KETO-ENOL TAUTOMERISM IN β-DICARBONYLS STUDIED BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

Thesis for the Degree of Ph. D.
MICHIGAN STATE UNIVERSITY
Jane Louise Burdett
1963

ABSTRACT

KETO-ENOL TAUTOMERISM IN β-DICARBONYLS STUDIED BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

by Jane Louise Burdett

A study of keto-enol tautomerism in β-dicarbonyls has been made by proton magnetic resonance techniques. Both β-diketone and β-ketoester molecules of the type RCOCH(R')COR" have been investigated with substitution of electron withdrawing and donating groups for R, R', and R".

Chemical shift measurements have been made for the pure compounds, and the effect of substituents on chemical shifts has been noted. Separate signals may be seen for the acetyl methyl protons of the enol and keto tautomers and for the α-protons of each tautomer. Occasionally the methylene protons of the alkoxy group give different chemical shifts for the two tautomeric forms. Identification of resonance peaks has been made possible by varying the tautomeric equilibrium through change of solvent and, in some cases, by the effect of temperature on the equilibrium.

The effect of solvent on chemical shifts has been studied and in most cases such measurements have been extended to give the chemical shifts at infinite dilution. In general the effect of the solvent is most pronounced on the keto and enolic α-protons and on the enolic OH proton which is involved in the intramolecular hydrogen bond. Specifically, dilution in various solvents has resulted in upfield shifts of the above-mentioned protons. Benzene represents the principal exception to this

result, and its behavior has been explained on the basis of complex formation.

Equilibrium constants have been determined for the pure compounds by integration of the relative areas under the resonance peaks of enol versus keto tautomers. The effect of substituent on the equilibrium constant has been noted and discussed. Extensive solvent studies have been made on the position of equilibrium, and it may be noted that the nonpolar solvents tend to increase the enolic tautomer, whereas polar solvents tend to decrease the enolic content.

Long-range spin-spin couplings in both enol and keto tautomers have been determined. These couplings are in general rather small. In the enol tautomer the spin-spin interaction between acetyl and α-protons increases over that in the keto as would be expected when the spin coupling is across a double bond.

Variable temperature studies have been undertaken. Low and high temperature effects on the chemical shift are concentrated principally on those protons involved directly in the equilibrium--the keto and enol α-protons and the enolic OH proton. High temperatures tend to cause an upfield shift of these protons and result in negligible shift of other protons.

The effect of temperature on the equilibrium constants has been observed. An increase in temperature results in a decrease in the enolic content. Low temperatures were particularly useful for studying compounds with low enolic content, but line broadening precluded extensive measurements.

Where feasible, the enthalpy of tautomerization has been obtained from the slope of the graph of ln([enol]/[keto]) versus $1/T$. Finally, free energies and entropies of enolization have been calculated.

KETO-ENOL TAUTOMERISM IN β-DICARBONYLS STUDIED BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

By

Jane Louise Burdett

A THESIS

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Chemistry

1963

To My Parents

ACKNOWLEDGMENTS

I would like to thank Professor Max T. Rogers for his continual support and encouragement during the investigation of this research.

Appreciation is expressed to Varian Associates for the use of their equipment and facilities at the Pittsburgh Sales Applications Office. In this connection I would like to thank Mr. Dennis Benefield, Dr. Norman Bhacca, Dr. Jerry Holcomb, Dr. Donald Hollis, Mr. Cappy Joller, and Mr. Robert Williams of the Varian staff for their assistance.

TABLE OF CONTENTS

	Page
HISTORICAL REVIEW	1
Introduction - Nature of the Equilibrium	1
Substituent Effects	3
Structure	4
Dipole Moments	4
Configuration of the Keto Tautomer	10
Configuration of the Enol Tautomer	12
Infrared Absorption	15
Ultraviolet Absorption	21
Summary of Structure Work on Keto-Enol Tautomers	22
Effect of Temperature and Pressure	24
Solvent Effects	27
Bromine Titration	27
Dipole Moments	27
Raman Spectroscopy	30
Infrared Spectroscopy	30
Ultraviolet Spectroscopy	33
Nuclear Magnetic Resonance Spectroscopy	36
Kinetics and Thermodynamics	36
Equilibrium Constants and Thermodynamic Quantities	37
Rates of Enolization	40
Rates of Ionization and Ionization Constants	41
Nuclear Magnetic Resonance Studies	48
Theoretical Studies	55
Stabilities of Metal Chelates	59
THEORETICAL CONSIDERATIONS	63
Nuclear Magnetic Moments	63
Chemical Shifts	63
Chemical Shift due to Bulk Susceptibility	64
Chemical Shift due to Anisotropy	65
Chemical Shift due to van der Waals Forces	70
Chemical Shift due to Polar Effects	72

TABLE OF CONTENTS - Continued

	Page
Hydrogen Bonding	75
Relaxation Mechanisms	77
Longitudinal Relaxation	77
Transverse Relaxation	78
Proton Exchange	78
Nuclear Spin-Spin Coupling	79
EXPERIMENTAL	81
Instrumental	81
Compound Preparation	82
Compound Purification	83
Preparation of Solutions	83
Physical Properties	84
Solvent Purification	84
RESULTS AND DISCUSSION	87
Nuclear Magnetic Resonance Spectra	87
Chemical Shifts	87
Structure	124
Tautomeric Equilibrium	125
Solvent Effects	129
Carbon Tetrachloride	129
Benzene	136
Hexane	143
Chloroform	147
Carbon Disulfide	150
Ether	150
Acetic Acid	150
Acetonitrile	154
Dimethylsulfoxide	154
Alcoholic Solvents	155
Triethylamine	155
Diethylamine	157
Other Bases	158
Solvent Effect on Keto-Enol Equilibrium	158
Long-Range Proton Spin-Spin Coupling	166
Variable Temperature Nuclear Magnetic Resonance	170

TABLE OF CONTENTS - Continued

	Page
Chemical Shift Measurements	170
Equilibrium Constant Measurements	173
SUMMARY	178
REFERENCES	179

LIST OF TABLES

TABLE		Page
I.	Percentage of Enol Tautomer in β-Dicarbonyls. . . .	2
II.	Effect of Substituents on Enolization in β-Dicarbonyls	5
III.	Influence of Halogen Substitution on Enolization in Ethyl Acetoacetates.	6
IV.	Calculated Dipole Moments for Acetylacetone and Ethyl Acetoacetate	7
V.	Percentages of Enol Tautomer, Dielectric Constants, and Apparent Dipole Moments for Ethyl Acetoacetate in Various Solvents.	11
VI.	Infrared Frequencies for β-Diketones	16
VII.	Infrared Frequencies for β-Ketoesters	17
VIII.	Ultraviolet Absorption for β-Dicarbonyls	18
IX.	Temperature Dependence of Keto-Enol Equilibrium in Some β-Dicarbonyls.	26
X.	Percentages of Enol Tautomer and Equilibrium Constants for Enolization of Acetylacetone and Ethyl Acetoacetate in Various Solvents	28
XI.	Percentages Enol Tautomer for α-Substituted Ethyl Acetoacetates in Various Solvents.	29
XII.	Free Energy of Tautomerization for β-Dicarbonyls in Various Solvents	31
XIII.	Enthalpy of Tautomerization for Acetylacetone and Ethyl Acetoacetate in Various Solvents	32

LIST OF TABLES - Continued

TABLE		Page
XIV.	Percentages of Enol Tautomer for β-Dicarbonyls in Various Solvents.	34
XV.	Percentages of Enol Tautomer for Ethyl Acetoacetate and Acetylacetone in Various Solvents	35
XVI.	Equilibrium Constants for β-Dicarbonyls.	38
XVII.	Free Energies of Tautomerization for β-Dicarbonyls	39
XVIII.	Rates of Enolization and Thermodynamic Constants for Tautomerization for Fluorinated β-Dicarbonyls .	42
XIX.	Ionization Constants for β-Dicarbonyls.	44
XX.	Rates of Ionization of Pseudo Acids at 25°C in Water	45
XXI.	Enthalpy and Entropy of Ionization of β-Dicarbonyls.	45
XXII.	Infinite Dilution Chemical Shifts of the Protons of Acetylacetone in Various Solvents.	49
XXIII.	Molecular Orbital Calculations for β-Di- and β-Triketones.	57
XXIV.	Infrared Frequencies of Groups in β-Diketones and Their Metal Chelates	60
XXV.	Infrared Frequencies and Force Constants for Groups for Copper Chelates of β-Diketones.	62
XXVI.	Physical Constants of β-Diketones	85
XXVII.	Physical Constants of β-Ketoesters	86
XXVIII.	Molecular Formulas of β-Diketones	88
XXIX.	Molecular Formulas of β-Ketoesters.	99
XXX.	Proton Chemical Shifts in Pure β-Diketones	116

LIST OF TABLES - Continued

TABLE		Page
XXXI.	Proton Chemical Shifts in Pure β-Ketoesters.	117
XXXII.	Chemical Shifts of Enol OH for β-Dicarbonyls in Order of Increasing Interaction between OH and C=O	121
XXXIII.	Percentages of Enol Tautomers and Equilibrium Constants for β-Diketones as Determined by Nuclear Magnetic Resonance.	126
XXXIV.	Percentages of Enol Tautomers and Equilibrium Constants for β-Ketoesters as Determined by Nuclear Magnetic Resonance	127
XXXV.	Infinite Dilution Proton Chemical Shifts in β-Diketones in Carbon Tetrachloride.	130
XXXVI.	Infinite Dilution Proton Chemical Shifts in β-Ketoesters in Carbon Tetrachloride	131
XXXVII.	Infinite Dilution Proton Chemical Shifts in β-Diketones in Benzene.	137
XXXVIII.	Infinite Dilution Proton Chemical Shifts in β-Ketoesters in Benzene	138
XXXIX.	Chemical Shifts of Protons in β-Dicarbonyls at Infinite Dilution in n-Hexane	144
XL.	Chemical Shifts of Protons in β-Dicarbonyls at Infinite Dilution in Chloroform	148
XLI.	Infinite Dilution Proton Chemical Shifts in Acetylacetone in Various Solvents.	152
XLII.	Infinite Dilution Proton Chemical Shifts in Ethyl Acetoacetate in Various Solvents.	153
XLIII.	Equilibrium Constants for Tautomerization of Acetylacetone in Various Solvents at 0.1 Mole Fraction of Solute.	159

LIST OF TABLES - Continued

TABLE		Page
XLIV.	Equilibrium Constants for Tautomerization of Ethyl Acetoacetate in Various Solvents at 0.1 Mole Fraction of Solute.	160
XLV.	Free Energies of Tautomerization of β-Dicarbonyls at 0.1 Mole Fraction in Various Solvents and Values of the Solvent Property.	165
XLVI.	Long Range Spin-Spin Coupling in β-Dicarbonyls . . .	169
XLVII.	Chemical Shifts of the Enol OH and of Keto and Enol α-Hydrogen Protons in β-Dicarbonyls at Various Temperatures.	172
XLVIII.	Thermodynamic Quantities for the Tautomerization Equilibria in β-Dicarbonyls	176

LIST OF FIGURES

FIGURE		Page
1.	Configurations of keto and enol tautomer in acetylacetone.	8
2.	Configurations of keto and enol tautomers in ethyl acetoacetate	9
3.	Configurations of keto tautomer in β-dicarbonyls . .	10
4.	Configurations of enol tautomer in β-dicarbonyls . .	12
5.	Possible structures for intramolecularly hydrogen-bonded molecules	19
6.	Conjugated structures for the enol tautomers in β-dicarbonyls.	20
7.	Enolate ion structure	47
8.	Structures of some β-triketones	52
9.	Keto and enol structures for hydroxymethylene compounds.	54
10.	Schematic representation of ring-current effect . . .	68
11.	Orientation of polar molecule relative to benzene ring in complex.	69
12.	Proton NMR spectrum of acetylacetone.	89
13.	Proton NMR spectrum of α-bromoacetylacetone. . .	90
14.	Proton NMR spectrum of α-chloroacetylacetone . . .	91
15a.	Proton NMR spectrum of cyclic isopropylidene malonate (in $CHCl_3$).	92

LIST OF FIGURES - Continued

FIGURE		Page
15b.	Proton NMR spectrum of hexafluoroacetylacetone. . .	92
16.	Proton NMR spectrum of dibenzoylmethane (in CCl_4) .	93
17.	Proton NMR spectrum of trifluoroacetylacetone. . . .	94
18a.	Proton NMR spectrum of 1, 3-indanedione (in $CHCl_3$) .	95
18b.	Proton NMR spectrum of α-methylacetylacetone . . .	95
19.	Proton NMR spectrum of 1-phenyl-1, 3-butanedione (in CCl_4).	96
20a.	Proton NMR spectrum of 2-phenyl-1, 3-indianedione (in acetone)	97
20b.	Porton NMR spectrum of β-bromoethyl acetoacetate .	97
21.	Proton NMR spectrum of thenoyltrifluoroacetone (in (CS_2).	98
22a.	Proton NMR spectrum of butylacetoacetate	100
22b.	Proton NMR spectrum of t-butyl acetoacetate.	100
23a.	Proton NMR spectrum of n-butyl α-chloroacetoacetate	101
23b.	Proton NMR spectrum of t-butyl α-chloroacetoacetete	101
24.	Proton NMR spectrum of ethyl acetoacetate.	102
25.	Proton NMR spectrum of ethyl α-allylacetoacetate . .	103
26.	Proton NMR spectrum of ethyl α-isoamylacetoacetate	104
27.	Proton NMR spectrum of ethyl benzoylacetate	105
28a.	Proton NMR spectrum of ethyl α-bromoacetoacetate .	106
28b.	Proton NMR spectrum of ethyl γ-bromoacetoacetate .	106

LIST OF FIGURES - Continued

FIGURE		Page
29a.	Proton NMR spectrum of ethyl α-isobutylaceto-acetate.	107
29b.	Proton NMR spectrum of ethyl α-n-butylacetoacetate	107
30.	Proton NMR spectrum of ethyl α-chloroacetoacetate.	108
31.	Proton NMR spectrum of ethyl α-cyanoacetoacetate .	109
32a.	Proton NMR spectrum of ethyl α-ethylacetoacetate. .	110
32b.	Proton NMR spectrum of ethyl trifluoroacetoacetate.	110
33.	Proton NMR spectrum of ethyl α-fluoroacetoacetate .	111
34a.	Proton NMR spectrum of ethyl α-methylaceto-acetate.	112
34b.	Proton NMR spectrum of ethyl α-isopropylaceto-acetate.	112
35a.	Proton NMR spectrum of ethyl α-n-propylaceto-acetate.	113
35b.	Proton NMR spectrum of methyl acetoacetate	113
36.	Proton NMR spectrum of ethyl α-chloroacetoacetate following distillation.	114
37.	Chemical shift of enol OH versus carbonyl stretching frequency for β-dicarbonyls.	123
38.	Possible enol tautomers for trifluoroacetylacetone .	124
39.	Chemical shift of protons of ethyl acetoacetate in benzene and carbon tetrachloride.	133
40.	Proton NMR spectrum of acetylacetone in carbon tetrachloride.	134

LIST OF FIGURES - Continued

FIGURE Page

41. Chemical shift relative to pure solute of OH proton in β-dicarbonyls at infinite dilution in carbon tetrachloride versus mole fraction solute. 135

42. Proton NMR spectrum of ethyl acetoacetate in benzene. 139

43. Chemical shift relative to pure solute of the OH proton in β-dicarbonyls at infinite dilution in benzene versus mole fraction solute. 140

44. Proposed complex of acetylacetone with benzene. . . 142

45. Proton NMR spectrum of butyl acetoacetate in n-hexane. 145

46. Proton NMR spectrum of t-butyl acetoacetate in chloroform. 146

47. Association of keto molecules in ethyl α-chloroacetoacetate. 147

48. Chemical shift of chloroform proton in β-dicarbonyls as donor solvents 151

49. Proton NMR spectrum of acetylacetone in methanol . 156

50. Percentage enol tautomer in acetylacetone in various solvents. 162

51. Percentage enol tautomer in ethyl acetoacetate in various solvents 163

52. Free Energy of tautomerization for acetylacetone versus solvent property. 167

53. Free energy of tautomerization for ethyl acetoacetate versus solvent property 168

54. Long range spin-spin coupling in ethyl acetoacetate. 171

55. Graph of log ([enol]/[keto]) versus 1/T for α-methylacetylacetone. 175

HISTORICAL REVIEW

Introduction--Nature of the Equilibrium

Keto-enol tautomerism in β-dicarbonyls may be considered as an equilibrium between keto and enol forms through the anion, as pictured below:

$$R\text{-}C^{=O}\text{-}CHR'\text{-}C^{=O}R'' \longleftrightarrow R\text{-}C^{O^-}=CR'\text{-}C^{=O}\text{-}R'' \longleftrightarrow R\text{-}C^{OH}=CR'\text{-}C^{=O}R'' . \quad (1)$$

As early as 1912 the keto-enol equilibrium in these compounds was studied by Meyer (1) using bromine titration. This method involves the reaction of the enolic tautomer with bromine, as seen in the following equations:

$$Me\text{-}C(OH)=CH\text{-}COOEt \xrightarrow{Br_2} MeCO\text{-}CHBr\text{-}COOEt \quad (2a)$$

$$MeCO\text{-}CHBr\text{-}COOEt \xrightarrow{H^+ + I^-} MeCOCH_2\text{-}COOEt + Br^- + I_2 \quad (2b)$$

$$I_2 + 2S_2O_3^{=} \longrightarrow 2I^- + S_4O_6^{=} . \quad (2c)$$

As stated by Meyer, one of the principal problems associated with this method involves the fact that during the reaction more enolic tautomer is formed and the end point is not sharp. For the molecule, R-CO-CHR'-CO-R", Meyer noted that the equilibrium is affected by substitution of various groups for R, R', and R" in Equation (1). The effects of both solvent and temperature on the equilibrium were observed. Polar solvents tended to decrease enolization, as did increased temperatures (2). Results are shown in Table I for pure compounds.

Bromine titration has also been used as a measure of the tautomeric equilibrium by Park et al. (3), Ratnakar (4), Malawski et al. (5),

Table I. Percentage of Enol Tautomer in β-Dicarbonyls

Compound	Percent Enol		Method	Reference
	Pure Liquid	Gas		
Acetylacetone	76		Br_2	1
	60		IR	30
	78	92	Br_2	55
	85		NMR	71
	81		NMR	23
		95	Br_2	51
Dibenzoylmethane	100		Br_2	1
Ethyl acetoacetate	7		Br_2	1
	8	46	Br_2	55
	7		NMR	58
		63	Br_2	52
Ethyl benzoylacetate	29		Br_2	1
Ethyl α-bromoacetoacetate		29	Br_2	50
Ethyl n-butylacetoacetate	6	14	Br_2	55
	2		Br_2	14
Ethyl α-chloroacetoacetate		46	Br_2	50
Ethyl ethylacetoacetate	3		Br_2	1
	3	10	Br_2	55
Ethyl methylacetoacetate	3		Br_2	1
	4	14	Br_2	55
Ethyl isopropylacetoacetate	5	6	Br_2	55
	1		Br_2	14
Ethyl n-propylacetoacetate	7	13	Br_2	55
Ethyl trifluoroacetoacetate	89		NMR	18
Methyl acetoacetate	5		Br_2	1
	6	54	Br_2	55
3-Methylacetylacetone	30		Br_2	1
	30	44	Br_2	55
1-Phenyl-1, 3-butanedione	100		Br_2	1

Eistert and Reiss (6,7), Kabachnik et al. (8-12), and Eistert and Geiss (13). Results from the literature for β-dicarbonyls included in the present study are given in Table I.

The keto-enol equilibrium is influenced by many factors, and several of these will now be considered.

Substituent Effects

Meyer (1) noted the effect of various substituents on the tautomeric equilibrium. He found increased enolization in the order OMe < OEt < OH < NHPh < Me < PH < COOR" for R" in Equation (1). For substitution in the α-position, enolization was decreased with an alkyl group and increased with an acyl group. However, if the unsubstituted compound is strongly enolized, an acyl group decreases enolization. He found that bromine in the α-position increased enolization.

Henecka (14) also found a decrease in enolization with alkyl α-substitution and explained this on the basis of a disturbance of the inductive and conjugative effects. He noted further that branching of the R (or R") [see Equation (1)] alkyl group of a β-dicarbonyl decreases enolization, which contrasts with the conclusions of Hammond (15).

Hammond has stated that branching of the end group reduces the keto content compared to acetylacetone (15). With large groups the carbonyl groups can only be rotated about 90° from the parallel coplanar configuration seen in Figure 3(a). In cyclic enols there is no serious interference with even a pair of terminal tertiary butyl groups. Intramolecular hydrogen bonding is not possible in cyclic β-dicarbonyls with both carbonyl groups in the ring.

The influence of branching of a hydrocarbon chain on enolization in derivatives of acetylacetone was studied by Rumpf and La Riviere (16),

and the percentage enol was obtained by bromine titration. Results are given in Table II. As reported by earlier workers, increased branching resulted in decreased enolization. The authors have stated that α-substitution prevents coplanarity not only of the enol, but also of the anion. Substitution of a more bulky group in the end position gave increased ketone form, in disagreement with Hammond et al. (17). The high degree of enolization in dipivaloylmethane has been explained by Hammond et al., by the fact that the end groups force the carbonyls into a position in which electrostatic repulsion is a maximum. Therefore, the enolic tautomer becomes energetically more favorable.

For a series of 2-phenylacetoacetic acid nitriles substituted in the 4'-position, Malawski et al. (5), have determined the keto-enol equilibrium by bromine titration. An electron attracting group in the 4'-position resulted in an increased enolic content, and an electron withdrawing group in decreased enolic form. This effect must be an electronic one, since a steric effect is not possible in this position, according to the authors.

Filler and Naqvi (18) have found by indirect bromine titration and by nuclear magnetic resonance that fluorine substitution on the acetyl methyl of ethyl acetoacetate results in increased enolization. The presence of the fluorine atoms probably makes the enols more acidic, so that there is increased proton donor capacity and stronger hydrogen bonding to the ester carbonyl oxygen. These results are shown in Table III.

Structure

Dipole Moments. Wolf (19) has determined the dipole moment of acetylacetone in benzene at 16°C as 2.78 ± 0.08 D. Wolf has also calculated dipole moments for each tautomer in several possible configurations, and these values are reproduced in Table IV. Zahn (20) measured

Table II.* Effect of Substituents on Enolization in β-Dicarbonyls

Compound	K_e**	pK_e
$CH_3COCH_2COCH_3$	0.24	8.23
$CH_3COCH_2COC_2H_5$	0.19	8.57
$CH_3COCH_2COCH(CH_3)_2$	0.09	8.33
$CH_3COCH_2CO[CHCH(CH_3)_2]$	0.09	8.88
$CH_3COCH_2CO(C_6H_5)$	0.38	8.12
$CH(CH_3)_2$-$COCH_2CH(CH_3)_2$	0.08	8.76
$CH_3COCH(CH_3)COCH_3$	0.03	9.2
$CH_3COCH(C_2H_5)COCH_3$	0.01	$\leq$ 9.5
$CH_3COCH[CH(CH_3)_2]COCH_3$	$\leq$ 0.003	$\leq$10.3
$CH_3COCH(C_6H_5)COCH_3$	0.09	$\leq$ 8.3
$CH_3COCH(CH_3)CO(C_6H_5)$	< 0.005	< 8.8

*From Rumpf and La Riviere (16)

**K_e ≠ [enol]/[keto]

Table III.* Influence of Halogen Substitution on Enolization in Ethyl Acetoacetates

Compound	Percent Enol in Pure Liquid	Method
Ethyl acetoacetate	6.0	NMR
Ethyl γ-fluoroacetoacetate	7.2	NMR
Ethyl γ, γ-difluoroacetoacetate	53 ± 4	NMR
Ethyl γ, γ, γ-trifluoroacetoacetate	89	NMR
Ethyl γ-chloroacetoacetate	11	Br_2**
Ethyl γ, γ, γ-trichloroacetoacetate	40-50	Br_2
Ethyl α-bromoacetoacetate	4	Br_2
Ethyl α, γ-difluoroacetoacetate	5	Br_2

*From Filler and Naqvi (18)

**Reported by authors from other references

Table IV.* Calculated Dipole Moments for Acetylacetone and Ethyl Acetoacetate

Configuration	Dipole Moment (D)	
	Acetylacetone	Ethyl Acetoacetate
Free diketone	3.7	3.2
Trans diketone	1.8	1.6
Diketone (a)**	3.2	2.8
Free enol; only CH_3CO or COOEt firm (b)**	3.0-2.8	2.3
Free	3.3-3.6	2.6-3.0
Chelate (c)**	3.4-4.0	2.7-3.2
Dienol (d)**	2.2-2.6	-

*From Zahn (20)

**Letters in parentheses refer to configuration shown on page 8.

the dipole moment of acetylacetone in the gas phase and has considered the structure of both the keto and the enol tautomers. Among the structures shown in Figure 1, Zahn has preferred (c) for the enol and (a) for the keto in which the carbonyl approaches the opposite methyl group.

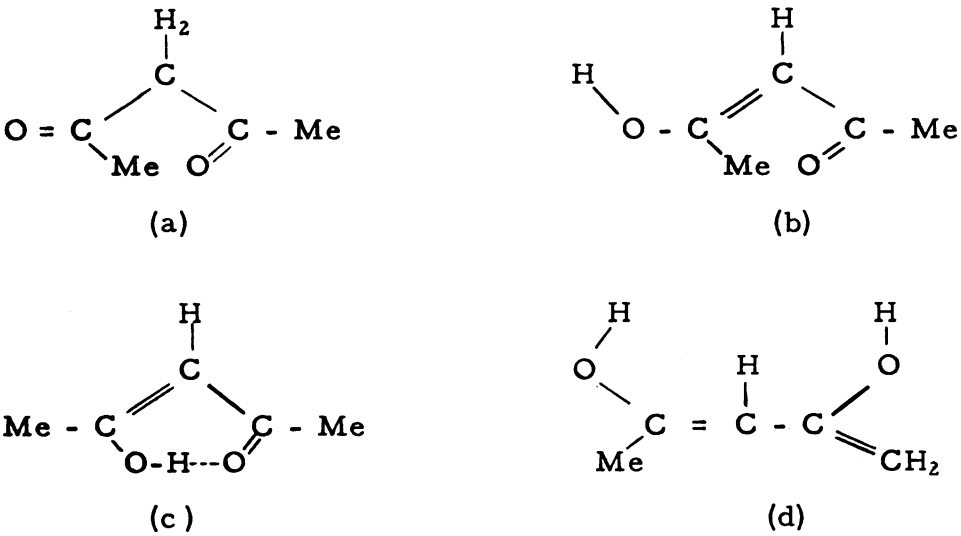


Figure 1. Configurations of keto and enol tautomers in acetylacetone.

These groups approach too closely to permit completely free rotation, according to Zahn. The author discounted the presence of either free enol or di-enol forms. The observed dipole moment was 3.00 D, which represents an average of enolic and ketone forms. Since the equilibrium in acetylacetone is very far in the direction of the enol form, one should compare the observed value with that calculated for the chelate form (c), 3.4-4.0 D. Temperature studies over the range 50-200°C by Zahn indicated a dipole moment independent of temperature. This is perhaps surprising when one realizes that increased temperature favors the keto form (2). Lack of temperature variation may be due either to completely free rotation or to completely hindered rotation.

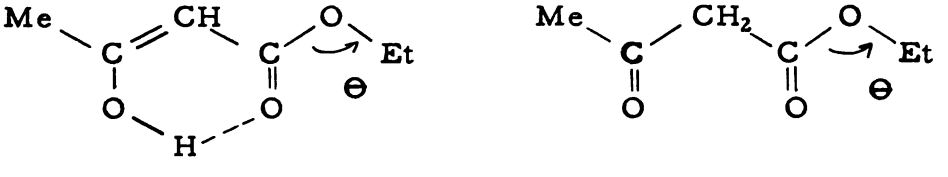
Similar calculations for ethyl acetoacetate gave dipole moments of 3.2 D for the ketone form (a) and 2.7-3.2 for enol form (c). The observed dipole moment in the gas phase was 2.9 D, and no temperature dependence of this moment was observed in the interval 394-431°K. It has been found that the tautomeric equilibrium of ethyl acetoacetate is independent of temperature (2).

Beyaert (21) attempted to determine the dipole moment of each tautomer of ethyl acetoacetate. The dipole moment of the ketone form as measured in benzene at room temperature was 3.22 D. The benzene solution contained 16.8 percent enol. The moment of the enolic form, as measured in carbon disulfide at -80°C, was 2.04 D. The amount of ketone under these conditions was considered negligible. These results do not show good agreement with the calculations of Zahn (20).

The square of the apparent dipole moment has been determined by Le Fevre and Welsh (22) for ethyl acetoacetate in several solvents. These workers have assumed the following relationship,

$$\mu^2 = X_e\mu_e^2 + X_k\mu_k^2 , \qquad (3)$$

where μ is the apparent dipole moment, X_e and X_k are mole fractions of enol and ketone tautomer, respectively, and μ_e and μ_k are dipole moments of enol and keto tautomers, respectively. Le Fevre and Welsh criticized Zahn's gas phase moment measurements, since the percentage of enol tautomer was not accurately known. They have assumed the structures in Figure 2 for enol and keto tautomers.

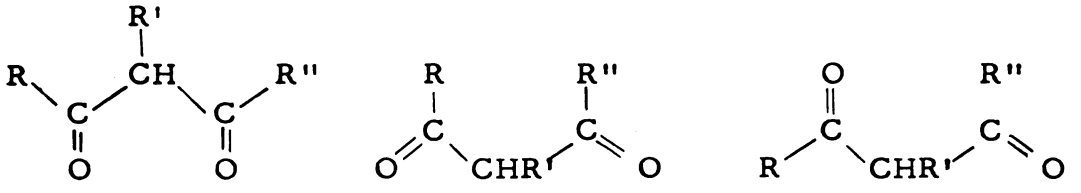


(a) (b)

Figure 2. Configurations of keto and enol tautomers in ethyl acetoacetate.

Structure (a) gave a calculated moment of 2.2 to 1.4 D, and structure (b) a moment of 3.5 to 2.7 D, for values of the angle Θ between 60° and 120°. Apparent moments are listed in Table V. Dielectric constant measurements in Le Fevre and Welsh's work have been converted from weight fractions to mole fractions for the purposes of this thesis. These values have been plotted graphically for several solvents. The graphs deviate from linearity as would be expected for a decrease of percentage keto tautomer on dilution.

Configuration of the Keto Tautomer. Possible structures for this tautomer are seen in Figure 3. Although Le Fevre and Welsh (22) have



(a) (b) (c)

Figure 3. Configurations of the keto tautomer of β-dicarbonyls.

pictured structure (a) for the keto tautomer, molecular models show that the carbonyls in this orientation have maximum electrostatic repulsion. Reeves (23) has pictured acetylacetone as structure (a) since the methyl groups are equivalent in the proton NMR spectrum. Hammond et al. (17), have suggested that acetylacetone exists as either (b), (c), or both. Bulky groups on the end positions tend to force the molecule into the enol form rather than into the less favorable keto configuration (a). For some compounds with bulky end alkyl groups the carbonyl groups may only be rotated about 90° from their parallel coplanar configuration in structure (b). Zahn has suggested structure (c) as the most important for the diketone form.

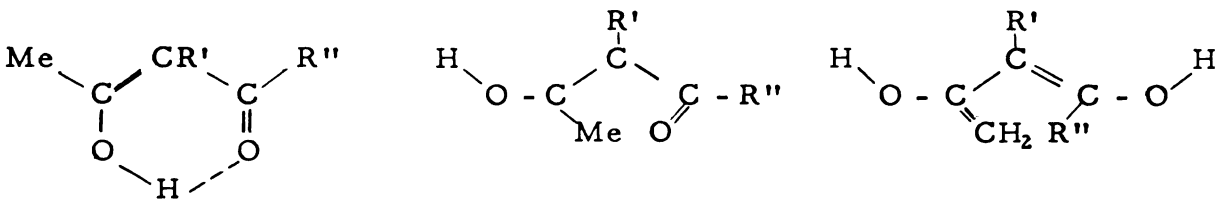
Table V.* Percentages of Enol Tautomer, Dielectric Constants, and Apparent Dipole Moments for Ethyl Acetoacetate in Various Solvents

Solvent	Percentage Enol		μ_{app}	$\epsilon_{solvent}$
	Observed	Calculated**		
Chloroform	0	-	3.36	-
Ether	14	19	2.42	4.27
Carbon tetrachloride	25	53	3.07	2.23
Benzene	25	52	2.93	2.27
Toluene	39	49	2.75	2.37
Carbon disulfide	43	44	2.60	2.63
Hexane	63	63	1.70	1.89

*From Le Fevre and Welsh (22), using literature values for observed enolic percentages.

**Calculated from Equation (6).

Configuration of the Enol Tautomer. The enol tautomer might exist in any of the forms seen in Figure 4.



(a) cis-enol (b) trans-enol (c) di-enol

Figure 4. Configuration of the enol tautomer in β-dicarbonyls.

The cis or intramolecularly hydrogen bonded species, (a), has been suggested by Sidgwick (24) and many workers since that time have assumed that this was the preferred configuration. Referring to Meyer's work, Sidgwick observed that the preference for the enolic tautomer in nonpolar solvents indicates the presence of a chelated enolic structure. According to Sidgwick's calculations, the sum of the angles in the chelate ring structure is 720° or that of a plane hexagon, which indicates a ring entirely free of strain. Sidgwick noted that the chelate enol tautomer is less polar than the diketone form and will have a lower boiling point than it or the free enolic tautomer. Hammond (15) stated that enols have a coplanar ring of six atoms which gives minimum electrostatic repulsion and maximum resonance stabilization. He has further suggested that α-methylacetylacetone may exist to some extent in the trans enol form, since infrared measurements show a weaker hydrogen bond than in acetylacetone.

Henecka (14) suggested the presence of trans enol in compounds with large groups in the α-position. Bromine titration indicated the presence of enol. However, the colorimetric reaction of ferric chloride, which involves only the cis enolic tautomer was negative. The fact that bromine titration indicates the presence of enol, but the ferric chloride

reaction negates the possibility of cis enol, lends support to the presence of a trans enol tautomer. In this reaction the iron atom replaces the proton in the intramolecular bond.

$$FeCl_3 + C_6H_9O_2 \cdot OH \longrightarrow FeCl_2C_6H_9O_3 + HCl \qquad (4)$$

Eistert et al. (25), have called attention to the possibility of two cis- and two trans-enolic forms for the molecule, $R'COCH_2COR$, where R and R' differ. In cis enols the chelate structure essentially eliminates the difference between the two forms. For β-ketoesters the keto carbonyl is predominantly enolized. These authors suggest the presence of a trans enol-solvent complex in a solution of acetylacetone in methanol.

Kabachnik et al. (8), hypothesized that the keto-enol equilibrium of trans-fixed β-dicarbonyl compounds is independent of solvent. Eistert and Geiss (13) found infrared and ultraviolet evidence indicating that these equilibria were actually dependent upon the solvent. In hydrophobic solvents enolic trans-fixed compounds were ketonized, whereas in hydrophilic solvents they were not. Kabachnik, et al. (9), extended this study to a series of compounds by ultraviolet and infrared spectroscopy and attempted to show the applicability of the relationship

$$K_e = EL + E'L', \qquad (5)$$

where K_e is the equilibrium constant, E and E' the cis and trans enolizability of the solute, and L and L' the tendency of the solvent to enhance cis and trans enolizability in the given solute. They have demonstrated that for β-dicarbonyls with bulky substituents in the α-position, the equilibrium is independent of the solvent. They have argued that a large percentage of trans enol exists in compounds with bulky α-substituents. In another work Kabachnik et al. (10), found that

enolization was essentially independent of the solvent for alkyl tetronic acids and for cyclic acetals of malonic acid. Only dimedone seemed to agree with Eistert and Geiss' hypothesis that the trans enol form predominated in hydrophilic solvents and the keto in hydrophobic solvents. They further examined (10) enolization in a number of compounds and showed that the equilibrium depended to a considerable extent upon the type of compound.

The keto-enol equilibrium of α-alkylacetylacetones has been investigated by Kabachnik et al.(11). Ultraviolet absorption spectra appear to indicate the presence of both cis and trans enolic forms, and the relative amounts of cis and trans forms are influenced by the solvent. For α-ethyl, α-propyl, α-butyl, and α-isobutyl acetylacetone, both cis and trans forms appear to be present. For α-methyl acetylacetone, only cis seems to exist, whereas in α-isopropyl and α-sec-butyl acetylacetone, only trans may be present. The amount of trans enol has been considered constant, and a graph of 1/L versus 1/I has been made, where L is the solvent enolizability toward cis enol and I the intensity of the absorption peak. This graph gives an approximately linear relationship for solutions in hexane, ethanol, ether, and in 67, 75, and 85 percent aqueous methanol. Values for λ_{max} and the extinction coefficients are given in Table VIII for ethyl-, isobutyl-, and isopropylacetoacetates.

Bratoz et al. (26), found infrared evidence in the form of a weak absorption band at 3570-3600 cm^{-1} which suggested the possibility of a small amount of trans enol in acetylacetone, but this has not been confirmed by others. Rasmussen et al. (27), have recognized that not only the formation of an intramolecular hydrogen bond but also the separation in space of the oxygen atoms may be important in influencing enolization of β-dicarbonyls. Certain trans-fixed β-diketones which cannot form intramolecular hydrogen bonds may form dimers involving the enolic tautomer.

Shigorin (28) has measured the frequencies and intensities of the infrared bands of the enol and keto forms of several β-dicarbonyls. Evidence was presented in support of the existence of dienol forms in equilibrium with enol forms. In a later work Shigorin (29) has introduced deuterium into β-dicarbonyls and has tabulated Raman frequencies for the C-D bond and for the C=CH and C=CD double bond. The presence of dienol was confirmed, according to the author.

Infrared Absorption. Infrared data are available for β-diketones in work by Mecke and Funck (30), Rasmussen et al. (27), Park et al. (3), Angell and Werner (31), Bellamy and Beecher (32), Bratoz et al. (26), Holtzclaw et al. (33), Hammond et al. (17), Tamm and Albrecht (34), Murthy et al. (35), Powling and Bernstein (36), Kuratani (37), Belford et al. (38), Shigorin (29), and in Sadtler Standard Spectra Nos. 3505, 5437, 5774, and 11982 (39). Spectra for β-ketoesters may be found in Le Fevre and Welsh (22), Rasmussen and Brattain (40), Hunsberger et al. (41), Bratoz et al. (26), Murthy et al. (35), Powling and Bernstein (36), Kuratani (42), Belford et al. (38), Shigorin (28), Shigorin (29), Bańkowska (43), and in Sadtler Standard Spectra Nos. 65, 101, 8013, 8017, 14640, 17508, and 18941 (39). Data from these references are summarized in Tables VI for β-diketones and in Table VII for β-ketoesters. In general the following frequencies may be listed for groups of principal interest in the tautomeric equilibrium.

Group	Frequency, cm^{-1}	Reference
Free OH intermolecular	3650-3590 sharp	Bellamy (44)
Intramolecular hydrogen bond	3570-3450 sharp	Bellamy (44)
Chelated OH	3200-2500 broad	Bellamy (44)
Normal conjugated carbonyl	1695-1672	Rasmussen et al. (27)
Carboxyl carbonyl	1733	Bellamy and Beecher (32)
Carbonyl not chelated	1709	Mecke and Funck (30)
Conjugated chelate carbonyl	1639-1538	Bellamy (44)
C=C	1650	Mecke and Funck (30)

Compound	Absorption Band (cm^{-1})				
	OH	Keto C=O	Chelate Enol C=O	C=C	Reference
Acetylacetone	3550	1725, 1708	1620	1633	38
		1720	1610		37
	2703		1639-1538*		27
	2700	1727, 1707	1616		30
	3460, 3380	1720, 1700	1618	1523	33
	2800		1610		26
	broad		1622		39
		1725	1625		36
		1725	1608		32
		1723	1655	1596	29
3-Chloroacetylacetone		1725	1613		33
	2730		1610		26
	2600		1604	1604	30
Dibenzoylmethane			1639-1538		27
	2604		1605		26
	broad		1610		39
			1600		32
Dimedone**	2632***	1730, $^{\rho}$1705$^{\rho}$	1640,* 1610$^{\rho}$		31
		1733, 1706$^{\pi}$			32
Hexafluoroacetylacetone	3120	1790, 1765	1680 or 1625		38
		1785	1711	1620	29
3-Methylacetylacetone	3400$^{\omega}$	1690			15
		1730, 1708	1615		33
1-Phenyl-1, 3, butanedione		1724	1600		32
	2640		1603		26
			1595		39
Trifluoroacetylacetone	3360	1775, 1745	1680		38
			1600		3

*Carbon tetrachloride; **Depends on solvent; ***Intermolecular hydrogen bond; ρ Chloroform
π Depends on concentration; ω Acyclic.

Table VII. Infrared Frequencies for β-Ketoesters

Compound	Absorption Band (cm^{-1})					
	OH	Keto COOR	Keto C=O	Chelate C=O	C=C	Reference
t-Butyl acetoacetate				1650-55		39
Ethyl acetoacetate		1740		1650		42
		1733	1709	1645		32
		1730			1640	71
				1634*		26
	broad			1640		39
				1640	1640-45	22
	3550	1735	1720	1640-50		38
		1742	1718	1650		40
		1740	1714		1632	29
Ethyl benzoylacetate	broad					39
Ethyl n-butylacetoacetate		1742	1714		1622	28
	broad			1645		39
Ethyl chloroacetoacetate				1610		26
		1760-1735		1644	1615	43
Ethyl ethylacetoacetate	broad			1650		39
Ethyl methylacetoacetate		1742	1718	1650		40
				1650		44
Ethyl isopropylacetoacetate		1745	1713		1623	28
	broad			1650		39
Ethyl trifluoroacetoacetate	3360	1650	1608	1562or1545		38
		1734	1786		1622	29
Methyl acetoacetate	broad			1635		39
		1751	1726	1655	1632	41
				1650		44

*Assignment uncertain.

Compound	Solvent	Molarity	λ_{max}(mμ)	ε	Reference
Acetylacetone	$CHCl_3$	4×10^{-5}	280	12,500±500	38
	Cyclohexane	-	-	11,100*	17

Table VIII. Ultraviolet Absorption for β-Dicarbonyls

Compound	Solvent	Molarity	λ_{max}(mμ)	ε	Reference
Acetylacetone	$CHCl_3$	$4x10^{-5}$	280	12,500±500	38
	Cyclohexane	-	-	11,100*	17
			-	12,000**	35
			270	10,000	27
α-Isobutylacetylacetone	MeOH	-	290^{ω}, 260^{γ}	4400^{ω}, 1800^{γ}	12
α-Isopropylacetylacetone	MeOH		260^{γ}	3650	12
Dibenzoylmethane	CH_3CN	$2.4x10^{-4}$	342	-	17
	hexane	-	339	-	17
Ethyl acetoacetate			-	16,000**	35
Ethyl α-chloroacetoacetate	heptane	0.14	264	3670***	43
Hexafluoroacetylacetone	$CHCl_3$	$4.0x10^{-5}$	273	7,800	38
Trifluoroacetylacetone	$CHCl_3$	$4.0x10^{-5}$	284	11,100±600	38

*Extrapolated to infinite dilution.
**Independent of concentration.
***Varies with solvent.
$^{\omega}$Cis enol tautomer.
$^{\gamma}$Trans enol tautomer.

In β-diketones Rasmussen (27) has found the OH frequency at about 2700 cm^{-1}. The OH peak is often very broad due to its chelated nature and may be masked by the strong CH stretch band near 3000 cm^{-1}. The strength of the hydrogen bond is given in some measure by the frequency, since a lower stretching frequency indicates a more nearly symmetrical bond, according to Rundle and Parasol (45). Rundle and Parasol have indicated that very broad bands which are characteristic of strong bonds become sharper as the bond becomes symmetrical. For a symmetrical bond, the OH bond length is longer, with a resulting lowering of the OH frequency. In compounds which appear symmetrical, such as nickel or palladium dimethylglyoxime, the OH frequencies are 1775 cm^{-1} and about 1600 cm^{-1}, respectively, and the peaks are sharp. With increased hydrogen bonding, the peaks become first broadened and finally sharp once again.

Mecke and Funck (30) showed that for the cis-enol form of acetylacetone the observed frequencies for the C=O and C=C bonds are between those for the normal CO and CC single and double bonds. Several structures have been written for the hydrogen-bonded species in Figure 5.

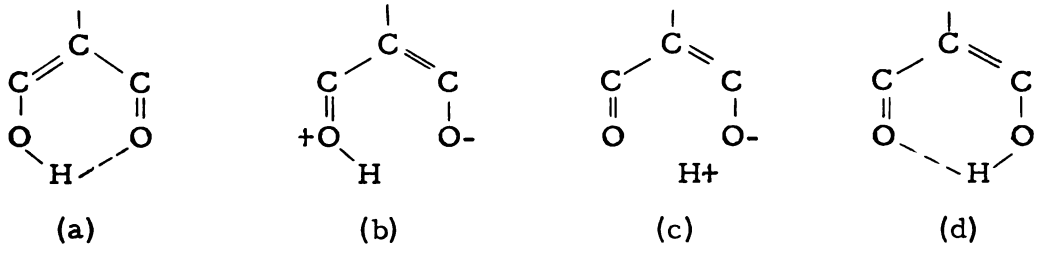


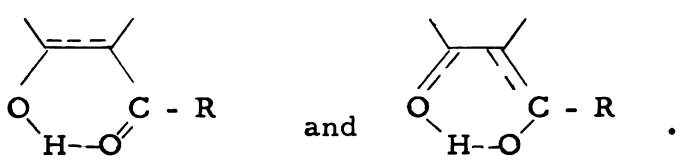
Figure 5. Possible structures for the intramolecularly hydrogen-bonded molecule.

Structures (a) and (d) together would lead to a symmetrical hydrogen bond. Forms (a) and (d) then could explain the lowering of the OH stretching frequency. Structures (b) and (c) might explain the displacement of the double bond frequency even though the hydrogen atom were

not symmetrically located according to these workers. Rasmussen et al. (27) have also suggested that structure (b) is stabilized by the hydrogen bond of (a).

Bellamy and Beecher (32) have pointed out that the frequencies of the carbonyl stretch are essentially the same for acetylacetone, benzoylacetone, dibenzoylmethane, α-thenoyltrifluoroacetone, and dimedone. These workers have assumed that the contribution of structure (b) [Figure 5] is the same in all these compounds. They have further calculated that form (b) contributes about 20-25 percent in aliphatic β-dicarbonyls. The authors have concluded that, since the equilibrium constants of enols vary widely, the proportion of resonant form (b) is not a determining factor in their ionization. Consequently, no relationship would be expected between the carbonyl frequencies and the equilibrium constants.

The chelated carbonyl stretching frequency occurs about 100 cm^{-1} below that for the normal conjugated carbonyl group and is a much more intense peak (27). Hunsberger et al. (41), have suggested that the difference in carbonyl stretching frequencies may depend on the relative importance of structures such as



(e) (f)

Figure 6. Conjugated structures for the enol tautomers in β-dicarbonyls.

The relationship between the carbonyl frequency and double-bond character has been investigated by these workers. A linear relationship has been found between the difference in chelated and unchelated stretching frequency and the double bond character, using Pauling's values for percentage double-bond character and neglecting ionic character.

Rasmussen and Brattain (40) have assigned the 1650 cm^{-1} band to the chelated carbonyl of ethyl acetoacetate, in disagreement with earlier Raman results. Rasmussen et al. (27), also noted a chelated carbonyl absorption band both intense and much shifted from the normal region. It was suggested that the greater participation of ionic structures leads to greater decrease in the double-bond character of the carbonyl bond than would occur for simple conjugation. The increased charge on the carbonyl oxygen results in the observed high intensity. It was assumed that the C=C stretching frequency is hidden under the carbonyl absorption. Bellamy and Beecher (32) have stated that the carbonyl frequencies are determined almost entirely by the character of the double bond involved since its length effectively determines the O. . .O distance. Unlike the results of Hunsberger et al. (41), a linear relationship between double bond character and the difference in carbonyl stretching frequency for a chelate and non-chelate bond was not found to hold for aliphatic compounds with unconjugated double bonds. A graph of double bond character of β-diketones versus the actual stretching frequency, however, shows a linear relationship. In assigning double-bond character, Pauling's values were used, and the contribution of ionic and Dewar forms to the resonance hybrid was ignored. For β-keto-esters such a plot is less satisfactory, probably because the second oxygen of the ester group has greater effect on the carbonyl to which it is attached.

Stretching frequencies have been measured by Raman spectroscopy by Shigorin (46) for several β-dicarbonyls. The results are seen in Tables VI and VII.

Ultraviolet Absorption. Ultraviolet absorption of β-dicarbonyls has been studied by Belford et al. (38), Hammond et al. (17), Murthy et al. (35), Rasmussen et al. (27), Bankowska (43), and Kabachnik et al. (11).

Values for λ_{max} and of extinction coefficients are given in Table VIII. Rasmussen, et al. (27), have pointed out that a simple conjugated system will have two maxima at 2350 and 3200 Å, with extinction coefficients of 10,000 and 40, respectively. For the conjugated chelate systems studied here, however, only one maximum of considerable intensity was observed.

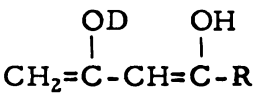
Summary of Structural Work on Keto-Enol Tautomers. (1) The Keto Tautomer. Dipole moment measurements for ethyl acetoacetate and acetylacetone appear to indicate the presence of structure (b), Figure 3. Structure (a) has been discounted because of strong electrostatic repulsion. Structure (c) would lead to a dipole moment substantially lower than the experimental values and lower than the enolic tautomer. However, the boiling point data would indicate that the enol form is less polar since it distils at a lower temperature. Also in favor of structure (b) is the fact that little rearrangement would be necessary in order to form the coplanar anion which has been proposed as an intermediate in the keto-enol equilibrium reaction. This writer's calculations for structure (b) give a dipole moment of 3.0 D, in good agreement with Zahn's calculations (20). The presence of a small amount of the trans structure (c) cannot be discounted as a possibility. However, compounds with large bulky groups on one or both ends show an increase in percentage of enol tautomer, presumably because of steric hindrance in structure (b) (Figure 3), whereas in structure (c) the non bonded interactions are negligible.

(2) The Enol Tautomer. The presence of the cis-enol form has been clearly established by both infrared and nuclear magnetic resonance measurements. Kabachnik's evidence for the existence of trans enol in α-alkyl substituted β-ketoesters depends on the absence of the chelated carbonyl absorption peak in infrared measurements (9). It is possible,

however, that the C=C absorption peak masks the chelate carbonyl absorption band. His assumption that the percentage of trans enol is independent of the solvent appears unsubstantiated since bromine titration is neither precise nor accurate as an analytical tool, and since the ultraviolet spectra and graphs of equilibrium constant versus enolizability of solvent toward cis enol both suggest the opposite conclusion. The present writer would prefer to have positive evidence in the form of free OH stretching bands in dilute nonpolar solvents. Ultraviolet evidence given by Kabachnik et al. (11), for isobutylacetylacetone does, however, appear to indicate two conjugated forms each of which depends upon solvent in both intensity and maximum wavelength. Shigorin's suggestion of a trans enol form for ethyl acetoacetate in inert solvents from infrared and Raman data does not appear to be proven by the facts (28). The present writer feels that additional solvent studies of the OH stretching frequency would be needed, and a clear distinction should be made between the intramolecular and intermolecular hydrogen bond in terms of stretching frequency and solvent dependency. Further studies of Shigorin (47, 48) do not appear to provide new evidence for the existence of trans enol in other β-dicarbonyl compounds. As has been mentioned, Bankowska (43) was unable to reproduce Shigorin's infrared evidence for free or intermolecularly linked OH bands for ethyl α-chloroacetoacetate.

Shigorin's Raman spectra of ethyl acetoacetate and acetylacetone do not appear to support the presence of dienol forms (28). The substitution of deuterium in β-dicarbonyls has provided evidence which may suggest the presence of a small amount of dienol structure (29). Shigorin has concluded that the low intensity of the O-D band in certain compounds indicates the presence of the dienol form. He also notes that the intensity of the C=C-H intensity increases in deuterated over that in the undeuterated compound. In a compound with mobile protons on the acetyl methyl and

in the α-position, these two facts together would substantiate Shigorin's claim. In this case, the data could only be explained by a structure such as the following:



However, there is no evidence from NMR that the acetyl methyl protons are labile. Dipole moment measurements indicate that the enol form of both acetylacetone and ethyl acetoacetate is an intramolecularly bonded species. A free hydroxyl group would result in a larger dipole moment than that for the keto tautomer, contrary to the evidence. The present writer has attempted to calculate the dipole moment for the enolic tautomer. If one considers the proton symmetrically placed between the oxygen atoms with an OHO angle of 150°, and takes the OH dipole moment from water, the calculated dipole moment is 3.5 D, higher than the observed value. If the dipole moment for the OH bond is taken as 1.7 D as in free hydroxyl groups, the calculated moment is 2.9 D.

Effects of Temperature and Pressure

Meyer's observation of an increase in keto tautomer in acetylacetone with an increase in temperature and the independence of the keto-enol equilibrium in ethyl acetoacetate from temperature changes have been noted. The latter observation does not agree with expected results or with the work of Briegleb (52). In a study of acetylacetone and ethyl acetoacetate in various solvents by bromine titration, Grossmann (49) has found that the keto concentration increases with a rise in temperature, although the rate of achieving equilibrium varied from 1-2 hours for alcohol solutions to 1-2 days for inert solvents.

Briegleb et al. (50), have studied the temperature dependence of the keto-enol equilibrium of α-chloro- and α-bromoacetoacetic ester in

the gas state. The enolic content of the α-chloro- and α-bromoacetoacetic ester over the range 0-160° and 0-100°, respectively, is less than that of ethyl acetoacetate itself at the same temperatures. Earlier work provides temperature studies on acetylacetone (51) and ethyl acetoacetate (52). Equilibrium constants and thermodynamic quantities for these compounds are given in Table IX.

The effect of pressure on the tautomeric equilibrium of acetoacetic ester was studied first by Kabachnik et al. (53). The equilibrium constants were determined in two percent solutions in various solvents. The observed shift of the equilibrium to the enol form with increased pressure in water and methanol has been interpreted as a solvation effect. The authors have assumed that the trans enol form, although low in concentration, is in greatest concentration in aqueous solvents and in methanol, and is most readily solvated. In ethanol and chloroform, increased pressure gave smaller equilibrium constants, and in the pure compound and in inert solvents, no effect was observed. Le Noble (54) has questioned whether the systems in Kabachnik's study were in equilibrium. In the pure liquid, Le Noble found for ethyl acetoacetate a decrease in the equilibrium constant from 0.0834 to 0.0685 from 1 atm to 3700 atm. For an equilibrium constant which is the ratio of enol to ketone tautomer, one would expect an increase in the equilibrium constant with increasing pressure, which was observed. Le Noble has pointed out that the molar volume of [-C(OH)=CH] is less than that of $COCH_2$, and that this difference is even greater for the intramolecularly hydrogen-bonded species. According to him the molar volume of the enol is greater than that of the diketone by about 1.0-1.5 ml/mole.

Table IX. Temperature Dependence of Keto-Enol Equilibrium in Some β-Dicarbonyls

Compound	T°K	Percent Enol	K_e*	ΔH kcal/ mole	ΔF kcal/ mole	TΔS kcal/ mole	ΔS kcal/ mole deg.	Reference
Acetylacetone	273.2	95	19.0	-1.78	-1.60	-0.18	-0.66	51
	413.2	79	--	-3.77	-1.06	-2.71	-6.55	
Ethyl acetoacetate	273.2	63	1.70	-3.71	-0.292	-3.41	-12.5	52
	453.2	14	0.163	-2.52	+1.63	-4.15	-9.17	
Ethyl α-chloroaceto-acetate	273.2	46	0.834	-3.66	0.099	-3.76	-13.8	50
	433	16	0.193	-0.10	1.41	-1.52	-3.50	
Ethyl α-bromoaceto-acetate	273.2	29	0.401	-1.51	0.50	-2.01	-7.4	50
	413.2	8	0.084	-3.83	2.03	-5.86	-14.2	

*K_e = [enol]/[keto]

Solvent Effects

Bromine Titration. Meyer (1) has studied the effect of solvent on enolization in acetylacetone and ethyl acetoacetate by bromine titration in 3-5 percent solutions in various solvents. The percentage of enol tautomer and equilibrium constants have been determined, and results are shown in Table X. A marked increase in the percentage of enol may be noted in the nonpolar solvent, hexane, over that in more polar solvents. Bromine titration has been used by Kabachnik (9) in a study of the effect of solvent on the tautomeric equilibrium in ethyl acetoacetate. Percentages of enols are given in Table XI, which indicates greatest enolization in nonpolar solvents. More recently Kabachnik et al. (10), followed the enolization of α-substituted β-keto-esters. These results are also shown in Table XI. For all compounds the greater enolization is in the direction

67 percent aqueous MeOH < MeOH < EtOH < benzene,

but it should be noted that concentrations are not recorded.

Dipole Moments. The effect of the solvent on the apparent dipole moment of ethyl acetoacetate has been noted by Le Fevre and Welsh (22). Percentages of the enol form have been taken from literature values and extrapolated to infinite dilution. The moments have been rearranged in order of increasing percentage of enol tautomer, as shown in Table V. Calculated values are those obtained from assuming a simple relationship between the solvent dielectric constant and the equilibrium constant, as shown in the following equation,

$$E = 100\, e^{-\mu_e (\epsilon - 1)/\mu_k}, \qquad (6)$$

Where E is the percentage enolic tautomer, μ_e and μ_k are dipole moments for the enol and keto tautomer, respectively, and ϵ is the

Table X.* Percentages of Enol Tautomer and Equilibrium Constants for Enolization of Acetylacetone and Ethyl Acetoacetate in Various Solvents

Solvent	T°C	Ethyl acetoacetate		Acetylacetone	
		Percent Enol	K_e**	Percent Enol	K_e**
Water	0	0.4	0.004	19	0.24
Formic acid	20	1.1	0.011	48	0.9
Methanol	0	6.9	0.074	72	2.6
Melt	20	7.4	0.079 0.084***	76	3.2
Chloroform	20	8.2	0.089 0.106***	79	3.8
Ethanol	0	12.7	0.15	84	5.3
Benzol	20	18.0	0.22	85	5.7
Heptane	--	--	0.92***	--	--
Hexane	20	48	0.9	92	12

*Bromine titration by Meyer (1) in 3-5 percent solutions.
**K_e = [enol]/[keto].
***From Kabachnik (9).

Table XI.* Percentages of Enol Tautomer for α-Substituted Ethyl Acetoacetates in Various Solvents

Substituent R in MeCOCHRCOOEt \ Solvent	67% MeOH	MeOH	EtOH	C_6H_6	$(Et)_2O$	CCl_4	$CHCl_3$	Hexane
H	2.0	7.1	11.4	18.3	29.1		8.7	54.3
CH_3	1.1	2.5	3.9	5.2				
C_2H_5	0.9	1.8	2.8	4.2				
n-C_3H_7	1.9	3.0	4.2	5.6				
n-C_4H_9	3.4	4.3	5.4	6.2				
i-C_3H_7	2.6	3.0	3.1	3.6				
i-C_4H_9	3.3	4.7	6.7	7.9				
s-C_4H_9	14.3	14.5	13.9	14.6		14.8		
s-C_5H_{11}	6.2	6.7	7.2	8.0	9.3			
C_6H_5	8.4	19.0	26.0	51.5			32.0	

*From Kabachnik (8, 9) by bromine titration.

dielectric constant of the solvent. There does not appear to be a good relationship between the solvent dielectric constant, as expressed in Equation (6), and the tautomeric equilibrium, although some agreement may be noted between observed and calculated values.

Raman Spectroscopy. From the vibrational spectrum of OH, Shigorin (28) has noted that an intermolecular bond between keto and enol forms is preferred in pure ethyl acetoacetate. In inert solvents such as hexane, carbon tetrachloride, and carbon disulfide at low concentrations, the enol tautomer forms an intramolecular hydrogen bond. The formation of this bond is then followed by displacement of the equilibrium toward the enol form (28). The present writer does not find adequate evidence for these conclusions.

Infrared Spectroscopy. Infrared techniques were used by Powling and Bernstein (36) to show the effect of solvent on the keto-enol equilibrium in acetylacetone, ethyl acetoacetate, benzoylacetone, and other compounds. Free energies and heats of tautomerization for these substances vary in a linear fashion with the solvent parameter $[(\epsilon-1)/2\epsilon+1)]$ (ρ/M). Tables XII and XIII for free energies and enthalpies of tautomerization, respectively, incorporate not only the authors' results but also values taken from the literature by them. For the purpose of this thesis values at infinite dilution have been extrapolated from figures in reference (36). The trend for both free energies and enthalpies is in the same general direction for all compounds, and algebraically smaller values are found in the gas phase, or in a nonpolar solvent such as hexane, than in polar solvents.

In an infrared study Kuratani has found ethyl acetoacetate more enolizable in the nonpolar solvents carbon disulfide, hexane, ether, and benzene than in methanol and pyridine (42). In a more recent work,

Table XII.* Free Energy of Tautomerization for β-Dicarbonyls in Various Solvents

Solvent \ Compound	25°C ΔF kcal/mole		
	Acetyl-acetone	Ethyl aceto-acetate	1-Phenyl-1, 3-butanedione
Gas phase	-1.4	+0.2	-
Ethanol	-1.0	+1.2	+1.0
Methanol	-0.6	+1.5	+1.5
Water	+0.5, +1.0	+3.3	-
Acetic acid	-0.6	+1.7	+1.7
Formic acid	-0.1	+2.7	-
n-Hexane**	-1.4	+0.2	-
Toluene**	-1.1	+0.8	+0.9
Benzene**	-1.0	+0.9	+1.2
Decalin**	-1.2	-	-
Hexachloroethylene**	-1.1	-	-
Chloroform**	-0.8	+1.4	+1.5
Bromoform**	-0.7	-	-
Acetone**	-0.5	+1.5	-

*Values interpolated from figures in Powling and Bernstein (36). Solutions were 0.1 M and were considered infinitely dilute.

**Solvent considered inert.

Table XIII.* Enthalpy of Tautomerization for Acetylacetone and Ethyl Acetoacetate in Various Solvents

Solvent	Compound ΔH kcal/mole Acetylacetone	Ethyl acetoacetate
Gas phase	-2.4	-2.0
Decalin	-2.3	-
Hexane	-	-2.0
Tetrachloroethylene	-2.2	-
Carbon tetrachloride	-	-1.3
Bromoform	-2.1	-
Ether	-	-1.0
n-Pentanol	-	-2.0
Ethanol	-	-1.6
Methanol	-	-1.3

*Values interpolated from figures in Powling and Bernstein (36). Solutions were 0.1 M and were considered infinitely dilute.

Kuratani has concluded that acetylacetone is also more enolizable in nonpolar solvents than in polar solvents (37).

Infrared studies of the effect of solvent on the tautomeric equilibrium in dimedone were made by Angell and Werner (31). For this compound the keto form is preferred in nonpolar solvents. The authors have concluded that, where intramolecular hydrogen bonding cannot stabilize the enol form, the keto form is preferred. In acetonitrile and dioxane both keto and enol forms are present.

Mecke and Funck (30), in infrared studies of acetylacetone, have found that the percentage of enol increased from an acetonitrile solution through the pure liquid to hexane solutions. These results are in Table XIV. The percentage enol has been determined for a number of β-dicarbonyls by Conant and Thompson (55) in absolute alcohol and in hexane, and these values are also in Table XIV.

Ultraviolet Spectroscopy. In an ultraviolet study of α-acylphenylacetonitriles, Russell (56) has concluded that in hydroxylic solvents, the keto-enol equilibrium is determined by solvation, whereas in non-hydroxylic solvents, it is determined by chelation.

The effect of solvent on the equilibrium constant for acetylacetone has been recorded by Hammond et al. (17). Where this constant is defined as [enol]/[keto], the values are 1.4 and 0.15 in acetonitrile and water, respectively.

Murthy et al. (35), have determined the tautomeric equilibrium of ethyl acetoacetate and acetylacetone in several solvents from the equation,

$$E = 100\left(\frac{\epsilon_o}{\epsilon_a}\right), \qquad (7)$$

where E is the percentage enol, ϵ_o is the observed molar extinction coefficient, and ϵ_a the assumed value for the enol tautomer. Results of these calculations are shown in Table XV. The authors have plotted

Table XIV. Percentages of Enol Tautomer for β-Dicarbonyls in Various Solvents

Compound	Percent Enol	Solvent	Molarity	Reference
Acetylacetone	90	hexane	1/10(vol)	30
	45	CH_3CN	1/10(vol)	30
	92	hexane	0.1	55
	83	ethanol*	0.1	55
Dibenzoylmethane	~100	ether	-	1
Ethyl α-butylacetoacetate	10	hexane	0.1	55
	6	ethanol	0.1	55
Ethyl α-ethylacetoacetate	15	hexane	0.1	55
	4	ethanol	0.1	55
Ethyl α-methylacetoacetate	12	hexane	0.1	55
	5	ethanol	0.1	55
Ethyl α-isopropylacetoacetate	6	hexane	0.1	55
Ethyl α-n-propylacetoacetate	14	hexane	0.1	55
Ethyl acetoacetate	49	hexane	0.1	55
	10	ethanol	0.1	55
	13	ether	-	1
1-Phenyl-1,3-butanedione	84	ether	-	1

*Absolute ethanol in all cases.

Table XV.* Percentages of Enol Tautomer for Ethyl Acetoacetate and Acetylacetone in Various Solvents

Solvent	Percentage Enol	
	Ethyl Acetoacetate	Acetylacetone
Cyclohexane	43	88
Dioxane	8	73
Diethyl ether	25	85
Ether/CH_3CN (50/50)	7	68
Ether/CH_3CN (75/25)	7	71
Acetonitrile	4	55
t-Butanol	10	80
i-Propanol	11	85
Ethanol	8	73
Methanol	6	70
Water	0.5	16

*From Murthy et al. (35), calculated from extinction coefficients.

the percentage of enol tautomer against the carbonyl stretching frequency and the $n \rightarrow \pi^*$ frequency in various solvents. The trends in both infrared and ultraviolet data indicate the stabilization of the carbonyl groups of the keto form by polar solvents. In the case of polar solvents which cannot donate protons, the solvent blue shifts are determined mainly by the dielectric constant of the solvent. In proton-donating solvents, however, the major contribution is hydrogen bonding.

Nuclear Magnetic Resonance Spectroscopy. Nuclear magnetic resonance (NMR) spectroscopy has been used by Reeves (23) for the determination of the keto-enol ratio for acetylacetone in various solvents. At infinite dilution the percentage enol was found to be 73 in acetic acid, 91 in cyclohexane, 58 in pyrrole, and 100 in triethylamine. In diethylamine only enol was observed, but keto may be present as an intermediate among rapidly interconverting forms, according to Reeves and Schneider (57). Giessner-Prettre (58) has observed the effect of solvents on the equilibrium in ethyl acetoacetate. In this compound an increase in enol content was noted in carbon tetrachloride, dichloroethylene, and benzene. No change in enol content was observed in either chloroform or pyridine. In pyrrole a decrease in the percentage of enol was found.

Kinetics and Thermodynamics

In a study of equilibrium constants over a range of solvents of different polarities, Kosower (59) has plotted graphically log K_{eq} versus Z, an empirical measure of solvent polarity. The source of equilibrium constant values is not given, but the figure shows that this basis of comparing the effect of various solvents on the equilibrium has some merit.

Equilibrium Constants and Thermodynamic Quantities. Equilibrium constants for enolization have been determined by Meyer (1), Kabachnik (9), and Hammond et al. (17). The present writer has calculated constants from the data of Conant and Thompson (55). For the purposes of comparison, equilibrium constants have also been calculated from nuclear magnetic resonance data of Reeves (23), Jarrett et al. (69), Giessner-Prettre (58), and Filler and Naqvi (18). These data are given in Table XVI.

Free energies of enolization have also been determined by Conant and Thompson (55) using indirect bromine titration. Measurements in the gas phase were made by noting the effect of a change of temperature on the composition of the distillate, but only over a short temperature range. Determinations were also made in the pure liquid and in hexane and alcohol solutions, and results are seen in Table XVII.

Dewar (60) has stated that, other things being equal, a ketone is more stable than the corresponding enol because the sum of bond energies in H-C-C=O is greater than that in C=C-O-H. Powling and Bernstein (36) estimate that the open chain end is about 18 kcal less stable than the diketone from bond energies. The present author has used Pauling's (61) bond energies to obtain a difference of 15 kcal/mole. In β-diketones where there is the possibility of intramolecular hydrogen bonding, one must consider the additional energy obtained from this hydrogen bond. Wheland (62) estimates that the intramolecular hydrogen bond of acetylacetone stabilizes the end tautomer by 5-10 kcal, and the conjugated system further stabilizes this tautomer by 2-3 kcal.

Powling and Bernstein (36) have determined the heats of tautomerization of acetylacetone in dilute solutions in decalin, tetrachloroethylene and bromoform, and in the gas phase. The optical densities of the enol and keto carbonyl stretching frequency bands were measured to obtain the concentrations of the tautomers. Measurements were made

Table XVI.* Equilibrium Constants for β-Dicarbonyls

Compound	K_e** Gas	Pure Liquid	0.1M Hexane	0.1M Alcohol
Acetylacetone	11	3.6	11.1	4.88
		4.4[23]		
		5.66[69]		
Ethyl acetoacetate	0.93	0.082	0.96	0.111
		0.0753[58]		
Ethyl α-n-butylacetoacetate	0.163	0.0650	0.111	0.0650
Ethyl α-ethylacetoacetate	0.11	0.031	0.170	0.0363
Ethyl α-methylacetoacetate	0.16	0.043	0.131	0.0537
Ethyl α-isopropylaceto-acetate	0.066	0.051	0.0638	-
Ethyl α-n-propylaceto-acetate	0.15	0.075	0.168	-
Ethyl trifluoroacetoacetate	-	8.09[18]	-	-
Methyl acetoacetate	1.19	0.062	-	-
3-Methylacetylacetone	0.79	0.44	1.44	0.460

*Calculated for purposes of this thesis from data in Conant and Thompson (55), and calculated from other references given as superscripts.

**K_e = enol/keto.

Table XVII.* Free Energies of Tautomerization for β-Dicarbonyls

Compound	$\Delta F^{25^\circ C}$ kcal/mole			
	Gas	Pure Liquid	0.1M Hexane	0.1M Alcohol
Acetylacetone	-1.3 -1.4,-1.8[36]	-0.7	-1.3	-1.0
Ethyl acetoacetate	0.1 +0.2-0[36]	1.5	0	1.2
Ethyl α-n-butylaceto-acetate	1.1	1.6	1.3	1.6
Ethyl α-ethylacetoacetate	1.3	2.1	1.1	2.0
Ethyl α-methylaceto-acetate	1.1	1.9	1.1	1.7
Ethyl α-isopropylaceto-acetate	1.6	1.8	1.6	-
Ethyl α-n-propylaceto-acetate	1.1	1.5	1.1	-
Methyl acetoacetate	-0.1	1.6	-	-
3-Methylacetylacetone	0.1	0.5	-0.2	0.4
1-Phenyl-1,3-butanedione	2.1[36]	-	-	-

*From Conant and Thomson by bromine titration at 25°C, unless specified by superscript, in which case values have been obtained from Powling and Bernstein (36) by extrapolation of figures to infinite dilution.

in the gas phase at 5 mm pressure, and in 0.1 M solution, which was assumed to be infinite dilution. Temperature ranges were 25-200° and 25-100° for the gas and solution determinations, respectively. It may be shown that the heat of isomerization in the gas phase is related to that in dilute solution by the equation,

$$\Delta H_{gas} = \Delta H_{soln} + \left(\frac{\epsilon - 1}{2\epsilon + 1}\right) \frac{\rho}{M_{soln}} (\mu_1^2 - \mu_2^2), \qquad (8)$$

where ϵ is the solvent dielectric constant, ρ the density of the solvent, M the molecular weight of the solvent, μ_1 and μ_2 the dipole moments of the less stable and more stable isomer of the solute, respectively. A plot of ΔH_{soln} against the solvent property will give a straight line with a slope equal to $-(\mu_1^2 - \mu_2^2)$ and the intercept ΔH_{gas}. Data have been plotted graphically for acetylacetone from measurements made by Powling and Bernstein, and the extrapolated value for ΔH_{gas}, -2.4 kcal/mole, agrees very well with that found experimentally. Literature values have supplied data for a plot of ethyl acetoacetate from which the extrapolated ΔH_{gas} is -2.0 kcal/mole. Literature values of ΔF were plotted versus the solvent property. ΔH and ΔF values, interpolated for the purposes of this thesis, are given in Tables XII and XIII, respectively, for 0.1M solutions in various solvents.

From nuclear magnetic resonance measurements of acetylacetone at various temperatures, Reeves (23) has found that increasing the temperature favors the keto form. By plotting $\log(c_1/c_2)$ versus $1/T^\circ K$, Reeves has determined the enthalpy difference between tautomers as -2.7 ± 0.1 kcal/mole.

Rates of Enolization. Reid and Calvin (63) have studied the rate of enolization in water for compounds with a trifluoromethyl group. These workers have found that the rate of formation of the enolate ion is the rate determining step in the reaction,

$$\frac{d\,[\text{keto}]}{dt} = -\,k_e\,[\text{keto}]\,. \qquad (9)$$

Rate constants for enolization and $\Delta H_{\text{activation}}$ for enolization are shown in Table XVIII. Also included in the table are values of ΔF^{o}_{25}, ΔS^{o}_{25}, and ΔH^{o} for enolization.

Bankowska (43) has studied the enolization of ethyl α- and γ-chloroacetoacetates. Following distillation, ethyl α-chloroacetoacetate reached the equilibrium mixture in alcohol and ether solution within a few days. In nonpolar solvents the enol concentration changed only slightly over several weeks, but pyridine catalyzed enolization in these solvents and also changed the position of equilibrium. Infrared spectra indicated the presence only of cis enol, in contrast to the work of Shigorin (28). Infrared and ultraviolet data are given in Tables VI-VII and VIII, respectively.

The enol content of ethyl α-chloroacetoacetate was measured bromometrically by Bankowska (64). A difference in the attainment of equilibrium following distillation was noted in various solvents. In polar solvents equilibrium was attained quickly, but in nonpolar solvents, the rate of approaching equilibrium was slow and increased with the addition of pyridine. Only cis enol appeared to be present both from infrared and ultraviolet spectra. The slow rate of tautomerization in nonpolar solvents has been explained by a weakening of the basicity of the α-chloroester from the inductive effect of the chlorine atom.

Rates of Ionization and Ionization Constants. Pearson and Mills (65) have determined the rate of ionization of β-dicarbonyls in water by measuring bromine uptake conductimetrically. The reactions are

$$H_2O + HA \underset{k_2}{\overset{k_1}{\rightleftharpoons}} H_3O^{+} + A^{-} \qquad (10a)$$

$$Br_2 + A^{-} \xrightarrow{k_3} ABr + Br^{-}, \qquad (10b)$$

Table XVIII.* Rates of Enolization and Thermodynamic Constants for Tautomerization for Fluorinated β-Dicarbonyls

Compound	Solvent	Molarity	T°C	k_e** sec^{-1}	ΔH_{act} kcal	K_e***	ΔF^o_{25} kcal/mole	ΔS^o_{25} kcal/mole deg.	ΔH^o kcal/mole
Trifluoroacetylacetone	water	0.0824	25	0.0149		0.011	+1.3	+0.7	+1.5
	water	0.0824	0	0.0009	+19.7				
	benzene	0.0825	25			35	-2.1	+4	-0.9
	benzene	0.0825	14			37			
Benzoyl trifluoroacetone	water	0.0093	25	0.0855		0.015			
	water	0.0082	14	0.0372	+13.0	0.023	+2.5	-30	-7
	benzene	0.102	25			17			
	benzene	0.0968	14			-	-	-	-
Thenoyl trifluoroacetone	water	0.0092	25	0.0101		0.016			
	water	0.0103	14	0.0030	+19.1	0.015	+2.4	-3	+1
	benzene	0.0669	25			17			
	benzene	0.100	14			26	-1.8	-7	-4

*From Reid and Calvin (63), using NaOH titration of aqueous ketone solutions for dissociation constants.
**See Equation (9).
***K_e = [enol]/[keto].

where Equation (10a) is the rate determining step, and the ionization constant is given by the following relationship:

$$K_e = K_{ion} \left(\frac{k_1}{k_2}\right). \qquad (11)$$

The rates of ionization were correlated with ionization constants, and these constants are shown in Table XIX. Rates of ionization are given in Table XX. The authors have calculated the changes in enthalpy and entropy from transition state theory for the forward and reverse ionization reactions for compounds where activation energies for ionization and heats of ionization are known (see Table XXI).

Pearson and Dillon (66) have extended the study of ionization rates of β-dicarbonyls in water. Ionization constants are shown in Table XIX and rates of ionization in Table XXI. A plot of log [rate constant] for ionization versus log [equilibrium constant] is approximately linear. Alkyl groups on the central carbon produce negative deviations, or have rates less than expected, and a fluorine atom on the central carbon has the opposite result.

Gould (67) has noted that the rate of enolization seems to be independent of acidity. Those substances which show more electron-withdrawing power by induction are, in general, more effective in stabilizing the anion than the activated complex leading to it.

The influence of branching of the chain on enolization and on the acidity of alkyl derivatives of acetylacetone has been studied by Rumpf and La Riviere (16). Acidity constants have been determined electrometrically, spectrophotometrically, and iodometrically. The acidity constant has been defined as

$$pK_e = pK_{app} - \log(1 + E) + \log E, \qquad (12)$$

where pK_e is the pK of the enol tautomer, pK_{app} is the observed pK,

Table XIX. Ionization Constants for β-Dicarbonyls

Compound	Ref. Eqn.	Ionization Constants* ($\times 10^{10}$)							
		70 (14)	65 (11)	66 (11)	16 (12)	69 (13)	15 (13)	17 (13)	68 (12)
Acetylacetone		1.99	11.7	10	59.5	10	0.054	-	-
Dibenzoylmethane								0.031	
Ethyl acetoacetate		0.063	0.21		0.16				0.22
Ethyl α-bromoacetoacetate			100						
Ethyl α-ethylacetoacetate			0.0018						0.0015
Ethyl α-n-butylacetoacetate									0.00063
Ethyl α-methylacetoacetate									0.0026
Ethyl α-isopropylacetoacetate									< 0.00001
Methyl acetoacetate									19.2
3-Methylacetylacetone			0.15	10	6.31				
1-Phenyl-1, 3-butanedione		1.58		4	76				
Thenoyltrifluoroacetone				8000					
Trifluoroacetylacetone		1990		200000					

*See text for definition of various constants in equations given above.

Table XX. Rates of Ionization of Pseudo Acids at 25°C in Water

Compound	$k_1(min^{-1})$	
	Pearson and Mills (65)	Pearson and Dillon (66)
Ethyl acetoacetate	$1.29x10^{-3}$	$7.2x10^{-2}$
Ethyl α-bromoacetoacetate	$1.59x10^{-2}$	$3.6x10^{-1}$
Ethyl α-ethylacetoacetate	$4.53x10^{-4}$	$4.5x10^{-4}$
Acetylacetone	$6.8x10^{-1}$	1.0
3-Methylacetylacetone	$4.97x10^{-3}$	$5x10^{-3}$
Benzoylacetone	-	$6.6x10^{-1}$
Trifluoroacetylacetone	-	$9.0x10^{-1}$
Thenoyl trifluoroacetone	-	$6.0x10^{-1}$

Table XXI.* Enthalpy and Entropy of Ionization of β-Dicarbonyls in Water

Compound	$\Delta H_2^{\ddagger}$ Kcal/mole	$\Delta S_2^{\ddagger}$ e.u.
Ethyl acetoacetate	13.6	-34.4
Ethyl α-ethylacetoacetate	14.9	-31.6
α-Methyl acetylacetone	17.4	-16

*From Pearson and Mills (65).

and **E** is the ratio of enol to keto tautomer. For this thesis, the pK_e values have been converted to K_e and are given in Table XIX. From the data it is seen that **α**-substitution results in an increase in pK_e, a decrease in **E**, and apparently prevents coplanarity not only of the enol, but also of the anion. This is an example of the steric inhibition of conjugation.

In a study of the acidity of β-dicarbonyls in aqueous solution, Rumpf and Reynaud (68) have concluded that the influence of alkyl substituents on ionization constants is comparable in acetylacetone and ethyl acetoacetate. Ionization constants for some β-ketoesters have been determined, and results are given in Table XIX. pK_e Values have again been converted for the purposes of this thesis to K_e values.

The potentiometric determination of dissociation constants for both acetylacetone and ethyl acetoacetate has been reported by Walisch et al. (9). The empirical dissociation constant has been defined as

$$K_b' = \frac{[H^+][A^-]}{[HA]} \qquad (13)$$

where [H] and [**A**] are activities, and [**HA**] is the total β-dicarbonyl content. Values for the constants are given in Table XIX.

Hammond (15, 17) has considered concentration acidity constants, Q_A, defined the same as K_b' in Equation (13), but using concentrations instead of activities. It may be noted that values for pK_a may be obtained by adding 1.55 to -log Q_A. For the purposes of this thesis the reported values of -log Q_A have been converted to values of $Q_A = K_b'$ and are given in Table XIX. Hammond observed that acetylacetone is a stronger acid than dibenzoylmethane, although the latter is more enolized. Hammond has defined acidity as the ability to form anions. Steric strain can be important in producing variations in acidity. For the enolate ion structure shown in Figure 7, a large R group introduces

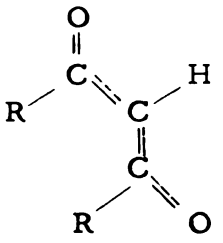


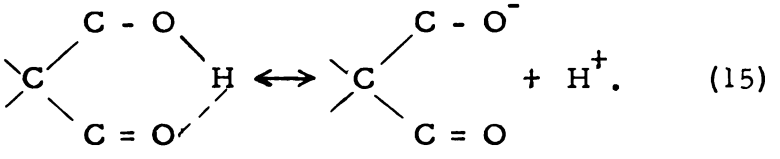
Figure 7. Enolate ion structure.

strain in the planar trans configuration which should ordinarily be the most stable form. For dibenzoylmethane the trans configuration of the ion can only be constructed with models if the benzene group is perpendicular to the plane of the dicarbonyl system.

Calvin and Wilson (70) have determined the constant, K_D, for several β-dicarbonyl compounds. This constant is defined as

$$K_D = \frac{[H^+][K_e^-]}{[HK_e]} \quad , \qquad (14)$$

where K_D represents the acid strength of the enol for the reaction



(15)

Values for the ionization constants are given in Table XIX. These values indicate that the anion of acetylacetone is more stable than that of ethyl acetoacetate. As noted earlier, Bellamy and Beecher (32) concluded from the work of Calvin and Wilson that the equilibrium constant is independent of the percentage double-bond character of the carbonyl bond.

Nuclear Magnetic Resonance Studies

The initial application of nuclear magnetic resonance techniques to β-dicarbonyls was by Jarrett, Sadler, and Shoolery (71). For both acetylacetone and 3-methylacetylacetone the 30 Mc proton spectra allowed integration of enol versus keto peaks for the calculation of the percentage of each tautomer. Jarrett et al., had assigned all acetyl methyl protons to one peak and $CH_3C(OH)=$ methyls to another. Assignment to the methyl absorption peaks was corrected by Reeves (23) using a 40 Mc instrument at variable temperatures. Reeves showed that both methyls are equivalent in the enol tautomer of acetylacetone, and that the two methyl resonance peaks are due to keto and enol tautomers.

Solvent studies of acetylacetone were performed by Reeves (23). Chemical shift measurements were made in pyrrole, cyclohexane, triethylamine, and acetic acid. Results are given in Table XXII. Their reported values have been converted to cps at a spectrometer frequency of 60 Mc and are referred to tetramethylsilane as a standard for purposes of this thesis. The use of a methyl group as an internal standard, as was done by Reeves, is advisable only with fairly inert solvents, such as cyclohexane. From chemical shift measurements both acetic acid and cyclohexane appear to be inert solvents toward acetylacetone in the sense that they do not change the chemical shifts of the various protons. In acetic acid the OH signal of the solute was broadened, but remained a separate resonance from that of the carboxyl OH group throughout the dilution range at room temperature. In pyrrole the OH peak was once again broadened. Here the keto α-methylene protons shifted upfield by 28 cps on dilution, while the enol OH protons shifted downfield by 33 cps. Triethylamine showed only the enol tautomer and gave a very large upfield shift of the enol

Table XXII.* Infinite Dilution Chemical Shifts of the Protons of Acetylacetone in Various Solvents

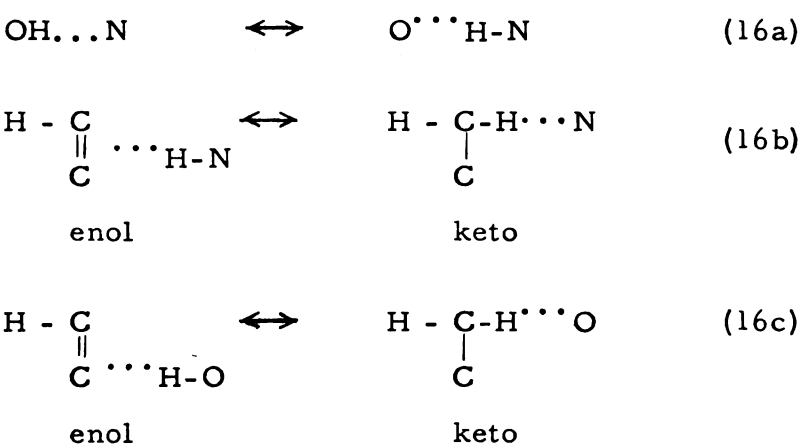
Solvent	Proton Resonance Peak				
	Enol CH_3**	Keto CH_3	Keto CH_2	Enol CH=	Enol OH
Pure	119	129	218	334	933
Pyrrole	119	124	190	333	966
Cyclohexane	119	127	212	331	935
Triethylamine	119	-	-	334	455
Acetic acid	119	130	218	334	919

*From Reeves (23), changed to cps at 60 Mc relative to tetramethylsilane.

**Used as an internal standard.

OH by 478 cps. This large shift was explained by Reeves as due to both breaking of the intramolecular hydrogen bond of acetylacetone and the formation of a hydrogen bond with the solvent. Both the enol OH and the enol α-proton resonances were broadened in this solvent.

Proton transfer in acetylacetone in diethylamine and triethylamine has been observed by Reeves and Schneider (57). Solutions in triethylamine are completely enolic. Amines not only change the keto-enol equilibrium, but also increase the keto-enol conversion rate. With diethylamine, the rate of exchange is sufficiently rapid to result in an averaged spectrum. Assignment of the OH, NH, and enol α-proton peaks was made from temperature studies. Broadening of the above peaks has indicated that there is exchange among all of these protons. The following exchange processes are proposed to explain the behavior in diethylamine:



(16a)

(16b)

(16c)

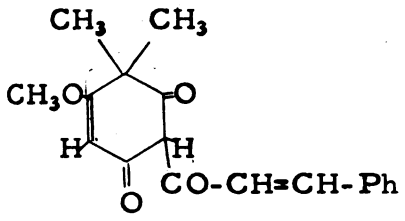
Proton exchange in hydrogen-bonded systems has been reviewed by Schneider and Reeves (72). A study of exchange in acetylacetone and acetic acid mixtures was made. The subject of proton transfer in such systems is covered in the theoretical section of this thesis (page 78).

Solvent studies of acetylacetone in pyridine, water, and mixtures of pyridine and water have been conducted by Balta Calleja (73).

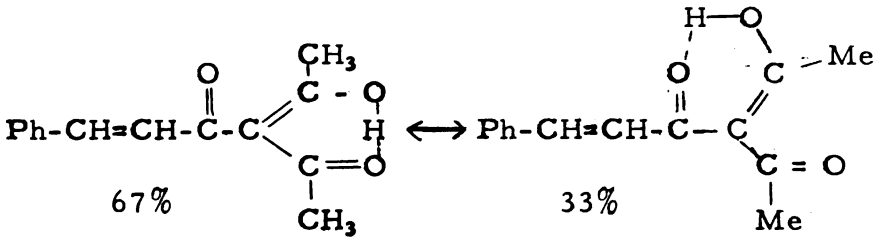
Measurements were made at 25 Mc relative to the enolic methyl protons as an internal standard. Only the enol OH proton showed a change in chemical shift in these solvents. With pyridine alone, no change was observed, but both with water and in mixtures, the enol OH proton showed a high-field shift. This shift has been explained on the basis of dissociation, but solubility limited the study of mole fractions above 0.6 M.

Enolized β-triketones have been extensively investigated by nuclear magnetic resonance by Forsen and Nilsson. In a study of triacetylmethane, 2-acylcyclohexane-1, 3-diones, and ceroptene (see Figure 8a), chemical shifts for the enol OH protons varied from 1040 cps (downfield from TMS) in triacetylmethane to 1130 cps in ceroptene. Two enolic tautomers are possible, and the NMR spectrum indicated a ratio of 1/4, but no attempt was made to distinguish between these forms. The presence of more than one enolic tautomer was detected in several compounds. Equilibrium constants were dependent on the solvent and are in the range 3-8, corresponding to a free energy change on enolization of less than 1 kcal/mole. The tautomeric forms are evidently similar, with hydrogen bonds of about equal strength. Infrared carbonyl stretching frequencies in the chelated forms were measured, and a linear correlation was observed between these frequencies and the chemical shift of the enolic proton. A lower stretching frequency was accompanied by a proton resonance at lower applied fields.

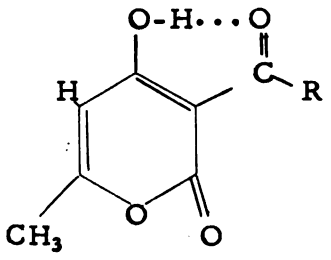
Forsen and Nilsson (75) further found complete enolization in methyl and ethyl diacetoacetate. The enol proton chemical shifts in these compounds occurred at lower applied fields than in triacetylmethane. Both ethyl cinnamoylacetoacetate (see Figure 8b), and 3-cinnamoylpentane-2, 4-dione indicated the presence of two enolic tautomers. The latter exhibited two separate signals for the enol



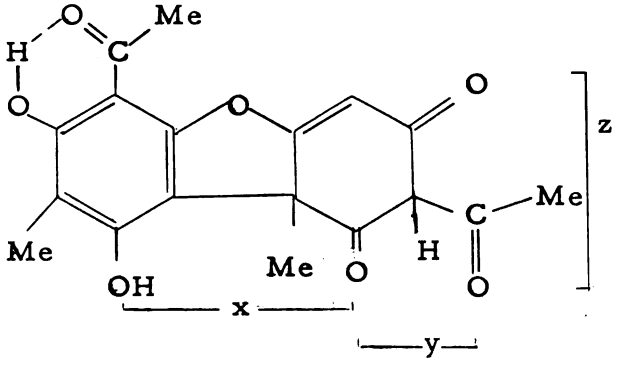
(a) ceroptene



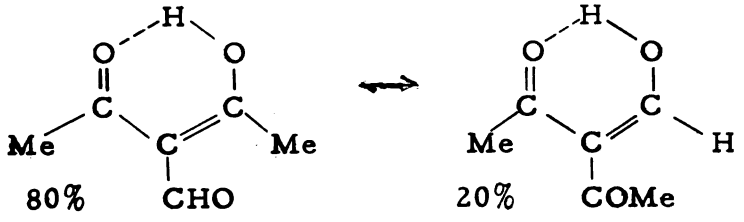
(b) ethyl cinnamoylacetoacetate



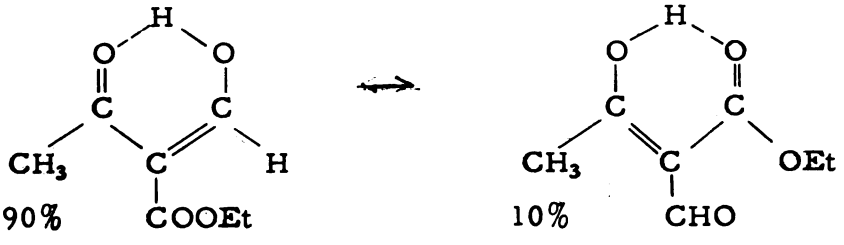
(c) dehydroacetic acid



(d) usnic acid



(e) diacetoacetaldehyde



(f) ethyl 2-acetyl-2-formylacetate

Figure 8. Structures of some β-triketones.

OH protons of these two tautomers, whereas in other β-triketones the lifetime in the two sites has been too short for detection by nuclear magnetic resonance. This separation of signals may also be explained by the ring current effect on the protons in different locations.

Both infrared and NMR evidence indicate that dehydroacetic acid (see Figure 8c) exists entirely in one enolic form (76). The intramolecular hydrogen bond in this compound was found to be weaker than those in other β-triketones studied, both from the chelate carbonyl frequency and the enol proton chemical shift measurements. The authors have suggested that the chelate system may be affected by the nature of the 4-5 double bond in the compound. Additional conjugation appears to give a stronger intramolecular hydrogen bond.

In usnic acid compounds (see Figure 8d), the enolic hydrogen bond appeared to be comparable in strength to that in ceroptene (77). Hydrogen bonding is possible at positions x, y, and z in the figure. Only one enolic tautomer is seen in the NMR spectrum. Neither infrared nor nuclear magnetic resonance were conclusive in determining which tautomer was present.

Nilsson (78) has extended the original correlation figure (74) between enol proton chemical shift and chelate carbonyl stretching frequency. Nilsson pointed out that, in a comparison of triacetylmethane and diacetoacetic esters and their conjugated analogues, the esters show stronger hydrogen bonds. Corrections were not made for magnetic anistropy effects. Whether this strengthening of the hydrogen bond is mostly due to inductive rather than resonance effects is not known. The effect of conjugation on such systems varies with the compound. The presence of an adjacent aromatic group appears to weaken the intramolecular hydrogen bond, whereas a non-aromatic ring seems to strengthen this bond. However, there are discrepancies between infrared and nuclear magnetic resonance results among such compounds.

Spin coupling effects have been observed by Forsen and Nilsson (79) in hydroxymethylene- and anilinomethylene compounds, which have possible structures as shown in Figure 9.

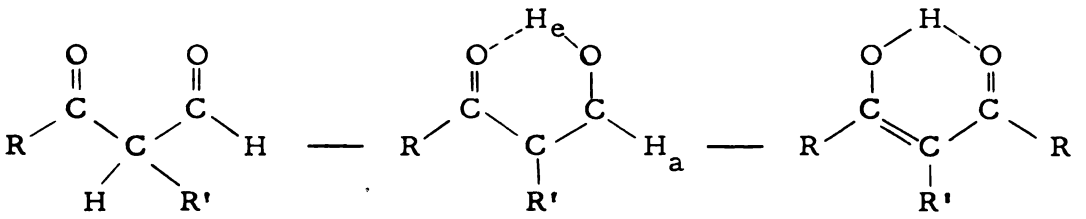


Figure 9. Keto and enol structures for hydroymethylene compounds.

These compounds are almost entirely enolized, and in many cases more than one enolic form is observed by nuclear magnetic resonance. Spin coupling was seen between the enol OH proton and the aldehydic proton. This coupling varied from about 6 cps in hydroxymethylene compounds to 12.5 cps in ethyl 2-formyl-2-phenylacetate. Spin coupling generally decreased with increased temperature and varied with concentration. For diacetoacetaldehyde two of the possible chelated enolic forms were seen in the nuclear magnetic resonance spectrum. The dominant form was the chelated 3-formyl-4-hydroxypent-3-en-2-one seen in Figure 8e. In ethyl 2-acetyl-2-formylacetate, two of six possible chelated enols was present. Spin-spin coupling constants and infrared spectra make possible the identification of these enols, shown in Figure 8f.

A review of nuclear magnetic resonance studies of hydrogen bonding in β-triketone systems has been written by Forsen (80).

In ethyl acetoacetate, Giessner-Prettre has shown by nuclear magnetic resonance studies at 25 Mc that carbon tetrachloride, benzene, and tetrachloroethylene increased enolization, whereas pyrrole decreased enolization on dilution. In pyridine and chloroform, no change

in the amount of enol tautomer was observed. In carbon tetrachloride, benzene, and tetrachloroethylene, the keto CH_2 resonance peak was displaced toward higher fields on dilution. This was interpreted as due to a breaking up of intermolecular associations between CH_2 and C=O. Basic solvents such as triethylamine and piperidine did not favor enolization, in contrast to the effect on acetylacetone observed by Reeves. Giessner-Prettre was unable to observe the OH resonance in binary solutions of ethyl acetoacetate with various solvents. There was approximately 50 percent enol at infinite dilution in carbon tetrachloride and tetrachloroethylene.

Dudek and Holm (81) have noted a decreased shielding of the enolic OH proton of acetylacetone in benzene and have suggested that there is some hydrogen bonding of the carbonyl group of the solute with the solvent. For bis(acetylacetone)-ethylenediimine there was a shift to high field of certain protons. The authors have explained this shift on the basis of the orientation of these protons above the plane of the benzene ring.

γ-Fluoro-β-ketoesters have been studied by Filler and Naqvi (18). The percentage of enol was determined, and an attempt was made to explain these percentages on the basis of the electron-withdrawing power of fluorine.

Theoretical Studies

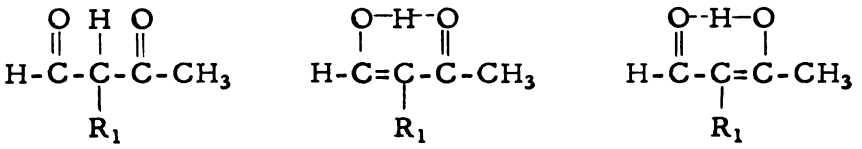
Forsen (82) has used a simple molecular orbital approach to calculate the effect of substituents on the carbonyl stretching frequency. He has calculated bond orders for the carbonyl bond and has neglected resonance and overlap integrals. A linear relationship was found between bond order and stretching frequency, and it was concluded that the inductive effects determine the stretching frequency in these compounds for the most part. A correlation was also found between the

charge on the oxygen atom (and the dipole moment) and the stretching frequency.

Molecular orbital calculations of the Hückel type have been carried out by Forsen (83) for some enolized di- and tri-ketones. For the keto and the various enol tautomers the total π-electron energy and the delocalization energy have been calculated. There appears to be a general correlation between the calculated difference in delocalization energy and the position of the keto-enol equilibrium, since smaller differences in delocalization energy accompany a higher enol content. Some results have been reproduced in Table XXIII. However, Forsen has pointed out that the molecular orbital calculations involve many uncertainties, and that entropy differences, energies of intramolecular hydrogen bonds, and solvent effects have been neglected.

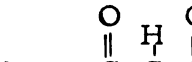
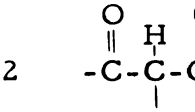
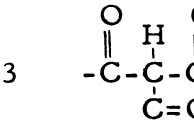
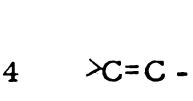
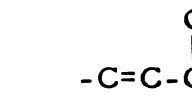
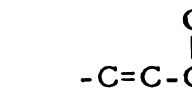
Forsen has extended the molecular orbital calculations to an estimation of charge distributions and bond orders in these compounds (84) (see Table XXIII). No definite correlation was found between the enol proton chemical shift and the calculated charge density on the carbonyl oxygen. Neither was good correlation discovered between the calculated bond order of the C=C bond in the chelate ring and the stretching frequency of the chelated carbonyl group. Forsen has suggested that the lack of correlation may be due to the fact that the Hückel method may not give an adequate description of relative charges in the electronic distribution among molecules.

In α-formyl ketones such calculations were used to predict which of the enolic tautomers pictures below is most stable (85).

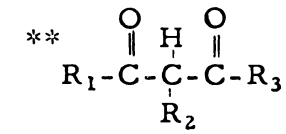


(a) (b) (c)

Table XXIII.* Molecular Orbital Calculations for β-Di and β-Tri-Ketones

	Skeleton**	Tautomer	Parameter Set I: Total π-Electron Energy	Delocalization Energy	Difference in Delocalization Energy between Keto and Enol Tautomers	Observed Enol Content
1		k	4α + 9.060β	6.260β	0.554β	76.4
		e	6α + 13.106β	5.706β		
2		k	6α + 11.060β	8.260β	0.126β	95
		e	8α + 15.534β	8.134β		
3		k	6α + 13.590β	9.390β	0.112β	-
		e	8α + 18.078β	9.278β		
4		k	6α + 11.516β	8.716β		-
		e	8α 15.612β	8.212β	0.504β	
		e	8α 15.526β	8.126β	0.590β	

*From Forsen and Nilsson (75, 76)

** 

IR (cm^{-1})	NMR OH (cps)	Chelate C=O Electron Density	Enolic Oxygen Electron Density	Bond Order Chelate C=O	Bond Order C=C	Excitation Energy of First $\pi \rightarrow \pi^*$ Transition
1608	-5.4	1.527	1.968	0.777	0.863	1.519β
1580	-7.4	1.518	1.961	0.792	0.766	1.480β

Several sets of parameters were tried, but the results of these calculations are inconclusive.

Stabilities of Metal Chelates

A brief discussion of metal chelates is included because of their interest in the separation of metal ions and because of possible correlations of stability with the β-dicarbonyls themselves. Calvin and Wilson (70) studied the stability of chelate compounds by titrating H^+ in a solution containing Cu(II), β-dicarbonyl, and excess H^+. Factors of importance in determining the stability of the chelate include not only coulombic effects but also resonance in the enolate ion. For increased resonance in the chelated form of the ion, increased stability of the chelate is expected.

Holtzclaw et al. (33), have studied the infrared absorption of metal chelate compounds of 1, 3-diketones. Stability was established by polarographic reduction of copper chelates. In the chelate ring of the enolic form, the basic effect of oxygen donor atoms is responsible for bonding. Stability is also determined by resonance in the chelate ring and by steric hindrance. Trifluoromethyl groups make the oxygen less basic, and the trifluoroacetylacetone chelate is between acetylacetone and hexafluoroacetylacetone in stability. The 2-thenoyltrifluoroacetone chelate is less stable than that of trifluoroacetylacetone since the thenoyl group is electron attracting and also interferes with resonance in the chelate ring. The order of increasing stability of metal chelates is hexafluoroacetylacetone > 2-thenoyltrifluoroacetone > trifluoroacetylacetone > 1-phenyl-1, 3-butanedione > 2, 4-pentanedione > 3-methylpentanedione. Infrared frequencies of interest are given in Table XXIV.

Nakamoto et al. (86), have studied the infrared spectra of metal chelate compounds and have determined the effect of substituents on

Table XXIV.* Infrared Frequencies of Groups in β-Diketones and Their Metal Chelates

Compound	Absorption Band (cm^{-1})				
	Hydroxyl OH	Keto C=O	Chelate C=O	Perturbed C=O	Perturbed C=C
Acetylacetone	3460w 3380w	1720s 1700s	1618s		
Cd(II)-acetylacetone				1613s**	1518s
3-Chloroacetylacetone		1725m, b	1613s, b		
Cu(II)-3-chloroacetyl-acetone				1571s	1520s
Dibenzoylmethane			1595s, b		
Cu(II)-dibenzoylmethane				1552s	1535s
Cu(II)-hexafluoroacetyl-acetone				1615s	1541a
Cu(II)-methylacetylacetone				1580s	1530w, 1515w
1-Phenyl-1, 3-butanedione			1604s, b		
Cu(II)-1-phenyl-1, 3-butane-dione				1561s	1525s
Thenoyltrifluoroacetone			1640s, b		
Cu(II)-thenoyltrifluoro-acetone				1570s	-
Cu(II)-trifluoroacetyl-acetone				1598s	1538s

*From Library of Congress, ADI 5129, referred to in Holtzclaw and Collman (33).

**Dependent upon concentration.

^{w}Weak

^{s}Strong

^{b}Broad

the spectra of metal acetylacetonates. Results for the copper chelates of hexafluoroacetylacetone, trifluoroacetylacetone, benzoylacetone, and dibenzoylmethane are given in Table XXV. Force constants have been calculated and are included in the table. The effect of the trifluoromethyl group is to increase the C=C and C=O bond distances and decrease the C-R and M-O (M=metal) bonds. Thus the strong inductive effect of the trifluoromethyl group strengthens the C=C and C=O bonds and weakens the M-O bonds. Phenyl substitution could lead to electron release and a strengthening of M-O bonds by an increase in the negative charge on oxygen. This effect strengthens the C-C and M-O bonds more than the C-O bond of the ring. These results differ from those of Holtzclaw, et al. (33), who said that the phenyl group weakens the M-O bond, since the C=O bond is weakened by conjugation with the ring. Stability constants agree with those found by Holtzclaw et al.

Table XXV. Infrared Frequencies and Force Constants for Groups in Copper Chelates of β-Diketones

Ligand	Frequency cm^{-1}		Force Constant 10^5 cyne/cm	
	C=C	C=O	C=C	C=O
Hexafluoroacetylacetone	1644	1614	5.81	7.90
Trifluoroacetylacetone	1611	1600		
Acetylacetone	1580	1548 1524	5.35	6.90
Benzoylacetone	1590	1554		
Dibenzoylmethane	1593	1544	5.49	6.82

*From Nakamoto et al. (86).

THEORETICAL CONSIDERATIONS

Nuclear Magnetic Moments

All nuclei with non-zero nuclear spin may be studied by nuclear magnetic resonance techniques. For a nuclear spin of 1/2, as in protons, the nuclear magnetic quantum number m may have the values $\pm$ 1/2. In the absence of a magnetic field, there will be equal populations of nuclei with m = 1/2 and m = -1/2. In the presence of a magnetic field those nuclei with m = +1/2 are the more favored state, and the distribution of nuclei between states with m = $\pm$ 1/2 may be expressed by the Boltzmann equation (87),

$$N = Ape^{-\epsilon/kT}, \tag{17}$$

where

$$\left.\begin{aligned} \epsilon &= -\mu_H H \\ \mu &= \frac{\gamma h}{2\pi} m, \end{aligned}\right\} \tag{18}$$

and μ_H is the component of the magnetic moment along the field axis, H is the magnetic field, and γ is the gyromagnetic ratio.

Chemical Shifts

In an applied magnetic field, the field at the nucleus is given by

$$H = H_o (1 - \sigma), \tag{19}$$

where H_o is the applied field and σ is the shielding constant. In liquids where molecular rotation is rapid, the shielding constant may be expressed as (88)

$$\sigma = \frac{1}{3}(\sigma_{11} + \sigma_{22} + \sigma_{33}), \tag{20}$$

where σ_{11}, σ_{22}, and σ_{33} represent the principal components of the shielding tensor.

An expression may be derived for the screening constant for a particular nucleus when the applied field is in the z-direction, as follows (88)

$$\sigma_{zz} = \frac{e^2}{2mc^2}\int \frac{x^2 + y^2}{r^3}\,\rho\, d\tau + \frac{e^2\hbar^2}{m^2c^2\Delta E}\left(0\left|\sum_{jk} r_k^{-3}\frac{\partial^2}{\partial\Phi_j\,\partial\Phi_k}\right|0\right). \tag{21}$$

In this equation ρ is the electron density, Φ_j is the azimuthal angle for rotation about the z-axis, and ΔE represents the average electronic excitation energy. The first term is positive and represents the local diamagnetic contribution, and the second is negative so is termed the contribution from local paramagnetic currents. From a practical standpoint, one is able to calculate the screening constant only for small molecules.

The shielding constant receives contributions from several sources and has been arbitrarily divided by Buckingham (89), and Buckingham et al. (90), into the following components,

$$\sigma = \sigma_b + \sigma_a + \sigma_w + \sigma_E, \tag{22}$$

where σ_b is the contribution from the bulk magnetic susceptibility of the medium, σ_a is due to anisotropy in the susceptibility of the solvent molecules, σ_w is due to van der Waals forces between solute and solvent, and σ_E is the polar effect.

Chemical Shift due to Bulk Susceptibility. The magnetic field experienced by a proton in a cylindrical sample is given by

$$H_{proton} = \sigma H_o (1 - 2\pi \chi_v/3), \tag{23}$$

where H_o is the applied field, σ is the shielding constant, and χ_v is the volume susceptibility. For the chemical shift between protons of two substances in a liquid mixture, the chemical shift becomes

$$\delta = \frac{\sigma_j - \sigma_i}{\sigma_i} \times 10^6, \tag{24}$$

where σ_j and σ_i are proton shielding constants for the reference and observed proton, respectively. For the case of Equation (24) the chemical shift is independent of volume susceptibility. Bothner-By and Glick (91) found good agreement between experimental values and those calculated by this equation for mixtures of methylene-chloride and methylenebromide.

Bothner-By and Glick (92) also studied the chemical shift of a given proton in media of different susceptibilities using the equation,

$$\delta = \frac{2\pi \Delta\chi_v}{3} \times 10^6, \tag{25}$$

where $\Delta\chi_v$ is the difference in susceptibility of the media. Agreement was only fair when the shape factor $2\pi/3$ was used. The error may be explained not only by experimental error, but also by unreliability of literature susceptibility values. As a result of these studies, Bothner-By and Glick suggested the use of the empirical equation for predicting the behavior of regular mixtures, as follows:

$$H = \sigma_i H_i^o (1 - 2.6 \chi_v). \tag{26}$$

Chemical Shift due to Anisotropy. The volume magnetic susceptibility is given by

$$\vec{M} = \chi_v \vec{H}, \tag{27}$$

where $\vec{M}$ is the magnetic moment per unit volume, $\vec{H}$ the magnetic field, and χ_v depends on the nature of the material. If $\chi_v > 0$ or the induced moment is parallel to the magnetic field, then the substance is paramagnetic, and if $\chi_v < 0$, it is diamagnetic. The susceptibility of a mixture is given by (88)

$$\chi_{M,\,mixt} = x_1 \chi_{M_1} + x_2 \chi_{M_2}, \tag{28}$$

where x_1 and x_2 are mole fractions, and χ_{M_1} and χ_{M_2} are susceptibilities of the pure compounds.

The diamagnetic susceptibility of a molecule has been expressed by Pascal (88) in the empirical equation,

$$\chi_M = \Sigma \chi_A + \lambda, \tag{29}$$

where χ_A are atomic susceptibilities and λ are constitutive corrections.

The susceptibility of a bond may be written in terms of components as follows:

$$\chi_m = 1/3(\chi_1 + \chi_2 + \chi_3), \tag{30}$$

where $\chi_{1,2,3}$ represent susceptibilities along the three axes of the bond. If the components are unequal, then the bond shows diamagnetic anisotropy. Similarly a molecule may show diamagnetic anisotropy if the components along principal axes differ.

It may be shown that the anisotropic contribution to the shielding constant is given by

$$\sigma_a = -n\frac{(\chi_{//} - \chi_{\perp})}{3R^3}/(3\cos^2\theta - 1), \qquad (31)$$

where n is the number of molecules within the range R, $\chi_{//,\perp}$, are susceptibilities parallel and perpendicular to the molecular axis, θ is the angle between the direction of principal susceptibility and the line from the molecular axis to the proton under observation, and R is the distance from the axis to the proton.

For disc or rod-shaped solvent molecules close to the solute, where θ is 0° and 90°, respectively, the shielding contribution reduces to:

$$\left.\begin{aligned} \sigma_{a(disc)} &= -2n(\chi_{//} - \chi_{\perp})/3R^3 \\ \sigma_{a(rod)} &= n(\chi_{//} - \chi_{\perp})/3R^3 . \end{aligned}\right\} \qquad (32)$$

In solvents with disc-like molecules, there is a resultant high-field shift of the solute protons, whereas for rod-like molecules with the largest susceptibility along the molecular axis, there is a low-field shift of the solute protons.

Calculations for methane in benzene give $\sigma_a = 1.3$ ppm, and for methane in carbon disulfide, $\sigma_a = -0.5$ ppm. Precise agreement with the observed values of 0.33 and -0.42 ppm is not expected because of the assumptions made in deriving Equation (31).

Bothner-By and Glick (93) studied aliphatic solutes in aromatic solvents and noted irregular behavior in solvents with large magnetic polarizability anisotropy. For the benzene protons extrapolated to infinite dilution in several solvents, the resonance position is at lower applied fields by 0.6-0.7 ppm than that calculated using Equation (25). The aromatic compounds have effective volume susceptibilities smaller by about $0.25\text{-}0.30 \times 10^{-6}$ than literature values. These effective susceptibilities when substituted into Equation (25), give a shape factor of 2.6 instead of the value $\frac{2\pi}{3}$ obtained from electromagnetic theory.

Chemical shifts of solutes in benzene move to higher applied fields as infinite dilution is approached, which indicates anomalous diamagnetic shielding by the aromatic ring (93). The size of the shift is irregular and depends on the specific solute. An approximate shift of 0.12 ppm has been calculated for a proton in the vicinity of a benzene molecule and directly above the ring. This calculation disregards factors such as statistical variation in intramolecular distances, the occurrence of interaction with more than one solvent molecule at a time, and the possibility of a solute molecule lying in the plane of the ring.

The large diamagnetic anisotropy of the benzene ring may be explained in terms of the ring current model, shown in Figure 10.

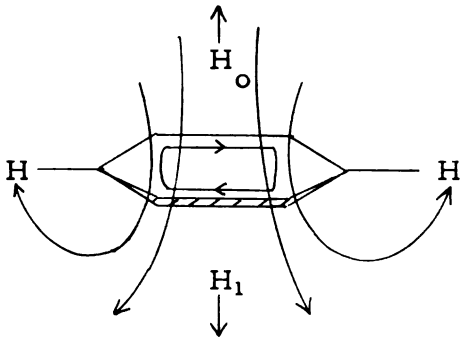


Figure 10. Schematic representation of ring-current effect.

Protons situated above or below the plane of the ring experience a magnetic field less than that elsewhere, and as a consequence require a greater applied magnetic field for resonance. Protons lying in the plane of the ring will experience a downfield shift by similar reasoning. In solutions concentrated in benzene, there is a greater chance for other benzene molecules to be above and below the plane of the ring than in the plane, with a resulting high field shift of the solute protons.

Johnson and Bovey (94) have calculated the magnetic field in the vicinity of the benzene ring and have determined the chemical shift for

a proton in any position relative to an aromatic ring. A plot is given for the diamagnetic and paramagnetic shift as a function of distance from the ring. Reeves and Schneider (95) have calculated the distance of chloroform molecules from the plane of the benzene ring for assumed complexes of the chloroform molecule with benzene. For an observed shift of 1.25 ppm in benzene, the chloroform proton may be calculated to be 3.43 Å above the plane of the ring. The chemical shift in ppm at the proton is given by:

$$\delta = \frac{3e^2a^2}{mc^2r^3} , \qquad (33)$$

where e is the charge on the electron, a is the radius of the benzene ring, m the mass of the electron, c the velocity of light, and r the distance of the proton from the center of the ring. Hatton and Schneider (96) have compared the behavior of polar molecules in toluene and methyl cyclohexane. It was suggested that the difference in solute chemical shift between solutions in these solvents made it possible to neglect the chemical shift due to van der Waals interactions and due to the reaction field since these would be the same. The observed chemical shift of the polar compound may then be explained by complex formation. The authors have proposed a complex in which the more positive end of the molecule is oriented above the plane of the ring, as shown in Figure 11.

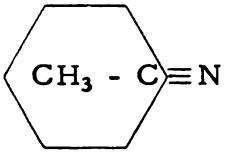


Figure 11. Orientation of a polar molecule with respect to the benzene ring.

Schneider (97) has investigated the effect of the shape of the solute molecule in benzene solutions by comparing chemical shifts for rod-like

and planar solute molecules. The results eliminate the possibility of a shape effect and support the proposed benzene-polar solute complex.

Stephen (98) has used statistical mechanics to study the effect of molecular interaction by treating molecules as point dipoles. For solvents whose molecules show a diamagnetic anisotropy two effects appear to be important. Magnetic moments induced in a solvent molecule produce a magnetic field at neighboring solute molecules. This effect is particularly important in aromatic compounds, and the contribution to the shielding constant from the magnetic anisotropy effect has been calculated to be 0.70×10^{-6} in aromatic solutions. The second effect is a change in the electronic distribution of a molecule by an induced electric field in a nearby molecule. This effect is most important in polar molecules, and its contribution to the shielding constant is larger and of opposite sign than the first effect. For water, this contribution is -4.5×10^{-6}.

Chemical Shift due to van der Waals Forces. Bothner-By (99) has calculated the shielding correction for a randomly oriented field due to London disperson forces as:

$$\Delta \sigma \cong - 10^{18} E^2, \tag{34}$$

where **E** is the electric field. For nonpolar liquids $\Delta\sigma$ is -0.1 ppm. Bothner-By has determined the 'liquid association shift' for several organic solvents. The term 'liquid association shift' was first introduced by Schneider, Bernstein, and Pople (100) in a study of gaseous and liquid hydride molecules. If the shift from a gas to a liquid is given accurately by the bulk susceptibility correction, then

$$\delta_{(calc)} = \delta_g + \frac{2\pi}{3} \chi_v \times 10^{-6}. \tag{35}$$

The liquid association shift, β_i^i, is defined as the difference between the observed shift and the calculated shift, as follows:

$$\beta_i^i = \delta_\ell - \delta_{\ell(\text{calc})}. \tag{36}$$

For neopentane, the liquid association shift has been calculated as -0.16 ppm. All β_i^j values are negative, so the "liquid association" term leads to a down-field shift as expected from an effect which is primarily due to van der Waals interactions.

Bothner-By has further suggested that the magnitudes of the anomalous shift may be calculated empirically using the equation

$$-\beta_i^j = x_i y_j, \tag{37}$$

where x_i and y_j are characteristic numbers assigned to the solute and solvent proton, respectively. The solvent parameter, y_j, is a measure of the electric field in the neighborhood of the solvent molecule which arises from instantaneous and from permanent moments in the molecule. The solute parameter, x_i, is the product of two factors. On the one hand is involved the accessibility of the solute proton to solvent molecules because of orientation of anisotropic solvent molecules. The second factor involves the sensitivity of the shielding of the solute protons to the surrounding electric field. The latter will be affected by the nature of the H-X bond and the ease of polarizability of the bond in the solute molecule.

Buckingham et al. (101), have chosen a nonpolar solute, methane, for study in nonassociated solvents relative to gaseous methane. Corrections have been applied for bulk diamagnetic susceptibility, and the shift should then be proportional to van der Waals forces and to the magnetic anisotropy of the solvent molecule.

Van der Waals forces involve interactions between permanent dipoles, between permanent and induced dipoles, and between neutral atoms or molecules. Qualitatively van der Waals forces for the solvent molecule involve two effects: (a) interaction between solute and solvent molecules in equilibrium configuration, resulting in electrons of the solute molecule being attracted by nuclei of surrounding solvent molecules to produce a low-field shift of solute protons, and (b) destruction of axial symmetry of the solute by departures from equilibrium solvent configurations. The contribution to the shielding constant due to van der Waals forces is negative, and thus the chemical shifts are low-field shifts.

Since the energy due to van der Waals forces cannot be evaluated directly, Buckingham et al. (90), have used an indirect measurement of molecular interaction and have compared the chemical shift of solute protons with the heat of vaporization of the solvent at the boiling point. A linear relationship was found for solvents in which only van der Waals effects are operating. For these solvents the expected low-field shift is observed with increasing interaction with the solvent as estimated from thermal data. Various solvents give anomalous shifts, and these may be explained on the basis of magnetic anisotropy.

Chemical Shift due to Polar Effects. The magnetic screening of the nucleus by electrons is reduced in all directions by a uniform electric field (102). According to Marshall and Pople, this reduction is only partly due to the paramagnetic term of Equation (21), since the diamagnetic Lamb-type term is also reduced. The paramagnetic term represents the effect of mixing the ground and excited states by the magnetic field. The effect of the electric field is expressed in the following equations for the parallel and perpendicular shielding constants:

$$\left.\begin{aligned} \sigma &= \frac{e^2}{3mc^2a}\left[1 - \frac{439}{40}\,\frac{a^4E^2}{e^2}\right] \\ \sigma &= \frac{e^2}{3mc^2a}\left[1 - \frac{193}{15}\,\frac{a^4E^2}{e^2}\right], \end{aligned}\right\} \qquad (38)$$

where σ_E is the electronic charge, m the nuclear mas, c the speed of light, a the atomic radius, and E the electric field.

The polar effect σ_E of Equation (22) can be computed from the reaction field introduced by Buckingham (90). When a polar molecule dissolves, it polarizes the surrounding medium, and this polarization leads to an electric field, the reaction field, at the solute. If the molecule is sufficiently symmetrical, it may be shown that the mean reaction field is parallel, and proportional to, its dipole moment, μ. The reaction field is given by

$$\overrightarrow{R} = \left[\frac{\epsilon - 1}{2\epsilon + 2.5}\right]\,\frac{\overrightarrow{\mu}}{a}\,, \qquad (39)$$

where a is the polarizability of the solute molecule, ϵ the dielectric constant of the medium, and μ the dipole moment. There are also local solvent effects on the solute proton. Fields from induced charges on the solvent molecules near polar groups probably produce electric fields at the solute even though the solvent itself may be nonpolar. In this case the reaction field is given by the approximation,

$$\overrightarrow{R} \simeq \frac{\epsilon - 1}{\epsilon + 1}\,. \qquad (40)$$

Therefore, the chemical shift will be linearly dependent upon the solvent parameter in Equation (40), if other effects such as anisotropy, van der Waals forces, difference in shape, or strong specific interactions are absent. The effect of the electric field on the screening constant is

given by Buckingham (89), as follows:

$$\sigma = 2x10^{-5} - 2x10^{-12}E_z - 10^{-18}E^2 - \ldots, \qquad (41)$$

where E_z is the component of the total field, E, along the X-H bond. For $E = 10^5$ esu (the field 7 Å from a proton), the term in Equation 41 proportional to E is about 0.2 ppm and is about twenty times that of the term proportional to E^2.

Buckingham et al., studied acetonitrile as a polar solute in various solvents. In order to consider the polar effect alone, magnetically anisotropic aromatic, rod-shaped and halogenated molecules were omitted. To allow for the shift due to van der Waals interactions in an approximate way, a five percent solution of acetonitrile in n-hexane was used as a reference. A plot of shift versus $(\epsilon-1)/(2\epsilon+2.5)$ showed a linear relationship for the solvents used. Some of the scatter may be due to inaccuracies of the bulk susceptibilities, but some is due to the assumption that van der Waals forces are the same for all solvents and equal to that of n-hexane. Buckingham et al., have calculated σ_E for acetonitrile in n-hexane as -0.11 ppm and in acetone as -0.50 ppm (90).

Abraham (103) in reference to Buckingham's study has suggested a direct comparison of chemical shifts of methane and acetonitrile. By referring shifts to n-hexane, corrected shifts are obtained which are a function of the reaction field of the solvent introduced by Buckingham. A plot of the corrected shift versus $(\epsilon-1)/(\epsilon+0.9)$ for the solvent gives good correlation except for benzene as a solvent.

Buckingham, Schaefer, and Schneider (101) measured the chemical shift of the acetonitrile protons in several solvents with neopentane as an internal standard. The results agree with those of Buckingham et al. (90), and Abraham (103).

With the exception of the magnetic anisotropy term σ_a for disc-shaped molecules and the polar contribution σ_E in some molecules, all contributions to the screening constant are negative, causing a shift to lower applied magnetic field. For solvents with large diamagnetic anisotropies and in the absence of hydrogen bonding, σ_a is larger than van der Waals and polar contributions.

Gas phase measurements of chemical shifts have been made by Rayne et al. (104), and their experimental results are in good agreement with calculations of shielding due to van der Waals forces and polar effects, when corrected for bulk diamagnetic susceptibility. Calculated contributions to the shielding constant show that the reaction field effect is from 3-4 times that calculated for van der Waals interactions for some gases, and ten times that calculated for van der Waals interactions for gases made up of polar molecules. The bulk susceptibility corrections represent about 80-90 percent of the medium effect within the pressure range used.

Diehl and Freeman (105) have derived an expression for the reaction field of a polarizable dipole in a non-spherical cavity. Measurements of acetonitrile and paraldehyde give support to the shape theory as more accurate than the earlier assumption of a spherical cavity made by Buckingham (96).

Hydrogen Bonding

The presence of hydrogen bonding is evidenced in nuclear magnetic resonance by a low-field shift of the proton involved in the hydrogen bond. If the lifetime in the associated and non-associated states is sufficiently long, then a separate signal is observed for each environment. For very short lifetimes, a signal which represents the average in these states is seen; this is the case with hydrogen-bonded and non hydrogen-bonded protons. Both solvent dilution and temperature changes

may affect the population of protons in the bonded and non-bonded states and thus will change the position of resonance, but a second resonance is never seen.

The resonance position of a proton which becomes involved in the hydrogen bond, XH···Y, is obviously affected by the induced electric currents in the hydrogen-bonded species. The magnetic field is affected by (1) induced currents in Y, and (2) by changes in currents in the XH bond (88).

Regarding the first effect, anisotropy in Y involves interatomic bond distances longer than ordinary intramolecular bond lengths. From Equation (32) it is seen that the shielding constant is inversely related to the cube of the bond length. Effects from the anisotropy of the Y atom will ordinarily result in a positive contribution to the shielding constant and a high-field shift of the bonded proton (106).

Free diamagnetic precession of electrons is possible only if their electrical environment is axially symmetrical about the direction of the magnetic field. The second effect increases the asymmetry of the molecule, and the screening is reduced. Calculations by Schneider show that a characteristic shift of 4 ppm due to a hydrogen bond may be produced by an electric field of 1.5×10^6 esu. Such a field would arise from an electron at 1.7 Å from the hydrogen-bonded proton and is in the correct order of magnitude.

The effect on the bond itself, caused by the presence of an electron-attracting Y atom, is complex. Pimentel and McClelland (107) state that, although the chemical shifts of the protons of water and hydrogen sulfide in the liquid state are approximately proportional to the electronegativities of the central atom, the proton chemical shifts of a number of gases are not qualitatively in the order of the electronegativity of the central atom. The association shifts ($\sigma_\ell - \sigma_g$) between the gas and liquid near the melting point are all negative and show greater shifts for substances forming strong hydrogen bonds.

In addition the diamagnetic circulation of the proton may be interferred with by the Y atom. This would cause deshielding, as seen by the Lamb formula for shielding due to diamagnetic currents:

$$\sigma_{\text{local diam}} = \frac{e^2}{3mc^2} \int \frac{\rho}{r} \, d\tau, \qquad (42)$$

where ρ is the electron density of the proton, and the integral is over all space.

Buckingham (89) has calculated the change in shielding caused by an electric field applied to a covalently bonded hydrogen atom. His calculations predict a deshielding of the proton on a hydrogen bond.

Stephen (98) states that a change in the intramolecular shielding constant will occur by distortion of the electronic distribution from nearby electric fields. For solutions in an isotropic solvent, measurement of the shielding constant leads to a correct intramolecular shielding contribution after correcting for bulk susceptibility and extrapolating to infinite dilution.

An excellent discussion of hydrogen bonding is found in an article by Cannon (108).

Relaxation Mechanisms

Longitudinal Relaxation. The spin-lattice relaxation time, T_1, is the half time for establishing thermal equilibrium along the magnetic field axis among nuclei of different magnetic quantum numbers (87). In liquids this time is 10^{-2} to 10^2 sec. Thermal equilibrium of spins occurs through interaction with local magnetic fields. Energy is transferred from nuclei to the lattice by this mechanism. The extent of interaction depends on the magnitude of the local fields and on the rate of change in these fields. Paramagnetic molecules reduce the spin-lattice relaxation time and cause line broadening.

Transverse Relaxation. The spin-spin relaxation time, T_2, results as precessing nuclei lose their phase coherence (87). One cause of transverse relaxation is the fact that different nuclei may experience different local fields, and there is a spread in the values of the resonance frequency with a consequent line broadening. Another method of producing transverse relaxation is spin-spin relaxation, which is an exchange of spin energy between two nuclei precessing at the same frequency. Inhomogeneity of the applied magnetic field contributes to phase incoherence and to a decrease in transverse relaxation time.

Proton Exchange

In a hydrogen bonded system the proton spends time in both XH···Y and X···HY states. If the lifetime is sufficiently long, two separate signals are seen, but if the lifetime is short or the exchange rapid, then an averaged signal may be seen. The spin-lattice relaxation time may be ignored if widths of signals for slow exchange are small compared with their difference in frequency.

As developed by Pople, Schneider, and Bernstein for the case of slow exchange (88), there is a broadened signal at ω_A with width given by:

$$\frac{1}{T'_{2A}} = \frac{1}{T_{2A}} + \frac{1}{\tau_A} , \qquad (43)$$

where T_{2A} is the transverse relaxation of nucleus A in the absence of exchange, and τ_A is the mean lifetime at site A.

For intermediate exchange assuming equal populations and lifetimes and large transverse relaxation times, the shape function depends only on

$$\tau | \nu_A - \nu_B | \equiv \tau \Delta\nu . \qquad (44)$$

If τ is the mean lifetime in one site, then the signals coalesce when

$$\tau \leq \frac{\sqrt{2}}{2\pi\Delta\nu} , \tag{45}$$

where $\Delta\nu$ is the separation of the two resonance signals in cps.

In the case of rapid exchange the mean frequency is

$$\omega_{mean} = p_A\omega_A + p_B\omega_B , \tag{46}$$

and the linewidth is given by

$$\frac{1}{T'_2} = \frac{p_A}{T_{2A}} + \frac{p_B}{T_{2B}} , \tag{47}$$

where p_A and p_B are fractional populations at sites A and B, respectively, and T_{2A} and T_{2B} are transverse relaxation times of nucleus A and B in the absence of exchange.

Nuclear Spin-Spin Coupling

Nuclear spin coupling involves the interaction between nuclear spins through coupling with the electron spins and the electron orbital motion (88). The so-called Fermi-contact coupling contributes the largest quantity to the coupling constant between protons not directly bonded. This contribution is given as

$$J^{(3)}_{NN'} = -\frac{2}{3h}\left(\frac{16\pi\beta\hbar}{3}\right)^2 \gamma_N \gamma_{N'} \frac{1}{\Delta E} \times \left[0 \left| \sum_k \sum_j \delta\ (r_{kN})\, \delta\ (r_{jN'}) S_k \cdot S_j \right| 0 \right], \tag{48}$$

and requires for its evaluation a knowledge of the ground state wave function.

McConnell (109) has used a molecular orbital approximation to calculate the spin-spin interactions. Contributions from interactions between electrons in non-s orbitals and nuclear moments have been considered to be negligible for protons. Orbital contributions for protons not directly bonded to one another are small. Electron-coupled spin-spin interaction of protons, then, arises primarily through the Fermi interaction expressed in Equation (48).

Valence bond calculations for nuclear spin interactions have been made by Karplus et al. (110). Such calculations give results in rather good agreement with experimental values. Contact electron spin coupling has been further investigated by Karplus (111). The assumption of perfect-pairing gives results which show some agreement with experiment and indicate that the contact term (Equation 48) is the principal factor in observed proton couplings.

An angular dependence of electron-coupled proton interactions has been pointed out by Gutowsky et al. (112). The coupling decreases with increasing HCH angle for protons bonded to the same carbon atom.

For nuclei other than the proton, there is a larger contribution of the dipole interaction between electronic and nuclear spins and of the interaction between the electron orbital motion and the nuclear moment. In particular for fluorine nuclei, the orbital contribution is still only a small fraction of the observed coupling (88).

EXPERIMENTAL

Instrumental

Nuclear magnetic resonance spectra were obtained on the Varian A-60 spectrometer (113). Chemical shift measurements were obtained with both the room temperature V-6303 probe and the variable temperature V-6031 probe (114). These measurements are reported to ±1 cps. Chemical shifts are reported in cps from tetramethylsilane. For dilution shifts, differences are given as positive for upfield and negative for downfield shifts. Resolution, or the linewidth at half-maximum amplitude, of 0.6 cps is possible with either probe. Integration of peak areas is used for the determination of equilibrium constants and percentage enol values are accurate to about ±2 percent.

Variable temperature work was performed with the Varian V-6057 variable temperature system with the V-6040 controller, with regulation to ±2°C at the sample. Low temperature calibration was checked by the use of the methanol chemical shift and at high temperature by the ethylene glycol shift. Measurements were made within about 2-3 minutes following introduction of the sample in the magnet. Temperature regulation at the sensor is ±1°C, and the temperature calibration accuracy is ±3°C.

A sweep width of 500 cps was used generally for recording spectra, although this was changed to 50 cps for coupling constant determinations. Coupling constant means were repeated at least six times to reduce error to ±0.03. For recorded spectra, the radiofrequency field and intensity were varied as necessary. An increase in either of these factors within a spectrum has been indicated by the initials, ii, on the particular resonance peak.

Compound Preparation

α-Chloroacetylacetone was synthesized according to the method of D'Amico (115). Fractional distillation at 14 mm and 41.0-44.5°C gave the product. α-Bromoacetylacetone was synthesized according to the method of Schwarzenbach and Felder (116) after preparing the copper complex of acetylacetone according to the method of Ciocca (117). The product was fractionally distilled as a yellow liquid at 13 mm and 60°C.

Both n-butyl α-chloroacetoacetate and t-butyl α-chloroacetoacetate were prepared by modifications of the procedure of D'Amico (115). Sulfuryl chloride (34 g.) was added dropwise to n-butyl acetoacetate (40 g.) with stirring at 0°C over a two hour period. The mixture was neutralized with ten percent aqueous sodium bicarbonate (150 ml.) and extracted with ether (150 ml) in three portions. The extract was dried, the ether removed by distillation, and the product vacuum distilled at 5 mm and 84-86°C as a pale yellow liquid. t-Butyl acetoacetate was treated in the same manner as n-butyl acetoacetate. The ether extract was washed with water to neutralize it and then dried. The ether was removed by distillation, and the product vacuum distilled at 3 mm and 59-61°C as a pale yellow liquid.

β-Bromoethyl acetoacetate was synthesized according to Donaruma (118) from β-bromoethanol and ethyl acetoacetate by ester exchange, using PbO as a catalyst. Fractional distillation at 8 mm and 114-119°C gave the product. Ethyl γ-bromoacetoacetate was prepared by the method of Burger and Ullyot (119). The product was distilled at 84-5°C and 5 mm as a pink liquid. Isohima's preparation, in which ketene is reacted with ethyl α-cyanoacetate, was used to make ethyl α-cyanoacetoacetate (120). The ethyl α-cyanoacetate, along with an equimolar amount of pyridine, was heated to 80° before introduction of ketene, and ketene was fed in for a period of three and

one-half hours. The reaction mixture was shaken occasionally. The solution was neutralized, and the pyridine removed by distillation. The compound was fractionally distilled at 88-89°C at 6 mm as a colorless liquid. Ethyl α-bromoacetoacetate was prepared according to the procedure of Kharasch et al. (121), by the action of bromine on the parent ester. The product was distilled at 94-94.5°C and 11 mm as a colorless liquid.

Other compounds were commercially available, and their source is indicated in Tables XXVI and XXVII for β-diketones and β-ketoesters, respectively.

Compound Purification

Compounds were purified by the usual recrystallization, fractional distillation, and vapor phase chromatographic techniques. Purity was checked by melting point, boiling point or refractive index measurement and by gas chromatography. Refractive indices were obtained on the Bausch and Lomb, Type 33-45-56 refractometer. Vapor phase chromatography was performed on the Perkin-Elmer Model 154A (20 percent silica column) and Aerograph Model A-700 (30 percent silica column).

Preparation of Solutions

Solutions were weighed on an analytical balance to ±0.1 mg, and mole fractions were determined to within ±0.001. Tetramethylsilane was added as an internal reference to each solution, and the quantity added was the same in each case and did not affect the calculated mole fraction to within 0.001. Spectra from unsealed and evacuated sealed sample tubes were compared, and no difference in linewidth or shape was found in most cases. For acetic acid solutions and those

using acetylacetone, tubes were evacuated and sealed but unsealed sample tubes were used in the remaining cases.

Physical Properties

Physical constants for the β-diketones and β-ketoesters used in this work are given in Tables XXVI and XXVII, respectively. Included among these constants are boiling points, melting points, and refractive indices.

Solvent Purification

Benzene, chloroform, acetic acid, and dioxane were purified according to Vogel (122). Other solvents were purified by fractional distillation, following drying.

Table XXVI. Physical Constants of β-Diketones

Compound	B.p. °C/mm	M.p. °C	$n_D^{°C}$	Source
Acetylacetone	38/10	-	$1.4003^{19.1}$	Eastman[α]
α-Bromoacetylacetone	60/13	-	-	Synthesized[3,4]
α-Chloroacetylacetone	200[v]	-	$1.4749^{20.3}$	Synthesized[2]
Dibenzoylmethane	-	70-5, 77, 78[*]	-	Eastman[α]
5, 5-Dimethyl-1, 3-cyclohexanedione		148-9	-	K and K[β]
Hexafluoroacetylacetone	95[v]	-	$1.3327^{20.4}$	Peninsular[γ]
Trifluoroacetylacetone	130[v]	-	$1.3883^{19.8}$	Columbia[δ]
1, 3-Indanedione	-	55/<1mm[s]	-	Aldrich[ε]
α-Methylacetylacetone	193[v]	-	$1.4378^{19.8}$	Chem. Proc.[σ]
1-Phenyl-1, 3-butanedione	-	40[s]	-	Eastman[α]
2-Phenyl-1, 3-indanedione	-	145	-	Aldrich[ε]
Thenoyltrifluoroacetone	-	30/<1mm[s]	-	Columbia[δ]

[v] Vapor phase chromatography
[s] Sublimation
[*] Enol, enol, keto, respectively
[α] Eastman Organic Chemicals, Distillation Products Industries
[β] K and K Laboratories, Inc.
[γ] Peninsular Chem. Research, Inc.
[δ] Columbia Organic Chemicals Co., Inc.
[ε] Aldrich Chem. Co., Inc.
[σ] Chemicals Procurement Labs., Inc.

Table XXVII. Physical Constants of β-Ketoesters

Compound	B.p. °C/mm	$n_D^{°C}$	Source
β-Bromoethylacetoacetate	112-4/7	$1.4750^{20.3}$	Synthesized[5]
Butyl acetoacetate	-	$1.4280^{20.0}$	Eastman[a]
t-Butyl acetoacetate	62/<1	$1.4198^{20.2}$	Aldrich Chem. Co., Inc.
Butyl α-chloroacetoacetate	84-5/3	$1.4463^{20.3}$	Adapted from D'Amico[2]
t-Butyl α-chloroacetoacetate	59-61/3	$1.4450^{20.3}$	Adapted from D'Amico[2]
Ethyl acetoacetate	47/2	$1.4175^{21.1}$	
Ethyl α-allylacetoacetate	67/<1	$1.4380^{17.6}$	Chem. Prov.[γ]
Ethyl α-isoamylacetoacetate	69/<1	$1.4349^{20.0}$	K and K Labs., Inc.
Ethyl benzoylacetate	132/1	$1.5208^{20.6}$	Eastman[a]
Ethyl α-bromoacetoacetate	94-5/11	$1.4622^{20.3}$	Synthesized[8]
Ethyl γ-bromoacetoacetate	84-5/5	-	Synthesized[6]
Ethyl α-isobutylacetoacetate	251[v]	$1.4288^{20.0}$	K and K Labs., Inc.
Ethyl α-n-butylacetoacetate	200[v]	$1.4330^{19.9}$	K and K Labs., Inc.
Ethyl α-chloroacetoacetate	68/<1	$1.4425^{20.8}$	Eastman[a]
Ethyl α-cyanoacetoacetate	88-9/6	$1.4710^{20.3}$	Synthesized[7]
Ethyl α-ethylacetoacetate	57/<1	$1.4220^{19.0}$	Bios Labs., Inc.
Ethyl α-fluoroacetoacetate	210[v]	$1.4085^{20.4}$	Chem. Proc.[γ]
Ethyl trifluoroacetoacetate	160[v]	$1.3762^{20.0}$	Peninsular[δ]
Ethyl α-methylacetoacetate	73/11	$1.4253^{20.0}$	Aldrich Chem. Co., Inc.
Ethyl α-isopropylacetoacetate	-	$1.4223^{21.6}$	Eastman[a]
Ethyl α-n-propylacetoacetate	70/2	$1.4251^{20.1}$	K and K Labs., Inc.
Methyl acetoacetate	62/<1	$1.4184^{20.5}$	Eastman[a]

[v] Vapor phase chromatography.
[a] Eastman Org. Chem., Distillation Products Ind. Butyl acetoacetate and ethyl α-isopropylacetoacetate were synthesized for us by Distillation Products Industries.
[γ] Chemicals Procurement Labs., Inc.
[δ] Peninsular Chem. Research, Inc.

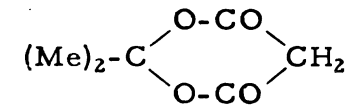
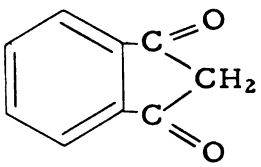
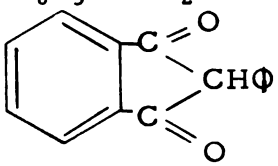
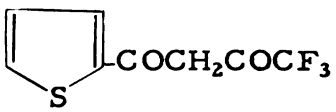
RESULTS AND DISCUSSION

Nuclear Magnetic Resonance Spectra

Chemical Shifts. A list of molecular formulas for the β-diketones studied is given in Table XXVIII, along with the numbers of the figures (Figure 12-Figure 20a) in which the corresponding proton resonance spectra are shown. Also numbers have been assigned to each compound for the purpose of identifying points on graphs in the thesis. Formulas for the β-ketoesters studied are shown in Table XXIX, with similar figure and numerical assignments. Figures 20b through 35b show proton magnetic resonance spectra for the β-ketoesters. Of the compounds studied nuclear magnetic resonance spectra have been recorded previously for acetylacetone (23, 71) α-methylacetylacetone (71), ethyl acetoacetate (58), 1, 3-indanedione (123), and thenoyl trifluoroacetone (123).

Assignment of resonance peaks to the various proton groups in a compound is indicated on the figure showing the NMR spectrum of that compound. These assignments have been verified by integration of peak areas and also, in some cases, by changing the position of equilibrium by addition of solvent. A case in point is the verification of the enolic resonance peaks in ethyl α-methylacetoacetate by the addition of hexane. For trifluoroacetylacetone and hexafluoroacetylacetone, the position of keto resonance peaks was confirmed by high temperature studies. Identification of enol versus keto resonance peaks has been aided occasionally by fractional distillation of the β-dicarbonyl. The first fraction is primarily enol tautomer, since the intramolecularly hydrogen-bonded enol tautomer is less polar than the keto tautomer. A spectrum taken shortly after vacuum distillation is seen in Figure 36

Table XXVIII. Molecular Formulas of β-Diketones

No.	Compound	Formula	Figure
1	Acetylacetone	$CH_3COCH_2COCH_3$	12
2	α-Bromoacetylacetone	$CH_3COCH(Br)COCH_3$	13
3	α-Chloroacetylacetone	$CH_3COCH(Cl)COCH_3$	14
4	Cyclic isopropylidene malonate(in $CHCl_3$)		15a
5	Dibenzoylmethane	$C_6H_5COCH_2COC_6H_5$	16
6	Hexafluoroacetylacetone	$CF_3COCH_2COCF_3$	15b
7	Trifluoroacetylacetone	$CF_3COCH_2COCH_3$	17
8	1, 3-Indanedione (in $CHCl_3$)		18a
9	α-Methylacetylacetone	$CH_3COCH(CH_3)COCH_3$	18b
10	1-Phenyl-1, 3-butanedione (in CCl_4)	$C_6H_5COCH_2COCH_3$	19
11	2-Φ-1, 3-Indanedione (in Acetone)		20a
12	Thenoyltrifluoroacetone (in CS_2)		21

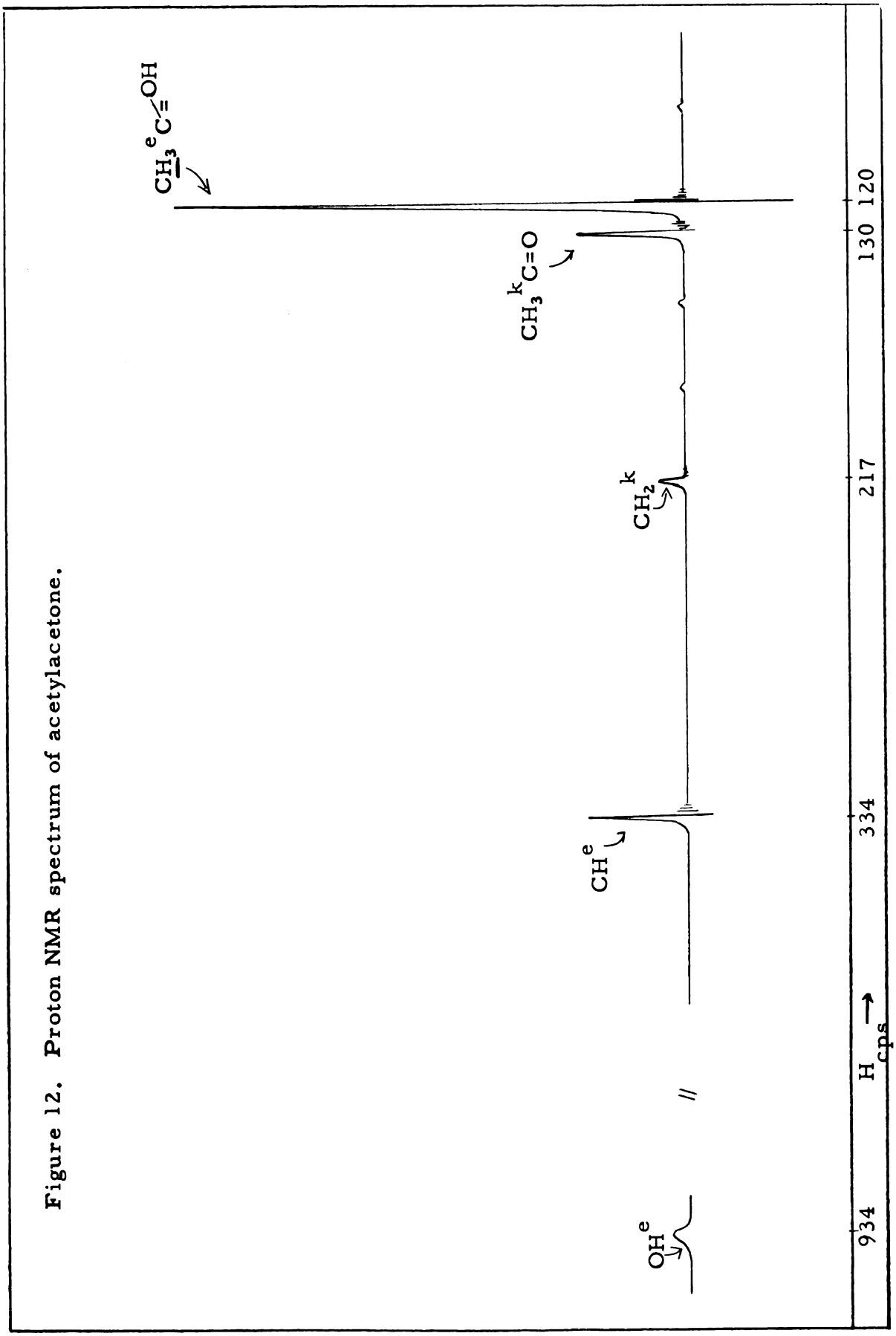


Figure 12. Proton NMR spectrum of acetylacetone.

Figure 13. Proton NMR spectrum of α-bromoacetylacetone.

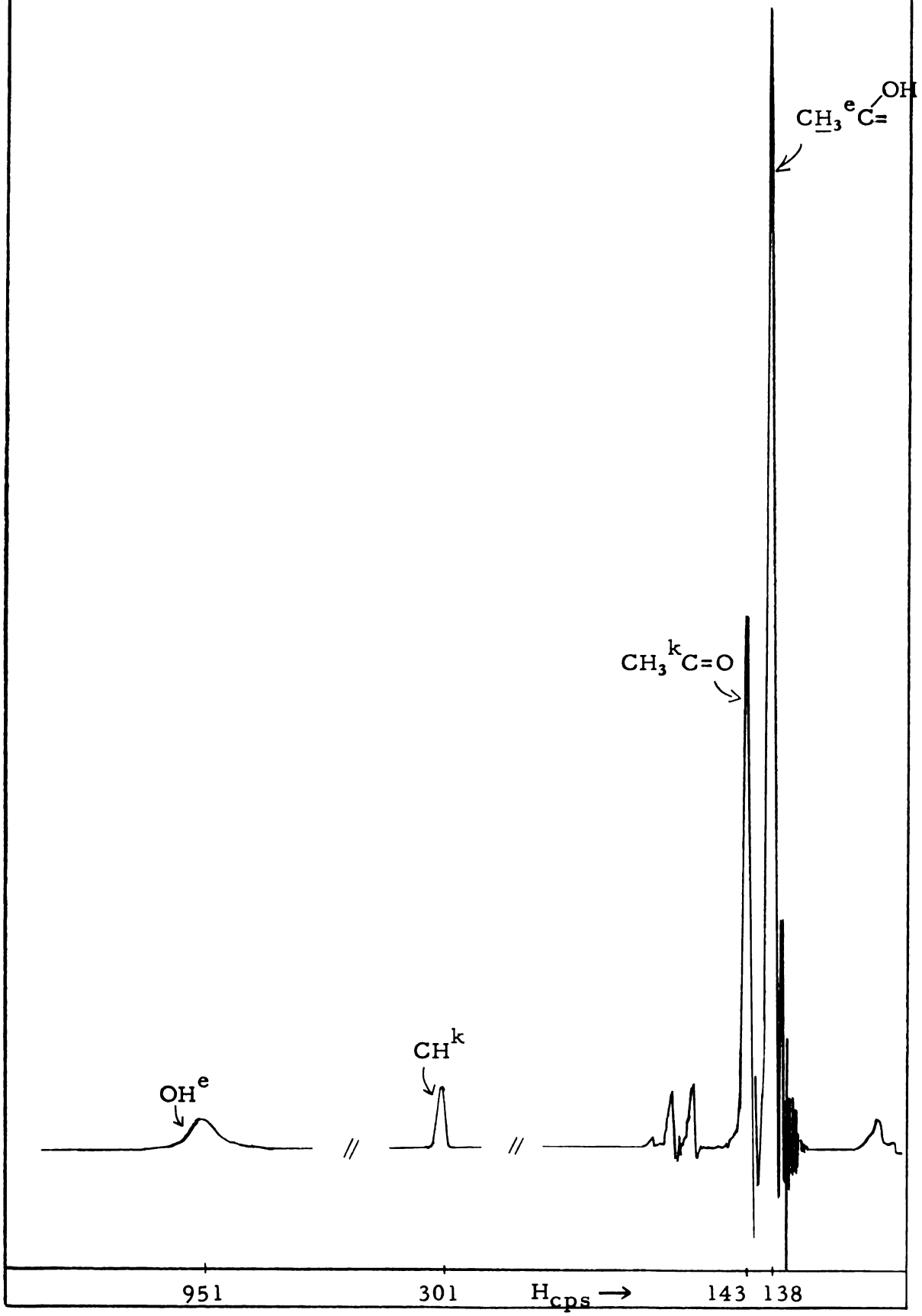
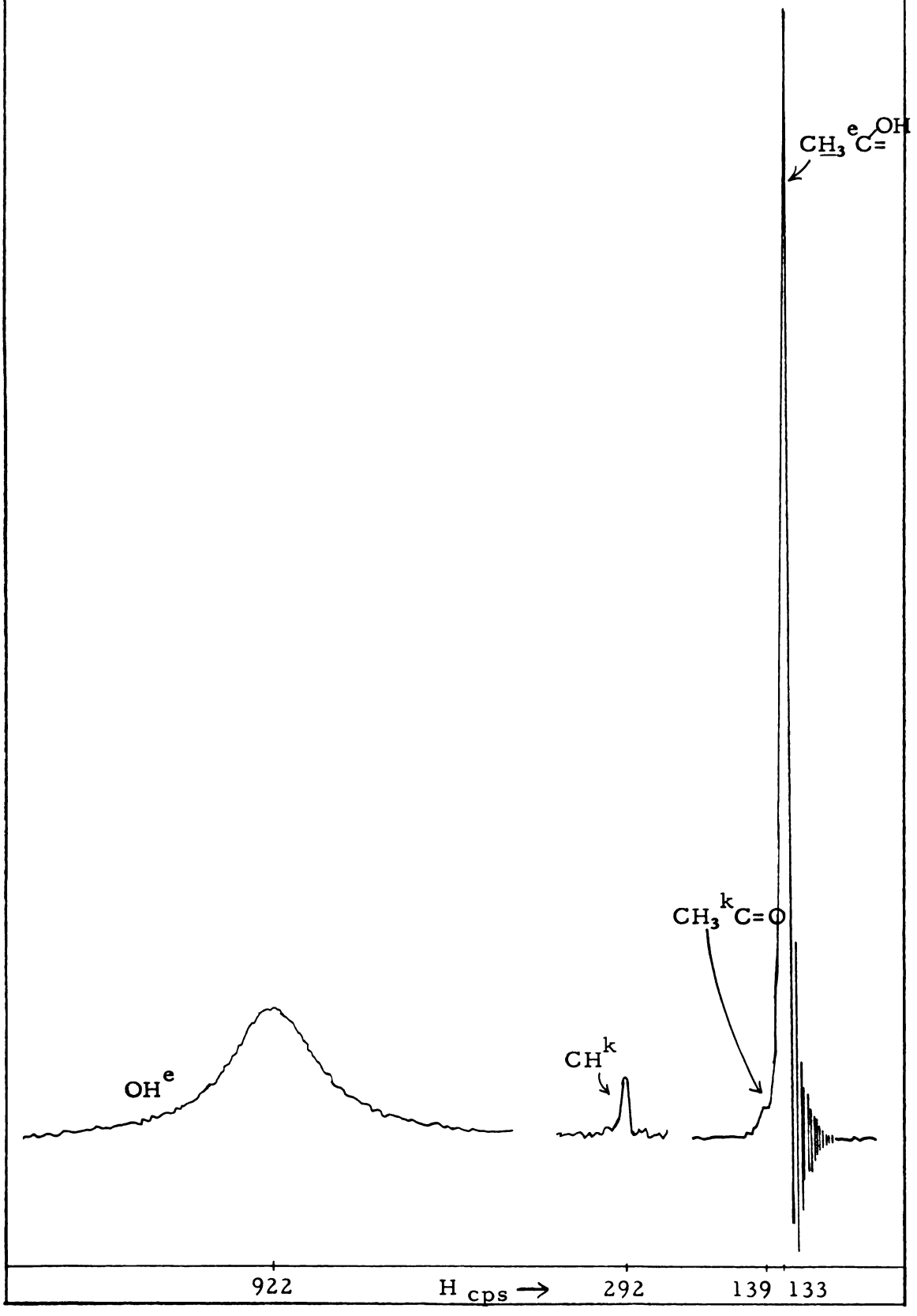


Figure 14. Proton NMR spectrum of α-chloroacetylacetone.



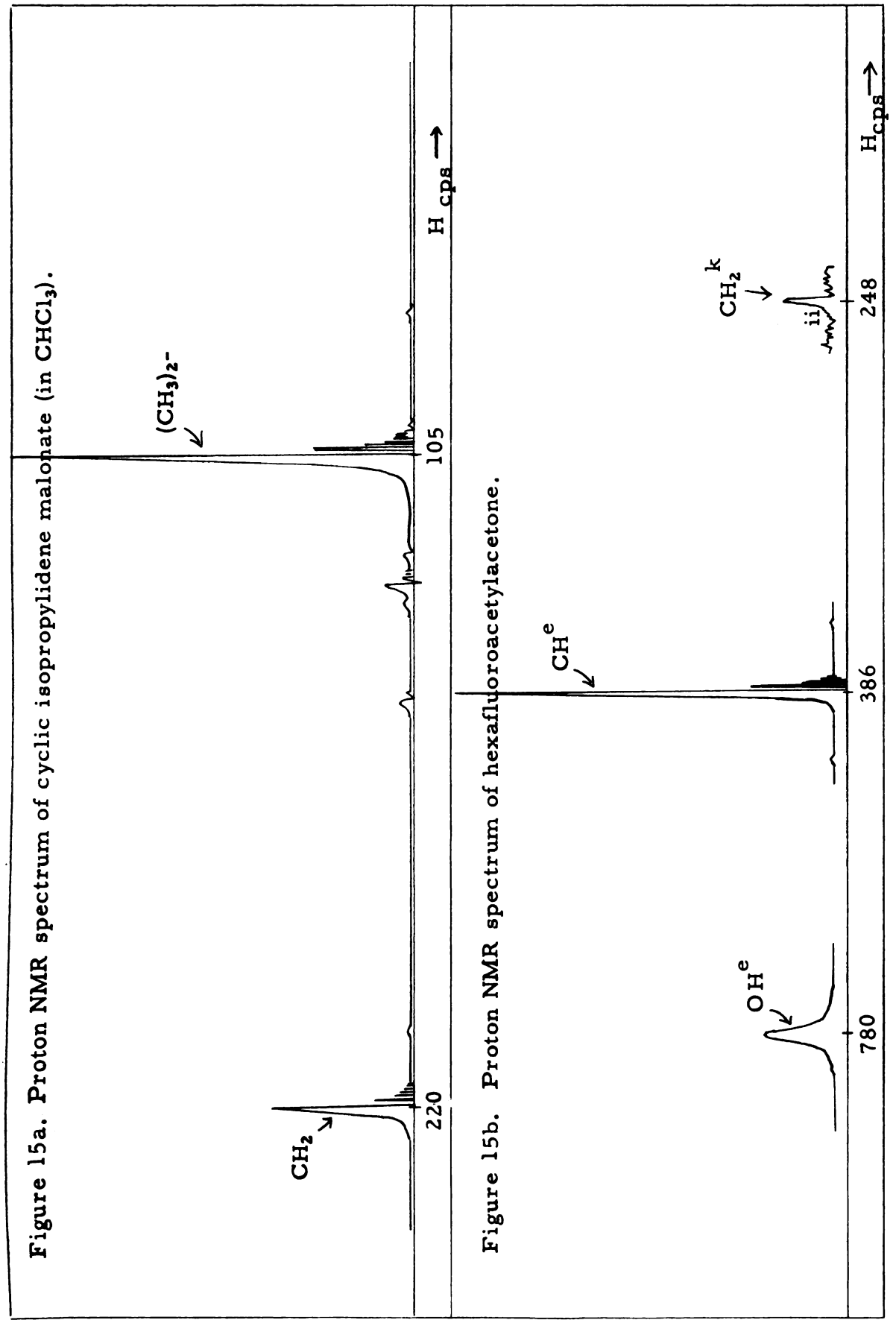
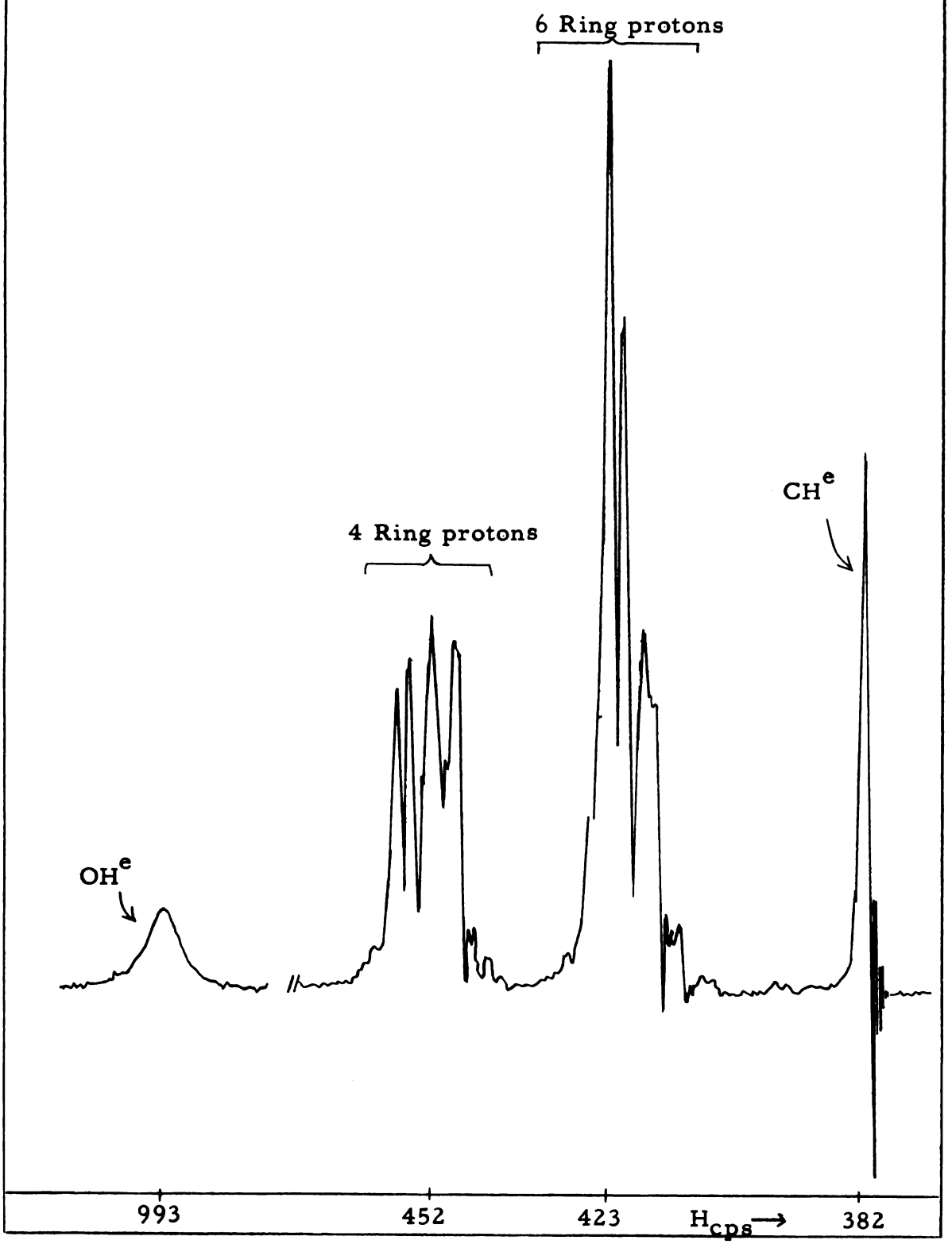


Figure 15a. Proton NMR spectrum of cyclic isopropylidene malonate (in $CHCl_3$).

Figure 15b. Proton NMR spectrum of hexafluoroacetylacetone.

Figure 16. Proton NMR spectrum of dibenzoylmethane (in CCl_4)



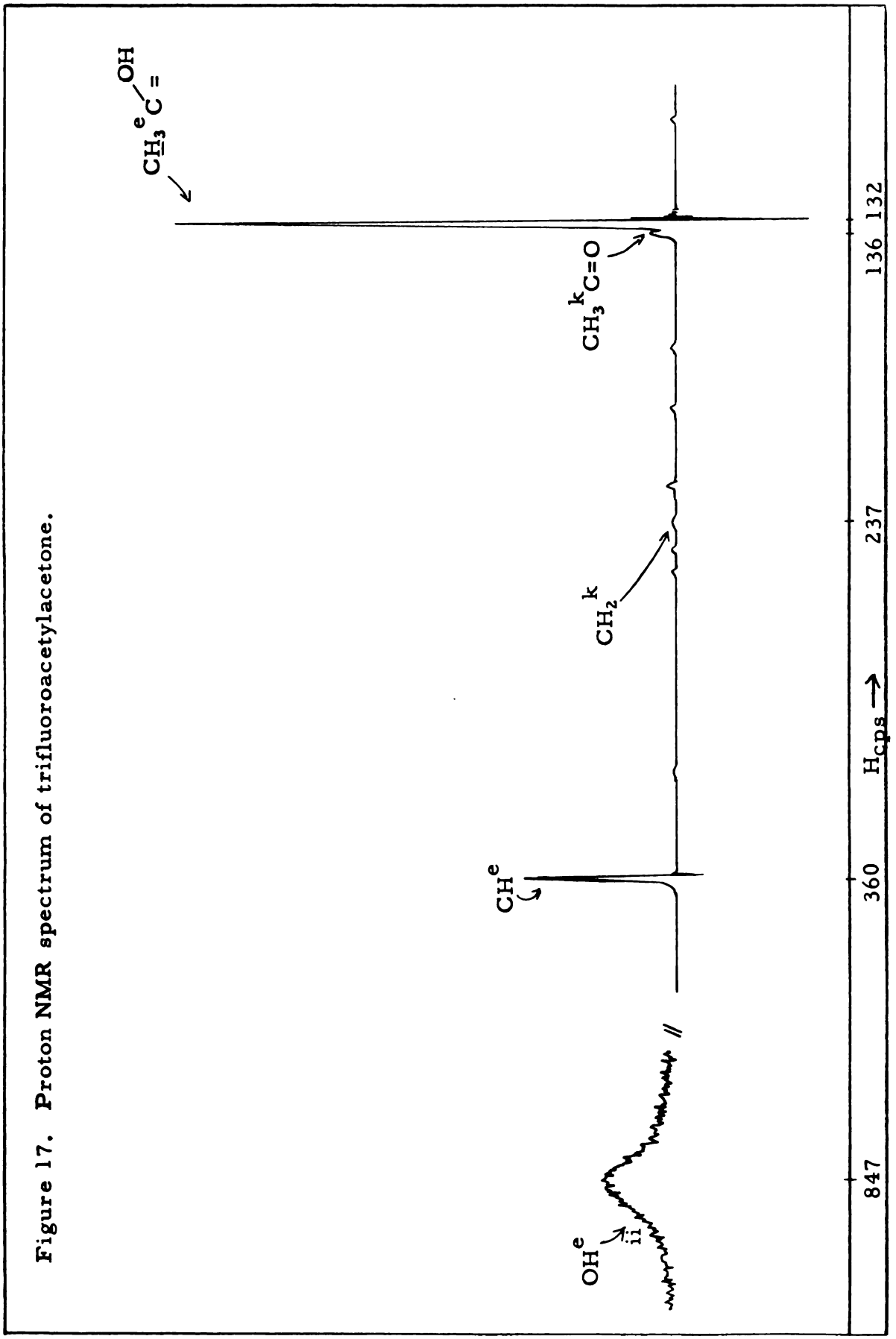


Figure 17. Proton NMR spectrum of trifluoroacetylacetone.

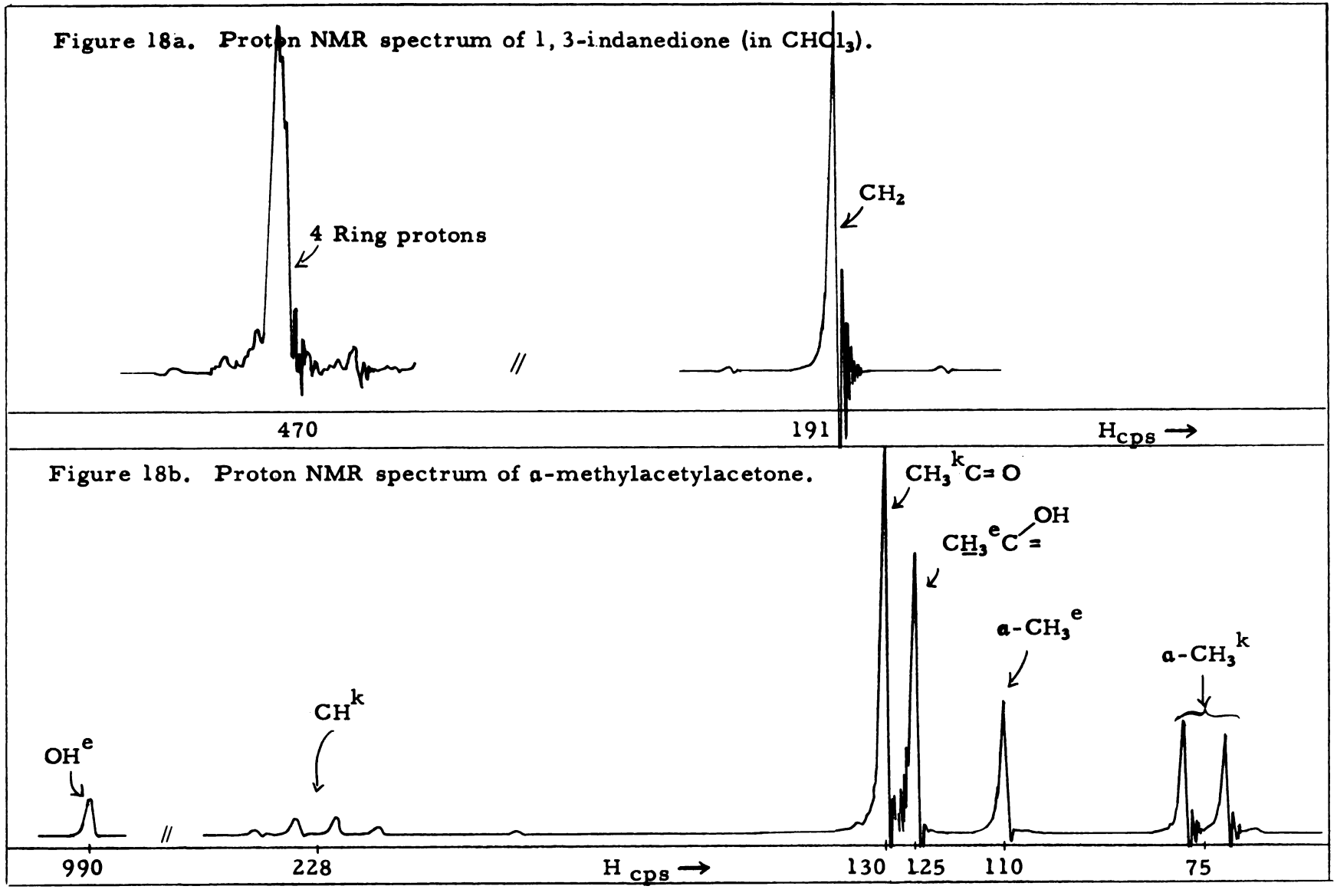


Figure 18a. Proton NMR spectrum of 1, 3-indanedione (in $CHCl_3$).

Figure 18b. Proton NMR spectrum of a-methylacetylacetone.

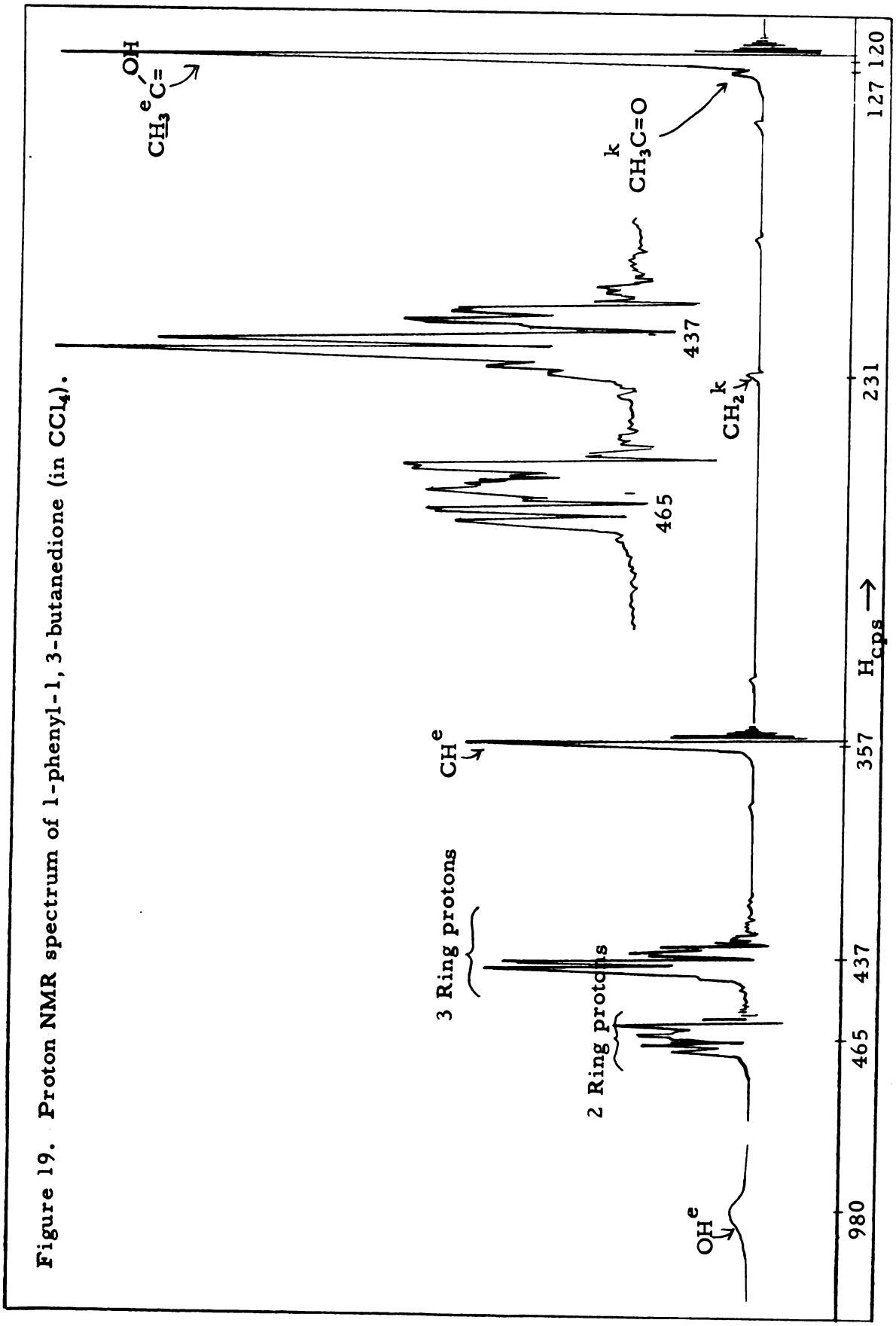


Figure 19. Proton NMR spectrum of 1-phenyl-1, 3-butanedione (in CCl_4).

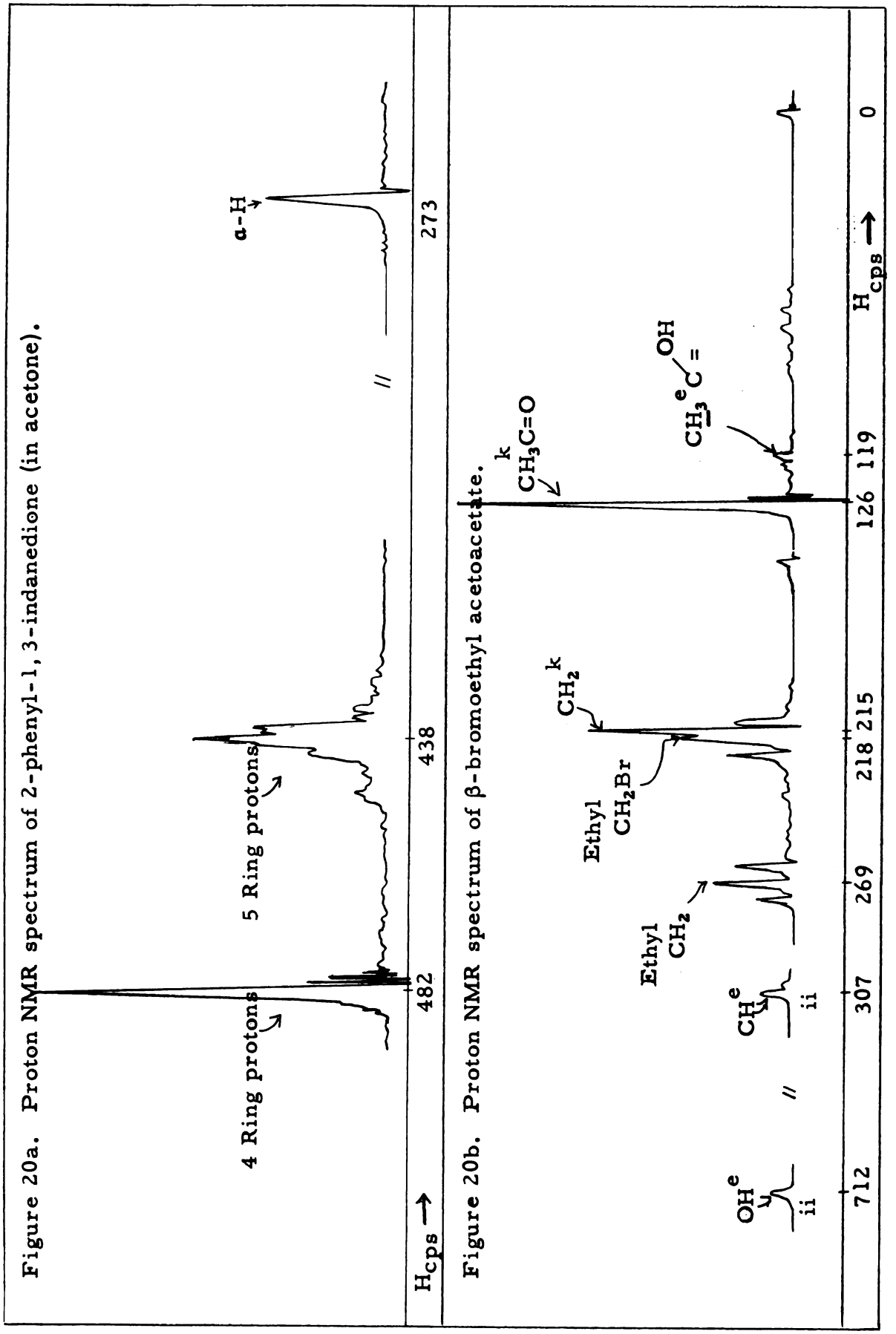


Figure 20a. Proton NMR spectrum of 2-phenyl-1,3-indanedione (in acetone).

Figure 20b. Proton NMR spectrum of β-bromoethyl acetoacetate.

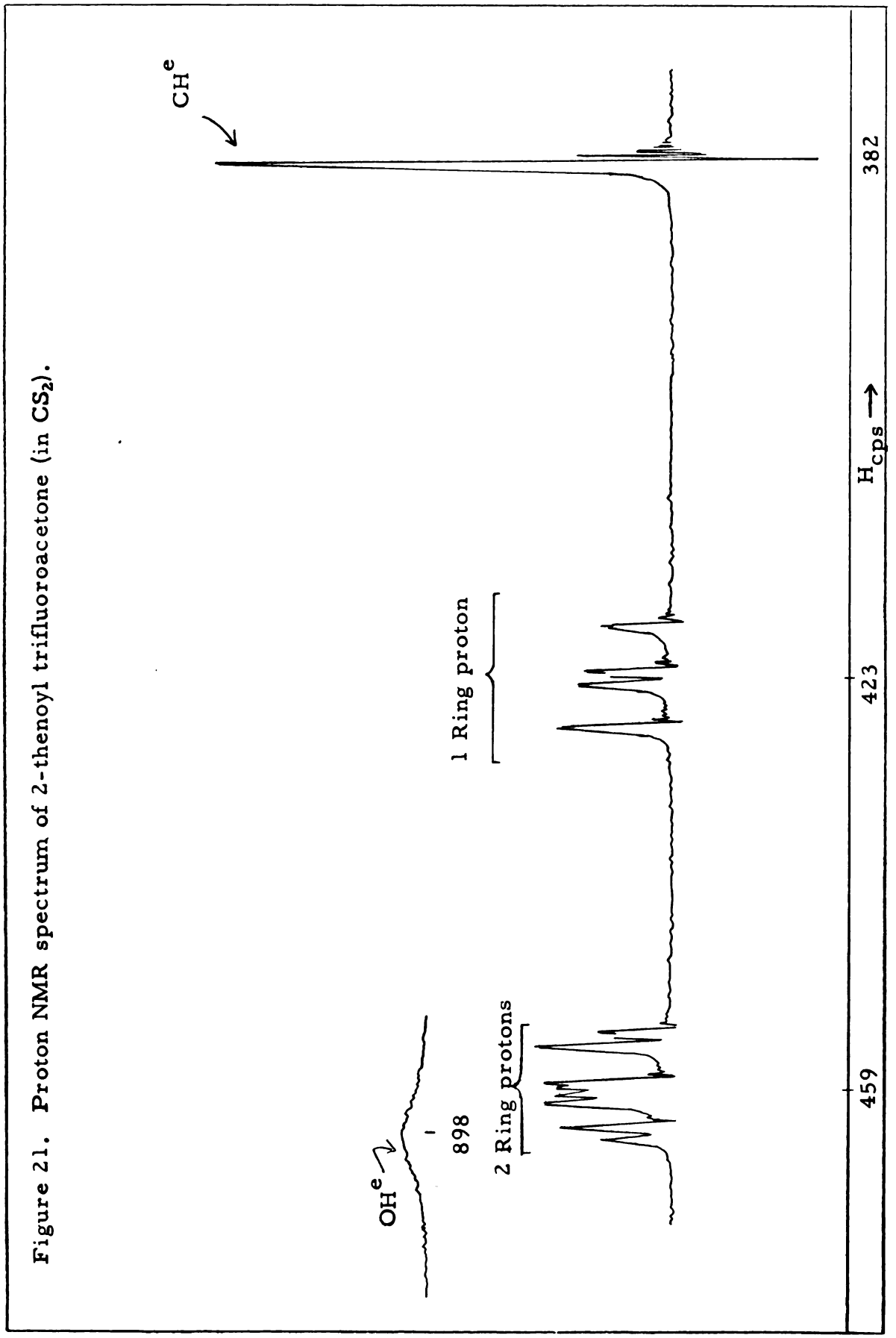


Figure 21. Proton NMR spectrum of 2-thenoyl trifluoroacetone (in CS_2).

Table XXIX. Molecular Formulas of β-Ketoesters

No.	Compound	Formula	Figure
13	β-Bromo ethyl acetoacetate	$CH_3COCH_2COOCH_2CH_2Br$	20b
14	Butyl acetoacetate	$CH_3COCH_2COO(CH_2)_3CH_3$	22a
15	t-Butyl acetoacetate	$CH_3COCH_2COOC(CH_3)_3$	22b
16	n-Butyl α-chloroacetoacetate	$CH_3COCH(Cl)COO(CH_2)_3CH_3$	23a
17	t-Butyl α-chloroacetoacetate	$CH_3COCH(Cl)COOC(CH_3)_3$	23b
18	Ethyl acetoacetate	$CH_3COCH_2COOCH_2CH_3$	24
19	Ethyl α-allylacetoacetate	$CH_3COCH(CH_2CH=CH_2)COOCH_2CH_3$	25
20	Ethyl α-isoamylacetoacetate	$CH_3COCH[(CH_2)_3-(CH_3)_2]COOCH_2CH_3$	26
21	Ethyl benzoylacetate	$C_6H_5COCH_2COOCH_2CH_3$	27
22	Ethyl α-bromoacetoacetate	$CH_3COCH(Br)COOCH_2CH_3$	28a
23	Ethyl γ-bromoacetoacetate	$CH_2(Br)COCH_2COOCH_2CH_3$	28b
24	Ethyl α-isobutylacetoacetate	$CH_3COCH[CH_2-CH(CH_3)_2]COOCH_2CH_3$	29a
25	Ethyl α-n-butylacetoacetate	$CH_3COCH[(CH_2)_3CH_3]COOCH_2CH_3$	29b
26	Ethyl α-chloroacetoacetate	$CH_3COCH(Cl)COOCH_2CH_3$	30
27	Ethyl α-cyanoacetoacetate	$CH_3COCH(CN)COOCH_2CH_3$	31
28	Ethyl α-ethylacetoacetate	$CH_3COCH(CH_2CH_3)COOCH_2CH_3$	32a
29	Ethyl α-fluoroacetoacetate	$CH_3COCH(F)COOCH_2CH_3$	33
30	Ethyl trifluoroacetoacetate	$CF_3COCH_2COOCH_2CH_3$	32b
31	Ethyl α-methylacetoacetate	$CH_3COCH(CH_3)COOCH_2CH_3$	34a
32	Ethyl α-isopropylacetoacetate	$CH_3COCH[CH(CH_3)_2]COOCH_2CH_3$	34b
33	Ethyl α-n-propylacetoacetate	$CH_3COCH[(CH_2)_2CH_3]COOCH_2CH_3$	35a
34	Methyl acetoacetate	$CH_3COCH_2COOCH_3$	35b

Figure 22a. Proton NMR spectrum of butyl acetoacetate.

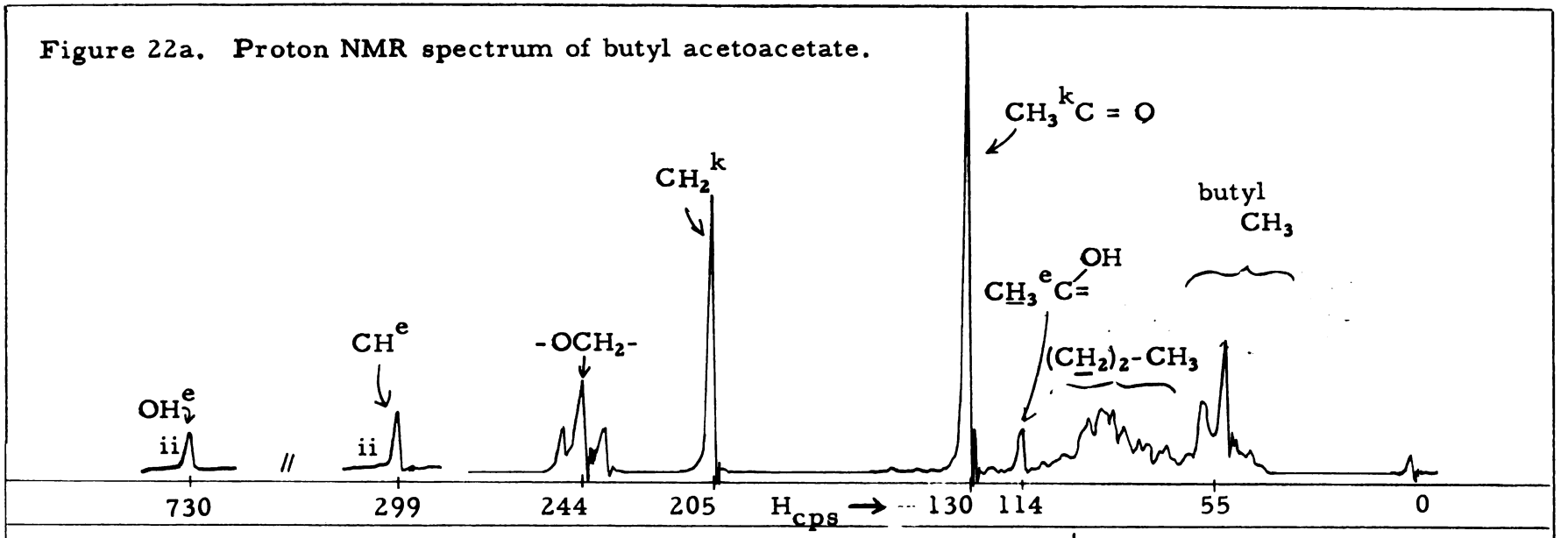
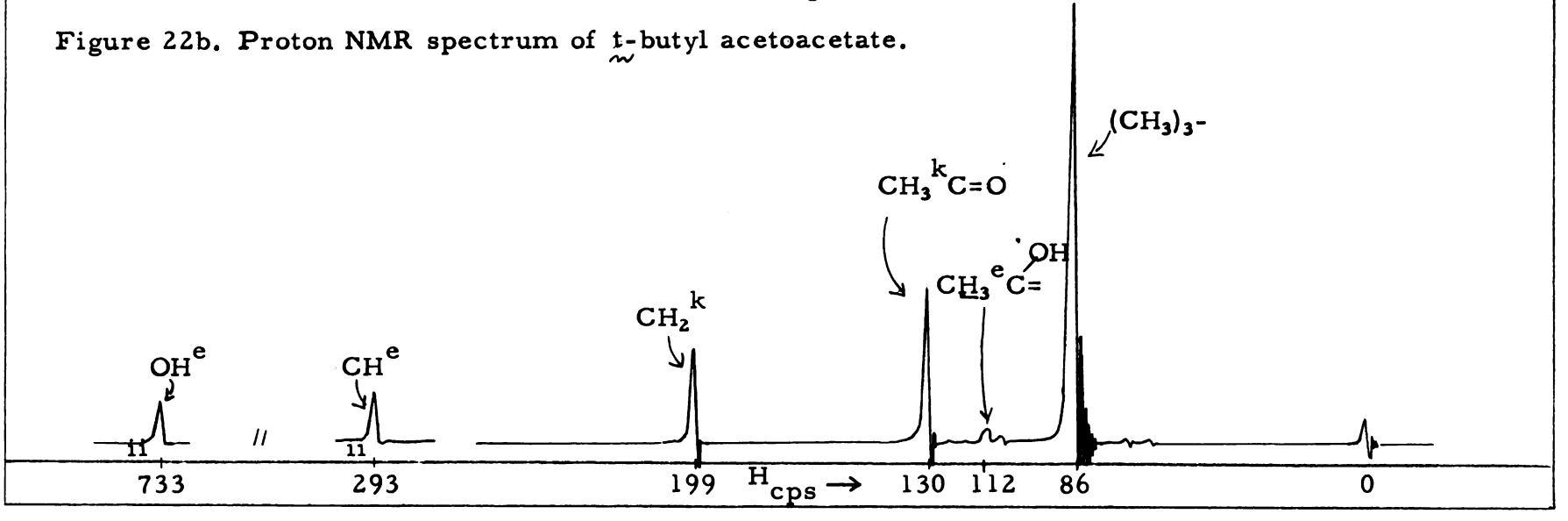


Figure 22b. Proton NMR spectrum of t-butyl acetoacetate.



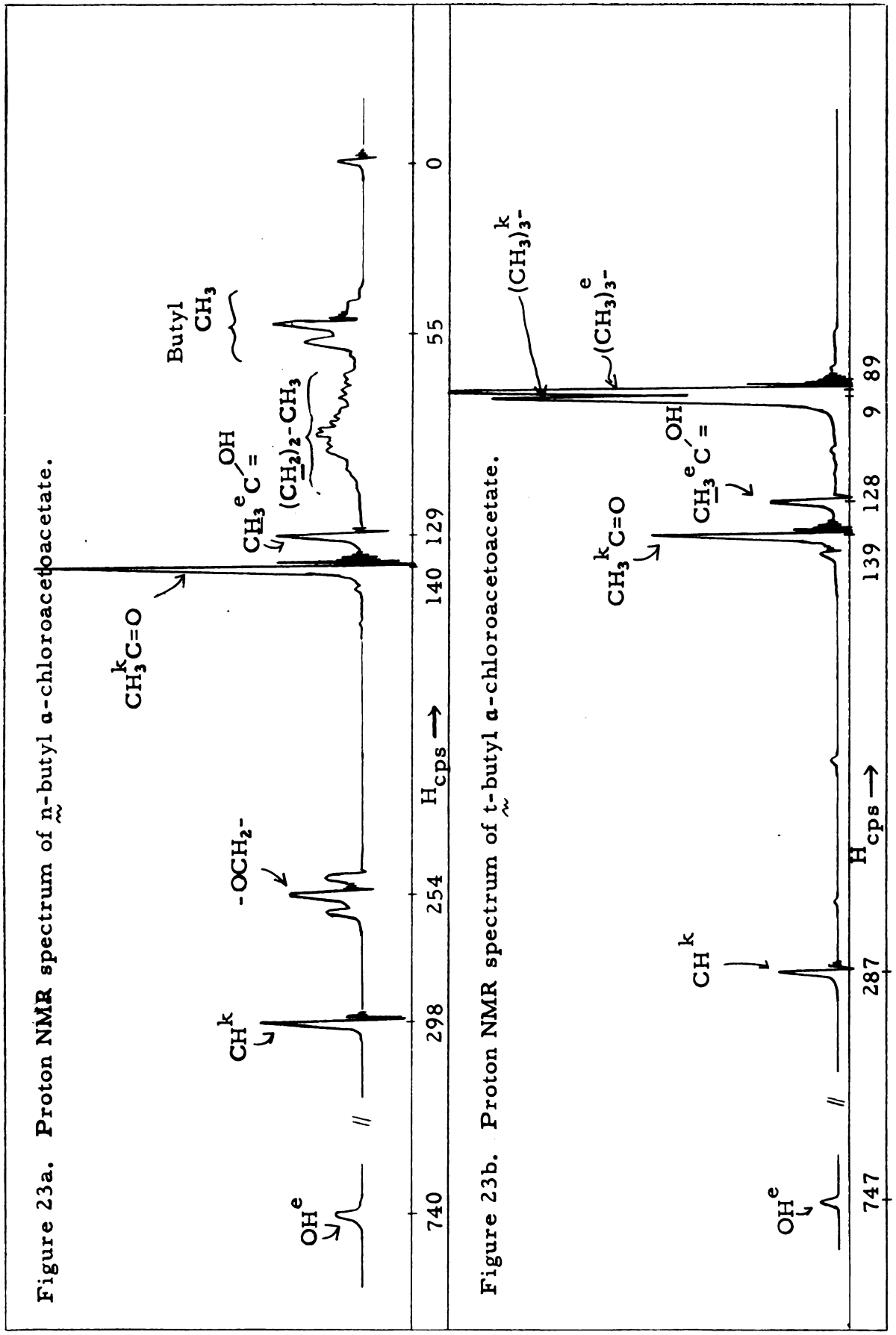


Figure 23a. Proton NMR spectrum of n-butyl α-chloroacetoacetate.

Figure 23b. Proton NMR spectrum of t-butyl α-chloroacetoacetate.

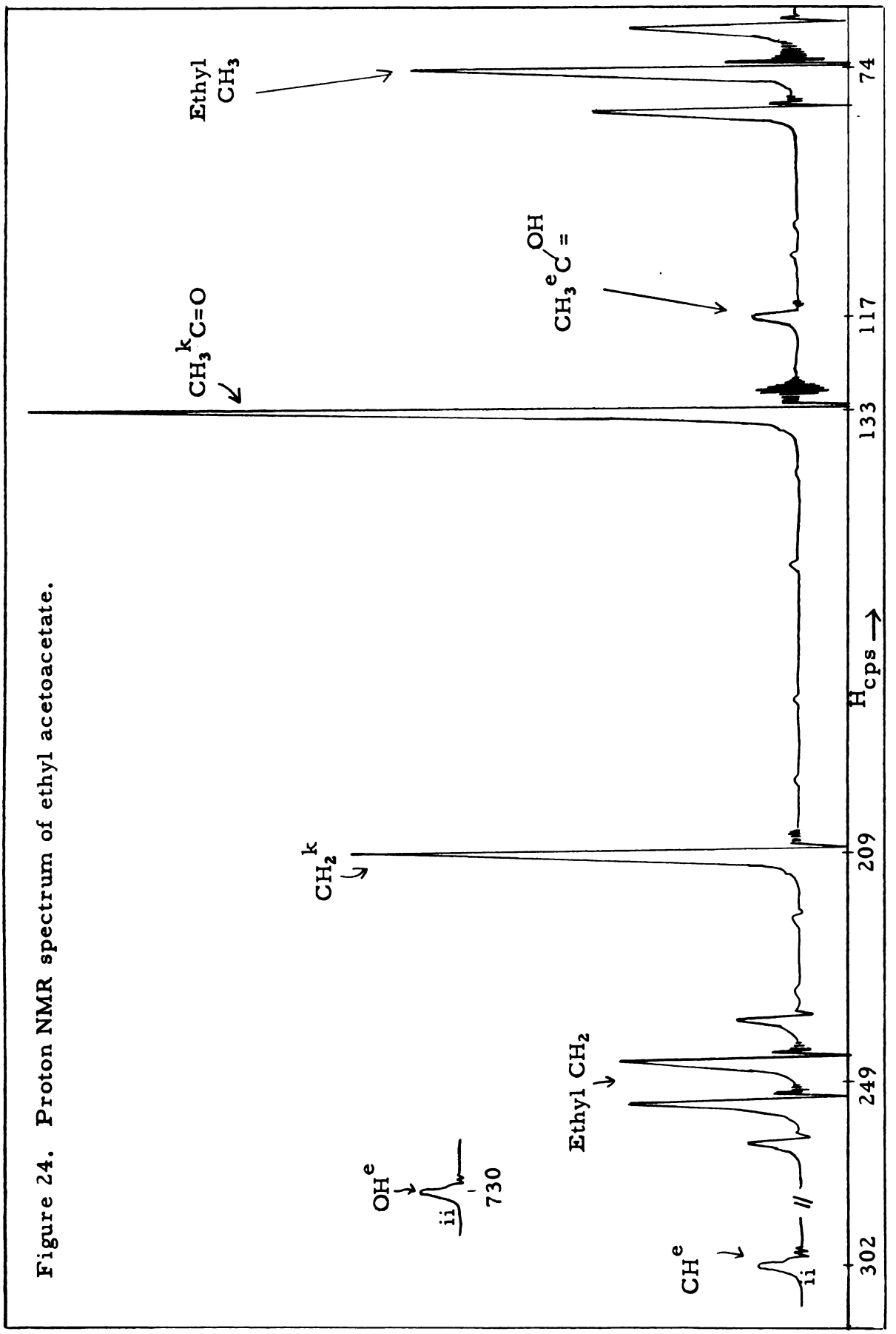


Figure 24. Proton NMR spectrum of ethyl acetoacetate.

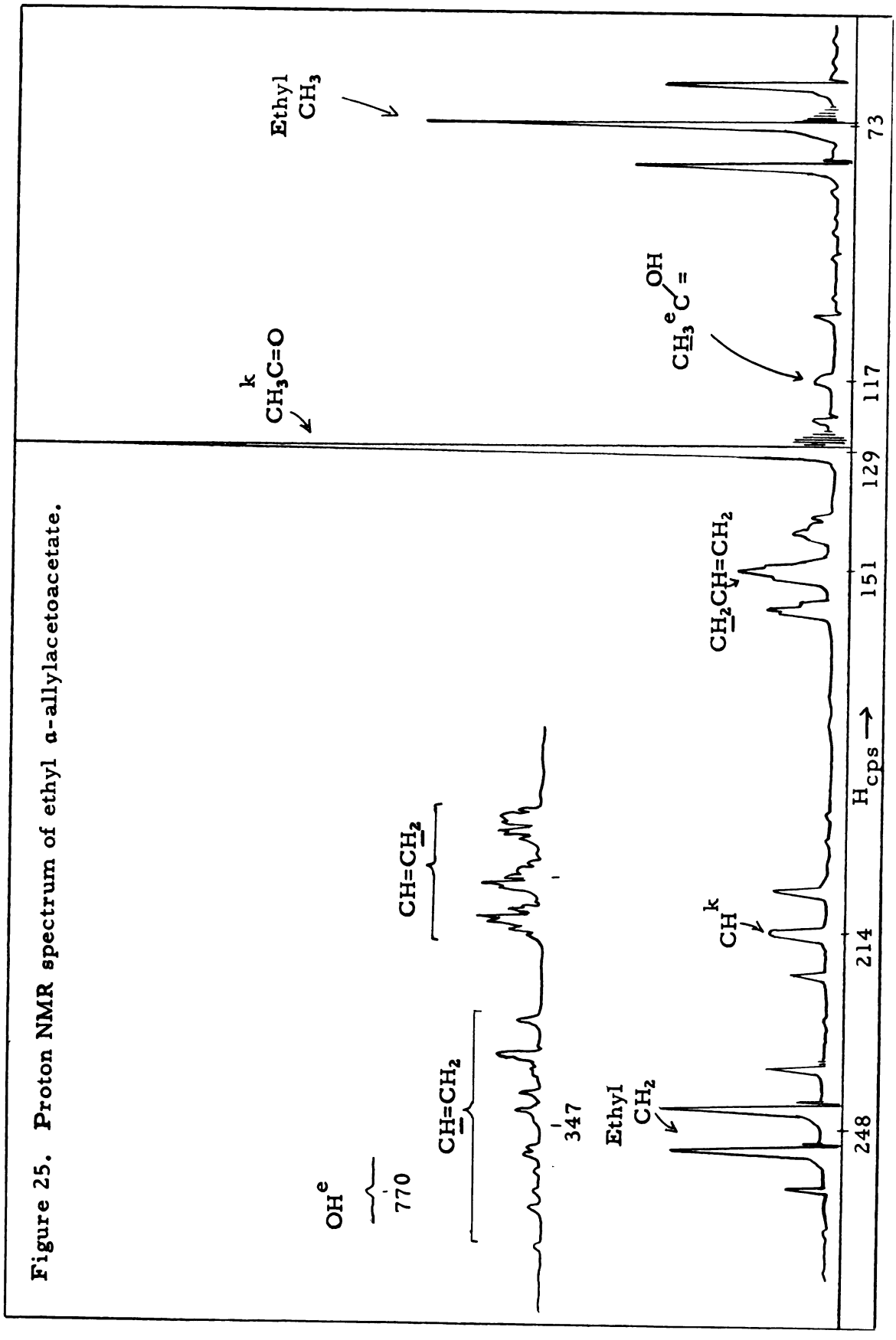


Figure 25. Proton NMR spectrum of ethyl α-allylacetoacetate.

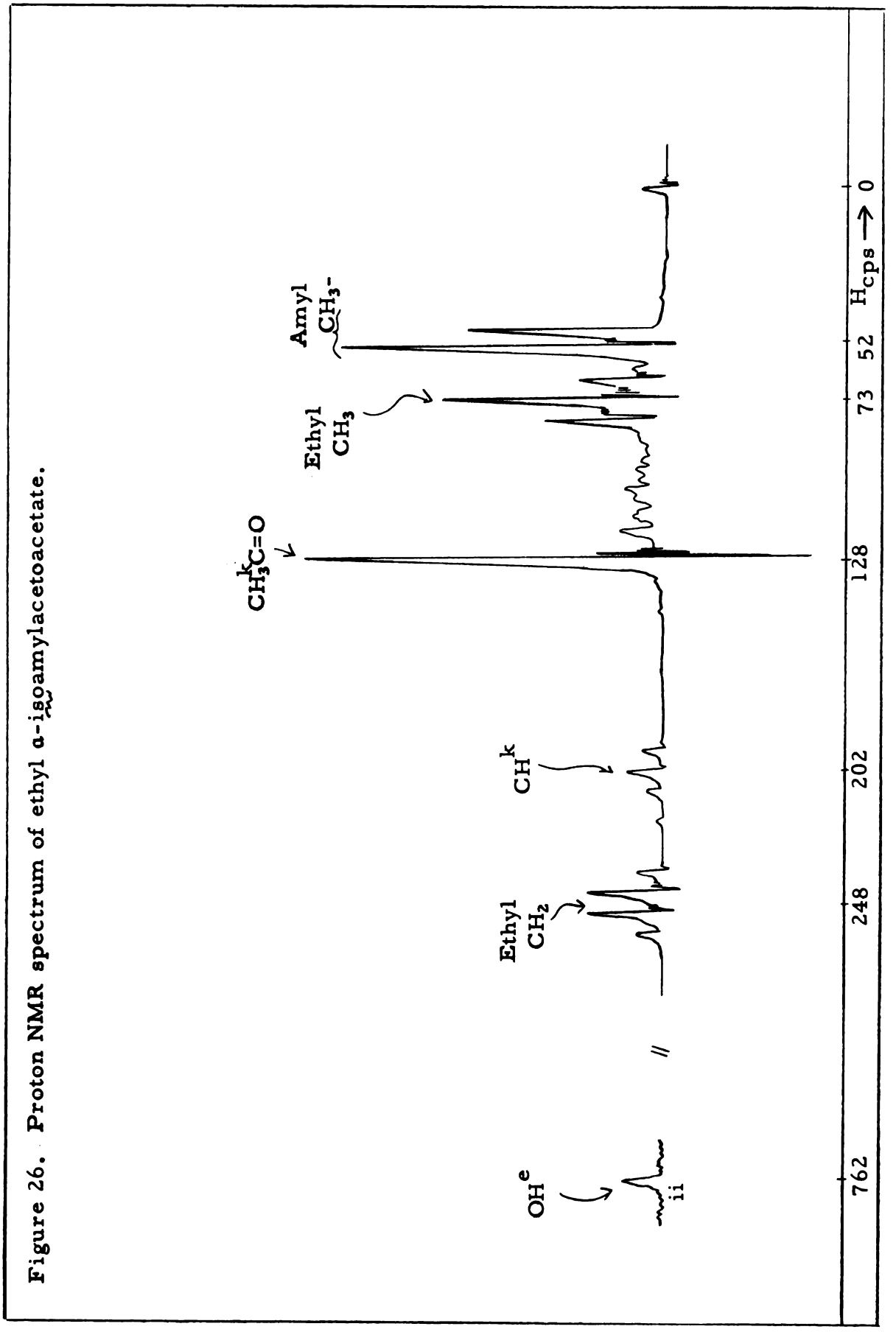


Figure 26. Proton NMR spectrum of ethyl α-isoamylacetoacetate.

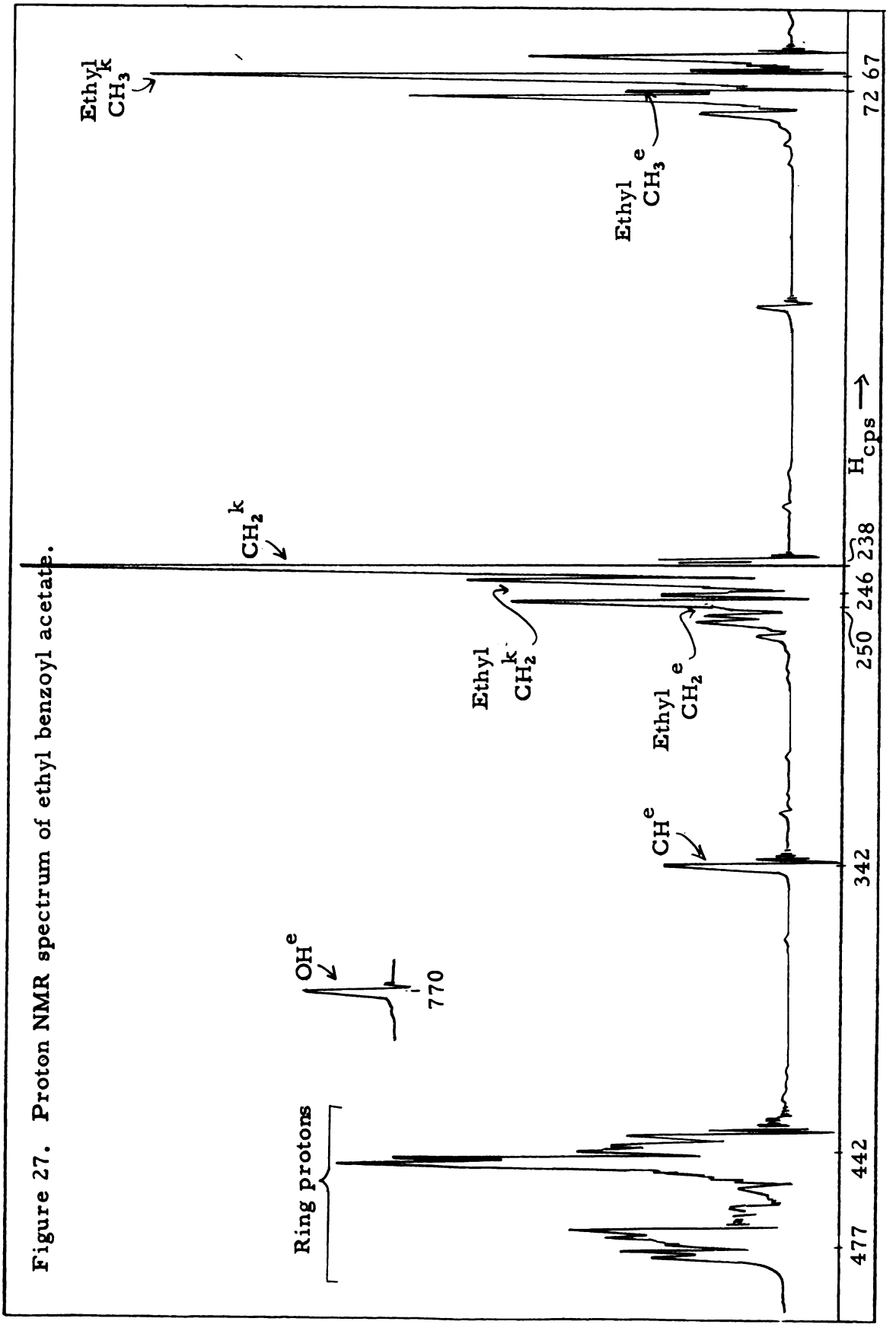


Figure 27. Proton NMR spectrum of ethyl benzoyl acetate.

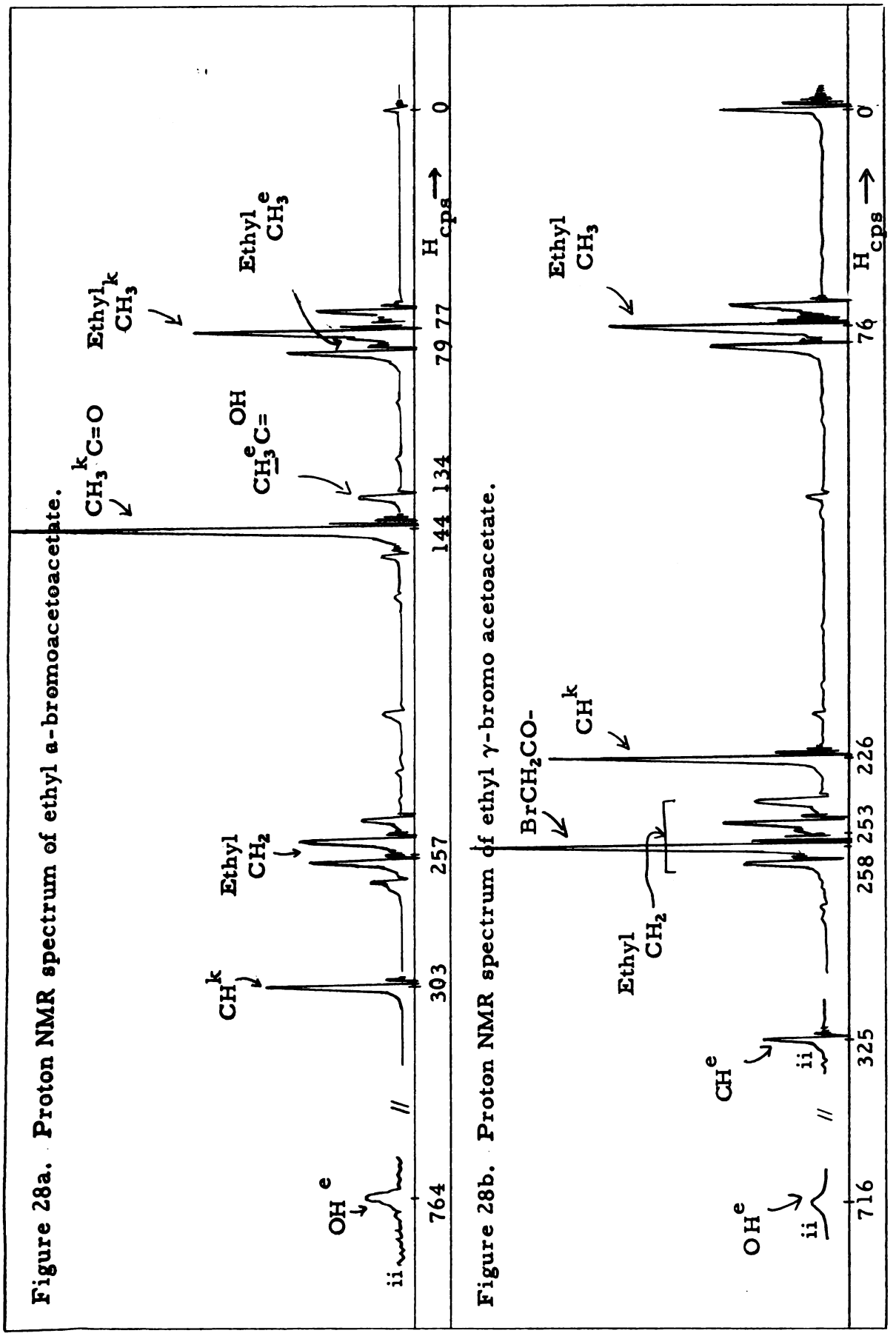
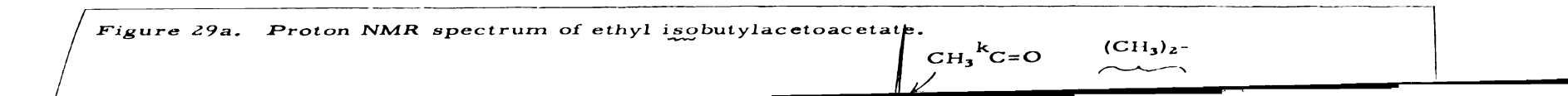


Figure 28a. Proton NMR spectrum of ethyl a-bromoacetoacetate.
$CH_3^kC=O$
Ethyl$_k$ CH_3
Ethyl^e CH_3
$CH_3^eC=$ OH
CH^k
Ethyl CH_2
OH^e
ii
764
303
257
144
134
79 77
0
H_{cps} →
Figure 28b. Proton NMR spectrum of ethyl γ-bromo acetoacetate.
Ethyl CH_3
$BrCH_2CO-$
CH^k
Ethyl CH_2
CH^e
OH^e
ii
716
325
258 253
226
76
0
H_{cps} →

Figure 29a. Proton NMR spectrum of ethyl isobutylacetoacetate.



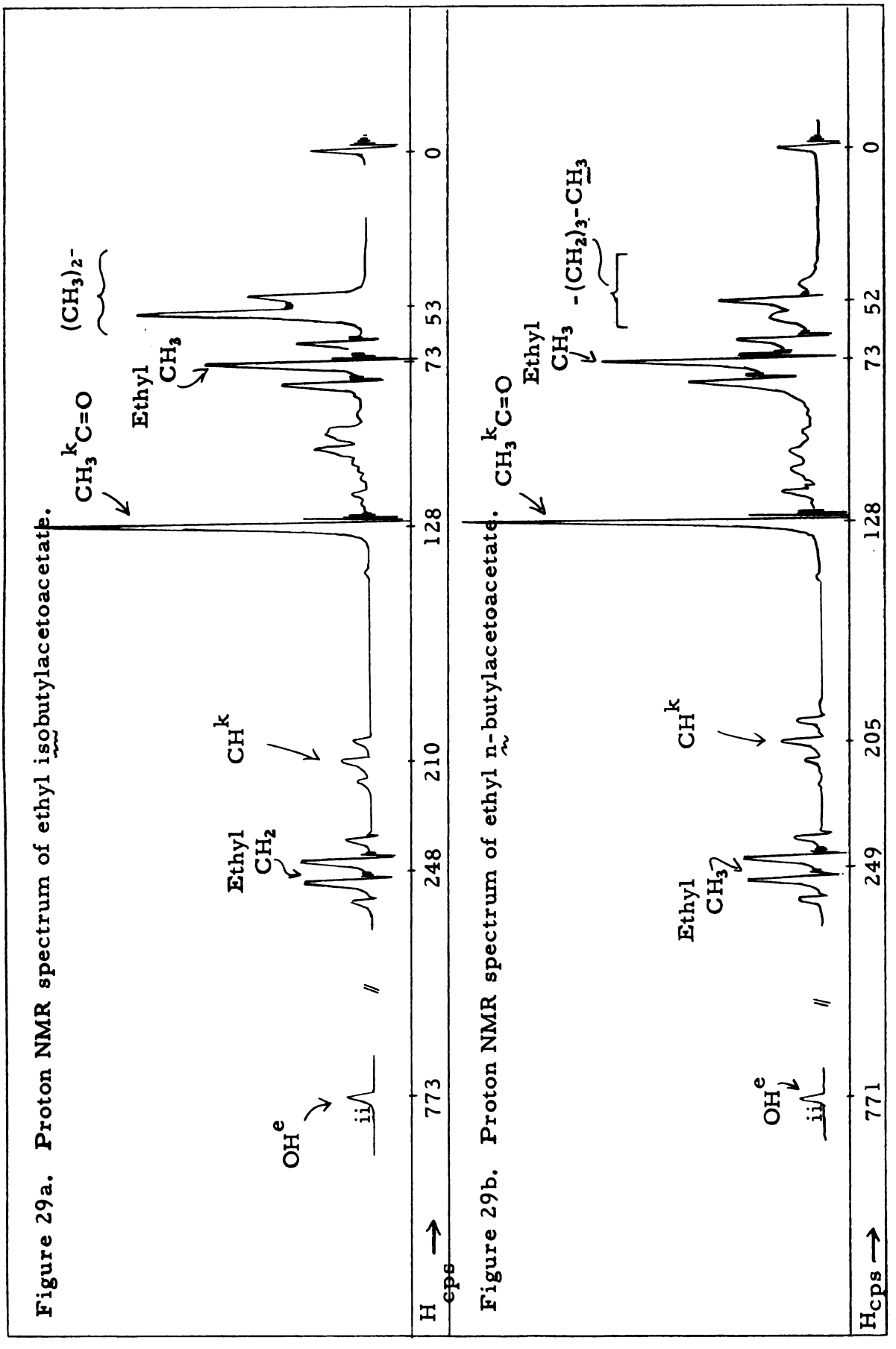


Figure 29a. Proton NMR spectrum of ethyl isobutylacetoacetate.
CH3 k C=O
Ethyl CH3
(CH3)2-
CH k
Ethyl CH2
OH e
H cps →
773
248
210
128
73
53
0
Figure 29b. Proton NMR spectrum of ethyl n-butylacetoacetate.
CH3 k C=O
Ethyl CH3
-(CH2)3-CH3
CH k
Ethyl CH2
OH e
Hcps →
771
249
205
128
73
52
0

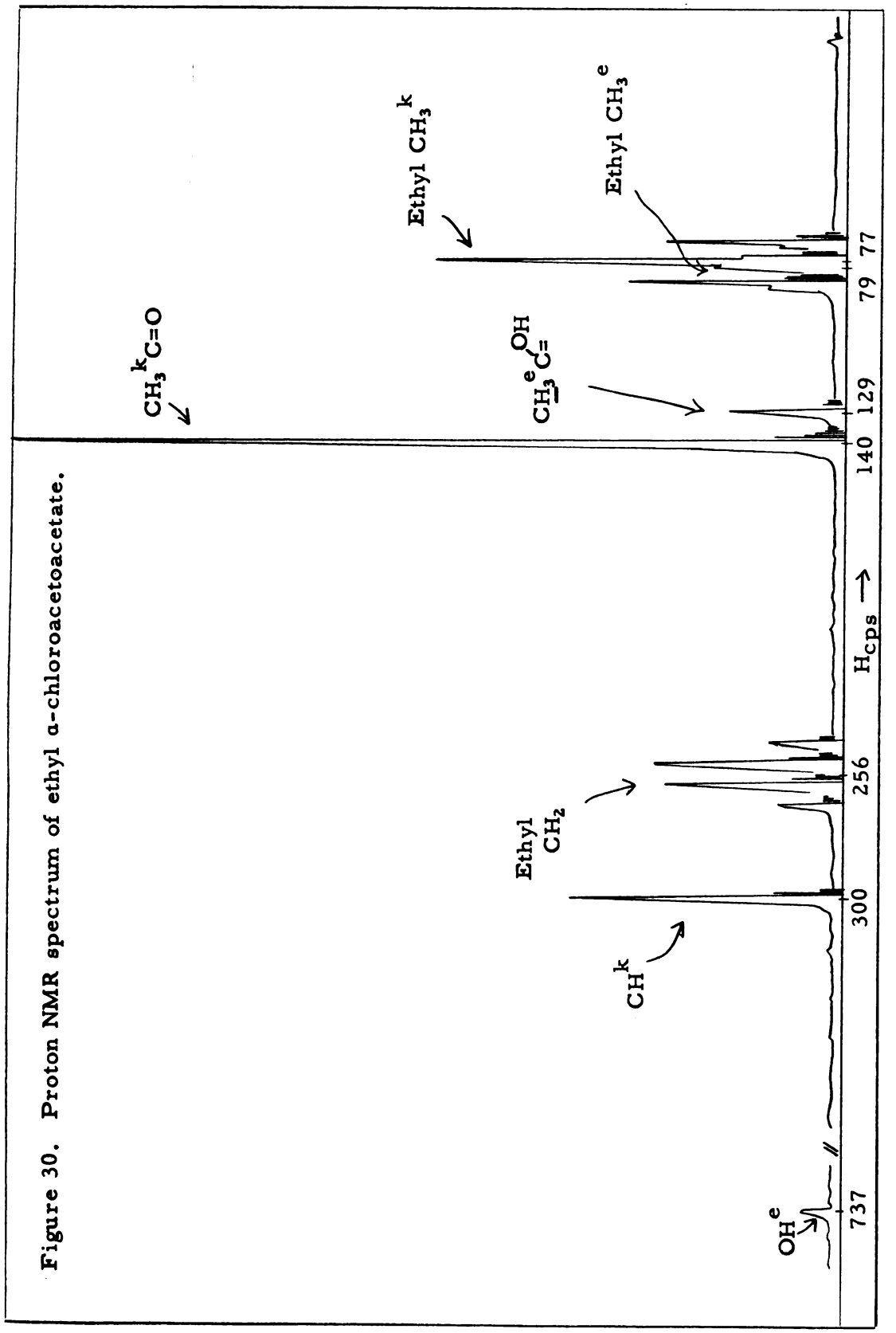


Figure 30. Proton NMR spectrum of ethyl α-chloroacetoacetate.

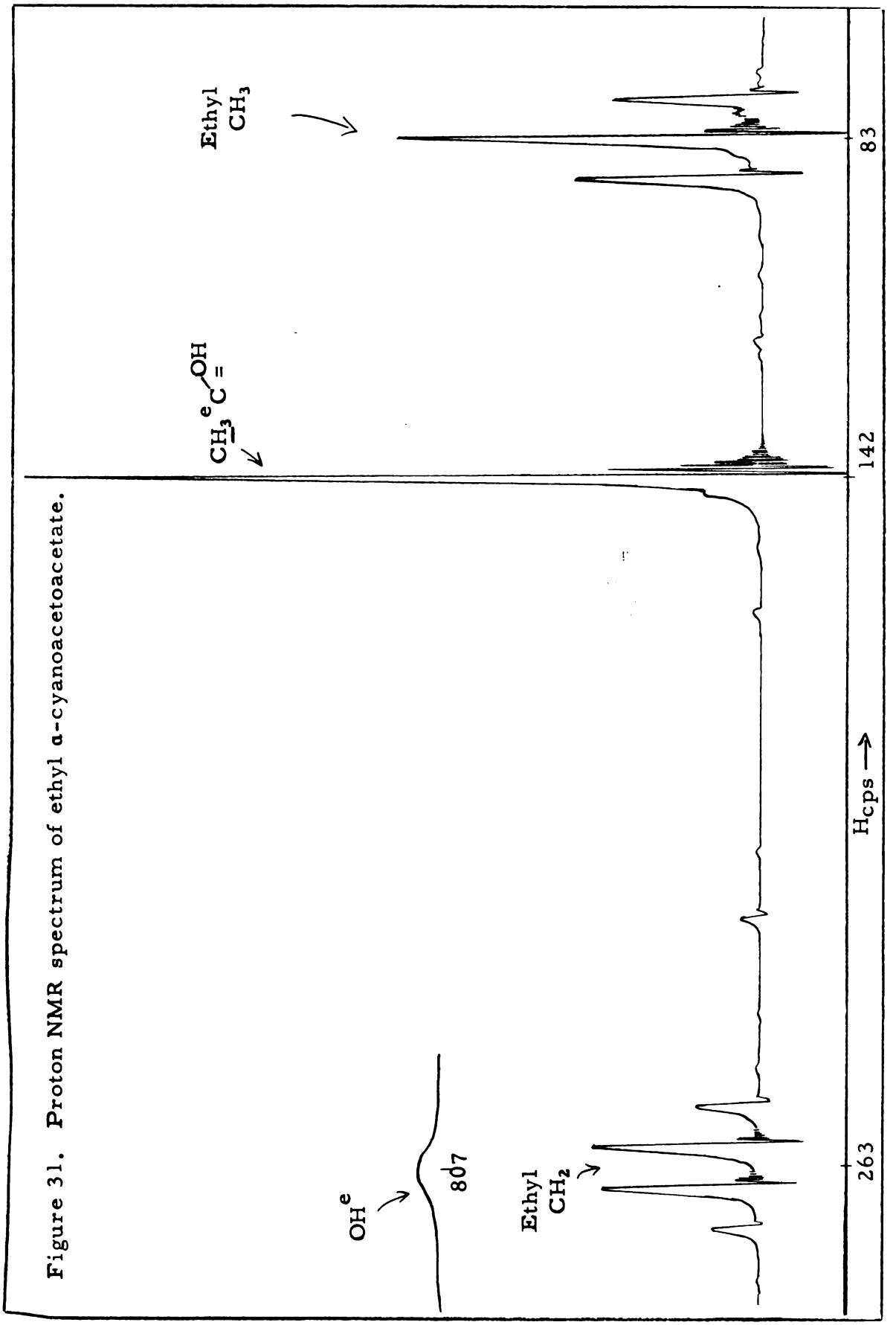


Figure 31. Proton NMR spectrum of ethyl α-cyanoacetoacetate.

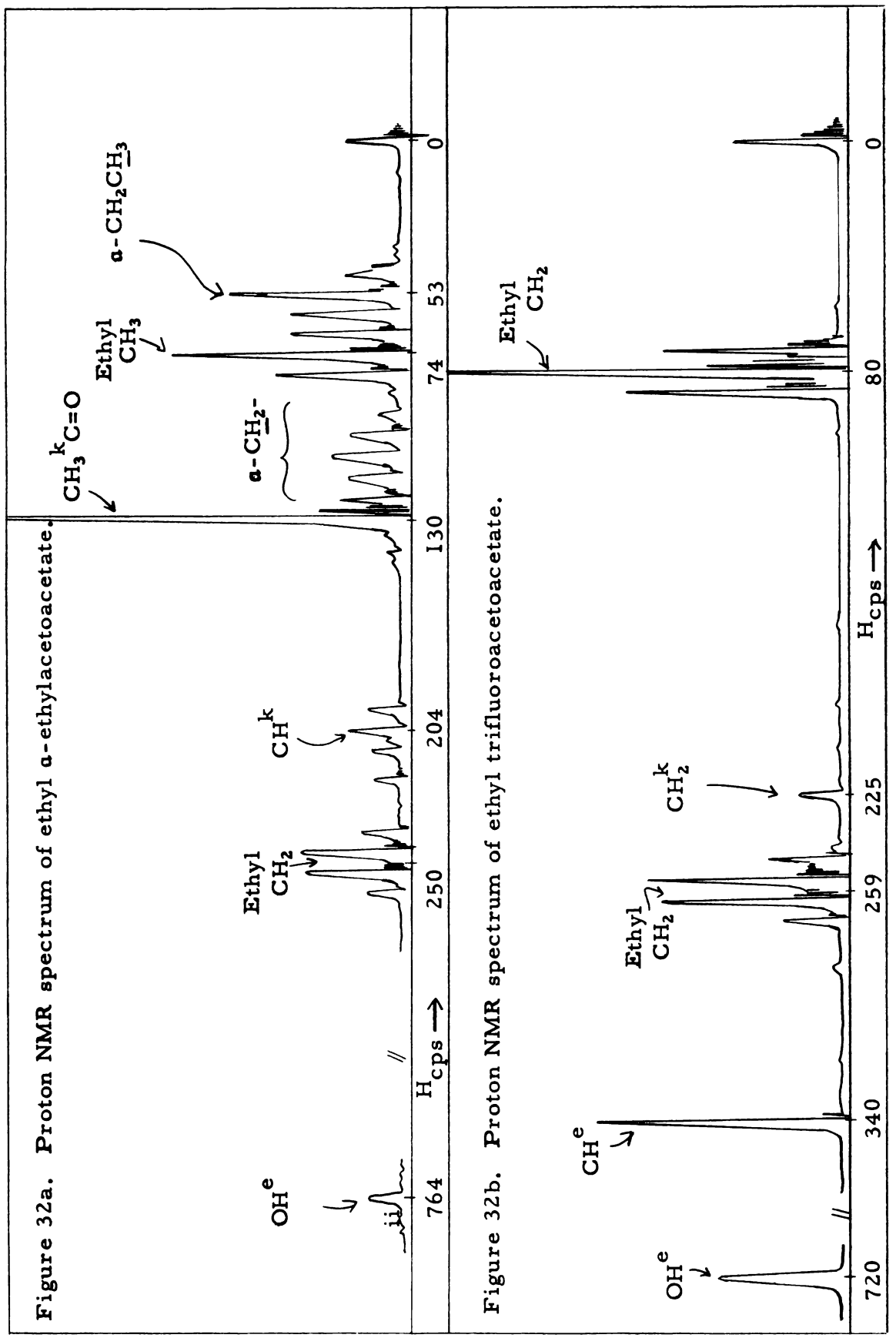


Figure 32b. Proton NMR spectrum of ethyl trifluoroacetoacetate.

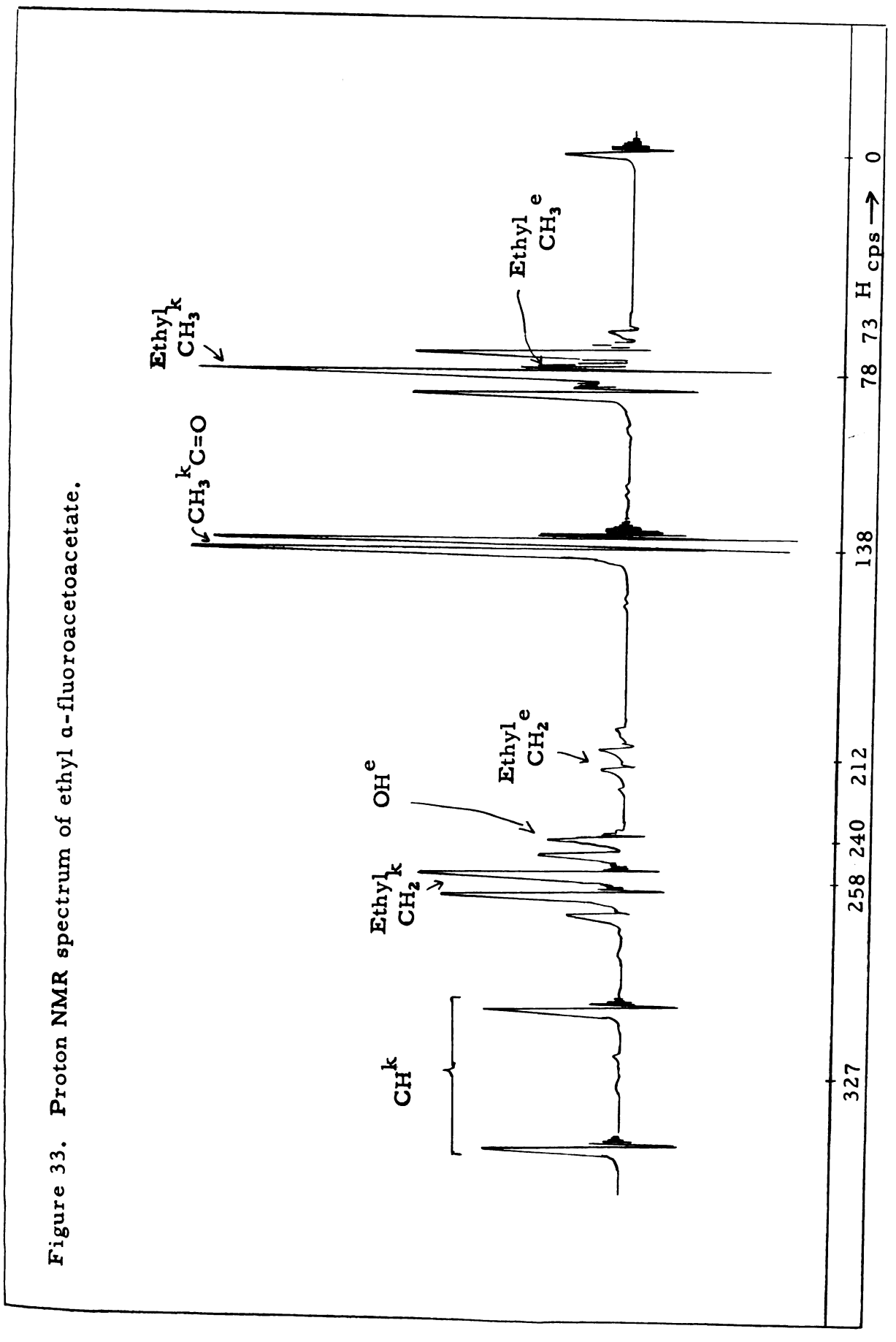


Figure 33. Proton NMR spectrum of ethyl α-fluoroacetoacetate.

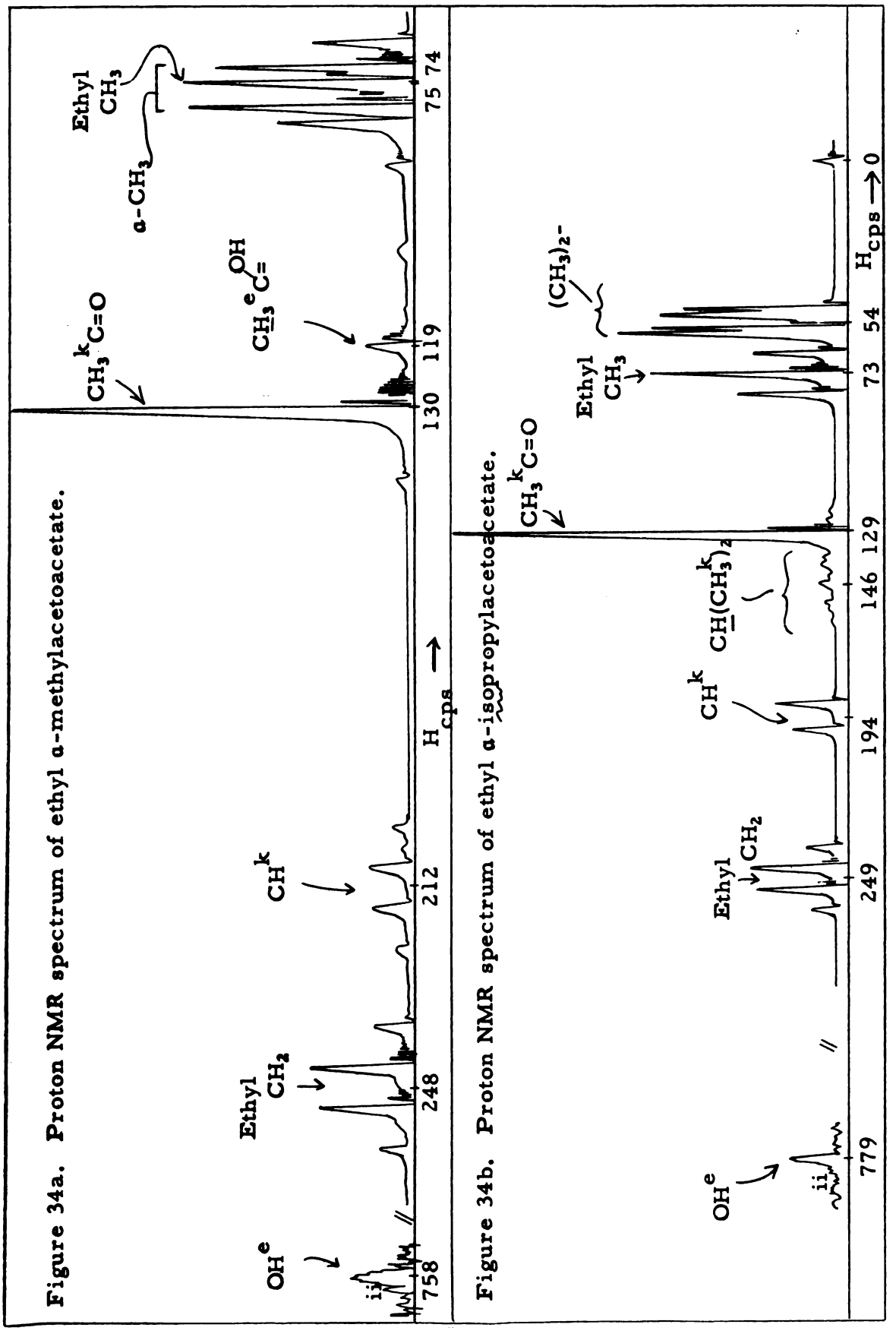


Figure 34a. Proton NMR spectrum of ethyl α-methylacetoacetate.

Figure 34b. Proton NMR spectrum of ethyl α-isopropylacetoacetate.

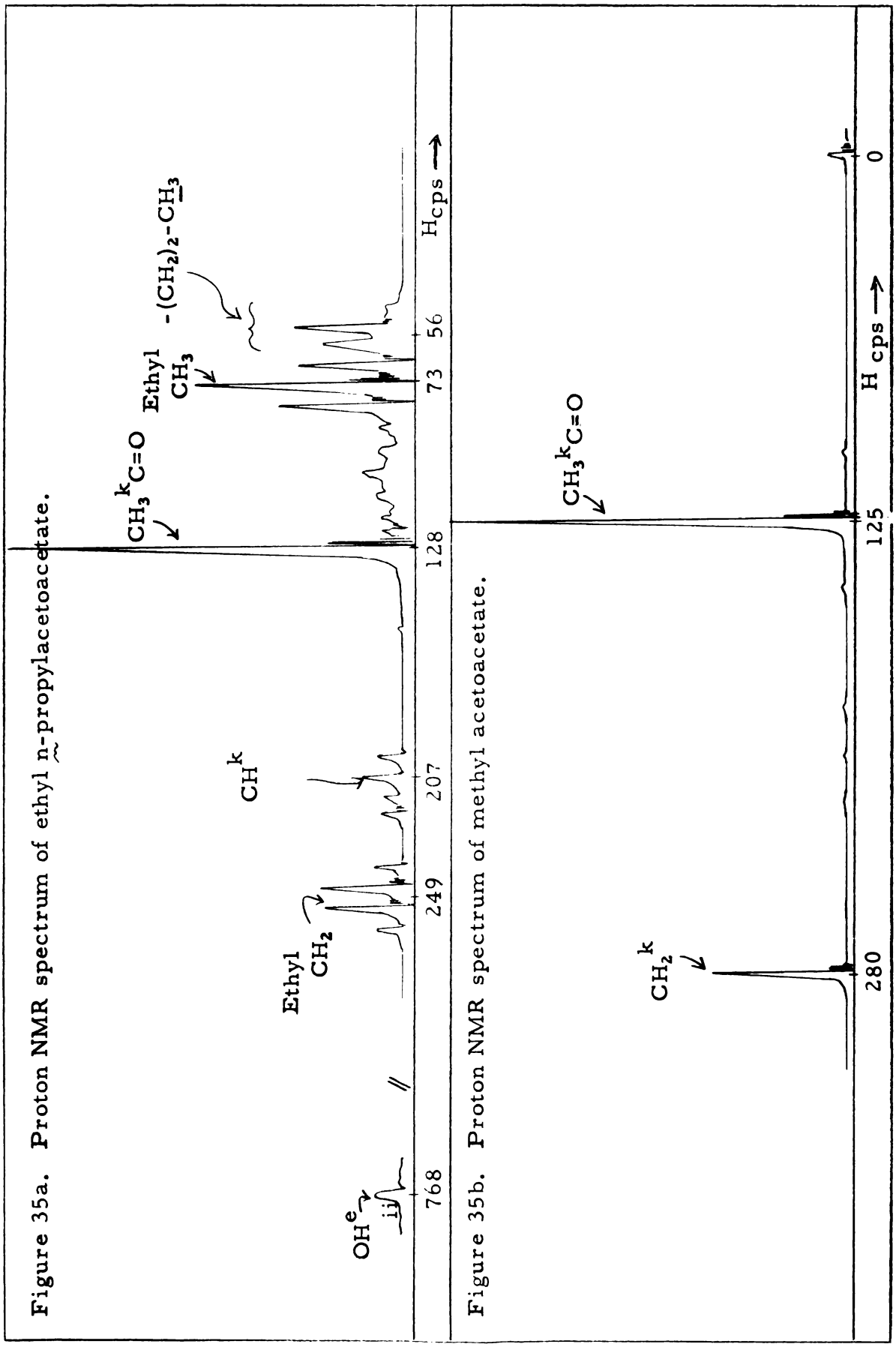


Figure 35a. Proton NMR spectrum of ethyl n-propylacetoacetate.

Figure 35b. Proton NMR spectrum of methyl acetoacetate.

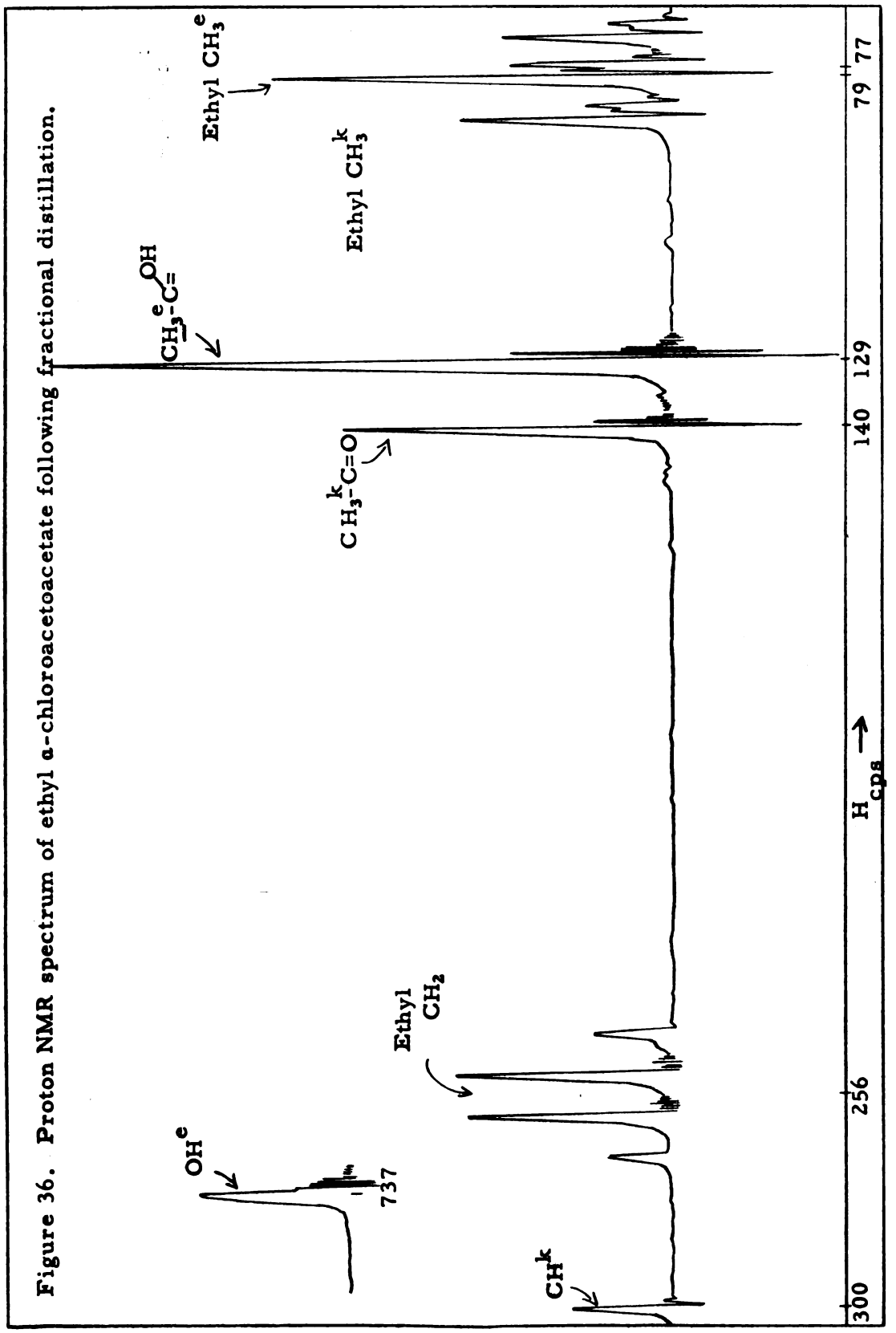


Figure 36. Proton NMR spectrum of ethyl α-chloroacetoacetate following fractional distillation.

for ethyl α-chloroacetoacetate and may be compared with that of the pure compound at equilibrium in Figure 30.

In general it may be noted that the tautomeric equilibrium lies on the side of the enol tautomer for β-diketones and far to the side of the keto tautomer for most β-ketoesters. Molecular models show that there is greater van der Waals non-bonded interaction in β-diketones between acetyl protons in the most favorable diketo configuration thus shifting the equilibrium toward the enol tautomer in these compounds.

Separate resonance signals are detected for the methyl protons of the acetyl groups of the keto and enol forms, as well as for the keto and enol α-protons and the enolic OH proton. Giessner-Prettre (58) has reported that the OH resonance line of ethyl acetoacetate is not visible in binary solutions without the addition of hydrochloric acid. The present study finds the OH resonance peak not only for ethyl acetoacetate, but also for all the α-substituted acetoacetates, both in pure form and in various solvents.

Chemical shift measurements for pure β-diketones and β-ketoesters (in cps from tetramethylsilane) are given in Tables XXX and XXXI, respectively. For the β-diketones and β-ketoesters neither the enol nor keto acetyl-methyl resonance peak varies appreciably in chemical shift. However, the deshielding effect of electron-withdrawing groups both in the α-position and on the acetyl group on the keto and enol α-proton is considerable. Resonances for the enolic OH proton occur at very low fields and show considerable variation among the compounds studied. For the most part the enolic OH resonance occurs at much lower field for β-diketones than for β-ketoesters.

Methyl protons of the ethoxy group show little variation among the β-ketoesters, whereas methylene protons are deshielded by electron-withdrawing groups in the α-position. Those compounds for which the ethoxy protons give different chemical shifts for enol and diketo

Table XXX. Proton Chemical Shifts in Pure β-Diketones

Compound	Acetyl		α-Proton			Alkyl		Other
	CH_3^e	CH_3^k	CH_2^k	CH^k	CH^e	OH^e	α-Group	
Acetylacetone	120	130	217	-	334	934	-	-
α-Chloroacetylacetone	133	137	-	292	-	922	-	-
α-Bromoacetylacetone	138	143	-	301	-	951	-	-
Cyclic isopropylidene malonate (in CCl_4)	-	-	107	-	-	-	-	105 $(CH_3)_2$
Dibenzoylmethane (in CCl_4)	-	-	-	-	382	1020	-	422 6 ring H's 455 4 ring H's
Hexafluoroacetylacetone	-	-	248	-	386	780	-	-
Trifluoroacetylacetone	132	136	237	-	360	847	-	-
1, 3-Indanedione (in dioxane)	-	-	191	-	-	-	-	-
α-Methylacetylacetone	125	130	-	228	-	990	75^k 110^e	-
1-Phenyl-1, 3-butanedione (0.401 M in CCl_4)	120	127	231	-	357	980	-	-
2-ϕ-1, 3-Indanedione	-	-	-	270	-	-	-	-
Thenoyltrifluoroacetone (0.301 M in CS_2)	-	-	-	-	382	898	-	-

k = keto
e = enol
* = Chemical shifts in cps from TMS.

Table XXXI. Proton Chemical Shifts in Pure β-Ketoesters*

Compound	Ethyl		Acetyl		α-Protons			OH[e]	Other
	CH_3	CH_2	CH_3[e]	CH_3[k]	CH_2[k]	CH[k]	CH[e]		
β-Bromo ethyl acetoacetate	-	269	119	126	215	-	307	712	218 ethyl CH_2Br
Butyl acetoacetate	-	-	114	130	205	-	299	730	244 butyl OCH_2 55 butyl CH_3 92 butyl $(CH_2)_2CH_3$
t-Butyl acetoacetate	-	-	112	130	199	-	293	733	86 $(CH_3)_3$[e, k]
n-Butyl α-chloroacetoacetate	-	-	129	140	-	298	-	740	254 butyl OCH_2 55 butyl CH_3
t-Butyl α-chloroacetoacetate	-	-	128	139	-	287	-	747	89 t-butyl[e] 92 t-butyl[k]
Ethyl acetoacetate	74	249	117	133	209	-	302	730	-
Ethyl α-allylacetoacetate	73	248	117	129	-	214	-	770	151 $C\underline{H}_2CH=CH_2$ 303 $CH=C\underline{H}_2$ 347 $C\underline{H}=CH_2$
Ethyl α-isoamylacetoacetate	73	248	m	128	-	202	-	762	50, 55 $(CH_3)_2$- 103 $(CH_2)_3$
Ethyl benzoylacetate	67[k] 73[e]	246[k] 253[e]	-	-	238		342	770	-
Ethyl α-bromoacetoacetate	77[k] 79[e]	257	134	144	-	303	-	764	-
Ethyl γ-bromoacetoacetate	76	253	-	-	226	-	325	716	258 Br-CH_2CO

Ethyl α-isobutylacetoacetate	73	248	m	128	-	210	-	773	50 CH(CH$_3$)$_2$ 56 103 CH$_2$CH
Ethyl α-n-butylacetoacetate	73	249	m	128	-	205	-	771	52 butyl CH$_3$ 72 (CH$_2$)$_2$CH$_3$ 108 (CH$_2$)$_2$CH$_3$
Ethyl α-chloroacetoacetate	77^k 79^e	256	129	140	-	300	-	737	-
Ethyl α-cyanoacetoacetate	83	263	142	–	-	-	-	807	-
Ethyl α-ethylacetoacetate	74	250	m	130	-	204	-	764	53 α-ethyl CH$_3$ 109 α-ethyl CH$_2$
Ethyl α-fluoroacetoacetate	78^k 73^e	258^k 212^e	-	138	-	327	-	-	-
Ethyl trifluoroacetoacetate	76^k 80^e	255^k 259^e	-	-	225	-	340	720	-
Ethyl α-methylacetoacetate	74	248	119	130	-	212	-	758	75 α-CH$_3$
Ethyl α-isopropylacetoacetate	73	249	132	129	-	194	-	779	54 CH(CH$_3$)$_2^k$ 73 CH(CH$_3$)$_2^e$ k 146 CH-CH(CH$_3$)$_2$ 301 CH(CH$_3$)$_2^e$
Ethyl α-n-propylacetoacetate	73	249	m	128	-	207	-	768	103 (CH$_2$)$_2$CH$_3$ 56 (CH$_2$)$_2$CH$_3$
Methyl acetoacetate	-	-	-	125	280	-	-	-	125 OCH$_3$

k = keto, e = enol, m = masked, * = Chemical shifts in cps from TMS.

tautomers include the α-bromo, α-fluoro, α-chloro, and the trifluoroethyl acetoacetates, along with ethyl benzoyl acetate.

Substitution of fluorine atoms for protons on the acetyl methyl group of β-diketones results in a deshielding of the α-protons for the keto tautomer of 20 and 30 cps in tri- and hexa-fluoroacetylacetone, respectively. Both chlorine and bromine in the α-position result in deshielding of the keto α-protons of about 80 cps from the resonance position in acetylacetone itself. In β-ketoesters the keto α-proton is once again deshielded by fluorine, chlorine, and bromine atoms in the α-position by 118, 91, and 94 cps, respectively, from its resonance in unsubstituted ethyl acetoacetate. Bromine substituted in the γ-position (on the acetyl group) deshields the β-proton only 15 cps, and in the β-position on the ethyl group has little effect. In β-bromo ethyl acetoacetate the α-proton is deshielded more than in ethyl γ-bromoacetoacetate. Among the α-alkyl substituted compounds little difference in the resonance position of the α-proton is observed. A trifluoro group in place of a methyl group only deshields the keto α-proton 16 cps for the β-ketoesters.

The enolic α-proton is deshielded in the trifluoro- and hexafluoroacetylacetone compounds by about 25 and 50 cps, respectively, from its position in acetylacetone. In thenoyltrifluoroacetone it is deshielded by nearly 50 cps. For the trifluoro-β-ketoesters the α-proton occurs 38 cps below its resonance position in ethyl acetoacetate. Bromine in the γ-position deshields this proton by about 20 cps, and a phenyl group in place of the acetyl methyl group deshields the α-proton by 40 cps.

For β-ketoesters the position of the OH resonance line varies over about 100 cps. For the series of compounds substituted in the α-position, greater deshielding occurs in the order chlorine > bromine > cyano. For alkyl substitution in the α-position the hydroxyl resonance peaks have chemical shifts in the range 720-773 cps with no apparent

general trend with increasing bulk. It appears surprising that an α-methyl group results in deshielding of the OH proton by 28 cps. The trifluoro compound shows some shielding of the OH proton from ethyl acetoacetate. In ethyl α-fluoroacetoacetate, there is evidence that some enol tautomer is present, but the enol OH does not appear at the expected low fields. There is a peak of the correct intensity at 240 cps which might be a non-intramolecularly-bonded OH resonance. However molecular models do not indicate any interference with the internally hydrogen bonded species. Variable temperature studies have not been helpful in assigning the enol OH resonance position.

Within the β-diketone compounds similar trends are observed. The position of OH resonance is at much lower applied fields than in the esters, and there is more variation among the compounds studied. A trifluoro and also hexafluoro group in place of the acetyl methyl group results in shielding of the OH proton. Deshielding of the OH proton occurs in the order α-chloro > α-bromo > α-methyl. That the substitution of a methyl group for an α-proton causes decreased shielding to the extent of 75 cps is surely puzzling.

Table XXXII indicates the enol OH chemical shift in cps from tetramethylsilane for pure compounds in the order of decreased shielding and presumably increasing interaction between OH and the carbonyl oxygen atom. Forsen and Nilsson (74) have plotted the carbonyl stretching frequency against chemical shift of the enol OH and found that a lower carbonyl stretching frequency corresponds to a lower chemical shift of the enol OH. They point out that a lower carbonyl stretching frequency is observed for cases of association of the type AH···C=O.

In Figure 37 the chemical shift of enol OH for β-dicarbonyls has been plotted against the stretching frequency for the enol chelate carbonyl. Chemical shift measurements for line A of the figure are

Table XXXII. Chemical Shifts of Enol OH for β-Dicarbonyls in Order of Increasing Interaction Between OH and C=O*

Compound	Chemical Shift
β-Bromo ethyl acetoacetate	712
Ethyl γ-bromoacetoacetate	716
Ethyl trifluoroacetoacetate	720
Butyl acetoacetate	730
Ethyl acetoacetate	730
t-Butyl acetoacetate	733
Ethyl α-chloroacetoacetate	737
n-Butyl α-chloroacetoacetate	740
t-Butyl α-chloroacetoacetate	747
Ethyl α-isoamylacetoacetate	754
Ethyl α-n-butylacetoacetate	757
Ethyl α-methylacetoacetate	758
Ethyl α-isoamylacetoacetate	762
Ethyl α-ethylacetoacetate	764
Ethyl α-bromoacetoacetate	764
Ethyl α-n-propylacetoacetate	768
Ethyl α-allylacetoacetate	770
Ethyl benzoylacetate	770
Ethyl α-n-butylacetoacetate	771
Ethyl α-isobutylacetoacetate	773
Ethyl α-isopropylacetoacetate	779
Hexafluoroacetylacetone	780
Ethyl α-cyanoacetoacetate	807
Trifluoroacetylacetone	847
Thenoyl trifluoroacetone (in CS_2)	898

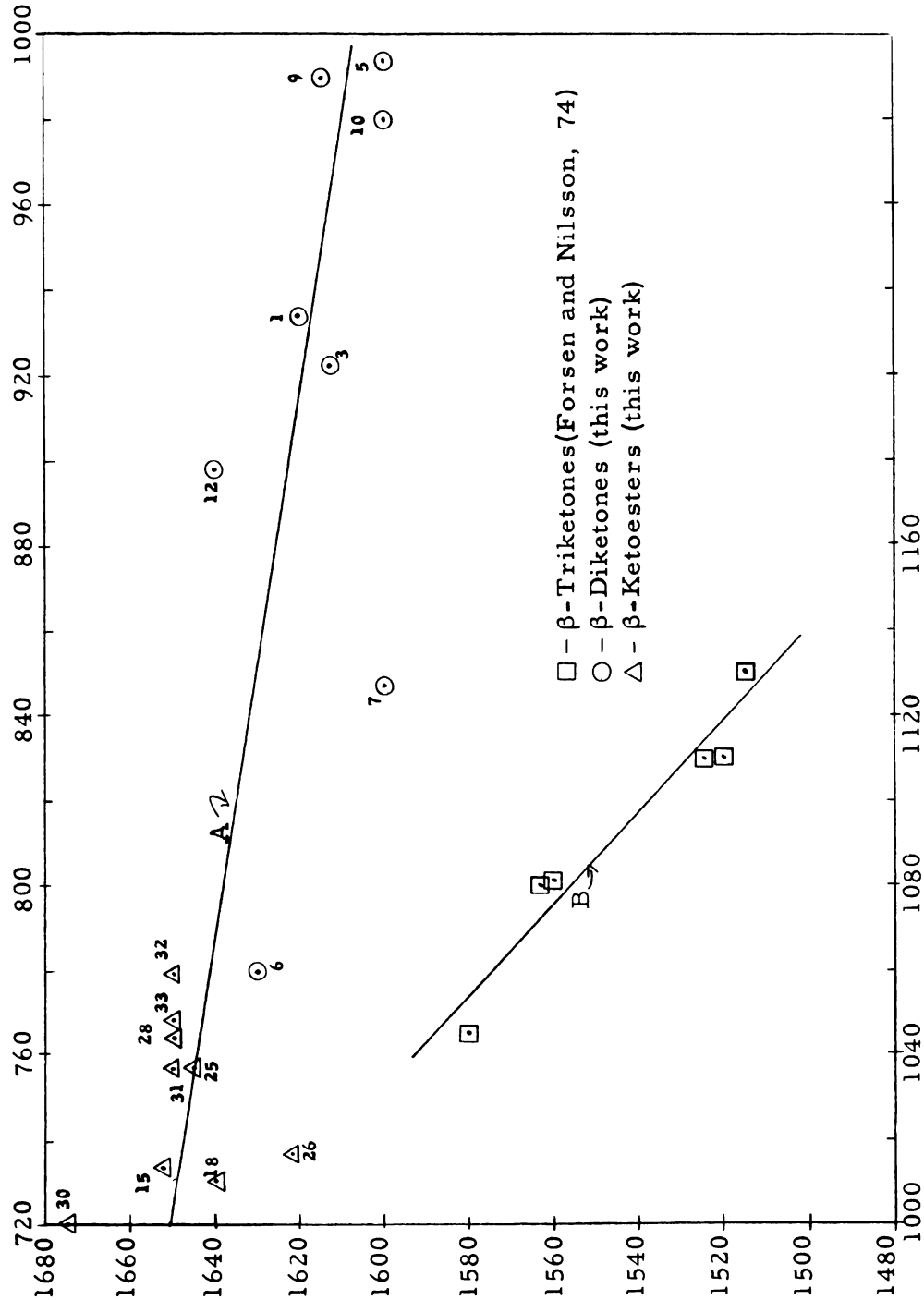
continued

Table XXXII - Continued

Compound	Chemical Shift
α-Chloroacetylacetone	922
α-Bromoacetylacetone	951
Acetylacetone	934
1-Phenyl-1, 3-butanedione (in CCl_4)	980
α-Methylacetylacetone	990
Dibenzoylmethane (in CCl_4)	993

*Chemical shifts are in cps from TMS.

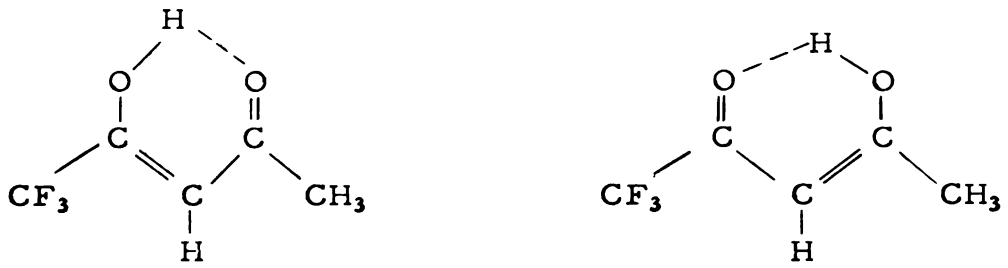
Figure 37. Chemical shift of enol OH versus carbonyl stretching frequency for β-dicarbonyls.*



*The numbers in the figure correspond to those in the table on page 88 for β-diketones and on page 99 for β-ketoesters.

taken from the present work, and an average value for the stretching frequencies has been taken from Tables VI and VII in the literature. Values of stretching frequencies for ethyl trifluoroacetoacetate, hexafluoroacetylacetone, and trifluoroacetylacetone obtained in the present work are 1675 cm^{-1}, 1629 cm^{-1}, and 1600 cm^{-1}, respectively. Line B of Figure 37 represents the results of Forsen and Nilsson (74). As may be seen from the figure, there is a general trend of increasing carbonyl frequency with a more shielded enol OH proton, in agreement with Forsen and Nilsson's results. However, the β-dicarbonyls in the present study do not give a strict linear relationship. Certain deviations from linearity may be noted, in particular ethyl trifluoroacetoacetate, trifluoroacetylacetone, and thenoyl trifluoroacetone.

Structure. Among the unsymmetrical β-diketones there is the possibility of two different enol tautomers, as shown in Figure 38 for trifluoroacetylacetone. Park et al. (3), prefer structure (a) with no justification given. Belford et al. (38), assume that structure (a) is



(a) (b)

Figure 38. Possible enol tautomers for trifluoroacetylacetone.

more acidic than (b), and that structure (b) is probably in greatest concentration. Bellamy and Beecher (32) state that the trifluoro group induces enolization of the adjacent keto group and that the trifluoro

group is then far removed from the carbonyl undergoing chelation. Thus they prefer structure (a). Nakamoto (86) has found that the trifluoro group strengthens the adjacent C=O bond for chelates, which would tend to favor structure (b). However, the infrared evidence is inconclusive.

Nuclear magnetic resonance studies to date do not give firm evidence to distinguish between structures (a) and (b). Chemical shift measurements for the series acetylacetone, trifluoro- and hexafluoroacetylacetone indicate that the resonance position of the OH proton for the trifluoro compound occurs midway between its position in the other two compounds. It appears possible that the proton is exchanging sites and that the resonance in trifluoroacetylacetone actually represents an average between structures (a) and (b).

For other unsymmetrical β-diketones observed in the present work, only one enol form appears to be present, although the possibility of rapid exchange is not precluded by the NMR evidence.

Tautomeric Equilibrium. The percentage enol tautomers in the β-diketones and β-ketoesters is given in Tables XXXIII and XXXIV, respectively, along with equilibrium constants at 33°C. For the β-diketones substitution of an electron-withdrawing group such as chlorine in the α-position results in increased enolization; however, bromine results in a marked decrease in enolization. Molecular models show that a chlorine atom is about the size of a methyl group. Steric considerations in the α-chloro- and α-methylacetylacetone should, therefore, be approximately equal. Bromine, however, is considerably larger, and van der Waals non-bonded interactions become far greater than with chlorine. Also bromine is less electronegative than chlorine and would consequently result in a less acidic α-hydrogen atom. The high enol content of both trifluoro- and hexafluoroacetylacetone indicates

Table XXXIII. Percentages of Enol Tautomers and Equilibrium Constants for β-Diketones as Determined by Nuclear Magnetic Resonance

Compound	Percent Enol	K_e*	Protons Integrated
Acetylacetone	81	4.3	CH^e/CH_2^k
α-Bromoacetylacetone	46	0.85	CH_3^e/CH_3^k
α-Chloroacetylacetone	94	16	CH_3^e/CH_3^k
Cyclic isopropylidene malonate (in CCl_4)	0	0	-
Dibenzoylmethane (in CCl_4)	100	-	-
Hexafluoroacetylacetone	100	-	-
Trifluoroacetylacetone	97	32	CH_3^e/CH_3^k
1, 3-Indanedione (in $CHCl_3$)	0	0	-
α-Methylacetylacetone	30	0.43	$\alpha\text{-}CH_3^e/\alpha\text{-}CH_3^k$
1-Phenyl-1, 3-butanedione (in CCl_4)	100	-	-
2-Phenyl-1, 3-indanedione (in dioxane)	0	0	-
Thenoyltrifluoroacetone (in CS_2)	100	-	-

*$K_e = \frac{[\text{enol}]}{[\text{keto}]}$, and all measurements are at 33 ± 2°C.

Table XXXIV. Percentage Enol Tautomers and Equilibrium Constants for β-Ketoesters as Determined by Nuclear Magnetic Resonance

Compound	Percent Enol	K_e*	Protons Integrated
β-Bromo ethyl acetoacetate	6	0.06	CH_3^e/CH_3^k
Butyl acetoacetate	15	0.18	CH^k/ethyl CH_2
t-Butyl acetoacetate	17	0.21	$(CH_3)_3^e/(CH_3)_3^k$
Butyl α-chloroacetoacetate	20	0.25	CH^k/OH^e
t-Butyl α-chloroacetoacetate	46	0.85	CH_3^e/CH_3^k
Ethyl acetoacetate	8	0.09	CH_3^e/CH_3^k
Ethyl α-allylacetoacetate	~3	~0.03	peak heights
Ethyl benzoylacetate	22	0.28	$CH^e/(CH_3)_3^{e+k}$
Ethyl α-isoamylacetoacetate	~3	~0.03	peak heights
Ethyl α-bromoacetoacetate	5	0.05	peak heights
Ethyl α-isobutylacetoacetate	~2	~0.02	peak heights
Ethyl α-n-butylacetoacetate	~2	~0.02	peak heights
Ethyl α-chloroacetoacetate	15	0.18	CH^k/ethyl CH_2
Ethyl α-cyanoacetoacetate	93	13	OH^e/CH_2^{e+k}
Ethyl α-ethylacetoacetate	~1	~0.01	peak heights
Ethyl α-fluoroacetoacetate	15	0.18	CH^k/ethyl CH_2
Ethyl trifluoroacetoacetate	89	8.1	CH^e/CH_2^k
Ethyl α-methylacetoacetate	5	0.05	CH^k/ethyl CH_2
Ethyl α-isopropylacetoacetate	~1	~0.01	peak heights
Ethyl α-n-propylacetoacetate	~1	~0.01	peak heights
Methyl acetoacetate	0	0	-

*$K_e = \frac{[\text{enol}]}{[\text{keto}]}$, and all measurements are at 33 ± 2°C.

that the electronegative fluorine atoms are successful in withdrawing electrons from the vicinity of the α-protons.

Park et al. (3), explain the very high enol content in compounds such as trifluoroacetylacetone by additional stabilization of the cis form by possible CH···F bonding and in the trans enol by OH···F bonding. Filler and Naqvi (18) point out, however, that the discontinuity in the observed percentage of tautomers precludes this explanation. They suggest the alternative explanation that the enols become increasingly acidic as the number of fluorine atoms increases which would lead to stronger hydrogen bonding.

In dibenzoylmethane, 1-phenyl-1, 3-butanedione, and thenoyltrifluoroacetone, the presence of the aromatic ring results in increased enolization. In each case, however, the aromatic ring is unable to assume a position parallel to the intramolecular six-membered ring of the enolic tautomer because of steric interaction with the enol α-proton. The conjugated system has evidently not been extended. Stabilization of the enol tautomer must then result from an electron-withdrawing effect of the rings. Neither 1, 3-indanedione nor 2-phenyl-1, 3-indanedione gives evidence of enolization in solvents such as chloroform, benzene, dioxane, and dichloroethane. This is not surprising in view of the fact that molecular models indicate the formation of an intramolecularly-bonded system is precluded by steric considerations. Likewise, cyclic isopropylidene malonate cannot form an intramolecular hydrogen bond and is completely ketonic in carbon disulfide, carbon tetrachloride, benzene, and chloroform.

Among the β-ketoesters a trend similar to that in the β-diketones is observed. Alkyl groups substituted in the α-position decrease the degree of enolization, whereas both fluorine and chlorine in this position increase the percentage of enol tautomer. However, bromine in the α-position results in less enol tautomer, and this decrease may be

explained as in the case of α-bromoacetylacetone. A larger alkyl group on the alkoxy end of the β-ketoester results in an increase in enolization, which may be explained by steric interaction between the alkoxy protons and those of the acetyl methyl group for the diketone tautomer. The substitution of a cyano group in the α-position results in very great increase of the enol form. A molecular model indicates that the possibility of N...H bonding in the enol tautomer is not a likely one. Further, no steric hindrance is apparent in the keto tautomer. It would appear that the equilibrium is shifted toward the enol form because of electron withdrawal from the vicinity of the α-proton.

Solvent Effects

Carbon Tetrachloride. Infinite dilution chemical shifts of protons of β-diketones and β-ketoesters in carbon tetrachloride solution are given in Tables XXXV and XXXVI, respectively. Chemical shift values are given in cps and are positive for a shift to high field on dilution. It may be mentioned that the addition of carbon tetrachloride to β-dicarbonyls results in an increase in the percentage of the enol tautomer. For the acetyl, alkoxy, and α-alkyl-group protons of both β-diketones and β-ketoesters there is little effect on chemical shift on dilution. The α-proton for the keto tautomer usually shows an upfield shift of about 10-15 cps, but in ethyl α-fluoroacetoacetate the upfield shift is 29 cps. Enol α-proton resonance peaks shift upfield on dilution by about the same amount as the keto α-protons. Exceptions are hexafluoro- and α-chloroacetylacetone in which no shift is observed. The enol OH proton resonance line moved upfield on dilution in carbon tetrachloride by from 6 to 21 cps in the β-dicarbonyls. Only α-chloro-, trifluoro-, and hexafluoro-acetylacetone do not show this upfield shift of the OH proton.

Table XXXV. Infinite Dilution Proton Chemical Shifts in β-Diketones in Carbon Tetrachloride*

Compound	Acetyl		α-H			
	CH_3^e	CH_3^k	H^k	H^e	OH^e	Other
Acetylacetone	2	1	10	12	21	-
α-Chloroacetylacetone	-2	0	18	-	3	-
Hexafluoroacetylacetone	-	-	-	0	1	-
Trifluoroacetylacetone	2	-	-	9	-2	-
α-Methylacetylacetone	0	3	18	-	16	0- α-$CH_3^{k,e}$

k = keto
e = enol
* = Chemical shifts are in cps relative to the pure compound.

Table XXXVI. Infinite Dilution Proton Chemical Shifts in β-Ketoesters in Carbon Tetrachloride*

Compound	Ethyl		Acetyl CH_3		α-H^k	α-H^e	OH^e	Alkyl α-Group	Other
	CH_3	CH_2	Enol	Keto					
Butyl acetoacetate	-	-	-1	-1	9	7	9	-	-1 bu CH_2
t-Butyl acetoacetate	-	-	0	0	6	2	9	-	-1 $(CH_3)_3^{e,k}$
Ethyl acetoacetate	-3	1	1	1	13	8	6	-	-
Ethyl α-allylacetoacetate	-3	0	1	1	13	-	10	1, 0, 2	-
Ethyl α-isoamylacetoacetate	-2	0	m	1	10	-	7	-1, -2, 0	-
Ethyl benzoylacetate	$-5^{k,e}$	$2^{k,e}$	-	-	11	9	20	-	-
Ethyl α-isobutylacetoacetate	-3	0	m	1	13	-	12	-1, 0, 2	-
Ethyl α-n-butylacetoacetate	-3	1	m	1	13	-	17	-3, 3, m	-
Ethyl α-chloroacetoacetate	0^k -1^e	2	1	2	8	-	6	-	-
Ethyl α-ethylacetoacetate	-1	1	m	3	15	-	12	-	-
Ethyl α-fluoroacetoacetate	-2	5	-	1	29	-	-	-	-
Ethyl trifluoroacetoacetate	-1^k 1^e	0^k 3^e	-	-	6	7	12	-	-
Ethyl α-methylacetoacetate	-1	0	4	2	12	-	7	2	-
Ethyl α-isopropylacetoacetate	0	1	0	2	13	-	11	0, 2, -2, 1, 1	-
Methyl acetoacetate	-	-	-	0	9	-	-	-	O-(OCH_3)

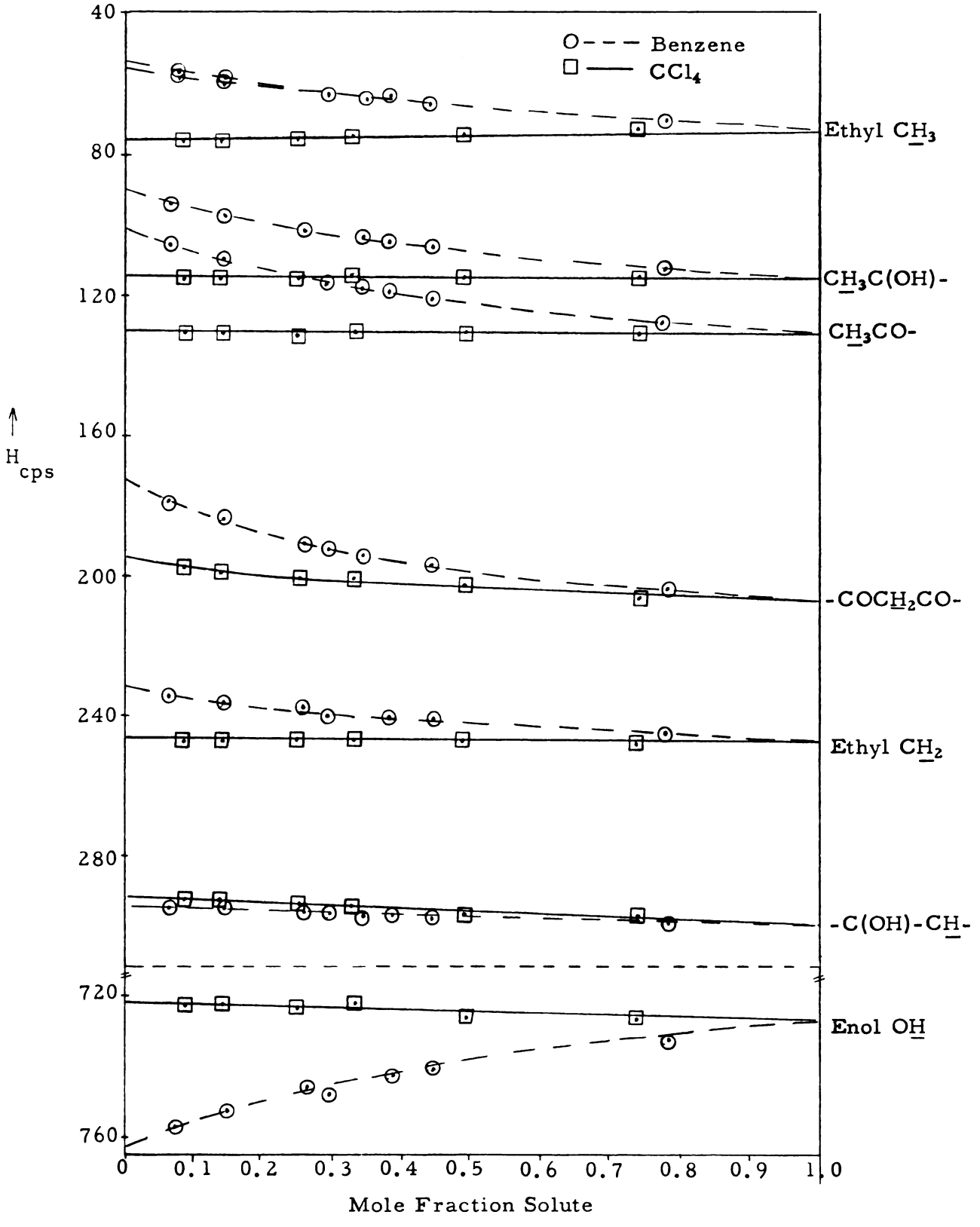
k = keto, e = enol, m = masked, * = chemical shifts are in cps relative to the pure compound.

Giessner-Prettre (58) explained the shielding of the keto α-CH_2 protons on the basis of breaking up of associated groups of ketone molecules which were assumed to be held together by means of intermolecular hydrogen bonds. However, the present study shows that the enol protons also become more shielded in nearly all β-dicarbonyls. Increased shielding of both the enol OH and enol α-CH protons may be explained as due to breaking up of the intramolecular hydrogen bonds on dilution. The keto protons, if involved in intermolecular hydrogen bonds, become dissociated on dilution to about the same extent as the intramolecular hydrogen bonds. In either case, one assumes that the respective peaks represent an average of the chelate and non-chelate enol form or of the bonded and non-bonded ketone form.

Figure 39 shows a graph of chemical shift in cps versus mole fraction for solutions of ethyl acetoacetate in carbon tetrachloride. A spectrum showing the effect of dilution on the proton resonance peaks of acetylacetone is shown in Figure 40. In Figure 41 are plotted chemical shifts in cps for the OH resonance peaks of a series of compounds at infinite dilution in carbon tetrachloride, relative to the OH resonance peak in the pure compound, versus mole fraction. In each case the shift is taken as positive if the proton is shielded relative to the OH peak for the pure compound. If the shielding does represent principally a breaking up of the intermolecular hydrogen bonds, then carbon tetrachloride affects this dissociation in the increasing order of hexafluoroacetylacetone (least), α-chloroacetylacetone, ethyl acetoacetate, ethyl α-allylacetoacetate, ethyl α-ethylacetoacetate, ethyl α-n-butylacetoacetate, α-methylacetylacetone, and acetylacetone (greatest).

1-Phenyl-1,3-butanedione on dilution in carbon tetrachloride shows a slight upfield shift for both enol and keto acetyl methyl protons, a negligible shift for keto and enol α-protons, and a downfield shift for the enol OH proton resonance line, which is a very broad resonance peak.

Figure 39. Chemical shift of protons of ethyl acetoacetate in benzene and carbon tetrachloride.



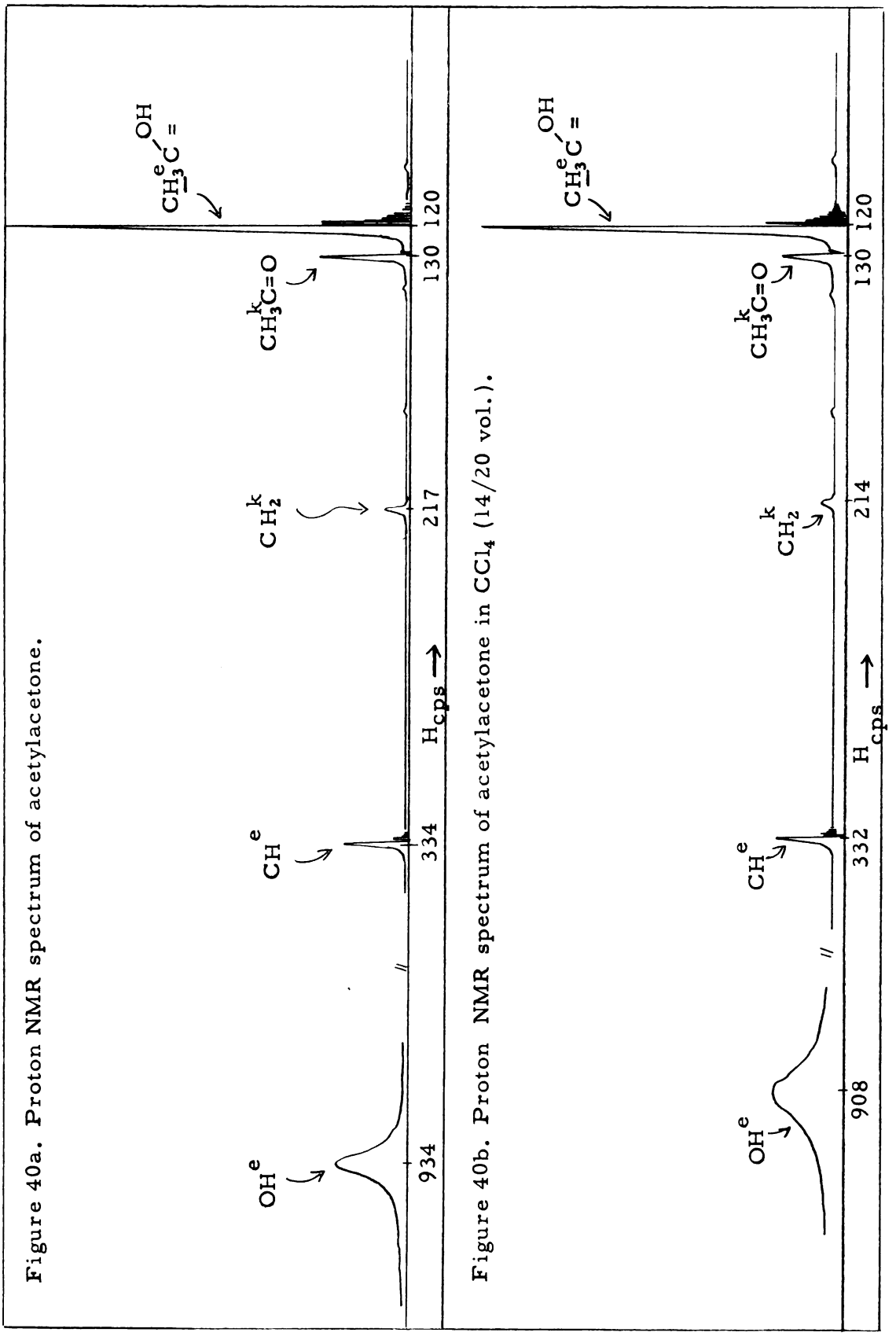
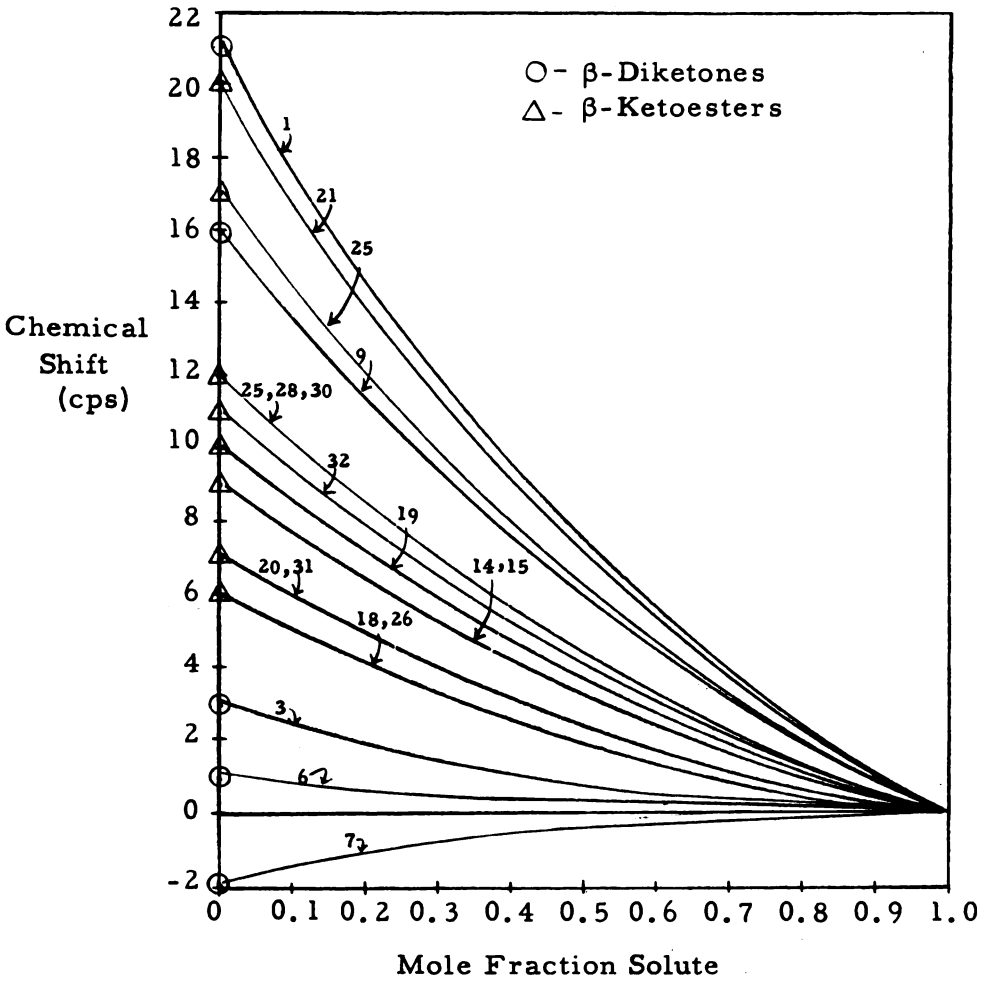


Figure 40a. Proton NMR spectrum of acetylacetone.

Figure 40b. Proton NMR spectrum of acetylacetone in CCl_4 (14/20 vol.).

Figure 41. Chemical shift relative to pure solute of the OH proton in β-dicarbonyls in carbon tetrachloride versus mole fraction solute.



Benzene. Chemical shift measurements of β-diketones and β-keto-esters at infinite dilution in benzene are summarized in Tables XXXVII and XXXVIII, respectively. The shielding of the protons caused by the usual ring current effect is illustrated by these tables, in which positive shifts refer to resonances which occur at higher applied magnetic fields. Alkoxy, acetyl, and α-keto protons are shifted upfield at infinite dilution by as much as 33, 57, and 50 cps, respectively. The enol α-proton among the esters shows only modest upfield shifts, but among the β-diketones it is shifted up to 46 cps at infinite dilution. Protons of the α-alkyl substituent show little ring current effect. Figure 42 shows a spectrum of ethyl acetoacetate in benzene to illustrate these points. .

1-Phenyl-1, 3-butanedione on dilution in benzene gives the usual upfield shifts of enol and keto acetyl methyl proton resonance lines. Both enol and keto α-protons are shielded on dilution.

The striking exception to increased shielding is seen in the enolic OH resonance position which becomes deshielded on dilution in benzene. For a series of β-dicarbonyls the infinite dilution shift of the OH proton is from -10 to -45 cps. In Figure 43 are shown infinite dilution chemical shifts relative to the pure OH resonance position for a series of β-dicarbonyls in benzene versus mole fraction solute. Exceptions to the downfield shift of enolic OH protons are observed in both trifluoro- and hexafluoroacetylacetone. This apparent anomaly will be discussed later.

The large downfield shift of the enolic OH proton resonance line, coupled with upfield shifts of other protons suggests that the solute molecule is so oriented that the OH proton lies approximately in the plane of the benzene ring. The upfield shift of other protons in β-dicarbonyls is explained by an orientation of the solute molecules which places these protons above or below the plane of the ring.

The formation of complexes with benzene is not without precedent. Reeves and Schneider (95) have proposed that a complex of benzene and

Table XXXVII. Infinite Dilution Proton Chemical Shifts in β-Diketones in Benzene*

Compound	Acetyl					
	CH_3^e	CH_3^k	$\alpha\text{-}H^k$	$\alpha\text{-}H^e$	OH^e	Other
Acetylacetone	25	33	50	39	-45	-
α-Chloroacetylacetone	25	29	39	-	-29	-
Hexafluoroacetylacetone	-	-	-	40	+37	-
Trifluoroacetylacetone	57	54	-	46	+27	-
α-Methylacetylacetone	24	29	47	-	-34	20 $\alpha\text{-}CH_3^k$ 32 $\alpha\text{-}CH_3^e$

k = keto

e = enol

* Chemical shifts are in cps relative to the pure compound.

Table XXXVIII. Infinite Dilution Proton Chemical Shifts in β-Ketoesters in Benzene*

Compound	Ethyl		Acetyl CH_3		α-H[k]	α-CH[e]	OH[e]	Alkyl α-group	Other
	CH_3	CH_2	Enol	Keto					
Butyl acetoacetate	-	-	23	29	28	5	-36	-	8-bu CH_2
t-Butyl acetoacetate	-	-	22	29	25	2	-37	-	8-$(CH_3)_3$[e] 5-$(CH_3)_3$[k]
Ethyl acetoacetate	19[k] 21[e]	16[k] 14[e]	25	31	35	8	-35	-	
Ethyl α-allylacetoacetate	22	17	15	20	19	-	-34	-1, 4, 5	-
Ethyl α-isoamylacetoacetate	18	14	m	15	13	-	-38	5, 5, -2	-
Ethyl benzoylacetate	14[k, e]	12[k] 14[e]	-	-	24	3	-22	-	-
Ethyl α-isobutylacetoacetate	20	16	m	16	9	-	-38	-2, 7, 8	-
Ethyl α-n-butylacetoacetate	20	16	m	17	13	-	-31	m	-
Ethyl α-chloroacetoacetate	30[k] 27[e]	30[k] 26[e]	21	32	43	-	-25	-	-
Ethyl α-ethylacetoacetate	21	15	m	19	20	-	-36	6, 0	-
Ethyl α-fluoroacetoacetate	28	29	-	28	44	-	-	-	-
Ethyl trifluoroacetoacetate	30[k] 32[e]	31[k] 33[e]	-	-	47	24	-10	-	-
Ethyl α-methylacetoacetate	23	18	-	24	28	-	-39	8	-
Ethyl α-isopropylacetoacetate	18	15	19	28	11	-	-33	(7, 3, -1)[k] (16, 6)[e]	-
Methyl acetoacetate	-	-	-	38	34	-	-	-	23-OCH_3

k = keto, e = enol, m = masked, * chemical shifts are in cps relative to the pure compound.

Figure 42a. Proton NMR spectrum of ethyl acetoacetate.

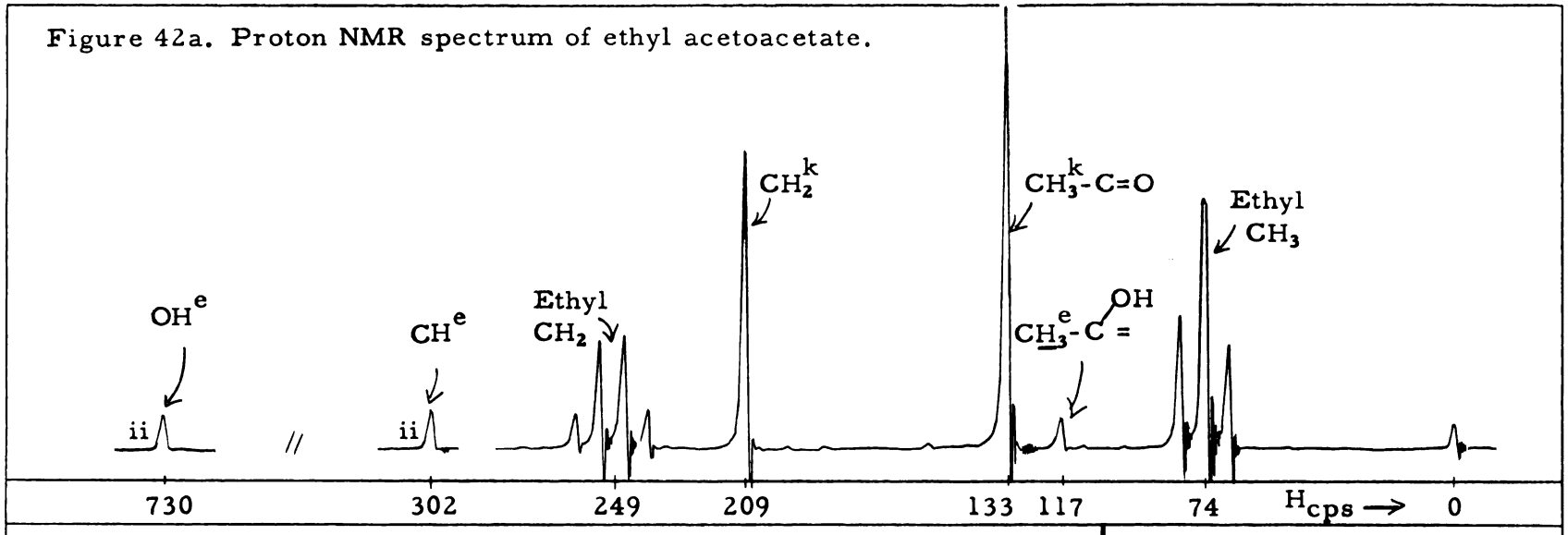


Figure 42b. Proton NMR spectrum of ethyl acetoacetate in benzene (3/31 vol.)

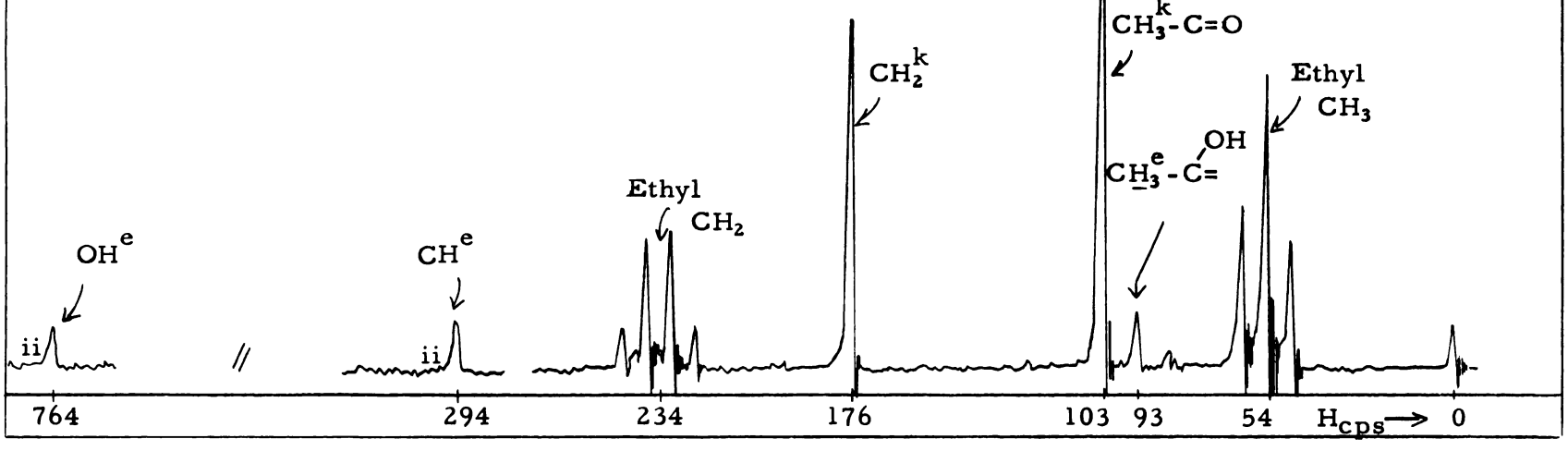
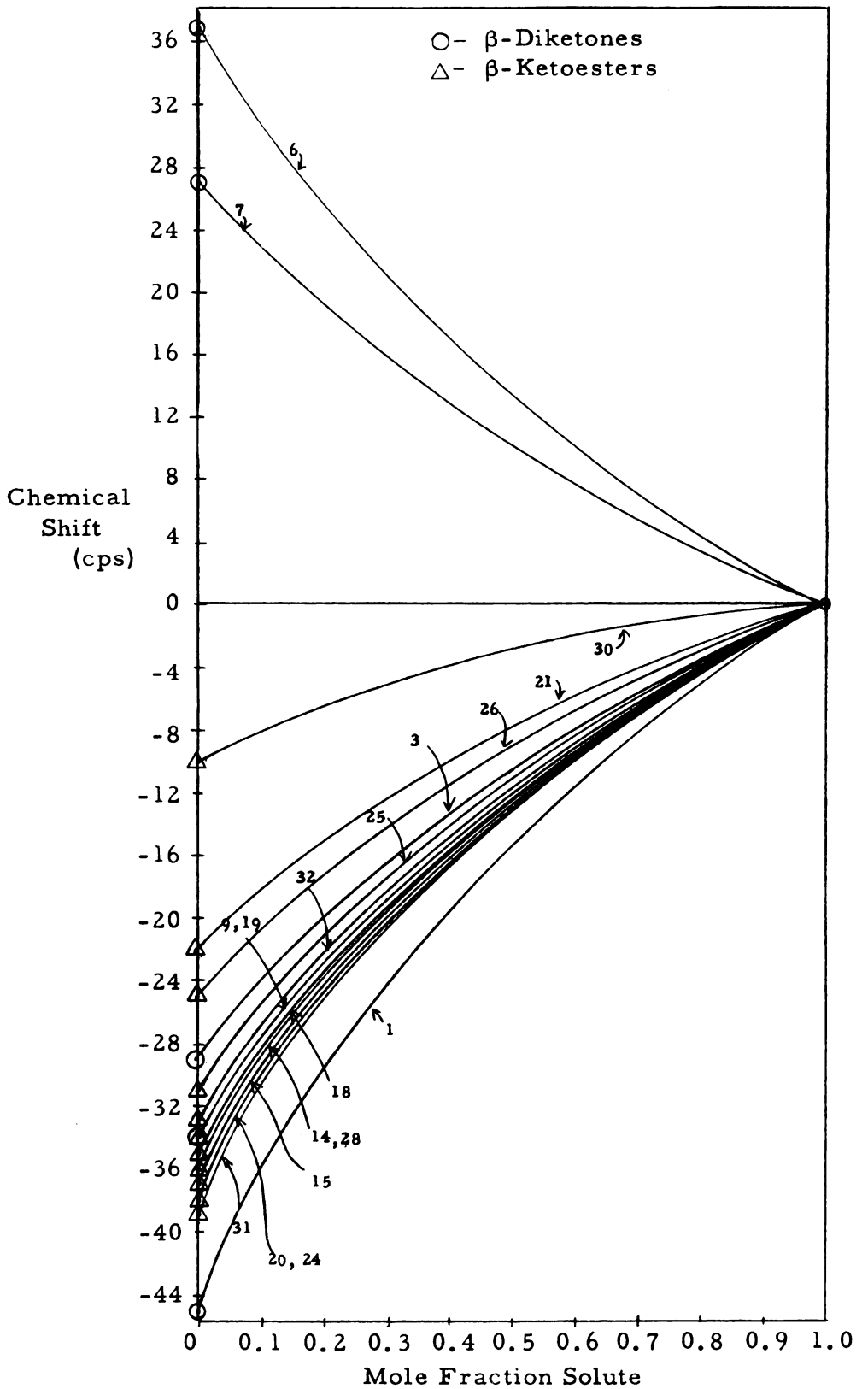


Figure 43. Chemical shift relative to pure solute of OH proton in β-dicarbonyls in benzene versus mole fraction solute.



chloroform exists. Hatton and Richards (124) concluded for amides in benzene solution that the more positive end (the methyl protons) of the amide lay above or below the plane of the ring and the more negative end (the carbonyl group) tended to be as removed from the π-electron cloud as possible. Hatton and Schneider (96) confirmed the existence of molecular complexes with benzene by measuring the temperature coefficients of solute chemical shifts. Schneider (97) determined, in a study of solute-solvent interactions in benzene, that a rough correlation exists between the ratio of dipole moment to molecular volume and the chemical shift of the solute molecule. A specific association of bis-(acetylacetone)-ethylenediimine in benzene was reported by Dudek and Holm (81).

An attempt was made to determine the nature of the orientation of β-dicarbonyls in complexes with benzene. Johnson and Bovey's tables for the calculation of chemical shifts of protons in the vicinity of the benzene ring (94) have been used to attempt to relate the solute molecule chemical shift measurements to distance from and angle with respect to the benzene ring. A comparison of the infinite dilution chemical shifts for ethyl acetoacetate has been made with the so-called 'isoshielding' lines around benzene and, with the tables of chemical shift versus Z and P distances (perpendicular and parallel to the benzene ring, respectively), gives a qualitative picture of the interaction. There is apparently no way of orienting the benzene ring with respect to the solute molecule in order to simultaneously give the large upfield shifts of both acetyl methyl and ethoxy protons, and the large downfield shift of the enolic OH proton. However, an association involving two molecules of benzene with each solute molecule does give a qualitative and quantitative explanation of the observed chamical shifts. With the aid of molecular models, the interaction proposed in illustrated in Figure 44, which pictures the acetylacetone-benzene complex. Reference to the

Figure 44. Proposed complex of acetylacetone with benzene.

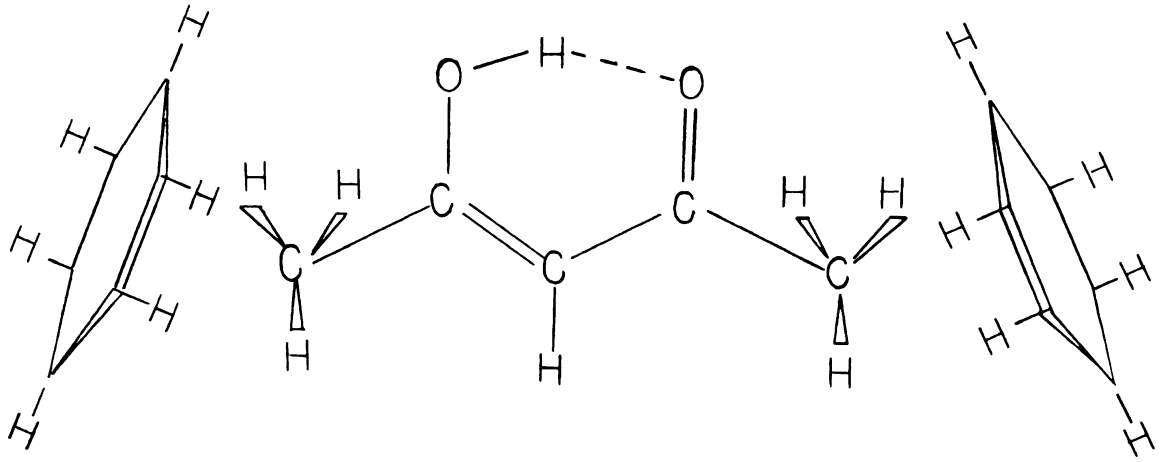


figure gives an explanation to the two exceptions noted above, namely the trifluoro- and hexafluoroacetylacetone molecules. The substitution of fluorine atoms for the methyl protons of the acetyl group would result in the highly electronegative atoms lying in the area of greatest π-electron density, which is a most electrostatically unfavorable situation. It may be noted that ethyl trifluoroacetoacetate gives the least deshielding of the enol OH proton, which may indicate association of benzene with only the alkoxy end of the solute molecule. Dilution in benzene results in an increase in the enol tautomer. It may be that the benzene- solute complex occurs only with the enol tautomer and shifts the equilibrium in favor of the enol tautomer.

Hexane. The chemical shifts of protons of β-dicarbonyls are given in Table XXXIX at infinite dilution in n-hexane. Figure 45 is a spectrum of butyl acetoacetate in n-hexane, and the resonance positions may be compared with those of pure butyl acetoacetate in Figure 22a. Negligible chemical shifts are observed for alkoxy protons. A small shielding effect is seen for the acetyl protons. Both enol and keto α-protons are shielded in solution to a considerable extent relative to the pure liquids. Generally the enol OH resonance peak is slightly shifted to lower fields in solution.

An association of the solute molecule with an inert solvent such as hexane appears rather unlikely. Upfield shifts of the α-protons in both enolic and keto tautomers might be explained by breaking up of intermolecular association of solute with solute molecule. However, such association does not appear to affect the intramolecular hydrogen bond. Very dilute solutions of β-dicarbonyls in hexane approximate the gas phase in terms of percentage of enol tautomer. At least we may say that the absence of upfield chemical shifts of the enol OH proton resonance peak indicates that strong hydrogen bonds exist in hexane

Table XXXIX. Chemical Shifts of Protons in β-Dicarbonyls at Infinite Dilution in n-Hexane*

Compound	Percent Enol at 0.5X**	Acetyl CH_3		Ethyl		α-Proton		OH[e]	Other
		Enol	Keto	CH_3	CH_2	CH^k	CH^e		
Ethyl α-chloroacetoacetate	35	3	5	m	5	28	-	-3	-
Ethyl α-methylacetoacetate	10	2	7	m	1	17	-	3	-
Ethyl acetoacetate	16	8	7	0	1	17	10	-3	-
Acetylacetone	91	8	7	-	-	17	16	6	-
Methyl acetoacetate	0	-	5	-	-	15	-	-	5($OOCH_3$)

**X is mole fraction solute

k - keto

e - enol

m - masked

*Chemical shifts are in cps relative to the pure compound.

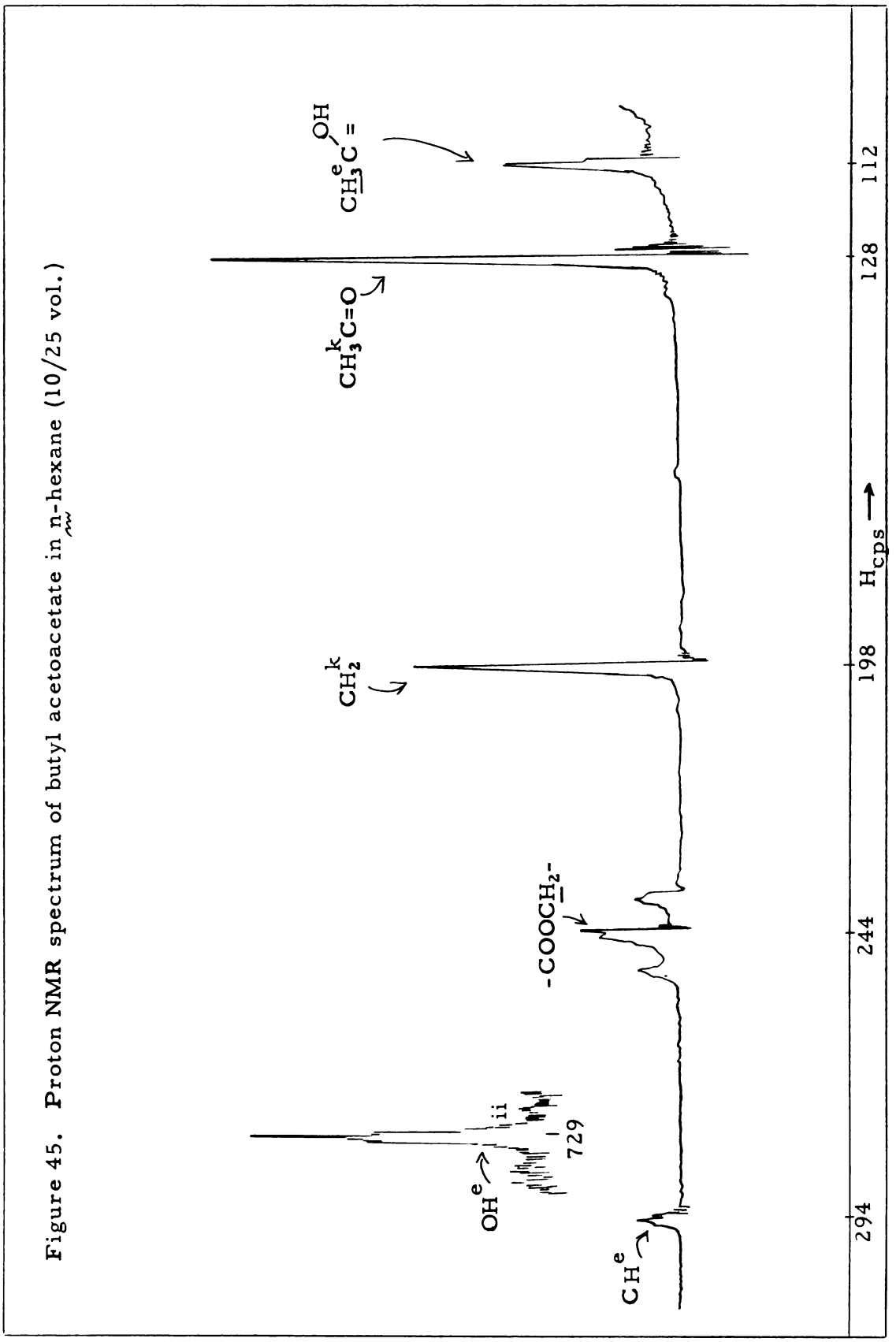


Figure 45. Proton NMR spectrum of butyl acetoacetate in n-hexane (10/25 vol.)

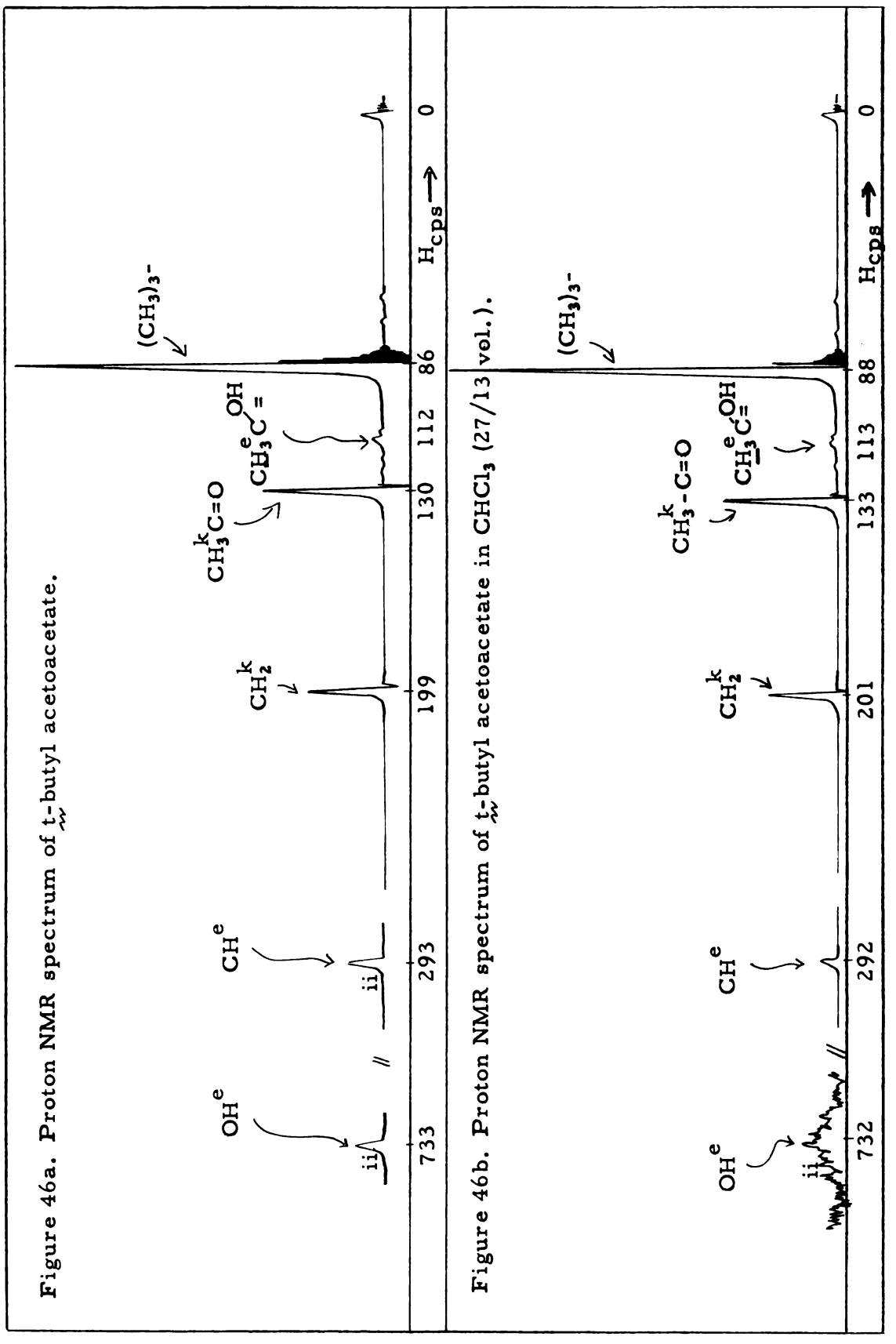


Figure 46a. Proton NMR spectrum of t-butyl acetoacetate.

Figure 46b. Proton NMR spectrum of t-butyl acetoacetate in $CHCl_3$ (27/13 vol.).

solutions and the position of the equilibrium, which favors the enol tautomer in this solvent, appears to support this interpretation.

Chloroform. Chemical shifts of protons of β-dicarbonyls at infinite dilution in chloroform are given in Table XL. A typical NMR spectrum is shown in Figure 46 for t-butyl acetoacetate in chloroform. Both alkoxy and acetyl protons show some deshielding in this solvent.

In general, there is little effect upon keto or enol α-protons on dilution in chloroform. However, the keto α-proton of ethyl α-chloroacetoacetate is considerably shielded on dilution, and this may be evidence for the existence of an intermolecular hydrogen bond. However, the enol OH proton resonance position does not appear affected by chloroform. Therefore, one might assume the intermolecular hydrogen bond of ethyl α-chloroacetoacetate to be between keto molecules, perhaps of the type shown in Figure 47.

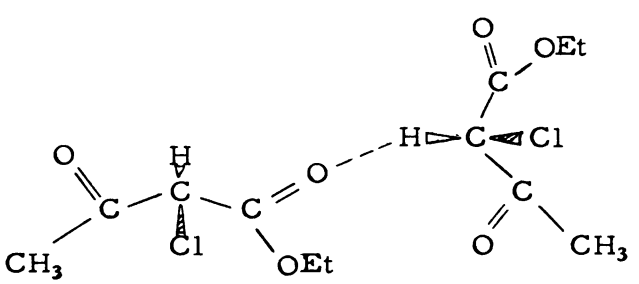


Figure 47. Association of keto molecules in ethyl α-chloroacetoacetate.

The effect of chloroform on the resonance position of the enol OH proton is in general negligible in β-ketoesters. The upfield shift of the enol OH proton in ethyl benzoyl acetate is unique among the β-ketoesters. In the β-diketones studied chloroform appears to cause shielding of the enol OH proton. The position of the enol OH resonance in β-ketoesters on dilution in chloroform appears to indicate that the intramolecular hydrogen

Table XL. Chemical Shifts of Protons in β-Dicarbonyls at Infinite Dilution in Chloroform*

Compound	Percent Enol	Ethyl		Acetyl		α-H			Other
		CH_3	CH_2	CH_3	CH_3				
				e	k	k	e	e	
Acetylacetone	88	-	-	-4	-5	0	2	20	-
t-Butylacetoacetate	-	-	-	3	5	-	-4	0	3 $(CH_3)_3$
Ethyl acetoacetate	7	-4	-5	0	-3	3	3	2	-
Ethyl benzoyl acetate	20	-10 k -5 e	-9 k -6 e	-	-	-2	-1	22	-
Ethyl α-chloroacetoacetate	19	-2 e, k	-3	-2	-3	15	-	-3	-
Ethyl α-methylacetoacetate	-	-6	-6	m	4	2	-	-2	-5 (α-CH_3)
Trifluoroacetylacetone	95	-	-	-2	-2	4	2	31	-

m - masked

e - enol

k - keto

* Chemical shifts are in cps relative to the pure compound.

bond is stronger than in carbon tetrachloride. For the β-diketones, however, this resonance peak is shielded to about the same extent as in carbon tetrachloride. Evidently chloroform does affect the intramolecular association of the β-diketones more than the esters. 1-Phenyl-1,3-butanedione shows little change in chemical shift except for the enol OH, which moves far upfield on dilution. Thenoyl trifluoroacetone also shows increasing shielding of the enol OH proton on dilution in chloroform.

Korinek and Schneider (125) have obtained the difference between the chemical shift of chloroform at infinite dilution in inert hydrocarbon solvents and in donor solvents. On the assumption that the donor molecules do not show self-association, the resultant difference in chemical shift is the association shift of chloroform and may be correlated with the hydrogen-bond strength and the relative donor strength of the solvent molecule. For the present study, it has been assumed that the β-dicarbonyls do not show appreciable intermolecular association. Further, the shift of the chloroform proton peak in inert hydrocarbon solvents relative to pure chloroform is constant at +10 cps at infinite dilution. Therefore, a graph of the chemical shift of the chloroform proton resonance at infinite dilution in β-dicarbonyls versus mole fraction of chloroform will be meaningful in a relative manner. It may be seen on the basis of such a plot in Figure 48 that the best donor molecule is ethyl acetoacetate and the poorest is trifluoroacetylacetone. It would appear then that the most extensive hydrogen bonding of chloroform with the solvent molecule occurs with ethyl acetoacetate.

In general it may be noted from Figure 48 that the β-ketoesters associate with chloroform to a greater extent than do the β-diketones. It will be recalled that the β-ketoesters exist for the most part as the keto tautomer, whereas the β-diketones are mostly enolic. It is suggested that chloroform tends to associate with the keto form of the

β-dicarbonyl molecule rather than with the enol tautomer. The absence of the upfield shift of the keto and enol α-proton as was observed in carbon tetrachloride may be taken as evidence that the α-proton is not involved in intermolecular hydrogen-bond formation. However, the β-dicarbonyl may be associating with the solvent through a hydrogen bond between the carbonyl group and the chloroform proton. The exception is ethyl α-chloroacetoacetate, in which the keto α-proton is shielded in solution relative to the pure compound. The position of this compound in Figure 48 indicates that it associates with chloroform to a greater extent than do other β-ketoesters, and it may be that such association is involved with the enol rather than the keto form.

Carbon Disulfide. Infinite dilution shifts for protons of acetylacetone and ethyl acetoacetate are given in Tables XLI and XLII, respectively. Once again little change in chemical shift occurs in the alkoxy or acetyl methyl protons, whereas the keto and enol α-protons and enol OH resonance peaks are shielded on dilution, as in carbon tetrachloride. This may indicate dissociation of both intra- and intermolecularly hydrogen-bonded groups. However, carbon disulfide favors the enol tautomer. Thenoyl trifluoroacetone shows shielding of the enol OH proton on dilution in carbon disulfide.

Ether. Infinite dilution shifts for protons of acetylacetone and ethyl acetoacetate are in Tables XLI and XLII, respectively. In this comparatively inert solvent, the enol and keto α-protons are shifted upfield on dilution. The enol OH resonance position moves to higher applied fields in the β-diketone, but not in the β-ketoester. Yet this solvent favors enolization over the pure compound in both cases.

Acetic Acid. Chemical shifts for this solvent are given in Tables XLI and XLII and show little change on dilution, except for the enol OH

Figure 48. Chemical shifts of chloroform proton in β-dicarbonyls as donor solvents.

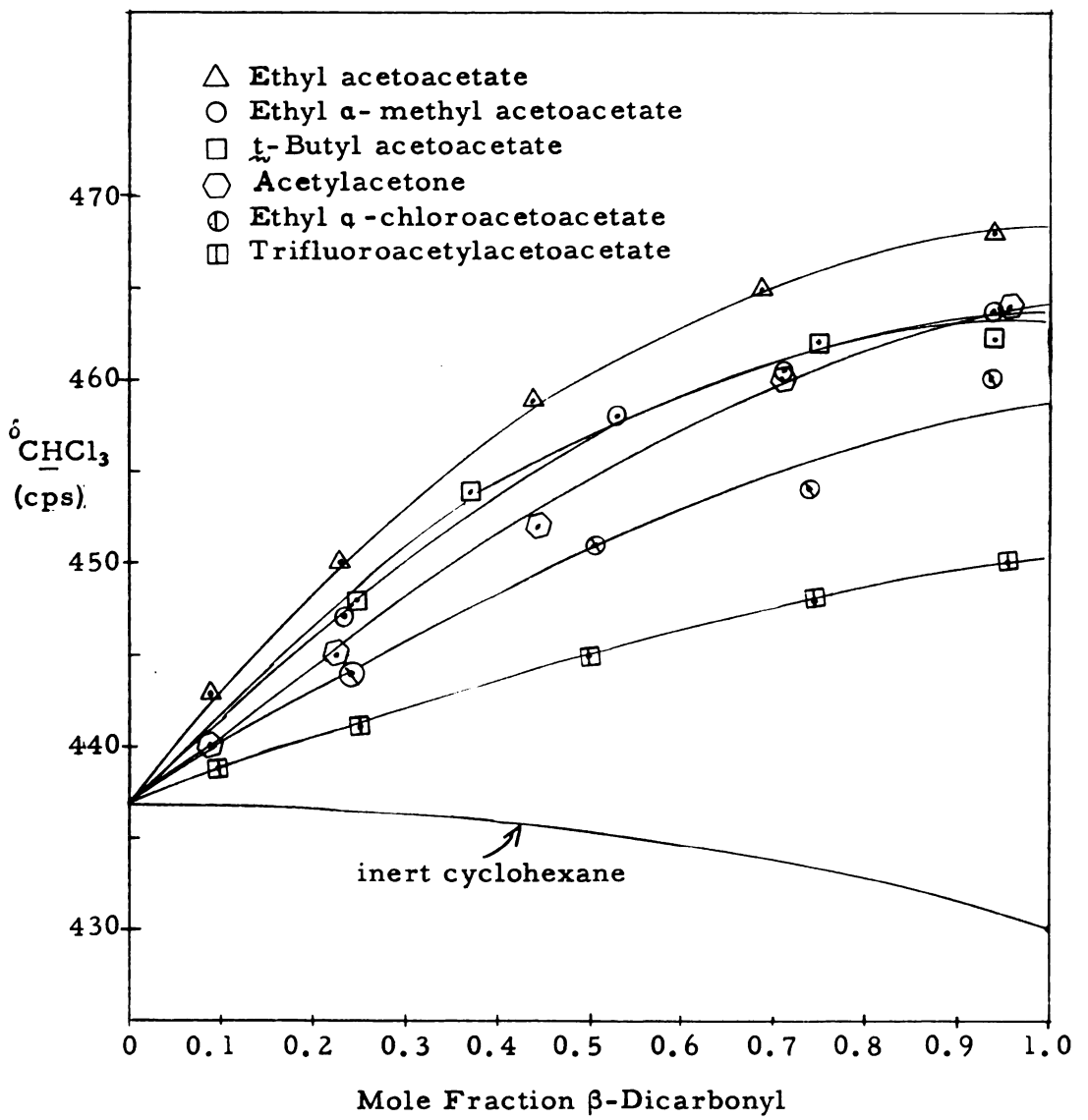


Table XLI. Infinite Dilution Proton Chemical Shifts in Acetylacetone in Various Solvents*

Solvent	Acetyl		α-Proton		OH[e]
	CH_3[e]	CH_3[k]	CH_2[k]	CH[e]	
Acetic acid	-1	-1	-2	0	32[b]
Acetonitrile	-1	0	0	-4	-10
Benzene	25	33	50	39	-41
Carbon disulfide	3	4	14	13	16
Carbon tetrachloride	2	1	10	12	21
Chloroform	-4	-5	0	2	20
Dimethylsulfoxide	-2	3	-5	-8	68[b]
Dioxane	1	2	m	2	38
Absolute ethanol	-1	-1	m	-1	595
95 Percent Ethanol	-3	-4	m	-4	605
Ether	3	4	m	7	21
Hexane	8	7	17	16	6
Methanol	-2	-3	-4	-3	625

e = enol, k = keto, b = broad, m = masked

*Chemical shifts are in cps relative to the pure compound.

Table XLII. Infinite Dilution Proton Chemical Shifts in Ethyl Acetoacetate in Various Solvents*

Solvent	Ethyl		Acetyl		α-Proton		
	CH_3	CH_2	CH_3^e	CH_3^k	CH_2^k	CH^e	OH^e
Acetic acid	-3	-3	1	-2	-4	2	4
Acetonitrile	0	0	m	1	-1	0	1
Benzene	19^k 17^e	15^k 13^e	26	32	36	9	-33
Carbon disulfide	1	$4^{k,e}$	4	5	13	9	8
Carbon tetrachloride	-2	0	2	2	14	9	8
Chloroform	-4	-5	0	-3	3	3	2
Dimethylsulfoxide	1	2	0	2	-6	-5	6
Dioxane	-1	1	2	3	3	2	2
Absolute ethanol	-2	-1	1	-1	-1	2	1
95 Percent Ethanol	-1	-2	-1	-3	-3	0	2
Ether	0	0	4	4	11	6	-3
Hexane	0	1	8	7	17	10	-3
Methanol	-1	-2	1	-1	-3	-1	1

k = keto, e = enol, m = masked, * Chemical shifts are in cps relative to the pure compound.

proton in acetylacetone which is shifted upfield and is very broad. Ethyl α-methylacetoacetate gives essentially the same results as ethyl acetoacetate. In dibenzoyl methane the OH peak is again very broad and is separate from the carboxyl proton peak of the solvent. Although an increase in percentage of keto tautomer is observed, only a slight upfield shift of the enol OH is observed. Trifluoroacetylacetone shows little effect, except for the enol OH proton resonance which has coalesced with the OH resonance peak of the solvent and consequently shows a dilution shift of close to 200 cps. Thenoyl trifluoroacetone gave results similar to those of the other β-diketones with separate resonance peaks for the enol OH and carboxyl OH groups of the solvent. Again little dilution effect is seen, other than for the enol OH resonance position. Protons of 1, 3-indanedione show little change from their position in chloroform. Little chemical shift is noted for the protons of 1-phenyl-1, 3-butanedione in acetic acid as compared with the same resonances in carbon tetrachloride solution. Further, no change is noted on dilution, except for the enol OH proton which moves slightly upfield.

Acetonitrile. As seen in Tables XLI and XLII, there is little effect upon resonance positions of protons in either ethyl acetoacetate or acetylacetone by dilution in this solvent. Yet acetonitrile favors the keto tautomer. Only the enol OH proton resonance position of acetylacetone varies on dilution, and this is deshielded somewhat with increasing dilution.

Dimethylsulfoxide. Chemical shifts in Tables XLI and XLII indicate little dilution effect for most proton resonances of either acetylacetone or ethyl acetoacetate. The solute enol OH proton does show considerable shielding upon dilution. One might expect competition for the enol OH proton by this solvent, especially since dimethylsulfoxide

favors the keto tautomer. The fact that this resonance peak becomes extremely broad does appear to indicate association with the solvent.

Alcoholic Solvents. Chemical shifts in absolute ethanol, methanol, and 95 percent ethanol are given in Tables XLI and XLII for acetylacetone and ethyl acetoacetate. Only methanol affects the position of the tautomeric equilibrium, and it causes a decrease in the percentage of enol tautomer. These solvents show little dilution effect on ethyl acetoacetate, but in acetylacetone the enol OH resonance signal is coalesced with the solvent OH resonance throughout the concentration range between the pure solute and infinite dilution. A spectrum of acetylacetone in methanol is shown in Figure 49. The half width of the coalesced OH signal becomes somewhat narrow on dilution. Calculations made from the shape of the OH signal indicate an exchange time of the order of 10^{-4} sec^{-1}, if one assumes equal relaxation times for OH protons of solute and solvent molecule.

Triethylamine. The proton resonances of methyl acetoacetate show no chemical shift in this solvent. t-Butyl acetoacetate and ethyl α-allylacetoacetate show only slight chemical shifts of enol and keto protons, but the enol OH resonance peak is evidently too broad for detection although the amount of enol tautomer increases on dilution. The keto α-protons are shielded somewhat on dilution. In ethyl acetoacetate only keto peaks appear visible, but these are considerably broadened, and there is evidence of chemical reaction by discoloration of the solution.

Among the β-diketones, acetylacetone has been studied by Reeves (23) and Reeves and Schneider (57) in this solvent. Results are comparable to the present study. Only the enol tautomer is found, and the most significant change in chemical shift on dilution occurs with the enol OH resonance peak, which moves upfield. In 1-phenyl-1, 3-butanedione

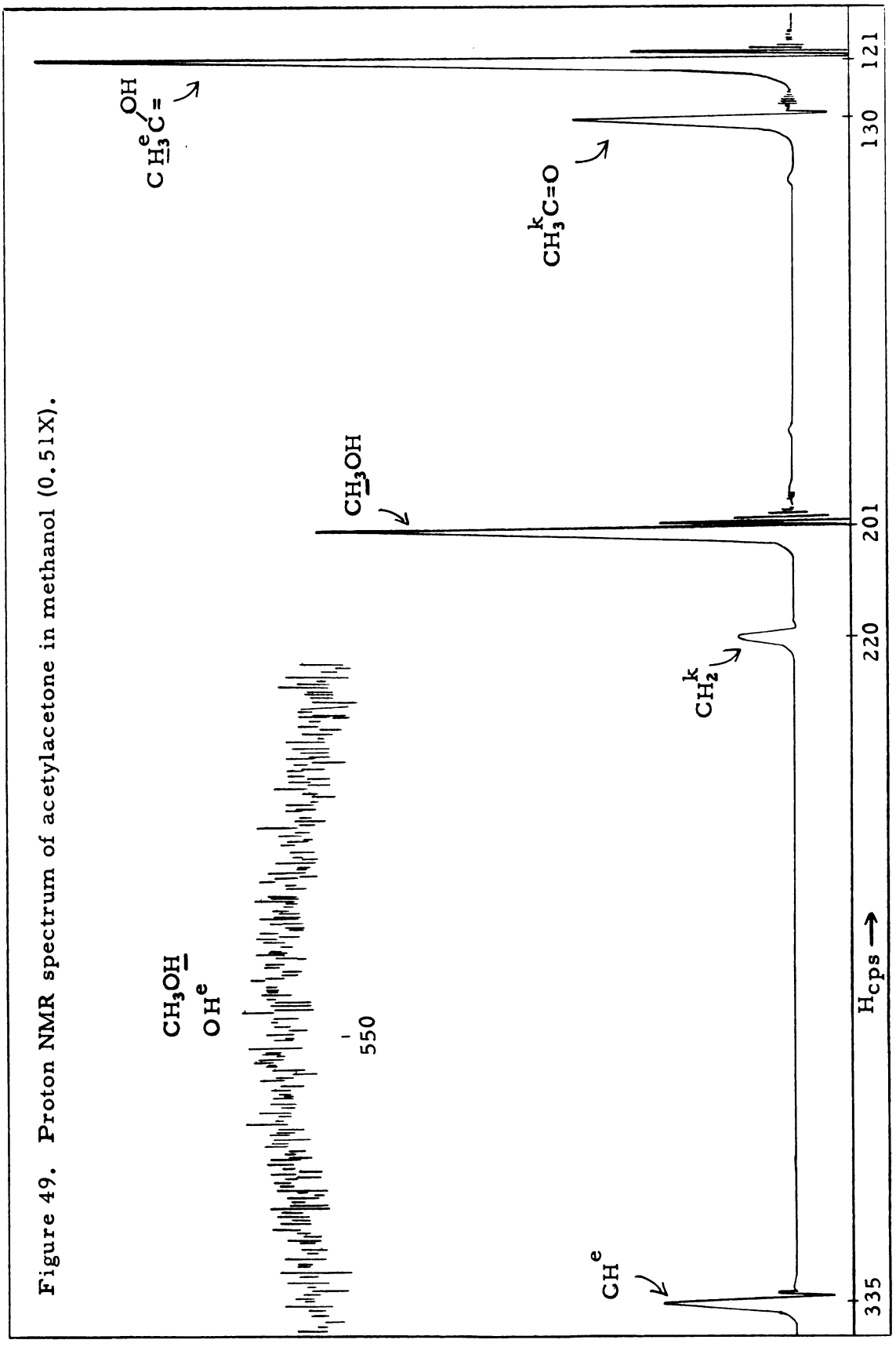


Figure 49. Proton NMR spectrum of acetylacetone in methanol (0.51X).

chemical shift changes on dilution are negligible except for the enol OH which in a saturated solution is 200 cps upfield of its value in carbon tetrachloride. In more dilute solutions this resonance peak broadens considerably. Dibenzoylmethane in a saturated solution of triethylamine shows little chemical shift effect on dilution, except for the enol OH which moves from the value of 993 cps in carbon tetrachloride to 660 cps in a saturated solution and to 267 cps in a more dilute solution. For thenoyl trifluoroacetone, the results are much the same as for other β-diketones, with only the chemical shift of the enol OH proton resonance peak being affected by the solvent.

Diethylamine. In 1-phenyl-1, 3-butanedione the enol form is present, but the enol OH is so broad as to preclude its detection. The enol α-proton is also broad and is increasingly shielded on dilution, but the keto α-proton is masked by this solvent. The amine proton on the nitrogen is deshielded on dilution. In dibenzoyl methane the enolic α-proton is not much affected by dilution in diethylamine either in line-width or in chemical shift. The NH proton resonance peak, in contrast to its behavior in 1-phenyl-1, 3-butanedione, moves upfield on dilution and becomes sharper. The enol OH proton resonance is too broad for detection. Among the β-ketoesters only methyl acetoacetate does not appear to be affected by diethylamine. In t-butyl acetoacetate and ethyl acetoacetate there is evidence of chemical reaction, since even the acetyl methyl proton resonance signal is broad. No enol tautomer is seen. Glickman and Cope (126) have reported the following reaction between a β-dicarbonyl and a secondary amine:

$$CH_3COCH_2COOEt + (CH_3)_2NH \longrightarrow CH_3\underset{\displaystyle N(CH_3)_2}{\overset{\displaystyle |}{C}}=CHCOOEt\ . \qquad (50)$$

For t-butyl acetoacetate in diethylamine the keto α-proton resonance signal has completely disappeared, but for ethyl acetoacetate it is very

much broadened and combined with the NH proton. On further dilution this coalesced signal moves upfield. In ethyl α-allyl- and α-isoamyl-acetoacetate, the equilibrium does not appear to be affected by this solvent, and the principal chemical shift effect is broadening of the keto α-proton. The NH proton resonance signal moves upfield on dilution in these solutes.

Acetylacetone has been studied in this solvent by Reeves (23) and Reeves and Schneider (57). The enol tautomer is favored, and there is evidence of complex formation with this tautomer. Thenoyl trifluoro-acetone apparently undergoes chemical reaction with this solvent.

Other Bases. In both pyrrole and pyridine the enol OH proton of thenoyl trifluoroacetone is considerably shielded on dilution.

Solvent Effect on Keto-Enol Equilibrium

In Table XLIII and XLIV are given equilibrium constants for acetylacetone and ethyl acetoacetate in various solvents at 0.1 mole fraction solute. For these β-dicarbonyls benzene, carbon tetrachloride, n-hexane, carbon disulfide, and ether increase the percentage of enol tautomer on dilution. This effect is greatest in n-hexane. The increase in the enol tautomer in these solvents is observed for all the β-dicarbonyls studied. For β-ketoesters with alkyl groups substituted in the α-position, this increase is less pronounced. In Table XXXIX the percentage enol is given for several β-dicarbonyls at 0.5 mole fraction in n-hexane. For chloroform the percentage enol at infinite dilution is given in Table XL.

Those solvents in which little effect is observed on the keto-enol equilibrium are dioxane, chloroform, absolute ethanol and 95 percent ethanol. Those solvents which result in a decrease in the enol content of β-dicarbonyls are methanol, acetic acid, acetonitrile, and dimethyl-sulfoxide. Equilibrium constants are given in Tables XLIII and XLIV.

Table XLIII. Equilibrium Constants for Tautomerization of Acetylacetone in Various Solvents at 0.1 Mole Fraction of Solute*

Solvent	Percent Enol	K_e*
Hexane	95	19
Carbon tetrachloride	96	24
Ether	95	19
Carbon disulfide	94	16
Benzene	89	8.1
Chloroform	87	6.7
Dioxane	82	4.6
Ethanol	82	4.6
Pure	81	4.3
95 Percent Ethanol	77	3.4
Methanol	74	2.8
Acetic acid	67	2.0
Acetonitrile	62	1.6
Dimethylsulfoxide	62	1.6

*Where $K_e = \frac{\text{enol}}{\text{keto}}$, and measurements are at $33 \pm 2^{\circ}C$.

Table XLIV. Equilibrium Constants for Tautomerization of Ethyl Acetoacetate in Various Solvents at 0.1 Mole Fraction of Solute *

Solvent	Percent Enol	K_e *
Hexane	39	0.64
Carbon tetrachloride	28	0.39
Ether	22	0.29
Carbon disulfide	20	0.25
Benzene	16	0.19
Dioxane	11	0.12
Absolute ethanol	10	0.11
Chloroform	7.5	0.081
Pure	7.5	0.081
95 Percent Ethanol	7.2	0.078
Methanol	5.8	0.062
Acetonitrile	4.9	0.052
Dimethylsulfoxide	2.2	0.023
Acetic acid	1.9	0.019

*$K_e = \frac{\text{enol}}{\text{keto}}$, and measurements are at $33 \pm 2^{\circ}C$.

Figures 50 and 51 give the percentage enol at various mole fractions for acetylacetone and ethyl acetoacetate, respectively, in several solvents. It may be seen that the percentage enol for ethyl acetoacetate extrapolated to infinite dilution in n-hexane is about 50 percent, that of the gas phase. This result may be compared with the findings of Powling and Bernstein (36) for hexane solutions of β-dicarbonyls in which the infinite dilution free energy of tautomerization approached that found in the gas phase.

A strict comparison of equilibrium constants obtained from nuclear magnetic resonance spectroscopy and from other methods is not possible, since the concentration of solutions is not indicated in the bromine titration and infrared techniques. However, Table X shows qualitative agreement for the percentages of enol tautomer in acetylacetone and ethyl acetoacetate by bromine titration with the results of Tables XLIII and XLIV by NMR. Qualitative agreement may also be noted between Kabachnik's (8, 9) results in Table XI for ethyl acetoacetate by bromine titration and Table XLIV by NMR.

Results from NMR do not show good agreement with those of Conant and Thompson (55) in Table XIV for α-alkyl substituted β-dicarbonyls. The present NMR study does not show appreciable increase in the percentage of enol tautomer in hexane for such compounds. Good qualitative agreement is found between the work of Murthy et al. (35), from ultraviolet spectroscopy in Table XV for the percentages of enol tautomer in acetylacetone and ethyl acetoacetate and the NMR results shown in Tables XLIII and XLIV.

Dewar (60) has stated that solvents with higher dielectric constants favor the keto form, since the carbonyl group of the keto tautomer is more polar than C=C-OH in the enol tautomer. Therefore, there is an increase in solvation energy for the more polar tautomer.

Figure 50. Percentage enol tautomer in acetylacetone in various solvents.

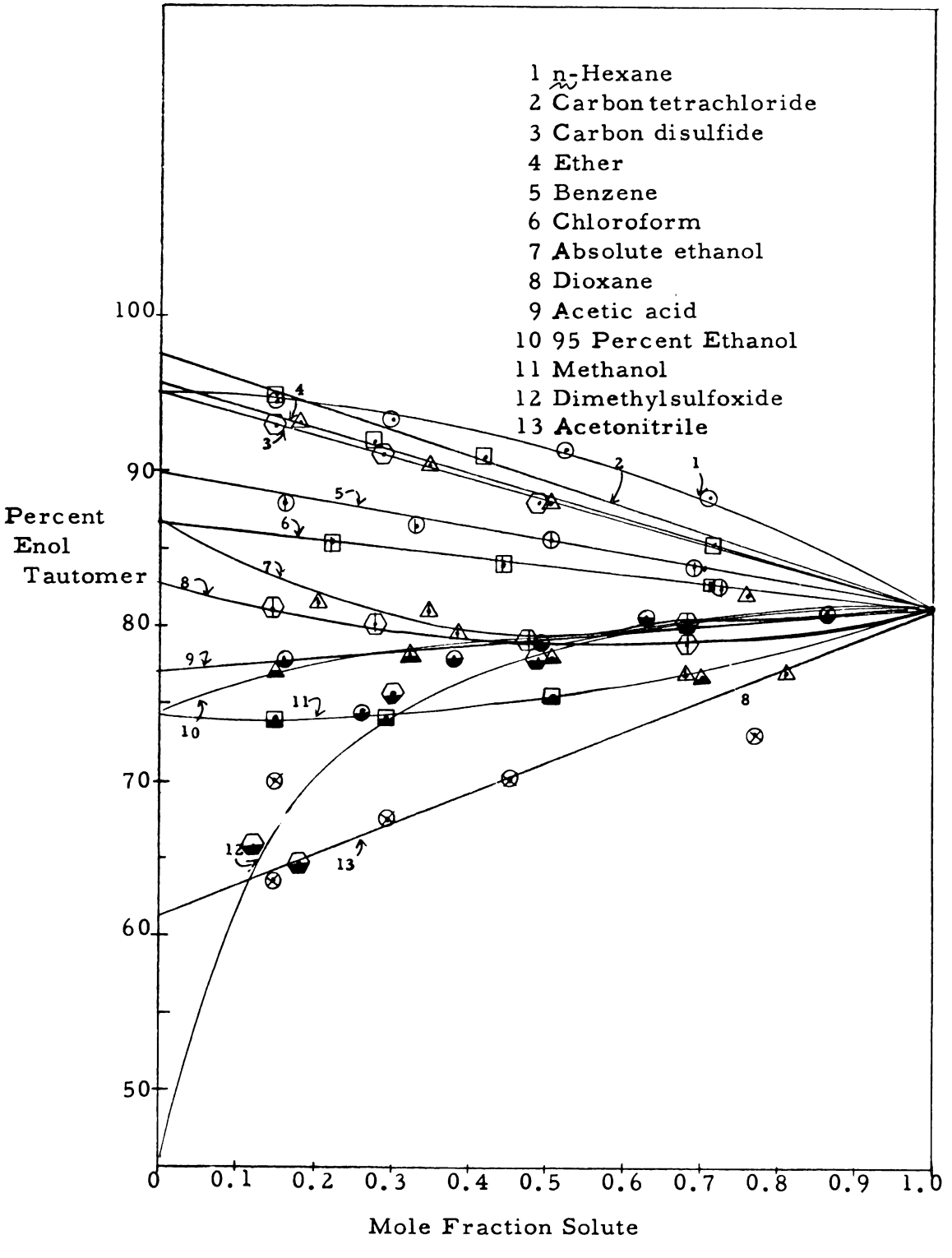
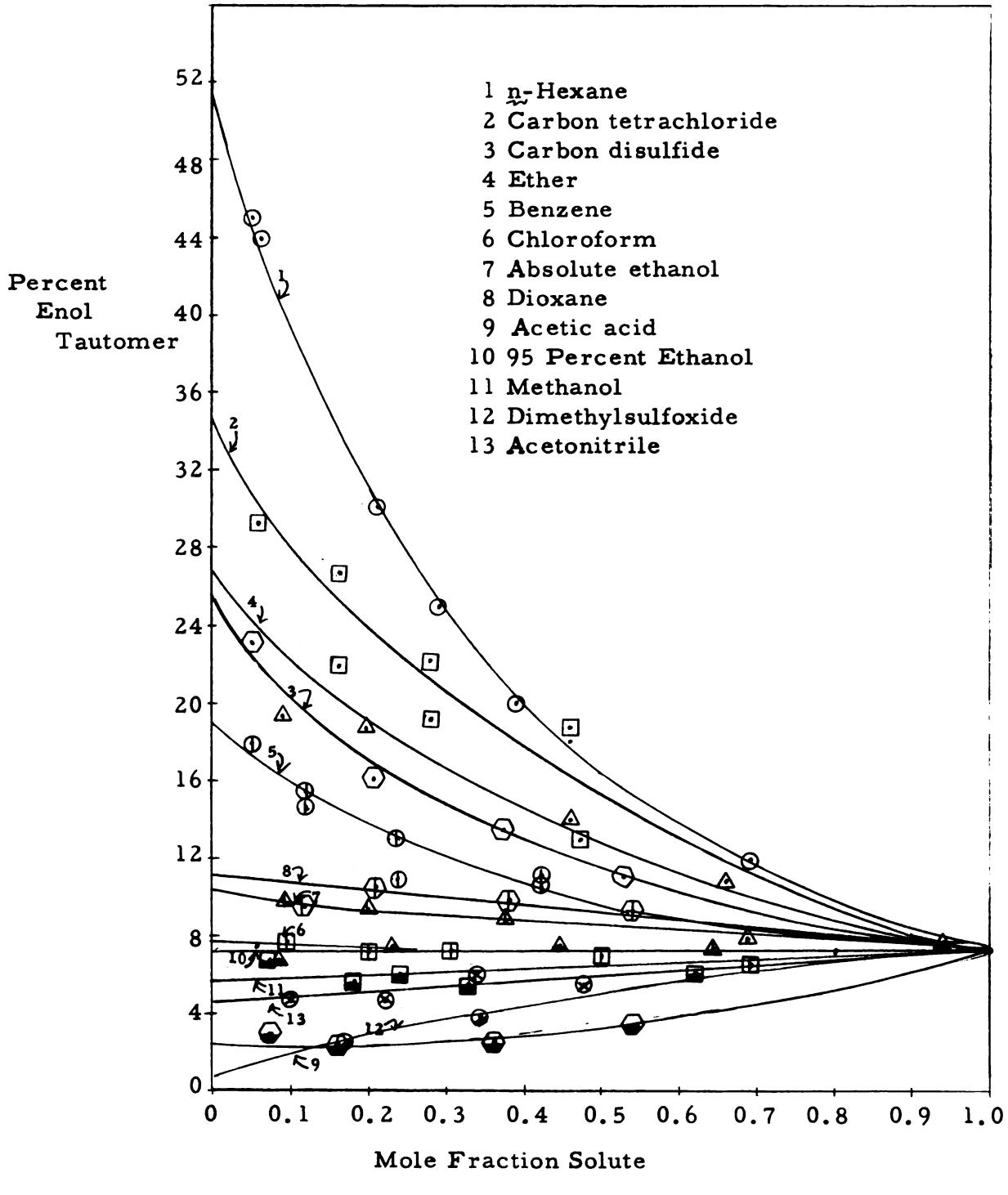


Figure 51. Percentage enol tautomer in ethyl acetoacetate in various solvents.



Wheland (62) has used the van't Hoff-Dimroth relation as an explanation of the increase in enolization in nonpolar solvents. This relation defines the quantity, G, as follows:

$$G \equiv \frac{[\text{enol}]/(\text{sol}_e)}{[\text{keto}]/(\text{sol}_k)} = K_e\left(\frac{\text{sol}_k}{\text{sol}_e}\right), \tag{51}$$

where K_e is the equilibrium constant for enolization, and sol_e and sol_k are solubilities of enol and keto tautomer, respectively. The quantity, G, is independent of the solvent if solubilities are not too large. Therefore, the solubility of enol relative to keto is greatest in the least polar solvents.

Powling and Bernstein (36, 127) have assumed that solvent interaction could be described on the basis of the reaction field of Onsager and have taken the cavity to be that occupied by the solvent molecule. The enthalpy of enolization in the gas phase is given by

$$\Delta H_g = \Delta H_{soln} + \left(\frac{\epsilon - 1}{2\epsilon+1}\frac{\rho}{M}\right)_{\text{solvent}}(\mu_1^2 - \mu_2^2), \tag{52}$$

where ΔH_{soln} is the enthalpy of tautomerization in solution, ϵ the dielectric constant of the solvent, ρ and M the density and molecular weight of the solvent, respectively, and μ_1 and μ_2 the dipole moments of enol and keto tautomers. Powling and Bernstein have obtained a linear relationship for the enthalpy and free energy of tautomerization in a graph of these thermodynamic quantities versus the solvent property of Equation (52). They have taken literature values for the free energies and enthalpies of tautomerization of the β-dicarbonyls. Their results are shown in Figures 52 and 53 for acetylacetone and ethyl acetoacetate, respectively. Also given in these figures are some results from the present study. The solvent property has been calculated according to Table XLV, using values in Lange's Handbook (128).

Table XLV. Free Energies of Tautomerization of β-Dicarbonyls at 0.1 Mole Fraction in Various Solvents and Values of the Solvent Property

Solvent	ϵ*	ρ*	$[(\frac{\epsilon - 1}{2\epsilon + 1})\frac{\rho}{M} \times 10^{-3}]$**	ΔF kcal/mole	
				Acetylacetone	Ethyl Acetoacetate
Acetic acid	6.15^{20°	1.05^{20°	6.67	-0.700	+1.700
Acetonitrile	37.5^{20°	0.783^{20°	9.14	-0.100	+2.080
Benzene	2.27^{25°	0.879^{20°	2.59	-1.000	+0.900
Carbon disulfide	2.64^{20°	1.26^{20°	4.35	-0.750	+1.250
Carbon tetrachloride	2.23^{25°	1.59^{20°	2.32	-1.100	+0.800
Chloroform	4.81^{20°	1.49^{20°	4.49	-0.800	+1.400
Dioxane	2.21^{25°	1.03^{20°	4.64	-0.750	+1.250
Ethanol	24.3^{25°	0.789^{20°	8.01	-1.000	+1.170
Ether	4.34^{20°	0.708^{25°	3.30	-0.850	+1.000
Hexane	1.89^{20°	0.654^{20°	1.41	-1.400	0.00
Methanol	32.6^{25°	0.792^{20°	11.8	-0.600	+1.550

*From Lange's Handbook (128).

**The quantity tabulated in column four is termed the solvent property.

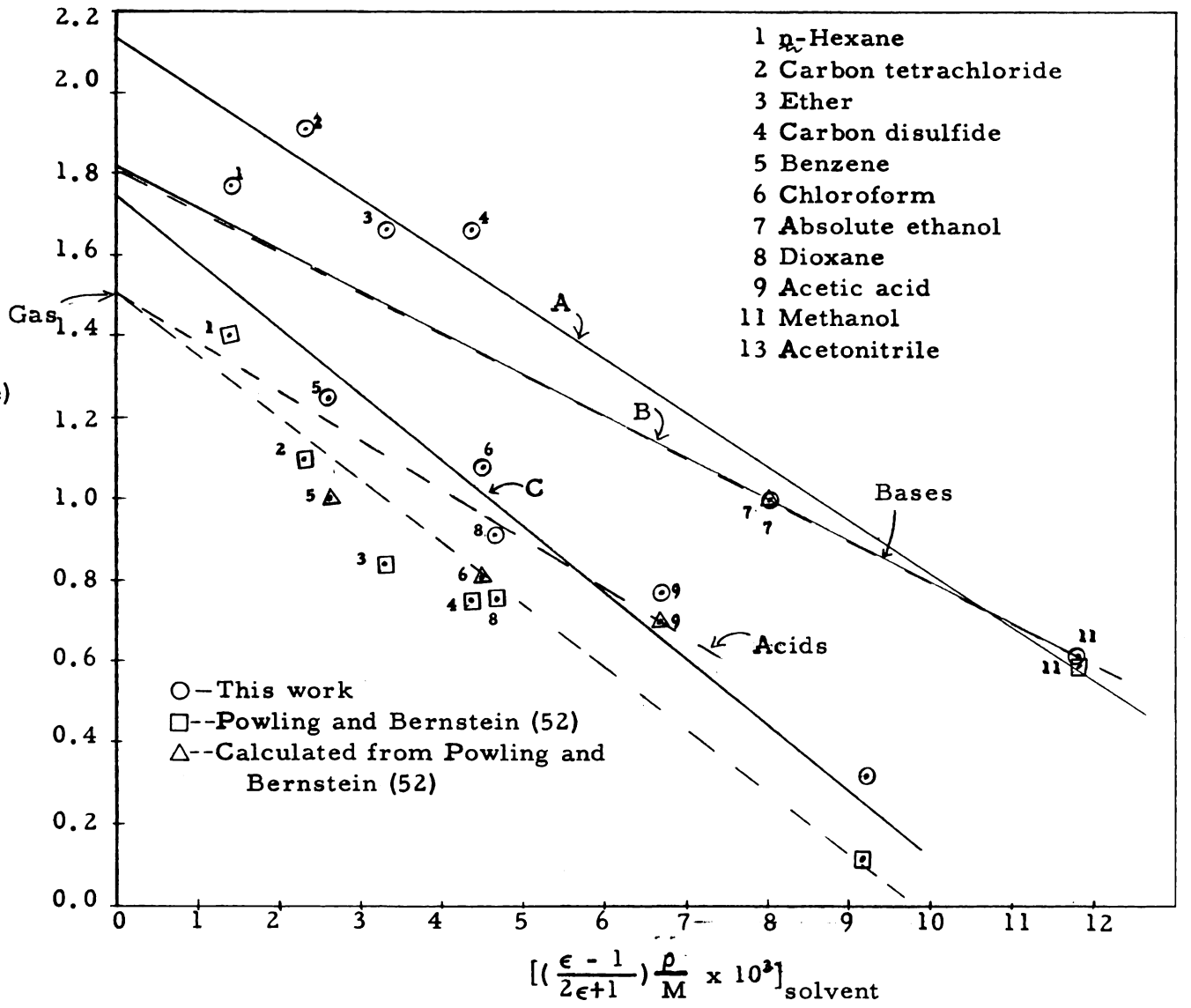
Free energies are those calculated from equilibrium constants in Tables XLIII and XLIV at 33°C. For acetylacetone in Figure 52, line **A** includes the so-called inert solvents. The free energy of tautomerization extrapolated to infinite dilution is -2.1 kcal/mole. Line B includes the alcoholic solvents and gives a free energy value at infinite dilution of -1.8 kcal/mole. Line C includes all other solvents, and the free energy of tautomerization value at infinite dilution is again -1.8 kcal/mole. For ethyl acetoacetate in Figure 53, the inert solvents (line **A**) may be extrapolated to give a free energy of tautomerization at infinite dilution of +0.1 kcal/mole, approaching the gas phase value. Alcoholic solvents (line B) give an extrapolated free energy of tautomerization at infinite dilution of +0.6 kcal/mole, and other solvents give +0.2 kcal/mole. In general, a strict comparison may not be made between results of Powling and Bernstein and those from nuclear magnetic resonance in the present study. Free energies used in Powling and Bernstein were taken from several sources, but principally bromine titration studies which are not too reliable.

Long-Range Proton Spin-Spin Coupling

Takahaski (129) has reported a long range proton spin-spin coupling constant, J_{AB}, for $CH_3^{A}COCH^{B}(CH_3)_2$ of 0.45±0.05 cps and for $CH_3CH_2^{A}COCH_3^{B}$ of 0.48±0.05 cps. Takahaski has observed that the long range coupling in these ketones may be due to π-electrons in the vicinity of the carbonyl group. Kowalewski and de Kowalewski (130) have measured long-range couplings in $HCOOCH_2CH_3$ as 0.85 and 0.57 cps for $J_{HCOO-CH_2}$ and $J_{HCOO-CH_3}$, respectively. In the present study of $CH_3COCH_2COOCH_2CH_3$, these couplings are 0.5 and 0.3 cps for $J_{C\underline{H}_2-COOC\underline{H}_2}$ and $J_{C\underline{H}_2-COOCH_2C\underline{H}_3}$, respectively.

Long range spin-spin coupling constants for the β-dicarbonyls are given in Table XLVI. The coupling constant, J_{AB}, between the

Figure 52. Free energy of tautomerization for acetylacetone versus solvent property.



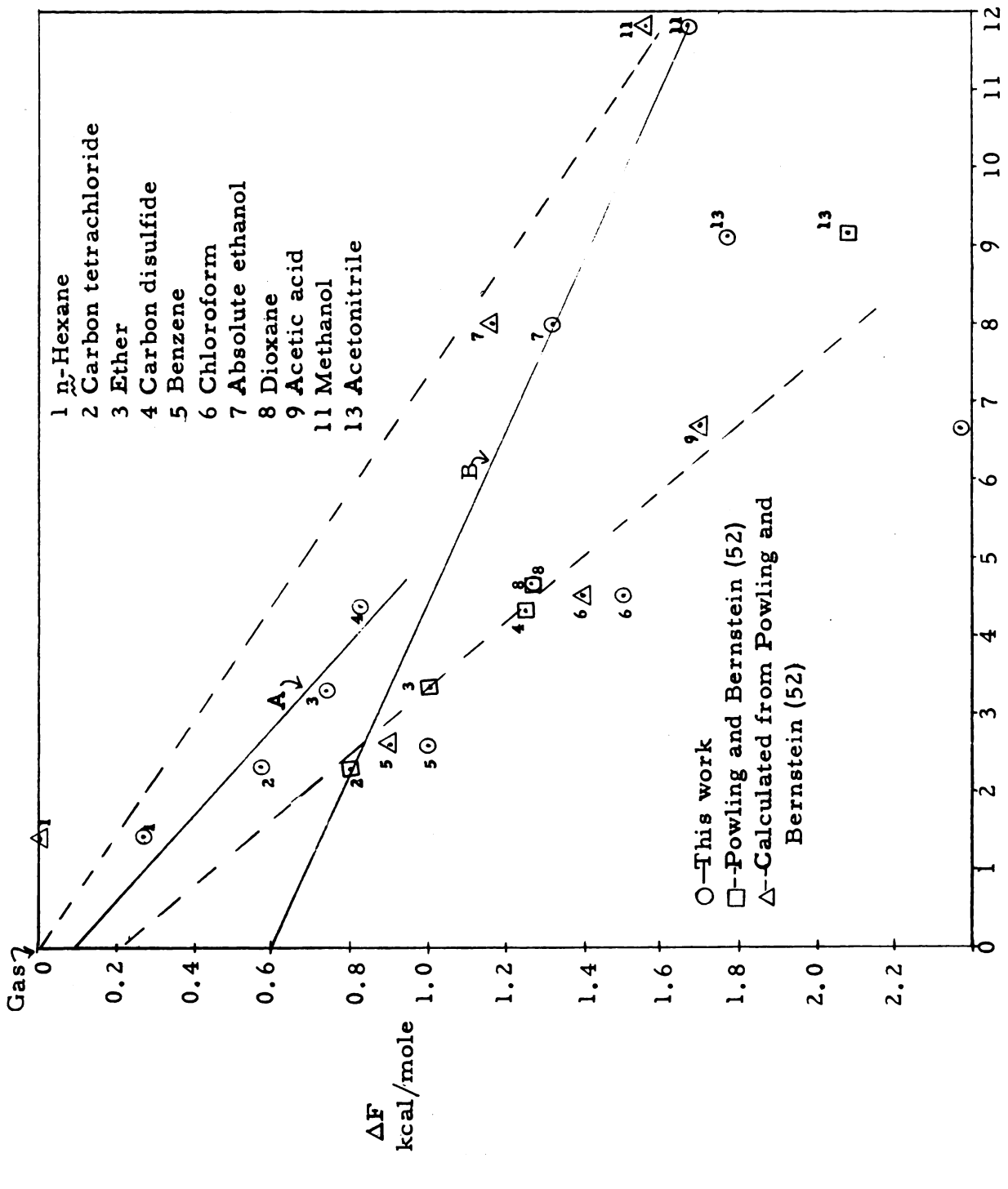


Figure 53. Free energy of tautomerization for ethyl acetoacetate versus solvent property.

Table XLVI. Long Range Spin-Spin Coupling in β-Dicarbonyls

Compound	Spin Coupling (in cps)*				
	J_{AB}	J_{CE}	J_{DE}	J_{CD}	Other
$CH_3COCH_2COCH_3$	0.44	-	-	-	
$CH_3COCH(CH_3)COCH_3$	0.40	-	$J_{A\text{-(enol }\alpha\text{-}CH_3)} = 0.27$		
$CH_3COCH_2COOCH_2CH_3$	0.43	0.71	0.71	0.78	
$CH_3COCH(CH_3)COOCH_2CH_3$	0.36	-	-	0.74	
$CH_3COCH(CH_2CH_3)COOCH_2CH_3$	0.33	-	-	-	
$CH_3COCH(Cl)COOC(CH_3)_3$	0.35	-	-	0.76	
$CH_3COCH(CH_2CH=CH_2)COOCH_2CH_3$	0.36	-	-	0.76	
$CH_3COCH(F)COOCH_2CH_3$	-	-	-	-	$J_{AF} = 3.75$ $J_{F(\alpha\text{-}H)} = 50$
$CF_3COCH_2COOCH_2CH_3$	-	-	-	-	$J_{BF} = 0.62$ $J_{EF} = 0.40$
$CH_3COCH_2COOC(CH_3)_3$	0.39	-	-	-	

*Keto: $CH_3^{A}\text{-}CO\text{-}CH_2^{B}\text{-}CO\text{-}R$

Enol: $CH_3^{C}\text{-}C(OH)=^{D}CH\text{-}^{E}CO\text{-}R$

acetyl methyl protons and the α-protons in the keto tautomer is small. In acetylacetone and ethyl acetoacetate, this constant is of comparable magnitude. With increasing substitution in the α-position, the size of the coupling constant is slightly decreased. However, these couplings generally occur at the limit of resolution of the A-60 spectrometer, so the precision is limited and generalizations based on small differences should be made only with caution.

For ethyl acetoacetate the coupling constant between the acetyl methyl protons and the α-proton of the enol tautomer (J_{CD}) is greater than in the keto form (J_{AB}). Long range couplings in this compound are shown in Figure 54. The peak for the acetyl methyl protons of the enol tautomer is seen as a triplet, but is actually a double doublet with $J_{C\underline{H}_3\text{-}COH=CH} = J_{C\underline{H}_3\text{-}COH=C\underline{H}}$. An instance of long range spin-spin interaction over five bonds has been detected in α-methyl acetylacetone between the acetyl methyl and α-methyl protons in the keto tautomer.

Fluorine-proton couplings where observed are also included in the table. For ethyl trifluoroacetoacetate the long range coupling between the trifluorogroup and the α-protons is larger in the keto than the enol tautomer, contrary to what might be expected. Other fluorine-proton couplings and proton-proton couplings in the enol tautomers are not reported, because the linewidths are too broad to allow complete resolution.

Variable Temperature Nuclear Magnetic Resonance

Chemical Shift Measurements. Variable temperature studies on β-dicarbonyls indicate that those protons which vary in chemical shift with temperature include the keto and enol α-protons as well as the enol OH proton. In all cases these protons are shifted upfield with increasing temperature. Table XLVII gives the chemical shift in cps and the

Figure 54. Long range spin-spin coupling in ethyl acetoacetate (0.79 x in CCl_4).

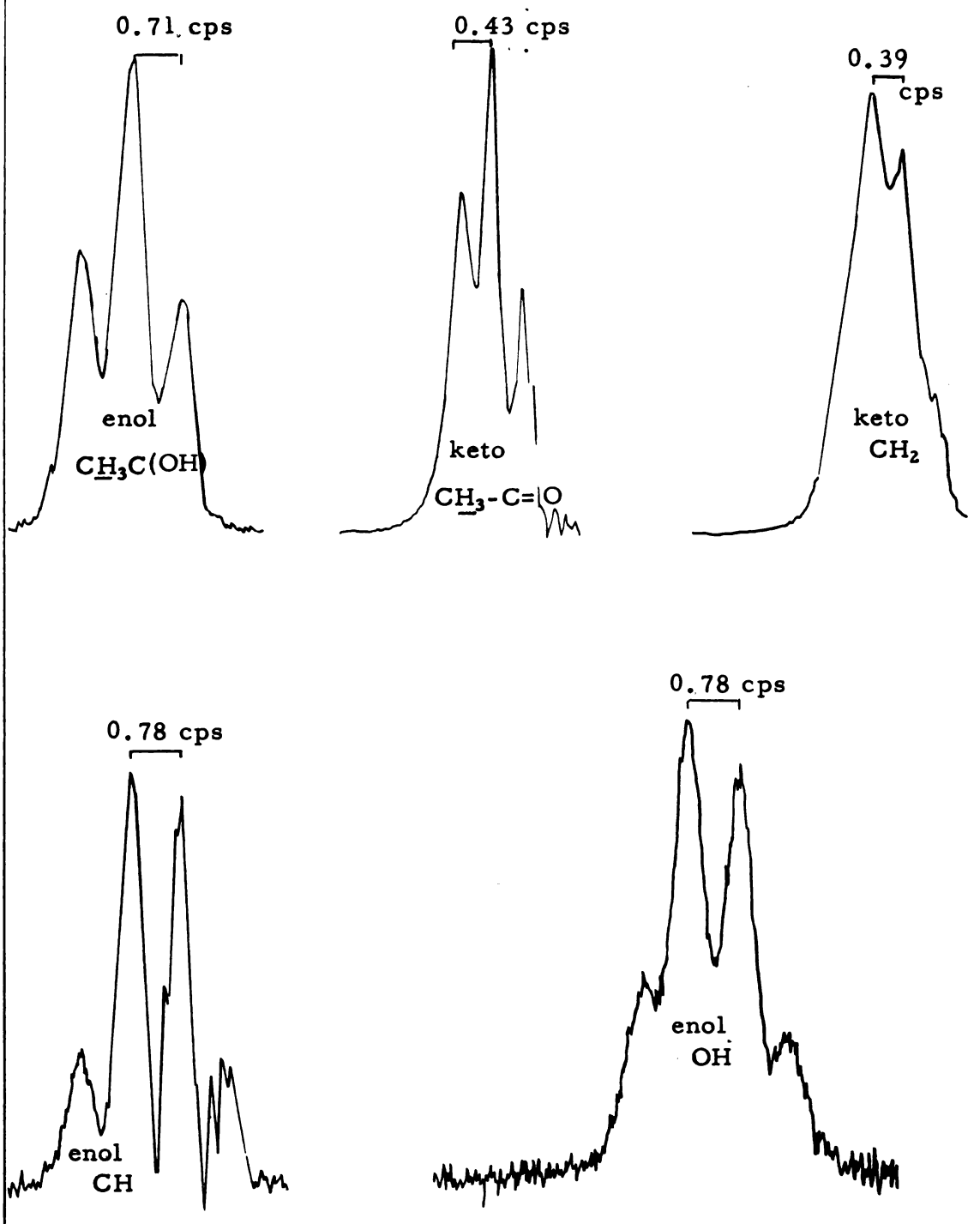


Table XLVII. Chemical Shifts of the Enol OH and of Keto and Enol α-Hydrogen Protons in β-Dicarbonyls at Various Temperatures

Compound	Temperature Range °C	Chemical Shift (cps)		
		Enol OH	Enol α-CH	Keto α-CH
Acetylacetone	-11 to 80	32[β]	1	3
Butyl acetoacetate	-11 to 33	0	2	5
t-Butyl acetoacetate	-33 to +80	5	2	5
t-Butyl α-chloroacetoacetate	-33 to 87	10	-	16
α-Chloroacetylacetone	-33 to 80	25	-	10
Ethyl acetoacetate	-33 to 80	3	3	6
Ethyl benzoyl acetate	+3 to 87	10	4	5
Ethyl α-bromoacetoacetate	-33 to 53	0[**]	-	10
Ethyl α-n-butylacetoacetate	-11 to 33	4[α]	-	2
Ethyl α-chloroacetoacetate	-33 to 106	8	-	16
Ethyl α-cyanoacetoacetate	+33 to 87	11	-	0
Ethyl α-ethyl acetoacetate	-33 to 33	4	-	3[δ]
Ethyl α-fluoroacetoacetate	-11 to 87	-	-	13
Ethyl trifluoroacetoacetate	-33 to 80	6	2	8
Ethyl α-methylacetoacetate	-11 to 80	0[*]	-	6
Hexafluoroacetylacetone	-33 to 59	5	3	-
Trifluoroacetylacetone	-33 to 80	37	0	9
Methyl acetoacetate	-33 to 33	-	-	3
α-Methylacetylacetone	-11 to 1-6	13[γ]	-	8

[*] +33 to 80°C

[**] -33 to 33°C

[α] -33 to 33

[β] -11 to 87

[γ] -11 to 80

[δ] -11 to 33

temperature range for the affected protons. Among the β-ketoesters, those compounds showing the greatest shift of the keto α-proton with temperature variation include ethyl α-fluoro, α-chloro, α-bromo-acetoacetate, ethyl trifluoroacetoacetate, and t-butyl α-chloroacetoacetate. For the β-diketones the effect is greatest in trifluoro-, α-methyl-, and α-chloroacetylacetone. The enol α-protons shows less temperature effect than the keto α-protons.

For the enol OH proton, the halogenated β-ketoesters show the most pronounced upfield shift. Ethyl α-cyanoacetoacetate has by far the greatest slope for chemical shift versus temperature. All the β-diketones show large shifts of the enol OH with increasing temperature.

These results appear to indicate a breaking up of the intramolecular hydrogen bond in β-dicarbonyls with increasing temperature. Furthermore the upfield shift of the keto α-protons with higher temperatures suggests that intermolecular association exists among these molecules and that these associated species are also dissociating. This association apparently does not involve the enol α-proton and probably is between keto molecules. This kind of behavior has been observed in the solvent studies, but in this case involved also the enol α-proton.

In no case was evidence found for the existence of trans enol or di-enol tautomers. There is no indication that coalescence of enol and keto resonance peaks will occur for these compounds within the available temperature range.

Equilibrium Constant Measurements. An increase in temperature results in lower enol content of the β-dicarbonyls. This is to be expected since high temperatures presumably break up the intramolecularly hydrogen-bonded species. Equilibrium constants have been determined at various temperatures, where percentages of enol are sufficient to make such measurements feasible.

From the relationship between equilibrium constant and absolute temperature,

$$\frac{d(\ln K_e)}{d(1/T)} = -\frac{\Delta H}{R}, \qquad (53)$$

the change in enthalpy for tautomerization may be obtained from the slope of a plot of log K_e versus $1/T$. Such a graph is shown in Figure 55 for α-methylacetylacetone. Enthalpies of tautomerization for several β-dicarbonyls obtained in this manner are given in Table XLVIII. The greatest change in the enthalpy of tautomerization occurs for α-chloroacetylacetone. On the other hand, there is comparatively little effect of temperature upon the position of equilibrium in ethyl α-chloroacetoacetate.

Free energies of tautomerization have been calculated from the relationship,

$$\Delta F^{33^\circ} = -RT\ln K_e . \qquad (54)$$

Finally, the change in entropy for tautomerization has been calculated by use of the equation,

$$\frac{\Delta H - \Delta F}{T} = \Delta S. \qquad (55)$$

Values of these thermodynamic quantities are listed in Table XLVIII for the systems studied.

The thermodynamic quantities determined by NMR may be compared with those in Table IX in the gas phase by Briegleb (50-52). Neither the free energies nor enthalpies of tautomerization agree even qualitatively. Free energies of tautomerization in the gas phase are understandably higher negative numbers, indicating an increased enol

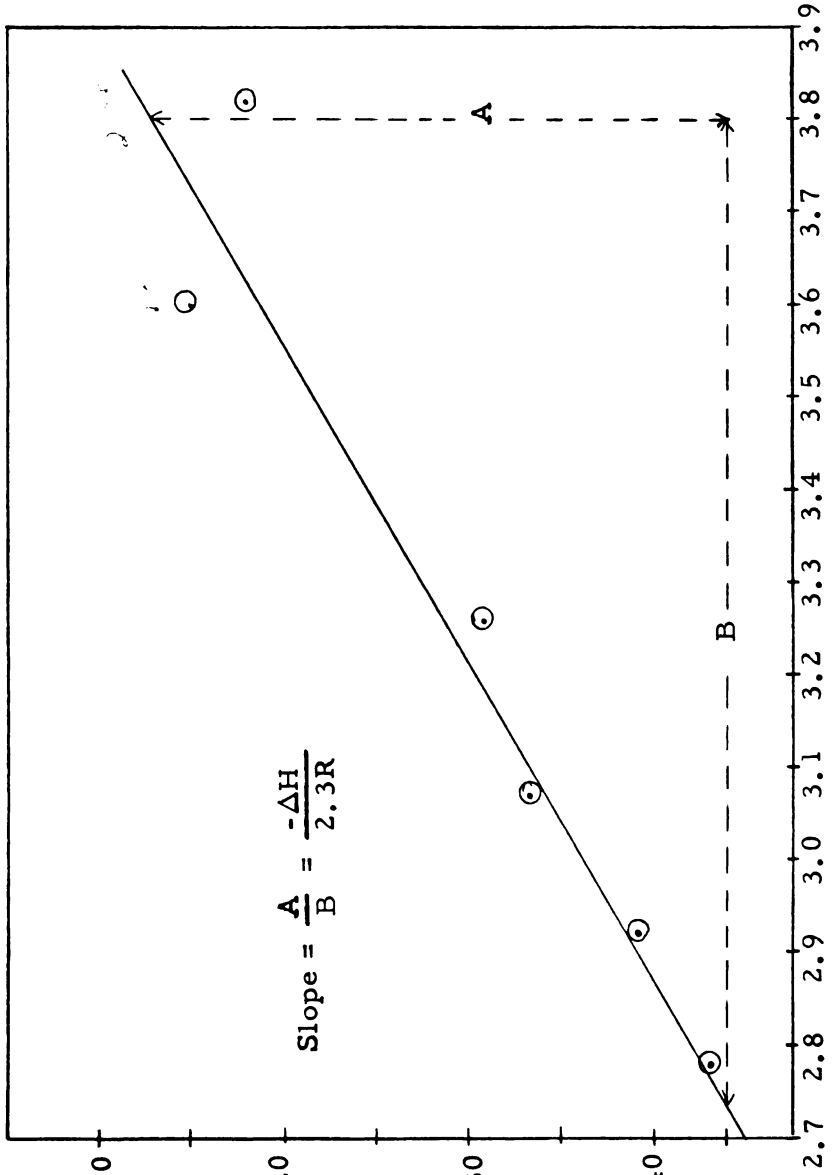


Figure 55. Graph of log ([enol]/[keto]) versus 1/T for α-methylacetylacetone.

Table XLVIII. Thermodynamic Quantities for the Tautomerization Equilibria in β-Dicarbonyls

Compound	Temperature Range (°C)	*Log $K^{33°}$	$\Delta F^{33°}$ cal/mole	ΔH cal/mole	$\Delta S^{33°}$ cal/mole deg.
Acetylacetone	-11 to 59	+0.570	-799±70	-2840±200	-6.66±0.88
α-Chloroacetylacetone	+33 to 80	+1.15	-1610±110	-5920±200	-14.1±1.01
Ethyl trifluoroacetoacetate	+5 to 80	+0.780	-1090±180	-3910±200	-9.21±1.24
Ethyl α-chloroacetoacetate	-33 to 105	-0.185	+259±100	-875±100	-3.69±0.57
α-Methylacetylacetone	-11 to 89	-0.285	+399±100	-1330±100	-5.65±0.45

*Taken from graph of log K_e versus 1/T

tautomer. The enthalpies of tautomerization are too high algebraically for acetylacetone and too low for ethyl α-chloroacetoacetate.

Entropies of tautomerization indicate a more ordered system for the enol tautomer as compared with the keto tautomer. Both α-chloroacetylacetone and ethyl trifluoroacetoacetate have fairly large negative entropies of tautomerization. It is suggested that these compounds have very strong intramolecularly hydrogen-bonded species.

SUMMARY

The tautomeric equilibria of β-dicarbonyls have been investigated by nuclear magnetic resonance spectroscopy. Chemical shift measurements have been made in a number of solvents, and equilibrium constants ([enol]/[keto]) have been determined. The equilibrium has been studied as a function of temperature, and thermodynamic quantities have been obtained from the experimental data in the case of several β-dicarbonyls.

REFERENCES

1. K. H. Meyer, Chem. Ber., 45, 2843 (1912).

2. K. H. Meyer, Chem. Ber., 44, 2718 (1911).

3. J. D. Park, H. A. Brown, and J. R. Lacher, J. Am. Chem. Soc., 75, 4753 (1953).

4. M. D. Ratnakar and K. K. Mahajan, Vikram, J. Vikram Univ., 2, 37 (1958).

5. M. J. Malawski and W. Czerska, Roczniki Chem., 34, 491 (1960).

6. B. Eistert and W. Reiss, Chem. Ber., 87, 92 (1954).

7. B. Eistert and W. Reiss, ibid., 87, 108 (1954).

8. M. I, Kabachnik, S. T. Yoffe and K. V. Vatsuro, Tetrahedron, 1, 317 (1957).

9. M. I. Kabachnik, S. T. Yoffe, E. M. Popov, and K. V. Vatsuro, ibid., 12, 76 (1961).

10. M. I. Kabachnik, S. T. Yoffe, E. M. Popov, and K. V. Vatsuro, Zh. Obshch. Khim., 31, 2122 (1961).

11. M. I. Kabachnik, et al., ibid., 31, 2682 (1961).

12. M. I. Kabachnik, et al., Dokl. Akad. Nauk SSSR, 144, 802 (1962).

13. B. Eistert and F. Geiss, Tetrahedron, 7, 1 (1959).

14. H. Henecka, Chem. Ber., 81, 189 (1948).

15. M. S. Newman, ed., Steric Effects in Organic Chemistry, John Wiley and Sons, Inc., New York, (1956).

16. P. Rumpf and E. La Riviere, Compt. Rend., 244, 902 (1957).

17. G. S. Hammond, W. G. Borduin, and G. A. Guter, J. Am. Chem. Soc., 81, 4682 (1959).

18. R. Filler and S. M. Naqvi, J. Org. Chem., 26, 2571 (1961).

19. K. L. Wolf, Physik, Z., 31, 227 (1930).

20. C. T. Zahn, Physik. Z., 34, 570 (1933).

21. M. Beyaert, Natuurw. Tijdschr., 18, 197 (1936).

22. R. J. W. Le Fevre and H. Welsh, J. Chem. Soc., 1909 (1949).

23. L. W. Reeves, Can. J. Chem., 35, 1351 (1957).

24. N. V. Sidgwick, J. Chem. Soc., 907 (1925).

25. B. Eistert, F. Arndt, L. Loewe, and E. Ayca, Chem. Ber., 84, 156 (1951).

26. S. Bratoz, D. Hadzi, and G. Rossmy, Trans. Faraday Soc., 52, 464 (1956).

27. R. S. Rasmussen, D. D. Tunnicliff, and R. R. Brattain, J. Am. Chem. Soc., 71, 1068 (1949).

28. D. N. Shigorin, Izv. Akad. Nauk SSSR, Ser. Fiz., 14, 395 (1950).

29. D. N. Shigorin, Zh. Fiz. Khim., 28, 584 (1954).

30. R. Mecke and E. Funck, Z. Elektrochem., 60, 1124 (1956).

31. C. L. Angell and R. L. Werner, Australian J. Chem., 6, 294 (1953).

32. L. J. Bellamy and L. Beecher, J. Chem. Soc., 4487 (1954).

33. H. F. Holtzclaw, Jr., and J. P. Collman, J. Am. Chem. Soc., 79, 3318 (1957).

34. Ch. Tamm and R. Albrecht, Helv. Chim. Acta, 43, 768 (1960).

35. A. S. N. Murthy, A. Balasubramanian, and C. N. R. Rao, Can. J. Chem., 40, 2267 (1962).

36. J. J. Powling and H. J. Bernstein, J. Am. Chem. Soc., 73, 4353 (1951).

37. K. Kuratani, Rep. Inst. Sci. Technol., Univ. Tokyo, 6, 217 (1952).

38. R. Belford, A. E. Martell, and M. Calvin, J. Inorg. Nucl. Chem., 2, 11 (1956).

39. Sadtler Standard Spectra, Sadtler Research Laboratories, Philadelphia, (1962).

40. R. S. Rasmussen and R. R. Brattain, J. Am. Chem. Soc., 71, 1073 (1949).

41. I. M. Hunsberger, R. Ketcham, and H. S. Gutowsky, J. Am. Chem. Soc., 74, 4839 (1952).

42. K. Kuratani, Rep. Inst. Sci. Technol., Univ. Tokyo, 5, 25 (1951).

43. Z. Bankowska, Bull. Acad. Polon. Sci., Ser. Sci. Chim., 10 401 (1962).

44. L. J. Bellamy, Infrared Spectra of Complex Molecules, John Wiley and Sons, Inc., New York, 2nd ed., (1958).

45. R. E. Rundle and M. Parasol, J. Chem. Phys., 20, 1487 (1952).

46. D. N. Shigorin, Dokl. Akad. Nauk SSSR, 96, 561 (1954).

47. D. N. Shigorin, Zh. Fiz. Khim., 24, 932 (1950).

48. D. N. Shigorin, ibid., 24, 954 (1950).

49. P. Grossmann, Z. Physik. Chem. (Leipzig), 109, 305 (1924).

50. G. Briegleb et al., Z. Naturforsch, 8b, 219 (1953).

51. G. Briegleb et al., ibid., 7b, 184 (1952).

52. G. Briegleb et al., ibid., 6b, 1 (1951).

53. M. I. Kabachnik et al., Dokl. Akad. Nauk SSSR, 96, 1169 (1954).

54. W. J. Le Noble, J. Am. Chem. Soc., 82, 5253 (1960).

55. J. B. Conant and A. F. Thompson, Jr., ibid., 54, 4039 (1932).

56. P. B. Russell, ibid., 74, 2654 (1952).

57. L. W. Reeves and W. G. Schneider, Can. J. Chem., 36, 793 (1958).

58. C. Giessner-Prettre, Compt. Rend., 250, 2547 (1960).

59. E. M. Kosower, J. Am. Chem. Soc., 80, 3267 (1958).

60. M. J. S. Dewar, Electronic Theory of Organic Chemistry, Clarendon Press, Oxford, (1949).

61. L. Pauling, Nature of the Chemical Bond, Cornell Univ. Press, Ithaca, 3rd ed., (1960).

62. G. W. Wheland, Advanced Organic Chemistry, John Wiley and Sons, New York, 3rd ed., (1960).

63. J. C. Reid and M. Calvin, J. Am. Chem. Soc., 72, 2948 (1950).

64. Z. Bankowska, Roczniki Chem., 36, 1159 (1962).

65. R. G. Pearson and J. M. Mills, J. Am. Chem. Soc., 72, 1692 (1950).

66. R. G. Pearson and R. L. Dillon, ibid., 75, 2439 (1953).

67. E. S. Gould, Mechanisms and Structure in Organic Chemistry, Holt and Co., New York, (1959).

68. P. Rumpf and R. Reynaud, Compt. Rend., 250, 1501 (1960).

69. W. Walisch and H. A. Ruppersberg, Ann. Univ. Saraviensis, Sci., 8, 1 (1959).

70. M. Calvin and K. W. Wilson, J. Am. Chem. Soc., 67, 2003 (1945).

71. H. S. Jarrett, M. S. Sadler, and J. N. Shoolery, J. Chem. Phys., 21, 2092 (1953).

72. W. G. Schneider and L. W. Reeves, Ann. N. Y. Acad. Sci., 70, 858 (1958).

73. F. J. Balta Calleja, Compt. Rend., 249, 1102 (1959).

74. S. Forsen and M. Nilsson, Acta Chem. Scand., 13, 1383 (1959).

75. S. Forsen and M. Nilsson, ibid., 14, 1333 (1960).

76. S. Forsen and M. Nilsson, Arkiv Kemi, 17, 523 (1961).

77. S. Forsen, M. Nilsson, and C. A. Wachtmeister, Acta Chem. Scand., 16, 583 (1962).

78. M. Nilsson, Svensk. Kem. Tidskr., 73, 447 (1961).

79. S. Forsen and M. Nilsson, Arkiv Kemi, 19, 569 (1962).

80. S. Forsen, Svensk Kem. Tidskr., 74, 439 (1962).

81. G. O. Dudek and R. H. Holm, J. Am. Chem. Soc., 83, 2099 (1961).

82. S. Forsen, Spectrochim. Acta, 18, 595 (1962).

83. S. Forsen, Arkiv Kemi, 20, 1 (1963).

84. S. Forsen, ibid., 20, 25 (1963).

85. S. Forsen, ibid., 20, 41 (1963).

86. K. Nakamoto, Y. Morimoto, and A. E. Martell, J. Phys. Chem., 66, 346 (1962).

87. J. D. Roberts, Nuclear Magnetic Resonance, McGraw-Hill Book Co., New York, (1959).

88. J. A. Pople, W. G. Schneider, and H. J. Bernstein, High-resolution Nuclear Magnetic Resonance, McGraw-Hill Book Co., New York, (1959).

89. A. D. Buckingham, Can. J. Chem., 38, 300 (1960).

90. A. D. Buckingham, T. Schaefer, and W. G. Schneider, J. Chem. Phys., 32, 1227 (1960).

91. A. A. Bothner-By and R. E. Glick, J. Am. Chem. Soc., 78, 1071 (1956).

92. A. A. Bothner-By and R. E. Glick, J. Chem. Phys., 26, 1657 (1957).

93. A. A. Bothner-By and R. E. Glick, ibid., 26, 1651 (1957).

94. C. E. Johnson, Jr., and F. A. Bovey, ibid., 29, 1012 (1958).

95. L. W. Reeves and W. G. Schneider, Can. J. Chem. 35, 251 (1957).

96. J. V. Hatton and W. G. Schneider, ibid., 40, 1285 (1962).

97. W. G. Schneider, J. Phys. Chem., 66, 2653 (1962).

98. M. J. Stephen, Mol. Phys., 1, 223 (1958).

99. A. A. Bothner-By, J. Mol. Spectry., 5, 52 (1960).

100. W. G. Schneider, H. J. Bernstein, and J. A. Pople, J. Chem. Phys., 28, 601 (1958).

101. A. D. Buckingham, T. Schaefer, and W. G. Schneider, J. Chem. Phys., 34, 1064 (1961).

102. T. W. Marshall and J. A. Pople, Mol. Phys., 1, 199 (1958).

103. R. J. Abraham, ibid., 34, 1062 (1961).

104. W. T. Raynes, A. D. Buckingham, and H. J. Bernstein, ibid., 36, 3481 (1962).

105. P. Diehl and R. Freeman, Mol. Phys., 4, 39 (1961).

106. W. G. Schneider, J. Chem. Phys., 28, 601 (1958).

107. G. C. Pimentel and A. L. McClellan, The Hydrogen Bond, Reinhold Publishing Corp., New York, (1960).

108. C. G. Cannon, Spectrochim. Acta, 10, 341 (1958).

109. H. M. McConnell, J. Chem. Phys., 24, 460 (1956).

110. M. Karplus and D. H. Anderson, ibid., 30, 6 (1959).

111. M. Karplus, ibid., 30, 11 (1959).

112. H. S. Gutowsky, M. Karplus, and D. M. Grant, ibid., 31, 1278 (1959).

113. Instruction Manual, Model A-60 Analytical NMR Spectrometer System, Publ. No. 87-100-030, Instrument Division, Varian Assoc., Palo Alto.

114. Preliminary Instruction Manual, V6057 Variable Temperature System for A-60 Analytical Spectrometers, Publ. No. 87-100-110, Instrument Division, Varian Assoc., Palo Alto.

115. J. J. D'Amico (to Monsanto Chemical Co.), U. S. Patent 2,704,761, Mar. 22, 1955.

116. G. Schwarzenbach and E. Felder, Helv. Chim. Acta, 27, 1044 (1944).

117. B. Ciocca, Gazz. Chim. Ital., 67, 346 (1937).

118. L. G. Donaruma, J. Org. Chem., 26, 4737 (1961).

119. A. Burger and G. E. Ullyot, ibid., 12, 342 (1947).

120. T. Isoshima, Nippon Kagaku Zasshi, 77, 425 (1956).

121. M. S. Kharasch, E. Sternfeld, and F. R. Mayo, J. Am. Chem. Soc., 59, 1655 (1937).

122. A. I. Vogel, Practical Organic Chemistry, John Wiley and Sons, Inc., New York, 3rd ed., (1956).

123. NMR Spectra Catalog, Varian Associates, National Press, (1962).

124. J. V. Hatton and R. E. Richards, Mol. Phys., 3, 253 (1960).

125. G. J. Korinek and W. G. Schneider, Can. J. Chem., 35, 1157 (1957).

126. S. A. Glickman and A. C. Cope, J. Am. Chem. Soc., 67, 1017 (1945).

127. J. Powling and H. J. Bernstein, J. Am. Chem. Soc., 73, 1815 (1951).

128. Lange's Handbook of Chemistry, Handbook Publishers, Inc., Sandusky, 9th ed., (1956).

129. I. Takahaski, Bull. Chem. Soc. Japan, 35, 1046 (1962).

130. V. J. Kowalewski and D. G. de Kowalewski, private communication.