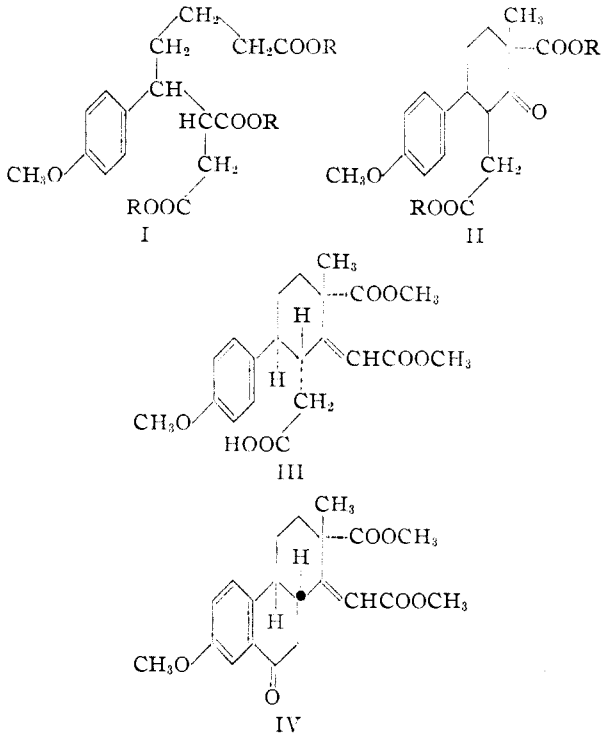

from the Stobbe condensation of diethyl succinate with ethyl γ-anisoylbutyrate (prepared *via* the Friedel–Crafts reaction of glutaric anhydride with anisole). Dieckmann cyclization of the trimethyl ester I (R = CH_3) and methylation *in situ* gave the keto diester II (R = CH_3), m.p. 95–95.5°, which was crystallized directly from the reaction mixture in 36% yield.

Reformatsky reaction of II (R = CH_3) with methyl bromoacetate gave a mixture of a lactone (m.p. 112.5–113°; *Anal.* Calcd. for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.67; H, 6.75) and hydroxy ester (m.p. 101.2–101.9°; *Anal.* Calcd. for $C_{22}H_{30}O_8$: C, 62.54; H, 7.16. Found: C, 62.63; H, 7.27), which was not separated but treated directly with formic acid (to lactonize the hydroxy ester) followed by dilute sodium hydroxide which converted the mixture of isomeric lactones into essentially one form of the unsaturated mono acid III, m.p. 121–122°; *Anal.* Calcd. for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.92; H, 6.78. Cyclization of III by the inverse Friedel–Crafts method[3] gave a single keto diester IV, m.p. 147.8–148.4°; *Anal.* Calcd. for $C_{21}H_{24}O_6$: C, 67.72; H, 6.50. Found: C, 68.02; H, 6.94. Hydrogenolysis of the keto group over palladium catalyst promoted by perchloric acid[4] yielded a single unsaturated diester IV (methylene in place of keto group), m.p. 112–112.2° (perhaps the same as Anner and Miescher's[5] isomer m.p. 113–115°), which on further hydrogenation in neutral medium gave practically exclusively, racemic dimethyl marrianolate methyl ether, m.p. 99.5–100° (reported,[5] 95–96°). At this stage all four of the asymmetric centers have been introduced, and the subsequent steps involve no stereochemical problems. Partial saponification and homologation by the Arndt–Eistert reaction afforded, as previously described,[5] homomarrianolic acid methyl ether, m.p. 224.2–225.8°, undepressed on admixture with authentic material.[6] Cyclization of the dibasic acid yielded *dl*-estrone methyl ether, m.p. 143.2–144.2°, undepressed on admixture with an authentic specimen.[6] The demethylation and resolution of this product have already been described.[5,6]

(3) W. S. Johnson and H. J. Glenn, THIS JOURNAL, **71**, 1092 (1949).

(4) The method of Kindler; see K. W. Rosenmund and E. Karg, *Ber.*, **75**, 1850 (1942).

(5) G. Anner and K. Miescher, *Helv. Chim. Acta*, **31**, 2173 (1948).

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VARIATION OF ELECTRIC DIPOLE MOMENT WITH BOND LENGTH

Sir:

A quantity of importance for the understanding of absorption intensities in the infrared is ϵ, the derivative of the electric dipole moment of a bond with respect to the bond length, evaluated at the equilibrium internuclear distance.[1] Bartholomé[2] has estimated ϵ for HCl, HBr and HI from absorption intensities; experimental difficulties make the values thus obtained somewhat uncertain.

Recently a new point of view as to the origin of electric dipole moments in molecules has been published.[3] It seems worth while to consider the variation of electric dipole moment with internuclear distance from the new point of view. According to equation (9) of the paper just mentioned, with accompanying discussion, a bond moment may be considered as arising from an internal field, E, of the form

$$E = e\left[\frac{Z_a}{R_a^2} - \frac{Z_b}{R_b^2}\right] \qquad (1)$$

where the symbols have the same significance as previously. The bond moment is then given by the product of this field and the longitudinal polarizability, b_1, so that

$$\epsilon = \frac{du}{dR} = b_1\frac{dE}{dR} + E\frac{db_1}{dR} \qquad (2)$$

Consider first

$$\frac{dE}{dR} = e\frac{d}{dR}\left(\frac{Z_a}{R_a^2}\right) - e\frac{d}{dR}\left(\frac{Z_b}{R_b^2}\right) \qquad (3)$$

This term we claim to be effectively zero or negligible compared to the other term composing ϵ; the reason for this is as follows. As was pointed out in the previous paper,[3] the quantity E is a small difference of two large quantities. Neglecting this small difference, we find

$$Z_a/R_a^2 \approx Z_b/R_b^2 \qquad (4)$$

for two atoms a and b; hence Z/R^2 must be approximately the same for different atoms. It therefore seems reasonable to assume that this quantity is approximately constant for the *same* atom when a

(1) L. Pauling and E. B. Wilson, Jr., "Introduction to Quantum Mechanics," McGraw-Hill Book Co., Inc., New York, N. Y., 1935, pp. 309–310.

(2) E. Bartholomé, *Z. physik. Chem.*, **B23**, 131 (1933).

(3) R. P. Smith, T. Ree, J. L. Magee, and H. Eyring, THIS JOURNAL, **73**, 2263 (1951).

bond, of which it is a part, is stretched, so that the right side of eq. (3) may be equated to zero, at least to good approximation for our purposes. Or, alternatively, we may simply say that the field, E, may be assumed constant for small stretchings of a bond, the change in the longitudinal polarizability being the more important quantity. With this assumption, together with equation (9) of the preceding paper,[3] eq. (2) reduces to

$$\epsilon = \frac{\mu}{b_1} \cdot \frac{db_1}{dR} \qquad (5)$$

For H–X molecules, Denbigh[4] found $b_t/b_1 = 0.75$. Assuming this relation to be satisfied as the bond is stretched, we find, using $\alpha = (1/3)(b_1 + 2b_t)$, that $db_1/dR = 1.20\ d\alpha/dR$. Hence we are now prepared to calculate values of ϵ for diatomic molecules for which μ, b_1, and $d\alpha/dR$ are known experimentally, namely, HCl and HBr. These data, together with calculated and observed values of ϵ, are summarized in Table I.

TABLE I

CALCULATED AND OBSERVED VALUES OF ϵ FOR HCl AND HBr

Molecule	μ, D	b_1, Å	$d\alpha/dR$, Å	ϵ(calcd.), e	ϵ(obs.), e
HCl	1.03	3.13	1.23	0.102	0.086
HBr	0.79	4.23	1.07	0.050	0.075

Since both the observed ϵ values and the $d\alpha/dR$ values are somewhat uncertain, the agreement between calculated and observed ϵ values seems satisfactory, and apparently adds justification to the use of the model we have proposed for the origin of electric dipole moments.

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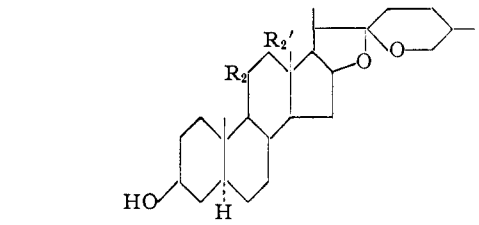
RECEIVED SEPTEMBER 24, 1951

(4) K. G. Denbigh, *Trans. Faraday Soc.*, **36**, 936 (1940).
(5) R. P. Bell, *ibid.*, **38**, 422 (1942).
(6) Department of Chemistry, Harvard University, Cambridge, Mass.

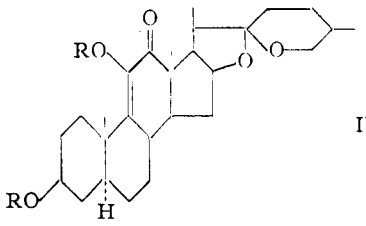
STEROIDAL SAPOGENINS. XV. EXPERIMENTS IN THE HECOGENIN SERIES (PART 3).[1] CONVERSION TO CORTISONE

Sir:

In two recent communications[2,3] there was recorded the partial synthesis of cortisone from ring C unsubstituted plant steroids such as diosgenin, ergosterol and stigmasterol. Another potentially very attractive starting material for the preparation of cortisone is the class of C-12 oxygenated steroidal sapogenins, as exemplified by hecogenin (I) (22-isoallospirostan-3β-ol-12-one), which occurs in a wide variety of *Agave's* indigenous to the southwestern part of the United States,[4] Mexico,[4] and East Africa.[5] We should now like to record the successful conversion of hecogenin to cortisone.



I $R_2 = H_2$, $R_2' = O$
II $R_2 = O$, $R_2' =$ 
III $R_2 = R_2' = O$
V $R_2 = O$, $R_2' = H_2$



IVa R = H
b R = Ac

Of the two most useful methods[6,7] employed in the bile acid series for shifting a keto group from position 12 to C-11, that of Kendall and co-workers[6] is inapplicable to hecogenin (I) and related sapogenins, because they do not possess the required steric configuration at C-3 (α) and C-5 (β); Gallagher's[7] procedure in its initial stages (bromination at C-11, followed by alkaline hydrolysis and isomerization to the 11-one-12β-ol) as applied[8] to hecogenin (I) leads in good yield to 22-isoallospirostan-3β,12β-diol-11-one (II), but the subsequent reaction of a 3-monoacylated-12-ol with phosphorus tribromide proceeds exceedingly poorly in the sapogenin series because of interaction with the spiroketal side chain. It has now been observed that bismuth oxide, a specific oxidizing agent for acyloins,[9] does not attack tigogenin (22-isoallospirostan-3β-ol), but reacts smoothly with a ketol such as methyl 3α,12β-dihydroxy-11-ketocholanate (Marker-Lawson acid)[10] to afford after acetylation the known[11] enol acetate of methyl 3α-acetoxy-11,12-diketocholanate (m.p. 130–132°, $[\alpha]^{20}D$ +117°, $\lambda_{max.}^{EtOH}$ 244 mμ, log ϵ 3.97; found: C, 69.31; H, 8.70). On applying the bismuth oxide oxidation (18 hrs. refluxing in acetic acid solution) to 22-isoallospirostan-3β,12β-diol-11-one (II),[8] there was obtained in over 70% yield 22-isoallospirostan-3β-ol-11,12-dione as a mixture of keto (III) and enol forms (m.p. 196–197°, dark green color with ferric chloride, $[\alpha]^{20}D$ −21° (all rotations in chloroform), $\lambda_{max.}^{EtOH}$ 282 mμ, log ϵ 3.28; found: C, 73.45; H, 9.40), further characterized by the exceedingly soluble enol acetate, Δ^9-22-isoallospirosten-3β,11-diol-12-one 3,11-diacetate (IVb) (m.p. 188–192°, $[\alpha]^{20}D$ +14°, $\lambda_{max.}^{EtOH}$ 244 mμ, log ϵ 4.05; found: C, 70.90; H, 8.31). Huang-Minlon reduction[12] of III yielded 22-isoallospirostan-3β-ol-11-one (V), contaminated by some of the 11-hydroxy derivative and purifica-

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(5) R. K. Callow, J. W. Cornforth and P. C. Spensley, *Chemistry and Industry*, 699 (1951).
(6) B. F. McKenzie, V. R. Mattox, L. L. Engel and E. C. Kendall, *J. Biol. Chem.*, **173**, 271 (1948), and earlier papers.
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(9) W. Rigby, *J. Chem. Soc.*, 793 (1951).
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(11) O. Wintersteiner and M. Moore, *ibid.*, **162**, 725 (1946).
(12) Huang-Minlon, THIS JOURNAL, **68**, 2487 (1946).