washed with aqueous sodium hydroxide containing ice and then with water. After drying the organic layer and evaporation of solvent, an oily residue was obtained. Without purification the crude product was dissolved in 15 ml. of methanol and 3.75 ml. of 6 *N* aqueous sulfuric acid was added, and the mixture was allowed to stand at room temperature for 3 days. After dilution with ethyl acetate and washing with cold dilute sodium hydroxide solution and water, the organic layer was dried and evaporated to give 123 mg. of oily material. Acetylation in the usual manner with acetic anhydride and pyridine and recrystallization from methanol gave 80 mg. of IX, m.p. 187–193°, as white plates. The analytical sample melted at 194–195°; $[\alpha]^{27}_{D}$ +15.2°.

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.77. Found: C, 70.46; H, 8.92.

Acknowledgment.—The authors wish to thank Dr. T. F. Gallagher for his support and interest in this work. They wish to thank Mrs. Beatrice Gallagher for the infrared spectra and their interpretation.

Studies in the Sandalwood-Oil Series. I. The Structure, Synthesis, and Configuration of the Lactone of Tricycloekasantalic Acid[1]

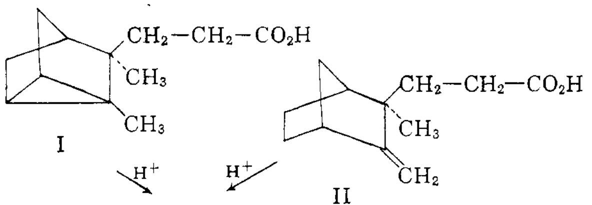
ASHARAM BHATI[2]

Department of Organic Chemistry, Indian Institute of Science, Bangalore, India

Received September 15, 1961

The structure, synthesis. and configuration of the lactone of tricycloekasantalic acid have been described. It has been shown that in the formation of this lactone (XII) from the acids (I) or (II) a rearrangement is involved.

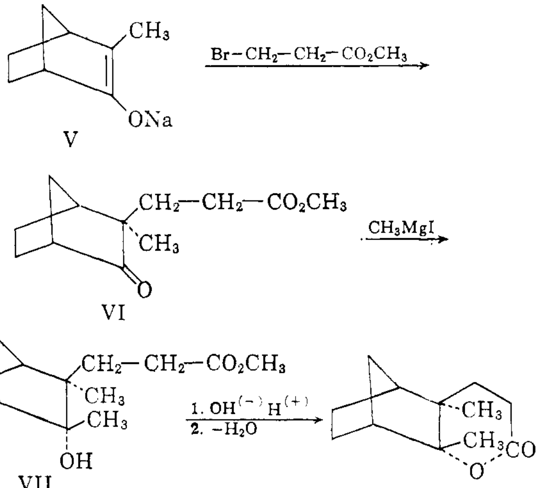
In an attempt to convert tricycloekasantalic acid (I) (a degradation product of α-santalol, the chief constituent of the East Indian sandalwood-oil) into the isomeric acid (II) by boiling with dilute sulfuric acid, Semmler and Bode[3] obtained an isomeric lactone for which two structures (III) and (IV) have been proposed.[4,5] Structure III is based on a synthesis of the lactone by Bhattacharyya.[4] In this synthesis sodionormethylcamphor (V) was condensed with methyl β-bromopropionate, and the resultant keto ester (VI) was converted into the lactone either *via* the hydroxy ester (VII) or directly by treatment with two moles of methylmagnesium iodide.



I

II

Lactone



V

VI

VII

III

Besides this synthesis, the structure (III) would appear to receive support from the fact that the same lactone is obtained by refluxing bicycloekasantalic acid (II) with formic acid.[6] Structure IV was suggested by Simonsen and Barton[5] by analogy with the lactone (VIII) prepared similarly[7] from teresantalic acid (IX). The formation of IV from bicycloekasantalic acid (II) was assumed by Simonsen and Barton to have involved a Wagner-Meerwein rearrangement.

The conflict between the structure (III), based on a straightforward synthesis, and that (IV) deduced from a reasonable analogy, prompted the present investigation.

The lactone gave, on hydrolysis with sodium hydroxide, the sodium salt of a hydroxy carboxylic acid which relactonized on acidification at 0°. If IV were correct then the hydroxy group of the acid, obtained on hydrolysis, ought to be second-

---

(1) The substance of this work was communicated to Professor P. de Mayo, and is briefly described by him in "The Mono- and Sesquiterpenoids," Interscience Publishers, Inc., New York, 1959, p. 128.

(2) Present address: Medical Research Council's Laboratory, The University, Perry Road, Exeter, England.

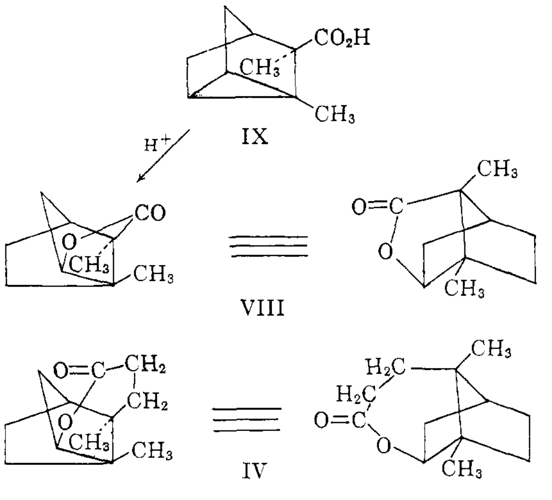
(3) F. W. Semmler and K. Bode, *Ber.*, **40**, 1124 (1907).

(4) S. C. Bhattacharyya, *Sci. and Culture* (Calcutta), **13**, 158–160 (1947).

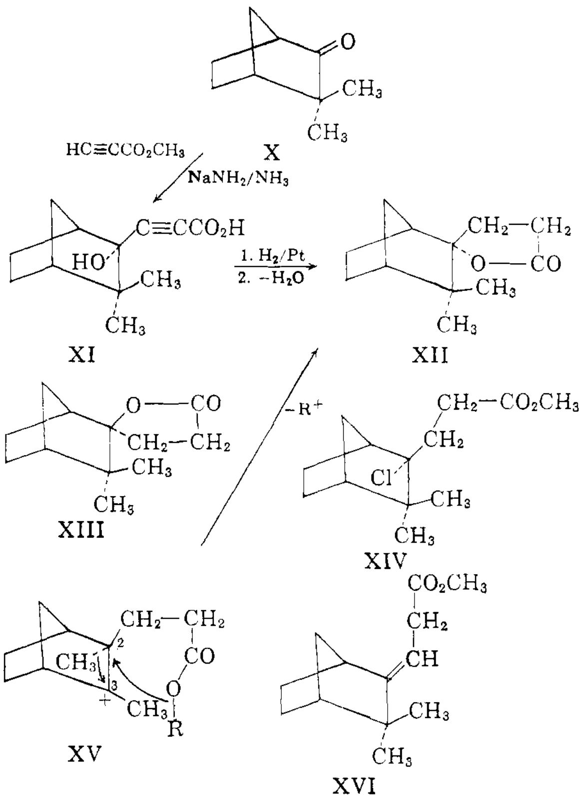
(5) J. L. Simonsen and D. H. R. Barton, "The Terpenes," 2nd ed. (1952), University Press, Cambridge, Vol. III, pp. 103–104. See also A. Bhati, Ph.D. thesis, Agra University (1952).

(6) L. Ruzicka and G. Thomann, *Helv. Chim. Acta*, **18**, 355 (1935).

(7) F. W. Semmler and K. Bartelt, *Ber.*, **40**, 4469 (1907).



ary, and it should, therefore, be possible to oxidize the hydroxy acid to the corresponding keto acid (as has been done[8] with the corresponding acid obtained from VIII). The sodium salt of the hydroxy acid was unchanged by permanganate even under fairly vigorous conditions. Structure IV, therefore, seems unlikely. If III were correct then it would seem possible to convert the lactone into the known bicycloekasantalic acid (II) or bicycloekasantalol. Attempts to effect such conversions were unsuccessful and led to mixtures of isomeric compounds. Thus, on treatment with acetic anhydride the sodium salt (and also the silver salt prepared from it) gave the lactone. The hydroxy ester, prepared from the silver salt and methyl iodide, decomposed during its isolation into the lactone and methanol. With methanolic hydrogen chloride the lactone gave a chloro ester which underwent partial dehydrochlorination on distillation, and gave a mixture of acids on treatment with alcoholic potassium hydroxide. The same acidic mixture[9] was obtained by first dehydrochlorinating the chloro ester with dimethylaniline and then by treating the resultant unsaturated ester with alcoholic alkali. The acidic mixture gave the lactone on heating with dilute sulfuric acid. The major component of this mixture was a crystalline acid which possesses a *gem*-dimethyl group and a trisubstituted double bond. The unsaturated ester, obtained on dehydrochlorination, gave, upon reduction with lithium aluminum hydride, a mixture of alcohols, one of which possesses a *gem*-dimethyl group and a trisubstituted double bond, and the other a >C=CH_2 group. The same alcoholic mixture was obtained by reducing[10] the lactone with lithium aluminum hydride, and dehydrating the resultant diol with acetic anhydride. On using an excess of the hydride and prolonging the reaction time, the lactone underwent hydrogenolysis and gave a saturated ether, $C_{12}H_{20}O$, possessing a *gem*-dimethyl group. The lactone showed[11] in carbon disulfide bands at 1775 cm.$^{-1}$ (CO of a γ- lactone), and 1366 cm.$^{-1}$ and 1386 cm.$^{-1}$ (doublet, *gem*-dimethyl group). These data ruled out structures III and IV and indicated XII, or its configurational isomer (XIII), as the correct structure. This was confirmed by synthesis.



Camphenilone (X) was condensed with methyl propiolate[12] in the presence of sodamide in liquid ammonia[13] and the resultant product hydrolyzed. The acetylenic acid (XI), so obtained, gave, on catalytic reduction, directly the lactone, lactonization having taken place during the isolation of the reduction product.

Structure XII for the lactone explains its reactions. The chloro ester derived from it must be

---

[8] T. Hasselström, *J. Am. Chem. Soc.*, **53**, 1097 (1931).

[9] The same acidic mixture was also obtained on heating the sodium salt with alumina at 240°.

[10] In conformity with Semmler's observation [*Ber.*, **41**, 1488 (1908)], the lactone could not be reduced with sodium and alcohol. Even the application of the improved Bouvealt and Blanc's method [V. L. Hansley, *Ind. Eng. Chem.*, **39**, 55 (1947)] for the reduction of esters failed to reduce the lactone.

[11] In carbon tetrachloride it showed γ-lactone CO at 1785 cm.$^{-1}$ and the *gem*-dimethyl group at 1395 and 1376 cm.$^{-1}$. These measurements were possible through the courtesy of Professors D. H. R. Barton and J. D. Roberts whom I thank very cordially. I am particularly grateful to Professor Barton for his keen interest in, and comments on, this particular piece of investigation.

[12] I am grateful to Professor D. K. Banerjee for directing my attention to the use of this reagent. Earlier attempts to introduce the propionic acid side chain by a Reformatsky reaction using β-bromopropionate [*cf.* Haberland *et al.*, *Ber.*, **72**, 1222 (1939)] or by the Stobbe condensation failed, although a model experiment with 2-methylcyclohexanone gave, on Reformatsky reaction, the expected product (*cf.* Experimental).

[13] W. E. Bachmann and E. K. Raunio, *J. Am. Chem. Soc.*, **72**, 2530 (1950).

XIV (or its configurational isomer) which partially rearranges on treatment with alcoholic alkali or dimethylaniline and, consequently, gives rise to a mixture of acids II and XVI or the corresponding methyl esters. The synthetic lactone behaves in exactly the same manner as the one prepared from tricycloekasantalic acid.

In the formation of the lactone from either tricycloekasantalic acid (I) or its bicyclo isomer (II) in protonic medium, the same carbonium ion (XV. R = H) is involved. By the process indicated this ion ultimately leads to the lactone. In the synthesis of the lactone by Bhattacharyya, a similar ion (XV. R = CH_3) is involved. That such a carbonium ion (with an ester grouping) can give rise to the lactone was ascertained by refluxing the methyl ester of the acid (I) with formic acid when the same lactone was obtained. Bhattacharryya's synthesis is thus explained. Simonsen and Barton's structure IV illustrates the difference in the behavior of two homologs (I) and (IX) when subjected to the same experimental conditions. This difference, as will be described in a subsequent paper, is due to the length, mode of folding, and configuration of the chain carrying the carboxyl group.

Only two configurations, XII and XIII, are possible for the lactone. Of these, XII seems to be correct from the following considerations: (1) Nucleophiles add[14] *exo* to the unsubstituted bicyclo-[2.2.1]heptan-7-one, and, therefore, in the synthesis of the lactone, the intermediate acetylenic acid (XI) (and hence the reduced acid) must have the carboxyl chain in the sterically less hindered *exo* position. (2) The propionic acid chain of tricyclo- and bicycloekasantalic acids (I and II, respectively) occupies[15] the *exo* position, and, as depicted in XV (R = H or CH_3), the lactone is formed by the front-side attack of the carboxylate anion at carbon 2, followed by the displacement of a methyl anion which migrates to carbon 3. It is known[16a] that such a process does not involve a change in configuration. (3) The reactions of the lactone are also compatible with XII.

Experimental[16b]

Preparation of the Lactone of Tricycloekasantalic Acid.—(1) The lactone was prepared by the method of Semmler and Bode[3] by refluxing tricycloekasantalic acid[17a] with dilute sulfuric acid. Yield, 70%, shiny white plates from petroleum ether, m.p., 103–104°. No optical rotation could be observed (c 5%, l 0.5 dm.).

(2) Methyl tricycloekasantalate (1.0 g.) [prepared by Semmler and Bode's method[3] and having b.p. 102.5°/2.5 mm.; n^{21} 1.4848; $[\alpha]^{21}{}_D$ +17.96°] was refluxed with 90% formic acid (9 ml.) for 75 min. The reaction mixture gave, on cooling and subsequent treatment with ice (50 g.), fine white crystals (0.83 g., 70%) which melted after two recrystallizations from petroleum ether at 103–104°; undepressed on admixture with the lactone as prepared above.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.22; H, 9.27; mol. wt., 194. Found: C, 74.08; H, 9.31; and mol. wt., 192.4 (by saponification).

Hydrolysis of the Lactone.—The lactone (45 g.) was refluxed with alcoholic sodium hydroxide (8 g., less than 1 equiv. of sodium hydroxide in 200 ml. of 95% ethanol) for about 40 hr. The thick sirupy residue, left after removal of alcohol, was dissolved in water (200 ml.) and the resultant mixture was repeatedly extracted with ether in order to remove the unchanged lactone. The aqueous solution gave, on complete removal of water, a waxy solid (38 g.).

Experiments with the Sodium Salt on the Hydroxy Acid.—The sodium salt gave back the lactone on treatment with dilute acid at 0°. It was unchanged by 4% aqueous potassium permanganate at 0° and at 25°. When the mixture was heated to *ca.* 100°, there was a spontaneous decolorization of the permanganate. The aqueous filtrate, obtained on removal of the manganese dioxide sludge, gave back the lactone on acidification. A sample of the sodium salt, dried at 150°/2 mm., gave, on treatment with freshly distilled acetic anhydride, the lactone, and sodium acetate.

Attempted Preparation of the Methyl Ester of the Hydroxy Acid. A. Preparation of the Silver Salt.—The sodium salt (4 g.), dissolved in distilled water (40 ml.), was treated with aqueous silver nitrate (3 g. in 15 ml. of water) in a brown beaker. The white precipitate of the silver salt was filtered, washed thoroughly with water, and dried at 24°/1 mm. Yield, 5.1 g., 94.4%. It decomposes completely at 158°.

Anal. Calcd. for $C_{12}H_{19}O_3Ag$, H_2O: C, 42.73; H, 6.23; Ag, 32.05. Found: C, 42.96; H, 6.35; Ag, 32.57.

On treatment with freshly distilled acetic anhydride it gave the lactone and silver acetate.

B. Treatment of the Silver Salt with Methyl Iodide.—To the silver salt (10 g.), suspended in absolute benzene (75 ml.), was added methyl iodide (4.5 g.) at room temperature under mechanical stirring. The resultant silver iodide (7 g.) was filtered off and the precipitate washed twice with pure benzene. The filtrate and the washings were combined. On distillation of the benzene a sweet-smelling semisolid (5.1 g.), which solidified on cooling, was obtained. This was found to be the lactone from its melting point and mixed melting point with the lactone of tricycloekasantalic acid. The recovered benzene was shaken with distilled water (25 ml.). The aqueous extract was distilled and the forerun (5 ml.) was treated with a red-hot copper gauze. The mixture contained formaldehyde, isolated and identified by its dimedone derivative, m.p 188°, undepressed on admixture with an authentic sample. The hydroxy ester, being unstable, thus decomposed into the lactone and methancl.

Preparation of the Chloro Ester from the Lactone.—A solution of the lactone (15 g.) in absolute methanol (140 ml.), contained in a thick-walled soda-water bottle, was saturated with dry hydrogen chloride at 0°. The bottle was corked and placed in an iron frame with a safety wire gauze around it. After allowing it to stand for 71 hr. at room temperature, it was again cooled in ice and then cautiously opened. The residual thick oil, left after removal of the volatile products *in vacuo* was poured into ice (100 g.) and the organic material was extracted with ether (3 × 100 ml.). The ether extract was washed with water (80 ml.), dried (Na$_2$-

---

[14] P. D. Bartlett *et al.*, *Ann.*, **623**, 217 (1959) and papers cited there.

[15] G. Ourrisson, *Bull. soc. chim. France*, 895 (1955).

[16] (a) P. D. Barlett, "Organic Chemistry, an Advance Treatise," Vol. III, H. Gilman, ed., J. Wiley and Sons, Inc., New York, 1953, pp. 37, 44. (b) All melting points are uncorrected. Petroleum ether refers to the fraction, b.p. 60–80°. Analyses by Mr. B. R. Seetharamiah, Department of Organic Chemistry, Indian Institute of Science.

[17] (a) The earlier supply of this acid was from Dr. S. C. Bhattacharyya whom I thank very warmly for this and also for introducing me to sandalwood-oil chemistry. (b) The ozonolysis mentioned in this and later experiments was done in carbon tetrachloride solution, and the formaldehyde obtained was characterized through the dimedone derivative. The yield of formaldehyde was not measured.

SO_4) and then freed from the solvent. The thick oil (18.0 g.), so obtained, gave, on distillation, a clear liquid, b.p. 134–140°/2 mm.; yield, 17.05 g. (90%). During its distillation the chloro ester was found to eliminate hydrogen chloride and consequently the distilled material contained only 8.3% of chlorine ($C_{13}H_{21}ClO_2$ required Cl, 14.86%).

Treatment of the Chloro Ester with 10% Alcoholic Potassium Hydroxide.—To boiling 10% alcoholic potassium hydroxide (150 ml.) a solution of the chloro ester (5.27 g.) in alcohol (50 ml.) was added in drops, and the mixture was refluxed for 3 hr. The residue, left after distillation of alcohol, was diluted with water (50 ml.) and the mixture extracted with ether. The ether extract gave a trace of a resinous product which was discarded. The alkaline solution was cooled in ice and then acidified with dilute hydrochloric acid. The liberated material was taken up in ether (300 ml.) and the ether extract was shaken with 5% sodium carbonate solution (2 × 100 ml.). The ether extract gave, on removal of the solvent, the lactone (0.4 g.) identical in melting point and mixed melting point with the starting material. The sodium–carbonate extract gave, on acidification with dilute hydrochloric acid at 0° and subsequent extraction with ether (300 ml.), an acidic product (4.14 g., m.p., 82–88°). This gave formaldehyde on ozonolysis.[17b] On three recrystallizations from petroleum ether it gave shiny white plates (1.6 g.), m.p., 105–106°.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.22; H, 9.27; equiv. wt., 194. Found: C, 74.20; H, 9.30; equiv. wt., 194.1.

The acidic product, m.p., 82–88°, gave back the lactone on refluxing with 25% dilute sulfuric acid.

Dehydrochlorination of the Chloro Ester with Dimethylaniline.—The chloro ester (5 g.) was refluxed with freshly distilled dimethylaniline (7.5 ml.) for 1 hr. The mixture was cooled in ice and treated with dilute hydrochloric acid in order to remove the base, and then taken up in ether (150 ml.) and washed successively with water, dilute hydrochloric acid, and water. On drying (Na_2SO_4) and removal of ether an oil (4.1 g.) was obtained. On distillation it gave a colorless, mobile liquid (3.83 g.), having b.p., 93°/1 mm.; $n^{26.5}$ 1.4810; $d^{26.5}_4$ 1.000, $[\alpha]_D$ −4.12 (l 5 cm.).

Anal. Calcd. for $C_{13}H_{20}O_2/\overline{\overline{1}}$: C, 75.00; H, 9.60; M_R, 59.02. Found: C, 74.93; H, 10.09; M_R, 59.23.

The above oil gave a yellow coloration with tetranitromethane and it decolorized bromine in chloroform. On hydrolysis with 10% alcoholic potassium hydroxide, it gave an acidic product similar to that obtained on simultaneous dehydrochlorination and hydrolysis of the chloro ester with alcoholic potassium hydroxide. The crystalline acid, obtained from this mixture, is also identical in melting point and mixed melting point with that (m.p. 105–106°) mentioned before. In the infrared (KBr wafer) the acid showed[18] bands at 1393 and 1379 cm.$^{-1}$ (*gem*-dimethyl) and at 816 cm.$^{-1}$ ($R_1R_2C = CHR_3$, trisubstituted double bond).

Lithium Aluminum Hydride Reduction of the Unsaturated Ester.—The unsaturated material (6.0 g.) (from the last experiment) was dissolved in ether (100 ml.) and added to an ice-cold slurry of lithium aluminum hydride (0.66 g. in 80 ml. of absolute ether). There was a feeble effervescence. After letting the mixture stand at room temperature for 2 hr., it was treated with ice water (20 ml.) and 10% sulfuric acid (30 ml.). The ether layer was separated, and the residue obtained on removal of ether was refluxed with 10% alcoholic potassium hydroxide (50 ml.) for 2 hr. On working up in the normal way, the mixture yielded a neutral product (1.62 g.) and an acidic mixture (2.42 g.), showing that the reduction was incomplete. The neutral product gave, on distillation, a pleasant smelling oil (1.45 g.), b.p., 93–96°/2 mm., n^{26} 1.4960, d^{26}_4 0.9720. In the infrared the product showed bands at 1374 and 1353 cm.$^{-1}$ (*gem*-dimethyl group), 881 cm.$^{-1}$ ($R_1R_2C{=}CH_2$) and 841 cm.$^{-1}$ ($R_1R_2C{=}CHR_3$), showing it to be a mixture of di- and trisubstituted double-bonded compounds. On ozonolysis the product gave formaldehyde, thus confirming the presence of an exocyclic double bond.

Anal. Calcd. for $C_{12}H_{20}O/\overline{\overline{1}}$: C, 80.00; H, 11.11; M_R, 54.27. Found: C, 80.06; H, 11.14; M_R, 54.17.

Reduction of the Lactone with Lithium Aluminum Hydride. A. Reduction to the Corresponding Diol.—To a slurry of lithium aluminum hydride (0.6 g.) in absolute ether (50 ml.), a solution of the lactone (2.5 g.) in ether (50 ml.) was gradually added under cooling with ice, and the mixture was refluxed for 3.5 hr. and then allowed to stand at room temperature for 16 hr., and finally treated with ice and dilute hydrochloric acid. The ether layer was removed and the acidic layer extracted with more ether (100 ml.). The two extracts were combined and then washed with water, dried (Na_2SO_4) and freed from ether, when a viscous product (2.2 g.) with a pleasant smell was obtained. On cooling, it deposited crystals of the unchanged lactone. The mixture was dissolved in petroleum ether (50 ml.) and the solution chilled in ice. The lactone (1.5 g.) which separated from the chilled solution was filtered. The filtrate gave, on removal of the solvent, a viscous oil (0.66 g.), b.p., 135–140°/1.5 mm.

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.72; H, 11.11. Found: C, 72.50; H, 11.00.

Dehydration of the Above Diol.—The above diol (0.5 g.) was refluxed with acetic anhydride (15 ml.) for 2 hr. The resultant solution was neutralized and then heated with an excess of alcoholic potassium hydroxide for 30 min. in order to saponify any acetyl derivative formed. The product (0.25 g.), isolated by extraction with ether, was a fairly viscous oil with a sweet smell, b.p, 108–112°/4.5 mm. It gave a yellow coloration with tetranitromethane and formaldehyde on ozonolysis. From these properties and also from its infrared spectrum it appeared similar to the alcoholic mixture obtained by reduction of the unsaturated ester mixture mentioned before. This had satisfactory analyses for carbon and hydrogen.

B. Hydrogenolysis—Reduction of the Lactone to the Corresponding Ether.—The lactone (10 g.), dissolved in absolute ether (150 ml.), was heated with lithium aluminum hydride (3 g., in 200 ml. of absolute ether) for 19 hr. The product gave, on working up as before, an oil (8.35 g.) which upon distillation gave a fragrant smelling liquid (7.4 g.), b.p., 103–104°/10.5 mm.; n^{26} 1.4800; d^{26}_4 0.9970.

Anal. Calcd. for $C_{12}H_{20}O/\overline{\overline{0}}$: C, 80.00; H, 11.11; M_R, 54.62. Found: C, 80.00; H, 11.10; M_R, 54.73.

Reformatsky Reaction with 2-Methylcyclohexanone and Ethyl β-Bromopropionate.—2-Methylcyclohexanone (5 g.), ethyl β-bromopropionate (8.1 g.), clean magnesium turnings (1.1 g.), and dry toluene (100 ml.) were mixed. A small amount (6 ml.) of the toluene was distilled in order to remove azeotropically any traces of water in the reactants. A few crystals of iodine were added and the mixture heated under reflux for 8 hr. A white complex separated. The mixture was allowed to stand overnight and then treated with ice and dilute sulfuric acid. The reaction product (7.0 g., a dark greenish liquid), isolated in the usual way, gave, on repeated fractionation, the following two fractions: (i) 0.75 g.; b.p. 60–70°/2 mm.; n^{23} 1.4460. This fraction gave a yellow coloration with tetranitromethane.

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.46; H, 10.20. Found: C, 73.20; H, 10.76.

Hence it is the unsaturated ester obtained by the dehydration of the expected product.

(ii) 2.0 g., b.p. 125–127°/2 mm.; $n^{22.5}$ 1.4820; $d^{22.5}_4$ 1.034.

Anal. Calcd. for $C_{12}H_{22}O_3$: C, 67.29; H, 10.28; M_R, 58.60. Found: C, 67.80; H, 10.40; M_R, 59.00.

The Reformatsky reaction was also conducted with *d*-camphor. The only product obtained was diethyl adipate. The Stobbe condensation of camphor did not take place. The same failure was encountered with *l*-camphenilone.

---

[18] All the infrared measurements, except that on the lactone prepared from tricycloekasantalic acid, were performed by Samuel P. Sadtler and Son, Inc., Philadelphia, through the kind arrangement of Professor D. K. Banerjee.

Synthesis of the Lactone (XII). Condensation of *l*-Camphenilone with Methyl Propiolate.—A solution of *l*-camphenilone[19] (2.5 g.), m.p. 37°, $[\alpha]^{92}_{D}$ −12.23° (*l* 1 dm.; *c* 6.946, benzene), and methyl propiolate[20] (1.68 g.) in absolute ether (30 ml.) was gradually added to a greyish suspension, prepared from ferric nitrate (100 mg.), liquid ammonia (500 ml.), and sodium (0.45 g.) under anhydrous conditions, with mechanical stirring in about 1 hr. The stirring was continued for another 2 hr. and the mixture was allowed to stand at room temperature overnight, during which time almost all the ammonia had evaporated. The mixture was treated with water (300 ml.). Extraction with ether (150 ml.) gave only a small amount of a neutral material which gave, on saponification with 10% alcoholic alkali, an acidic product (0.10 g.) and unchanged camphenilone (0.8 g.). The alkaline solution from the condensation was acidified with dilute hydrochloric acid and the liberated acid (1.87 g.) was isolated by extraction with ether (350 ml.). The two acidic portions were combined. Yield, 1.97 g. It is a viscous gum.

Catalytic Reduction of the Acid (XI).—A mixture of the acid (1.96 g.), platinic oxide (100 mg.), and 96% methanol (50 ml.) was shaken with hydrogen at room temperature under 20 atmospheric pressure[21] for 4 hr. The methanolic solution, left after filtering off the catalyst, gave, on removal of the solvent, a solid (1.5 g.), m.p. *ca.* 95°, which was probably the expected lactone mixed with some impurity. It was, therefore, refluxed with 10% alcoholic potassium hydroxide (35 ml.) for 3 hr. The alcohol was distilled and the alkaline solution diluted with water (50 ml.) and then extracted with ether (100 ml.). The ether extract gave a small amount (0.05 g.) of a gummy product with a camphoraceous smell. The alkaline solution was acidified under ice-cooling with dilute hydrochloric acid, and the organic matter taken up in ether (100 ml.); the ether extract was shaken with 5% sodium carbonate solution (50 ml.). The neutral ether extract gave the lactone (0.45 g.), m.p., 98–100°. The sodium carbonate extract was acidified and the liberated material (0.72 g.) heated with acetic anhydride (5 ml.) on the steam bath for 1 hr. The residue left on removal of the acetic anhydride at *ca.* 110°/50 mm. was boiled with water (10 ml.) for 1 hr. and the product (0.60 g.) was extracted with ether, m.p., 98–100°. The two samples were combined and the mixture (1.05 g., 57.3%) gave, on crystallizing twice from petroleum ether, shiny white plates, m.p., 103–104°, $[\alpha]^{21}_{D}$ −5.6 (alcohol, *c* 4.642; *l* 0.5 dm., α, 0–130°) identical in melting point, mixed melting point and infrared spectrum with the lactone of tricycloekasantalic acid.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.22; H, 9.27. Found: C, 74.77; H, 9.22.

The synthetic lactone (1 g.) gave, on treatment with methanolic hydrogen chloride, a chloro ester (1.28 g.) which, upon dehydrochlorination with dimethylaniline (as described previously in the case of the lactone of tricyclosantalic acid), furnished an unsaturated ester (1.04 g.) which gave, upon distillation, a colorless liquid (0.869 g.), b.p. 93°/1 mm., n^{22} 1.4800; d^{22}_{4} 1.002 $[\alpha]^{22}_{D}$ −9.38° (pure oil, *l* 0.5 dm.).

Anal. Calcd. for $C_{13}H_{20}O_2/\overline{1}$: C, 75.00; H, 9.61; M_R, 59.02. Found: C, 75.51; H, 9.70; M_R, 59.33.

The above ester gave, on hydrolysis, an acid,[22] m.p. 105–106°, undepressed on admixture with the corresponding acid from the lactone of tricycloekasantalic acid.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.22; H, 9.27; equiv. wt., 194. Found: C, 73.80; H, 9.27; equiv. wt., 195.

This acid gave the lactone on refluxing with dilute sulfuric acid. Hence, the behavior of the synthetic lactone is similar to that of the lactone from tricycloekasantalic acid.

Acknowledgment.—This work was carried out partly during the tenure of a Research Scholarship of the Institute and partly whilst holding an I.C.I. Research Fellowship, for which the author offers his sincere thanks to the governing Councils of the Indian Institute of Science, Bangalore, and the National Institute of Sciences of India, New Delhi.

---

[19] It was prepared from *l*-camphene, $[\alpha]^{22}_{D}$ −15.2° (petroleum ether; *c* 6.000; *l* 1 dm., m.p. 48°), by treating it with nitrogen tetroxide (*cf.* Cohen and Calvert, *J. Chem. Soc., Trans.*, **71**, 1052 (1891)) and then decomposing the resultant product with alcoholic potassium hydroxide (*cf.* W. Hückel, *Ann.*, **549**, 186 (1941) and papers cited there).

[20] Prepared by using the experimental conditions of C. K. Ingold, *J. Chem. Soc., Trans.*, **127**, 1202 (1925).

[21] The uptake of hydrogen at the ordinary pressure was found to be very slow.

[22] Compare the preparation of this acid by G. Longlois, *Ann. Chem.* [9] **12**, 290 (1919), Elsevier's "Encyclopedia of Org. Chem.," **12A**, 624.

Bromochlorovanillins: Some Substitution Reactions

STEWART E. HAZLET AND JOE LEHMAN, JR.

Department of Chemistry, Washington State University, Pullman, Wash.

Received January 16, 1962

The previously unreported monobromomonochlorovanillins and dibromomonochloro- and monobromodichlorovanillins have been prepared. Some direct substitution reactions with related molecules have been accomplished under conditions whch are more favorable for these changes than those which had been employed earlier.

The objectives of this study involved the preparation of previously unreported bromochloro derivatives of vanillin and information concerning ease of bromination or chlorination of certain substituted vanillins and vanillin derivatives.

Of the six possible monobromomonochlorovanillins, all but 2-bromo-6-chloro- and 6-bromo-2-chlorovanillin have been reported,[1,2] but of the six possible dibromomonochloro- and monobromodichlorovanillins, only 5-bromo-2,6-dichlorovanillin[1] has been described. The preparations in this work include the remaining possibilities: the two monobromomonochlorovanillins named above, 2,5-dibromo-6-chloro-, 5,6-dibromo-2-chloro-, 2,6-dibromo-5-chloro-, 6-bromo-2,5-dichloro-, and 2-

---

[1] L. C. Raiford and J. G. Lichty, *J. Am. Chem. Soc.*, **52**, 4576 (1930).

[2] 2-Bromo-5-chlorovanillin (m.p. 175–176°) has been prepared (D. E. Floyd, thesis, State University of Iowa, 1943) from 2-amino-5-chlorovanillin[1] in 75% yield by a Sandmeyer reaction.