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Synthesis of Poly Substituted *cis*-Hydrindanes[1]

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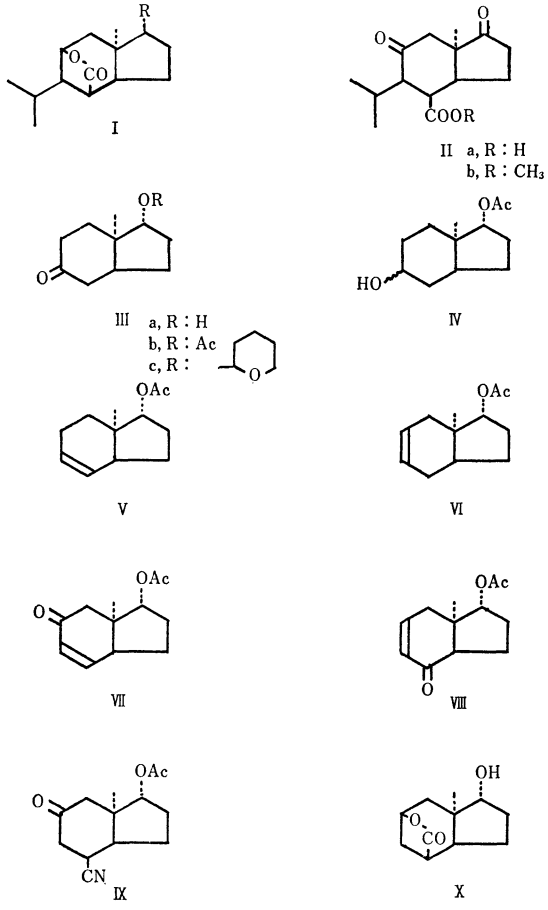
cis-4-Carboxy-5-isopropyl-8-methylhydrindane-1,6-dione was synthesized from *cis*-1-hydroxy-8-methylhydrindanone-5 as a useful intermediate for the synthesis of picrotoxin and dendrobine.

cis-4-Carboxy-6-hydroxy-5-isopropyl-8-methylhydrindane lactone-4,6 (I) is a moiety of picrotoxinin, picrotin, tutin, coriamytrin, dendrobine and related alkaloids which are known as peculiar sesquiterpene and sesquiterpene alkaloid.[2] *cis*-4-Carboxy-5-isopropyl-8-methylhydrindane-1,6-dione (II) may be regarded as a possible intermediate on the way to the synthesis of these compounds. We have studied the procedure to derive compound II from *cis*-1-hydroxy-8-methylhydrindanone-5 (III), which was prepared according to Boyce's method.[3]

Formation of γ-lactone on six membered ring of *cis*-hydrindane was first studied. Sodium borohydride reduction of acetate IIIb gave an alcohol in good yield. Dehydration of alcohol IV gave a mixture of olefins V and VI, which could not be separated from each other by means of gas chromatography or TLC. Allylic oxidation of the mixture of olefins with *t*-butyl chromate afforded a mixture of α,β-unsaturated ketones VII (75%) and VIII (25%). Pure compound VII was isolated by chromatography on silica gel. Hydrocyanation of compound VII gave a cyanoketone and a pure epimeric isomer was separated (mp 105—107°C) by chromatography on silica gel. Their stereochemistry was determined by the fact that reduction with sodium borohydride and subsequent hydrolysis gave a γ-lactone (IR: 1760 cm^{-1}). An attempt to introduce an isopropyl group at C_5-position of compound VII was unsuccessful, but we were able to ascertain the procedure of the formation of lactone. We therefore dealt with 5-isopropyl-8-



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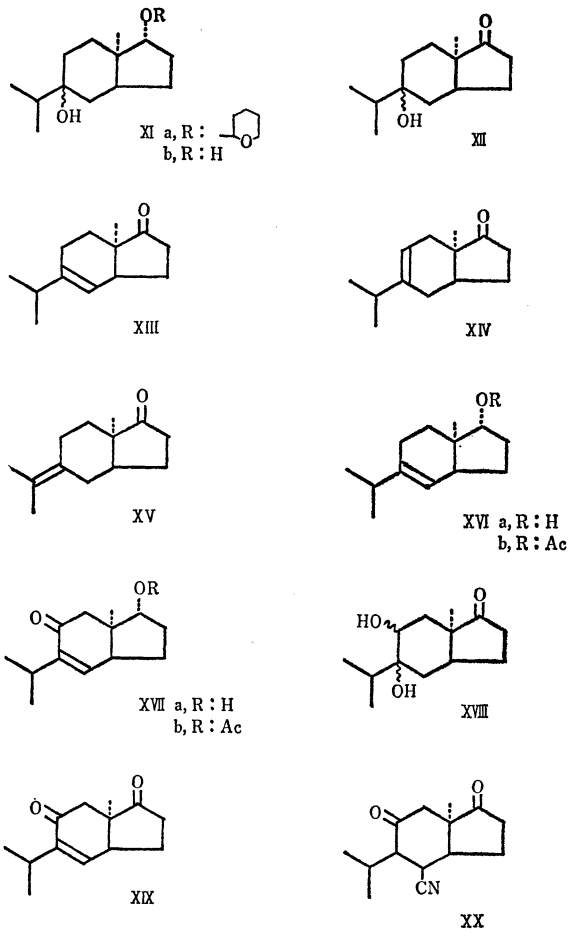
2) L. A. Poter, *Chem. Rev.*, **67**, 441 (1967).

3) C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, **1960**, 4547.



methylhydrindane derivatives in an analogous way.

To introduce the isopropyl group at C_5-position, compound III was treated with dihydropyran and a few drops of concentrated hydrochloric acid to give a pyranyl ether IIIc in good yield. Compound IIIc was treated repeatedly with isopropyllithium in petroleum ether to afford compound XIa in 52% yield. Dialcohol XIb, obtained from compound XIa by treatment with 2 N hydrochloric acid in tetrahydrofuran, was oxidized with chromium trioxide in a mixture of acetone and acetic acid to give a keto alcohol XII.

A Δ^4-olefinic compound will be obtained predominantly by dehydration of compound XII because a Δ^4-olefinic compound is more stable than a Δ^5-olefinic compound in *cis*-8-methylhydrindane system.[4]

A mixture of keto olefins was obtained from compound XII by heating at 200°C with potassium hydrogensulfate. VPC analysis of dehydration products showed three peaks with the ratio 7 : 3 : 1 (retention time: 2.7, 3.8, and 5.5 min, respectively). The main product was isolated by column chromatography using silica gel treated with silver nitrate.[5,6] The remaining isomers were separated by preparative gas chromatography. The structure of the main product XIII was confirmed by NMR spectra which showed olefinic proton at 5.32 ppm (d, 1H, J=2.5 Hz). The structures of the two other keto olefins were elucidated also by NMR spectra. Isomer XIV showed olefinic proton at 5.30 ppm (m, 1H), while isomer XV had no absorption of olefinic proton but olefinic methyl groups at 1.65 ppm (s, 6H).

Three other methods were investigated in order to increase the yield of XIII. Dehydration of XII by treatment with phosphorus oxychloride in pyridine gave XIII : XIV : XV=6 : 3 : 1. Dehydration by treatment with iodine-hydrochloric acid in benzene gave 6 : 3 : 1 and dehydration by heating on alumina which was treated with pyridine[7,8] gave 10 : 5 : 1. Evidently the most useful method was dehydration with potassium hydrogensulfate. Isomerization from XIV and XV to XIII did not occur under the conditions of sodium ethoxide or hydrochloric acid in ethanol.

For the preparation of compound XVII, allylic oxidation of compound XIII was studied. Direct oxidation of XIII with *t*-butyl chromate in benzene afforded an α,β-unsaturated ketone XIX in only 5% yield. On the other hand, reduction of XIII with lithium aluminum hydride in ether and successive acetylation gave compound XVIb in 90% yield. Oxidation of acetyl derivative XVIb with selenium oxide gave compound XVIIb in 19% yield and also gave a small amount of isomerized compound. Oxidation of XVIb with *t*-butyl chromate in benzene under reflux for 60 hr afforded a mixture, which was separated by silica gel chromatography to give compound XVIIb in 11% yield and recovered material XVIb in 50% yield. Therefore the latter route (XIII→XVIb→XVIIb) was useful for the preparation of the compound XVIIb.

Compound XVIIb was hydrolyzed with 2 N sodium hydroxide in methanol and then oxidized with Jones' reagent[9] to give compound XIX in good yield. Its structure was confirmed by the following synthetic route. Isomer XIV was treated with performic acid to afford diol XVIII in 30% yield. By subsequent oxidation with Jones' reagent and dehydration with iodine-hydrochloric acid in benzene under reflux, diol XVIII gave compound XIX in 60% yield. Hydrocyanation of diketo olefin XIX with potassium cyanide and ammonium chloride in dimethylformamide[10] afforded an isomeric mixture of cyanoketone, which showed three spot in TLC (R_f: 0.01, 0.41, and 0.38, ethyl acetate: benzene=3 : 10), in 85% yield. The main product (mp 117—118°C, R_f 0.38) separated by recrystallization, was recognized as an isomer XXi having an axial cyano group and an equatorial isopropyl group, since absorption of α-proton of cyano group appeared at 3.36 ppm (d-d) and their coupling constant was 3.5—1 Hz in NMR spectrum.[11] The conformation of the second isomer

4) L. Velluz, J. Valls, and G. Nonime, *Angew. Chem.*, **77**, 185 (1965).
5) B. de Vries, *Chem. Ind.* (London), **1962**, 1049.
6) A. S. Gupta and S. Dev, *J. Chromatog.*, **12**, 189 (1963).
7) E. J. Corey and A. G. Hortmann, *J. Amer. Chem. Soc.*, **87**, 5736 (1965).
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9) A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *J. Chem. Soc.*, **1953**, 2548.
10) W. Nagata, S. Hirai, H. Itazaki, and K. Takeda, *J. Org. Chem.*, **26**, 2413 (1961).
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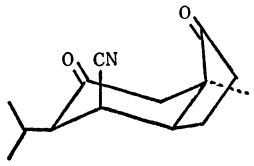
(mp 115—116°C, R_f 0.61) obtained by silica gel chromatography of the mother liquor, was suggested to be an isomer XXii by NMR spectrum which showed absorption of α-proton of cyano group at 2.8 ppm and methyl protons of isopropyl group at a lower field than that of XXi. The third isomer XXiii which was expected to have equatorial cyano and isopropyl groups could not be isolated in a pure state. Hydrolysis of the isomeric mixture of cyanoketone XX with 6N sulfuric acid in acetic acid under reflux for 100 hr afforded an isomeric mixture of carboxylic acid IIa. Separation of the isomeric mixture as its methyl ester IIb by chromatography on silica gel resulted in the isolation of an isomer (mp 93—94°C), which was identical with the isomer derived from XXi by TLC and gas chromatography in the same way.

Treatment of the isomer of IIb with methanolic sodium methoxide yielded an equilibrium mixture of IIb and diastereomer having epimeric configuration of carbomethoxyl group.



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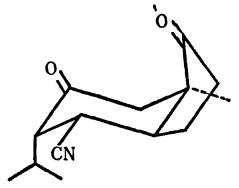
i



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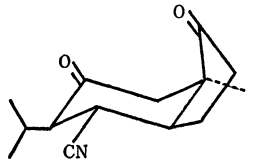

iii

Although the compound we aimed at was synthesized, it takes a long time to purify the intermediate and the method is troublesome. Studies of other methods to synthesize these compounds and the methods available for introduction of carbon chain at C_1-position are in progress.

Experimental

Preparation of 2-Methylcyclopentane-1,3-dione. 2-Methylcyclopentane-1,3-dione was prepared from diethyl oxalate *via* ester condensation according to Boyce's method.[12] Recently Grenda developed a convenient method for its preparation in a large amount from succinic anhydride and 2-buten-2-ol acetate.[13]

12) C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, **1959**, 2022.

13) V. J. Grenda, G. W. Lindberg, N. L. Wendler, and S. H. Pines, *J. Org. Chem.*, **32**, 1236 (1967).

cis-1-Hydroxy-8-methylhydrindanone-5 (IIIa). This was prepared by Boyce's method, mp 80—83°C.

cis-1-Acetoxy-8-methylhydrindanone-5 (IIIb). A mixture of IIIa (33.6 g), acetic anhydride (30.6 g), and pyridine (150 m*l*) was allowed to stand overnight, water was added and the separated organic layer was extracted with ether. The ethereal extract was washed and dried. The solvent was removed and the residual oil was distilled, bp 113—116°C/1 mmHg, 37 g (87%). IR: ν^{neat} 1740, 1710 cm^{-1}.

Found: C, 68.25; H, 8.64%. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63%.

cis-1-Acetoxy-8-methylhydrindan-5-ol (IV). To a solution of IIIb (36.8 g) in ethanol (100 m*l*) was added dropwise a solution of sodium borohydride (3 g) in ethanol (200 m*l*), and the reaction mixture was stirred for 10 hr at room temperature. Water and acetic acid were added to the reaction mixture which was then concentrated *in vacuo*. Water was added to the residue which was extracted with ether. The ethereal extract was washed and dried. The solvent was removed and the residual oil was distilled to give IV (32 g, 87%), bp 120—125°C/1 mmHg. IR: ν^{neat} 3400, 1740 cm^{-1}.

Found: C, 67.71; H, 9.47%. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50%.

cis-1-Acetoxy-8-methyl-6,7,8,9-tetrahydroindane (V and VI). To a solution of IV (21 g) in pyridine (100 m*l*) was added dropwise a mixture of phosphorus oxychloride (23 g) and pyridine (30 m*l*) under ice cooling. The reaction mixture was allowed to stand overnight at room temperature and then heated at 80°C for 4 hr. Ice was added to the cooled mixture and separated organic layer was extracted with ether. The ethereal extract was washed successively with 2N hydrochloric acid, sodium hydrogencarbonate solution and water and dried. The solvent was removed and the residual oil was distilled, bp 124°C/28 mmHg, 10.5 g (56%). IR: ν^{neat} 1740 cm^{-1}. NMR: $\delta(CCl_4)$ 5.62 (m, 2H), 2.0 ppm (s, 3H).

Found: C, 73.70; H, 9.27%. Calcd for $C_{18}H_{18}O_2$: C, 74.19; H, 9.34%.

This oil was a mixture of $\Delta^{4(5)}$- and $\Delta^{5(6)}$-olefin.

cis-1-Acetoxy-8-methyl-6,7,8,9-tetrahydroindanone-6 (VII). To a solution of a mixture of olefin (V and VI, 11.4 g) in benzene (100 m*l*) was added dropwise a solution of *t*-butyl chromate (prepared from 18.5 g of chromium trioxide) in acetic acid (4.5 g) and acetic anhydride (7.5 g) under reflux. After the reaction mixture was heated with stirring under reflux for 20 hr, water was added. Excess reagent was decomposed by addition of oxalic acid and separated organic layer was extracted with benzene. The benzene solution was washed with sodium hydrogencarbonate solution and water, and dried. On removing the solvent, the residual oil gave on distillation a mixture of VII and VIII, bp 124—128°C/3 mmHg, 4 g. The oil was chromatographed on silica gel and the fraction eluted with benzene gave pure VII. IR: ν^{neat} 1740, 1680 cm^{-1}. NMR: $\delta(CCl_4)$ 5.85 (d, 1H, J=10 Hz), 6.80 (d-d, 1H, J=10.5 Hz), 2.00 ppm (s, 3H).

Found: C, 69.47; H, 7.55%. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.71%.

cis-1-Acetoxy-4-cyano-8-methylhydrindanone-6 (IX). To a solution of VII (1.27 g) in dimethylformamide (30 m*l*) and water (10 m*l*) was added a solution of potassium cyanide (0.54 g) and ammonium chloride (0.46 g) in water (15 m*l*). The reaction mixture was heated at 90°C for 20 hr and then the solvent was removed. To the residue was added water and it was extracted with chloroform. The chloroform solution was washed and dried. On evaporation of the solvent,

the residue was chromatographed on silica gel. The fraction eluted benzene-ether gave 350 mg of a crystalline substance, mp 105—107°C.

Found: C, 66.04; H, 7.19%. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28%.

Reduction and Subsequent Hydrolysis of IX. Above cyanoketone IX (350 mg) was dissolved in ethanol and reduced with sodium borohydride in the usual way. The reaction mixture was evaporated *in vacuo*. Acetic acid and 6N sulfuric acid (3 : 1) were added to the residue and then it was heated under reflux for 30 hr. The hydrolyzate was extracted with ether and dried. On evaporation of the solvent, the residue showed IR absorption band at 1760 cm^{-1}.

cis-8-Methyl-1-tetrahydropyranyloxyhydrindanone-5 (IIIc). The ketol IIIa (17 g) was dissolved in 2,3-dihydropyran (50 m*l*) and then a few drops of concentrated hydrochloric acid were added. The reaction mixture was allowed to stand overnight at room temperature. Ether was added and the ether solution was washed with saturated sodium hydrogencarbonate solution and water, and dried. The solvent was removed and residual oil was distilled, 130—135°C/0.001 mmHg, 22 g (93%). IR; ν^{neat} 1720 cm^{-1} (cyclohexanone carbonyl).

Found: C, 71.15; H, 9.51%. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59%.

cis-1-Tetrahydropyranyloxy-5-hydroxy-5-isopropyl-8-methylhydrindane (XIa). To a solution of IIIc (25 g) in olefin free petroleum ether (50 m*l*), was added a solution of isopropyllithium (prepared from 2.1 g of lithium metal and 12 g of isopropyl chloride) in olefin free petroleum ether under nitrogen. After stirring for 3 hr under reflux, the reaction mixture was decomposed by the addition of 10% ammonium chloride solution (70 m*l*). The separated aqueous layer was extracted with ether. The combined organic layers were washed with saturated sodium chloride solution and dried. The solvent was removed and the remaining viscous yellow oil showed only 30% conversion to alcohol XIa in IR spectra. After three such treatments, the product was distilled, bp 140—145°C/0.001 mmHg, 15.4 g (total yield 52%). IR: ν^{neat} 3400 cm^{-1}. NMR: $\delta(CCl_4)$ 0.92 (d, 3H, J=7 Hz), 0.87 (d, 3H, J=7 Hz), 0.88 (s, 3H), 4.57 ppm (s, 1H).

Found: C, 72.36; H, 10.56%. Calcd for $C_{18}H_{32}O_3$: C, 72.93; H, 10.88%.

cis-5-Hydroxy-5-isopropyl-8-methylhydrindanone-1 (XII). To a solution of XIa (36.7 g) in tetrahydrofuran (120 m*l*), was added 2N hydrochloric acid (100 m*l*). After the solution was stirred for 5 hr at room temperature, 2N sodium hydroxide (100 m*l*) was added. The organic layer was separated and the aqueous layer was extracted with ether. The combined extracts were washed with water and dried. The solvent was removed and the residual oil was distilled to give a diol XIb (25 g), bp 135—138°C/0.001 mmHg. IR: ν^{neat} 3400 cm^{-1}. To a solution of XIb in acetone (50 m*l*) and acetic acid (100 m*l*), was added a solution of water (10 m*l*) and acetic acid (90 m*l*) containing chromium trioxide (13 g) under ice cooling. After stirring for 2 days at room temperature, ice (150 g) was added. The aqueous layer was extracted with ether. The ethereal extract was washed with saturated sodium hydrogencarbonate solution, and dried. The solvent was removed and the residual oil was distilled to give a ketol XII (20.5 g, 81%), bp 110—115°C/0.01 mmHg. IR: ν^{neat} 3450, 1740 cm^{-1} (cyclopentanone carbonyl). NMR: $\delta(CCl_4)$ 0.97 (s, 3H), 0.87 ppm (d, 6H, J=7 Hz).

Found: C, 74.24; H, 10.54%. Calcd for $C_{13}H_{22}O_2$: C, 74.11; H, 10.28%.

Dehydration of XII. i) XII (21 g) and potassium hydrogensulfate (2 g) were placed in a Claisen flask and then heated at 200°C for 30 min. After removal of the resulting water, the residue was subjected to distillation to give a mixture of olefins (16 g, 84%), bp 75—77°C/0.1 mmHg.

Found: C, 80.68; H, 10.40%. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48%.

The product showed no absorption of hydroxy group in IR spectra but three peaks by VPC analysis (P.E.G. 6000; their ratio was 7 : 3 : 1). The main product XIII (1.5 g) was isolated from the olefinic mixture (4.0 g) in a pure state by chromatography using silica gel pretreated with silver nitrate. IR: ν^{neat} 1740 cm^{-1}. NMR: $\delta(CCl_4)$ 0.96 (d, 6H, J=7 Hz), 0.94 (d, 3H), 5.32 ppm (d, 1H, J= 2.5 Hz). The second and the third isomer were obtained by preparative VPC (Carbowax-20M, at 170°C). $\Delta^{5(6)}$-Olefin XIV: NMR: δ (CCl_4) 0.94 (s, 3H), 1.02 (d, 6H, J=7 Hz), 5.30 ppm (m, 1H). Isopropylideneindanone XV: NMR: $\delta(CCl_4)$ 1.03 (s, 3H), 1.65 ppm (s, 6H).

ii) To a solution of XII (20 g) in pyridine (200 m*l*) was added phosphorus oxychloride (30.8 g) under ice cooling. The solution was warmed at 50°C for 3 hr. After cooling the solution was poured into ice-water (500 m*l*) and ex tracted with ether. The ethereal extract was washed with 5% hydrochloric acid, 10% sodium hydrogencarbonate solution and water, and dried. The solvent was removed and the residual oil was distilled to give a mixture of olefins (15 g, 84%). The ratio of XIII, XIV, and XV was 6 : 3 : 1 by VPC analysis.

iii) A mixture of XII (2.6 g) and alumina (8.0 g, Woelm grade I neutral, pretreated with 2% solution of pyridine) was evenly distributed on a glass "boat" consisting of a 20 cm glass tube. The glass boat was heated to 230°C by Corey's method under nitrogen. After 5 min, the product began to undergo distillation. The distillate was dissolved in ether and the ether solution was washed with water and dried. The solvent was removed and residual oil was distilled to give a mixture of XIII, XIV, and XV (2.1 g, 80%). Their ratio was 10 : 5 : 1 by VPC analysis.

cis-1-Acetoxy-5-isopropyl-8-methyl-6,7,8,9-tetrahydroindane (XVIb). A solution of XIII (13.5 g) in anhydrous ether (75 m*l*) was added to a stirred suspension of lithium aluminum hydride (1.4 g) in anhydrous ether (250 m*l*). The mixture was stirred for 4 hr at room temperature and then the required amount of ethyl acetate and water was added in order to decompose excess lithium aluminum hydride. The organic layer was separated and the aqueous layer was extracted with ether. The combined ethereal extracts were washed with water, and dried. The solvent was removed and the residual viscous oil was dissolved in pyridine (70 m*l*), and acetic anhydride (8 g) was then added under ice cooling with stirring. The reaction mixture was allowed to stand at room temperature overnight and then poured into ice-water. The organic material was extracted with ether and the ethereal extract was washed with water, and dried. The oil obtained by evaporating the solvent was distilled to give an acetate XVIb (14.8 g, 90%), bp 95—97°C/0.1 mmHg. IR: ν^{neat} 1745, 1380, 1240 cm^{-1}. NMR: $\delta(CCl_4)$ 0.97 (s, 3H), 1.0 (d, 6H, J=7 Hz), 2.0 (s, 3H), 4.8 (t, 1H), 5.37 ppm (d, 1H, J=2 Hz).

Found: C, 76.43; H, 10.22%. Calcd for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24%.

cis-1-Acetoxy-5-isopropyl-8-methyl-6,7,8,9-tetrahydroindanone-6 (XVIIb). i) To a solution of XVIb (14.8 g) in anhydrous benzene (80 m*l*) was added a mixture of *t*-butyl chromate (prepared from 19 g of chromium trioxide, 13 g of acetic acid and 17.5 g of acetic anhydride) with stirring

at 70°C over 8 hr. After stirring for 40 hr at the same temperature, a solution of oxalic acid (20 g) in water (100 m*l*) was added to the cooled reaction mixture. The organic material was extracted with ether and the extract was washed successively with water, 5% sodium hydrogencarbonate solution and water. The residue obtained by evaporating the solvent was distilled to give 7.5 g of recovered starting material (bp 95°C/0.1 mmHg) and 6.1 g of XVIIb (bp 100—130°C/0.1 mmHg), which was purified by chromatography on silica gel (eluted by petroleum ether : ether= 9 : 1). XVIIb was obtained in a pure state, 1.6 g (11%). IR: ν^{neat} 1745, 1680, 1240 cm^{-1}. UV: λ_{max}^{EtOH} 240 mμ (ε 8600). NMR: $\delta(CCl_4)$ 0.98 (d, 6H, J=7 Hz), 1.08 (s, 3H), 1.82 (s, 3H), 4.75 (broad 1H), 6.24 ppm (d, 1H, J=3.5 Hz).

Found: C, 71.97; H, 8.86%. Calcd for $C_{15}H_{22}O_3$: C, 71.91; H, 8.76%.

ii) To a solution of XVIb (7.5 g) in benzene (60 m*l*) was quickly added selenium oxide (6 g), water (2.4 m*l*) and acetic acid (120 m*l*). The mixture was heated at 80°C for 1 hr. The reaction mixture was cooled to room temperature and added sodium acetate (24 g) and heated at 80°C for 5 min. After cooling, the deposited selenium was filtered off and the filtrate was poured into the saturated sodium chloride solution (240 m*l*). The aqueous layer was extracted with ether. The crude oil (8 g) obtained by evaporating the solvent was dissolved in a mixture of acetone (40 m*l*) and acetic acid (50 m*l*). To this solution was added a mixture of water (2 m*l*) and acetic acid (7 m*l*) containing chromium trioxide (2.5 g). After stirring for 12 hr at room temperature, the solution was poured into 100 g of ice and then extracted with ether. The ethereal extract was washed with saturated sodium hydrogencarbonate solution and water, and dried. The crude oil (5.5 g), obtained by removal of the solvent, gave an α,β-unsaturated ketone XVIIb (1.5 g, 19%) by purification of silica gel chromatography (eluted by petroleum ether : ether=10 : 1).

cis-5-Isopropyl-8-methyl-6,7,8,9-tetrahydroindane-1,6-dione (XIX). i) To a solution of XVIIb (1.4 g) in methanol (30 m*l*), was added 2N sodium hydroxide (30 m*l*). The solution was stirred for 4 hr at room temperature and then allowed to stand overnight. The solution was neutralized with acetic acid and evaporated. The residue was extracted with ether and the ethereal extract was washed with saturated sodium chloride solution, and dried. The residual oil obtained by evaporating the solvent was dissolved in acetone (30 m*l*). Jones' reagent (1.6 m*l*) was added to this solution with stirring under ice-cooling. After stirring for 20 min at room temperature, excess reagent was decomposed with methanol. The solvent was evaporated *in vacuo* and water was added to the residue which was extracted with ether. The ethereal extract was dried and evaporated. The residual oil was distilled to give a diketone XIX (1.2 g, 95%), bp 110°C/0.1 mmHg (bath temp.). IR: ν^{neat} 1740, 1680, 1630, 1410 cm^{-1}. NMR: $\delta(CCl_4)$ 0.98 (d, 3H, J=7 Hz), 1.02 (d, 3H, J=7 Hz), 1.10 (s, 3H), 6.47 ppm (d, 1H, J=3.5 Hz).

Found: C, 74.90; H, 8.70%. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80%.

ii) To a solution of XIII (5.3 g) in anhydrous benzene (30 m*l*) was added a solution of *t*-butyl chromate (prepared from 8 g of chromium trioxide, 5.3 g of acetic acid and 7 g of acetic anhydride) over 6 hr at 50—60°C with stirring. After stirring for an additional 30 hr at the same temperature, the solution was allowed to stand at room temperature overnight. A solution of oxalic acid (8 g) in water (50 m*l*) was added to the ice-cooled reaction mixture and the separated aqueous layer was extracted with ether. The combined extracts were washed with saturated sodium hydrogencarbonate solution and water, and dried. The residual oil obtained by removal of the solvent was purified by chromatography on silica gel (eluted by petroleum ether : ether=10 : 1) to yield a diketone XIX (250 mg, 4.5%).

iii) To a solution of XVIII (500 mg) in acetone (10 m*l*) was added 0.8 m*l* of Jones' reagent with stirring under ice-cooling. After stirring for 15 min at room temperature, excess reagent was decomposed with methanol (5 m*l*). Water was added and the solution was extracted with ether. The extract was washed with water and dried. The residual oil (450 mg) obtained by removal of the solvent was dissolved in benzene (10 m*l*) and to this solution was added iodine (10 mg) and a few drops of concentrated hydrochloric acid. The mixture was heated under reflux for 20 hr. After cooling, the organic layer was washed with saturated sodium thiosulfate solution and water, and dried. On distillation 300 mg of XIX (68%) was obtained.

cis-5,6-Dihydroxy-5-isopropyl-8-methylhydrindanone-1 (XVIII). To a mixture of formic acid (25 m*l*) and 30% hydrogen peroxide (3 m*l*) was added XIV (1.5 g) with stirring at 40°C. After stirring for an additional 4 hr at the same temperature, the reaction mixture was allowed to stand at room temperature overnight. After removal of excess formic acid, the remaining solution was added to a mixture of 10% sodium hydroxide solution (10 m*l*) and dioxane (40 m*l*) and then allowed to stand for one day at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was extracted with ether. The ethereal extract was washed with water and dried. The crystals obtained by evaporating the solvent were recrystallized from ether to give XVIII (100 mg), mp 140—141°C. IR: ν^{nujol} 3450, 1735, 1415, 1380 cm^{-1}.

Found: C, 69.11; H, 9.75%. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80%. Concentration of the mother liquors gave an oily diol (450 mg).

cis-4-Cyano-5-isopropyl-8-methylhydrindane-1,6-dione (XX). A solution of XIX (1.5 g) in dimethylformamide (45 m*l*) was treated with a solution of potassium cyanide (0.94 g) and ammonium chloride (0.59 g) in water (15 m*l*). After stirring at 100°C for 20 hr, the solution was concentrated under reduced pressure and extracted with chloroform. The extract was washed with water and dried. The residue obtained by evaporating the solvent was crystallized from ether to give XXi (0.50 g), mp 117—118°C. IR: ν^{nujol} 2240, 1745, 1720, 1410, 1380 cm^{-1}. NMR: $\delta(CDCl_3)$ 1.0 (d, 6H, J=7 Hz), 1.26 (s, 3H), 3.36 ppm (d-d, 1H, J=3.5—1 Hz).

Found: C, 72.10; H, 8.20; N, 5.97%. Calcd for $C_{14}H_{19}O_2N$: C, 72.07; H, 8.21; N, 6.00%. Concentration of the mother liquor yielded 1.05 g of oil, from which an isomer XXii (20 mg) was separated by silica gel chromatography (eluted by petroleum ether : ether=10 : 1), mp 115—116°C. IR: ν^{nujol} 2250, 1740, 1715, 1410, 1380 cm^{-1}. NMR: δ ($CDCl_3$) 1.08 (d, 6H, J=7 Hz), 1.25 (s, 3H), 2.8 ppm (m, 1H).

cis-4-Carboxy-5-isopropyl-8-methylhydrindane-1,6-dione (IIa). A solution of the isomer XXi (400 mg) in a mixture of acetic acid (7 m*l*) and 6N sulfuric acid (20 m*l*) was heated under reflux for 100 hr. After cooling, the reaction mixture was extracted with chloroform. The extract was washed with water and dried. The crystals obtained by evaporating the solvent were recrystallized from ethyl acetate to give an acid IIa (300 mg, 65%), mp 162—163°C. IR: ν^{nujol} 3500—2500, 1740, 1720, 1690, 1410, 1380, 1185 cm^{-1}. NMR: $\delta(CDCl_3)$ 0.93 (d, 6H, J=7 Hz), 1.15 (s, 3H), 8.95 ppm

(s, 1H).

Found: C, 66.62; H, 7.95%. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99%. Its methyl ester had mp 93—94°C.

cis-*4-Carbomethoxy-5-isopropyl-8-methylhydrindane-1,6-dione (IIb)*. A stereoisomeric mixture of XX (750 mg) was hydrolyzed and followed by esterification with ethereal diazomethane. The methyl ester was obtained by distillation, bp 150°C (bath temp.)/0.1 mmHg, 650 mg (80%). The main isomer was isolated by silica gel chromatography (eluted by petroleum ether : ether=200 : 25), 450 mg, which was recrystallized from ether, mp 93—94°C. IR: ν^{nujol} 1750, 1740, 1710, 1405, 1380, 1170 cm^{-1}. NMR: $\delta(CDCl_3)$ 0.95 (d, 3H, J=7 Hz), 1.04 (d, 3H, J=7 Hz), 1.13 (s, 3H), 3.79 ppm (s, 3H).

Found: C, 67.64; H, 8.33%. Calcd for $C_{15}H_{22}O_4$: C, 67.99; H, 8.33%.