communication reports an unambiguous synthesis of apogossypol hexamethyl ether, identical in all respects with that obtained from I (natural product m.p. 277–278°; synthetic product m.p. 277–279°; mixed m.p. 277–278°; infrared spectra indistinguishable),[5] which establishes conclusively the correctness of the original Adams formulation. Compound II was synthesized by the oxidative coupling of 5-isopropyl-6,7-dimethoxy-3-methyl-1-naphthol (III) m.p. 129–130°, found; C, 73.76; H, 7.78)[6] with ferric chloride in dioxane as the solvent and subsequent methylation of the resulting 2,2′ - bi - 1 - (5 - isopropyl - 6,7 - dimethoxy - 3-methyl)-naphthol (m.p. 271–275°, found: C, 74.21; H, 7.39). Consideration of models demonstrates that no coupling in the 4-position of III can occur due to steric hindrance.

Compound III was prepared in the following manner: formylation of 3-isopropyl-1,2-dimethoxybenzene[7,8] gave 2-isopropyl-3,4-dimethoxybenzaldehyde (IV), b.p. 98–102° (0.13 mm.) (2,4-dinitrophenylhydrazone, m.p. 190–192°, found: C, 55.79; H, 5.58). Oxidation of IV gave 2-isopropyl-3,4-dimethoxybenzoic acid as shown by comparison with an authentic sample.[9] The Stobbe reaction of IV and diethyl succinate with subsequent ring closure (sodium acetate and acetic anhydride) and saponification in the conventional manner gave 1-hydroxy-5-isopropyl-6,7-dimethoxy-3-naphthoic acid (m.p. 226–227°, found: C, 66.32; H, 6.34). Reduction with lithium aluminum hydride gave 3-hydroxymethyl-5-isopropyl-6,7-dimethoxy-1-naphthol (m.p. 207–209°, found: C, 69.71; H, 7.20). Hydrogenolysis with palladium on charcoal in methanol with a trace of hydrochloric acid gave III.

The interest and encouragement of Professor R. B. Turner is gratefully acknowledged.

[5] Perkin–Elmer Model 21 Spectrophotometer, 0.11-mm. cells, solvent chloroform, concn. 7%.

[6] All analyses by Huffman Microanalytical Laboratories, Wheatridge, Colorado.

[7] R. Adams, M. Hunt and R. C. Morris, THIS JOURNAL, **60**, 2972 (1938).

[8] J. D. Edwards, Jr., and J. L. Cashaw, *J. Org. Chem.*, **20**, 847 (1955).

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RESEARCH LABORATORIES
VETERANS ADMINISTRATION HOSPITAL
HOUSTON, TEXAS
J. D. EDWARDS, JR.
J. L. CASHAW

RECEIVED MAY 21, 1956

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## NUCLEAR MAGNETIC RESONANCE STERIC SHIFTS IN –CH GROUPS

*Sir:*

Sterically interfering hydrogen atoms in the 4–5 position of phenanthrene and many similar molecules shows up strongly in high resolution nuclear magnetic resonance experiments. Since the work of Arnold, *et al.*,[1] on the steric effects of methylene groups in hydrindene and tetralin with $\alpha$-substituents in the aromatic ring shows clearly that the interaction is much greater when both rings are six-membered than when one of them is five-membered, it is of interest to investigate the effect of ring size on the nuclear magnetic resonance signals. Accordingly, the proton signals from a number of polycyclic compounds have been examined (Table I). The shifts are measured relative to the main peak due to the rest of the aromatic hydrogens. Usually the distance of the two peaks from a standard marker (cyclohexane or decalin when the latter was used as solvent) were measured. The strong interaction found in benzophenanthrene is considerably weakened by the change in angle introduced by the 5-membered ring in dibenzofluorene, and the initially weaker phenanthrene interaction is similarly much reduced in fluorene and completely removed in fluoranthene, where the hydrogen atoms are even farther apart.

TABLE I

| | H–H distance A | Shift, cycles |
|---|---|---|
| 3,4-Benzophenanthrene | 0.53 | 68 |
| 1,2,5,6-Dibenzanthracene | 1.71 | 45 |
| 1,2,5,6-Dibenzfluorene | 1.73 | 40 |
| Phenanthrene | 1.76 | 42 |
| Fluorene | 2.72 | 12 uncertain |
| Fluoranthene | 2.95 | 0 uncertain |

A fairly simple relation exists between the nuclear magnetic resonance shift and the hydrogen–hydrogen distance. However, since the H–H distances are calculated on the basis of a planar molecule and the H–H repulsion must distort the molecule somewhat out of plane, these values are not the true equilibrium H–H distances. Allowance for this fact would increase the small H–H distances proportionally more than the large ones.

A consideration of other molecules with interacting protons shows some interesting effects. Perylene with two sterically interfering pairs each tending to twist the molecule out of plane about the central pair of bonds shows a shift of only 25 cycles, about half that observed for phenanthrene. The doubled torque has clearly effected an increased twist, so that the protons in each pair are considerably farther apart than in phenanthrene. Chrysene also has two interacting pairs, but now the torque is across a 3-bond rather than a two-bond system. Correspondingly we find a shift intermediate between that of phenanthrene and perylene (35 cycles). A more detailed examination of this kind of structural effect will be published shortly.

One is easily convinced from the molecular models that the 4–5 proton repulsion in phenanthrene puts the maximum strain on the $C_9$–$C_{10}$ bond. The anomalously high "K region" reactivity which is greater than predicted by molecular orbital theory based on a planar molecule is no doubt due to this fact. A study of the shifts in carcinogenic hydrocarbons is also in progress.

It has been pointed out to the author[2] that the closeness of the proton to two aromatic rings rather than one may result in the kind of shift observed. An investigation of the relative importance of the two factors is under way.

The work reported here was done using a Varian Associates Model V4300 spectrometer working at

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[1] R. T. Arnold, V. J. Webers and R. M. Dodson, THIS JOURNAL, **74**, 368 (1952).

[2] W. G. Schneider, H. J. Bernstein and J. A. Pople, private communication.

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DEPARTMENT OF CHEMISTRY
UNIVERSITY OF BRITISH COLUMBIA
VANCOUVER, CANADA
C. REID

RECEIVED MAY 1, 1956

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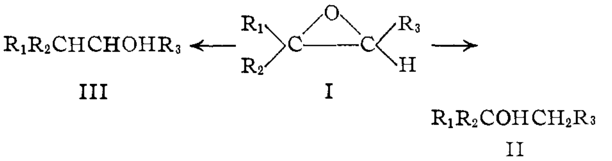
## ANOMALOUS REDUCTION OF EPOXIDES WITH LITHIUM ALUMINUM HYDRIDE

*Sir:*

Lithium aluminum hydride attacks unsymmetrically substituted epoxides predominantly at the least substituted carbon atom to give the more highly substituted alcohol.[1-3] Thus primary–secondary epoxides (I, $R_1$ = alkyl, $R_2 = R_3$ = H) give secondary alcohols (II, same), and primary–tertiary or secondary–tertiary epoxides (I, $R_1$, $R_2$ = alkyl, $R_3$ = H or alkyl) give tertiary alcohols (II,



same). Representative examples from the literature and from our own work are listed in the table (entries 1, 3, 4, 5, 8, 10, 12).

TABLE I

REDUCTION OF EPOXIDES WITH LITHIUM ALUMINUM HYDRIDE

| Entry | compound | $R_1$ | $R_2$ | $R_3$ | Moles LAH | Moles $AlX_3$ | Yield, % | Products % II | % III | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Propylene oxide | Me | H | H | 0.3 | 0 | 60 | 100 | 0 | *a* |
| 2 | Propylene oxide | Me | H | H | .25 | 1[b] | *ca.* 42 | *ca.* 80 | *ca.* 20 | *a* |
| 3 | 1,2-Epoxydecane | Oct | H | H | .25 | 0 | 90 | 100 | 0 | 2 |
| 4 | Styrene oxide | Ph | H | H | .25+ | 0 | 94 | 100 | 0 | 3 |
| 5 | Styrene oxide | Ph | H | H | .3 | 0 | 82 | 90–95 | 5–10 | *a* |
| 6 | Styrene oxide | Ph | H | H | .25 | 1[b] | 87 | 2–10 | 90–98 | *a* |
| 7 | Styrene oxide | Ph | H | H | 1.5 | *c* | 80 | 71 | 28 | *a* |
| 8 | Isobutylene oxide | Me | Me | H | 0.3 | 0 | 26 | 95–98 | 2–5 | *a* |
| 9 | Isobutylene oxide | Me | Me | H | .25 | 1[b] | 55 | 5–7 | 93–95 | *a* |
| 10 | 1,1-Diphenylethylene oxide | Ph | Ph | H | .4 | 0 | 97 | 100 | 0 | *a* |
| 11 | 1,1-Diphenylethylene oxide | Ph | Ph | H | 2.4 | *c* | 85 | 14 | 86 | *a* |
| 12 | 1,1,2-Triphenylethylene oxide | Ph | Ph | Ph | 2.2 | 0 | 11.5[d] | 100 | 0 | *a* |
| 13 | 1,1,2-Triphenylethylene oxide | Ph | Ph | Ph | 2.4 | *c* | 91 | 0 | 100 | *a* |

[a] This work. [b] Aluminum chloride. [c] Generated *in situ* from 1 mole of allyl bromide. [d] Also recovered 81% starting material.

In contrast, we have now found that *reversal* of the direction of ring opening occurs (I → III) when the reduction is carried out in the presence of aluminum chloride or bromide. Substantially complete reversal is achieved in phenyl-substituted epoxides (entries 6, 11, 13) and in isobutylene oxide (entry 9). With propylene oxide (entry 2) only partial reversal occurred and the crude reaction product contained halohydrins. No aliphatic secondary–tertiary epoxide has as yet been studied.

The reductions were carried out in the customary way.[1] Water-soluble products were isolated by continuous ether extraction. Mixtures of solid products (entries 10–13) were analyzed by chromatographic separation. Liquid mixtures (entries 1, 2, 5–9) were analyzed by mass spectrometry; in most cases the analyses were checked by infrared comparison with synthetic mixtures. The reduction mixture for experiments 2, 6, 7, 9, 11 and 13 was obtained by adding standardized ethereal lithium aluminum hydride to cold ethereal aluminum chloride, or by adding allyl bromide in ether to the standardized hydride solution prior to addition of the epoxide.

We are presently studying the mechanism of the abnormal ring opening as well as extensions of the method to other epoxides, including alicyclic and steroid cases.

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DEPARTMENT OF CHEMISTRY
UNIVERSITY OF NOTRE DAME
NOTRE DAME, INDIANA
ERNEST L. ELIEL
DAVID W. DELMONTE[4]

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[1] W. G. Brown in R. Adams, "Organic Reactions," John Wiley and Sons, Inc., New York, Vol. VI, 1951, p. 476; L. W. Trevoy and W. G. Brown, THIS JOURNAL, **71**, 1675 (1949); R. Fuchs and C. A. VanderWerf, *ibid.*, **74**, 5917 (1952); E. L. Eliel and J. P. Freeman, *ibid.*, **74**, 923 (1952).

[2] M. S. Newman, G. Underwood and M. Renoll, *ibid.*, **71**, 3362 (1949).

[3] R. F. Nystrom and W. G. Brown, *ibid.*, **70**, 3738 (1948).

[4] Shell Research Fellow, 1955–1956.

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## THE RADIATION CHEMISTRY OF WATER VAPOR. THE INDIRECT EFFECT ON DEUTERIUM[1]

*Sir:*

The rate of formation of hydrogen deuteride in gaseous mixtures of tritium–water (0.284 hydrogen-atom % tritium) and deuterium is a direct measure of the rate of formation of hydrogen atoms. Samples containing 0.185 g. of tritium–water vapor and deuterium gas at mole fractions in the range $10^{-3}$ to $10^{-2}$ were heated in sealed Pyrex tubes (238 ml., 47 mm. i.d.) at temperatures from 120 to 165° and total pressures of 1000 millimeters. Evolution of foreign gases from the tube walls was kept negligibly small by heating and pumping on the tubes for at least 12 hours at 510° followed by 12 hours at 440° before admission of the reactants. Isotopic analysis of the hydrogen was performed on a mass spectrometer. No exchange was observed in the absence of tritium–water. $G$(HD)

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[1] Based on work performed under the auspices of the U. S. Atomic Energy Commission.