chromatography as described above) in 320 ml of acetic acid and 11 ml of water was stirred and warmed at 65° for 4 hr under nitrogen. The solution was cooled in an ice–water bath, neutralized to pH 9 with 10% sodium hydroxide, and the product was isolated by ether extraction (three 500-ml portions): yield, 19.5 g of **6** plus **2**: vpc analysis showed **6–3** ≅75:25; λ_{max} 249 mμ (ε 11,790). Material from combined runs totaling 25.3 g was chromatographed on Florisil (100–200 mesh, 1520 g, solvent system petroleum ether–benzene–ethyl acetate). Early fractions from 2–4% ethyl acetate–benzene contained mostly **2** (4.6 g) and mixed fractions of **2** and **6**. The major fraction from 4% ethyl acetate–benzene contained 11.1 g of enedione **6** which slowly solidified on cooling and scratching and which was crystallized from methanol–water or petroleum ether cooled to −20°. The analytical sample of **6** was obtained as colorless needles from petroleum ether and dried at room temperature *in vacuo* (0.03 mm) for 6 hr: mp 38–41°; λ_{max} 249 mμ (ε 12,500); ν_{max} 1716, 1655 cm^{-1}; δ 1.07 (7aβ-methyl), 1.18 ppm (1β-*t*-butyl).

Anal. Calcd for $C_{19}H_{30}O_3$ (306.43): C, 74.47; H, 9.87. Found: C, 74.76; H, 10.21.

(±)-17β-Hydroxy-Δ$^{9(10)}$-des-A-androsten-5-one (8).—To a prereduced suspension of 1.32 g of 10% palladium–barium sulfate in 28 ml of absolute ethyl alcohol was added 3.0 g of enedione **6** in 28 ml of ethyl alcohol and the mixture was shaken under hydrogen at room temperature and essentially atmospheric pressure. After 50 min, 120% of the theoretical amount of hydrogen had been consumed. The solvent was removed *in vacuo* and the residue (3.0 g, no ultraviolet absorption) was dissolved in 120 ml of methanol containing 12 ml of 1 *N* sodium methoxide and allowed to equilibrate under nitrogen for 15 min. The solution was neutralized with ammonium chloride and extracted with three 100-ml portions of ether. Cyclization and hydrolysis of the crude product (3.0 g) was achieved by refluxing under nitrogen for 6.5 hr in 150 ml of ethyl alcohol containing 30 ml of 3 *N* hydrochloric acid. The mixture was neutralized with 5% sodium bicarbonate, the solvent was removed *in vacuo*, and the crude product (2.0 g) was obtained by methylene chloride extraction. Crystallization from ether–petroleum ether afforded 1.16 g of the BCD tricyclic compound **8**: λ_{max} 248 mμ (ε 15,000); essentially pure by vpc. The melting range of such preparations is not an indication of purity since a typical melting point would be *ca.* 120–127° with sintering. An analytical sample of **8** was prepared by chromatography on Florisil with benzene and crystallization from ether: mp 132.5–135.5°; λ_{max} 248.5 mμ (ε 15,400); ν_{max} 3650 and 3450–3550, 1665, 1605 cm^{-1}; δ 0.91 (13-CH_3), 1.79 ppm (10-CH_3).

Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 77.02; H, 9.52.

(±)-Δ$^{9(10)}$-Des-A-androstene-5,17-dione (9).—The keto alcohol **8** (117 mg) was dissolved in 21 ml of acetone (distilled from potassium permanganate), cooled and stirred at −12°, and treated with 0.14 ml of 8 *N* chromic anhydride in sulfuric acid under nitrogen.[13] After 15 min, 10 ml of saturated sodium chloride solution was added and the mixture was extracted twice with ethyl acetate and once with ether. The organic phase was washed (1 *N* sodium bicarbonate) and worked up in the usual manner: yield, 115 mg of an oil that crystallized on scratching. Crystallization from ether–petroleum ether gave 95 mg of the tricyclic diketone **9**: mp 95–97.5°; λ_{max} 247 mμ (ε 15,900); ν_{max} 1740, 1665, 1605 cm^{-1}; δ 1.03 (13β-CH_3), 1.80 ppm (10-CH_3). Recrystallization from ether gave the pure sample of **9**, mp 98.5–100° (lit.[4] mp 98–100°).

Registry No.—**2**, 13652-01-2; **3**, 13652-02-3; **4**, 13699-65-5; **5**, 13652-03-4; **6**, 13652-04-5; **8**, 13652-05-6; **9**, 13652-06-7.

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(13) C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

The Synthesis of Racemic and (3*R*)-Methylcyclopentane-1,2-dicarboxylic Acids (Nepetic Acids)[1a]

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The Favorskii-type rearrangement of (+)-methyl 3-bromo-4-methyl-2-oxocyclohexanecarboxylate (**11a**) derived from (+)-pulegone (**8**) provides a convenient synthesis of the optically active (3*R*)-methylcyclopentane-1,2-dicarboxylic acids (**12a**, **13a**, **14a**, and **15a**). The purification of these acids was accomplished by fractional precipitation of their barium salts and preparative gas chromatography separation of their methyl esters. The correlation of the (−)-*cis,cis* acid, **15a**, derived from (+)-pulegone (**8**), with genipin (**16**) is described. The four racemic 3-methylcyclopentane-1,2-dicarboxylic acids (**12c**, **13c**, **14c**, and **15c**) were readily prepared from the racemic keto ester **11c**.

The racemic 3-methylcyclopentane-1,2-dicarboxylic acids have been synthesized, and their properties have been described.[2] Optically active acids having this carbon skeleton and the (3*S*)-methyl absolute configuration[3a,b] are known as nepetic acids. Two of these nepetic acids, the *trans,trans* isomer **4** and the *cis,trans* isomer **6**, were previously obtained as degradation products of nepetalactone (**1a**)[3c] *via* nepetonic acid (**2**) and the enol lactone **3** as shown in Chart I.[4]

A third nepetic acid, the *trans,cis* isomer **5**, was obtained from epinepetalactone **1b**.[3b] The remaining member of this series, *cis,cis*-nepetic acid (**7**), has not been described. Certain members of the enantiomeric series of 3-methylcyclopentane-1,2-dicarboxylic acids having the (3*R*)-methyl configuration were first en-

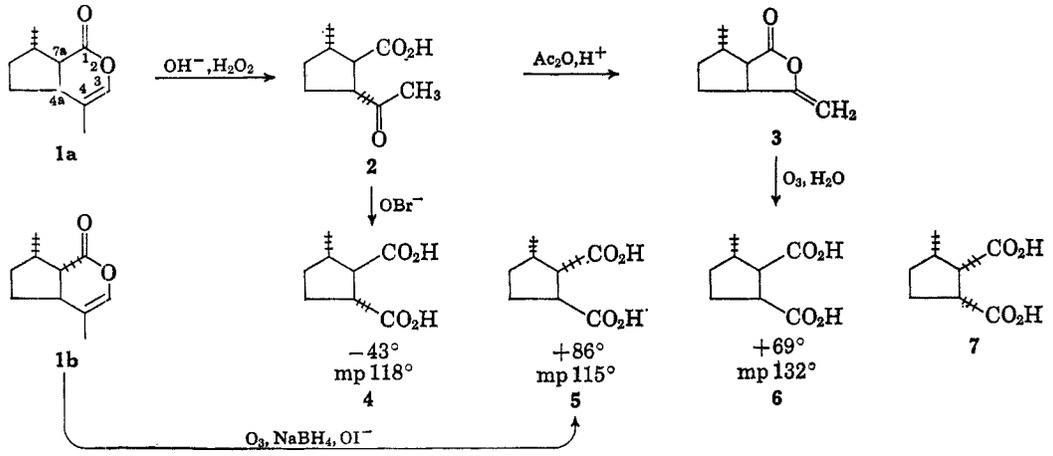
(1) (a) E. J. Eisenbraun, P. G. Hanel, K. S. Schorno, J. Osiecki, and Sr. St. F. Dilgen, Abstracts, 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966, K-14. (b) P. G. Hanel, M.S. Thesis, Oklahoma State University, 1966; American Petroleum Institute Research Project 58A Graduate Research Assistant, 1963–1965. (c) Participant in the National Science Foundation Research Participation Program for College Teachers, Oklahoma State University, summer 1963; (d) Dr. Osiecki's contribution was made from the Department of Chemistry, Stanford University, during 1960–1962. This portion of the research was partially supported by National Science Foundation Grant 13115 to E. J. E.

(2) (a) R. B. Bates, E. J. Eisenbraun, and S. M. McElvain, *J. Am. Chem. Soc.*, **80**, 3413 (1958); (b) A. T. Blomquist, J. Wolinsky, Y. C. Meinwald, and D. T. Longone, *ibid.*, **78**, 6057 (1956).

(3) (a) E. J. Eisenbraun and S. M. McElvain, *ibid.*, **77**, 3383 (1955). (b) R. B. Bates, E. J. Eisenbraun, and S. M. McElvain, *ibid.*, **80**, 3420 (1958). (c) We thank Dr. K. Loening, Chemical Abstracts Service, for advice in selection of the numbering system for this series.

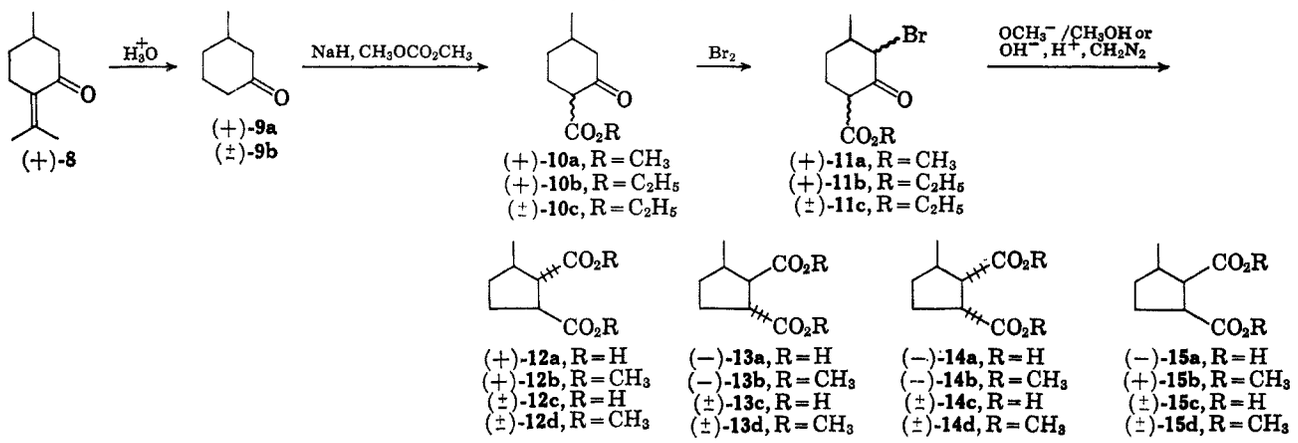
(4) (a) S. M. McElvain and E. J. Eisenbraun, *J. Am. Chem. Soc.*, **77**, 1599 (1955); (b) S. M. McElvain, R. D. Bright, and P. R. Johnson, *ibid.*, **63**, 1558 (1941).

CHART I[a]



[a] −43°, +86°, and +69° are $[\alpha]_D$ values for compounds **4**, **5**, and **6**, respectively.

CHART II



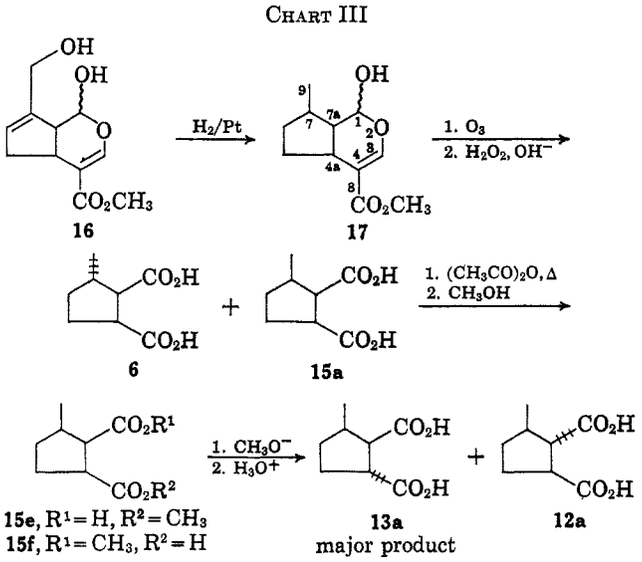
countered as impure degradation products of genipin. Their structures, **13a** and **15a**, along with those of the remaining acids of this series, **12a** and **14a**, are shown in Chart II.

Aside from extensive instrumental studies, the earlier structure and absolute configuration proof for genipin (**16**) rests largely on the isolation in 32% yield of crystalline **17**, mp 81.5–83°, from the mixture of hydrogenation products of **16** and its subsequent degradation with ozone and hydrogen peroxide to 3-methylcyclopentane-1,2-dicarboxylic acid (**15a**), mp 136–137°, which has a plain positive optical rotatory dispersion (ORD) curve.[5] These conversions are shown in Chart III. Our current studies show that synthetic **15a** gives a positive Cotton effect curve. The ORD curve of **15a** is similar to the curve obtained from **15a** from genipin.

A nepetalactone-derived nepetic acid was not available for comparison; consequently **15a** obtained from genipin (**16**) was identified[5] by conversion to **13a**, and the latter, although impure, was considered to be the antipode of (+)-*trans,cis*-(3*S*)-methylcyclopentane-1,2-dicarboxylic acid (**5**) derived from nepetalactone.[3b]

The properties of the nepetalactone-derived *cis,trans*-nepetic acid (**6**)[3b] and the infrared spectrum of the racemic acid **14c**[2a] were used to help establish the absolute configuration, stereochemistry, and structure of monotropein (**18**).[6] Monotropein (**18**) and genipin (**16**)

CHART III



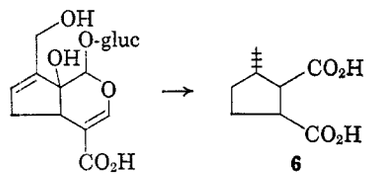
are closely related in that each structure contains a hydroxymethyl group, attached at C-7 to the cyclopentene ring. The system can be hydrogenolyzed and hydrogenated to a methylcyclopentane ring. It is to be expected that as additional monoterpenoids having this function are discovered, the utilization of this hydrogenolysis reaction will become common, and a greater need for the (*R*)-, (*S*)-, and racemic 3-methyl-

(5) C. Djerassi, T. Nakano, A. N. James, L. H. Zalkow, E. J. Eisenbraun, and J. N. Shoolery, *J. Org. Chem.*, **26**, 1192 (1961).

(6) H. Inouye, T. Arai, Y. Miyoshi, and Y. Yaoi, *Tetrahedron Letters*, 1031 (1963)

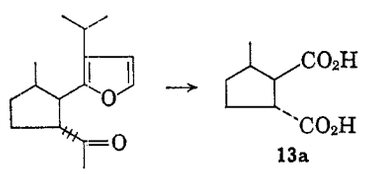
cyclopentane-1,2-dicarboxylic acids as reference compounds will arise.

The newly synthesized (−)-(3*R*)-*trans,cis*-methylcyclopentane-1,2-dicarboxylic acid (**13a**) derived from (+)-pulegone (**8**) was used in establishing the structure, absolute configuration, and stereochemistry of furopelargone A (**19**) from *Geranium bourbon*.[7] These



18

6



19

13a

correlations and our interest in obtaining the (3*R*)-methylcyclopentane-1,2-dicarboxylic acids having the absolute configuration opposite that of the nepetic acids obtained from nepetalactone (**1a**) prompted our completing the synthesis sequence shown in Chart II to provide all the acids of this group having the (3*R*)-methyl absolute configuration. Aside from the simplicity and convenience of this synthesis, the major advantage is that the starting material is optically pure and of rigorously established absolute configuration.[3a] Thus the need for resolution, a weak point of our earlier synthesis of nepetic acids, is avoided.[2a]

While we did not question the correctness of the structure, stereochemistry, and absolute configuration assignment to genipin (**16**) and its degradation products, it was recognized that the key degradation product **13a** from genipin (**16**) used for comparison with the antipodal nepetic acid **5** was not homogeneous and probably contained **6**.[5] The relevant structures are shown in Charts I, II, and III.

With the availability of the newly synthesized **13a**, **14a**, and **15a** for comparison, it seemed worthwhile to repeat the degradation of genipin to provide materials for direct comparison and rigorous confirmation of the earlier studies. The degradation followed essentially the previously described route. In one experiment, 9-deoxy-6,7-dihydrogenipin (**17**)[3c] was isolated by chromatography on a column of Merck acid-washed alumina and was found to melt at 81–82° after recrystallization.[5] In another procedure, the entire hydrogenation reaction product from genipin (**16**) was ozonized, and, after the reaction mixture was treated with basic peroxide, the *cis* acids were isolated as insoluble barium salts.[8] These barium salts were converted to acids and, after recrystallization, the mixture was found to melt at 136–138°. The filtrate from the barium hydroxide treatment was acidified, extracted with ether, and treated with diazomethane. A gas chromatogram from a packed 10 ft × 0.25 in. phenyldiethanolamine succinate column showed **6** and **15a** were present as a mixture in a 1:2.5 ratio. The retention time of the major component corresponded with that of **15b** and that of the minor component with **14b** (antipode of **6b**). When the *cis*-dimethyl esters obtained from genipin (**16**) were individually mixed with **14b** and **15b** obtained from (+)-pulegone (**8**), the same two, and only two, peaks were obtained. Thus, the presence of **6** is explained; the hydrogenation of genipin takes place to some extent on the more hindered side of the molecule.[5]

The recrystallized product from the ozonolysis of **17**, consisting mainly of the *cis,cis* acid **15a**, was converted as shown in Chart III *via* the anhydride to a mixture of the methyl half-esters **15e** and **15f**. This mixture was epimerized and then hydrolyzed. The product, a mixture of **12a** and **13a**, was treated with diazomethane. Gas chromatography of the resulting mixture of dimethyl esters showed, by comparison with those obtained from (+)-pulegone (**8**), that the mixture contained the *trans* acids **12a** and **13a** in a ratio of 1:5.3.

Brenner's conversion of ethyl 2-oxocyclohexanecarboxylate (**20b**) *via* the bromo keto ester **21b** to *trans*-1,2-dicarboxylic acid (**22a**) appears to be the sole citation of this Favorskii-type rearrangement.[9,10] We were interested in determining whether differences existed in the Favorskii-type rearrangement of **11b** and **21b**, and, therefore, the original reaction was repeated and the reaction products from **21b** (Chart IV) were examined in detail. Gas chromatographic analysis of methyl esters of the acidic products showed the presence of *trans*-cyclopentane-1,2-dicarboxylic acid (**22a**) and *cis*-cyclopentane-1,2-dicarboxylic acid (**23a**) as well as cyclopentene-1,2-dicarboxylic acid (**24a**) in the ratio of 4:1:2. The retention times of **22b**, **23b** and **24b** at 190° on the 10 ft × 0.25 in. Carbowax 20 M column using a 75 cc/min flow of helium were 23, 30, and 41 min, respectively.

The structures of **24a** and **24b** were established by their infrared, mass, nmr, and ultraviolet spectra. During the course of the structure proof of **24a**, **25a** was eliminated as a possible acidic reaction product from **21a** by converting the entire acidic fraction of the Favorskii-type rearrangement to a mixture of methyl esters, equilibrating this mixture of esters by use of methoxide ion in anhydrous methanol, and showing by gas chromatography analysis that **22b** and **23b** were present in the ratio of 90:10.[11] This ratio is the equilibrium value for **22b** and **23b** and, therefore, it may be safely assumed that none or little of **25b** is present, even though **23b** and **25b** were indistinguishable by the gas chromatography studies.

Additional evidence for the structure of **24b** was obtained from the catalytic hydrogenation of **24b** in the presence of PtO_2 catalyst in acetic acid solvent. The peak due to **24b** was not present in the chromatogram after hydrogenation and only the peaks due to **22b** and **23b**, in the ratio of 11:89, were observed.

The identity of the precursors to **24a** and **24b** is under study. At present, a dibromo derivative of **20a** is

(7) G. Lukas, J. C. N. Ma, J. A. McCloskey, and R. E. Wolff, *Tetrahedron*, **20**, 1789 (1964).

(8) Five pairs of substituted *cis*- and *trans*-cyclopentane-1,2-dicarboxylic acids show the barium salt of each *cis* isomer to be considerably less soluble in water than that of the *trans* isomer. *Cf.* E. J. Eisenbraun, "The Structure of Nepetalic Acid," Ph.D. Thesis, University of Wisconsin, 1955.

(9) J. E. Brenner, *J. Org. Chem.*, **26**, 22 (1961).

(10) A. S. Kende, *Org. Reactions*, **11**, 261 (1960).

(11) G. J. Fonken and S. J. Shiengthong, *J. Org. Chem.*, **28**, 3435 (1963).

CHART IV

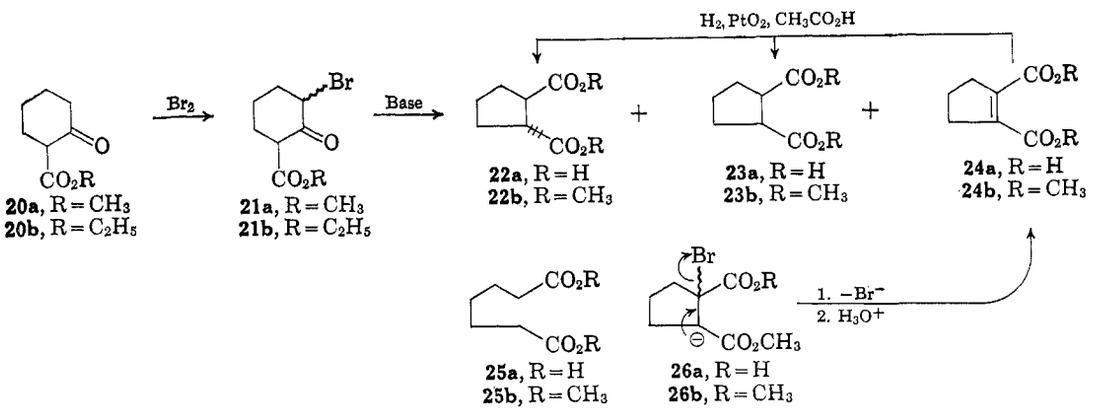
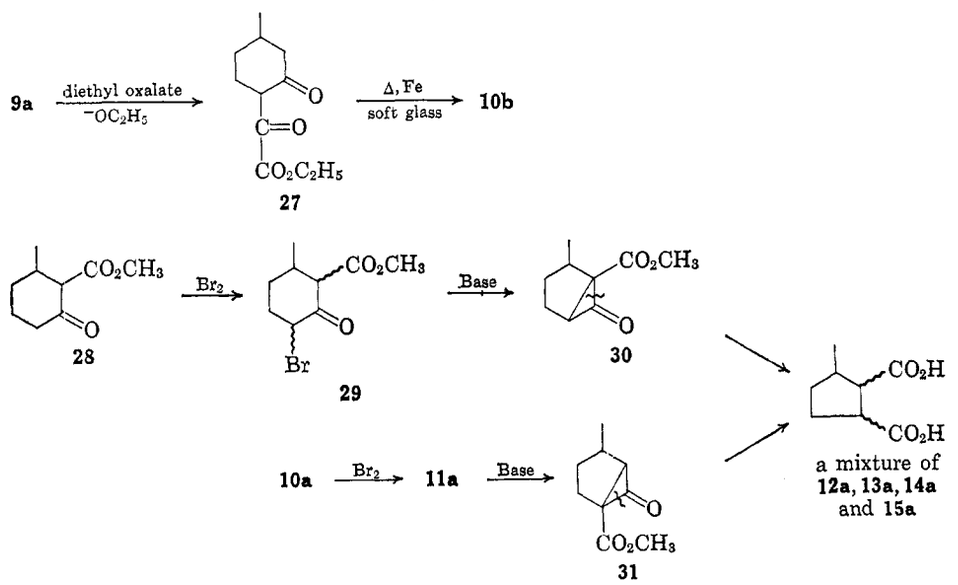


CHART V



favored and the intermediates **26a** or **26b** which lose a bromide ion are considered likely.

The identification of **24a** and **24b** as reaction products from **21a** suggests that similar products should accompany **12a**, **13a**, **14a**, and **15a** from **11a**. Indeed, extra peaks having gas chromatographic retention times proportional to the retention time of **24b** are observed, and it is assumed these are due to unsaturated methyl esters. Their identity remains under study.

The Corey method for carbomethoxylation of cyclic ketones to form β-keto esters is ideally suited for the second step of Chart II.[12] We compared this reaction with the two-step sequence involving formation and decarboxylation of the α,γ-diketo ester **27** to give **10b**.[13] Using the Corey method with some modification and on a larger scale, the yield for the conversion of ketone **9a** to β-keto ester increased from about 70 to 85%.

It is our opinion that **10a** results from carbalkoxylation of **9a** and that little of the isomer **28** is formed. We feel this is true for the formation of **10b** as well.

If intermediates **30** and **31** serve in the formation of the four acids **12a**, **13a**, **14a**, and **15a**, it is immaterial whether **28** accompanies **10a** in their formation. However, the possibility of the existence of two intermediates to the formation of these acids provides an intriguing stereochemical problem which is being examined in detail. Our preliminary results[1] show that if aqueous alkali is used for the Favorskii-type rearrangement of **11a** to the acids **12a**, **13a**, **14a**, and **15a**, a high percentage of the thermodynamically less stable *cis* acids **14a** and **15a** result. Conversely, when anhydrous methanol is used as reaction solvent, the product ratio is dramatically altered to favor the *trans* esters **12b** and **13b**. This result corresponds essentially with the equilibrium mixture of their methyl esters. A similar study involving **20a** showed that **22b** and **23b** formed in a 90:10 ratio, which is essentially the known equilibrium value of these esters.[11]

Though the acids **12a**, **13a**, **14a**, and **15a** could be roughly separated through selective precipitation of the barium salts[8] of **14a** and **15a**, the production of pure isomers required the use of preparative gas chromatography of the methyl esters.[14]

Application of the reaction sequence shown in Chart II to (±)-**9b** provided the (±) acids **12c**, **13c**, **14c**, and **15c** and their respective methyl esters.[2a] The entire

(12) E. J. Corey, R. B. Mitra, and H. Uda, *J. Am. Chem. Soc.*, **86**, 485 (1964).

(13) H. R. Snyder, L. A. Brooks, and S. H. Shapiro, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p 531.

(14) A. B. Carel and G. Perkins, Jr., *Anal. Chim. Acta*, **34**, 83 (1966). We are grateful to the Continental Oil Co. for use of their large-diameter preparative gas chromatography columns which enabled us to separate completely the methyl esters **12b**, **13b**, **14b**, and **15b**.

effort using a 0.1 mole of (±)-**9b** requires about 10 hr; using the commercially available (±)-**10c** about 2 hr is needed.

Experimental Section

General.—The elemental analyses were obtained from the Galbraith Laboratories, Knoxville, Tenn. Infrared and ultraviolet spectra were determined with a Beckman IR5A spectrometer. The infrared spectra of the acids **12a**, **13a**, **14a**, and **15a**, as well as those of the dimethyl esters **12b**, **13b**, **14b**, and **15b**, are sufficiently similar to the previously described spectra of racemic acids and esters that description will not be made of these at this time.[2a] Esterifications were accomplished, unless otherwise stated, by adding a cold ethereal solution of the acid to a cold ethereal solution of diazomethane.[15a]

Gas Chromatography.—Gas chromatographic analyses employing packed 10 ft × 0.25 or 0.125 in. columns carried out with an F & M 700 or Beckman GC2A instrument. The columns usually contained LAC 886 as a 20% coating on 80–100 mesh, acid-washed Chromosorb W.

The preparative separations were made by injecting 7–20 ml of a partially separated mixture of dimethyl esters onto a large-diameter column (12 ft × 4 in.) containing 20% Apiezon L or 20% LAC 886 coated on 80–100 mesh, acid-washed Chromosorb W.[14]

(+)-3-Methylcyclohexanone (9a) from (+)-Pulegone (8).—To 1.8 l. of concentrated hydrochloric acid was added 1650 ml (1540 g, 10 moles) of oil of pennyroyal (Fritzche Brothers) containing about 85% pulegone. The mixture was heated and agitated vigorously with a magnetic stirrer. The material which distilled slowly between 56 and 80° (~7 hr) consisted mainly of acetone. Steam was then passed into the reaction mixture until organic material ceased to appear in the condensate (approximately 8 hr). The steam distillate was saturated with sodium chloride and the organic layer separated to give crude (+)-3-methylcyclohexanone (**9a**) as a pale yellow liquid. The crude product was dried over anhydrous magnesium sulfate, filtered, and distilled to give 722 ml (661 g) of colorless **9a**, boiling at 168° or 58–60° (13 mm), $\alpha^{24}D$ +11.4° (neat).[3a] The semicarbazone was prepared and found to melt at 181°. Gas chromatography analysis shows that oil of pennyroyal contains compounds besides pulegone. However, if it is considered to have been 85% pulegone, the reaction yield is 69%.

(+)-Methyl 4-Methyl-2-oxocyclohexanecarboxylate (10a) from (+)-3-Methylcyclohexanone (9a).—The preparation of **10a** from **9a** was carried out essentially as described by Corey[12] except that a larger scale using 100 g (2.3 moles) of 56% sodium hydride mineral oil dispersion, 1 l. of dry dioxane, 560 ml (9 moles) of dimethyl carbonate, and 153 ml (140 g, 1.25 moles) of (+)-3-methylcyclohexanone was used. The product was distilled at 74° (2 mm) to give 181 g (85% yield) of methyl 4-methyl-2-oxocyclohexanecarboxylate (**10a**), mp 22°. A recrystallized sample, mp 41°, $[\alpha]^{23}D$ +101.5° (*c* 0.5, $CHCl_3$), $\lambda_{max}^{CHCl_3}$ 255 mμ (log ε 3.8), was analyzed.

Anal. Calcd for $C_9H_{14}O_2$: C, 63.51; H, 8.29. Found: C, 63.93; H, 8.11.

Small-scale runs were carried out under a nitrogen atmosphere. This was omitted for those runs larger than 1 mole.

(+)-Methyl 3-Bromo-4-methyl-2-oxocyclohexanecarboxylate (11a) from 10a.—A 170-g (1 mole) sample of methyl 4-methyl-2-oxocyclohexanecarboxylate (**10a**) was added to 90 ml of cold dry ether. Bromine (168 g, 1.05 moles) was added dropwise with stirring and cooling over a period of 65 min. Upon completion of addition, the reaction mixture was stirred for an additional 15 min. Evolution of hydrogen bromide was apparent. The reaction mixture was then diluted with ether and poured over 160 g of sodium bicarbonate in ice water. This mixture was allowed to stand for 30 min, with occasional stirring. The organic layer was separated and the aqueous layer extracted three times with ether. The combined ether extracts were dried with anhydrous magnesium sulfate and filtered, and the ether was distilled, giving a crude mixture of (+)-methyl 3-bromo-4-methyl-2-oxocyclohexanecarboxylate (**11a**).

An attempt was made to distil the bromo keto ester **11a**. However, decomposition took place and no further attempts were made to purify or isolate **11a** for preparative work.

Preparation of the Four 3-Methylcyclopentane-1,2-dicarboxylic Acids (12a, 13a, 14a, and 15a) from (+)-Methyl 3-Bromo-4-methyl-2-oxocyclohexanecarboxylate (11a).—The reaction product mixture containing the bromo keto ester **11a** (from 0.9 mole of **10a**) was added to 4 l. of 95% ethanol. To this was added a solution of 230 g of sodium hydroxide in 770 ml of water. The reaction mixture was heated at reflux temperature for 3 hr under a nitrogen atmosphere. After cooling, the sodium bromide was filtered out and washed well with ether. The filtrate and ether washings were combined and then distilled to remove ethanol and ether. The remaining aqueous solution was strongly acidified with concentrated hydrochloric acid. Continuous extraction with ether for 24 hr and work-up yielded 104 g (66%) of crude acids. It was necessary to keep the aqueous layer strongly acidic during the continuous extraction to ensure complete removal of the acids.

Preparation of a Mixture of the Dimethyl Esters 12b, 13b, 14b, and 15b.—A 22-g sample of the mixture of acids from the preceding experiment was added to 34 ml of methanol, 80 ml of methylene chloride, and 6 ml of concentrated sulfuric acid and the mixture was heated at the reflux temperature for 15 hr. The cooled reaction mixture was washed successively with water, twice with a saturated sodium bicarbonate solution, and again with water.[15b] The methylene chloride was evaporated through a rotary evaporator at water aspirator pressure. Distillation yielded 22 g (87%) of a mixture of the dimethyl esters, bp 63–67° (48 mm).

Separation of (+)-*trans,trans*-Dimethyl 3-Methylcyclopentane-1,2-dicarboxylate (12b) and (−)-*trans,cis*-Dimethyl 3-Methylcyclopentane-1,2-dicarboxylate (13b) Using Preparative Gas Chromatography Employing Large-Diameter Columns.—A description of preparative gas chromatography using the large-scale unit employing 4-in.-diameter columns developed by Continental Oil Co. is presented elsewhere.[14] The materials and conditions used to separate and purify **12b** and **13b** were 20% Apiezon L on 60–80 mesh, acid-washed Chromosorb W, helium flow 9 l./min at 10 psi, injection port temperature 250°, column temperture 200°, and thermal detector temperature 250°.

The *cis* acids **14a** and **15a**, as well as any methylcyclopentene-1,2-dicarboxylic acid, were previously removed as the anhydrides. A total of 65 g of mixtures containing approximately 65% of **12b** and 35% of **13b** were injected in 7- to 20-ml portions. The collection traps were cooled by an ice bath. The materials collected were as follows: 1 g of compound represented by a leading unidentified peak, 26 g of 99% pure *trans,trans*-dimethyl ester **12b**, 13 g of 99% pure *trans,cis*-dimethyl ester **13b**, and 4 g of a mixture of **12b** and **13b** from the by-pass trap. The total recovery was 67%. The sample containing **12b** was distilled at 69° (1.0 mm) and collected. The sample of **13b** was distilled at 72° (1.1 mm). The dimethyl esters **12b** and **13b** showed $[\alpha]^{23}D$ +36 and −52° (*c* 2.5, $CHCl_3$), respectively. Their mass spectra showed a parent ion *m/e* 200.

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found for **12b**: C, 60.14; H, 8.09. Found for **13b**: C, 60.10; H, 8.18.

The infrared spectra of **12b** and **13b** were essentially the same as those reported for the dimethyl esters of their racemic counterparts.[2a]

(+)-*trans,trans*-3-Methylcyclopentane-1,2-dicarboxylic Acid (12a).—To 10 g of *trans,trans*-dimethyl ester **12b**, purified through preparative gas chromatography, was added 250 ml of a 5% sodium hydroxide solution and 175 ml of methanol. The solution was heated at reflux temperature for 3 hr and the methanol was distilled under reduced pressure. The remaining solution was acidified with hydrochloric acid and extracted with ether three times and then continuously extracted for 28 hr. The combined ether extracts were dried with magnesium sulfate and filtered, and the ether was evaporated, giving 10.3 g of a light yellow oil which crystallized upon scratching. Recrystallization from a mixture of ether and petroleum ether gave 3.5 g of (+)-*trans,trans*-3-methylcyclopentane-1,2-dicarboxylic acid (**12a**), mp 119–120°, $[\alpha]^{23}D$ +43° (*c* 2.1, $CHCl_3$). Evaporation of the solvents from the mother liquor and recrystallization from a mixture of ether and petroleum ether yielded an additional 3.6 g of acid **12a**. *trans,trans*-Nepetic acid (**4**) melts at 118° and shows $[\alpha]D$ −43°.[3a] The total yield of the *trans,trans* acid **12a** was 83%.

Anal. Calcd for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 55.69; H, 6.86.

(−)-*trans,cis*-3-Methylcyclopentane-1,2-dicarboxylic Acid (13a).—Saponification of 8.0 g of *trans,cis*-dimethyl ester **13b**

(15) (a) J. A. Moore and D. E. Reed, *Org. Syn.*, **41**, 16 (1961); (b) R. O. Clinton and S. C. Laskowski, *J. Am. Chem. Soc.*, **70**, 3135 (1948).

and work-up as described for the *trans,trans* acid **12a** yielded 7.8 g of a light yellow solid. A single recrystallization from ether and petroleum ether yielded 2.0 g of (−)-*trans,cis*-3-methylcyclopentane-1,2-dicarboxylic acid (**13a**), mp 113–115°, $[\alpha]^{25}D$ −88° (*c* 2.1, $CHCl_3$). The catnip *trans,cis*-nepetic acid (**5**) melts at 114–115° and has $[\alpha]D$ +86°.[3a] An admixture of **13a** with the acid obtained as a degradation product of furopelargone A (**19**) showed no depression in melting point.[7]

Anal. Calcd for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 55.74; H, 7.07.

***cis* Anhydrides from a Crude 3-Methylcyclopentane-1,2-dicarboxylic Acid Mixture.**—A 275-g sample of a crude mixture of acids **12a**, **13a**, **14a**, and **15a** was mixed with 1500 ml of acetic anhydride, and the mixture was heated at reflux temperature for 14 hr. The acetic acid formed by the reaction was distilled periodically. After the heating period, the acetic anhydride was distilled at 139° and the remaining mixture was distilled at 83° (0.3 mm) to yield 165 g of a crude mixture of *cis,trans* and *cis,cis* anhydrides of **14a** and **15a** in 67% yield.

Isolation, Separation, and Purification of the (−)-*cis,trans*- and (−)-*cis,cis*-3-Methylcyclopentane-1,2-dicarboxylic Acids (14a and 15a) from a Mixture of *cis* Anhydrides.—A 160-g (1.04 moles) mixture of *cis,trans*- and *cis,cis*-3-methylcyclopentane-1,2-dicarboxylic acid anhydrides was treated with a saturated solution of aqueous barium hydroxide until additional precipitate or cloudiness failed to appear on further addition. The barium salts were filtered and washed with water. The filtered barium salt mixture was acidified with concentrated hydrochloric acid to release *cis* acids.[4a,8] This solution was extracted five times with ether. The combined ether extracts were dried and evaporated to give 112 g (64% yield) of a crude mixture of **14a** and **15a**. This mixture was allowed to crystallize for 3 days. The crystals were removed by filtration and washed with petroleum ether followed by a small volume of cold ether to give 29 g of crude *cis,trans* acid **14a**, mp 124–126°. Gas chromatography of the dimethyl ester of this crude acid showed it to contain 95% **14a** and 5% **15a**. Two additional recrystallizations from ether–petroleum–ether gave (−)-*cis,trans*-3-methylcyclopentane-1,2-dicarboxylic acid (**14a**), mp 131–132°, $[\alpha]^{23}D$ −67° (*c* 2, $CHCl_3$). Gas chromatography of the dimethyl ester **14b** showed it to be free of other isomers.

Anal. Calcd for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 55.94; H, 6.98.

Esterification of **14a** with diazomethane[15a] gave (−)-*cis,trans*-dimethyl 3-methylcyclopentane-1,2-dicarboxylate (**14b**), bp 115° (oil-bath temperature at 1 mm), $[\alpha]^{23}D$ −54° (*c* 1.3 $CHCl_3$), *m/e* 200.

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.82; H, 8.13.

The retained aqueous solutions containing a mixture of barium salts of *cis*-acids **14a** and **15a** were combined, strongly acidified, and extracted continuously with ether for 12 hr. The ether extract was dried over anhydrous magnesium sulfate, filtered, and concentrated to give 56 g of a crude mixture of the *cis* acids **14a** and **15a** in 32% yield. The over-all yield of recovered *cis* acids was 96%.

This latter crude mixture of *cis* acids **14a** and **15a** was treated a second time with saturated aqueous barium hydroxide solution. The resulting barium salt precipitate was filtered out immediately, and the filtrate was allowed to stand at room temperature for 15 hr at which time an additional crop of barium salts was obtained on filtration. This crop was treated with hydrochloric acid and extracted with ether, and the ether extract was dried and evaporated to give 7.6 g of crude *cis* acids enriched with *cis,cis* acid **15a** as shown by gas chromatography of the dimethyl esters. The 7.6-g sample was seeded with a small crystal of **15a** obtained from degradation of genipin (**16**). On standing for 4 days, 1.55 g of needle-shaped crystals of **15a**, mp 132–134°, was deposited. The crude acid was recrystallized from a mixture of ether and petroleum ether to give 0.9 g of pure (−)-*cis,cis*-3-methylcyclopentane-1,2-dicarboxylic acid (**15a**), mp 140–140.5°, $[\alpha]D$ −4.7° (*c* 1.0, $CHCl_3$), $[\alpha]D$ 37° (*c* 0.54, CH_3OH).

Anal. Calcd for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 56.02; H, 6.98.

An admixture of **15a** with the *cis,cis* acid **15a** from genipin (**16**) showed no depression in melting point.

Esterification of 0.104 g of **15a** with diazomethane and distillation by heating in a 115° oil bath at 1 mm gave 0.1 ml of (+)-*cis,cis*-dimethyl 3-methylcyclopentane-1,2-dicarboxylate (**15b**), $[\alpha]^{23}D$ +32° (*c* 0.6, $CHCl_3$).

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.07; H, 8.11.

Isomerization of (+)-*cis,cis*-Dimethyl Nepetate (15b) during Saponification.—A 0.1-g sample of **15a** was added to a solution of 5% sodium hydroxide containing a small amount of methanol, and the resulting mixture was heated at reflux temperature for 3 hr. The methanol was stripped and the remaining aqueous solution was acidified with dilute hydrochloric acid, saturated with sodium chloride, and extracted continuously with ether for 24 hr. The ether extract was dried with magnesium sulfate and filtered, and the ether was evaporated, giving a light brown solid. Esterification *via* diazomethane followed by gas chromatography analysis showed the brown solid to be a mixture of all four nepetic acid isomers with the *trans,trans* isomer **12a** as the major component.

(+)-Ethyl 4-Methyl-2-oxocyclohexanecarboxylate (10b) from 8 *via* 9a and 27.—The condensation of 448 g (4 moles) of **9a**, bp 168–169° (759 mm), and 584 g (4 moles) of diethyl oxalate in the presence of 92 g (4 g-atoms) of sodium was carried out, and the product was isolated as previously described to give 266 g of colorless ethyl 4-methyl-2-oxocyclohexaneglyoxylate (**27**), bp 110–130° (7 mm), in 74% yield after a second distillation.[13] Some **10b** may have resulted from pyrolysis during the distillation of **27**.

Powdered soft glass (2.5 g) and a trace of iron were added to 411 g of **27** in a 1-l. distillation flask heated by an oil bath, and stirred with a magnetic stirrer. The oil bath was heated to and held at 170°, and at this temperature, 341 g of ethyl 4-methyl-2-oxocyclohexanecarboxylate (**10b**) was distilled at 110–130° at varying unknown pressures.[13,16a] The product was redistilled at 75–80° (1–1.5 mm) and showed $n^{24}D$ 1.4735, $[\alpha]^{28}D$ +86° (*c* 1.3, $CHCl_3$), $[\alpha]D$ 84.2° (ethanol).[16b]

(+)-Ethyl 3-Bromo-4-methyl-2-oxocyclohexanecarboxylate (11b) from 10b.—One mole (184 g) of the keto ester **10b** was brominated as described for the preparation of **11a** to give a crude mixture of ethyl 3-bromo-4-methyl-2-oxocyclohexanecarboxylate (**11b**) which was distilled at 130° (0.4 mm), $[\alpha]^{24}D$ +91° (*c* 4.4, $CHCl_3$). A center cut was analyzed.

Anal. Calcd for $C_{10}H_{15}O_3Br$: C, 45.62; H, 5.75; Br, 30.36. Found: C, 45.47; H, 5.49; Br, 30.64.

3-Methylcyclopentane-1,2-dicarboxylic Acids (12a, 13a, 14a, and 15a) from (+)-Ethyl 3-Bromo-4-methyl-2-oxocyclohexanecarboxylate (11b).—The bromo keto ester **11b** obtained from 92 g (0.5 mole) of the keto ester **10b** from the preceding step was added over a period of 10 min to a solution of 260 g of sodium hydroxide in 1 l. of water and 3 l. of 95% ethanol. Nitrogen was passed over the reaction mixture as it was heated with agitation. After 75 min, the mixture began to reflux and the remainder of the bromo keto ester **11b** was added *via* a dropping funnel over a period of 20 min. The reaction was heated at the reflux temperature for an additional hour. Ethanol was then removed by stripping with a water aspirator and heating on the steam bath. The reaction mixture was cooled, then acidified with concentrated hydrochloric acid, and extracted continuously with ethyl ether for 8 hr. The combined ether extracts were extracted with a solution of sodium bicarbonate. Extraction was continued until the last two extracts were basic to pH paper.

The sodium bicarbonate insoluble, ether-soluble layer yielded 10 g of a dark brown liquid with a phenolic odor.[17] The combined sodium bicarbonate extracts were acidified with 6 *N* hydrochloric acid and extracted with ether. The aqueous solution was continuously extracted with ether for 8 hr. The ether extracts were combined, dried with magnesium sulfate, and filtered, and the ether was distilled to give 113 g of a crude oily mixture of 3-methylcyclopentane-1,2-dicarboxylic acids (**12a**, **13a**, **14a**, and **15a**).

To remove remaining phenolic material, 12 g of the crude reaction product was treated with a dilute potassium permanganate solution until no more manganese dioxide formed. The mixture was made basic with a 10% sodium hydroxide solution and then filtered. The filtrate was acidified with 6 *N* hydrochloric acid and extracted with ether. The combined ether extracts were dried and the ether removed on a rotary evaporator at water aspirator pressure yielding 10.2 g of a mixture of the four acids *trans,trans* **12a**, *trans,cis* **13a**, *cis,trans* **14a**, and *cis,cis* **15a** and some minor

(16) (a) C. Black, G. L. Buchanan, and A. W. Jarvil, *J. Chem. Soc.*, 2971 (1956); (b) W. H. Perkins, Jr., and H. Watson, *ibid.*, **97**, 1756 (1910).

(17) The β-keto esters **10a** and **10c** prepared through the Corey method[13] appeared to be free of phenolic impurities.

impurities. The yield of crude acid mixture based on keto ester **10b** was 56%.

The oily mixture crystallized to a slurry. Filtration gave solid material consisting mainly of the *trans* acids **12a** and **13a**, while the filtrate (and the major portion) remained a mixture of **12a**, **13a**, **14a**, and **15a**.

Pimelic Acid (25a) from Ethyl 2-Oxocyclohexanecarboxylate (20b).—Pimelic acid (**25a**) was prepared from 10 g of **20b** essentially as previously reported[13] to give 6.3 g (67%) of **25a**, mp 97–100°. The dimethyl ester **25b** was prepared.[15a]

Favorskii-type Rearrangement Products from 21b.—The bromination and Favorskii-type rearrangement of 14.1 g of **20b** was carried out as previously described to give 8.6 g (66% yield) of crude acids.[9]

Part of the crude reaction product was treated with diazomethane and analyzed by gas chromatography on a 10 ft × 0.25 in. column of acid-washed Chromosorb W, 80–100 mesh, coated with 15% Carbowax 20 M, which showed the presence of three components at retention times of 23, 30, and 41 min and relative peak areas of 4:1:2. The column was operated at 190° using helium carrier gas at 75 cc/min. These peaks were found to be due to **22b**, **23b**, and **24b**, respectively. Preparative separation using this column was carried out to obtain pure samples of **22b**, **23b**, and **24b**.

Crystallization of the crude mixture from ether gave pure *trans* acid **22a**, mp 159–160°.[9] Ether–petroleum ether recrystallization of the remainder gave more acid with a lower melting point. The remainder of the crude mixture was esterified with diazomethane, and preparative gas chromatography separation of a 10 ft × 0.25 in. column of 80–100 mesh Chromosorb W coated with 15% Carbowax 20 M gave pure fractions of **22b**, **23b** and **24b**. The identity of **24b** was established by infrared, mass, and nmr spectroscopy: λ_{max}^{neat} 5.82 and 6.11 μ; *m/e* 184; singlet at δ 3.7 (6 H), triplet at δ 2.7 (4 H), quartet at δ 2.0 (2 H).

Saponification of **24b** with alkali in aqueous methanol gave **24a**, mp 171–172°, after recrystallization from a mixture of ether and benzene.[18]

A 0.08-g sample of **24b** was hydrogenated in the presence of 0.05 g of PtO_2 catalyst suspended in 5 ml of acetic acid. The catalyst was filtered out, the sample was dissolved in ether, and the ether solution was washed with bicarbonate solution and then analyzed on the Carbowax gas chromatography column. The chromatogram showed that the peak due to **24b** had disappeared and only those peaks due to **22b** and **23b** (11:89) remained.

Hydrogenation of Genipin (16).—A solution of 15 g (0.067 mole) of genipin (**16**)[19] in 125 ml of glacial acetic acid was hydrogenated at room temperature and atmospheric pressure in the presence of 3 g of prereduced platinum oxide catalyst. During 19 hr, the solution absorbed approximately 0.084 mole of hydrogen, or 63% of the expected 2 equiv. The catalyst was removed by filtration and the solution was treated twice with Norite. The solution was then hydrogenated a second time in the presence of prereduced platinum oxide and found to absorb 0.027 mole of hydrogen during 7 hr. The total uptake of hydrogen was 0.111 mole or 83% of the expected. After the catalyst was removed, the acetic acid was distilled under vacuum and the residue was taken up in ether and washed with sodium bicarbonate solution until the washings were basic. The ether solution was dried over anhydrous magnesium sulfate and evaporated to yield 10.6 g of orange oil.

A small sample of the oil was subjected to thin layer chromatography. The mixture was spotted on a silica gel plate and eluted with a 4:2:1 mixture of petroleum ether (bp 60–68°), benzene, and 95% ethanol. Development with iodine vapor showed six spots, two of which were much larger than the rest. Comparison of the R_f values of the two main components with those of samples of 9-deoxy-6,7-dihydrogenipin (**17**) and 1,9-anhydro-6,7-dihydrogenipin[5] determined under the same conditions indicated that these substances were the major reaction products. The sample apparently contained only a small amount of genipin despite the incomplete reduction. Its preferential solubility in water probably caused it to be removed during the washings. All of the components gave brown spots with iodine except genipin which gave a light purple spot.

(18) R. Willstätter, *Ber.*, **25**, 660 (1895).

(19) We thank Dr. C. Djerassi, Department of Chemistry, Stanford University, for the genipin.

In an earlier experiment,[1d] a solution of 11.7 g of genipin (**16**) in 150 ml of glacial acetic acid was hydrogenated at room temperature (20°) and atmospheric pressure by adding the solution to 2.34 g of platinum oxide which had been reduced for 30 min in 25 ml of glacial acetic acid. The hydrogen uptake, about 2500 ml, took 3 hr. This is a faster hydrogen absorption than previously reported.[5] The catalyst was removed by filtration and the acetic acid was evaporated *in vacuo*. The residue taken up in ether was washed with aqueous sodium carbonate and water and dried, and the ether was evaporated. Crystallization from ether–petroleum ether failed.

The crude product, 10.3 g, was chromatographed on a column of 135 g of Merck acid-washed alumina packed with benzene. Elution with 200 ml of benzene–ether, 9:1, gave the first crystals. Five 100-ml fractions were eluted with polarity ranging to ether and 9:1 ether–methanol for the last cut. These fractions gave 6.8 g of crystals which were combined and recrystallized from petroleum ether and ether to give **17**, mp 81–82°. The remaining five cuts ranging in polarity to 3:1 ether–methanol yielded 2.1 g of oil.

Ozonolysis of a Crude Mixture of 9-Deoxy-6,7-dihydrogenipin (17) to the *cis,cis* Acid 15a.—A solution of 10.6 g of the total reduction product of genipin (**16**) in 50 ml of methylene chloride was cooled to −70° and ozone in oxygen was added until the solution turned blue. This required approximately 1 hr. The solution was then added dropwise to a mixture of 50 ml of 10% sodium hydroxide and 42 ml of 30% hydrogen peroxide. The mixture was stirred for 30 min and then methylene chloride was evaporated at reduced pressure. An additional 70 ml of 30% hydrogen peroxide was added and the solution stirred overnight. This solution was acidified with concentrated hydrochloric acid and sodium sulfite was added. Solid sodium chloride was then added until the solution appeared saturated, after which it was extracted five times with ether and the ethereal solution was dried over anhydrous magnesium sulfate. Evaporation yielded a colorless oil which was basified with saturated barium hydroxide solution. The precipitate which formed was filtered and then acidified with 6 *N* hydrochloric acid. After the addition of solid sodium chloride, the solution was extracted three times with ether. The ether extract was dried over magnesium sulfate and evaporated. A solid was obtained upon trituration of the resulting oil with petroleum ether. This was recrystallized from ether–petroleum ether to give 0.75 g of solid, mp 131–135°. A second recrystallization yielded 0.5 g of *cis,cis* acid **15a**, mp 136–138°. A sample melting at 140–141° was obtained through additional recrystallizations. There was no depression in melting point when this acid was mixed with **15a** synthesized from (+)-pulegone (**8**). The filtrates from this and similar ozonolysis experiments were combined and evaporated. The barium hydroxide precipitation and work-up were repeated and a sample of the semisolid which was obtained was treated with diazomethane. Gas chromatography of the resulting esters indicated the presence of the dimethyl esters of *cis,trans* acid **6** and *cis,cis* acid **15a** in a ratio of 1:2.5.

Epimerization of *cis,cis* Acid 15a from Genipin (16).—A solution of 0.7 g of the *cis,cis* acid **15a** in 4 ml of reagent grade acetic anhydride was heated at reflux for 6 hr. The excess acetic anhydride and acetic acid were removed under vacuum, 4.2 ml of absolute methanol was added, and the solution was heated at reflux temperature for 2 hr, after which part of the methanol was distilled to remove any methyl acetate which might have formed. This solution was then poured into a solution prepared by the reaction of 0.4 g of sodium with 10 ml of absolute methanol. The mixture was heated at reflux temperature for 30 min. After the addition of 4 ml of water, the solution was heated for 1 hr longer. The methanol was removed under vacuum and water was added. This was partially removed under vacuum, water and benzene were added, and the mixture was again evaporated. Sufficient water was then added to dissolve the salts which had precipitated. The solution was acidified and extracted four times with ether, and the ether extract was dried and evaporated. The residual oil solidified when treated with petroleum ether to yield 0.6 g of white solid melting broadly below 100°. This was recrystallized from ether–petroleum ether to give 0.35 g of white solid, mp 90–97°. The filtrate and solid were blended by means of ether and evaporated to give 0.57 g of solid. This was dissolved in ether and treated with diazomethane. After removal of solvent, the resulting mixture of esters was analyzed by gas chromatography and found, by comparison and mixing with the corresponding previously prepared esters, to contain the *trans,*-

trans ester **12b** and the *trans,cis* ester **13b** in a ratio of 1:5.25.

Registry No.—**4**, 13350-94-2; **5**, 13368-63-3; **6**, 13368-64-4; **9a**, 13368-65-5; **10a**, 13368-66-6; **10b**, 13368-67-7; **11a**, 13368-68-8; **11b**, 13368-69-9; **12a**, 13368-70-2; **12b**, 13368-71-3; **13a**, 13368-72-4; **13b**, 13428-14-3; **14a**, 13368-94-6; **14b**, 13428-15-4; **15a**, 13368-76-8; **15b**, 13396-39-9; **17**, 13368-77-9; **22a**, 1461-97-8; **24b**, 13368-79-1; **25a**, 111-16-0.

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The Crystal and Molecular Structure of 2,6-Diphenyl-3-benzyl-2H-thiopyran-5-carboxaldehyde ($C_{25}H_{20}OS$)

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The structure of 2,6-diphenyl-3-benzyl-2H-thiopyran-5-carboxaldehyde ($C_{25}H_{20}OS$) has been solved by an X-ray diffraction study. The crystals are monoclinic with lattice parameters, a = 11.00, b = 11.06, c = 16.86 A, β = 96.5°, and Z = 4. The space group is $P2_1/n$ with one molecule in the asymmetric unit. The crystal structure was solved from the Patterson function by location of the sulfur atom and by five subsequent Fouriers. Anisotropic full matrix least-squares refinement using 906 reflections has reduced the R to 10.3%. The thiopyran ring is nonplanar. One of the sulfur–carbon distances of 1.74 A indicates a partial double bond. Other bond distances and angles are normal.

A yellow crystalline compound ($C_{25}H_{20}OS$) was synthesized by Latif, *et al.*,[1] by the treatment of benzaldehyde with sodium polysulfide in aqueous ethyl alcohol at reflux temperature. The presence of three Ph–C groups, a sulfide linkage, and a ketone group were found by them. Later Cremer and Subbaratnam[2] prepared the same compound under similar conditions and by chemical, nmr, mass spectral, and ultraviolet studies suggested a number of possible five- and six-membered ring structures which were consistent with the data. An X-ray study on this compound was undertaken by us to determine the structure unequivocally and add to the knowledge of sulfur heterocyclic compounds. When we first obtained the crystals,[3] only the molecular formula was known for certain. The X-ray study[4] showed the compound to be 2,6-diphenyl-3-benzyl-2H-thiopyran-5-carboxaldehyde. Cremer and Subbaratnam[4] found this structure consistent with their spectroscopic and chemical studies.

Experimental Section

A crystal of approximate dimensions 0.1 × 0.2 × 1.0 mm was selected and used for collection of the data. 2,6-Diphenyl-3-benzyl-2H-thiopyran-5-carboxaldehyde, $C_{25}H_{20}OS$, has a molecular weight of 368.3. It is monoclinic with lattice parameters, a = 11.00 ± 0.01, b = 11.06 ± 0.01, c = 16.86 ± 0.01 A, and β = 96.5° ± 10′. The systematic absences were confined to $k \neq 2n$ for the $0k0$ reflections and $h + l = 2n$ for the $h0l$ zone; thus the space group is $P2_1/n$: V = 2038.5 A^3, d_o = 1.145 ± 0.005 g cm^{-3}, Z = 4, d_c = 1.199 g cm^{-3}. The absorption coefficient for Cu Kα radiation is μ = 14.4 cm^{-1}. Total number of electrons in the unit cell is $F(000)$ = 776.

Multiple film Weissenberg photographs were taken with Cu Kα radiation for k = 0 to 8 for oscillation of the crystal around the b axis. Intensities of 906 independent reflections were measured visually by comparing with a standard intensity strip. The data were corrected for Lorentz and polarization factors using a data reduction program[5] which also gives a Wilson plot for pre-

TABLE I

ATOMIC COORDINATES AND THEIR STANDARD DEVIATIONS

Atom	x/a	y/b	z/c
S(1)	0.2322(4)[a]	0.0575(4)	0.1817(3)
C(2)	0.3726(14)	−0.0344(15)	0.2139(10)
C(3)	0.3572(21)	−0.0905(19)	0.2978(13)
C(4)	0.2500(17)	−0.1198(15)	0.3210(10)
C(5)	0.1251(15)	−0.1040(17)	0.2767(11)
C(6)	0.1108(13)	−0.0175(15)	0.2176(9)
C(7)	0.3900(16)	−0.1338(16)	0.1506(11)
C(8)	0.4772(17)	−0.0950(18)	0.0969(15)
C(9)	0.5028(17)	−0.1829(20)	0.0356(11)
C(10)	0.4397(20)	−0.2897(21)	0.0288(10)
C(11)	0.3592(16)	−0.3189(15)	0.0834(13)
C(12)	0.3316(14)	−0.2397(14)	0.1479(11)
C(13)	0.4772(14)	−0.1203(16)	0.3454(10)
C(14)	0.5436(19)	−0.0035(22)	0.3794(10)
C(15)	0.6746(20)	−0.0166(25)	0.3983(15)
C(16)	0.7379(23)	0.0939(27)	0.4311(16)
C(17)	0.6749(25)	0.2011(27)	0.4436(12)
C(18)	0.5441(25)	0.2051(25)	0.4221(16)
C(19)	0.4820(19)	0.1029(27)	0.3902(12)
C(20)	0.0192(17)	−0.1800(19)	0.2926(13)
C(21)	0.0341(13)	−0.2576(13)	0.3472(9)
C(22)	0.9874(15)	0.0324(15)	0.1826(11)
C(23)	0.9056(16)	0.0711(16)	0.2388(12)
C(24)	0.7868(19)	0.1224(19)	0.2108(13)
C(25)	0.7536(19)	0.1317(17)	0.1297(14)
C(26)	0.8342(19)	0.1017(21)	0.0766(14)
C(27)	0.9533(18)	0.0492(17)	0.0966(13)

[a] The number in parenthesis is the standard deviation and refers to the least significant digits.

(1) K. A. Latif, M. A. Razzaq, S. K. Adhikari, and M. M. Eunus, *J. Indian Chem. Soc.*, **36**, 209 (1959); K. A. Latif, S. K. Adhikari, and M. M. Eunus, *ibid.*, **36**, 212 (1959).

(2) S. E. Cremer and A. V. Subbaratnam, *Chem. Commun.*, **1**, 33 (1967).

(3) The crystals were produced by S. E. Cremer at the Illinois Institute of Technology. Preliminary studies were made by S. E. Cremer and A. V. Subbaratnam. Because of difficulty in unequivocally assigning the structure from their studies, they suggested to us that an X-ray study be undertaken and provided us with a sample of the material.

(4) M.-U. Haque and C. N. Caughlan, *Chem. Commun.*, **1**, 34 (1967).

(5) All programs used except least-squares refinement were those from the Montana State University Library for Crystallographic Computing for the IBM 1620, written by C. T. Li, G. Svetich, C. N. Caughlan, R. D. Witters, and K. Watenpaugh.