Acknowledgment.—We are indebted to Dr. Amira Sattar for valuable discussions of this work. In addition, we thank Mr. Don Miles and Mrs. Kreuvul Sophasan for carrying out two of the acetylation experiments and Mrs. Catherine Maxey for performing some of the rate calculations.

Studies of the Synthesis of the B, C, and D Rings of Gibberellic Acid[1]

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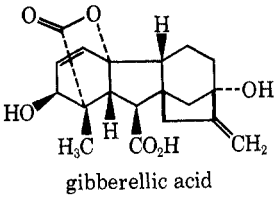
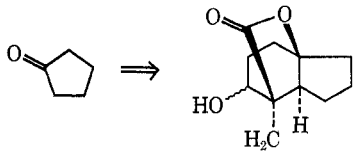
Cyclopentenones **3** and **7** have been condensed with butadiene to give the tetrahydroindene **4** and tetrahydro-1-indanone **8** derivatives, respectively. The tetrahydroindene **4** results from condensation on the enolic double bond of the enol form of **3** and is of no use for the synthesis of gibberellic acid. The tetrahydro-1-indanone **8** was saponified and subjected to iodolactonization to give iodolactone **10**. Removal of the iodine gave keto lactone **16** which was condensed with the anion of dimethyl sulfone to give the β-keto sulfone **17**. Oxidation of **17** afforded the triketone **18** which cyclized smoothly with base to give the tricyclic sulfone **19** possessing the skeleton of the B, C, and D rings of gibberellic acid. Attempts to remove the extraneous D ring keto group from sulfone met with failure. An alternative elaboration of **17** was carried out. The extraneous keto group of the β-keto sulfone moiety was removed by a six-step sequence to give the diketo sulfone **29**. However, cyclization of **29** failed to give tricyclic material and the corresponding methyl ester, **32**, cyclized to an undesired β-keto sulfone **33**.

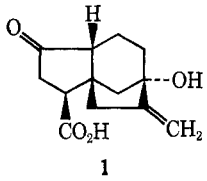
The total synthesis of the gibberellins has attracted a great deal of attention in the past several years. In considering the problem, it is attractive to construct the A ring in the final stages of the synthesis because of its great chemical sensitivity. Our earlier model studies provided an attractive approach for assembling the A ring as illustrated by the elaboration of cyclopentanone into the AB ring system of gibberellic acid.[5]



gibberellic acid



Therefore, our synthetic target is the tricyclic compound **1**.[6] Our general approach to this problem is to



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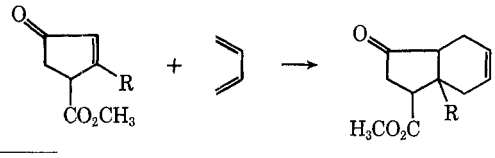
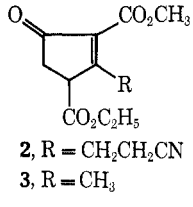
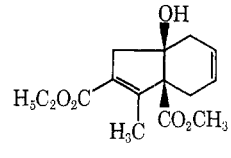
begin with a substituted cyclopentenone and generate the BC rings by means of a Diels–Alder reaction. Our first effort involved the condensation of cyclopentenone **2** with 2-methoxybutadiene, a reaction which gives a monocyclic product.[7] In a further attempt, the condensation of butadiene with the more easily obtained cyclopentenone **3** was examined. A simple adduct was obtained in good yields, but the material proved to have structure **4** rather than the expected structure **5**. This result appears to be another manifestation of the enolic character of **2** and **3**.





2, R = CH_2CH_2CN
3, R = CH_3



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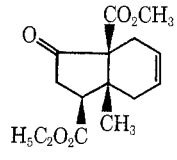

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The structure follows from both spectroscopic examination and chemical transformations. The ultraviolet spectrum shows λ_{max}^{EtOH} 231 nm (ε 6550) as found for similar compounds.[7] The infrared spectrum shows hydroxyl absorption, and the material did not form a 2,4-dinitrophenylhydrazone. The pmr spectrum shows the methyl group as a triplet (J = 2 Hz) owing to homoallylic coupling as previously observed in related compounds.[7] Saponification affords the corresponding dibasic acid and catalytic hydrogenation readily reduces the disubstituted double bond. Reduction of the dihydro derivative with potassium in liquid ammonia affords the saturated dibasic acid. Treatment of **4** with a

(1) The authors gratefully acknowledge financial support from the National Science Foundation (Grant GP 9427) and a Public Health Service Career Program Award (1-K3-NB-28,105) from the National Institute of Neurological Disease and Blindness.

(2) Alfred P. Sloan Research Fellow, 1965–1967.

(3) National Institutes of Health Postdoctoral Fellow, Fellowship 1-F2-GM-39,115-01.

(4) NDEA Predoctoral Fellow, 1966–1969.

(5) L. J. Dolby and R. J. Milligan, *J. Amer. Chem. Soc.*, **88**, 4536 (1966).

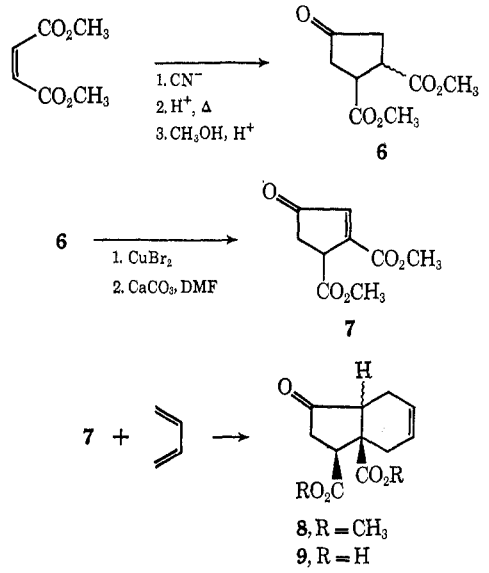
(6) All asymmetric synthetic products described are racemic mixtures. Only one enantiomorph for each is drawn for convenience of representation and discussion. Nomenclature is for the enantiomorph indicated.

(7) L. J. Dolby, C. A. Elliger, S. Esfandiari, and K. S. Marshall, *J. Org. Chem.*, **33**, 4508 (1968).

solution of sodium iodide and acetic acid in refluxing diglyme yielded a mixture of *cis*- and *trans*-1-methyl-2-carboxyindan. This mixture and the corresponding mixture of methyl esters were identified by comparison with authentic material.

Since our efforts to elaborate **2** met with failure, we turned to a new cyclopentenone derivative, 3,4-dicarbomethoxycyclopent-2-enone. This material may be obtained in large quantity and serves well as a dienophile (Scheme I).

SCHEME I

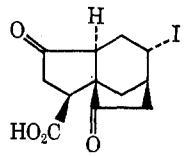


The structure and purity of the material from the dimerization of dimethyl maleate with sodium cyanide are uncertain.[8] The spectra are complicated by the presence of enolic material and a number of stereoisomers is possible. However, all of the possible structures would lead to a mixture of *cis*- and *trans*-cyclopentanone-3,4-dicarboxylic acid on vigorous acid hydrolysis. The trans isomer can be obtained from the mixture by crystallization.[8] In practice it is most convenient to esterify the mixture of acids and use the ester mixture in the next steps. Bromination of the ester mixture with cupric bromide gives a mixture of bromo ketones which is dehydrohalogenated by the action of calcium carbonate in *N*,*N*-dimethylformamide to give the desired 3,4-dicarbomethoxycyclopent-2-enone. The yield of the unsaturated ketone is about 25% based on dimethyl maleate.

The Diels–Alder condensation of the unsaturated ketone with butadiene proceeds smoothly to give a mixture of the tetrahydro-1-indanone diesters **8**. Although the kinetic products would be anticipated to possess cis-ring junctures, the isolated products also contain trans-fused material (14%), owing to epimerization under the reaction conditions. Under similar conditions, cyclopentenone and butadiene produce both diastereomers of the expected tetrahydro-1-indanone.[9]

Saponification of the crude reaction mixture gives a mixture (75% cis to 25% trans) of the corresponding diacids **9** in 77% yield based on cyclopentenone **7**. A pure sample, mp 176–177.5° dec, is easily isolated by crystallization and contains the same cis to trans ratio of diacids.

The next stages of the synthesis required selective oxygenation of the double bond to introduce the bridgehead oxygen of the CD ring of gibberellic acid and subsequent elaboration of the ring juncture carbonyl function. Selective oxygenation of the double bond was accomplished by iodolactonization to give **10**. The structure and stereochemistry of this material were established by X-ray crystallography.[10]



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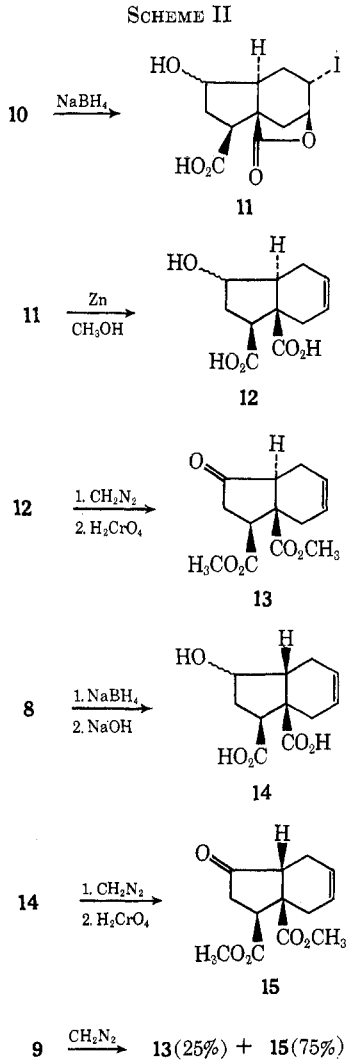
With the relative stereochemistry of the iodolactone **10** established, it is possible to determine the stereochemistry of the Diels–Alder adducts **8** and their corresponding diacids **9** (Scheme II).

SCHEME II



The tetrahydro-1-indanone **13** with a known trans-ring juncture is prepared from the *trans*-hydroxy diacid

(8) A. Michael and J. Ross, *J. Amer. Chem. Soc.*, **53**, 2394 (1931).
(9) H. O. House and G. H. Rasmusson, *J. Org. Chem.*, **28**, 31 (1963).
(10) The authors are indebted to Professor Ian Paul and his collaborators of the University of Illinois for the X-ray crystallographic study of the iodolactone **10**: C. A. Maier, J. A. Kapecki, and I. C. Paul, *ibid.*, **36**, 1299 (1971).

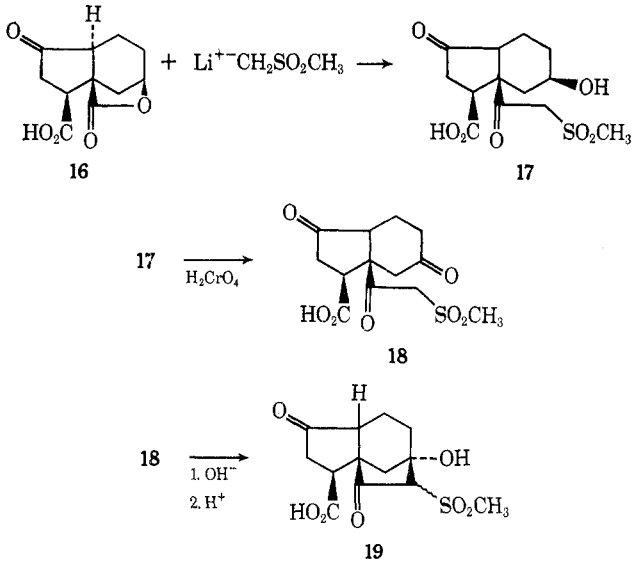
12, mp 170–171°, an intermediate in the degradation of the iodolactone **10** (see Scheme II). The pmr spectrum of **13** shows two 3 H singlets at δ 3.68 and 3.70 for the carbomethoxy protons. Sodium borohydride reduction of a pure sample of the Diels–Alder adducts **8** followed by saponification leads to the *cis*-hydroxy diacid **14**, mp 154–156°. Chromic acid oxidation of the esterified diacid **14** gives the tetrahydro-1-indanone **15** with a cis-ring juncture. The pmr spectrum shows two 3 H singlets at δ 3.70 and 3.72 for the carbomethoxy protons. The cis isomer **15** can also be isolated from the diazomethane esterified keto diacid **9** by crystallization.

The pmr spectrum of the purified Diels–Alder adduct **8** indicates the presence of 86% of the cis isomer and 14% of the trans isomer. Examination (pmr) of the diazomethane esterified diacids **9** indicates an isomeric mixture of 75% cis and 25% trans. The yields (19–25%) of **10** are the same starting with either crude or purified diacid. It is apparent that only the trans isomer undergoes iodolactonization.

The synthesis was continued from compound **10** in spite of the fact that it possesses a trans-ring juncture, whereas the corresponding fusion in gibberellic acid is cis. Since the keto group of the five-membered ring makes all of the intermediates subject to epimerization at the ring juncture, this synthetic approach is foredoomed to failure unless the cis-fused isomer of the critical intermediate **1** is at least comparable in stability to the trans-fused isomer. We take the optimistic view of this situation.

Accordingly, the iodine was efficiently replaced by hydrogen through the action of tri-*n*-butyltin hydride.[11] The keto lactone **16** was then elaborated following the method developed by House and his collaborators[12] (Scheme III). The condensation of **16** with dimethyl

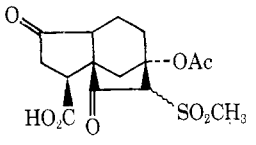
SCHEME III



sulfone proceeds smoothly to give the β-keto sulfone **17** in 55% yield. Both compounds **17** and **18** obtained by chromic acid oxidation of **17** exist at least in part as lactols as indicated by an absorption at 1780 cm^{-1} in their infrared spectra.

(11) H. G. Kuivila, *Advan. Organometal. Chem.*, **1**, 47 (1964).
(12) H. O. House and J. K. Larsen, *J. Org. Chem.*, **33**, 61 (1968).

Due to the possibility of base-induced epimerization of the ring juncture during the formation of **17**, the stereochemistry at the ring juncture is not definitely known beyond the keto lactone **16**. The triketone **18** is smoothly cyclized to **19**, obtained in 68% yield, by action of methanolic potassium hydroxide. This is in contrast to the cyclization of a very closely related compound with a cis-ring juncture which gave an equilibrium mixture containing only 10% of tricyclic material.[12] The structure of **19** follows from its spectral properties and subsequent transformations. The pmr spectrum of **18** shows a broad multiplet at δ 4.60 (two protons) which is ascribed to the methylene protons adjacent to the sulfone. This absorption is absent from the spectrum of **19**, but a sharp singlet appears at δ 4.44 (one proton) attributed to the methine proton adjacent to the sulfone. Moreover, the bridgehead hydroxy group was acetylated with acetyl chloride to give the tricyclic acetate **20** which was esterified with diazomethane to yield the ester **21**. The spectral properties of these materials were in agreement with structure **19**.



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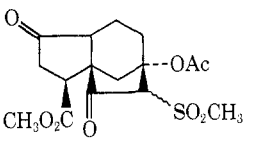

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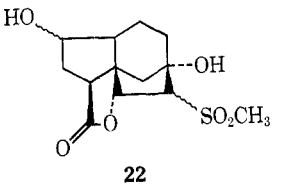
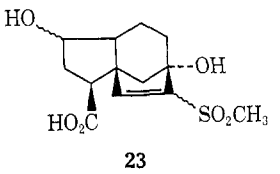
The next problem in elaborating compound **19** was the removal of the extraneous oxygen of the D ring. We hoped that reduction of **19** would lead to lactone **22**. The action of strong base in **22** would then likely give the vinyl sulfone **23**. However, reduction of **19** with sodium borohydride afforded an intractable mixture of



22



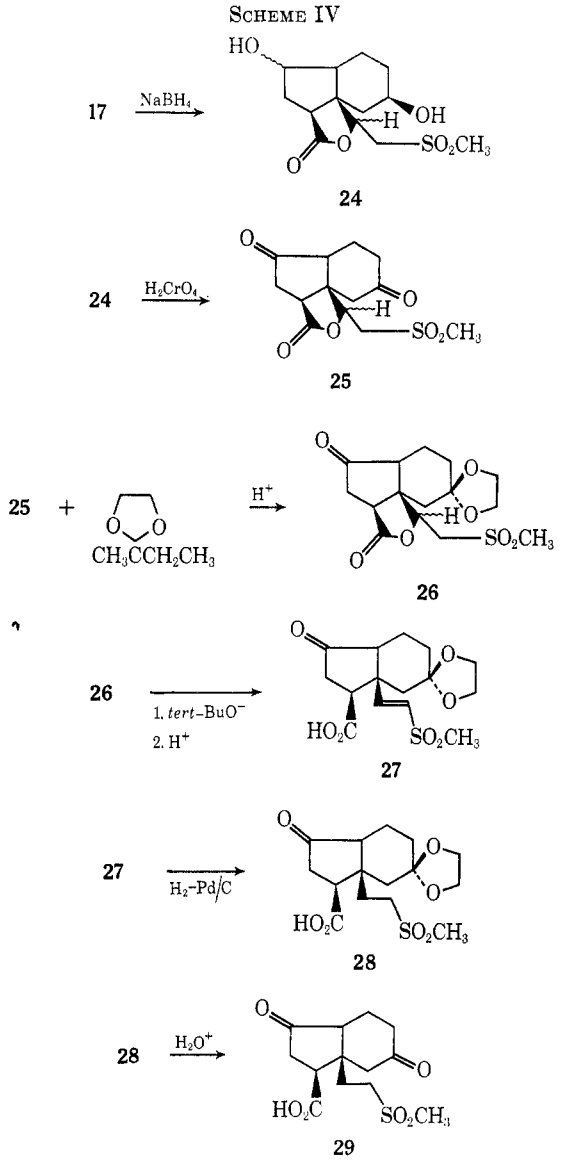
23

no less than seven compounds, and we were unable to characterize any of the products. This approach was abandoned in favor of a sequence involving removal of the offending oxygen prior to closure of the D ring (Scheme IV).

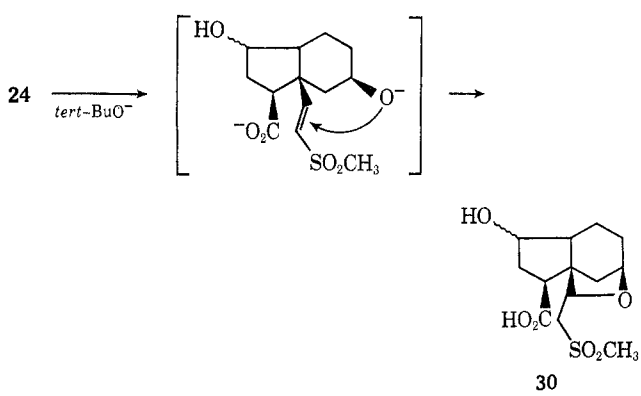
The transformations of Scheme IV are unexceptional for the most part. Ketal formation from the diketo lactone **25** gave very good yields (87%) of the monoketal **26**. The spectroscopic evidence clearly showed that only the six-membered ring carbonyl was involved in ketal formation. The pmr spectrum in perdeuteriodimethyl sulfoxide of the vinyl sulfone **27** showed a singlet at δ 6.85 which changed to an AB quartet (J = 15 Hz) in perdeuterioacetone. Accordingly, the double bond is assigned the trans configuration. Hydrogenation and hydrolysis of **27** proceeded smoothly although surprisingly vigorous conditions were required to remove the protecting group.

The overall transformation accomplished in Scheme IV could have been accomplished in fewer steps if base-induced elimination could have been successfully car-

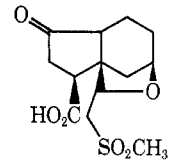
SCHEME IV



ried out on the dihydroxy lactone **24** or the diketone **25**. Treatment of **24** with potassium *tert*-butoxide afforded a cyclic ether to which we assign structure **30**. It appears that the desired vinyl sulfone is formed but then suffers nucleophilic addition to the double bond.

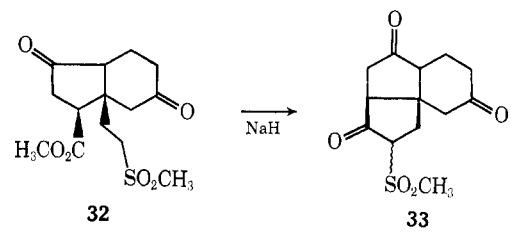


The spectral properties of **30** are in accord with the assigned structure; in particular, the pmr spectrum shows no vinyl protons although **30** is clearly a carboxylic acid. Oxidation of **30** with chromic acid affords only a monoketone **31**, and the infrared spectrum of this material shows a new maximum at 1740 cm^{-1} as expected on the basis of structure **30**.



Attempted elimination of the diketone **25** resulted in a deep seated rearrangement. The product, $C_{12}H_{16}O_4S$, has lost the carboxyl group with the appearance of an α,β-unsaturated ketone grouping. Moreover, the pmr spectrum showed absorption which could be ascribed to a methyl group attached to a methine carbon. Although the structure of this product has not been established, it is clearly not the desired vinyl sulfone.

The successful completion of the transformations of Scheme IV provided the desired diketo sulfone **29** for cyclization. Unfortunately, all of our attempts to cyclize **29** met with failure, and only starting material could be isolated. Since the strongly alkaline conditions converted the carboxyl group of **29** to carboxylate, it was considered that this negative charge might be inhibiting the desired cyclization. Accordingly, **29** was esterified and treatment of the ester with sodium hydride produced a new compound. However, the new compound is clearly not the desired tricyclic system and its properties are consistent with structure **33**.



Experimental Section[13]

cis-**2-Carbethoxy-3aβ-carbomethoxy-7aβ-hydroxy-3-methyl-3a,4,7,7a-tetrahydroindene** (**4**).—A solution of 56.4 g (0.25 mol) of cyclopentenone **3**, benzene (120 ml), 80 ml of liquid 1,3-butadiene, and 2.5 g of 2,6-di-*tert*-butylphenol (added as an inhibitor) was heated at 180° in a sealed bomb for 42 hr. The resulting yellow mixture was concentrated under reduced pressure to leave a viscous yellow oil (99 g). This oil was mixed with 1500 ml of 40% potassium carbonate solution and extracted with three 500-ml portions of ether. The basic aqueous layer was acidified with concentrated hydrochloric acid to pH 2 and extracted with three 200-ml portions of ether. These extracts were dried and concentrated to give 15.0 g of **3**. The ethereal solution of neutral material was washed with water, dried, and concentrated under vacuum. Distillation of the residual oil in a modified Hickman molecular still [bath temperature 110–120°

(13) All melting and boiling points are uncorrected. Unless otherwise stated, magnesium sulfate was employed as a drying agent. Reactions involving strong bases or organometallic reagents were carried out under nitrogen. Infrared spectra were determined with a Beckman IR-5A infrared spectrophotometer. Unless otherwise stated, the ultraviolet spectra were determined in 95% ethanol with a Cary Model 15 recording spectrophotometer. The nuclear magnetic resonance spectra were determined at 60 MHz with a Varian Model A-60 nmr spectrometer. The chemical shift values are expressed in δ values (ppm) relative to a tetramethylsilane internal standard. The mass spectra were obtained with a CEC, Model 21-110 mass spectrometer equipped with a direct inlet system at an ionizing potential of 70 eV. The microanalyses were performed either by Berkeley Analytical Laboratory, Berkeley, Calif., Chemalytics, Inc., Tempe, Ariz., or Micro-Tech Laboratories Inc., Skokie, Ill.

(0.15 mm)] separated 24.0 g (34%) of crude **4** as a colorless viscous oil. A pure sample of the **4** was obtained by glc on a 1.5-m column packed with 10% silicone on Chromosorb W at 200°: ir $\tilde{\nu}_{max}^{CCl_4}$ 3590, 3520, 1735, 1715, and 1645 cm^{-1} (weak); pmr (CCl_4) δ 1.28 (t, J = 7 Hz, 3 H), 2.1 (t, J = 2 Hz, 3 H), 2.02–3.20 (complex multiplets, 5 H), 2.7 (q, J = 2 Hz, 2 H), 3.72 (s, 3 H), 4.20 (q, J = 7 Hz, 2 H), and 5.83 (broad singlet, 2 H); uv λ_{max}^{EtOH} 231 nm (ϵ 6550).

Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.28; H, 7.14. Found: C, 64.48; H, 7.08.

***cis*-2-Carbethoxy-3aβ-carbomethoxy-7aβ-hydroxy-3-methyl-3a,4,5,6,7,7a-hexahydroindene.**—A sample of **4** (1.4 g, 5.0 mmol) was hydrogenated (1 atm) in ethanol over 0.1 g of 10% Pd/C. Filtration of the resulting mixture, followed by removal of the solvent, gave 1.41 g (100%) of the title compound as a colorless oil: ir $\tilde{\nu}_{max}^{CCl_4}$ 3600–3400 (broad), 1730, 1710, and 1640 cm^{-1}; pmr ($CDCl_3$) δ 1.28 (t, J = 7 Hz, 3 H), 0.85–2.9 (complex multiplets, 9 H), 2.16 (t, J = 2 Hz, 3 H), 2.68 (q, J = 2 Hz, 2 H), 3.74 (s, 3 H), and 4.20 (q, J = 7 Hz, 2 H); uv λ_{max}^{EtOH} 231 nm (ϵ 5200).

Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 64.42; H, 7.85.

***cis*-2,3aβ-Dicarboxy-7aβ-hydroxy-3-methyl-3a,4,7,7a-tetrahydroindene.**—A mixture of 2.80 g (10.0 mmol) of **4**, 2 N aqueous sodium hydroxide (100 ml), and 95% ethanol (50 ml) was refluxed for 1 hr. The reaction mixture was concentrated under reduced pressure, diluted with 50 ml of water, and extracted with ether. The aqueous phase was then acidified with hydrochloric acid to pH 2 and extracted with two 100-ml portions of ether. The ether was washed with 200 ml of brine and dried. Evaporation of the solvent and trituration with chloroform gave 0.75 g (31.4%) of diacid: mp 183–184°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600–2800 (broad), 1740, 1710, and 1640 cm^{-1}; pmr [$(CD_3)_2CO$–$(CD_3)_2SO$, 9:1] δ 1.83–2.65 (complex multiplets, 5 H) 2.10 (t, J = 2 Hz, 3 H), 2.73 (q, J = 2 Hz, 2 H), and 5.79 (broad, 2 H); uv λ_{max}^{EtOH} 233 nm (ϵ 7710).

Anal. Calcd for $C_{12}H_{14}O_5$: C, 60.51; H, 5.88. Found: C, 60.14; H, 5.83.

***cis*-2,3aβ-Dicarboxy-7aβ-hydroxy-3-methyl-3a,4,5,6,7,7a-hexahydroindene.**—In 75 ml of ethanol and 0.2 g of 10% Pd/C was dissolved 0.476 g (2.0 mmol) of *cis*-2,3aβ-dicarboxy-7aβ-hydroxy-3-methyl-3a,4,7,7a-tetrahydroindene. The hydrogenation was carried out at room temperature and at atmospheric pressure until the hydrogen uptake ceased. Filtration of the catalyst, followed by removal of the solvent and trituration with chloroform, gave 0.39 g (81%) of the diacid. A sample was purified by sublimination (150°, 0.01 mm) and crystallization from acetonitrile: mp 213–214°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600–2700 (broad), 1730, and 1710 cm^{-1}; pmr [$(CD_3)_2SO$] δ 0.85–2.8 (complex multiplets, 9 H), 2.02 (t, J = 2 Hz, 3 H), and 2.58 (q, J = 2 Hz, 2 H); uv λ_{max}^{EtOH} 233 nm (ϵ 7380).

Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.96; H, 6.71. Found: C, 59.71; H, 7.06.

Birch Reduction of *cis*-2,3aβ-Dicarboxy-7aβ-hydroxy-3-methyl-3a,4,5,6,7,7a-hexahydroindene.—In a 50-ml flask was placed 0.24 g (0.001 mol) of the diacid in liquid ammonia (25 ml) at −80° and 0.4 g (0.01 g-atom) of potassium metal was added with rapid stirring. The stirring was continued for 10 min after the final addition and then 7 ml of dry 2-propanol was added during 15 min. The cooling bath was removed and the stirring was continued until the ammonia had evaporated. The reaction mixture was diluted with water (30 ml), cooled in ice, and acidified with concentrated hydrochloric acid to pH 2. The resulting mixture was extracted with two 100-ml portions of ethyl acetate. The ethyl acetate was dried and evaporated. Trituration with chloroform gave 0.183 g (75.6%) of *cis*-2,9β-dicarboxy-8β-hydroxy-3-methylhydrindan. Recrystallization from benzene–ethyl acetate afforded the pure diacid as white crystals: mp 186–188°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3700–2700 (broad), 1730, and 1710 cm^{-1}; pmr [CD_3CN–$(CD_3)_2SO$, 9:1] δ 0.8–3.2 (complex multiplets, 13 H), 1.07 (d, J = 6 Hz, 3 H), and 8.75 (broad singlet, 2 H).

Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.11; H, 7.57.

1-Methyl-2-carboxyindan.—To 3.92 g (14 mmol) of **4** was added 10.5 g (70 mmol) of sodium iodide, 10 ml of glacial acetic acid, and 60 ml of freshly distilled diglyme. The reaction mixture was refluxed for 2 hr during which carbon dioxide evolved. The reaction mixture was then poured onto ice (200 g) and extracted with two 200-ml portions of ether. The ether was dried and concentrated under reduced pressure. The residue was saponified in a refluxing solution of 40% aqueous sodium hydroxide (5 ml) and of methanol (50 ml) for 30 min. The solvent was removed under reduced pressure and the residue was diluted with water (200 ml) and extracted with three 60-ml portions of ether. The aqueous phase was acidified with concentrated hydrochloric acid and extracted with three 100-ml portions of ether. The ether was dried and concentrated under reduced pressure. Distillation of the residue in a modified Hickman molecular still gave 0.75 g (30.4%) of *cis*- and *trans*-1-methyl-2-carboxyindan as a colorless oil which solidified on standing. The solid was sublimed [170° (0.5 mm)] and recrystallized from ethanol–water to give a mixture of cis and trans acids as white crystals: mp 68–73°; mp 77–80° after recrystallization from hot water (lit.[14] mp 82°); ir $\tilde{\nu}_{max}^{CCl_4}$ 1700 cm^{-1}; pmr (CCl_4) δ 1.20 and 1.42 (two sets of doublets, J = 6.5 Hz, 3 H), 2.50–3.80 (complex multiplets, 4 H), 7.10 (s, 4 H), and 11.95 (s, 1 H); uv λ_{max}^{EtOH} 272 nm (ϵ 2357), 266 (1947), and 260 (1400).

Anal. Calcd for $C_{11}H_{12}O_2$: C, 75.00; H, 6.82. Found: C, 74.83; H, 6.96.

Treatment of the acid mixture in ether solution with excess ethereal diazomethane gave the corresponding methyl esters as a colorless oil. Gas chromatography (1.5-m column packed with 10% silicone on Fluoropak at 200°) purified a sample of this ester which was found to be identical with an authentic sample prepared by the method of Roser[14] by comparison of their glc retention times (33 min), ir, and pmr spectra: ir $\tilde{\nu}_{min}^{CCl_4}$ 1730 cm^{-1}; pmr (CCl_4) δ 1.1 and 1.4 (two sets of doublets, J = 7 Hz, 3 H), 2.5–3.65 (complex multiplet, 4 H), 3.69 and 3.72 (two singlets, 3 H), and 7.13 (s, 4 H).

Condensation of Dimethyl Maleate with Sodium Cyanide.—Dimethyl maleate (14.4 g, 50 mmol) was refluxed for 6 hr with stirring with sodium cyanide (2.45 g, 50 mmol) in dry methanol (100 ml). The solvent was removed under reduced pressure and the residue was taken up in water (200 ml). The aqueous solution was washed with two 100-ml portions of ether to remove starting material after which it was acidified with concentrated hydrochloric acid to pH 2 and extracted with three 100-ml portions of ethyl acetate. The ethyl acetate solution was washed twice with 100-ml portions of saturated salt solution, dried, and evaporated under pressure to give 10.5 g (73%) of crude cyanotricarbomethoxycyclopentanone. Distillation of the residue through a short-path still gave a colorless viscous oil: bp 173–176° (1.5 mm) [lit.[8] bp 190–200° (4 mm)]; ir $\tilde{\nu}_{max}^{CHCl_3}$ 3500–2700 (very broad) and 1735 cm^{-1}; pmr ($CDCl_3$) δ 2.8 (complex multiplets, 2 H), 3.43 and 3.48 (two singlets, 1 H), 3.75 (two sets of four singlets, 9 H), 4.2 (complex multiplet, $^2/_3$ H), and 10.0 (s, $^1/_3$ H).

Large-Scale Preparation of the Diester Mixture 6.—In a 2000-ml flask equipped with a reflux condenser were placed sodium cyanide (73.5 g, 1.5 mol) and anhydrous methanol (750 ml). The cyanide was partially dissolved with swirling and diethyl maleate (516 g, 3.0 mol) was added. The resulting mixture heated at reflux overnight and then 650–700 ml of methanol was removed by simple distillation, and water (500 ml) was added to the dark brown residue. To the resulting solution was slowly added concentrated hydrochloric acid (500 ml) (CAUTION: HCN) and the mixture was refluxed for 3 hr after which 900 ml of water and hydrogen chloride was removed by simple distillation. The residue was diluted with 500 ml of water and saturated with 150 g of ammonium sulfate followed by a 12–20-hr continuous extraction with ethyl acetate. The ethyl acetate solution was dried and evaporated under reduced pressure to give the crude mixture of cyclopentanone-3,4-dicarboxylic acids. Without further purification, the crude diacid was dissolved in 1000 ml of dry methanol and placed in a 2000-ml flask equipped with a mechanical stirrer and Soxhlet extractor containing 3-Å molecular sieves. To this stirring solution was added 90 g of Dowex 50 W-X8 acidic ion exchange resin and the mixture was refluxed for 24 hr. (The esterification has also been done by allowing the methanol solution of the diacid to stand overnight with 5% by weight anhydrous hydrogen chloride.) The acidic ion exchange resin was filtered off and the excess methanol removed under reduced pressure to give a crude yellow oil. Fractionation of the crude diester through a 70-cm Podbielniak tantalum spiral column gave 150 g (50%) of a cis and trans mixture of the diester **6**; bp 125–155° (1.5 mm). The overall yield for the three steps varied from 45 to 55%.

(14) W. Roser, *Justus Liebigs Ann. Chem.*, **247**, 157 (1888).

3,4-Dicarbomethoxycyclopent-2-enone (7).—In a 1000-ml flask equipped with a mechanical stirrer and a reflux condenser were placed 40 g (0.20 mol) of the keto diester **6**, cupric bromide (98.12 g, 0.44 mol), and tetrahydrofuran (600 ml). The heterogeneous mixture was refluxed with vigorous stirring for 2 hr. The cuprous bromide was filtered off and the solvent was removed under pressure to give the crude bromo ketone as a green oil.

The crude bromo ketone was dissolved in dimethylformamide (50 ml) and placed in a 250-ml flask equipped with a magnetic stirrer. To this stirring solution was added 22 g (0.22 mol) of calcium carbonate and the resulting mixture was kept at 90–100° for 1 hr. The very dark brown reaction mixture was poured over 250 g of crushed ice and the precipitate was filtered off. The aqueous mixture was then extracted with four 200-ml portions of ethyl acetate. The ethyl acetate solution was dried and evaporated under reduced pressure to give 40 g of a very dark brown oil. Distillation gave 21 g (53%) of the α,β-unsaturated ketone **7** as a pale yellow oil: bp 120–125° (1.5 mm); ir $\tilde{\nu}_{max}^{CCl_4}$ 1735 and 1620 cm^{-1}; pmr (CCl_4) δ 2.6 (complex multiplets, 2 H), 3.7 (s, 3 H), 3.82 (s, 3 H), 4.0 (complex multiplet, 1 H), and 6.8 (d, J = 2 Hz, 1 H); uv λ_{max}^{EtOH} 227 nm (ϵ 5530), and $\lambda_{max}^{EtOH-NaOH}$ 245 nm (ϵ 2880) and 297 (6930).

Anal. Calcd for $C_9H_{10}O_5$: C, 54.55; H, 5.09. Found: C, 54.62; H, 5.51.

3β,3aβ-Dicarbomethoxy-3a,4,7,7a-tetrahydro-1-indanone (8).—Into a stainless steel bomb cooled to 0° were placed the diester **7** (80.0 g, 0.404 mol), dry benzene (100 ml), 2,6-di-*tert*-butylphenol (6.0 g), and 1,3-butadiene (218 g, 330 ml, 4.04 mol). The bomb was sealed and heated at 130–135° for 3 days. After cooling, the contents were concentrated under reduced pressure to give 211.4 g of gummy residue. The crude diester was separated from the butadiene polymer by vigorously extracting the residue with five 200-ml portions of boiling methanol. The boiling methanol mixture was filtered through a 1/2-in. Celite bed and concentrated under reduced pressure to give 76.1 g of crude orange oil. Fractionation of the oil gave 50.0 g (48.9%) of a mixture of the indanone diesters **8** as a colorless oil: bp 131–133° (1.0 mm); ir $\tilde{\nu}_{max}^{CHCl_3}$ 1745 and 1730 cm^{-1}; nmr ($CDCl_3$) 1.80–3.42 (complex multiplets, 8 H), 3.72 (s, 0.42 H), 3.80 (s, 2.54 H), 3.82 (s, 2.54 H), 3.91 (s, 0.50 H), and 5.78 (m, 2 H).

3β,3aβ-Dicarboxy-3a,4,7,7a-tetrahydro-1-indanone (9).—The crude product from a condensation similar to the one described above was refluxed for 8 hr with 15% aqueous potassium hydroxide (1200 ml) and ethanol (250 ml). The basic solution was separated from the rubbery polymer and extracted with two 300-ml portions of chloroform after which it was acidified with concentrated hydrochloric acid to pH 2 and extracted with four 300-ml portions of ethyl acetate. The ethyl acetate solution was dried and concentrated to give 69.5 g (77.5%) of crude diacid **9**, as a brown viscous oil which crystallized on standing. A small sample was recrystallized once from ethyl acetate and twice from acetone: mp 180–182° dec; ir $\tilde{\nu}_{max}^{KBr}$ 3300–2500 (broad), 1730, and 1690 cm^{-1}; pmr [$(CD_3)_2CO$] δ 1.83–3.5 (complex multiplets, 8 H), 5.65 (broad doublet, 2 H), and 6.38 (broad singlet, 2 H).

Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 58.77; H, 5.29.

A sample recrystallized only once from ethyl acetate, mp 176–177.5°, was esterified with an ethereal solution of diazomethane. The composition of the mixture of the tetrahydro-1-indanones was 75% of the cis isomer **15** and 25% of the trans isomer **13**.

***trans*-3β,9β-Dicarboxy-5β-hydroxy-6α-iodo-8α-1-hydrindanone-9β→5β-lactone (10).**—To a solution of iodine (50.8 g, 0.2 mol) and of potassium iodide (99.6 g, 0.6 mol) in 300 ml of water was added diacid **9** (44.8 g, 0.2 mol) dissolved in 1000 ml of 0.5 *M* sodium bicarbonate solution. The mixture was stored in the dark at room temperature for 20 hr. This mixture was mixed with ethyl acetate (400 ml), cooled to 0°, and acidified with 2 *N* sulfuric acid to pH 2. The ethyl acetate layer was separated and the aqueous solution was extracted with three 400-ml portions of ethyl acetate. The combined ethyl acetate fractions were washed with four 200-ml portions of 10% aqueous sodium thiosulfate, dried, and evaporated to give a dark orange solid–liquid mixture. Ethyl acetate (50 ml) was added and the mixture was cooled to 0° and filtered to give 17.5 g (25%) of the iodolactone **10** as a light brown solid, mp (iodine evolution) 165°, melting to dark oil at 180°. Recrystallization from acetone afforded pure iodolactone as white crystals: mp (iodine evolution) 170°, melting to dark oil at 184°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600–2700 (broad), 1775, 1740, and 1705 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.7–3.9 (complex multiplets, 8 H), 4.67 (broad triplet, J = 3.5 Hz, 1 H), 5.0 (broad triplet, J = 4.0 Hz, 1 H), and 12.7 (broad singlet, 1 H).

Anal. Calcd for $C_{11}H_{11}IO_5$: C, 37.74; H, 3.17; I, 36.25. Found: C, 37.63; H, 3.21; I, 36.06.

***trans*-3β,9β-Dicarboxy-1,5β-dihydroxy-6α-iodo-8α-hydrindan-9β→5β-lactone (11).**—The keto iodolactone **10** (4.47 g, 12.7 mmol) was partially dissolved in a solution of methanol (200 ml) and water (30 ml) and cooled to 0° with an ice bath. To this stirring, cooled suspension was added a solution of sodium borohydride (1.46 g, 38.4 mmol) dissolved in methanol (200 ml) and ice (50 g). After vigorous gas evolution had ceased, the clear solution was stirred at 0° for 4 hr and then at room temperature overnight. The slightly cloudy reaction mixture was carefully acidified to pH 1 with concentrated hydrochloric acid and the excess methanol removed under reduced pressure. Water (200 ml) was added to the residue and the mixture saturated with ammonium sulfate. The saturated solution was extracted with five 100-ml portions of ethyl acetate. The combined ethyl acetate layers were washed once with brine, dried, and concentrated to give 1.98 g (44.2%) of crude **11** as a white solid. Material recrystallized from acetone gave very small white crystals: mp (iodine evolution) 170–173°, 175–176° dec; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600, 3200, 1783, and 1740 cm^{-1}; pmr [$(CD_3)_2CO$–$(CD_3)_2SO$, 4:1] δ 1.80–3.20 (complex multiplets, 9 H), 4.18 (broad t, J = 5 Hz, 1 H), and 4.76 (m, 2 H).

Anal. Calcd for $C_{11}H_{13}IO_5$: C, 37.52; H, 3.72; I, 36.04. Found: C, 37.76; H, 3.51; I, 35.62.

***trans*-3β,3aβ-Dicarboxy-1-hydroxy-3a,4,7,7aα-tetrahydroindan (12).**—In a 50-ml flask equipped with a magnetic stirrer and a reflux condenser were placed the hydroxyiodo lactone **11** (570 mg, 1.62 mmol), zinc dust (210 mg, 3.24 mg-atoms), and anhydrous methanol (30 ml). The resulting mixture was refluxed for 20 hr. After the reaction mixture was allowed to cool to room temperature, it was carefully acidified with 2 *N* sulfuric acid (6.0 ml) and the excess zinc filtered off. The excess methanol was removed and the ammonium sulfate saturated aqueous layer was extracted with four 30-ml portions of ethyl acetate. The combined ethyl acetate layers washed once with brine, dried, and concentrated gave 344 mg (94.0%) of crude **12**. Recrystallization from ethyl acetate gave pure diacid **12** as very small crystals: mp 170–171°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3500, 3250–2850, and 1745 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.53–3.1 (complex multiplets, 8 H), 4.10 (broad t, J = 5 Hz, 1 H), and 5.68 (m, 3 H).

Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.32; H, 6.12.

***trans*-3β,3aβ-Dicarbomethoxy-3a,4,7,7aα-tetrahydro-1-indanone (13).**—In a 50-ml flask were placed the hydroxy diacid **12** (57.9 mg, 0.256 mmol) and freshly distilled tetrahydrofuran (5.0 ml). The magnetically stirred solution was cooled to 0° with an ice bath. Excess ethereal diazomethane was added and the slightly yellow solution was stirred 15 min at 0° and overnight at room temperature. The colorless solution was concentrated to give 64.8 mg (100%) of *trans*-3β,3aβ-dicarbomethoxy-1-hydroxy-3a,4,7,7aα-tetrahydroindan as a colorless oil: ir $\tilde{\nu}_{max}^{CHCl_3}$ 3450, 3040, 2980, 2850, and 1735 cm^{-1}; pmr ($CDCl_3$) δ 1.8–3.4 (complex multiplets, 8 H), 3.68 (s, 3 H), 3.70 (s, 3 H), 4.28 (m, 2 H), and 5.72 (m, 2 H).

The hydroxy diester was taken up in acetone (5.0 ml, distilled from potassium permanganate) and cooled to 0° with an ice bath. To this solution was added 0.2 ml of 8 *N* Jones reagent and the resulting mixture was stirred at 0° for 75 min. The excess reagent was destroyed with 2-propanol (10 ml), and the chromium salts were filtered off. The green solution was concentrated and the residue was taken up in hot ethyl acetate (5.0 ml), dried, and concentrated to yield 43.0 mg (66.7%) of crystalline *trans*-keto diester **13**. Material recrystallized from benzene–hexane gave small needles: mp 108–110°; ir $\tilde{\nu}_{max}^{CHCl_3}$ 3040, 2960, 2850, 1745, and 1735 cm^{-1}; pmr ($CDCl_3$) δ 1.8–4.25 (complex multiplets, 8 H), 3.62 (s, 3 H), 3.73 (s, 3 H), and 5.72 (m, 2 H).

Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 62.15; H, 6.50.

***cis*-3β,3aβ-Dicarboxy-1-hydroxy-3a,4,7,7aβ-tetrahydroindan (14).**—A pure sample of the Diels–Alder adducts **8** (5.52 g, 12.8 mmol) was taken up in methanol (50 ml), placed in a 250-ml erlenmeyer flask, and cooled to 0° with an ice bath. A solution of sodium borohydride (1.24 g, 32.8 mmol) in methanol (30 ml) and ice (20 g) was slowly added at 0°. The resulting solution was stirred 2 hr at 0° and then overnight at room temperature. Water (100 ml) was added and the methanol removed under reduced pressure. The aqueous mixture was extracted with

four 30-ml portions of ether. The combined ethereal layers were dried and concentrated to give 4.25 g (76.5%) of crude 3β,3aβ-dicarbomethoxy-1-hydroxy-3a,4,7,7a-tetrahydroindan as a light yellow oil: ir $\tilde{\nu}_{max}^{CHCl_3}$ 3500, 3040, 2960, 2850, and 1735 cm^{-1}; pmr ($CDCl_3$) δ 1.60–3.30 (complex multiplets, 8 H), 3.56 (broad s, 6 H), 4.10–4.50 (m, 1 H), and 5.71 (m, 2 H).

Without further purification, the crude hydroxy diester (2.31 g, 9.1 mmol) was taken up in 95% ethanol (10 ml) and placed in a 100-ml flask equipped with a magnetic stirrer and reflux condenser. To this light yellow solution was added 15% sodium hydroxide (50 ml) and the resulting mixture refluxed 12 hr. The reaction mixture was allowed to cool to room temperature and extracted with three 50-ml portions of chloroform. The aqueous layer was carefully acidified to pH 1 with concentrated hydrochloric acid. The acidic, ammonium sulfate saturated mixture was extracted with three 50-ml portions of ethyl acetate. The combined ethyl acetate layers were dried and concentrated to yield 1.99 g (97%) of hydroxy diacid **14** as a white foam. The foam was taken up in 5.0 ml of hot ethyl acetate and allowed to crystallize: mp 154–156°; ir $\tilde{\nu}_{max}^{CHCl_3}$ 3500, 3250–2850, and 1742 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.32–3.80 (complex multiplets 8 H), 4.12 (m, 1 H), and 5.62 (m, 3 H).

Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.79; H, 6.21.

***cis*-3β,3aβ-Dicarbomethoxy-3a,4,7,7aβ-tetrahydro-1-indanone (15).**—In a 50-ml flask equipped with a magnetic stirrer were placed the hydroxy diacid **14** (178 mg, 0.79 mmol) and freshly distilled tetrahydrofuran (8.0 ml). The resulting solution was cooled to 0° and excess ethereal diazomethane was added. The yellow solution was stirred at 0° for 15 min and then overnight at room temperature. The colorless solution was concentrated to give 200 mg (99.1%) of *cis*-3β,3aβ-dicarbomethoxy-1-hydroxy-3a,4,7,7aβ-tetrahydroindan as a colorless oil: ir $\tilde{\nu}_{max}^{CHCl_3}$ 3600, 3500, 3040, 3029, 2980, 2940, 2850, and 1735 cm^{-1}; pmr ($CDCl_3$) δ 1.7–3.4 (complex multiplets, 8 H), 3.68 (broad s, 6 H), 3.7–4.4 (m, 2 H), and 5.70 (m, 2 H).

The hydroxy diester was taken up in acetone (5.0 ml, distilled from potassium permanganate) and cooled to 0° with an ice bath. To the stirring solution was added 8 *N* Jones reagent (0.6 ml) at 0° and the mixture stirred at 0° for 75 min. The excess reagent was destroyed with 2-propanol (15 ml) and the chromium salts were filtered off. The concentrated residue was taken up in hot ethyl acetate (15 ml), dried, and concentrated to give 149 mg (75.0%) of *cis*-keto diester **15** as a slightly yellow oil, which was crystallized from benzene–hexane: mp 62.5–63°; ir $\tilde{\nu}_{max}^{CHCl_3}$ 3040, 2960, 2920, 2850, 1745 (sh), and 1735 cm^{-1}; pmr ($CDCl_3$) δ 1.80–3.43 (complex multiplets, 8 H), 3.70 (s, 3 H), 3.72 (s, 3 H), and 5.71 (m, 2 H).

Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.92; H, 6.26.

The *cis*-keto diester **15** was also prepared from the diazomethane treatment of the keto diacids **9**, mp 176–177.5°, followed by selective crystallization of the cis isomer away from the minor trans isomer.

***trans*-3β,9β-Dicarboxy-5β-hydroxy-8α-1-hydrindanone-9β→5β-lactone (16).**—In a 500-ml flask equipped with a magnetic stirrer were placed iodolactone **10** (17.5 g, 50 mmol) and freshly distilled tetrahydrofuran (200 ml). The suspension was cooled to 5° and 44 g (0.15 mol) of tri-*n*-butyltin hydride was added with stirring over 15 min. The cooling bath was removed and the mixture was allowed to warm to room temperature during which time a clear solution was obtained. After stirring, at room temperature, for an additional 12 hr, the solvent was removed under reduced pressure and the residue was taken up in ethyl acetate (200 ml). The ethyl acetate solution was extracted with three 100-ml portions of saturated sodium carbonate solution. The carbonate solutions were cooled to 0°, acidified with 2 *N* sulfuric acid, and extracted with three 250-ml portions of ethyl acetate. The ethyl acetate solutions were combined and washed twice with 150-ml portions of 10% sodium thiosulfate solution and once with 200-ml of brine. After drying and removal of solvent, the residue was taken up in ethyl acetate (25 ml), cooled, and filtered to give 8.52 g (76%) of keto lactone **16** as a light tan solid, mp 193–195°. The crude keto lactone was recrystallized twice from acetone to give pure keto lactone: mp 195–197°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600–2500 (broad), 1775, and 1740 cm^{-1}; pmr (CD_3CN) δ 1.0–3.7 (complex multiplets, 10 H), 4.9 (complex multiplet, 1 H), and 8.2 (broad singlet, 1 H).

Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 58.68; H, 5.51.

3β-Carboxy-5β-hydroxy-9β-(1′-oxo-2′-(methylsulfonyl)ethyl)-1-hydrindanone (17).—In a 1000-ml flask equipped with a reflux condenser, a magnetic stirrer, a dropping funnel, and a septum were placed 15.04 g (0.16 mol) of dimethyl sulfone and freshly distilled tetrahydrofuran (600 ml). Air was excluded from the flask and a 1.6 *M* hexane solution of *n*-butyllithium (100 ml, 0.16 mol) was injected through the septum. The milky suspension was refluxed with stirring for 2 hr and then keto lactone **16** (8.96 g, 40 mmol) and dry tetrahydrofuran (100 ml) was added over 30 min. The stirring mixture was refluxed for 16 hr, cooled to room temperature, and acidified with concentrated hydrochloric acid (20 ml). This solution was concentrated on 30 g of silica gel under reduced pressure. The solid material was placed on a column of silica gel (50 g) packed in a water jacketted continuous chromatography column. The excess dimethyl sulfone was eluted with chloroform. The crude sulfone was eluted with 50% ethyl acetate–chloroform. Removal of the solvent left 12.0 g of a light tan foam. Trituration of this foam with ethyl acetate (20 ml) gave 7.0 g (55%) of the sulfone **17** as a white solid. Recrystallization from acetone afforded pure **17**: mp 184–186°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600–2700 (broad), 1780, 1740, and 1315 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.0–3.4 (complex multiplets, 12 H), 2.95 (s, 3 H), 3.85 (broad singlet, 1 H), and 4.75 (broad doublet, 2 H).

Anal. Calcd for $C_{13}H_{18}O_7S$: C, 49.06; H, 5.70; S, 10.05. Found: C, 48.79; H, 5.72; S, 10.02.

3β-Carboxy-9β-(1′-oxo-2′-(methylsulfonyl)ethyl)-1,5-hydrindanone (18).—To a cold (0°) solution of 5.57 g (17.5 mmol) of **17** in acetone (250 ml) was added dropwise with stirring 5 ml of aqueous 8 *N* chromic acid solution. The reaction mixture was stirred at 0° for 90 min and then the excess oxidant was destroyed with excess 2-propanol. The chromium salts were filtered off and washed with hot acetone, and then the green solution was concentrated under reduced pressure. The residue was taken up in hot ethyl acetate, dried, and concentrated to give 5.5 g of a white foam. The white foam was crystallized from ethyl acetate to afford 4.5 g (88.5%) of **18** as white crystals: mp 176–178°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3700–2700 (broad), 1780, 1740, 1720, and 1315 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.8–3.6 (complex multiplets, 11 H), 3.08 (s, 3 H), and 4.6 (broad doublet, 2 H); mass spectrum molecular ion peak at *m/e* 316 (calcd mol wt, 316.3).

Anal. Calcd for $C_{13}H_{16}O_7S$: C, 49.37; H, 5.10; S, 10.12. Found: C, 49.23; H, 5.12; S, 9.94.

2β-Carboxy-8α-hydroxy-9-(methylsulfonyl)tricyclo[6.2.1.0^{1,5}]-undecane-4,10-dione (19).—A solution of the triketo sulfone **18** (4.4 g, 13.9 mmol) in anhydrous methanol (100 ml) and potassium hydroxide (5.0 g) was refluxed for 1 hr, during which a precipitate formed. The resulting mixture was cooled, acidified with concentrated hydrochloric acid, and concentrated under reduced pressure. The residue was taken up in hot ethyl acetate, dried, and concentrated to give 4.4 g of a foam. Crystallization from ethyl acetate (3 days at room temperature) afforded 3.0 g (68.2%) of **19** as white crystals: mp 234–236°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3700–2700 (broad), 1740, 1310, and 1140 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.5–3.8 (complex multiplets, 11 H), 3.08 (s, 3 H), 4.44 (s, 1 H); mass spectrum molecular ion peak at *m/e* 316 (calcd mol wt, 316.3).

Anal. Calcd for $C_{13}H_{16}O_7S$: C, 49.37; H, 5.10; S, 10.12. Found: C, 49.39; H, 5.21; S, 9.95.

8α-Acetoxy-2β-carboxy-9-(methylsulfonyl)tricyclo[6.2.1.0^{1,5}]-undecane-4,10-dione (20).—A solution of **19** (0.95 g, 3.0 mmol) in acetyl chloride (75 ml) was refluxed for 19 hr. The excess acetyl chloride was removed under reduced pressure followed by the addition and evaporation of two 100-ml portions of ethyl acetate to give the crude acetate as a solid. Crystallization from ethyl acetate afforded 0.46 g (43%) of the tricyclic sulfone acetate as white crystals: mp 261° dec; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600–2900 (broad), 1740, and 1320 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.6–3.8 (complex multiplets, 10 H), 2.05 (s, 3 H), 3.08 (s, 3 H), and 4.65 (s, 1 H)

Anal. Calcd for $C_{15}H_{18}O_8S$: C, 50.28; H, 5.06; S, 8.93. Found: C, 50.52; H, 5.01; S, 8.87.

8α-Acetoxy-2β-carbomethoxy-9-(methylsulfonyl)tricyclo[6.2.-1.0^{1,5}]undecane-4,10-dione (21).—To a solution of 0.1074 g (0.3 mmol) of the tricyclic acetate **20** in dry tetrahydrofuran (20 ml) was added 0.08 *M* ethereal diazomethane (10.0 ml) at 0°. The solvents were removed and the residue crystallized from ethyl acetate to give 0.085 g (76%) of the methyl ester **21**: mp 216–220°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600, 3500, 1745, 1315, 1240, and 1150 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.65–3.80 (complex multiplets, 10 H), 2.08 (s, 3 H), 3.15 (s, 3 H), 3.65 (s, 3 H), and 4.88 (s, 1 H).

Anal. Calcd for $C_{16}H_{20}O_8S$: C, 51.61; H, 5.41; S, 8.59. Found: C, 51.45; H, 5.38; S, 8.68.

3β-Carboxy-1,5β-dihydroxy-9β-(1′-hydroxy-2′-(methylsulfonyl)ethyl)-hydrindan-3β→1′-lactone (24).—To a cold (0°) solution of the sulfone **17** (4.14 g, 13 mmol) absolute ethanol (200 ml) was added with stirring sodium borohydride (4.94 g, 0.13 mol) in 200 ml of absolute ethanol over a period of 30 min. The reaction mixture was stirred at room temperature for 9 hr, acidified with anhydrous hydrogen chloride to pH 2, and stirred for an additional 1 hr. The reaction mixture was concentrated on 15 g of silica gel under reduced pressure. The solid material was placed on top of a silica gel (35 g) chromatography column packed in chloroform. The column was washed with ethyl acetate (2 l.) and the ethyl acetate solution was concentrated to give 3.20 g of a white foam. Crystallization of this foam from ethyl acetate afforded 1.2 g (30.4%) of the dihydroxy lactone **24** as white crystals: mp 187–189°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3540, 1780, 1305, and 1135 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.0–5.0 (complex multiplets, 17 H), and 2.98 (s, 3 H); mass spectrum molecular ion peak at *m/e* 304 (calcd mol wt, 304.3).

Anal. Calcd for $C_{13}H_{20}O_6S$: C, 51.30; H, 6.62; S, 10.53. Found: C, 51.39; H, 6.60; S, 10.34.

3β-Carboxy-9β-(1′-hydroxy-2′-(methylsulfonyl)ethyl)-1,5-hydrindandione-3β→1′-lactone (25).—To a cold solution of 3.22 g (10.6 mmol) of crude **24** in acetone (200 ml) was added dropwise with stirring 2 ml of aqueous 8 *N* chromic acid solution. The reaction mixture was stirred at 0° for 60 min and then the excess oxidant was destroyed with 2-propanol. After the chromium salts were filtered off and washed with hot acetone, the green organic solution was concentrated under reduced pressure. The residue was taken up in hot ethyl acetate (250 ml), dried, and concentrated to give 3.01 g of a white foam. The white foam was crystallized from ethyl acetate to give **25** (1.4 g, 44% from **17**) as white crystals: mp 197–198°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 1780, 1740, 1720, 1305, and 1138 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.90–4.30 (complex multiplets, 12 H), 3.05 (s, 3 H), 5.0 (two sets of doublets, J = 3 Hz, 1 H).

Anal. Calcd for $C_{13}H_{16}O_6S$: C, 52.00; H, 5.37. Found: C, 51.92; H, 5.25.

3′β-Carboxy-9′β-(1′′-hydroxy-2′′-(methylsulfonyl)ethyl)spiro-(1,3-dioxolane-2,5′-1′-hydrindanone)-3′β→1′′-lactone (26).—A mixture of **25** (1.5 g, 5.0 mmol), *p*-toluenesulfonic acid monohydrate (40 mg), and 50 ml of 2-ethyl-2-methyl-1,3-dioxolane[15] was heated and the liberated 2-butanone admixed with the dioxolane reagent distilled through a short-path column at such a rate that 20 ml of distillate was collected over a period of 4 hr; 20 ml of dioxolane reagent was added; and the mixture was refluxed for 20 hr. The excess dioxolane reagent was removed under reduced pressure and the solid residue was crystallized from acetonitrile to give the monoketal **26** (1.5 g, 87%) as white crystals: mp 252–254°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 1780, 1740, 1310, and 1135 cm^{-1}; pmr [$(CD_3)_2SO$] δ 0.9–4.4 (complex multiplets, 12 H), 3.05 (s, 3 H), 3.91 (s, 4 H), and 4.9 (m, 1 H); mass spectrum molecular ion peak at *m/e* 344 (calcd mol wt, 344.4).

Anal. Calcd for $C_{15}H_{20}O_7S$: C, 52.33; H, 5.85; S, 9.29. Found: C, 52.31; H, 5.89; S, 9.00.

3′β-Carboxy-9′β-(*trans*-2′′-(methylsulfonyl)ethynyl)spiro(1,3-dioxolane-2,5′-1′-hydrindanone) (27).—A sample of the monoketal **26** (1.20 g, 3.5 mmol) was refluxed for 5 hr in 0.17 *N* potassium *tert*-butoxide in *tert*-butyl alcohol (200 ml). The cooled reaction mixture was acidified with concentrated hydrochloric acid (3.5 ml) and concentrated under reduced pressure. The residue was taken up in ethyl acetate, dried, and evaporated to afford the crude sulfone **27** (1.12 g) which was crystallized from ethyl acetate to give pure material (0.71 g, 59%): mp 203–205°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600–2800 (broad), 1740 (broad), 1630 (weak), 1305, and 1138 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.0–3.5 (complex multiplets, 10 H), 3.0 (s, 3 H), 3.92 (s, 4 H), 6.85 (s, by the addition of deuterated acetone, this singlet was converted to an AB quartet, J = 15 Hz, 2 H); uv λ_{max}^{EtOH} shoulder at 205 nm (ε 2900); mass spectrum molecular ion peak at *m/e* 344 (calcd mol wt, 344.4).

Anal. Calcd for $C_{15}H_{20}O_7S$: C, 52.33; H, 5.85; S, 9.29. Found: C, 52.27; H, 5.55; S, 9.32.

3′β-Carboxy-9′β-(2′′-(methylsulfonyl)ethyl)spiro(1,3-dioxolane-2,5′-1′-hydrindanone) (28).—A solution of (0.516 g, 1.5 mmol) in absolute methanol (150 ml) with 10% Pd/C (200 mg) was hydrogenated at atmospheric pressure and room temperature until the hydrogen uptake ceased. The reaction time for pure material was usually 5 min; however, for crude material several hours were needed. Filtration of the catalyst followed by removal of the solvent gave a white solid (0.501 g). Crystallization from benzene–ethyl acetate afforded 0.42 g (81%) of the keto sulfone **28**: mp 174–175°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600–2800 (broad), 1740, 1305, and 1138 cm^{-1}; pmr [$(CD_3)_2CO$–$(CD_3)_2SO$, 9:1] δ 0.9–3.6 (complex multiplets, 14 H), 2.92 (s, 3 H), 3.92 (unsymmetrical doublet, J = 1.5 Hz, 4 H), and 6.6 (broad singlet, 1 H); mass spectrum molecular ion peak at *m/e* 346 (calcd mol wt, 346.4).

Anal. Calcd for $C_{15}H_{22}O_7S$: C, 52.02; H, 6.40; S, 9.24. Found: C, 51.81; H, 6.28; S, 9.48.

3β-Carboxy-9β-(2′-(methylsulfonyl)ethyl)-1,5-hydrindandione (29).—Keto sulfone **28** (0.97 g, 2.8 mmol) was refluxed with 3 *N* hydrochloric acid (20 ml) for 9 hr. The product was isolated with ethyl acetate and crystallized from benzene–ethyl acetate to give pure **28** (0.57 g, 68%): mp 138–139°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600–2800 (broad), 1740, 1720, 1305, and 1140 cm^{-1}; pmr [$(CD_3)_2CO$] δ 1.0–3.6 (complex multiplets, 14 H), 2.97 (s, 3 H), and 8.13 (s, 1 H); mass spectrum molecular ion peak at *m/e* 302 (calcd mol wt, 302.3).

Anal. Calcd for $C_{13}H_{18}O_6S$: C, 51.66; H, 6.00; S, 10.60. Found: C, 51.33; H, 5.83; S, 10.54.

3β-Carbomethoxy-9β-(2′-(methylsulfonyl)ethyl)-1,5-hydrindandione (32).—Diketo sulfone **29** (0.302 g, 1 mmol) was heated under reflux for 24 hr with anhydrous methanol (150 ml) and anhydrous hydrogen chloride (15 g). The solvent was removed under reduced pressure and the residue was crystallized from ethyl acetate to give pure ester (0.196 g, 62%): mp 151–152°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 1725 (broad), 1305, and 1140 cm^{-1}; pmr (CD_3CN) δ 1.6–3.5 (complex multiplets, 14 H), 2.89 (s, 3 H), and 3.73 (s, 3 H).

Anal. Calcd for $C_{14}H_{20}O_6S$: C, 53.16; H, 6.37; S, 10.11. Found: C, 53.29; H, 6.24; S, 10.24.

2β-Carboxy-4-hydroxy-10-((methylsulfonyl)methyl)-8α-9-oxatricyclo[6.2.1.0^{1,5}]undecane (30).—A sample of **24** (1.0 g, 3.3 mmol) was refluxed with 0.132 *N* potassium *tert*-butoxide in *tert*-butyl alcohol (100 ml) for 6 hr. The cooled reaction mixture was acidified with concentrated hydrochloric acid and concentrated under reduced pressure. The residue was taken up in ethyl acetate, dried, and crystallized from ethyl acetate to give **30** (0.81 g, 81%) as white crystals: mp 189–191°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3550, 3480–3000 (broad), 1730, 1300, 1160, and 1135 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.2–4.0 (complex multiplets, 14 H), 2.95 (s, 3 H), and 4.0–4.35 (complex multiplets, 2 H).

Anal. Calcd for $C_{13}H_{20}O_6S$: C, 51.31; H, 6.62. Found: C, 50.98; H, 6.76.

2β-Carboxy-10-((methylsulfonyl)methyl)-8α-9-oxatricyclo[6.2.1.0^{1,5}]undecan-4-one (31).—A sample of **30** (0.456 g, 1.5 mmol) in acetone (50 ml) was treated with 8 *N* chromic acid solution (1 ml). After stirring at 0° for 2 hr the excess chromic acid was destroyed with 2-propanol and the chromium salts were filtered and washed with hot acetone. The acetone solution was evaporated under reduced pressure and the residue was crystallized from benzene–ethyl acetate to give **31** (0.36 g, 79%) as white crystals: mp 184–186°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3600–2700 (broad), 1740 (broad), 1300, 1185, and 1135 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.0–3.9 (complex multiplets, 12 H), 3.02 (s, 3 H), 4.15–4.7 (complex multiplet, 2 H); mass spectrum molecular ion peak at *m/e* 302 (calcd mol wt, 302.3).

Anal. Calcd for $C_{13}H_{18}O_6S$: C, 51.66; H, 6.00. Found: C, 51.63; H, 6.02.

Reaction of the Diketo Lactone 25 with Potassium *tert*-Butoxide.—A sample of diketo lactone **25** (1.2 g, 4.0 mmol) was refluxed with 0.16 *N* potassium *tert*-butoxide in *tert*-butyl alcohol for 3 hr. The resulting solution was acidified with hydrochloric acid and concentrated on silicic acid (15 g) under reduced pressure. The residue was placed on top of a column of silicic acid (50 g) and eluted with 25% ethyl acetate–chloroform (2:1). Evaporation of the effluent afforded 0.6 g of a dark red oil which was crystallized from ethyl acetate to give 0.31 g (30%) of red crystalline material which was further crystallized twice from acetone to give white crystals: mp 145–146°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 1700, 1295, and 1135 cm^{-1}; pmr [$(CD_3)_2SO$] δ 1.25 (d, J = 7 Hz, 3 H), 1.7–3.8 (complex multiplets, 9 H), 3.0 (s, 3 H), and 4.55 (broad triplet, J = 5 Hz, 1 H); uv λ_{max}^{EtOH} 234 nm (ε 11,600); mass spectrum very weak molecular ion peak at *m/e* 256 and abundant fragment peak at *m/e* 177 (M − CH_3SO_2·) (calcd mol wt, 256.3).

Anal. Calcd for $C_{12}H_{16}O_4S$: C, 56.25; H, 6.29; S, 12.48. Found: C, 56.10; H, 6.13; S, 12.60.

(15) H. J. Dauben, Jr., B. Löken, and H. J. Ringold, *J. Amer. Chem. Soc.*, **76**, 1359 (1954).

11-(Methylsulfonyl)-9α-tricyclo[7.3.0.0^{1,6}]dodecane-3,7,10-trione (**33**).—A sample of **32** (95 mg, 0.3 mmol) in dry glyme (20 ml) was added to a suspension of oil-free sodium hydride (0.144 g, 0.60 mmol) in glyme (40 ml), and the mixture was refluxed for 8 hr. The cooled reaction mixture was acidified with concentrated hydrochloric acid and evaporated under reduced pressure. The residue was leached with hot ethyl acetate and concentrated to give 0.091 g of light brown foam which was separated on a 20 × 20 silica gel (PF_{254}) thin layer plate eluted with ethyl acetate. Collection of two components (R_f 0.48 and 0.54) gave an isomeric mixture of **33** (47 mg, 45%) which crystallized from ethyl acetate: mp 166–169°; ir $\tilde{\nu}_{max}^{CH_3CN}$ 3700–3400 (broad, partly as enol form), 1745, 1720, 1310, and 1145 cm^{-1}; pmr (CD_3CN) δ 1.7–2.9 (complex multiplets, 12 H), 3.08, 3.16 (two singlets because of the two isomeric forms, 3 H), and 4.3 (complex multiplet, 1 H); mass spectrum molecular ion peak at *m/e* 284. The exact molecular weight determined by high resolution mass spectrometry was 284.078 (calcd for $C_{13}H_{16}O_5S$, 284.075) and for M − CH_3SO_2· was 205.092 (calcd for $C_{12}H_{13}O_3$, 205.089).

Registry No.—**4**, 28269-01-4; *cis*-**6**, 28269-02-5; *trans*-**6**, 28269-03-6; **7**, 26269-04-7; *cis*-**8**, 28269-05-8; *trans*-**8**, 28269-06-9; *cis*-**9**, 28269-07-0; *trans*-**9**, 28269-08-1; **10**, 28269-09-2; **11**, 28269-10-5; **12**, 28269-11-6; **14**, 28269-12-7; **16**, 28269-13-8; **17**, 28269-14-9; **18**, 28269-15-0; **19**, 28269-16-1; **20**, 28392-70-3; **21**, 28269-17-2; **24**, 28269-18-3; **25**, 28269-19-4; **26**, 28269-20-7; **27**, 28269-21-8; **28**, 28392-71-4; **29**, 28278-27-5; **30**, 28278-28-6; **31**, 28278-29-7; **32**, 28278-30-0; 11α-**33**, 28278-31-1; 11β-**33**, 28278-32-2; *cis*-2-carbethoxy-3aβ-carbomethoxy-7aβ-hydroxy-3-methyl-3a,4,5,6,7,7a-hexahydroindene, 28278-33-3; *cis*-2,3aβ-dicarboxy-7aβ-hydroxy-3-methyl-3a,4,7,7a-tetrahydroindene, 28278-34-4; *cis*-2,3aβ-dicarboxy-7aβ-hydroxy-3-methyl-3a,4,5,6,7,7a-hexahydroindene, 28278-35-5; *cis*-2,9β-dicarboxy-8β-hydroxy-3-methylhydrindan, 28278-36-6; *cis*-1-methyl-2-carboxyindene, 28278-37-7; *trans*-1-methyl-2-carboxyindan, 28278-38-8; *trans*-3β,3aβ-dicarbomethoxy-1-hydroxy-3a,4,7,7aα-tetrahydroindan, 28278-39-9; 3β,3aβ-dicarbomethoxy-1-hydroxy-3a,4,7,7a-tetrahydroindan, 28278-40-2; *cis*-3β,3aβ-dicarbomethoxy-1-hydroxy-3a,4,7,7aβ-tetrahydroindan, 28278-41-3.

Synthesis and Properties of Some 1-Halophospholenes[1]

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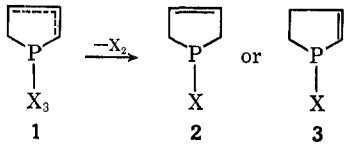
Two methods have been devised for preparing the previously unknown 1-halophospholenes. These compounds, which are formally cyclic phosphinous halides, resulted from reduction (dehalogenation) of diene–phosphorus trihalide cycloadducts with triphenylphosphine, as well as from reduction with hexachlorodisilane of 1-halophospholene oxides. Examples of both 2- and 3-phospholene derivatives were prepared. Structures were assigned from nmr spectral data. Of particular value was the exceptionally large (over 40 Hz) value for coupling of ^{31}P with the vinyl proton at the 2 position of the 2-phospholene derivatives. The halophospholenes were hydrolyzed to give cyclic secondary phosphine oxides (characterized as their chloral adducts). Successful displacement of halogen with a secondary amine as well as with a Grignard reagent demonstrates further the synthetic utility of these substances in phospholene chemistry.

The discovery of the cycloaddition of dienes with phosphonous dihalides[2] has made possible the synthesis of a number of derivatives of the phospholene ring system and stimulated a considerable amount of work on this family of compounds.[3] To date no 1-halophospholenes, where phosphorus is trivalent, have been prepared; yet these compounds, which may be classed as cyclic phosphinous halides, should be particularly valuable as synthetic intermediates in this family. We report in this paper two methods which have made these compounds available, and describe several reactions leading to new phospholene derivatives.

Reduction of Diene–Phosphorus Trihalide Cycloadducts.—We have previously shown that the diene–phosphonous dihalide cycloadducts may be reduced (dehalogenated) with magnesium in tetrahydrofuran to form 1-alkyl- or arylphospholenes.[4] Application of this reaction to cycloadducts from phosphorus trihalides[5] (**1**; the position of the double bond is uncertain) should provide the desired 1-halophospholenes (**2** or **3**).



1 **2** **3**

However, the magnesium–THF system, when applied to isoprene–PCl_3 or PBr_3 cycloadducts, provided none of the desired product; the only material isolated was the 1,4-dihalobutane from cleavage of the solvent.[6] It was then found that the dehalogenation could be successfully accomplished with triphenylphosphine in methylene chloride as solvent. The other product of the reaction, presumably the dihalotriphenylphosphorane, is partially soluble in the reaction medium, but is precipitated with pentane. Its removal from the reaction medium was considered desirable as the halogen exchange process is probably reversible. Unreacted cycloadduct is also precipitated in this step. The halophospholenes are then recovered by distillation. Products and yields are included in Table I. The halides are highly reactive substances, sensitive to air and to water; even protected from these, some products proved to be unstable, precipitating orange solids on standing. The most unstable was compound **3a** which began to decompose in the receiver even before distillation was complete, and was obtained in only 5% yield. On the other hand, compound **2a** remained unchanged on standing for several weeks; it was obtained in 79%

(1) Supported by Public Health Service Research Grant CA-05507 from the National Cancer Institute.

(2) W. B. McCormack, U. S. Patents, 2,663,736 and 2,663,737 (Dec 22, 1953).

(3) For a review, see L. D. Quin in "1,4-Cycloaddition Reactions," J. Hamer, Ed., Academic Press, New York, N. Y., 1967, Chapter 3.

(4) L. D. Quin and D. A. Mathewes, *J. Org. Chem.*, **29**, 836 (1964).

(5) U. Hasserodt, K. Hunger, and F. Korte, *Tetrahedron*, **19**, 1563 (1963).

(6) A. G. Anderson and F. J. Freenor, *J. Amer. Chem. Soc.*, **86**, 5037 (1964), have reported a similar cleavage of THF by dibromotriphenylphosphorane.