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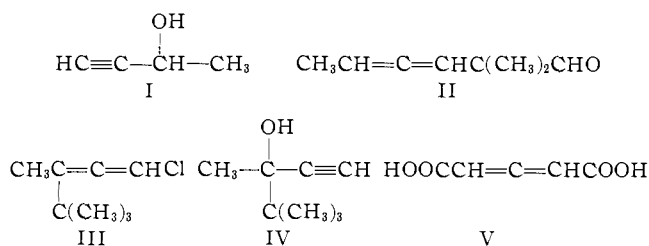
The Absolute Configuration of Pentadienoic Acid¹

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RECEIVED DECEMBER 23, 1963

The Diels–Alder reaction of (–)-pentadienoic acid (V) with cyclopentadiene yields (–)-X. In separate experiments (–)-X has been degraded to (–)-norcamphor, isolated as its dinitrophenylhydrazone. The known absolute configuration of norcamphor permits the conclusion that (–)-pentadienoic acid has the absolute geometry shown in XIII.

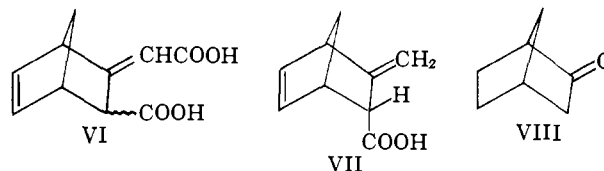
Although the number of optically active allenes has increased considerably in recent years,³ the absolute configurations of only two such compounds have been determined. Jones, Loder, and Whiting stereospecifically converted active but-3-yn-2-ol (I) into the allenic aldehyde II,⁴ and Landor and Taylor-Smith prepared the active chloroallene III from IV.⁵ Since in each case the absolute configuration of the starting alcohol was known⁴ or later deduced,⁶ the absolute



stereochemistry of the product allenes could be assigned on mechanistic grounds.

Both these correlations depend on stereospecific synthesis of the optically active allene from a precursor containing an asymmetric carbon atom. It appeared to us worthwhile to investigate the possibility of determining the configuration of a pre-existing active allene, that is, of reversing the above steps and transforming an asymmetric allenic system into a substance with asymmetrically substituted carbon.⁷ Some method of this type might eventually find use in assigning the stereochemistry of naturally occurring allenes.⁸ For such an investigation we chose to work with the symmetrical dicarboxylic acid derived from allene,

pentadienoic (glutinic) acid (V),⁹ a choice motivated not only by the simplicity of structure of this substance and anticipated ease of resolution as an alkaloid salt, but also by the hope that it might be capable of relation to other allenes through transformations of the reactive carboxyl groups. For conversion of this allene into a compound possessing an asymmetric carbon, we elected to employ its reaction with cyclopentadiene. The Diels–Alder addition of cyclopentadiene to glutinic acid is known to occur readily in high yield,¹⁰ and the adduct has been assigned structure VI with-out stereochemical implications in analogy to the reaction between cyclopentadiene and buta-2,3-dienoic acid, the product from which was rigorously shown to be VII.¹⁰ It seemed to us that a substance of the gross structure VI could be degraded rather readily to norcamphor (VIII) by reduction of the endocyclic



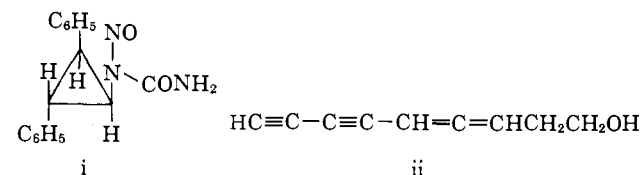
unsaturation followed by oxidative fission of the remaining double bond and decarboxylation of the resulting β -ketoacid. The absolute geometry of norcamphor could be investigated, in turn, by any of a number of well established techniques.^{11,12}

There are four substances of structure VI (IX, X, XI, and XII), any or all of which are, *a priori*, possible products in the Diels–Alder reaction we wish to utilize. The steric relations depicted in XIII indicate that IX is the product predicted by application of the Alder–Stein rules^{10,13} in conjunction with simple steric considerations. That is, in XIII there is maximum overlap of cyclopentadiene with the carbonyl conjugated with the reacting double bond, and the diene is approaching from the top, where it is hindered only by the out-of-plane hydrogen atom, rather than from the bottom, which is shielded by a carboxyl group. Adduct X would originate from failure of the Alder–Stein rules, a fairly common occurrence,¹⁴ but with the

(1) A preliminary report of a portion of this work has appeared: W. C. Agosta, *J. Am. Chem. Soc.*, **84**, 110 (1962). The configurational assignment made in this earlier communication is incorrect (see footnote 26).

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(3) Two interesting examples from the current literature are (a) the lithium ethoxide promoted decomposition of the active N-nitrosourea i to (+)-1,3-diphenylallene (W. M. Jones, J. W. Wilson, Jr., and F. B. Tutwiler, *J. Am. Chem. Soc.*, **85**, 3309 (1963)), and (b) the isolation from natural sources of the dextrorotatory diacetylenic allene ii, the enantiomorph of which had previously been described (R. C. Cambie, A. Hirschberg, E. R. H. Jones, and G. Lowe, *J. Chem. Soc.*, 4120 (1963); G. Bendz, *Arkiv Kemi*, **14**, 305 (1959)).



(4) E. R. H. Jones, J. D. Loder, and M. C. Whiting, *Proc. Chem. Soc.*, 180 (1960).

(5) S. R. Landor and R. Taylor-Smith, *ibid.*, 154 (1959).

(6) E. L. Eliel, *Tetrahedron Letters*, No. 8, 16 (1960); R. J. D. Evans and S. R. Landor, *Proc. Chem. Soc.*, 182 (1962).

(7) Cf. D. W. Dicker, D. Phil. Thesis, University of Oxford, 1957.

(8) Cf. ref. 3b and references cited therein.

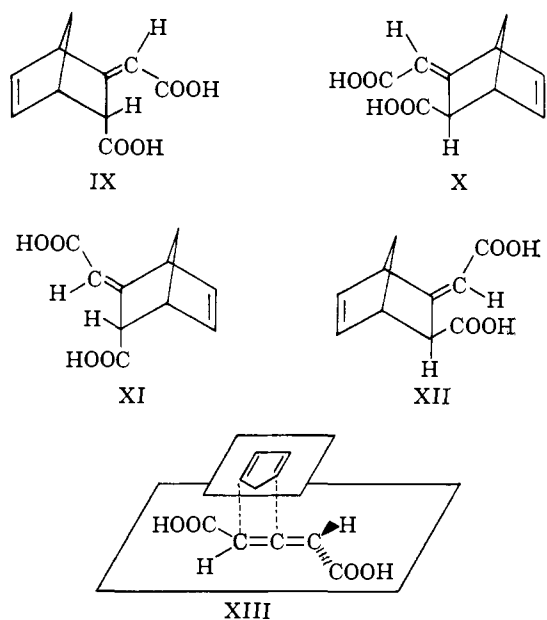
(9) E. R. H. Jones, G. H. Mansfield, and M. C. Whiting, *J. Chem. Soc.* 3208 (1954).

(10) E. R. H. Jones, G. H. Mansfield, and M. C. Whiting, *ibid.*, 4073 (1956).

(11) (a) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, Chapter 10; (b) V. Prelog, *Bull. soc. chim. France*, 987 (1956); (c) J. A. Mills and W. Klyne, *Progr. Stereochem.*, **1**, 177 (1954).

(12) At the time this investigation was begun the absolute configuration of norcamphor was unknown; its determination by Berson is mentioned below.

(13) K. Alder and G. Stein, *Ann.*, **514**, 1 (1934); *Angew. Chem.*, **50**, 510 (1937).



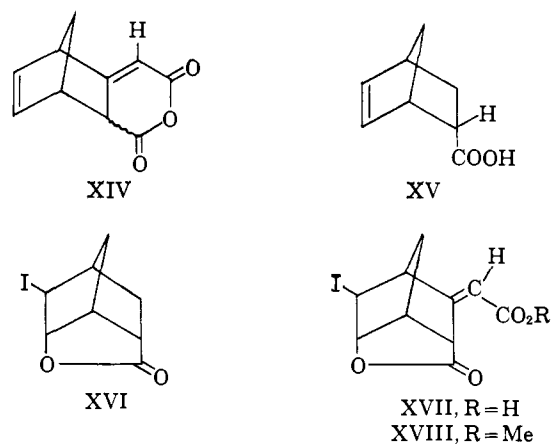
sterically favored approach, while the remaining two possibilities would result from the sterically less likely combination with (for XI) and without (for XII) maximum overlap. If this reaction is considered for optically active material, there arise two further points of importance. First, the adducts from a single optical isomer of glutinic acid, as is shown in XIII, belong to both possible enantiomorphous series. This is evident in structures IX, X, XI, and XII, each of which is derived from the isomer of glutinic acid in XIII. Clearly it will be of paramount importance firmly to establish the structure of the adduct used for degradation to norcamphor, for either enantiomorph of norcamphor can result from a given isomer of the allene. Secondly, in a single optical isomer of the symmetrically substituted allene, the double bonds are sterically equivalent. That is, the same optical isomer of any of the adducts IX–XII will result from addition of cyclopentadiene to either of the chemically equivalent double bonds of the antipode of glutinic acid depicted in XIII.

In order to test the feasibility of this scheme and also to define the unsettled stereochemical features of adduct VI, we first carried out reactions with racemic pentadienioic acid. The addition with cyclopentadiene proceeded smoothly as reported¹⁰ and yielded a material which we found could be separated by fractional crystallization from water or nitromethane into approximately equal amounts of two isomeric compounds, one melting 205–207°, and the other 245–246°. The transformations recounted below demonstrate that the lower melting adduct possesses structure IX and that the higher melting material is X.

The two sterically less likely possibilities, XI and XII, fell from further consideration when we found that treatment of either adduct with warm acetic anhydride produced a monomeric anhydride (XIV). This dehydration could be reversed by heating the anhydride in aqueous dioxane containing a trace of acetic acid, conditions which yielded largely the low melting diacid accompanied by a small amount of its

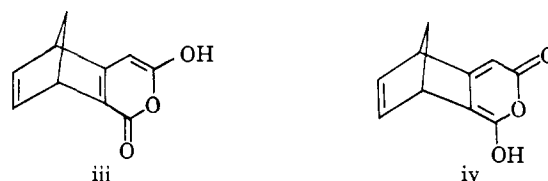
higher melting isomer. The *endo* or *exo* orientation of the carbonyl in XIV remains an open question. Both adducts give the anhydride in moderate yield, but the product melts sharply only after sublimation. That epimerization occurs rather easily under conditions of both formation and hydrolysis of this substance is not surprising, since it is a glutaconic anhydride.¹⁵

There is then only the decision between *endo* and *exo* configuration for the carboxyl group in the two adducts themselves. We first sought an answer to this question in the treatment of the two compounds with iodine and sodium bicarbonate.¹⁶ This procedure has been found particularly useful in determining the *endo/exo* ratios in the adducts of cyclopentadiene with various acrylic acids^{17,18} and in separating these stereoisomers. The *endo* isomer (as XV) is converted to an iodolactone (as XVI), while the *exo* epimer customarily remains unchanged. This latter feature gives the reaction a definite superiority over the analogous procedure using bromine, which may result in formation of rearranged bromolactones¹⁷ or vicinal dibromides¹⁸ from *exo*-acids. The *endo*-acid may be regenerated by zinc–acetic acid reduction of the iodolactone.¹⁷ In consonance with these earlier reports we obtained an iodolactone in good yield on solution of the lower melting adduct in dilute sodium



bicarbonate and treatment with iodine. Physical and chemical properties supported structure XVII for this compound. Its infrared spectrum showed a split lactone carbonyl band (5.54 and 5.58 μ), an acid carbonyl (5.89 μ), and a double bond (6.01 μ); treatment with excess diazomethane gave a monomethyl ester (XVIII) which had infrared absorption appropriate for a strained γ -lactone and acrylic ester (5.52,

(15) To the extent of our observations, however, XIV otherwise behaves as a normal saturated anhydride. Thus it is hydrolyzed under very mild acidic conditions, and its infrared spectrum shows typical anhydride absorption in the carbonyl region with no evidence of a hydroxyl group. These properties may be rationalized by noting that the enolic structures typical of glutaconic anhydrides (iii and iv) here impose additional steric strain in an already quite strained system (*cf.* ref. 10).



(16) E. E. van Tamelen and M. Shamma, *J. Am. Chem. Soc.*, **76**, 2315 (1954).

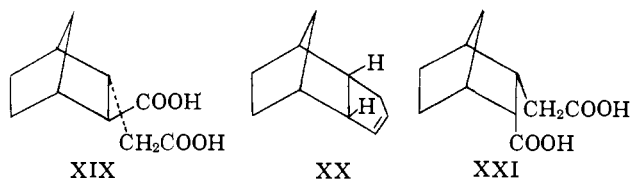
(17) C. S. Rondestvedt, Jr., and C. D. Ver Nooy, *ibid.*, **77**, 4878 (1955).

(18) K. Alder and W. Günzl, *Chem. Ber.*, **93**, 809 (1960).

(14) *Cf. inter alia* (a) K. Alder, R. Hartmann, and W. Roth, *Chem. Ber.*, **93**, 2271 (1960), and references cited therein; (b) J. A. Berson, Z. Hamlet, and W. A. Mueller, *J. Am. Chem. Soc.*, **84**, 297 (1962).

5.57, 5.78, 5.99 μ). In addition the n.m.r. spectrum of XVIII indicated one olefinic proton. Two further results, however, made us reluctant to accept these observations as a final basis for assigning *endo* structure IX to the low melting adduct. In the first place, the isomeric adduct (*i.e.*, presumably X) also absorbed iodine from bicarbonate solution, although the infrared spectrum of the crude product gave no indication that an iodolactone had been formed. Indeed, no pure compound was ever isolated from this reaction. Secondly, reduction of iodolactone XVII with zinc in acetic acid failed to regenerate the original unsaturated acid. Although we believe that these departures from the usual experience^{17,18} with the formation and reduction of iodolactones may be ascribed to the presence in IX and X of the reactive exocyclic acrylic acid grouping, we nevertheless desired to gather additional evidence before leaving this question.

The point was settled by reduction of the higher melting adduct with hydrogen (approximately 4.5 atm.) in the presence of Adams catalyst to give the known¹⁹ saturated bicyclic acid XIX. The purified material isolated from the hydrogenation proved identical in melting point, mixture melting point, and solid state infrared spectrum with an authentic sample prepared¹⁹ by oxidation of dihydrodicyclopentadiene (XX) to the *endo,endo*-diacid XXI, followed by ethoxide-catalyzed epimerization of the corresponding dimethyl ester in hot ethanol, and then saponification.²⁰ This correlation indicates conclusively that the doubly unsaturated starting material must have an *exo*-carboxyl and, in conjunction with the previous transformations and the ultimate degradation of both adducts to norcamphor (VIII), permits a reliable assignment of structure to the two adducts.²¹

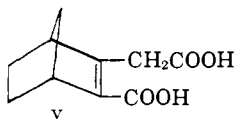


It is this conversion to norcamphor to which we next turn our attention. With palladium-on-carbon as catalyst it was possible to achieve selective hydrogenation of the reactive double bond of IX, although

(19) K. Alder, H. Wirtz, and H. Koppelberg, *Ann.*, **601**, 138 (1956).

(20) In agreement with K. Alder's report,¹⁹ we obtained XXI, m.p. 136.5–137.5°, and XIX, m.p. 110–111.5°, both from nitromethane. We are therefore unable to confirm the recent observation that oxidation of XX gives XXI, melting 97–98.5° (R. W. Alder and M. C. Whiting, *J. Chem. Soc.*, 4595 (1963); Dr. Whiting has informed us privately that he believes his material may have been XIX, either impure or as a different polymorph).

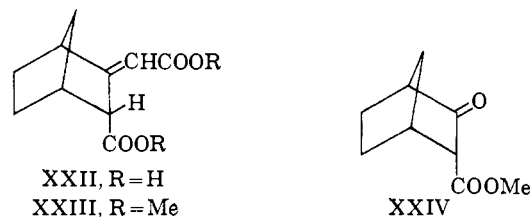
(21) We may note here that similar hydrogenation of the isomeric adduct IX would presumably lead to XXI. For our purposes, however, we could not consider such an observation conclusive. There is the possibility that, after rapid saturation of the extremely reactive isolated double bond, the catalyst may promote isomerization of XXII to v. The anticipated *exo* addition of hydrogen^{19,22} would then lead to XXI, regardless of the original location of the carboxyl group. Indeed, the low yield of purified XIX may well be due to an analogous process in the reduction of X. The formation of XIX itself is open to no such ambiguity of interpretation.



(22) G. Komppa and S. Beckmann, *Ann.*, **512**, 172 (1934)

even at 1 atm. it was necessary to interrupt the reaction after absorption of 1 equiv. of hydrogen to avoid slow further reduction. With excess diazomethane the hydrogenation product XXII gave a dimethyl ester (XXIII). The presence of absorption for one vinyl proton in the n.m.r. spectrum of XXIII confirmed that the desired *exo*-double bond had not been isomerized into the ring.²¹ This ester was ozonized in methanol solution at -78° and the mixture treated at this temperature with potassium iodide-acetic acid.²³ The crude ketoester XXIV thus obtained was hydrolyzed and decarboxylated directly by heating with concentrated hydrochloric acid.²⁴ The volatile product obtained was treated with 2,4-dinitrophenylhydrazine without purification; there resulted a bright red-orange compound which was identical in all respects with authentic norcamphor 2,4-dinitrophenylhydrazone²⁵ prepared from VIII. A parallel sequence of reactions starting with adduct X also ended with this derivative of norcamphor.

With this demonstration of the possibility of correlating glutinic acid with norcamphor, we now concerned ourselves with the preparation and reactions of the allene in optically active form. We were able to



effect a partial resolution of glutinic acid as its quinine salt. Recrystallization of this material from aqueous methanol brought about both optical purification and general decomposition; a single crystallization of the initially amorphous salt from water, however, permitted recovery of a workable amount of crude material (23%) with a rotation of -53° . The Diels-Alder reaction of levorotatory glutinic acid $[\alpha]_D -45.6^\circ$ with cyclopentadiene gave a mixture from which levorotatory X was separated by fractional crystallization ($[\alpha]_D -29.6^\circ$ after purification).²⁶

(23) These conditions are known to result in formation of camphenilone (vi) in good yield from camphene (vii). Various other conditions lead to rearrangement. Cf. P. S. Bailey, *Chem. Ber.*, **88**, 795 (1955).



(24) L. Ruzicka, *Helv. Chim. Acta*, **3**, 748 (1920).

(25) K. Alder, H. K. Schäfer, H. Esser, H. Krieger, and R. Reubke, *Ann.*, **593**, 23 (1955).

(26) Adduct IX formed in this reaction was clearly dextrorotatory, although it could not be purified without almost total loss in optical activity. While the solid state infrared spectrum of the material before final purification was identical with that of racemic IX, its melting point was high (196–220°), indicating contamination with X. Optically active IX and X apparently have solubility properties sufficiently different from those of the racemates to render difficult the purification of IX. Since these products obtained from (–)-pentadiendioic acid rotate in opposite directions, this small impurity should not affect the conclusion that IX is dextrorotatory. Experience with the racemates has indicated that no other reaction products are expected to interfere with the separation of IX and X. It was precisely due to this contamination, however, that the initial assignment of absolute configuration of glutinic acid (see ref. 1) was incorrect. Starting with dextro-

Although in earlier work optically active material from the Diels–Alder reaction was itself degraded to norcamphor, it has proved much more convenient to resolve both IX and X directly and then carry out the conversion to norcamphor. In each case we found the quinine salt suitable for effecting partial resolution. Dextrorotatory IX ($[\alpha]_D^{25} 39^\circ$) was degraded by the pathway outlined above for its racemate to dextrorotatory norcamphor dinitrophenylhydrazone ($[\alpha]_D^{25} 9^\circ$). A parallel sequence starting with levorotatory X ($[\alpha]_D^{25} -53^\circ$) gave a dinitrophenylhydrazone of opposite rotation ($[\alpha]_D^{25} -14.1^\circ$).

While this work was in hand, Berson demonstrated the absolute configuration of VIII for (+)-norcamphor,²⁷ and we have found the dinitrophenylhydrazone prepared from his ketone also to be dextrorotatory.²⁸ We can therefore assign structure VIII in the absolute sense to the norcamphor formed in excess on the degradation of dextrorotatory IX and accept the absolute geometry of IX for this enantiomer of the adduct. Similarly, levorotatory X, which leads to (–)-norcamphor (enantiomer of VIII), must possess the absolute configuration shown in X. This same antipode of adduct X arises from (–)-pentadiendioic acid, and the allene must, therefore, be that enantiomer depicted in XIII.²⁹

Experimental³⁰

endo- and exo-3-Carboxy-5-norbornene- Δ^2,α -acetic Acid (IX and X).—The Diels–Alder reaction was carried out as detailed by Jones, *et al.*¹⁰ The crude product could be purified by fractional crystallization from either water or nitromethane. The most convenient procedure found is given in detail: the crude adduct (8.8 g.), dissolved in a minimum amount of hot methanol, was treated with 495 ml. of water and the solution concentrated to 360 ml. to remove most of the methanol. On cooling, there deposited 3.76 g. of colorless crystals, m.p. 237–246°. Repeated recrystallization from water gave X, m.p. 245–246°.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19. Found: C, 61.76; H, 5.31.

On evaporation of the mother liquor from the initial separation above, there was recovered 4.14 g. of crude IX, m.p. 206.5–209.5°. Recrystallization from nitromethane yielded 4.13 g., m.p. 205–207°.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19. Found: C, 62.01; H, 5.39.

3-Carboxy-5-norbornene- Δ^2,α -acetic Acid, Cyclic Anhydride (XIV). **A.** From *endo*-Acid IX.—A solution of 100 mg. of IX in 1.5 ml. of acetic anhydride was heated at 60° for 55 min. Removal of the solvent *in vacuo* left a brownish oil which crystallized. The product was recrystallized with difficulty from benzene–cyclohexane and then sublimed at 70° (0.02 mm.) to give 48 mg. of hard colorless crystals (53%), m.p. 80–81°.

Anal. Calcd. for $C_{10}H_8O_5$: C, 68.18; H, 4.58. Found: C, 67.83; H, 4.63.

B. From *exo*-Acid X.—In a manner similar to that above, 74 mg. of X was dehydrated in 1.0 ml. of acetic anhydride. After recrystallization and sublimation twice, the product amounted to 39 mg. (58%), m.p. 79–79.5°. The infrared spectra of the

rotatory allene of much lower optical activity we isolated a sample of IX with a very small positive rotation. It now appears that this rotation was due to contaminating X rather than IX, and that purified IX from this experiment would have been levorotatory.

(27) J. A. Berson, J. S. Walla, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff, and D. Willner, *J. Am. Chem. Soc.*, **83**, 3986 (1961).

(28) This experiment was carried out by Prof. R. L. Autrey at the Department of Chemistry, University of Rochester, Rochester, N. Y.

(29) Clearly, if we accept the rather less rigorous evidence that (–)-pentadiendioic acid leads to (+)-IX (*cf.* footnote 26), we reach the same conclusion by a second, independent route.

(30) Melting points are corrected; boiling points are uncorrected. Nuclear magnetic resonance spectra were determined in deuteriochloroform at 60 Mc. and are reported in c.p.s. downfield from tetramethylsilane. Rotations were determined in methanol unless otherwise noted.

two samples measured in dichloromethane were identical; carbonyl absorption was present at 5.54 and 5.71 μ .

Hydrolysis of Anhydride XIV.—A solution of 42 mg. of anhydride XIV, 1 ml. of water, 0.3 ml. of purified dioxane, and 2 drops of acetic acid was heated in a water bath at 70–80° for 4 hr. and then allowed to stand overnight. The solution was decanted from 7 mg. (15%) of crystals, shown by solid state infrared spectrum and m.p. to be X. Removal of solvent from the decanted solution left 37 mg. (80%) of crystals. These were recrystallized from nitromethane, after which they were shown by m.p., mixture m.p., and solid state infrared spectrum to be IX.

Formation of Iodolactone XVII.—A solution of 50 mg. of IX in 3 ml. of saturated aqueous sodium bicarbonate was treated with 400 μ l. of iodine solution prepared from 10.0 g. of potassium iodide, 5.00 g. of iodine, and 30.0 ml. of water. The iodine was added slowly over a 30-min. period with occasional swirling. After the last 20 μ l. of iodine solution was added, the mixture stood 1 hr. The very small amount of iodine remaining was destroyed with a few drops of aqueous sodium thiosulfate and the clear solution acidified with 5 *N* sulfuric acid. The product precipitated as almost colorless crystals which were washed with water and dried *in vacuo*; 65 mg. (79%). Material recrystallized from benzene melted 209.5–211°. A sample was dried 40 hr. at 65° (0.02 mm.) for analysis. The infrared spectrum in dichloromethane had bands at 5.54, 5.58, 5.89, and 6.01 μ .

Anal. Calcd. for $C_{10}H_8O_4I$: C, 37.52; H, 2.84. Found: C, 37.69; H, 3.07.

Iodolactone Methyl Ester XVIII.—Dissolved in a minimum volume of dichloromethane, 125 mg. of iodolactone XVII was esterified with excess distilled diazomethane in ether. Removal of solvent left a colorless oil which crystallized spontaneously. Two recrystallizations from benzene–cyclohexane gave material melting 127–128°.

Anal. Calcd. for $C_{11}H_{11}O_4I$: C, 39.54; H, 3.32. Found: C, 39.50; H, 3.34.

The n.m.r. spectrum had bands of the indicated chemical shifts and areas: 358 (0.8), 316 (2.0), 221 (6.1), 136 (2.1). The infrared spectrum in chloroform showed absorption at 5.52, 5.57, 5.78, and 5.99 μ ; hydroxyl absorption was absent.

exo-3-Carboxynorbornane-endo-2-acetic Acid (XIX). **A.** From Adduct X.—A solution of 155 mg. of X in 10 ml. of methanol containing 35 mg. of platinum dioxide was shaken overnight in an atmosphere of approximately 4.5 atm. of hydrogen. After removal of the catalyst by filtration through Celite and evaporation of the solvent there remained a colorless oil which crystallized partially only after seeding with authentic XIX. Two recrystallizations from nitromethane gave 29 mg., m.p. and mixture m.p. with authentic XIX, 109.5–111°. The infrared spectra of the two samples measured in potassium bromide were identical.

B. Authentic Sample.—This sample was prepared following the procedure of Alder.¹⁹ In essential agreement with that report, our authentic sample melted 110–111.5° after two recrystallizations from nitromethane.

endo-3-Carboxynorbornane- Δ^2,α -acetic Acid (XXII).—A solution of 50 mg. of IX in 3 ml. of methanol containing 3 mg. of 5% palladium-on-carbon was stirred at room temperature under 1 atm. of hydrogen. In the first 3 min., 5.8 cc. of hydrogen was absorbed, while during the following 4 min., only 0.6 cc. more of hydrogen was consumed. The reaction was interrupted, catalyst removed by Celite filtration, and the solvent evaporated. Although the m.p. of this material increased from 170–175° to 191.5–195° with five recrystallizations from nitromethane, its infrared spectrum remained unchanged. The broad m.p. may indicate the persistence of a small amount of isomeric impurity (*cf.* ref. 21).

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.40; H, 6.41.

Methyl endo-3-Carbomethoxynorbornane- Δ^2,α -acetate (XXIII).—A methanolic solution of 75 mg. of XXII was esterified with an excess of distilled diazomethane in ether. Molecular distillation at 80° (0.01 mm.) of the mobile oil recovered on removal of solvent gave analytically pure material. The n.m.r. spectrum contained a band at 350 c.p.s. with an area equivalent to 0.85 proton.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.06; H, 7.07.

Methyl endo-3-Carbomethoxy-5-norbornene- Δ^2,α -acetate.—A solution of 100 mg. of IX was esterified with diazomethane and purified as described for XXII above. The n.m.r. spectrum

possessed the following bands with indicated areas: 368 (2.9), 220 (9.1), 98 (2.0).

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.63; H, 6.28.

exo-3-Carboxynorbornane- Δ^2,α -acetic Acid.—This dihydro compound was prepared from X just as its epimer XXII was prepared from IX. The analytical sample melted at 210–213° after several recrystallizations from nitromethane.

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.43; H, 6.29.

Norcamphor Dinitrophenylhydrazone. A. From XXIII.—A solution of 117 mg. of XXIII in 10 ml. of methanol was ozonized at -78° during 4 hr. A cooled mixture of 10 ml. of methanol, 2 ml. of acetic acid, and 4 g. of potassium iodide was then added and the solution shaken for several minutes. The liberated iodine was destroyed with a small amount of aqueous sodium thiosulfate, the mixture diluted with ether and then water, and the aqueous layer separated. This was extracted several times with more ether, and the combined ether extracts washed with aqueous sodium thiosulfate, aqueous sodium bicarbonate, water, and brine. The ether was dried over sodium sulfate and removed to leave 75 mg. of crude ketoester (XXIV, infrared bands in chloroform at 5.68, 5.81 μ). A solution of 66 mg. of this oily intermediate in 3 ml. of concentrated hydrochloric acid was heated at reflux for 5 hr. The cooled solution was diluted with water and extracted exhaustively with ether. The combined ether extracts were washed with aqueous sodium hydroxide, water, and brine. Careful removal of ether through a Vigreux column left 20 mg. of crude norcamphor. This was converted to the dinitrophenylhydrazone as described for the authentic sample below. There was recovered 26 mg. (20% based on XXIII) of derivative. Recrystallization twice gave material melting 128.5–130°, unchanged on admixture with authentic material. The carbon tetrachloride infrared spectrum was identical with that of the authentic derivative.

B. From the *exo* Epimer of XXIII.—The *exo* epimer of XXII was esterified with diazomethane and the crude diester subjected to the ozonolysis reaction as described above. In this case 112 mg. of diester yielded 62 mg. (74%) of unpurified ozonolysis product, which ultimately gave 13 mg. of norcamphor dinitrophenylhydrazone.

C. Authentic sample²⁵ was prepared by treating 20 mg. of authentic norcamphor with a warm solution of 43 mg. of 2,4-dinitrophenylhydrazine in 2 ml. of methanol containing 0.2 ml. of concentrated hydrochloric acid. Filtration gave 50 mg. (95%) of crude derivative. Recrystallization from ethanol or aqueous methanol gave material melting 128.5–129.5° (lit.²⁵ 130°).

Partial Resolution of Pentadiendioic Acid.—A solution of 200 mg. of pentadiendioic acid (V) in 32 ml. of ether was added dropwise to a solution of 504 mg. of quinine in 100 ml. of ether. The white amorphous salt was filtered off and dried *in vacuo*; it amounted to 644 mg. (91%), $[\alpha]_D -141^\circ$. Trituration of the salt (611 mg.) with water gave 315 mg. of cream crystals, $[\alpha]_D -167^\circ$. This material was recrystallized by dissolving in a minimum volume of methanol and adding water until tan crystals appeared; 230 mg. Rotation on this material was difficult to measure, since the salt decomposes somewhat on recrystallization; an approximate value of $[\alpha]_D -187 \pm 7^\circ$ was obtained. This 230 mg. of salt was dissolved in aqueous methanol and aqueous sodium carbonate added to pH 9. The resulting milky precipitate of quinine was extracted with chloroform. Solution pH was adjusted to 2 with 5 *M* sulfuric acid and pentadiendioic acid extracted with six portions of ether. The dried ether solution yielded 25 mg. of crude crystalline material, shown to be pentadiendioic acid by solid state infrared spectrum, $[\alpha]_D -104^\circ$.

This resolution was repeated on a larger scale using 1.48 g. of pentadiendioic acid and 4.17 g. of quinine in 200 and 800 ml. of ether, respectively. The 5.14 g. of crude amorphous salt was crystallized from water and decomposed directly to alkaloid and acid. There was thereby obtained 348 mg. of crude allene, $[\alpha]_D -53^\circ$, which was combined with the above 25 mg., $[\alpha]_D -104^\circ$, for purification. Recrystallization from dichloromethane–ether gave 271 mg. of pentadiendioic acid in two crops, $[\alpha]_D -45.6 \pm 0.3^\circ$, infrared spectrum in potassium bromide virtually superposable on that of authentic racemic material.

Optically Active *endo*- and *exo*-3-Carboxy-5-norbornene- Δ^2,α -acetic Acid (IX and X) from (–)-Pentadiendioic Acid.—The Diels–Alder reaction was carried out as previously reported,¹⁰ but using 270 mg. of partially resolved pentadiendioic acid, $[\alpha]_D -45.6 \pm 0.3^\circ$. Recrystallization of the crude adduct from

aqueous methanol gave 157 mg. (40%) of *exo* adduct X, m.p. 227–247° dec., $[\alpha]_D -50^\circ$, solid state infrared spectrum identical with that of racemic X. Recrystallization of this material from aqueous methanol gave 94 mg., m.p. 238–248° dec., $[\alpha]_D -29.6 \pm 0.7^\circ$.

From the mother liquors of the first recrystallization above there was recovered 215 mg. (55%). Two recrystallizations from methanol–nitromethane gave 130 mg. of off-white crystals, m.p. 200–235°. Crystallization of this material from a minimum of methanol yielded 41 mg. of virtually racemic IX, $[\alpha]_D +1^\circ$, m.p. 205–209°. The mother liquors from this separation were taken to dryness to leave 90 mg., m.p. 196–220°, $[\alpha]_D +10.5 \pm 0.3^\circ$. Two further recrystallizations removed the remaining high melting impurity and most of the optically active material; recovered 42 mg., $[\alpha]_D +1.5 \pm 0.4^\circ$, m.p. 194–206°.

Resolution of *exo*-3-Carboxy-5-norbornene- Δ^2,α -acetic Acid (X).

—In methanol solution 500 mg. of adduct acid and 835 mg. of quinine were mixed, and the solution was then taken to dryness to leave a colorless foam, $[\alpha]_D -113^\circ$. This material separated from solution in ethyl acetate as small needles, 858 mg. (64%). Recrystallization from ethyl acetate–methanol gave 608 mg. (45%), $[\alpha]_D -160.0 \pm 0.3^\circ$. This salt was decomposed to quinine and the dicarboxylic acid as detailed below for the isomeric adduct. There was recovered 105 mg. (44%), $[\alpha]_D -67^\circ$. Recrystallization from aqueous methanol gave 78 mg., $[\alpha]_D -81 \pm 2^\circ$, m.p. 237–244°, infrared spectrum identical with authentic racemic material.

Resolution of *endo*-3-Carboxy-5-norbornene- Δ^2,α -acetic Acid (IX).

—Solutions of 1.00 g. of IX and 1.67 g. of quinine, each in 10 ml. of methanol, were mixed and taken to dryness *in vacuo*. The residual white foam was crystallized from ethyl acetate to give a first crop of 2.35 g. of fluffy white needles, $[\alpha]_D -53^\circ$ ($CHCl_3$). This material was carried through four further recrystallizations, from ethyl acetate at first and later from ethyl acetate containing a small amount of methanol. This yielded 675 mg. of needles, $[\alpha]_D -87^\circ$ ($CHCl_3$). To regenerate IX this salt was dissolved in a minimum volume of methanol, treated with 2.30 ml. of 5% aqueous sodium hydroxide solution (approximately 10% excess), and then diluted with water. Chloroform extraction removed the precipitated quinine, and the resulting clear solution was acidified with 5.83 ml. of 0.5 *M* hydrochloric acid. The water was removed at reduced pressure to leave 426 mg. of white crystals, a mixture of IX and sodium chloride. This residue was dissolved in 12 ml. of water and extracted continuously with ether for 7 hr. Removal of ether after drying left 257 mg. This was recrystallized from nitromethane to give 202 mg. (80%), m.p. 189–191°, $[\alpha]_D -122^\circ$. The solid state infrared spectrum of this active material was quite similar to, but not identical with, that of racemic IX. This was the most active sample of IX obtained.

From the mother liquors of the above partial resolution there was isolated by the same procedure 788 mg. of dextrorotatory diacid, m.p. 198–206°, $[\alpha]_D +39.4 \pm 0.2^\circ$.

(+)-Norcamphor Dinitrophenylhydrazone. A. From (+)-IX.

—The above-described 788 mg. of dextrorotatory IX was carried through the sequence detailed above to give ultimately 344 mg. of norcamphor dinitrophenylhydrazone (29% over-all from IX), m.p. 129–131.5°, $[\alpha]_D +9^\circ$ ($CHCl_3$). The infrared spectrum of this material in carbon tetrachloride was identical with that of the authentic racemic derivative.

B. From (+)-Norcamphor.^{27,28}—Authentic norcamphor, $[\alpha]_D^{20} +17.0^\circ$ ($CHCl_3$), was converted to the derivative as described above for the racemic compound. Two recrystallizations gave material of m.p. 129–131°, $[\alpha]_D^{25} +30^\circ$ ($CHCl_3$).

(–)-Norcamphor Dinitrophenylhydrazone.—The degradation sequence was applied to 217 mg. of X, $[\alpha]_D -53 \pm 1^\circ$, to yield 33 mg. (10%) of norcamphor dinitrophenylhydrazone. Two recrystallizations from aqueous methanol gave 23 mg., m.p. 127.5–130°, $[\alpha]_D -14.1 \pm 0.7^\circ$ ($CHCl_3$).

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