THE JOURNAL OF Organic Chemistry®

VOLUME 38, NUMBER 8 | APRIL 20, 1973

The Synthesis of Dicyclopenta[*ef,kl*]heptalene (Azupyrene). I. Routes to 1,6,7,8,9,9a-Hexahydro-2*H*-benzo[*c,d*]azulen-6-one[1,2]

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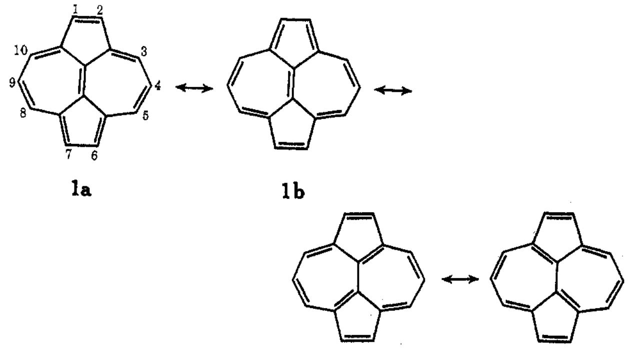
Received August 4, 1972

As the first phase in the synthesis of dicyclopenta[*ef,kl*]heptalene, four routes to 1,6,7,8,9,9a-hexahydro-2*H*-benzo[*c,d*]azulen-6-one (**19**) *via* the intermediate 4-(1-indanyl)butanoic acid (**3**) have been investigated: (i) *via* a Reformatsky reaction of 1-indanone with methyl 4-bromo-2-butenoate; (ii) *via* a Reformatsky reaction of 1-indanone with ethyl bromoacetate and subsequent chain lengthening by a malonic ester alkylation sequence; (iii) *via* reaction of 1-indanone with 3-methoxy-1-propylmagnesium chloride and subsequent chain lengthening by carbonation of a Grignard reagent; (iv) by reaction of sodio indene with 1-chloro-3-bromopropane and a subsequent Grignard carbonation sequence. Route iv proved to be the shortest, most adaptable to relatively large runs, and gave the best overall yields. The melting point of **3** in the literature was found to be incorrect. The acid-catalyzed cyclization of **3** or its acid chloride to **19** was accompanied by the formation of 1,2,3,4-tetrahydro-5*H*-fluoren-4-one (**20**).

The dicyclopenta[*ef,kl*]heptalene structure (**1**), for which we have proposed the common name azupyrene,[1] represents a cyclocondensed, conjugate-unsaturated, convex, nonalternant hydrocarbon having no benzenoid components. Two of the valence-bond resonance formulas (**1a**, **1b**) possess a 14-π-electron system peripheral to a central 2-π-electron moiety, whereas the other two noncharge-separated formulas (**1c**, **1d**) do not. Azupyrene therefore provides a new, nonbenzenoid system for the further tests of structural theories of aromaticity, especially that of Platt[6,7a] wherein a stable (*i.e.*, $4n + 2$) π-electron "shell" will be separated from inner π electrons by circular nodes such that the two loci of unsaturation will consist of more or less discrete molecular orbitals. This concept, a modification of an earlier one based on the free-electron model,[7,8] has afforded an explanation of the aromatic character of benzenoid cyclocondensed hydrocarbons (*e.g.*, pyrene, coronene, and ovalene, for which extension of the Hückel rule has not been satisfactory), and of acepleiadylene (as contrasted with pleiadiene and acepleiadiene).[9]



1a **1b** **1c** **1d**

The azupyrene structure is also symmetric[10] such that Craig's rules[11] may be formally applied to any of the Kekule structures with either of the two axes of symmetry. The result in each case is that $f + g$ is an even number and the valence-bond ground state is therefore predicted to be totally symmetric and, consequently, to have normal aromatic stability. A calculated value of 0.38 β has been determined for the specific delocalization energy per electron for azupy-

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(1) A preliminary announcement of the synthesis has appeared: A. G. Anderson, Jr., A. A. MacDonald, and A. F. Montana, *J. Amer. Chem. Soc.*, **90**, 2993 (1968).

(2) Taken in part from the Ph.D. Theses of G. M. M. and A. F. M., University of Washington.

(3) University of Washington.

(4) NIH Predoctoral Fellow, 1968–1970.

(5) Seattle Pacific College.

(6) J. R. Platt, *J. Chem. Phys.*, **22**, 1448 (1954).

(7) (a) J. R. Platt, *ibid.*, **17**, 484 (1949); (b) W. T. Simpson, *ibid.*, **17**, 1218 (1949).

(8) N. S. Bayliss, *ibid.*, **16**, 287 (1948); H. Kuhn, *ibid.*, **16**, 840 (1948); F. D. Rice and E. Teller, "The Structure of Matter," Wiley, New York, N. Y., 1949, p 110.

(9) V. Boekelheide, W. E. Langeland, and C.-T. Liu, *J. Amer. Chem. Soc.*, **73**, 2432 (1951); V. Boekelheide and G. K. Vick, *ibid.*, **73**, 653 (1951).

(10) One other compound of this type is known: the isomeric pentaleno-[1,6,5-*def*]heptalene, which is less symmetrical. K. Hafner, R. Fleischer, and K. Fritz, *Angew. Chem., Int. Ed. Engl.*, **4**, 69 (1965).

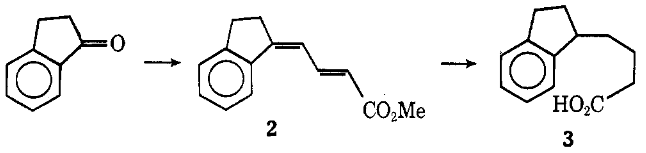
(11) D. P. Craig, *J. Chem. Soc.*, 3175 (1951); D. P. Craig and A. Macoll, *ibid.*, 964 (1949). Azupyrene may have an abnormal symmetry in this regard, however.[12]

rene[12] as compared to 0.41 β for pyrene, 0.38 β for anthracene, and 0.37 β for naphthalene.

The general route selected for the synthesis resolved into three quite distinct parts in the laboratory: (i) the preparation of 1,6,7,8,9,9a-hexahydro-2*H*-benzo[*c,d*]azulen-6-one (**19**), (ii) the preparation of 1,5,6,-6a,7,8,9,9a-octahydro-2*H*-indeno[5,4,3-*cde*]azulene, and (iii) the conversion of the octahydroindenoazulene to azupyrene. The present paper presents the results of the first part of the study.

Route 1. ***Via*** **a Reformatsky Reaction of 1-Indanone and Methyl 4-Bromo-2-butenoate.**—The first synthesis carried out was that shown in Scheme I. A Reformatsky reaction involving 1-indanone and methyl 4-bromo-2-butenoate formed the hydroxy ester plus some dehydrated ester (**2**) and 2-(1-indanylidene)-1-indanone (the ketol condensation product from 1-indanone). Treatment of this mixture with hydrogen and W-6 Raney nickel gave incomplete reduction, and subsequent dehydration with potassium bisulfate, hydrogenation (platinum catalyst), and saponification gave **3** in only *ca.* 14% overall yield. It was then found that distillation of the crude Reformatsky product mixture in the presence of *p*-toluenesulfonic acid effected complete dehydration and the product thus formed could be converted to **3** in good (80%) yield (36–42% overall) by reduction (platinum catalyst) and hydrolysis. Thus, in practice, this route as developed involved just three operational steps with the isolation of but one intermediate (**2**). There were, however, two major disadvantages: it was difficult to carry out the Reformatsky reaction on larger than a 0.5 *M* scale, and extensive polymerization occurred if the acid-catalyzed dehydration was performed on more than 25 g.

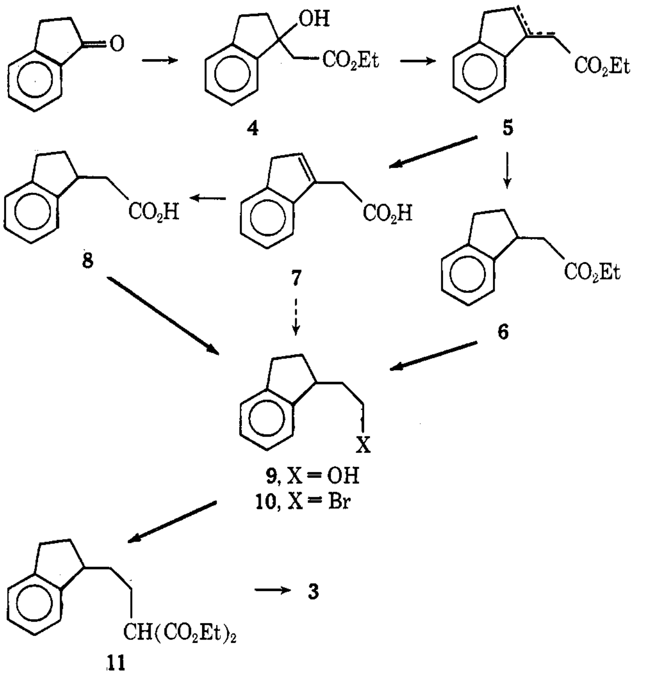
SCHEME I



Route 2. ***Via*** **a Reformatsky Reaction of 1-Indanone and Ethyl Bromoacetate. Scheme II.**—The product (**3**) obtained from route 1 melted at 72–73°, whereas von Braun, *et al.*,[13] had reported a value of 92°. Though our product and its amide derivative gave correct analyses, it was considered advisable to repeat the von Braun synthesis[13,14] to be certain that the products were indeed the same and to compare the two routes, since little yield data had been reported in the earlier work.

A Reformatsky reaction of 1-indanone with ethyl bromoacetate gave the hydroxy ester **4** (71%). Distillation of **4** in the presence of *p*-toluenesulfonic acid or treatment with thionyl chloride and pyridine gave incomplete dehydration, but heating with anhydrous formic acid gave $\geq 90\%$ yields of the unsaturated ester **5**, the ultraviolet spectrum of which indicated the presence of a considerable fraction having the exocyclic double bond. Catalytic (platinum) reduction of **5** afforded **6** (93%). Reduction of **6** to **9** with lithium aluminum hydride (in place of sodium–alcohol) increased the yield in this step from 40% to 94%.

SCHEME II



The alternative path of hydrolysis of the unsaturated ester **5** to the corresponding acid **7** and reduction of the latter to **9** was also examined. Unexpectedly,[15] reaction of **7** with lithium aluminum hydride gave incomplete reduction, but catalytic (platinum) hydrogenation gave **8** (72%) and subsequent hydride reduction formed **9** (79%). This path thus proved to be one step longer and to give lower yields.

Reaction of **9** with excess hydrogen bromide formed **10** (82%), which, upon treatment with sodiomalonic ester gave **11** (76%), and hydrolysis and then decarboxylation of **11** formed **3** (75%, 28% overall). The shorter and better path for this route involved seven operational steps with six isolated intermediates. It was judged to be inferior to Scheme I, as it also contained a Reformatsky reaction, for which large runs gave lower yields, and gave a lower overall yield. The product (**3**) obtained was identical with that from Scheme I; so the melting point reported[13] was incorrect.

Route 3. ***Via*** **the Reaction of 1-Indanone with 3-Methoxy-1-propylmagnesium Chloride. Scheme III.**—Smith and Sprung[16] had studied the use of 3-alkoxypropyl halides for the introduction of a three-carbon chain bearing a terminal functional group and found that methoxy was cleaved more readily than ethoxy. Accordingly, a Grignard reaction of 1-indanone and 3-methoxy-1-propylmagnesium chloride yielded 1-hydroxy-1-(3-methoxypropyl)indan (**12**) (41%), which after dehydration afforded 3-(3-methoxypropyl)indene (**13**) (63%). The assignment of the double bond position in **13** was based on comparison of the ultraviolet spectrum with those of 3-methyl-

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[12] A. Rosowsky, H. Fleischer, S. T. Young, R. Partch, W. H. Saunders, Jr., and V. Boekelheide, *Tetrahedron*, **11**, 121 (1960); B. A. Hess, Jr., and L. J. Schaal, *J. Org. Chem.*, **36**, 3418 (1971), give 0.353 β for azupyrene.

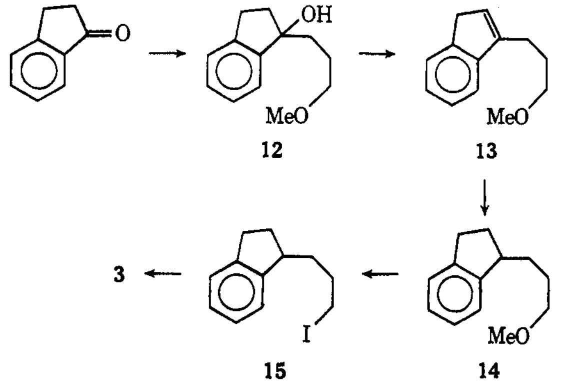
[13] J. von Braun and E. Rath, *Chem. Ber.*, **60B**, 1182 (1927).

[14] J. von Braun, E. Danziger, and Z. Koehler, *ibid.*, **50**, 56 (1917).

[15] R. F. Nystrom and W. B. Brown, *J. Amer. Chem. Soc.*, **69**, 2548 (1947), reported that $LiAlH_4$ effected the conversion of cinnamic acid to 3-phenyl-1-propanol.

[16] L. I. Smith and J. A. Sprung, *ibid.*, **65**, 1276 (1943).

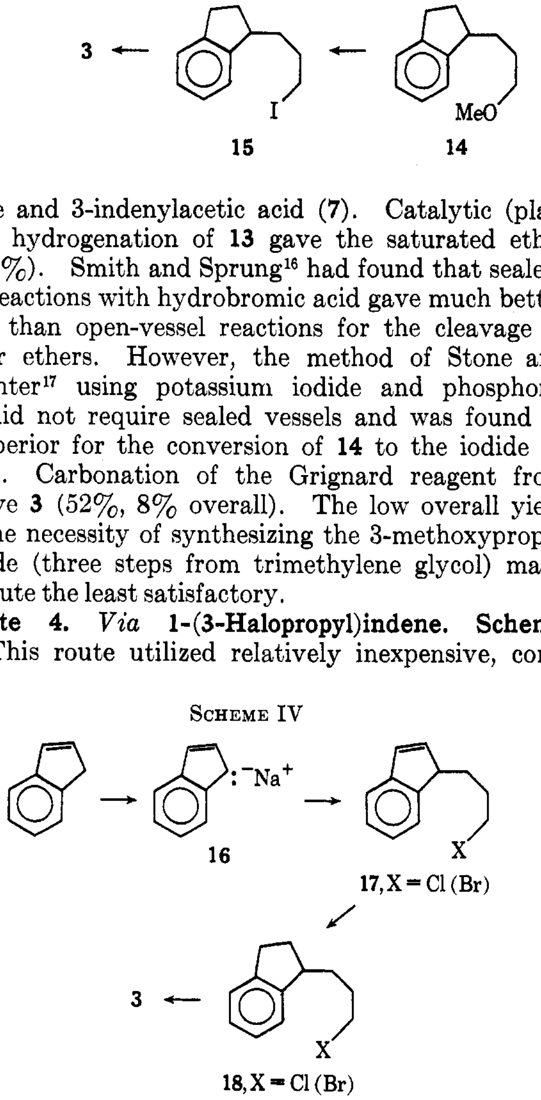
SCHEME III



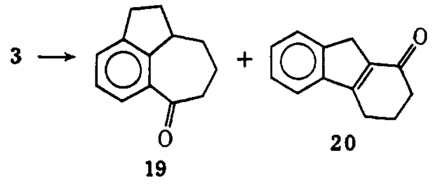
indene and 3-indenylacetic acid (**7**). Catalytic (platinum) hydrogenation of **13** gave the saturated ether **14** (87%). Smith and Sprung[16] had found that sealed-tube reactions with hydrobromic acid gave much better yields than open-vessel reactions for the cleavage of similar ethers. However, the method of Stone and Schechter[17] using potassium iodide and phosphoric acid did not require sealed vessels and was found to be superior for the conversion of **14** to the iodide **15** (62%). Carbonation of the Grignard reagent from **15** gave **3** (52%, 8% overall). The low overall yield and the necessity of synthesizing the 3-methoxypropyl chloride (three steps from trimethylene glycol) made this route the least satisfactory.

Route 4. ***Via*** **1-(3-Halopropyl)indene. Scheme IV.**—This route utilized relatively inexpensive, commercially available reagents and it was hoped that the reactions involved would be adaptable to relatively large runs. In practice, the source and purity of the indene proved to be important[18] and, independent of this factor, the yields of **17** (obtained as a mixture of the chloride and bromide from the reaction of **16** with 1-chloro-3-bromopropane) varied considerably for reasons which could not be determined. Efforts to resolve these difficulties led to three procedures for the preparation of **16** and its conversion to **17**. One procedure required very pure indene, yet formed considerable by-product. The most satisfactory method (68%, 75% net) did not require such pure indene and gave little of the by-product. High yields (>90%) of **18** were obtained from **17** and carbonation of the Grignard reagent from **18** produced **3** (70–81%, 43–52% overall). This route involved three operation steps and the isolation of two intermediates (**17** and **18**). It was considered to be the best with respect to practical convenience, especially for relatively large runs, as well as for the overall yield despite the uncertainties with regard to the behavior of the indene.

SCHEME IV



von Braun and Rath[13] had reported a low (15%) yield for the inverse Friedel–Crafts cyclization of the acid chloride of **3** to **19** and noted that, in contrast, this method gave good yields of 1-indanone and 1-tetralone. We have found that a high-dilution technique using carbon disulfide gives 45–52% yields. The convenience of the one-step ring closure with polyphosphoric acid was attractive, but with the commercial reagent yields of 30% or less were usually obtained, plus appreciable amounts of a by-product (**20**) which was also isolated from cyclization of the acid chloride in tetrachloroethane. The latter product was both unexpected and undesirable and its source was investigated. The ketone **19** was shown to be stable to polyphosphoric acid; so an impurity in **3** was suspected. A sample of **3** was converted to the methyl ester and the derivative was purified by preparative gas–liquid chromatography. Reaction of the pure acid **3** obtained from this ester with polyphosphoric acid, and of the acid chloride with aluminum chloride, gave **20** along with **19**. Thus **20** is formed from **3** and a likely intermediate is 4-(3-indenyl)butanoic acid,[19] formed *via* acid abstraction of hydride from the tertiary benzylic carbon.



The inconsistent results in the cyclizations with different batches of commercial polyphosphoric acid led to a study of the yield of **19** as a function of the composition of the reagent. It was found that the reaction was very sensitive to the percentage of P_2O_5 and that *ca.* 45% yields of **19** could be obtained with 80% P_2O_5 regent,[20] and this became the method of choice.

Experimental Section

Melting points were taken in capillary tubes using an aluminum block and are corrected. Boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 21 recording spectrophotometer using NaCl prisms and cells. Ultraviolet spectra were taken on a Cary Model 115 spectrophotom-

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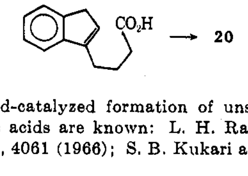
[17] H. Stone and H. Schecter, *J. Org. Chem.*, **15**, 491 (1950).

[18] Other workers have had similar experiences with indene: Professor H. Rapoport, University of California, Berkeley, personal communication, 1958.

[19] The action of an acid catalyst on 4-(3-indenyl)butanoic acid would lead to **20**; *cf.* F. H. Howell and D. A. H. Taylor, *J. Chem. Soc.*, 3011 (1957).



Other examples of acid-catalyzed formation of unsaturated ketones from alkenes and carboxylic acids are known: L. H. Rand and R. J. Dolinski, *J. Org. Chem.*, **31**, 3063, 4061 (1966); S. B. Kukari and S. Dev, *Tetrahedron*, **24**, 545 (1968).

[20] R. C. Gilmore and W. J. Horton, *J. Amer. Chem. Soc.*, **73**, 1411 (1951), found 79.8% P_2O_5 content optimum for the analogous cyclization of 4-(1,2,3,4-tetrahydro-1-naphthyl)butanoic acid. The high yields (92–94%) in this case may be due to the difference in reactivity of the position ortho to a six-membered rather than a five-membered ring.

eter. Elementary analyses were performed by B. Nist and C. H. Ludwig.

1-Indanone.—A modification of the method of Cope[21] was used. A mixture of 450 g (3.0 mol) of 3-phenylpropanoic acid and 450 g (3.8 mol) of thionyl chloride was refluxed for 2 hr. Distillation gave 471 g (94%) of 3-phenylpropanoyl chloride, bp 112–115° (15 mm) [lit.[22] bp 121–122° (22.5 mm)]. The acid chloride (168 g, 1 mol) was added rapidly (10 min) to a well-stirred suspension of 175 g (1.3 mol) of aluminum chloride in 400 ml of petroleum ether (bp 60–90°). The mixture was stirred for 15 min after HCl evolution had ceased and then a solution of 30 ml of concentrated hydrochloric acid in 1 l. of H_2O was cautiously added. Distillation of the residue from the washed (5% sodium bicarbonate), dried (magnesium sulfate), combined ethereal layers from the extraction of the mixture with four 200-ml portions of ether gave 106 g (80%) of 1-indanone, bp 88–90° (*ca.* 1 mm) [lit.[23] bp 125–126° (17 mm)].

4-(1-Indanyl)butanoic Acid (3) *Via* a Reformatsky Reaction of 1-Indanone and Methyl 4-Bromo-2-butenoate.—A mixture of 100 g of granular (20 mesh), purified[24] Zn, 225 ml of anhydrous benzene, and 5 g of $HgCl_2$ was stirred vigorously for 15 min under a N_2 atmosphere in a flask equipped with an efficient condenser with a drying tube and a stirrer which extended to the bottom of the flask. A solution of 66 g (0.5 mol) of 1-indanone, 90 g of methyl 4-bromo-2-butenoate, 75 ml of dry benzene, and 225 ml of dry ether and then an iodine crystal were added. The application of external heat started a vigorous exothermic reaction which was controlled by cooling (ice bath). After the reaction had been moderated (30 min), the mixture was heated and stirred under gentle reflux. Three additions of 30 g of methyl 4-bromo-2-butenoate, 50 g of Zn, and an iodine crystal were made at 90-min intervals. After an additional 3 hr, the mixture was cooled to room temperature and poured into a solution of 70 ml of glacial acetic acid and 500 ml of H_2O. The separated aqueous layer was extracted several times with ether, and the combined organic layer and ethereal extracts were washed with 10% ammonium hydroxide until the alkaline extracts were only slightly colored (6–8 times) and then with saturated NaCl solution. Removal of the solvents and unreacted starting materials by distillation at *ca.* 10 mm left a yellow oil which appeared to consist of methyl 4-[1-(1-hydroxy)indanyl]-2-butenoate (ir 3390 cm^{-1}), methyl 4-(1-indanylidene)-2-butenoate (**2**) [uv (ethanol) 243, 350, and 338 nm], and a small amount of 2-(1-indanylidene)-1-indanone.[25]

Rapid distillation of one-half of the yellow oil (*ca.* 25 g)[27] in the presence of 50 mg of *p*-toluenesulfonic acid from a pear-shaped flask and through an air-cooled tube gave 23.4 g (44% from 1-indanone) of **2** as a yellow oil: bp 125–145° (*ca.* 1 mm); uv (ethanol) 243 nm (log ϵ 3.95), 250 (3.92), and 338 (4.04); ir (neat) 1724 and 1628 cm^{-1}. The yields for four runs using 0.5–1 mol of indanone ranged from 41 to 58%; larger runs gave lower yields of the Reformatsky products.

A mixture of 12 g (0.056 mol) of **2**, 100 ml of absolute ethanol, and 0.1 g of prereduced PtO_2 in a Parr flask was treated with H_2 (3 atm). The uptake of H_2 ceased at the theoretical amount (0.11 mol) and the catalyst was removed by filtration. The filtrate was divided into two equal fractions and each half was diluted to 150 ml with ethanol and treated separately as follows. A solution of 6 g (0.107 mol) of KOH in 150 ml of H_2O was added to the alcoholic solution and the mixture was heated (reflux) for 3.5 hr under N_2. The alcohol was removed by distillation and the cooled alkaline solution was extracted with ether, treated with Norit, filtered, and acidified with 6 *N* hydrochloric acid. The tan crystals of crude **3** (4.6 g, 80% from **2**, 36–42% overall), mp 70–73°, after recrystallization from *n*-hexane gave colorless needles: mp 72–73°;[28] uv (ethanol) 260 nm (log ϵ 2.88), 266 (3.08), and 273 (3.14).

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.25; H, 7.79.

4-(1-Indanyl)butanamide.—One gram of **3** was refluxed with 5 ml of thionyl chloride for 30 min. The cooled mixture was poured into 15 ml of cold, concentrated ammonium hydroxide. Filtration separated the colorless precipitate, which after recrystallization from water melted at 95–96°.

Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43. Found: C, 76.92; H, 8.39.

4-(1-Indanyl)butanoic Acid (3) *Via* a Reformatsky Reaction of 1-Indanone and Ethyl Bromoacetate.[29]—A mixture of 200 g of purified,[24] granular (20 mesh) Zn, 10 g of $HgCl_2$, and 600 ml of dry benzene was stirred in the apparatus and as described for the above Reformatsky reaction. A solution of 132 g (1.0 mol) of 1-indanone, 280 ml of ethyl bromoacetate, and 500 ml of dry ether and then an iodine crystal were added with stirring and the reaction was initiated, controlled, and maintained as before. Two further additions of 100 g of Zn, 50 ml of ethyl bromoacetate, and an iodine crystal were made at 2-hr intervals. Reflux was continued for 2 hr after the last addition and then the cooled mixture was poured into 1 l. of 6 *N* sulfuric acid and worked up as described above to give 157 g (71%) of ethyl 2-[1-(1-hydroxy)-indanyl]acetate (**4**) as a light yellow oil, bp 120–125° (0.5 mm) [lit.[14] bp 180° (18 mm)].

The hydroxy ester **4** (20 g, 91 mmol) was heated (steam bath) with 115 ml of anhydrous formic acid for 15 min.[30] The cooled reaction mixture was taken up in 200 ml of H_2O and 100 ml of benzene and the separated aqueous layer was extracted with two 50-ml portions of ether. Removal of the solvents (distillation) from the combined, washed (5% $NaHCO_3$, H_2O), dried ($CaSO_4$) organic layers and distillation of the residue gave 16.7 g (90%) of the unsaturated ester **5**: bp 130–140° (2.5 mm) [lit.[14] bp 166–168° (10 mm)]; uv (ethanol) 226 nm (log ϵ 3.89), 232 (3.81), 263 (3.85), 271 (3.92), 278 (3.95), 290 (3.98), 308 (3.94), and 319 (sh, 3.89). Runs using 60 g of the hydroxy ester gave up to 96% yields.

A mixture of 22 g (0.11 mol) of the unsaturated ester **5**, 30 g (0.52 mol) of KOH, 500 ml of ethanol, and 600 ml of H_2O was heated under reflux for 3 hr and the alcohol was removed by distillation. The cooled red alkaline solution was extracted with ether, treated with Norit, and then acidified with concentrated hydrochloric acid. Recrystallization of the collected precipitate from *n*-hexane gave 15 g (79%) of the indenylacetic acid **7**, mp 87–94° (lit.[14] mp 85–86°) and 87–95° after a second recrystallization, as a mixture of needles and prisms, uv (ethanol) 254 nm (log ϵ 2.97) and 280 (2.3).

A Parr flask was charged with 19.5 g (0.11 mol) of the unsaturated acid **7**, 100 ml of absolute ethanol, 0.2 g of PtO_2, and H_2 (3 atm). After the H_2 uptake had ceased at the theoretical amount, the mixture was filtered and the solvent was removed under reduced pressure to give, after two recrystallizations from petroleum ether (bp 30–60°), 15.1 g (72%) of α-(1-indanyl)acetic acid (**8**), mp 58–61° (lit.[14] mp 60–61°).

A solution of 356 g (1.76 mol) of the unsaturated ester **5**, 350 ml of absolute ethanol, and 1 g of prereduced PtO_2 in a large Parr flask was treated with H_2 at 3 atm. After the H_2 uptake ceased, an additional 0.3 g of PtO_2 was added, whereupon H_2 uptake resumed. When the H_2 uptake again ceased a second portion of 0.3 g of PtO_2 was added. After the H_2 pressure became constant, the solution was decanted from the catalyst, the solvent was removed, and the residue was distilled to give 334 g (93%) of ethyl α-(1-indanyl)acetate (**6**), bp 93–95° (*ca.* 0.5 mm) or 124–125° (3 mm) [lit.[14] bp 149–150° (12 mm)]. The uv and ir spectra showed no absorption for nonbenzenoid C=C. Yields of 94–96% were obtained in smaller (*ca.* 0.2 mol) runs.

To a stirred solution of 4.75 g (0.125 mol) of $LiAlH_4$ in 180 ml of dry ether in a 1-l. three-necked flask equipped with a condenser with a drying tube, a mechanical stirrer, and a dropping funnel was added a solution of 15.1 g (86 mmol) of the saturated acid **8** in 150 ml of dry ether at a rate which caused gentle refluxing (45 min). The mixture was stirred for an additional 15 min and then cooled. H_2O (cautiously to decompose excess hydride) and then 150 ml of 10% sulfuric acid were added. The separated ethereal layer was washed with 5% $NaHCO_3$ and then saturated NaCl solutions and dried ($CaSO_4$). Removal of the solvent and

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[21] A. C. Cope, *J. Amer. Chem. Soc.*, **72**, 3056 (1950).

[22] R. A. Pacaud and C. F. H. Allan, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 336.

[23] H. F. Greef, Ph.D. Thesis, University of Washington, 1951.

[24] J. von Braun and W. Eberlein, *Chem. Ber.*, **45**, 384 (1912).

[25] When the washed and dried organic layer and extracts from one run were allowed to stand for 2 months, light green crystals (*ca.* 4 g) separated. Recrystallization four times from benzene with the addition of Norit the first two times followed by sublimation and drying over P_2O_5 gave yellow needles, mp 144–144.4° (lit.[26] mp 142°).

[26] F. S. Kipping, *J. Chem. Soc.*, **65**, 480, 495 (1894).

[27] Larger batches gave lower yields.

[28] The melting point of 92° reported by J. von Braun and E. Rath[13] is incorrect.

[29] The procedures are in part modifications of those given by J. von Braun, *et al.*,[13,14] who reported little yield data.

[30] W. E. Bachmann and R. O. Edgerton, *J. Amer. Chem. Soc.*, **62**, 2970 (1940).

distillation of the residue gave 11 g (79%) of β-(1-indanyl)ethyl alcohol (**9**), bp 118–124° (6 mm) [lit.[14] bp 150–152° (11 mm)].

In the manner described for the above reduction of **8** except that the reaction mixture was stirred for 2 hr after completion of the addition, 370 g (1.81 mol) of ethyl α-(1-indanyl)acetate (**6**) was treated with 45 g (1.27 mol) of $LiAlH_4$ in 1.4 l. of dry ether. Hydrolysis was effected with 200 ml of H_2O and 1200 ml of 10% sulfuric acid. There was obtained 294 g (94%) of **9**, bp 97–100° (0.5 mm).

In a 500-ml, three-necked flask equipped with a mechanical stirrer, a gas inlet tube reaching the bottom of the flask, a thermometer, and an exit tube connected through a trap into a tared flask containing H_2O was placed 267 g (1.78 mol) of the saturated alcohol **9**. The flask was heated to 120° (oil bath), and dry HBr was added through the inlet tube. The exothermic reaction caused the temperature to rise to 130°. When excess HBr increased the weight of the tared flask (5 hr), the addition was stopped and the mixture was cooled to and then held at room temperature for 24 hr. The mixture was washed with 600 ml of 6 *M* sulfuric acid and the acid washings were extracted with two 300-ml portions of ether. Removal of the solvent from the combined, washed (two 300-ml portions of H_2O, 300 ml of 50% methyl alcohol, and 300 ml of saturated NaCl solution), dried ($MgSO_4$) organic layers and then distillation gave 398 g (82%) of β-(1-indanyl)ethyl bromide (**10**), bp 99–100 (1 mm) [lit.[13] bp 145–147° (16 mm)].

To a stirred, gently refluxing solution of sodiomalonic ester prepared from 44.5 g (1.95 g-atom) of Na, 1300 ml of dry ethanol, and 312 g (1.95 mol) of redistilled ethyl malonate in a 3-l. flask equipped with a condenser with a drying tube, a dropping funnel, and a mechanical stirrer was added 327 g (1.45 mol) of the above bromide **10** over a period of 3 hr, during which period NaBr precipitated. The mixture was refluxed for 10 hr and then allowed to stand at room temperature for 24 hr. Alcohol (*ca.* 1.2 l.) was removed by distillation, the mixture was cooled, and the NaBr was dissolved by adding 1 l. of H_2O. The layers were separated and the aqueous layer was extracted with four 300-ml portions of ether. Removal of the solvent from the combined, washed (saturated NaCl solution), and dried ($MgSO_4$) organic layers and then distillation gave 336 g (76%) of diethyl β-(1-indanyl)ethylmalonate (**11**), bp 143–145° (0.2 mm) [lit.[13] bp 212° (12 mm)].

To a solution of 240 g of KOH dissolved in 250 ml of H_2O in a flask fitted with a condenser was added 336 g (1.1 mol) of the above diester **11** and 400 ml of ethanol, and, after the initial vigorous reaction had subsided, the mixture was refluxed for 8 hr. The solvent was removed by distillation, and the cooled solution was acidified with concentrated hydrochloric acid. The collected, dried precipitate was heated in a flask at 160° (oil bath) until the evolution of CO_2 ceased (5 hr) and then cooled. Recrystallization of the crude acid from hexane gave 168 g (75% from **11** and *ca.* 28% from 1-indanone) of 4-(1-indanyl)butanoic acid (**3**) as colorless crystals, mp 72–73° [no depression on admixture with samples prepared *via* other routes (*vide supra* and *infra*)].

4-(1-Indanyl)butanoic Acid (3) *via* the Reaction of 1-Indanone with 3-Methoxy-1-propylmagnesium Chloride.—To a flame-dried flask equipped with a mechanical stirrer, a condenser with a drying tube, and a pressure-equalizing dropping funnel, and containing 8 g (0.33 g-atom) of Mg turnings and an iodine crystal, were added with stirring and under a N_2 atmosphere 75 ml of dry ether and a solution of 36.2 g (0.33 mol) of 3-methoxy-1-chloropropane[31] in 55 ml of dry ether, the latter at a rate to maintain gentle refluxing. The mixture was refluxed for 30 min after the addition was complete, then cooled to below 10°. A solution of 43 g (0.33 mol) of 1-indanone in 200 ml of dry ether was added slowly and the mixture was then refluxed for 1 hr. The cooled mixture was poured into a solution of 8 ml of concentrated sulfuric acid in 150 ml of ice water. The separated aqueous layer was extracted with ether. The solvent was removed from the combined, washed (5% $NaHCO_3$ and saturated NaCl solutions), dried ($CaSO_4$) organic layers and distillation of the residue gave 27.8 g (41%) of 1-hydroxy-1-(3-methoxypropyl)indan (**12**), bp 133–135° (1.5 mm), $n^{25.5}\mathrm{D}$ 1.5320.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.80; H, 8.61.

A mixture of 20 g (98 mmol) or the above alcohol **12** and 60 g of potassium pyrosulfate was heated at 155–160° (oil bath) for 1 hr. The cooled mixture was extracted with ether several times and the combined ethereal layers were dried ($MgSO_4$). Removal of the solvent and distillation of the residue gave 11.5 g (63%) of 3-(3-methoxypropyl)indene (**13**): bp 85–77° (0.3 mm); $n^{26.5}\mathrm{D}$ 1.5423; uv (ethanol) 252 nm ($\log \epsilon$ 4.02), 280 (2.94), and 290 (1.70).

Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.98; H, 8.74.

A suspension of 11 g (59 mmol) of the above unsaturated ether **13**, and 0.1 g of prereduced PtO_2 in 100 ml of absolute ethanol was treated with H_2 at 30 psi in a Parr apparatus. After H_2 uptake ceased (2 hr), the mixture was filtered. Distillation of the filtrate gave 9.74 g (87%) of 1-(3-methoxypropyl)indan (**14**), bp 91–92° (0.3 mm), $n^{25.5}\mathrm{D}$ 1.5215.

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.96; H, 9.55.

A mixture of 8 g (42 mmol) of the above saturated ether **14**, 18.74 g (0.113 mol) of KI, and 95% phosphoric acid (from 4.3 g of P_2O_5 and 33.1 ml of 85% phosphoric acid) was heated with vigorous stirring at 150° (oil bath) for 5 hr.[17] The cooled mixture was extracted with ether several times and the combined extracts were washed with 10% $NaHCO_3$ 10% $NaHSO_3$, and saturated NaCl solutions and then dried ($CaSO_4$). Removal of the solvent and distillation of the residue gave 12 g (62%) of 1-(3-iodopropyl)indan (**15**), bp 100–105° (0.05 mm), $n^{25.5}\mathrm{D}$ 1.5889.

Anal. Calcd for $C_{12}H_{15}I$: C, 50.37; H, 5.28. Found: C, 50.31; H, 5.40.

In an oven-dried flask equipped with a condenser with a drying tube, a mechanical stirrer, and a dropping funnel were placed 0.25 g (10.3 mg-atom) of Mg turnings and 5 ml of dry ether. A solution of 2.86 g (10 mmol) of the above iodide **15** in 10 ml of dry ether was added with stirring at a rate to maintain gentle refluxing (30 min) and the mixture then was refluxed for an additional 30 min. The mixture was cooled to 10–15° and poured over 5 g of powdered CO_2. After the excess CO_2 had evaporated, a solution of 2 ml of concentrated hydrochloric acid in 15 ml of H_2O was added. The separated aqueous layer was extracted with ether and the combined organic layers were extracted with two 10-ml portions of saturated $NaHCO_3$ solution. Acidification of the combined alkaline extracts with dilute hydrochloric acid, filtration, and drying of the collected precipitate gave 1.05 g (51.5%) of 4-(1-indanyl)butanoic acid (**3**), mp 71.5–72.5° [no depression on admixture with samples prepared *via* other routes (*vide supra*)].

4-(1-Indanyl)butanoic Acid (3) *Via* 1-(3-Halopropyl)indene (17). Method A.—To a stirred, refluxing suspension of 40 g (0.87 mol) of NaH (52%)–mineral oil in a solution of 350 g (2.22 mol) of 1-chloro-3-bromopropane and 2 l. of K-dried tetrahydrofuran under a N_2 atmosphere was added 80 g (0.69 mol) of indene[32] and the mixture was stirred under reflux for *ca.* 20 hr (including the time for indene addition). The cooled mixture was filtered and the filtrate was washed with 10% hydrochloric acid, 5% $NaHCO_3$, and saturated NaCl solutions. Distillation of the dried ($MgSO_4$) solution removed the solvent and unchanged indene and then afforded 83 g (62%) of **17**, bp 120–130° (2 mm), which was indicated by analysis to be principally the chloro compound.[33] This material was converted to **18** as described below.

Method B.—A solution of 260 g (2.24 mol) of indene[34] in 200 ml of tetrahydrofuran was added over a 30-min period to a stirred, refluxing suspension of 90 g (2 mol) of NaH (53.2%)–mineral oil in 1 l. of K-dried tetrahydrofuran under a N_2 atmosphere. During the addition the mixture changed from green to red-violet. It was refluxed for 12 hr, diluted with 1 l. of tetrahydrofuran, and then added over a 15-hr period to a stirred, refluxing solution of 784 g (5 mol) of 1-chloro-3-bromopropene in 1 l. of tetrahydrofuran under a N_2 atmosphere. Work-up as described in A gave 209 g (54%) of **17**, bp 120–130° (2 mm), as obtained in A.[35]

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[31] Prepared in 51% yield by the method of R. L. Letsinger and A. W. Schnizer, *J. Org. Chem.*, **16**, 704 (1951), from 3-methoxy-1-propanol which was prepared in 65% yield by the method of L. I. Smith and J. A. Sprung.[16]

[32] Neville Chemical Co. or Rütgenswerke-Aktingesellschaft. These products were *ca.* 100% pure as shown by vpc analysis. Indene from Aldrich Chemical Co. or from Matheson was impure and unsatisfactory. The yield of product was independent of the rate of addition of the indene.

[33] This method gave inconsistent results (30–62% yields) from a large number of runs for reasons which were not apparent. Appreciable quantities (up to 20 g) of red oil were obtained as the distillation residue. The use of Na, $NaNH_2$, or LiH in place of NaH was less satisfactory.

[34] Matheson Scientific, Inc.

[35] Several runs gave yields of 37–54%. The reasons for the variation were not apparent.

Method C.—To a stirred, refluxing solution of 450 g (2.87 mol) of 1-chloro-3-bromopropane and 80 g of indene[36] in 2 l. of tetrahydrofuran (distilled from $LiAlH_4$) under a N_2 atmosphere was added 40 g (0.87 mol) of a NaH (52%)-mineral oil suspension in *ca.* 1 g portions over a period of 3-4 hr and reflux was then maintained for 10-12 hr. Work-up as described in A gave 91 g (68%) of **17**, bp 120-130° (2 mm), as obtained in A. The yield based on recovered indene was 75%. The product was converted to **18** as described below.

In a large Parr bomb 354 g (1.83 mol) of the unsaturated halide **17**, 500 ml of absolute ethanol, and 1 g of prereduced PtO_2 were treated with H_2 at 3-atm pressure until H_2 uptake ceased. An additional 0.2 g of PtO_2 was added. The theoretical amount (1.83 mol) of H_2 was taken up. Decantation of the solution from the catalyst and distillation gave 325 g (91%) of the corresponding 1-(3-halopropyl)indan (**18**), bp 97-100° (0.9 mm).[37] One-fourth of a solution of this product (327 g, 1.69 mol) in 100 ml of dry ether was added to 43 g (1.77 g-atoms) of Mg turnings[38] and 850 ml of dry ether under a N_2 atmosphere in a flask equipped with a stirrer, a condenser with a drying tube, and a dropping funnel. After the reaction had begun, the remaining solution was added at a rate to maintain gentle refluxing (*ca.* 90 min) and the mixture was refluxed for an additional 3 hr. The cooled mixture was poured, a little at a time and with stirring, onto excess freshly crushed Dry Ice in five 500-ml filter flasks. After the excess Dry Ice had evaporated, hydrolysis was effected with 1 l. of 5% hydrochloric acid. Ether (750 ml) was then added, the separated aqueous layer was extracted with 300 ml of ether, and the combined ethereal solutions were washed with water and then extracted with 10% aqueous KOH. Acidification of the alkaline extracts with concentrated hydrochloric acid formed an oil which solidified on standing. The crude product was dried *in vacuo* over P_2O_5 and then recrystallized from hexane to give 232-279 g (70-81%) of 4-(1-indanyl)butanoic acid (**3**), mp 71-73° (no depression on admixture with samples prepared *via* the other routes described above).

Cyclization of 4(1-Indanyl)butanoic Acid (3). Method A.—A mixture of 30 g (0.147 mol) of **3** and 30 g (0.25 mol) of thionyl chloride was refluxed for 1 hr and then distilled. The acid chloride of **3** (29 g, 89%) was collected at 116-118° (0.5 mm) [lit.[13] bp 172° (12 mm)].

A solution of 12.2 g (0.05 mol) of the acid chloride in 1 l. of anhydrous carbon disulfide was added over a 5-hr period to a stirred suspension of 9.5 g (0.07 mol) of powdered $AlCl_3$ in 1 l. of dry carbon disulfide and the mixture was then refluxed with stirring for 3 hr. Ice water (800 ml) was added cautiously to the deep red mixture, the carbon disulfide was removed by distillation (water bath), and the residual material was extracted with ether. Removal of the solvent from the combined, washed (6 *N* hydrochloric acid, 7% $NaHCO_3$, and then saturated NaCl), dried ($MgSO_4$) extracts and then distillation gave 4.97 g (52%) of 1,6,7,8,9,9a-hexahydro-2*H*-benzo[*c,d*]azulen-6-one (**19**), bp 110-112° (0.5 mm) [lit.[13] bp 172° (12 mm)].[39]

Anal. Calcd for $C_{13}H_{14}O$: C, 83.84; H, 7.58 Found: C, 83.55; H, 7.58.

Method B.—To polyphosphoric acid (79.8% in P_2O_5), prepared by the cautious, slow addition with swirling of 920 ml of 85% phosphoric acid to 1430 g of P_2O_5, maintained at 80-90° (water bath), was added 57.4 g (0.282 mol) of finely powdered **3** with swirling. This temperature and vigorous, frequent swirling were continued for 15 min, during which time the color of the mixture changed from orange to dark red-brown. The mixture was poured immediately onto 4 l. of crushed ice and stirred until the dark, viscous mass had completely hydrolyzed. The hydrolysate was divided into two equal portions, the volume of each was brought to 3 l. with H_2O, and the yellow suspensions which resulted were extracted with ether until the extracts were colorless. Removal of the solvent from the combined, washed (H_2O, saturated $NaHCO_3$, saturated NaCl), dried ($MgSO_4$) extracts left 48.4 g of amber oil which was chromatographed on acidic alumina (1.5 lb in a 5.5-cm diameter column). An oily forerun (4.73 g) was eluted with hexane, 10:1 hexane-ethyl acetate then removed **19** as a pale yellow oil, and finally 1,2,3,4-tetrahydro-5*H*-fluoren-4-one (**20**) was eluted with 1:1 hexane-ethyl acetate. Crystallization of **19** from methanol at −25° gave 24.2 g (46%) of colorless prisms: mp 40.0-41.5°; uv (cyclohexane) 243 nm (log ϵ 4.03), 291 (3.77), and 322 (sh, 1.95); ir (CCl_4) 1709 cm^{-1}.

Recrystallization of the yellow solid **20** from hexane gave 11.3 g (22%) as colorless plates: mp 106-106.5° (lit.[40] mp 104-106°); uv (cyclohexane) 225 nm (log ϵ 3.88), 232 (4.07), 238 (4.07), 290 (sh, 4.29), 296 (4.30), and 307 (sh, 4.16).

Anal. Calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.77; H, 6.38.

Registry No.—**2**, 38425-60-4; **3**, 38425-61-5; **4**, 1620-02-6; **5**, 38386-68-4; **6**, 22339-45-3; **7**, 1620-00-4; **8**, 38425-65-9; **9**, 38425-66-0; **10**, 38434-35-4; **11**, 38434-36-5; **12**, 38434-37-6; **13**, 38434-38-7; **14**, 38434-39-8; **15**, 38434-40-1; **17** (X = Cl), 38521-62-9; **18** (X = Cl), 38434-41-2; **19**, 14528-87-1; **20**, 7235-16-7; 1-indanone, 83-33-0; 3-phenylpropanoic acid, 501-52-0; 3-phenylpropanoyl chloride, 645-45-4; methyl 4-bromo-2-butenoate, 1117-71-1; 4-(1-indanyl)butanamide, 38434-44-5; ethyl bromoacetate, 105-36-2; sodiomalonic ester, ethyl, 28290-06-4; 3-methoxy-1-chloropropane, 36215-07-3; 1-chloro-3-bromopropane, 109-70-6; indene, 95-13-6; 4-(1-indanyl)butanoic acid, chloride, 38434-46-7.

Acknowledgments.—This investigation was supported in part by grants from the National Science Foundation. The authors wish to thank Robert Hathaway, Ruth Ann Henrikson, Imadel James, and Gerald Klein for valuable assistance.

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[36] Either pure indene[32] or 90% indene (Aldrich Chemical Co.) was satisfactory. This method also gave lower yields (43-60%) in some runs for reasons which could not be determined.

[37] In a large number of runs yields varied from 90 to 95%.

[38] Ground in a dry mortar and pestle just prior to using. The addition of ethyl- or methylmagnesium iodide was sometimes necessary to initiate the reaction.

[39] A procedure using tetrachloroethane as the solvent at room temperature gave 26-34% of **19** and *ca.* 9% of **20**, bp 120-125° (0.5 mm).

[40] A. G. Anderson, Jr., and S. Y. Wang, *J. Org. Chem.*, **19**, 277 (1954).