[CONTRIBUTION FROM INDIAN ASSOCIATION FOR THE CULTIVATION OF SCIENCE]

Synthesis of a Stereoisomer of the $C_{12}H_{18}O_6$ Tricarboxylic Acid from Abietic Acid*

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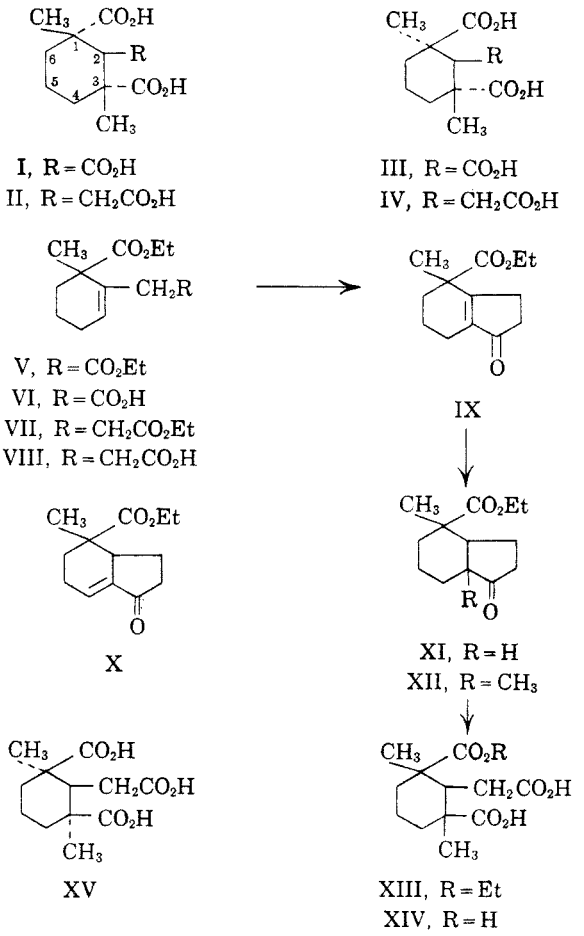
A stereoisomer of the tricarboxylic acid $C_{12}H_{18}O_6$, obtained from the oxidation of abietic acid, has been synthesized. The synthetic product, although having the same melting point as the natural one, depressed its melting point and showed differences in infrared absorption spectrum.

Abietic acid on energetic oxidation with potassium permanganate, on vigorous ozonolysis,[1,2] and on oxidation with nitric acid,[3] gives two homologous tricarboxylic acids, $C_{11}H_{16}O_6$ of m.p. 219° and $C_{12}H_{18}O_6$ of m.p. 213°, which have been assigned structures I and II respectively.[4–7] The important part played by these acids in the elucidation of the structure and stereochemistry of the A/C ring junction of abietic and related resin acids is well known. The fact that these acids are optically inactive[8] settled the relative configurations of the two asymmetric carbon atoms 1 and 3 substituted by methyl and carboxyl groups. Determination of the configuration of the substituents at the carbon atom 2 in the C_{11}- and C_{12}-acids offered considerable difficulty. However, Barton and Schmeidler[7] from a study of the thermodynamic dissociation constants of the C_{11}-acid and its mono and dimethyl esters arrived at the conclusion that the C_{11}-acid has *trans-meso* structure I. Accordingly the C_{12} acid is assigned the *trans-meso* structure II.

Mention should also be made of optically active C_{11}- and C_{12}-acids which were obtained by Ruzicka and Bernold[9] as a mixture, by the oxidation of agathenedicarboxylic acid. Although these acids were not obtained in a pure state, the very fact that their ester mixture showed optical activity, along with the evidence that the stereochemistry of the A/C ring junction of agathenedicarboxylic acid is the same as that of abietic acid, led Ruzicka[9] to assign the stereostructures III and IV for the active C_{11}- and C_{12}-acids, respectively.



In view of the important part played by the C_{11}- and C_{12}-acids in the elucidation of the structures of diterpenoid resin acids, there have been attempts to provide confirmation of their structures by synthesis. Mention may be made of the unsuccessful attempts of Arbusov and Schapschinskaja[10] and of Mukherjee[11] for the synthesis of C_{11}- and C_{12}-acids, respectively.

2-Methyl-2-carbethoxycyclohexanone was subjected to a Reformatsky reaction with ethyl bromo-

* Taken from a thesis submitted by P. N. Rao for the degree of Doctor of Philosophy (Science) of the University of Calcutta, June 1953.

(1) L. Ruzicka, J. Meyer, and M. Pfeiffer, *Helv. Chim. Acta*, **8**, 632 (1925).

(2) L. Ruzicka, M. W. Goldberg, H. W. Huyser, and C. F. Seidel, *Helv. Chim. Acta*, **14**, 545 (1931).

(3) P. Levy, *Ber.*, **62**, 2497 (1929).

(4) L. Ruzicka and H. Waldmann, *Helv. Chim. Acta*, **16**, 842 (1933).

(5) F. Vocke, *Ann.*, **497**, 247 (1932).

(6) H. N. Rydon, *J. Chem. Soc.*, 257 (1937).

(7) D. H. R. Barton and G. A. Schmeidler, *J. Chem. Soc.*, 1197 (1948).

(8) L. Ruzicka and L. Sternbach, *Helv. Chim. Acta*, **21**, 565 (1938).

(9) L. Ruzicka and E. Bernold, *Helv. Chim. Acta*, **24**, 931 (1941).

(10) B. A. Arbusov and O. M. Schapschinskaja, *Ber.*, **68**, 437 (1935).

(11) S. M. Mukherjee, *J. Indian Chem. Soc.*, **24**, 495 (1947).

acetate[12,13] in benzene and the hydroxyester obtained in 70% yield was dehydrated in good yield by refluxing with phosphorus pentoxide in benzene. The product of dehydration should be considered as consisting of a mixture of α,β- and β,γ-isomers in which the latter predominates[14] and hence was assigned the structure V. The primary carbethoxyl group of the diester (V) was hydrolyzed by refluxing with one equivalent of sodium hydroxide in ethanol solution to give 6-methyl-6-carbethoxycyclohexenylacetic acid (VI) as a colorless viscous oil, which failed to crystallize. It may be recalled that Chwang, Tien, and Huang[12] prepared an acid by a similar sequence of reactions with the exception that the dehydration of the hydroxyester was effected with the help of thionyl chloride and pyridine and they obtained an acid of m.p. 93°, which perhaps represents the α,β-isomer, since the dehydrating agent employed by the Chinese workers is known to give a higher percentage of the α,β-isomer. Another evidence for the predominant β,γ-structure of our unsaturated acid is the fact that it could be homologated by the Arndt-Eistert method, whereas the method has been shown to fail in the case of α,β-unsaturated acids.[15] The ester-acid VI, on Arndt-Eistert homologation in the usual manner, gave ethyl β-(6-methyl-6-carbethoxycyclohexenyl) propionate (VII) in about 40% yield. The primary carbethoxyl group of the diethyl ester (VII) was hydrolyzed by refluxing with just one equivalent of sodium hydroxide in ethanol solution to furnish β-(6-methyl-6-carbethoxycyclohexenyl)propionic acid (VIII) as a colorless oil. This unsaturated acid was cyclized by refluxing in an atmosphere of nitrogen with a mixture of acetic anhydride and acetic acid containing catalytic quantities of zinc chloride.[16] The cyclized product obtained in about 50% yield was assigned the structure IX and not the alternative structure X since its ultraviolet absorption spectrum shows absorption maximum at 235 mμ (log ϵ = 3.98) which is expected for the $\Delta^{5,9}$-hydrinden-1-one, as against absorption maximum above 240 mμ for a $\Delta^{7,8}$-hydrinden-1-one.[17] Some lactonic product was invariably formed during this cyclization and could be separated by extracting with ice cold 5% sodium hydroxide solution. The unsaturated keto ester IX underwent smooth catalytic hydrogenation over palladium charcoal (5%) to give 4-methyl-4-carbethoxyhydrindan-1-one (XI).

In view of the well known fact that in the case of hydrindan-1-ones a *cis* fusion of the rings represents the energetically favored configuration, the compound XI should be assumed to have a *cis* structure at the ring junction. The stereochemical disposition of the groups at C_4, however, remains uncertain. Nevertheless, we believe that XI is essentially homogeneous since its semicarbazone, m.p. 206° (dec.), did not show any rise in melting point on repeated crystallization.

An angular methyl group was then introduced into XI by methylation with potassium *tert*-butoxide and methyl iodide in a nitrogen atmosphere, following the procedure of Birch and Robinson[18] by first protecting the active methylene group with an *N*-methylanilinomethylene group and subsequent removal of it by hydrolysis, giving an acid, which on esterification with ethanol and sulphuric acid furnished 4,8-dimethyl-4-carbethoxyhydrindan-1-one (XII), a colorless liquid with camphoraceous smell, in about 45% yield. Its semicarbazone obtained in 90% yield by the usual pyridine method was also subjected to fractional crystallization from ethanol to study whether the methylated keto ester XII was a mixture of stereoisomers. But there was absolutely no rise in the melting point of the semicarbazone from one crystallization to another. This suggests that the keto ester (XII) was a homogeneous product and there was no evidence of the formation of more than one stereoisomer in the methylation step. It has been shown by Birch, Jaeger, and Robinson[19] that angular methylation of *cis*-hydrindan-1-one according to the above procedure invariably leads to the *cis*-isomer. In analogy with the above observation keto ester XII should be considered to have a *cis*-hydrindan-1-one structure, with uncertain stereochemical disposition of groups attached to C_4. XII was then oxidized by warming under reflux with concentrated nitric acid (*d* 1.4)[20] to give 1,3-dimethyl-1-carbethoxy-3-carboxycyclohexane-2-acetic acid (XIII) which was not isolated but directly hydrolyzed with ethanolic potassium hydroxide solution to 1,3-dimethyl-1,3-dicarboxycyclohexane-2-acetic acid (XIV). This acid was at first obtained as a glass which subsequently crystallized from glacial acetic acid in small clusters of needles. The analytical sample melted at 213–214° (dec.) and analyzed correctly for $C_{12}H_{18}O_6$.

For direct comparison with the synthetic acid (XIV) an authentic specimen of Ruzicka's C_{12}-acid was prepared by oxidation of abietic acid. The oxidation was carried out with a mixture of concentrated

(12) C. K. Chuang, Y. L. Tien, and Y. T. Huang, *Ber.*, **68**, 866 (1935).
(13) W. E. Bachmann and S. Kushner, *J. Am. Chem. Soc.*, **65**, 1963 (1943).
(14) G. A. R. Kon and K. S. Nargund, *J. Chem. Soc.*, 2461 (1932).
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(16) W. S. Johnson, H. C. E. Johnson, and J. W. Peterson, *J. Am. Chem. Soc.*, **67**, 1360 (1945).
(17) E. A. Braude and J. A. Coles, *J. Chem. Soc.*, 1430 (1952).
(18) A. J. Birch and R. Robertson, *J. Chem. Soc.*, 501 (1944).
(19) A. J. Birch, R. Jaeger, and R. Robinson, *J. Chem. Soc.*, 582 (1945).
(20) G. A. R. Kon, R. P. Linstead, and C. Simons, *J. Chem. Soc.*, 814 (1937).

and fuming nitric acids in the presence of a catalytic quantity of vanadium pentoxide.[8] The crystalline C_{11}-acid from the oxidation product was separated, and the residue was then worked up exactly as recommended by Ruzicka[2] for the product of oxidation of abietic acid obtained by oxidation first with potassium permanganate and then with nitric acid. Ultimately a small quantity of C_{12}-acid of m.p. 213° (dec.) was isolated which analyzed correctly for $C_{12}H_{18}O_6$.

It is interesting to note that the synthetic acid (XIV) and Ruzicka's C_{12}-acid from abietic acid have identical melting points. But the mixed melting point of these two showed about 7° depression and melted at 206–208°. This suggests that the synthetic acid is not identical with the natural one, and must be a stereoisomer, a fact which has been confirmed from a study of their infrared spectra (in Nujol mull) shown in Figure 1, *A* and *B*.

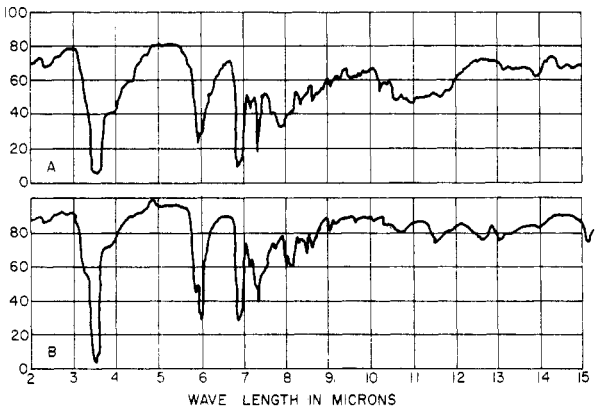

FIG. 1. INFRARED ABSORPTION SPECTRA: Curve A, natural C_{12}-acid from abietic acid: Curve B, synthetic C_{12}-acid.

From what has been previously said regarding the stereochemistry of the intermediate (XII) the acetic acid group and one of the carboxyl groups in the synthetic acid (XIV) must be related *cis* to each other, and the two possible stereostructures for the synthetic C_{12}-acid are *cis*-meso (XV) and racemic (IV). In the latter case, the synthetic acid should be capable of resolution into its antipodes one of which should correspond to the optically active C_{12}-acid obtained from agathenedicarboxylic acid.

The configuration of the other tertiary carboxyl group at C_1-position, however, could reasonably be guessed from a consideration of the theories of catalytic hydrogenation[21] of aromatic compounds which postulate that the hydrogen atoms preferably add to the site of reduction from the sterically less hindered side. In other words, the organic molecule will be adsorbed on the catalyst surface in such a way that the bulky groups are away from the catalyst surface and that the hydrogen atoms are added at the unsaturation from the same side. If we assume that similar phenomena had taken place during the reduction of the unsaturated keto ester (IX) it could be easily visualized that the more bulky carbethoxy group was away from the catalyst surface during hydrogenation and the entering hydrogen atoms took up the *cis*-position with respect to the methyl group at C_4-position with the result that the synthetic C_{12}-acid should have the *cis*-meso configuration (XV). It must be made clear, however, that the arguments put forward in favor of the configuration (XV) for the synthetic C_{12}-acid are based on analogy and hence the assigned configuration should be accepted only with a high degree of probability and not with certainty.

(21) R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine, and R. R. Whetstone, *J. Am. Chem. Soc.*, 64, 1985 (1942).

EXPERIMENTAL

All melting points and boiling points are uncorrected.

Ethyl 1-hydroxy-2-methyl-2-carbethoxycyclohexylacetate was prepared according to the method recommended by previous workers[12,13] with the exception that thiophene-free dry benzene was employed as the solvent in the place of ether-benzene mixture and for one mole of the keto ester, two gram atoms of zinc wool and 1.3 mole of ethyl bromoacetate were used. We obtained consistently a little over 70% yield of the Reformatsky product.

Ethyl 6-methyl-6-carbethoxycyclohexenylacetate (V). To a mixture of the above mentioned Reformatsky ester (29.5 g.) and dry benzene (100 ml.), phosphorus pentoxide was added in three lots (15 g., 5 g., and 5 g.) at intervals of 15 min., and the contents were refluxed under anhydrous conditions on a steam bath for 3 hr. with occasional shaking. The contents were cooled, the benzene solution decanted from the phosphorus pentoxide, and crushed ice and water were added to decompose it. The aqueous solution was extracted with ether and the ether extract was added to the benzene solution. The combined extract was washed with water, sodium bicarbonate solution (5%), and again with water, and dried over anhydrous sodium sulfate. The solvent was then removed and the product distilled under reduced pressure. Ethyl 6-methyl-6-carbethoxycyclohexenylacetate (22 g., 88%) was obtained as a colorless oil, b.p. 132–138°/4 mm. [(lit.[15] b.p. 154–155°/10 mm.)] n_D^{28} 1.4636.

Anal. Calcd. for $C_{14}H_{22}O_4$: C, 66.14; H, 8.66. Found: C, 65.84; H, 8.50.

A drop of the above dehydrated ester readily decolorized bromine in carbon tetrachloride solution.

6-Methyl-6-carbethoxycyclohexenylacetic acid (VI). To a solution of ethyl 6-methyl-6-carbethoxycyclohexenylacetate (22 g.) in ethanol (350 ml.), 1.1*N* aqueous sodium hydroxide solution (83.2 ml.) was added and the contents were refluxed on a water bath for 5 hr. Ethanol was removed under reduced pressure, the residue was dissolved in water, and the solution extracted with ether to remove the neutral material. The aqueous solution was cooled and acidified with dilute hydrochloric acid whereby a heavy oil separated. The mixture was saturated with salt and extracted with ether. The ether extract was dried over anhydrous sodium sulfate, the solvent was removed, and the product was distilled in vacuum. 6-Methyl-6-carbethoxycyclohexenylacetic acid (18.1 g.) was obtained, b.p. 170–174°/3–4 mm., n_D^{27} 1.4820, as a colorless viscous oil. All attempts to induce crystallization were unsuccessful.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.71; H, 7.96. Found: C, 63.50; H, 8.20.

Ethyl β-(6-methyl-6-carbethoxycyclohexenyl)propionate (VII). (*a*) *Preparation of acid chloride of* (VI). To a solution of acid ester (9.1 g.) in thiophene-free dry benzene (10 ml.) cooled in ice water, two drops of dry pyridine and purified thionyl chloride (5.5 ml.) were added and the contents were

mixed intimately by swirling. Reaction took place immediately. The contents were left at room temperature for 4 hr. and then the mixture was warmed at 45° for 15 min. after which the solvent and excess thionyl chloride were removed under reduced pressure. Ten ml. of dry benzene were added to the residual acid chloride and removed again by a second evaporation to remove last traces of thionyl chloride.

(*b*) *Preparation of diazomethane solution.* An ethereal solution (300 ml.) of diazomethane was prepared from *N*-nitroso-*N*-methyl urea (30 g.), carefully distilled, and the distillate containing the diazomethane was dried over pellets of potassium hydroxide and then over sodium to remove last traces of moisture.

(*c*) *Preparation of the diazoketone and its conversion to the homologous ester.* The dried ethereal solution of diazomethane was taken in a round bottom flask and cooled in a freezing mixture. A solution of the acid chloride in dry ether (30 ml.) was then added dropwise with constant swirling to the diazomethane solution and the contents were left overnight at room temperature. Then the ether and excess of diazomethane were removed under reduced pressure (water pump) at room temperature. To the orange colored oily diazoketone in absolute ethanol (100 ml.) a slurry of silver oxide (obtained from 10% silver nitrate solution, 40 ml.) in absolute ethanol was added and the contents refluxed on a water bath. Brisk evolution of nitrogen took place and after 0.5 hr. another lot of silver oxide (0.2 g.) was added and the refluxing continued for 2 hr. more. The solution was then boiled with Norit, filtered, and the filtrate was evaporated under reduced pressure. The liquid diethyl ester left in the flask was then distilled in vacuum. Ethyl β-(6-methyl-6-carbethoxycyclohexenyl)propionate was obtained (4.3 g., 40%) as a colorless oil, b.p. 137–140°/3 mm., n_D^{28} 1.4715. [A low boiling product 70–80°/3 mm. (1.5 g.) was invariably obtained but this was not investigated.]

Anal. Calcd. for $C_{15}H_{24}O_4$: C, 67.16; H, 8.96. Found: C, 66.97; H, 9.04.

β-(6-Methyl-6-carbethoxycyclohexenyl)propionic acid (VIII). To a mixture of ethyl β-(6-methyl-6-carbethoxycyclohexenyl)propionate (25.3 g.) and ethanol (500 ml.) was added 1.109*N* aqueous sodium hydroxide solution (85.2 ml.) and the contents were refluxed on a steam bath for 5 hr. Ethanol was removed under reduced pressure, the residue dissolved in water and extracted with ether to remove any unhydrolyzed ester. The aqueous layer was separated, cooled, and acidified with ice cold dilute hydrochloric acid. The mixture was saturated with salt and extracted with ether. The ether extract was dried over anhydrous sodium sulfate, the solvent was removed and the residue was distilled in vacuum. β-(6-Methyl-6-carbethoxycyclohexenyl)propionic acid (20 g.) distilled at 180–184°/4 mm., n_D^{22} 1.4860, as a colorless viscous oil. All attempts to induce crystallization were unsuccessful.

Anal. Calcd. for $C_{13}H_{20}O_4$: C, 65.00; H, 8.33. Found: C, 64.70; H, 8.36.

4-Methyl-4-carbethoxyhydrind-Δ^{8,9}-en-1-one (IX). To a solution of β-(6-methyl-6-carbethoxycyclohexenyl)propionic acid (4.3 g.) in glacial acetic acid (17 ml.) were added freshly distilled acetic anhydride (70 ml.) and a solution of acetic acid containing zinc chloride (17 ml., fused zinc chloride 20 mg. per ml. of glacial acetic acid) and the contents were refluxed in an atmosphere of nitrogen for 5 hr. The solution gradually turned dark brown in color. After the refluxing was completed, excess acetic anhydride was decomposed with careful addition of water and the acetic acid was removed under reduced pressure. The dark brown residue left in the flask was taken up in ether, the ether extract was washed with water, and then with ice cold 5% sodium hydroxide solution to remove any lactone formed, and again with water until it was free from alkali, and dried over anhydrous sodium sulfate. The solvent was then removed and the residue distilled in vacuum. 4-Methyl-4-carbethoxyhydrind-Δ^{3,9}-en-1-one (2.4 g.) distilled at 144–150°/2–3 mm., n_D^{22} 1.5021.

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.27; H, 8.10. Found: C, 70.10; H, 8.34.

The ultraviolet absorption spectrum of the unsaturated keto ester (XI) showed λ_{max}^{alc} 235 mμ, log ε = 3.98.

Semicarbazone. To a mixture of semicarbazide hydrochloride (0.8 g.) and pyridine (1 ml.) in ethanol (10 ml.) 4-methyl-4-carbethoxyhydrind-Δ^{8,9}-en-1-one (0.45 g.) was added and the mixture was warmed at 70–75° (water bath) for 2 hr. Water was added to the mixture and the precipitated semicarbazone (0.4 g.) (crude m.p. 219–221°) crystallized from ethanol. The analytical sample melted at 220–222° (dec.).

Anal. Calcd. for $C_{14}H_{21}O_3N_3$: N, 15.05. Found: N, 14.80.

4-Methyl-4-carbethoxyhydrindan-1-one (XI). To palladium-charcoal (5% Pd, 1 g.) in ethanol (50 ml.) the above unsaturated keto ester (7 g.) was added and the contents were stirred under hydrogen at room temperature. After the theoretical amount of hydrogen had been consumed (15 hr. stirring), the alcoholic solution was filtered from the catalyst, the solvent was removed, and the product was distilled in vacuum. 4-Methyl-4-carbethoxyhydrindan-1-one distilled at 140–142°/3 mm., $n_D^{22.5}$ 1.4770, as a colorless oil with a sweet camphoraceous odor (6.3 g.).

Anal. Calcd. for $C_{13}H_{20}O_3$: C, 69.64; H, 8.93. Found: C, 69.25; H, 8.80.

The *semicarbazone* was prepared from 0.3 g. of the keto-ester as described above (crude m.p. 202–204°). After two crystallizations from ethanol, the analytical sample melted at 206° (dec.).

Anal. Calcd. for $C_{14}H_{23}O_3N_3$: C, 59.79; H, 8.19. Found: C, 59.88; H, 8.07.

4,8-Dimethyl-4-carbethoxyhydrindan-1-one (XII). (*a*) *Formylation.* Sodium ethoxide was prepared by slow addition of ethanol (3.5 ml.) to a cooled suspension of powdered sodium (1.25 g.) in dry benzene (50 ml.). After the reaction was complete the benzene was removed under reduced pressure. Twenty ml. of dry benzene were added to the sodium ethoxide and removed by a second evaporation. To the cooled suspension of sodium ethoxide in dry benzene (50 ml.) kept under nitrogen, were added ethyl formate (5 ml.) and 4-methyl-4-carbethoxyhydrindan-1-one (6 g.). The mixture was kept under nitrogen for 24 hr. with occasional shaking. The sodium ethoxide gradually disappeared and the solution became viscous and turned deep orange in color. The product was decomposed with ice water and the benzene layer was separated and washed twice with dilute sodium hydroxide solution (5%). The combined aqueous solution was acidified with cold dilute hydrochloric acid and the liberated oil was taken up in ether. The ether extracted was dried over anhydrous sodium sulfate and after removing the solvent the formyl derivative (crude 6.6 g.) was obtained. It gave a deep violet color with alcoholic ferric chloride solution.

(*b*) *N-methylanilino derivative.* To the aforementioned crude formyl compound (6.6 g.) in benzene (100 ml.) *N*-methylaniline (4 g.) was added and the mixture was refluxed on a steam bath for 2 hr. The water formed in the reaction was removed with the help of a Dean-Starke water separator. The solvent was then evaporated under reduced pressure and the residue was evaporatively distilled in high vacuum (from an air bath at 170° and pressure 0.4 mm.). The *N*-methylanilino compound was obtained as a very viscous gum, yellowish brown in color (7.6 g.).

(*c*) *Methylation.* To a cooled solution of potassium (5 g.) in *tert*-butyl alcohol in a 3-necked flask, fitted with a mechanical stirrer, reflux condenser, and a dropping funnel and filled with dry nitrogen, was added the solution of N-methylanilino compound (7.6 g.) in *tert*-butyl alcohol (10 ml.) and the contents were stirred. After 2 min. methyl iodide (25 ml.) was added and the stirring continued at room temperature for 2 hr. Gradually the dark brown color of the mixture disappeared and potassium iodide separated. The contents were refluxed for 2 hr., most of the solvent removed under reduced pressure and the residue diluted

with water, and extracted with ether and the solvent was removed.

(d) Hydrolysis. The above residue was refluxed for 2 hr. with a mixture of water (100 ml.), ethanol (60 ml.), and concentrated sulfuric acid (15 ml.). The product was extracted with ether, and the residue after the removal of the solvent was refluxed with 5% sodium hydroxide solution (150 ml.) for 4 hr. The reaction mixture was cooled and acidified with dilute hydrochloric acid and the liberated keto acid was taken up in ether. The solvent was removed and the residue was esterified by refluxing with a mixture of ethanol (30 ml.) and concentrated sulfuric acid (4 g., d. 1.84) for 10 hr. Crushed ice and water were added and the solution saturated with ammonium sulfate, and extracted with ether. After removing the solvent the residue was distilled in vacuum. 4,8-Dimethyl-4-carbethoxyhydrindan-1-one distilled at 145–150°/2–3 mm., n_D^{21} 1.4837, as a colorless mobile oil (3 g.) with a pleasant camphoraceous smell which was distinctly different from that of the unmethylated keto ester.

Anal. Calcd. for $C_{14}H_{22}O_3$: C, 70.59; H, 9.24. Found: C, 70.70; H, 9.30.

The *semicarbazone* was prepared from 0.4 g. of the keto ester (XII) as described previously. The crude semicarbazone (0.47 g.) m.p. 230–232° (dec.) amounting to 90% was obtained. The derivative was fractionally crystallized from ethanol but it was observed that the melting point was practically the same after each crystallization. The analytical sample was obtained as small leaflets, m.p. 232–233° (dec.).

Anal. Calcd. for $C_{15}H_{25}O_3N_3$: C, 61.02; H, 8.47. Found: C, 61.03; H, 8.72.

1,3-Dimethyl-1,3-dicarboxycyclohexan-2-acetic acid (XIV). 4,8-Dimethyl-4-carbethoxyhydrindan-1-one (2 g.) was heated under reflux on a water bath with concentrated nitric acid (8 ml., d. 1.4) for 1 hr. and then 2 hr. more with the addition of water (6.5 ml.). The contents were cooled and the nitric acid and water were removed by keeping the flask in a vacuum desiccator over potassium hydroxide for 48 hr. The crystalline solid along with the adhering oil left in the flask was directly hydrolyzed by refluxing with a solution of potassium hydroxide (4 g.) in ethanol (20 ml.) for 5 hr. The alcohol was removed and the residue dissolved in water and acidified with 2*N* hydrochloric acid, and extracted with ether after saturating with ammonium sulfate. The solvent was removed and the residue which was obtained as a glass was dissolved in glacial acetic acid (5 ml.) when gradually clusters of stout needles began to separate after two days. They were filtered and washed with a little cold acetic acid. The first crop of crystals amounted to 0.3 g.; crude m.p. 211–213° (dec.). After some days another crop of crystals was obtained (0.15 g.) from the mother liquor. The analytical sample melted at 213–214° (dec.) after two crystallizations from glacial acetic acid.

Anal. Calcd. for $C_{12}H_{18}O_6$: C, 55.81; H, 6.98. Found: C, 55.90; H, 7.26.

The melting point was determined according to the direction given by Ruzicka.[2]

Preparation of authentic $C_{12}H_{18}O_6$ tricarboxylic acid from abietic acid. Abietic acid was prepared from colophony according to the method of Palkin and Harris,[22] the acid sodium salt ($C_{19}H_{29}COONa \cdot 3C_{20}H_{30}O_2$) was crystallized from ethanol only once and the abietic acid liberated from it melted at 163–167°.

Abietic acid was oxidized with a mixture of concentrated and fuming nitric acids to which 0.2% (on the weight of abietic acid) of vanadium pentoxide was added as a catalyst as suggested by Barton.[3] After the oxidation was complete the nitric acid was removed by evaporation on a water bath, and the resinous residue was dissolved in acetone and kept in a refrigerator. The $C_{11}H_{16}O_6$-tricarboxylic acid crystallized out in nearly pure form and was further purified by recrystallization from acetone, m.p. 219° (dec.). Mixed melting point with an authentic specimen kindly supplied by Professor Ruzicka showed no depression. To the residue (250 g.) obtained after separation of the crystallized C_{11}-acid, was added a mixture of absolute methanol (500 ml.) and concentrated sulfuric acid (125 g., d. 1.84) and the contents were refluxed on a water bath for 10 hr. Half the quantity of methanol was removed under reduced pressure, water was added, and the product separated into acidic and neutral fractions with sodium carbonate solution and ether. The neutral fraction obtained from the ether extract was carefully fractionated in high vacuum and the fraction distilling at 135–155°/0.5 mm. (27.1 g.) was collected. The ester (27.1 g.) was hydrolyzed by heating under reflux at 130° with concentrated hydrochloric acid (250 ml.) for 20 hr. The crystalline product (12.2 g.) obtained after the hydrolysis was esterified by refluxing with a mixture of absolute methanol (100 ml.) and concentrated sulfuric acid (5 g.) for 40 hr. Again the reaction product was separated into acidic and neutral fractions, as described above. The neutral fraction was distilled in vacuum and the fraction distilling at 130–135°/0.1 mm. was collected (3.1 g.) and again hydrolyzed with concentrated hydrochloric acid. The acid so obtained (1.2 g.) was found to melt at 208–210°. This suggested that the acid was still a mixture of C_{11}- and C_{12}-acids and the pure C_{12}-acid was separated as the triester by re-esterifying the acid mixture (1.2 g.) of m.p. 208–210°, with 5% methanolic hydrochloric acid (30 ml.). The neutral fraction on hydrolysis with concentrated hydrochloric acid gave the C_{12}-acid (0.6 g.) and the analytical sample after two crystallizations from acetone melted at 213° (dec.). Mixed melting point with the authentic C_{11}-acid was found to be 205–207° (lit.[2] states mixed m.p. 205–207°). The melting point was determined as described by Ruzicka.[2]

Anal. Calcd. for $C_{12}H_{18}O_6$: C, 55.81; H, 6.98. Found: C, 55.90, 56.01; H, 7.02, 6.99.

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