The brick-red **2,4-dinitrophenylhydrazone** had m.p. 121–123° dec. (from nitromethane).

Anal. Calcd. for $C_{22}H_{26}N_4O_7$: N, 12.22. Found: N, 12.48.

(b) **In Dioxane.**—The olefin (13.1 g.), selenious acid (6.5 g.) and dioxane (10 ml.) were refluxed for 8 hr. After the usual work-up, the crude product whose infrared spectrum showed that it contained both the allylic alcohol and the desired α,β-ethylenic ketone [2.92 μ (OH), 5.99 μ (C═O)], was dissolved in pyridine (50 ml.) and hydroxylamine hydrochloride (10 g.) and absolute ethanol (10 ml.) were added. The mixture was refluxed for 4 hr. and then subjected to steam distillation. The crude oxime of the desired ketone remained behind. Refluxing the oxime with dilute hydrochloric acid for 4 hr. and ether extraction afforded the ketone whose semicarbazone (6.4 g., 38%), had m.p. 174–175° dec. and was identical with the product described above.

Benzoylation of the portion volatile with steam, with an equal weight of benzoyl chloride in a tenfold weight of pyridine, permitted separation of the allylic alcohol from a small amount of unreacted olefin.

Steam distillation of the benzoylation mixture afforded only the olefin (1.6 g.) as the volatile fraction. The benzoate could be saponified with excess ethanolic potassium hydroxide and the resulting crude allylic alcohol (4.7 g.) could be oxidized further either by the Oppenauer method or the method described below.

Oxidation of 2-(2′,3′,4′-Trimethoxyphenyl)-cyclohept-2-en-1-ol with Active Manganese Dioxide.—The alcohol (1 g.), b.p. 170–173° at 5 mm., was dissolved in chloroform (25 ml.) and the solution was shaken with active manganese dioxide[3] for 24 hr. at room temperature. After removal of the inorganic material by filtration and the chloroform by distillation under vacuum, the residue was treated with semicarbazide hydrochloride in ethanol-pyridine. The semicarbazone of 2-(2′,3′,4′-trimethoxyphenyl)-cyclohept-2-enone (410 mg., 34%), m.p. and mixed m.p. 174–175°, was obtained.

1,2,3-Trimethoxy-6,6a,7,8,9,10,11,11a-octahydro-5,11-dioxo-5H-cyclohept[a]naphthalene. (a) **Michael Condensation.**—The conditions used were analogous to those previously described.[7] The ketone IIb (5 g.), ethyl malonate (8 g.) and potassium *t*-butoxide (prepared from 0.14 g. of potassium and 3 ml. of *t*-butyl alcohol) afforded after acid saponification and decarboxylation as described,[7] **3-oxo-2-(2′,3′,4′-trimethoxyphenyl)-cycloheptaneacetic acid** (4.4 g., 72%), as an oil.

Anal. Calcd. for $C_{18}H_{24}O_6$: neut. equiv., 336.4. Found: neut. equiv., 330.

(b) **Cyclization.**—The above acid (3.4 g.) was dissolved in anhydrous hydrogen fluoride. The tricyclic diketone III formed colorless needles (2.6 g., 81%), m.p. 110° (from petroleum ether).

Anal. Calcd. for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.59; H, 6.61.

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(7) D. Ginsburg and R. Pappo, *J. Chem. Soc.*, **938** (1951).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Configuration of α-Methoxyadipic Acid

BY DONALD S. NOYCE AND JAMES H. CANFIELD

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α-Methoxyadipic acid has been prepared and resolved. From ethyl γ-chlorobutyrate and sodio-dimethylmalonate, there was obtained diethyl α-carboethoxyadipate, which by bromination, decarboxylation and replacement with methoxyl afforded α-methoxyadipic acid. (+)α-Methoxyadipic acid afforded (+)2-methoxy-1,6-hexanediol on reduction with lithium aluminum hydride, whose bis-tosylate on further reduction afforded (+)2-methoxyhexane, which has been configurationally related to glyceraldehyde.

Current interest in the absolute configuration of broad series of natural products has produced a great deal of progress in recent years.[1–4] We have been interested in effecting a direct chemical relationship between the sugars (glyceraldehyde) and the monoterpenes. Such a relationship involving the common reference compound (−)*cis*-3-hydroxycyclohexanecarboxylic acid (I) has been undertaken. The degradation of (−)-I to (+)3-methylcyclohexanone (II) has been reported previously,[5] and more recently the degradation of (−)-I to (−)α-methoxyadipic acid (III).[6] The present report is concerned with the last stage of the stereochemical interrelationship, that of relating (−)α-methoxyadipic acid to glyceraldehyde.

For the preparation of III the method reported by von Braun and Meyer[7] for the preparation of α-bromoadipic acid (IV) has been used with some modification. Treatment of γ-butyrolactone with ethanolic hydrogen chloride afforded ethyl γ-chlorobutyrate (V) in 91% yield. When V was allowed to react with sodiomalonic ester, catalyzed by sodium iodide,[8] diethyl α-carboethoxyadipate (VI) was obtained in 73% yield. VI was hydrolyzed to the malonic acid, which was treated with one mole of bromine, and decarboxylated to afford α-bromoadipic acid (IV). Esterification of IV with diazomethane and treatment with sodium methoxide in methanol afforded dimethyl α-methoxyadipate (VII), which was thence hydrolyzed to α-methoxyadipic acid (*dl*-III).

The resolution of III proved reasonably tedious. Using the cinchonidine salt, the (−)-form concentrated in the head fractions, and after several crystallizations, nearly completely resolved (−)-III was obtained after cleavage of the salt. This material proved to be identical with that obtained previously by the degradation of (−)-I,[6] by comparison of the infrared spectra of the Nujol mulls, whereas the spectrum of *dl*-III differed in details.

Reduction of (−)-III afforded (−)2-methoxy-1,6-hexanediol ((−)-VIII). Formation of the bis-*p*-toluenesulfonate and reduction with lithium alu-

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(1) A. Fredga, "The Svedberg Memorial Volume," Almquist and Wiksells, Boktryckeri, Upsala, 1944, p. 261; see also *Acta Chem. Scand.*, **1**, 361 (1947).

(2) S. Bergstrom, A. Lardon and T. Reichstein, *Helv. Chim. Acta*, **32**, 3, 1613, 1617, 2003 (1949).

(3) W. G. Dauben, D. F. Dickel, O. Jeger and V. Prelog, *ibid.*, **36**, 325 (1953).

(4) A. Furst, O. Jeger, R. B. Woodward, *et al.*, THIS JOURNAL, **76**, 314 (1954).

(5) D. S. Noyce and D. B. Denney, *ibid.*, **74**, 5912 (1952).

(6) D. S. Noyce and D. B. Denney, *ibid.*, **76**, 768 (1954).

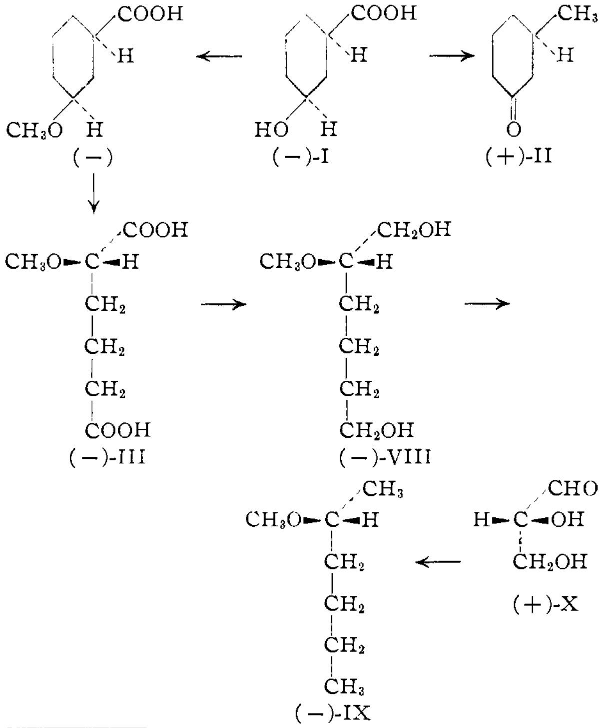
(7) J. von Braun and F. Meyer, *Ber.*, **74**, 19 (1941).

(8) U. S. Patent 2,415,261; *C. A.*, **41**, 3119 (1947).

minum hydride afforded crude 2-methoxyhexane (IX) with a negative rotation but an insufficient quantity for further purification.

Reduction of partially resolved (+)-III from the mother liquors of the cinchonidine resolutions was likewise carried out with lithium aluminum hydride to afford (+)-VIII, which was converted to the bis-*p*-toluenesulfonate and reduced further with lithium aluminum hydride to (+)-IX. (+)-IX was identified by comparison of the infrared spectrum with the spectrum of an authentic sample of 2-methoxyhexane prepared by the reaction of 2-hexanol with methyl iodide through the sodium salt.

Since (−)2-methoxyhexane has been shown by Levene[9] to be configurationally related to D(+)-glyceraldehyde (X), one may draw the spatial formulas as in the accompanying diagram and flow sheet and be representing absolute configurations. These conclusions are in agreement with the tentative conclusions drawn earlier,[6] and also with the results of Freudenberg and Hohmann[10] which have been reported recently. Likewise in accord with these conclusions is the work of Fredga[1] wherein relationship between the terpenes and sugars was suggested on the basis of phase diagrams of "quasi-racemates." It is also of interest that these conclusions lend support to the usefulness and validity of the method of molecular rotation differences as applied by Klyne[11] and Mills,[12] and thus perhaps support the suggestion that the absolute configuration of the natural steroids may be more appropriately represented as normally drawn, rather than inverted as suggested by Bergstrom, Lardon and Reichstein.[2,12a]



Experimental[13]

Ethyl γ-Chlorobutyrate (V).—Anhydrous hydrogen chloride was bubbled into a cooled solution of 86 g. (1.0 mole) of butyrolactone in 600 ml. of absolute alcohol until the mixture was saturated with hydrogen chloride. After standing at room temperature for 48 hours, the solution was poured into excess ice-water, and the crude ethyl γ-chlorobutyrate separated. The aqueous layer was extracted with four 100-ml. portions of chloroform and the combined extracts washed with sodium bicarbonate solution. After drying (magnesium sulfate), distillation afforded 128 g. (91%) of (V), b.p. 94–95° (37 mm.),[14] $n^{25}\mathrm{D}$ 1.4298.

Anal. Calcd. for $C_6H_{11}O_2Cl$: Cl, 23.54. Found: Cl, 23.55.

Diethyl α-Carboethoxyadipate (VI).—Sodium iodide (21 g., 0.125 mole) was dissolved in 500 ml. of absolute alcohol and 12.6 g. (0.55 mole) of sodium was added. This was followed by 144 g. (0.90 mole) of diethyl malonate. To this solution there was added slowly from a dropping funnel 75.3 g. (0.50 mole) of V, and the mixture was heated under reflux for 18 hours. The excess base was neutralized with acetic acid, water added to dissolve the inorganic salts, and the layers separated. Extraction of the aqueous layer with a small portion of benzene and combination of this with the above crude ester was followed by drying and distillation. There was obtained 101 g. (73%) of diethyl α-carboethoxyadipate (VI), b.p. 134–137° (1.5 mm.), $n^{25}\mathrm{D}$ 1.4362. von Braun and Meyer[7] report b.p. 172–174° (13 mm.).

α-Carboxyadipic Acid.—VI was hydrolyzed by heating under reflux briefly with 30% sodium hydroxide. The initial reaction was quite vigorous. After acidification with 6 *N* sulfuric acid, the acidic solution was continuously extracted with ether. The ether extracts were dried, and the ether removed by distillation to afford 64 g. (92%) of α-carboxyadipic acid, m.p. 136–140° with evolution of CO_2.

Anal. Calcd. for $C_7H_{10}O_6$: neut. equiv., 63.4. Found: neut. equiv., 66.2.

α-Bromoadipic Acid (IV).—To a stirred suspension of 155 g. (0.82 mole) of α-carboxyadipic acid in 700 ml. of ether in a 2-liter flask equipped with a stirrer and a trap for exit gases, 127 g. (41 ml.) of bromine in 700 ml. of carbon tetrachloride was added dropwise at such a rate that the temperature of the reaction mixture did not rise above 25°. After all of the bromine had been added, the solvents and hydrogen bromide were removed by distillation. There was obtained 215 g. (95%) of crude α-bromo-α-carboxyadipic acid as a light tan powder.

Heating this crude acid at 135–140° for one hour resulted in the loss of the theoretical weight corresponding to decarboxylation. There was obtained in this fashion 179 g. (98%) of crude α-bromoadipic acid. Some hydrogen bromide was also evolved during the course of the decarboxylation. Solution of the crude IV in ether and treatment with decolorizing charcoal gave after evaporation of the ether 174 g. (94%) of a slightly tan IV, neut. equiv. 101 (calculated 112.5). Two crystallizations from ether–carbon tetrachloride afforded 138 g. (75%) of IV, m.p. 118–121°, neut. equiv. 111. von Braun and Meyer[7] report m.p. 126°.

α-Methoxyadipic Acid (III).—Diazomethane was used to esterify 43 g. (0.191 mole) of IV to afford 45.5 g. (94%) of dimethyl α-bromoadipate. To a solution of 8 g. of sodium in 220 ml. of absolute methanol was added the above crude ester, and the mixture heated under reflux for 12 hours. Following the addition of 50 g. of 50% sodium hydroxide, the mixture was heated under reflux for an additional three

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[9] P. A. Levene and H. S. Haller, *J. Biol. Chem.*, **65**, 49 (1925); **67**, 329 (1926); **69**, 165 (1926); P. A. Levene, A. Walti and H. S. Haller, *ibid.*, **71**, 465 (1927).

[10] K. Freudenberg and W. Hohmann, *Ann.*, **584**, 54 (1954).

[11] W. Klyne, *J. Chem. Soc.*, 2916 (1952).

[12] J. A. Mills, *ibid.*, 4976 (1953).

[12a] NOTE ADDED IN PROOF.—The absolute configurations of the steroids and lanostenol have been determined: B. Riniker, D. Arigoni and O. Jeger, *Helv. Chim. Acta*, **37**, 546 (1954); R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives and R. B. Kelly, THIS JOURNAL, **76**, 2852 (1954).

[13] Melting points are corrected; boiling points are uncorrected. Analyses are by the Microanalytical Laboratory of the University of California. We wish to thank Mr. Charles Huggins and Mr. Roger Millikan for their assistance in the determination and interpretation of the infrared spectra.

[14] F. F. Blicke, W. B. Wright, Jr., and M. F. Zienty, THIS JOURNAL, **63**, 2488 (1941), report b.p. 70–71° (10 mm.).

hours. Removal of the methanol, acidification and continuous extraction afforded 27 g. (77%) of crude III. Two crystallizations from benzene–isopropyl ether gave 23 g. (67%) of III, m.p. 76–79° (reported[15] 78–79°).

Anal. Calcd. for $C_7H_{12}O_5$: neut. equiv., 88.1. Found: neut. equiv., 87.

Resolution of III.—Cinchonidine, when mixed with III in the molar proportions of two-to-one gave a salt which crystallized readily from water, m.p. 181–182° dec.

Anal. Calcd. for $C_{45}H_{56}O_7N_4$: C, 70.65; H, 7.38; N, 7.32. Found: C, 70.42; H, 7.27; H, 7.50.

After several crystallizations, the α-methoxyadipic acid regenerated from the head fractions had m.p. 80–85°, $[\alpha]^{23}D$ −6.85° (*c* 2 in ethyl acetate). Crystallization from methanol–ethyl acetate was also feasible, and using this solvent pair, resolution proceeded somewhat further. From 200 g. of salt there was obtained after fractional crystallization 4.5 g. of (−)α-methoxyadipic acid from the head fraction of the salt, m.p. 90–97°, which when further purified by partition chromatography on silicic acid[6] had m.p. 94.5–97°, $[\alpha]^{22.5}D$ −50.6° (*c* 2 in ethyl acetate), neut. equiv., 88.0. This material showed an infrared spectrum identical with that obtained by Noyce and Denney.[6] From the second fraction there was obtained 2.2 g. of (−)III, m.p. 84–95°, $[\alpha]^{20.5}D$ −47.8° (*c* 2 in ethyl acetate).

From the appropriate mother liquors there was obtained 16.7 g. of partially resolved (+)-III, m.p. 76–81°, $[\alpha]^{20}D$ +4.75°.

Reduction of III.—*dl*-α-Methoxyadipic acid, 10 g. (0.057 mole), esterified with diazomethane, was reduced with a slurry of 4.5 g. of lithium aluminum hydride in 200 ml. of ether. The mixture was allowed to reflux overnight. Water (20 ml.) was added cautiously to destroy excess reducing agent, and the mixture was acidified with 6 *N* sulfuric acid. The 2-methoxy-1,6-hexanediol was recovered by continuous ether extraction for 36 hours. It was necessary to add methanol to the ether after extraction to obtain an homogeneous solution. After drying and removal of the volatile solvents, distillation afforded 4.5 g. (53%) of 2-methoxy-1,6-hexanediol, b.p. 125° (0.5 mm.), as a very viscous sirup.

The bis-*p*-nitrobenzoate was prepared in the usual fashion and crystallized from ethanol, m.p. 73.0–74.2°.

Anal. Calcd. for $C_{21}H_{22}N_2O_9$: C, 56.60; H, 4.97; N, 6.28. Found: C, 56.68; H, 4.85; N, 6.37.

In a similar manner 1.5 g. of (−)-III ($[\alpha]D$ −50.6°) was reduced *via* the ester to give 0.5 g. (40%) of (−)2-methoxy-1,6-hexanediol, b.p. 122–124° (0.5 mm.), $[\alpha]^{17}D$ −3.0° (*c* 2 in methanol).

Likewise, 15.0 g. of (+)-III, $[\alpha]D$ +4.75°, was reduced with lithium aluminum hydride to give 5.5 g. (44%) of (+)VIII, b.p. 120–123°, $[\alpha]^{21.5}D$ 0.28° (*c* 5 in methanol). The bis-*p*-nitrobenzoate, crystallized from ethanol, m.p. 69.6–71.0°, but had no observable rotation.

Anal. Found: C, 56.44; H, 5.00; N, 6.06.

Formation of the Bis-*p*-toluenesulfonate of VIII.—To a cooled solution of VII in 20 ml. of pyridine, 5.7 g. of *p*-toluenesulfonyl chloride was added. The mixture was stirred at room temperature for five hours, added to water, and acidified with 6 *N* sulfuric acid. The aqueous solution was extracted with benzene, and the benzene extract dried and the benzene removed by distillation. There was obtained 2 g. (32%) of an oil which slowly crystallized. Crystallization from ether–pentane afforded the bis-*p*-toluenesulfonate of VIII, m.p. 63.0–64.4°.

Anal. Calcd. for $C_{21}H_{28}O_7S_2$: C, 55.24; H, 6.18; S, 14.04. Found: C, 55.27; H, 6.28; S, 14.19.

In a similar fashion the bis-*p*-toluenesulfonate of (+)-VIII was obtained as an oil which was used immediately, before crystallization occurred.

Reduction of the Bis-*p*-toluenesulfonate of VIII: Formation of 2-Methoxyhexane (IX).—A solution of 1.7 g. of crude bis-*p*-toluenesulfonate of VIII in benzene was added to a slurry of 2.0 g. of lithium aluminum hydride in 50 ml. of di-*n*-propyl ether. The mixture was heated under reflux for 3 days. At the end of this time, the excess lithium aluminum hydride was decomposed with 10 ml. of water, and acidified with 6 *N* sulfuric acid. The ether layer was separated, washed with dilute sodium hydroxide solution, dried and fractionated through a two-foot modified Podbielniak column. There was obtained 0.10 g. of *dl*-2-methoxyhexane (22%), b.p. 115°. The infrared spectrum of this material was indistinguishable from the infrared spectrum of 2-methoxyhexane obtained from 2-hexanol, by methylation with methyl iodide.

In a similar manner, 5.0 g. of the crude bis-*p*-toluenesulfonate of (+)-VIII was reduced to afford after distillation through a modified Lecky–Ewell column, 0.55 g. of (+)2-methoxyhexane, b.p. 114–115°, $[\alpha]^{18.5}D$ +0.37° (homog., *l* 1) which was characterized by infrared spectrum. The infrared spectrum of the (+)2-methoxyhexane was essentially identical with the spectrum of the material obtained above, except for the presence of two weak bands characteristic of toluene at 728 and 694 cm.$^{-1}$.

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[15] W. Meyer and M. B. Neymeyr, *Ann.*, **572**, 212 (1951).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Synthetic Routes to *trans*-2-Decalone

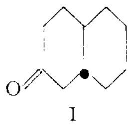
BY EUGENE E. VAN TAMELEN AND WILLIAM C. PROOST, JR.

RECEIVED FEBRUARY 24, 1954

Various possible routes to *trans*-2-decalone from readily available starting materials have been investigated. Several reported transformations of certain $\Delta^{1,9}$-2-octalones to *trans*-2-decalone involving catalytic hydrogenations have been shown to yield instead *cis*-2-decalone. Two new methods for the production of the *trans*-isomer from the octalone have been developed: (1) catalytic hydrogenation of the enol ethyl ether followed by hydrolysis of the resulting dihydro derivative or, preferably, (2) reduction with excess lithium in liquid ammonia and subsequent chromic acid oxidation of the unisolated intermediate decalol.

In connection with the prosecution of certain research programs in this Laboratory[1a] as well as in others,[1b] the need for *trans*-2-decalone (I) encouraged us to develop a convenient preparative method for this substance. The purpose of this report is to describe such a method and also to present our experimental evaluations of other possible routes to the same compound—both those attempted for the first time in this Laboratory as well as those described in the previous literature.

Although the 105°-melting *cis*-2-decalol, convertible to *cis*-2-decalone (II) by chromic acid oxidation, can be readily obtained from 2-naphthol by



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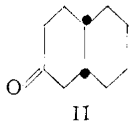

II

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[1] (a) E. E. van Tamelen and M. Shamma, THIS JOURNAL, **76**, 950 (1954); (b) *e.g.* A. R. Pinder and R. Robinson, *J. Chem. Soc.*, 1221 (1952).