

The 7-nitro compound, IV, is an exceedingly active substance (Table I), showing *in vitro* activity at least four times that of I against the assay organism.² The 9-nitro isomer, V, on the contrary, shows only a fraction of the activity² of I. Catalytic hydrogenation of the two nitro isomers yields the corresponding amino compounds (VI and VII), which exhibit *in vitro* activity quite comparable to each other and to I.

TABLE I
Biological assay versus *Klebsiella pneumoniae* in oxytetracycline units per mg.²

Compound	Biological assay versus <i>Klebsiella pneumoniae</i> in oxytetracycline units per mg. ²
I	900
II	1300
III	25
IV	4600
V	200
VI	760
VII	975
VIII	<10

Nitration of 6-deoxy-5-oxytetracycline¹ yields the 9-nitro compound³ [VIII, $\lambda_{\text{max}}^{(\text{MeOH}-0.01N \text{ HCl})}$ 263 m μ , 358 m μ ; $\lambda_{\text{max}}^{(\text{MeOH}-0.01N \text{ NaOH})}$ 241 m μ , 280 m μ , 352 m μ , 420 m μ] which like III and V is relatively inactive.²

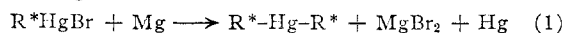
These data suggest that the phenolic hydroxyl group in the tetracycline molecule plays an essential role in the microbial inhibition process which is inhibited by hydrogen bonding with an ortho nitro substituent.

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CONVERSION OF ALKYL MERCURIC SALTS TO DIALKYL MERCURY COMPOUNDS WITH RETENTION OF CONFIGURATION IN BOTH ALKYL GROUPS¹

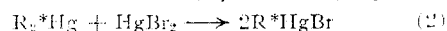
Sir:

This report concerns the finding that stereoisomeric alkylmercuric salts are reduced stereospecifically by magnesium to give dialkylmercury compounds with retention (85-97%) of configuration (1). The mechanism of the reaction has been investigated.



The reduction has been carried out with *cis*- and *trans*-4-methylcyclohexylmercuric bromides² to yield di-4-methylcyclohexylmercury with, respectively, 89% retention of configuration (96% yield) and 97% retention of configuration (93% yield). The reaction with L-(-)-*sec*-butylmercuric bromide^{3,4} gives di-L-(-)-*sec*-butylmercury with 89-93% retention of configuration (yields to 98%). In a typical experiment, L-(-)-*sec*-butylmercuric bromide, $[\alpha]^{25D} -5.05^\circ$, gave di-L-(-)-*sec*-butyl-

mercury, $[\alpha]^{25D} -7.57^\circ$, which upon cleavage with mercuric bromide (equation 2) gave L-

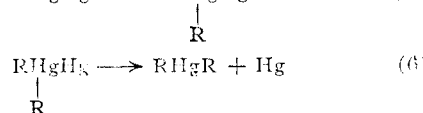
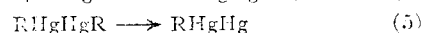


(-)-*sec*-butylmercuric bromide, $[\alpha]^{25D} -4.60^\circ$. Although evidence has been given previously which indicates that reaction (2) occurs with retention of configuration,^{4,5} the results of cleaving the above compounds provide additional proof of the correctness of the assigned stereochemical course.

In previous related work, α -bromomercuricamphor and *l*-menthyl α -bromomercuriphenylacetate were converted stereospecifically to the corresponding optically active dialkylmercury compounds by the addition of certain complexing agents.^{6,7} For these compounds reaction (2) is reversible and the complexing agent acts on the mercuric bromide. No example of the reversal of reaction (2) where R- is a simple alkyl group has been reported.

Evidence relating to the mechanism of reaction (1) is given: (a) when the reaction is conducted in a carbon dioxide atmosphere or in the presence of 1-butanol no carboxylic acid or hydrocarbon is produced; (b) the reaction may be carried out in the presence of styrene and the styrene may be recovered unchanged from the reaction mixture; (c) the reactions with *cis*- and *trans*-2-methoxycyclohexylmercuric bromide yield only cyclohexene and no dialkylmercury compound; and (d) the stereochemical course is retention of configuration. The above evidence eliminates possible intervention of R^- , $RMgBr$, and $R\cdot$ as reaction intermediates. The simplest intermediate which would lead to olefin in a compound containing an adjacent methoxyl group (item c) is RHg^- .

The mechanism proposed to account for the results is given below; however, possible intervention of RHg in a chain reaction is not rigorously excluded. In order to give retention of configura-



tion, the alkyl group in the organomercurous compound⁸ must migrate with retention of configuration.

The reverse of reactions (6) and (5) represent an attractive mechanism for the exchange of Hg^{2+} with organomercurials, which is known to proceed with retention of configuration.⁹ Other reactions which might involve intermediates having Hg-Hg bonds and involve alkyl migrations on mercury, analogous to reaction 5, are the cleavage of di-

(5) H. B. Charman, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 2530 (1959).

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(9) O. A. Reutov, P. Knoll and Yan-Tsei U, *Doklady Akad. Nauk S.S.S.R.*, **120**, 1052 (1958) (*C. A.*, **52**, 20003 (1958)); O. A. Reutov, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 684 (1959) (*C. A.*, **52**, 20004 (1958)).

(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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alkylmercury compounds by mercuric bromide (reaction 2), and the exchange of alkyl groups in dialkylmercury compounds in the presence of alkylmercuric salts.¹⁰

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CHEMICAL EVIDENCE FOR AT LEAST TWO
DIFFERENT PRECURSORS TO CYCLOHEXENE
FORMED BY ELECTRON IRRADIATION OF
CYCLOHEXANE

Sir:

By observation of the cyclohexene yield, $G(\text{C}_6\text{H}_{10})$, obtained by electron irradiation of cyclohexane containing a number of solutes, we have shown that there are at least two different modes for the formation of cyclohexene. Table I contains the experimental results.

TABLE I
 $G(\text{C}_6\text{H}_{10})$ IN THE PRESENCE OF SOLUTES^a

Solute	Concn., M	Dose $\times 10^{-20}$ ev./ml.	$G(\text{C}_6\text{H}_{10})$
None	..	3.55	2.3
Iodine	0.02	3.55	1.1
	.05	3.55	0.9
Benzyl chloride	.05 ^b	5.54	1.3
	.11 ^b	5.68	0.9
	.20	5.73	.8
	.55	5.73	.8
	3.48	5.97	.3
Toluene	0.097	4.84	1.8

^a Irradiations were carried out on deoxygenated samples unless noted. ^b Irradiated both in the presence and absence of air, with the same results within experimental error.

The high-energy source used in this work was a 2-Mev. G. E. Resonant Transformer delivering 1 ma. beam current. Irradiations were performed in a multiple-cell sample holder previously described.¹ Dosimetry was accomplished by means of a flow calorimeter developed in this Laboratory. Cyclohexene was analyzed by means of quantitative gas-liquid chromatography. A 20-ft. column of 15% tricresyl phosphate on 30-60 mesh acid-washed Chromosorb, operated at 65°, separated cyclohexene from all other products.

It is postulated that cyclohexene is produced by processes other than thermalized radical reactions. Cyclohexyl radicals do not disproportionate efficiently to form cyclohexene.^{2,3} We have found that for pure cyclohexane $G(\text{C}_6\text{H}_{10}) = 2.3 \pm 0.2$ (Table I), in agreement with Dewhurst's value.⁴ When the irradiation is carried out on samples containing 0.02 M iodine in cyclohexane the G -yield drops to 1.1. As suggested by the work of Burton, *et al.*,⁵ this result clearly shows that iodine

(0.02 M) does not completely prevent the formation of cyclohexene. Benzyl chloride (0.1 M) has an effect similar to that of iodine, reducing $G(\text{C}_6\text{H}_{10})$ to about 1.0. When the benzyl chloride concentration is varied from 0.05 M to 3.48 M (25% benzyl chloride by volume), $G(\text{C}_6\text{H}_{10})$ is decreased from 1.3 to 0.3. The reduction in cyclohexene is not linear with solute concentration. It drops rapidly with the initial addition of 0.05 M benzyl chloride, and then decreases slowly as the concentration is raised to 3.48 M . The fast initial drop of cyclohexene yield followed by the slow reduction on further addition of solute indicates that at least two different processes lead to cyclohexene. Addition of solutes quenches the formation of cyclohexene from one of these intermediates.

There is a gradation of effectiveness of different solutes with regard to ability to inhibit cyclohexene formation. The data in Table I demonstrate that at the same concentration iodine is more efficient than benzyl chloride which in turn is more effective than toluene.

At present, speculation as to the nature of these species is of little value and will be deferred until more of the variables have been studied (*e.g.*, effect of temperature, phase, viscosity, etc.).⁶

(6) Results similar to these have been published recently, see H. A. Dewhurst, *J. Phys. Chem.*, **63**, 813 (1959).

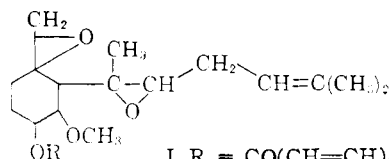
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RECEIVED JULY 2, 1959

THE STRUCTURE OF FUMAGILLIN¹

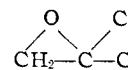
Sir:

Consideration of previous information²⁻¹⁰ and of results now presented shows that fumagillin and its neutral saponification product "alcohol-I" possess structures I and II.



I, R = $\text{CO}(\text{CH}=\text{CH})_4\text{COOH}$
II, R = H

The presence in II of the epoxide group^{5,6,10}



(1) Supported in part by Grant E-1138 of the U. S. Public Health Service.

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