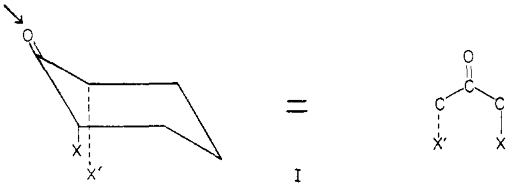
the chlorine or bromine is to the *left* (I, X′ = Cl or Br) the effect will be *negative*.[8]



I

Since the axially-oriented bromine or chlorine substituent in α-halocyclohexanones is often the more stable one,[9] the presently described method for the determination of absolute configuration of such ketones should be rather widely applicable. The steps to be taken are simple and particularly if the first one can be omitted, the entire sequence can be carried out on a micro-scale without using up any material: (a) if both α and α′ positions can be substituted and the exact location of the halogen atom does not follow from its mode of preparation (*e.g.*, epoxide opening followed by oxidation), then this must be established chemically—usually by dehydrohalogenation; (b) the axial orientation[10] of the α-halocyclohexanone must be confirmed by ultraviolet[7] and infrared[9,11] measurements; (c) the rotatory dispersion curve must be measured. It is then possible to determine in the manner illustrated above (*cf.* I) which one of the two absolute configurations leads to the observed (positive or negative) Cotton effect.

Attention should be called to two further applications of rotatory dispersion measurements among α-halocyclohexanones. If the absolute configuration of the parent ketone is known but the location (α or α′) of the axial halogen atom is not, then the rotatory dispersion curve will provide the answer. Conversely, if information concerning the absolute configuration of the ketone and the location of the halogen substituent is available, but spectroscopic determination of the orientation of the halogen atom is obscured by additional carbonyl groups, a decision may be reached by means of the rotatory dispersion curve. An interesting example is provided by the two epimeric methyl 3α-acetoxy-11-bromo-12-ketocholanates[12] which possess virtually identical rotations ($[\gamma]_{\mathrm{D}}$ +44° and +40°) at the conventional sodium D line. However, the rotatory dispersion curves[4] disclose that once rotation measurements are continued in the ultraviolet range, a marked change is noted. In agreement with the postulates made in this paper, the equatorial 11α-bromo isomer exhibits a positive Cotton effect (peak[6] at 295 mμ, [α] +498°) as does the halogen-free 11-ketone,[13] while the axial 11β-isomer shows a strong negative Cotton effect (trough[6] at 337.5 mμ, [α] −1020°).

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[8] This effect may be so pronounced that it may carry over into the visible range of the spectrum. Consequently, at times even comparisons of molecular rotation differences (based only on $[\alpha]_{\mathrm{D}}$ values) with steroid reference compounds may be used as has been done in the friedelin series (E. J. Corey and J. J. Ursprung, THIS JOURNAL, **78**, 5041 (1956)).

[9] E. J. Corey and H. J. Burke, *ibid.*, **77**, 5418 (1955), and earlier papers. See, however, W. D. Kumler and A. C. Huitric, *ibid.*, **78**, 3369 (1956).

[10] It appears (ref. 4) that even if the equatorial orientation is the more stable one it might still be possible to use this method if the corresponding *gem*-dihalo ketone is available since one of the halogen atoms must now be axial.

[11] R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1952).

[12] Kindly provided by Dr. T. F. Gallagher, Sloan-Kettering Institute for Cancer Research.

[13] C. Djerassi and W. Closson, THIS JOURNAL, **78**, 3761 (1956).

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RECEIVED FEBRUARY 14, 1957

MULTILAYER MEMBRANE ELECTRODES[1]

Sir:

We have prepared a new membrane which is permeable almost exclusively to certain ions in the presence of other ions of the same charge. These membranes are multilayers, where transport of the potential-determining ion is *transverse* to the axis of orientation.

Membranes were constructed by cracking a standard slide in half, so as to insure a nearly perfect fit, because the effective membrane pore width was 2.5 × 10^{-5} cm. Each glass half-slide was coated with 50 Y-type monolayers of barium stearate, the two halves fitted together and cemented in place between slides having holes in their centers, arms were attached for solutions and the potential measured between saturated calomel electrodes.

The resistance of this membrane was 5.8 × 10^7 ohms. Accordingly, a highly sensitive Keithley Model 200 B vacuum-tube voltmeter accurate to ± 1% was used with proper shielding. A constant asymmetry potential of 1–3 mv. for identical barium chloride solutions was read; constant and stable potential readings were obtained rapidly.

Preliminary results obtained with this Multilayer Membrane Electrode are given. Experimentally determined potentials were corrected for asymmetry. Calculated e.m.f. values were obtained using the tabulated data of Conway[2]; at higher concentrations, mean activity coefficients were used. For dilute (< 0.02 *M*) solution pairs whose concentration ratio was less than 2:1, calculated e.m.f. values were reasonably accurate.

Multilayer Membrane Electrodes are shown to be reversible to barium ions, even in the presence of high concentrations of sodium ions. A real measure of this specificity cannot be obtained from potential measurements, but is being determined using transport, exchange, and other methods.

The ability of Multilayer Membrane Electrodes to concentrate a specific ionic species without completely immobilizing that species is responsible for its specific function. The glass electrode is an example. This ideal or nearly ideal degree of specificity results from its highly oriented or semi-crystalline state. Pores, in the usual sense, are not present. Transport probably takes place by exchange between adjacent barium ions. Multilayer Membrane Electrodes specific for other cat-

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[1] We wish to thank the Office of Naval Research and the U. S. Public Health Service for the support given this work.

[2] B. E. Conway, "Electrochemical Data," Elsevier Publishing Co., New York, N. Y., 1952, p. 102.

TABLE I

POTENTIALS OF BARIUM STEARATE MULTILAYER MEMBRANE ELECTRODES

Chain S.C.E.||Solution 1 |Membrane |Solution 2||S.C.E.
Temperature, 25°

Solution 1 *M*	Solution 2 *M*	Experimental e.m.f. (corr.), mv.	Calcd. e.m.f., mv.
0.002 $BaCl_2$	0.001 $BaCl_2$	7.65	7.88
0.02 $BaCl_2$	0.01 $BaCl_2$	6.65	6.55
0.01 $BaCl_2$	0.001 $BaCl_2$	25.15	24.21
1.0 $BaCl_2$	0.5 $BaCl_2$	5.28	4.96
0.02 $BaCl_2$	0.01 $BaCl_2$ 0.005 NaCl	6.85	7.01
0.02 $BaCl_2$	0.01 $BaCl_2$ 0.02 NaCl	8.10	8.22
1.0 $BaCl_2$	0.5 $BaCl_2$ 2.0 NaCl	3.27	. .

ions or anions could in principle be prepared from insoluble or non-ionized salts which formed multilayers; further work in this direction is in progress.

The specific resistance of the multilayer *transverse* to the axis of orientation was 1.9 × 10^4 ohm cm. A Multilayer Membrane 50 Å. thick (10 molecule multilayer row) would have a resistance of 0.01 ohm cm.^{2}, a value which approximates that of ion-specific natural membranes.

Multilayer Membrane Electrodes can be used to measure activities of ions in mixed electrolytes. Problems of biochemical interest similarly can be attacked, such as the determination of calcium ion activities, the so-called "unbound" calcium concentration, in blood and other biological fluids.

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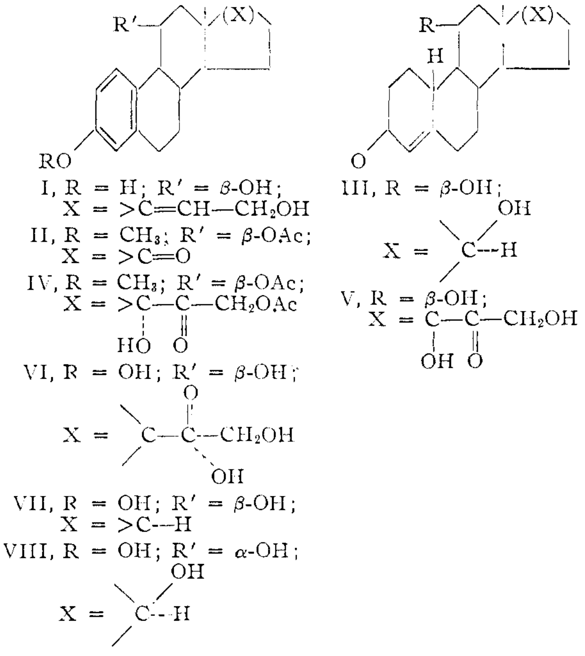
RECEIVED FEBRUARY 6, 1957

SYNTHESIS OF THE NOVEL 11-OXYGENATED 1,3,5-(10)-ESTRATRIENES

Sir:

Although aromatic A ring steroids are well known, their 11-oxygenated analogs have not been described.[1] We have prepared several members of this novel class of steroids and also have converted them to 11-oxygenated 19-norsteroids hitherto only available through the 11-hydroxylation of the corresponding 11-desoxy-19-norsteroids.[2,7]

The key intermediate for these chemical transformations is 19-nor-1,3,5(10),17(20)-pregnatetraene-3,11β,21-triol (I), m.p. 200–202°; $[\alpha]_D$ + 110° (acetone); λ_{max}^{EtOH} 281 mμ, a_M 2,000; (*Anal.* Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.35. Found: C, 76.62; H, 8.66). The surprising stability of the 11β-hydroxyl group under pyrolytic conditions was demonstrated by the conversion of 11β,21-dihydroxy-1,4,17(20)-[*cis*]-pregnatrien-3-one[3] to I in 15% yield at 575° in a mineral oil suspension.[4] Methylation of I yielded the 3-methyl ether, m.p. 143–144°; $[\alpha]_D$ + 122° (chloroform); (*Anal.* Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.94; H, 8.74). Acetylation gave the oily 11,21-diacetate[5] which when ozonized furnished the 11β-acetoxy-3-methoxy-1,3,5(10)-estratrien-17-one (II). m.p. 236–238°; $[\alpha]_D$ + 117° (chloroform); (*Anal.* Calcd. for $C_{20}H_{26}O_4$: C, 73.66; H, 7.65. Found: C, 73.46; H, 7.60). The structure of II and therefore also that of I was established by the conversion of II, using a lithium aluminum hydride reduction followed by a Birch type reduction, to 11β-hydroxy-19-nortestosterone (III).[6] This is the first described synthesis of an 11-oxygenated 19-norsteroid wherein the 11-hydroxyl group was present during the chemical modification of Ring A.



I, R = H; R' = β-OH; X = $>C{=}CH{-}CH_2OH$
II, R = CH_3; R' = β-OAc; X = $>C{=}O$
IV, R = CH_3; R' = β-OAc; X = $>\underset{\mathrm{HO}}{\underset{|}{C}}-\underset{\mathrm{O}}{\underset{\|}{C}}-CH_2OAc$
VI, R = OH; R' = β-OH; X = $>\underset{\mathrm{OH}}{C}-\overset{\mathrm{O}}{\overset{\|}{C}}-CH_2OH$
VII, R = OH; R' = β-OH; X = $>C{-}H$
VIII, R = OH; R' = α-OH; X = $>\overset{\mathrm{OH}}{C}-H$
III, R = β-OH; X = $>\overset{\mathrm{OH}}{C}-H$
V, R = β-OH; X = $\underset{\mathrm{OH}}{\underset{|}{C}}-\underset{\mathrm{O}}{\underset{\|}{C}}-CH_2OH$

A novel reaction was encountered when II was reduced with lithium in ammonia in the presence of alcohol. The expected product III was not detected, but a compound was isolated to which the following structure is assigned: 1-(α-hydroxyethyl)-11β,17β-dihydroxy-4-pregnen-3-one, m.p. 221–222°, λ_{max}^{EtOH} 247 mμ, a_M = 15,000; (*Anal.* Calcd. for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 72.04; H, 8.90; C-Methyl 2). Oxidation of this compound gave an oily tetraone which showed a maximum in the ultraviolet at 240 mμ, thus ruling out a hydroxyethyl substituent at 2 or 4. We postulate that this unique compound may be formed by an internal Claisen type transfer of the

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[1] 11-Ketoequilenin, which has *both* aromatic A and B rings was described by R. E. Marker and E. Rohrman, THIS JOURNAL, **61**, 3314 (1939).

[2] The 11α-hydroxyl group was introduced into a 19-norsteroid by a microbiological procedure, R. L. Pederson, J. A. Campbell, J. C. Babcock, S. H. Eppstein, H. C. Murray, A. Weintraub, R. C. Meeks, P. D. Meister, L. M. Reineke and D. H. Peterson, *ibid.*, **78**, 1512 (1956). The 11β-hydroxyl group was introduced by an adrenal perfusion technique, F. B. Colton and J. W. Ralls, U. S. Patent 2,694,080 (1954).

[3] J. A. Hogg, F. H. Lincoln, A. H. Nathan, A. R. Hanze, B. J. Magerlein, W. P. Schneider, P. F. Beal and J. Korman, THIS JOURNAL, **77**, 4436 (1955).

[4] E. B. Hershberg, M. Rubin and E. Schwenk, *J. Org. Chem.*, **15**, 292 (1950).

[5] The 11β-hydroxyl group is acylated with acetic anhydride-pyridine at room temperature in the 19-nor series. See also ref. 8, footnote 7.

[6] We are indebted to J. A. Campbell and J. C. Babcock, of the Upjohn Company, for a known sample of 11β-hydroxy-19-nortestosterone, whose preparation was described by J. C. Babcock at the 129th Meeting of the American Chemical Society, Dallas, Texas, April 8–13, 1956. See p. 29M of the Abstracts.