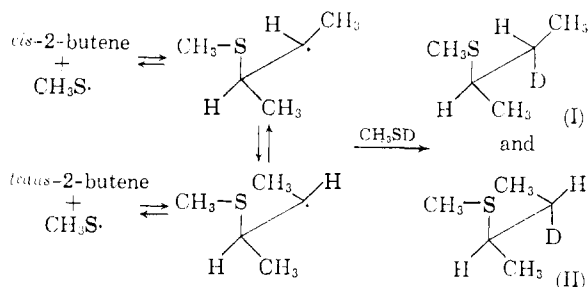


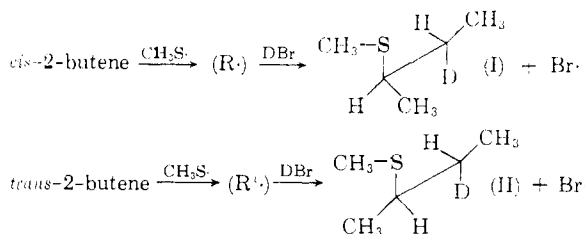
isomerization, the products are the same mixture of *erythro*- and *threo*-3-deuterio-2-methylthiobutane starting with either olefin. Rationalization of these observations requires an open chain radical which isomerizes more rapidly than the transfer of a deuterium atom from CH_3SD .



In the liquid phase at -78° , product analyses for the reaction of HBr , CH_3SH and *cis*-2-butene (1:2:1) yielded an apparent relative rate of hydrogen atom transfer to $\text{CH}_3\text{-CHX-}\dot{\text{C}}\text{H-CH}_3$ of $k_{\text{HBr}}/k_{\text{CH}_3\text{SH}} = 1.94$. Thus it was deemed advisable to examine the stereospecificity of CH_3SD additions in the presence of DBr . Under these conditions the formation of the 3-deuterio-2-bromobutanes is stereospecific, as it is in the absence of methyl mercaptan.³ The 3-deuterio-2-methylthiobutanes are also produced by stereospecific *trans* additions, *cis*- and *trans*-2-butenes yielding *threo* (I) and *erythro* (II) products, respectively. Evidence for structure and purity was obtained through syntheses of the thioethers by reactions of CH_3SNa with pure *erythro*- and *threo*-3-deuterio-2-bromobutanes, inversions at C-2 being assumed. Examination of infrared spectra provides no evidence of isomer intercontamination for the radical additions.¹⁰

These results require that (1) DBr be the sole transfer agent with radicals $\text{CH}_3\text{-CHX-}\dot{\text{C}}\text{H-CH}_3$, and (2) equilibration $\text{Br}\cdot + \text{CH}_3\text{SD} \rightarrow \text{DBr} + \text{CH}_3\text{S}\cdot$ be more rapid than additions of $\text{Br}\cdot$ and $\text{CH}_3\text{S}\cdot$ to these olefins.

Steric control of mercaptan addition is achieved by the rapid reaction of the diastereomerically related 3-methylthio-2-butyl radicals with hydrogen bromide, a reaction which is more rapid than the isomerizations of the radicals.



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(10) Throughout, vapor phase chromatography homogeneous samples were examined neat. Less than 5% intercontamination might have escaped detection.

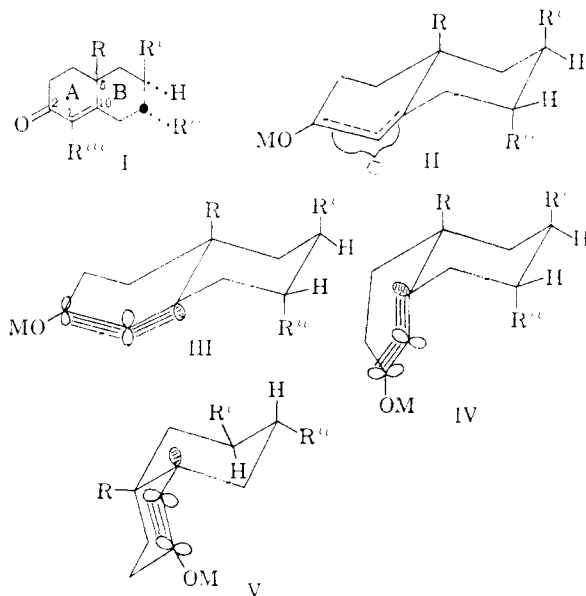
(11) This research was supported by the United States Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command, under contract No. AF 49(638)-457.

STEREOCHEMISTRY OF THE LITHIUM-AMMONIA REDUCTION OF α,β -UNSATURATED KETONES

Sir:

It has been proposed that the reduction of an α,β -unsaturated ketone with lithium in ammonia leads to the more stable epimer at the β -carbon atom.¹ Results in this Laboratory have led us to reexamine these conclusions. We will illustrate the argument by reference to the reduction of octalones such as I. The transition state for protonation of the intermediate anion II must have considerable tetrahedral character at the β -carbon atom (C_{10}): if the β -carbon atom were still trigonal in the transition state for protonation (*cf.* II) approach of the proton source would be at least as easy to give a *cis* as a *trans* product and considerable quantities of *cis* decalones would be expected. This is contrary to experience. Even though the transition state has considerable tetrahedral character at C_{10} , the developing orbital at that carbon will be expected to overlap continually with the double bond, *i.e.*, must remain perpendicular to it (*cf.* III and IV). This leads to introduction of the C_{10} hydrogen *axially* to ring A. It is in the recognition of the necessity of continual overlap of the β -orbital with the enolate double bond that the picture differs from that previously suggested.¹

We are thus led to the following rule: In reduction of an octalone system with lithium in ammonia the product will be the more stable of the two isomers (*cis* or *trans*) having the newly introduced hydrogen axial to the ketone ring. The conformation of the *cis* form of a β -decalone which is not permitted in the transition state (*cf.* V) is in many



cases more stable than the conformation of the *trans* isomer, whereas the permitted *cis* form is in general less stable than the *trans*. The product of the reduction of an octalone such as I will thus often be exclusively the *trans*- β -decalone even when the *cis*-decalone would be expected to be the more stable isomer.

(1) D. H. R. Barton and C. H. Robinson, *J. Chem. Soc.*, 3045 (1954).

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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RECEIVED JANUARY 22, 1960

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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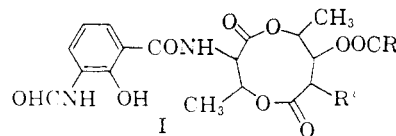
A. STREITWIESER, JR.
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L. REIF

RECEIVED JANUARY 18, 1960

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*-C₆H₁₃

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).