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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(10) G. Calingaert, H. Soroos and V. Hnizda, THIS JOURNAL, **62**, 1107 (1940).

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RECEIVED DECEMBER 23, 1959

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

Sir:

By observation of the cyclohexene yield, $G(C_6H_{10})$, 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

$G(C_6H_{10})$ IN THE PRESENCE OF SOLUTES[a]

Solute	Concn., *M*	Dose $\times 10^{-20}$ ev./ml.	$G(C_6H_{10})$
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 $G(C_6H_{10}) = 2.3 \pm 0.2$ (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 $G(C_6H_{10})$ to about 1.0. When the benzyl chloride concentration is varied from 0.05 *M* to 3.48 *M* (25% benzyl chloride by volume), $G(C_6H_{10})$ 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]

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(1) A. MacLachlan, *Rev. Sci. Instr.*, **29**, 790 (1958).

(2) E. H. Farmer and C. G. Moore, *J. Chem. Soc.*, 131 (1958).

(3) C. G. Swain, L. J. Schaad and A. J. Kresge, THIS JOURNAL, **80**, 5313 (1958).

(4) H. A. Dewhurst, *J. Chem. Phys.*, **24**, 1254 (1956).

(5) M. Burton, J. Chang, S. Lipsky and M. P. Reddy, ***Radiation Research***, **8**, 203 (1958).

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

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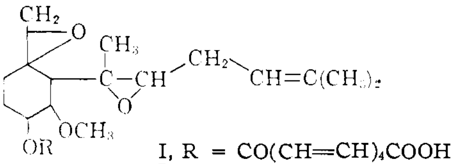
RECEIVED JULY 2, 1959

THE STRUCTURE OF FUMAGILLIN[1]

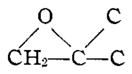
Sir:

Consideration of previous information[2–10] and of results now presented shows that fumagillin and its neutral saponification product "alcohol-I" possess structures I and II.



I, R = CO(CH=CH)$_4$COOH
II, R = H

The presence in II of the epoxide group[5,6,10]



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

(2) J. R. Schenck, M. P. Hargie, D. S. Tarbell and P. Hoffman, THIS JOURNAL, **75**, 2274 (1953).

(3) J. R. Schenck, M. P. Hargie and A. Isarasena, *ibid.*, **77**, 5606 (1955).

(4) D. S. Tarbell, P. Hoffman, H. R. Al-Kazimi, G. A. Page, J. M. Ross, H. R. Vogt and B. Wargotz, *ibid.*, **77**, 5610 (1955).

(5) J. K. Landquist, *J. Chem. Soc.*, 4237 (1956).

(6) J. M. Ross, D. S. Tarbell, W. E. Lovett and A. D. Cross, THIS JOURNAL, **78**, 4675 (1956).

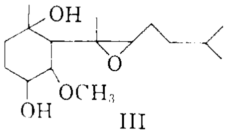
(7) J. G. McNally, Jr., and D. S. Tarbell, *ibid.*, **80**, 3676 (1958).

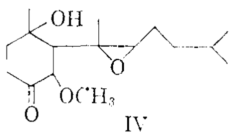
(8) D. D. Chapman and D. S. Tarbell, *ibid.*, **80**, 3679 (1958).

(9) A. D. Cross and D. S. Tarbell, *ibid.*, **80**, 3682 (1958).

(10) R. M. Carman, D. D. Chapman, N. J. McCorkindale, D. S. Tarbell, F. H. L. Varino, R. L. West and D. J. Wilson, *ibid.*, **81**, 3151 (1959).

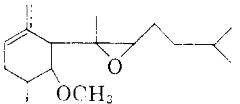
the $-CH_2CHOH$-group as part of a ring system,[7] the isopropylidene group,[3,5] the $-CHCH_2CH_2$-$CH(CH_3)_2$ group,[4,6] (in the reduced alcohol-I) and the methoxyl group[3,4] have been established, and are supported by n.m.r. data.

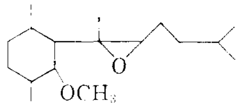

III

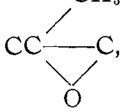

IV

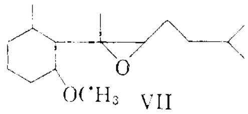
The ketone IV,[4,6] derived from tetrahydroalcohol-I (III),[4,6] contains the $-CH_2CO-CHOCH_3$ group, shown by deuterium exchange experiments on the monofurfurylidene derivative and by the high carbonyl frequency (1724 cm.$^{-1}$)[11] of the ketone IV, among other reasons. *t*-Butoxide–*t*-butanol converts IV to a *crystalline isomer*,[12] m.p. 78°; the non-elimination of water or methanol from IV by base is significant.

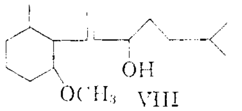
Reduction with rhodium–hydrogen of the two unsaturated acetates[10] (prepared from the acetate of III with thionyl chloride–pyridine) gives the desoxy compound VI, still containing one epoxide group. The unsaturated compounds V contain the side-chain as shown, because they yield isocapraldehyde (and formaldehyde) with periodic acid and with sodium periodate, due to hydration of the side-chain epoxide and cleavage.[13] A tabulation of n.m.r. data for II and fourteen derivatives shows clearly the presence of *three* epoxide protons in II and derivative of II in which the side-chain double bond is reduced, a single epoxide proton,[14] τ 7.20–7.65, in the other compounds in which only the second ether ring is intact, and its absence in the hexahydroalcohol IX in which the epoxide ring has been opened.


V.R = $COCH_3$

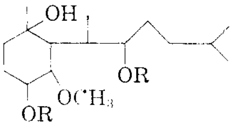

VI.R = $COCH_3$
VIa.R = H
VIb.R = Ts

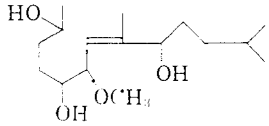
The didesoxy compound VII (formed from tosylate VIb with lithium aluminum hydride) gives with dilute mineral acid the isomeric allylic alcohol VIII (terminal methylene group in infrared[15]); VIII is oxidized to an α,β-unsaturated ketone, (λ_{max} 222 mμ; ε, 7000; carbonyl band, 1680 cm.$^{-1}$), which is reduced back to VIII. The didesoxy compound VII shows unsplit methyl protons at τ 8.90, due to  $\overset{CH_3}{CC}\underset{O}{-}C$, and this group disappears in VIII, with the appearance of two vinyl protons.

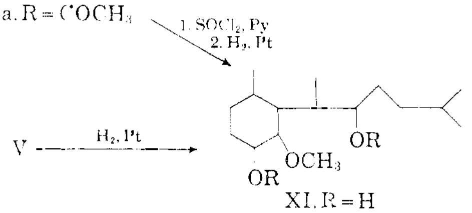

VII


VIII

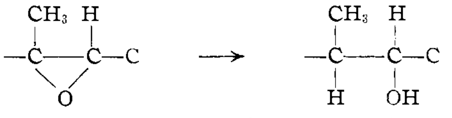
Lithium aluminum hydride with III gives two triols, the α- and β-hexahydroalcohols IX and X; the latter is an open chain compound, formed by an isomerization reaction.[16] That IX is formed from III without rearrangement is shown by conversion of IXa by dehydration and reduction to the crystalline desoxy compound XI, m.p. 84°; this compound also is obtained by hydrogenation of the anhydro compounds V, with hydrogen–platinum, followed by saponification. This gives XIa by hydrogenolysis, in addition to VI. Since the formation of V from III has been proved to proceed without rearrangement,[10] and since catalytic reduction of V may be assumed to do the same, it is concluded that IX and XI are formed from III without rearrangement. Oxidation of XI gives a diketone, with two carbonyl peaks (1725, 1705 cm.$^{-1}$), which is not a β-diketone, and which does not lose methanol; hence the methoxyl is not beta to either carbonyl. The n.m.r. spectrum of III shows two unsplit CH_3-C-O groups; IXa shows only one CH_3-C-O, but shows now four peaks in the CH_3-C region corresponding to nine protons. Six of these are in the gem dimethyl group, and the new CH_3CH has been formed by opening the side-chain epoxide reductively


IX.R = H
IXa.R = $COCH_3$

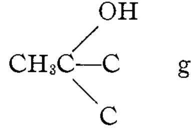

X



XI.R = H
XIa.R = $COCH_3$



$$-\overset{CH_3}{C}\overset{H}{-}C-C \longrightarrow -\underset{H}{\overset{CH_3}{C}}-\underset{OH}{\overset{H}{C}}-C$$

The side-chain accounts for eight carbons of III leaving seven (plus methoxyl) for the ring system; one  $CH_3\overset{OH}{C}\underset{C}{-}C$ group is present and, since a carbocyclic ring is present, it must be a six-mem-

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[11] *Cf.* R. N. Jones, *et al.*, *ibid.*, **70**, 2024 (1948); **74**, 2828 (1952); C. Sandris and G. Ourisson, *Bull. Soc. Chim.*, [5] **23**, 958 (1956).

[12] A reasonable structure can be proposed: K. R. Huffman and D. S. Tarbell, unpublished.

[13] The isocapraldehyde obtained previously[10] from the diol derived from V (isomer with endocyclic double bond) was thus formed by opening the second epoxide group in the side-chain; the precursor V did not have the structure $RC(CH_3){=}CHCH_2CH_2CH(CH_3)_2$ as postulated.[10] The more reactive epoxide in II is thus the spiro one, and the less reactive is in the side-chain.

[14] G. V. Tiers, "Tables of τ Values"; C. Y. Hopkins and H. J. Bernstein, *Can. J. Chem.*, **37**, 775 (1959).

[15] Isomerization of epoxides to allylic alcohols by acids is reported by W. J. Hickinbottom, *J. Chem. Soc.*, 1331 (1948); L. F. Fieser and T. Goto, quoted in L. F. Fieser and M. Fieser, "Steroids," Reinhold Publ. Corp., New York, N. Y., 1959, p. 243.

[16] R. M. Carman and D. S. Tarbell, unpublished; X, but not IX, was described in an earlier account[6] of hydride reduction of III.

bered ring. The facts that in III the tertiary hydroxyl and the methoxyl cannot be beta to the secondary hydroxyl, and that IX does not react with periodate, severely limit the possible arrangements of the three oxygen functions on the ring in III. The conversion of IX to perhydrobenzofuran derivatives, the structure of one of which is established by synthesis,[17] indicates the correctness of structures IX, III and II.

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[17] D. D. Chapman, *et al.*, THIS JOURNAL, **82**, 1009 (1960).

[18] Abbott Laboratories Fellow, 1957–1958.

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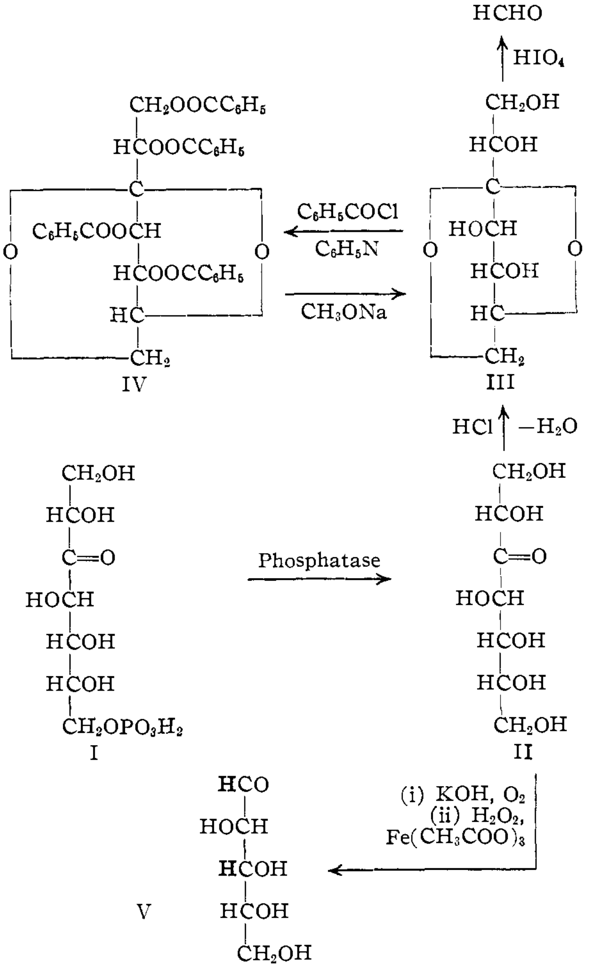
RECEIVED JANUARY 4, 1960

3-KETO-D-ARABOHEPTOSE PHOSPHATE: PROPOSED STRUCTURE FOR A NEW HEPTULOSE PHOSPHATE[1]

Sir:

In a previous communication,[2] we reported the isolation of a new heptulose phosphate from a digest of rat liver supernatant plus glucose 6-phosphate (G6P) as well as some properties of the heptulose, its phosphate, anhydride and anhydride tetrabenzoate. Evidence supporting its structure as 3-keto-D-*arabo*heptose phosphate (I) is now presented.

Phosphatase ("polidase") hydrolysis of I (free of other sugar phosphates) yielded the free sugar II which exhibits positive color reactions for ketose (resorcinol HCl; naphthoresorcinol-HCl and α-naphthylamine phosphoric acid) and for keto-heptose by the orcinol trichloroacetic acid reagent. II was degraded first by alkali oxidation[3] and then by ferric acetate–H_2O_2[4] to a pentose V. This was identified as arabinose by circular paper chromatography in two separate solvent systems[5] and by its crystalline diphenylhydrazone (2 mg.) m.p. 202.5°. The mixed melting point with authentic D-arabinose diphenylhydrazone (m.p. 202.5°) was not depressed. Acid treatment[6] of II yielded an anhydride III which was converted to the pure crystalline tetrabenzoate derivative[2] IV. Debenzoylation of IV (3 mg.) with sodium methoxide reagent produced III, which was oxidized with periodate to yield an equimolar amount of formaldehyde.[7] Gluco- and mannoheptulose[8] exhibited a rate of migration on paper different from II in butanol–pyridine–water (6:4:3).



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RECEIVED DECEMBER 28, 1959

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[1] Supported by research grants (P-106, P-107) from the American Cancer Society, Inc., New York, and (C-3213) from the National Cancer Institute, National Institutes of Health, Bethesda, Md.

[2] H.-G. Sie, V. N. Nigam and W. H. Fishman, THIS JOURNAL, **81**, 6083 (1959).

[3] N. K. Richtmyer, R. M. Mann and C. S. Hudson, *ibid.*, **61**, 343 (1939).

[4] H. G. Fletcher, Jr., H. D. Diehl and C. S. Hudson, *ibid.*, **72**, 4246 (1950).

[5] Acetone:butanol:water (7:2:1) and butanol:pyridine:water (6:4:3) separate ribose and arabinose completely in six hours. The pentose consistently occupied the arabinose position. The conditions of degradation were ones which yield ribose only from sedoheptulose[8] and this fact was confirmed in this laboratory with both solvent systems.

[6] H.-G. Sie, V. N. Nigam and W. H. Fishman, *J. Biol. Chem.*, **234**, 1955 (1959).

[7] D. A. McFadyen, *ibid.*, **158**, 107 (1945).

[8] We thank Dr. H. S. Isbell, National Bureau of Standards, Washington, D. C., for making these reference sugars available to us.

NOVEL THERMAL REARRANGEMENTS ACCOMPANYING ACETATE PYROLYSIS IN SMALL RING SYSTEMS

Sir:

Pursuant to the preparation and the polymerization of vinylcycloalkanes, the acetate pyrolysis procedure[1,2] was applied to esters of secondary alcohols bearing an alpha carbocyclic group. We wish to report the discovery that the principal product from the pyrolysis of 1-cyclopropylethyl acetate was *cyclopentene* and that from 1-cyclobutylethyl acetate was *cyclohexene*. The pyrolysis of 1-cyclopentylethyl acetate proceeded in the reported manner[3] while the pyrolysis of 3-cyclohexenylmethyl acetate yielded 4-methylenecyclohexene, 60%, toluene, 24%, and methylenecyclohexene, 3%.

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[1] C. G. Overberger and D. Tanner, THIS JOURNAL, **77**, 369 (1955).

[2] W. J. Bailey and W. F. Hale, *ibid.*, 647 (1959), and previous references.

[3] J. R. van der Bij and E. C. Kooijman, *Rec. trav. chim.*, **71**, 837 (1952).