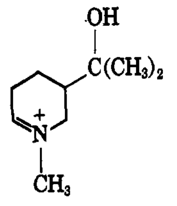
g., were not identified but shown by their infrared spectra to have terminal vinyl groups.

Mass Spectra of *cis*- and *trans*-α,α,1,6-Tetramethyl-3-piperidinemethanol.—Mass spectra were obtained for the major and minor Clarke–Eschweiler products using a C.E.C. Type 21-130 spectrometer. For the minor component the sample was prepared by vapor phase chromatography of a 90% mixture on a 60-cm. silicone rubber column. There is no significant difference in the spectra of the two isomers. The molecular-ion peak appears at m/e 171 and the base peak at M − 15. Two stable ions, **12** and **13**, could result from loss of CH_3; both probably are formed. There are two remaining strong peaks at m/e >100, M − 33 and M − 59. The first probably corresponds to loss of water from **12**. The second is presumably the result of loss of the hydroxypropyl radical from the molecular ion.



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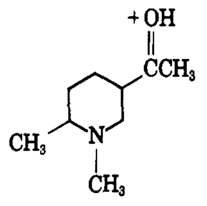

13

N.m.r. spectra were obtained using the Varian Model A-60 spectrometer. Tetramethylsilane, for carbon tetrachloride solutions, and the sodium salt of γ-trimethylsilylpropanesulfonic acid, for deuterium oxide solutions, were the internal standards.

Conformational Analysis. XLIV. The Dependence of Some Physical Properties of Acetophenone Derivatives on the Conformation of the Side Chain[1-3]

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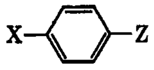
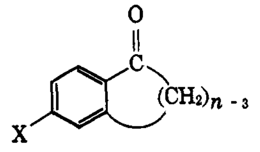
A series of compounds (II, X = H, F, NH_2, OH, or COOH with n = 5–8) have been studied with respect to pK values and n.m.r. (for X = F) and ultraviolet spectra. Earlier conclusions regarding the interpretation of the data on the ρσ basis are confirmed for the most part, but it is shown that the ultraviolet data cannot be so correlated reliably. The theoretical implications of these facts are considered.

The effect of a substituent (Z) located on a benzene ring *para* to a reaction site (X) as in I is one of the most thoroughly studied phenomena in the field of organic chemistry, much of the study being summarized in terms of the Hammett ρσ relationship.[4-6] Typically, Z (and hence σ) is varied over a series of atoms or groups, and various values of ρ are obtained depending on the property being studied at the reaction site. The property being examined is always a function of the difference between two states (one may be a transition site in the case of rate phenomena), transitions between which are under examination. It was originally thought that, for a given Z, there would be a single σ constant, or perhaps a few constants, which would be applicable to different kinds of situations. When the mechanism of the effective action of Z on X is examined, it appears that in most, if not all, cases that the effect of Z is simply to increase or decrease the electronic charge at X in the states under observation. Thus it seems reasonable *a priori* that, since this distribution will vary depending on the demands of the states of X in question, σ should not be a constant, but rather a function of the property being examined, and hence to the next approximation a function of ρ as well as of X. That this is in fact the case is shown by the profusion of σ constants, and of ways of defining and measuring them, which have become available in recent years.



I

There would be certain advantages to being able to study a system in which it was possible to vary Z in a systematic continuous fashion, rather than by large uncontrollable increments (such as from nitro to bromo to hydroxyl). One way in which such a variation might be brought about would be to have a group, say acetyl, in which the properties examined were a function of the rotational orientation about the bond joining it to the benzene ring, and then to vary systematically the conformation of the side chain relative to the ring. Such substituted acetophenones would allow one to deal with a minimum of variables, but they cannot, unfortunately, have their side chains held in various definite, arbitrary arrangements relative to the ring while the properties of interest are being studied. If the acetophenone is further substituted with groups of varying sizes, the side chain can be effectively held. This has been done in the past in various studies,[6-8] and, while such a technique is useful, there are usually too many variables in the system to evaluate some of the points of interest accurately. The present work is concerned with a study of benzocyclanones (II) in which one can come about as close as is



II

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[1] Paper XLIII: N. L. Allinger and L. A. Tushaus, *J. Org. Chem.*, **30**, 1945 (1965).

[2] This research was supported by Grant No. DA-ARO(D)-31-124-G375 from the U. S. Army Research Office.

[3] Abstracted from the Ph.D. Dissertation of E. S. J., presented to the Graduate School of Wayne State University, 1960.

[4] H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

[5] R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 556.

[6] H. Van Bekkum, P. E. Verkade, and B. M. Wepster, *Rec. trav. Chim.*, **78**, 815 (1959).

[7] B. M. Wepster in "Progress in Stereochemistry," Vol. 2, W. Klyne and P. B. D. de la Mare, Ed., Academic Press Inc., New York, N. Y., 1958, p. 99.

[8] E. A. Braude in "Determination of Organic Structures by Physical Methods," E. A. Braude and F. C. Nachod, Ed., Academic Press Inc., New York, N. Y., 1955.

physically possible to the ideal situation. While it is not possible to fix the orientation of the carbonyl at continuous arbitrary orientations, by changing the size of the ring one can achieve a number of orientations which, according to the literature, have known geometries.[9-11] The effect of the attachment of the other end of the side chain to the benzene ring at the position *meta* to X should be essentially constant.[12]

The most simple case is the situation where X = H, and here there are a number of properties that one might conceivably examine. The ultraviolet and infrared spectra are among the more easily measured properties, and studies on those properties have previously been reported for these compounds.[9-11] As the benzocyclopentanone (II, $n = 2$) must necessarily be planar (or very close to it), the carbonyl is conjugated with the benzene ring. As n increases the carbonyl is forced out of the plane of the ring as a result of the conformational restrictions imposed by the unfavorable dihedral angles in the acyclic ring. The carbonyl group is thus twisted from the plane of the aromatic ring and deconjugated. The infrared carbonyl stretching frequency thus first decreases (because of the change in bond angle at the carbonyl carbon) and then increases with increasing n owing to the interruption of conjugation.

The behavior of the ultraviolet spectra of the series II (X = H) as a function of n has been discussed by previous workers, and the assumption made was that, for such a series of compounds, the extinction coefficient (properly the oscillator strength) of the K band decreases, approximately proportionately to the square of the cosine of the angle of torsion.[9-11] So far as the present authors have been able to determine, there is no good experimental or theoretical justification for this widely used relationship. It was introduced as an empirical relationship by Klevens and Platt,[13] and was intended to correlate angles of twist which were themselves unknown. That the resonance energy gained from the conjugation of two resonating systems would show such a proportionality was derived for p-orbitals of hydrocarbon systems by perturbation theory.[14] This extra energy is simply the conjugation energy of the ground state, and the $\cos^2$ relationship does not necessarily refer to the transition energy, although it may in certain cases, nor does it refer to the ratio of the extinction coefficients in the nonplanar and planar cases. The extinction coefficients are determined by the transition moments, which vary according to the difference in electron distribution between the ground state and the excited state being considered, and have in general no simple relationship to the angle in question.[15,16] Guy showed many years ago that for twisted biphenyls the relationship is more complicated than the $\cos^2$ proportionality would indicate.[17] More recently, from the rather thoroughly studied case butadiene,[18] it can be seen that none of the transition energies and none of the extinction coefficients vary as the square of the cosine of the angle of twist. Since these $\cos^2$ curves are ordinarily deduced by knowing the value of the extinction coefficients at 0 and 90°, they will (as will any continuous single valued monotonous function) give *qualitatively* the observed results between 0 and 90°. The interplanar angles derived from such a relationship cannot, however, be expected to be any more than qualitatively ordered.[19]

Detailed quantum-mechanical calculations of the ultraviolet spectra of nonplanar acetophenones as a function of the dihedral angle about the carbonyl group will make it possible to deduce the interplanar angles from the ultraviolet spectra. Such calculations are in progress and will be reported later. For the present it will simply be noted that the ultraviolet spectra of such compounds, which involve an excited molecular state and are hence distinct from the other properties which are commonly correlated by $\rho\sigma$ treatments, and which involve only ground (or transition) states, are not expected to correlate with these other properties. Experimentally, in the cases studied here, it is found that in fact they do not correlate. In the past it has been widely assumed that dihedral angles can be determined by correlation between the extinction coefficients for various series of compounds.[6-8,13,19,20] All such correlations are definitely suspect, but they will not be discussed in further detail here.[21]

Results and Discussion

At the outset of this investigation it was intended to calculate the angles of twist for the accessible compounds from the ultraviolet spectra and extrapolate to an angle of twist of 90°, at which point only the inductive part of the σ constant should be operative. From these data a separation of σ into resonance and inductive portions would be possible. This approach to a separation of the components of σ failed because of the failure of ϵ to show the type of behavior that earlier workers had indicated that it should show; thus plots of ϵ *vs.* the other properties studied for II as a function of n do not give straight lines. In the meantime, a paper by Taft appeared[22] which showed that in substituted fluorobenzenes the chemical shift of the fluorine in the n.m.r. spectrum could be used as a measure of the electron density supplied to the fluorine by the aromatic system. The transitions being examined in this case involve two nuclear states which do not differ to any noticeable extent in chemical properties or electron distribution, and this seemed to be a better standard to which to refer the other properties. The chemical shift of the fluorine was therefore determined for compounds II (X = F) as a function of ring size. As will be discussed below, many properties do correlate well with the chemical shifts. Taft showed that a separation of σ into its components could be made from the n.m.r. spectra of substituted

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(9) R. Huisgen, *Angew. Chem.*, **69**, 341 (1957).

(10) G. D. Hedden and W. G. Brown, *J. Am. Chem. Soc.*, **75**, 3744 (1953).

(11) E. A. Braude and F. Sondheimer, *J. Chem. Soc.*, 3754 (1955).

(12) R. T. Arnold and W. L. Truett, *J. Am. Chem. Soc.*, **73**, 5508 (1951); G. Baddeley and M. Gordon, *J. Chem. Soc.*, 2190 (1952).

(13) H. B. Klevens and J. R. Platt, *J. Am. Chem. Soc.*, **71**, 1714 (1949).

(14) M. J. S. Dewar, *ibid.*, **74**, 3345 (1952).

(15) E. Heilbronner and R. Gerdil, *Helv. Chem. Acta*, **39**, 1996 (1956).

(16) J. N. Murrell, *J. Chem. Soc.*, 3779 (1956).

(17) M. J. Guy, *J. chim. phys.*, **46**, 469 (1949).

(18) N. L. Allinger and M. A. Miller, *J. Am. Chem. Soc.*, **86**, 2811 (1964).

(19) (a) C. Dickinson, J. R. Holden, and M. J. Kamlet, *Proc. Chem. Soc.*, 232 (1964); (b) J. E. Bloor and A. Burawoy, *Tetrahedron*, **20**, 861 (1964); (c) H. Suzuki, *Bull. Chem. Soc. Japan*, **32**, 1350 (1959); **33**, 613, 619 (1960); (d) H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1962, p. 384.

(20) B. M. Wepster, *Rec. trav. chim.*, **76**, 335, 357 (1957).

(21) See also L. A. Cohen and W. M. Jones, *J. Am. Chem. Soc.*, **85**, 3402 (1963), and references therein.

(22) R. W. Taft, Jr., *ibid.*, **79**, 1045 (1957).

fluorobenzenes, and he has tabulated the resonance (σ_R) and inductive (σ_I) components for various substituents.[22] Taft values were therefore utilized in the present work.

The compounds (II) studied in the present work had $n = 5$–8, and $X = H, F, NH_2, OH$, and COOH. The properties studied were the fluorine resonance in the n.m.r. spectrum for $X = F$, the ultraviolet spectrum for $X = H$, and the pK_a values for the other compounds. The syntheses of the compounds have previously been described.[23] The experimental data are summarized in Tables I–V.

TABLE I

APPARENT IONIZATION CONSTANTS OF BENZOIC ACIDS[a]

Compd.	pK_a	pK_a (lit.)
Benzoic acid	5.59 ± 0.05	5.73,[b] 5.65[c]
p-Acetobenzoic acid	5.03 ± 0.03	5.10[b]
5-Carboxy-1-indanone	4.93 ± 0.04	...
6-Carboxy-1-tetralone	5.06 ± 0.04	...
7-Carboxy-1-benzosuberone	5.20 ± 0.04	...
8-Carboxy-1-benzocyclooctanone	5.30 ± 0.03	...

[a] In 50% aqueous ethanol at 25°; $\rho = 1.464$. [b] Reference 7. [c] H. H. Szmant and G. Suld, *J. Am. Chem. Soc.*, **78**, 3400 (1956).

TABLE II

APPARENT IONIZATION CONSTANTS OF PHENOLS[a]

Compd.	pK_a	pK_a (lit.)
Phenol	11.12 ± 0.08	11.28[b]
p-Acetophenol	9.04 ± 0.05	9.21[b]
5-Hydroxy-1-indanone	8.70 ± 0.02	...
6-Hydroxy-1-tetralone	8.98 ± 0.03	...
7-Hydroxy-1-benzosuberone	9.40 ± 0.03	...
8-Hydroxy-1-benzocyclooctanone	9.36 ± 0.02	...

[a] In 50% aqueous ethanol at 25°; $\rho = 2.545$. [b] Reference 7.

TABLE III

APPARENT IONIZATION CONSTANTS OF ANILINIUM IONS[a]

Compd.	pK_a
Aniline	4.41 ± 0.05
p-Aminoacetophenone	1.83 ± 0.03
5-Amino-1-indanone	1.47 ± 0.01
6-Amino-1-tetralone	1.76 ± 0.02
7-Amino-1-benzosuberone	2.29 ± 0.02
8-Amino-1-benzocyclooctanone	2.34 ± 0.03

[a] In 30% aqueous ethanol at 25°; $\rho = 3.435$.

TABLE IV

ULTRAVIOLET SPECTRA OF THE BENZOCYCLANONES[a]

Compd.	λ_{max}, mμ	ε
Abs. Ethanol Solvent		
Acetophenone	241	12,300
1-Indanone	244	12,200
1-Tetralone	247	11,300
1-Benzosuberone	246	9,300
1-Benzocyclooctanone	248	5,800
p-Acetobenzoic acid	249	18,300
5-Carboxy-1-indanone	251	18,600
6-Carboxy-1-tetralone	255	18,000
7-Carboxy-1-benzosuberone	253	15,100
8-Carboxy-1-benzocyclooctanone	246	9,500
p-Fluoroacetophenone	243	11,800
5-Fluoro-1-indanone	244	11,300
6-Fluoro-1-tetralone	248	11,400
7-Fluoro-1-benzosuberone	247	9,200
8-Fluoro-1-benzocyclooctanone	249	7,700
p-Aminoacetophenone	317	20,800
5-Amino-1-indanone	322	22,800
6-Amino-1-tetralone	323	22,100
7-Amino-1-benzosuberone	318	17,200
8-Amino-1-benzocyclooctanone	321	18,900
p-Hydroxyacetophenone	277	14,900
5-Hydroxy-1-indanone	293	11,400
	269	13,000
6-Hydroxy-1-tetralone	278	14,500
7-Hydroxy-1-benzosuberone	276	12,300
8-Hydroxy-1-benzocyclooctanone	282	12,800
0.1 *N* NaOH Solvent		
p-Hydroxyacetophenone	325	23,300
5-Hydroxy-1-indanone	323	28,300
6-Hydroxy-1-tetralone	330	25,500
7-Hydroxy-1-benzosuberone	327	20,000
8-Hydroxy-1-benzocyclooctanone	331	18,900

TABLE V

NUCLEAR MAGNETIC SHIELDING PARAMETERS FOR THE *para*-SUBSTITUTED FLUOROBENZENES

Compd.	δ[a]
5-Fluoro-1-indanone	0.839
6-Fluoro-1-tetralone	0.701
p-Fluoroacetophenone	0.672[b]
7-Fluoro-1-benzosuberone	0.459
8-Fluoro-1-benzocyclooctanone	0.390

[a] Relative to fluorobenzene. [b] Reported value, 0.66.[24]

For any property, p, one can write the Hammett relationship as

$$p = \rho(a\sigma_I + b\sigma_R) + c \tag{1}$$

where $(a\sigma_I + b\sigma_R) = \sigma$. Ordinarily a and b are equal to 1. Taft has written an equation for the chemical shift of a p-fluorine, δ, as

$$\delta = 0.583\sigma_I + 1.88\sigma_R - 0.08 \tag{2}$$

The π electrons are thus more effective in shielding the fluorine nucleus than are the σ electrons, while quantities such as pK depend on the total electron density. For the Hammett equation in its more usual form (3) we can use the usual values of ρ for the ionization of benzoic acids, anilinium salts, and phenols as given in Tables I–III.

$$\log k/k_0 = \rho\,(\sigma_I + \sigma_R) \tag{3}$$

The value for σ_I can be taken[22] as constant for the whole series, independent of both X and n, and equal to the sum of the values for p-acetyl and m-methyl, +0.22. We can then evaluate σ_R as a function of X with the angle of the carbonyl group remaining 0°, and also as a function of the angle with X remaining constant. It is to be expected from theory, and it has been experimentally demonstrated previously, that σ_R in eq. 3 should vary with the nature of X. In the present case, considering only the planar compounds (II, $n = 2$), we find that to fit the data σ_R must vary significantly, having values of 0.23, 0.42, 0.63, and 0.73 for the acids, fluorides, amines, and phenols, respectively. These numbers span a range which is in satisfactory agreement with the values given by Taft for σ_R and σ_R^- (0.25 and 0.60), and they are in the qualitative order one might expect, thus the larger the electron-donating power of X, the greater the response of the acyl group toward accepting electrons.[22,24]

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(23) N. L. Allinger and E. S. Jones, *J. Org. Chem.*, **27**, 70 (1962).

(24) R. W. Taft, Jr., S. Ehrenson, I. C. Lewis, and R. E. Glick, *J. Am. Chem. Soc.*, **81**, 5352 (1959); R. W. Taft, Jr., and I. C. Lewis, *ibid.*, **81**, 5343 (1959).

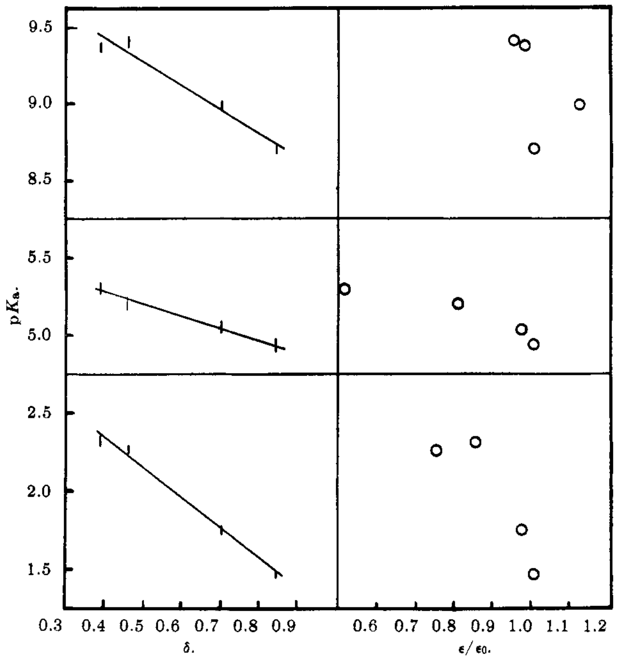

Figure 1.—Plots of the pK values of a series of compounds (II) for X = OH, COOH, and NH_2 *vs.* the δ values for X = F, and the same pK_a data plotted against the ϵ/ϵ_0 value of the strongest absorption bands of the same compounds (ϵ_0 from n = 5).

Next one can look at the variation of the effect of σ_R with the angle between the plane of the ring and the carbonyl, and these data are summarized in Table VI. In eq. 1, σ_R is taken as independent of angle and the constant b varies with angle between the limits of 1 (where σ_R exerts its full effect) and 0 (where the substituent exerts no resonance effect). It might be supposed that for substituents (X) which can resonate strongly with the carbonyl group, more conjugation energy will be obtained than with substituents which cannot resonate as well, and therefore the system might be expected to flatten out for the amines and phenols, relative to what is found for the carboxylic acids. Such a flattening out has been suggested previously.[5,25] In the present case it is opposed mainly by torsional barriers, and these lead to energies which change only rather slowly with change in dihedral angle. The flattening-out effect should therefore be seen more clearly here than in cases where the opposing force is a van der Waals repulsion. From the data $b\sigma_R$ was calculated as a function of n for each series of compounds. It was expected that b would vary continuously from the value one at θ = 0°, to zero at θ = 90°, and a smaller value for b corresponds to a larger value of θ. (No attempt will be made to specify what function relates b and θ at this time.) Table VI shows that for the amines and phenols, where the resonance is very much more effective in one state (amine or phenolate ions) than in the other (ammonium salt or phenol), b falls slowly with increasing n, going down by about 40% by the time n = 8. For the fluorides the resonance is less effective and b falls more rapidly, losing 60% of its initial effect at n = 8. For compounds like the acids, σ_R does lead to stabilization of the anion and increased acidity, but the effect is not great, and σ_R is small. The tendency for the ring to be planar is also therefore expected to be small, and b has been reduced to zero (within experimental error) at n = 8.

TABLE VI

$b\sigma_R$ VALUES FOR THE *para*-SUBSTITUTED BENZOCYCLANONES

	X			
Compd. II	F	NH_2	OH	CO_2H
5	0.42	63	73	0.23
6	0.35	55	62	0.14
7	0.22	40	45	0.05
8	0.18	38	47	−0.02

We are able to reach a number of conclusions from the present work. First, from evidence with quite a different basis from that used by Taft, it can be concluded that one component of the σ value of an acyl group shows an angular dependence which can be identified with Taft σ_R. Second, accepting Taft values for σ_I and σ_R, one can ascertain the extent to which σ_R contributes to compounds of structure II, both as functions of n and X. Third, σ_R is seen not to be a constant, but is a function of X and n. These conclusions have been reached by others, but few of them have been as clearly established as in the present work.

More important, perhaps, is the variation of the ultraviolet spectra for these series of compounds. If a plot is made of the pK values of any single series against the δ values for the corresponding series (Figure 1[26]), a straight line is obtained. On the other hand, if similar plots of extinction coefficients of these series are made against the same values, no particular correlation is obtained. (The use of oscillator strengths instead of extinction coefficients does not improve the correlation.) Thus theory suggests and experiment supports the fact that there is no simple correlation between the ultraviolet extinction coefficients of these compounds and other properties of the sort discussed here, and the so-called "angles of twist" deduced for systems of this type of earlier workers from the data on extinction coefficients in the ultraviolet are really only qualitatively meaningful at best.

It appears to the authors that all of the experimental properties discussed herein, including the ultraviolet spectra, are probably now calculable by the semiempirical quantum-mechanical methods presently available.[27] The σρ type of treatment is essentially an empirical way of applying perturbation approximations to systems of interest. We suggest that enough is now known about the principles involved actually to do the calculations for spectroscopic observables and probably also for equilibria, and the elaboration of the ρσ approach has probably reached if not gone well past the point of diminishing returns. The experimental data presented here in fact offer something of a challenge to organic quantum chemistry, a challenge which will be taken up in a later paper.

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(25) R. O. C. Norman, G. K. Radda, D. A. Brimacombe, P. D. Ralph, and E. M. Smith, *J. Chem. Soc.*, 3247 (1961).

(26) It is noted that for the compounds with n = 8, the carboxylic acid is weaker, the ammonium salt stronger, and the phenol much stronger than required by a straight-line relationship with the n.m.r. While the data are not completely definitive, this is consistent with appreciable differences in ring flattening here, compared to the smaller, more rigid rings.

(27) For example, see E. G. McRae and L. Goodman, *Mol. Spectr.*, **2**, 464 (1958), and ref. 18.

Experimental

Apparent Ionization Constants.—All measurements on the acids and phenols were made in aqueous alcohol which was prepared from carbon dioxide-free water and Commercial Solvents Co. Gold Shield alcohol, mixed in equal parts by volume. Samples of about 30 μmoles of compound in 75 ml. of 50% alcohol were titrated with standard 0.05 *N* sodium hydroxide solution made up in the same solvent. The titrations were done under an atmosphere of purified nitrogen at 25 ± 1° using a Leeds and Northrup pH meter, Model 77664, equipped with glass and saturated calomel electrodes. The meter was standardized with aqueous buffers. The $\mathrm{p}K_a$ values were calculated from the Henderson equation[28] and are the average of two independent determinations at approximately 20, 40, and 60% neutralization. Tables I–II give the $\mathrm{p}K_a$ values measured for the acids and phenols.

The values of the apparent ionization constants of the anilinium ions were measured in 30% alcohol by a spectrophotometric method. The amine (about 50 μmoles) was dissolved in 50 ml. of 30% ethanol to give a stock solution. Aliquots of this stock solution (1 ml.) were diluted with 50 ml. of 30% alcohol and with 1 *N* hydrochloric acid in 30% alcohol to secure the amine in the forms of the free base and anilinium salt, respectively. Aliquots (1 ml.) of the amine solutions were also diluted to 50 ml. with a dilute hydrochloric acid solution having a pH within 0.5 units of the expected $\mathrm{p}K_a$ value. Absorption curves were then obtained using a Beckman DU spectrophotometer equipped with a Warren Spectrocord automatic recording attachment. The pH of the dilute acid solutions were determined at 25 ± 1° using a Leeds and Northrup pH meter standardized against a saturated solution of potassium hydrogen tartrate. The $\mathrm{p}K_a$ values were determined from the equation: $\mathrm{p}K_a = \mathrm{pH} + \log (\mathrm{RNH_3^+}/\mathrm{RNH_2})$. The quantity $\log (\mathrm{RNH_3^+}/\mathrm{RNH_2})$ was obtained from the relationship $\mathrm{RNH_3^+}/\mathrm{RNH_2} = (A_b - A)/(A - A_a)$ where A_a, A_b, and A are the absorbancies of the acid, base, and dilute acid solutions at $\lambda_{\max}$ for the free amine. The $\mathrm{p}K_a$ values listed in Table III are the average of two determinations.

Ultraviolet Absorption Spectra.—The spectra for the compounds were determined in absolute ethanol using a Beckman Model DU spectrophotometer equipped with a Warren Spectrocord automatic recording attachment. The spectra of the phenols were also obtained in 0.1 *N* sodium hydroxide solution, and the spectra of the amines were also determined in 0.1 *N* hydrochloric acid solution. The results are tabulated in Table IV.

N.m.r. Shielding Parameters for the Fluorocyclanones.—The n.m.r. spectra were determined in dilute carbon tetrachloride solution using fluorobenzene as an internal standard, and the results are tabulated in Table VI. The spectrometer employed was a Varian Associates n.m.r. spectrometer, Model HR-60.

Acknowledgment.—The authors are indebted to Dr. L. A. Freiberg and to Mr. B. Shoulders (University of Illinois) for determining the spectra reported herein.

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(28) F. G. Bordwell and G. D. Cooper, *J. Am. Chem. Soc.*, **74**, 1058 (1952).

The Synthesis of 11,12-Oxygenated Progesterones

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The rearrangement of 9α-bromo-11-ketoprogesterone with hydroxide ion gives 12α-hydroxy-11-ketoprogesterone. The syntheses of two other 11,12-ketols, *viz.*, 11α-hydroxy-12-ketoprogesterone and 12β-hydroxy-11-ketoprogesterone are also described, and their alkaline equilibration is discussed. The four possible 11,12-dihydroxyprogesterones have been prepared as well as the acetonides of the 11α,12α, 11β,12β, and 11α,12β isomers.

The reaction of 9α-halo-11-keto steroids with nucleophilic reagents leading to 12α-substituted 11-keto steroids has been the subject of a number of recent publications.[2] In 1961 the reaction of 9α-bromo-11-ketoprogesterone (I) with methoxide ion yielding 12α-methoxy-11-ketoprogesterone was reported[2b] from this laboratory. We would now like to report the reaction of I with hydroxide ion and the conversion of the product of this reaction to other 11,12-oxygenated progesterones.

The reaction of 9α-bromo-11-ketoprogesterone with sodium hydroxide under mild conditions gave a bromine-free compound which showed a correct analysis for $C_{21}H_{28}O_4$. That this compound was 12α-hydroxy-11-ketoprogesterone (II) and not one of the other isomeric 11,12-ketols which might have been formed under these alkaline conditions was confirmed by both chemical and physical methods. Reaction of 11β,12β-oxidoprogesterone[3] (III) with perchloric acid gave 11β,12α-dihydroxyprogesterone[4] (IV) which on acetylation gave only a monoacetate, the 12α-acetate (IVa). Oxidation of IVa with Jones reagent[5a] gave 12α-acetoxy-11-ketoprogesterone (IIa), identical with the acetylation product of II. That the structural assignments for these compounds were correct was also supported by the n.m.r. spectra of these compounds (*cf.* Table I) and the hydrogen bonding detectable in both the infrared and proton magnetic resonance spectra.[5b] The 11α and 12β protons of IV appeared at τ 5.75 ($W_{1/2}$ = 8.5 c.p.s.) and 6.10 ($W_{1/2}$ = 7.5 c.p.s.), respectively, and for IVa appeared at τ 5.77 ($W_{1/2}$ = 8 c.p.s.) and 4.96 (d, J = 2.5 c.p.s.). The doublet and small coupling constant of the 12β proton in the latter case indicated the diequatorial relationship of the C-12 proton to the C-11 proton. In II and IIa the 12β proton appeared at τ 6.10 (d, J = 3.5 c.p.s.) and 5.21 (s), respectively, the singlet of IIa confirming that no vicinal proton was present. That the carbonyl groups of II and IIa are at position 11 and not at 12 was evident by the resonance bands for the 18-methyl

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