

For example, reduction of the octalone I² (R = CH₃, R' = OCH₃, R'', R''' = H) with lithium-ammonia in the presence of alcohol, then without separation of intermediates an oxidation and Wolff-Kishner reduction gave a 2-methoxy-10-methyldecalin in 65% over-all yield from the octalone. Vapor phase chromatography showed two components (A = 84 ± 3%; B = 16 ± 3%) which are both *trans*-decalins³: degradation of A and B separately by acetolysis with anhydrous hydrogen bromide in acetic acid, hydrolysis to the 10-methyl-2-decalol and oxidation with nitric acid readily gave in both cases *trans*-1-methylcyclohexane-1,2-diacetic acid, m.p. 197.4–198.8°,⁴ undepressed on admixture with authentic material, but depressed to 164° when mixed with the pure *cis* isomer,⁵ m.p. 191.2–192.9°.

Similarly, the octalone I² (R, R'' = CH₃, R' = OCH₃, R''' = H) gave by the same sequence of steps as outlined above substances of the *trans* decalin series: nitric acid oxidation of the final hydroxy compound gave again pure *trans*-1-methylcyclohexane-1,2-diacetic acid, m.p. and mixed m.p. 193.9–195.8°.

One last case may be mentioned from the literature⁶: Reduction of the optically active octalone I (R, R''' = CH₃, R'' = *i*-Pr, R' = H) with lithium and ammonia gave a decalone which was shown to be *trans* by rotatory dispersion.⁷

In the first of these three cases, the *cis* and *trans* decalones should be of roughly equal energy while in the last two cases the *cis* isomer should be the more stable one by between three and four kilocalories and thermodynamic stability of the products is clearly not controlling. The results are, however, in agreement with the formation of the more stable of the two isomers with the C₁₀ hydrogen axial to the ketone ring.

(2) The synthesis of these substances is unexceptional and will be detailed in our full paper.

(3) These two substances differ in the relative stereochemistry of the methyl and methoxyl groups and reflect a similar mixture in their octalone precursor. The latter was made by methyl vinyl ketone addition to 2-methyl-4-methoxycyclohexanone and the major component is undoubtedly that resulting from (unhindered) axial addition of methyl vinyl ketone to the anion of the cyclohexanone. In this isomer the methyl and methoxyl groups are *cis*.

(4) Some confusion exists in the literature on the properties of this substance. Our authentic material was made by nitric acid oxidation of crystalline *trans*-5-methyl-2-decalol and gave correct analytical values.

(5) R. P. Linstead, A. F. Millidge and A. L. Walpole, *J. Chem. Soc.*, 1140 (1937).

(6) R. Howe and F. J. McQuillin, *ibid.*, 2670 (1956).

(7) Private communication from Professor Carl Djerassi.

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STEREOCHEMISTRY OF A BASE-CATALYZED EXCHANGE OF ETHYLBENZENE- α -*d*

Sir:

Cram, Kingsbury and Rickborn¹ recently have reported a high degree of retention of configuration in the replacement of a tertiary hydrogen by deuterium or *vice versa* in reaction with potassium

(1) D. J. Cram, C. C. Kingsbury and B. Rickborn, *THIS JOURNAL*, **81**, 5835 (1959).

t-butoxide in *t*-butyl alcohol. We report herewith that similar results are obtained for replacement of a secondary hydrogen by hydrogen in cyclohexylamine as solvent.

Optically active ethylbenzene- α -*d* both loses deuterium and racemizes with lithium cyclohexylamide in cyclohexylamine. Racemization can occur from replacement of deuterium by hydrogen (k_D) and in some fraction, λ , of the replacements of the α -hydrogen by hydrogen (k_H)

$$k_{\text{rac}} = k_D + \lambda k_H \quad (1)$$

Determination of λ characterizes the stereochemistry of the reaction; $\lambda = 0, 1$ or 2 for complete retention, racemization or inversion, respectively.

At 49.9° with 0.049 *M* lithium cyclohexylamide and 0.71 *M* ethylbenzene- α -*d*, good pseudo-first order kinetics are obeyed using vacuum line techniques; k_{rac} and k_D are 3.0×10^{-5} and 1.07×10^{-5} sec.⁻¹, respectively. k_H cannot be measured directly but this rate constant can be determined from the primary isotope effect using tritium. Under similar conditions a mixture of ethylbenzene- α -*d* and ethylbenzene- α -*t* gave $k_D/k_T = 3.0 \pm 0.3$.² From the treatment of Swain, *et al.*,³ we can derive

$$k_H/k_D = (k_D/k_T)^{2.26} \quad (2)$$

whence $k_H/k_D = 12 \pm 3$.

All of the rate constants in equation 1 are now known. Evaluation of λ gives 0.17; *i.e.*, the replacement of the α -hydrogen by hydrogen under these conditions occurs with 17% racemization and 83% net retention of configuration. This relatively large degree of retention agrees with Cram's evaluation of amines as "retention solvents" in some other reactions thought to proceed through intermediates of the carbanion type.⁴

(2) This relatively large value has been confirmed recently with toluene- α -*d* and toluene- α -*t*, for which $k_D/k_T = 2.75, 2.98$ (W. C. Langworthy).

(3) C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr., and L. J. Schaad, *THIS JOURNAL*, **80**, 5888 (1958).

(4) D. J. Cram, A. Langemann, J. Allinger and K. P. Kopecky, *ibid.*, **81**, 5740 (1959).

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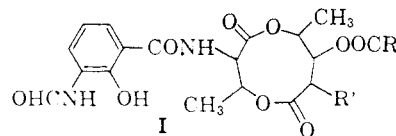
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THE CHEMISTRY OF ANTIMYCIN A. IX. STRUCTURE OF THE ANTIMYCINS

Sir:

As the culmination of our extended structural studies on the members of the antimycin complex,¹



R = CH₂CH(CH₃)₂
(a) R' = *n*-C₄H₉
(b) R' = *n*-C₅H₁₁

we present findings which permit assignment of the generalized expression I to this group of closely related *Streptomyces* antibiotics.

(1) For paper VIII and preceding references, see W. Liu, E. E. van Tamelen and F. M. Strong, *THIS JOURNAL*, **82**, April 5 (1960).