[CONTRIBUTION FROM CHANDLER AND HAVEMEYER LABORATORIES, COLUMBIA UNIVERSITY]

On the Decarbonmonoxylation Reaction

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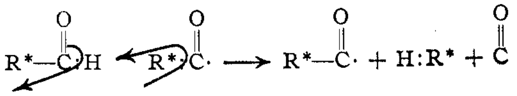
Optically active methylethylisobutylacetaldehyde, bicyclo[2.2.2]octane-2-carboxaldehyde and apocamphane-1-carboxaldehyde have been decarbonmonoxylated to the corresponding hydrocarbons. From these events, it is concluded that an alkyl free radical is incapable of sustaining optical activity, is not prone to rearrangement and is not of prohibitively high energy when situated in a bridgehead.

In the course of divers investigations, the liquid phase decarbonmonoxylation reaction developed by Winstein and Seubold[1] has been applied to three aldehydes, the specific structural features of which are such that the results are pertinent both to the mechanism of the reaction and the properties of free radicals.

Optically active methylethylisobutylacetaldehyde (I) was prepared in two steps from active methylethylisobutylacetic acid (II)[2] by reduction with lithium aluminum hydride to active 2,4-dimethyl-2-ethylpentanol-1 (III) which was then oxidized by *t*-butyl chromate, the reagent discovered by Oppenauer and Oberrauch.[3] The optical purity of II used in these experiments being 6.4%, it is reasonably assumed that the carbinol III and the aldehyde I are of the same degree of purity. The decomposition of I, induced by *t*-butyl peroxide, afforded 2,4-dimethylhexane (IV) with no optical activity. On the basis of the specific rotation of 18.7° given by Levene and Marker[4] for optically pure IV, the product of this reaction could have had a rotation as high as 1.2°. It is therefore concluded that an intermediate stage in the decarbonmonoxylation is unable to sustain asymmetry. In particular, the free radical scheme proposed by Winstein and Seubold[1] is consistent, whereas the alternative free radical displacement (*a*), whether rear or front, is very probably not.

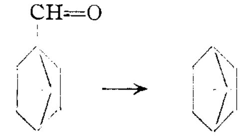
(a) 

$$R^*{-}\overset{O}{\overset{\|}{C}}H \; R^*\overset{O}{\overset{\|}{C}}\cdot \longrightarrow R^*{-}\overset{O}{\overset{\|}{C}}\cdot + H{:}R^* + \overset{O}{\overset{\|}{C}}$$

On the hypothesis that free radicals are involved in the reaction[5] the stereochemical result can be considered as evidence for the theory that carbon free radicals cannot support asymmetry (under the condition of this experiment).

Bicyclo[2.2.2]octane-2-carboxaldehyde (V), prepared by the direct hydrogenation of the Diels-Alder adduct of acrolein and cyclohexadiene,[6] loses carbon monoxide on heating with *t*-butyl peroxide giving bicyclo[2.2.2]octane (VI), apparently uncontaminated with rearranged hydrocarbon, bicyclo[1.2.3]octane. In another work it has been found that 2-bromobicyclo[2.2.2]octane rearranges to 2-bromobicyclo[1.2.3]octane with extraordinary ease, so weak an acid as silver bromide being sufficient catalyst.[7] It is of interest that the bicyclo[2.2.2]octyl system, so easily rearranged when electron deficient, does not rearrange as a free radical, a fact to be compared with the partial rearrangement of the neophyl radical where participation by phenyl may constitute a driving force for rearrangement.

Finally, the behavior of a bicyclic bridgehead aldehyde was examined. 10-Hydroxycamphane, prepared from apocamphane-1-carboxylic acid by lithium aluminum hydride reduction,[8] was oxidized with chromic anhydride in acetic acid, essentially according to Asahina and Ishidate,[9] to apocamphane-1-carboxaldehyde (VII). This aldehyde reacted normally giving apocamphane (VIII), indicating that there is no particular inhibition to a bridgehead free radical.



VII VIII

Experimental

2,4-Dimethyl-2-ethylpentanol-1 (III).—Methylethylisobutylacetic acid (II, 47 g.; $[\alpha]^{26}D$ −1.39°) was added to 14. g. of lithium aluminum hydride in 250 cc. of dry ether. The resulting mixture was stirred for 4 hr. and treated with dilute hydrochloric acid. The dried ether extract was distilled giving 37 g. (87%) of III; b.p. 187–189°; $n^{25}D$ 1.4380; d^{25} 0.837; $[\alpha]^{25}D$ +0.09° (neat); *M*D, calcd., 45.29; found, 45.32.

Anal. Calcd. for $C_9H_{20}O$: C, 74.9; H, 14.0. Found: C, 75.2; H, 13.8.

Methylethylisobutylacetaldehyde (I).—The solution resulting from adding 56.5 g. of chromium trioxide to 110 g. of *t*-butyl alcohol with cooling followed by the addition of 450 cc. of pentane was dried over anhydrous sodium sulfate. The addition of 29 g. of III ($[\alpha]^{25}D$ +0.09°) in 100 cc. of pentane at 0° caused the solution to turn from red to dark brown. After 5 days at room temperature, the solution was treated with 350 cc. of cold water and oxalic acid in small portions until carbon dioxide ceased to be evolved. Then 76 cc. of concd. sulfuric acid in 150 cc. of glacial acetic acid was added slowly with stirring. The pentane layer was separated, washed with 10% sodium carbonate solution and dried over anhydrous sodium sulfate.

Distillation gave 10 g. (37%) of I; b.p. 165–168°; $n^{25}D$ 1.4224; d^{25}_4 0.827; $[\alpha]^{30}D$ −0.18° (neat); *M*D, calcd., 43.77; found, 43.73.

Anal. Calcd. for $C_9H_{18}O$: C, 76.0; H, 12.7. Found: C, 76.1; H, 13.2.

A sample of *dl*-I was converted to the 2,4-dinitrophenylhydrazone, m.p. 127–127.5° after crystallization from ethanol–water.

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(1) S. Winstein and F. H. Seubold, THIS JOURNAL, **69**, 2916 (1947).

(2) W. von E. Doering and K. B. Wiberg, *ibid.*, **72**, 2608 (1950).

(3) R. V. Oppenauer and H. Oberrauch, *Anales asoc. quim. argentina*, **37**, 246 (1949).

(4) P. A. Levene and R. E. Marker, *J. Biol. Chem.*, **91**, 405 (1931).

(5) This hypothesis is supported by the nature of the inducing reagent and the structure of other products formed [see Winstein and Seubold[1] and F. F. Rust, F. H. Seubold and W. E. Vaughn, THIS JOURNAL, **70**, 95, 3258, 4253 (1948)].

(6) O. Diels and K. Alder, *Ann.*, **478**, 137 (1930).

(7) W. von Doering and M. Farber, THIS JOURNAL, **71**, 1514 (1949).

(8) M. Levitz, Ph.D. Dissertation, 1951, Columbia University.

(9) Y. Asahina and M. Ishidate, *Ber.*, **67**, 1202 (1934).

Anal. Calcd. for $C_{18}H_{22}N_4O_4$: C, 55.9; H, 6.8; N, 17.4. Found: C, 55.8; H, 6.8; N, 17.2.

Decarbonmonoxylation of I.—A solution of 8 g. of I ($[\alpha]^{30}\text{D}$ −0.18°) and 0.5 g. of *t*-butyl peroxide was refluxed in a 20-cm. Vigreux column fitted with a total condensation, variable take-off head with the heating bath at 180°. Material boiling below 115° was collected. After three additions of 0.1 g. of peroxide over a three-hour period, evolution of carbon monoxide had ceased. The distillate was washed with concentrated sulfuric acid, distilled from sodium and redistilled from potassium to give 2.2 g. of 2,4-dimethylhexane; b.p. 108–110°; $n^{25}\text{D}$ 1.3928; d^{25}_4 0.695; $[\alpha]^{22}\text{D}$ 0.00 ± 0.01° (reported[4] b.p. 110–111° and d^{21}_4 0.703).[10]

Decarbonmonoxylation of Bicyclo[2.2.2]octane-2-carboxaldehyde (V).—Following Diels and Alder,[6] 128 g. of cyclohexadiene and 180 g. of acrolein was heated 18 hr. at 120° in an autoclave. Distillation yielded 139.3 g. of Δ^5-bicyclo[2.2.2]octene-2-carboxaldehyde, the semicarbazone of which melted 165.5–167° after recrystallization from methanol–water (reported[6] m.p. 176–177°) and could be hydrogenated to the saturated semicarbazone, m.p. 191–192° (reported[6] m.p. 191–192°). Hydrogenation of the unsaturated aldehyde with platinum oxide in glacial acetic acid afforded crude V which was purified through the bisulfite addition product and, somewhat wastefully, by distillation.

Pure V (m.p. 75.5–77°, 6 g.) was refluxed with *t*-butyl peroxide as described above. The product which had sublimed extensively was removed mechanically and sublimed from phosphorus pentoxide and then from sodium to give bicyclo[2.2.2]octane (VI), m.p. 174.5–175°.

Anal. Calcd. for C_8H_{14}: C, 87.2; H, 12.8. Found: 87.0; H, 12.8.

Apocamphane-1-carboxaldehyde (VII).—Following the method of Asahina and Ishidate,[9] a solution of 6 g. of 10-hydroxycamphane, m.p. 199–200°, in 40 cc. of glacial acetic acid was treated with 4 g. of potassium dichromate and shaken for 1 hr. at 80–90°. The reaction mixture was diluted with water and extracted with 5 portions of pentane. The pentane extracts were washed with 3 portions of 10% aqueous sodium carbonate solution and then with saturated sodium chloride, and concentrated to a viscous residue from which 6.6 g. (81%) of VII semicarbazone, m.p. 206–209°, was obtained. Repeated recrystallization from ethanol raised the m.p. to 208–209°, a value considerably below that reported by Asahina and Ishidate,[9] m.p. 220–221°. It is mentionable that the clear melt clouds and decomposes at 210–211°, in part to a solid which melts completely from 245–250°.

Anal. Calcd. for $C_{11}H_{19}N_3O$: C, 63.1; H, 9.2; N, 20.1. Found: C, 63.2; H, 9.3; N, 19.8.

Steam distillation of VII semicarbazone from 7% phosphoric acid followed by extraction with pentane, washing with sodium carbonate, and drying, afforded the aldehyde VII, m.p. 186–188° (reported[9] m.p. 187–189°).

Decarbonmonoxylation of VII.—A mixture of 1.0 g. of VII and 0.8 cc. of *t*-butyl peroxide was heated at 140–150° under reflux in a nitrogen atmosphere, an additional 0.1 cc. of peroxide being added after 1.5 and 2.5 hr., respectively. After 2.75 hr. the vigorous gas evolution having diminished, the temperature was raised to 180° for 10 min. Following distillation of most of the di-*t*-butyl peroxide, the residue was transferred in a little pentane and evaporatively distilled at 100° and 30 mm. The partly solid distillate was dissolved in pentane, washed with aqueous sodium carbonate (from which 5 mg. of apocamphane-1-carboxylic acid was recovered), with aqueous semicarbazide solution, with water, then repeatedly with cold, concentrated sulfuric acid until discoloration ceased, again with water and finally with saturated sodium chloride solution. Careful distillation of the pentane followed by sublimation at 50–60° and 50 mm. yielded 108 mg. of apocamphane (VIII), m.p. 82–87.5° (sealed tube). Resublimation (m.p. 85.5–87.5°), crystallization from methanol, and resublimation from phosphorus pentoxide gave pure material, m.p. 89.5–90.5° (sealed tube).[11] The poor yield is at least in part to be ascribed to the exceptional volatility of the hydrocarbon.

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(10) The physical constants, $n^{25}\text{D}$ 1.3925, d^{25}_4 0.694, b.p. 110°, were calculated from the data of A. W. Francis, *Ind. Eng. Chem.*, **33**, 554 (1941).

(11) G. Komppa and T. Hasselström, *Ann.*, **496**, 164 (1932), report m.p. 86° for unrecrystallized VIII.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, LOS ANGELES]

Flavanones and Related Compounds. VII. The Formation of 4,6,3',4'-Tetrahydroxy-2-benzylcoumaranone-3 by the Sodium Hydrosulfite Reduction of Quercetin

BY T. A. GEISSMAN AND HAROLD LISCHNER

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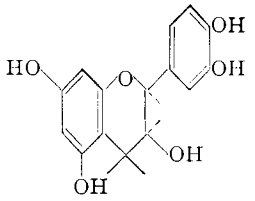
The sodium hydrosulfite reduction of quercetin yields, besides the previously described 2,3-dihydroquercetin, 4,6,3',4'-tetrahydroxy-2-benzylcoumaranone-3. This was shown to be identical with the compound reported in the literature to have the structure 3,4,3',4'-pentahydroxy-2-benzylcoumarane.

In the course of experiments aimed at devising a convenient route to the difficultly accessible epicatechin (I) a study has been made of the reduction of certain flavonoid compounds. Since epicatechin has the configuration shown,[1] it was hoped that its synthesis might be accomplished by a reduction of quercetin (II) in which a catalytic reduction of the 2,3-double bond would comprise the step leading to the desired *cis* configuration of the substituents in the 2,3-positions.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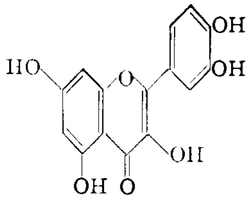
II

It has been reported that quercetin does not absorb hydrogen when platinum oxide is used as the catalyst.[2-4] While our experience did not confirm this, the reduction which occurred appeared to be non-specific. The yellow color of the solution had not disappeared after three moles of hydrogen had been adsorbed, and no homogeneous product was isolated.

In order to examine the catalytic reduction of dihydroquercetin (III), the latter substance was prepared by the hydrosulfite reduction of quercetin as described by Pew.[4] The flavanonol was formed

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(1) K. Freudenberg and M. Harder, *Ann.*, **451**, 213 (1927); W. Hückel, *ibid.*, **477**, 159 (1929).

(2) K. Freudenberg and A. Kammuller, *ibid.*, **451**, 209 (1927).

(3) R. Mozingo and H. Adkins, THIS JOURNAL, **60**, 669 (1938).

(4) J. C. Pew, *ibid.*, **70**, 3031 (1948).