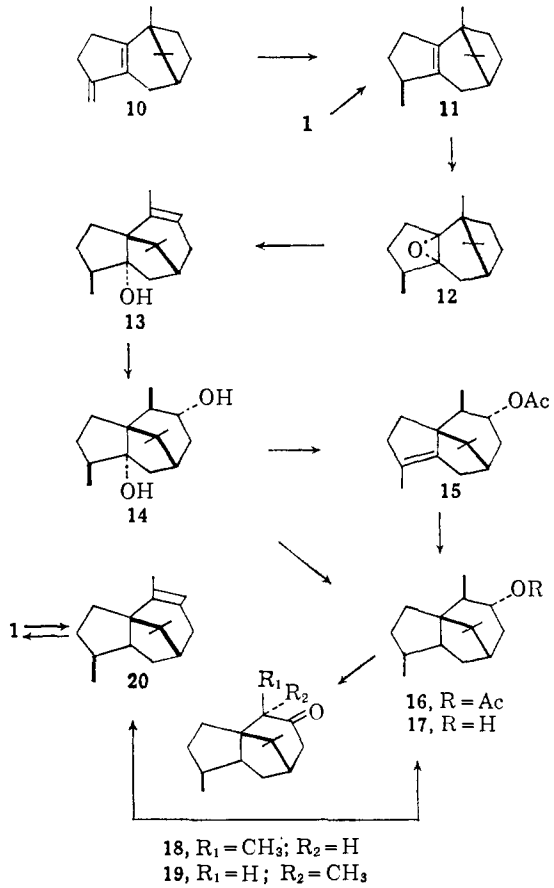
n.m.r. at 4.57 broad ($>C=C<^{H}$); 7.73 (OH), 8.38 ($CH_3-\overset{|}{C}=\overset{|}{C}-$), doublet centered at 9.0 (J 6 cs., $CH_3-\overset{|}{C}H$), 9.05, 9.14τ ($CH_3-\overset{|}{C}-CH_3$). Hydroboration–oxidation led to the diol (**14**) (45%), m.p. 112–113°, $[\alpha]_D$ −2° subsequently transformed to the liquid acetate (**15**) (87%), $[\alpha]_D$ +39° with acetic anhydride in hot pyridine. The position of the double bond in **15** was revealed by its n.m.r. spectrum: doublet at 5.4 (1H, J 6 cs.), 8.15 (3H), 8.55 (3H), doublet at 8.85 (3H, J 6 cs.), 8.97, 9.20 τ (6H) with no olefinic protons. Catalytic reduction of **15** afforded the liquid acetate (**16**) (98%), $[\alpha]_D$ −3° which with lithium aluminum hydride gave the alcohol (**17**) (87%) m.p. 97–97.5°, $[\alpha]_D$ −7° identical in every respect with an alcohol obtained from α-patchoulene (**20**) by hydroboration–oxidation. Catalytic reduction of the diol (**14**) over platinum in acetic acid containing some perchloric acid yielded the alcohol (**17**) in one operation.



The synthesis of patchoulione (**19**) was completed by chromic acid oxidation of **17** to the ketone (**18**) (97%), m.p. 25–26°, $[\alpha]_D$ +13° followed by epimerization with alkali to **19** (60%), m.p. 48–50° identical (infrared, mixture m.p. and rotation) with an authentic sample of patchoulione (**19**). Pyrolysis of **16** at 350° afforded a mixture of two liquid olefins in a ratio of 4:1. The major isomer, $[\alpha]_D$ +51° had n.m.r. at 4.95 (broad, $-\overset{|}{C}=\overset{|}{C}-H$); 8.37 ($CH_3-\overset{|}{C}=\overset{|}{C}-$); doublet centered at 9.10 (J 6 cs.) 9.05; 9.11 τ ($CH_3-\overset{|}{C}-CH_3$) and was spectroscopically (infrared and n.m.r.), vapor chromatographically and polarimetrically identical with authentic α-patchoulene (**20**). Preferential formation of **20** agrees with the postulate of double bond character in the transition state of the pyrolytic elimination[8] because the other isomer is destabilized by 1,3-methyl interaction. We have previously described[1] a conversion of α-patchoulene (**20**) to patchouli alcohol (**1**) and since total syntheses of (+)-camphor have been accomplished the transformations[9] described constitute a total synthesis.

Financial support by the National Institutes of Health (RG9186) and by Firmenich and Cie, Geneva, is gratefully acknowledged.

(8) C. H. DePuy and R. W. King, *Chem. Revs.*, **60**, 431 (1960).
(9) G. Komppa, *Ber.*, **36**, 4332 (1903); *Ann.*, **370**, 209 (1909).
(10) National Institutes of Health Predoctoral Fellow 1960–1962.

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STEROIDS. CC.[1] SPECTRA AND STEREOCHEMISTRY, PART III.[2] STEROIDAL 5,6-EPOXIDES

Sir:

Epoxidation of Δ^5-steroids frequently produces both the 5α,6α- and 5β,6β-epoxides, the former stereochemistry normally being assigned to that isomer which preponderates. Proof of structure has hitherto rested on further chemical reactions and molecular rotation differences.[3]

An examination of Dreiding models of the stereoisomeric 5,6-epoxides suggested that the angles (ϕ) subtended by the epoxidic C—H bonds with the C—H bonds at C_7 (Table I) are sufficiently different to permit a differentiation between the α- and β-epoxides to be made through a study of J_{HH} values, providing that the Karplus correlation,[5] relating J_{HH} to ϕ is valid for these cases.[6]

(1) Steroids. CXCIX, L. H. Knox, E. Velarde, S. Berger and D. Cuadriello, *Chem. and Ind.*, in press, 1962.
(2) Part II, A. D. Cross and P. W. Landis, *J. Am. Chem. Soc.*, **84**, 1736 (1962).
(3) A survey of the literature and collected data[4] reveals that the β-epoxide is more dextrorotatory than the α. However, this requires both compounds for the comparison. An apparent exception concerns the epoxides of 17β-carboxy-$\Delta^{5,16}$-androstadiene-3β-ol acetate methyl ester, where the correct specific rotation of the β-epoxide, −7° (ref. 4c, p. 1167), is erroneously given as −70° (ref. 4c, p. 1171) and repeated elsewhere as the incorrect value (ref. 4a, p. 78).
(4) (a) A. Petit and J. P. Mathieu, "Tables de Constantes et Données Numériques. 6. Constantes Sélectionnées. Pouvoir Rotatoire Naturel. I. Stéroïdes," Masson et Cie., Paris, 1956; (b) A. Bowers, L. C. Ibáñez and H. J. Ringold, *Tetrahedron*, **7**, 138 (1959); (c) L. Ruzicka, E. Hardegger and C. Kauter, *Helv. Chim. Acta*, **27**, 1164 (1944).
(5) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).
(6) It has been shown recently[7] that in the rigid steroid molecule, the constants of the Karplus equations need to be much larger, at least for the steroidal 2- and 4-acetoxy-3-ketones examined. Table I also includes therefore calculated J values according to these modified equations.[7]
(7) K. L. Williamson and W. S. Johnson, *J. Am. Chem. Soc.*, **83**, 4623 (1961).

Noticeable differences in the chemical shifts of the 19-methyl protons for α- and β-epoxides were also anticipated.[8]

Eight $5\alpha,6\alpha$-epoxides and seven $5\beta,6\beta$-epoxides, all having either an ethylene ketal or a 3β-acetoxy substituent at C-3, were examined.[13,14] In no compound were there C=C or C=O functions which could give rise to long-range shielding of either the 19-protons or the epoxidic proton. For the α-epoxide-3-ketals the 6β-proton resonance always appeared within the range 169.5–171.5 c./s. from the TMS reference as a doublet, J, 3.3–4.1 c./s., while the 6α-proton resonance of the β-epoxide-3-ketals appeared at 183.0–185.4 c./s. from TMS,[15] J, 2.1–2.7 c./s. Replacement of the 3-ketal by 3β-OAc raises the epoxidic proton absorption range by *ca.* 5 c./s. for the α-epoxides and by *ca.* 2 c./s. for the β-epoxides. A comparison of observed and calculated J values is given in Table I. It is of note that these epoxides constitute very rigid systems, yet the observed J values for the epoxidic protons are *lower* than either set of calculated values. The agreement of the observed values and those calculated from the Karplus equations[5] is however acceptable. The range of J values is conveniently narrow in each case and coupled with the value of the chemical shift *completely defines the epoxide stereochemistry.* That each proton absorption appears as a doublet agrees well with the implications[5,7] that for ϕ = 70–110°, J is quite small. In both epoxides only *one* 6,7-proton coupling is observed.

From the positions of the 19-proton resonances it was possible to calculate additivity values[9,10,17] of + 15.0 c./s. for the α-epoxide, + 2.5 c./s. for the β-epoxide, and + 2 c./s. for the 3-ketal of the β-epoxide.[18] Thus, after epoxidation of a series of Δ^5-steroid 3-ethylene ketals the 19-protons resonated at 64.4–65.6 c./s. for five α-epoxides and at 60.2–60.7 c./s. for four β-epoxides. Agreement of calculated and observed 19-proton frequencies is a further criterion for the epoxide stereochemistry. Moreover, if the epoxide bears a 3β-hydroxy or 3β-acyloxy function, the 3α-proton is shifted 25–30 c./s. away from the TMS frequency in the α-epoxides only.[19]

TABLE I.

CALCULATED AND OBSERVED COUPLING CONSTANTS FOR 6-PROTONS OF STEROID 5,6-EPOXIDES[13,15]

$5\alpha,6\alpha$-epoxide	ϕ[a]	J^6, c/s	J^7, c/s	Observed J, c/s
6βH–7αH	94 ± 4°	0.28– 0.1	0.0–0.27	.....
6βH–7βH	28 ± 4°	5.8 – 6.8	7.2–8.3	3.3–4.1
$5\beta,6\beta$-epoxide				
6αH–7αH	75 ± 4°	0.03–0.62	0.36–1.06	.....
6αH–7βH	49 ± 4°	2.8 –4.0	3.6 –5.0	2.1–2.7

[a] These values of ϕ are measured from models. Twelve measurements were made in each case and the majority fell well within the limiting range of ±4°.

We consider it important to note that additivity values for steroid methyl proton frequency shifts are applicable *only when the introduction of further substituents into the steroid nucleus does not cause serious alterations of the relative positions and orientations of the methyls and substituents capable of long-range shielding.* This is particularly important for unsaturated and keto steroids. Thus, additivity generally holds for steroids containing a $\Delta^{9(11)}$ double bond or a $5\beta,6\beta$-epoxide, but when both groups are present this is no longer true since now ring B is forced into a half-boat form and the position of the 19-methyl relative to both groups is changed. For example, $5\beta,6\beta$-epoxy-$\Delta^{9(11)}$-pregnene-3,20-dione-17α,21-diol diacetate 3-ethylene ketal has calculated and observed 19-proton resonances of 70.0 and 73.7 c./s. respectively, a disparity considerably larger than the agreement normally observable.[9,10,11]

We thank the Universidad Nacional Autónoma de México and Prof. A. Sandoval for time on the A-60 spectrometer.

(8) The chemical shift of the methyl protons at C_{19} or C_{18} in steroids is determined by the overall shielding experienced, which is a net effect of the position and orientation of all neighboring single and double bonds, plus long-range shielding effects due to magnetic anisotropy of more distant groups of electrons. *Changes in stereochemistry can lead to considerable changes in long-range shielding* effects.[7,9,10] Failure to consider fully these effects has led to errors in interpretation in recently published work.[10,11] A more detailed discussion of some new aspects will appear shortly.[12]

(9) A. D. Cross and P. W. Landis, unpublished results.

(10) R. F. Zürcher, *Helv. Chim. Acta*, **44**, 1380 (1961).

(11) J. Jacquesy, J. Lehn and J. Levisalles, *Bull. Soc. chim. France*, 2444 (1961).

(12) A. D. Cross, forthcoming publication.

(13) N.m.r. spectra were obtained for purified chloroform solutions at 60 Mc. using tetramethylsilane (TMS) as an internal reference. A Varian A-60 spectrometer was employed, but final calibration is against spectra run on a Varian HR-60 instrument, suitably equipped for calibration by the standard side-band technique. Accuracy limits are of the order of ±1 c./s. for chemical shifts and ±0.3 c./s. for J values.

(14) The α-epoxides were: $5\alpha,6\alpha$-epoxy-androstan-$3\beta,17\beta$-diol diacetate, $5\alpha,6\alpha$-epoxy-androstan-17-one-3β-ol acetate, $5\alpha,6\alpha$-epoxy-androstan-3-one-17β-ol-17-acetate 3-ethylene ketal, $5\alpha,6\alpha$-epoxy-pregnan-3,20-dione 3,20-diethylene ketal, $5\alpha,6\alpha$-epoxy-pregnan-3,20-dione-21-ol 3,20-diethylene ketal, $5\alpha,6\alpha$-epoxy-pregnan-3,20-dione 3-ethylene ketal, $5\alpha,6\alpha$-epoxy-pregnan-3,20-dione-21-ol 3-ethylene ketal 21-acetate, and $5\alpha,6\alpha$-epoxy-pregnan-3,20-dione-17α,21-diol 3-ethylene ketal 17α,21-diacetate. The β-epoxides were: $5\beta,6\beta$-epoxy-pregnan-3,20-dione-21-ol 3-ethylene ketal 21-acetate, $5\beta,6\beta$-epoxy-pregnan-3,20-dione 3,20-diethylene ketal, $5\beta,6\beta$-epoxy-pregnan-3,20-dione-17α,21-diol 3,20-diethylene ketal 17α,21-diacetate, $5\beta,6\beta$-epoxy-androstan-17-one-3β-ol acetate, $5\beta,6\beta$-epoxy-17α-ethinylandrostan-$3\beta,17\beta$-diol 3β-acetate, $5\beta,6\beta$-epoxy-androstan-$3\beta,17\beta$-diol diacetate, and $5\beta,6\beta$-epoxy-androstan-3-one-17β-ol 17-acetate 3-ethylene ketal.

(15) On the τ scale[16] the α-epoxide 6β-proton is *ca.* 7.2 and the β-epoxide 6α-proton is *ca.* 6.9.

(16) G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

(17) J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958).

(18) Positive shifts are *away* from TMS, for the 19-proton resonance frequency, due to the extra deshielding induced by these functional groups, relative to 5α- or 5β-androstane, according to stereochemistry at C_5.

(19) Shifts of the 3α-H resonance have been noted for the other steroids with a highly polar 5α bond.[9]

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THE ANODIC OXIDATION OF TRIPHENYLMETHANE DYES

Sir:

We wish to report an unusual electrochemical reaction, which is exhibited in the anodic oxidation of crystal violet and related triphenylmethane dyes.