Perhydroindan Derivatives. IX. The Diels-Alder Reaction with 7-Methylindene Derivatives[1a]

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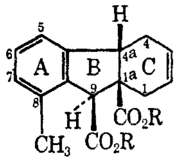
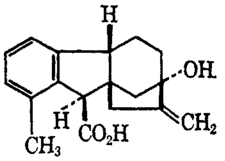
1,2-Dicarbomethoxy-7-methylindene (**3**) has been synthesized. The Diels-Alder reaction of this indene derivative **3** with butadiene has been found to occur without migration of the carbon-carbon double bond to form the tetrahydrofluorene derivative **1**.

In continuing our study of synthetic routes to the gibberellins and related molecules,[2] we wished to prepare the unsaturated diacid **1a** since model studies[2a] had suggested that this intermediate might be a suitable precursor for epiallogibberic acid **2**. A useful synthesis of this diacid **1a** has been accomplished and is described in this paper. At the same time, we initiated studies directed toward the synthesis of a diacid analogous to **1a** except that the 8-methyl group is replaced by a 7-methoxyl function. These studies, described in an accompanying paper,[3] led to an interesting complication in the Diels-Alder reaction used to add the C ring.



1a, R = H
b, R = CH_3



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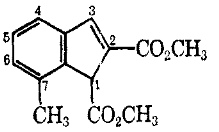

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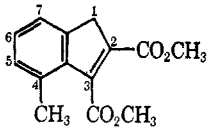

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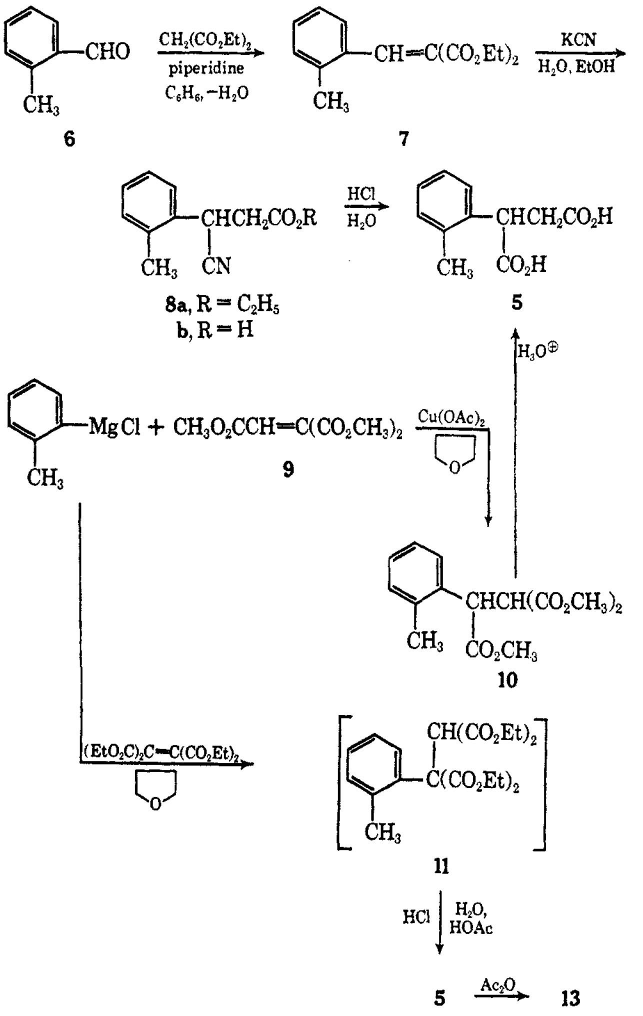
Our synthetic plan was to use a Diels-Alder reaction between butadiene and the indene diester **3** to obtain the diacid derivative **1** with a *cis* fusion between the B and C rings. Since it was not clear at the outset which of the unsaturated esters **3** or **4** would be more stable, we sought a synthetic route which would hopefully allow us to obtain the diester **3** even if it was less stable than its double-bond isomer **4**. Scheme I summarizes several routes which were used to obtain the succinic acid intermediate **5** required in subsequent steps. This diacid **5** was converted into keto diester **12** (Scheme II) employing a modification of a previously described procedure.[4] Attempts to reduce the carbonyl function of this enolic keto diester **12** to an alcohol were unsuccessful in spite of the fact that a comparable reaction was successful in the analogous methoxyindanone series.[3] This problem was overcome by catalytic hydrogenation of the related enol acetate **15** over a platinum catalyst. The resulting acetoxy diester underwent an acid-catalyzed elimination of acetic acid to form the unsaturated ester **3**. Treatment of this ester **3** with acid catalysts under conditions known to effect equilibration of double-bond isomers in related compounds[3] lead to recovery of the diester **3** in which not more than 5% of the isomeric diester **4** could have been present. We therefore conclude that the desired olefin **3** is substantially more stable than its double-bond isomer **4**.

SCHEME I



Reaction of the unsaturated ester **3** with 1,3-butadiene at elevated temperatures yielded the desired Diels-Alder adduct **1** (Scheme III). Base-catalyzed hydrogen-deuterium exchange at C-9 of the diester **1b** demonstrated that the product isolated has the more stable configuration at this center. Heating the diacid **1a** readily formed a cyclic anhydride **17**. Since the five-membered cyclic anhydride is formed under equilibrating conditions, the product formed will clearly be the more stable epimer **17** with the two five-membered

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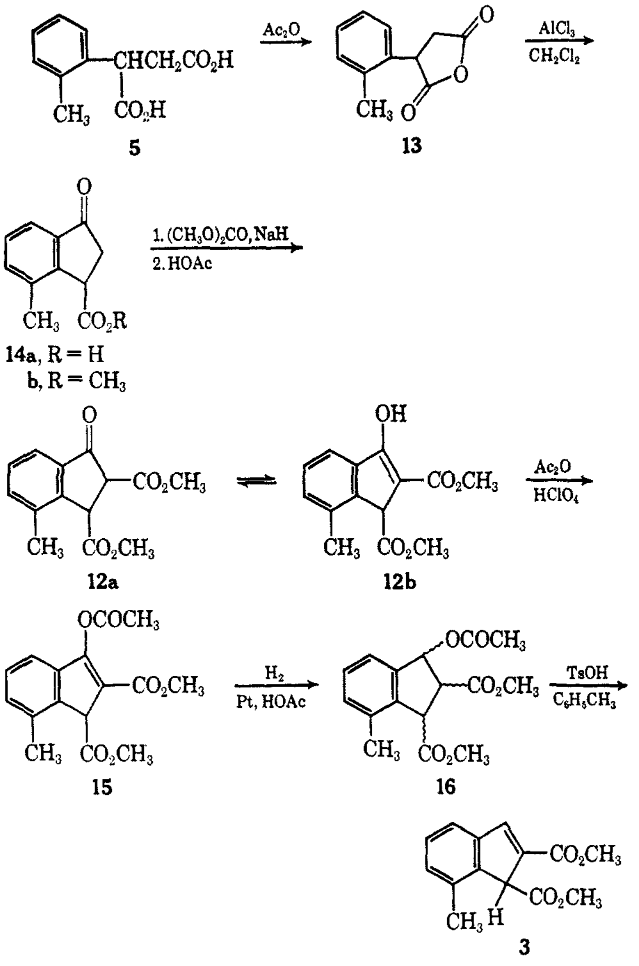
(2) (a) H. O. House and J. K. Larson, *J. Org. Chem.*, **33**, 448 (1968); (b) H. O. House and R. Darms, *ibid.*, **30**, 2528 (1965), and references therein.

(3) H. O. House, J. K. Larson, and H. C. Müller, *ibid.*, **33**, 961 (1968).

(4) K. Mori, M. Matsui, and Y. Sumiki, *Agr. Biol. Chem.* (Tokyo), **27**, 27 (1963).

Scheme II



rings *cis* fused. Reconversion of this anhydride into the diester **1b** under neutral conditions allowed us to assign the indicated configurations at C-9 to the acid derivatives **1**. Since the diester **1b** was not epimerized when treated with methanolic sodium methoxide, the indicated stereochemical arrangement with both carbomethoxy groups *cis* is also the more stable epimer.

The fact that the Diels–Alder adduct had the structure **1** (from unsaturated ester **3**) and not the isomeric structure **20** which would result from reaction of butadiene with the double-bond isomer **4** was indicated from the nmr spectrum of **1**. The assignment was verified by decarboxylation and dehydrogenation of the diacid **1a** to form the known 1-methylfluorene **18**. The isomeric adduct would be expected[3] to yield 4-methylfluorene **21** when subjected to this degradation.

Experimental Section[5]

***o*-Tolualdehyde** (6). **A. From *o*-Xylene.**—Following a general bromination procedure described previously,[6] treatment of 64.0 g (0.603 mol) of *o*-xylene with 110 g (0.618 mol) of N-bromosuccinimide and 2.0 g (8.3 mmol) of benzoyl peroxide in 600 ml of carbon tetrachloride yielded 73.6–84.0 g (66–75%) of α-bromo-*o*-xylene, bp 70–72° (2.8 mm) [lit. bp 102° (15 mm),[7] 215–218° (760 mm)[8]]. The procedure of Hass and Bender[9] was applied to α-bromo-*o*-xylene to give a 66–71% yield of *o*-tolualdehyde (6), bp 60–66° (3.5–5.0 mm) [lit.[9] bp 68–72° (6 mm)]; the 2,4-dinitrophenylhydrazone was crystallized as orange needles from an ethanol–ethyl acetate mixture, mp 194–195° (lit.[10] mp 193–194°).

B. From *o*-Toluic Acid.—*o*-Toluic acid was converted into N,N-dimethyl-*o*-toluamide, yield 93%, bp 124–125° (5 mm) [lit.[11] bp 115–118° (4.8 mm)], as previously described.[11] A cold (−10°) solution of 400 g (2.45 moles) of this dimethylamide in 2.0 l. of ether was reduced with the lithium diethoxyaluminum hydride reagent[12] prepared from 51.2 g (1.35 moles) of $LiAlH_4$ and 117 g (1.35 mole) of ethyl acetate. Following the usual isolation procedure,[12] the *o*-tolualdehyde (6) was collected as 218.6 g (74.2%) of colorless liquid, bp 70–72° (4.6 mm).

***o*-Tolylsuccinic Acid** (5). **A. From *o*-Tolualdehyde** (6).—Following previous directions,[4] *o*-tolualdehyde (6) was condensed with diethyl malonate to give the pure[13] diethyl *o*-methylbenzalmalonate (7) in 98% yield: bp 145–150° (*ca.* 1 mm) [lit.[4] bp 148–149° (4 mm)]; ir (CCl_4), 1735 (conjugated ester C=O) and 1630 cm^{-1} (conjugated (C=C); nmr (CCl_4), δ 7.82 (1 H singlet, vinyl CH), 6.9–7.4 (4 H multiplet, aryl CH), 4.24 and 4.13 (4 H, two overlapping quadruplets with J = 7 cps, ethoxy CH_2), 2.36 (3 H singlet, aryl CH_3), and 1.32 and 1.11 (6 H, two overlapping triplets, J = 7 cps, ethoxyl CH_3). Following previous directions,[4] 297.7 g (1.13 moles) of this unsaturated ester **7** was treated with potassium cyanide in aqueous ethanol and the crude mixture of cyano acid **8b** and ester **8a** was hydrolyzed with aqueous HCl to give 181.7 g (77%) of the crude diacid **5** as pale yellow prisms, mp 172–179°. Recrystallization from aqueous ethanol afforded the diacid **5** as white prisms, mp 179.5–180.5°. The material separated from diisopropyl ether as white prisms: mp 184–185° (lit.[4] mp 184–185°); ir (Nujol mull), 2500–3000 (carboxyl OH) and 1700 cm^{-1} (carboxyl C=O).

B. From 1,1,2-Tricarbomethoxyethylene (9).—The reaction of 153 g (1.0 mol) of methyl bromoacetate with the enolate anion formed from 264.2 g (2.0 mol) of dimethyl malonate, 23.0 g (1.0 g-atom) of sodium, and 1.0 l. of methanol yielded, after the usual isolation procedure, 111.9 g (58%) of pure[13] **1,1,2-tricarbomethoxyethane** as a colorless liquid: bp 86–95° (0.2–0.4 mm) [lit. bp 120–122° (5 mm),[14a] 98–102° (0.5 mm),[14b] mp 34°,[14a] 34–35°[15]]; ir (CCl_4), 1750 cm^{-1} (ester C=O). To a cold (0°) solution of 102.1 g (0.50 mol) of this triester in 170 ml of methylene chloride was added, dropwise and with stirring, a solution of 27.2 ml (0.50 mol) of bromine in 71 ml of methylene chloride. After the addition was complete, the mixture was stirred for 30 min at reflux. The resulting solution was washed successively with aqueous Na_2CO_3, with water, and with saturated aqueous NaCl and then dried, concentrated, and distilled. The **1-bromo-1,1,2-tricarbomethoxyethane**, collected at 90–93° (0.15–0.17 mm) [lit.[15] bp 148.5–149.5° (9 mm)], amounted to 130.6 g (92.2%): ir (CCl_4), 1750 and 1775 (shoulder) cm^{-1} (ester C=O); nmr (CCl_4), singlets at δ 3.37 (2 H, $-CH_2-CO$), 3.71 (3 H, $-CO_2CH_3$), and 3.83 (6 H, CO_2CH_3). A solution of 127.3 g (0.45 mole) of this bromo ester in 450 ml of pyridine was heated to 95–100° for 1 hr and then cooled and poured into water. The resulting mixture was extracted with ether and the ethereal extract was washed successively with dilute, aqueous HCl, with aqueous $NaHCO_3$, and with saturated, aqueous NaCl. After the ethereal solution had been dried and concentrated, distillation afforded 57.8 g (64%) of **1,1,2-tricarbomethoxyethylene** (9), bp 88–90°

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(5) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated, magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin-Elmer, Model 237, infrared recording spectrophotometer fitted with a grating. Unless otherwise stated, the ultraviolet spectra were determined in 95% ethanol with a Cary recording spectrophotometer, Model 14. The nmr spectra were determined at 60 Mc with a Varian Model A-60, nmr spectrometer. The chemical shift values are expressed either in cycles per second (cps) or δ values (ppm) relative to a tetramethylsilane internal standard. The mass spectra were obtained with either a CEC Model 21–130 or a Hitachi (Perkin-Elmer) mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates. All reactions involving organometallic reagents or other strong bases (metal alkoxides, sodium hydride) were performed under a nitrogen atmosphere.

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(8) E. F. J. Atkinson and J. F. Thorpe, *J. Chem. Soc.*, **91**, 1687 (1907).

(9) H. B. Hass and M. L. Bender, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p 932.

(10) B. O. Field and J. Grundy, *J. Chem. Soc.*, 1110 (1955).

(11) H. O. House and W. M. Bryant, *J. Org. Chem.*, **31**, 3482 (1966).

(12) H. C. Brown and A. Tsukamoto, *J. Amer. Chem. Soc.*, **86**, 1089 (1964).

(13) A gas chromatography column packed with silicone gum, no. SE-30, suspended on Chromosorb P was employed for this analysis.

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(15) T. Gradowska, A. Krynicki, and R. Malachowski, *Bull. Inter. Acad. Polonaise Sci., Classe Sci. Math. Nat.*, **1933A**, 552; *Chem. Abstr.*, **28**, 4383 (1934).

(0.2 mm). This triester **9** crystallized from an ether–pentane mixture as 22 g (24%) of white prisms: mp 39.5–41.5° [lit.[15] mp 40–41°, bp 141° (12 mm)]; ir (CCl_4), 1735 cm^{-1} (conjugated ester C=O); nmr (CCl_4), δ 6.82 (1 H singlet, vinyl C–H) and three partially resolved singlets at δ 3.77, 3.82, and 3.84 (9 H, CO_2CH_3); uv maximum (*n*-heptane), 204 mμ (ε 14,500); mass spectrum, no molecular ion peak, abundant fragment peaks at *m/e* 173, 59, 53, 39, 31, 30, 29, and 28.

To a solution of *o*-tolylmagnesium chloride, prepared from 30.38 g (0.24 mol) of *o*-chlorotoluene, 5.35 g (0.22 g-atom) of magnesium, and 200 ml of tetrahydrofuran, was added, dropwise and with stirring, a solution of 20.22 g (0.10 mol) of the unsaturated ester **9** and 2.0 g (0.010 mol) of anhydrous cupric acetate in 230 ml of tetrahydrofuran. After the addition was complete, the reaction mixture was stirred for 1 hr and then hydrolyzed with saturated, aqueous ammonium chloride. The ether layer was combined with the ethereal extract of the aqueous phase and then dried and concentrated. Distillation of the residual liquid separated 17.4 g (59%) of the crude ester **10**, bp 132–133° (0.2 mm). Crystallization of the product from a pentane–ether mixture afforded 11.25 g (39%) of the ester **10** as white crystals: mp 83.5–85° (recrystallization raised the melting point to 84.5–85°); ir (CCl_4), 1745 and 1760 cm^{-1} (ester C=O); uv maxima, series in the region 250–275 mμ (ε 430 or less); nmr (CCl_4), δ 7.05 (4 H, aryl C–H), 2.40 (3 H singlet, aryl CH_3), 3.28, 3.53, and 3.67 (three 3 H singlets, CO_2CH_3 functions), and two doublets (J = 12 cps, an AB pattern) with the chemical shift positions estimated to be δ 4.12 and 4.52 (2 H, aliphatic CH); mass spectrum, molecular ion peak at *m/e* 294, abundant fragment peaks at *m/e* 203, 135, 116, 115, 91, 59, and 39.

Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.21; H, 6.17. Found: C, 61.37; H, 6.21.

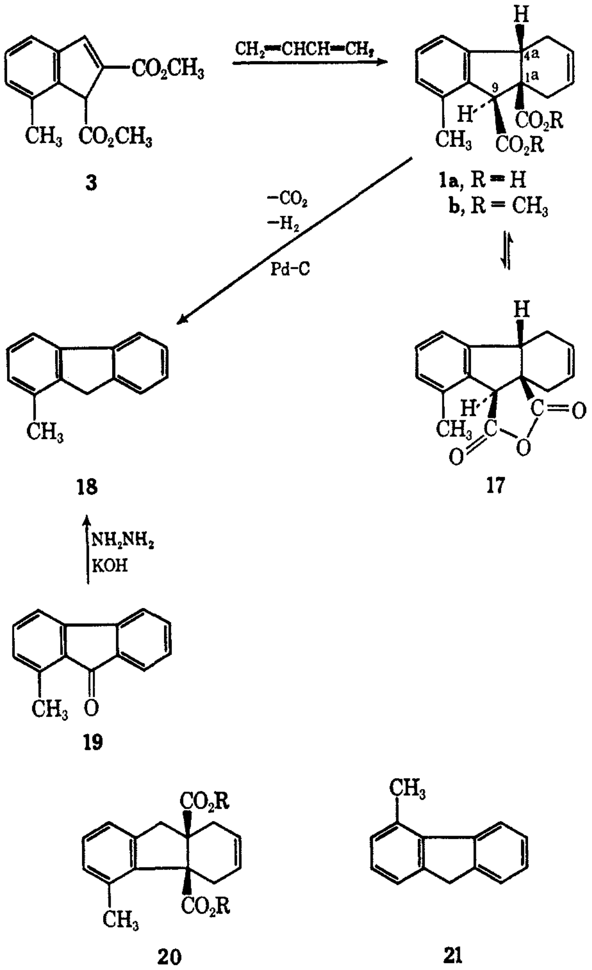
A mixture of 5.88 g (20 mmol) of this triester **10** and 20 ml of concentrated aqueous HCl was refluxed for 18 hr. The resulting mixture was partitioned between ether and water and the ethereal solution was extracted with aqueous NaOH. Acidification of this aqueous extract precipitated 3.96 g (95%) of the diacid **5**, mp 179.5–181°, identified with the previously described sample by comparison of infrared spectra.

C. **From Tetracarboethoxyethylene.**—To 20.0 ml of a tetrahydrofuran solution containing 25.6 mmol of *o*-tolylmagnesium chloride was added, dropwise and with stirring, over a 1-hr period, a solution of 8.30 g (26.2 mmol) of tetracarboethoxyethylene[16] in 20 ml of tetrahydrofuran. After the reddish brown reaction solution had been refluxed for 15 min, it was washed successively with saturated aqueous NH_4Cl, with water, and with aqueous NaCl, and then dried and concentrated to leave 10.9 g of the crude tetraester **11** as a viscous yellow oil. A 9.82-g portion of this crude ester **11** was treated with refluxing concentrated aqueous HCl for 18 hr and then 75 ml of acetic acid was added and refluxing was continued for 14 hr. The resulting mixture was concentrated under reduced pressure and then partitioned between water and ether. The ethereal layer was extracted with aqueous NaOH and this aqueous phase was acidified and extracted with ether. After this ether extract had been dried and concentrated, the crude residual diacid **5** (2.20 g of brown semisolid) was heated to 120° with 10 ml of acetic anhydride for 30 min and then distilled to separate 1.45 g (33% based on the starting tetraester) of the anhydride **13** as a viscous yellow liquid, bp 155–160° (0.5 mm). This sample was identified with the subsequently described sample of the anhydride **13** by comparison of infrared spectra.

***o*-Tolylsuccinic Anhydride (13).**—A mixture of 208.2 g (1.0 mol) of the diacid **5** and 500 ml of acetic anhydride was refluxed for 1.5 hr and then distilled. The anhydride was collected as 160.5 g (84.3%) of a very viscous yellow liquid: bp 158–160° (0.5 mm) [lit.[4] bp 174–176° (5 mm)]; ir (liquid film), 1790 and 1860 cm^{-1} (C=O of five-membered cyclic anhydride). In one preparation, the anhydride **13** crystallized on standing as white prisms, mp 45.3–46.3°.

3-Carboxy-4-methyl-1-indanone (14a).—To a cold (ice bath) solution of 23.50 g (0.124 mol) of the anhydride **13** in 450 ml of methylene chloride was added, portionwise with stirring and cooling, 36.00 g (0.271 mol) of anhydrous aluminum chloride. After the addition was complete, the reaction mixture was stirred for 1 hr with cooling and then the ice bath was removed and the mixture was stirred for 12 hr at room temperature. The initially yellow reaction mixture turned red and finally brown in color. After the reaction complex had been decomposed by the addition of ice and hydrochloric acid, the organic layer was washed successively with water and aqueous NaCl and then dried and concentrated. The crude keto acid **5** remained as 21.50 g (91.5%) of brown prisms: mp 155–157° (lit.[4] mp 155–156.5°); ir (Nujol mull), 2600–3300, (carboxyl associated O–H), 1730 (C=O of an intramolecularly bonded carboxyl function), 1685 cm^{-1} (C=O of a hydrogen-bonded conjugated ketone in a five-membered ring); uv maxima, 249 mμ (ε 10,000) and 293 mμ (ε 2040).

SCHEME III



3-Carbomethoxy-4-methyl-1-indanone (14b).—A solution of 21.0 g (0.111 mol) of the keto acid **14a** and 2.0 ml of concentrated sulfuric acid in 120 ml of methanol was refluxed for 20 hr and then cooled, diluted with aqueous $NaHCO_3$, and extracted with ether. The ethereal extract was washed successively with aqueous $NaHCO_3$ and aqueous NaCl and then dried and concentrated. The residual oil was distilled in a short-path still to separate 18.52 g (82.5%) of the keto ester **14b**, bp 117–122° (0.15 mm), which crystallized on cooling as white prisms: mp 50–52° [lit.[4] mp 53–54°, bp 140–150° (5 mm)]; ir (CCl_4), 1745 (ester C=O) and 1730 cm^{-1} (conjugated C=O in a five-membered ring); uv maxima, 249 mμ (ε 12,200) and 292 mμ (ε 2000); nmr (CCl_4), δ 3.55 (3 H singlet, O–CH_3), 2.26 (3 H singlet, aryl C–CH_3), 7.0–7.6 (3 H multiplet, aryl C–H), 4.07 (triplet, line separation 5.5 cps, Ar–CH–CO), and δ 2.67 (2 H multiplet, AB part of ABX pattern, –CH_2–CO); mass spectrum, molecular ion peak at *m/e* 204, abundant fragment peaks at *m/e* 145 (M − CO_2CH_3), 144, 115, 91, and 39.

2,3-Dicarbomethoxy-4-methyl-1-indanone (12).—A mineral oil dispersion containing 48.0 g (2 mol) of sodium hydride was washed free of mineral oil with pentane and then 700 ml of benzene and 360 g (4.0 mol) of dimethyl carbonate were added. This suspension was warmed to 60° and a solution of 115.4 g (0.565 mole) of the keto ester **14b** in 150 ml of benzene was added, dropwise and with stirring over a 2.5-hr period. The resulting suspension was heated to 60° with stirring for 2 hr

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[16] This material was purchased from the J. T. Baker Co.

and then cooled to room temperature and treated with 250 ml of acetic acid with concurrent cooling and stirring. The resulting mixture was poured onto crushed ice and the organic layer was separated. The aqueous phase was extracted with benzene and the combined benzene solutions were washed successively with aqueous $NaHCO_3$ and saturated, aqueous NaCl. After the organic solution had been dried and concentrated, the residual solid was washed with methanol to leave 115.2 g of the diester **12** as tan prisms, mp 94–97°. An additional 8.3 g (total yield 83.4%) crop, mp 92–96°, was separated from the mother liquors. A portion of this material was taken up in diisopropyl ether, decolorized with Norit, and cooled to deposit the keto diester **12** as white prisms: mp 92–94° (lit.[4] mp 96–97°); ir (CCl_4), 1745 (strong, ester C=O), 1730 (shoulder), 1715 (shoulder), 1660 (medium), 1620 (weak), and 1580 cm^{-1} (medium, enolic β-keto ester); nmr (CCl_4), δ 2.43 (3 H, partially resolved doublet, aryl CH_3-C), 7.3–7.9 (3 H multiplet, aryl C-H), 4.4–4.9 (1 H multiplet, Ar-CH-CO-), and 3.6–4.0 (7 H multiplet, CH_3-O and -CH-CO-). The shapes and relative intensities of the peaks in the regions δ 3.6–4.0 (shifted to δ 3.8–4.3) and 4.4–4.9 were altered when the sample was measured in deuteriochloroform suggesting that the solutions contain mixtures of *cis* and *trans* keto isomers as well as the enol tautomer. The highest peak in the mass spectrum is at *m/e* 230 (M − 32); abundant fragment peaks are found at *m/e* 145, 91, 44, 32, and 31.

An attempt to reduce 262.4 mg of the keto diester **12** with 11.0 mg of sodium borohydride in 35 ml of isopropyl alcohol at room temperature for 2.5 hr resulted in recovery of 244.2 mg (93%) of the crude starting material identified by its infrared absorption.

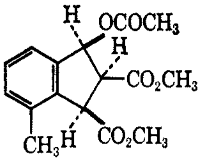
3-Acetoxy-1,2-dicarbomethoxy-7-methylindene (15).—A vigorously stirred solution of 85.7 g (0.328 mol) of the keto diester **12** and 200 g (1.96 mol) of acetic anhydride in 200 ml of benzene was treated with 3 drops of aqueous 70% perchloric acid and the resulting solution was stirred at 25° for 5 hr. The resulting solution was washed successively with aqueous $NaHCO_3$ and aqueous NaCl and then dried and concentrated. The residual brown oil was diluted with 400 ml of ether and then cooled and concentrated. The crystalline enol acetate **15** which separated was collected and washed with a benzene–hexane mixture (1:10 v/v) to leave 86.3 g (86.9%) of white prisms, mp 101.1–103°. Recrystallization from an ethyl acetate–hexane mixture afforded the pure enol acetate **15**: mp 102–103°; ir (CCl_4), 1785 (enol ester C=O), 1740 (ester C=O), 1720 (conjugated ester C=O), and 1625 cm^{-1} (conjugated C=C); nmr ($CDCl_3$), δ 7.0–7.4 (3 H multiplet, aryl CH), 4.67 (1 H singlet, benzylic CH), 3.79 (3 H singlet, OCH_3), 3.67 (3 H singlet, OCH_3), 2.38 and and 2.41 (two 3 H singlets, aryl CH_3 and $COCH_3$); uv maxima, 209 mμ (ϵ 17,600), 228 (13,200), 235 (shoulder, 10,800), and 290 (18,100).

Anal. Calcd for $C_{16}H_{16}O_6$: C, 63.15; H, 5.30; mol wt, 304. Found: C, 63.16; H, 5.17; mol wt, 304 (mass spectrum).

3-Acetoxy-1,2-dicarbomethoxy-7-methylindan (16).—A solution of 20.0 g (65.8 mmoles) of the enol acetate **15** in 250 ml of acetic acid was hydrogenated at atmospheric pressure and 23.6° over the catalyst from 3.0 g of platinum oxide. After 40 min (hydrogen uptake 1920 ml or 1.2 equiv) the reaction was stopped and the mixture was filtered and concentrated under reduced pressure. The residual oil was crystallized from a benzene–hexane mixture to separate 13.61 g (67.7%) of one stereoisomer of the acetoxy diester **16** as fluffy white needles melting in the range 109–111°. Recrystallization separated the pure acetoxy diester **16**: mp 111.5–112°; ir (CCl_4), 1745 (shoulder) and 1738 cm^{-1} (ester C=O); uv maxima, 265 mμ (ϵ 306), 268 (shoulder, 288), 274 (260), and 293 (64); nmr ($CDCl_3$), δ 7.0–7.4 (3 H multiplet, aryl CH), 6.46 (1 H doublet, J = 6 cps, aryl >CH-O), 4.25 (1 H doublet, J = 8.5 cps, benzylic CH), 3.5–3.8 (7 H multiplet, two OCH_3 and CH-CO_2R), 2.29 and 2.00 (two 3 H singlets, aryl CH_3 and CO-CH_3).

Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92; mol wt, 306. Found: C, 62.82; H, 5.83; mol wt, 306 (mass spectrum).

The oily material remaining in the mother liquors from this reaction appeared to be a mixture of the starting enol acetate and hydrogenolysis products. We were unsuccessful in isolating any additional pure material from the mixture. Both the nmr coupling constants (6 and 8.5 cps)[17] and the mode of preparation would suggest that the major product, the stereoisomer, mp 111.5–112°, possesses the stereochemistry illustrated in structure **16a**.



16a

1,2-Dicarbomethoxy-7-methylindene (3).—A solution of 9.8 g (33 mmol) of the acetoxy diester **16** and 1.0 g of *p*-toluenesulfonic acid in 500 ml of toluene was boiled for 3.5 hr during which time 250 ml of toluene was allowed to distil from the mixture. The resulting toluene solution was washed with water, dried, and concentrated under reduced pressure. The residual white solid was recrystallized from hexane to separate 7.8 g (98%) of indene **3** as colorless prisms: mp 78–80° (recrystallization raised the melting point to 79.9–81°); ir (CCl_4), 1745 (ester C=O), 1720 (conjugated ester C=O), and 1610 cm^{-1} (conjugated C=C); uv maxima, 230 mμ (ϵ 12,200), 237 (10,900), and 293 (16,300); nmr (CCl_4), δ 7.49 (1 H doublet, J = 1.5 cps, vinyl CH), 6.8–7.3 (3 H multiplet, aryl CH), 4.38 (1 H doublet, J = 1.5 cps, benzylic CH), 3.72 (3 H singlet, OCH_3), 3.54 (3 H singlet, OCH_3) and 2.33 (3 H singlet, aryl CH_3).

Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73; mol wt, 246. Found: C, 68.52; H, 5.89; mol wt, 246 (mass spectrum).

A solution of 247 mg (1.0 mmol) of the diester **3** and 59 mg (0.3 mmol) of *p*-toluenesulfonic acid in 20 ml of methanol was refluxed for 72 hr and then the crude neutral product (205 mg or 83% of white prisms, mp 60–78°) was recovered. The nmr spectrum (CCl_4) of this crude product corresponded to the nmr spectrum for the pure diester **3** (see above) except for the presence of an additional very weak peak at δ 4.92 which may be attributable to the signal from one of the methoxy functions in diester **4**. Comparison of these spectra with the spectra of known mixtures of analogous indene diesters[3] indicates that this crude product does not contain more than 5% of the diester **4**.

Diels–Alder Reaction with the Indene 3.—A mixture of 6.6 g (27 mmoles) of the diester **3**, 0.6 g of phenothiazine (as a radical inhibitor), 40 ml of cold (−70°) liquid 1,3-butadiene, and 50 ml of benzene was placed in an autoclave and heated to 180–190° for 18 hr. The mixture was cooled, an additional 40 ml of liquid butadiene was added, and the mixture was heated to 180–190° for an additional 36 hr. The resulting yellow solution was concentrated under reduced pressure and extracted repeatedly with portions of boiling methanol to remove the methanol-soluble product from the methanol-insoluble polymer. The methanol extracts were concentrated and the residue was treated with 100 ml of refluxing aqueous 10% NaOH for 14 hr. After the basic solution had been extracted with ether, it was acidified and the crude diacid **1a** which separated was collected. Recrystallization of the crude product from ether afforded 2.9 g (31%) of the **ether solvate of the diacid 1a** as colorless prisms: mp 75° dec; ir ($CHCl_3$), 2500–3300 (carboxyl OH) and 1715 cm^{-1} (carboxyl C=O); uv maxima, 266.5 mμ (ϵ 279), 270 (shoulder, 226) and 275 (199); nmr ($CDCl_3$), δ 12.60 (2 H singlet, COOH), 6.9–7.3 (3 H multiplet, aryl CH), 5.3–6.0 (2 H multiplet, vinyl CH), 4.2–4.5 (1 H multiplet, benzylic CH), 3.95 (1 H singlet, benzylic CH), 3.50 (4 H quadruplet, J = 7 cps, ethoxyl CH_2), 2.40 (3 H singlet, aryl CH_3), 1.6–3.0 (4 H multiplet, aliphatic CH), and 1.21 (6 H triplet, J = 7 cps, ethoxyl CH_3).

Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.57. Found: C, 69.27; H, 7.35.

A solution of this solvate in hexane, when heated, deposited the solvent free diacid **1a** as white needles: mp 214° dec; ir ($CHCl_3$), 2500–3200 (carboxyl OH) and 1710 cm^{-1} (carboxyl C=O); uv maxima, 266 mμ (ϵ 282), 270 (shoulder, 228) and 274.5 (205); nmr ($CDCl_3$), δ 12.60 (2 H singlet, COOH), 6.8–7.4 (3 H multiplet, aryl CH), 5.2–6.0 (2 H multiplet, vinyl CH), 4.1–4.5 (1 H multiplet, benzylic CH), 3.92 (1 H singlet, benzylic CH), 2.37 (3 H singlet, aryl CH_3) and 1.6–3.0 (4 H multiplet, aliphatic CH).

Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.31; H, 6.20.

Reaction of 982 mg (2.84 mmol) of the diacid etherate **1a** with excess ethereal diazomethane yielded 859 mg (100%) of the crude diester **1b** as white prisms, mp 84–87°. Recrystal-

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[17] E. Lustig and E. P. Ragelis [*J. Org. Chem.*, **32**, 1398 (1967)] have reported values of 8.45 and 3.37 cps for the *cis* and *trans* vicinal coupling constants in 1-indanone.

lization from methanol afforded the pure diester **1b** as colorless prisms: mp 86–87°; ir (CCl_4), 1740 (ester C=O) and 1660 cm^{-1} (weak, C=C); uv maxima, 266 mμ (ε 274), 270 (shoulder, 223), and 274.5 (200); nmr (CCl_4), δ 6.7–7.2 (3 H multiplet, aryl CH), 5.1–5.9 (2 H multiplet, vinyl CH), 4.0–4.3 (1 H multiplet, benzylic CH), 3.79 (1 H singlet, benzylic CH), 3.63 (3 H singlet, OCH_3), 3.53 (3 H singlet, OCH_3), 2.28 (3 H singlet, aryl CH_3), and 1.6–2.9 (4 H multiplet, aliphatic CH); mass spectrum, molecular ion peak at *m/e* 300, abundant fragment peaks at *m/e* 181, 180, 166, and 165.

Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.86; H, 6.81.

A solution of 172 mg (0.51 mmol) of the diester **1b** and the sodium methoxide from 75 mg (3.3 mg-atom) of sodium in 3.0 ml of methanol-d_1 was refluxed for 3 days and poured into a mixture of deuterium oxide and acetic acid-d_1. The resulting mixture was concentrated under reduced pressure and an ether solution of the residue was washed successively with aqueous $NaHCO_3$ and aqueous NaCl and then dried and concentrated to leave 159 mg (93%) of the crude partially deuterated diester **1b**, mp 76–82°. Recrystallization from methanol afforded 94 mg of the ester **1b**, mp 84–85°, which contained 16% d_0 species and 84% d_1 species. The nmr spectrum of this material corresponded to the spectrum previously described except that the singlet at δ 3.79 (benzylic CH) was markedly reduced in intensity.

A mixture of 1.064 g (3.08 mmol) of the etherate of the diacid **1a** and 632 mg of a 30% palladium-on-carbon catalyst was heated to 235° under a slow stream of nitrogen for 2.25 hr. The resulting mixture was extracted with boiling chloroform and the chloroform extract was filtered and concentrated. Recrystallization of the residual white solid from ethanol separated 243 mg (50.5%) of 1-methylfluorene (**18**) as white prisms, mp 83–84.5°; after sublimation at 80° (3 mm), the material melted at 85–87° (lit. mp 85°,[18a] 86°[18b]).[19] This material was identified with a subsequently described sample by a mixture melting point determination and by comparison of infrared and mass spectra.

To obtain an authentic sample of the fluorene **18**, a 300-mg (1.76 mmol) sample of the ketone **19**[20] was reduced with 1.5 ml of hydrazine hydrate and 0.60 g (11 mmol) of KOH in 20 ml of diethylene glycol for 3 hr at 175° and 0.5 hr at 250°. The crude neutral product (180 mg), isolated in the usual way, was recrystallized from ethanol to separate 120 mg of the fluorene **18**, mp 83.6–85.6°. After sublimation at 70° (0.2 mm), the product melted at 85–86°.

Preparation of the Anhydride 17.—The ether solvate of the diacid **1a** (1.448 g or 4.19 mmol) was distilled twice in a short-path still (0.2 mm and 180–190° bath) to yield 1.010 g (84%) of the anhydride **17** as a colorless liquid. The anhydride **17** crystallized on standing as white prisms: mp 99.6–101.6°; ir (CCl_4), 1790 and 1855 cm^{-1} (anhydride C=O in a five-membered ring); uv maxima (CH_3CN), 265 mμ (ε 307), 270 (shoulder, 246), and 274 (238); nmr ($CDCl_3$), δ 6.9–7.3 (3 H multiplet, aryl CH), 5.8–6.0 (2 H multiplet, vinyl CH), 4.29 (1 H singlet, benzylic CH), 3.84–4.1 (1 H multiplet, benzylic CH), 2.52 (3 H singlet, aryl CH_3), and 2.2–2.9 (4 H multiplet, aliphatic CH).

Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.70; H, 5.59.

A solution of 254 mg (1.0 mmol) of the anhydride **17** in 10 ml of methanol was refluxed for 3 hr and then concentrated under reduced pressure. The residual monomethyl ester(s) was esterified with excess ethereal diazomethane. The crude neutral product was recrystallized from methanol to separate 130 mg (43%) of the diester **1b**, mp 85–88°, identified with the previously described sample by a mixture melting point and comparison of infrared spectra. An additional 50 mg (17%) of the diester **1b**, mp 85–87°, was recovered from the mother liquor.

Registry No.—**1a**, 15448-20-1; ether solvate of **1a**, 15448-21-2; **1b**, 15448-22-3; **1b**, *C-9-d*$_1$, 15544-45-3; **3**, 15448-23-4; **10**, 15448-24-5; **15**, 15448-25-6; **16a**, 15448-29-0; **16**, 15448-26-7.

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[18] (a) L. A. Pinck and G. E. Hilbert, *J. Amer. Chem. Soc.*, **68**, 751 (1946); (b) W. C. Lothrup and P. A. Goodwin, *ibid.*, **65**, 363 (1943).

[19] The other possible product would have been 4-methylfluorene (**21**) which is reported to melt at 71.5–72.5° [M. Orchin and E. O. Woolfolk, *ibid.*, **67**, 122 (1945)] and 70.4–71.2° [L. J. E. Hofer and W. C. Peebles, *Anal. Chem.*, **23**, 690 (1951)].

[20] H. O. House, R. G. Carlson, H. Müller, A. W. Noltes, and C. D. Slater, *J. Amer. Chem. Soc.*, **84**, 2614 (1962).

Perhydroindan Derivatives. X. The Diels–Alder Reaction with 6-Methoxyindene Derivatives[1a]

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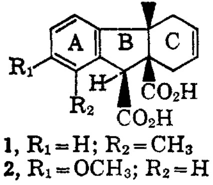
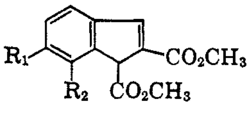
Both of the double-bond isomers of 1,2-dicarbomethoxy-6-methoxyindene (**4** and **17**) and 1,2-dicarbomethoxyindene (**19** and **20**) have been synthesized. In each case the less highly substituted double isomer **4** or **20** is the more stable. However, derivatives of each of these indenes react with 1,3-butadiene to give the Diels–Alder adduct derived from the more highly substituted double-bond isomer.

As noted in the accompanying paper,[2] we wished to synthesize the tetrahydrofluorene diacids **1** and **2** as potential precursors for epiallogibberic acid and gibberellin derivatives in which the A ring is nonaromatic.



1, $R_1 = H$; $R_2 = CH_3$
2, $R_1 = OCH_3$; $R_2 = H$



3, $R_1 = H$; $R_2 = CH_3$
4, $R_1 = OCH_3$; $R_2 = H$

It was our intention to use the indenes **3** and **4** as reactants with 1,3-butadiene to produce these acids **1** and **2**. The accompanying paper[2] describes the successful conversion of the indene **3** into the diacid **1**. In this manuscript, we describe the synthesis of the indene **4**. However, the reaction of this indene **4** with 1,3-butadiene did not yield the desired diacid **2**, but rather a structurally isomeric product.

The synthetic route (Scheme I) used for the indene derivative **4** followed the general pattern described[2] for the indene **3**. Differences were observed in the Friedel–Crafts cyclization of the anhydride **9** where the major product **11** was accompanied by lesser amounts (10–20%) of the alternative cyclization product **10**. The structure of the major product **11** was confirmed by oxidation to form the known phthalic acid derivative **12**. Unlike the result obtained in the previous study[2] with the 7-methylindanone derivative, the keto diester

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[2] H. O. House, F. J. Sauter, W. G. Kenyon, and J. J. Riehl, *J. Org. Chem.*, **33**, 957 (1968).