PART 1
PROTON-^{13}C SPIN-SPIN COUPLING
PART 11
CARBONIUM ION REARRANGEMENTS IN THE *n*-PROPYL AND NEOPENTYL SYSTEMS

Thesis for the Degree of Ph. D.
MICHIGAN STATE UNIVERSITY
Chester E. Orzech, Jr.
1968

This is to certify that the

thesis entitled
PART I
PROTON-^{13}C SPIN-SPIN COUPLING
PART II
CARBONIUM ION REARRANGEMENTS IN THE
n-PROPYL AND NEOPENTYL SYSTEMS
presented by

Chester E. Orzech, Jr.

has been accepted towards fulfillment
of the requirements for

Ph.D. **degree in** Chemistry

G. J. Karabatsos
Major professor

Date December 15, 1967

ABSTRACT

PART I

PROTON-^{13}C SPIN-SPIN COUPLING

PART II

CARBONIUM ION REARRANGEMENTS IN THE *n*-PROPYL AND NEOPENTYL SYSTEMS

by Chester E. Orzech, Jr.

PART I

Several investigations have been directed toward elucidation of the factors affecting proton-^{13}C couplings over one, two, and three bonds both in saturated and unsaturated systems. The short-range coupling, $J_{^{13}CH}$, has been studied extensively on account of the relative ease of detection by high resolution n.m.r. of the natural occurring 1% ^{13}C. The general linearity between $J_{^{13}CH}$ and fractional s-character of the ^{13}C hybrid atomic orbital has led to the conclusion that the Fermi contact term is essentially the sole contributor to the coupling (1).

Long-range proton-^{13}C coupling has been studied less extensively. In this case ^{13}C enriched (>10%) compounds must be used. Several workers (2,3) in the field concluded that $J_{^{13}CCH}$ follows s-character when the ^{13}CCH angle is tetrahedral only. No correlation has been found for $J_{^{13}CCCH}$.

A synthesis of many ^{13}C enriched compounds was undertaken in order to measure their proton-^{13}C couplings and attempt a correlation. The compounds were either prepared from lithium or magnesium alkyls and $^{13}CO_2$ obtained from enriched barium carbonate or purchased directly. The compounds were purified either by vapor phase chromatography or recrystallization.

One-, two-, and three-bond couplings were studied. The one- and three-bond couplings were measured together in neopentyl ($-^{13}CH_2-$) compounds and the two-bond couplings in acetyl ($^{13}C=O$) compounds. A Varian Associates A-60 n.m.r. spectrometer was used at about 38°C (ambient) to measure the proton-^{13}C couplings from the proton spectra.

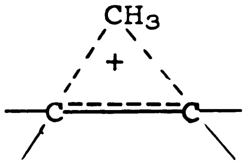
The one- and two-bond couplings, $J_{^{13}CH}$ and $J_{^{13}CCH}$, follow s-character fairly well, with one exception. When the substituent is a group with angular-dependent atomic orbitals (p,d,f), both $J_{^{13}CH}$ and $J_{^{13}CCH}$ do not behave in a linear fashion with s-character.

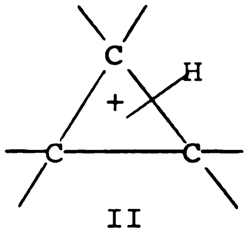
In the case of the three-bond coupling, $J_{^{13}CCCH}$, no linear relation is obtained at all. Dihedral angle effects have been shown to be of little significance, whereas it appears $J_{^{13}CCH}$ is extremely sensitive to the HCC and $CC^{13}C$ angles. Also a bent-bond approach seems to correlate very well qualitatively with the data.

PART II

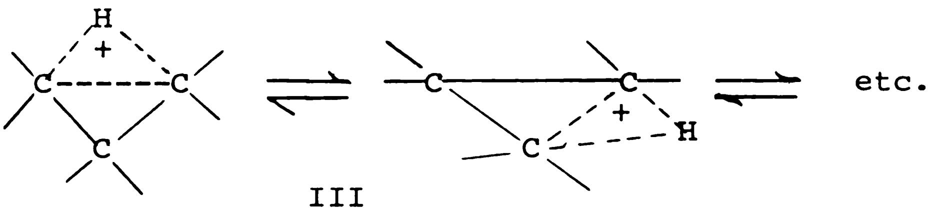
In reactions which are known to generate carbonium ions the neopentyl system always gives products resulting from the t-amyl cation. t-Amyl products and iso-pentenes, but no 1,1-dimethylcyclopropane, are found. The 1-propyl system on generation of a carbonium ion leads to 1- and 2-propyl products, propene, and cyclopropane.

It has been suggested that many carbonium ion rearrangements proceed via methyl-bridged nonclassical ions (I) or protonated cyclopropanes (II), since cyclopropanes are found


I


II

to be products of many of these reactions. Evidence for methyl-bridged nonclassical carbonium ions and protonated cyclopropanes has been scarce. By appropriately labeling 1-propyl and neopentyl compounds, generating the carbonium ions, and analyzing the products for label position and percent, protonated cyclopropanes, symmetrical (II) or bridged (III), could be detected, if formed.



III

For studying the 1-propyl system, 1-propylammonium-1,1-$\underline{d}_2$ and 1-propylammonium-2,2-$\underline{d}_2$ perchlorates were prepared and deaminated with nitrous acid. For the neopentyl system, neopentylammonium-1,1-$\underline{d}_2$ and neopentylammonium-1-^{13}C perchlorates were prepared and deaminated. Also studied by solvolysis were neopentyl-1,1-$\underline{d}_2$ and neopentyl-1-^{13}C tosylates, and neopentyl-1-^{13}C iodide.

Mass spectral analysis of the 1-propanol obtained from the deamination of 1-propylammonium-1,1-$\underline{d}_2$ perchlorate gave the following isotopic composition for the α-carbon: 96.1% $\underline{d}_2$, 0.8% $\underline{d}_1$, and 3.1% $\underline{d}_0$. The 1-propanol from 1-propylammonium-2,2-$\underline{d}_2$ perchlorate gave: 1.2% $\underline{d}_2$, 0.9% $\underline{d}_1$, and 97.9% $\underline{d}_0$. Since protium-deuterium positional rearrangements occurred, and reversible 1,2-shifts are ruled out on the basis of the percentage ratios of the products and the fact that 2-aminopropane did not yield any 1-propanol, a protonated cyclopropane (II) or bridged ion (III) accommodates the results quite well. About 5% of the 1-propanol was found to be rearranged at 40° and 3% at 0°.

The $\underline{t}$-amyl alcohol obtained from the deaminations and solvolyses was found by mass spectral analysis to contain all the label at C-3. This eliminates the possibility of protonated cyclopropane intermediates. If a protonated cyclopropane had formed some of the label would have been found at C-4. Also, no 1,3-hydride shifts occurred, because no label was found at C-1. Apparently the only reaction occurring is a 1,2-methyl shift on account of the very favorable primary to tertiary ion rearrangement.

REFERENCES

1. M. Karplus and D. Grant, Proc. Natl. Acad. Sci. U. S., 45, 1269 (1959).

2. G. J. Karabatsos, J. D. Graham, and F. Vane, J. Phys. Chem., 65, 1657 (1961).

3. J. Ranft, Ann. Physik, 9, 124 (1962); 10, 399 (1963).

PART I

PROTON-^{13}C SPIN-SPIN COUPLING

PART II

CARBONIUM ION REARRANGEMENTS IN THE *n*-PROPYL AND NEOPENTYL SYSTEMS

By

Chester E. Orzech, Jr.

A THESIS

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

DOCTOR OF PHILOSOPHY

Department of Chemistry

1968

ACKNOWLEDGMENTS

The author desires to express his most earnest appreciation to Dr. Gerasimos J. Karabatsos for his guidance and interest during the course of this study.

Grateful acknowledgment is given to the Petroleum Research Fund of the American Chemical Society whose grant provided financial aid from June 1961 to August 1961 and to the National Science Foundation for the period September 1961 to June 1962 and whose fellowship program provided funds from September 1962 to August 1964.

Appreciation is also extended to Seymour Meyerson of the American Oil Company for the numerous mass spectral analyses.

****

TABLE OF CONTENTS

Page

PART I

PROTON-^{13}C SPIN-SPIN COUPLING

PART II

CARBONIUM ION REARRANGEMENTS IN THE *n*-PROPYL AND NEOPENTYL SYSTEMS

EXPERIMENTAL

LIST OF TABLES

PART I

PART II

LIST OF FIGURES

PART I

PART II

PART I

PROTON-^{13}C SPIN-SPIN COUPLING

INTRODUCTION

Several investigations have been directed toward elucidation of the factors affecting proton-^{13}C coupling over one (1-15), two (16-19), and three (10,16-20) bonds both in saturated and unsaturated systems. The short-range coupling, $J^{13}{}_{CH}$, has been studied extensively. The general linearity between $J^{13}{}_{CH}$ and fractional s-character of the ^{13}C hybrid atomic orbital has led to the conclusion that the Fermi contact term is essentially the sole contributor to the coupling, as suggested from valence bond theory (21). Schoolery (2) has plotted values of $J^{13}{}_{CH}$ versus percent s-character (see Figure 1) to obtain a linear relation.

Muller and Pritchard (3), and Gutowsky and Juan (8) have derived the following relationship (equation 1) from valence

$$J^{13}{}_{CH} = 500\ \alpha^2_H \quad \text{c.p.s.} \tag{1}$$

bond theory, making several approximations, between $J^{13}{}_{CH}$ and fractional s-character (α^2_H) of the carbon hybrid orbital used in the C-H bond.

Additivity relations of substituent effects on $J^{13}{}_{CH}$ in substituted methanes (6) and formyl (7) compounds have been discovered and interpreted as a direct relation between $J^{13}{}_{CH}$ and s-character (8). On the assumption therefore that the

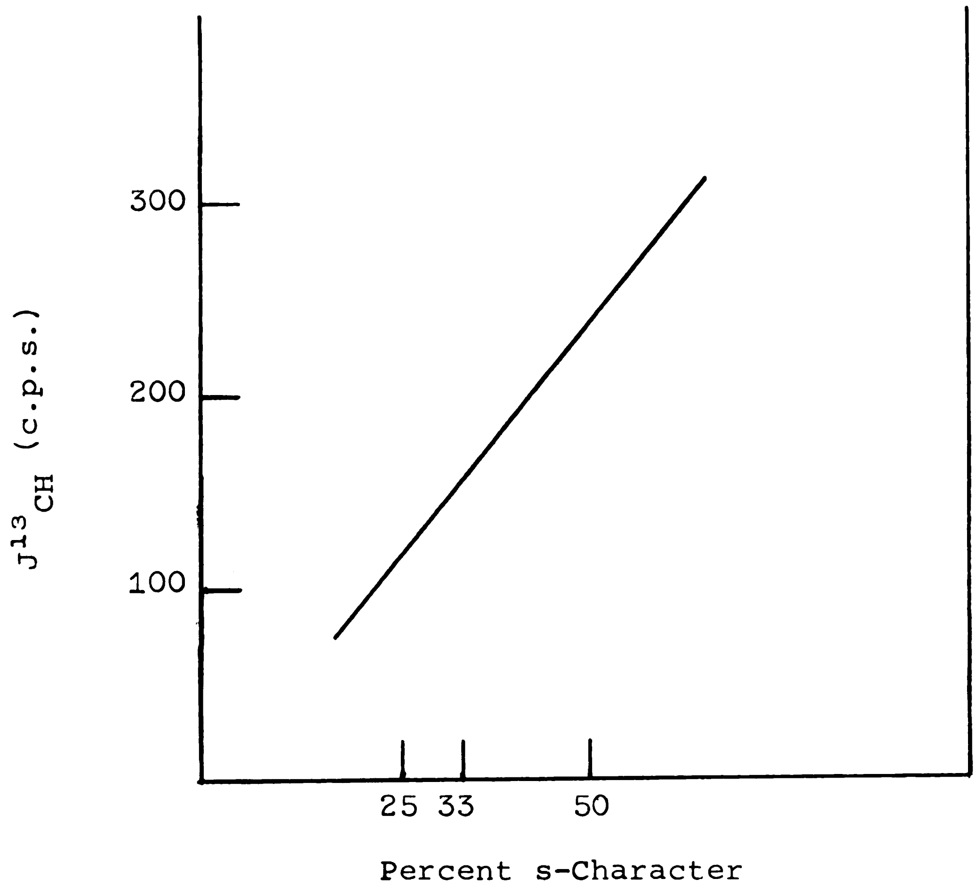


Figure 1. One-bond proton-^{13}C coupling versus s-character (sp^3, sp^2, sp) of various compounds (2).

contact term is essentially the sole contributor to the coupling, fractional s-characters have been calculated, usually in three significant figures, from experimental $J^{13}{}_{CH}$ values. Deviations from the additivity relations have been observed (5,11,12) especially for highly electronegative substituents such as -F and $-OCH_3$. Douglas (12) has suggested an empirical correction but offers no interpretation.

Foote (13) and Mislow (14) have obtained linear empirical relations between $J^{13}{}_{CH}$ and the C-C-C interatomic angle of saturated cyclic hydrocarbons from C_3 to C_{12}.

Long-range proton-^{13}C coupling has enjoyed less attention than $J^{13}{}_{CH}$. From an approximate treatment of $J^{13}{}_{CCH}$, and the linearity between $J^{13}{}_{CCH}$ and fractional s-character of the ^{13}C hybrid atomic orbital (Figure 2), Karabatsos and co-workers (17) concluded that contact interaction dominates this coupling when the ^{13}C-C-H angle is tetrahedral. The same conclusion was also reached by Ranft (10,19) and Smith (24). No simple correlation has been found between the three-bond coupling, $J^{13}{}_{CCCH}$, and the s-character of the ^{13}C atomic orbital (18,20).

Elucidation of the factors affecting long-range proton-^{13}C coupling has been hampered by lack of sufficient and pertinent data. The goal of this research project was therefore to synthesize a large number of suitably substituted ^{13}C enriched compounds, to measure the one-, two-, and three-bond proton-^{13}C coupling wherever applicable, and attempt to interpret the data.

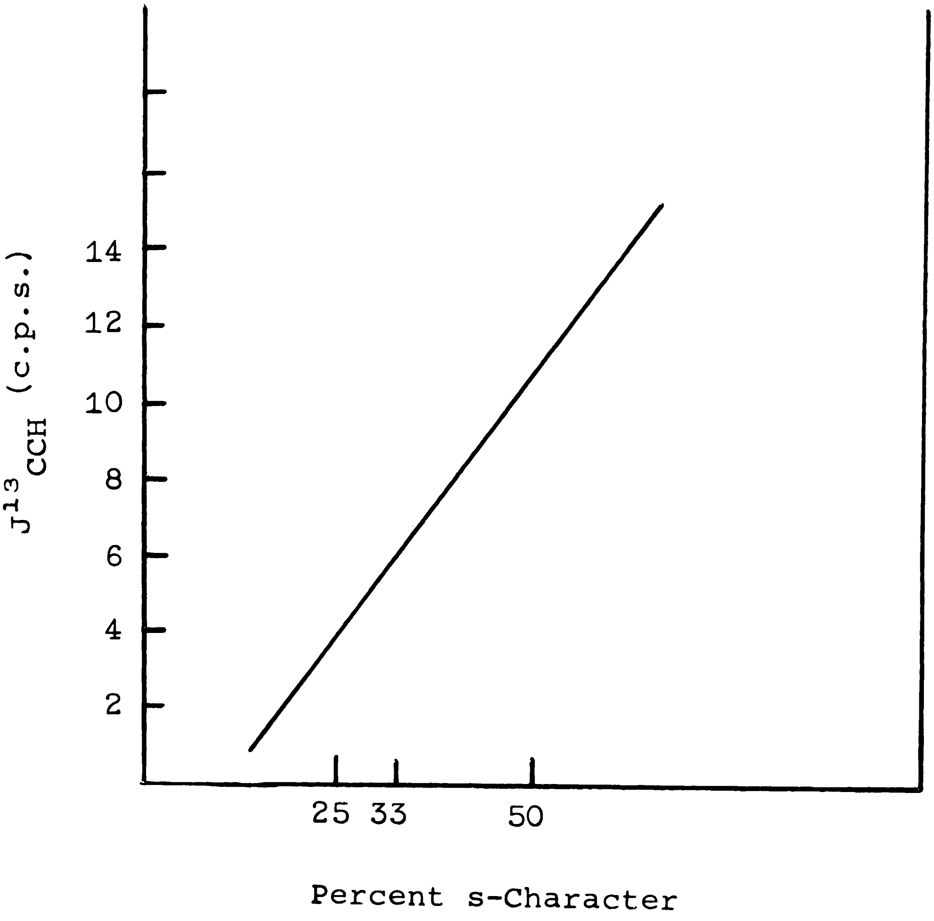


Figure 2. Two-bond proton-^{13}C coupling versus s-character of various compounds (17).

RESULTS

Table I summarizes the two-bond coupling constants and Table II the one- and three-bond coupling constants that were obtained with a Varian Associates A-60 n.m.r. spectrometer at about 36°C. The values for the long-range constants, determined at 50 c.p.s. sweep width, are averages of at least three measurements with precision of ± 0.03 c.p.s. They were checked against acetaldehyde, J_{HH} = 2.85 c.p.s. (22,23), and should be accurate to ± 0.05 c.p.s. Short-range constants, determined at 250 c.p.s. sweep widths, are also averages of at least three determinations with precision of ± 0.2 c.p.s. They should be accurate to ± 0.5 c.p.s. The choice of compounds with structure I for the two-bond couplings and structure II for the one-bond and three-bond couplings was dictated

$CH_3-{}^{13}C$ I $\qquad$ $(CH_3)_3C-{}^{13}C$ II

by convenience and by the simplicity inherent in first-order spectra. All spectra had simple, first-order appearance (Figure 3). Neopentyl sulfite and neopentyl chlorosulfite, as a consequence of nonplanar sulfur, showed nonequivalent methylene protons (25).

The syn and anti methyls of acetoxime and acetone 2,4-dinitrophenylhydrazone were assigned according to

Table I. Proton-^{13}C Couplings of Various Compounds[a]

Compound	$J_{^{13}CCH}$ (c.p.s.)
1. $(CH_3)_2{}^{13}C{=}O$	5.90
2. $(CH_3)_2{}^{13}C{=}NOH$	
syn	6.27[c]
anti	6.76[c]
3. $(CH_3)_2{}^{13}C{=}NNC_6H_3(NO_2)_2$-2,4	
syn	5.90[b]
anti	7.04[b]
4. $CH_3[C(CH_3)_3]{}^{13}C{=}O$	5.76
5. $CH_3[C(CH_3)_3]{}^{13}C{=}NNHC_6H_3(NO_2)_2$-2,4	6.40[b]
6. $CH_3{}^{13}CO_2H$	6.80
7. $CH_3{}^{13}CONH_2$	6.01
8. $CH_3{}^{13}COCl$	7.58
9. $CH_3{}^{13}COBr$	7.60
10. $CH_3{}^{13}COI$	7.30
11. $CH_3{}^{13}CO_2C_6H_4OCH_3$-p	7.00[b]
12. $CH_3{}^{13}CO_2C_6H_5$	7.04[b]
13. $CH_3{}^{13}CO_2C_6H_4NO_2$-p	7.16[b]
14. $CH_3{}^{13}CO_2CH_3$	4.00
15. $CH_3{}^{13}CO_2C_2H_5$	4.00
16. $CH_3{}^{13}CO_2CH(CH_3)_2$	4.00
17. $CH_3{}^{13}CO_2CH_2C(CH_3)_3$	4.00
18. $CH_3{}^{13}CO_2CH_2C_6H_5$	4.00
19. $CH_3{}^{13}CO_2CH[C(CH_3)_3]_2$	4.00
20. $CH_3{}^{13}CONHC_6H_5$	6.24[d]
21. $CH_3{}^{13}C[(CH_3)_3C]{=}CH_2$	6.40
22. $(CH_3)_2{}^{13}C(OH)C(CH_3)_3$	3.94
23. $(CH_3)_3{}^{13}COH$	4.25
24. $(CH_3)_3{}^{13}CI$	4.43

---

[a] Unless otherwise noted, spectra were taken in carbon tetrachloride solution.

[b] Benzene solution.

[c] 25% Benzene-75% carbon tetrachloride solution, v/v.

[d] 50% Benzene-50% dimethylsulfoxide solution, v/v.

Table II. Proton-^{13}C Couplings of $(CH_3)_3C^{13}C$ Compounds[a,e]

Compound	$J_{^{13}CCCH}$ (c.p.s.)	$J_{^{13}CH}$ (c.p.s.)
1. $R-^{13}CH_3$	4.65	123.3
2. $R-^{13}CH_2CD_2OH$	4.13	124.0
3. $R-^{13}CH_2CD_2OAc$	4.21	127.2
4. $R-^{13}CH_2CD_2Br$	4.36	131.0
5. $R-^{13}CH_2CO_2H$	4.44	126.4
6. $R-^{13}CH_2OH$	4.48[a,b,f]	139.9
7. $R-^{13}CH_2OAc$	4.83	146.1
8. $R-^{13}CH_2OCOC_6H_4OCH_3$-p	4.74	145.7
9. $R-^{13}CH_2OCOC_6H_5$	4.81	146.1
10. $R-^{13}CH_2OCOC_6H_4NO_2$-p	4.91	146.8
11. $R-^{13}CH_2OTs$	5.17	147.9
12. $(R-^{13}CH_2O)_2SO$	5.16	146.3
13. $R-^{13}CH_2OSOCl$	5.42	150.0
14. $R-^{13}CH_2OSi(CH_3)_3$	4.79	139.3
15. $R-^{13}CH_2N^+H_3ClO_4^-$	5.01[g]	143.0
16. $R-^{13}CH_2Cl$	5.63	147.9
17. $R-^{13}CH_2Br$	5.84	149.1
18. $R-^{13}CH_2I$	5.99	148.0
19. $R_2{}^{13}CHOH$	3.80	136.8
20. $R_2{}^{13}CHOAc$	3.99	147.5
21. $R-^{13}C(CH_3)_2OH$	3.59	
22. $R_3{}^{13}COH$	3.80	
23. $R_3{}^{13}COAc$	3.96	
24. $R-^{13}CH=CD_2$	4.23	
25. $R-^{13}C(CH_3)=CH_2$	4.00	
26. $R-^{13}CHO$	4.60	171.7
27. $R-^{13}COCH_3$	4.20	
28. $R_2{}^{13}CO$	3.72	
29. $R-^{13}CO_2H$	4.38	
30. $R-^{13}CO_2^-K^+$	4.36[g]	

Continued

Table II - Continued

Compound	$J_{^{13}CCCH}$ (c.p.s.)	$J_{^{13}CH}$ (c.p.s.)
31. $R\text{-}^{13}CO_2CH_3$	4.11	
32. $R\text{-}^{13}CO_2CH_2C(CH_3)_3$	4.10	
33. $R\text{-}^{13}CO_2C_6H_4OCH_3\text{-}p$	4.58	
34. $R\text{-}^{13}CO_2C_6H_5$	4.60	
35. $R\text{-}^{13}CO_2C_6H_4NO_2\text{-}p$	4.76	
36. $R\text{-}^{13}CONH_2$	4.07	
37. $R\text{-}^{13}CONHC_6H_5$	4.38	
38. $R\text{-}^{13}COCl$	5.99	
39. $R\text{-}^{13}COBr$	6.43	
40. $R\text{-}^{13}CH{=}NNHC_6H_3(NO_2)_2\text{-}2,4$	4.40	166.2
41. $R\text{-}^{13}C(CH_3){=}NNHC_6H_3(NO_2)_2\text{-}2,4$	3.91	
42. $R\text{-}^{13}CN$	5.38	

---

[a] Unless otherwise noted, spectra were taken in carbon tetrachloride solution.

[b] Benzene solution.

[c] 25% Benzene-75% carbon tetrachloride solution, v/v.

[d] 50% Benzene-50% dimethylsulfoxide solution, v/v.

[e] R stands for $(CH_3)_3C$-

[f] Dimethylsulfoxide solution.

[g] Deuterium oxide solution.

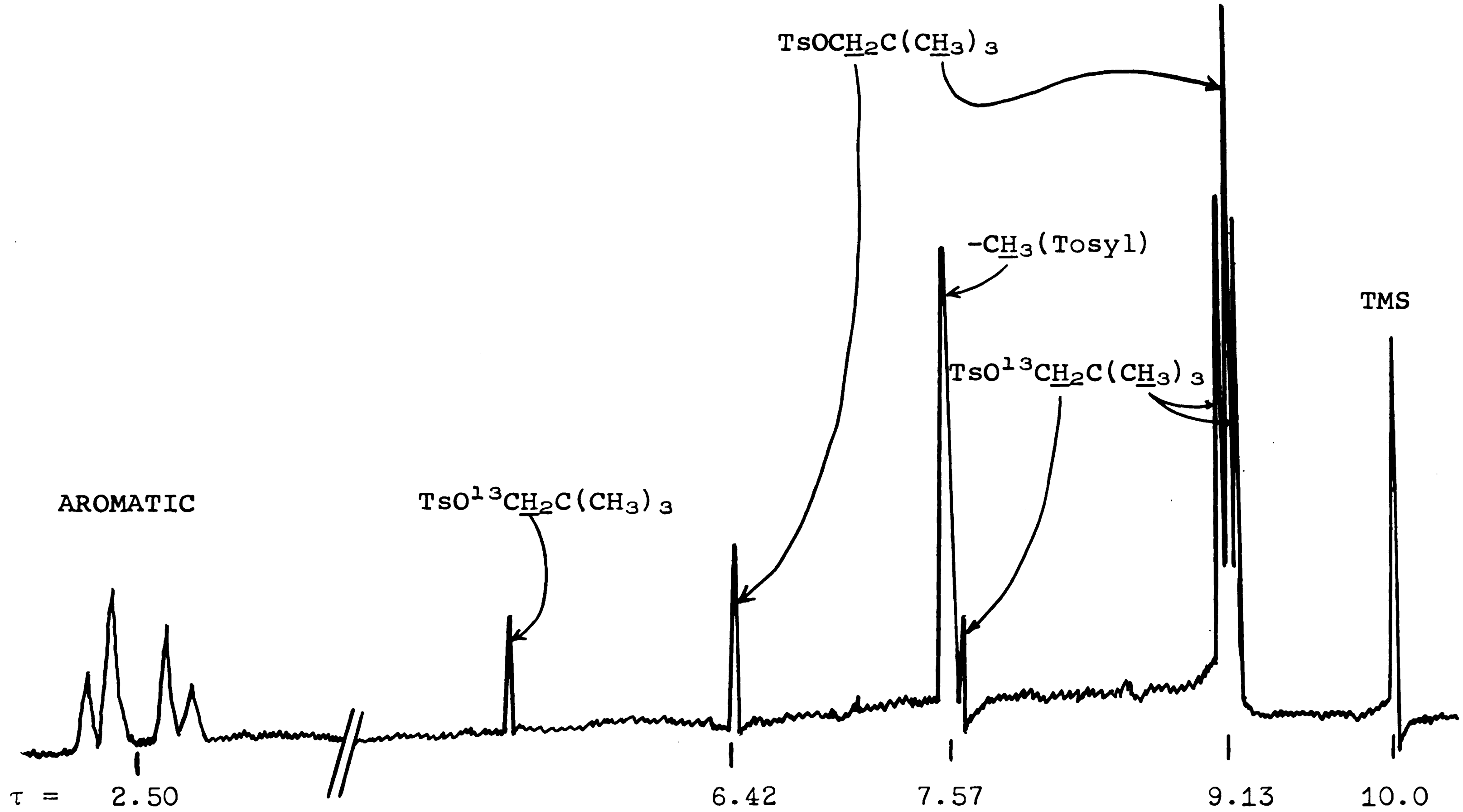


Figure 3. Proton n.m.r. spectrum of neopentyl-1-^{13}C (ca. 50%) tosylate in carbon tetrachloride.

Karabatsos and co-workers (26). The cis and trans hydrogens of styrene were assigned according to Pople _et al_. (27).

DISCUSSION

One-bond Coupling

As the electronegativity, X_a, of the group attached to the ^{13}C increases, $J_{^{13}CH}$ increases in a fairly linear fashion (since X_a's from various sources were used by necessity, some deviations are noted (see Figure 4)). Also, for the neopentyl-1-^{13}C benzoates, as the para substituent changes from methoxy to hydrogen to nitro, $J_{^{13}CH}$ changes linearly from 145.7 to 146.1 to 146.8 c.p.s. However, for the neopentyl-1-^{13}C halides $J_{^{13}CH}$ changes from 147.9 (chloro) to 149.1 (bromo) to 148.0 c.p.s. (iodo) in a non-linear fashion. Methyl halides show the same trend (1-9): 150 (chloro), 152 (bromo), 151 c.p.s. (iodo). This non-linear relationship has been previously interpreted (3) in terms of increases in the percent s-character of the carbon atomic orbital of the C-X bond as the C-X interatomic distance increases.

When the ^{13}C is sp^2 hybridized, $J_{^{13}CH}$ values are unusually high when a halogen or oxygen is bonded to it; e.g., for formyl fluoride (4) and methyl formate (4), $J_{^{13}CH}$ values are 267 and 226 c.p.s., respectively. That the effect may be detectable even when the halogen is not directly bonded to the ^{13}C is shown by the higher $J_{^{13}CH}$ values of ortho-substituted benzaldehydes when the ortho substituent is a group with

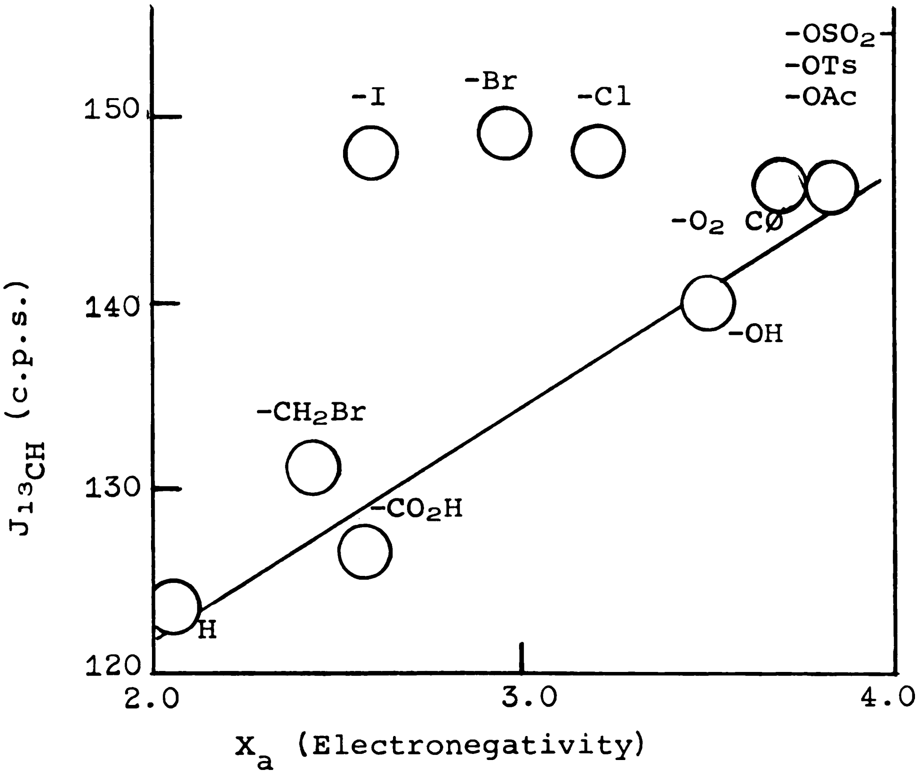


Figure 4. $J_{^{13}CH}$ of compounds of structure $(CH_3)_3C^{13}CH_2X$ versus electronegativity.

angular-dependent atomic orbitals (p,d,f); e.g., see compounds 1; 2,3, and 4; 5 and 6; 10 and 11; and 12, 13, and 14 of Table III. On the basis of the non-linear relationship between X_a and $J_{^{13}CH}$ for the halogens, the large couplings in some sp^2 compounds, and effects of ortho substituents on $J_{^{13}CH}$ of various benzaldehydes, it is evident that s-characters calculated from $J_{^{13}CH}$ can be unreliable and misleading when substituents having angular dependent orbitals are involved. Therefore, contact interaction may not be the only important coupling mechanism (27).

Two-bond Coupling

As one can see from Table I, $J_{^{13}CCH}$ follows s-character, i.e., as the electronegativity of the substituents increases $J_{^{13}CCH}$ increases, e.g., 1, 6, 7, 11, 12, and 13. This is what is to be expected from valence-bond theory (10,17,19). However, as in the case of the one-bond coupling, $J_{^{13}CCH}$ of the compounds containing substituents with angular-dependent atomic orbitals does not follow electronegativity, e.g., 8, 9, and 10. Here again, the contact interaction may not be the only coupling mechanism operative and fractional s-character cannot be obtained with certainty.

Table III. $J_{^{13}C\text{-aldehydic proton}}$ of Substituted Benzaldehydes

Compound	$J_{^{13}CH}$(c.p.s.)
1. C_6H_5CHO	174.4
2. o-$CH_3C_6H_4CHO$	173.2
3. m-$CH_3C_6H_4CHO$	173.7
4. p-$CH_3C_6H_4CHO$	173.2
5. o-ClC_6H_4CHO	182.1[a]
6. m-ClC_6H_4CHO	176.2
7. o-$CH_3OC_6H_4CHO$	179.8
8. m-$CH_3OC_6H_4CHO$	175.4
9. p-$CH_3OC_6H_4CHO$	172.7
10. o-BrC_6H_4CHO	182.4
11. m-BrC_6H_4CHO	177.6
12. o-FC_6H_4CHO	182.0
13. m-FC_6H_4CHO	177.7
14. p-FC_6H_4CHO	175.7
15. o-$C_2H_5OC_6H_4CHO$	180.2
16. p-HOC_6H_4CHO	177[b]

---

[a] All liquid samples run neat. Solids run in carbon tetrachloride solution.

[b] Value from Dr. G. J. Karabatsos.

Three-bond Coupling

From Table II the failure of a single factor (substituent electronegativity, angle deformation, hybridization) to accommodate the data is obvious. The most striking observations are: unusually high values for the halogen compounds; increase of these values in the order chloro < bromo < iodo, whereas the reverse order is expected (see para-substituted neopentyl benzoates and phenyl pivalates); and some higher values for sp^3 and sp^2 compounds than for the sp compound (compare 17, 18, 38, 39, and 42). This and the extensive variation of $J_{^{13}CCCH}$ (from 3.59 to 5.99 c.p.s. when the ^{13}C is sp^3 hybridized, 3.72 to 6.43 c.p.s. when sp^2 hybridized, and the value of 5.38 c.p.s. when sp hybridized) clearly indicates that in addition to the s-character of the ^{13}C hybrid atomic orbital, other factors must significantly affect this coupling. Also, if $J_{^{13}CH}$ is plotted versus $J_{^{13}CCCH}$ for the sp^3 neopentyl compounds (Figure 6), no linear relation is obtained. Since $J_{^{13}CH}$ follows electronegativity (Figure 1), except for the halogens, one can readily see that s-character is not the only important factor affecting $J_{^{13}CCCH}$. Increasing electronegativity should increase $J_{^{13}CCCH}$ by virtue of increasing the s-character (28) of the ^{13}C atomic orbital used in ^{13}C-C bond. The values obtained from the para-substituted neopentyl benzoates (entries 8, 9, and 10 in Table II) and phenyl pivalates (entries 33, 34, and 35), where the effects of factors other than electronegativity are kept constant,

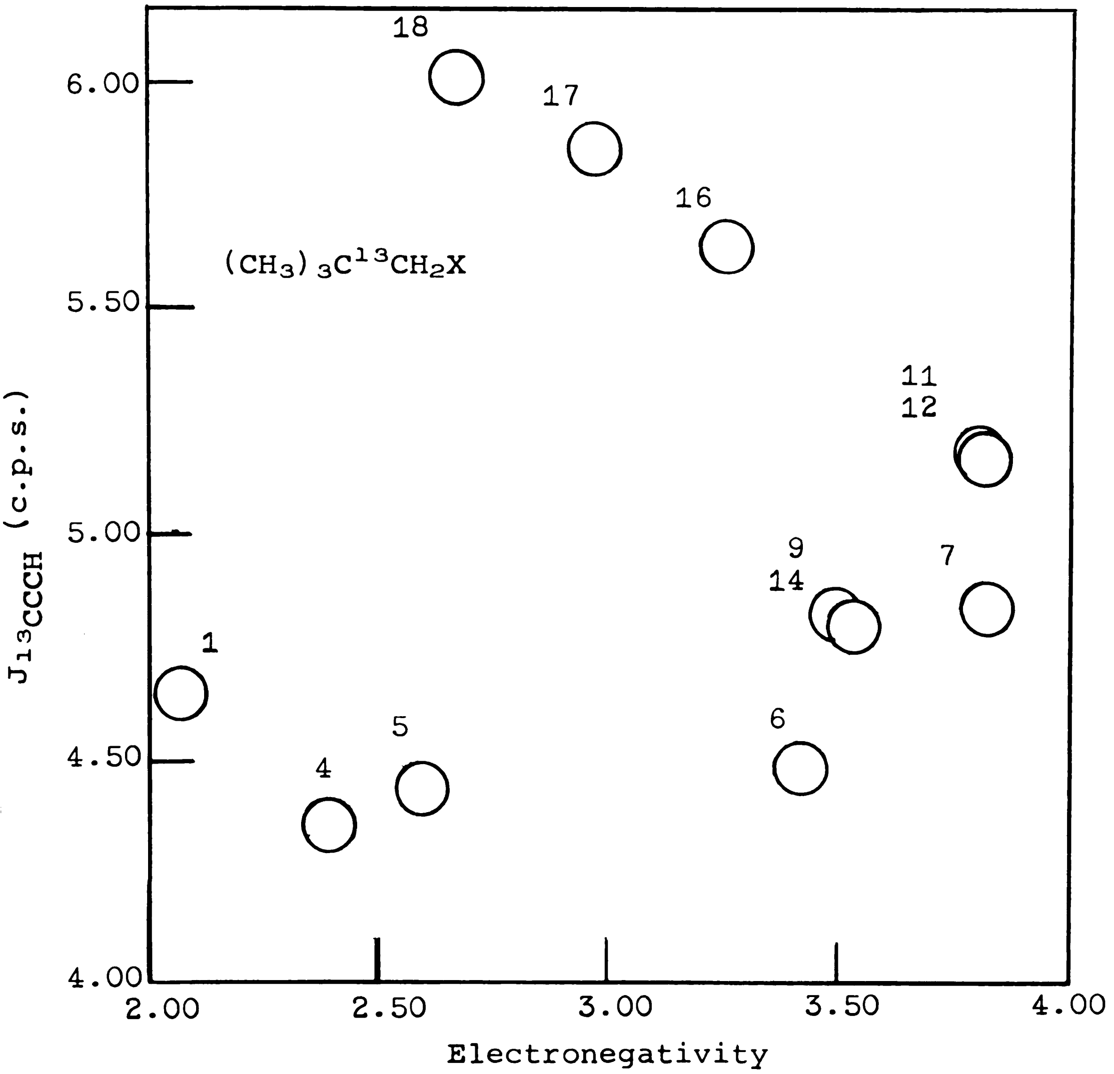


Figure 5. Three-bond proton-^{13}C coupling of neopentyl-1-^{13}C compounds versus substituent electronegativity.

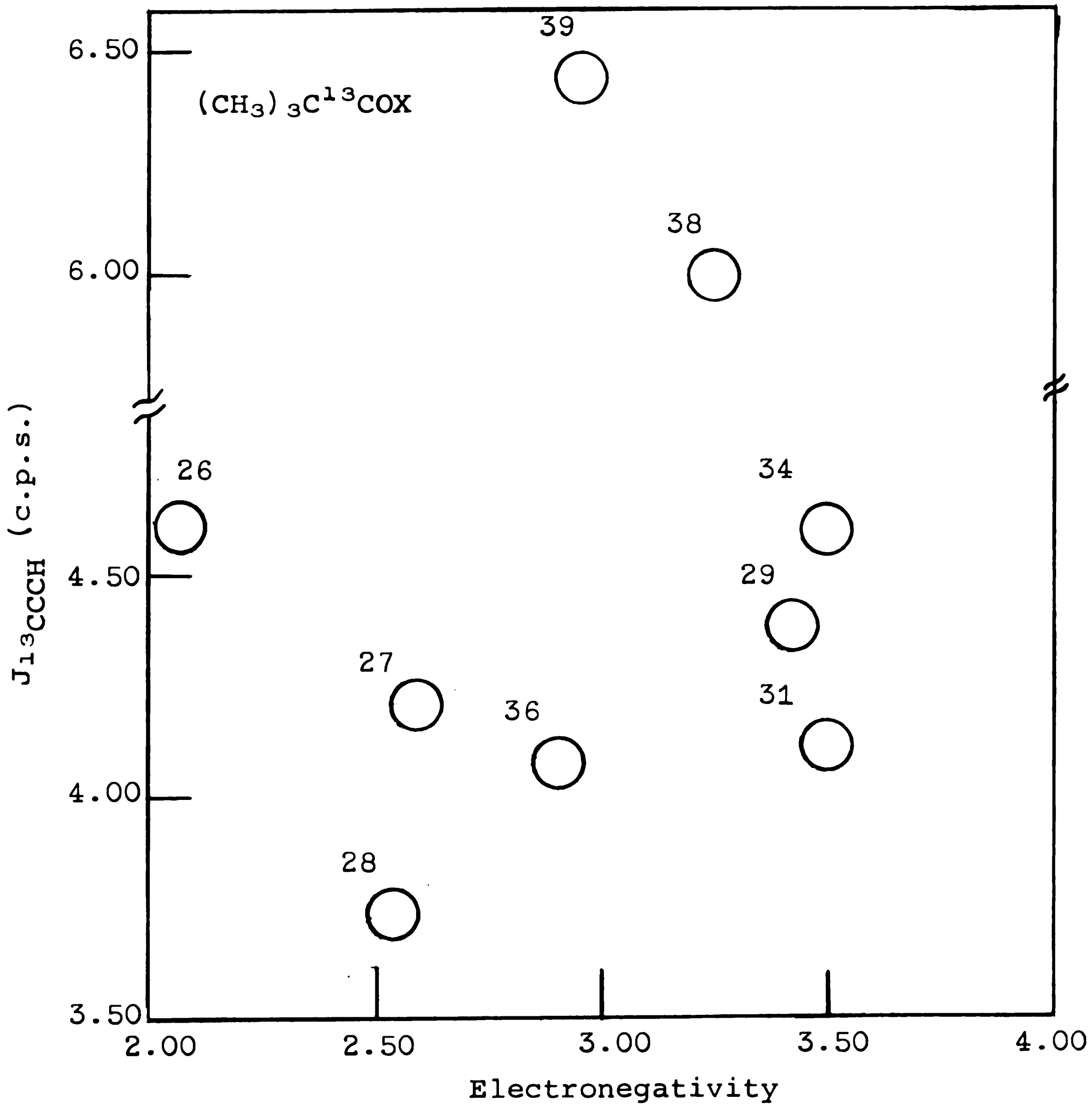


Figure 6. Three-bond proton-^{13}C coupling of trimethylacetyl (^{13}C=O) compounds versus substituent electronegativity.

Electronegativity references for figures 4, 5, and 6

Number (see Table II)	Group	Reference
1	H	105
4	CH_2Br	106
5	CO_2H	107
6	OH	107
7	OAc	108
9	$O_2CC_6H_5$	109
11	OTs	108
12	OSO_2	108
14	OSi	105
16	Cl	107
17	Br	107
18	I	107
26	H	105
27	CH_3	3
28	$C(CH_3)_3$	3
29	OH	107
31	OCH_3	110
34	OC_6H_5	110
36	NH_2	107
38	Cl	107
39	Br	107

Ω

v

d

i

c

a

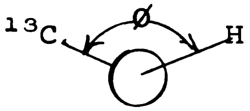
va

sh

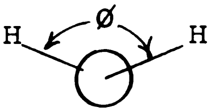
bear out this prediction. The contribution of electronegativity can be readily masked by the effects of other factors.

Possible factors which cause this non first-order dependence of $J_{^{13}CCCH}$ on s-character might be:

(A) Dihedral Angle. - Although the dependence of $J_{^{13}CCCH}$ on ϕ(III) has yet to be experimentally demonstrated, it is

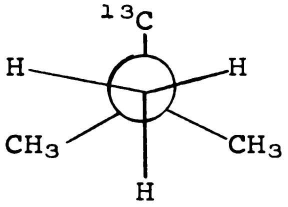


III

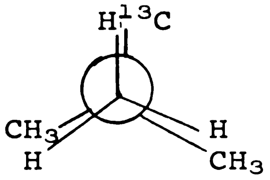


IV

reasonable to assume that the relation between J_{HCCH} and ϕ(IV) (29) qualitatively applies to $J_{^{13}CCCH}$ and ϕ(III). Any variation in the present data, however, as a result of such dependence can be readily discounted. First, it is highly improbable that any of the compounds examined exists in conformations other than V. Second, even if extreme conformational differences (ranging from V to VI) existed between the



V



VI

various compounds, the experimentally determined constants should be independent of conformation. Consider J_{HCCH} of a

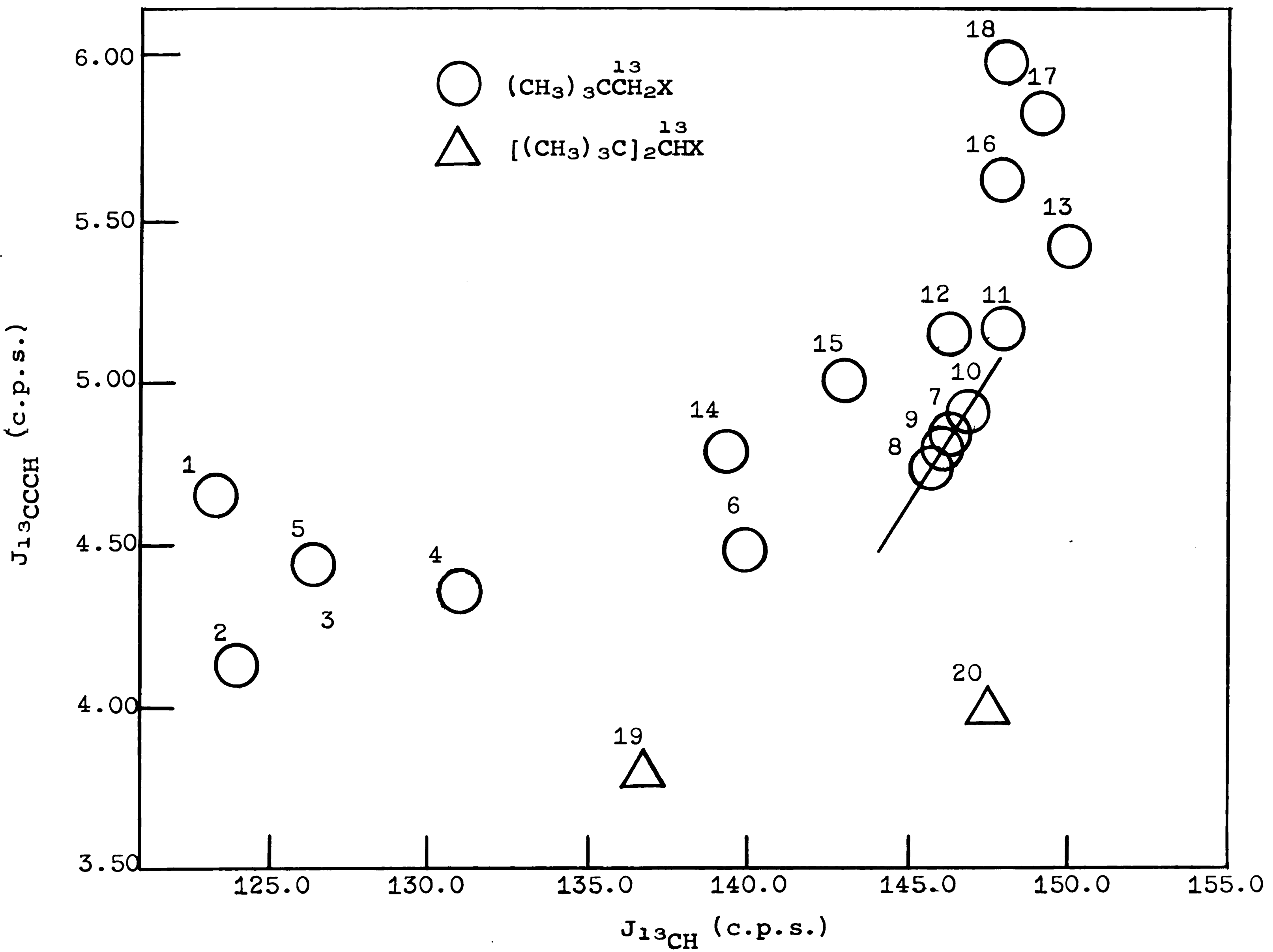


Figure 7. One-bond proton-^{13}C coupling versus three-bond proton-^{13}C coupling of neopentyl-1-^{13}C compounds.

C

t

th

in

J_{HC}

θ'

for

θ a

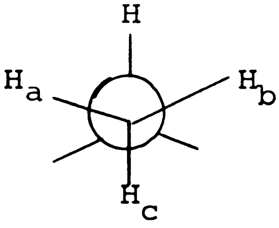
known

made

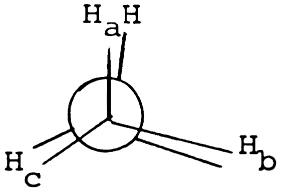
The m

attach

CH_3CH group as the conformation varies from VII (staggered) to VIII (eclipsed). Using equation 2 (29) one finds that



VII

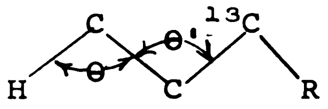


VIII

$$J_{HH'} = A + B\cos\emptyset + C\cos 2\emptyset \qquad (2)$$

the average coupling, J_{HH}(avg.) = $(J_{HH_a} + J_{HH_b} + J_{HH_c})/3$, is independent of conformation.

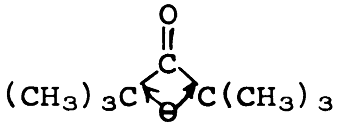
(B) Angle θ and θ'. - Vicinal proton-proton couplings, $J_{HCC'H'}$ decrease with increase in angles θ and θ' (θ = < HCC', θ' = < HC'C) (27,29-35). It is reasonable to assume, therefore, that $J_{^{13}CCCH}$ might be affected similarly by changes in θ and θ' (θ = < HCC, θ' = $<^{13}$CCC. Although θ and θ' are not



IX

known for the compounds studied, reasonable guesses can be made as to what structural features might increase these angles. The most plausible feature is increase in the size of groups attached to the ^{13}C, e.g., as R increases in size (IX), θ and

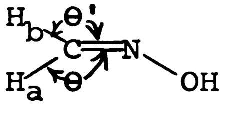
θ' should increase on account of nonbonded repulsions. On this assumption several trends and apparent inconsistencies in the data can be qualitatively accounted for. For example, compare the rather large coupling of neopentane (small repulsions) with the relatively small couplings of all other compounds (large repulsions). Specifically, compare entries (Table II) 1, 19, 21, and 22; 24 and 25; 26, 27, and 28; and 40 and 41. From the low carbonyl stretching frequency of di-t-butyl ketone it was suggested (36) that θ(X) should be 130-137°. Such an angle requires an s-character of 0.39-0.42 for the ^{13}C atomic orbital used in the ^{13}C-C bond. Assuming the ^{13}C atomic orbital of neopentane to have 0.25 s-character, and using contact interaction, a coupling constant of 7.3-7.8 c.p.s. is calculated for di-t-butyl ketone. The experimental value is only 3.72 c.p.s. It would seem, therefore, that $J_{^{13}CCCH}$ is extremely sensitive to θ and θ'.



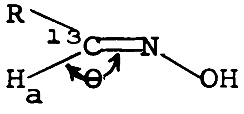
X

(C) Bent Bonds. - Theoretical and experimental investigations have recently emphasized that the maximum electron density of a sigma-bond may not lie along the internuclear straight line (37-41). Although the effect of bond bending on spin-spin coupling has not been evaluated, it is reasonable to expect that it would decrease contact contribution. With respect to the data discussed, bond bending would introduce the same effects as increases in angles Θ and Θ'.

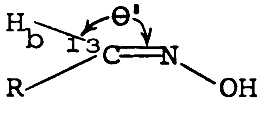
The following data seem to be best interpreted if certain bonds are assumed to be bent. From the values (42) of $\Theta(121^{\circ}46')$ and $\Theta'(115^{\circ}33')$ of formaldoxime (XI) the



XI



XII



XIII

s-characters of the carbon atomic orbitals used in the C-H_a and C-H_b bonds are 0.40 and 0.31. $J_{^{13}CH_a}$ should therefore be larger than $J_{^{13}CH_b}$ by about 30%. Yet, from XII and XIII, $J_{^{13}CH_a}$ (162 c.p.s.) $<$ $J_{^{13}CH_b}$ (174 c.p.s.) (43). The assumption is made that Θ(XII) $>$ Θ' (XIII). Similarly, for vinyl chloride (XIV) $J_{^{13}CH_a}$ (160 c.p.s.) $<$ $J_{^{13}CH_b}$ (161 c.p.s.) although, based on the 0.34 and 0.32 s-characters ($\Theta = 121^{\circ}1'$ and $\Theta' = 119^{\circ}\ 32'$) (45) of the carbon atomic orbitals used in the C-H_a and C-H_b bonds, $J_{^{13}CH_a}$ should be greater than $J_{^{13}CH_b}$ by about 6%. Smaller $J_{^{13}CH_b}$ values have been also observed for XV, $J_{^{13}CH_a} = 156$ c.p.s. and $J_{^{13}CH_b} = 178$ c.p.s. (46). The above results can be satisfactorily rationalized if, as a result of nonbonded repulsions, the C-H_a bond is assumed to be bent. In addition to decreasing $J_{^{13}CH_a}$ such bending should lead to internuclear Θ values that are larger than the interhybrid ones. In the course of this work proton-^{13}C coupling constants were measured for styrene (XVI), acetone oxime r

a

o

b

7

c.

(5

Th

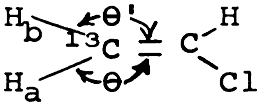
13

co

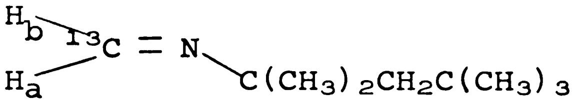
e.g

cre

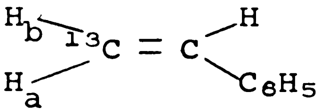
(XVII), and acetone 2,4-dinitrophenylhydrazone (XVIII) (see Table IV).



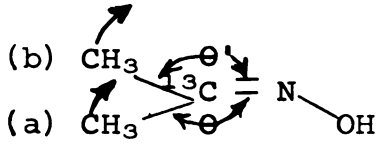
XIV



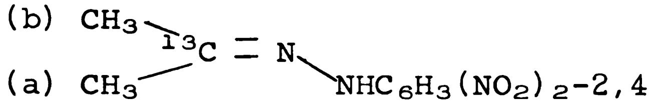
XV



XVI



XVII



XVIII

Consistent with the bent bond concept are several long-range proton-^{13}C couplings. From $\theta(131^{o})$ and $\theta'(113^{o})$ of acetoxime (47) (XVII) and s-characters of the ^{13}C atomic orbitals used in the ^{13}C-CH_3(a) and ^{13}C-CH_3(b) bonds should be 0.42 and 0.21. Consequently, $J_{^{13}CCH_a}$ should be about 7.5 c.p.s. and $J_{^{13}CCH_b}$ about 3.8 c.p.s. Yet, $J_{^{13}CCH_a}$ (6.27 c.p.s.) $<$ $J_{^{13}CCH_b}$ (6.76 c.p.s.). Similar values, $J_{^{13}CCH_a}$ (5.90 c.p.s.) $<$ $J_{^{13}CCH_b}$ (7.04 c.p.s.), are obtained for XVIII. These results can again be rationalized by assuming that the ^{13}C-CH_3 bonds are bent in the direction shown in XVII.

Table IV summarizes a few more long-range proton-^{13}C couplings that are consistent with the concept of bent bonds; e.g., as the nonbonded repulsions between alkyl groups increase the coupling decreases.

Table IV. Proton-^{13}C Couplings of Various Compounds

Compound	$J_{^{13}C-CH_3}$ (c.p.s.)	$J_{^{13}C-C-CH_3}$ (c.p.s.)
1. $(CH_3)_3C^{13}CH_2OH$		4.48
2. $(CH_3)_3{}^{13}COH$	4.25	
3. $[(CH_3)_3C]_3{}^{13}COH$		3.80
4. $(CH_3)_3C^{13}C(CH_3)_2OH$	3.94	3.59
5. $(CH_3)_3C^{13}CHO$		4.60
6. $(CH_3)_3C^{13}C(CH_3)=O$	5.76	4.20
7. $(CH_3)_2{}^{13}C=O$	5.90	
8. $[(CH_3)_3C]_2{}^{13}C=O$		3.72
9. $(CH_3)_2{}^{13}C=NOH$		
syn	6.27	
anti	6.76	
10. $(CH_3)_2{}^{13}C=NNHC_6H_3(NO_2)_2$-2,4		
syn	5.90	
anti	7.04	

v

2

Er

ac

sc

of

EXPERIMENTAL

Acetoxime ($^{13}C=N$) (48)

To 0.50 g. (0.0086 mole) of acetone was added 2.09 g. (0.030 mole) of hydroxylamine hydrochloride in 6 ml. of water and 1.40 g. (0.025 mole) of potassium hydroxide in 4 ml. of water. The mixture was heated on a steam bath for 10 min., cooled, saturated with sodium chloride, and extracted with three 50 ml. portions of ether. The ether was dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. The remaining acetoxime was sublimed. Yield: 0.49 g. (77.8%); m.p. 61°.

Acetone-2,4-dinitrophenylhydrazone ($^{13}C=N$)

To a solution of 2,4-dinitrophenylhydrazine reagent (49) was added 5 drops of acetone. The resulting solid was washed with cold ethanol and vacuum dried.

2,4-Dinitrophenylhydrazine reagent

To 0.4 g. of 2,4-dinitrophenylhydrazine in a 25 ml. Erlenmeyer flask was added 2 ml. of concentrated sulfuric acid. Water (3 ml.) was added dropwise, with swirling until solution was complete. To this warm solution was added 10 ml. of 95% ethanol (49).

t-Butylmethyl ketone ($^{13}C=O$)

To a 1 ml. carbon tetrachloride solution of 2,3,3-trimethyl-2-^{13}C-butene-1, prepared in a previous experiment, was added 15 ml. of methylene chloride. The solution was cooled to -30° and ozone was bubbled in until a blue solution persisted for 5 min. The solution was hydrolyzed with a small amount of 30% hydrogen peroxide and 5% hydrochloric acid. The methylene chloride solution was dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. The small amount of ketone remaining was pulled over under vacuum (1 mm of Hg) into a trap cooled in liquid nitrogen.

t-Butyl methyl ketone-2,4-dinitrophenylhydrazone ($^{13}C=N$)

To a portion of 2,4-dinitrophenylhydrazine reagent (49) solution were added a few drops of the *t*-butyl methyl ketone ($^{13}C=O$). The precipitate was filtered, washed with cold ethanol and vacuum dried.

Acetic acid-1-^{13}C

To 24.31 g. (1.00 mole) of magnesium metal in 600 ml. of ether was added dropwise 118.3 g. (0.83 mole) of methyl iodide with a crystal of iodine to initiate the reaction. After forming the Grignard reagent at 0°, carbon dioxide-^{13}C (30% enriched) was bubbled into it at 0°. The carbon dioxide was generated by dropping 136.8 g. (1.36 moles) of 70%

perchloric acid on 107.6 g. (0.545 mole) of 30% enriched barium carbonate-^{13}C. The reaction mixture was warmed to room temperature, hydrolyzed with 10% hydrochloric acid, saturated with sodium chloride, dried over anhydrous magnesium sulfate, and distilled. Yield: 20.15 g. (61.4%).

Acetamide (^{13}C=O)

To 5 drops of acetyl-1-^{13}C bromide was added excess concentrated ammonium hydroxide. The aqueous solution was used as such.

Acetyl-1-^{13}C bromide (50)

To 2.0 g. (0.034 mole) of acetic-1-^{13}C acid was added 9.2 g. (0.034 mole) of phosphorus tribromide. After heating for 1 hr. on a steam bath and cooling, the top layer was removed and used as such.

Acetyl-1-^{13}C chloride

See acetyl-1-^{13}C bromide for procedure. Phosphorus trichloride and a 0.038 mole quantity of acetic acid were used.

Acetyl-1-^{13}C iodide

A mixture of 2.02 g. (0.034 mole) of acetic-1-^{13}C acid and 4.60 g. (0.011 mole) of phosphorus triiodide (51) was heated on a steam bath for 1 hr. After cooling, the top layer contained 45% iodide and 55% acid. The mixture was used as such.

Phenyl acetate (^{13}C=O)

To 0.25 g. (0.0032 mole) of acetyl-1-^{13}C chloride was added 0.30 g. (0.0032 mole) of phenol. The mixture was heated on a steam bath for 1 hr., extracted with 25 ml. of ether, washed with 10% sodium carbonate solution, dried over anhydrous magnesium sulfate, filtered, and the ether evaporated on a steam bath. The remaining acetate was used without further purification.

p-Methoxyphenyl acetate (^{13}C=O)

See phenyl acetate (^{13}C=O) for procedure. The same mole quantities were used.

p-Nitrophenyl acetate (^{13}C=O)

See phenyl acetate (^{13}C=O) for procedure. The same mole quantities were used.

N-Phenylacetamide (^{13}C=O)

See phenyl acetate (^{13}C=O) for procedure. Aniline and the same mole quantities were used.

t-Butyl alcohol (^{13}COH)

To 10.13 g. (0.17 mole) of acetic acid-1-^{13}C in 100 ml. of ether was added 320 ml. of ether solution of diazomethane (52) prepared from 32.6 g. (0.316 mole) of N-methyl-N-nitrosourea. After drying with anhydrous magnesium sulfate, this solution was added to a solution of methyl magnesium iodide prepared from 12.3 g. (0.51 mole) of magnesium metal and 72.0 g. (0.507 mole) of methyl iodide. One liter of ether was used to make the Grignard reagent. The reaction mixture was hydrolyzed with 81 ml. of an aqueous saturated ammonium chloride solution. After drying with anhydrous magnesium sulfate the ether and alcohol were separated by fractional distillation.

Methyl acetate-1-^{13}C

See *t*-butyl alcohol (^{13}COH) for procedure.

Alkyl and aryl acetates (^{13}C=O)

The following acetates were prepared by adding a slight excess of the alcohol to a few drops of acetyl-1-^{13}C chloride and warming at 50° for $\frac{1}{2}$ hr.: ethyl, 2-propyl, neopentyl, benzyl, and di-*t*-butylcarbinyl. The reaction mixtures were cooled and used as such.

2,3,3-Trimethyl-2-^{13}C-butene-1

To 0.80 g. (0.0069 mole) of 2,3,3-trimethyl-2-butanol-2-^{13}C was added 5.4 g. (0.0043 mole) of oxalyl chloride and 10 ml. of quinoline. To the oil-bath heated vessel was attached a trap cooled in liquid nitrogen. By heating to 150° all of the olefin formed was caught in the cold trap. It was taken up in 1 ml. of carbon tetrachloride and used as such.

2,3,3-Trimethyl-2-butanol-2-^{13}C

To 4.26 g. (0.03 mole) of methyl iodide in 100 ml. of ether was added 0.73 g. (0.03 mole) of magnesium turnings at room temperature. After the Grignard reagent was formed, it was added to 1.04 g. (0.009 mole) of methyl trimethylacetate-1-^{13}C in 250 ml. of ether. The reaction mixture was hydrolyzed with 10 ml. of saturated ammonium chloride solution. The ether was decanted from the solid, the solid was washed three times with 50 ml. portions of ether, and the ether solutions were combined and dried over anhydrous magnesium sulfate. Fractional distillation gave 0.80 g. (77.0%) of the alcohol.

t-Butyl iodide (^{13}C-I)

To 0.5 ml. of *t*-butyl alcohol (^{13}COH) was added 3 ml. of 47% hydroiodic acid. The mixture was heated on a steam bath for 5 min. and cooled. The upper layer was dried over anhydrous potassium carbonate and used as such.

Neopentane (-^{13}CH)

To 1.00 g. (0.0065 mole) of neopentyl-1-^{13}C bromide in 25 ml. of tetrahydrofuran was added 0.16 g. (0.0065 mole) of magnesium turnings. By initiating with an iodine crystal and heating to 50° the Grignard reagent was formed. Addition of a small amount of 5% sulfuric acid dissolved all the solids. The mixture was fractionally distilled with only the first milliliter being collected in a liquid nitrogen cooled trap and added to 1 ml. of carbon tetrachloride. The solution was stored in a sealed ampoule.

3

i

d

A

l

c

fr

3,

d_2

Th

an

3,3

d_2-

of

was

wate

and

ing

used

3,3-D

300 r

3,3-Dimethylbutanol-1,1-$\underline{d}_2$-2-^{13}C

To 1.87 g. (0.045 mole) of lithium aluminum deuteride in 200 ml. of ether was added 3.50 g. (0.032 mole) of 3,3-dimethylbutyric-2-^{13}C acid in 100 ml. of ether at 0°. After refluxing for 1 hr. the reaction mixture was hydrolyzed with 6 ml. of 5% sulfuric acid. The ether was decanted off, dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. Yield: 2.92 g. (91%).

3,3-Dimethylbutyl-1,1-$\underline{d}_2$-2-^{13}C acetate

To 1.00 g. (0.0096 mole) of 3,3-dimethylbutanol-1,1-$\underline{d}_2$-2-^{13}C was added 0.79 g. (0.01 mole) of acetyl chloride. The mixture was heated on a steam bath for 1 hr., cooled, and used as such.

3,3-Dimethylbutyl-1,1-$\underline{d}_2$-2-^{13}C bromide

To 0.69 g. (0.0066 mole) of 3,3-dimethylbutanol-1,1-$\underline{d}_2$-2-^{13}C in 5 ml. of benzene was added 0.60 g. (0.0022 mole) of phosphorus tribromide in 5 ml. of benzene. The mixture was refluxed for 1 hr., the benzene layer was washed with water, dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. The remaining material containing some benzene was taken up in carbon tetrachloride and used as such.

3,3-Dimethylbutyric-2-^{13}C acid

To 6.10 g. (0.040 mole) of neopentyl-1-^{13}C bromide in 300 ml. of ether was added 1.08 g. (0.045 mole) of magnesium metal. After formation of the Grignard reagent at room temperature, anhydrous carbon dioxide was bubbled in until reaction ceased. All solid material was dissolved with concentrated hydrochloric acid. The ether was removed, dried over anhydrous magnesium sulfate, filtered and fractionally distilled. Yield: 3.50 g. (71.5%).

See PART II EXPERIMENTAL for the following compounds:

Trimethylacetic-1-^{13}C acid
Neopentyl-1-^{13}C alcohol
Neopentyl-1-^{13}C tosylate
Neopentyl-1-^{13}C iodide
Neopentyl-1-^{13}C chloride
Neopentyl-1-^{13}C-ammonium perchlorate
Trimethylacetamide-1-^{13}C
Trimethylacetonitrile-1-^{13}C
Di-_t_-butylketone (see trimethylacetic-1-^{13}C acid)
Tri-_t_-butyl carbinol (see trimethylacetic-1-^{13}C acid)

Neopentyl-1-^{13}C acetate

To 0.50 g. (0.0057 mole) of neopentyl-1-^{13}C alcohol was added 0.42 g. (0.0057 mole) of acetyl chloride. The mixture was refluxed on a steam bath for 1 hr., dissolved in 50 ml. of ether, and washed with 10% sodium carbonate solution. The ether was dried over anhydrous magnesium sulfate, filtered, and fractionally distilled from the acetate. The acetate was collected under vacuum (1 mm.) in a trap cooled in liquid nitrogen. Yield: 0.50 g. (68.0%).

Neopentyl-1-^{13}C p-methoxybenzoate

To 0.50 g. (0.0057 mole) of neopentyl alcohol was added 0.97 g. (0.0056 mole) of freshly distilled p-methoxybenzoyl chloride, b.p. 105-107° (1 mm.). The mixture was heated on a steam bath for 1 hr., cooled, dissolved in ether and washed with 10% sodium carbonate solution. The ether solution was dried over anhydrous magnesium sulfate, filtered, and evaporated on a steam bath. The resulting oil was distilled under vacuum (1 mm.) in a short-path apparatus.

Neopentyl-1-^{13}C benzoate

To 0.50 g. (0.0057 mole) of neopentyl alcohol was added 0.80 g. (0.0057 mole) of benzoylchloride. The mixture was heated for 2 hrs. on a steam bath, cooled, taken up into carbon tetrachloride, and used as such.

Neopentyl-1-^{13}C p-nitrobenzoate

To 0.50 g. (0.0057 mole) of neopentyl alcohol was added 1.05 g. (0.0057 mole) of p-nitrobenzoyl chloride. The mixture was heated on a steam bath for 24 hrs., cooled, and crystallized from ethanol. M.p.: 54°.

Neopentyl-1-^{13}C sulfite (53)

To 0.50 g. (0.0057 mole) of neopentyl alcohol and 0.45 g. (0.0057 mole) of pyridine in 2.0 ml. of ether was added dropwise at -15° 0.34 g. (0.0028 mole) of thionyl chloride in 1.5 ml. of ether. The reaction mixture was warmed to room temperature, washed with water, dried with anhydrous magnesium sulfate, filtered and fractionally distilled. The remaining sulfite was used as such.

Neopentyl-1-^{13}C chlorosulfite (53)

To 0.50 g. (0.0057 mole) of neopentyl alcohol in 1.5 ml. of ether was added dropwise at -15° 1.07 g. (0.009 mole) of thionyl chloride. The reaction mixture was warmed to 70° over a 1 hr. period, cooled, and fractionally distilled. The remaining chlorosulfite was used without further purification.

Neopentyl-1-^{13}C trimethylsilyl ether (54)

To 0.50 g. (0.0057 mole) of neopentyl-1-^{13}C alcohol was added 0.62 g. (0.0057 mole) of trimethylsilyl chloride and 0.45 g. (0.0057 mole) of pyridine. The reaction mixture was heated on a steam bath for ½ hr., cooled, taken up into 50 ml. of ether, and washed with 10% sodium carbonate and 5% hydrochloric acid. The ether was then dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. The remaining silyl ether was used as such.

Neopentyl-1-^{13}C bromide

To 10.66 g. (0.12 mole) of neopentyl-1-^{13}C alcohol was added 20.60 g. (0.12 mole) of benzyl bromide and 37.50 g. (0.12 mole) of triphenylphosphite. The mixture was kept at

140° for 46 hrs. After cooling, the mixture was vacuum distilled into a trap cooled in liquid nitrogen. The product was taken up into 250 ml. of ether, washed with 10% sodium hydroxide, dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. No yield was recorded.

Di-*t*-butylcarbinol (^{13}CHOH)

To 0.38 g. (0.01 mole) of lithium aluminum hydride in 25 ml. of ether was added dropwise, at 0°, 0.26 g. (0.0018 mole) of di-*t*-butyl ketone in 25 ml. of ether. The reaction mixture was heated to reflux for 1 hr., cooled, and hydrolyzed with 5% sulfuric acid. The ether solution was dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. The remaining alcohol was purified by v.p.c. on the 10 ft. Carbowax 20M column.

Di-*t*-butylcarbinyl acetate ($^{13}\mathrm{C{-}O{-}}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}$)

To a few drops of acetyl chloride were added a few drops of di-*t*-butylcarbinol (^{13}COH). After warming at 50° for a few minutes, the reaction mixture was cooled and used as such.

Tri-*t*-butylcarbinyl acetate ($^{13}\mathrm{C{-}O{-}}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}$)

This compound was prepared in the same way as the di-*t*-butylcarbinyl acetate ($^{13}\mathrm{C{-}O{-}}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}$).

t-Butylethylene-1-^{13}C-2,2-d_2

To 1.4 g. (0.0096 mole) of 3,3-dimethylbutyl-1,1-d_2-2-^{13}C acetate was added 25 ml. of benzene. This mixture was percolated through a glass helices packed column heated at 500°. The bottom of the column was connected to a one-necked ₮ 24/40 500 ml. round-bottomed flask which was cooled in liquid nitrogen. After the product and benzene were collected and transferred to a small fractional distillation set-up, the olefin was distilled off from the benzene. A small amount was obtained and was taken up in carbon tetrachloride.

Trimethylacetaldehyde (^{13}C=O) (55)

Dry nitrogen gas was slowly passed (15 cc./min.) over 2 g. of neopentyl alcohol entraining it into a 10 in. x 3/4 in. I.D. Vycor tube. The tube was tightly packed with copper turnings and placed in a tube furnace at 315°. The resulting aldehyde was entrained into a trap cooled in liquid nitrogen. A 100% yield of aldehyde was obtained.

Methyl trimethylacetate-1-^{13}C

To 1.00 g. (0.01 mole) of trimethyl-1-^{13}C acid in 10 ml. of ether was added a 100 ml. ether solution of diazomethane (52) prepared from 2.06 g. (0.02 mole) of N-methyl-N-nitrosourea. The ether was dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. The remaining ester was used as such.

Neopentyl trimethylacetate (^{13}C=O)

To 0.5 g. (0.0041 mole) of trimethylacetyl-1-^{13}C chloride was added 0.36 g. (0.0041 mole) of neopentyl alcohol.

The mixture was heated on a steam bath for 1 hr. and cooled. The material was used without further purification.

Phenyl trimethylacetate ($^{13}C=O$)

To 0.16 g. (0.001 mole) of trimethylacetyl bromide ($^{13}C=O$) was added 0.09 g. (0.001 mole) of phenol. The mixture was heated on a steam bath for 1 hr., taken up into carbon tetrachloride, and used as such.

p-Methoxyphenyl trimethylacetate ($^{13}C=O$)

The same procedure and mole amounts were used as in the synthesis of phenyl trimethylacetate ($^{13}C=O$).

p-Nitrophenyltrimethylacetate ($^{13}C=O$)

The same procedure and mole amounts were used as in the synthesis of phenyl trimethylacetate ($^{13}C=O$).

N-Phenyl trimethylacetamide-1-^{13}C

To 0.10 g. (0.00083 mole) of trimethylacetyl-1-^{13}C chloride was added 0.16 g. (0.0017 mole) of aniline. The mixture was heated on a steam bath for 5 min., cooled, extracted with ether and washed with water. The ether was dried with anhydrous magnesium sulfate, filtered, and removed on a steam bath. The resulting solid was used as such.

Trimethylacetyl chloride ($^{13}C=O$)

To 1.04 g. (0.01 mole) of trimethyl acetic acid was added 1.33 g. (0.01 mole) of thionyl chloride. The reaction mixture was heated on a steam bath for 1 hr., cooled, and used without further purification.

Trimethylacetyl bromide ($^{13}C=O$)

To 0.77 g. (0.0075 mole) of trimethylacetic acid was added 0.68 g. (0.0025 mole) of phosphorus tribromide. After heating on a steam bath for 1 hr., the reaction mixture was extracted with ether and the ether was fractionally distilled. The remaining acid bromide was used as such.

Trimethylacetaldehyde-2,4-dinitrophenylhydrazone ($^{13}C=N$) (49,56)

To a solution of 2,4-dinitrophenylhydrazine reagent were added 5 drops of trimethylacetaldehyde. The resulting solid was washed with some cold ethanol and vacuum dried.

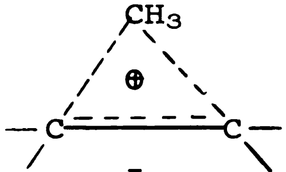
PART II

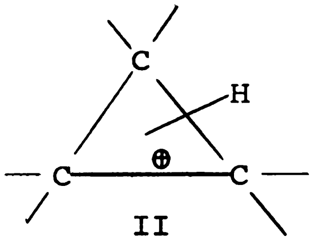
CARBONIUM ION REARRANGEMENTS IN THE n-PROPYL AND NEOPENTYL SYSTEMS

INTRODUCTION

In reactions which are known to generate carbonium ions the neopentyl system always gives products resulting from the t-amyl cation. The deamination of the amine (57,58), solvolysis of the tosylate (57-59), solvolysis of the chloride (58) and iodide (60), deoxidation of the alcohol (57), and bromination of the alcohol with hydrobromic acid (61) all lead to t-amyl products and iso-pentenes. Thus, it appears that in the neopentyl system, the Wagner-Meerwein rearrangement leading to a tertiary cation from a primary one is completely favored over nucleophilic attack on the primary cation.

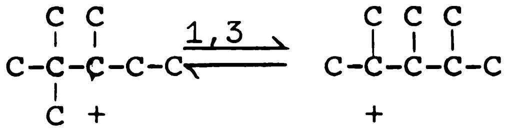
It has been suggested (59,62-68) that many carbonium ion rearrangements proceed by way of methyl-bridged non-classical carbonium ions (I). Protonated cyclopropane intermediates (57,69-72) (II) have also been postulated since


I


II

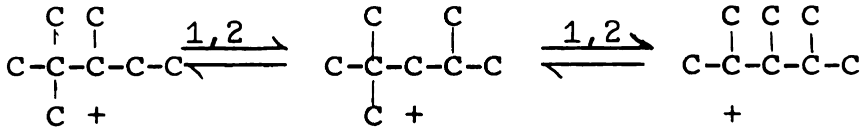
cyclopropanes are found to be products of many of these reactions (57,62,68,73,74). The intermediacy of protonated cyclopropanes in gas-phase ionic decompositions in the mass spectrometer is well documented (72,75,76). The suggestion that such species may intervene as intermediates in liquid-phase carbonium ion rearrangements, however, has not been substantiated. Evidence for methyl-bridged non-classical carbonium ions (64,67,68) and protonated cyclopropanes (70-72) has been none too plentiful and evidence against them in many systems (58,61,77,78) has been given.

The occurrence of Wagner-Meerwein 1,3-shifts in open-chain systems has eluded unambiguous confirmation. Such shifts have been proposed (79-81) in mechanistic interpretations of product formation in carbonium ion reactions, e.g., (1) has been suggested (79). However, the products can always be rationalized equally well by postulating successive 1,2-shifts, (2). Nevertheless, the reported 1,3-hydride



$$\mathrm{C{-}\overset{C}{\underset{C}{C}}{-}\overset{C}{\underset{+}{C}}{-}C{-}C} \xrightleftharpoons{1,3} \mathrm{C{-}\overset{C}{\underset{+}{C}}{-}\overset{C}{C}{-}\overset{C}{C}{-}C}$$

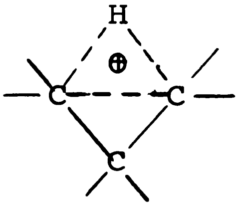
(1)



$$\mathrm{C{-}\overset{C}{\underset{C}{C}}{-}\overset{C}{\underset{+}{C}}{-}C{-}C} \xrightleftharpoons{1,2} \mathrm{C{-}\overset{C}{\underset{C}{C}}{-}\underset{+}{C}{-}\overset{C}{C}{-}C} \xrightleftharpoons{1,2} \mathrm{C{-}\overset{C}{\underset{+}{C}}{-}\overset{C}{C}{-}\overset{C}{C}{-}C}$$

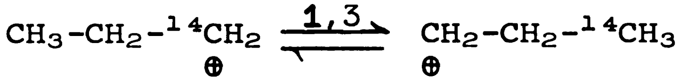
(2)

shifts (74,86) and proton exchange between cyclopropane and sulfuric acid (83) might be interpreted in terms of protonated cyclopropanes, either symmetrical (II) or hydrogen bridged (III).

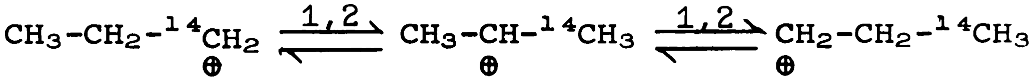


III

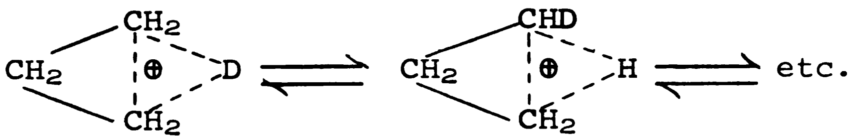
In the simplest system where it is possible to generate a methyl-bridged cation or protonated cyclopropane, or have a 1,3-hydride shift occur, the n-propyl system, cyclopropane is a product in the deamination of the amine (57) and deoxidation of the alcohol (57). It has been reported (77,84,85) that the nitrous acid deamination of the perchlorate salt of n-propylamine-1-^{14}C leads to labeled 1-propanol and 2-propanol, the label in 1-propanol being at C-1 and C-3 only. Solvolysis of cyclopropane in deuterated sulfuric acid (83) leads to 1-propanol containing deuterium at C-1, C-2, and C-3. Treatment of unlabeled 1-propanol under the same conditions leads to no incorporation of the label. The deamination of the amine suggests a 1,3-hydride shift (3) or successive 1,2-shifts (4) whereas the solvolysis of the cyclopropane suggests a protonated cyclopropane (5).



$$CH_3\text{-}CH_2\text{-}\underset{\oplus}{^{14}CH_2} \underset{}{\overset{1,3}{\rightleftharpoons}} \underset{\oplus}{CH_2}\text{-}CH_2\text{-}^{14}CH_3 \qquad (\underline{3})$$

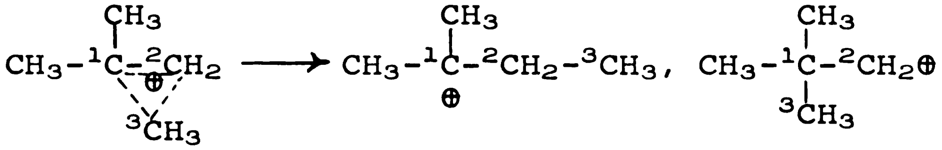


$$CH_3\text{-}CH_2\text{-}\underset{\oplus}{^{14}CH_2} \overset{1,2}{\rightleftharpoons} CH_3\text{-}\underset{\oplus}{CH}\text{-}^{14}CH_3 \overset{1,2}{\rightleftharpoons} \underset{\oplus}{CH_2}\text{-}CH_2\text{-}^{14}CH_3 \qquad (\underline{4})$$

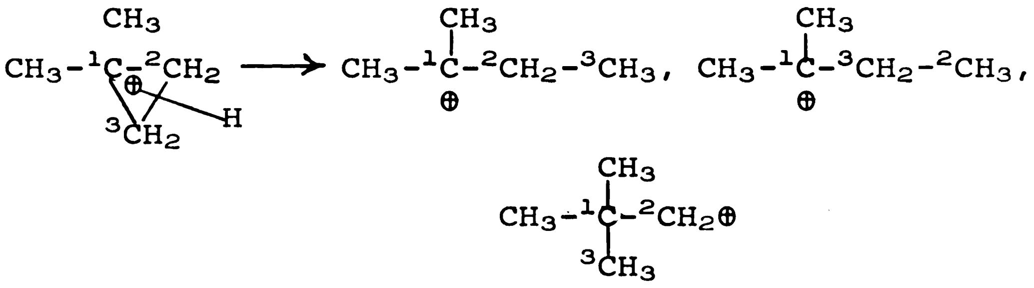


(5)

In the neopentyl system cyclopropanes have never been found (58,61-63,73). However this does not remove the possibility of forming a methyl-bridged non-classical carbonium ion or protonated cyclopropane intermediate which decomposes to the tert-amyl cation. The non-classical carbonium ion has only two modes of decomposition, one leading to a primary ion and the other to a tertiary ion (6).


(6)

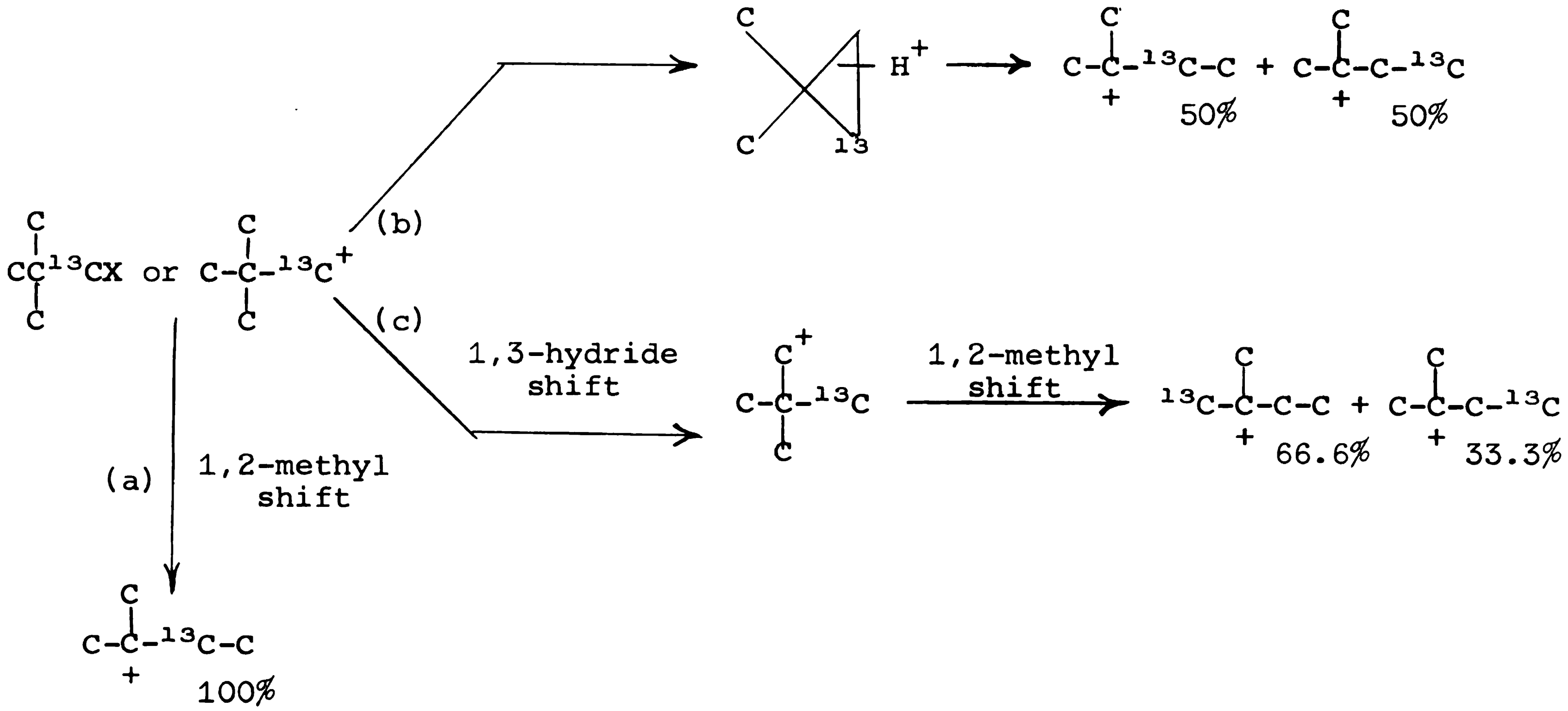
If a non-classical ion is formed it can only be deduced indirectly, by kinetics (67) for example, and not by any direct means such as labeling. If a protonated cyclopropane is formed it has three modes of decomposition (7), one leading


(7)

to a primary ion and two leading to tertiary ions. In (6) and (7) the primary ion can be discounted since no primary product is found.

The path of the rearrangement can be elucidated by suitably labeling the neopentyl group and locating the isotope in the t-amyl group. Chart I summarizes the isotopic distributions predicted for various paths on the assumption

CHART I


(a)
1,2-methyl shift
100%
(b)
H+
50%
50%
(c)
1,3-hydride shift
1,2-methyl shift
66.6%
33.3%

that isotope effects are negligible and that no further scrambling of atoms occurs once the t-amyl structure is attained. Path a, a 1,2-methyl shift, leads to a t-amyl cation labeled solely at C-3; path b, involving a protonated cyclopropane, distributes the label equally between C-3 and C-4; path c, a single 1,3-hydride shift followed by a 1,2-methyl shift, distributes the label between C-1 and C-4 in a 2:1 ratio.

The n-propyl and neopentyl systems were chosen for study due to their simplicity and absence of interfering groups. The path of decomposition, possibly involving 1,2-hydride shifts, 1,3-hydride shifts, and protonated cyclopropanes, to be studied by means of suitably labeled compounds is the subject of this part of the thesis.

RESULTS

n-Propyl System

1-Propylammonium-1,1-$\underline{d}_2$ perchlorate

The 1-propanol obtained from the deamination at 40° of 1-propylammonium-1,1-$\underline{d}_2$ perchlorate (96.6% $\underline{d}_2$ and 3.4% $\underline{d}_1$) was converted with hexamethyldisilazane to the trimethylsilyl ether. Isotopic composition of the silyl ether, calculated from the parent-less-methyl peaks, was 96.4% $\underline{d}_2$ and 3.6% $\underline{d}_1$. The isotopic composition of the amine was obtained from the mass spectral analysis of its diacetamide. Good agreement between the values from the diacetamide and the silyl ether supports the view that methyl loss occurs solely from the trimethylsilyl group and that no deuterium-protium exchange occurs between substrate and solvent during the reaction. The parent-less-ethyl ion of the silyl ether had the composition 91.6% $\underline{d}_2$, 4.9% $\underline{d}_1$, and 3.5% $\underline{d}_0$. These values correspond to the isotopic composition of the α-methylene group of the 1-propanol.

The mass spectral analysis of the trimethylsilyl ethers of 1-propanol-1,1-$\underline{d}_2$ prepared from the reduction of propionic anhydride (a and b), propionic acid (c) and propionyl chloride by lithium aluminum deuteride (d) gave the results summarized in Table I.

Table I. Mass Spectral Analysis of the Trimethylsilyl Ethers of 1-Propanol-1,1-$\underline{d}_2$ Prepared by Lithium Aluminum Deuteride Reduction

	Parent-less-methyl			Parent-less-ethyl		
	$\underline{d}_2$	$\underline{d}_1$	$\underline{d}_0$	$\underline{d}_2$	$\underline{d}_1$	$\underline{d}_0$
(a)	98.8	1.2	0.0	98.3	1.6	0.1
(b)	99.0	1.0	0.0	98.3	1.6	0.1
(c)	88.4	11.5	0.1	87.7	12.0	0.3
(d)	88.4	11.4	0.2	87.5	12.1	0.4

As can be seen from Table I, the composition of the α-methylene group of the trimethylsilyl ether of the 1-propanol obtained from the deamination of the 1-propylammonium-1,1-$\underline{d}_2$ perchlorate needs to be corrected. On the average, the $\underline{d}_1$ and $\underline{d}_0$ intensities of the parent-less-ethyl ions are 0.6% and 0.2% larger and the $\underline{d}_2$ 0.7% smaller than those values obtained from the parent-less-methyl ions. This indicates that this much rearrangement is taking place in the mass spectrometer in the cleavage of the ethyl group. Therefore, the isotopic composition of the α-methylene group of the 1-propanol obtained from the deamination should be 92.4% $\underline{d}_2$, 4.3% $\underline{d}_1$, and 3.3% $\underline{d}_0$.

Since the parent-less-methyl peaks of the trimethylsilyl ether of the 1-propanol from the deamination shows that there is 3.6% $\underline{d}_1$ amine in our starting material, it must be subtracted in order to put our final composition of trimethylsilyl ether on a 100% d_2 basis of the starting amine. Since there is about 95% unrearranged alcohol in the reaction, the 3.6% d_1 amine contributes 3.4% d_1 and 0.2% d_0 to the 1-propanol. Subtracting this amount (3.4% d_1 and 0.2% d_0) from the trimethylsilyl ether a composition of 92.4% d_2, 0.9% d_1, and 3.1% d_0 is arrived at. Putting the composition on a 100% basis yields 95.9% d_2, 0.9% d_1, and 3.2% d_0.

A second run at 40° gave 1-propanol having a composition of 98.0% d_2 and 2.0% d_1 from the parent-less-methyl ion and 93.6% d_2, 3.2% d_1, and 3.2% d_0 from the parent-less-ethyl ion. Applying all corrections as before, the 1-propanol becomes 96.3% d_2, 0.7% d_1, and 3.0% d_0.

A run at 0° gave 1-propanol having a composition of 98.2% d_2 and 1.8% d_1, from the parent-less-methyl ion and 95.4% d_2, 2.8% d_1, and 1.8% d_0 from the parent-less-ethyl ion. Applying all corrections as before, the 1-propanol becomes 98.0% d_2, 0.5% d_1, and 1.5% d_0.

1-Propylammonium-2,2-d_2 perchlorate

Isotopic analysis of the trimethylsilyl ether of the 1-propanol obtained from the deamination of the perchlorate at 40° gave 98.0% d_2 and 2.0% d_1 from the parent-less-methyl ion and 1.4% d_2, 1.1% d_1, and 97.5% d_0 from the parent-less ethyl ion. The silyl ether of authentic 1-propanol-2,2-d_2 gave the following results: 98.4% d_2 and 1.6% d_1 from the parent-less-methyl ion and 0.2% d_2, 0.2% d_1, and 99.6% d_0 from the parent-less-ethyl ion. The correction factors for deuterium and protium rearrangement in the mass spectrometer to be added to the parent-less-ethyl isotope analysis of the 1-propanol from the deamination of the amine are: -0.2% $\underline{d}_2$, -0.2% $\underline{d}_1$, and +0.4% $\underline{d}_0$. The parent-less-ethyl peak thus becomes 1.2% $\underline{d}_2$, 0.9% $\underline{d}_1$, and 97.9% $\underline{d}_0$. Subtracting out the $\underline{d}_1$ present in the starting material in order to have the analysis on $\underline{d}_2$ starting material only, the analysis becomes 1.2% $\underline{d}_2$, 0.9% $\underline{d}_1$, and 96.0% $\underline{d}_0$. Putting this on a 100% basis, the final values become 1.2% $\underline{d}_2$, 0.9% $\underline{d}_1$, and 97.9% $\underline{d}_0$.

The results are summarized by ($\underline{8}$) and ($\underline{9}$).

$$\begin{array}{cccccc} \mathrm{CH_3CH_2CD_2NH_2} & \xrightarrow{40^{\circ}} & \mathrm{C_2H_5\text{-}CD_2OH} & + & \mathrm{C_2H_4D\text{-}CHDOH} & + \\ 100\%\ \underline{d}_2 & & \text{IV, } 96.1\% & & \text{V, } 0.8\% & \\ & & & & \mathrm{C_2H_3D_2\text{-}CH_2OH} & \\ & & & & \text{VI, } 3.1\% & \end{array} \qquad (\underline{8})$$

$$\begin{array}{cccccc} \mathrm{CH_3CD_2CH_2NH_2} & \xrightarrow{40^{\circ}} & \mathrm{C_2H_5\text{-}CD_2OH} & + & \mathrm{C_2H_4D\text{-}CHDOH} & + \\ 100\%\ \underline{d}_2 & & \text{IV', } 1.2\% & & \text{V', } 0.9\% & \\ & & & & \mathrm{C_2H_3D_2\text{-}CH_2OH} & \\ & & & & \text{VI', } 97.9\% & \end{array} \qquad (\underline{9})$$

The Neopentyl System

The t-amyl alcohol obtained from the deamination of neopentyl-1-^{13}C and neopentyl-1,1-d_2-amines, from the solvolysis of neopentyl-1-^{13}C and neopentyl-1,1-d_2 tosylates, and from the solvolysis of neopentyl-1-^{13}C iodide were analyzed by n.m.r. (60 Mc.) and mass spectrometry. The t-amyl chloride obtained from the reaction of neopentyl-1-^{13}C alcohol with triphenyl phosphite and benzyl chloride was analyzed by n.m.r. The preparation of neopentyl iodide (86, 87) (triphenyl phosphite and methyl iodide) yielded no detectable (n.m.r. analysis) rearrangement to t-amyl iodide while the preparation of the chloride gave a 50-50 mixture of neopentyl chloride and t-amyl chloride.

Isotopic composition of the ^{13}C-labeled neopentyl compounds was determined by integration of the $-^{12}CH_2-$ and $-^{13}CH_2-$signals. The values, believed to be accurate to ±4%, in terms of percent labeled molecules are: neopentyl-1-^{13}C-ammonium perchlorate, 31.5%; neopentyl-1-^{13}C tosylate, 55.8%; neopentyl-1-^{13}C iodide, 54.3%; and neopentyl-1-^{13}C chloride, 53.7%. Neopentyl-1,1-d_2-ammonium perchlorate and neopentyl-1,1-d_2 tosylate were estimated to be at least 96% d_2. Fig. 1 shows typical spectra.

The t-amyl alcohols isolated from the rearrangement of the d_2-labeled neopentyl compounds showed no protium at C-3 (less than 5%). Those obtained from the ^{13}C-labeled compounds showed no ^{13}C at C-1 or C-4. From integration of the $-^{13}CH_2-$signals at 7.4 versus other signals (OH, $-^{12}CH_2-$) the amount of ^{13}C at C-3 from deamination was estimated to be 30.6%; from tosylate solvolysis, 53.2-57%; and from iodide solvolysis, 53.8%. The t-amyl chloride also showed no ^{13}C

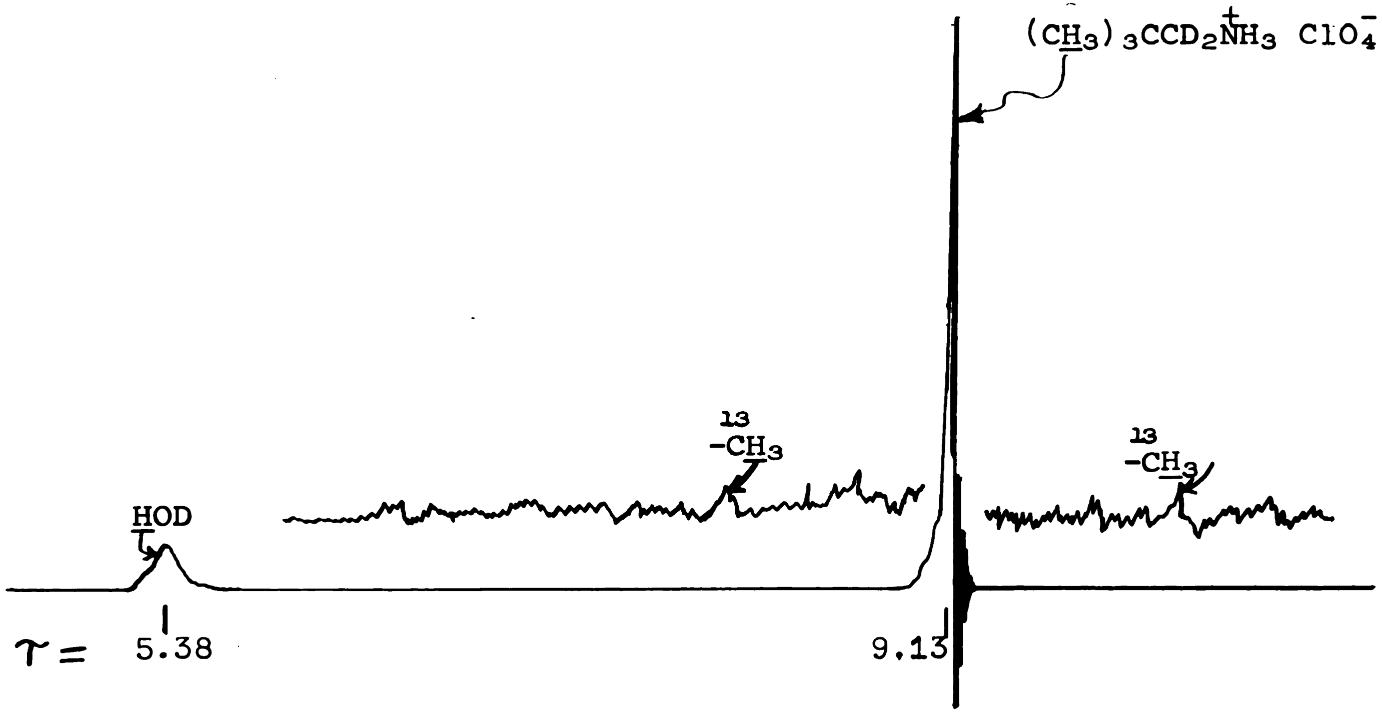


Fig. 1. Proton n.m.r. spectrum of neopentyl-1,1-$\underline{d}_2$-ammonium perchlorate in deuterium oxide.

at C-1 or C-4. Typical spectra are shown in Fig. 2. Apparently all the labeled atoms-deuterium and ^{13}C-in the t-amyl compounds are confined to the C-3 position.

Table II shows partial spectra of t-amyl alcohols obtained from the rearrangement of labeled neopentyl compounds. Analysis (92) of these spectra gives the following results: retention of ^{13}C label in the $C_5H_{11}^+$ ion, parent-less-hydroxyl, is 30, 55, and 54% for the alcohols obtained from the deamination solvolysis of tosylate, and solvolysis of iodide, respectively. Retention of ^{13}C label in the $C_4H_9O^+$ ion, parent-less-methyl, is 29.4, 56.3, and 56.2%; in the $C_4H_7^+$ ion, parent-less-methyl-and-water, it is 29, 55, and 54%. Hence no label is at C-1. ^{13}C retention in the $C_3H_7O^+$ ion, parent-less-ethyl, is not more than 0.2, 0.2, and 0.2%. If intensities at masses 74 and 75 in the spectra of the deuterated alcohols are attributed solely to $C_4H_9O^+$-d_1 and -d_2, respectively, and if unlabeled $C_4H_9O^+$ is assumed absent, an estimate can be made of the isotopic distribution of this fragment-ion and, by inference, of the parent molecule: 3.6% d_1 and 96.4% d_2 in both alcohols. Deuterium retention in the $C_3H_7O^+$ ion is essentially zero. All the ^{13}C and deuterium, therefore, is confined to the ethyl groups.

The n.m.r. and mass spectral data are in good agreement, and the combination of the two leads to the conclusion that all label originally at C-1 of the neopentyl compounds ends up at C-3 of the t-amyl compounds. Table III summarizes the results.

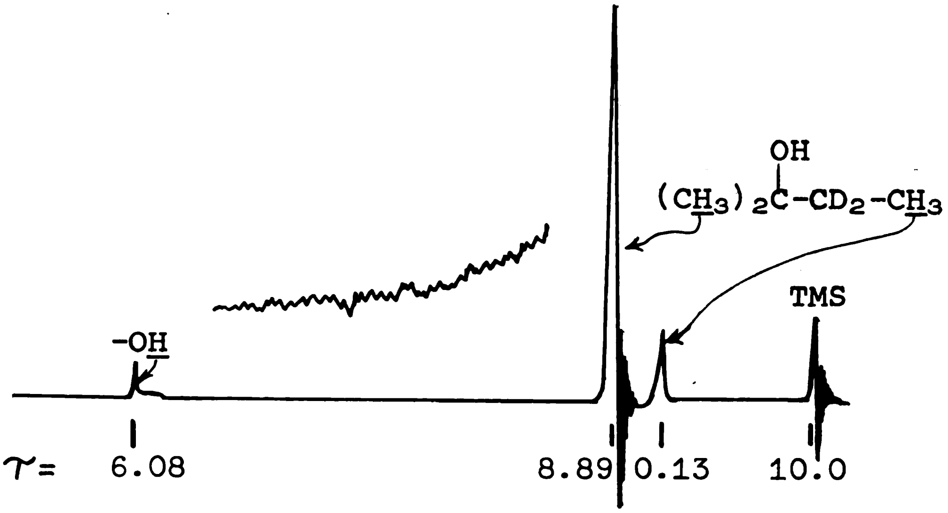


Fig. 2a. Proton n.m.r. spectrum in carbon tetrachloride of t-amyl alcohol obtained from the deamination of neopentyl-1,1-d_2-ammonium perchlorate.

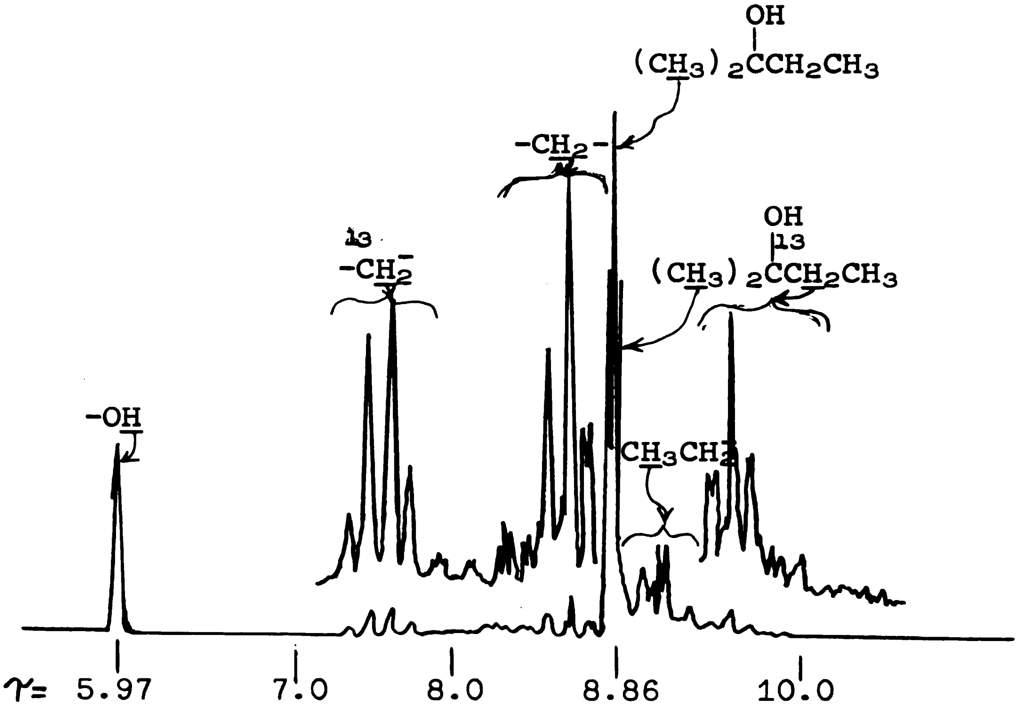


Fig. 2b. Proton n.m.r. spectrum in carbon tetrachloride of t-amyl alcohol obtained from the solvolysis of neopentyl-1-^{13}C tosylate.

Table II. Partial Mass Spectra of t-Amyl Alcohols

	Relative Intensity[a]						
Mass	I[b]	II[c]	III[d]	IV[b]	V[e]	VI[f]	VII[g]
53	3.10	2.33	1.62	3.84	2.06	1.09	1.09
54	0.60	1.24	1.82	0.74	2.38	1.83	1.84
55	41.6	29.1	18.4	47.8	22.1	3.19	3.16
56	0.47	11.8	22.4	0.41	26.0	11.1	11.3
57	2.62	2.20	1.68	2.75	1.64	36.0	36.3
58	1.82	2.28	2.45	1.76	2.33	2.13	2.12
59	100.0	100.0	100.0	100.0	100.0	100.0	100.0
60	0.10	0.24	0.20	0.05	0.18	2.27	2.29
61	0.12	0.09	0.08	0.17	0.13	0.10	0.11
69	0.81	0.69	0.39	1.01	0.47	0.17	0.17
70	3.80	2.65	1.96	5.87	3.04	0.43	0.41
71	5.46	4.97	4.37	5.62	5.61	2.24	2.25
72	0.20	1.83	3.22	0.14	3.16	3.58	3.63
73	55.6	39.1	24.4	55.3	24.6	5.66	5.62
74	0.07	16.3	31.4	0.05	31.6	2.14	2.14
75	0.0	0.0	0.0	0.0	0.0	57.9	57.5
76	0.0	0.0	0.0	0.0	0.0	0.79	0.80

[a] Contributions from ions containing heavy isotopes in natural abundance have been removed.

[b] Unlabeled. Interpretation of spectra of labeled compounds requires comparison with spectra of the corresponding unlabeled species measured consecutively or nearly so to ensure constant instrument operating characteristics. The spectra shown here were measured in two groups at different times. Hence two spectra, I and IV, are reported for the unlabeled alcohol. Spectrum I was measured at the same time as II and III, IV at the same time as V, VI, and VII.

[c] From the deamination of neopentyl-1-^{13}C-amine.

[d] From the solvolysis of neopentyl-1-^{13}C tosylate.

[e] From the solvolysis of neopentyl-1-^{13}C iodide.

[f] From the deamination of neopentyl-1,1-d_2 amine.

[g] From the solvolysis of neopentyl-1,1-d_2 tosylate.

Table III. Percentage Distribution of Label in the t-Amyl Compounds Obtained from the Rearrangement of Neopentyl Compounds

Neopentyl compound	Reaction	Product	Label in t-amyl compounds, Percent C-1	C-2	C-3	C-4
$(CH_3)_3C^{13}CH_2N^+H_3ClO_4^-$	Deamination	t-Amyl alcohol	0	0	100	0
$(CH_3)_3CCD_2N^+H_3ClO_4^-$	Deamination	t-Amyl alcohol	0	...	100	0
$(CH_3)_3C^{13}CH_2OTs$	Solvolysis	t-Amyl alcohol	0	0	100	0
$(CH_3)_3CCD_2OTs$	Solvolysis	t-Amyl alcohol	0	...	100	0
$(CH_3)_3C^{13}CH_2I$	Solvolysis	t-Amyl alcohol	0	0	100	0
$(CH_3)_3C^{13}CH_2OH$	Reaction with $(C_6H_5O)_3P$ + $C_6H_5CH_2Cl$	t-Amyl chloride			>96[a]	
$(CH_3)_3C^{13}CH_2OH$	Reaction with HBr	Pentenes + t-Amyl bromide			>96[b]	
$(CH_3)_3CCD_2OH$	Deoxidation	Pentenes			>96[c]	

[a] Calculated from the n.m.r. spectrum.

[b] Ref. 61.

[c] Ref. 63.

DISCUSSION

The n-Propyl System

The data provide evidence that the 1-propanol arises mainly from a path leading to isotopically unrearranged alcohol and partly from a path leading to extensively rearranged alcohol. The higher concentration of IV' over V' rules out reversible 1,2-hydride shifts as the rearrangement path. If complete scrambling of label by 1,2-shifts had taken place statistically the ratio of IV' to V' would have been 1:10. Experimentally this ratio is found to be 1:0.75. Also, in a mechanism involving only partial scrambling by 1,2-shifts V' should be in excess of IV' on account of V' being formed first and being a precursor of IV' (see (10)).

$$\begin{tikzcd}
CH_3CD_2\overset{+}{C}H_2 \arrow[r, shift left, "\sim D"] & CH_3\overset{+}{C}DCH_2D \arrow[l, shift left] \arrow[r, shift left, "\sim H"] & \underset{\text{V}'}{CH_3CHD\overset{+}{C}HD} \arrow[l, shift left] \arrow[d, shift left, "\sim D"] \\
 & \underset{\text{IV}'}{CH_3CH_2\overset{+}{C}D_2} \arrow[r, shift left, "\sim H"] & CH_3\overset{+}{C}HCHD_2 \arrow[l, shift left] \arrow[u, shift left]
\end{tikzcd} \qquad (10)$$

2-Aminopropane has been shown to yield no 1-propanol. This too helps to rule out reversible 1,2-shifts. 1,3-Shifts can be ruled out on the basis that 1-aminopropane-2,2-d_2

forms 1-propanol with label in the 1-position. Since [V]=[V'], 1-aminopropane-1,1-$\underline{d}_2$ and 1-aminopropane-2,2-$\underline{d}_2$ must lead to the same isotope position intermediate, or its equivalent, prior to the formation of isotopically rearranged 1-propanol. This intermediate (Chart II) accommodates the results, provided the following are true: (a) from [V]= [V'], VII $\rightleftharpoons$ VII' is much faster than reaction of these ions with solvent to form 1-propanol. In terms of isotope position rearrangement, this is indistinguishable from a symmetrical protonated cyclopropane. [b] From [IV'] > [V'], VII $\rightleftharpoons$ VIII is slower than VII $\rightleftharpoons$ VII' and competitive with reaction of the ions with solvent. Mechanism I is therefore ruled out, because it requires assumptions already excluded by solvolytic studies of cyclopropane in deuteriosulfuric acid (88,89).

Mechanism II (Chart III), either A or B, is consistent with the results and those of Baird and Aboderin (88,89). For path A to be correct, X must go to VII and VII' as fast as or faster than it reacts with solvent to give 1-propanol. For path B (formation of VII and VII' without the intervention of X) to be correct, VII and VII' must arise in the same ratio from either labeled species. Neither path requires the excluded (88,89) condition that VII $\rightleftharpoons$ VIII be slower than VII $\rightleftharpoons$ VII'.

In conclusion, the results indicate that at 40° about 5% (1.2% IV, 0.9% V, and 3.2% VI) of the 1-propanol arises from protonated cyclopropanes and 95% from an intermediate, or

CHART II

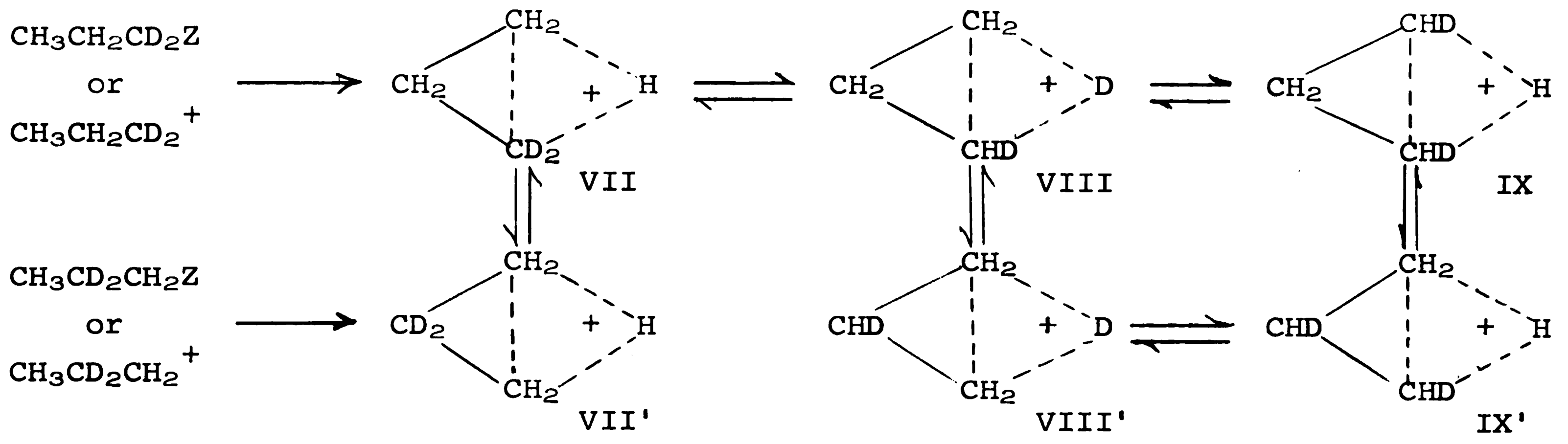
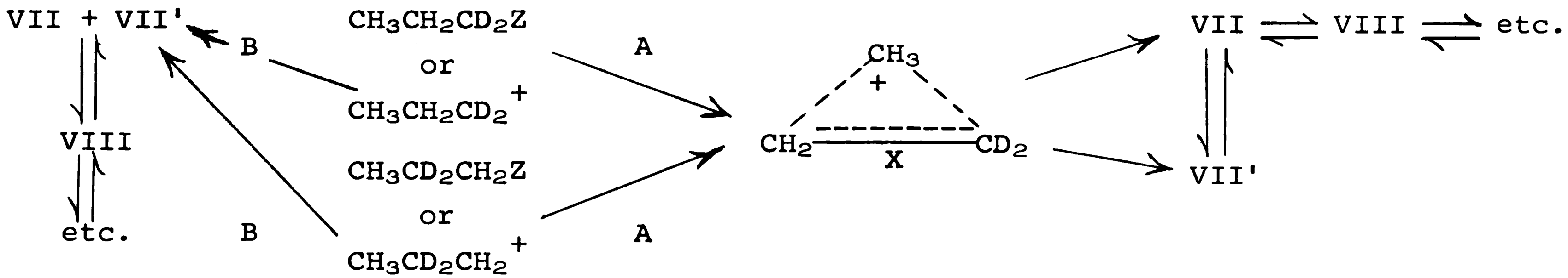


CHART III

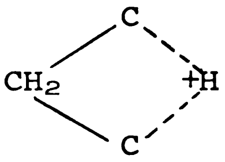


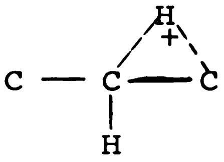
intermediates, leading to isotopically unrearranged alcohol. At 0° the contribution of the protonated cyclopropane path is about 3%.

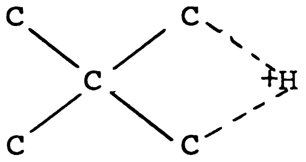
Our results are in good agreement with those of Lee and co-workers (90, 91) who have studied ^{14}C and tritium labeled 1-aminopropane.

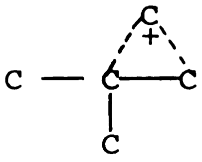
The Neopentyl System

In the liquid phase reactions, regardless of experimental conditions, neopentyl compounds rearrange to t-amyl compounds without the intervention of 1,3-hydride shifts, protonated cyclopropanes, or hydrogen-bridged ions. The ability of 1,3-hydride shifts to compete with 1,2-shifts in the n-propyl system (IV vs. V) but not in the neopentyl system (VI vs. VII) can be rationalized in terms of formation of a tertiary carbonium ion in VII but only a secondary in V, and in terms of greater release of nonbonded interactions in going from the neopentyl group to VII than from the n-propyl to V.

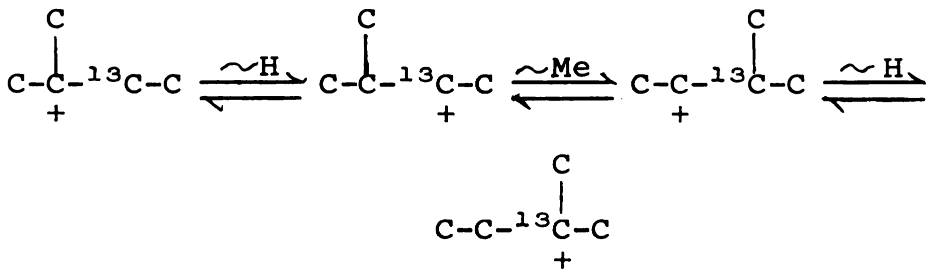

IV


V


VI


VII

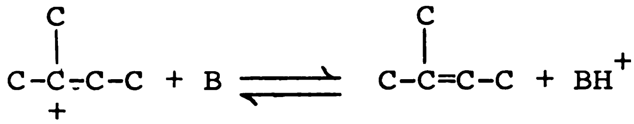
The results exclude the occurrence of 8, a reaction sequence that is significant in the reactions of t-amyl



$$\mathrm{C{-}\overset{C}{\underset{+}{C}}{-}{}^{13}C{-}C} \xrightleftharpoons{\sim H} \mathrm{C{-}\overset{C}{C}{-}{}^{13}\underset{+}{C}{-}C} \xrightleftharpoons{\sim Me} \mathrm{C{-}\underset{+}{C}{-}{}^{13}\overset{C}{C}{-}C} \xrightleftharpoons{\sim H} \mathrm{C{-}C{-}{}^{13}\overset{C}{\underset{+}{C}}{-}C} \qquad (\underline{8})$$

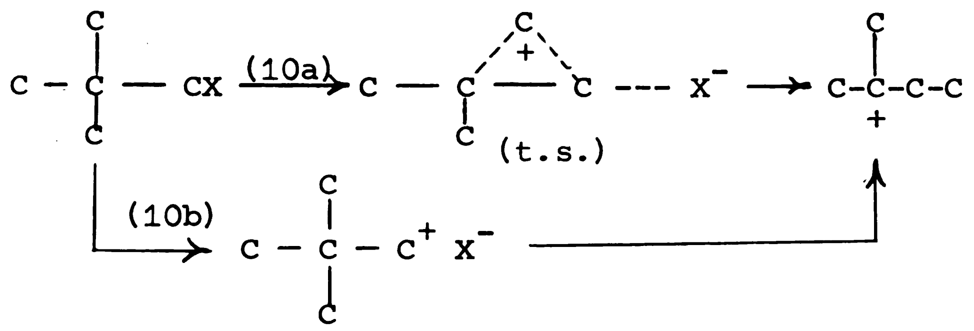
halides with aluminum halides (92, 93). This difference in the behavior of the t-amyl cation is reasonable. Under the present experimental conditions the cation is irreversibly captured by nucleophile at rates approaching those of collision reactions. Consequently rearrangement to the secondary carbonium ion, which requires at least 11 kcal./mole of activation energy, cannot compete favorably with nucleophilic capture or with proton elimination. Under the conditions of alkyl-Lewis acid reactions, however, competition becomes effective because the carbonium ions are long lived.

Retention of all deuterium in the t-amyl products also excludes the reversibility of 9.



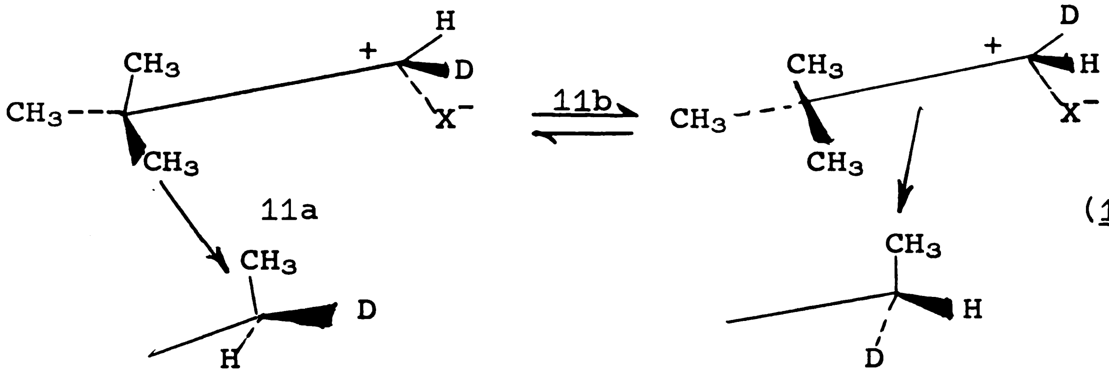
$$\mathrm{C{-}\overset{C}{\underset{+}{C}}{-}C{-}C} + \mathrm{B} \rightleftharpoons \mathrm{C{-}\overset{C}{C}{=}C{-}C} + \mathrm{BH}^{+} \qquad (\underline{9})$$

The methyl shift can proceed either by a synchronous C-X breaking and methyl migration, path 10a, or by a two-step process that involves the intermediacy of the neopentyl cation, path 10b. Mechanisms intermediate between these



(<u>10</u>)

extremes can also be visualized. The relative merits of 10a and 10b in terms of X have been recently discussed (58,94). In most cases the available data bar a choice between the two mechanisms. Path 10b apparently intervenes in the reaction of neopentyl iodide with silver nitrate. In this case optically active neopentyl-1-d iodide leads to inactive t-amyl alcohol (94). Path 10a has been implicated (94) in the deoxidation of neopentyl alcohol, because optically active (presumably inverted) 2-methyl-1-butene-3-d results from optically active neopentyl-1-d alcohol. The results, however, are equally compatible with path 10b provided the methyl rearrangement (11a) is faster than or competes favorably with rotation of the -CHD group with



(<u>11</u>)

respect to X (11b). These differences in the behavior of neopentyl cations may reflect the importance of X in product control rather than a change from a two-step to a concerted mechanism. Vibrationally excited neopentyl cations, e.g., those formed from deamination and deoxidation, may underto rearrangement faster than rotation about the $-\overset{+}{C}HD$ group with respect to X. Recent publications have focused attention on the importance of counter ion X and solvent in the competition between product formation and conformational changes of carbonium ions (95,96).

EXPERIMENTAL

Purification of liquid products

The propanols, the _t_-amyl alcohols, the trimethylsilyl ethers, and the diacetamides were all purified for mass spectral and n.m.r. analysis by vapor phase chromatography, by using a 10 ft. x ¼ in. 20% Carbowax 20M on 60/80 Chromosorb W column for the alcohols and ethers and a 6 ft. x ¼ in. 20% Carbowax 20M on 60/80 Chromosorb W column for the diacetamides. The alcohols were run at about 80°, the ethers at 50°, and the diacetamides at 155°. An Aerograph A-90-P gas chromatograph was used.

The _t_-amyl chloride and neopentyl chloride were separated by vapor phase chromatography using a 7 ft. x ¼ in. 15% Bentone 34 and 5% SE-52 on 60/80 Chromosorb W column at 70°. Fifty to seventy microliter injections were used in all cases.

Preparation of trimethylsilyl ethers (97)

By using small glassware (₮ 14/20), 0.1 to 0.5 g. of the alcohol was refluxed on a steam bath for two hrs. with one-half the molar amount of hexamethyldisilazane and one drop of trimethylsilyl chloride. The cooled reaction mixture was used directly for VPC purification and then mass spectral analysis.

1-Propyl-N,N-diacetamide (98)

To 3.0 g. (0.02 mole) of the perchlorate salt of the amine was added 5.6 g. (0.1 mole) of potassium hydroxide and 15 ml. of water. The solution was immediately distilled (the amine comes over first) into 10 ml. of toluene. The toluene was dried with anhydrous magnesium sulfate. To the toluene solution was then added 3.1 g. (0.04 mole) of acetyl chloride and 3.17 g. (0.04 mole) of pyridine in 10 ml. of toluene. The mixture was refluxed on a steam bath for 1 hr., cooled, washed with three 25 ml. portions of water, dried, and distilled. The remaining diacetamide was purified by VPC.

1-Propyl-N,N-diacetamide-1,1-d_2

The same procedure as for the unlabeled amine was used. A 0.019 mole quantity of starting material was used.

1-Propanol-1,1-d_2

To 6.20 g. (0.048 mole) of propionic anhydride in 25 ml. of dry ether was added, at 0°, 2.00 g. (0.048 mole) of lithium aluminum deuteride in 100 ml. of ether. The mixture was warmed to room temperature slowly and then refluxed on a steam bath for 3 hrs. After cooling, 4 ml. of water and 4 ml. of 5% sodium hydroxide solution were added. The ether layer was decanted, dried over anhydrous magnesium sulfate, and fractionally distilled. Yield: 3.02 g. (51.0%).

1-Propylammonium-2,2-d_2 perchlorate

To 13.30 g. (0.35 mole) of lithium aluminum hydride in 250 ml. of ether was added dropwise 14.24 g. (0.25 mole) of propionitrile-α,α-d_2 in 50 ml. of ether. The mixture was refluxed on a steam bath for 3 hrs., cooled, worked up with 100 ml. of water, and distilled into 35.8 g. (0.25 mole) of 70% perchloric acid. The ether, water, and perchloric acid were removed under vacuum. The remaining solid was crystallized (84) from *n*-heptyl alcohol and *n*-pentane. Yield: 25.73 g. (75.2%).

1-Propylammonium-1,1-d_2 perchlorate

The procedure used was exactly the same as that for the 1-propylammonium-2,2-d_2 perchlorate. A 0.2 mole quantity of starting materials was used.

Methylmalonic acid (99)

Shake 149.8 g. (0.86 mole) of methylmalonic acid diethyl ester with 10 g. of sodium hydroxide in 30 ml. of water at 0° for one minute to remove any malonic acid diethyl ester present. Wash once with 100 ml. of water. Add to the ester in a 3-necked ₸ 24/40 1 liter round-bottomed flask equipped with a condenser, stirrer, and thermometer 137.6 g. (3.44 mole) of sodium hydroxide in 400 ml. of cold water. Heat with stirring on a steam bath to 80° and maintain for 1 hr. Cool, extract three times with 100 ml. portions of ether, make acidic (pH $<$ 1) with cold concentrated hydrochloric acid and extract with three 100 ml. portions of ether and salt out with sodium chloride. Dry the ether solution with anhydrous magnesium sulfate, filter, and remove the ether under vacuum using a warm water bath (50°). The yield after one crystallization from ethyl acetate was 65.1 g. (72.8%).

Methylmalonic acid-α-*d*-carboxyl-*d*$_2$ (100)

Fifty g. of methylmalonic acid was dissolved in 100 ml. of deuterium oxide in a stoppered 250 ml. 1-neck § 24/40 round-bottomed flask and kept at 55° for 18 hrs. After removing the water by heating to 55° under vacuum, another 100 ml. of deuterium oxide was added. After a total of eight exchanges, approximately 1% of protium remained.

Propionic acid-α,α-*d*$_2$

The methylmalonic acid-α-d-carboxyl-*d*$_2$ was distilled at atmospheric pressure and then redistilled to give pure propionic acid-α,α-*d*$_2$.

Propionamide-α,α-*d*$_2$

To 35.00 g. (0.46 mole) of propionic acid-α,α-*d*$_2$ was added 54.8 g. (0.46 mole) of purified thionyl chloride (101). The mixture was refluxed for 1 hr. on a steam bath, cooled, and taken up into 800 ml. of dry ether. The ether solution was poured into a 2 liter 3-necked round-bottom flask equipped with a gas inlet tube, dry ice cold finger condenser, and a paddle stirrer. Anhydrous ammonia gas was introduced above the ether solution. On condensing the ammonia dripped into the ether solution. The solid formed was filtered off and the ether and ammonia were removed by fractional distillation. The remaining solid was purified by crystallization from ether. Yield: 25.9 g. (79%), m.p. 78-79°.

Propionitrile-α,α-d$_2$

To 25.9 g. (0.345 mole) of propionamide-α,α-d$_2$ was added 61.6 g. (0.518 mole) of thionyl chloride. The mixture was heated on a steam bath for 2 hrs., taken up into 300 ml. of ether, washed with 50 ml. of 10% sodium carbonate solution saturated with sodium chloride, dried over anhydrous magnesium sulfate, and distilled. Yield: 14.24 g. (72.4%), b.p. 97°.

1-Propanol-2,2-d$_2$

To 11.40 g. (0.30 mole) of lithium aluminum hydride in 200 ml. of ether was added dropwise 20.12 g. (0.26 mole) of propionic acid-α,α-d$_2$ in 50 ml. of ether. After refluxing on a steam bath for 2 hrs., 33 g. of water was added and the solid was washed with ether. Upon fractional distillation of the ether 15.23 g. (95.2%) of 1-propanol-2,2-d$_2$ was obtained.

Deamination of 1-propylammonium-1,1-d$_2$ perchlorate (84)

To 9,52 g. (0.06 mole) of 1-propylammonium-1,1-d$_2$ perchlorate dissolved in 10 ml. of water and 7.15 g. (0.05 mole) of 70% perchloric acid was added dropwise with constant stirring over a 1 hr. period a solution of 8.80 g.

(0.127 mole) of sodium nitrite in 15 ml. of water. The reaction mixture was distilled into a receiver cooled in ice. When approximately 2/3 of the solution was distilled over, the distillation was stopped and the distillate was saturated with potassium fluoride and extracted with three 50 ml. portions of ether. The ether was dried over anhydrous magnesium sulfate and fractionally distilled. The yield of 1- and 2-propanol was 1.56 g.

Deamination of 1-propylammonium-2,2-$\underline{d}_2$ perchlorate (84)

The procedure was the same as that used in the deamination of 1-propylammonium-1,1-$\underline{d}_2$ perchlorate. A 0.08 mole quantity of the amine salt was used. Yield: 0.86 g. of 1- and 2-propanol.

Deamination of 2-propylammonium perchlorate (84)

The procedure was the same as that used in the deamination of 1-propylammonium-1,1-$\underline{d}_2$ perchlorate. Twenty g. (0.126 mole) of the amine salt, 17.6 ml. of 35% perchloric acid, and 18.6 g. (0.27 mole) of sodium nitrite in 25 ml. of water yielded 5.2 g. of alcohol.

Neopentyl-1,1-$\underline{d}_2$ ammonium perchlorate

To 3.00 g. (0.072 mole) of lithium aluminum deuteride in 200 ml. of ether was added dropwise over a 1 hr. period with stirring, at 0°, 6.25 g. (0.075 mole) of *t*-butyl cyanide in 30 ml. of ether. The reaction mixture was then slowly warmed and refluxed for 3 hrs. The reaction mixture was successively hydrolyzed with 3 ml. of water, 3 ml. of 20% aqueous sodium hydroxide, and 10 ml. of water. The ether layer was decanted from the solid material, the solid was repeatedly washed with ether, and the extracts were combined. To the ether was added 10.76 g. (0.075 mole) of 70% perchloric acid with subsequent vigorous shaking. The ether and water were removed under vacuum and the perchlorate salt was purified by precipitation from n-heptyl alcohol with n-heptane (84). Yield: 13.77 g. (72.6%), m.p. 168-169°.

Deamination of neopentyl-1,1-d_2-ammonium perchlorate

The procedure was similar to that used in the deamination of 1-propylammonium-1,1-d_2 perchlorate. The reaction mixture was extracted directly with ether and without the use of potassium fluoride. The reaction of 11.55 g. (0.062 mole) of the amine salt in 10 ml. of water and 4.4 ml. of 70% perchloric acid with 9.15 g. (0.133 mole) of sodium nitrite in 13 ml. of water yielded 2.90 g. (53.5%) of t-amyl alcohol.

Neopentyl-1,1-d_2 alcohol

To 2.79 g. (0.067 mole) of lithium aluminum deuteride in 200 ml. of ether was added dropwise with stirring, at 0°, 6.79 g. (0.067 mole) of trimethylacetic acid in 50 ml. of ether. The reaction mixture was refluxed for 3 hrs. and then hydrolyzed with 5% sulfuric acid. The ether layer was dried with anhydrous magnesium sulfate and fractionally distilled. Yield: 5.28 g. (88.0%), m.p. 46-47°.

Neopentyl-1,1-$\underline{d}_2$ tosylate (67,102)

To 6.27 g. (0.07 mole) of neopentyl-1,1-$\underline{d}_2$ alcohol in 25 ml. of pyridine was added 13.3 g. (0.07 mole) of tosyl chloride in 25 ml. of pyridine. The reaction was run at room temperature and allowed to stand for 90 hrs. After extraction with ether and 10% sulfuric acid, crystallization from n-pentane gave 14.96 g. (88.2%, m.p. 42-44°) of the tosylate.

Solvolysis of neopentyl-1,1-$\underline{d}_2$ tosylate (58)

To a mixture of 100 ml. of water, 100 ml. of glacial acetic acid, and 7.7 g. of potassium acetate was added 14.96 g. (0.06 mole) of the tosylate. The reaction mixture was kept at 90° with stirring for 297 hrs. Upon neutralization of the acid with 20% aqueous sodium hydroxide, extraction with 150 ml. of ether, and fractional distillation, 0.80 g. (14.5%) of t-amyl alcohol was obtained.

t-Butyllithium (103)

In a 250 ml. glass-stoppered Erlenmeyer flask containing 50 ml. of mineral oil, 5.20 g. (0.750 mole) of lithium metal was heated to 210° and shaken vigorously until the temperature was about 150°. The lithium sand and oil were cooled to room temperature and 150 ml. of dry ether was added. The lithium was filtered off in a funnel containing a glass wool plug. The lithium was washed with dry ether and added to 500 ml. 3-necked ₸ 24/40 round-bottomed flask equipped with a nichrome wire stirrer with a ground-glass seal, a condenser containing a suspended thermometer, and a dropping funnel. To the top of the condenser were consecutively attached an anhydrous magnesium perchlorate trap, an aqueous saturated barium hydroxide trap, and a potassium hydroxide (pellets) trap. To the lithium in 200 ml. of dry ether was added dropwise with stirring 27.8 g. (0.30 mole) of t-butyl chloride in 75 ml. of dry ether at -35 to -40°. The reaction mixture was dark grey in color.

Trimethylacetic-1-^{13}C acid (103)

To 27.25 g. (0.138 mole) of 56.5% enriched barium carbonate (Bio-Rad Laboratories) was added dropwise 71.8 g. (0.500 mole) of 70% perchloric acid. The resulting carbon dioxide was passed through two gas washing bottles containing concentrated sulfuric acid and bubbled into the t-butyl lithium-ether solution (0.75 mole), with the temperature being kept between -50 and -60°. After the addition of all the perchloric acid, the system was flushed with dry nitrogen. The reaction mixture was then hydrolyzed with 10% hydrochloric acid at -50° and then let warm to room temperature. The ether layer was extracted with 10% sodium carbonate and dried over anhydrous magnesium sulfate. Upon distillation of the ether solution, approximately 1 g. of a 50-50 mixture of tri-t-butylcarbinol (^{13}COH) and di-t-butyl ketone (^{13}C=O) was obtained. These were separated by VPC on a 10 ft. x $\frac{1}{4}$ in. Carbowax 20 M on 60/80 Chromasorb W column. Upon acidification of the sodium carbonate extract, extraction with ether, and fractional distillation, 12.81 g. (90.8%, b.p. 162-164°) of trimethylacetic-1-^{13}C acid was obtained.

Neopentyl-1-^{13}C alcohol

To 10.0 g. (0.25 mole) of lithium aluminum hydride in 200 ml. of ether was added dropwise with stirring, at 0°, 9.89 g. (0.10 mole) of trimethylacetic-1-^{13}C acid in 50 ml. of ether. The reaction mixture was refluxed for 3 hrs. and hydrolyzed with 10% sulfuric acid. The product was vacuum distilled to give 7.84 g. (92.8%, m.p. 53-54°) of alcohol.

Neopentyl-1-^{13}C tosylate (67,102)

The procedure was the same as that used in the preparation of neopentyl-1,1-$\underline{d}_2$ tosylate. Five g. (0.056 mole) of alcohol and 10.72 g. (0.056 mole) of tosyl chloride were used. Yield: 11.59 g. (92.3%, m.p. 46-47°).

Solvolysis of neopentyl-1-^{13}C tosylate (58)

The procedure was the same as that used in the solvolysis of neopentyl-1,1-$\underline{d}_2$ tosylate. About 11.6 g. (0.048 mole) of the tosylate gave 0.4 g. of $\underline{t}$-amyl alcohol.

Trimethylacetamide-1-^{13}C (104)

To 5.00 g. (0.05 mole) of trimethylacetic-1-^{13}C acid was added 8.45 g. (0.07 mole) of thionyl chloride. The reaction mixture was refluxed for 3 hrs., cooled to 0°, and added dropwise to 200 ml. of concentrated ammonium hydroxide. Crystallization of the amide from 50-50 v/v petroleum ether-ethyl acetate gave 4.90 g. (99.0%) of the amide melting at 156-157°.

Trimethylacetonitrile-1-^{13}C

To 4.90 g. (0.048 mole) of trimethylacetamide-1-^{13}C was added 8.60 g. (0.07 mole) of thionyl chloride (101). The reaction mixture was refluxed for 1 hr. and distilled. Yield: 1.09 g. (27.0%, I.R. 4.50 μ, 4.60 μ).

Neopentyl-1-^{13}C-ammonium perchlorate

The procedure was the same as that used in the synthesis of neopentyl-1,1-$\underline{d}_2$-ammonium perchlorate. The reaction of 3.80 g. (0.10 mole) of lithium aluminum hydride in 150 ml. of ether with 1.0 g. (0.01 mole) of trimethylacetonitrile-1-^{13}C in 50 ml. of dry ether, followed by the reaction of the resulting amine with 1.72 g. (0.01 mole) of 70% perchloric acid yielded 1.70 g. (75.6%, m.p. 168-169°) of the perchlorate.

Deamination of neopentyl-1-^{13}C-ammonium perchlorate

The procedure was the same as that used in the deamination of neopentyl-1,1-$\underline{d}_2$-ammonium perchlorate. The reaction of 3.10 g (0.017 mole) of the perchlorate with 2.5 ml. of 35% perchloric acid and 2.45 g. (0.036 mole) of sodium nitrite in 10 ml. of water gave 0.6 g. of $\underline{t}$-amyl alcohol.

Neopentyl-1-^{13}C iodide (86)

To 15.5 g. (0.05 mole) of triphenylphosphite was added 10.5 g. (0.074 mole) of methyl iodide. The mixture was refluxed for 30 hrs., cooled, and washed with dry petroleum ether. To 12.1 g. (0.038 mole) of the methyl triphenylphosphonium iodide was added 2.88 g. (0.027 mole) of neopentyl-1-^{13}C alcohol. The mixture was refluxed for 24 hrs. After extracting with 150 ml. of ether and washing with 100 ml. of 20% aqueous sodium hydroxide, the ether solution was dried and fractionally distilled to give 4.68 g. (88.3%) of the iodide.

Solvolysis of neopentyl-1-^{13}C iodide (60)

To 20 ml. of water containing 2.75 g. (0.016 mole) of silver nitrate was added 2.68 g. (0.014 mole) of the iodide. The reaction mixture was stirred for 12 hrs., saturated with sodium chloride, and extracted with 150 ml. of ether. The ether extract was dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. Yield: 0.79 g. (65.8%) of *t*-amyl alcohol.

Neopentyl-1-^{13}C chloride (86)

To 34.00 g. (0.110 mole) of triphenylphosphite was added 13.00 g. (0.103 mole) of benzyl chloride. The mixture was heated at 175° for 90 hrs. After cooling, the mixture was extracted with 300 ml. of dry ether. To 30.7 g. (0.07 mole) of the solid benzyltriphenylphosphonium iodide, remaining after the ether extraction, was added 5.00 g. (0.056 mole) of neopentyl-1-^{13}C alcohol. The mixture was heated at 60° for 60 hrs. and then distilled under reduced pressure (1 mm. of Hg) into a receiver cooled in liquid nitrogen. The phenol and unreacted alcohol solidified on the walls of the distilling head with only the chlorides being collected in the receiver. A 50-50 mixture of neopentyl and _t_-amyl chloride (2.65 g.) was collected, characterized, and separated by vapor phase chromatography.

REFERENCES

1. P. C. Lauterbur, *J. Chem. Phys.*, *26*, 217 (1957); *J. Am. Chem. Soc.*, *83*, 1838, 1846 (1961).
2. J. N. Shoolery, *J. Chem. Phys.*, *31*, 1427 (1959).
3. N. Muller and D. E. Pritchard, *ibid.*, *31*, 768, 1471 (1959).
4. N. Muller, *ibid.*, *36*, 359 (1962).
5. N. Muller and P. I. Rose, *J. Am. Chem. Soc.*, *84*, 3973 (1962).
6. E. R. Malinowski, *ibid.*, *83*, 4479 (1961).
7. E. R. Malinowski, L. Z. Pollara, and J. P. Larmann, *ibid.*, *84*, 2649 (1962).
8. H. S. Gutowsky and C. S. Juan, *ibid.*, *84*, 307 (1962); *J. Chem. Phys.*, *37*, 2198 (1962).
9. H. Dreeskamp and E. Sackmann, *Z. Physik. Chem. (Frankfurt)*, *27*, 136 (1961); *34*, 273 (1962).
10. J. Ranft, *Ann. Physik*, *9*, 124 (1962); *10*, 399 (1963).
11. S. G. Frankiss, *J. Phys. Chem.*, *67*, 752 (1963).
12. A. W. Douglas, *J. Chem. Phys.*, *40*, 2413 (1964).
13. C. S. Foote, *Tetrahedron Letters*, *9*, 579 (1963).
14. K. Mislow, *ibid.*, *22*, 1415 (1964).
15. G. P. van der Kelen and Z. Eeckhut, *J. Mol. Spectry.*, *10*, 141 (1963).
16. G. J. Karabatsos, *J. Am. Chem. Soc.*, *83*, 1230 (1961).
17. G. J. Karabatsos, J. D. Graham, and F. Vane, *J. Phys. Chem.*, *65*, 1657 (1961).

18. G. J. Karabatsos, J. D. Graham, and F. Vane, *J. Am. Chem. Soc.*, *84*, 37 (1962).

19. J. Ranft, *Ann. Physik*, *10*, 399 (1963).

20. G. J. Karabatsos, J. D. Graham, and F. Vane, *J. Am. Chem. Soc.*, *83*, 2778 (1961).

21. M. Karplus and D. Grant, *Proc. Natl. Acad. Sci. U. S.*, *45*, 1269 (1959).

22. R. J. Abraham and J. A. Pople, *Mol. Phys.*, *3*, 609 (1960).

23. J. G. Powles and J. H. Strange, *Mol. Phys.*, *5*, 329 (1962); *Diss. Fara. Soc.*, *34*, 30 (1962).

24. G. W. Smith, *J. Chem. Phys.*, *39*, 2031 (1963); *40*, 2037 (1964).

25. For Magnetically nonequivalent methylene protons of sulfites see: (a) H. Finegold, *Proc. Chem. Soc.*, 283 (1960); (b) F. Kaplan and J. D. Roberts, *J. Am. Chem. Soc.*, 83, 4666 (1961); (c) J. G. Pritchard and P. C. Lauterbur, *ibid.*, *83*, 2105 (1961).

26. G. J. Karabatsos, R. A. Taller, and F. M. Vane, *J. Am. Chem. Soc.*, *85*, 2326 (1963).

27. J. A. Pople, W. G. Schneider, and H. J. Bernstein, *High-Resolution Nuclear Magnetic Resonance*, McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 195.

28. H. A. Bent, *Chem. Rev.*, *61*, 275 (1961).

29. M. Karplus, *J. Am. Chem. Soc.*, *85*, 2870 (1963); and previous references by the same author.

30. H. S. Gutowsky and A. L. Porte, *J. Chem. Phys.*, *35* 839 (1961).

31. R. J. Abraham and H. J. Bernstein, *Can. J. Chem.*, *39*, 905 (1961).

32. J. D. Graham and M. T. Rogers, *J. Am. Chem. Soc.*, *84*, 2249 (1962).

33. O. L. Chapman, *ibid.*, *85*, 2014 (1963).

34. G. V. Smith and H. Kriloff, *ibid.*, *85*, 2016 (1963).

35. P. Laszlo and P. von R. Schleyer, *ibid.*, *85*, 2018 (1963).

36. J. O. Halford, *J. Chem. Phys.*, *24*, 830 (1956).

37. D. Peters, *J. Chem. Soc.*, 2003 (1963).

38. A. Veillard and G. Del Re, *Theoret. Chim. Acta*, *2*, 55 (1964).

39. U. Blukis, P. H. Kasai, and R. J. Myers, *J. Chem. Phys.*, *38*, 2753 (1963).

40. L. S. Bartell, B. L. Carroll, and J. P. Guillory, *Tetrahedron Letters*, *13*, 705 (1964).

41. For further references see the recent review by W. H. Flygare, *Science*, 140, 1179 (1963).

42. I. N. Levine, *J. Chem. Phys.*, *38*, 2326 (1963).

43. G. J. Karabatsos, F. M. Vane, and R. A. Taller, *J. Am. Chem. Soc.*, *85*, 2327 (1963).

44. E. B. Whipple, W. E. Stewart, G. S. Reddy, and J. H. Goldstein, *J. Chem. Phys.*, *34*, 2136 (1961).

45. D. Kivelson, E. B. Wilson, Jr., and D. R. Lide, Jr., *ibid.*, *32*, 205 (1960).

46. Dr. B. L. Shapiro, private communication.

47. T. K. Bierlein and E. C. Lingafelter, *Acta Cryst.*, *4*, 450 (1951).

48. C. R. Walter, Jr., *J. Am. Chem. Soc.*, *74*, 5185 (1952).

49. R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *The Systematic Identification of Organic Compounds*, John Wiley and Sons, New York, N. Y., 4th ed., 1948, p. 219.

50. T. M. Burton and E. F. Degering, *J. Am. Chem. Soc.*, *62*, 227 (1940).

51. R. E. Dodd and P. L. Robinson, *Experimental Inorganic Chemistry*, Elsevier Publishing Co., New York, N. Y.,

52. *Organic Synthesis, Collective Volume II*, John Wiley and Sons, New York, N. Y., 1943, pp. 165-166.

53. W. Gerrard, A. Nechvatal, and B. M. Wilson, *J. Chem. Soc.*, 2088 (1950).

54. W. Gerrard and P. Tolcher, J. Chem. Soc., 3640 (1954).

55. J. B. Conant, C. N. Webb, and W. C. Mendum, J. Am. Chem. Soc., 51, 1246 (1929).

56. F. C. Whitmore, J. Am. Chem. Soc., 63, 2633 (1941).

57. P. S. Skell and I. Starer, J. Am. Chem. Soc., 82, 2971 (1960).

58. M. S. Silver, J. Am. Chem. Soc., 83, 3482 (1961).

59. S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber, and J. Corse, J. Am. Chem. Soc., 74, 1113 (1952).

60. F. C. Whitmore, E. L. Wittle, and A. H. Popkin, J. Am. Chem. Soc., 61, 1585 (1939).

61. G. J. Karabatsos and J. D. Graham, J. Am. Chem. Soc., 82, 5250 (1960).

62. M. S. Silver, J. Am. Chem. Soc., 82, 2971 (1960).

63. P. S. Skell, I. Starer, and A. P. Krapcho, J. Am. Chem. Soc., 82, 5257 (1960).

64. D. J. Cram and J. E. McCarty, J. Am. Chem. Soc., 79, 2866 (1957).

65. C. L. Arcus, Chemistry and Industry, 442 (1947).

66. A. J. Finlayson and C. C. Lee, Can. J. Chem., 37, 940 (1959).

67. A. P. Krapcho and M. Benzon, J. Am. Chem. Soc., 84, 1036 (1962).

68. W. G. Dauben and J. B. Rogan, J. Am. Chem. Soc., 79, 5002 (1957).

69. J. D. Roberts and J. A. Yancy, J. Am. Chem. Soc., 75 3165 (1953).

70. D. P. Steveson, C. D. Wagner, O. Beech, and J. W. Otwos, J. Am. Chem. Soc., 74, 3269 (1952).

71. J. D. Roberts, C. C. Lee, and W. H. Saunders, J. Am. Chem. Soc., 76, 4501 (1954).

72. P. N. Rylander and S. Meyerson, J. Am. Chem. Soc., 78, 5799 (1956).

73. P. S. Skell and I. Starer, J. Am. Chem. Soc., 81, 4117 (1959).

74. P. S. Skell and R. J. Maxwell, J. Am. Chem. Soc., 84, 3963 (1962).

75. S. Meyerson and H. Hart, J. Am. Chem. Soc., 85, 2358 (1963).

76. H. M. Grubb and S. Meyerson in The Mass Spectrometry of Organic Ions, F. W. McLafferty, ed., Academic Press, Inc., New York, N. Y., 1963, p. 453.

77. O. A. Reutov and T. N. Shatkina, Tetrahedron, 18, 237 (1962).

78. S. Winstein and B. K. Morse, J. Am. Chem. Soc., 74, 1133 (1952).

79. F. C. Whitmore, K. C. Laughlin, J. F. Matuszeski, and J. D. Surmatis, J. Am. Chem. Soc., 63, 756 (1941).

80. F. C. Whitmore and W. A. Mosher, J. Am. Chem. Soc., 68, 281 (1946).

81. W. A. Mosher and J. C. Cox, J. Am. Chem. Soc., 72, 3701 (1950).

82. P. S. Skell and I. Starer, J. Am. Chem. Soc., 84, 3962 (1962).

83. R. L. Baird and A. Aboderin, Tetrahedron Letters, 4, 235 (1963).

84. J. D. Roberts and M. Halman, J. Am. Chem. Soc., 75, 5759 (1953).

85. O. A. Reutov and T. N. Shatkina, Dokl. Akad. Nauk. S. S. S. R., 133, 606 (1960).

86. S. R. Landauer and H. N. Rydon, J. Chem. Soc., 2224 (1953).

87. N. Kornblum and D. C. Iffland, J. Am. Chem. Soc., 77, 6653 (1955).

88. R. L. Baird and A. A. Aboderin, J. Am. Chem. Soc., 86, 252 (1964).

89. A. A. Aboderin and R. L. Baird, J. Am. Chem. Soc., 86, 2300 (1964).

90. C. C. Lee, J. E. Kruger, and E. W. C. Wong, J. Am. Chem. Soc., 87, 3985 (1965).

91. C. C. Lee and J. E. Kruger, J. Am. Chem. Soc., 87, 3986 (1965).

92. G. J. Karabatsos, F. M. Vane, and S. Meyerson, J. Am. Chem. Soc., 85, 733 (1963).

93. J. D. Roberts, R. E. McMahon, and J. S. Hine, J. Am. Chem. Soc., 72, 4237 (1950).

94. W. A. Sanderson and H. S. Mosher, J. Am. Chem. Soc., 83, 5033 (1961).

95. D. J. Cram and M. R. V. Sahyun, J. Am. Chem. Soc., 85, 1257 (1963).

96. P. S. Skell and W. L. Hall, J. Am. Chem. Soc., 85, 2851 (1963).

97. S. H. Langer, S. Connell, and I. Wender, J. Org. Chem., 23, 50 (1958).

98. D. M. Smith and W. M. D. Bryant, J. Am. Chem. Soc., 57, 61 (1935).

99. Organic Synthesis, Collective Volume II, John Wiley and Sons, New York, N. Y., 1943, p. 279, note 6.

100. A. Kruis and W. Schanzer, Zeit. fur Physik Chemie, 191A, 303 (1942).

101. L. F. Fieser, Experiments in Organic Chemistry, D. C. Heath and Co., Boston, Mass., 3rd ed., 1955, p. 345.

102. R. S. Tipson, J. Org. Chem., 9, 235 (1944).

103. P. D. Bartlett and E. B. Lefferts, J. Am. Chem. Soc., 77, 2804, 2806 (1955).

104. F. C. Whitmore and D. P. Langlois, J. Am. Chem. Soc., 54, 3438 (1932).

105. M. L. Huggins, J. Am. Chem. Soc., 75, 4123 (1953).

106. J. Hinze, M. A. Whitehead and H. H. Jaffé, J. Am. Chem. Soc., 85, 148 (1963).

107. J. R. Cavanaugh and B. P. Dailey, J. Chem. Phys., 34, 1099 (1961).

108. B. P. Dailey and J. N. Shoolery, J. Am. Chem. Soc., 77, 3977 (1955).

109. R. E. Glick and A. A. Bothner-By, J. Chem. Phys., 25, 362 (1956).

110. T. Schaefer, Can. J. Chem., 40, 1 (1962).