The dimer half-ester acid **35** or **36** (68 mg) was dissolved in methanol (5 ml) and hydrogenated over PtO_2 (10 mg) for 3 hr. The catalyst and solvent were removed, and the oily residue (68 mg) was crystallized. Recrystallization from ether–petroleum ether gave 22 mg, mp 105–107°. This substance gave an intense dark green color with $FeCl_3$. On heating at the melting point gas was evolved, and after cessation of bubbling, the $FeCl_3$ test was redetermined and was negative.

Dimer Diacid 37 or 38.—The diketo ester **30** (4.0 g) was dissolved in water and 40 drops of 45% aqueous KOH was added until the pH rose to 10.5. The solution was stirred for 1 hr at room temperature and then passed through Dowex 50W X12 (H^+ form) column. The eluates (1 l.) were freeze dried, and the lyophilisate (2.7 g) was allowed to stand in ethyl acetate; crystals (740 mg, mp 192–195°) were deposited. Recrystallization (MeOH) gave compound **37** or **38**: mp 194–195°; ir (Nujol) 3500 (m), 1735 (s), 1710 (s), 1685 (m), 1628 cm^{-1} (m).

Anal. Calcd for $C_{14}H_{16}O_6$: C, 59.56; H, 6.43. Found: C, 59.60; H, 6.11.

Registry No.—**7**, 31235-77-5; **8**, 31281-12-6; **8** diacid, 31235-94-6; **9**, 32777-42-7; **10**, 31235-78-6; **11**, 31235-79-7; **13**, 23131-62-6; **14**, 23029-38-1; **14** bisdimethyl amide, 31235-81-1; **15**, 23029-39-2; **16**, 31235-83-3; **17**, 23029-40-5; **18**, 31281-14-8; **19**, 23029-36-9; **20**, 23029-37-0; **22**, 31281-15-9; **23**, 31235-87-7; **24**, 31235-88-8; **25**, 31235-89-9; **26**, 3288-67-5; **27**, 31235-91-3; **28** Cu complex, 31235-92-4; **30**, 31235-93-5; **33–34**, 31228-76-9; **35–36**, 31228-77-0; **37–38**, 31228-78-1.

Acknowledgment.—We wish to acknowledge the support and encouragement of Dr. George deStevens and helpful discussions with Mr. L. Dorfman, whose staff we thank for microanalyses and spectra.

Studies on Terpenes. IV.[1] The Synthesis of a Bridged Tricyclic Ketone Embodying the BCD Ring System of Diterpenes of the Kaurene Class[2]

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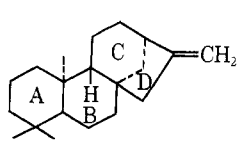
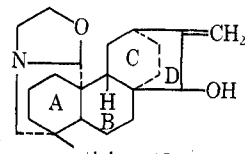
A stereoselective synthesis of *dl*-12-oxo-7,9-ethano-*cis*-$\Delta^{1,2}$-octalin (**4**) is described. This unsaturated tricyclic ketone comprises the BCD ring skeleton present in the kaurene (**1**) class of diterpenes and is a potentially suitable intermediate for the total synthesis of several natural products. Of particular interest is the successful application of the Nagata reagent (Et_2Al/HCN) for effecting the 1,6 addition of HCN to conjugated dienone **24**.

We have previously[1] outlined our concern for the total synthesis of diterpenes which contain, for rings C and D, a bicyclo[3.2.1]- or -[2.2.2]octane moiety. The hydrocarbon (−)-kaurene (**1**) and the alkaloid atisine (**2**) are typical of those members of this class which possess a *trans–anti–cis* fusion of rings ABC. Although a fair number of CD-bridged diterpenes have yielded to total synthesis,[4] the number of suitable synthetic targets remains large and grows rapidly.[5]

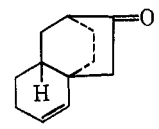


(−)-kaurene (**1**)

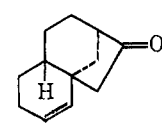


atisine (**2**)

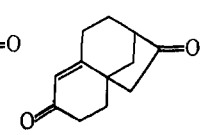
Our work in this field has been based on a ring construction sequence BCDA in contrast to the more commonly employed ABCD sequence[4a,c,d] and has focused on the preparation of compounds **3**, **4**, and **5** as BCD models.[6] In the synthesis of **3**, which has been reported in detail,[1] 6-carbethoxyoctalone (**6**) served as



3



4



5

a convenient starting material. As we intended to make use of a parallel series of reactions for the preparation of **4**, our attention turned to the obtention of isomeric octalone **7**. Although **6** was readily available from the condensation of methyl vinyl ketone with ethyl 4-ketocyclohexanecarboxylate, we anticipated that the analogous reaction with the 3-keto ester **8** would lead to a mixture of octalones (**7** and **9**) (Scheme I) and, accordingly, we embarked initially on an unambiguous, though lengthier, preparation of **7**.

The sequence of reactions which led to **7** is outlined in Scheme II and requires only brief comment. That the cyclization of **11** to **12** occurred in the expected direction was shown by the conversion of the derived tetralin, **13**, to a series of known 2,7-disubstituted naphthalene der vatives, **16**, **16a**, and **16b**, whose physical properties distinguished them from their 1,6 isomers. Lithium–ammonia reduction of **13**, followed by hydrolysis of the resultant enol ether, provided only poor yields of **7**, probably owing to complicating ammonolysis reactions. However, when the corresponding acid, **13a**, was reduced, and the crude enol ether was hydrolyzed under conditions which simultaneously effected reesterification, a satisfactory yield of a mix-

(1) Previous paper in this series: R. A. Finnegan and P. L. Bachman, *J. Org. Chem.*, **30**, 4145 (1965).

(2) This work was supported in part by Research Grants GM-11412 and RG-8004 from the Division of General Medical Sciences, National Institutes of Health, U. S. Public Health Service, Bethesda, Md. Preliminary announcement of this work has been made before the Organic Division at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965, Abstracts, p 25S.

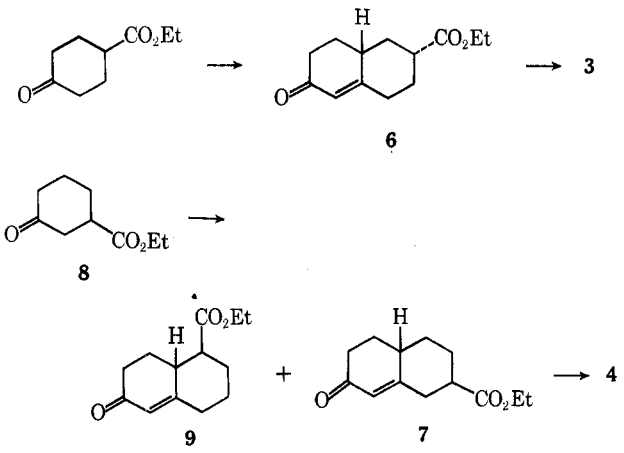
(3) Public Health Service Predoctoral Fellow, 1962–1965. This paper is based on a portion of a thesis submitted by P. L. Bachman to the Department of Chemistry, The Ohio State University, in partial fulfillment of the requirements for the Doctor of Philosophy degree, June 1965.

(4) For example, kaurene: (a) R. A. Bell, R. E. Ireland, and R. A. Partyka, *J. Org. Chem.*, **31**, 2530 (1966); (b) S. Masamune, *J. Amer. Chem. Soc.*, **86**, 289 (1964). Atisine: (c) W. Nagata, *et al.*, *J. Amer. Chem. Soc.*, **89**, 1483 (1967); (d) R. W. Guthrie, Z. Valenta, and K. Wiesner, *Tetrahedron Lett.*, 4645 (1966); (e) S. Mansamune, *J. Amer. Chem. Soc.*, **86**, 291 (1964).

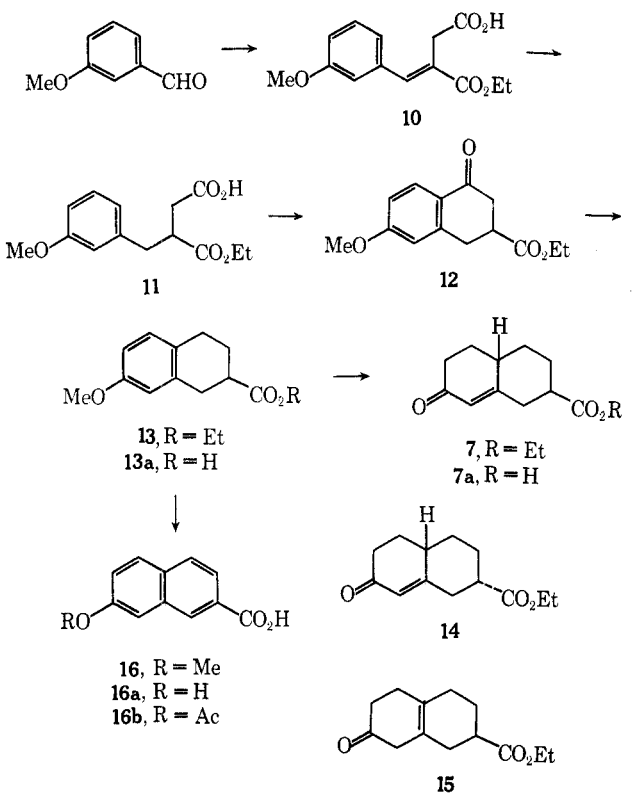
(5) J. R. Hanson, *Progr. Phytochem.*, **1**, 161 (1968); E. Fujita, *Bull. Inst. Chem. Res., Kyoto Univ.*, **48**, 111 (1970), and previous papers in this series.

(6) Compound **5** has been reported recently by D. J. Beames and L. N. Mander, *J. Chem. Soc. D*, 498 (1969).

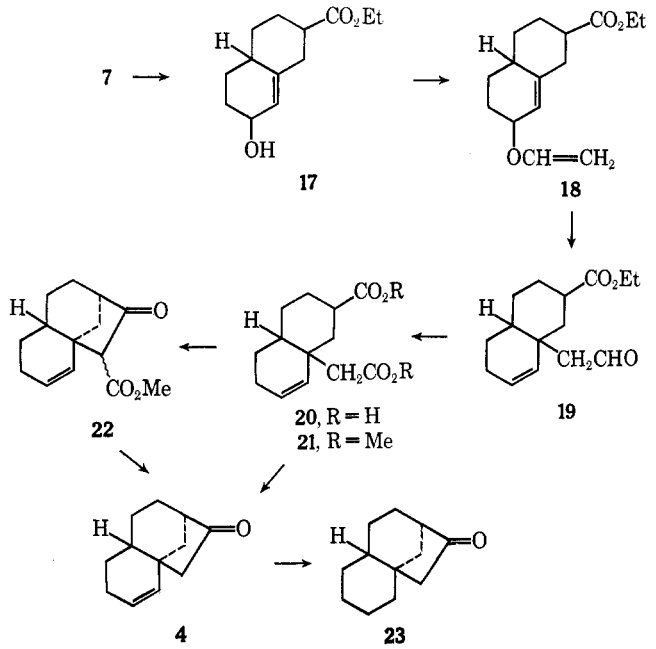
SCHEME I



SCHEME II



SCHEME III



ture of **7**, **14**, and **15** was produced. The mixture contained 75% of the desired octalone, **7**, which could be separated from its isomers by fractional crystallization at low temperature. Equilibration of the mother liquors with acid provided an additional quantity of **7** so that it was obtained pure in 42% yield from the tetralin acid. The stereochemistry implied in formula **7** was assigned on the basis of arguments exactly analogous to those used for the assignment of **6**[1] and need not be reproduced here.

The pathway by which we were able to transform octalone **7** into the tricyclic material **4** is illustrated in Scheme III and follows the identical course employed previously[1] for the conversion of **6** into **3**. It may be noted that, in this instance, the Dieckmann cyclization (**21** → **22**) occurred with much greater facility and yield than in the prior example on the route to **3**. The reasons for this have been discussed in detail.[1]

The structure and stereochemistry of **4** were secured not only on the basis of the usual physical measurements but also are required by its mode of synthesis, the steric course of the key reduction (**7** → **17**) and Claisen rearrangement (**18** → **19**) steps having been amply documented.[1] At this point, however, we were able to append an additional piece of evidence for **4**. The occasion for this was the publication of Masamune's masterful series[4b,e,7] on diterpene total synthesis in which was mentioned the saturated tricyclic ketone **23**.[8] This ketone appeared as an intermediate in a sequence of reactions which resulted in a rigorous proof of its stereochemistry. Thereupon, catalytic reduction of **4** provided a sample of **23** which was spectroscopically indistinguishable from the compound encountered by Masamune. Finally, we note the more recent preparation of **23** by Quasseem, Rogers, and Othman.[9]

Having established the utility of **7** as a starting point for the synthesis of **4**, we returned to the question raised at the beginning of this discussion and illustrated in Scheme I. Condensation of methyl vinyl ketone with the morpholine enamine of keto ester **8** did, indeed, produce a mixture of octalones **7** and **9** in 58% yield. Gas chromatographic analysis indicated that the unwanted isomer, **9**, predominated by a ratio of 2:1 and after a lengthy separation procedure, compound **7** could be obtained pure in only about 10% yield. The reasons for this apparent imbalance in the composition of the enamine mixture derived from **8** are not clear, although the electron-withdrawing effect of the carbethoxy group may be implicated.

In conclusion, it seems appropriate to record here the results of a new line of experiments[10] which, though still incompletely studied, nonetheless offer promise of a direct and efficient method for the preparation of **7**. This route is illustrated in Scheme IV and began with

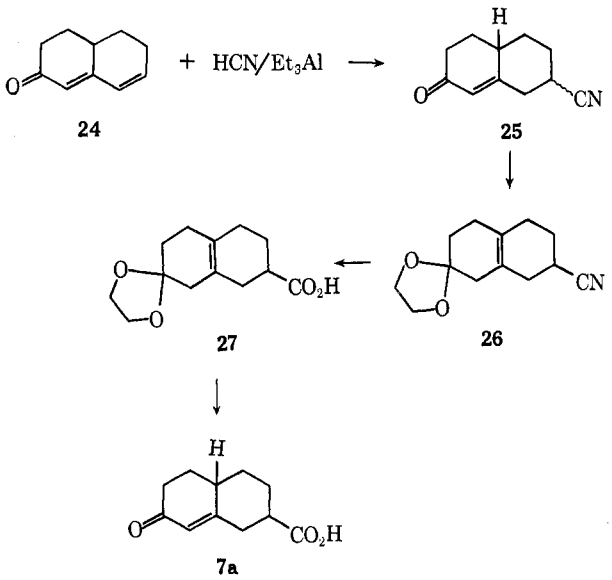
(7) (a) S. Masamune, *J. Amer. Chem. Soc.*, **86**, 288 (1964); (b) *ibid.*, **86**, 290 (1964).

(8) Footnote 7 in ref 7a.

(9) M. A. Quasseem, N. A. J. Rogers, and A. A. Othman, *Tetrahedron*, **24**, 4535 (1968).

(10) These experiments were conducted by Walter J. Ranus.

SCHEME IV



a study of the addition of HCN to the hexalone **24**. At the outset, it could be expected that the monoadduct, **25**, might well be a more reactive HCN acceptor than **24** itself. Indeed, after a very large number of experiments using classical procedures, in which the solvent, temperature, and reactant ratios were varied, no evidence for the persistence of **25**, either as an intermediate or as a product, could be adduced.[11,12] When, almost in desperation, we applied the Nagata procedure[4c,13] using triethylaluminum, we were delighted to find that the cyanoenone **25** was the major product and could be isolated in 48% yield. Subsequent transformations as shown in Scheme IV afforded the octalone acid **7a**, which was already in hand following the saponification of the ethyl ester **7** (Scheme II). This successful monohydrocyanation of a conjugated dienone appears to be without precedent and will, no doubt, serve to expand the utility of the Nagata reagent in organic synthesis.

Experimental Section[14]

3-Carbethoxy-4-(*m*-methoxyphenyl)-3-butenoic Acid (10).—To a dry, 1-l. reaction flask equipped with mechanical stirrer, reflux condenser, and addition funnel was added 450 ml of dry *tert*-butyl alcohol and 19.4 g (0.49 g-atom) of potassium cut into small pieces. When the potassium had all dissolved, the solution was heated to reflux and the system was flushed with nitrogen. A solution of 60.4 g (0.46 mol) of *m*-methoxybenzaldehyde (Eastman) and 108 ml (0.62 mol) of diethyl succinate was added over 18 min with stirring to the gently refluxing solution. After refluxing under nitrogen for an additional 30 min the reaction mixture was concentrated under reduced pressure to one-half its original volume and diluted with 200 ml of 3 *N* hydrochloric acid, and the remaining alcohol was then removed under reduced pressure. After cooling to room temperature the organic phase was separated and the aqueous phase was then extracted with three 100-ml portions of ether. The organic phase and ether extracts were combined, washed with water until neutral, and then extracted with saturated sodium bicarbonate solution. The bicarbonate extract was acidified with concentrated hydrochloric acid and extracted with four 100-ml portions of ether, which were combined, washed with water until neutral, and dried over anhydrous magnesium sulfate. Removal of the ether under reduced pressure yielded 73.3 g (62%) of yellow, nearly immobile oil. No attempt was made to further purify the oil. The yield averaged 70% in six experiments: ir (film) 1724–1695 (broad), 1639, 1600, 1587 cm^{-1}; neut equiv, 263 (calcd for $C_{14}H_{16}O_5$, 264).

3-Carbethoxy-4-(*m*-methoxyphenyl)butanoic Acid (11).—A solution of 73.3 g (0.278 mol) of **10** in 350 ml of absolute ethanol containing 4 g of 5% palladium on charcoal was reduced at atmospheric pressure. Hydrogen uptake was complete in 9 hr. The mixture was filtered through Supercel and the ethanol was removed under reduced pressure, yielding 67.4 g (92%) of viscous yellow oil which was used without further purification: ir (film) 1724–1695 (broad), 1600, 1587 cm^{-1}.

3-Carbethoxy-6-methoxy-1-tetralone (12).—To a 2-l. reaction flask equipped with mechanical stirrer and addition funnel and containing a solution of 67.4 g (0.254 mol) of **11** in 300 ml of dry, thiophene-free benzene was added 82 g (0.38 mol) of powdered phosphorus pentachloride with stirring and cooling during 1 hr. When most of the phosphorus pentachloride had dissolved, the flask was warmed with hot water until solution was complete and the evolution of hydrogen chloride had ceased. The solution was then cooled to 0° and a cold solution of 60 ml (0.51 mol) of anhydrous stannic chloride in 200 ml of dry, thiophene-free benzene was added rapidly with vigorous stirring, while maintaining the temperature below 30°. After stirring for 10 min, 100 ml of crushed ice, 75 ml of ether, and 180 ml of concentrated hydrochloric acid were added, and as soon as all the complex had dissolved the two phases were separated. The aqueous phase was extracted with three 100-ml portions of benzene, which were combined with the organic phase and washed with 60 ml of dilute hydrochloric acid followed by washing with water until neutral. The organic phase was then washed with four 100-ml portions of 5% sodium hydroxide solution followed by washing with water until neutral and finally dried over anhydrous magnesium sulfate. Removal of solvent under reduced pressure yielded 54 g (86%) of a dark, viscous oil. A small portion of the oil was distilled: bp 132° (0.03 mm); ir (film) 1730, 1678, 1603 cm^{-1}.

Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50; O, 25.78; mol wt, 248. Found: C, 67.54; H, 6.39; O, 26.04; mol wt, 255.

A deep red 2,4-dinitrophenylhydrazone derivative was prepared,[15] mp 206–207°.

Anal. Calcd for $C_{20}H_{20}N_4O_7$: N, 13.08. Found: N, 12.90.

2-Carbethoxy-7-methoxytetralin (13).—A solution of 52.8 g of crude tetralone, **12**, in 600 ml of absolute ethanol containing 6.1 g of 5% palladium on charcoal was reduced at atmospheric pressure. The hydrogen uptake (11.4 l.) was complete in 35 hr. The solution was filtered through Supercel and the ethanol was removed under reduced pressure, yielding 42.2 g of dark oil. The oil was distilled, bp 119° (0.25 mm), to yield 32.1 g (64.5%) of light yellow oil: ir (film) 1730, 1610 cm^{-1}; uv (MeOH) 220, 282 mμ (ε 7300, 2000); vpc (211°, 120 cc/min) retention time[14] 10.75 min. A portion of the oil was redistilled for analysis.

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74; O, 20.49; mol wt, 234. Found: C, 71.61; H, 7.93; O, 20.54; mol wt, 235.

7-Methoxy-2-naphthoic Acid (16), 7-Hydroxy-2-naphthoic Acid (16a), and 7-Acetoxy-2-naphthoic Acid (16b).—These derivatives were obtained in standard fashion from the tetralin ester

(11) R. A. Finnegan and W. J. Ranus, unpublished observations.

(12) No less than seven crystalline products were isolated, all the result of multiple addition of HCN followed by partial hydrolysis.[11] The report of O. R. Rodig and N. J. Johnston, *J. Org. Chem.*, **34**, 1949 (1969), on the addition of HCN to the 1,10-dimethyl derivative of **24** nicely complements and illuminates our experience with **24**.

(13) W. Nagata, *Nippon Kagaku Zasshi*, **90**, 837 (1969).

(14) The infrared spectra were measured on the Perkin-Elmer Model 237 spectrophotometer and the ultraviolet spectra were taken on the Perkin-Elmer Model 202 spectrophotometer. The proton magnetic resonance spectra were made on the Varian Associates A-60 spectrometer. Chemical shifts are measured in parts per million (ppm) using deuteriochloroform or carbon tetrachloride as solvent and containing tetramethylsilane as an internal reference standard. Analyses were performed by Dr. A. Bernhardt and Dornis and Kolbe, Mülheim, Germany. Melting points were observed on a Fisher–Johns melting point block and are uncorrected. Gas chromatography was carried out using a Wilkens Aerograph instrument, with helium as carrier gas, and equipped with a 5 ft × 0.25 in. column packed with 20% SF-96 silicone on firebrick and using a 60-ml/min flowr ate, unless otherwise stated. Retention times were measured from the air peak.

All solvents and liquid reagents were distilled before use. Solid reagents were generally analytical grade and were used without further purification.

(15) All DNP derivatives were washed in benzene through a column of Fisher A-540 alumina and recrystallized from a chloroform–isohexane solution, unless otherwise noted.

13 by dehydrogenation and saponification followed by demethylation and acetylation. Full details are given by Bachman.[16] The products and the ir properties follow: **16**, mp 194.5–197.5° (lit.[17,18] mp 195.5–196°); **16a**, mp 264–275° (lit.[17,19] mp 269–270°, 274–275°); **16b**, mp 207–208° (lit.[17,19] mp 210.5–211.5°, 209–210°). The melting point reported[19] for 5-hydroxy-2-naphthoic acid is 211–212° and for 5-acetoxy-2-naphthoic acid, 214–215°.[19]

7-Methoxytetralin-2-carboxylic Acid (13a).—A mixture of 54.6 g of tetralin ester **13**, 18 g of sodium hydroxide, 100 ml of ethanol, and 100 ml of water was refluxed under nitrogen for 4 hr. The reaction mixture was cooled, washed with a little chloroform, acidified with concentrated hydrochloric acid, and extracted with chloroform. The chloroform extract was washed with water until neutral and dried over anhydrous magnesium sulfate. The dried chloroform extract was then concentrated on a steam bath to *ca.* 200 ml, diluted with 200 ml of isohexane, cooled, and filtered to yield 33.9 g of **13a** (71%), mp 125–127°. Several recrystallizations from chloroform–isohexane afforded an analytical sample of light tan crystals, mp 127.0–127.5°.

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.55; H, 6.85.

7β-Carbethoxy-$\Delta^{1,9}$-octalin-2-one (7).—To a 5-l. reaction flask equipped with mechanical stirrer and Dry Ice condensers was added 10.0 g (42.7 mol) of tetralin acid **13a**, 130 ml of dry glyme, and 3 l. of liquid ammonia. The flask was cooled in Dry Ice and 11 g (1.6 g-atom) of lithium, cut into small pieces, was added over 0.5 hr with rapid stirring. The mixture was stirred for an additional 20 min and then 300 ml of absolute ethanol was added as rapidly as possible (*ca.* 8 min) with vigorous stirring. When the blue color discharged, the external cooling was removed and the ammonia was allowed to evaporate for about 9 hr with continuous stirring. When nearly all the ammonia had evaporated and before the reaction mixture could warm, the flask was cooled in an ice bath and 300 ml of ethanolic sulfuric acid (1:1) was added dropwise with stirring followed by an additional 300 ml of absolute ethanol and 300 ml of chloroform. An additional 100 ml of ethanolic sulfuric acid (1:1) was then added and the colorless ammonium sulfate slurry was stirred under nitrogen for 17 hr at room temperature. The slurry was then cooled in an ice bath and 1 l. of water was added with vigorous stirring over a 15-min period. After all the ammonium sulfate had dissolved, the two phases were separated and the aqueous phase was extracted with three 200-ml portions of chloroform. The combined organic phase was then washed with three 500-ml portions of water, which were combined and backwashed with several portions of chloroform totaling 400 ml. The combined chloroform extract and washings were dried over anhydrous magnesium sulfate and concentrated under reduced pressure, yielding 11.7 g of dark oil.

The oil from three such reductions was combined, dissolved in ether, and washed with saturated sodium bicarbonate solution, then with water until neutral. The ether was dried over anhydrous magnesium sulfate and concentrated to yield 31.2 g of dark, neutral oil. The oil was chromatographed on a 766-g Merck acid-washed alumina column measuring 2 × 19 in., and was eluted with 2.75 l. of isohexane–benzene (1:1), 2 l. of benzene–ether (9:1), and 2 l. (4:1), 1 l. (7:3), and 1 l. of chloroform–ethanol (1:1), respectively. The final 1.5 l. of isohexane–benzene through and including the benzene–ether (4:1) afforded 19.7 g of crude keto ester as a yellow oil which distilled at 130° (0.05 mm) to give 18.7 g (58%) of a light yellow oil, uv (EtOH) 239 mμ (ε 13,500).

The oil was crystallized from 120 ml of ether–isohexane (*ca.* 3:1) at −70° and a single recrystallization from 50 ml of solution afforded 9.52 g of nearly pure keto ester **7** as determined by gas chromatography. The concentrated filtrate was again crystallized, twice from 60 ml and then from 40 ml of solution, to afford an additional 1.8 g of purified keto ester. The remaining 7.2 g of crude oil was dissolved in 50 ml of absolute ethanol and 0.20 g of dry hydrogen chloride was then added. After standing for 2 days the solution was made weakly basic with saturated bicarbonate solution and then diluted with 60 ml of water. The solution was then extracted with several portions of ether which were combined, washed with water until neutral, and dried over anhydrous magnesium sulfate. Removal of the ether afforded 6.8 g of dark oil which was distilled as above to yield 6.5 g of yellow oil. Two recrystallizations from ether–isohexane afforded an additional 2.2 g of purified keto ester for a total of 13.5 g of **7** (42%): uv (EtOH) 238 mμ (ε 14,600); ir (film) 1736, 1684, 1631 cm^{-1}.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16; O, 21.59; mol wt, 222. Found: C, 70.15; H, 8.08; O, 21.81; mol wt, 210.

A deep red 1,4-dinitrophenylhydrazone[15] was prepared, mp 177–179°.

Anal. Calcd for $C_{19}H_{22}O_6N_4$: C, 56.71; H, 5.51; N, 13.92. Found: C, 56.77; H, 5.66; N, 14.05.

Ethyl 3-Ketocyclohexanecarboxylate (8).—This substance was prepared from ethyl *m*-hydroxybenzoate by the procedure used previously for the preparation of the corresponding 4-keto ester.[1] The product had bp 80–83° (0.6 mm), [lit.[20] bp 138° (18 mm)]. The 2,4-dinitrophenylhydrazone[15] derivative was obtained as orange needles, mp 121–122°.

Anal. Calcd for $C_{15}H_{18}O_6N_4$: C, 51.42; H, 5.18; N, 15.99. Found: C, 51.38; H, 5.13; N, 15.80.

The Reaction of Ethyl 3-Ketocyclohexanecarboxylate (8) with Methyl Vinyl Ketone. The Formation of Octalones 7 and 9.—A solution of 50 g (0.296 mol) of **8**, 25.8 g (0.296 mol) of morpholine, and 150 ml of benzene in a 500-ml round-bottomed flask equipped with a Dean–Stark water separator was refluxed overnight under a nitrogen atmosphere, during which time 5.5 ml (0.306 mol) of water was removed. The solvent and excess morpholine were removed under reduced pressure and the remaining orange oil was cooled to room temperature and dissolved in 100 ml of dry, thiophene-free benzene. To this solution was added, over a 40-min period, a solution of 21.2 g (0.30 mol) of freshly distilled methyl vinyl ketone in 50 ml of dry, thiophene-free benzene. The resulting solution was slowly heated, and then refluxed for 3 hr under a nitrogen atmosphere. The benzene (130 ml) was then removed by distillation, a solution of water (140 ml) and ethanol (110 ml) was added, and the resulting mixture was refluxed for 17 hr under an atmosphere of nitrogen. The reaction mixture was then cooled, diluted with 400 ml of water, and extracted with two 150-ml portions and one 50-ml portion of ether. The combined ether extract was washed with 40 ml of 2 *N* hydrochloric acid and then with water until neutral. The combined acid and aqueous washings were backwashed with three 50-ml portions of ether, which were combined, washed with water until neutral, and combined with the rest of the ether extract. After drying over anhydrous magnesium sulfate, the ether was removed under reduced pressure to give 49.7 g of yellow oil: ir (film) 1730, 1678, 1623 cm^{-1}. Gas chromatography[14] (205°) showed three peaks: 2.2 min (**8**, 8%), 9.7 min (**9**, 61%), and 11.6 min (**7**, 31%). A lengthy and rather inefficient procedure was used to separate these components and need not be recounted here (see ref 16 for details). Suffice it to note that only 6.2 g (9.5%) of **7** was obtained in a pure state. This sample was shown to be identical with the previously prepared **7** by spectroscopic and gas chromatographic comparisons, as well as by mixture melting point determinations (no depression) on their respective 2,4-dinitrophenylhydrazone derivatives.

The isomeric octalone **9** was obtained in a purity of only 90%, being contaminated by **7**. The structure of **9** was assured, however, by its method of formation and the fact that it was a conjugated ketone: ir (film) 1730, 1678, 1623 cm^{-1}; uv (EtOH) 237 mμ (ε 15,800), distinguishable by gas chromatography from **7** and **14**. Furthermore, a 2,4-dinitrophenylhydrazone[15] derivative was obtained, deep red crystals, mp 123.5–125.5°.

Anal. Calcd for $C_{19}H_{22}N_4O_6$: C, 56.71; H, 5.51. Found: C, 56.67; H, 5.62.

$\Delta^{1,9}$-Octalin-2-one-β-carboxylic Acid (7a). Saponification of 7.—A solution of 136 mg of purified keto ester **7**, 3 ml of methanol, 3 ml of water, and 200 mg of anhydrous potassium carbonate was refluxed under nitrogen overnight. The solution was cooled, diluted with water, and washed with a little ether. The solution was then acidified with concentrated hydrochloric acid and extracted with four portions of chloroform totaling approximately 15 ml. The extracts were combined, washed with water until neutral, and dried over anhydrous magnesium sulfate. The chloroform solution was then concentrated on a steam bath and the acid was crystallized by the addition of isohexane, 69 mp 136–147°. Several recrystallizations followed by sublima-

(16) F. L. Bachman, Ph.D. Thesis, The Ohio State University, 1965.
(17) H. L. Holmes and L. W. Trevoy, *Can. J. Res.*, **22B**, 56 (1944).
(18) W. H. Perkin and G. Tattersall, *J. Chem. Soc.*, **91**, 486 (1907).
(19) C. Butler and F. A. Royle, *ibid.*, **123**, 1649 (1923).
(20) A. Einhorn, *Justus Liebigs Ann. Chem.*, **291**, 301 (1896).

tion at 106° (0.06 mm) afforded an analytical sample, mp 146–148°.

Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02, H, 7.27. Found: C, 67.73; H, 7.21.

7β-Carbethoxy-Δ^{1,9}-octalin-2β-ol (17).—To a thoroughly dried 500-ml round-bottomed flask equipped with magnetic stirrer was added 250 ml of dry tetrahydrofuran (freshly distilled from lithium aluminum hydride) and 19 g (92 mmol) of lithium tri-*tert*-butoxyaluminum hydride. The resulting opaque solution was cooled to 0° and a solution of 5.16 g (23 mmol) of keto ester **7** in 150 ml of tetrahydrofuran was then added dropwise with stirring and under nitrogen during 40 min. Stirring was continued for 0.5 hr with cooling and then for 1 hr while warming to room temperature. The reaction mixture was then poured into a mixture of 500 ml of water, 32 ml of concentrated hydrochloric acid, and 800 ml of crushed ice. The resulting solution was saturated with sodium chloride and extracted with one 160-ml portion and ten 100-ml portions of ether. The combined ether extract, which was kept cold, was then washed with four 100-ml portions of saturated sodium chloride solution, which were combined and back-washed with four 50-ml portions of ether. The ether extract and washings were combined and dried over Drierite. Removal of solvent under reduced pressure afforded 5.2 g of yellow oil, which was distilled (air bath) at 115° (0.10 mm) to yield 4.81 g (92%) of colorless hydroxy ester: ir (film) 3413, 1736, 1669 cm^{-1}. The nmr spectrum of **17** showed the vinyl hydrogen signal as a broad singlet (half-width 5 cps) at 5.48 ppm. In accordance with previous arguments,[1] this small coupling of the vinyl hydrogen with the adjacent carbinol proton verifies the assignment of the quasiequatorial position to the hydroxyl group.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99; O, 21.40. Found: C, 69.45; H, 8.92; O, 21.59.

Preparation of Vinyl Ether 18.—To a dry 250-ml round-bottomed flask equipped with magnetic stirrer and reflux condenser was added a solution of 4.46 g (20 mmol) of freshly distilled hydroxy ester **17** in 120 ml of destabilized,[1] freshly distilled ethyl vinyl ether and 1 g of mercuric acetate. The solution was gently refluxed with stirring under nitrogen for 18 hr. Approximately 100-mg portions of mercuric acetate were added at about 3-hr intervals for the first 9 hr. The solution was cooled, quickly washed twice with cold, dilute sodium carbonate solution, and dried over anhydrous potassium carbonate. Removal of the ether on a steam bath under a stream of nitrogen yielded 5.57 g of pale yellow oil. The oil was rapidly chromatographed over 50 g of Woelm neutral alumina, grade 1, with 1.5 l. of isohexane. Removal of the isohexane under reduced pressure yielded 3.38 g (68%) of vinyl ether **18** as a clear, yellow oil: ir (film) 1736, 1637, 1613 cm^{-1}.

Pyrolysis of 18. The Preparation of Aldehyde 19.—A heavy-walled, Pyrex tube containing 3.17 g of vinyl ether **18** sealed under nitrogen was heated in a refluxing ethylene glycol bath at 196° for 4 hr. After cooling to room temperature, the oil was carefully chromatographed on a column of 83 g of 100–200 mesh florisil measuring 1 × 14 in. The oil was eluted with 1.7 l. of isohexane, 0.25 l. of isohexane–benzene (9:1), and 0.25 l. of benzene–ethanol (9:1), respectively, and the separation was followed by gas chromatography of the concentrated eluents. The isohexane–benzene and benzene–ethanol fractions yielded 2.80 g of crude aldehyde as a yellow oil which was distilled (air bath) at 105° (0.06 mm) to afford 2.64 g (83%) of colorless aldehyde: ir (CCl_4) 2747, 1739, 1727 cm^{-1}; vpc[14] retention time (218°) 11.8 min. Repeated microanalysis provided consistently low (1–2%) values for carbon.

The 2,4-dinitrophenylhydrazone derivative, yellow crystals, had mp 124–127°.

Anal. Calcd for $C_{21}H_{26}N_4O_6$: N, 13.02. Found: N, 13.37.

Oxidation of the Aldehyde 19. Preparation of the Diacid 20.—To a solution of 2.28 g (9.3 mmol) of aldehyde **19**, 58 of ethanol, and 20 ml (11.3 mmol) of silver nitrate solution (3.70 g dissolved in 39 ml of water) was added 75 ml of sodium hydroxide solution (3.72 g dissolved in 150 ml of water) in 30 min with stirring, under a nitrogen atmosphere. The mixture was stirred overnight (13 hr) and then filtered, acidified with concentrated hydrochloric acid, diluted with 100 ml of water, and extracted with two 50-ml and three 25-ml portions of chloroform. The chloroform extract was washed with water and dried over anhydrous magnesium sulfate. The chloroform was then removed under reduced pressure to give 2.27 g (104%) of a yellow glass, which was triturated with isohexane containing a little chloroform and filtered to afford 2.21 g of flocculant white solid, mp 100–120°. Recrystallization from isohexane–ethyl acetate yielded 0.88 g of fine white powder, mp 176.5–179.0°. A second crop afforded an additional 0.42 g for a total of 1.20 g (55%). The remaining 1 g of resinous acid could not be crystallized. Three additional recrystallizations from boiling acetonitrile afforded an analytical sample, mp 182.5–183°.

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53, H, 7.61; mol wt, 238.3. Found: C, 65.75; H, 7.67; mol wt, 236.

Attempts to convert the diacid directly into the bridged ketone **4**, either by pyrolysis of its barium salt or with acetic anhydride, were not satisfactory. Ketone **4** was obtained in only 12% yield.[16]

The Diester 21.—A solution of 0.77 g of diacid **20** in a few milliliters of ether–methanol (1:1) was treated with a freshly prepared ethereal solution of diazomethane. The resulting solution was concentrated on a steam bath, and the residue was distilled (air bath) at 125° (0.05 mm) to give 0.86 g of colorless diester **21**, ir (CCl_4) 1742 cm^{-1}, vpc[14] retention time (223°) 9.0 min. A sample was redistilled for analysis.

Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33; O, 24.03; mol wt, 266.3. Found: C, 67.68; H, 8.36; O, 24.22; mol wt, 256.

Dieckmann Cyclization of Diester 21. 11-Carbomethoxy-12-oxo-7,9-ethano-*cis*-Δ^{1,2}-octalin (22).—To a slurry of sodium methoxide (6.74 mmol) in 10 ml of benzene, contained in a 50-ml round-bottomed flask equipped with a magnetic stirring bar, was added, during 25 min, a solution of 0.862 g (3.24 mmol) of diester **21** in 20 ml of benzene. The flask was then placed in an oil bath preheated to 92°, and the stirred slurry was gently refluxed for 18 hr under an atmosphere of nitrogen. After cooling to room temperature, the amber-colored slurry was quickly poured with rapid stirring into an ice-cold solution of 50 ml of water and 5 ml of glacial acetic acid, and when the color had been discharged, the phases were separated. The aqueous phase was saturated with sodium chloride and extracted with four 10-ml portion of benzene, which were combined with the original benzene phase and washed with three 20-ml portions of water. The combined washings were back-washed with one 10-ml portion of benzene, which was combined with the rest of the benzene phase and dried over anhydrous magnesium sulfate. Removal of the benzene under reduced pressure gave 740 mg (97%) of yellow oil which was distilled (air bath) at 95° (0.08 mm) to furnish 471 mg (62%) of colorless β-keto ester **22** which gave a deep green color with ferric chloride: ir ($CHCl_3$) 1751, 1727 cm^{-1}.

12-Oxo-7,9-ethano-*cis*-Δ^{1,2}-octalin (4).—A solution of 205 mg of β-keto ester **22**, 3.5 ml of *p*-dioxane, 1 ml of water, and 0.5 ml of concentrated hydrochloric acid was refluxed for 13.5 hr under an atmosphere of nitrogen. The dark solution was cooled to room temperature, diluted to 50 ml with water, and extracted repeatedly with small portions of ether totaling 30 ml. The combined ether extract was washed with two small portions of dilute aqueous sodium carbonate solution and then with water until neutral. The combined carbonate and water washings were then back-washed with a little ether, which was combined with the rest of the ether and dried over anhydrous magnesium sulfate. The ether was removed on a steam bath under a stream of nitrogen to give 150 mg (97.5%) of yellow oil which was distilled (air bath) at 60° (0.19 mm) to afford 131 mg (85%) of colorless ketone, **4**, ir (CCl_4) 1748 cm^{-1}, vpc retention time[14] (212°), 4.6 min. Additional retention times, also measured at 212° and a flow rate of 60 cc/min, were as follows: 13.4 min (6 ft × 0.25 in. 20% DEGS on firebrick); 21.2 min (6 ft × 0.25 in. 20% NPGS on firebrick). The nmr spectrum showed a 14-proton multiplet between 1.0 and 1.3 ppm and a 2-proton multiplet between 5.3 and 5.8 ppm. In close analogy with the spectrum previously discussed for **3**,[1] the vinyl multiplet could be analyzed as an AB quartet (J = 10 cps) with the lower field pair further split (*ca.* 2 cps) by allylic coupling.

In spite of repeated redistillation and gas chromatographic purification, microanalysis (three determinations) provided consistantly low (*ca.* 1.4%) values for carbon. The molecular ion at m/e 176 in the mass spectrum,[21] however, assured its proper formulation.

Anal. Calcd[22] for $C_{12}H_{16}O$: rel intensity (M + 1/M) × 100, 13.3; (M + 2/M) × 100, 1.1. Found: (M + 1/M) × 100, 13.3; (M + 2/M) × 100, 1.3.

(21) Morgan Schaffer Corp., Montreal, Quebec, Canada.

(22) K. Biemann, "Mass Spectrometry," McGraw-Hill, New York, N. Y., 1962, pp 63, 64.

Preparation of a 2,4-dinitrophenylhydrozone derivative[15] provided a mixture of orange and yellow crystals, mp 180–201°. Repeated crystallization from methanol did not alter the melting point.

Anal. Calcd for $C_{18}H_{20}O_4N_4$: C, 60.67; H, 5.66; N, 15.72. Found: C, 60.47; H, 5.58; N, 15.97.

Two additional recrystallizations, however, from 95% ethanol afforded yellow needles, mp 201–201.5°.

Anal. Found: N, 16.19.

12-Oxo-7,9-ethano-*cis*-decalin (23).—A solution of 80 mg of ketone **4** in 2 ml of methanol, containing 7 mg of 5% palladium on carbon, was reduced at atmospheric pressure. Hydrogen uptake was complete in 1 hr. The solution was filtered and the carbon was washed with a little methanol. The filtrate was then concentrated under reduced pressure at room temperature to afford 81 mg of colorless oil which was distilled (air bath) at 60° (0.05 mm) to give 70 mg (88%) of colorless **23**, ir (film) 1748 cm^{-1}. The ir ($CHCl_3$) was indistinguishable from that of a sample of **23** independently prepared by Masamune.[8] We thank Professor Masamune for graciously providing us with this spectrum.

7-Cyano-$\Delta^{1,9}$-octalin-2-one (25).[10]—To a 1-l. round-bottomed flask fitted with a mechanical stirrer, dropping funnel, and condenser, and containing 425 ml of anhydrous ether, 11.5 g (0.1 mol) of triethylaluminum, and 5.4 g (0.2 mol) of HCN, was added over 15 min with stirring, cooling at 0°, and under nitrogen, a solution in ether (50 ml) of 14 g (0.095 mol) of hexalone **24**.[23] After 1 hr, the ice bath was removed, the solution was allowed to warm to room temperature, and stirring was continued for 6 days. After 2 days, the solution became dark and gummy solid began adhering to the walls of the flask. After the sixth day, 20 ml of ethanol was cautiously added to the mixture, followed by dropwise addition of 40 ml of 2 *N* HCl. The gummy residue dissolved and the ether layer was separated and washed with two 200-ml portions of water, dried ($MgSO_4$), and evaporated to give 10 g of yellow solid, mp 65–83°. This material was chromatographed on a column of 350 g silica gel and from the chloroform eluates were obtained 8 g (48%) of nitrile **25**. Four recrystallizations from isohexane–benzene provided analytically pure material: mp 118–119°; ir (KBr) 2227, 1667, 1623 cm^{-1}; uv (EtOH) 236 mμ (ε 15,700); nmr[14] 1.6–2.9 (m, 11 H), 3.23 (broad s, 1 H, CHCN), 5.99 ppm (s, 1 H, C=CH).

Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.41; H, 7.54; N, 8.10.

The Ketal 26.[10]—A solution of 1.7 g of cyanooctalone **25**, 1.0 g of ethylene glycol, and 15 mg of *p*-toluenesulfonic acid in 15 ml of benzene was heated at reflux in a 25-ml round-bottomed flask fitted with a Dean–Stark water separator. After 12 hr, the solution was cooled, washed with 5 ml of water, dried ($MgSO_4$), and evaporated. The residue (1.9 g) was distilled (air bath) at 140–143° (0.05 mm) to give 1.5 g (71%) of **26** as a colorless oil: ir (film) 2240 cm^{-1}; nmr[14] 1.7–2.3 (m, 11 H), 2.8 (very broad s, 1 H, CHCN), 4.0 ppm (s, 4 H, $-OCH_2CH_2O-$).

Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.10; H, 7.74; N, 6.53.

Hydrolysis of Cyano Ketal 26. The Ketal Acid 27.[10]—A solution of 15 ml of 95% ethanol containing 2.0 g of nitrile **26** and 1.5 g of KOH was heated at reflux under a nitrogen atmosphere for 36 hr. After being cooled, the reaction mixture was poured onto ice and extracted with chloroform. From the chloroform solution, after being dried and evaporated, there was obtained a small amount of solid which was recrystallized from ethyl acetate, mp 143–144°, and identified spectroscopically as the amide corresponding to the acid **27**. From the aqueous layer, after acidification with concentrated HCl, extraction with chloroform, and drying and evaporation of the organic extract, there was obtained 1.9 g of crude acid, **27**, mp 95–110°. Recrystallization from a benzene–isohexane mixture afforded 1.4 g (66%) of acid **27**: mp 113–114°; ir (KBr) 2840, 2560, 1684 cm^{-1}; nmr[14] 1.7–2.6 (m, 13 H), 4.0 (s, 4 H, $-OCH_2CH_2O-$), 10 ppm (broad s, 1 exchangeable H, COOH).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.55; H, 8.20.

Hydrolysis of Ketal 27. The Octalone Acid 7a.[10]—A solution in 75% aqueous acetone of 300 mg of ketal acid **27** and 3 drops of concentrated HCl was maintained at room temperature for 17 hr. The mixture was then concentrated and extracted with ether. After the ether extract was dried and evaporated, there was obtained 198 mg (81.5%) of crude acid **7a**, mp 119–127°. Recrystallization from benzene–isohexane solution provided material with mp 128–129° whose ir (KBr) was somewhat different from that of the sample of **7a**, mp 146–148°, previously obtained (see above) from the hydrolysis of ester **7**. There was no depression of melting point on admixture of the two specimens (137–144°) and the ir spectra of the two samples in chloroform solution were indistinguishable, indicating that they are dimorphs.

Registry No.—**4**, 31129-07-4; **4** 2,4-DNP, 31129-08-5; **7**, 31129-09-6; **7** 2,4-DNP, 31129-10-9; **7a**, 31129-11-0; **8** 2,4-DNP, 31129-12-1; **9**, 31081-93-3; **9** 2,4-DNP, 31129-13-2; **10**, 31129-14-3; **11**, 31129-15-4; **12**, 31129-16-5; **12** 2,4-DNP, 31129-17-6; **13**, 31129-18-7; **13a**, 31129-19-8; **17**, 31129-20-1; **19**, 31129-21-2; **19** 2,4-DNP, 31129-22-3; **20**, 31129-23-4; **21**, 31129-24-5; **22**, 31081-94-4; **23**, 31129-25-6; **25**, 31129-26-7; **26**, 31129-27-8; **27**, 31129-28-9.

(23) This compound was prepared by reduction of 2-methoxynaphthalene according to the procedure of A. J. Birch, A. R. Murray, and H. Smith, *J. Chem. Soc.*, 1945 (1951).