I. THE ELECTRIC MOMENTS OF SOME DERIVATIVES OF AZOBENZENE

II. THE ELECTRIC MOMENTS OF SOME STEROLS

By

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A THESIS

Submitted to the School of Graduate Studies of Michigan
State College of Agriculture and Applied Science
in partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Chemistry

1954

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ACKNOWLEDGEMENTS

The writer gratefully acknowledges the friendly, discerning advice and guidance of Dr. Max T. Rogers under whose supervision this investigation was undertaken.

Sincerest thanks is due Dr. John L. Speirs, who constructed the dielectric constant cell used for the sterols.

The writer deeply appreciates the generous fellowship grant from the Upjohn Pharmaceutical Company during the academic year 1952-53, and acknowledges the kind cooperation of Dr. E. R. Garrett and his associates who provided pure samples of many of the steroids used here.

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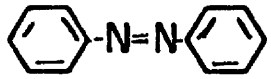
INTRODUCTION

The primary aim of this work has been the correlation of electric dipole moment and structure for two general types of organic molecules, some derivatives of azobenzene and a group of steroids. In both series the electric moment was calculated from dielectric constant and density data for dilute solutions of the substances in non-polar solvents. However, interpretation of the data required the application of quite different concepts, which are discussed below.

The azobenzene molecule



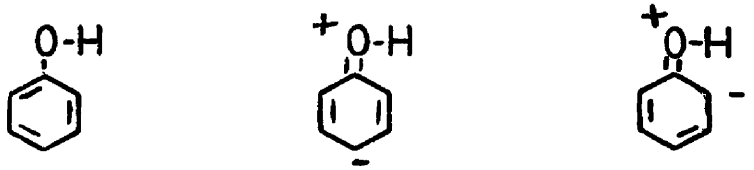
has a number of conjugated double bonds, a situation conducive to the existence of resonance. This phenomenon can be simply illustrated in the case of benzene for which several structures can be written, the two most important being

This method of representation does not imply independent existence of the forms which can possibly be written. These forms are intellectual constructions while the molecule behaves like a composite of these forms, rather than like any single one which can be drawn. In the language of quantum mechanics, upon which the theory of resonance is based,

$$\psi = k_1 \phi_1 + k_2 \phi_2 .$$

The wave function, ψ, a mathematical function of time and coordinates for all the particles constituting the system, represents a stationary state of the molecule. In theory ψ can be obtained as a solution of the Schrödinger wave equation but the complications involved make an approximation method more feasible. One can assume, as above, that ψ is a linear combination of known functions ϕ_1 and ϕ_2. The closeness with which ψ approximates the solution of the wave equation for the molecule depends upon the number of functions, ϕ_n, and the judgment exercised in choosing them. When $\phi_1, \phi_2, \ldots \phi_n$ can be correlated with certain structures of the molecule under consideration, the molecule can be said to resonate among these structures. In the case of benzene the equivalence of the two major structures means that neither ϕ_1 nor ϕ_2 alone is a good approximation to the eigenfunction desired; rather a function intermediate between them is used. As long as undue physical significance is not attached to these resonating structures, they are quite useful, and were used here.

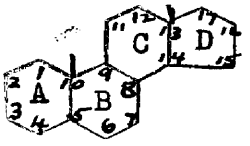
When polar groups are substituted on the benzene nucleus, it is often possible to find evidence for resonance from the properties of the resulting molecule. Thus phenol is a stronger acid than aliphatic alcohols and also tends to direct many second substituents entering the ring to the ortho and para positions. Both effects are understandable in light of the resonance structures,



The positive charge on the oxygen repels the proton increasing the acidic character while the accumulation of negative charge in the ortho and para positions seems to account for the directive effects.

Much dipole moment evidence for resonance is based in general on changes in moments for compounds containing a given polar group as one goes from aliphatic to benzenoid character. In this work comparison was made between analogous benzene and azobenzene compounds. Incidental to this work, the group moment and angle of the dimethylamino group was determined in both series of compounds studied.

By way of contrast to the azo compounds, there is no opportunity for resonance in the saturated steroids, having the common ring system



They often have two or more polar groups in various positions on the carbon skeleton or side chains. Their similarity causes difficulty in isolation of naturally occurring steroids or synthesis from less complex starting materials. On the other hand, relatively slight changes in the molecule often have large effects on the properties thereof. Thus the reactivity of epimers may differ greatly, epimers being chemically identical but differing in the position of one group with respect to the methyl group at C_{10}. This group is assigned the position above the plane of the ring. Therefore, groups on the same side are β -oriented, those on the opposite side, α -oriented. The reason for differences in reactions of epimers has been ascribed to steric hindrance, especially at C_{11}. Measurement of angles between polar groups in a molecular model,

calculation of the electric moment anticipated on the basis of these angles and known group moments, and comparison of this value with the observed moment could be used to verify or disprove this contention.

The type geometrical isomerism exhibited by cyclohexane

probably occurs in relatively flexible A ring of some saturated steroids. Comparison of moments found by angle measurement for each form with the observed value could be used to calculate the percent of each form in the equilibrium mixture.

There is also the possibility of correlating structural changes such as double bonds in various positions, with changes in electric moment. The changes in optical rotation and ultraviolet spectra have been correlated with structural differences in just such a way. Epimers might be distinguishable by differences in their electric moments.

In short, the scarcity of electric moment data for steroids and the potential applications of this sort of information made this work seem desirable. In addition, the methods used for treatment of the data were different than those used for the azo molecules. Thus the two sets of compounds provided a broader view of the end uses of electric moment data.

THEORY

When a chemical bond is formed between two atoms differing in electronegativity, the more electronegative atom tends to accumulate negative charge, leaving the other atom more positive. Such a bond constitutes an electric dipole, two equal charges of opposite sign separated by some distance, r. Labeling the charges +q and -q, the electric dipole moment is qr by definition.[1] This electric moment (μ) is a vector having both magnitude and direction. Since the electronic charge is of the order 4.8×10^{-10} esu and internuclear distances are usually listed in Ångstrom units ($1\text{Å} = 1 \times 10^{-8}$ cm.) most dipole moments have a magnitude of about 10^{-18} esu or one Debye unit. For polyatomic molecules with several such dipoles, the resultant moment may be considered the vector sum of the individual bond moments. This sum is what one observes experimentally and is useful in discussing the geometry of molecules and character of valence bonds.

The theoretical basis for the evaluation of electric moments is the concept of polarization of dielectrics. From classical electrostatics the electric field in a parallel-plate capacitor, with plates of area large compared with the distance between them, is

$$\underline{E} = 4\pi\sigma \qquad (1)$$

where σ is the density of charge per unit area. Now <u>in vacuo</u> this condenser has a capacitance C_o, while experiment shows that the introduction of a dielectric between the plates increases the capacitance

by a factor ε. Thus

$$C = \varepsilon C_o \tag{2}$$

where C and Co are capacitances with and without dielectric, respectively, and the proportionality constant ε is the dielectric constant. Since the electric field, $\underline{E}$, is inversely proportional to the capacitance, the field must be correspondingly reduced by ε from the value *in vacuo* upon substitution of the dielectric substance,

$$E = \frac{E_o}{\varepsilon} \tag{3}$$

The molecular theory of dielectric polarization leads to a reasonable explanation for this lowering of the field strength. Application of an electric field to a dielectric results in a tendency of molecules with permanent dipoles to align themselves in the field direction, this orientation effect being opposed by thermal agitation of the molecules. The field also induces dipoles in the molecules of the dielectric in a direction opposing the inducing field. Both effects will lower the strength of the applied field.[2] By a consideration of Gauss' Law for dielectrics, one finds the field therein to be

$$\underline{E} = \underline{D} - 4\pi \underline{P} \tag{4}$$

where $\underline{D}$ is the electric displacement and $\underline{P}$ is the polarization (electric moment per unit volume).

The polarization of a dielectric will be the sum of polarizations due to the induced separation of charge (distortion) and to the alignment tendency of the permanent dipoles (orientation). For isotropic substances the induced moment, $\underline{m}$, is proportional to the local field intensity, $\underline{F}$, the equation being

$$\underline{m} = \alpha \underline{F} \tag{5}$$

where the constant of proportionality is α, the polarizability or induced moment per unit field strength. The local field intensity $\underline{F}$ differs from the impressed value $\underline{E}$ by

$$\underline{F} = \underline{E} + \frac{4\pi P_D}{3} \tag{6}$$

where P_D is the distortion polarization.

If permanent dipoles are momentarily disregarded, one finds that

$$P_D = n\bar{m} \tag{7}$$

where n is the number of molecules per cc. and $\bar{m}$ is the average moment induced. It follows from (5) and (6) that

$$P_D = n\alpha\left(\underline{E} + \frac{4\pi P_D}{3}\right). \tag{8}$$

Use of (4) and the relation, $\underline{D} = \varepsilon \underline{E}$ gives the equation

$$4\pi P_D = \underline{E}(\varepsilon - 1) \tag{9}$$

which, when solved for P_D and inserted in (8), leads to

$$\frac{\varepsilon - 1}{\varepsilon + 2} = \frac{4\pi n\alpha}{3} \tag{10}$$

or multiplying both sides by M/d, ratio of molecular weight to density,

$$\frac{\varepsilon - 1}{\varepsilon + 2}\ \frac{M}{d} = \frac{4\pi N\alpha}{3} \tag{11}$$

where the right hand side is the molar polarization.

Any thermal collision which disturbs the position of a non-polar molecule has no lasting effect, since the field immediately induces the dipole again. However, for permanent dipoles, random thermal collisions oppose the tendency for them to align with the field. Thus the average component of the permanent dipole in the field direction as a function

of temperature must be computed.[3] If there is no field, all orientations are equally probable and the number of dipoles directed within the confines of a given solid angle, $d\Omega$, is $Ad\Omega$, where A is a constant depending on the number of molecules considered. If a dipole with a moment, μ, is oriented at an angle θ with a field of strength F, its potential energy is

$$V = -\mu F \cos \theta \tag{12}$$

and according to Boltzmann's Law the number of dipoles oriented in the solid angle is

$$A \exp(-V/kT)d\Omega = A \exp(\mu F \cos \theta/kT)d\Omega \tag{13}$$

where k is the Boltzmann constant and T is absolute temperature. The average moment for one molecule in the field direction is

$$\bar{m} = \frac{\int A \exp(\mu F \cos \theta/kT)\mu \cos \theta \, d\Omega}{\int A \exp(\mu F \cos \theta/kT)d\Omega} \tag{14}$$

Letting $\mu F/kT = x$, $\cos \theta = y$, and noting that $d\Omega = 2\pi \sin \theta d\theta = 2\pi dy$, (14) becomes

$$\frac{\bar{m}}{\mu} = \frac{\int_{-1}^{+1} \exp(xy)\, y dy}{\int_{-1}^{+1} \exp(xy)\, dy} \equiv \frac{\int dz/dx}{\int z} \tag{15}$$

Evaluating the denominator

$$z = \frac{(e^{x}-e^{-x})}{x} \tag{16}$$

and numerator, dz/dx, and combining

$$\frac{m}{\mu} = (\coth x - \frac{1}{x}) = L(x) \tag{17}$$

where L(x) is the Langevin function. Expansion of the terms of this function in power series gives, for small x values,

$$L(x) = \frac{x}{3} = \frac{\mu F}{3kT} \tag{18}$$

and

$$\bar{m} = \frac{\mu^2 F}{3kT} \tag{19}$$

This is the contribution of the permanent dipoles to the total polarizability and when added to the distortion polarizability, α, leads to a total polarization

$$P_M = \frac{4\pi N}{3}(\alpha + \mu^2/3kT). \tag{20}$$

But by (11), we can obtain a value of P_M experimentally by measuring dielectric constants over a range of temperatures. Then a plot of P_M against $1/T$ permits simultaneous evaluation of μ and α from slope and intercept.

In the absence of permanent dipoles there are two contributions to the total polarization to consider. These are the atomic (P_A) and electronic (P_E) polarizations caused by displacement of nuclei and electrons by the impressed field. To use (20) in calculating the dipole moment, we must either eliminate or evaluate these quantities. This is done in practice by measuring the dielectric constant in an alternating field of frequency sufficiently high to cause the atomic polarization to disappear. For polar molecules the orientation polarization will also disappear at such frequencies. These facts are the basis for one common experimental method for measuring dipole moments, the refractivity method, described below.[4]

At long wave lengths in the infrared the Maxwell relation

$$\varepsilon = n^2 \tag{21}$$

holds and the total polarization can be expressed by

$$P_T = \frac{n^2-1}{n^2+2}\frac{M}{d} \cong MR_D \qquad (22)$$

which is seen to be equal to the molar refraction as defined by the Lorenz-Lorentz equation.

Now the molar refraction is essentially constant since there is no orientation term involved. Thus, by determination of the total polarization from dielectric constant and density values, and of molar refraction from the refractive index in a portion of the infrared region where no absorption occurs, one can get the orientation polarization by difference. Experimental difficulties make it more expedient to use the sodium D line for refractive index measurements and to take the resultant molar refraction to be $P_A + P_E$. The P_A term is usually small and either neglected or estimated to be about ten percent of P_E. Since the orientation polarization term is $\frac{4\pi N \mu^2}{9kT}$,

we see that $$P_T - MR_D = \frac{4\pi N \mu^2}{9kT} \qquad (23)$$

or in terms of μ and known constants

$$\mu = 0.0128 \sqrt{(P_T - MR_D)T}. \qquad (24)$$

The preceding discussion applies to gases or vapors. Since many compounds are not obtainable as such, dilute solutions of polar solutes in non-polar solvents are used and give much useful information. This entails some modification of the Clasuius-Mosotti relation. Thus, the molar polarization for the solution is

$$P_{12} = \frac{\varepsilon_{12}-1}{\varepsilon_{12}+2}\frac{M_2 f_2 + M_1 f_1}{d_{12}} \qquad (25)$$

where subscripts 1, 2, and 12 refer to solvent, solute, and solution respectively, and f is mole fraction. Now

$$P_{12} = P_1 f_1 + P_2 f_2 \tag{26}$$

so solving for P_2 and using the fact that $f_1 = 1-f_2$, one finds that

$$P_2 = \frac{P_{12}-P_1}{f_2} - P_1, \tag{27}$$

is the molar polarization of the solute in terms of molar polarizations of solvent and solution and mole fraction of solute. By using a series of solutions containing low concentrations of solute, the corresponding P_2 values are obtained, plotted graphically as a function of concentration and the best line through the points extrapolated to zero concentration to give the true polarization P^o_2 of the solute in the absence of solvent effects. Substitution of n^2 for ε in (25) gives the molar refraction of the solution. Then

$$MR_{D_{12}} = MR_{D_1} f_1 + MR_{D_2} f_2 \tag{28}$$

and

$$MR_{D_2} = \frac{MR_{D_{12}}-MR_{D_1}}{f_2} - MR_{D_1} \tag{29}$$

and the best line through the points on the MR_{D_2} - concentration graph is extrapolated to infinite dilution giving the molar refraction of the solute. Then the difference $(P^o_2 - MR^o_{D_2})$ is used in (24) to compute the dipole moment.

EXPERIMENTAL

Densities

The density values were determined at 25°C, using a modified Ostwald pycnometer.[8] All weights were corrected for the buoyant effect arising when weighing in air with brass weights.

Dielectric Constants

Dielectric constants were measured using the heterodyne beat method, in which the frequencies of two oscillating circuits are made identical. One circuit contains known elements of resistance, capacitance and inductance, while the other contains the experimental cell with the solution. The oscillations from the two circuits are fed into a mixer tube (6SA7), the emerging frequency being the difference between the two impressed frequencies.

This signal, when amplified, can be heard through a speaker, the pitch decreasing to a null point when the frequencies are matched. For sharper, more sensitive detection of this condition, a visual method employing a "Magic Eye" indicator tube (6E5) was used.

The circuit used was essentially that described by Chien[9]. It had a two-hundred kilocycle quartz crystal as a control element in the fixed frequency oscillator. The experimental cell, a calibrated variable precision condenser (General Radio, Type 722D), and an inductance are connected in parallel in one of the tuned circuits of the variable frequency oscillator. The frequency of this second circuit is

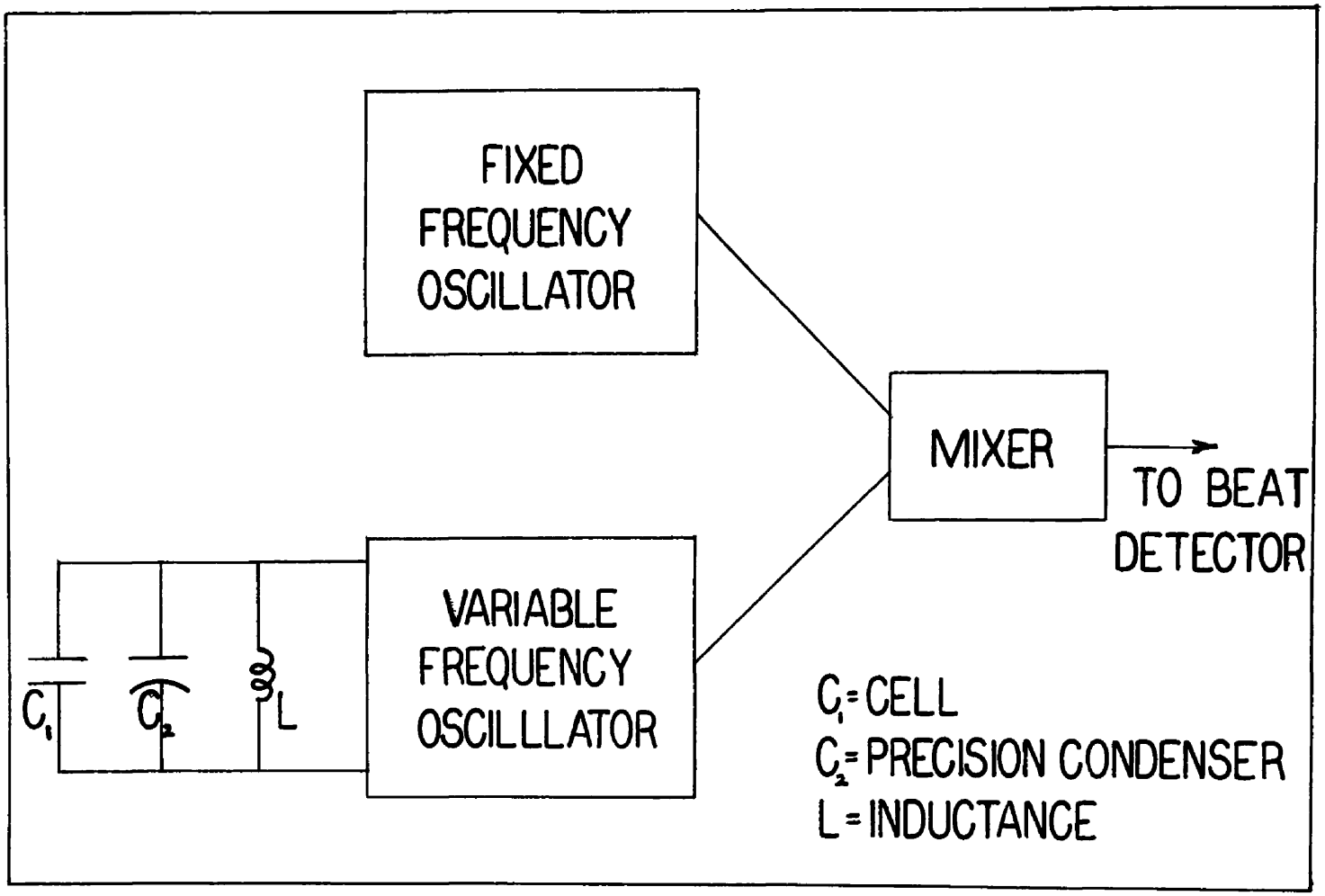


Figure 1. A block diagram of the circuit used in measuring the dielectric constants of the solutions.

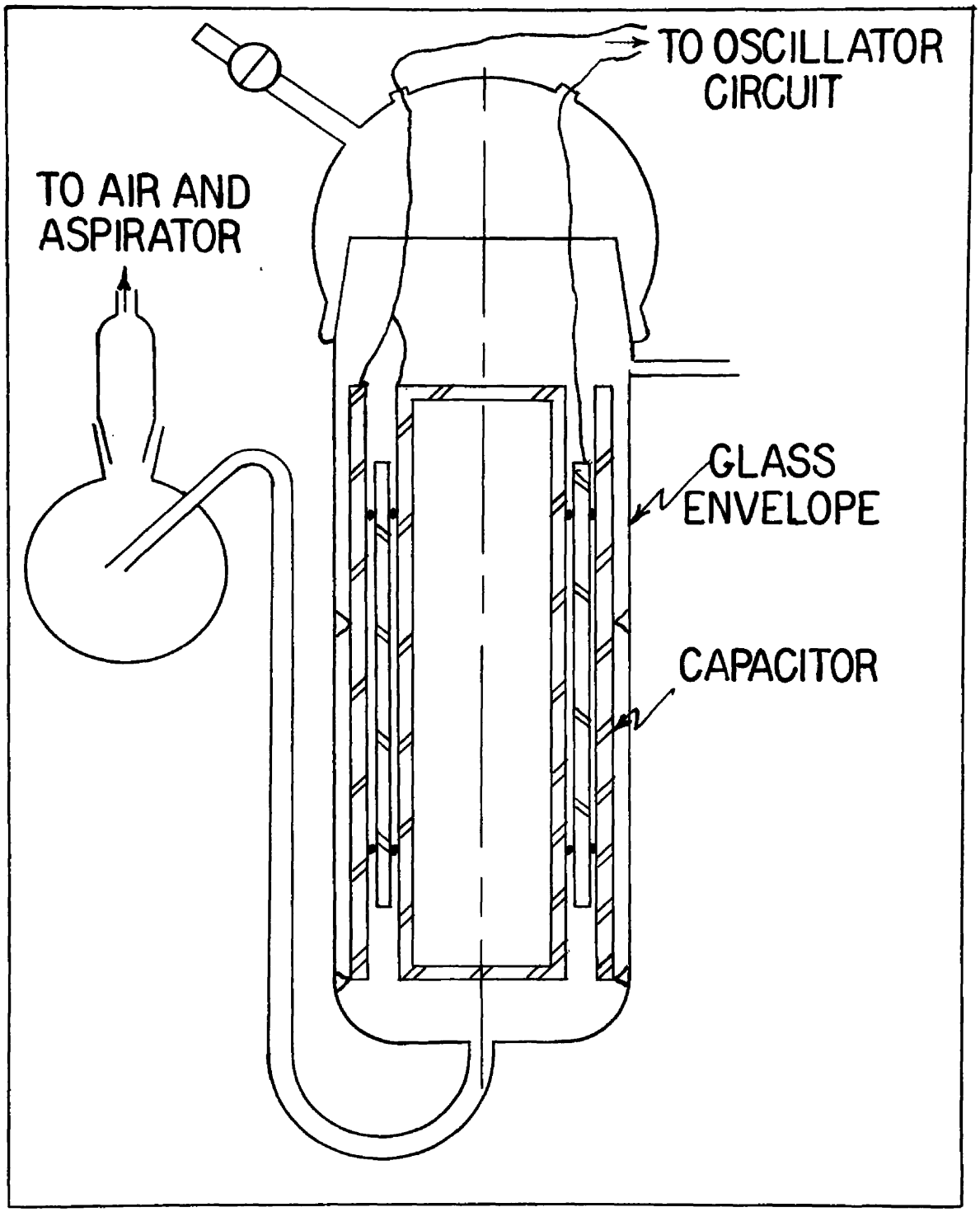


Figure 2. The experimental cell used in dielectric constant measurements.

$$\nu = 1/2 \sqrt{LC},$$

where L is inductance and C is capacitance, so changes in the cell capacitance must be matched by a compensating change in the precision condenser setting for the null condition to be retained. Figure 1 is a block diagram of the circuit used in the dielectric constant measurements.

The experimental dielectric constant cell consists of three concentric, rhodium-plated, brass cylinders which are separated by glass spacers. The middle cylinder is at high potential and shorter than the outer and inner cylinders, which are grounded, (see Figure 2). This geometry helps to eliminate the edge effect which causes inhomogeneity in the electric field between the plates.[10] The cell and glass envelope require fifty milliliters of solution for measurement.

The temperature was maintained at 25.00 ± 0.01°C. by using a thyratron-controlled thermoregulator device in conjunction with a knife heater, and a motor-driven stirrer to minimize temperature gradients within the bath. The General Radio condenser was calibrated by the National Bureau of Standards and the corrections indicated by their calibration chart were applied to each capacitance reading. In a typical experiment, six dilute solutions ranging in concentration from 0.0001 to 0.001 mole fraction were prepared. The measurements on any set of six were completed in a single day to assure reasonably constant conditions.

Most of the compounds used were prepared by Dr. T.W. Campbell, the exceptions being noted under the section entitled "Preparation of Compounds". They were recrystallized from acetone, ethyl alcohol, or isopropyl alcohol, or any two of these which proved satisfactory, until the melting points after two consecutive recrystallisations were identical. All melting points are corrected.

The non-polar solvent used was benzene, purified by freezing a major portion of some C.P. thiophene-free material, filtering, remelting the solid residue, and repeating the process. The solvent obtained in this manner was then distilled and stored over sodium. It was found to have a refractive index of 1.4980 and density of 0.87343, both measured at 25°C.

Preparation of Compounds

p-Aminoazobenzene. This compound was an Eastman Kodak Company product which was purified to give a melting point of 124°C. The literature value for the melting point is 126°C.

p-Nitroazobenzene. This was prepared by condensation of p-nitraniline with nitrosobenzene[11,12] in concentrated alcohol solution containing a drop of acetic acid. The compound melted at 134°C. The literature value for the melting point is 134°C.

p-p'-Dinitroazobenzene. This was prepared by reducing p-dinitrobenzene with glucose in an alcohol solution made alkaline by two grams of sodium hydroxide. The product was allowed to stand twenty-four hours in the reaction medium, then isolated,[15] the melting point being 223-24°C.

Tetramethyl-p-phenylenediamine. This compound was also Eastman Kodak Company White Label material which had a melting point, on purification, of 49°C, the melting point in the literature being 50°C.

p-p'-Tetramethyldiaminoazobenzene. This could not be isolated by methods suggested in the literature,[13] so it was prepared by the action of lithium aluminum hydride on an ether solution of p-nitrodimethylaniline

and extracted with hydrochloric acid from which the free amine was recovered by neutralization with ammonia. The crude product was extracted with dioxane and reprecipitated by water. A melting point of 260-61°C was observed.

p-Benzalaminoazobenzene. This was the product resulting from the condensation of benzaldehyde with p-aminoazobenzene.[14] It melted at 128°C; the value reported in the literature was 129°C.

p-Tolualaminoazobenzene. This compound was obtained from the reaction between p-aminoazobenzene and p-tolualdehyde in boiling alcohol containing a drop of acetic acid. The melting point was 117°C, and in the literature was 120°C.

p-(p-Dimethylaminobenzalamino)-azobenzene. This compound was prepared by mixing concentrated alcoholic solutions of p-aminoazobenzene and p-dimethylaminobenzaldehyde. The melting point was 176°C; the literature value is 176°C.

CALCULATIONS

Following a suggestion by Halverstadt and Kumler,[5] the method of calculating the total polarization discussed above was revised in an effort to eliminate accumulation of error. These workers have shown that both dielectric constant and specific volume (1/d) are linear functions of weight fraction of solute in a majority of cases, the relation being of the form

$$\varepsilon_{12} = \varepsilon_1 + \alpha W_2$$

$$v_{12} = v_1 + \beta W_2$$

where the subscripts have the same meaning as before while α and β are the slopes of the lines obtained when ε_{12} and v_{12} respectively are plotted against weight fraction, W_2; also ε_1 and v_1 are the corresponding intercepts at infinite dilution.

Substitution of these values of ε_{12} and v_{12} in the expression for the specific solute polarization, P_{12}, where

$$P_{12} = \frac{(\varepsilon_{12}-1)\ 1}{(\varepsilon_{12}+2)\ d}$$

gives, in terms of mole fraction, instead of weight fraction,

$$P^{o}_{2} = \frac{3\alpha' v_1 M_1}{(\varepsilon_1+2)^2} + (M_2 v_1 + M_1 \beta') \frac{\varepsilon_1 - 1}{\varepsilon_1 + 2} \quad . \qquad (30)$$

This equation was used in all calculations reported here.

The extrapolated values of ε_{12} and v_{12} should agree fairly well with those found for the pure solvent. Often, however, deviations not attributable to experimental error are noted. It has been asserted that

discrepancies indicate absorption of water by the solutions in the handling process and that these values should be used in lieu of the experimental data for the pure solvent. This viewpoint has been contested and some workers[6] advocate inclusion of accepted values of the pure solvent as points on the ϵ_{12}-f_2 and v_{12}-f_2 graphs. We have chosen to use the extrapolated values, with the accepted values used as a guide in plotting.

In the calculation of molar refraction using refractive index data the relation $\epsilon = n^2$ is assumed to be valid. However, this is subject to several restrictions, one of which is that the molecule must not absorb near the wave length used for the measurement. The compounds used here were all colored, and since the Abbe refractometer available is useful only for sodium D line, refractive index data seemed to be of doubtful value. Instead, the additivity of bond refractions was assumed and literature values[7] of these used to arrive at a figure for the molar refraction.

Before measuring the dielectric constant, it is necessary to get the cell constant for the experimental cell. This is done by measuring the capacitance of the cell at 25°C. with air, then benzene, as dielectrics. Then

$$\text{Cell Constant} = \frac{C_{air} - C_{bz}}{\epsilon_{bz} - 1} \qquad \text{Where} \qquad \epsilon_{bz} = 2.2725.$$

With this cell constant and capacitance readings for air and a solution of given concentration, the dielectric constant is

$$\epsilon_{12} = \frac{(C_{air} - C_{Sol'n}) + \text{Cell Const.}}{\text{Cell Const.}}$$

The density of each solution was determined at 25°C. Then plots

of ε_{12} and v_{12} against f_2 produced two sets of points lying along straight lines, within experimental error. The slopes of the best straight lines are α' and β' respectively and are used in the equation of Halverstadt and Kumler for computing molar polarization.

RESULTS

The experimentally determined dielectric constants (ϵ_{12}) and specific volumes (v_{12}) of the benzene solutions at 25°C are compiled in Table I. The graphical plots of dielectric constant and specific volume versus mole fraction (f_2) are shown in Figures 3-11. The slopes α' and β', and the intercepts at infinite dilution ϵ_1 and v_1 of the straight lines so obtained are listed in Table II along with values of the molar polarization of the solute at infinite dilution (P^o_2) calculated using Equation 30. The molar refractions ($MR^o_{D_2}$) calculated from empirical constants and the dipole moments (μ) obtained using Equation 24 are also listed in Table II.

RESULTS

TABLE 1

DIELECTRIC CONSTANTS AND SPECIFIC VOLUMES OF THE BENZENE SOLUTIONS AT 25°C

p-Aminoazobenzene		
f_2	ε_{12}	v_{12}
0.002008	2.2928	1.14338
.001510	2.2886	1.14372
.001126	2.2847	1.14405
.000645	2.2799	1.14440
.000462	2.2778	1.14464
.000214	2.2751	1.14469

p-Nitroazobenzene		
f_2	ε_{12}	v_{12}
0.002040	2.3306	1.14282
.001738	2.3232	1.14296
.001517	2.3174	1.14325
.001336	2.3089	1.14352
.001234	2.3077	1.14360
.000803	2.2957	1.14397
.000554	2.2894	1.14423

TABLE I continued

Tetra-methyl-p-phenylene diamine		
f_2	ε_{12}	ν_{12}
0.002186	2.2794	1.14441
.001617	2.2781	1.14456
.001098	2.2767	1.14473
.000632	2.2762	1.14478
.000360	2.2750	1.14483

p-Nitroazobenzene		
f_2	ε_{12}	ν_{12}
0.002272	2.3348	1.14292
.001887	2.3236	1.14333
.001572	2.3151	1.14375
.001191	2.3047	1.14402
.000787	2.2925	1.14443
.000351	2.2802	1.14482

p,p'-Dinitroazobenzene		
f_2	ε_{12}	ν_{12}
0.001292	2.2775	1.14299
.000990	2.2770	1.14337
.000836	2.2764	1.14365
.000641	2.2764	1.14394
.000377	2.2760	1.14433
.000219	2.2763	1.14462

TABLE I continued

p,p'-Tetramethyldiamino azobenzene		
f_2	ε_{12}	ν_{12}
0.001555	2.2847	1.14343
.001003	2.2814	1.14396
.000565	2.2785	1.14439
.000435	2.2762	1.14452
.000280	2.2764	1.14468
.000152	2.2751	1.14475

p-Benzalaminoazobenzene		
f_2	ε_{12}	ν_{12}
0.001316	2.2829	1.14352
.000644	2.2792	1.14422
.000304	2.2756	1.14464
.000098	2.2735	1.14471
.001126	2.2798	1.14385
.000914	2.2788	1.14402
.000495	2.2763	1.14449
.000247	2.2749	1.14471

TABLE I Continued

p-(p-Dimethylaminobenzalamino)azobenzene

f_2	ε_{12}	ν_{12}
0.000977	2.3038	1.14369
.000876	2.2983	1.14379
.000710	2.2950	1.14397
.000529	2.2892	1.14428
.000353	2.2847	1.14454
.000169	2.2802	1.14475

p-(p-Toulualamino)-azobenzene

f_2	ε_{12}	ν_{12}
0.001228	2.2845	1.14362
.001013	2.2824	1.14385
.000555	2.2786	1.14433
.000365	2.2754	1.14457
.000165	2.2740	1.14481

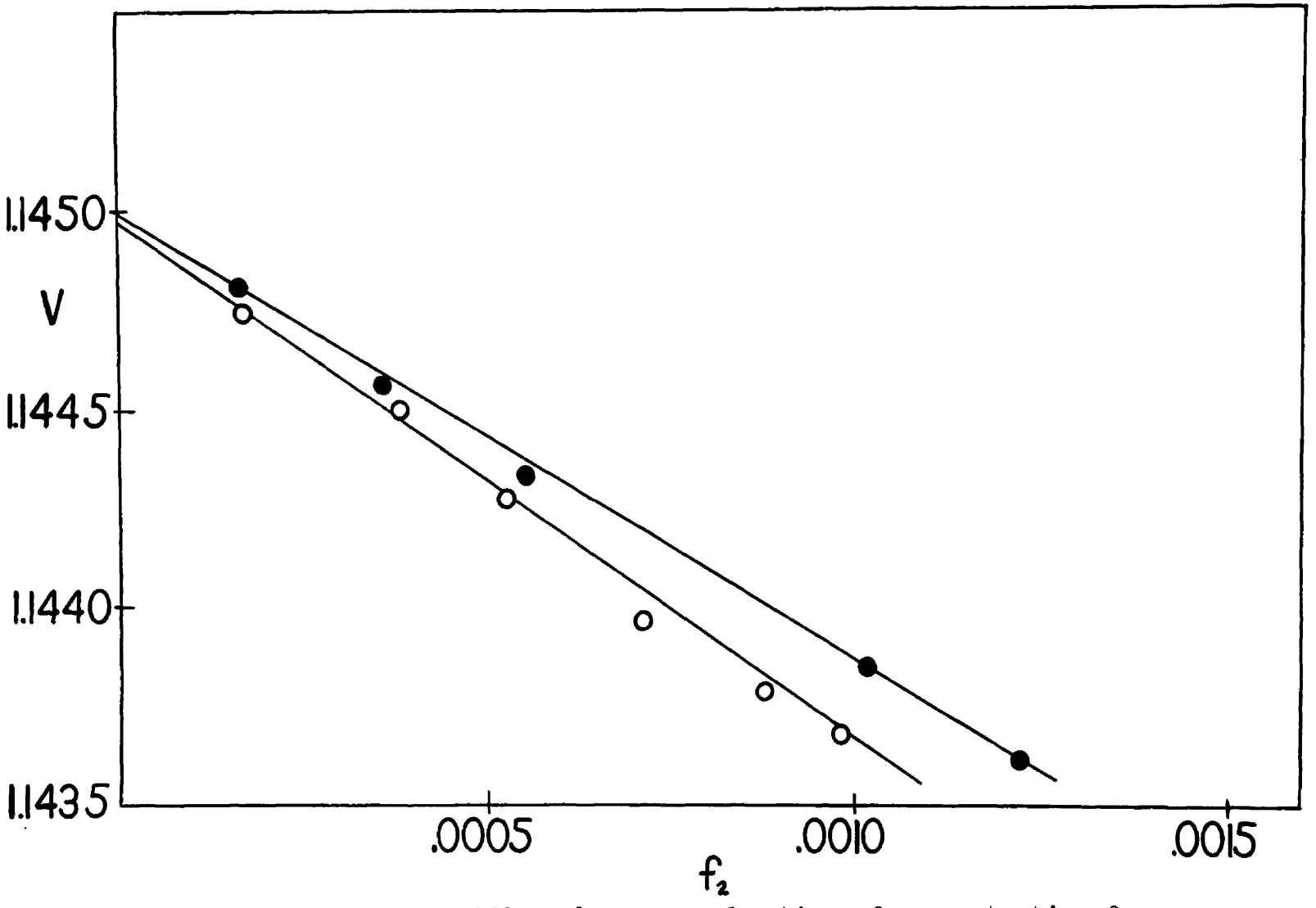


Figure 3. Specific volume as a function of concentration for benzene solutions of ● p-(p-tolualamino)-azobenzene and O p-(p-dimethylaminobenzalamino)-azobenzene.

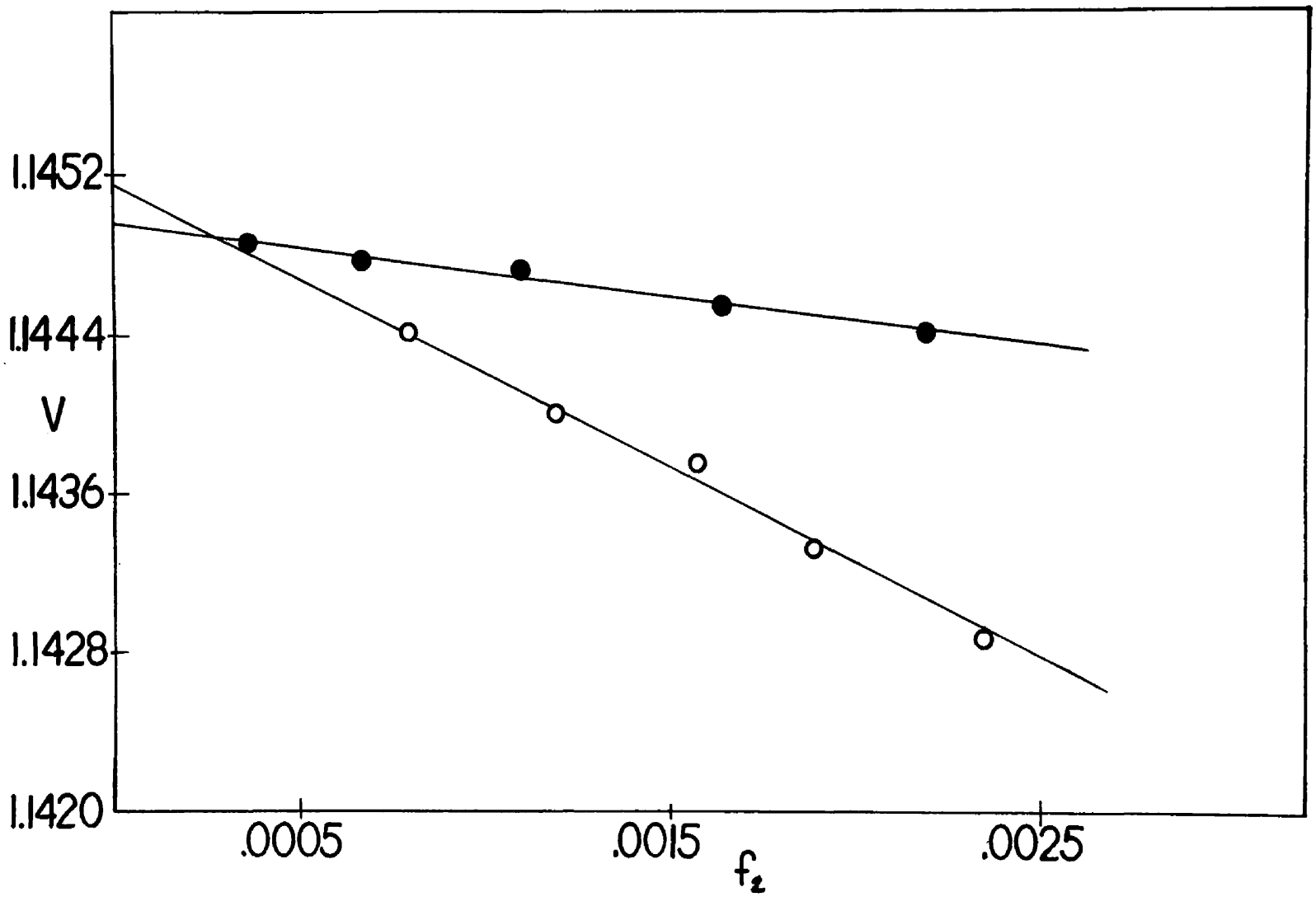


Figure 4. Specific volume as a function of concentration for benzene solutions of ● tetramethyl-p-phenylene-diamine and ○ p-nitroazobenzene.

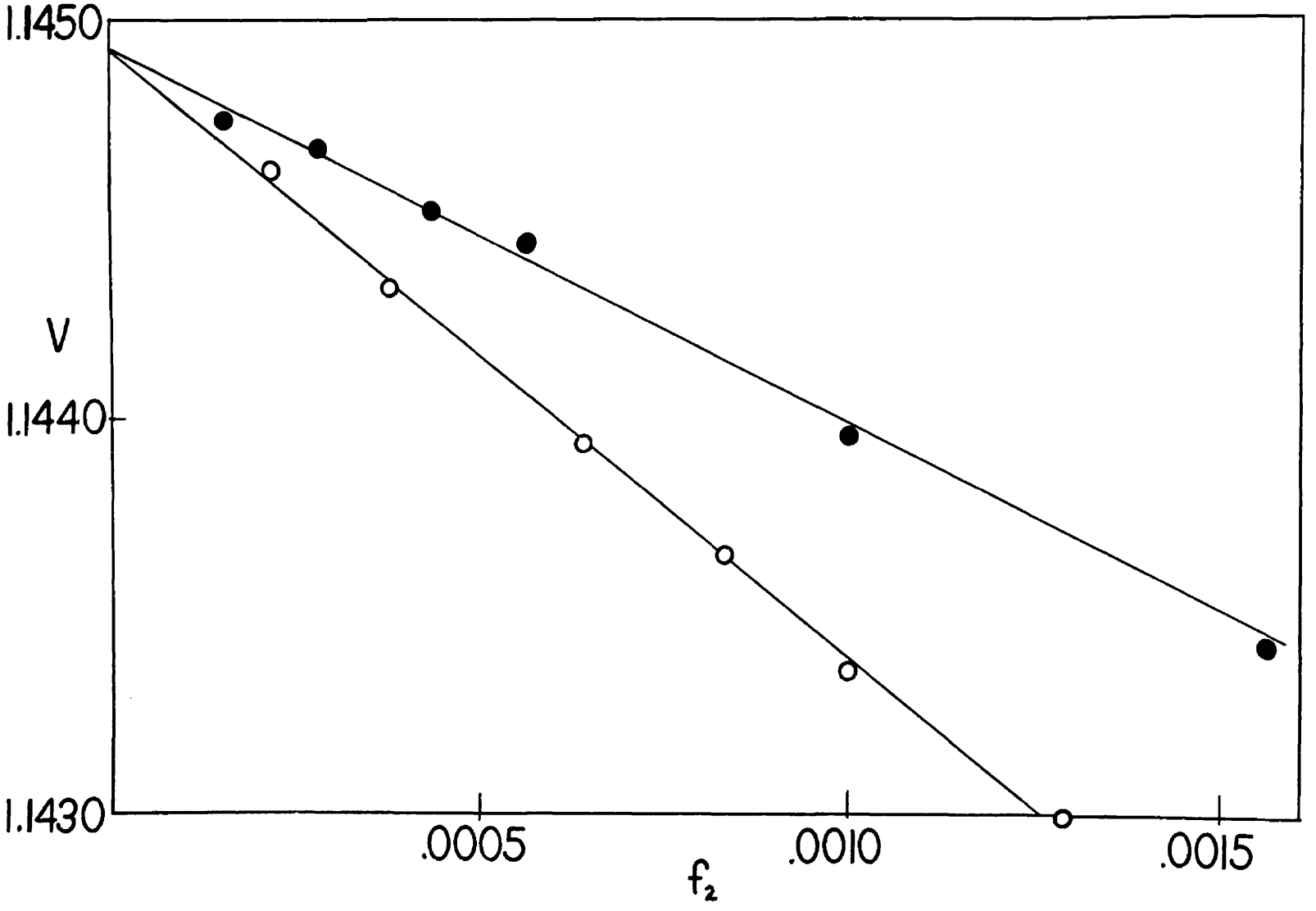


Figure 5. Specific volume as a function of concentration for benzene solutions of ● p,p'-tetramethyldiaminoazobenzene and ○ p,p'-dinitroazobenzene.

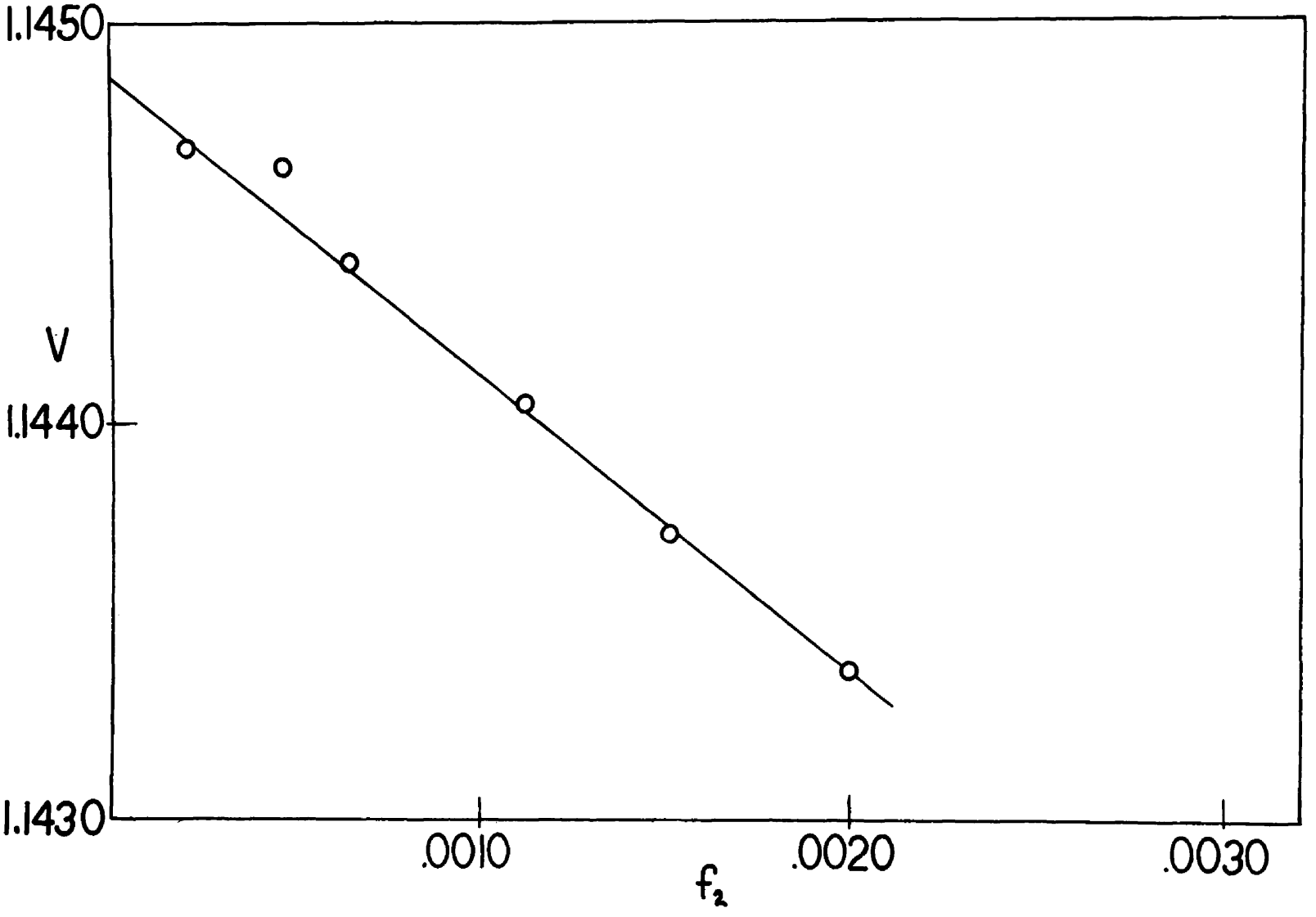


Figure 6. Specific volume as a function of concentration for benzene solutions of p-aminoazobenzene.

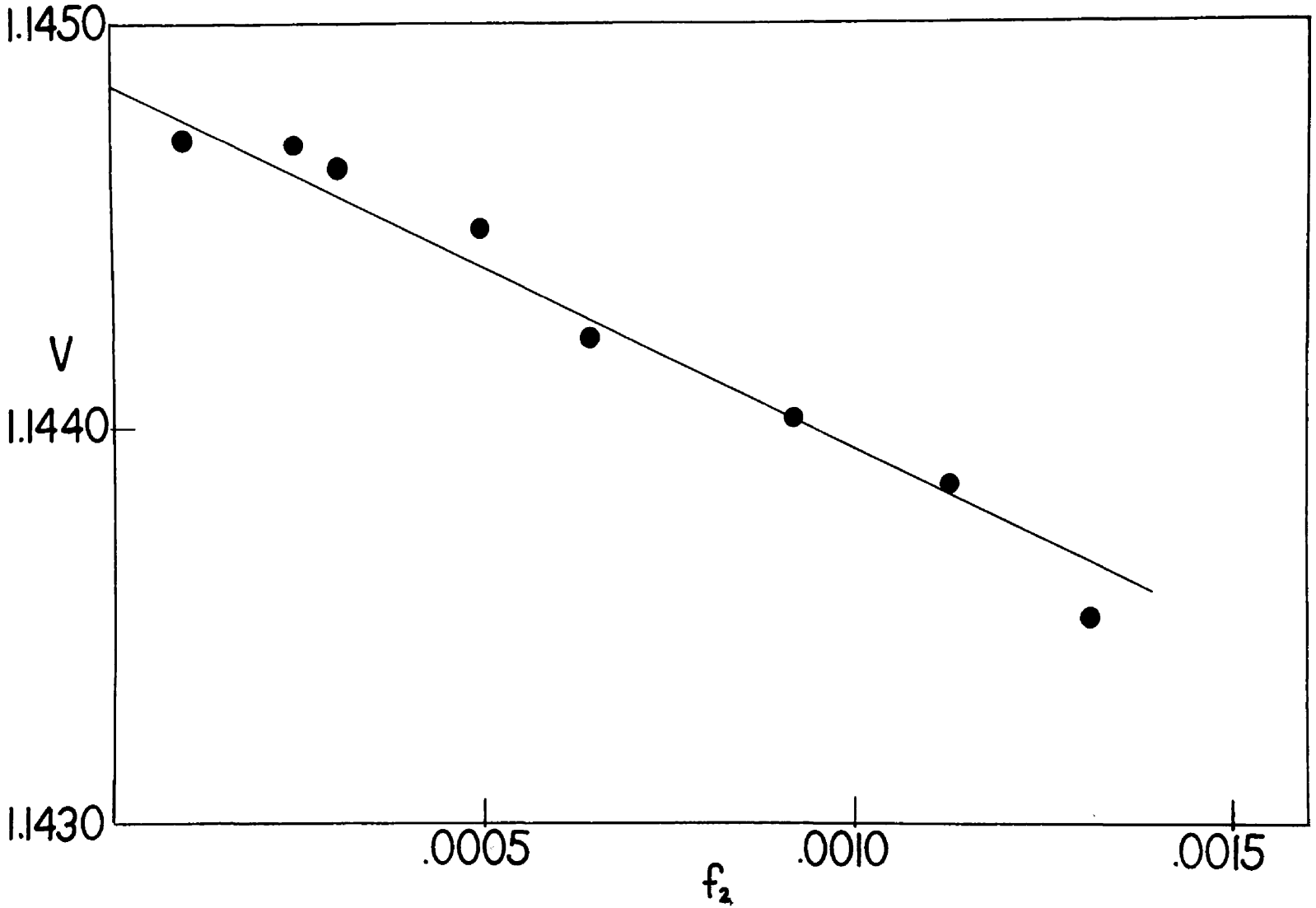


Figure 7. Specific volume as a function of concentration for benzene solutions of p-benzalaminoazobenzene.

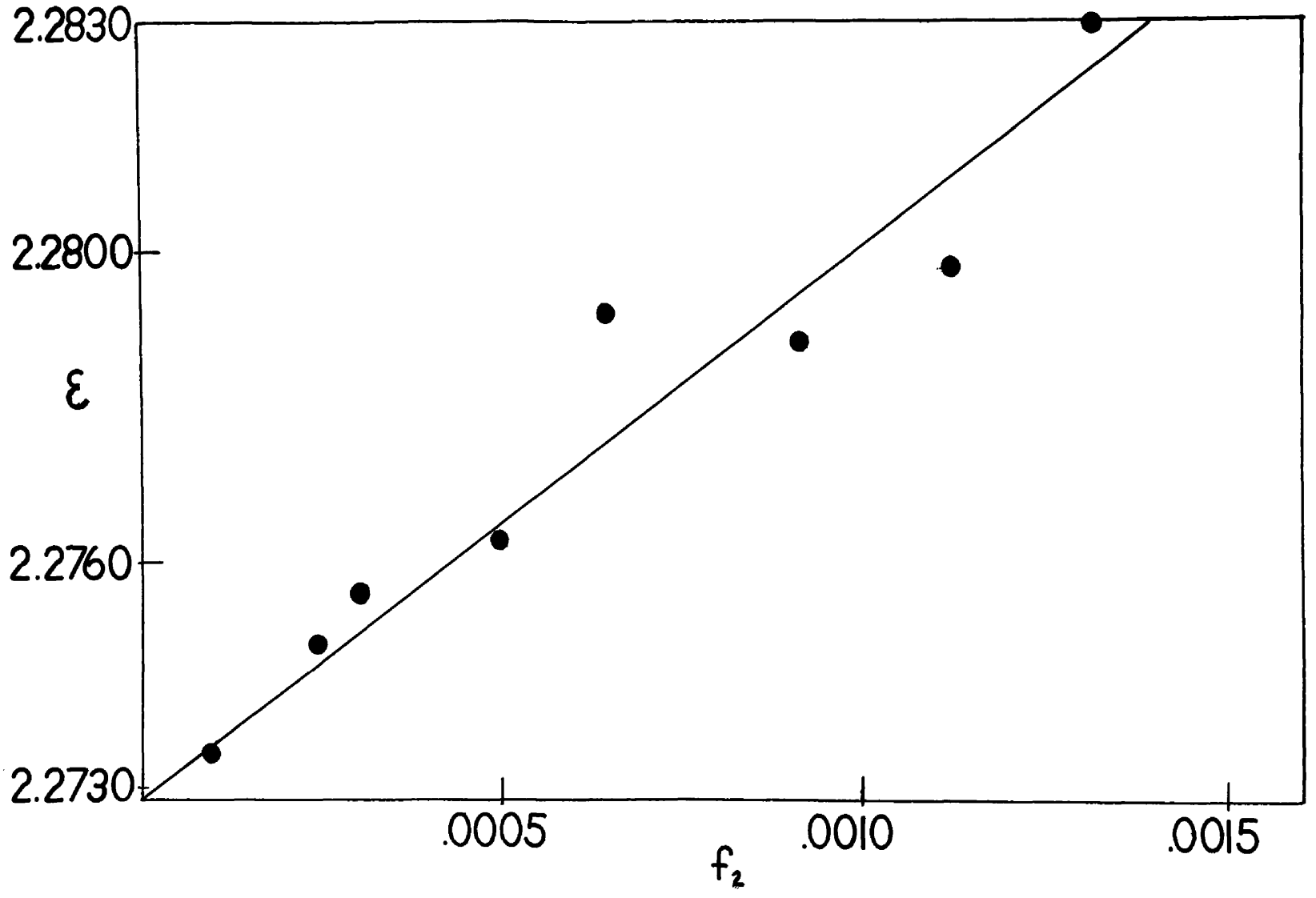


Figure 8. Dielectric constant as a function of concentration for benzene solutions of p-benzalaminoazobenzene.

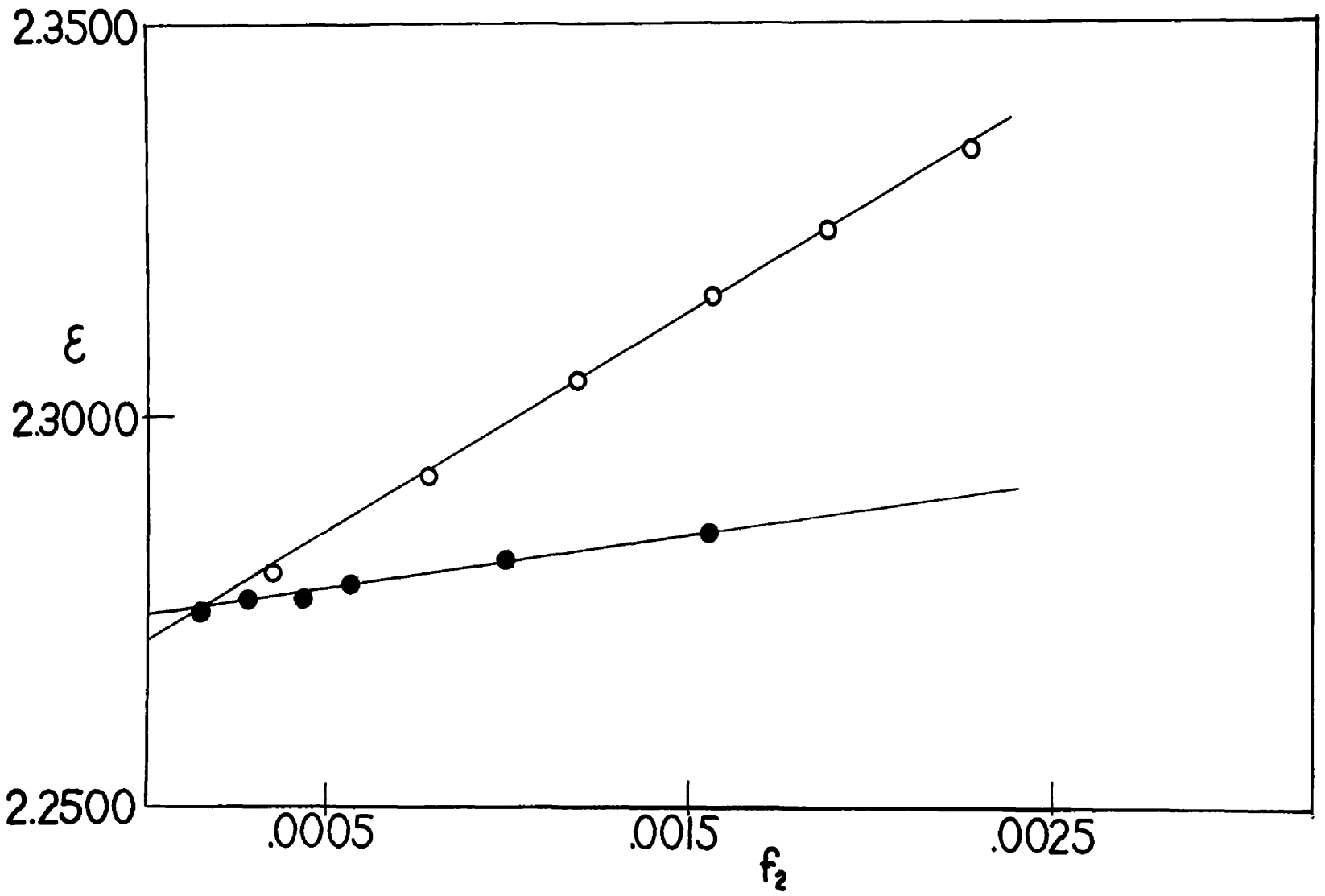


Figure 9. Dielectric constant as a function of concentration for benzene solutions of ○ p-nitroazobenzene and ● p,p'-tetramethyldiaminoazobenzene.

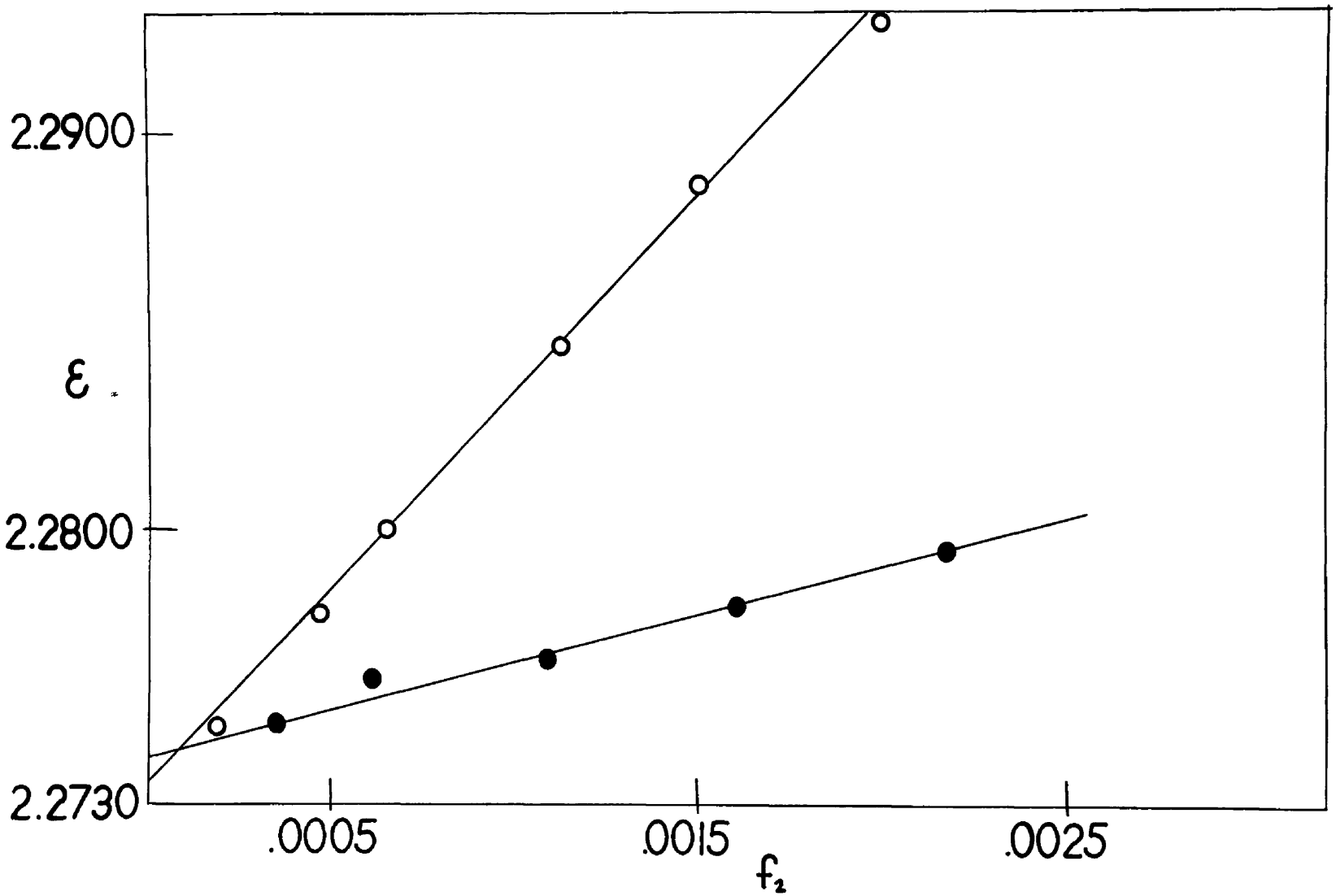


Figure 10. Dielectric constant as a function of concentration for benzene solutions of ○ p-aminoazobenzene and ● tetramethyl-p-phenylenediamine.

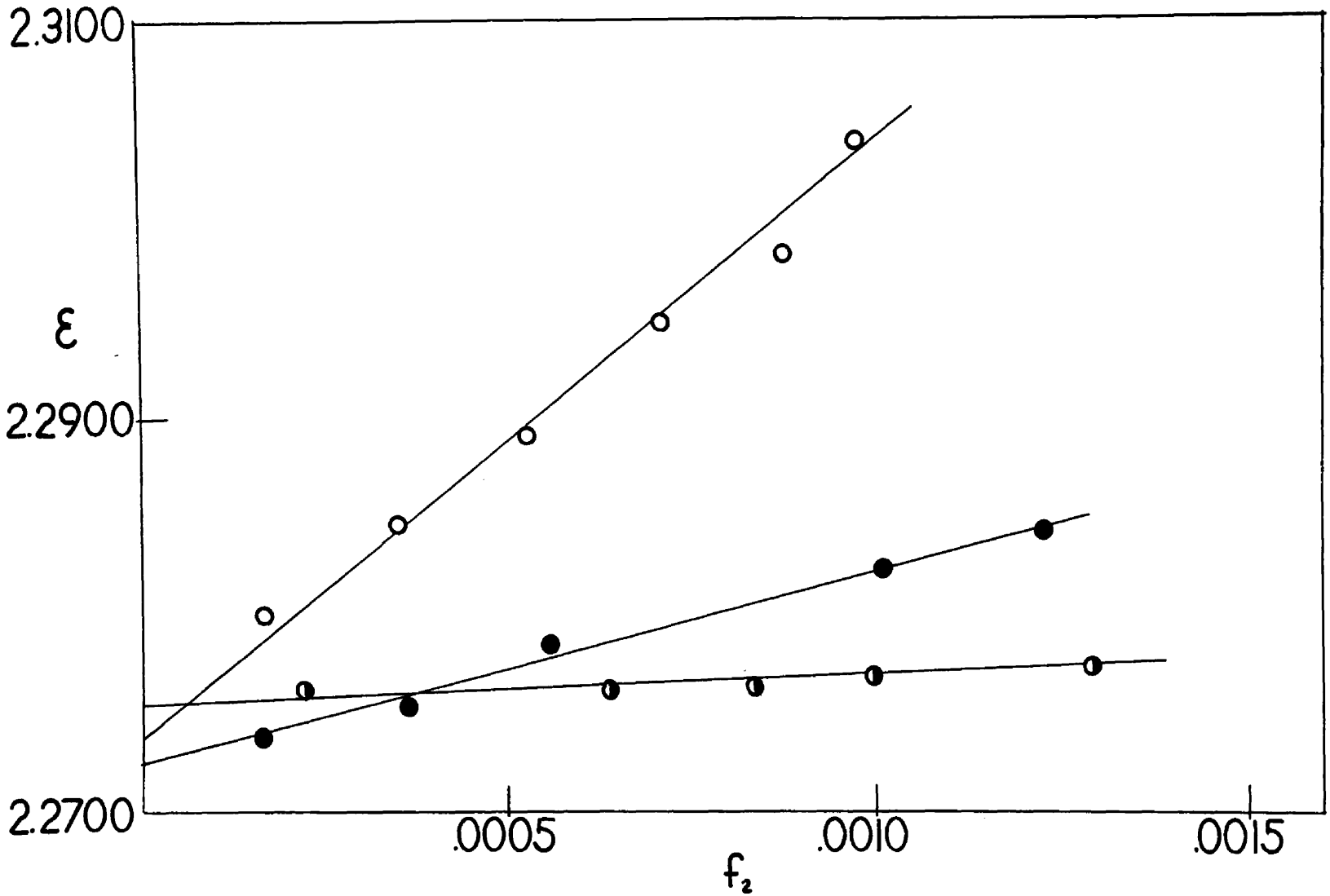


Figure 11. Dielectric constant as a function of concentration for benzene solutions of ○ p-(p-dimethylaminobenzalamino)-azobenzene, ● p-(tolualamino)-azobenzene, and ◐ p,p'-dinitroazobenzene.

TABLE II

DIELECTRIC CONSTANTS, SPECIFIC VOLUMES, MOLECULAR REFRACTIONS, AND DIPOLE MOMENTS IN BENZENE AT 25°C

ε_1	α'	v_1	β'	P^0_2	MR^0_{D2}	μ
			p-Aminoazobenzene			
2.2735	9.65	1.14487	-0.755	191.5	65.42	2.48
			p-Nitroazobenzene			
2.2721	27.62	1.14515	-0.9780	460.84	67.54	4.38
2.2737	27.60	1.14478	-0.9706	460.26	67.54	4.38
			p-p'-Dinitroazobenzene			
2.2755	1.467	1.14491	-1.486	79.9	73.03	0(0.78)
			Tetramethyl-p-phenylenediamine			
2.2742	2.477	1.14494	-0.2406	86.8	52.57	1.29
			p-p'-Tetramethyldiaminoazobenzene			
2.2746	6.48	1.14492	-0.9583	167.12	88.36	1.95
			p-Benzalaminoazobenzene			
2.2729	7.217	1.14484	-0.913	182.1	97.8	2.03
			p-(p-Tolualamino)-azobenzene			
2.2725	9.74	1.14498	-1.111	208.9	102.42	2.47
			p-(p-Dimethylaminobenzalamino)-azobenzene			
2.2736	30.19	1.14497	-1.320	527.5	110.93	4.51

DISCUSSION

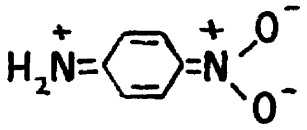
The theory of resonance[16] has greatly facilitated the interpretation of electric moment data for certain types of complex organic molecules. The observed moment is compared with that calculated from bond or group moments by vector methods, assuming free rotation about single bonds.[17,18] Any appreciable deviation from the calculated value is taken to indicate that steric factors or contributions from resonance structures or a combination of these are important.

These principles have been used in the present work, the study of the electric moments of some derivatives of azobenzene and related compounds substituted in one or both para positions. Azobenzene itself exists in *cis* and *trans* forms having electric moments of 3.0 D[19] and zero[20] respectively. However, the *cis* isomer is relatively unstable, being produced from *trans*-azobenzene by the action of ultraviolet light. It has been assumed that the azobenzene derivatives used here had the *trans* configuration, precautions having been taken to shield the compounds from light except for the duration of the measurements.

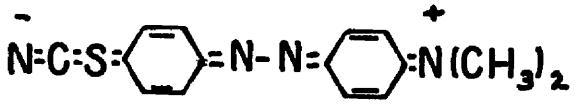
Some electric moments have been reported for various simple para-substituted derivatives of azobenzene.[21,22] The values noted were close to those for analogous benzene derivatives with several exceptions: p-aminoazobenzene and p-dimethylaminoazobenzene had moments much larger than aniline and dimethylaniline, respectively. These facts led to an investigation of some derivatives of dimethylaminoazobenzene substituted

in the p'-position.[23] It was found that an enhancement of resonance occurred when groups such as NO_2, SCN or halogens which are strong electron acceptors were para to the dimethylamino group.

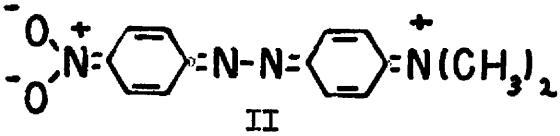
Enhancement of resonance is observed in certain benzene derivatives, a common example of which is p-nitroaniline. In this compound the amino and nitro group moments are not collinear since the former group is not axial. Thus, one would expect the moment of p-nitroaniline to be less than the sum of the moments of aniline and nitrobenzene, which are 1.53 D and 3.95 D, respectively, when measured in benzene solution.[24] Values reported for this substance in the vapor and in various solvents are in the range 6.0-7.0 D,[25,26] greater than the calculated sum (5.48 D). The amino group, which tends to repel electrons toward the ring, and the nitro group, which is electron-attracting, reinforce one another and a fairly large contribution from the structure,



is indicated. A similar situation exists for p-nitrodimethylaniline,[27] and for comparable azobenzene compounds the effect should be more pronounced since the charge separation in the corresponding resonance forms would be over twice as great. This can be illustrated by structures proposed to explain the high values of the electric moments of p-thiocyano-p-dimethylaminoazobenzene (I) and p-nitro-p'-dimethylaminoazobenzene (II).[23]

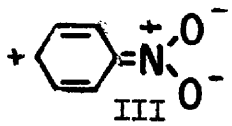


I

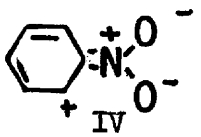


II

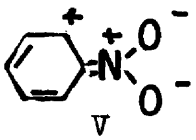
In the compounds studied here there is further evidence for this exaltation of the dipole moment. Thus the moment of nitrobenzene is 3.96 D[27] in benzene solution, an increase of about 0.4 D over the aliphatic nitro compound, nitromethane. This is due to the large moments of the relatively unstable structures, (III, IV and V).



III



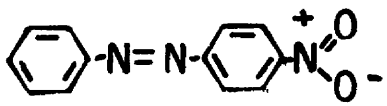
IV



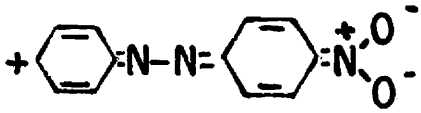
V

in which a large charge separation occurs. In the aliphatic series there is no possibility of resonance structures of this sort and only nitro group resonance and inductive effects contribute to the electric moment.

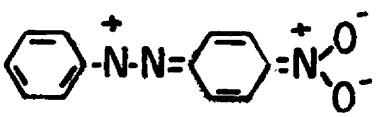
The substance p-nitroazobenzene investigated here has another ring and two more nitrogen atoms over which the charge may be distributed. This leads to structures in which the charge separation is even larger and the observed moment of 4.38 D is larger than nitrobenzene., (VI, VII, VIII).



VI

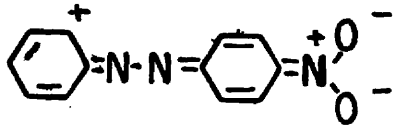


VII



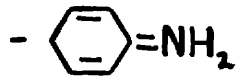
VIII

There are also equivalent structures in which the charge is at the ortho positions of either ring, IX being one example.

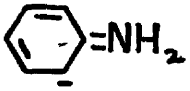


IX

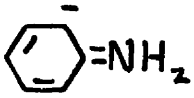
As mentioned above, aniline has an electric moment of 1.53 D,[24] with structures such as X, XI, XII, contributing.



X

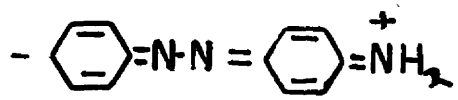


XI

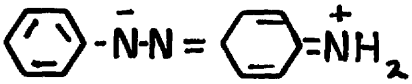


XII

For the corresponding azo compound a value of 2.48 D was found in this work indicating stabilisation of the molecule by resonance involving the phenylazo group, as in XIII and XIV.



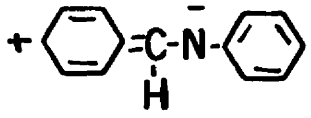
XIII



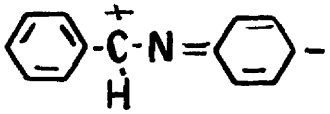
XIV

Three of the compounds studied had in common the benzalaminoazobenzene group, which can best be studied by analogy with the benzalaniline series of compounds.

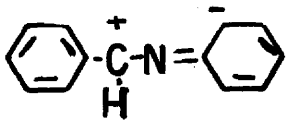
The dipole moments of benzalaniline and some of its derivatives have been investigated[28] and benzalaniline has been reported to have a moment (1.55D) essentially equal to that of aniline (1.53 D). Contributions from structures such as XV, XVI, and XVII



XV



XVI



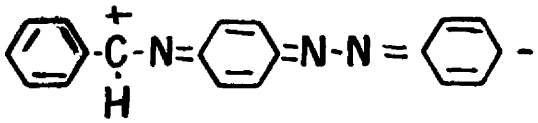
XVII

where the charge separation is not notably different from that in aniline itself, could explain this agreement.[29]

Evidence indicating that the above compounds have the <u>trans</u> configuration about the -C=N bond is found in the moment of p-chlorobenzylidene p-chloraniline, (1.56 D),[30] which is the same as benzalaniline. The phenylazo derivatives of these compounds, which were studied here, have been assumed to have the <u>trans</u> configuration.

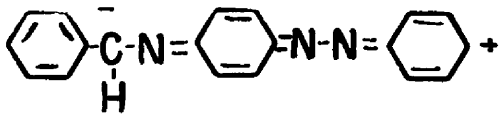
Benzalaminoazobenzene has a moment of 2.03 D, as found in this work, this being larger than that of benzalaniline by 0.48 D. This increment is only half as large as the increment observed for aminoazobenzene over aniline and may be traced to the replacement of amino hydrogen atoms by the benzal group. This group may participate in resonance through such structures as XVIII and XIX.

XVIII



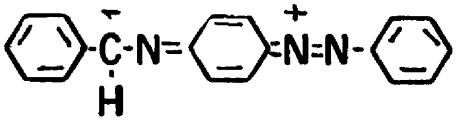
XIX

a contribution from a structure placing a negative charge on the benzal carbon atom (XX) also being possible.



XX

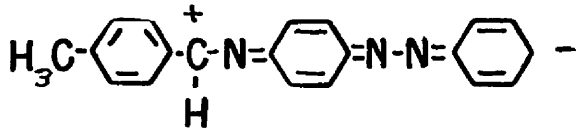
The last structure would not be as significant as the others since the electronegativity of nitrogen is greater than that of carbon. However, it could contribute enough to account for the observed difference in increment since it produces a moment in opposition to those noted in other polar structures. Other structures can be written which tend to place a negative charge on this carbon, e.g.,



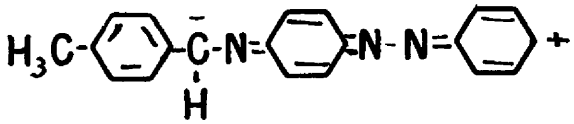
XXI

These would imply an axial symmetry[31] through the adjacent double bonds and this is not found by an X-ray investigation of azobenzene.[32] Such structures evidently make no contribution to the ground state of the molecule.

In p-(p-tolualamino)-azobenzene the observed moment, 2.47 D, is larger than that calculated for p-tolualaniline (about 1.95 D), indicating that structures such as



XXII

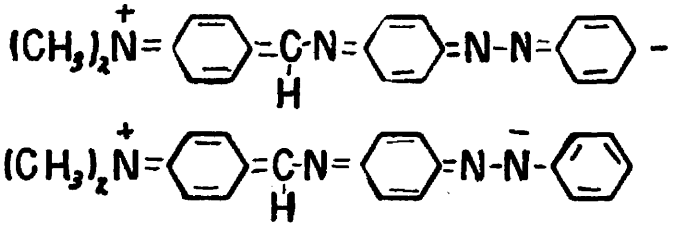


XXIII

which are analogous to those postulated for benzalaminoazobenzene itself, contribute appreciably to the ground state of the molecule.

Since the moment observed is higher than that for benzalamino azobenzene by 0.4 D, the moment assumed for the methyl group, the structure in which the carbon assumes positive character must make a more significant contribution.

The substance p-(p-dimethylaminobenzalamino)-azobenzene has a moment (4.51 D) which is larger than that of p-dimethylaminobenzal-aniline (3.60 D).[28] This reflects the increased ability of benzalaniline to accept electrons as a result of its conjugation with the phenylazo group. Structures with large charge separations would account for the



increment of 0.9 D over the benzalaniline compound.

The compound p,p'-dinitroazobenzene was studied to obtain evidence that these substances were really in the trans form. Since the nitro groups are coplanar with the ring, the resultant moment should be zero. There are probably several reasons that the value observed, 0.78 D, should be considered not fundamentally different from zero. As noted in the theoretical section, the molar refraction should be measured in the infra-red region of the spectrum. When sodium D line is used, one assumes the molar refraction to equal the sum of electronic and atomic polarizations. This causes no serious difficulty until the moment is below 1.0 D, in which case the latter quantity can be significant. Many workers, especially

in England, assume that the atomic polarization is ten percent of the value found for the molar refraction. Since we used molar refractions calculated from bond refractions instead of refractive index values, and the moment is less than 1.0 D, this latter correction should be applied. The result is a value of 7.3 cc. for the atomic polarization. This is quite close to the value for the difference between molar polarization and molar refraction, 6.9 cc., used to get the final dipole moment. On this basis the electric moment of p,p'-dinitroazobenzene is indistinguishable from zero. The fact that the nitrobenzene itself has a reported atomic polarization of 3.8 cc.,[33] and 1,3,5, trinitrobenzene a value of 12.0 cc.,[34] makes the figure of 7.3 cc. for the dinitroazobenzene compound appear not an unreasonable one.

In addition to such considerations, the low solubility of the substance in benzene made the experimental error greater than normal. The solutions were all saturated solutions and the concentration may have been altered by slight precipitation of solute during the measurements, although this could not be detected.

In such solutions the benzene solvent may associate with dinitroazobenzene to form a molecular compound. Then interaction of the nitro groups with the π electrons of the benzene ring could disturb the symmetry of the azo compound and give the small moment noted. Unfortunately, the magnitude of such an effect is hard to determine quantitatively, while the atomic polarization contribution estimated from the molar refraction has some foundation in experimental work and is to be preferred in explaining the discrepancy.

One aim of electric moment studies is the computation of the moments due to individual groups or bonds in different environments. Such data,

when available, assist in the calculation of moments to be expected for molecules, containing the group or groups in question. The moment of p,p'-tetramethyldiaminoazobenzene (1.95) was used in conjunction with that found for dimethylaminoazobenzene[23] (3.22) to calculate the moment of the dimethylamino group in azobenzene compounds.

The procedure involves application of the Law of Cosines for vectors to the group moments and resultant total moments in each compound. Assuming free rotation the equation

$$\mu^2 = m_1^2 + m_2^2 + 2m_1m_2 \cos\sigma \cos\phi_1 \cos\phi_2$$ is obtained.

Where μ = total moment, m_1 and m_2 are bond or group moments, σ is the angle between the axes about which free rotation occurs and ϕ_1 and ϕ_2 the angles which the rotating vectors make with the axes of rotation. For p-p'-tetramethyldiaminoazobenzene, this equation becomes

$$(1.95)^2 = 3.80 = 2m^2-2m^2 \cos^2\phi$$

while for p-p'-dimethylaminoazobenzene the equation becomes

$$(3.22)^2 = 10.40 = (0.4)^2 + m^2-0.8m \cos\phi$$

since the moment of the C-H bond is estimated to be 0.4 D[35] with $\phi_1 = 0^0$ (the negative end of the dipole being toward the ring).

By eliminating ϕ between these equations and solving the resulting expression

$$m^4-21.12m^2 + 101.71 = 0$$

for m, it was found that the roots were $m = \pm 3.70$ and $m = \pm 2.73$. Negative values of the group moments were disregarded as lacking physical meaning and the positive values were used to calculate the angle ϕ.

This was $22^{0}2'$ for m = 3.70 and $30^{0}7'$ for m = 2.73.

In a similar manner, the moments of tetramethyl-p-phenylenediamine (1.29) and dimethylaniline (1.58)[26] were used to get a value for the dimethylamino group moment in benzenoid compounds. The values obtained were m = 1.92, $\phi = 28^{0}7'$, and m = 1.28, $\phi = 45^{0}10'$.

The fact that the original set of simultaneous equations is satisfied by two different group moments and their corresponding angles poses a problem in that there is no apparent basis for choosing either moment-angle pair as the desired one. However, in neither azo nor benzenoid type compounds is the group moment along the direction of the nitrogen to aromatic carbon bond, regardless of the moment and angle used. The failure to obtain a unique solution of the equations may lie in the assumption of complete freedom of rotation which determines the equations to be solved for group moment and angle. Although molecular models give no indication of steric hindrance in these substances, there may be relative spatial positions of the dimethylamino groups which minimize the potential energy of the system. In such a case the equation for the dipole moment assuming free rotation would be altered in some unknown manner, which could give two results instead of the single unambiguous solution desired, i.e., one angle and moment for the dimethylamino group.

The estimation of an electric moment for p-tolualaniline, for subsequent comparison with p-(p-tolualamino)-azobenzene, presented a problem since benzalaniline can participate in resonance. A calculation of a group moment for Ph-C(H) = N- from two derivatives (p-chloro and p-nitrobenzalaniline, for example) is not feasible. Therefore, the p-tolual compound

was assumed to have a moment 0.4 D greater than that of benzalaniline ($\mu = 1.55$). Then the resulting value of 1.95 D was compared with p-(p-tolualamino)-azobenzene ($\mu = 2.47$).

The data for p-nitroazobenzene were used to determine the effect of observational errors on the values found for molar polarization and electric moment. The estimated errors are $\pm$ 5.30 cc. for the molar polarization and $\pm$ 0.06 D for the electric moment (see Appendix). Only a general statement can be made concerning the accuracy of these measurements since the effect of the solvent on the final moment is unknown. Values obtained in the gas phase are assumed to be best since the molecules are so far apart as to make interaction negligible. When gas and solution data are available for the same compound, the difference noted is from 0 to 0.3 D in a great number of cases. The compounds used here could not be conveniently studied as gases so it was assumed that the electric moments observed are correct to several tenths of a Debye. In reality, the absolute values are less important for the purpose of this work than their magnitude as compared with similar benzenoid type substances.

APPENDIX

Using the data for p-nitroazobenzene the deviations of the experimental values of dielectric constant versus concentration (Figure 9) and specific volume versus concentration (Figure 4) from those on the best straight line through these points was noted. From these figures the average deviation for a single reading was calculated. A summary of these results is presented in Table III with the absolute values of the individual deviations used to get the average.

The effect of such errors in the final value for molar polarization is estimated by using the total differential form for expressing P as a function of ε and v,

$$dP = \frac{\partial P}{\partial \varepsilon} d\varepsilon + \frac{\partial P}{\partial v} dv$$

By combining equations (28) and (27) one sees that

$$P_2 = \frac{\varepsilon_{12}-1}{\varepsilon_{12}+1} \frac{M_2 f_2 + M_1 f_1}{d_{12} f_2} \frac{P_1 f_1}{f_2}$$

which, on partial differentiation, leads to

$$\frac{\partial P_2}{\partial \varepsilon_{12}} = \frac{3v_{12}}{(\varepsilon_{12}+2)^2} \frac{M_2 f_2 + M_1 f_1}{f_2}$$

Choosing from Table I values of a dielectric constant (2.3151) and specific volume (1.14375) for a given intermediate solute concentration (0.001572), it was found that

TABLE III

OBSERVED AND CALCULATED VALUES OF DIELECTRIC CONSTANT AND SPECIFIC VOLUME OF P-NITROAZOBENZENE IN BENZENE AT 25°C

Dielectric Constant			Specific Volume		
Observed	Least Squares	Deviation	Observed	Least Squares	Deviation
2.3348	2.3346	.0002	1.14292	1.14297	.00005
.3236	.3240	.0004	.14333	.14334	.00001
.3151	.3152	.0001	.14375	.14365	.00010
.3047	.3047	.0000	.14402	.14402	.00000
.2925	.2944	.0019	.14443	.14440	.00003
.2802	.2815	.0013	.14482	.14482	.00000
2.3306	2.3305	.0001	1.14282	1.14278	.00005
.3232	.3221	.0011	.14296	.14307	.00011
.3174	.3160	.0014	.14325	.14328	.00003
.3089	.3087	.0002	.14352	.14347	.00005
.3077	.3079	.0002	.14360	.14357	.00003
.2957	.2968	.0009	.14397	.14398	.00001
.2894	.2894	.0000	.14423	.14425	.00002
	Average	0.0005		Average	0.00005

$$\frac{\partial P_2}{\partial \varepsilon_{12}} = 9100.$$

The dependence of molar polarization on specific volume is found to be

$$\frac{\partial P_2}{\partial v_{12}} = \frac{\varepsilon_{12}-1}{\varepsilon_{12}+2} \frac{M_2 f_2 + M_1 f_1}{f_2} = 14900.$$

Then, since $d\varepsilon = .0005$ and $dv = .00005$,

$$dP_2 = 9100\ (.0005) + 14900\ (.00005) = 5.30 \text{ c.c.}$$

The effect of such an error in molar polarization on the final moment is determined by considering the moment to be a function of the polarization only, i.e.,

$$d\mu = \frac{\partial \mu}{\partial P_2} dP_2 .$$

Since

$$\mu = 0.0128 \sqrt{(P_2 - MR_{D2})T},$$

$$\frac{\partial \mu}{\partial P_2} = \frac{0.0128}{2} \sqrt{\frac{T}{P_2 - MR_{D2}}}$$

which, on substitution, gives

$$\frac{\partial \mu}{\partial P_2} = 0.0056.$$

This in turn leads to an estimated error in dipole moment due to uncertainty of the polarization value,

$$d\mu = \pm 0.03 \text{ Debyes.}$$

The molar refraction is also a polarization term which does not include the orientation effect and the equations for molar polarization and refraction are of the same form as shown in the theory section.

Thus, in the absence of refractive index data, it was necessary to assume the molar refractions calculated by adding bond refractions to be subject to the same error as the molar polarization, $\pm$ 5.30 c.c. This results in another 0.03 D error in electric moment if it is considered as a function of molar refraction alone. The over-all result is a value of the electric moment with a probable deviation of $\pm$ 0.06 D, for compounds with moments of about 4.50 D.

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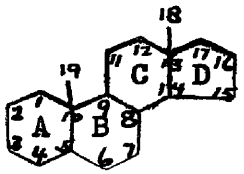
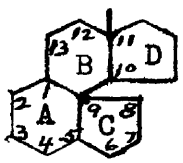
HISTORICAL

The sterols are a class of compounds having in common the perhydro-1,2-cyclopentanophenanthrene ring system



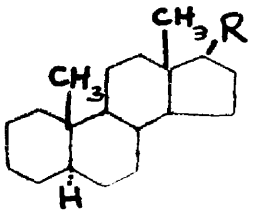
and usually containing one or more secondary alcohol groups. In addition these solid alcohols are completely saturated in many cases, the result being a molecule in which considerable departure from planarity occurs. This puckering is necessary to relieve the strain which would exist if the molecules were to be planar, as in benzenoid compounds. Thus a planar cyclohexane ring would have greater C-C-C angles than the tetrahedral angle of 109°28', a tendency relieved by puckering.

The accepted structure of the steroid nucleus presented above is the culmination of considerable research involving, among other work, Bernal's crystal studies[1] and studies of the dehydrogenation of sterols by Diels.[2] The former experiments led to the conclusion that the sterols were essentially flat, lath-shaped molecules. Dehydrogenation of some sterols gave chrysene as one of the products. These pieces of evidence were used by Rosenheim and King[3] to propose the phenanthrene-type nucleus above, a revision of the original structure of Wieland and Windaus.[4]

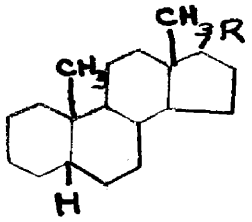


The description of steroids used here is that proposed by Fieser[5] and extended by Reichstein and Shoppee.[5] This representation includes both the number of the position and the position of groups above (β) or below (α) the general plane of the ring system.

Now the perhydro-1,2-cyclopentenophenanthrene system has six centers of asymmetry associated with the carbon atoms of the A/B, B/C, and C/D ring fusions. The number of optical isomers is given by 2^n, where n is the number of asymmetric carbon atoms, there being a possibility of sixty-four stereoisomers in this instance. Despite this potential source of difficulty in separation and identification, nearly all naturally occurring steroids are related to one of two C_5 isomers, cholestane and coprostane.



Cholestane

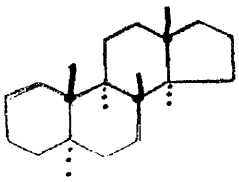


Coprostane

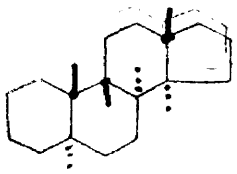
Solid lines indicate that the atom involved is above (β), dotted lines that it is below (α), the plane of the ring system. The two series of compounds exemplified by cholestane and coprostane are the allo and normal series, respectively.

Isolation and study of products obtained in reactions or degradations involving sterols led to the conclusion that the A/B, B/C, and C/D ring fusions are trans, trans, trans in the allo series and cis, trans, trans in the normal series, respectively.[6] Optical and X-ray diffraction data tend to confirm these configurational restrictions which reduce the number of possible isomers from sixty-four to eight, these eight forms differing in the individual orientations of the three ring junctions. The stereochemistry of the nucleus requires correlation of the asymmetric centers at C_8 and C_9 with those at C_{10} and C_{14}. In other words, the orientations of the groups attached to these carbon atoms must be determined.

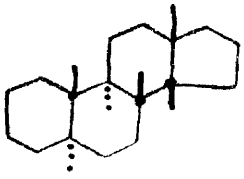
The reference point for such a discussion is the C_{10} methyl group which is assigned the β configuration. If androstane is taken as an example, there is a choice of four structures, shown below as I, II, III and IV, each of which has a mirror image.



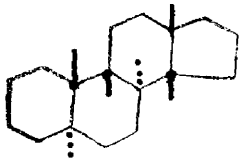
I



II



III



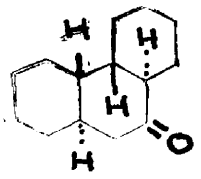
IV

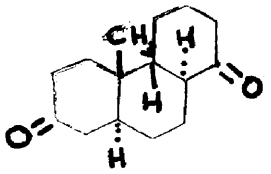
X-ray diffraction results and ease of dehydration of 11-β-hydroxy isomers as compared with the analogous α-forms indicate I to be the correct structure for androsterone.[6]

The geometry of sterols is largely dependent upon the constituent rings involved, so a consideration of the structure of cyclohexane is important. Cyclohexane exists in two "strainless" ring forms, the chair (Z) and boat (C). These stereoisomers result from the necessity for minimizing the strain which would be present in a planar saturated ring of this size.

Of the two forms, the chair is the more stable by some 5-10 kilocal./mole.[7] This is not surprising in view of the mutual repulsion of the hydrogens[8] which are much nearer in the C form.

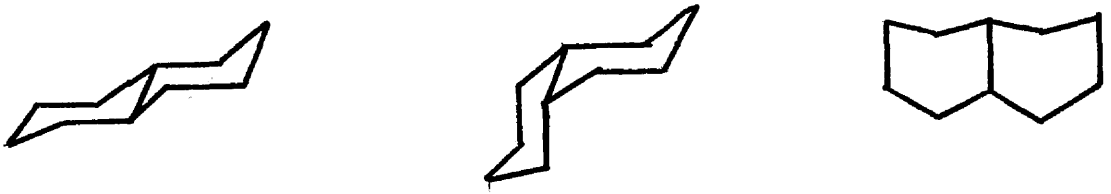
One interesting feature of both forms of cyclohexane is the fact that the hydrogen atoms fall into two distinct classes, polar and equatorial.[9] The polar bonds are alternately above and below the plane of the ring and perpendicular to this plane. Thus there are three such bonds on each side of the ring. The equatorial bonds lie essentially in the plane of the ring in all six cases. In the boat form, the two bond types are distinguishable only when occurring as a stereochemically unambiguous structure with double locking, i.e., when incorporated in a tricyclic structure. In such a system, four polar bonds are directed nearly vertically in one sense and the remainder are vertical in the opposite sense. The trans-α-decalones given below appear to be examples.[10]





Now in the cholestane, or allo, series of sterols, X-ray crystallography work indicates that carbon atoms 2, 3, 5, 7, 8, and 10 lie in a plane separated by 0.77Å* from another containing carbons 1, 9, 11, 13, and 14. This arrangement corresponds to the androstane structure discussed above and implies that rings A, B, and C all possess the Sachse-Mohr chair configuration,[11] at least in the crystalline state. However, by thermal bombardment, ring A can pass over to the boat form with ends at C_3 and C_{10} by relative motion of C_2, C_3, and C_4 without disturbing the remainder of the carbon skeleton.

In the A/B-cis series the only unambiguous structure is one (b) in which the rings are chairs though the union is cis. This configuration is favored by Bastiansen and Hassel[12] on the basis of their electron diffraction results. It has the disadvantage of predicting an L-shaped molecule rather than the flat lathe deduced from a previous X-ray analysis.[13] However, Barton has found that for the cis and trans decalins,[14] the stability sequence is a > b > c.



a b c

This is in agreement with thermal data[15] and the above-mentioned electron diffraction results. The difficulty could be resolved if one assumes form b the more stable in solution while intermolecular forces act to make form c the favored isomer in the solid.

The low energy barrier inhibiting chair-boat interconversion in cyclohexane argues for the existence of an equilibrium mixture of the two forms. In support of this, it was found that the calculated electric moments of cyclohexane-1,4-dione in Z and C forms are zero and 4.1 D respectively, while the observed value is 1.2 D.[16] From these data it was deduced that the chair form constitutes ninety percent of the equilibrium mixture. In some sterols the A ring doubtless participates in such an equilibrium so the ratio of the two forms should be detectable by similar measurements. This sort of experiment has been done for one pair of compounds with the result that ring A was found to be eighty-six percent Z form.[17]

A major share of the structural information concerning steroids is derived from studies of their reactions and degradation products obtained. However, the methods of a physical-chemical nature have also been valuable and are becoming more so. Thus Bernal's[13] crystallographic studies led to a significant revision of structure while electron diffraction results[12] have contributed greatly to the basic ideas concerning the geometry of the sterol nucleus. As anticipated in molecules with asymmetric carbon atoms, optical rotation has been an important factor in distinguishing between isomers. Indeed, a method based on molecular rotation differences has been useful in elucidating the structures of some unsaturated sterols.[18]

In sterols with polyene, unsaturated ketone, dienone, and like groupings, the position and intensity of the principal absorption maximum in the ultraviolet region have been correlated with structural features.[19] However, the infrared spectrum has been the source of more specific information of a different type, namely the association of various absorption bands with motions of the substituents and the positions of these groups in the molecule.[20] This technique is used as a criterion for the purity of sterols. These are prepared by reaction sequences which almost inevitably produce contaminating impurities that must be removed from the desired compound. Completeness of such removal is reflected in the infrared spectrum of the desired material.

The preceding physical methods all depend on optical properties, in a sense. A somewhat different sort of measurement, that of electric moments of sterols, has been used in recent years also. Thus, the electric moments of several large groups of sterols and bile acids are recorded in the literature.[21] These data and other work mentioned above[17] made electric moment studies of other such molecules appear to be a useful method for learning more about the structures of the steroids.

EXPERIMENTAL

Densities

The density values were determined at 25°C, using a modified Ostwald pycnometer. All weights were corrected for the buoyant effect arising when weighing in air with brass weights.

Dielectric Constants

The dielectric constants were measured by the heterodyne beat method, the details of which were discussed in the experimental section of Part I of this thesis.

Since the weight of sterols obtainable was 0.5 grams in most instances, smaller volumes of solution were necessary to achieve a desirable range of concentrations for the measurements. Consequently, the fifty milliliters required for dielectric constant measurements in available cells was excessive, so that a new cell had to be constructed. It consists of three concentric nickel cylinders with the middle cylinder at high potential and shorter in length than the two grounded cylinders. In contrast to the cell used previously, the outer nickel cylinder also served as the external wall, no glass envelope being required. The cell required a volume of ten milliliters of solution for a measurement. As is evident from Figure I, the solution was added from the top of the experimental cell which was evacuated before addition of the solution. This latter precaution was found to result in more reproducible condenser readings,

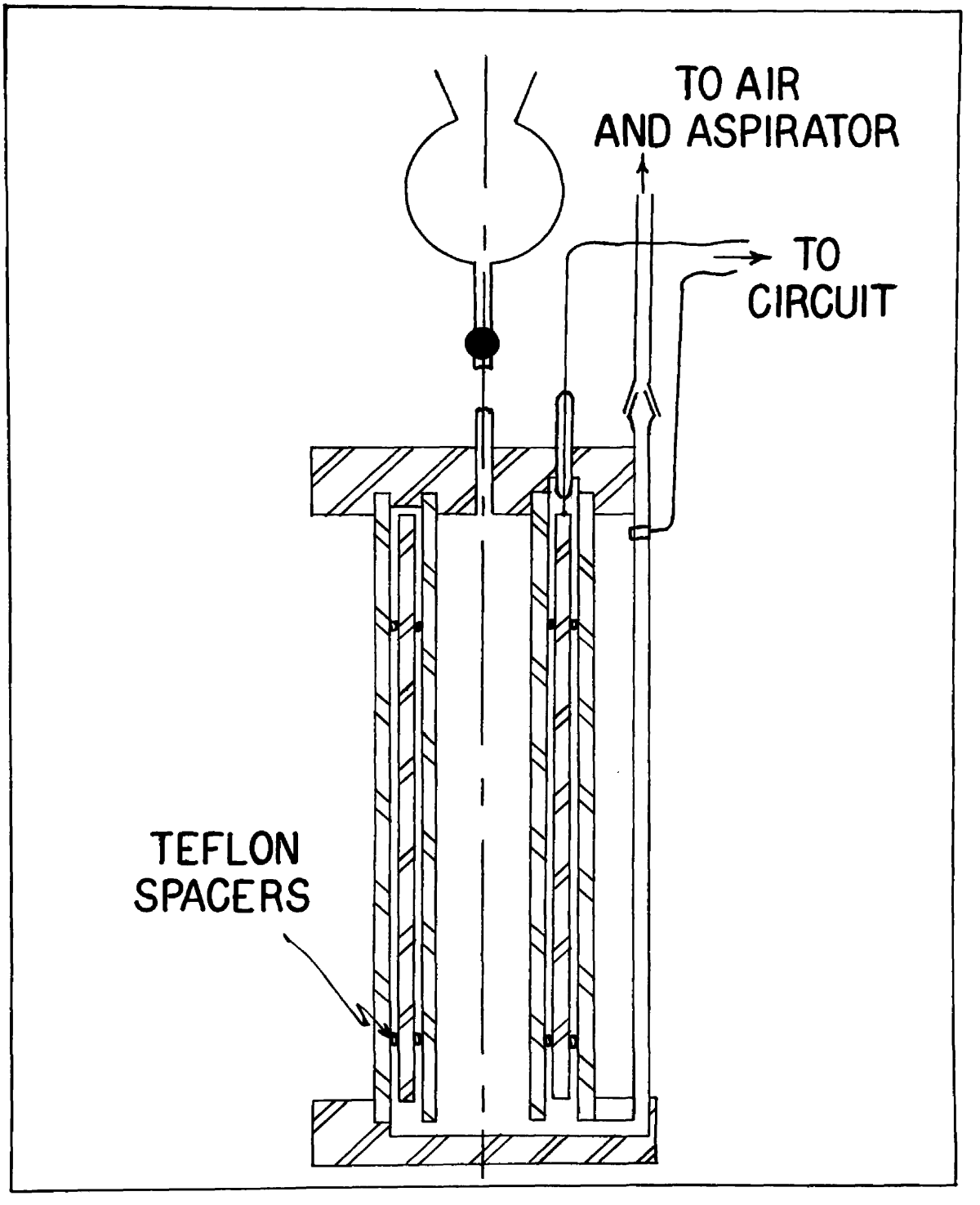


Figure 1. The experimental cell used for dielectric constant measurements.

probably by preventing air bubble formation. Since bubbles were unobservable if formed, three condenser readings were taken on each solution. The average of these values was taken to give the dielectric constant of the solution involved.

The solvent used for these compounds was dioxane obtained as practical grade material and purified by the method of Fieser[22] to give a product of density 1.0278 and refractive index 1.4200, both measured at 25°C. The purification method involves acid hydrolysis under nitrogen for twenty-four hours, followed by neutralization with potassium hydroxide pellets and separation of the resulting two layers. The dioxane layer was then refluxed over sodium for twelve hours and stored over sodium in a dark bottle until required. The affinity of dioxane for water made frequent checks on the density of this solvent mandatory.

The compounds were obtained from the Upjohn Company and General Biochemicals Company. They were used without further purification, since they had already been purified by chromatographic separation and the amount of sample was too small to sustain the losses involved in any further treatment of this sort. However, the melting points were checked on many of the compounds and in all cases were found to be quite close to known literature values. All melting points are uncorrected (Table III).

CALCULATIONS

As in Part One of this thesis, the calculations of molar polarisations were made with the aid of Equation 30. The dielectric constant and density data required were obtained from measurements on five or six dioxane solutions of the sterols in the concentration range 0.0001 - 0.001 molar, all measurements on a given group being taken on a single day.

RESULTS

The experimentally determined dielectric constants (ε_{12}) and specific volumes (v_{12}) of the dioxane solutions at 25°C are compiled in Table I. The graphical plots of dielectric constant and specific volume versus mole fraction of solute (f_2) are shown in Figures 2-31. The slopes α' and β' and the intercepts at infinite dilution ε_1 and v_1 of the straight lines so obtained are listed in Table II along with the values of molar polarization of solute at infinite dilution (P°_2) calculated using Equation (30). The molar refractions ($MR^{\circ}_{D_2}$) calculated from empirical constants and the electric moments obtained using Equation 24 are also listed in Table II.

RESULTS

TABLE I

DIELECTRIC CONSTANTS AND SPECIFIC VOLUMES OF THE DIOXANE SOLUTIONS AT 25°C

f_2	ϵ_{12}	v_{12}
Progesterone		
0.003226	2.2452	0.97208
.002668	2.2405	.07207
.001589	2.2261	.97231
.001111	2.2211	.97253
.000672	2.2154	.97262
11 α-Hydroxyprogesterone		
0.002995	2.2773	0.97147
.002321	2.2621	.97195
.001475	2.2462	.97216
.001061	2.2334	.97228
.000521	2.2214	.97265

TABLE I continued

f_2	ε_{12}	ν_{12}
11 β -Hydroxyprogesterone		
0.003654	2.2781	0.97130
.002890	2.2731	.97169
.001762	2.2496	.97207
.001036	2.2328	.97286
.000668	2.2284	.97264
11-Ketoprogesterone		
0.003177	2.2912	0.97134
.002605	2.2774	.97163
.002040	2.2582	.97182
.001770	2.2553	.97190
.001168	2.2376	.97222
.000731	2.2277	.97218
17 α -Hydroxyprogesterone		
0.003364	2.2701	0.97125
.002617	2.2558	.97164
.002019	2.2437	.97177
.001564	2.2364	.97208
.000547	2.2182	.97230

TABLE I continued

11 α , 17 α -Dihydroxyprogesterone

f_2	ε_{12}	v_{12}
0.003023	2.2935	0.97063
.002226	2.2711	.97128
.001794	2.2578	.97146
.001071	2.2386	.97180
.000533	2.2243	.97214

11 α -Acetoxyprogesterone

f_2	ε_{12}	v_{12}
0.002788	2.2451	0.97134
.002089	2.2355	.97170
.001617	2.2299	.97196
.001177	2.2226	.97209
.000708	2.2175	.97233
.000262	2.2100	.97269

Pregnane-3,20-dione

f_2	ε_{12}	v_{12}
0.003148	2.2269	0.97194
.002687	2.2283	.97230
.002054	2.2203	.97233
.001467	2.2175	.97269
.001165	2.2160	.97256
.000469	2.2116	.97227

TABLE I continued

Pregnane-3,11,20-trione		
f_2	ε_{12}	v_{12}
0.003201	2.2621	0.97137
.002676	2.2532	.97148
.001975	2.2415	.97193
.001560	2.2330	.97212
.001060	2.2250	.97235
.000593	2.2184	.97246

11α -Hydroxypregnane-3,20-dione		
f_2	ε_{12}	v_{12}
0.003162	2.2553	0.97165
.002541	2.2450	.97177
.001442	2.2294	.97221
.000955	2.2218	.97235
.000414	2.2140	.97251

3α,17α-Dihydroxy-21-bromo-pregnane-11,20-dione		
f_2	ε_{12}	v_{12}
0.002348	2.2764	0.96982
.001968	2.2665	.97032
.001077	2.2382	.97134
.000789	2.2327	.97157
.000461	2.2213	.97162

TABLE I continued

f_2	ε_{12}	ν_{12}
3 β ,17 α -Dihydroxy-21-bromo-pregnane-11,20-dione		
0.001665	2.2606	0.97053
.001242	2.2489	.97110
.000988	2.2416	.97124
.000633	2.2289	.97171
.000417	2.2241	.97222
4-Chloro-17 α -hydroxyprogenane-3,11,20-trione		
0.002744	2.2890	0.97036
.002314	2.2746	.97074
.001728	2.2581	.97122
.001280	2.2453	.97160
.000903	2.2348	.97191
4-Chloro-21-bromo-17 α -hydroxypregnane-3,11,20-trione		
0.002228	2.2748	0.96948
.001847	2.2538	.96999
.001469	2.2438	.97056
.001048	2.2322	.97111
.000758	2.2240	.97149
.000428	2.2170	.97214

TABLE I continued

4-Bromo-17α-hydroxy-21-acetoxypregnane-3,11-20-trione		
f_2	ε_{12}	γ_{12}
0.002161	2.2765	0.96949
.001809	2.2642	.96990
.001396	2.2524	.97067
.001094	2.2428	.97099
.000704	2.2322	.97222
.000306	2.2178	.97217

4-Chloro-17α-hydroxy-21-acetoxypregnane-3,11-20-trione		
f_2	ε_{12}	γ_{12}
0.002253	2.2782	0.97024
.001962	2.2704	.97071
.001558	2.2555	.97087
.001115	2.2430	.97142
.000741	2.2296	.97199
.000416	2.2208	.97215

Allopregnane-3,20-dione		
f_2	ε_{12}	γ_{12}
0.003233	2.2307	0.97225
.002622	2.2246	.97208
.002120	2.2222	.97226
.001514	2.2218	.97184
.000983	2.2145	.97249
.000659	2.2118	.97242

TABLE I continued

Allopregnane-3,11,20-trione

f_2	ε_{12}	ν_{12}
0.003100	2.2699	0.97155
.002396	2.2579	.97189
.001731	2.2457	.97204
.001356	2.2349	.97203
.000992	2.2271	.97242
.000383	2.2152	.97243

11 α -Hydroxyallopregnane-3,20-dione

f_2	ε_{12}	ν_{12}
0.003160	2.2543	0.97141
.002713	2.2463	.97150
.001985	2.2362	.97192
.001442	2.2295	.97194
.00948	2.2210	.97228
.000410	2.2162	.97251

21-Acetoxyallopregnanedione

f_2	ε_{12}	ν_{12}
0.002672	2.2373	0.97228
.002274	2.2339	.97206
.001790	2.2280	.97230
.001321	2.2244	.97251
.000809	2.2186	.97265
.000401	2.2141	.97276

TABLE I continued

Pregnenolone		
f_2	ϵ_{12}	γ_{12}
0.003144	2.2561	0.97256
.002603	2.2469	.97263
.002131	2.2384	.97257
.001475	2.2308	.97276
.000928	2.2232	.97264
.000506	2.2180	.97325

Pregnenolone-3-methyl ether		
f_2	ϵ_{12}	γ_{12}
0.003059	2.2538	0.97275
.002504	2.2448	.97280
.002018	2.2385	.97278
.001552	2.2321	.97282
.000931	2.2241	.97293
.000423	2.2175	.97298

Pregnenolone acetate		
f_2	ϵ_{12}	γ_{12}
0.002751	2.2374	0.97240
.002334	2.2323	.97255
.001807	2.2267	.97271
.001342	2.2224	.97272
.000856	2.2183	.97283
.000399	2.2133	.97297

TABLE I continued

21-Acetoxypregnenolone		
f_2	ϵ_{12}	r_{12}
0.002679	2.2513	0.97183
.002530	2.2429	.97204
.001795	2.2371	.97215
.001323	2.2286	.97237
.000861	2.2206	.97255
.000491	2.2168	.97274

21-Acetoxypregnenolone acetate		
f_2	ϵ_{12}	r_{12}
0.002288	2.2332	0.97211
.001940	2.2293	.97218
.001607	2.2255	.97237
.001174	2.2214	.97249
.000716	2.2177	.97270
.000452	2.2139	.97293

16-Dehydropregnenolone		
f_2	ϵ_{12}	r_{12}
0.003234	2.2645	0.97208
.002639	2.2539	.97242
.002092	2.2438	.97243
.001649	2.2356	.97276
.001107	2.2273	.97274
.000600	2.2177	.97282

TABLE I continued

Desoxycorticosterone		
f_2	ϵ_{12}	v_{12}
0.003039	2.2406	0.97175
.002433	2.2305	.97215
.002005	2.2276	.97186
.001447	2.2254	.97244
.000884	2.2186	.97264
.000475	2.2146	.97268

Estrone		
f_2	ϵ_{12}	v_{12}
0.003822	2.2777	0.97160
.003137	2.2648	.97228
.002550	2.2542	.97213
.001916	2.2415	.97253
.001283	2.2336	.97255
.000517	2.2205	.97296

α -Estradiol		
f_2	ϵ_{12}	v_{12}
0.003737	2.2497	0.97172
.002993	2.2417	.97214
.002424	2.2331	.97220
.001822	2.2266	.97239
.001052	2.2188	.97260
.000572	2.2139	.97293

TABLE I continued

Dehydroisoandrosterone		
f_2	ϵ_{12}	v_{12}
0.003529	2.2512	0.97267
.002889	2.2451	.97268
.002332	2.2369	.97236
.001665	2.2284	.97278
.001046	2.2223	.97280
.000524	2.2159	.97305

Stigmasteryl acetate		
f_2	ϵ_{12}	v_{12}
0.002251	2.2222	0.97379
.001801	2.2197	.97362
.001474	2.2192	.97375
.001093	2.2165	.97354
.000642	2.2143	.97303
.000379	2.2114	.97300
.002105	2.2228	.97333
.001658	2.2202	.97341
.001330	2.2176	.97323
.000914	2.2156	.97327
.000543	2.2134	.97266

TABLE I continued

Adrenosterone		
f_2	ε_{12}	ν_{12}
0.003444	2.3379	0.97143
.002753	2.3123	.97149
.002155	2.2912	.97197
.001589	2.2684	.97228
.001059	2.2478	.97262
.000601	2.2326	.97286

Dehydroisoandrosterone acetate		
f_2	ε_{12}	ν_{12}
0.003055	ε_{12} vs. f_2	0.97254
.002573		.97244
.002145	plot	.97273
.001565	was not	.97282
.000883	linear	.97280
.000433		.97318
.002879	2.2540	.97230
.002333	2.2445	.97262
.001541	2.2338	.97267
.001000	2.2256	.97293
.000536	2.2178	.97267

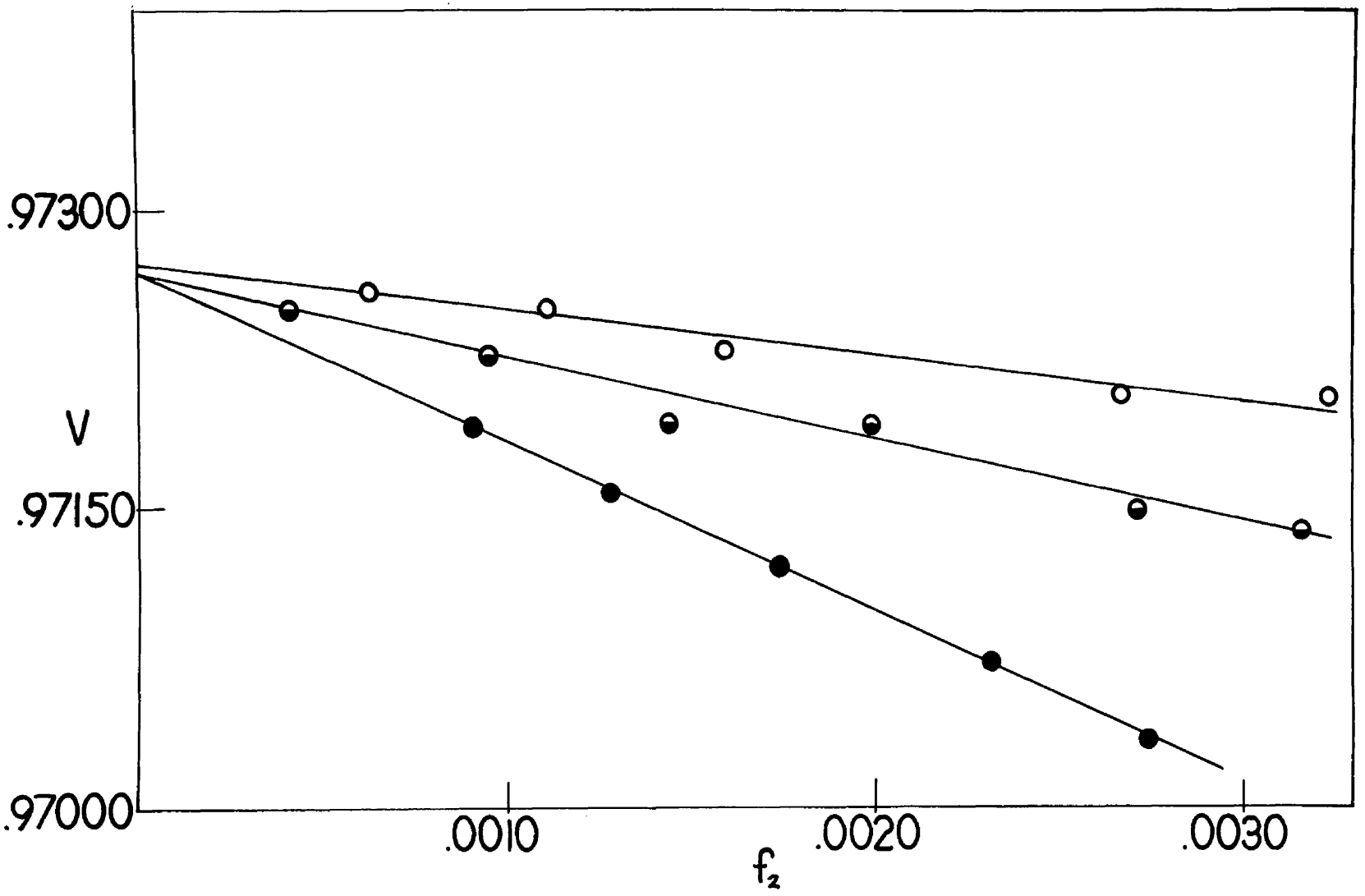


Figure 2. Specific volume as a function of concentration for dioxane solutions of ○ progesterone, ● 4-chloro-17α-hydroxypregnane-3,11,20-trione and ◒ 11α-hydroxyallopregnane-3,20-dione.

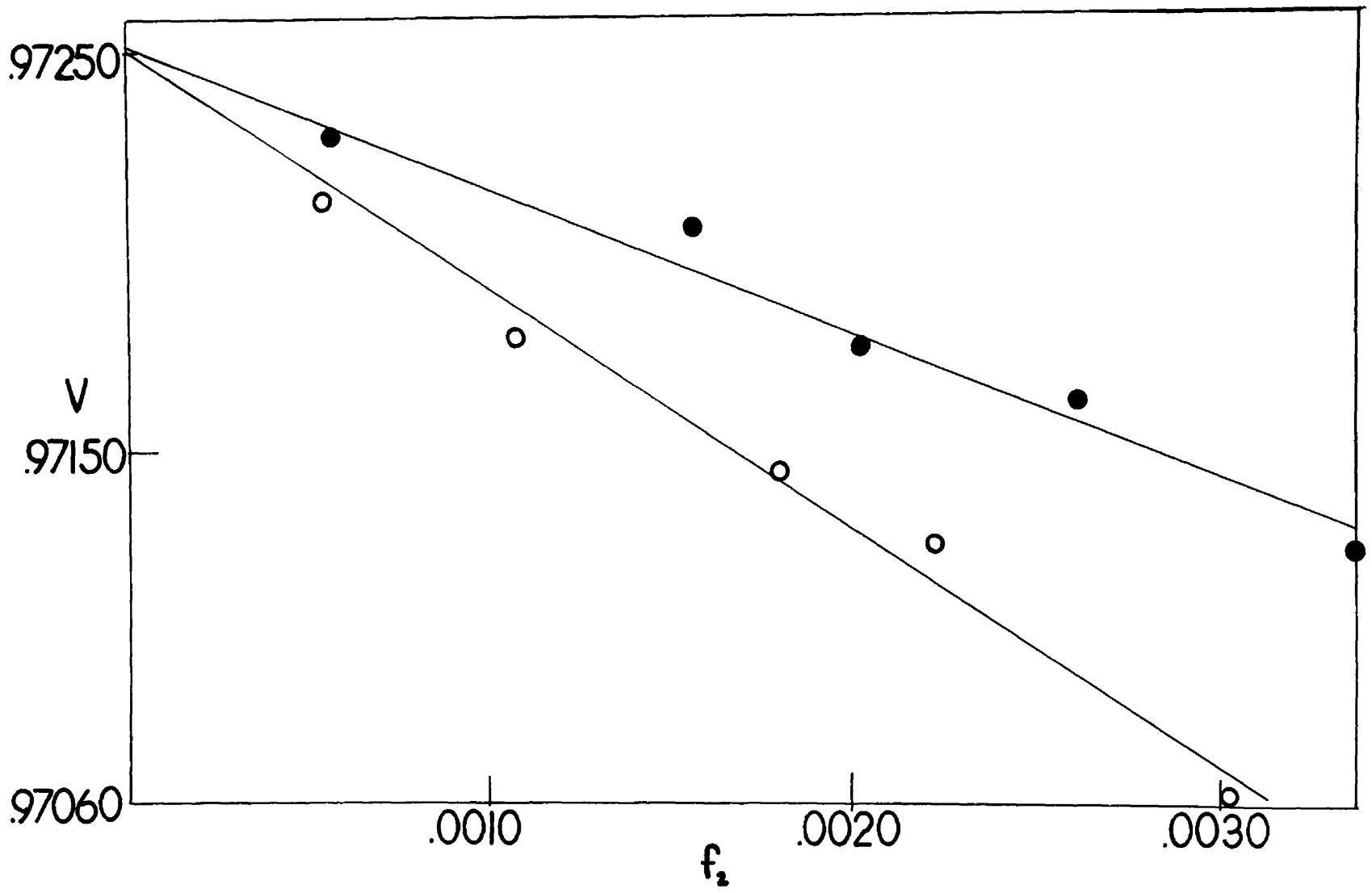


Figure 3. Specific volume as a function of concentration for dioxane solutions of ○ 11α, 17α-dihydroxyprogesterone and ● 17α-hydroxyprogesterone.

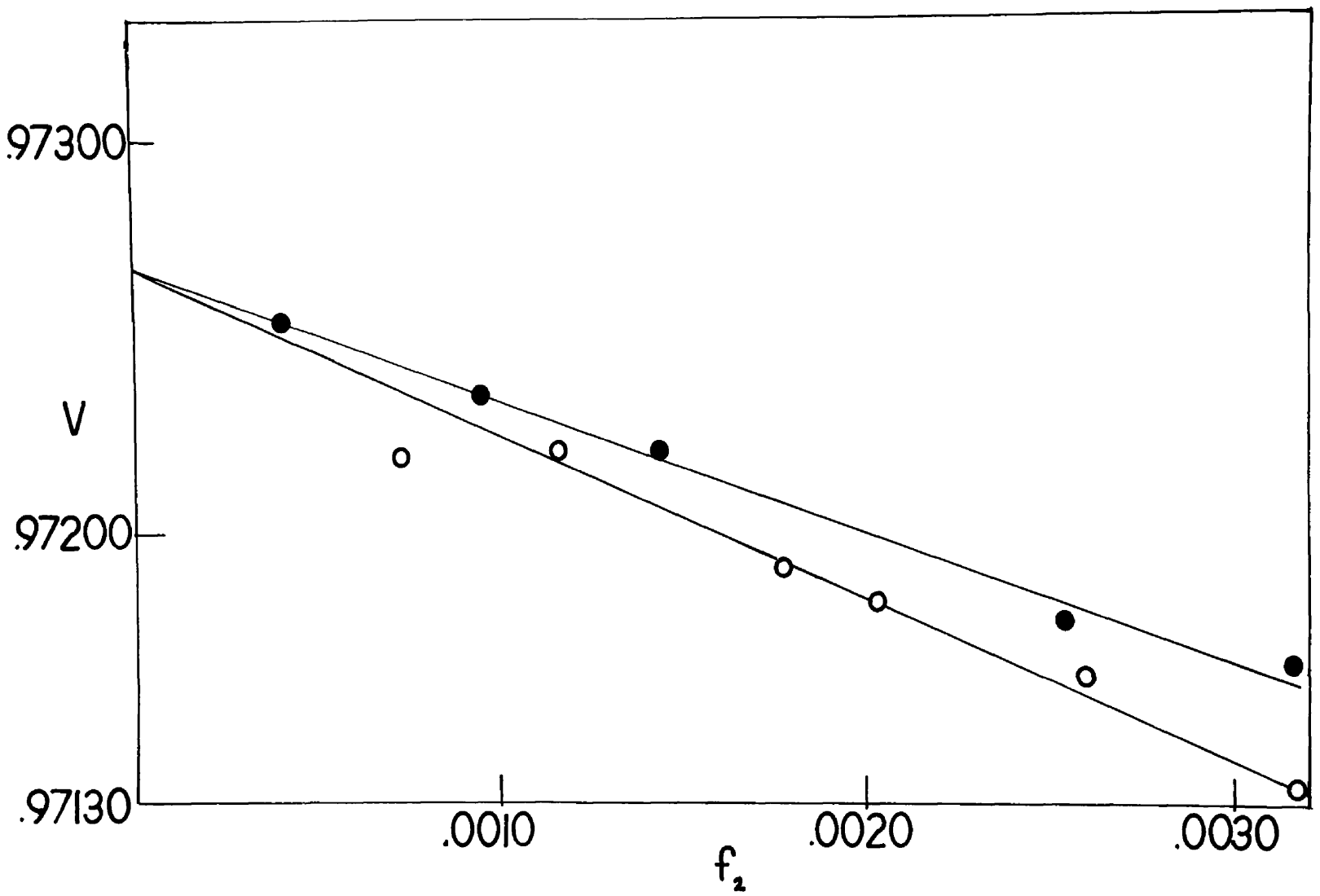


Figure 4. Specific volume as a function of concentration for dioxane solutions of O 11-ketoprogesterone and ● 11α-hydroxypregnane -3,20-dione.

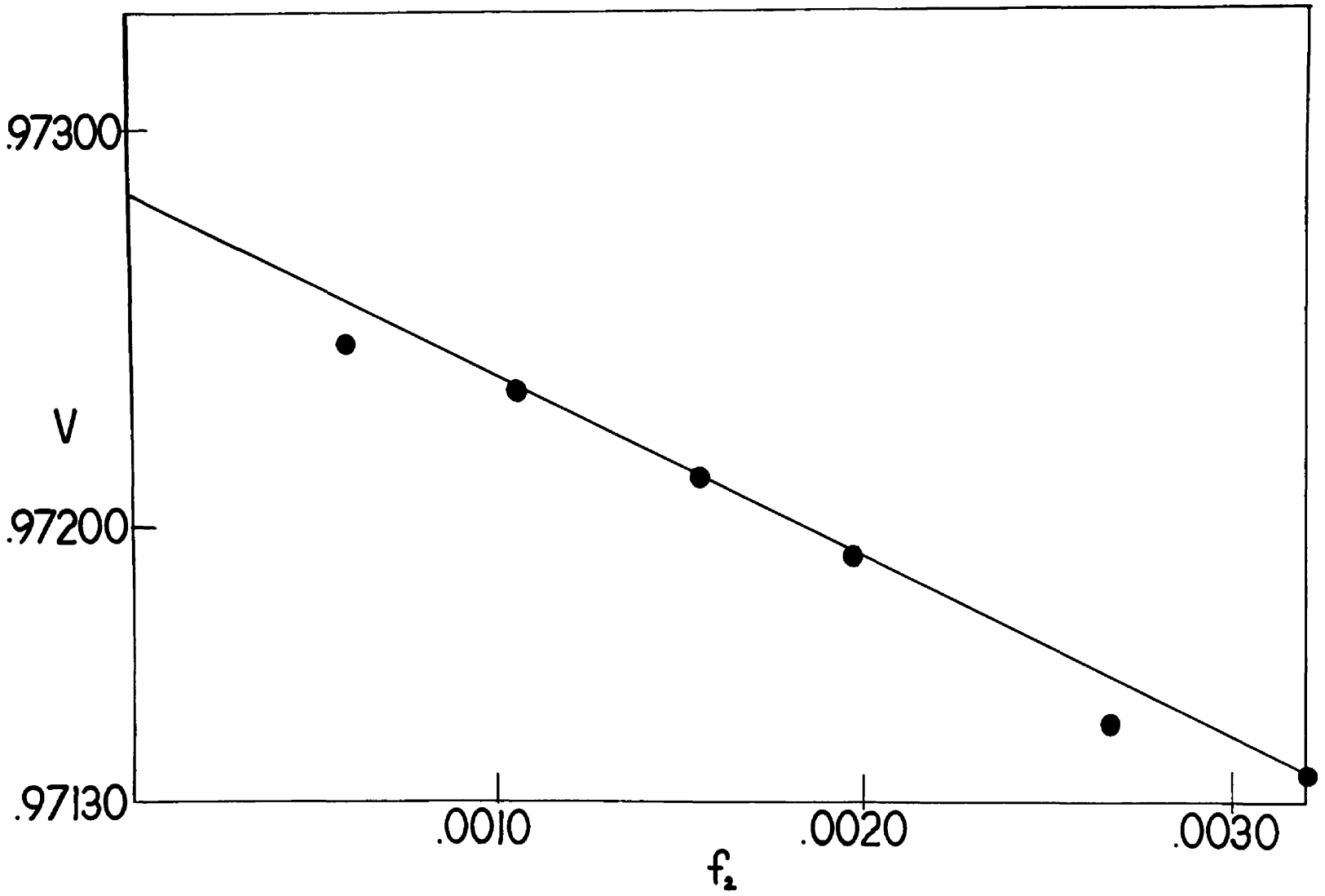


Figure 5. Specific volume as a function of concentration for dioxane solutions of pregnane-3,11,20-trione.

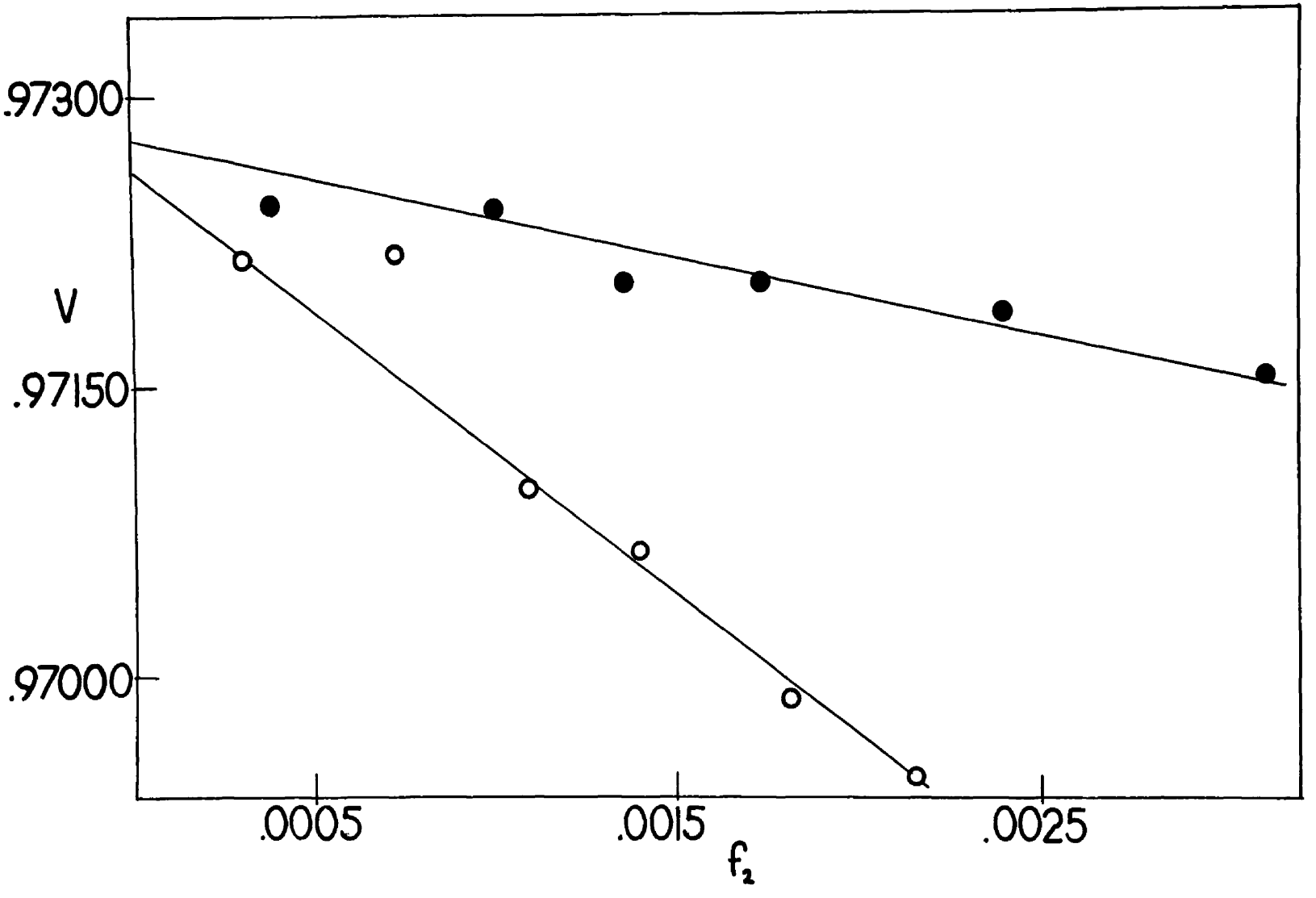


Figure 6. Specific volume as a function of concentration for dioxane solutions of ○ 4-bromo-17α-hydroxy-21-acetoxypregnane-3,11,20-trione and ● allopregnane-3,11,20-trione.

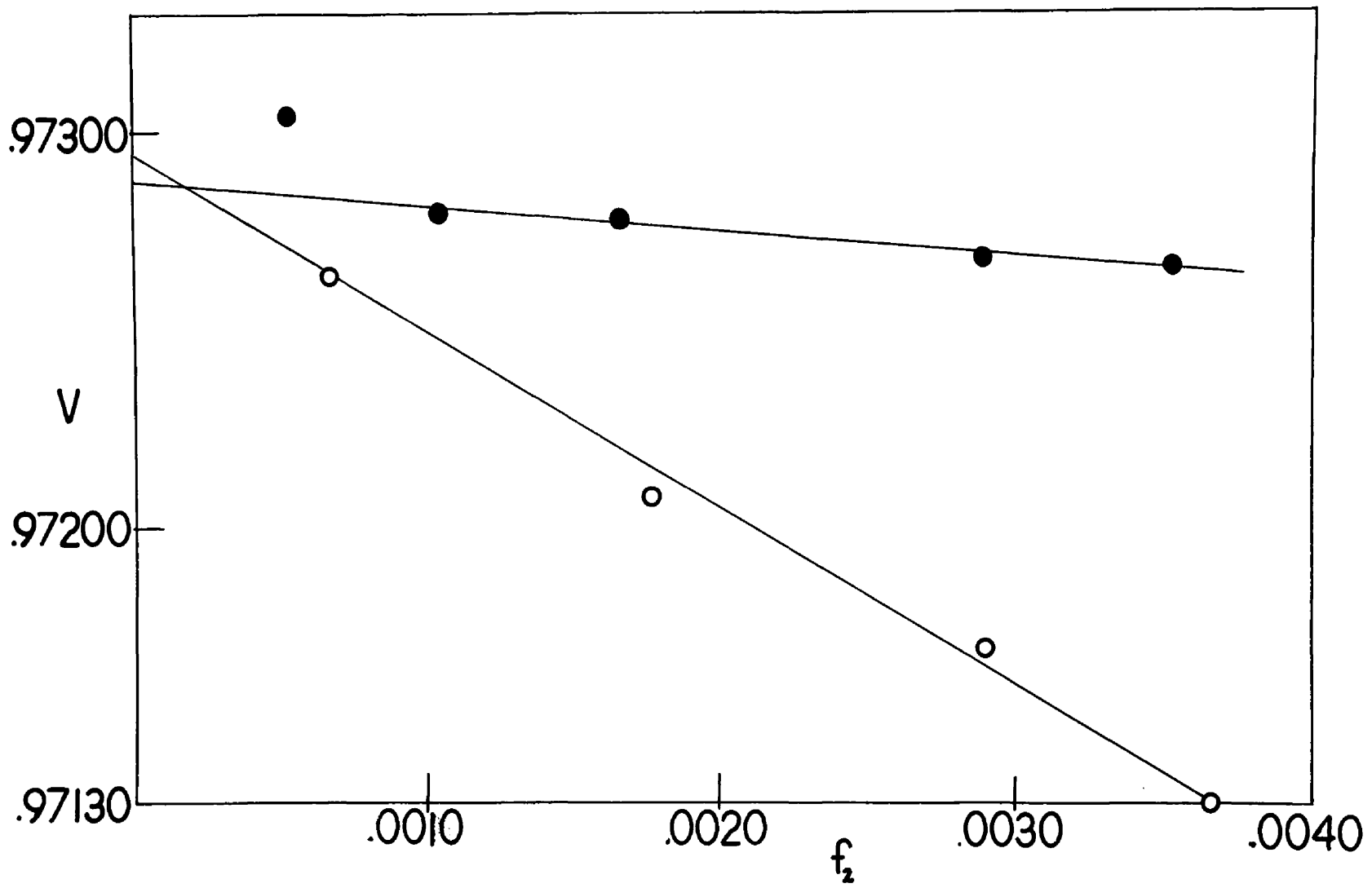


Figure 7. Specific volume as a function of concentration for dioxane solutions of O 11β- hydroxyprogesterone and ● dehydroisoandrosterone.

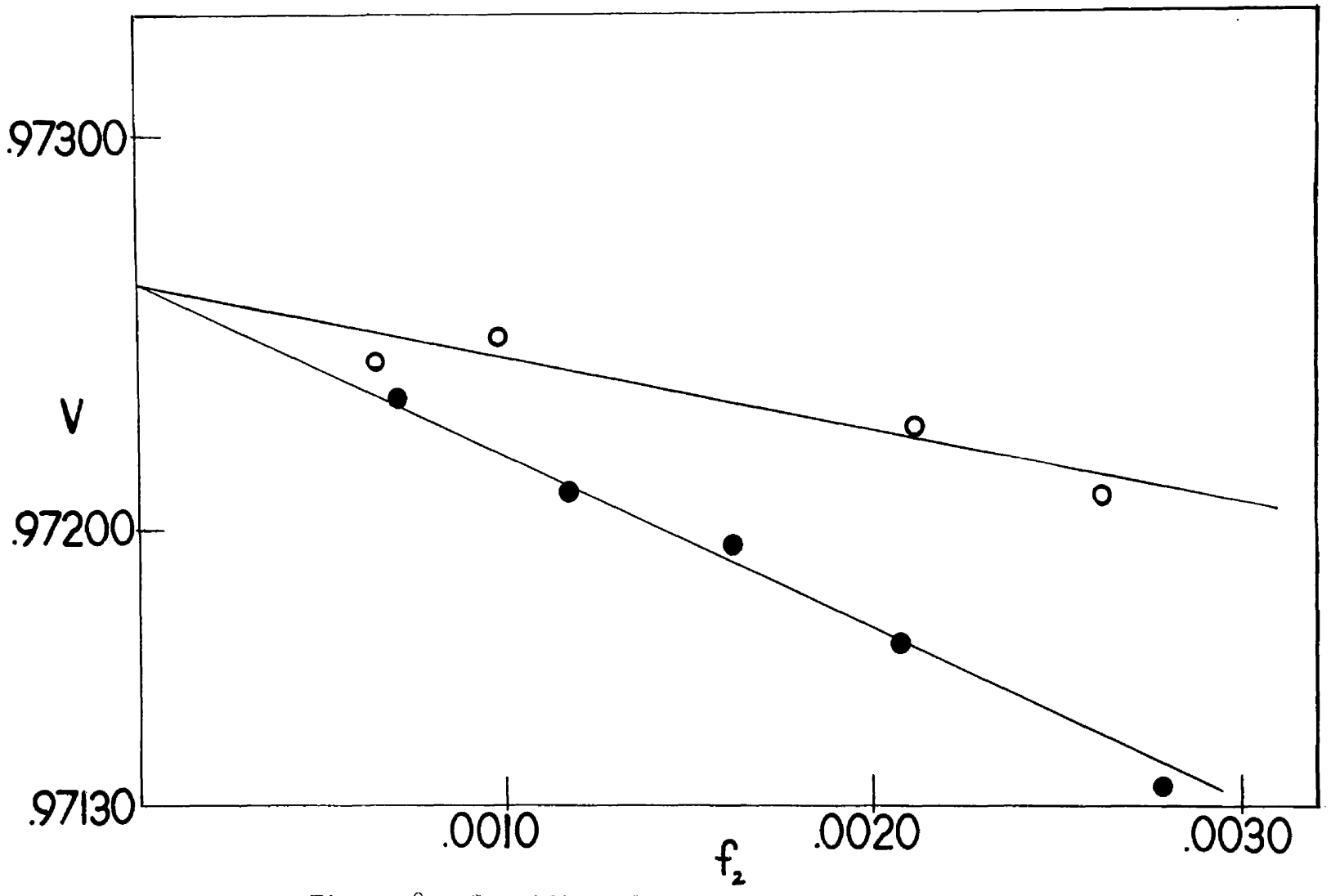


Figure 8. Specific volume as a function of concentration for dioxane solutions of ○ allopregnane-3,20-dione and ● 11α -acetoxyprogesterone.

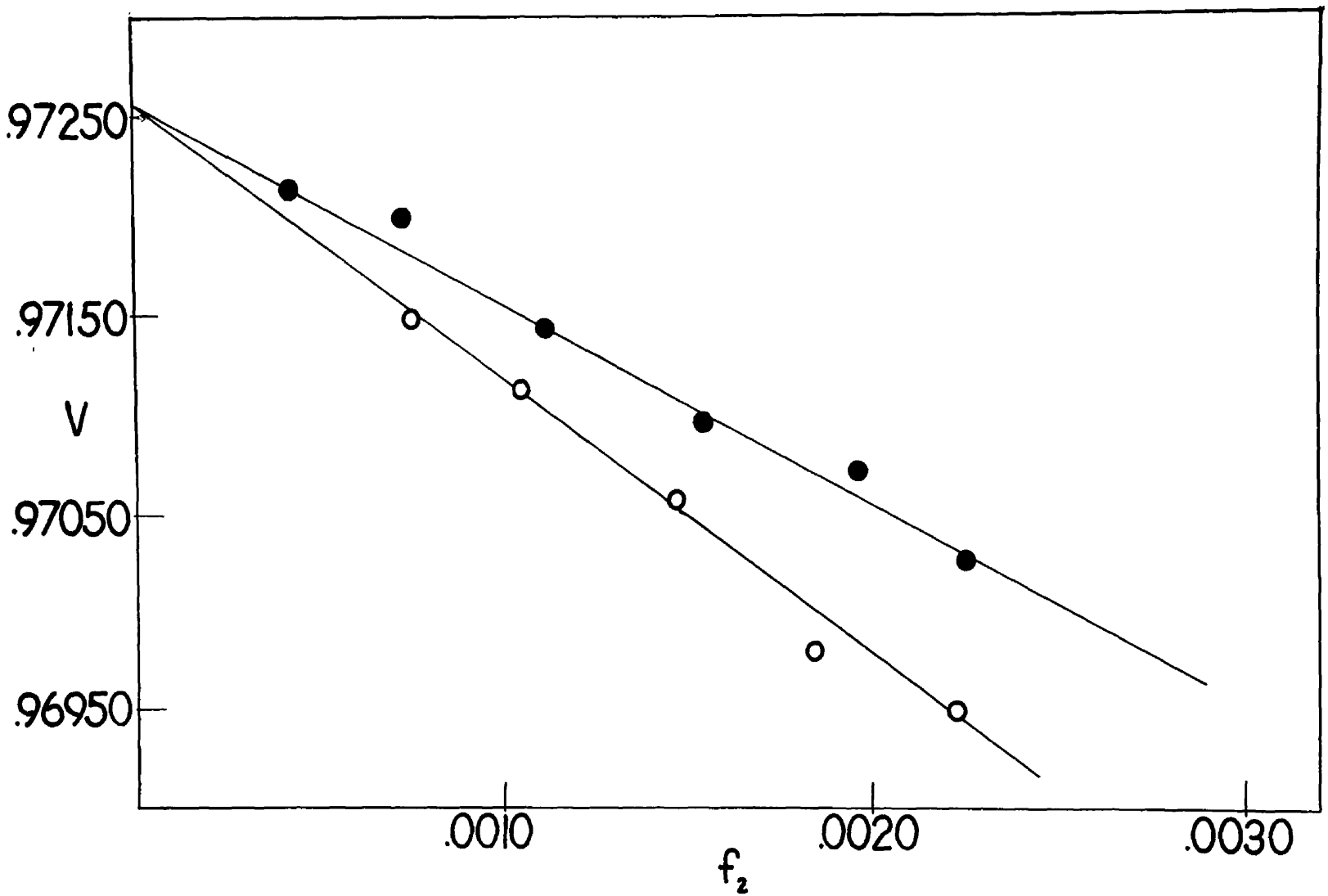


Figure 9. Specific volume as a function of concentration for dioxane solutions of ○ 4-chloro-21-bromo-17α-hydroxypregnane-3,11,20-trione and ● 4-chloro-17α-hydroxy-21-acetoxypregnane-3,11,20-trione.

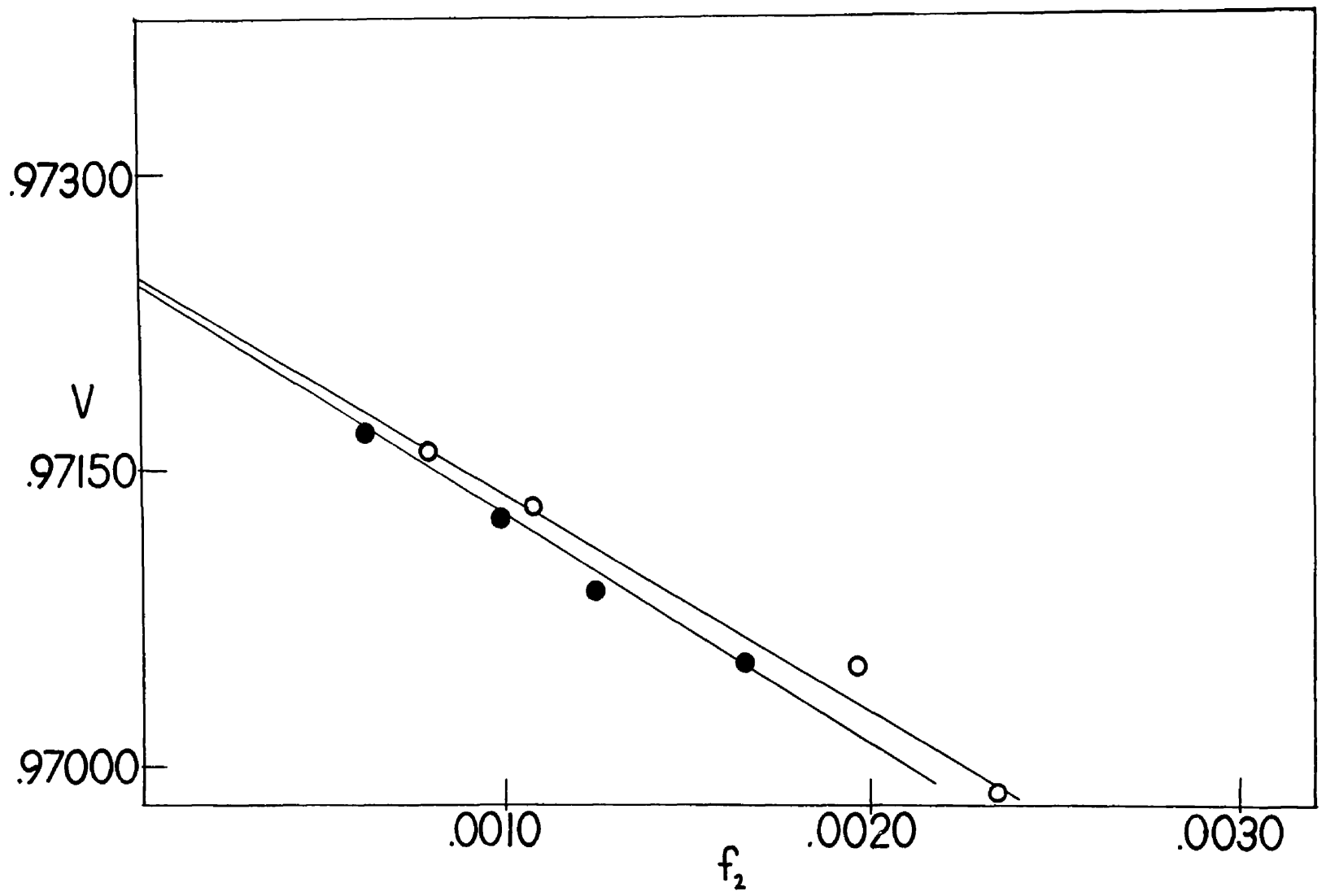


Figure 10. Specific volume as a function of concentration for dioxane solutions of ○ 3α,17α-dihydroxy-21-bromopregnane-11,20-dione and ● 3β,17α-dihydroxy-21-bromopregnane-11,20-dione.

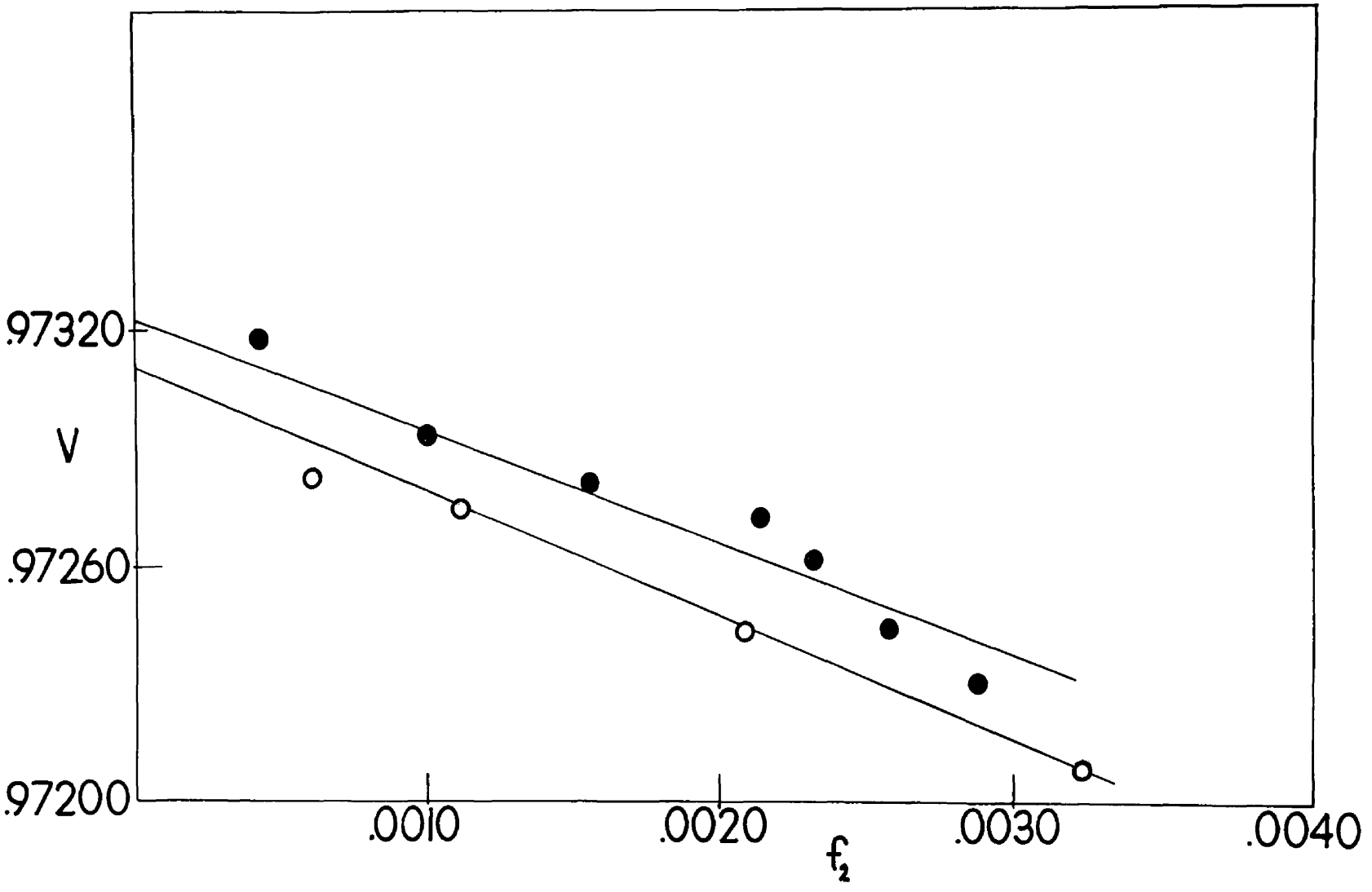


Figure 11. Specific volume as a function of concentration for dioxane solutions of ○ 16-dehydropregnenolone and ● dehydroisoandrosterone acetate.

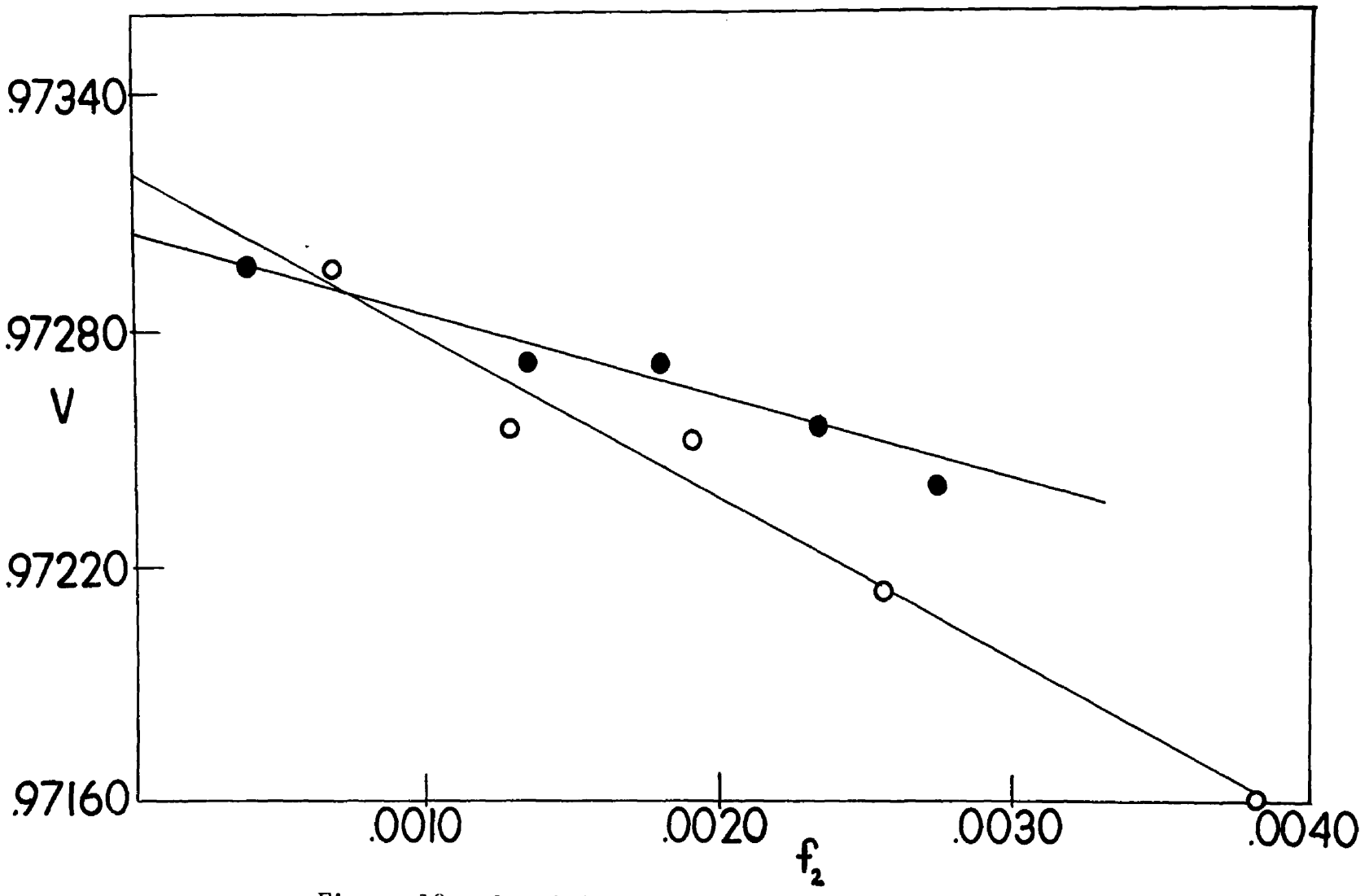


Figure 12. Specific volume as a function of concentration for dioxane solutions of ○ estrone and ● pregnenolone acetate.

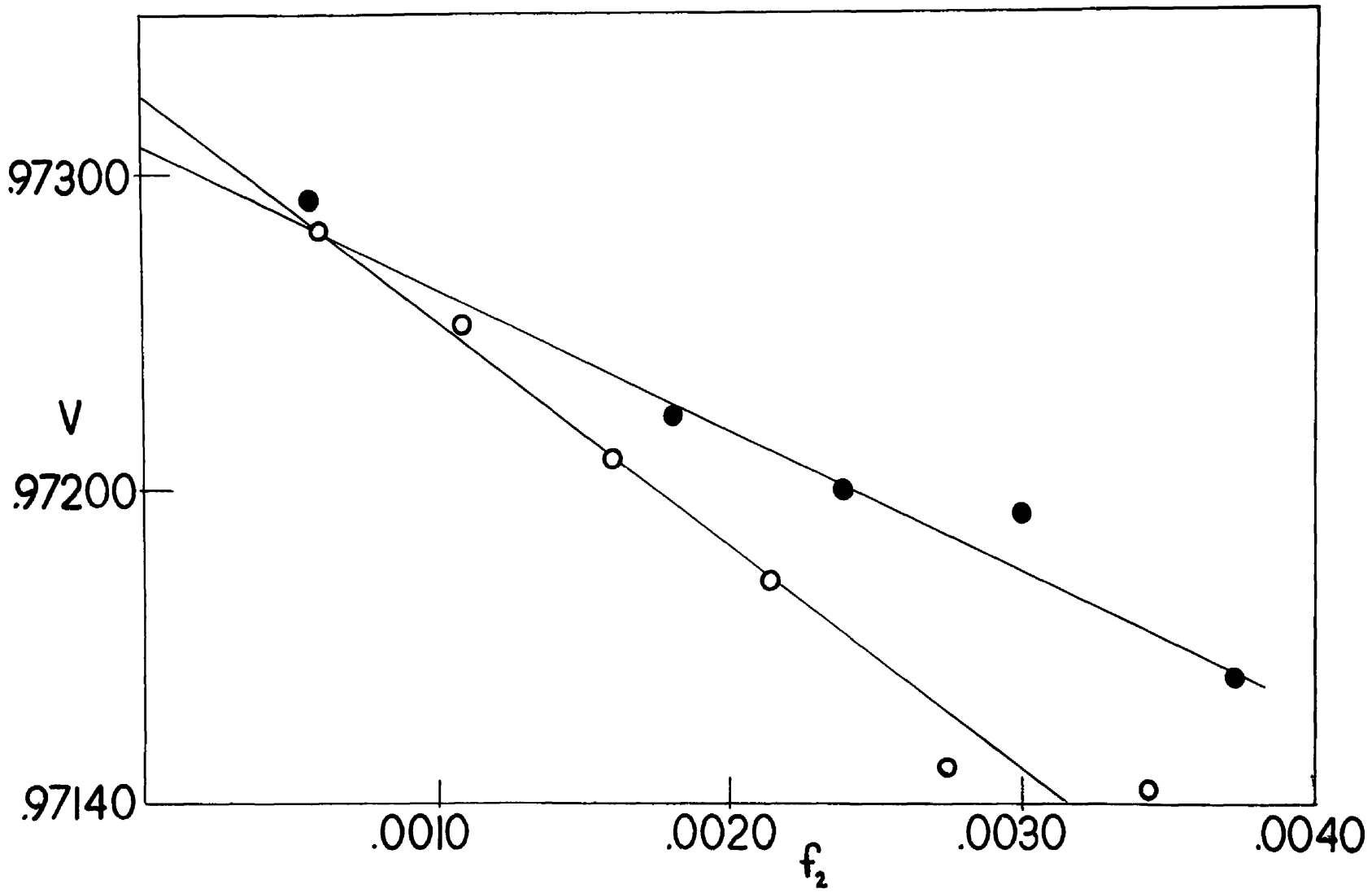


Figure 13. Specific volume as a function of concentration for dioxane solutions of O adrenosterone and ● α-estradiol.

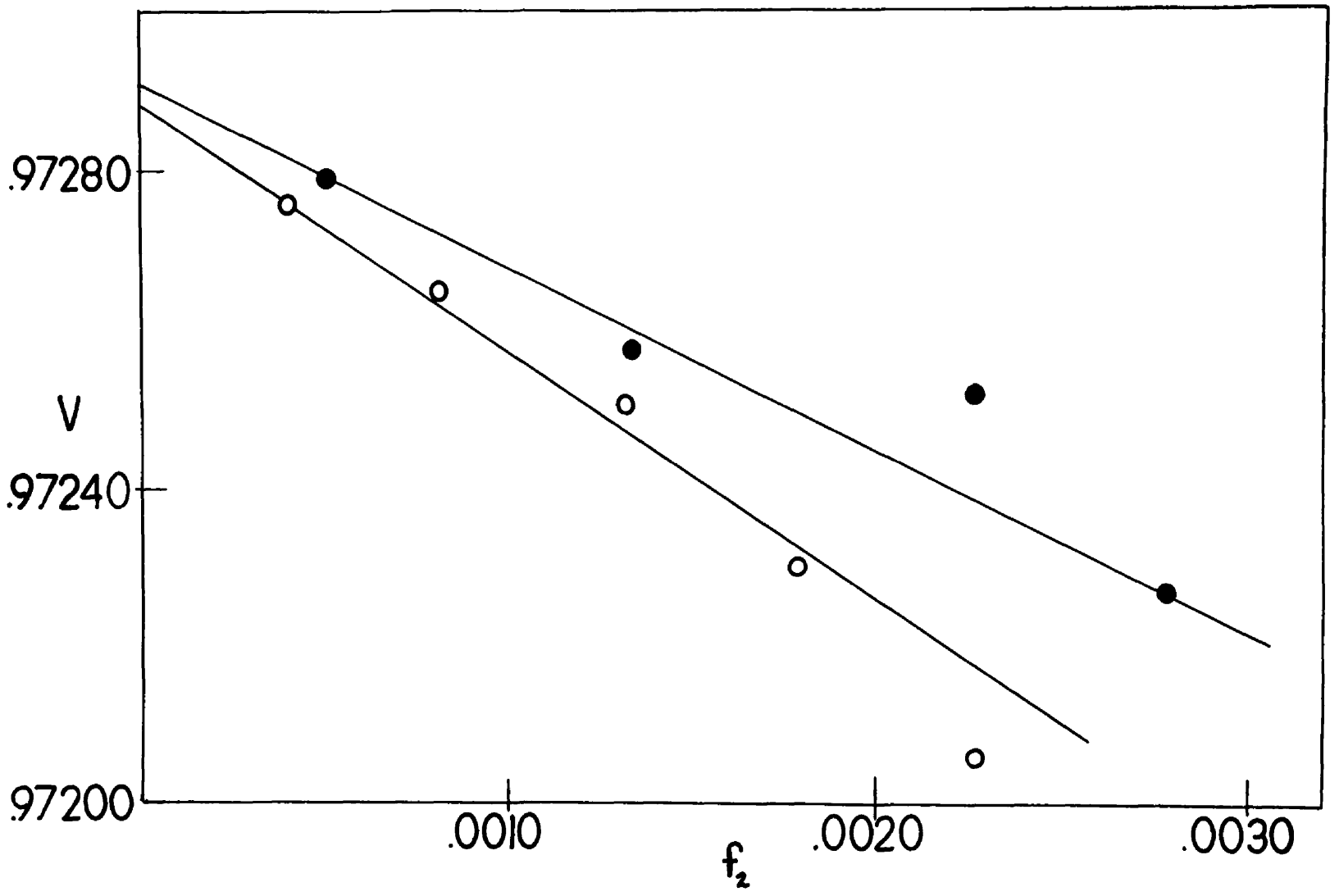


Figure 14. Specific volume as a function of concentration for dioxane solutions of ○ 21-acetoxyallopregnanedione and ● 16-dehydropregnenolone acetate.

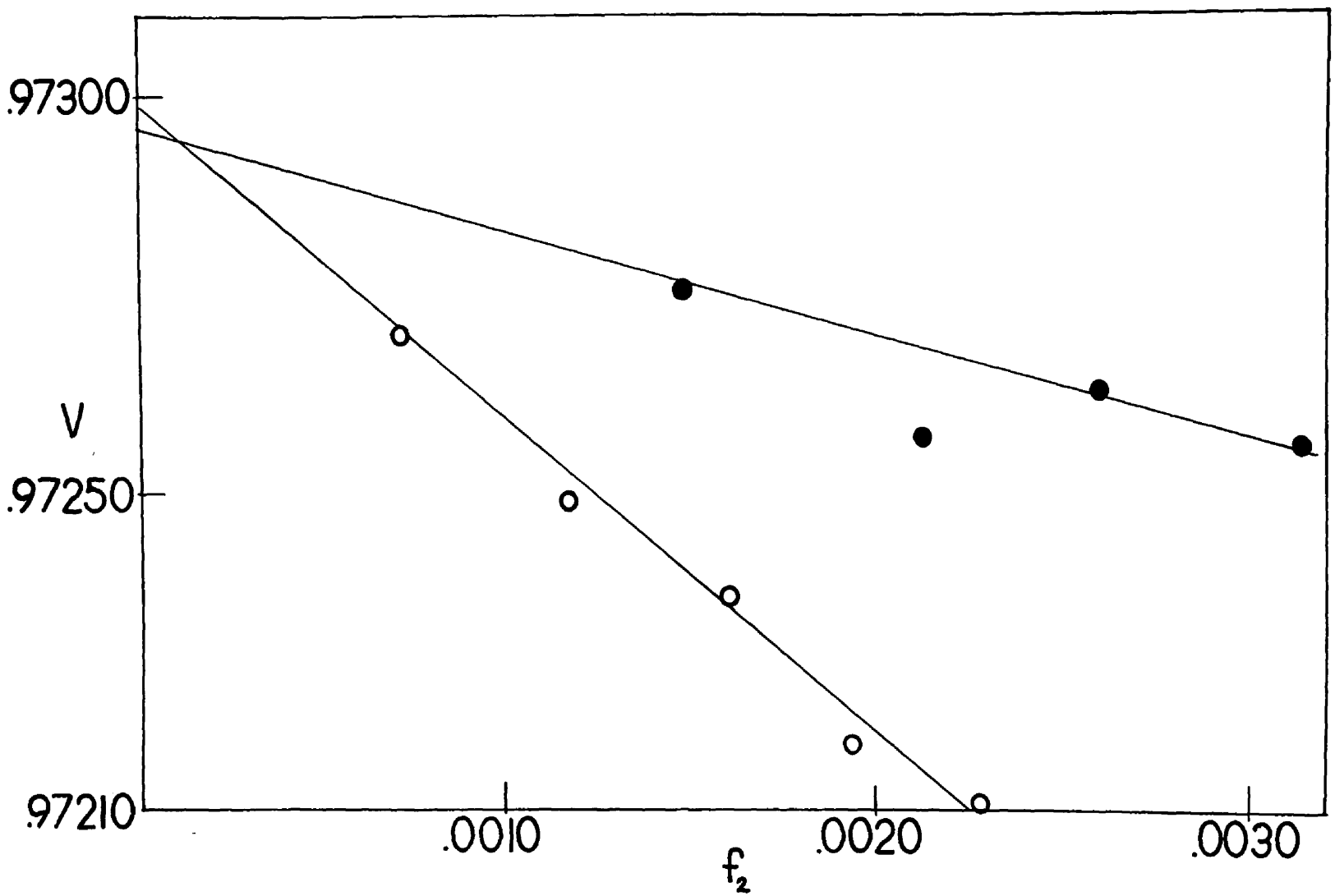


Figure 15. Specific volume as a function of concentration for dioxane solutions of ○ 21-acetoxypregnenolone acetate and ● pregnenolone.

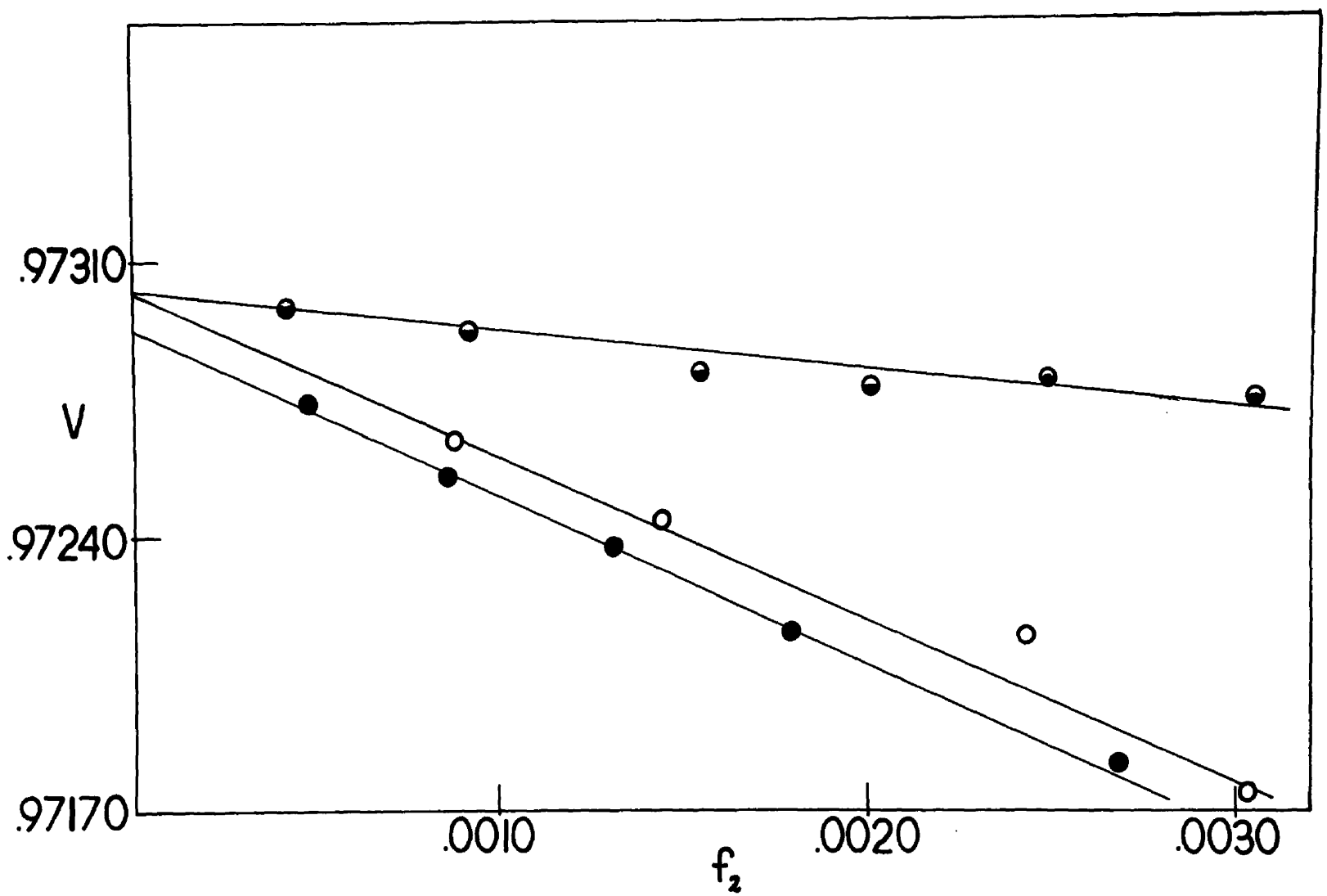


Figure 16. Specific volume as a function of concentration for dioxane solutions of O desoxycorticosterone, ● 21-acetoxypregnenolone, and ◒ pregnenolone-3-methyl ether.

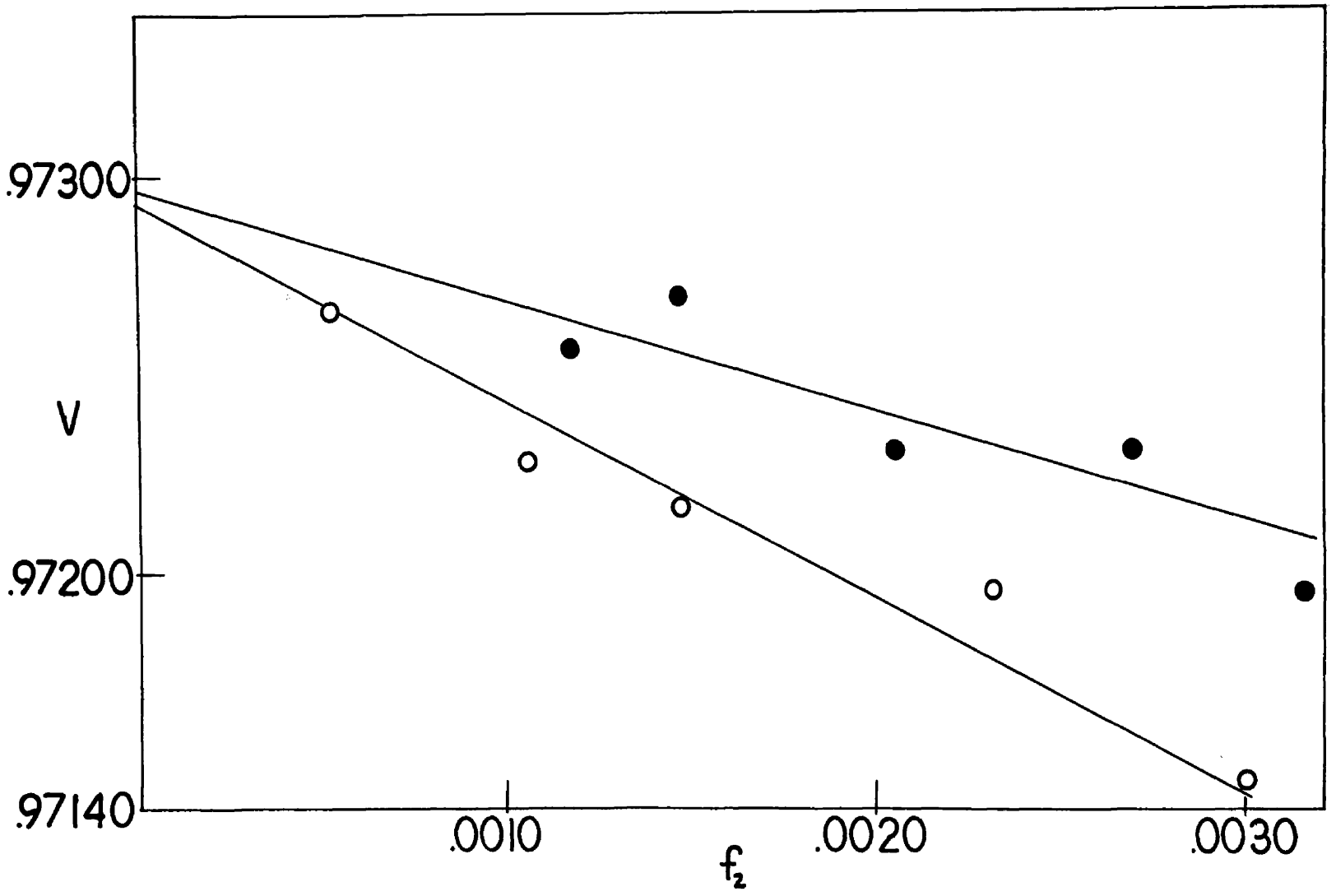


Figure 17. Specific volume as a function of concentration for dioxane solutions of ○ 11α-hydroxyprogesterone and ● pregnane-3,20-dione.

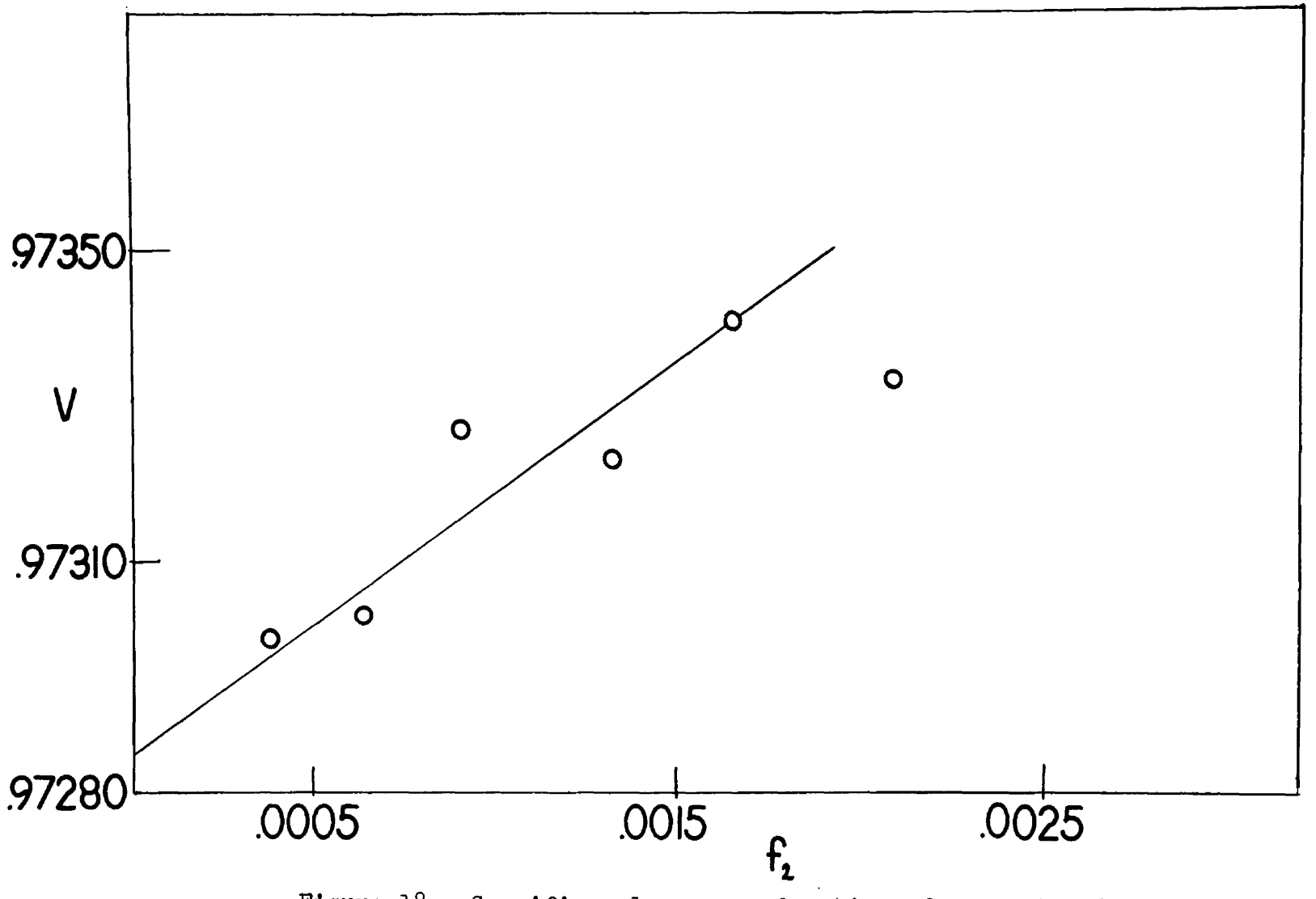


Figure 18. Specific volume as a function of concentration for dioxane solutions of stigmasteryl acetate.

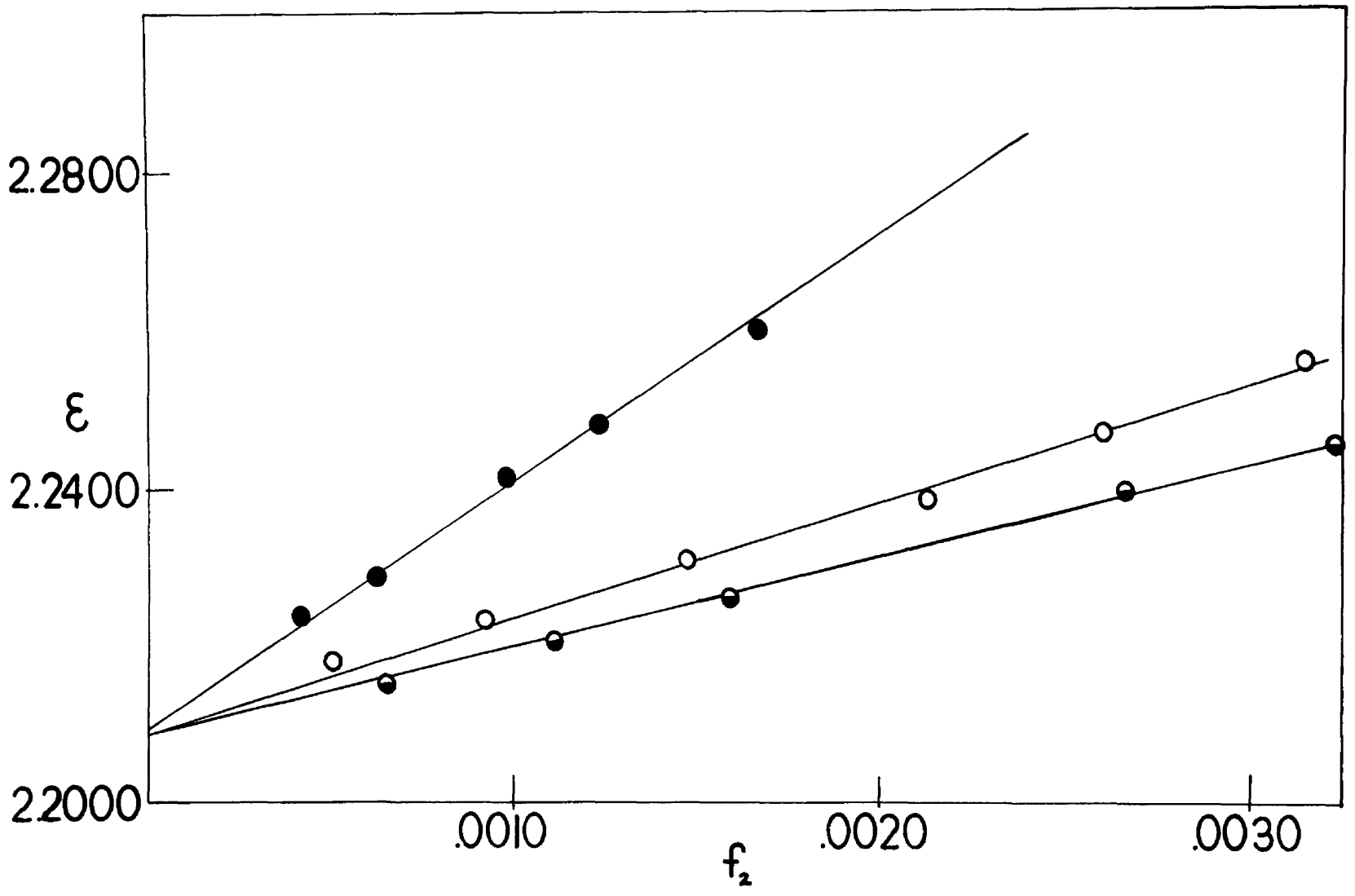


Figure 19. Dielectric constant as a function of concentration for dioxane solutions of ○ pregnenolone, ● 3β, 17α -dihydroxy-21-bromopregnane-11,20-dione and ◒ progesterone.

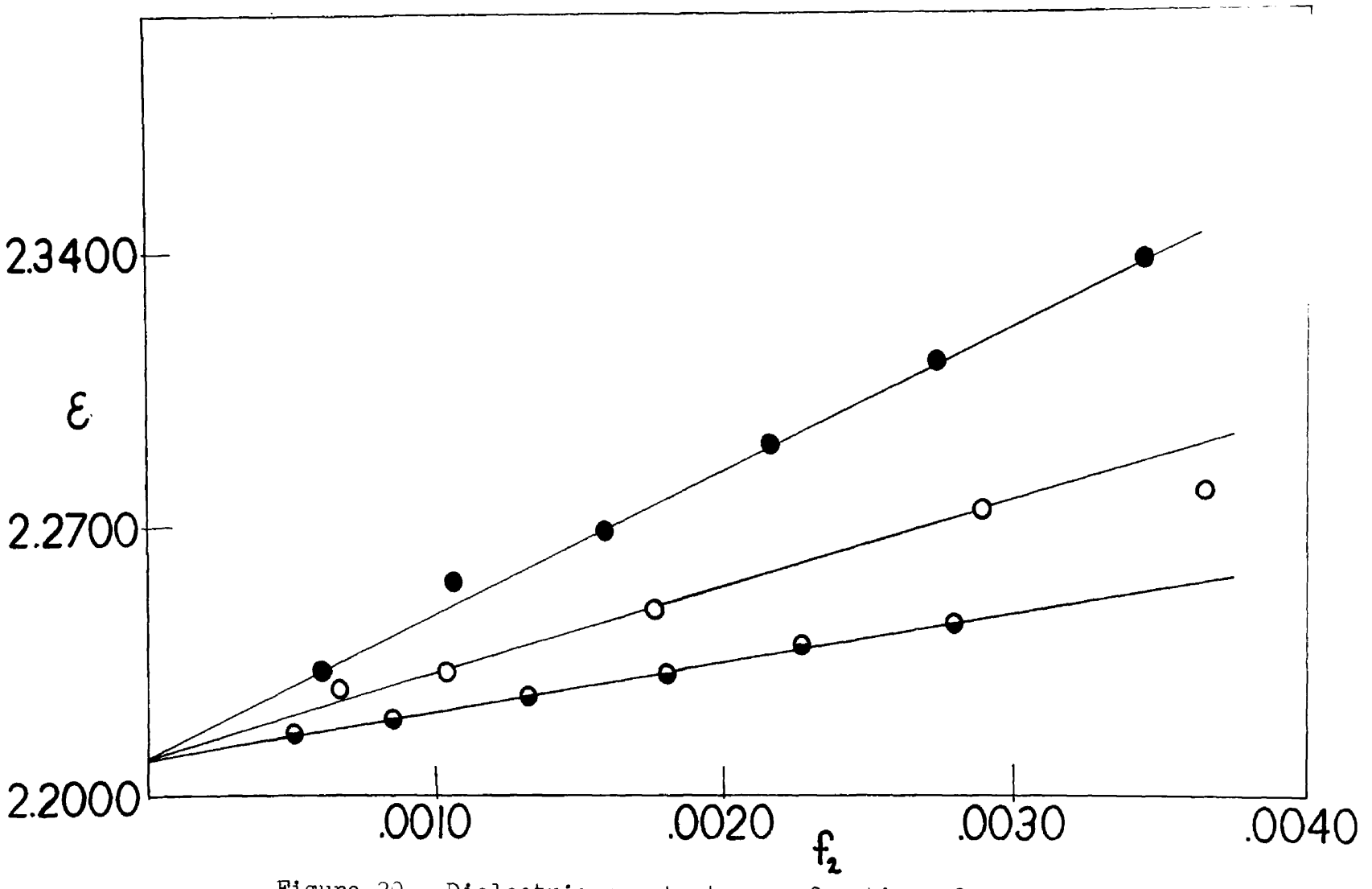


Figure 20. Dielectric constant as a function of concentration for dioxane solutions of ○ 11α -hydroxyprogesterone, ● adrenosterone, and ⊖ 16-dehydropregnenolone acetate.

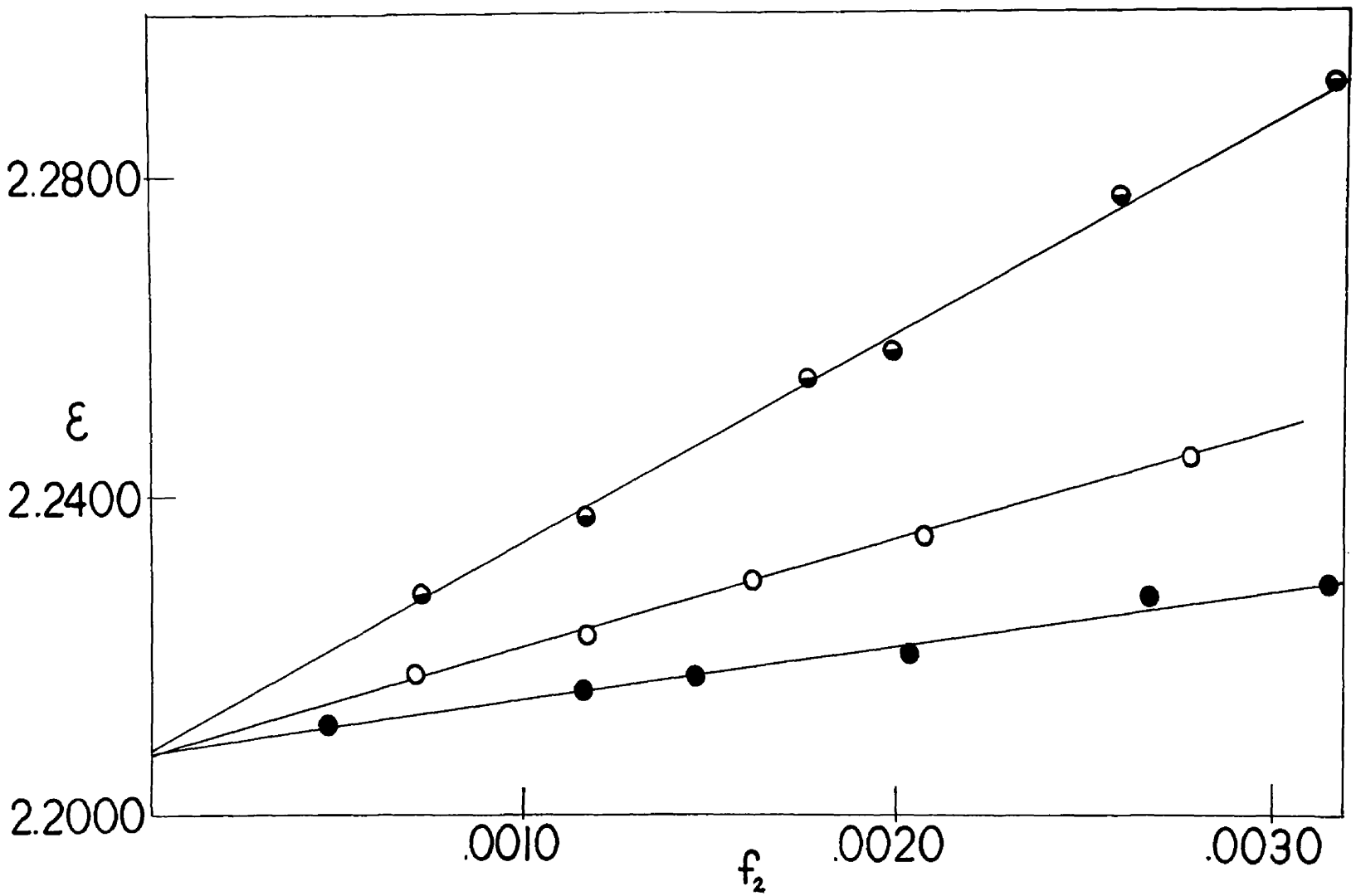


Figure 21. Dielectric constant as a function of concentration for dioxane solutions of ○ 11α-acetoxyprogesterone, ● pregnane-3,20-dione, and ◒ 11-ketoprogesterone.

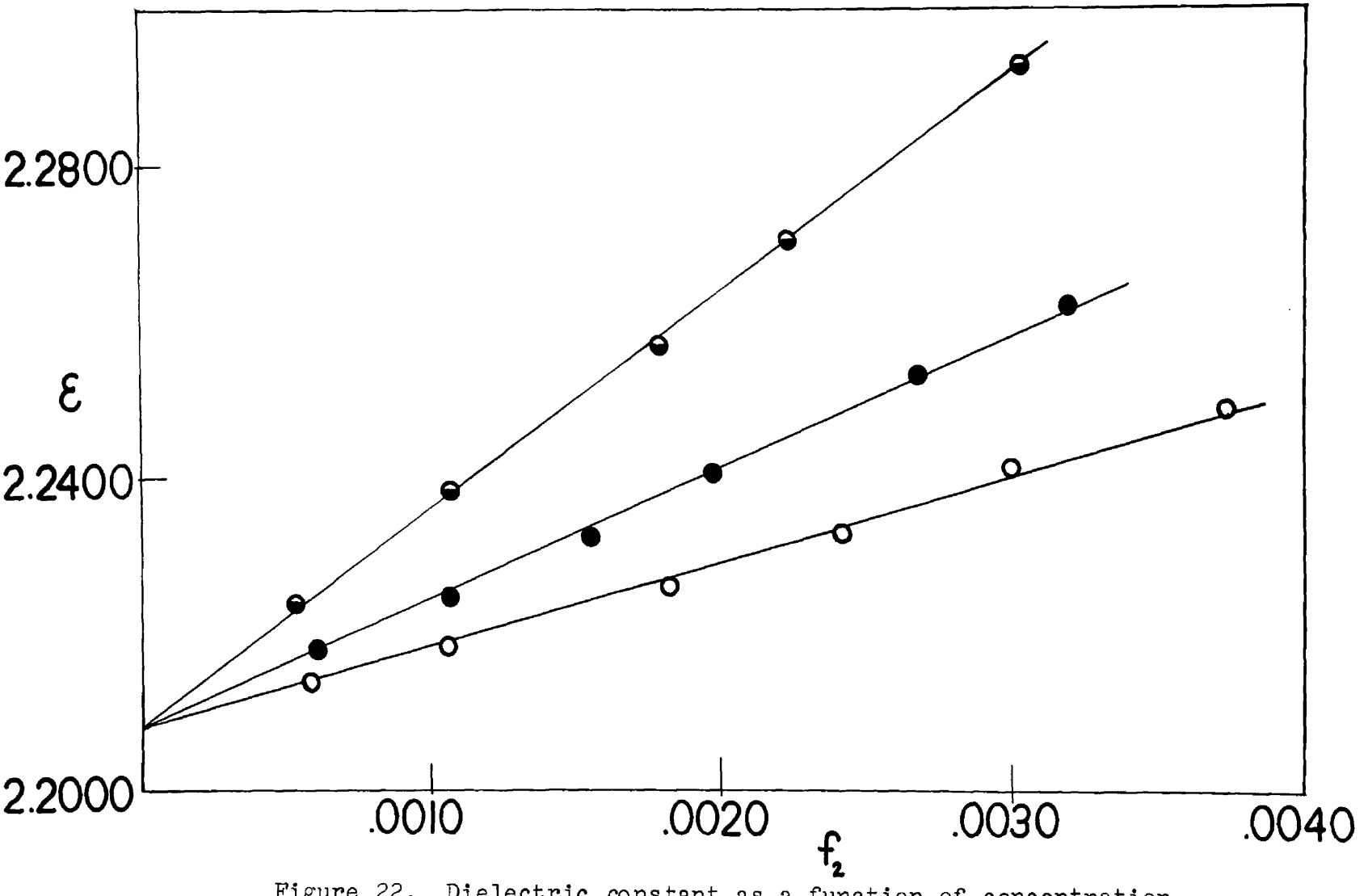


Figure 22. Dielectric constant as a function of concentration for dioxane solutions of ○ α-estradiol, ● pregnane-3,11,20-trione, and ◒ 11α,17α-dihydroxyprogesterone.

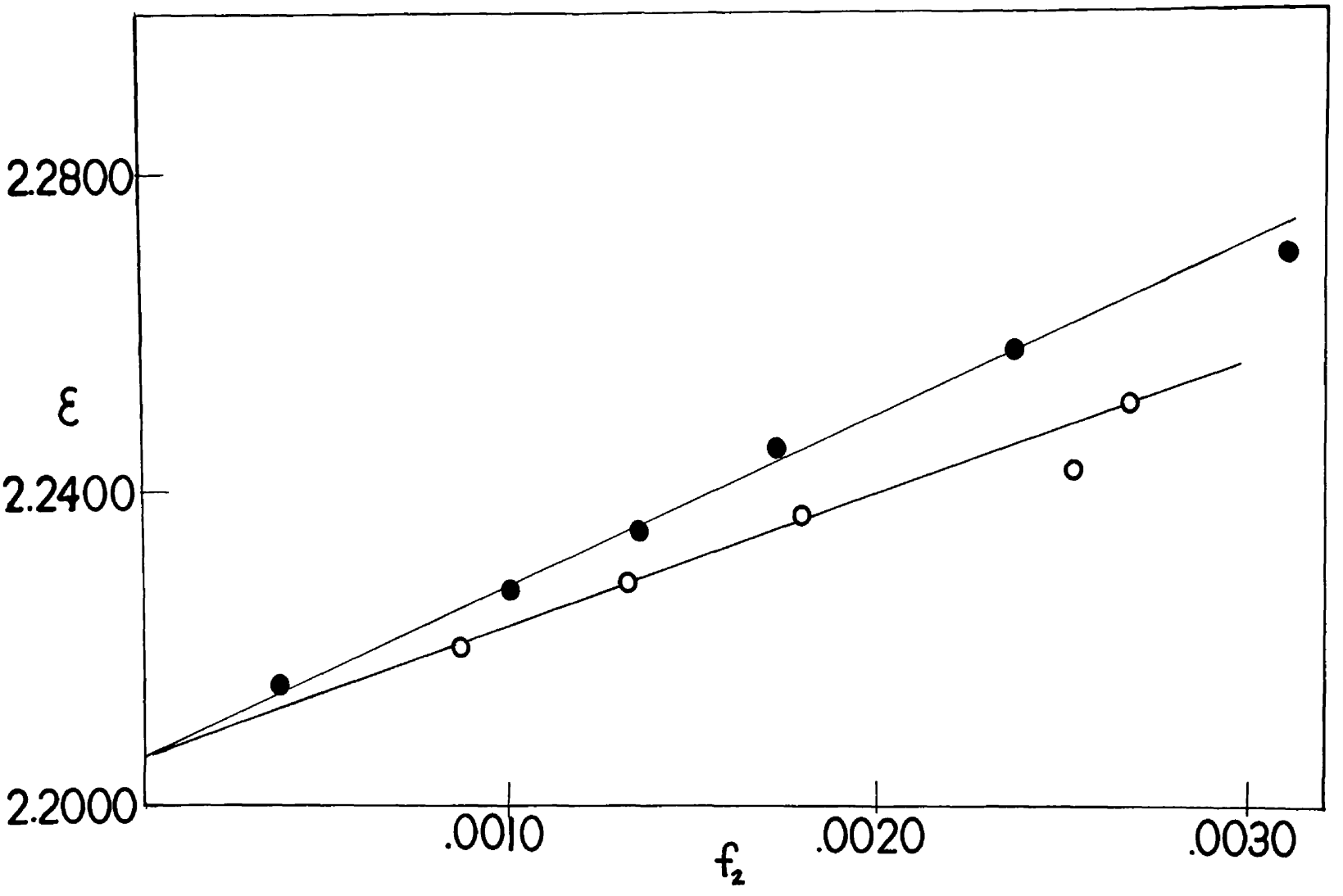


Figure 23. Dielectric constant as a function of concentration for dioxane solutions of O 21-acetoxypregnenolone and ● allopregnane-3,11,20-trione.

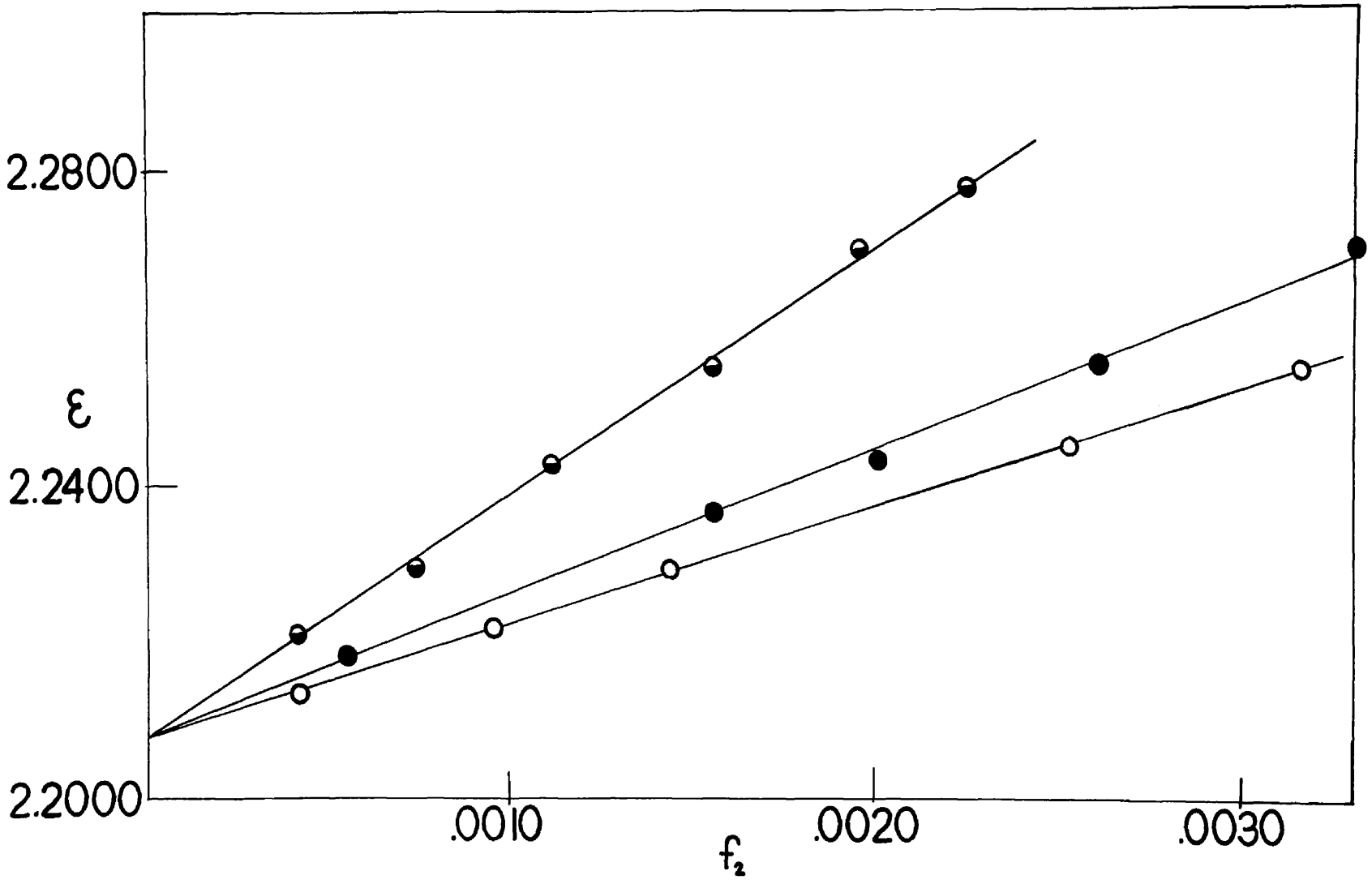


Figure 24. Dielectric constant as a function of concentration for dioxane solutions of ○ 11α-hydroxypregnane-3,20-dione, ● 17α-hydroxyprogesterone, and ⊖ 4-chloro-17α-hydroxy-21-acetoxypregnane-3,11,20-trione.

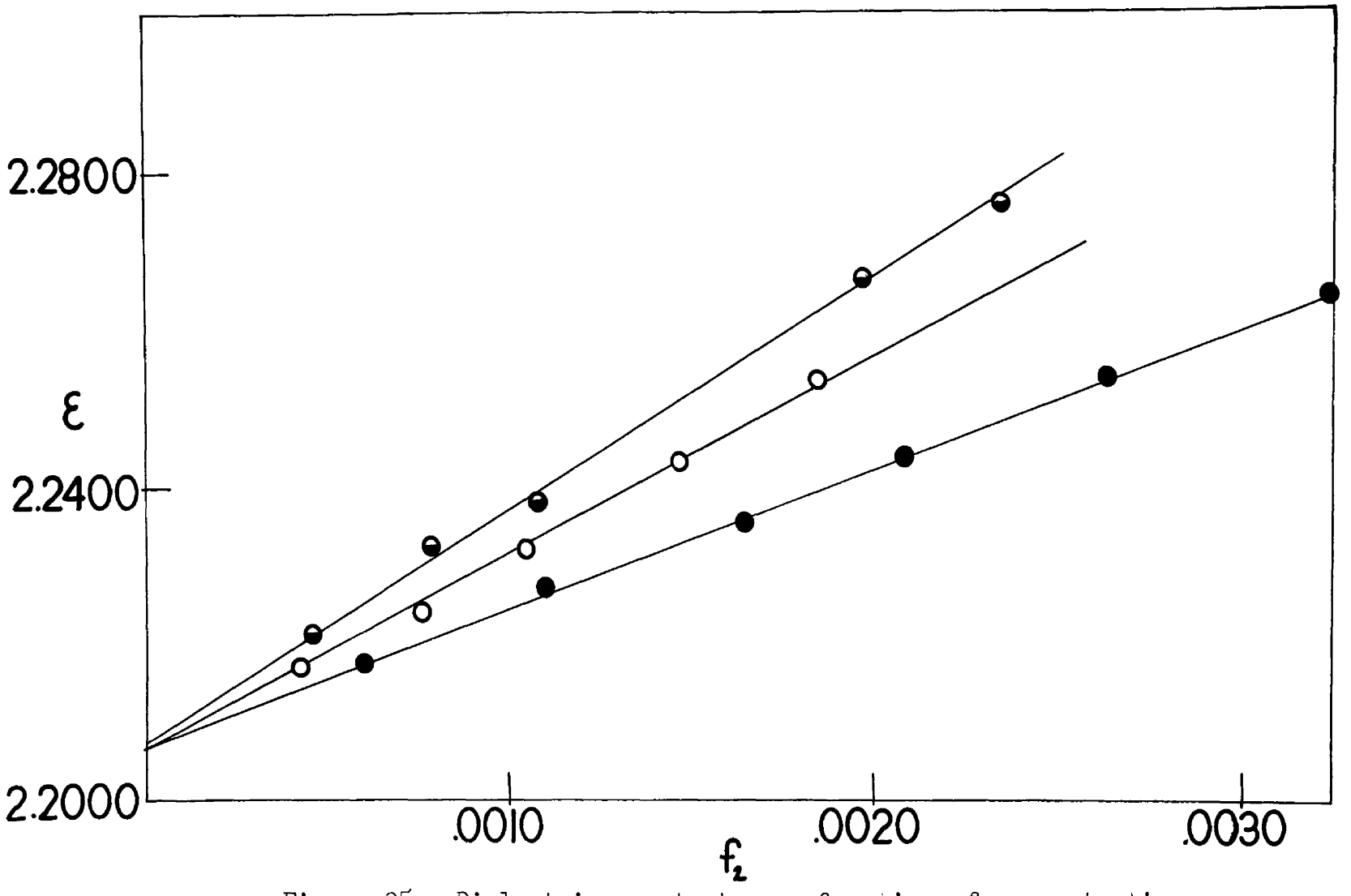


Figure 25. Dielectric constant as a function of concentration for dioxane solutions of ○ 4-chloro-21-bromo-17α-hydroxypregnane-3,11,20-trione, ● 16-dehydropregnenolone, and ⊖ 3α,17α-dihydroxy-21-bromopregnane-3,11,20-trione.

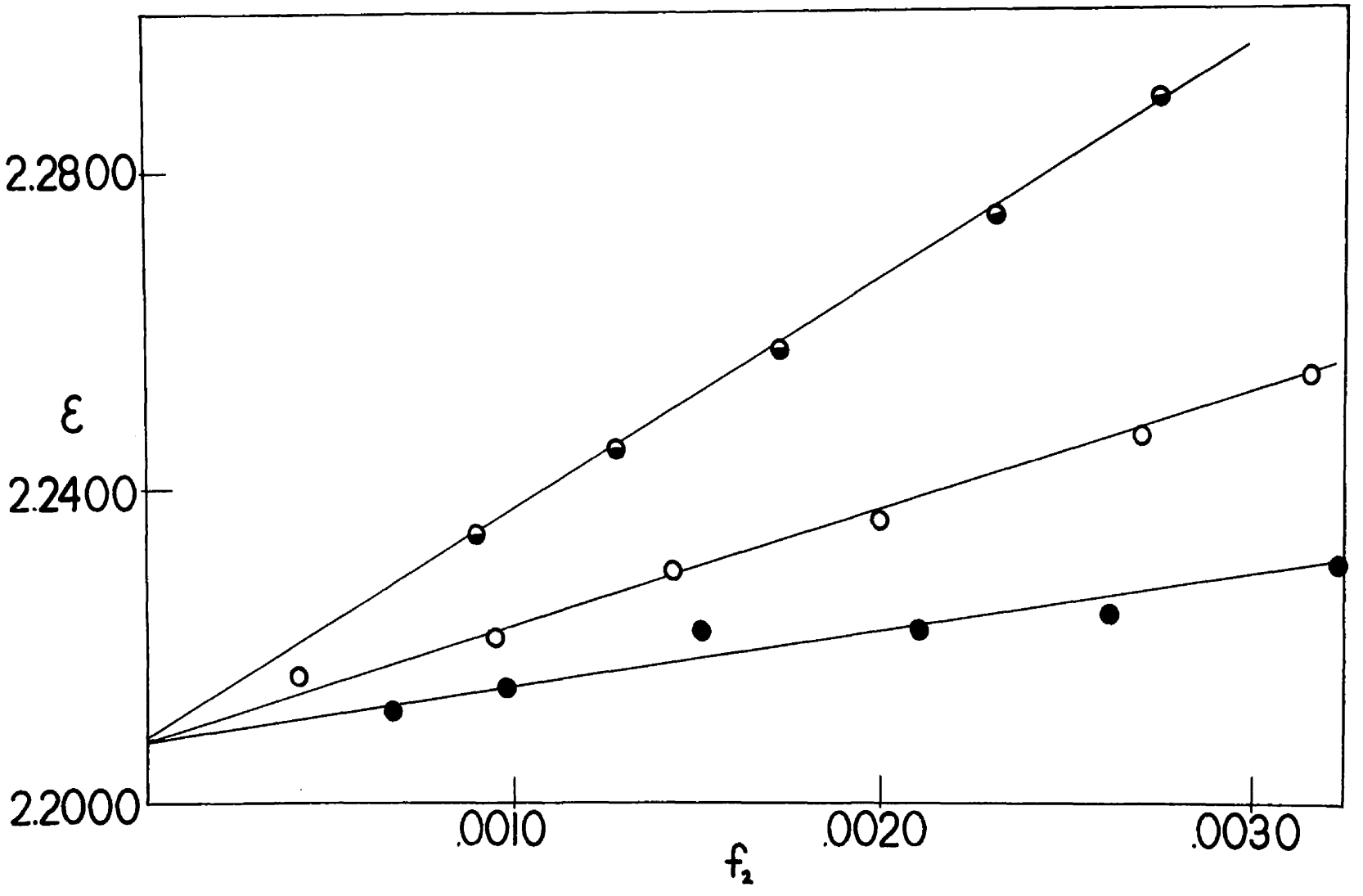


Figure 20. Dielectric constant as a function of concentration for dioxane solutions of ○ 11α-hydroxyallopregnane-3,20-dione, ● allopregnane-3,20-dione, and ◒ 4-chloro-17α-hydroxypregnane-3,11-20-trione.

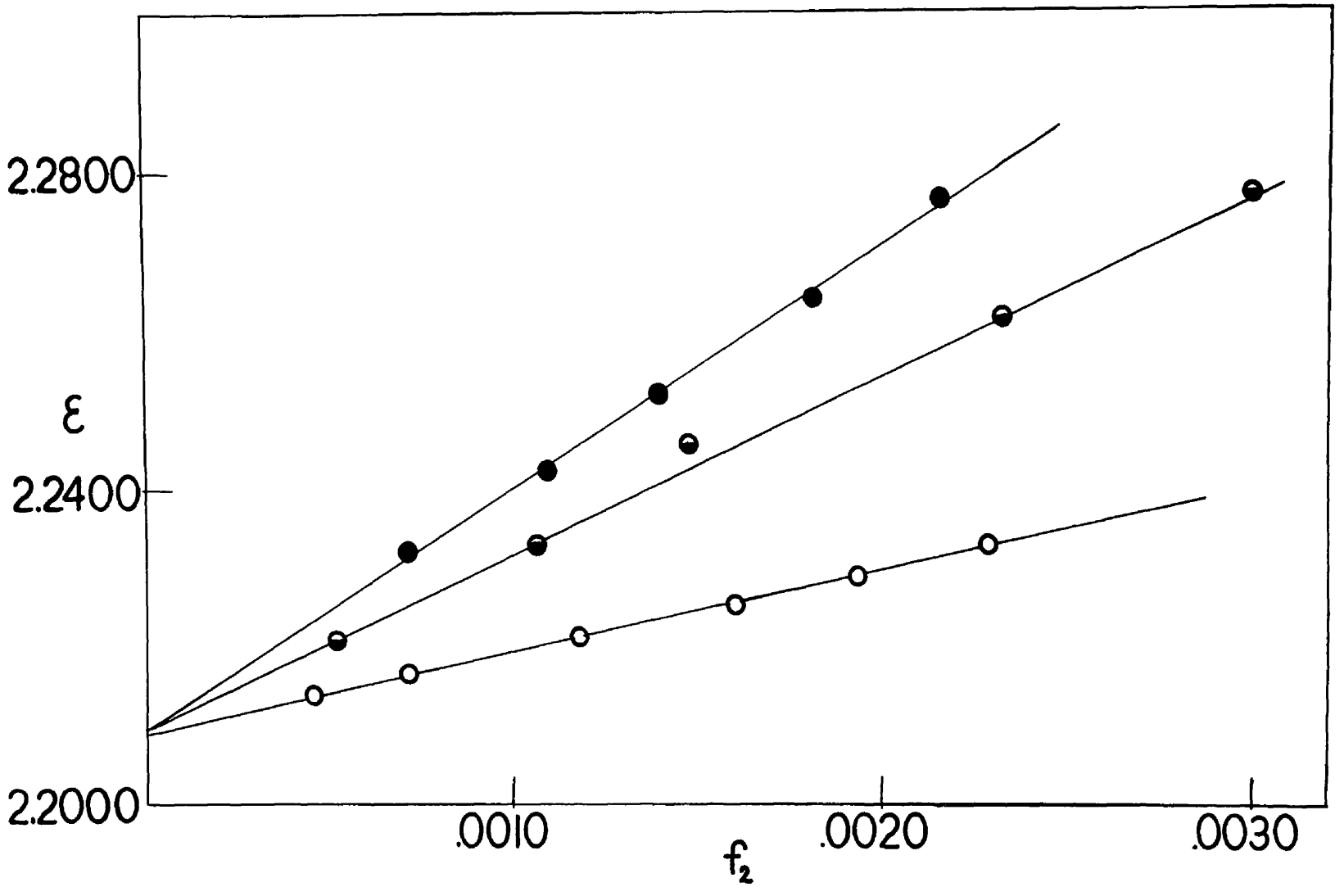


Figure 27. Dielectric constant as a function of concentration for dioxane solutions of ○ 21-acetoxypregnenolone acetate, ● 4-bromo-17α-hydroxy-21-acetoxypregnane-3,11,20-trione, and ◒ 11α-hydroxyprogesterone.

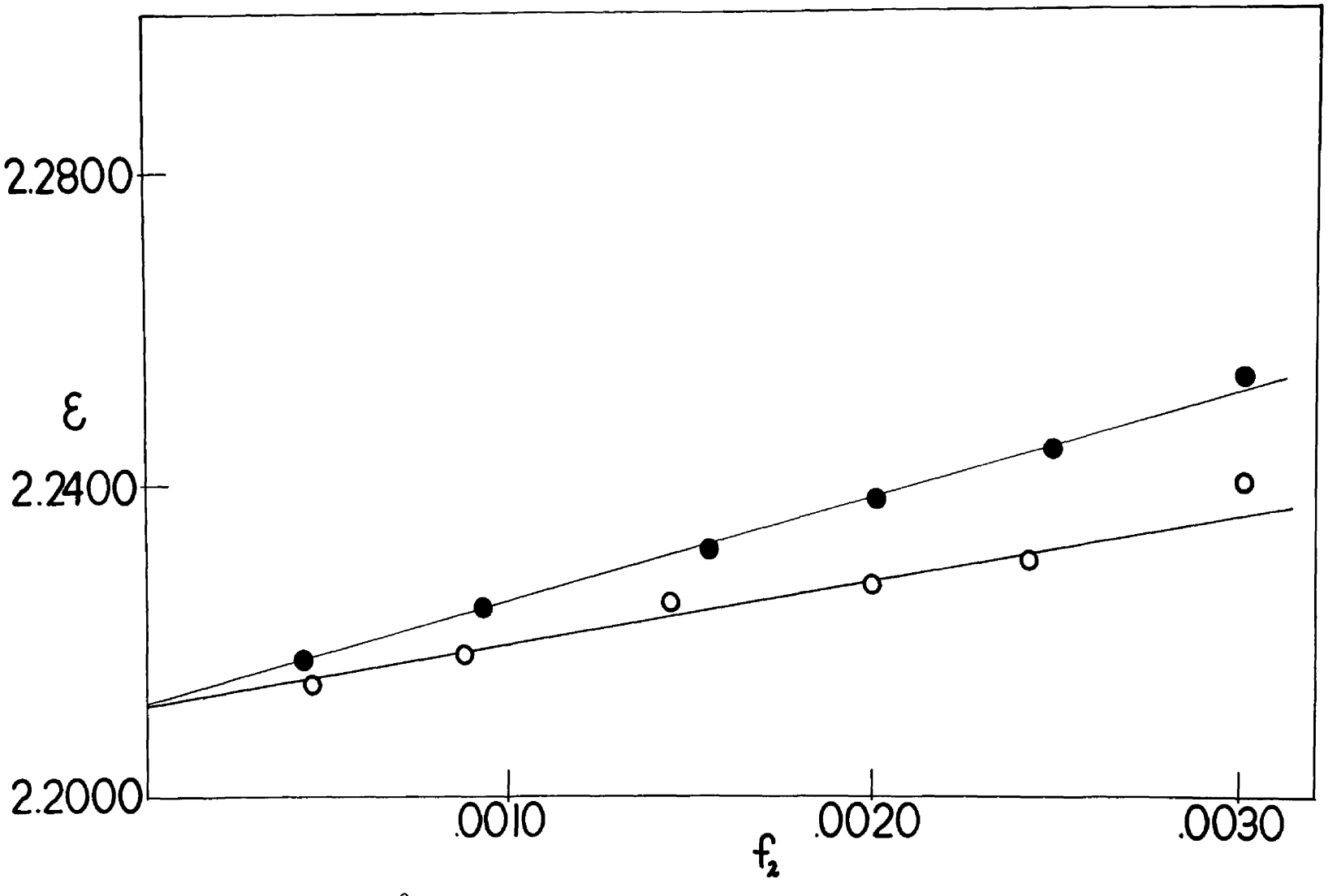


Figure 28. Dielectric constant as a function of concentration for dioxane solutions of ○ desoxycorticosterone and ● pregnenolone-3-methyl ether.

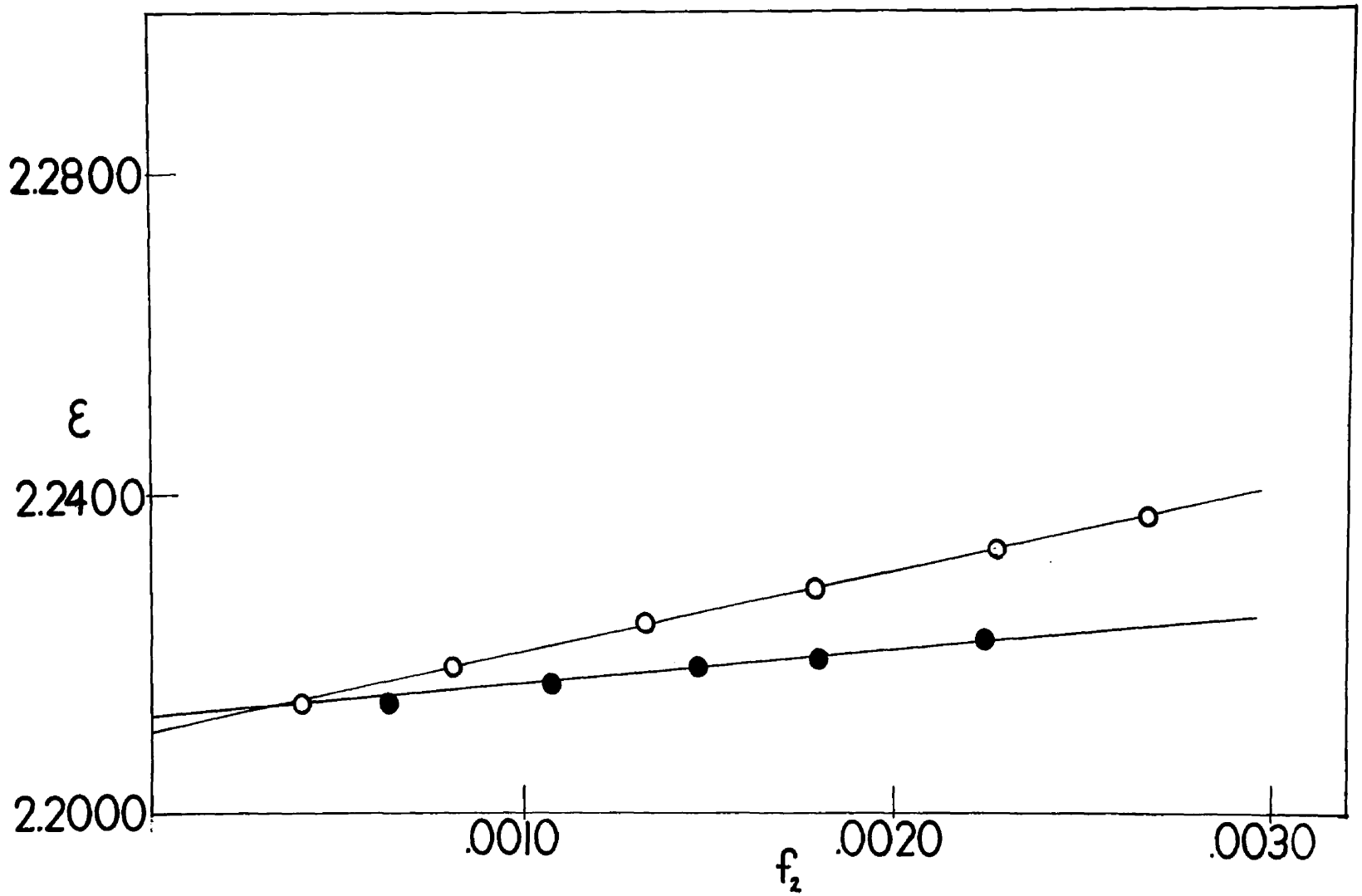


Figure 29. Dielectric constant as a function of concentration for dioxane solutions of ○ 21-acetoxyallopregnanedione and ● stigmasteryl acetate.

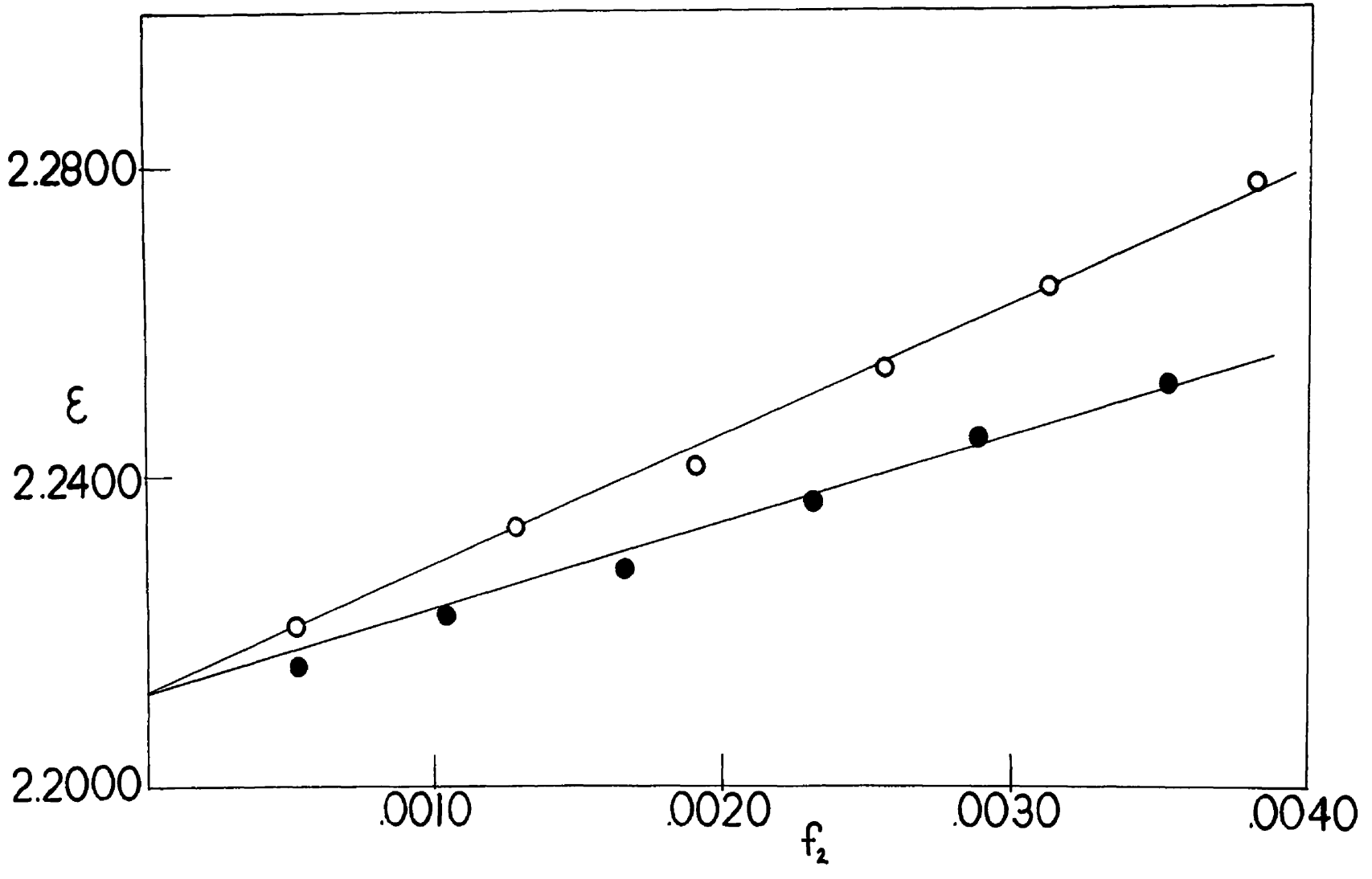


Figure 30. Dielectric constant as a function of concentration for dioxane solutions of O estrone and ● dehydroisoandrosterone.

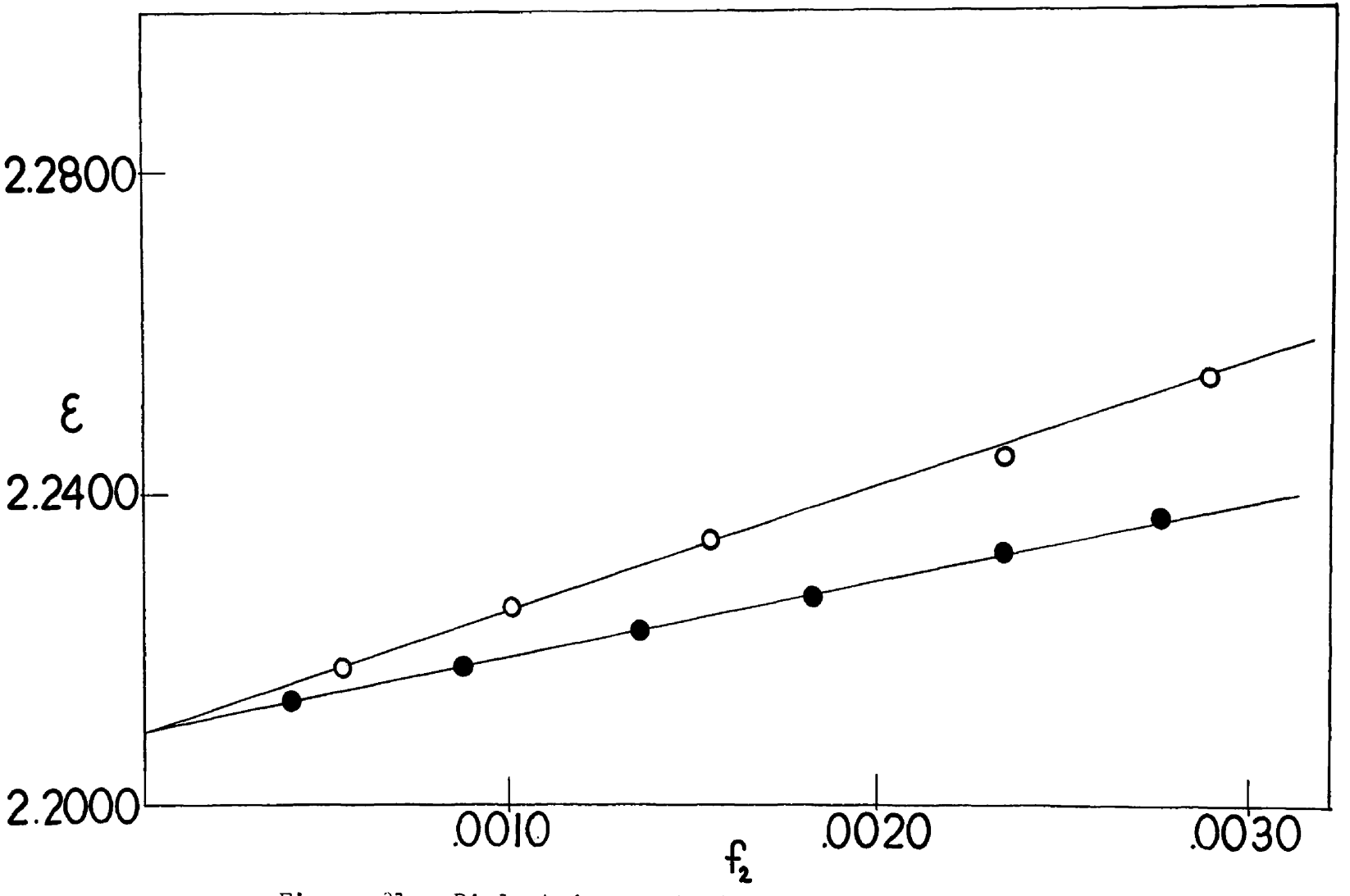


Figure 31. Dielectric constant as a function of concentration for dioxane solutions of ○ dehydroisoandrosterone acetate and ● pregnenolone acetate.

TABLE II

DIELECTRIC CONSTANTS, SPECIFIC VOLUMES, MOLECULAR REFRACTIONS, AND DIPOLE MOMENTS IN DIOXANE AT 25°C

ε_1	α'	v_1	β'	P°_2	MR°_{D2}	μ
			Progesterone			
2.2087	11.34	0.97274	-0.2031	247.31	89.93	2.77
			11 α -Hydroxyprogesterone			
2.2097	22.60	0.97293	-0.4900	409.00	91.46	3.94
			11 β -Hydroxyprogesterone			
2.2097	22.37	0.97295	-0.4490	409.00	91.46	3.92
			11-Ketoprogesterone			
2.2084	26.20	0.97266	-0.4038	462.09	91.04	4.26
			17 α -Hydroxyprogesterone			
2.2077	18.58	0.97253	-0.3794	352.40	91.46	3.57
			11 α ,17 α -Dihydroxyprogesterone			
2.2085	27.95	0.97252	-0.6095	486.55	92.98	4.38
			11 α -Acetoxyprogesterone			
2.2078	13.38	0.97261	-0.4355	287.23	100.71	3.02
			Pregnane-3,20-dione			
2.2082	6.75	0.97296	-0.3082	179.25	90.40	2.08
			Pregnane-3,11,20-trione			
2.2082	16.84	0.97284	-0.4594	325.19	90.41	3.39

TABLE II continued

ε_1	α'	v_1	β'	P°_2	MR°_{D2}	μ
11 α -Hydroxypregnane-3,20-dione						
2.2075	15.00	0.97267	-0.3405	302.03	91.94	3.20
3 α ,17 α -Dihydroxy-21-bromopregnane-11,20-dione						
2.2077	29.26	0.97249	-1.119	515.79	101.23	4.50
3 β ,17 α -Dihydroxy-21-bromopregnane-11,20-dione						
2.2094	31.94	0.97246	-1.147	582.42	101.23	4.85
4-Chloro-17 α -hydroxypregnane-3,11,20-trione						
2.2087	24.70	0.97268	-0.8480	443.44	96.80	4.12
4-Chloro-21-bromo-17 α -hydroxypregnane-3,11,20-trione						
2.2074	23.90	0.97256	-1.380	440.51	104.57	4.05
4-Bromo-17 α -hydroxyl-21-acetoxypregnane-3,11,20-trione						
2.2096	30.42	0.97260	-1.446	539.77	111.16	4.58
4-Chloro-17 α -hydroxy-21-acetoxypregnane-3,11,20-trione						
2.2078	30.77	0.97256	-1.004	543.84	108.26	4.61
Allopregnane-3,20-dione						
2.2083	6.61	0.97262	-0.1891	179.54	90.40	2.09
Allopregnane-3,11,20-trione						
2.2068	21.45	0.97278	-0.3806	394.25	90.41	3.85
11 α -Hydroxyallopregnane-3,11,20-trione						
2.2080	14.46	2.97268	-0.0854	300.62	91.94	3.18

TABLE II continued

ε_1	α'	v_1	β'	P°_2	MR°_{D2}	μ
			21-Acetoxyallopregnanedione			
2.2100	10.22	0.97288	-0.2710	264.12	103.50	2.64
			Pregnenolone			
2.2087	15.08	0.97297	-0.1320	304.03	91.45	3.22
			Pregnenolone-3-methyl ether			
2.2120	13.40	0.97302	-0.0883	280.18	96.18	3.00
			Pregnenolone acetate			
2.2095	10.00	0.97305	-0.2301	239.50	100.61	2.60
			21-Acetoxypregnenolone			
2.2065	16.87	0.97293	-0.4106	339.30	102.37	3.40
			21-Acetoxypregnenolone acetate			
2.2088	10.57	0.97299	-0.4047	266.96	113.26	2.74
			16-Dehydropregnenolone			
2.2075	17.58	0.97311	-0.3185	331.15	91.01	3.43
			16-Dehydropregnenolone acetate			
2.2100	12.53	0.97291	-0.2338	275.55	100.35	2.93
			Desoxycorticosterone			
2.2100	10.15	0.97302	-0.4133	229.22	89.73	2.61
			Estrone			
2.2120	17.07	0.97320	-0.4188	348.24	76.66	3.64
			α-Estradiol			
2.2080	10.80	0.97307	-0.3628	223.60	78.17	2.66

TABLE II continued

ε_1	α'	v_1	β'	P°_2	MR°_{D2}	μ
			Adrenosterone			
2.2100	37.14	0.97320	-0.5688	608.62	80.71	5.09
			Dehydroisoandrosterone			
2.2100	11.74	0.97288	-0.0635	249.36	82.21	2.86
			Dehydroisoandrosterone acetate			
2.2095	14.56	0.97322	-0.2848	309.62	91.58	3.26
			Stigmasteryl acetate			
2.2127	4.798	0.97286	-0.5550	210.98	133.81	1.94

TABLE III

LIST OF STEROLS

		Melting Point (°C)	
		Observed	Literature
1.	Progesterone	128	128
2.	11 α -Hydroxyprogesterone	166-7	166-7
3.	11 β -Hydroxyprogesterone	182-4	
4.	11-Ketoprogesterone	175-7	172-5
5.	11 α -Acetoxyprogesterone	175-6	175-7
6.	17 α -Hydroxyprogesterone		213-15
7.	11 α ,17 α -Dihydroxyprogesterone		220-3
8.	Pregnane-3,20-dione		123
9.	Allopregnane-3,20-dione		200.5
10.	Pregnane-3,11,20-trione	159-160	158-60
11.	Allopregnane-3,11,20-trione	213-214	211-5
12.	11 α -Hydroxypregnane-3,20-dione		106-10
13.	11 α -Hydroxyallopregnane-3,20-dione		197-200
14.	3 α ,17 α -Dihydroxy-21-bromo-pregnane-11,20-dione		
15.	3 β ,17 α -Dihydroxy-21-bromo-allopregnane-11,20-dione		238-40
16.	4-Chloro-17 α -hydroxy-21-acetoxy-pregnane-3,11,20-trione		
17.	4-Bromo-17 α -hydroxy-21-acetoxy-pregnane-3,11,20-trione		

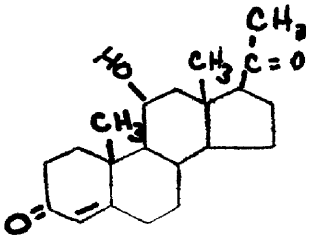
TABLE III continued

		Melting Point (°C) Observed	Literature
18.	4-Chloro-17 α -hydroxypregnane-3,11,20-trione		
19.	4-Chloro-21-bromo-17 α -hydroxy-pregnane-3,11,20-trione		
20.	Adrenosterone		217-20
21.	21-Acetoxyallopregnanedione	195-6	
22.	α -Estradiol	174	176-7
23.	Pregnenolone	189-90	190
24.	16-Dehydropregnenolone	213-14	213-14
25.	21-Acetoxypregnenolone	185-7	184-85
26.	16-Dehydropregnenolone acetate	173-4	176
27.	Pregnenolone acetate	144-5	146-7
28.	Pregnenolone-3-methyl ether	123-4	124-5
29.	Desoxycorticosterone	137-8	141-2
30.	Estrone	254-5	256
31.	Dehydroisoandrosterone	145-7	148
32.	Dehydroisoandrosterone acetate	166.5-167.5	
33.	Stigmasteryl acetate	138-9	
34.	21-Acetoxypregnenolone acetate		

The compounds numbered 1-20 were obtained from the Upjohn Pharmaceutical Company; the remaining sterols were procured from General Biochemicals Company.

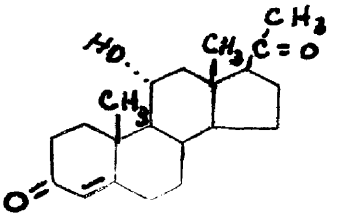
DISCUSSION

Some general conclusions can be drawn concerning the structure of sterols from an examination of the observed electric moments. An attempt to use differences in electric moment as a criterion for identifying epimers was singularly unsuccessful for several such pairs investigated here. Thus, the observed moments of 11α- and 11β-hydroxyprogesterone were essentially identical.



11β-Hydroxyprogesterone

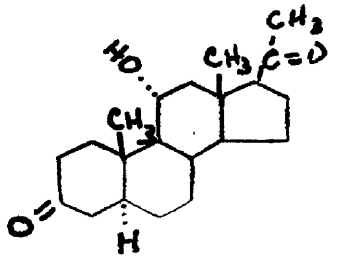
μ = 3.92 D



11α-Hydroxyprogesterone

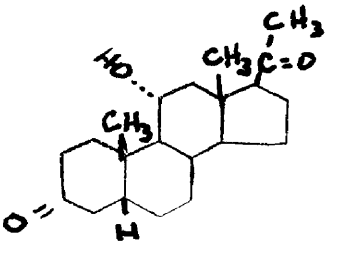
μ = 3.94 D

The normal and allo forms of 11α-hydroxypregnane exhibited a similar equality of moment.



11α-Hydroxyallopregnane-3,20-dione

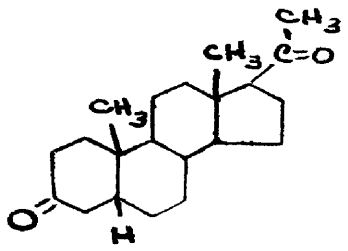
μ = 3.18 D



11α-Hydroxypregnane-3,20-dione

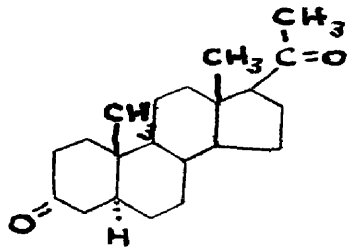
μ = 3.20 D

Still a third set, the normal and allopregnane-3,20-diones had equal moments.



Pregnane-3,20-dione

μ = 2.68 D

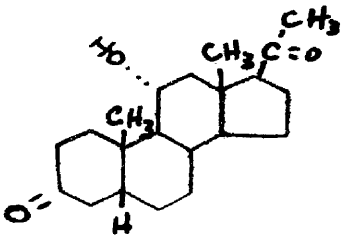


Allopregnane-3,20-dione

μ = 2.69 D

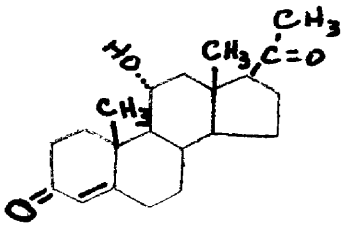
Although the agreement might be judged fortuitous if one set were considered alone, the subsequent pairs rule out such a conclusion. From the data for the pregnanediones, one would surmise that the angles formed by the group vectors are equal, despite the significantly different spatial arrangements of the A rings in allo and normal series. From the 11 α-and 11 β-hydroxyprogesterones it would seem that the hydroxyl groups are free to rotate in either configuration although the β-epimer might be hindered by the nearby methyl groups. This will be discussed in detail later.

A trend in the electric moment with variations in structural features is evident in the above compounds also. Dehydrogenation of either allo or normal 11 α-hydroxypregnane-3,20-dione to give a Δ^4 double bond (a double bond between C_4 and C_5) yields 11 α-hydroxyprogesterone with a moment 0.75 D greater than the saturated molecules.



11 α-Hydroxypregnane-3,20-dione

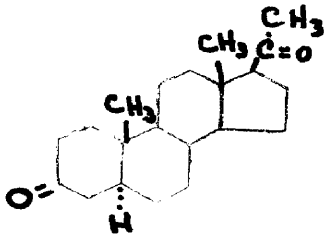
μ = 3.20 D



11 α-Hydroxyprogesterone

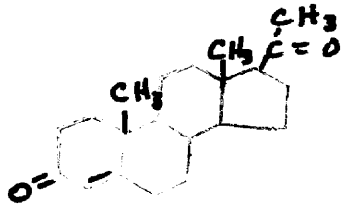
μ = 3.94 D

A comparison of the pregnane-3,20-diones with progesterone indicates an increase of 0.68 D, from 2.09 D to 2.77 D, resulting from the formation of the Δ^4 double bond.



Allopregnane-3,20-dione

μ = 2.09 D



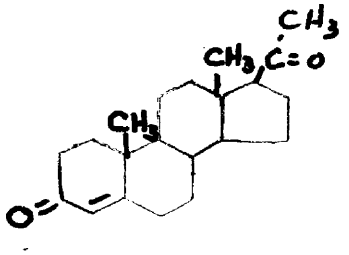
Progesterone

μ = 2.77 D

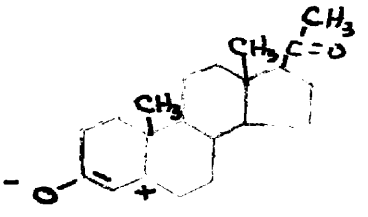
Thus, a sterol with a double bond in the 4,5 position appears to have an electric moment 0.7-0.8 D greater than the corresponding saturated molecule.

Although a slight change in the angular relationships of the polar groups occurs upon introduction of the double bond, the increase in the total moment is probably due principally to resonance in the A ring. Using Progesterone (I) as an example, the result is a structure in which a charge

separation occurs (II), contributes to the ground state of the molecule.

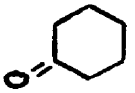


I



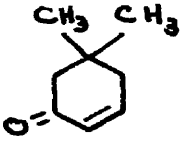
II

Previous evidence for such a resonance effect is to be found in the electric moments of cyclohexanone[24] and isophorone[21]



Cyclohexanone

μ = 2.90 D

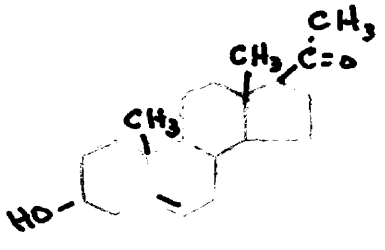


Isophorone

μ = 3.97 D

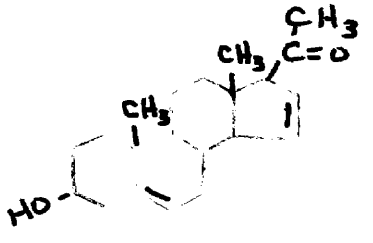
where a similar, though slightly larger, increase was noted for the unsaturated molecule.

Two pairs of sterols differ only in the presence of a double bond in the D ring.



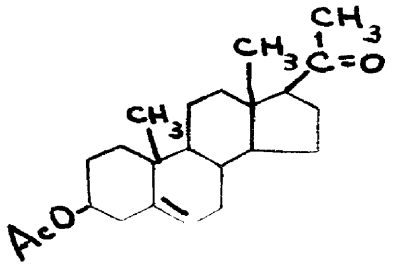
Pregnenolone

μ = 3.22 D



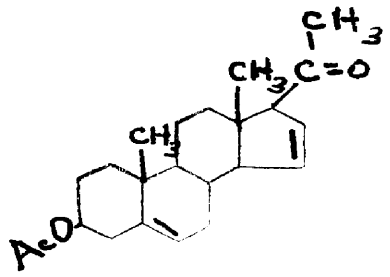
16-Dehydropregnenolone

μ = 3.43 D



Pregnenolone acetate

μ = 2.60 D

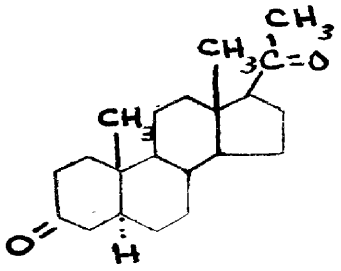


16-Dehydropregnenolone acetate

μ = 2.93 D

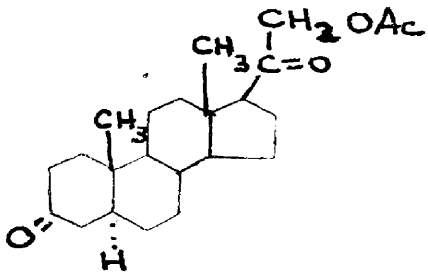
The moments increase by 0.21 D and 0.33 D respectively, upon insertion of the Δ^{16} double bond. This is doubtless a result of a change in the angular relationship between the polar groups since the distortion of the five-membered ring when the double bond is present changes the position of the keto group with respect to the 3-acetoxy group.

The effect of introducing an acetoxy group in the side chain of either allo or normal pregnanes at C_{21} may be estimated from the moments observed for the four compounds,



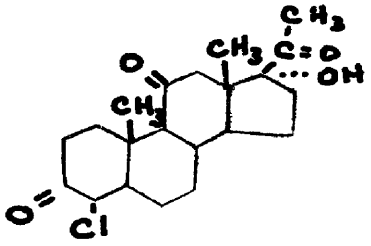
Allopregnane-3,20-dione

μ = 2.09 D



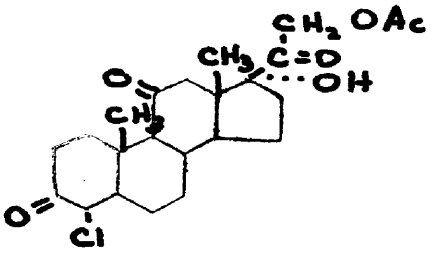
21-Acetoxyallopregnane-3,20-dione

μ = 2.64 D



4-Chloro-17 α -hydroxypregnane-3,11-20-trione

μ = 4.32 D

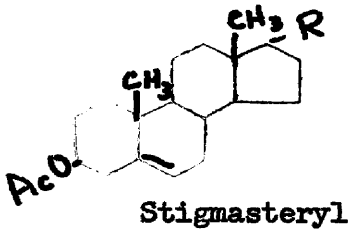


4-Chloro-17 α -hydroxy-21-acetoxy-pregnane-3,11g20-triene

μ = 4.61 D

wherein increases of 0.55 and 0.49 D respectively, are noted upon substitution of acetoxy for hydrogen. The agreement is quite good if one considers the much greater degree of substitution in the latter pair.

The electric moment of Stigmasteryl acetate, 1.94 D,



Stigmasteryl acetate

(where R is $CH\text{-}CH_3\text{-}C\text{=}CH_2\text{-}CH(CH_3)_2$ with C_2H_5) was of interest since some of the sterols studied here were acetoxy derivatives. This value agrees well with other observed values of compounds in which there is an acetoxy group as the only polar group.[24]

The preceding comparisons are qualitative in nature, being conclusions based solely on observed electric moments. Calculation of the total moment expected for the groups and angles involved should point up unusual structural features in the sterols. This was carried out using the group moments

TABLE IV

GROUP MOMENTS
FROM THE LITERATURE

Group	μ	Reference
Keto (cyclohexanone)	2.90	21
Keto (cyclopentanone)	3.00	25
Δ^4-3-Keto	3.97	21
17 α-Hydroxy	2.00	21
Δ^5-3-Hydroxy	2.00	21
Aromatic hydroxy	1.70	24
Other saturated alcohols	1.80	21
Acetoxy	1.80	26

recorded in Table IV, along with angles measured on molecular models of the Brode-Hurd-Boord type. These latter measurements were made with reference to a coordinate system fixed in the model. The components of the various group moments in Table IV on the coordinate axes were estimated with the help of these angles. Addition of the respective x, y and z components for all fixed polar groups in a molecule produces a total moment used as a basis for comparison with the observed figure. This procedure does not apply where groups capable of rotation are present so these compounds, usually containing hydroxyl groups, will be considered separately.

The components m_x, m_y and m_z of the group moments, for the groups encountered here, are listed in Table V. The angles measured for the 3-keto group were used with the moment of cyclohexanone (2.9 D) to get the components for the 3-keto group. Using the moment of isophorone (3.97 D) these same angles gave the components of the Δ^4-3-keto grouping. For the hindered 17 β-acetyl group there are two good positions, characterized by maximum distances of this group from the interfering C_{13} methyl and D ring hydrogens. However, only one of these positions predicts reasonable values for all of the compounds in which the 17 β-acetyl group occurs. Similarly, several positions were possible in some instances where hydroxyl groups were restricted. The position giving the best agreement of calculated and observed moments was used in such situations. Application to individual sterols will serve to illustrate these points.

The steroids used here fall into two general classes from the standpoint of calculation of the moments; those in which all the dipoles are fixed and those in which free rotation should be possible. In both categories

TABLE V

GROUP MOMENTS FOR CARBONYL AND HYDROXYL GROUPS
IN VARIOUS POSITIONS IN STEROID MOLECULES

Group	m_x	m_y	m_z
3-Keto	-2.47	0.00	-1.54
11-Keto	-1.37	+1.87	+2.23
17-Keto	+2.14	+2.17	-0.47
3-Keto boat (Allo)	-2.47	0.00	+1.54
3-Keto boat (Normal)	+2.47	0.00	-1.54
$\triangle^{4}$-3-Keto	-3.38	0.00	-2.12
17 β -Acetyl	+1.18	-1.09	+2.47
11 α -Hydroxy	0.00	0.00	+2.00
11 β -Hydroxy	0.00	-2.00	0.00
17 β -Hydroxy	-0.90	-1.48	-0.28
3 β -Hydroxy	0.00	-2.00	0.00
17 α -Hydroxy	-1.29	-0.85	-1.15
3 α -Acetoxy	-1.34	+1.34	0.00
3 β -Acetoxy	+1.34	+1.34	0.00
11 α -Acetoxy	0.00	+0.33	+1.80

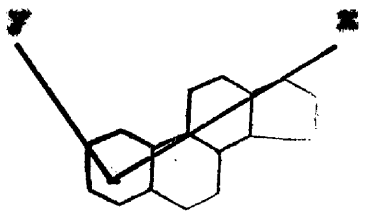
TABLE V - continued

The m_x, m_y and m_z values listed above were computed using the appropriate group moments (m) from Table IV and the angles formed by these vectors with the axes of a set of coordinates fixed in the molecular model. Thus, the x component is

$$m_x = m \cos \theta_x$$

θ_x being the angle between the x-axis and the direction of the group vector.

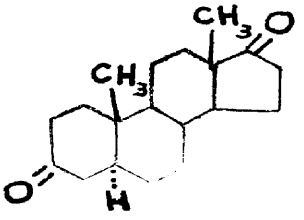
The coordinates were arranged as shown below



with the positive z axis being above and perpendicular to the plane of the paper. By this means $m_y = 0$ for any substituent at C_3 and simplifies measurement and calculation procedures whenever this group is involved. The keto moments listed are for the chair form unless otherwise stated.

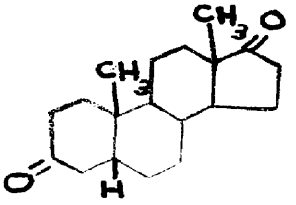
electric moments were calculated for sterols, for which dipole moments have been reported in the literature[21] but no interpretation of the values offered. These were considered in addition to the compounds listed in Table III and provided a test of the method of calculation, as well as being useful for interpretative purposes. The observed and calculated moments, along with conclusions, are compiled in Tables VI and VII.

Thus, the moments have been recorded for a pair of 3,17-diones recently.[17]



Androstane-3,17-dione

μ = 3.10 D



Etiocholane-3,17-dione

μ = 3.50 D

Addition of the components determined above resulted in values of 2.95 D for both of these. Since the boat conformation should be possible for both molecules, calculations were made to ascertain the percent boat form which might explain the observed differences. This was calculated from the equation

$$\mu^2 = X\mu_c^2 + (1-X)\mu_b^2$$

where μ is the observed moment, μ_c and μ_b the values calculated for chair and boat forms respectively, and X the fraction of molecules in the chair configuration. The results indicate that the allo compound exists with the A ring essentially all in the chair form while the A ring has sixteen percent boat form in the normal compound.

TABLE VI

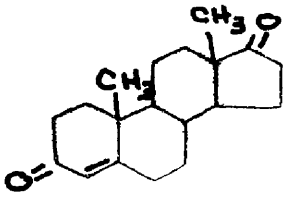
OBSERVED AND CALCULATED MOMENTS OF THE STEROLS WITH ONLY FIXED GROUPS

Compound	$\mu_{obs.}$	$\mu_{calc.}$	Remarks
Androstane-3,17-dione	3.10	2.95	No boat form
Etiocholane-3,17-dione	3.50	2.95	16% boat form
Δ^{4}-Androstene-3,17-dione	3.82	3.59	No boat form
Pregnane-3,20-dione	2.08	1.93	5% boat form
Allopregnane-3,20-dione	2.09	1.93	8% boat form
Pregnane-3,11,20-trione	3.39	4.20	No boat form
Allopregnane-3,11,20-trione	3.65	4.20	No boat form
11-Ketoprogesterone	4.26	4.20	No boat form
Progesterone	2.77	2.46	8% boat form
Adrenosterone	5.09	4.84	16% boat form

The calculated values were obtained assuming the molecule to be in the all chair form. The amounts of boat form listed in the last column were required to explain the discrepancy between calculated and observed moments.

This figure is in fairly good agreement with the value of fourteen percent computed by Nace and Turner,[17] for these sterols.

For Δ^4-androstene-3,17-dione

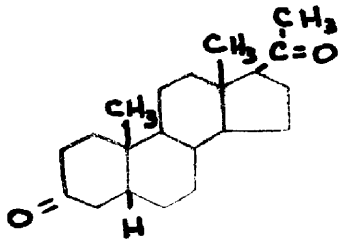


Δ^4-Androstene-3,17-dione

μ = 3.32 D (calc'd = 3.59 D)

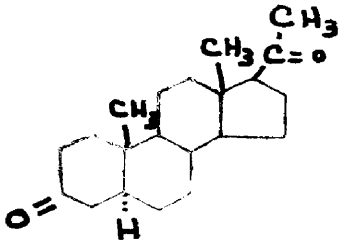
the value observed by Kumler (3.32 D)[21] is lower than calculated (3.59 D) so no contribution from the highly polar boat form (6.23 D) was expected or found.

For the pregnanediones



Pregnane-3,20-dione

μ = 2.08 D

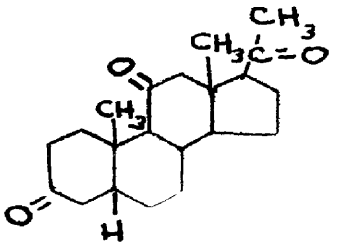


Allopregnane-3,20-dione

μ = 2.09 D

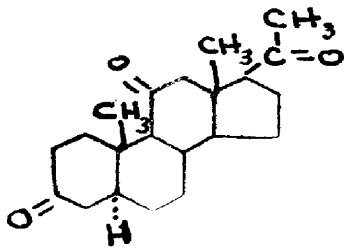
the value calculated for the chair structure is 1.93 D in both cases. The discrepancies can be attributed to five and two percent boat isomer in the normal and allo substances, respectively.

Normal and allopregnane-3,11,20-trione both have a calculated value of 4.20 D, which is higher than observed for either.



Pregnane-3,11,20-trione

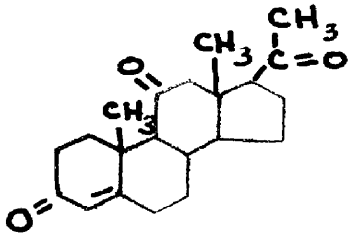
μ = 3.39 D



Allopregnane-3,11,20-trione

μ = 3.85 D

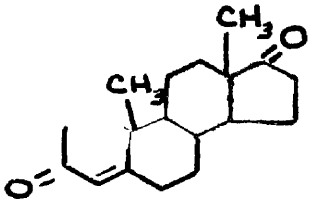
The boat forms have calculated moments of 3.96 D (normal) and 6.82 D (allo) both higher than observed so these should not be a factor in explaining the lower moments observed. Also, there is no apparent reason for the values observed to differ as they do. Other sets differing only in the orientation of the A ring were found to have identical electric moments. The calculated value of 4.20 D is probably not too much in error since the observed moment for 11-ketoprogesterone



is 4.26 D, in good agreement with the former value. The reason for the low observed values is not apparent so no ready explanation can be given here.

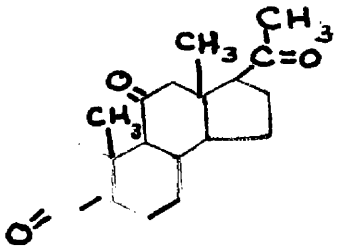
Although molecules with Δ^4 double bond do not have allo and normal forms, the unsaturation limits the A ring to a configuration resembling that of an allo steroid, chair and boat forms being possible therein. For these substances the moment of isophorone and the angles determined for the boat 3-keto grouping were used to compute the components necessary for estimation of percent boat form present in the equilibrium mixture.

Then for Δ^4-androstene-3,17-dione[21] and 11-ketoprogesterone



Δ^4-Androstene-3,17-dione

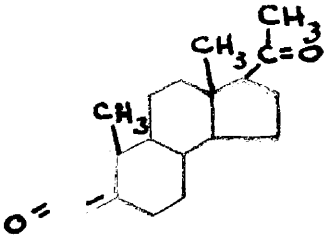
μ = 3.82 D



11-Ketoprogesterone

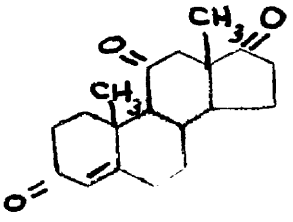
μ = 4.26 D

calculations, using the calculated values listed in Table VI, predict no boat form present. However, for progesterone and adrenosterone



Progesterone

μ = 2.77 D



Adrenosterone

μ = 5.09 D

eight and sixteen percent boat form, respectively, are indicated in the A ring equilibrium mixture.

From the preceding discussion it is clear that the electric moments of sterols with only fixed and hindered substituents can be interpreted in terms of structural features of the molecules. In sterols containing fixed or greatly hindered substituents or a Δ^4 double bond, or both, the use of a fixed position for the hindered group and the inclusion of the resonance effect in the A ring (by using the moment of isophorone) gave values close to the observed figures in most instances. Remaining differences after this operation could be attributed mainly to contributions from the boat form of the A ring. Thus, the effects considered in the calculation of the electric moments are correct in principle and of the right order of magnitude.

For sterols containing the rotatable hydroxyl group, the effective angle between the C-O axis and the group moment is close to ninety degrees, so this value was used in this work. This simplification reduces the calculation of the electric moment to addition of the squares of the individual group moments present, i.e., the cosine term disappears in the equation

$$\mu^2 = m_1^2 + m_2^2 + g m_1 m_2 \cos\sigma \cos\phi_1 \cos\phi_2.$$

In this equation the terms have the same meaning as that given in Part I of this thesis. This method was applied to the moments of sterols reported by other investigators also and the moments and conclusions are summarized in Table VII.

For testosterone and cis-testosterone

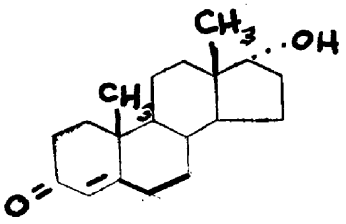
TABLE VII

OBSERVED AND CALCULATED MOMENTS OF THE STEROLS WITH GROUPS CAPABLE OF FREE ROTATION

Compound	$\mu_{obs.}$	$\mu_{calc.}$	Remarks
3 β ,17 α -Androstanediol	2.99	2.69	Free rotation
Δ^5-Androstenediol-3 β ,17 α	2.89	2.69	Free rotation
Δ^5-Androstenediol-3 β ,17 β	2.70	2.69	Free rotation
Cholestanediol-3 β ,7 α	2.31	2.55	Free rotation
Cholestanediol-3 β ,7 β	2.55	2.55	Free rotation
α -Estradiol	2.66	2.62	Free rotation
17-Methyl Δ^5-androstanediol-3 β ,17 α	2.78	2.69	Free rotation
Estrone	3.61	3.46	Resonance in A Ring
11 α -Hydroxypregnane-3,20-dione	3.19	2.64	Restriction of rotation by equatorial hydrogens
11 α -Hydroxyallopregnane-3,20-dione	3.20	2.64	Restricted rotation for the 11 α -hydroxyl
11 β -Hydroxyprogesterone	3.92	3.06	Essentially fixed position for 11 β -group
11 α -Hydroxyprogesterone	3.94	3.06	Less restricted than the 11 β -epimer
17 α -Hydroxyprogesterone	3.57	3.18	Hydroxyl repulsed by C_{20} methyl group
Pregnenolone	3.22	3.52	Slightly hindered
Pregnenolone-3-methyl ether	3.00	3.14	Slightly hindered

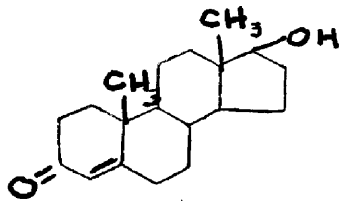
TABLE VII - continued

Compound	$\mu_{obs.}$	$\mu_{calc.}$	Remarks
16-Dehydropregnenolone	3.43	3.52	Slightly hindered
11 α-Acetoxyprogesterone	3.02	3.14	Probably a combination of steric effects and resonance.
Pregnenolone Acetate	2.60	3.14	Probably a combination
16-Dehydropregnenolone acetate	2.93	3.62	of steric effects and
Dehydroisoandrosterone acetate	3.26	3.72	resonance.
Testosterone	4.32	4.45	Free rotation
cis-Testosterone	5.17	4.36	17 β-hydroxyl restricted
17 α-Methyltestosterone	4.17	4.45	17 α-hydroxyl hindered slightly
Androsterone	3.70	3.50	Free rotation
β-Androsterone	2.95	3.50	3 β-hydroxyl restricted
Dehydroisoandrosterone	2.86	3.60	Partial free rotation
Δ^5-Cholestanol-3 β-one-7	3.79	4.44	Some oscillation probable
3 α ,17 α-Androstanediol	2.29	2.69	Essentially free rotation



Testosterone

μ = 4.32 D (Calc'd. = 4.45 D)

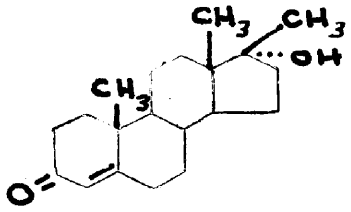


Cis-Testosterone

μ = 5.17 D (Calc'd. = 4.36 D)

the agreement noted in the former compound indicating virtually free rotation for the 11 α -hydroxy group. Such is not the case for the 11 β -isomer, where the OH group is much nearer the methyl group at the C/D ring juncture. Using one of two best possible fixed positions for this group, a value of 5.17 D was calculated. Such exact agreement is fortuitous but serves to indicate that the hydroxyl group is confined to a narrow space by steric repulsion.

For 17α -methyltestosterone



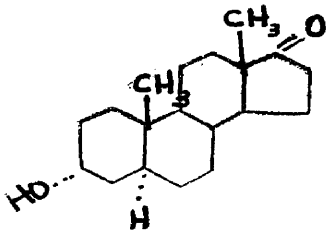
17 α -Methyltestosterone

μ = 4.17 D (Calc'd. = 4.45 D)

the observed value would suggest a hindrance of the alcohol group, undetectable on examination of the models. However, the mutual repulsion of the two bulky methyl groups could conceivably distort the D ring enough

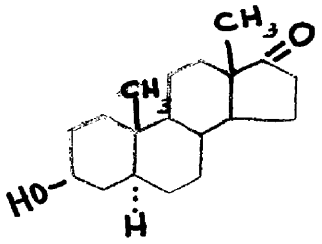
to cause interference of the hydrogen atoms with the alcohol group. The models used lack the flexibility required for observation of such an effect if it is important.

Androsterone and its β -isomer have equal calculated moments but different experimental values were found



Androsterone

μ = 3.70 D (Calc'd. = 3.50 D)

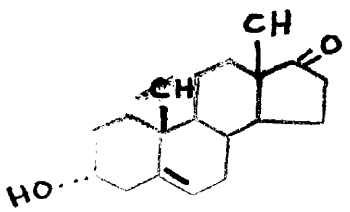


β -Androsterone

μ = 2.95 D (Calc'd. = 3.50 D)

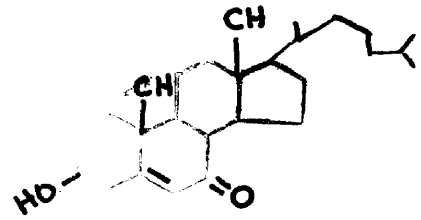
For the former molecule, the 3 α -hydroxy group is essentially free to rotate but the larger discrepancy in the β -androsterone values implies restriction of the β -hydroxy group. A calculation based on this assumption gave a moment of 2.28 D, which is lower than the observed figure and indicates that restriction of rotation exists to some degree.

Further evidence for restricted rotation in sterols was deduced from the data for dehydroisoandrosterone and Δ^5-cholestanol-3 β-one-7



Dehydroisoandrosterone

μ = 2.86 D (Calc'd. = 3.60 D)

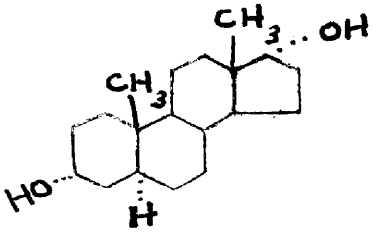


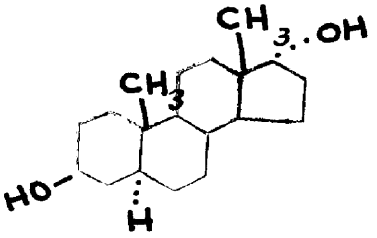
Δ^5-Cholestanol-3 β -one-7

μ = 3.79 D (Calc'd. = 4.44 D)

Using likely fixed positions for the alcohol groups at C_3, values of 2.24 D and 3.36 D respectively, were found. Since the figures obtained assuming free rotation and assuming a fixed position bracket the observed moments, the hydroxyl group is probably restricted to oscillation over a limited range.

Several pairs of diols were considered here also, the androstanediols below having moments less or greater than calculated, when the 3-hydroxy group is α - or β - oriented, respectively.





3 α,17 α-Androstanediol

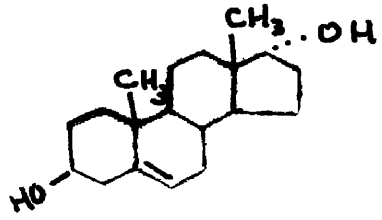
μ = 2.29 (Calc'd. = 2.69 D)

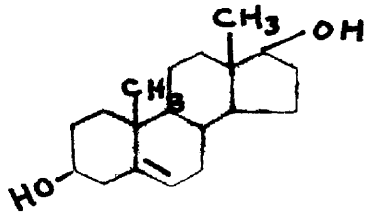
3 β,17 α-Androstanediol

μ = 2.99 D (Calc'd. = 2.69 D)

For the 3 α epimer, the best fixed position of the hydroxyl group gave a calculated moment of 1.05 D - much too low to account for the observed difference of 0.4 D noted above - so the groups are probably essentially free to rotate. For the 3 β modification a calculated value, assuming fixed hydroxyl groups, is 3.40 D so there may be slight hindrance at the 3 β position.

The structurally similar Δ^5-Androstenediols had moments in good agreement with those calculated for the free rotation.

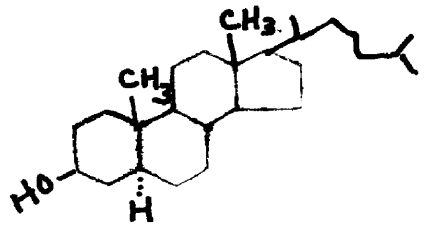


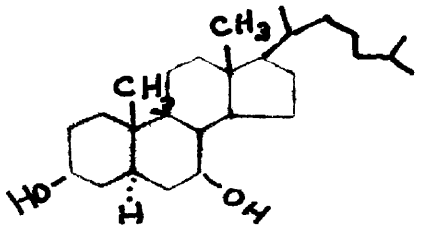


Δ^5-Androstenediol-3β,17α μ = 2.89 D (calc'd. = 2.69 D)

Δ^5-Androstenediol-3β,17β μ = 2.70 D (2.69 D)

The calculated and observed moments for the cholestanediols are also comparable in magnitude.





Cholestanediol-3β,7α μ = 2.31 D (calc'd. = 2.55 D)

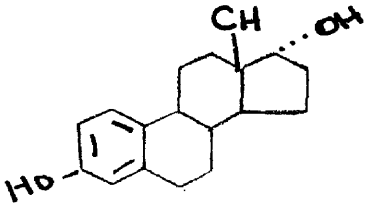
Cholestanediol-3β,7β μ = 2.55 D (calc'd. = 2.55 D)

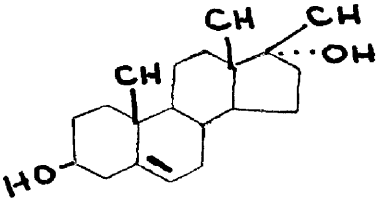
The values obtained for the Δ^5-epimers were interpreted as indicating free rotation, the unsaturation possibly altering the geometry of the molecule enough to permit freedom for the 3β-hydroxyl group. The cholestanediols probably have unhindered hydroxyl groups, though the difference noted for the 7α-isomer might be interpreted as due to hindrance at the 7α-position.

From the preceding discussion it is evident that the electric moments of alcohols are often ambiguous. This is especially true in a solvent like

dioxane which, though non-polar, can participate in hydrogen bonding with the sterols of this type. The extent to which such association might occur is difficult to assess in most instances. A comparison of the electric moments of these polyhydric sterols in dioxane and benzene might be of some value but many sterols are difficultly soluble in the latter solvent. Lacking such information, it was necessary to neglect effects due to the solvent.

Two other diols which should be included with this group are α - estradiol and 17-methyl- Δ^5-androstanediol-3 β,17α





α -Estradiol

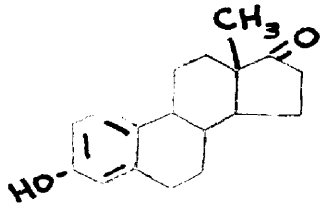
μ = 2.66 D (Calc'd. = 2.62 D)

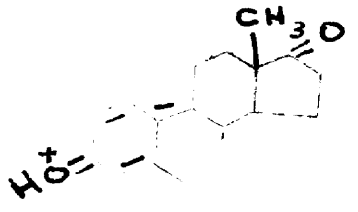
17-Methyl- Δ^5-androstanediol-3 β ,17α

μ = 2.78 D (Calc'd. = 2.69 D)

Here again it is highly probable that the hydroxyl groups are free to rotate.

For estrone the data agree well justifying the use of the moment of phenol in the calculation and suggesting resonance involving a charge separation as shown in II.





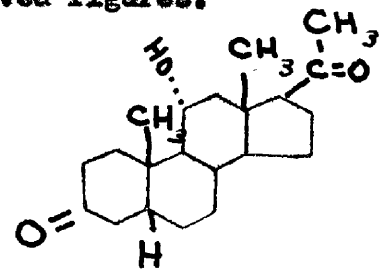
I

II

Estrone

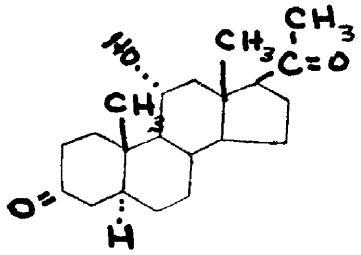
μ = 3.64 D (Calc'd. = 3.46 D)

In the hydroxypregnane and progesterone molecules, the appropriate hydroxy group moment and the moment calculated for the parent compounds (progesterone and pregnane-3,20-dione) were used to calculate moments assuming free rotation of the hydroxyl group. Application of this method to the 11 α-hydroxypregnanediones led to estimated electric moments which were identical for allo and normal isomers, although somewhat lower than the observed figures.



11 α-Hydroxypregnane-3,20-dione

μ = 3.19 D (Calc'd. = 2.64 D)

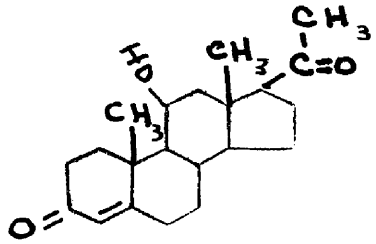


11 α-Hydroxyallopregnane-3,20-dione

μ = 3.20 D (Calc'd. = 2.64 D)

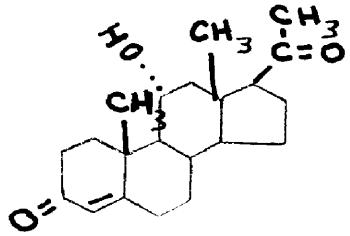
Choosing a fixed position for the hydroxyl group in which the latter is as far as possible from the interfering equatorial hydrogens and calculating the moment for this configuration, a value of 3.50 D is obtained. This indicates that there is some freedom to rotate, the extent to which this is possible being the same for both series since the environments are essentially the same for both and the observed moments are equal.

The molecules 11 α- and 11 β-hydroxyprogesterone have identical observed moments also.



11 β-Hydroxyprogesterone

μ = 3.92 D (Calc'd. = 3.06 D)

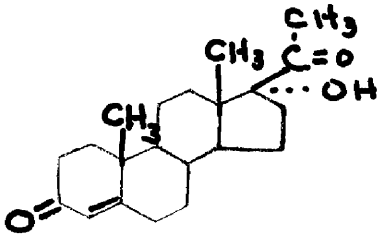


11 α-Hydroxyprogesterone

μ = 3.94 D (Calc'd. = 3.06 D)

In an effort to account for the higher figures obtained experimentally, fixed positions were assumed and the moments recalculated. For the ldirected away from the large methyl groups at C_{10} and C_{13}. The likely con-directed away from the large methyl groups at C_{10} and C_{13}. The likely conclusion is that the 11β -hydroxy group is fixed in this general orientation. The 11α -hydroxy molecule was found to have a maximum calculated moment of 3.40 D in a fixed conformation. It appears to be less restricted since it is hindered by only nearby equatorial hydrogen atoms which occupy less space than the methyl groups inhibiting rotation of the 11β -hydroxy-progesterone.

For 17α -hydroxyprogesterone, the observed value is again greater than that calculated assuming free rotation.

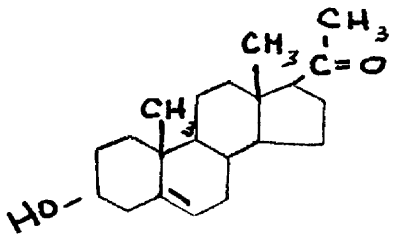


17α -Hydroxyprogesterone

μ = 3.57 D (calc'd. = 3.18 D)

The most probable fixed position led to a calculated moment of 4.07 D so some freedom of rotation is retained. The greatest interference comes from the C_{20} methyl group.

Pregnenolone had an observed electric moment of 3.22 D, about 0.3 D less than calculated

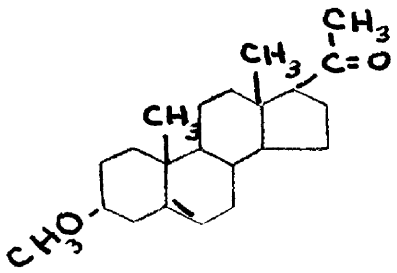


Pregnenolone

μ = 3.22 D (Calc'd. = 3.52 D)

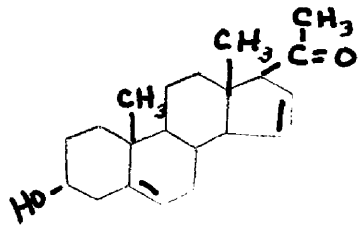
Calculations for two fixed positions gave values of 2.83 and 2.90 D so evidently there is some hindrance to free rotation of the 3β-hydroxy group.

Pregnenolone-3-methyl ether and 16-dehydropregnenolone also have slightly lower observed moments than those calculated assuming free rotation.



Pregnenolone-3-methyl ether

μ = 3.00 D (Calc'd. = 3.14 D)



16-Dehydropregnenolone

μ = 3.43 D (Calc'd. = 3.52 D)

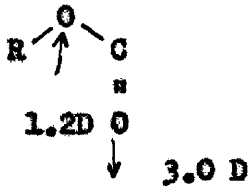
If the hydroxyl group in pregnenolone is not entirely free to rotate, the methyl group of the C_3 ether linkage must also be hindered but this could not be concluded from the small difference between observed and calculated moments of the latter. The Δ^{16}-pregnenolone might be considered as either freely rotating or slightly hindered. The slight difference between observed and calculated moment would indicate free rotation of the hydroxyl group. This difficulty was noted for many of the molecules in which two

polar groups, neither of which are fixed, are present. Evidence from other compounds not having this feature would favor slight hindrance in molecules like these pregnenolone derivatives.

An attempt was also made to relate electric moment to structure for some acetoxy compounds. For esters formed between saturated monocarboxylic acids and monohydric alcohols, the electric moments are found to lie in the range 1.7-1.9 D.[26] This has been interpreted as evidence that the ester is held in a planar configuration due to resonance between structures

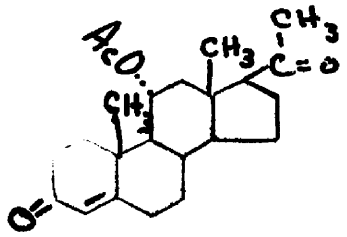
Then the double bond character conferred on the ether linkage opposes rotation about this bond and leads to the narrow range of electric moments observed for esters.

For sterols containing the acetoxy group, the resultant moment of the ester group was assumed to lie along the carbonyl group. This seemed justified since the difference between the keto and ether moments gives a total moment of 1.8 D, typical of esters.



By assuming fixed positions for the acetoxy group, moments were calculated for sterols containing this group.

The data for 11α-acetoxyprogesterone were in good agreement

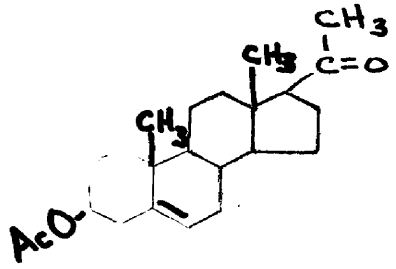


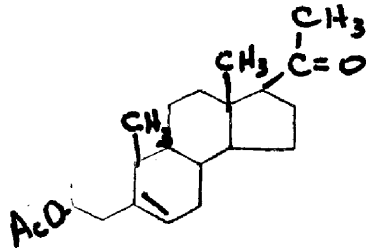
11 α-Acetoxyprogesterone

μ = 3.02 D (calc'd. = 3.14 D)

probably because the group is hindered by several adjacent atoms and groups and planarity is virtually assured.

However, for pregnenolone acetate and the Δ^{16}-derivative





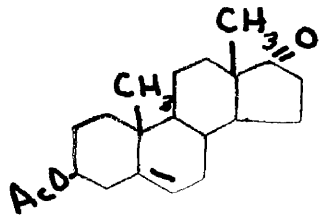
Pregnenolone acetate

μ = 2.60 D (calc'd. = 3.62 D)

16-Dehydropregnenolone acetate

μ = 2.93 D (calc'd. = 3.62 D)

the agreement is not nearly so good. For dehydroisoandrosterone acetate the observed and calculated values differed by about 0.5 D.



Dehydroisoandrosterone acetate

μ = 3.26 D (Calc'd. = 3.72 D)

The fact that the calculated moment is greater than experimental for the above sterols suggests that the resonance structure

$$R'-\underset{\underset{O^-}{|}}{C}=O^+-R$$

is important and augments the keto group moment. This in turn argues for a planar configuration of the acetoxy group. However, the steric and resonance effects are so interdependent in this group that entirely unambiguous conclusions are hard to formulate.

In sterols with only fixed groups, the accuracy with which the angles can be measured determines the degree to which the calculated electric moments are correct for a certain assumed conformation. The molecular models used were the best which were readily available but required modification in the highly distorted D ring. Thus, the strain, which is probably absorbed throughout the carbon skeleton in the molecule, is localized in this five-membered ring. The actual precision of the angle measurements was found to be $\pm$ 2° so the effect of such an error on the calculated moment was estimated using the data for androstane-3,17-dione. It was assumed that the angles locating the 3-keto group

in the reference system were really 2.0° higher than observed, while the 17-keto angles were 2.0° less than found by measurement. Use of the angles resulting from these assumptions led to the following components of the two keto groups.

	m_x	m_y	m_z
3-Keto	-2.40	0	-1.45
17-Keto	+2.20	+2.23	-0.57

The electric moment calculated using these data is 3.01 D, which is to be compared with the 2.95 D actually obtained. Thus, one would conclude that an error of $\pm$ 0.06 D is associated with the measurement of angles on molecular models of sterols with a total moment of about 3.0 D.

For sterols with freely rotating hydroxyl groups, the error involved in neglecting the cosine term is a measure of the accuracy of the calculated electric moment. A value of 75° is given in the literature for the angle between the C-O bond and the group moment of the hydroxyl group.[21] Now for 3β,17α-androstanediol, the angle between the polar groups was 106°. Then with $\phi_1 = \phi_2 = 75°$ and $\sigma = 106°$, the equation

$$\mu^2 = m_1^2 + m_2^2 + 2m_1m_2 \cos \sigma \cos \phi_1 \cos \phi_2$$

is used and gives a calculated value of 2.72 D for the electric moment. This compares quite favorably with the 2.69 D found assuming the angle between the C-O bond and hydroxy group moment to be 90° and apparently justifies the use of this latter assumption.

SUMMARY

The electric moments have been determined at 25°C for eight derivatives of azobenzene and thirty-four sterols using the refractivity method. The experimental data were collected on dilute solutions of the compounds in non-polar solvents; benzene was used for the azobenzene derivatives and dioxane for the sterols. Dielectric constant and density values for six different concentrations were plotted graphically and extrapolated to zero concentration to obtain data for the pure solute. These data in turn were used, along with calculated molar refractions, to compute the molar orientation polarizations and electric moments of the solute molecules.

The final values so obtained were interpreted from the standpoint of the theory of resonance, qualitative ideas concerning steric hindrance or some combination of these. The azobenzene compounds were found to have moments greater than their benzene analogues; this effect was attributed to resonance structures involving large charge separations. Extension of the azo ring system by conjugation with a benzalamino group led to further increases in moment presumably for the same reason.

Some of the data were used to calculate the moment and angle for the dimethylamino group in both benzene and azobenzene compounds. The fact that the electric moment of p,p'-dinitroazobenzene was found to be essentially zero has been construed as evidence that the azo derivatives have the trans configuration.

The sterols were investigated with the intention of correlating structural features with dipole moment. The angles between groups, from

which the electric moments could be calculated, were found for various conformations of the sterol molecules by direct measurements on molecular models. Comparison of the observed values with those calculated in this way provided information concerning the restriction of rotation of groups substituted in the various positions and the existence of chair-boat type geometrical isomerism in the rings.

In the pregnane and progesterone type sterols, it was necessary to postulate that from two to sixteen percent of the molecules in solution had the boat form of the A ring to explain the data obtained. For sterols with groups capable of free rotation the calculated values were often within experimental error of the observed values and rarely differed from the latter by more than 0.8 D. Where the electric moments calculated for free rotation differed considerably from the observed values it was concluded that the groups were restricted. Further calculations, based on molecular models, for various fixed positions of the groups indicate the source of the hindrance for the various positions. The 11 α, 11 β, and 17 α positions were presumably greatly hindered since the large methyl substituents or hydrogens attached directly to the ring in known fixed positions interfered physically with free rotation in these positions. For 11 - hydroxyprogesterones and pregnandiones the values calculated for fixed positions of the hydroxyl groups were in best agreement with experimentally determined moments, suggesting that the freedom of these groups to rotate has been seriously impaired.

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