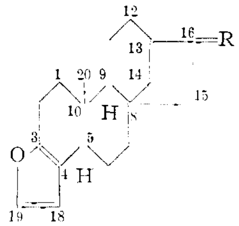
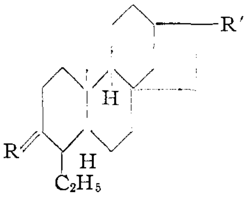
Further evidence for the location of the angular methyl group at C-10[2] rather than C-5[7] could be provided by bromination experiments. If the angular methyl group were located at C-5, the monobromo derivative of the ketone V should be the axial isomer[12] as demonstrated in the case of friedelin[13] and 19-nor-androstan-17β-ol-3-one acetate (present authors). On the other hand, if the angular methyl group is situated at C-10, an equatorial bromo derivative would be predicted[12] as was indeed found to be the case in the monobromination of the model 4α-ethyl-cholestan-3-one (m.p. 112–114°, $[\alpha]_D$ +33°, no u.v. shift but $\lambda_{max.}^{CHCl_3}$ 5.75 μ, found for $C_{29}H_{49}BrO$: C, 70.56; H, 9.73; Br, 16.49) and of the ketone V (m.p. 127–127.5°, $\lambda_{max.}^{CHCl_3}$ 5.73 μ, equatorial type bromo-ketone R.D. curve,[14] found for $C_{19}H_{29}BrO$: C, 64.84; H, 8.21; O, 4.71).



I, R = $\overset{\text{OH}}{|}\text{—CH}_2\text{OH}$
II, R = O
III, R = H_2
IV, R = $\overset{\text{H}}{|}\text{—CH}_3$



V, R = O; R′ = **H**
VI, R = O; R′ = CH_3
VII, R = $\overset{\text{H}}{\vdots}\text{...OH}$; R′ = **H**

The negative Cotton effect of the rotatory dispersion curves of V, VI and the corresponding mono-bromo derivative requires *that the A/B ring juncture is antipodal to that of the other polyterpenes and steroids* and this apparently also applies[5] to the other members of the phyllocladene group including the *Garrya* alkaloids. That diterpenes with the "wrong" absolute configuration are more common than has hitherto been assumed was demonstrated recently with eperuic acid,[15] which possesses an unrearranged diterpene skeleton. The possible biogenetic significance of this unexpected stereochemical feature and additional evidence in favor of stereoformula I for cafestol will be discussed in a detailed paper.

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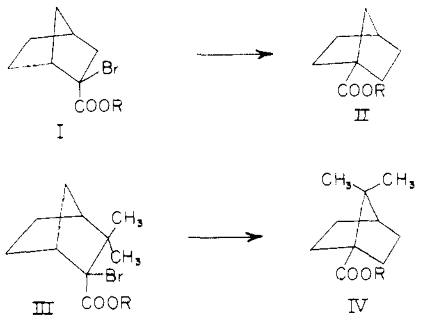
THE OBSERVATION OF REARRANGEMENT DURING HYDROGENOLYSIS; A NEW METHOD OF PREPARING BRIDGEHEAD CARBOXYLIC ACIDS

Sir:

Previous studies on the mechanism of hydrogenolysis by means of metals have stressed the occurrence of retained configuration.[1–6] For these cases ionic reaction mechanisms have been suggested. In contrast, the occurrence of almost complete racemization as a result of the hydrogenolysis of carbon–sulfur bonds has been attributed to the intermediacy of free radicals.[7,8] We wish to report the incidence of rearrangement accompanying the hydrogenolysis of carbon–halogen bonds in certain bicyclo[2,2,1]heptane compounds. Well characterized cases of rearrangement during hydrogenolysis have not been discussed previously, to the best of our knowledge.

This observation also affords a novel and a comparatively simple route to the synthesis of bridgehead compounds of bicyclo[2,2,1]heptane, and very possibly other bicyclic skeletons. These substances heretofore have been available only through rather lengthy sequences of reaction.[9,10] Good yields of product were obtained in each of the cases examined. Thus, the bromoacid I (R = H),[11]



when shaken under 40 lb. hydrogen pressure with 10% palladium–charcoal in dilute methanolic potassium hydroxide[12] and the product worked up in the customary manner, gave II (R = H), m.p. 112–113° after one recrystallization from pentane. An elemental analysis, mixed melting point and comparison of infrared spectrum with that of an authentic sample[13] established the identity of the product. The bromoester I (R = CH_3), when treated with powdered zinc in glacial acetic acid

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[1] W. A. Bonner, J. A. Zderic and G. S. Casaletto, THIS JOURNAL, **74**, 5086 (1952).

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[10] P. D. Bartlett and L. H. Knox, *ibid.*, **61**, 3189 (1939).

[11] The structures of the compounds I and II have been established and will be discussed in a forthcoming publication, from this laboratory.

[12] According to the directions of reference 6 and L. F. Fieser and Wei-Tuan Huang, THIS JOURNAL, **75**, 4837 (1953).

[13] We are indebted to Dr. W. von E. Doering for supplying this reference compound.

under the mild conditions described by Ott and Kramer,[9] yielded a colorless liquid on fractional distillation of the product; b.p. 52–53° at 1.8 mm., $n^{17}D$ 1.4670, identical in these properties as well as infrared spectrum with a sample of methyl ester prepared from II (R = H) by reaction with diazomethane. The bromoacid III (R = H) and the bromoester III (R = CH_3) gave results entirely similar to the above when treated, respectively, under hydrogenolysis conditions with palladium–hydrogen and zinc–acetic acid. The acid IV (R = H) obtained *via* palladium hydrogenolysis was identical with the apocamphane-1-carboxylic acid described by Bartlett and Knox[10]; m.p. 218° after recrystallization from methanol–water and petroleum ether, amide[14] m.p. 185° (lit.[10] 184–185°). The ester IV (R = CH_3) obtained from the zinc hydrogenolysis was recovered as a colorless liquid, b.p. 55° at 0.4 mm, $n^{25}D$ 1.4690, which when saponified gave the pure acid IV, m.p. 219–220° on recrystallization from petroleum ether, which showed no depression of m.p. on admixture with the acid sample resulting from the palladium reaction and had an identical infrared spectrum.

We are presently studying the circumstances required for the occurrence or absence of rearrangement to correlate such factors with details of the mechanism of related hydrogenolysis reactions.

Support of this research by the U. S. Rubber Co. is gratefully acknowledged.

[14] Identical with a sample kindly provided by Dr. P. D. Bartlett.

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RECEIVED NOVEMBER 20, 1957

SEPARATION OF POLYUNSATURATED FATTY ACID METHYL ESTERS BY GAS CHROMATOGRAPHY

Sir:

The partial separation of methyl esters of high molecular weight fatty acids by gas chromatography has been reported.[1–4] This analysis has great importance to the study of fat nutrition and metabolic processes involving fats. The above mentioned work included the separation of methyl oleate and methyl stearate and the partial separation of methyl oleate and methyl linoleate. Separation of methyl linoleate from methyl linolenate and other polyunsaturates has not been reported. The above work was done at 197 to 256° and used, as the partition medium, Apiezon M or L vacuum grease.[4] The retention times under conditions optimum for good resolution were of the order of 2 to 3 hours for the C_{18} fraction.

We wish to report the complete separation of the methyl esters of the commonly known fatty acids including the polyunsaturated materials. This includes the complete separation of the methyl esters of the following acids: palmitic, palmitoleic, stearic, oleic, linoleic, linolenic, arachidic, and erucic. The time required for an analysis has been much shortened, evidenced by the fact that methyl stearate has an emergence time of 27 minutes compared to approximately two hours in the previous work.

Using the column and conditions described below, the fatty esters in each carbon number class emerge from the column in times which increase with the number of double bonds in the compound. Thus, the order of emergence is reversed compared to that obtained with Apiezon L and other non-polar partition media. Table I gives the retention volumes for those materials for which data have been obtained thus far.

Work currently in progress indicates that further improvements in resolution are possible and that the retention times can be reduced further without seriously harming resolution.

Plots of the logarithm of the retention volume *versus* the number of carbon atoms in the fatty acid chain or the number of double bonds in the fatty acid chain of a given length, give straight lines which allow the prediction of approximate retention volumes for some of the less abundant fatty esters such as methyl arachidonate (methyl eicosatetraenoate) and methyl eicosapentaenoate.

Experimental conditions: column, copper 1/4" o.d., 12 ft. in length; partition medium, 23.1 g. of packing, consisting of 30% Reoplex 400 Plasticizer[5] on Johns–Mansville Celite 545[6] (80–100 mesh); detector, Gow-Mac Filament Thermal Conductivity Cell (Model 9285 - Pretzel geometry); flow rate, 75 ml. per minute of helium measured at column exit and at room temperature; column and cell temperature, 240°; pressure drop across column, 30 p.s.i.g.; sample size, 10 microliters.

TABLE I

Compound	Retention vol. (ml.) (V'_R)[7]
Methyl caprylate	140
Methyl caprate	245
Methyl laurate	420
Methyl myristate	710
Methyl palmitate	1220
Methyl palmitoleate	1340
Methyl stearate	2000
Methyl oleate	2180
Methyl linoleate	2520
Methyl linolenate	3040
Methyl arachidate	3400
Methyl erucate	(6000)

It is planned to determine retention volumes under similar conditions on this and other polar partition media for these and other known fatty acid esters and report a more complete list of data in a forthcoming publication.

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[3] William Insull, Jr., and A. T. James, American Chemical Society Meeting, New York City, September, 1957.

[4] S. R. Lipsky, private communication.

[5] Geigy Chemical Company, Dyestuffs Division, Yonkers, New York.

[6] The Celite was acid washed, neutralized, rinsed and dried according to Lipsky.[4]

[7] V'_R values are calculated for a flow rate of 75 ml./min. and under these conditions V_R for air is 94 ml.