vent in a vacuum gave an oil which did not crystallize. The oil was rechromatographed on a column of alumina, and the fractions eluted with 65 ml. of a petroleum ether–benzene mixture (7/3) yielded an oil which gave by treating with acetone–methanol crystals mixed with oil. Repeated recrystallizations from acetone–methanol gave 6 mg. of IX as fine needles, m.p. 129–130°, $\lambda_{max.}$ 272, 276.5 and 281.5 mμ (ϵ 720, 634 and 774), $\lambda_{max.}$ 5.74 (strong), 11.44 (moderate) and 11.60 μ (moderate).

Anal. Calcd. for $C_{19}H_{23}OCl$: C, 75.35; H, 7.65; Cl, 11.71. Found: C, 75.21; H, 7.47; Cl, 11.17.

The Influence of Temperature on the Dehydrobromination of 7-Bromocholesterol.—Cholesteryl acetate was brominated in a solution of refluxing petroleum ether using 120% of the calculated amount of freshly crystallized and dried N-bromosuccinimide.[9] General Electric RSP-2 Photospot lamps were used for illumination. After the mixture had refluxed for 15 min., it was cooled, filtered and evaporated to dryness at reduced pressure. The resulting crude 7-bromocholesterol was dissolved in the appropriate solvent (solvent/steroid = 4/1) and added dropwise to a hot, well-mixed solution of the same amount of solvent and a 300% excess of *s*-collidine (distilled from sodium). The approximate times required to obtain the percentage recoveries of collidine hydrobromide indicated below were determined empirically by carrying out the reactions for various intervals of time and weighing the recovered *s*-collidine hydrobromide. In the experiments listed below the percentage of conjugated diene or triene was measured spectrophotometrically using the maxima at 239, 282 and 305 mμ for the $\Delta^{4,6}$-, $\Delta^{5,7}$- and the $\Delta^{2,4,6}$-compounds, respectively.

When the dehydrobromination was carried out at 140° in the presence of dimethylaniline instead of *s*-collidine, none of the 4,6-isomer could be detected spectrophotometrically in the reaction mixture. However, strong absorption occurred in the 296–320 mμ region which was not present when *s*-collidine was used at the same temperature. This latter absorption is presumably attributable to 2,4,6-cholestatriene. The 5,7-diene was observable spectrophotometrically and apparently was not affected by the dimethylaniline.

Temp., °C.	Solvent	Time, hr.	No. of runs	C_8H_{12}-BrN recovd., %	% 4,6-diene	% 5,7-diene	% 2,4,6-triene	Total unsatd. mater., %
37	Toluene	99	1	100	60	6.3	..	66
55	Toluene	42	1	84	48	10	..	58
55	Toluene	19	1	79	53	8.3	..	61
68	Hexane	24	1	81	60	9.2	..	69
80	Benzene	5	2	89	65	17	..	72
91	Toluene	3	2	87	62	19	..	81
109	Toluene	2	4	86	38	51	..	89
140	Xylene	1	3	90	41	55	..	96
167	Decalin	0.5	2	96	46	44	13	103
174	Decalin	0.5	4	94	14	45	28	87

2,4,6-Cholestatriene.—Seventy-five grams of cholesteryl acetate was brominated with N-bromosuccinimide and dehydrobrominated with *s*-collidine in the manner described under the preparation of 7-dehydrocholesteryl acetate. After the *s*-collidine hydrobromide had been filtered off, the filtrate was evaporated in a vacuum on the steam-bath. A qualitative ultraviolet analysis on the residual oil showed characteristic peaks at 272, 282 and 295 mμ for 7-dehydrocholesteryl acetate and new peaks at 310 and 320 mμ; there was little or no absorption present at 239 mμ for the 4,6-isomer. The oil was crystallized from acetone giving 12.0 g. of crystals. The mother liquor was evaporated to dryness yielding 63 g. of material which was adsorbed on a column of 375 g. of Florisil in a mixture of benzene–petroleum ether (1/4). Elution with 2.5 l. of the same solvent mixture yielded an oil which was crystallized twice from acetone–methanol to give 3.7 g. of needles, m.p. 71–73.5°. One recrystallization from acetone–methanol gave thin needles, m.p. 72–74°, $[\alpha]D$ +3.4°, $\lambda_{max}^{isooctane}$ 296, 305 mμ and λ_{infl} 320 mμ (ϵ 14,380, 13,640 and 8,720)[6] (Fig. 2).

Anal. Calcd. for $C_{27}H_{42}$: C, 88.45; H, 11.55. Found: C, 88.74; H, 11.44.

BETHESDA, MARYLAND

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

Optical Rotatory Dispersion Studies. IV.[1] Steroidal Sapogenins[2]

BY CARL DJERASSI AND ROBERT EHRLICH

RECEIVED AUGUST 29, 1955

The rotatory dispersion curves of a variety of steroidal sapogenins are given and the changes produced by the introduction of carbonyl groups, halogen atoms and double bonds are discussed. The application to certain analytical problems also is mentioned.

In the preceding three papers[1,3,4] of this series, there was given the theoretical and experimental background to this study, which is concerned with an attempted correlation of the rotatory dispersion curves and certain structural features of steroids. The present investigation covers a series of closely related steroidal sapogenins, without, however, carrying out the earlier mathematical treatment[1] since it did not offer any advantages insofar as the correlation of chemical structure and rotatory dispersion is concerned.

The experimental procedure and definition of terms already has been outlined in detail[3] and has been followed in this paper as well. In contrast to the steroidal hydrocarbon, androstane, which showed[3] practically zero rotation over the spectral range (700–300 mμ) studied, the basic sapogenin skeleton, represented by 22a,25a,5α-spirostan (desoxytigogenin) (I)[5] shows an increasingly negative rotation (Fig. 1) down to the limit of measurement ($[\alpha]_{290}$ −358°). This curve should be considered the background against which the structural changes in the sapogenin molecule are to be discussed. The strong negative drift in the rotation is apparently a reflection of the spiroketal system attached to ring D and, as seen below, overshadows the possible recognition of more subtle effects which might be exerted by the introduction of

(1) Paper III, A. E. Lippman, E. W. Foltz and C. Djerassi, THIS JOURNAL, **77**, 4364 (1955).

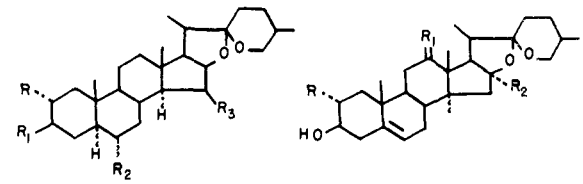
(2) Supported by a research grant from the Damon Runyon Memorial Fund for Cancer Research. We are indebted to the National Science Foundation for funds covering the purchase of the spectropolarimeter.

(3) Paper I, C. Djerassi, E. W. Foltz and A. E. Lippman, THIS JOURNAL, **77**, 4354 (1955).

(4) Paper II, E. W. Foltz, A. E. Lippman and C. Djerassi, *ibid.*, **77**, 4359 (1955).

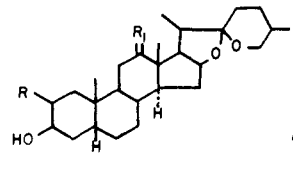
(5) For nomenclature, *cf.* C. Djerassi and J. Fishman, *ibid.*, **77**, 4291 (1955).

weak, optically active chromophores such as hydroxyl groups.

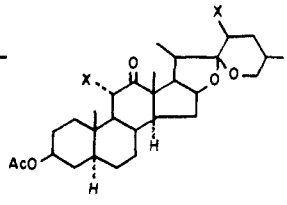


I $R=R_1=R_2=R_3=H$
II $R_1=OH$, $R=R_2=R_3=H$
III $R=R_1=OH$, $R_2=R_3=H$
IV $R_1=R_2=OH$, $R=R_3=H$
V $R=R_1=R_3=OH$, $R_2=H$

VI $R=R_1=R_2=H$
VII $R=R_1=H$, $R_2=OH$
VIII $R=OH$, $R_1=R_2=H$
IX $R=OH$, $R_1=O$, $R_2=H$



X $R=H$, $R_1=H_2$
XI $R=OH$, $R_1=H_2$
XII $R=OH$, $R_1=O$



XIII X = H
XIV X = Br

Figure 1 includes rotatory dispersion curves of only a few of the sapogenins which have been measured. The shapes of the curves are sufficiently similar in all cases so that for the majority of sapogenins lacking strong chromophores, only certain rotation values (usually the two extreme wave length limits—700 mμ and 290–300 mμ—and at the sodium D line) are listed in the experimental portion from which rough dispersion curves can be constructed. Introduction of a single hydroxyl group at C-3 (tigogenin, II), two adjacent hydroxyl groups (gitogenin, III) or two hydroxyl groups separated from each other (chlorogenin (IV), digitogenin (V)) causes no particular changes as compared to the desoxy derivative I and some typical examples are illustrated in Fig. 1. Introduction of a double bond in the 5,6-position, as in diosgenin (VI) (Fig. 1), produced the anticipated[1] negative shift, but did not change the shape of the curve. Addition of hydroxyl groups in presumably "sensitive" positions of the diosgenin molecule such as C-2 (yuccagenin, VIII) (Fig. 2) or C-16 (pennogenin, VII), had no effect, the pronounced negative drift toward lower wave length apparently overshadowing any possible minor contributions. Changes in the A/B ring juncture as found in smilagenin, samogenin (XI)[5] or sarsasapogenin (Xa)[6] do not affect the rotatory dispersion curve to any appreciable extent. In conclusion, it can be stated that in the series of sapogenins which possess only *weak* chromophores such as hydroxyl groups or isolated double bonds, measurement of the rotatory dispersion curve (over the range 700–300 mμ) offers no advantage over single measurements at the sodium D line or some other single, convenient wave length, since in those instances the method of molecular rotation differences will afford all the available information. Additional examples to support this statement are given in the experimental portion of this paper.

(6) Sarsasapogenin (Xa) differs from smilagenin in the configuration at C-25 (*cf.* I. Scheer, R. B. Kostic and E. Mosettig, THIS JOURNAL, **77**, 641 (1955)) and possibly also at C-22.

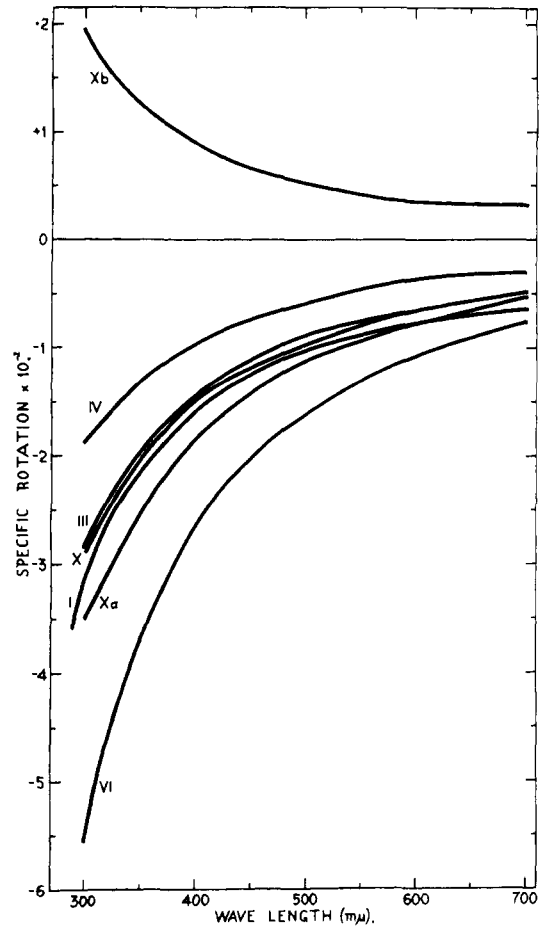


Fig. 1.—Rotatory dispersion curves of: desoxytigogenin (22a,25a,5α-spirostan (I)), gitogenin (22a,25a,5α-spirostan-2α,3β-diol (III)), chlorogenin (22a,25a,5α-spirostan-3β,6α-diol (IV)), diosgenin (Δ⁵-22a,25a-spirosten-3β-ol (VI)), smilagenin (22a,25a-spirostan-3β-ol (X)), sarsasapogenin (22b,25b-spirostan-3β-ol (Xa)), cyclo-ψ-sarsasapogenin (Xb).

There seems to exist only one exception, but the importance of it is as yet difficult to assess. Sapogenins (spirostans) are readily converted to ψ-sapogenins (furostens), which in turn regenerate the starting sapogenin upon treatment with strong acid. Recently,[7] it was observed that under mild conditions, a new series of sapogenins, cyclo-ψ-sapogenins,[8] can be produced which differs from the usual sapogenins only in the configuration at C-20 and possibly also at C-22. Attention has been called to the fact[7c] that while the specific rotations of sapogenins and cyclo-ψ-sapogenins are quite similar in those instances possessing the side chain of smilagenin (X), a considerable change can be noticed in analogous pairs of the sarsasapo-

(7) *Inter al.*, (a) J. B. Ziegler, W. E. Rosen and A. C. Shabica, *ibid.*, **77**, 1223 (1955); (b) M. E. Wall, S. Serota and C. R. Eddy, *ibid.*, **77**, 1230 (1955); (c) R. K. Callow, D. H. W. Dickson, J. Elks, R. M. Evans, V. H. T. James, A. G. Long, J. F. Oughton and J. E. Page, *J. Chem. Soc.*, 1966 (1955).

(8) D. A. H. Taylor, *Chemistry & Industry*, 1066 (1954).

genin (Xa)[6] series. This is illustrated in a particularly striking manner in this paper where the rotatory dispersion curves of cyclo-ψ-diosgenin[9] and cyclo-ψ-smilagenin are essentially identical (see Experimental section) with those of the parent sapogenins while the dispersion curves of sarsasapogenin (Xa) and cyclo-ψ-sarsasapogenin (Xb) are roughly mirror images. This would suggest either an unusual vicinal effect[7c] in the latter case or that the change Xa → Xb differs (stereochemically) in some respect from that observed with the other sapogenins.

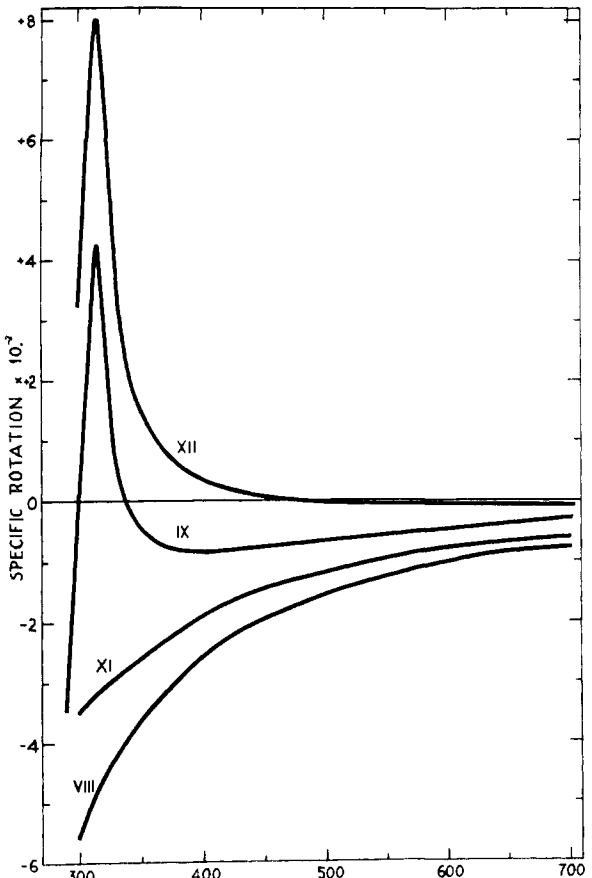


Fig. 2.—Rotatory dispersion curves of: yuccagenin (Δ^5-22a,25a-spirosten-2α,3β-diol (VIII)), kammogenin (Δ^5-22a,25a-spirosten-2α,3β-diol-12-one (IX)), samogenin (22a,-25a-spirostan-2β,3β-diol (XI)), mexogenin (22a,25a-spirostan-2β,3β-diol-12-one (XII)).

It has already been shown in the earlier papers of this series[1,3,4] that the most significant effects upon rotatory dispersion curves which lend themselves most readily to correlation with specific structural moieties are those in which strong chromophores notably carbonyl groups are present. Consequently, a number of naturally occurring as well as synthetically available keto-sapogenins have been investigated and the results are shown in Figs. 2–6. We were particularly interested in examining the validity of our earlier correlations to the sapogenin series, where the contribution of the carbonyl function would have to offset the strongly negative "background" rotation of the sapogenin skeleton, a feature which was absent in the other steroids[1,3,4] under investigation.

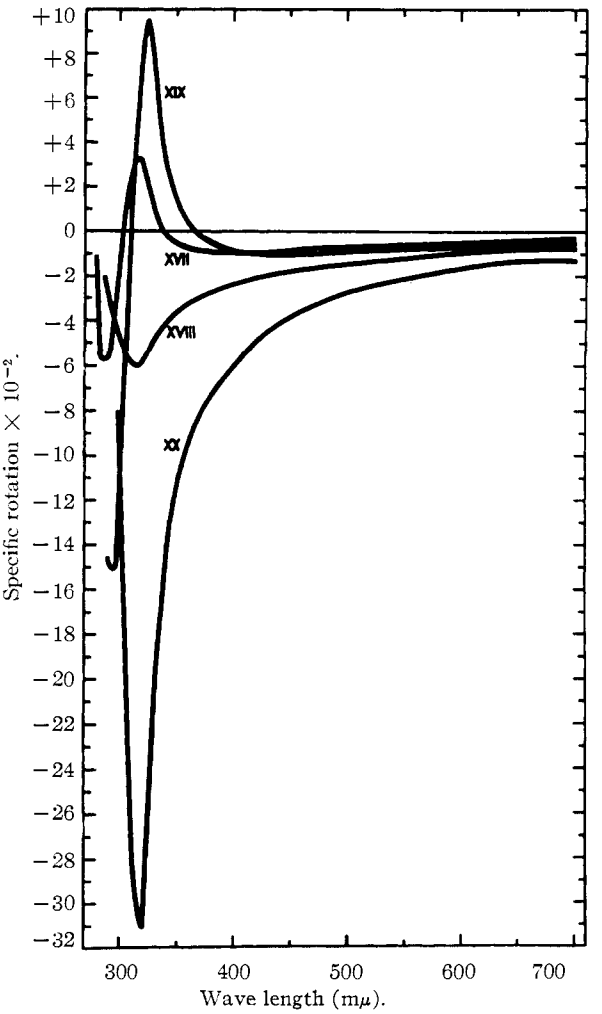
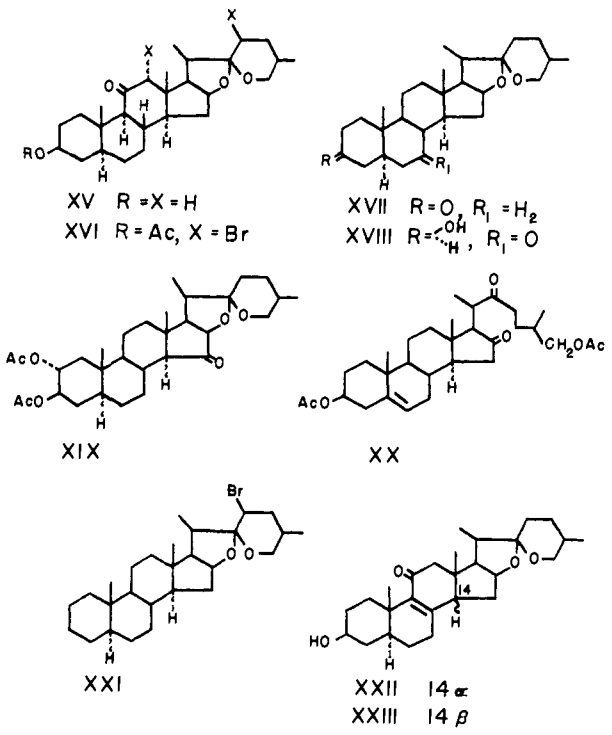


Fig. 3.—Rotatory dispersion curves of: tigogenone (22a,25a,5α-spirostan-3-one (XVII)), 22a,25a,5α-spirostan-3β-ol-7-one (XVIII), 22a,25a,5α-spirostan-2α,3β-diol-15-one diacetate (XIX), kryptogenin diacetate (Δ^5-cholesten-3β,26-diol-16,22-dione diacetate (XX)).

The changes produced when a carbonyl group is introduced at position 12 are illustrated in Fig. 2, where yuccagenin (VIII) and samogenin (XI) are compared with their 12-keto derivatives kammogenin (IX) and mexogenin (XII).[5] In each instance, the negative rotation is offset by a strongly positive one and both compounds show "maxima" at 315 mμ. While the negative peak could not be measured, it is clear that the 12-keto group is optically active and corresponds to an optically active absorption band at *ca.* 290–300 mμ as determined by the rough procedure of extrapolation through the zero rotation line. This value is in reasonable agreement with the observed ultraviolet absorption maximum of these substances around 280 mμ. Precisely the same type of curve is observed with hecogenin acetate (XIII) (Fig. 4) and it seems, therefore, that this type of carbonyl

(9) We are indebted to Dr. W. E. Rosen (Ciba Pharmaceutical Products, Inc., Summit, N. J.) for the cyclo-ψ-sapogenins.



group can be recognized quite readily by means of its rotatory dispersion curve.[9a]

Additional examples of isolated carbonyl groups are collected in Fig. 3. An interesting comparison is afforded between the 3-ketone, tigogenone (XVII) ("maximum" 315 mμ, "minimum" 285 mμ, optically active absorption band 300 mμ), and the 15-ketone, 22a,25a,5α-spirostane-2α,3β-diol-15-one diacetate (XIX)[10] ("maximum" 325 mμ, "minimum" 295 mμ, optically active absorption band 310 mμ), which completely parallels the results in the androstane series[3] between a 6-membered (androstan-3-one) and 5-membered (androstan-17-one) ring ketone. In each instance, the dispersion curves are quite similar, except that the cyclopentanone is more strongly active and gives rise to a much higher "maximum" which thus serves as a means of differentiation. The optically active absorption band of the 15-ketone XIX occurs at a slightly higher wave length (310 mμ), than that of the 3-ketone XVII (300 mμ) which again is in agreement with theory.[3] The carbonyl group at C-7 as in 7-ketotigogenin (XVIII) is also optically active, but in this case there occurs first a "minimum" and this has been found to be typical of other 7-keto 5α-steroids.[11] Thus while the location of the carbonyl group in saturated 3-keto- and 7-keto steroids cannot be predicted on the basis of the infrared absorption spectrum, this would appear to be a simple matter by means of the rotatory dispersion curve. Kryptogenin acetate (XX) is characterized by an extremely negative "minimum" ($[\alpha]_{320}$ −3105°) and this is almost certainly due mainly to the 16-carbonyl function since a very similar effect has been noted[11] with coprostan-16-one.

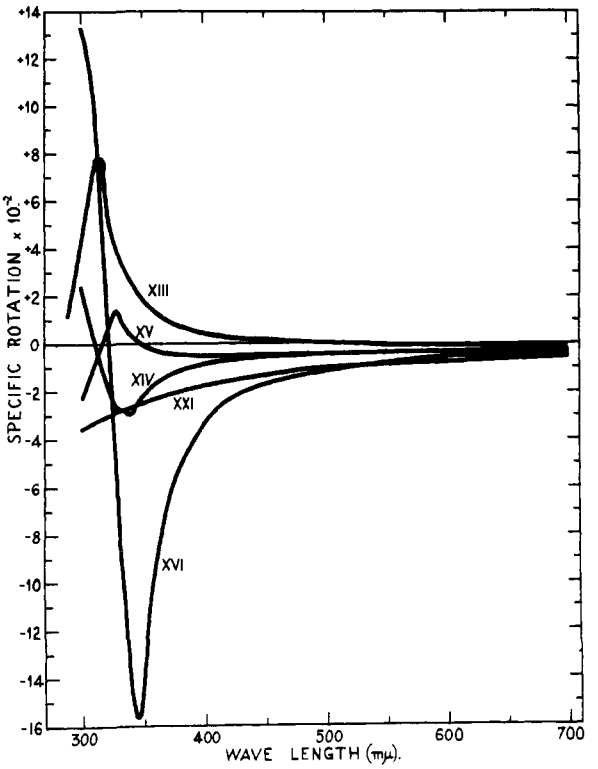


Fig. 4.—Rotatory dispersion curves of: hecogenin acetate (22a,25a,5α-spirostan-3β-ol-12-one acetate (XIII)), 11α,23-dibromo-22a,25a,5α-spirostan-3β-ol-12-one acetate (XIV), 22a,25a,5α-spirostan-3β-ol-11-one (XV), 12α,23-dibromo-22a,25a,5α-spirostan-3β-ol-11-one acetate (XVI), 23-bromo-desoxytigogenin (23-bromo-22a,25a,5α-spirostan (XXI)).

It seems pertinent at this point to emphasize another potentially very useful application of these rotatory dispersion measurements. In addition to utilizing the curves for the recognition of certain structural features, the availability of the dispersion curves may at times offer certain striking advantages for analytical purposes. For instance, in the commercial extraction of hecogenin (XIII), the crude sapogenin is usually accompanied by some tigogenin (II) and it is often cumbersome to determine the relative proportion of these sapogenins in such a mixture. While the rotations of the two substances (or their acetates as listed in the experimental section) differ by only 53° at the sodium D line (where specific rotations are usually measured), an inspection of Figs. 1 and 4 shows that their rotations differ by 1051° at 312.5 mμ. Consequently, the composition of a mixture of tigogenin and hecogenin (or their acetates) can be ascertained with a rather good degree of accuracy by simply determining the specific rotation at that wave length (in this instance 312.5 mμ) at which the rotations of the individual components of the mixture differ by the largest factor.

(9a) Since submission of this manuscript, we have obtained a sample of botogenin acetate (gentrogenin acetate) through the courtesy of Dr. M. E. Wall (THIS JOURNAL, **77**, 5196 (1955)) and as is to be expected, its rotatory dispersion curve (see experimental) is very similar to that of kammogenin (IX).

(10) C. Djerassi, T. T. Grossnickle and L. B. High, *Chemistry & Industry*, 473 (1955); C. Djerassi, L. B. High, J. Fried and E. F. Sabo, THIS JOURNAL, **77**, 3673 (1955).

(11) To be published.

This analytical application might prove useful in many other steroid mixtures, such as diosgenin (VI)–kryptogenin (XX) which differ in their rotations at 320 mμ by *ca.* 2600° (as compared to only 70° at 589 mμ), which often occur together in the same plant.

Cookson[12] recently has reported on a study of the ultraviolet absorption spectra of a series of steroidal ketones and their α-bromo derivatives and concluded that an equatorial bromine produces a hypsochromic shift of *ca.* 5 mμ while a strong bathochromic effect (*ca.* 28 mμ) is observed with the axially oriented epimer. It appeared of interest to examine whether this effect is also noticeable in the rotatory dispersion curve and Fig. 4 summarizes the data insofar as they are applicable to steroidal sapogenins. Since bromination in the sapogenin series invariably results in side chain substitution,[13] it was first necessary to establish that introduction of a halogen atom at C-23 would have no effect on the rotatory dispersion curve. That this assumption is correct is clearly shown by the curve of 23-bromo-22a,25a,5α-spirostan (XXI) (Fig. 4) which is essentially identical with that of the halogen-free parent compound I (Fig. 1). The two sapogenin ketones for which the relevant halo derivatives were available[14] and which were also studied by Cookson[12] are hecogenin (XIII) and

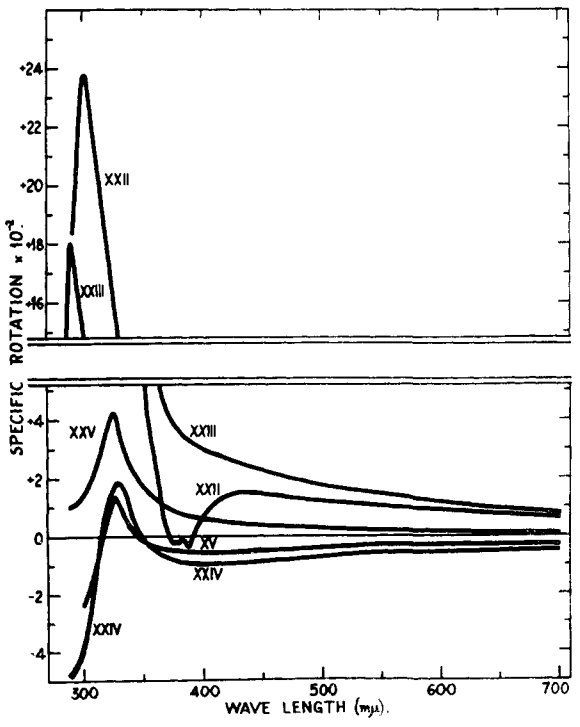


Fig. 5.—Rotatory dispersion curves of: 22a,25a,5α-spirostan-3β-ol-11-one (XV), Δ⁸-22a,25a,5α-spirosten-3β-ol-11-one (XXII), Δ⁸-22a,25a,5α,14β-spirosten-3β-ol-11-one (XXIII), 22a,25a,5α,8α-spirostan-3β-ol-11-one (XXIV), 22a,25a,5α,14β-spirostan-3β-ol-11-one (XXV).

11-ketotigogenin (XV). The curves of the two parent compounds XIII and XV are reproduced in Fig. 4 and while that of the 12-ketone, hecogenin acetate (XIII) ("maximum" $[\alpha]_{312.5}$ +783°) already has been discussed above, it is pertinent to point out that the 11-ketone XV exhibits the typical features—lower optical activity and bathochromic shift ("maximum" $[\alpha]_{325}$ +133°)—which have earlier[4] been associated with the isolated 11-ketone function. This represents a further example that generalizations concerning the relationship of carbonyl groups with dispersion curves appear to hold irrespective of the nature of the steroid skeleton.

In contrast to the situation observed with the ultraviolet absorption spectra,[12] the introduction of either an equatorial (XIV) or axial (XVI)[15] bromine atom adjacent to the carbonyl group produces practically the same change in the rotatory dispersion curve—namely, a pronounced inversion of the curve, the initial peak being 1000–1500° more negative than that of the halogen-free compound. Furthermore, the positions of the "minimum" are practically identical (340 and 345 mμ) and the points of intersection of the zero axis (presumably corresponding to the optically active absorption band and roughly related to the ultraviolet absorption maximum) differ to only a small extent (312 *vs.* 322 mμ). In either the equatorial (XIII *vs.* XIV) or axial (XV *vs.* XVI) case a bathochromic shift is produced irrespective of whether the position of the "minimum" or of the optically active absorption band is utilized for comparison purposes. The rotatory dispersion curves of a large number of steroidal halo ketones are now being measured in our laboratory and a general conclusion concerning the effect of α-halogen substitution is not justified until that study is complete.

The availability in this Laboratory[16] of 11-keto sapogenins differing only in the nature of the B/C or C/D ring juncture has prompted us to examine the possible effect of such a stereochemical alteration upon the rotatory dispersion curve and the relevant data are collected in Fig. 5. Changes in the C/D juncture could be examined in two pairs. In the first instance, Δ⁸-22a,25a,5α-spirosten-3β-ol-11-one (XXII) was compared with its 14β-isomer XXIII and two changes could be noted. The former exhibits fine structure in the 350–450 mμ region reminiscent of the rotatory dispersion curves of Δ⁴-3-keto steroids[1,3,4] and this feature is much less pronounced in the 14β-derivative XXIII. Furthermore, inversion at C-14 usually has been associated[16] with an increase in the rotation at the sodium D line, but a significant reversal of this trend is noticeable at the point (290–300 mμ) of maximum rotation.

The rotatory dispersion curves of three, isomeric, saturated 11-keto steroids are reproduced in Fig. 5. Here inversion at C-14 (XV *vs.* XXV) involves a

(12) R. C. Cookson, *J. Chem. Soc.*, 282 (1954).

(13) *Cf.* R. E. Marker and E. Rohrmann, THIS JOURNAL, **61**, 846 (1939).

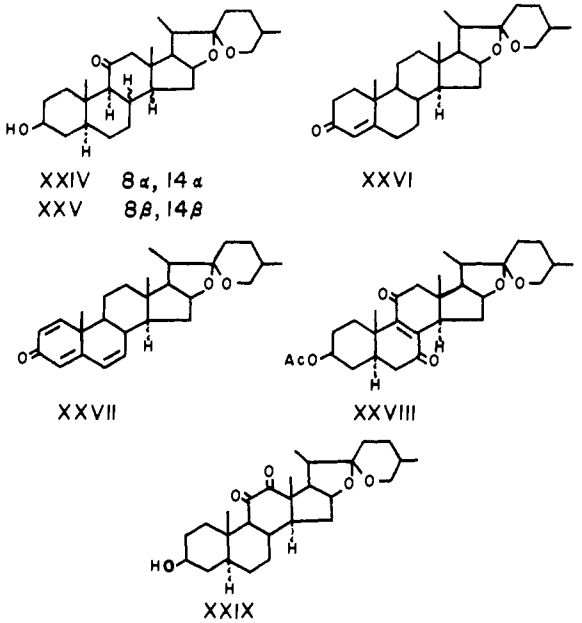
(14) J. W. Cornforth, J. M. Osbond and G. H. Phillips, *J. Chem. Soc.*, 907 (1954), and references cited. We are grateful to Dr. Cornforth for providing us with samples of the two bromo ketones.

(15) The fact that the parent substance XV was measured as the free alcohol and the bromo derivative as the 3-acetate XVI should have no bearing on the validity of the comparison, since it has been found with numerous sapogenin alcohols that acetylation produces no change in the shape of the dispersion curve (see Experimental section).

(16) C. Djerassi and G. H. Thomas, *Chemistry & Industry*, 1228 (1954); C. Djerassi, W. Frick, G. Rosenkranz and F. Sondheimer, THIS JOURNAL, **75**, 3496 (1953).

shift to higher rotation throughout the measured spectral range, the only difference being the position of the optically active absorption band (*i.e.* intersection of zero axis) associated with the 11-keto group[3] which in the 14β-isomer XXV has been shifted from 314 to below 300 mμ, an observation which is not paralleled by the ultraviolet absorption spectra. Inversion at C-8 (XV *vs.* XXIV) produces no particular change in the position of the "maximum" or the optically active absorption band other than that the 8α-isomer possesses a more negative rotation at the sodium D line but a more positive one at the "maximum." In conclusion, it can be stated that while isomerization at C-8 or C-14 produces some changes in the rotary dispersion curve, they are of a sufficiently subtle nature so that a considerable number of cases would have to be presented before some generalizations can be made.

In Fig. 6 are collected the curves of some miscellaneous unsaturated ketones. Δ^4-22a,25a-Spirosten-3-one (XXVI) and the corresponding 1,4,6-trienone XXVII were selected because the rotatory dispersion curves of other steroids[1,3,4] possessing the same chromophores exhibit very characteristic fine structures in the 350-400 mμ region. These features are clearly typical of such chromophores although no direct correlation with their ultraviolet absorption spectra is possible at this time.[3] It was of interest to determine whether these features would be recognizable in the case of sapogenins where they would be superimposed upon the strongly negative "background" rotation. An inspection of the curves and of the positions of the "maxima" and "minima" over the 350-400 mμ range listed in the Experimental portion show a striking coincidence with the earlier described[3] curves and values, in spite of the presence of the spiroketal system, thus demonstrating that fairly broad empirical correlations of dispersion curve shapes with certain structural groupings can be made safely throughout the steroid series. The remaining two compounds, the Δ^8-7,11-dione XXVIII and the 11,12-dione XXIX, are the first representatives of such chromophores for which dispersion curves have been constructed and no generalizations can be made at the present time. However, the rather sharp "maxima" and "minima" of the 11,12-diketone XXIX in the 300–400 mμ region are quite unusual and are probably associated with the diketone and/or enol moiety.



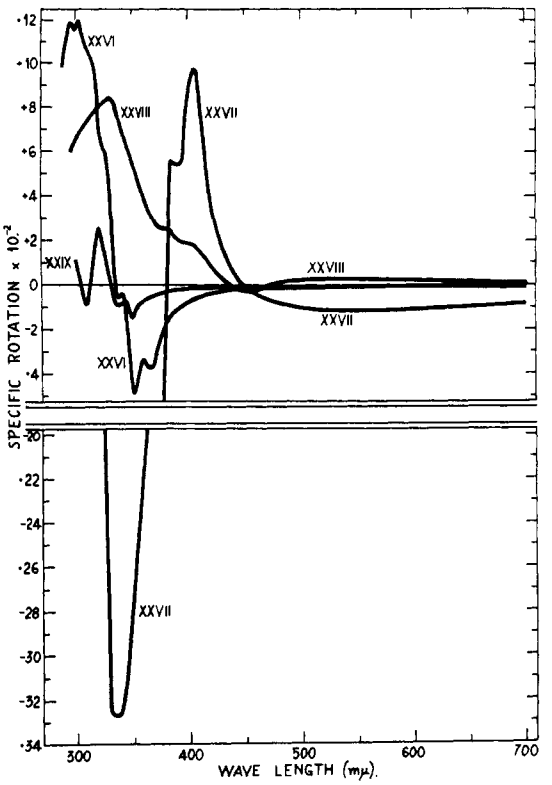


Fig. 6.—Rotatory dispersion curves of: Δ^4-22a,25a-spirosten-3-one (XXVI), $\Delta^{1,4,6}$-22a,25a-spirostatrien-3-one (XXVII), Δ^8-22a,25a,5α-spirosten-3β-ol-7,11-dione acetate (XXVIII), 11-ketohecogenin (22a,25a,5α-spirostan-3β-ol-11,12-dione (XXIX)).

Experimental[17]

Desoxytigogenin (I).—R.D. (Fig. 1.): $[\alpha]_{700}$ −65°, $[\alpha]_{589}$ −80°, $[\alpha]_{290}$ −358°; *c* 0.10, temp. 26°.

Tigogenin (II).—R.D.: $[\alpha]_{700}$ −37°, $[\alpha]_{589}$ −58°, $[\alpha]_{300}$ −248°; *c* 0.10, temp. 29°.

Tigogenin Acetate.—R.D.: $[\alpha]_{700}$ −52°, $[\alpha]_{589}$ −63°, $[\alpha]_{300}$ −297°; *c* 0.11, temp. 25°.

Gitogenin (III).—R.D. (Fig. 1): $[\alpha]_{700}$ −48°, $[\alpha]_{589}$ −68°, $[\alpha]_{300}$ −285°; *c* 0.09, temp. 25°.

Chlorogenin (IV).—R.D. (Fig. 1): $[\alpha]_{700}$ −32°, $[\alpha]_{589}$ −39°, $[\alpha]_{300}$ −187°; *c* 0.10, temp. 24°.

Digitogenin (V).—R.D.: $[\alpha]_{700}$ −57°, $[\alpha]_{589}$ −72°, $[\alpha]_{300}$ −341°; *c*, 0.10, temp. 24°.

Diosgenin (VI).—R.D. (Fig. 1): $[\alpha]_{700}$ −77°, $[\alpha]_{589}$ −113°, $[\alpha]_{300}$ −556°; *c* 0.10, temp. 25°.

Cyclo-ψ-diosgenin.—R.D.: $[\alpha]_{700}$ −76°, $[\alpha]_{589}$ −105°, $[\alpha]_{300}$ −475°; *c* 0.09, temp. 25°.

Pennogenin (VII).—R.D.: $[\alpha]_{700}$ −87°, $[\alpha]_{589}$ −111°, $[\alpha]_{300}$ −512°; *c* 0.10, temp. 24°.

Smilagenin (X).—R.D. (Fig. 1): $[\alpha]_{700}$ −49°, $[\alpha]_{589}$ −69°, $[\alpha]_{300}$ −289°; *c* 0.10, temp. 24°.

(17) All measurements were carried out in dioxane solution by the procedure outlined in ref. 3. With the exception of the substances listed in ref. 9 and 14, all other sapogenins came from the collection of C. D.

Cyclo-ψ-smilagenin: R.D.: $[\alpha]_{700}$ −50°, $[\alpha]_{589}$ −62°, $[\alpha]_{300}$ −305°; *c* 0.10, temp. 25°.

Sarsasapogenin (Xa).—R.D. (Fig. 1): $[\alpha]_{700}$ −53°, $[\alpha]_{589}$ −82°, $[\alpha]_{300}$ −351°; *c* 0.08, temp. 30°.

Cyclo-ψ-sarsasapogenin (Xb).—R.D. (Fig. 1): $[\alpha]_{700}$ +32°, $[\alpha]_{589}$ +37°, $[\alpha]_{300}$ +196°; *c* 0.11, temp. 24°.

Yuccagenin (VIII).—R.D. (Fig. 2): $[\alpha]_{700}$ −80°, $[\alpha]_{589}$ −108°, $[\alpha]_{300}$ −556°; *c* 0.11, temp. 25°.

Yuccagenin Diacetate.—R.D.: $[\alpha]_{700}$ −98°, $[\alpha]_{589}$ −134°, $[\alpha]_{300}$ −643°; *c* 0.11, temp. 30°.

Kammogenin (IX).—R.D. (Fig. 2): $[\alpha]_{700}$ −28°, $[\alpha]_{589}$ −51°, $[\alpha]_{290}$ −337°; "min." $[\alpha]_{385}$ −84°; "max." $[\alpha]_{315}$ +424°; *c* 0.10, temp. 25°; u.v. λ_{max} 288 mμ, log ε 1.65.

Samogenin (XI).—R.D. (Fig. 2): $[\alpha]_{700}$ −60°, $[\alpha]_{589}$ −82°, $[\alpha]_{300}$ −350°; *c* 0.08, temp. 24°.

Mexogenin (XII).—R.D. (Fig. 2): $[\alpha]_{700}$ −7°, $[\alpha]_{589}$ −6°, $[\alpha]_{300}$ +324°; "max." $[\alpha]_{315}$ +802°; *c* 0.10, temp. 25°; u.v. λ_{max} 290 mμ, log ε 1.62.

Tigogenone (XVII).—R.D. (Fig. 3): $[\alpha]_{700}$ −39°, $[\alpha]_{589}$ −56°, $[\alpha]_{280}$ −175°; "min." $[\alpha]_{395}$ −99°; "max." $[\alpha]_{315}$ +326°; "min." $[\alpha]_{295}$ −569°; *c* 0.08, temp. 24°.

22a,25a,5α-Spirostan-3β-ol-7-one (XVIII).—R.D. (Fig. 3): $[\alpha]_{700}$ −78°, $[\alpha]_{589}$ −103°, $[\alpha]_{290}$ −286°; "min." $[\alpha]_{315}$ −598°; *c* 0.10, temp. 30°; u.v. λ_{max} 284 mμ, log ε 1.53.

22a,25a,5α-Spirostan-2α,3β-diol-15-one Diacetate (XIX).—R.D. (Fig. 3): $[\alpha]_{700}$ −55°, $[\alpha]_{589}$ −74°, $[\alpha]_{290}$ −1472°; "min." $[\alpha]_{450}$ −103°; "max." $[\alpha]_{325}$ +949°; "min." $[\alpha]_{295}$ −1510°; *c* 0.09, temp. 25°; u.v. flat λ 280–305 mμ, log ε 1.55.

Kryptogenin Diacetate (XX).—R.D. (Fig. 3): $[\alpha]_{700}$ −133°, $[\alpha]_{589}$ −182°, $[\alpha]_{300}$ −960°; "min." $[\alpha]_{320}$ −3105°; *c* 0.08, temp. 23°.

Hecogenin Acetate (XIII).—R.D. (Fig. 4): $[\alpha]_{700}$ −13°, $[\alpha]_{589}$ −10°, $[\alpha]_{290}$ + 154°; "max." $[\alpha]_{312.5}$ +783°; *c* 0.09, temp. 28°; u.v. λ_{max} 280 mμ, log ε 1.79.

11α,23-Dibromo-hecogenin Acetate (XIV).—R.D. (Fig. 4): $[\alpha]_{700}$ −21°, $[\alpha]_{589}$ −26°, $[\alpha]_{300}$ +227°; "min." $[\alpha]_{340}$ −287°; *c* 0.08, temp. 25°; u.v. flat λ 275–288 mμ, log ε 1.90.

12α,23-Dibromo-11-keto-tigogenin Acetate (XVI).—R.D. (Fig. 4): $[\alpha]_{700}$ −41°, $[\alpha]_{589}$ −70°, $[\alpha]_{300}$ +1319°; "min." $[\alpha]_{345}$ −1566°; *c* 0.07, temp. 29°; u.v. λ_{max} 316 mμ, log ε 2.21.

23-Bromo-desoxytigogenin (XXI).—R.D. (Fig. 4): $[\alpha]_{700}$ −54°, $[\alpha]_{589}$ −82°, $[\alpha]_{300}$ −358°; *c* 0.07, temp. 28°.

11-Keto-tigogenin (XV).—R.D. (Fig. 5): $[\alpha]_{700}$ −32°, $[\alpha]_{589}$ −31°, $[\alpha]_{300}$ −226°; "min." $[\alpha]_{410}$ −57°; "max." $[\alpha]_{325}$ + 133°; *c* 0.11, temp. 26°; u.v. λ_{max} 290 mμ, log ε 1.62.

Δ⁵-22a,25a,5α-Spirosten-3β-ol-11-one (XXII).—R.D. (Fig. 5): $[\alpha]_{700}$ +63°, $[\alpha]_{589}$ +89°, $[\alpha]_{290}$ +1707°; "max." $[\alpha]_{450}$ + 144°; "min." $[\alpha]_{445}$ + 137°; "max." $[\alpha]_{440}$ +144°; "min." $[\alpha]_{425}$ +132°; "max." $[\alpha]_{420}$ +143°; "min." $[\alpha]_{387.5}$ −36°; "max." $[\alpha]_{382.5}$ −11°; "min." $[\alpha]_{380}$ −28°; "max." $[\alpha]_{377.5}$ −26°; "min." $[\alpha]_{375}$ −29°; "max." $[\alpha]_{300}$ +2371°; *c* 0.08, temp. 29°; u.v. flat λ 314–333 mμ, log ε 1.89.

Δ⁵-22a,25a,5α,14β-Spirosten-3β-ol-11-one (XXIII).—R.D. (Fig. 5): $[\alpha]_{700}$ +75°, $[\alpha]_{589}$ +116°, $[\alpha]_{285}$ +1204°; "max." $[\alpha]_{427.5}$ +258°; "min." $[\alpha]_{425}$ +255°; "max." $[\alpha]_{405}$ +304°; "min." $[\alpha]_{400}$ +302°; "max." $[\alpha]_{397.5}$ +312°; "min." $[\alpha]_{395}$ +307°; "max." $[\alpha]_{290}$ +1799°; *c* 0.06, temp. 30°; u.v. λ_{max} 330 mμ, log ε 1.81.

22a,25a,5α,8α-Spirostan-3β-ol-11-one (XXIV).—R.D. (Fig. 5): $[\alpha]_{700}$ −51°, $[\alpha]_{589}$ −60°, $[\alpha]_{290}$ −490°; "min." $[\alpha]_{400}$ −100°; "max." $[\alpha]_{330}$ +183°; *c* 0.10, temp. 28°.

22a,25a,5α,14β-Spirostan-3β-ol-11-one (XXV).—R.D. (Fig. 5): $[\alpha]_{700}$ +8°, $[\alpha]_{589}$ +10°, $[\alpha]_{290}$ +97°; "max." $[\alpha]_{325}$ +419°; *c* 0.11, temp. 24°; u.v. flat λ 296–308 mμ, log ε 1.62.

Δ⁴-22a,25a-Spirosten-3-one (XXVI).—R.D. (Fig. 6): $[\alpha]_{700}$ +7°, $[\alpha]_{589}$ −14°, $[\alpha]_{290}$ +1014°; "min." $[\alpha]_{365}$ −371°; "max." $[\alpha]_{360}$ −339°, "min." $[\alpha]_{352.5}$ −479°; "max." $[\alpha]_{340}$ −41°; "min." $[\alpha]_{337.5}$ −58°, "max." $[\alpha]_{302.5}$ +1191°; "min." $[\alpha]_{300}$ +1157°; "max." $[\alpha]_{295}$ +1182°; *c* 0.04, temp. 27°.

Δ¹,⁴,⁶-22a,25a-Spirostatrien-3-one (XXVII).—R.D. (Fig. 6): $[\alpha]_{700}$ −87°, $[\alpha]_{589}$ −114°, $[\alpha]_{300}$ −105°; "min." $[\alpha]_{550}$ −121°; "max." $[\alpha]_{405}$ +973°; "min." $[\alpha]_{390}$ +536°; "max." $[\alpha]_{385}$ +554°; "min." $[\alpha]_{335}$ −3272°; "max." $[\alpha]_{320}$ −5°; *c* 0.06, temp. 24°.

Δ⁵-22a,25a,5α-Spirosten-3β-ol-7,11-dione Acetate (XXVIII).—R.D. (Fig. 6): $[\alpha]_{700}$ +12°, $[\alpha]_{589}$ +19°, $[\alpha]_{300}$ +650°; "max." $[\alpha]_{520}$ +25°; "min." $[\alpha]_{450}$ −37°; "max." $[\alpha]_{330}$ +840°; *c* 0.06, temp. 25°.

11-Ketohecogenin (XXIX).—R.D. (Fig. 6): $[\alpha]_{700}$ −16°, $[\alpha]_{589}$ −8°, $[\alpha]_{300}$ −102°; "min." $[\alpha]_{365}$ −62°; "max." $[\alpha]_{362.5}$ −60°, "min." $[\alpha]_{350}$ −100°; "max." $[\alpha]_{345}$ −79°; "min." $[\alpha]_{340}$ −88°; "max." $[\alpha]_{320}$ +249°; "min." $[\alpha]_{305}$ −88°; *c* 0.09, temp. 25°.

Botogenin Acetate (Gentrogenin Acetate[9a]).—R. D.: $[\alpha]_{700}$ −53°, $[\alpha]_{589}$ −70°, $[\alpha]_{285}$ −896°; "min." $[\alpha]_{410}$ −116°, "max." $[\alpha]_{315}$ +585°; *c* 0.1, temp. 25°.

DETROIT, MICHIGAN

[CONTRIBUTION NO. 191 FROM JACKSON LABORATORY, E. I. DU PONT DE NEMOURS & CO.]

Condensation of Phthalideneacetic Acid with Naphthalenes to Form Benzopyrenequinones

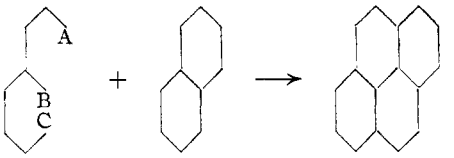
BY H. E. SCHROEDER, F. B. STILMAR AND F. S. PALMER

RECEIVED JUNE 22, 1955

An unusual and remarkably simple one-step synthesis of benzopyrenequinones has been found in the condensation of phthalideneacetic acid with naphthalenes in the presence of anhydrous hydrogen fluoride at moderate temperatures. It is applicable to naphthalene and homologs, fluoranthene and anthracene.

Studies of polynuclear substances frequently are hampered by the difficulty of synthesizing the specific derivatives needed. Furthermore, because of the many steps involved, customary procedures which involve cyclization of properly fashioned side chains into *ortho* or peri positions usually give inadequate yields of products.

In a search for more effective reactions for synthesis of polynuclear compounds, which would permit joining of larger fragments in a specific manner, attention was focused on simultaneous attack at the 1-, 2- and 8-positions in a naphthalene nucleus by use of six-membered carbon chains with functional groups appropriately situated as indicated.



Phthalideneacetic acid[1] appeared particularly well suited to such an approach since it should afford a 3,4-benzopyrene-1,5-quinone (benzo[a]pyrene-6,12-dione) as schematically illustrated by

(1) S. Gabriel and A. Michael, *Ber.*, **10**, 1554 (1877); S. Gabriel and A. Neumann, *ibid.*, **26**, 952 (1893).