

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY]

Oxidation of Camphor with Peracetic Acid

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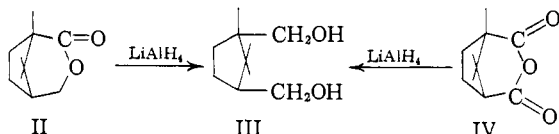
Oxidation of camphor with peracetic acid followed different courses depending on the acidity. In weakly acidic solution, lactone V was formed in high yield. In the presence of strong acid, a 30% yield of α -campholide (II) was isolated. A modification of the Criegee mechanism is proposed to explain these results.

In 1899, Baeyer and Villiger¹ reported that the action of Caro's acid on camphor (I) gave α -campholide (II) and an unidentified $C_{10}H_{16}O_4$ lactone. In view of recent reports on the Baeyer-Villiger



reaction²⁻⁶ which indicate that the expected order of alkyl migration is $3^\circ > 2^\circ > 1^\circ$, we decided to re-investigate the action of peracid on camphor.

The original¹ results could be duplicated on treatment of camphor with an excess of 40% peracetic acid⁷ in a 40:60 solution of sulfuric acid-acetic acid. Chromatography of the crude product gave a 30% yield of a product whose physical properties agreed with those published for α -campholide (II).⁸ Chemically, lactone II could be converted to the known diol III by lithium aluminum hydride



reduction. Comparison of the diol with an authentic sample prepared from camphoric anhydride (IV) established its identity.

On the other hand, when camphor was treated with peracetic acid in acetic acid containing sodium acetate, no isolable α -campholide (II) could be detected in the product. The product, isolated in good yield, consisted of another 6-membered lactone which was *a priori* assigned structure V.⁹

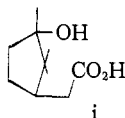
The structure of lactone V was established in two ways. Since V is a lactone derived from α -campholenic acid (VII) it should be readily iso-

(1) A. Baeyer and V. Villiger, *Ber.*, **32**, 3625 (1899).

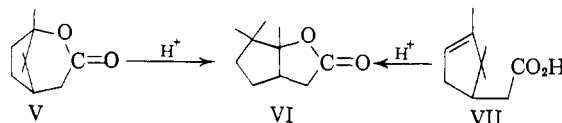
(2) For a recent review see C. H. Hassall in "Organic Reactions," Vol. IX, John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 73-106.

(3) W. D. Emmons and G. B. Lucas, *THIS JOURNAL*, **77**, 2287 (1955).(4) J. W. Wilt and A. Danielzadeh, *J. Org. Chem.*, **23**, 920 (1958).(5) G. Büchi and I. M. Goldman, *THIS JOURNAL*, **79**, 4741 (1957).(6) W. von E. Doering and L. Speers, *ibid.*, **72**, 5515 (1950).

(7) Obtained from the Becco Chemical Division, Buffalo, N. Y. This material contains 1% sulfuric acid.

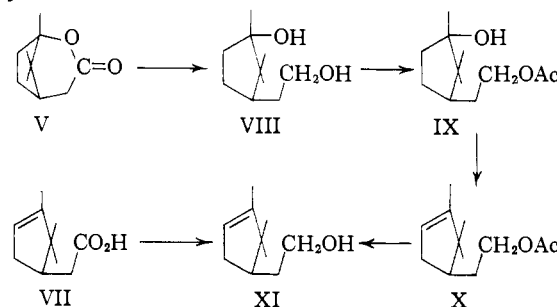
(8) Although no other pure compounds could be isolated, oils and some semi-crystalline material were obtained which probably contained the $C_{10}H_{16}O_4$ lactone.(9) An hydroxy acid assigned structure i was isolated by W. A. Mosher and E. O. Langerak, *ibid.*, **73**, 1302 (1951), as a product of the chromic acid oxidation of isoborneol. The hydroxyl group and the carboxymethyl group are probably *trans* in this compound since it appeared to be stable to lactonization.

merized by acid to dihydro- β -campholenolactone (VI).¹⁰ This conversion was, in fact, carried out in 87% yield on treatment of V with dilute sulfuric acid in acetic acid. The structure of VI was established by comparison with an authentic sample



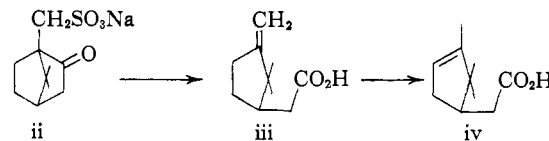
prepared from α -campholenic acid.¹¹

A more formal structure proof involved conversion of lactone V to alcohol XI. Lithium aluminum hydride reduction of V gave the diol VIII which could be monoacetylated to give hydroxyacetate IX. Phosphorous oxychloride-pyridine dehydration gave the acetate X which could be converted to XI on treatment with lithium aluminum hydride



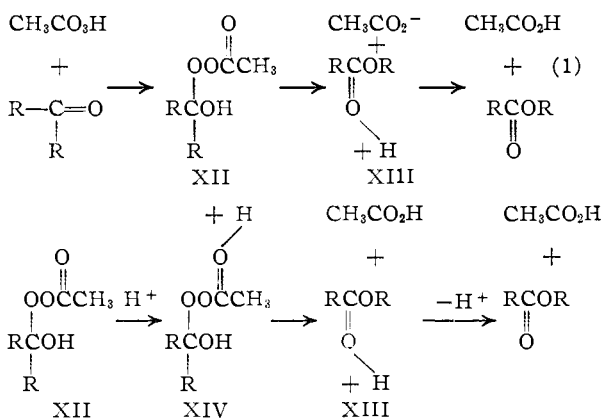
The structure of alcohol XI was confirmed by comparison of its infrared spectrum and vapor phase chromatogram with those of a sample prepared from α -campholenic acid.

These results represent the first well-defined data on the change in product composition with change in acidity in the Baeyer-Villiger reaction.¹² Al-

(10) F. Tiemann, *Ber.*, **28**, 2166 (1895); **30**, 405 (1897).(11) α -Campholenic acid was prepared from camphor oxime by the method of F. Tiemann, *ibid.*, **29c**, 3006 (1896). A more convenient method was that of J. Brecht, Rochussen and Heusch, *ibid.*, **35**, 1290 (1902), which involves fusion of sodium 10-camphorsulfonate (ii) with potassium hydroxide. Apparently, the exocyclic isomer iii is formed first and isomerized by base to give α -campholenic acid (iv) (*cf.* D. S. Tarbell and F. C. Loveless, *THIS JOURNAL*, **80**, 1963 (1958)). Further, the acid produced from camphor oxime probably was not homogeneous (see Experimental).(12) The earlier results of Doering and Speers⁶ and S. L. Friess, *ibid.*, **71**, 14 (1949), with acetophenone are not comparable since the oxidants and solvents were different. The low yields (4-7%) of benzoic acid isolated by the former authors render precarious any interpretations of these results.

though simple acid catalysis had been noted previously,^{6,13} only the *rate* of oxidation was changed, not the *products*.¹⁴ Thus, it appeared possible that lactone V was formed initially under both sets of conditions but that under the reaction conditions was converted to α -campholide (II).¹⁵ Treatment of either lactone V or VI with peracetic acid and strong sulfuric acid under the conditions of the reaction gave no detectable α -campholide but instead an oil which showed strong hydroxyl and carbonyl absorption in the infrared. These oils had spectra very similar to the more polar products isolated as by-products in the preparation of II and probably are indicative of the fate of any V produced during that reaction.

Consequently, the Criegee mechanism¹⁶ (equation 1) requires modification in strongly acidic solutions. One possible modification would involve protonation of the intermediate hydroxyperester XII prior to its decomposition to products (equation 2). This would probably have the effect of lowering the activation energies of the rearrangement steps, since in equation 1, separation of a positively charged species (XIII) from a negatively charged species (acetate ion) is involved; whereas in equation 2, positively charged XIII would separate from electrically neutral acetic acid.



This lowering of the activation energies would result in a compression¹⁷ of the energy scale for rearrangement thereby allowing alternate reactions to compete more successfully. In other words, the transition state for rearrangement is shifted toward the reactant XIV with consequent de-emphasis of the importance of electronic stabilization of the migrating group.

Alternate explanations^{6,18} for the formation of α -campholide are no longer applicable although they may contribute to the various forces involved.

(13) S. L. Friess and P. E. Frankenburg, *THIS JOURNAL*, **74**, 2679 (1952).

(14) It should be noted that Doering and Speers⁸ pointed out that the effect of acid on the Baeyer-Villiger reaction was more complicated than simple first order dependence.

(15) An analogy would be the carboxyl transfer observed by J. Meinwald, *THIS JOURNAL*, **77**, 1617 (1955), during the cinenic acid rearrangement.

(16) R. Criegee, *Ann.*, **560**, 127 (1948).

(17) Analogous to the arguments advanced by A. Streitwieser, Jr., and W. D. Schaeffer, *THIS JOURNAL*, **79**, 2888 (1957), to explain the differences in products between solvolysis and deamination reactions.

(18) M. F. Murray, B. A. Johnson, R. L. Pederson and A. C. Ott, *ibid.*, **78**, 981 (1956).

Acknowledgments.—We are indebted to Drs. W. J. Farrissey and D. B. Denney for interesting discussions on this problem. Especial thanks are due Dr. R. J. Gall and the Becco Chemical Division for helpful suggestions and gifts of the peracetic acid.

Experimental

All melting points are corrected. Infrared spectra were determined on a Perkin-Elmer Infracord, model 137, in chloroform solution unless otherwise noted; usually, the values quoted are averages of several determinations. Rotations were determined in chloroform. Petroleum ether refers to hydrocarbons boiling from 40–60°. Analyses are by G. Robertson, Florham Park, N. J.

α -Campholide (II).—A solution of 3.0 g. (0.02 mole) of *d*-camphor in 15 ml. of glacial acetic acid containing 6 ml. of concentrated sulfuric acid was treated with 6 ml. (0.036 mole) of 40% peracetic acid over a period of 10 minutes. The solution was kept in the dark at 27° for 5 days. Isolation of the product was accomplished by pouring the solution into a mixture of 200 ml. of ice and water followed by ether extraction. The ether was washed with sodium bicarbonate solution, once with water and dried over sodium sulfate. A dark semi-solid mass (2.85 g.) was obtained after removal of the ether. Chromatography on alumina (washed with ethyl acetate) gave only α -campholide in the petroleum ether eluates. Crystallization from petroleum ether gave two crops of white needles: 0.70 g. (21%), m.p. 209.5–211.5°, $[\alpha]_D^{25}$ -26° ; 0.27 g. (9%), m.p. 205–210° (lit., m.p. 210–211°¹⁹; $[\alpha]_D$ -22° ,¹⁹ -20° ,²⁰ -34° ²¹). Strong carbonyl absorption appeared at 5.73 μ .

Further elution with chloroform-petroleum ether mixtures gave oils and semi-crystalline masses (ca. 1 g.) which showed carbonyl (ca. 5.55 μ) and hydroxyl (ca. 2.62 and 2.72 μ) absorption.

Diol III.—Reduction of 4.0 g. of α -campholide with 2.0 g. of lithium aluminum hydride in 200 ml. of dry ether gave 3.86 g. (94%) of diol III, m.p. 134.5–137.5°. Crystallization from methylene chloride-petroleum ether raised the melting point to 135.5–137.5° (lit., m.p. 137°²² and 130°²³), λ_{max} 2.70, 2.80 μ .

Similar treatment of *d*-camphoric anhydride gave the same diol (III) m.p. 135.5–137.5°; mixture m.p. 136–137°. The infrared spectra of the two samples were identical.

Lactone V.—To a solution of 30 g. (0.2 mole) of *d*-camphor in 150 ml. of glacial acetic acid was added 10 g. of sodium acetate followed by dropwise addition of 60 ml. (0.36 mole) of peracetic acid. The slurry was stirred vigorously and allowed to stand in the dark at 27° for 14 days. Dilution with 1.4 l. of water was followed by ether extraction. The ether extracts were washed with sodium bicarbonate solution, acidic ferrous sulfate solution, sodium bicarbonate solution and water. Removal of the ether *in vacuo* gave 27.5 g. (82%) of crude lactone V, m.p. 163–167°. No α -campholide could be isolated by chromatography of this material. Crystallization from petroleum ether raised the melting point to 172–174°; on standing, the melting point dropped to 168.5–171.5°, λ_{max} 5.73 μ , $[\alpha]_D^{25}$ -37° .

Anal. Calcd. for C₁₀H₁₆O₂: C, 71.39; H, 9.57. Found: C, 71.21; H, 9.46.

Repetition of the above experiment in unbuffered solution gave mixtures of lactones V and VI.

Isomerization of Lactone V to Lactone VI.—A solution of 1.38 g. of lactone V in 30 ml. of glacial acetic acid was treated with 2 ml. of concentrated sulfuric acid and allowed to stand at 27° for 17 hours. The mixture was poured into 300 ml. of water followed by ether extraction. After washing with sodium bicarbonate solution and water, the extracts were dried and evaporated to give 1.2 g. (87%) of dihydro- β -campholenolactone. From comparisons of the infrared spectrum of the crude product with those of mixtures of II and VI, it was estimated that this product contained no more than 10% of II. No II could be isolated in chromatography.

(19) J. Tafel and H. Bublitz, *Ber.*, **38**, 3806 (1905).

(20) J. Vène, *Bull. soc. chim. France*, **9**, 776 (1942).

(21) J. Bredt, *J. prakt. Chem.*, [2] **95**, 73 (1917).

(22) A. Franke and E. Gigerl, *Monatsh.*, **49**, 8 (1928).

(23) H. Rupe and A. Jäggi, *Helv. Chim. Acta*, **3**, 654 (1920).

Reduction of the product in ether with lithium aluminum hydride gave the corresponding diol, m.p. 144.5–145.5°; mixture m.p. with authentic diol (see below) 145–146°.

Diol VIII.—Reduction of lactone V with lithium aluminum hydride in ether gave the diol in quantitative yield as a semisolid. Crystallization from benzene–petroleum ether gave a low yield of needles, m.p. 91–93°.

Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.62; H, 11.57.

Diol Acetate IX.—Eight grams of once-crystallized lactone V were reduced to diol VIII by stirring overnight in a slurry of 5 g. of lithium aluminum hydride in 200 ml. of ether. Cautious addition of water followed by filtration of the precipitated salts and evaporation of the ether gave 8.2 g. of crude diol. Acetylation was accomplished by treating the diol with 40 ml. of acetic anhydride in 80 ml. of pyridine. After 16 hours at 27° the mixture was poured into 1 l. of ice and water. The product was extracted into ether which was washed with water and dried. Evaporation of the ether and distillation of the crude oil gave 8.2 g. (80%) of acetate IX, b.p. 99° (0.37 mm.) to 100.5° (0.35 mm.), n_D^{25} 1.4652. Strong hydroxyl absorption (film) appeared at 2.77 μ and acetate absorption at 5.70 and 8.00 μ .

Anal. Calcd. for $C_{12}H_{22}O_4$: C, 67.25; H, 10.35. Found: C, 67.49; H, 10.41.

Unsaturated Acetate X.—To a solution of 6.0 g. (0.028 mole) of acetate IX in 90 ml. of pyridine was added slowly 18 ml. of phosphorus oxychloride with stirring and cooling. The mixture was allowed to stand at 27° for 15 hours after which it was poured cautiously into 1 l. of ice–water mixture. Ether extraction followed by rapid washing with cold, dilute hydrochloric acid, sodium bicarbonate solution and water gave an ether solution from which was obtained 3.25 g. (59%) of acetate X, b.p. 65° (0.46 mm.), n_D^{25} 1.4541, λ_{max}^{film} 5.72 and 8.03 μ (acetate), 6.07 μ (C=C) and 12.43 μ (=CH).

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.07. Found: C, 73.42; H, 10.16.

Unsaturated Alcohol XI.—Reduction of 2.65 g. (0.0135 mole) of acetate X with 1.0 g. of lithium aluminum hydride in 75 ml. of ether gave 1.8 g. (86%) of alcohol XI, b.p. 65° (0.48 mm.), n_D^{25} 1.4708, λ_{max}^{film} 2.92 μ (O–H), 12.43 μ (=CH). This compound exhibited a single sharp peak in a vapor phase chromatogram at 8.1 minutes.²⁴

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.86; H, 11.76.

α -Campholenic Acid (VII).—To 100 g. (1.79 moles) of fused potassium hydroxide in a porcelain casserole was added slowly with stirring 100 g. (0.39 mole) of sodium *dl*-10-camphorsulfonate. The molten mass was heated for ca. 20 minutes after the completion of the addition. Upon cooling, the mass was diluted with 800 ml. of water. After extraction with ether and methylene chloride, the acid was liberated by addition of dilute hydrochloric acid. Extrac-

tion into ether followed by evaporation and distillation gave 34.4 g. (52%) of *dl*- α -campholenic acid, b.p. 95.5° (0.54 mm.) to 97.5° (0.65 mm.), n_D^{25} 1.4695 (lit. b.p. 137° (1 mm.),²⁵ n_D^{25} 1.4682²⁶). The infrared spectrum (liquid film) showed broad absorption in the O–H region, carbonyl absorption at 5.74 μ and =CH absorption at 12.43 μ . The spectrum of a sample of α -campholenic acid (b.p. 90° (0.2 mm.), n_D^{25} 1.4698) prepared from *d*-camphor oxime¹¹ was virtually superimposable on this sample save for slightly decreased intensity at 11.23 μ .

The benzylisothiuronium salt crystallized as colorless needles from aqueous ethanol, m.p. 154–156°.

Anal. Calcd. for $C_{18}H_{28}O_2N_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.80; H, 7.61; N, 8.41.

Dihydro- β -campholenolactone (VI).—A solution of 19.5 g. of *dl*- α -campholenic acid in 150 ml. of glacial acetic acid containing 10 ml. of concentrated sulfuric acid was allowed to stand for 24 hours at 27°. Isolation of the lactone was effected by dilution with water followed by ether extraction. The extracts were washed with sodium bicarbonate solution and water, dried and evaporated. The resulting oil was distilled at 78.5° (0.52 mm.) to 75.5° (0.58 mm.) to give 16 g. (82%) of dihydro- β -campholenolactone (lit.²⁷ b.p. 126° (13 mm.)), λ_{max} 5.60 μ .

Reduction of this lactone with lithium aluminum hydride in ether gave the corresponding diol, m.p. 145–145.5° (lit.²⁸ m.p. 145°).

Alcohol XI (from α -Campholenic Acid).—The methyl ester of α -campholenic acid was prepared by treatment of the acid with ethereal diazomethane and had b.p. 104.5–109° (17 mm.), n_D^{25} 1.4550. Reduction of 5.3 g. of ester with 2.0 g. of lithium aluminum hydride gave 3.7 g. (82%) of alcohol XI, b.p. 64° (0.47 mm.) to 60° (0.33 mm.), n_D^{25} 1.4693. Analysis of this compound by vapor phase chromatography indicated that a small amount (ca. 5–10%) of impurity was present (probably the result of contamination the α -campholenic acid with β -campholenic acid).^{10,11} The major peak was at 8.2 minutes.²⁴ The infrared spectrum of this material was identical with the sample prepared from lactone V (above) except for a small peak at 11.32 μ in the latter.

Control Experiment.—A solution of 1.8 g. of lactone V in 9 ml. of glacial acetic acid was treated with 1.2 ml. of concentrated sulfuric acid followed by 1.2 ml. of peracetic acid. The mixture was allowed to stand at 27° for 5 days. On work-up there was obtained 1.3 g. of an oil which showed carbonyl absorption at 5.65 μ (broad) and hydroxyl absorption at ca. 2.8 and 2.9 μ . Trituration of the oil with petroleum ether gave 0.26 g. of an oil which could not be purified by crystallization, λ_{max} 5.65 and 5.78 μ (ca. equal intensity).

Lactone VI gave similar results.

NEW BRUNSWICK, N. J.

(25) F. R. Goss and C. K. Ingold, *J. Chem. Soc.*, **127**, 2780 (1925).

(26) C. Walling and S. A. Buckler, *THIS JOURNAL*, **77**, 6039 (1955).

(27) G. Ciamician and F. Silber, *Ber.*, **43**, 1340 (1910).

(28) A. Béhal, *Bull. soc. chim. France*, [3] **31**, 179 (1904).

(24) Carried out at 182° on a 2' column of silicone grease on Celite at a flow rate of 43–44 ml./minute.