The Synthesis of Dicyclopenta[*ef,kl*]heptalene (Azupyrene). II. Routes from 1,6,7,8,9,9a-Hexahydro-2*H*-benzo[*c,d*]azulen-6-one and 5-Phenylpentanoic Acid[1,2]

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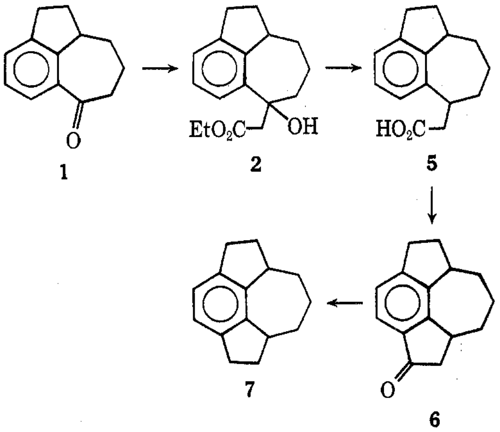
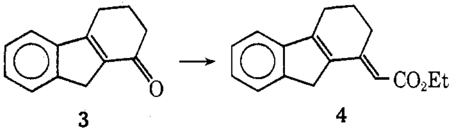
In the second phase of the synthesis of azupyrene, two routes *via* the intermediate 1,5,6,6a,7,8,9a-heptahydro-2*H*-indeno[5,4,3-*cde*]azulene (**7**) have been investigated: (i) from 1,6,7,8,9,9a-hexahydro-2*H*-benzo[*c,d*]azulen-6-one (**1**) as depicted in Schemes I, II, and III, and (ii) from 5-phenylpentanoic acid (**23**) as depicted in Scheme IV. The best route afforded **7** as the cis isomer (**19**) in *ca.* 43% overall yield from **1** and involved just three operational steps. This provided a seven-step synthesis of **19** from indene in 8–9% overall yield. Reaction of **19** with ethyl diazoacetate, saponification, and then concomitant decarboxylation and dehydrogenation formed azupyrene (3.8%).

The previous paper[1] described the first phase in the synthesis of azupyrene: routes to 1,6,7,8,9,9a-hexahydro-2*H*-benzo[*c,d*]azulen-6-one (**1**). The present paper describes the synthesis of 1,5,6,6a,7,8,9,9a-octahydro-2*H*-indeno[5,4,3-*cde*]azulene (**7**) and its conversion to azupyrene (**25**). Two routes to **7** were investigated: (i) from **1** and (ii) from benzocycloheptene (**22**).

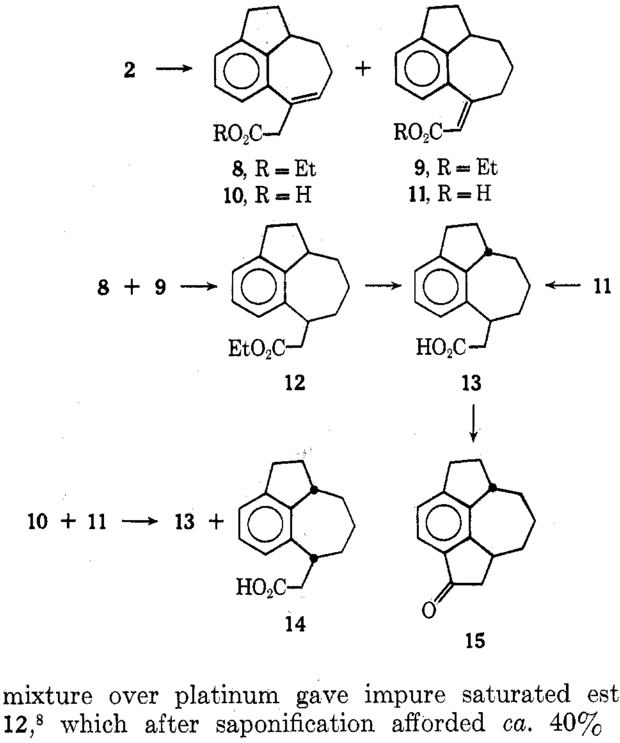
Route 1. From 1,6,7,8,9,9a-Hexahydro-2*H*-benzo-[*c,d*]azulen-6-one (1).—The general plan of this route is shown in Scheme I. The initial objectives were the conversion of **1** to **2** (77%) by a Reformatsky reaction and then dehydration, hydrogenation, and hydrolysis to form **5**. Treatment of **2** with 6 *N* sulfuric acid effected hydrolysis but not dehydration, and distillation in the presence of *p*-toluenesulfonic acid gave incomplete loss of water. The stability of **2** is characteristic of Reformatsky esters derived from benzocyclohepten-1-ones.[6] Initially the Reformatsky reaction was carried out on impure **1** containing **3**[1] and the product consisted of a mixture of **2** and **4** which did not separate on distillation. The absorption spectrum of **4** led to the erroneous conclusion that the dehydration of **2** had occurred. Subsequently this difficulty was overcome by the chromatographic separation of **1** and **3**. Three methods were found to effect the dehydration of **2**: (i) treatment with thionyl chloride and pyridine (84%); (ii) refluxing with *p*-toluenesulfonic acid in toluene (93%); and (iii) heating with anhydrous formic acid (97.5%). The infrared (two carbonyl peaks) and the nuclear magnetic resonance (vinylic singlet superimposed on a triplet) spectra of the dehydration product showed the presence of two species (**8** and **9**, Scheme II).[7] Hydrogenation of the mixture over platinum gave impure saturated ester **12**,[8] which after saponification afforded *ca.* 40% of

SCHEME I





SCHEME II



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[1] Paper I: A. G. Anderson, Jr., G. M. Masada, and A. F. Montana, *J. Org. Chem.*, **38**, 1439 (1973).

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

[3] University of Washington.

[4] Seattle Pacific College.

[5] NIH Predoctoral Fellow, 1968–1970.

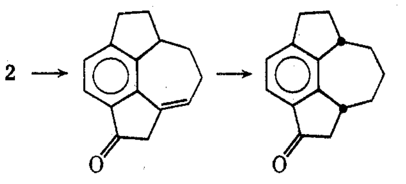
[6] R. C. Gilmore and W. J. Horton, *J. Amer. Chem. Soc.*, **73**, 1411 (1951); H. F. Greef, Ph.D. Thesis, University of Washington, 1951.

[7] Molecular models of **8–11** indicate that structures having the double bond in the endo position would be sterically less strained. The stabilization by conjugation in the exo-unsaturated structures is thus of comparable magnitude.

[8] The product also contained **9**, which reacted very slowly. Repeated hydrogenation of the mixture did not completely reduce this isomer.

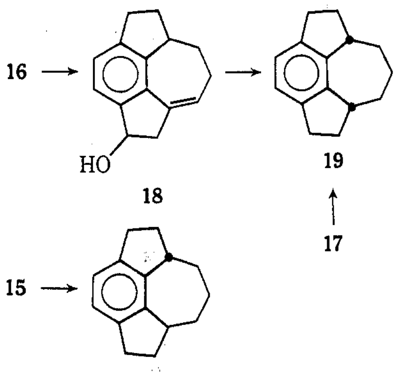
13. A mixture of **13** and **14** (42%) was usually obtained when **8** and **9** were first converted to the unsaturated acids **10** and **11** and the latter mixture reduced. The proportion of isomers varied and some runs afforded very predominantly (*ca.* 90%) **11** (λ_{max} 269 nm). Hydrogenation of isolated **11** gave pure **13** (98%) and treatment of the latter with polyphosphoric acid (93%) or thionyl chloride and then aluminum chloride (55%) formed the trans tetracyclic ketone **15**. The assignments of the structures for the isomers will be discussed later.

The reactions of Scheme II were not considered to be satisfactory. It was evident that hydrogenolysis of the benzylic hydroxyl group in **2** would avoid the problem of reduction of a mixture of **8** and **9** or **10** and **11** and also shorten the route by one step. Treatment of **2** with hydrogen and palladium or platinum catalysts, however, gave no reaction and attempted reduction by reaction with phosphorus and iodine in acetic acid[9] or with concentrated hydriodic acid in acetic acid[10] failed to give the desired transformation. The direct cyclization of **2**, with the possibility of concomitant removal of the hydroxyl, was considered next. Gilmore had found that the yield of ketone was the same from the cyclization of 5-phenylpentanoic acid or its methyl ester with polyphosphoric acid.[11] Reaction of **2** with this reagent at 80–90° for but 5 min[12] effected cyclization and dehydration to give a single product (**16**), a rather unstable substance, in 84% yield. The position of the carbon–carbon double bond in **16** was shown by the absorption spectra: a maximum at 247 nm, and pmr signals for a weakly split singlet at 2.92 (methylene adjacent to the carbonyl) and a triplet at 5.75 ppm (vinylic hydrogen). This intermediate, however, was inert to hydrogen in the presence of palladium on charcoal or platinum in ethanol, and platinum in acetic acid gave only 33% of **6** as the cis isomer (**17**). An attempted reduction with diborane using a method previously employed successfully on azulenic ketones[13] produced only yellow oils. Thus, although this new path eliminated the dehydration and ester hydrolysis steps, an alternative to the catalytic reduction was needed.



16 **17**

SCHEME III



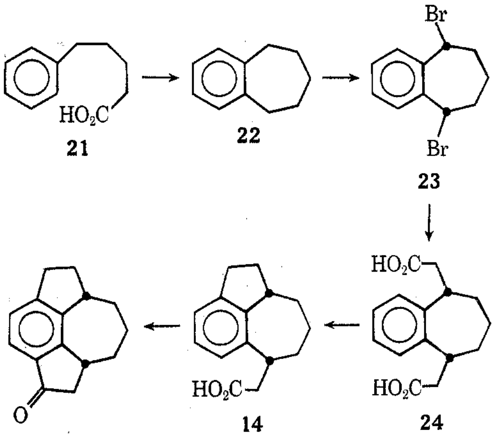
18 **19** **17** **20**

The existence of the Brown catalyst, supported platinum generated by the *in situ* reduction of platinum salts by borohydride,[14] led to the development of a new reaction sequence (Scheme III) wherein **16** was treated with excess sodium borohydride to reduce the carbonyl group. Decolorizing carbon and chloroplatinic acid were then added, any excess borohydride was destroyed, and the solution was brought to the required acidity with hydrochloric acid, and hydrogenative reduction of the carbon–carbon double bond and cleavage of the benzylic hydroxyl were all effected in one continuous operation to give **7** as the cis isomer (**19**) in 66% yield. The intermediate alcohol **18** could be isolated and was characterized. Pure **18** could be converted to **19** by hydrogenation with platinum in acetic acid, but in lower yield (56.5%). Wolff-Kishner reduction of **17** also gave, as expected, **19**, whereas the trans isomer (**20**) was obtained from **15**.

The best route from **1** to **7** now involved just three operational steps and gave an overall yield of the cis isomer (**19**) of *ca.* 43%. This made the overall yield from indene 8–9% for nine reactions and seven operational steps.

Route 2. From 5-Phenylpentanoic Acid (21) (Scheme IV).—An additional route to **7** patterned after the synthesis of tetrahydropyracene from tetralin[15] was investigated concurrently with the above studies. The initial intermediate needed for this approach was 5-phenylpentanoic acid (**21**), and three methods of preparation were compared. The first, Doebner condensation of cinnamaldehyde with malonic acid to give 5-phenylpenta-2,4-dienoic acid and then reduction with Raney nickel alloy and base, gave 90–95% overall yields[16] but the product was sometimes ob-

SCHEME IV



21 **22** **23** **24** **14** **17**

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[9] C. S. Marvel, F. D. Hager, and E. C. Caudle, "Organic Syntheses," Collect. Vol. I, Wiley, New York, N. Y., 1941, p 224.

[10] M. Orchin and L. Reggel, *J. Amer. Chem. Soc.*, **73**, 436 (1951).

[11] R. C. Gilmore, *ibid.*, **73**, 5879 (1951).

[12] No reaction occurred at lower temperatures, and longer times resulted in appreciable decomposition.

[13] A. G. Anderson, Jr. and R. D. Breazeale, *J. Org. Chem.*, **34**, 2375 (1969).

[14] H. C. Brown and C. A. Brown, *J. Amer. Chem. Soc.*, **84**, 2827 (1962); *Tetrahedron, Suppl. 8*, **22** (1), 149 (1966).

[15] A. G. Anderson, Jr., and R. G. Anderson, *J. Amer. Chem. Soc.*, **79**, 1197 (1957).

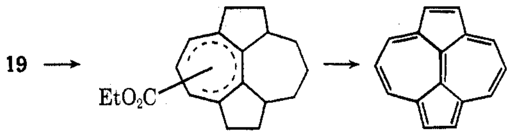
[16] A. G. Anderson, Jr., and S. Y. Wang, *J. Org. Chem.*, **19**, 277 (1954).

tained as an oil which was difficult to purify. The second, a Knoevenagel reaction of cinnamaldehyde with malonic ester followed by saponification, Raney nickel alloy–base reduction, and decarboxylation, gave *ca.* 50% overall yields and an oil product difficult to purify. The third, Friedel–Crafts reaction of benzene with glutaric anhydride and then Clemmensen reduction of the keto acid, gave *ca.* 80% of crystalline **21** and was considered to be the best.

Conversion of **21** to benzocycloheptene (**22**) was effected by Friedel–Crafts cyclization of the acid chloride from **21** and Clemmensen reduction of the resultant cyclic ketone in 60–70% overall yield. The bromination of tetralin with *N*-bromosuccinimide is vigorously exothermic.[15] In contrast, the reaction with **22** was very slow and heat, light, and azobisisobutyronitrile were needed to achieve a moderate rate. Molecular models showed that just two of the four benzylic hydrogens would be reactive and that these would be sterically less favorably oriented than the corresponding tetralin hydrogens.[17] Analysis of the product indicated it to be a mixture of **23** and the monobromo compound. Reaction of this material with sodiomalonic ester and then saponification gave a mixture of acids which was partially separated before thermal decarboxylation. The sequence afforded only 5% of the desired benzocycloheptene-1,5-diacetic acid (**24**). This route was therefore of no value for the synthesis of **7** but it provided pure samples of tricyclic acid **14** and tetracyclic ketone **17** which were isomers of those (**13** and **15**) obtained from the previous synthesis (Scheme II). Cyclization of **24** with polyphosphoric acid and then Clemmensen reduction[18] gave **14** (48%), and cyclization of the latter afforded **17** (60%).

The assignment of the stereochemistry to the trans (**13** and **15**) and cis (**14**, **17**, **24**) isomers was based on indirect evidence. Molecular models indicated that the two sterically less hindered benzylic positions on **22** and **23** were cis. The appreciably greater hindrance for a trans substituent made it seem likely that the malonic ester and, consequently, the acetic acid substituents would occupy the cis positions also. Models of the tetracyclic ketones (**15** and **17**) showed that the carbonyl of the cis isomer was slightly more nearly in the plane of the benzene ring than in the trans isomer. In agreement with this, the absorption maximum for **17** (264 nm) was at a longer wavelength than that (261 nm) for **15**. A similar difference (1705 and 1720 cm^{-1}) in the same direction was observed in the infrared spectra. Also, the more planar stuctures (**14**, **17**, and **24**) would be expected to have higher melting points than their isomers, and this was found to be so.

Conversion of 19 to Azupyrene (25).—The final phase of the synthesis was the conversion of **19** to azupyrene (**25**). Diazomethane was considered first for the ring-enlargement step, as dehydrogenation of the product would give azupyrene. Trial reactions were conducted on prehnitene (1,2,3,4-tetramethylbenzene) as a model system. Reactions of prehnitene with diazomethane, neat or in solution, catalyzed by cuprous ion,[19] bis(acetylacetonato)copper(II),[20] or cupric ion[21] gave low yields of cycloheptatriene product and a satisfactory separation of the mixture by liquid-phase column chromatography was not achieved. The use of diiodomethane or ethyl diiodoacetate with a zinc–copper couple, and of ethyl diiodoacetate with diethylzinc, were also unsatisfactory. Heating of prehnitene with ethyl diazoacetate[22] in the presence of bis(acetylacetonato)copper(II) or cupric ion gave mostly diethyl fumarate and diethyl maleate, but the reaction in the absence of a catalyst gave a separable ester fraction which exhibited pmr absorption for vinylic hydrogens. Treatment of **19** with the diazo ester gave two ester fractions which could be separated from unchanged hydrocarbon. That these were isomeric was indicated by the virtual identity of their nuclear magnetic resonance spectra and the fact that one became identical in all respects with the other upon standing.



25

Hydrolysis of the ester product afforded the corresponding acid. The low volatility of this substance made the use of a liquid-phase dehydrogenation method possible with methyl oleate as the solvent and hydrogen acceptor and a specially prepared palladium on carbon[23] as the catalyst. It was hoped that decarboxylation would occur concomitantly and a trail reaction with 1,2,3,6-tetrahydro-6-azuloic acid[24] was found to give azulene in 12% yield. Application of the procedure to the tetracyclic acid gave azupyrene (**25**; 3.8% from **19**) as thermally stable, bronze crystals.

The structure and aromatic character of **25** were confirmed by its spectra. The infrared spectrum showed absorption characteristic for aromatic CH and C=C, and a band at 1377 cm^{-1} very similar to that exhibited by azulene. The nuclear magnetic resonance spectrum showed a four-proton singlet, a four-proton doublet, and a two-proton triplet with a 1000-cycle sweep width, and with a 50-cycle sweep width eight lines of a characteristic AB$_2$ pattern were revealed. The value for the dimagnetic susceptibility of $\Lambda/\Lambda_{bz} = 3.9 \pm 0.3$ measured with a Faraday balance[25] was comparable with that (4.2 ± 0.1) obtained for pyrene.[26] The electron spin resonance spectrum of the 17-electron anion radical[27] showed the hyper-

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[17] The configuration of the radical intermediate from benzocycloheptene would provide less resonance stabilization.

[18] Wolff–Kishner reduction of the intermediate keto acid gave poor yields.

[19] E. Muller, H. Fricke, and H. Kessler, *Tetrahedron Lett.*, 1501 (1963); 1525 (1964). E. Muller, B. Zech, R. Heischkeil, H. Fricke, and H. Suhr, *Justus Liebigs Ann. Chem.*, **662**, 38 (1963).

[20] H. Nozake, S. Moriuti, M. Yamabe, and R. Noyori, *Tetrahedron Lett.*, 59 (1966); S. Kida, *Bull. Chem. Soc. Jap.*, **29**, 805 (1956).

[21] D. O. Cowan, M. H. Couch, K. R. Kopecky, and G. S. Hammond, *J. Org. Chem.*, **29**, 1922 (1964).

[22] An excess of the diazo compound was used, in contrast to the usual excess of hydrocarbon, in all reactions with prehnitene and **19**, since it was not feasible to use an excess of the latter. This was not a limiting factor, as unchanged hydrocarbon was always recovered.

[23] A. G. Anderson, Jr., W. F. Harrison, and R. G. Anderson, *J. Amer. Chem. Soc.*, **85**, 3448 (1963).

[24] E. J. Cowles, Ph.D. Thesis, University of Washington, 1953.

[25] We thank Drs. J. D. Wilson and C. E. Scott for this measurement.

[26] H. J. Dauben, Jr., J. D. Wilson, and J. L. Laity, *J. Amer. Chem. Soc.*, **90**, 811 (1968).

[27] These experiments were performed by G. Scott Owen and Dr. Gershon Vincow. The McConnell relationship was used for the calculated hyperfine splitting values.

fine splittings $a_{H^1} = 0.64 \pm 0.01$ G, $a_{H^3} = -4.23 \pm 0.01$ G, and $a_{H^4} = 0.94 \pm 0.01$ G as compared with respective calculated values of 0.10, −4.71, and 1.25 G. The *g* value was 2.00258. These data are consistent with the structure of **25**.

The diamagnetic susceptibility for a planar, cyclic 14 π electron structure, *trans*-15,16-dimethyl-15,16-dihydropyrene,[28] has been measured as $\Lambda/\Lambda_{bz} = 5.5 \pm 1$.[29] Thus the value for **25** is somewhat less than might be anticipated on the basis of a completely node-separated peripheral π system,[30] and suggests some participation of the central unsaturation.

The melting point (250–258°) of **25** is appreciably higher than those of pyrene (150–151°), acepleiadylene (156–162°), cyclohepta[*bc*]acenaphthylene (142.5–143.5°), or naphtha[2,1,8-*cde*]azulene (197–200°), with which it is isomeric. In the hope of finding an explanation for this in the crystal structure or in the molecular dimensions, an X-ray structural determination was attempted.[31] The crystal, however, exhibited a degree of disorder prohibiting meaningful analysis.

Experimental Section

Melting points were taken on an Eimer and Amend block and are corrected unless otherwise noted. 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 14 spectrophotometer. Pmr spectra were recorded on a Varian Model A-60, T-60, or DA 60-II spectrophotometer in CCl_4 with tetramethylsilane as internal reference standard unless noted otherwise. Volume ratios are given for mixed solvents for chromatography. Elemental analyses were performed by Dr. A. Bernhardt, Max-Plank-Institut für Kohlenforschung, Mülheim (Ruhr), West Germany, and Chemalytics, Inc., Tempe, Ariz.

Ethyl 6-Hydroxy-1,6,7,8,9,9a-hexahydro-2*H*-benzo[*cd*]azulenyl-6-acetate (2).—A mixture of 30 g of purified,[32] amalgamated, granular Zn and 250 ml of dry benzene was stirred under reflux (N_2 atmosphere) for 15 min. A portion (50 ml) of the benzene was withdrawn and added to a solution of 29.9 g (0.161 mol) of 1,6,7,8,9,9a-hexahydro-2*H*-benzo[*cd*]azulen-6-one (1) and 44 ml of ethyl bromoacetate and the whole was added to the original mixture. After the exothermic reaction had subsided, gentle refluxing was resumed, three portions of 6 g of zinc and 7 ml of ethyl bromoacetate were added at hourly intervals, and refluxing was continued for 30 min after the last addition. The cooled solution was then stirred with 150 ml of 6 *N* sulfuric acid for 15 min, the separated aqueous layer was washed with ether until clear, and the combined organic layers were washed with 6 *N* sulfuric acid, then with 10% aqueous ammonia until no appreciable color was extracted, and finally with saturated NaCl. Chromatography of the red-brown oil, obtained after removal of the solvent from the dried ($MgSO_4$) solution, on acidic alumina with 7:1 hexane–ethyl acetate gave **2** as a yellow oil which crystallized from hexane as colorless prisms (34.1 g, 77%): mp 72–72.5°; uv (cyclohexane) 263 nm (sh, log ϵ 2.77), 268 (2.95), and 276 (3.00); ir (CCl_4) 1723 cm^{-1}.

Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.37; H, 8.20.

Ethyl 1,2,3,4-Tetrahydro-5*H*-fluorenylidene-4-acetate (4).—In the manner described for the preparation of **2**, from the reaction of 3.02 g (16.4 mmol) of 1,2,3,4-tetrahydro-5*H*-fluoren-4-one (**3**), 6.5 ml (4.4 ml plus three 0.7-ml portions) of ethyl bromoacetate, and 6.8 g (5 g plus three 0.6-g portions) of Zn with 25 ml of benzene as solvent but with 7:1 petroleum ether (bp 30–60°)–ethyl acetate as the eluent was obtained 2.18 g (56% net) of **4** as colorless needles: mp 74.5–76°; uv (cyclohexane) 229 nm (log ϵ 3.94), 236 (3.96), 243 (4.05), 252 (3.96), and 330 (4.49).

Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.38; H, 7.02.

Dehydration of Ethyl 6-Hydroxy-1,6,7,8,9,9a-hexahydro-2*H*-benzo[*cd*]azulenyl-6-acetate (2). Method A.—Following the method of Chuang, *et al.*,[33] from 10 g (37 mmol) of **2**, 5.04 g (40 mmol) of thionyl chloride, and 7 g (90 mmol) of pyridine was obtained 9.4 g (84%) of a mixture of ethyl 1,8,9,9a-tetrahydro-2*H*-benzo[*cd*]azulenyl-6-acetate (**8**) and ethyl 1,6,7,8,9,9a-hexahydro-2*H*-benzo[*cd*]azulenylidene-6-acetate (**9**): bp 154–156° (0.5 mm); $n^{25.5}D$ 1.5641; uv (ethanol) 256 nm (log ϵ 3.97); ir (neat) 1717 and 1735 cm^{-1}.

Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.68; H, 7.86. Found: C, 79.43; H, 8.13.

Method B.—A solution of 4.28 g (15.6 mmol) of **2**, 100 mg of *p*-toluenesulfonic acid, and 50 ml of toluene was refluxed until no more H_2O was observed to collect in a Dean–Stark trap (2.5 hr). The cooled solution was washed with H_2O until the wash was no longer acidic to litmus and the solvent was then removed. Removal of the solvent from a dried ($MgSO_4$) ethereal solution of the residual oil left 3.72 g (93%) of product identical (ir and nmr) with that obtained in A.

Method C.—Following the method of Gilmore and Horton,[34] from 10 g (37 mmol) of **2** and 70 ml of 98–100% formic acid was obtained 9.2 g (97.5%) of product identical (ir and nmr) with that in A.

1,6,7,8,9,9a-Hexahydro-2*H*-benzo[*cd*]azulenylidene-6-acetic Acid (11).[35]—A solution of 6.5 g (25.3 mmol) of a mixture of **8** and (mostly) **9**, 130 ml of ethanol, 6.5 g (0.116 mol) of KOH, and 150 ml of H_2O was refluxed for 3 hr under a N_2 atmosphere and the solvent was then removed by distillation. The solution was extracted with ether, treated with Norit, and acidified with 6 *N* hydrochloric acid to give an impure solid. Recrystallization from *n*-hexane gave 5.25 g (91%) of **11** as colorless needles: mp 104–107.5°; uv (ethanol) 269 nm (log ϵ 4.04).

Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.07. Found: C, 78.86; H, 6.79.

***trans*-1,6,7,8,9,9a-Hexahydro-2*H*-benzo[*cd*]azulenyl-5-acetic Acid (13). Method A.**—A solution of 6 g (27.3 mmol) of the unsaturated acid **11** in 150 ml of absolute ethanol took up the theoretical amount of H_2 at 2 atm in the presence of 0.1 g of prereduced platinum oxide in 2 hr. Filtration, removal of the solvent, and recrystallization of the crude product from *n*-hexane or acetonitrile gave 6 g (98%) of **13** as colorless plates, mp 139.5–140.5°.

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.07; H, 7.67.

Method B.—A solution of 3.72 g (14.5 mmol) of the unsaturated esters **8** and **9** in absolute ethanol was treated with H_2 at *ca.* 4 atm over *ca.* 0.1 g of prereduced platinum oxide for 14 hr. Removal of the solvent and catalyst left 3.68 g (98%) of saturated ester **12** containing a small amount of **9** (nmr spectrum). A solution of 3.03 g (11.8 mmol) of this product, 3 g of KOH, 65 ml of ethanol, and 75 ml of H_2O was refluxed for 3 hr. The ethanol was removed by distillation and the aqueous solution was washed with ether and then acidified with 6 *N* hydrochloric acid. The oil which separated was extracted with ether. Distillation of the solvent from the ethereal layer and crystallization of the residual oil from acetonitrile gave 0.95 g of **13**, mp 137–140° (uncorrected), and a second crop of 0.121 g (40% total yield), mp 132–138° (uncorrected).

***trans*-1,5,6,6a,7,8,9,9a-Octahydro-2*H*-indeno[5,4,3-*cde*]azulen-5-one (15). Method A.**—A mixture of 5 g (21.8 mmol) of the trans saturated acid **13** and 6 g (50 mmol) of thionyl chloride was allowed to stand at room temperature for 1 hr and then refluxed for 15 min. Distillation gave 4 g (16 mmol) (75%) of the acid chloride, bp 139–143° (0.4 mm). A solution of this product in 20 ml of dry benzene was added dropwise (90 min) to a stirred suspension of 2.66 g (20 mmol) of $AlCl_3$ in 35 ml of dry benzene at 5–10°. The mixture was allowed to come to room temperature slowly (12 hr). Ether (10 ml) was added followed by 50 ml of 6 *N* hydrochloric acid. The separated aqueous layer was extracted with ether. Removal of the solvent from the combined, washed

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[28] V. Boekelheide and J. B. Phillips, *J. Amer. Chem. Soc.*, **89**, 1695 (1967).

[29] J. L. Laity, Ph.D. Thesis, University of Washington, 1968.

[30] See the discussion in ref 1.

[31] This experiment was performed by Dr. H. L. Ammon.

[32] J. von Braun and O. Kruber, *Ber.*, **45**, 384 (1912).

[33] C.-K. Chuang, Y.-L. Tien, and Y.-T-Huang, *Chem. Ber.*, **68**, 867 (1935).

[34] R. C. Gilmore and W. J. Horton, *J. Amer. Chem. Soc.*, **73**, 1411 (1951).

[35] The saponification of the mixture of **8** and **9** often obtained afforded a mixture of **10** and **11** having a broad melting range (*e.g.*, 83–140°), and catalytic (Pt) reduction of this material gave a corresponding mixture of **13** and **14**, mp 113–142° (42%).

(10% hydrochloric acid, 5% sodium bicarbonate, saturated NaCl), and dried ($MgSO_4$) extracts and recrystallization of the crude residual ketone from aqueous ethanol gave 2.5 g (55%) of **15** as colorless needles: mp 112–114° (uncorrected); uv (ethanol) 261 nm; ir (CCl_4) 1720 cm^{-1}.

Anal. Calcd for $C_{15}H_{16}O$: C, 84.83; H, 7.60. Found: C, 84.74; H, 7.57.

Method B.—A mixture of 1.71 g (7.44 mmol) of **13** and 38 g of commercial (84.3% P_2O_5) polyphosphoric acid in a flask loosely stoppered with glass wool was stirred and heated at 90° for 35 min, during which time the color became red-brown. Ice water (100 ml) was added, the light yellow solid which separated was extracted into ether, and the ethereal layer was washed with saturated sodium bicarbonate (acidification of the basic layer and recrystallization of the precipitate from acetonitrile gave 0.345 g of unchanged **13**) and saturated NaCl. Removal of the solvent and chromatography of the residue on acidic alumina with 10:1 hexane–ethyl acetate gave a small amount of yellow oil and then 0.797 g (63%) of **15**, mp 109.5–112° after recrystallization from *n*-hexane. Smaller runs (*ca.* 200 mg of **13**) heated for 25 min gave higher (up to 93%) yields.

1,5,6,8,9,9a-Hexahydro-2*H*-indeno[5,4,3-*cde*]azulen-5-one (16).—Finely powdered hydroxy ester **2** (12 g, 43.8 mmol) was mixed thoroughly with 250 g of commercial (84.3% P_2O_5) polyphosphoric acid. The mixture was heated with vigorous stirring in a water bath maintained at 92–95° for exactly 5 min (color change from orange to red-brown), then immediately poured onto 1 l. of crushed ice and stirred until the hydrolysis was complete. The collected (Büchner funnel with coarse filter paper) yellow-green precipitate was washed with water until the washings were neutral to litmus. A solution of the dried (air and then vacuum desiccator), grey-green solid in the minimal amount of benzene was chromatographed on acidic alumina. *n*-Hexane–ethyl acetate (10:1) removed an amber oil and 7:1 *n*-hexane–ethyl acetate eluted 7.72 g (84%) of **16**, obtained as a yellow solid, mp 132–145°, sufficiently pure for conversion to **17**. This material decomposed on standing but could be stored at −25° under N_2. Chromatography on silica gel using 10:1 *n*-hexane–ethyl acetate gave colorless plates: mp 140.5–142°; uv (cyclohexane) 242 nm (sh, log ϵ 4.37), 247 (4.51), 257 (sh, 4.36), 268 (4.29), 278 (4.15), 305 (3.11), 318 (3.32), 343 (sh, 2.39), and 336 (1.79); ir (CCl_4) 1710 cm^{-1}; nmr δ 2.92 (s, 1, α-CH_2) and 5.75 ppm (5, 1, vinylic H).

Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.42; H, 6.61.

A 2,4-dinitrophenylhydrazone precipitated from ethanol and recrystallized from ethyl acetate as deep red microcrystals, mp 264–265° dec (uncorrected).

***cis*-1,5,6,6a,7,8,9,9a-Octahydro-2*H*-indeno[5,4,3-*cde*]azulen-5-one (17). Method A.**—A 32.4-mg (0.14 mmol) sample of tricyclic acid **14** was treated with polyphosphoric acid as described in method B for the preparation of the trans ketone **15**. Chromatography of the crude, yellow product on neutral alumina with dichloromethane gave 20 mg (60%) of **17** as colorless needles, mp 117–118° (uncorrected), ir (Nujol) 1705 cm^{-1}.

Anal. Calcd for $C_{15}H_{16}O$: C, 84.83; H, 7.60. Found: C, 84.68; H, 7.52.

Method B.—A mixture of 0.45 g (2.1 mmol) of **16**, 30 ml of acetic acid, and 57 mg of prereduced platinum oxide was treated with H_2 at 3 atm for 4 hr. A fresh portion of platinum oxide was added and the hydrogenation was continued overnight. The oil remaining after removal of the catalyst and solvent was chromatographed on neutral, activity II alumina. Elution with *n*-hexane and then 7:1 *n*-hexane–ethyl acetate removed a small oily fraction followed by two solids. Recrystallization of the second solid from *n*-hexane gave 0.15 g (33%) of **17**, mp 119.5–121.5°, identical (ir and nmr) with the product from A.

***cis*-1,5,6,6a,7,8,9,9a-Octahydro-2*H*-indeno[5,4,3-*cde*]azulene (19). Method A.**—To a cooled (ice bath), stirred mixture of 7.52 g (35.8 mmol) of crude ketone **16** and 100 ml of absolute ethanol was added 1.01 g (26.4 mmol) of sodium borohydride. The ice bath was then removed and the mixture was allowed to come to room temperature. After the ketone and borohydride had completely dissolved to give a clear amber solution, a thick suspension of white crystals of *cis*-5-hydroxy-1,5,6,8,9,9a-hexahydro-2*H*-indeno[5,4,3-*cde*]azulene (**18**) formed. [In one run the crystals were collected and washed with cold, absolute ethanol, mp 174–176° (uncorrected). *Anal.* Calcd for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 84.32; H, 7.34.] After 3 hr, 40 ml of ethanol (to dissolve the precipitate) and 2 g of Darco carbon were added followed by 2 ml of *ca.* 0.2 *M* chloroplatinic acid hexahydrate. Excess borohydride was destroyed and the solution was made acidic by the addition of 8 ml of concentrated hydrochloric acid and the mixture was treated with H_2 at 3 atm until the uptake of H_2 ceased (4.5 hr). After filtration and removal of the solvent from the filtrate, a solution of the residual amber oil (which slowly crystallized on standing) in the minimal amount of petroleum ether was chromatographed on a column (3.6-cm diameter) containing a bottom layer (9 cm) of neutral, activity I alumina separated from a top layer (8 cm) of basic alumina. Elution with petroleum ether afforded 4.7 g (66%) of **19** as colorless crystals: mp 75–76°; uv (cyclohexane) 262 nm (sh, log ϵ 2.66), 265 (2.75), 269 (2.96), 274 (2.85), and 278 (3.09); ir (CCl_4) 1870 and 1724 cm^{-1} (1,2,3,4-tetraalkylbenzene); nmr (CCl_4) 6.78 (s, 2, aromatic), 3.3–2.5 (m, 6, benzylic), and 2.5–0.8 ppm (m, 10, methylene).

Anal. Calcd for $C_{15}H_{18}$: C, 90.85; H, 9.15. Found: C, 91.03; H, 8.83.

Method B.—A solution of 0.148 g (0.698 mmol) of ketone **17**, 1 ml of 99–100% hydrazine hydrate, and 2 ml of ethanol was refluxed for 1.5 hr. The condenser was removed, 2.5 ml of diethylene glycol was added, and the mixture was heated to 180° over a 20-min period. One pellet (*ca.* 0.13 g) of KOH was added to the cooled solution and heating was then resumed until N_2 evolution ceased. The cooled solution was diluted with 40 ml of H_2O and extracted with ether. Removal of the solvent from the combined, washed (saturated NaCl), dried ($MgSO_4$) solution and chromatography of the residue on neutral, activity I alumina with *n*-hexane gave 13.5 mg (10%) of **19**, mp 71–74° alone and when mixed with the product from A.

***trans*-1,5,6,6a,7,8,9,9a-Octahydro-2*H*-indeno[5,4,3-*cde*]azulene (20).**—In the manner described in B for the conversion of **17** to **19**, from 0.5 g (23.6 mmol) of trans ketone **15** was obtained 0.38 g (80%) of **20** as colorless needles: mp 61–62.5°; uv (ethanol) 269 nm (log ϵ 3.21) and 278 (3.18).

Anal. Calcd for $C_{15}H_{18}$: C, 90.85; H, 9.15. Found: C, 90.81; H, 8.84.

5-Phenylpentanoic Acid (21).—A solution of 278 g (2.44 mol) of glutaric anhydride in 700 ml of anhydrous benzene was added over a period of 90 min to a cooled (5°), stirred suspension of 650 g (4.88 mol) of $AlCl_3$ in 550 ml of benzene. The mixture was allowed to come slowly (1 hr) to room temperature and was then refluxed for 1 hr before removing the solvent by distillation. Ice water (1 l.) was added cautiously to the residue and remaining traces of solvent were removed by steam distillation. After cooling and filtration, the residue was taken up in 10% sodium carbonate. Acidification of the alkaline solution with concentrated hydrochloric acid gave 405 g (86%) of 5-phenyl-5-oxopentanoic acid of sufficient purity for conversion to **21**. Recrystallization of a sample from *n*-hexane resulted in colorless plates, mp 130–132° (uncorrected) (lit.[36] mp 132°).

A mixture of 146 g (0.75 mol) of the oxopentanoic acid, 275 ml of H_2O, 625 ml of concentrated hydrochloric acid, 360 g of freshly prepared amalgamated zinc, and 300 ml of toluene was heated under reflux, four additional portions of 180 ml of concentrated hydrochloric acid were added at 6-hr intervals, and refluxing was continued for 12 hr after the last addition. Ether extracts of the separated aqueous layer were combined with the original organic layer and the whole was extracted with 10% KOH. After treatment with Norit, acidification of the alkaline solution with concentrated hydrochloric acid gave 124 g (93%) of **21**, mp 56–58° (uncorrected) (lit.[37] mp 57°).

Benzocycloheptene (22).—A mixture of 91 g (0.46 mol) of acid **21** and 91 g (0.77 mol) of thionyl chloride was refluxed for 2 hr and then distilled to give 72 g (73%) of 5-phenylpentanoyl chloride, bp 104° (0.6 mm) [lit.[36] bp 155° (22 mm)]. A solution of 70 g (0.45 mol) of the acid chloride in 550 ml of CS_2 was added dropwise (4 hr) to a refluxing mixture of 57.5 g (0.43 mol) of $AlCl_3$ in 175 ml of CS_2 and reflux was maintained for an additional 4 hr. After distillative removal of the CS_2, 400 g of ice water was added and the mixture was steam distilled. The distillate was saturated with NaCl and extracted with ether. Removal of the solvent from the dried ($CaSO_4$) extracts and distillation gave 49.6 g (92%) of 6,7,8,9-tetrahydro-5*H*-cycloheptabenzen-5-one,

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(36) A. Ali, R. D. Desai, R. F. Hunter, and S. M. M. Muhammad, *J. Chem. Soc.*, 1013 (1937).

(37) W. Borsche and W. Eberlein, *Chem. Ber.*, **47**, 1465 (1962).

bp 82–84° (0.3 mm), n^{25}_{D} 1.5636 [lit.[38,39] bp 138–139° (12 mm), n^{20}_{D} 1.5636].

In the manner described above for the reduction of 5-phenyl-5-oxopentanoic acid to **21** except that the mixture was refluxed for 48 hr after the final addition of hydrochloric acid, from 49 g (0.33 mol) of the above ketone was obtained 44.3 g (91%) of **22**, bp 118–122° (33 mm), n^{25}_{D} 1.5487 [lit.[39] bp 98–100° (13 mm), n^{20}_{D} 1.5520].

Benzocycloheptene-1,5-diacetic Acid (24).—A mixture of 10 g (68 mmol) of benzocycloheptene (**22**), 26.2 g (0.154 mol) of recrystallized *N*-bromosuccinimide, 0.05 g of benzoyl peroxide, 0.02 g of azobisisobutyronitrile, and 75 ml of CCl_4 in a Pyrex flask was irradiated with uv light and refluxed for 1 hr and then cooled. The separated succinimide (14.5 g, 0.147 mol) was washed with 25 ml of cold CCl_4. Removal of the solvent from the combined organic solutions left a red oil (20.4 g). Chromatography over acidic alumina with 2:1 benzene–hexane gave a light yellow oil which darkened on standing. It was washed thoroughly with cold (10°) *n*-hexane to completely remove CCl_4. Analysis indicated the product to be **23** contaminated with *ca.* 20% of the corresponding monobromo compound.

A solution of 11.55 g of the yellow oil in 25 ml of anhydrous xylene was added dropwise (90 min) to a stirred suspension of sodiomalonic ester (from 1.75 g of Na and 39.5 g of ethyl malonate) in 50 ml of dry xylene and the mixture was then refluxed for 2 hr. Water (75 ml) was added to the cooled mixture, the separated aqueous layer was extracted with two 50-ml portions of ether, and the combined organic solutions were washed with H_2O and saturated NaCl. Drying ($MgSO_4$) and distillative removal of the solvent (25 mm) and excess ethyl malonate [bp 80–84° (10 mm)] left 13.7 g of crude ester product. This material was refluxed with 11 g of KOH, 40 ml of ethanol, and 20 ml of H_2O for 6 hr under N_2. The alcohol was removed (distillation), and the aqueous residue was diluted to 100 ml with H_2O before extraction with four 25-ml portions of ether. Acidification with 6 *N* hydrochloric acid gave a red, gummy precipitate which was separated and extracted with two 75-ml portions of H_2O. The combined aqueous solutions were continuously extracted with ether for 48 hr. Removal of the solvent from the dried ($MgSO_4$) ethereal solution left a red oil which was heated at 140° for 30 min and then at 180° for 10 min (CO_2 evolution). The cooled product was taken up in 10% KOH and the solution was extracted with ether. Treatment of the aqueous solution with Norite followed by acidification with 10% hydrochloric acid gave 2.75 g of brown oil. Crystallization from acetonitrile afforded 0.5 g (5%) of **24** as colorless plates, mp 254.5–255.5°.

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.50; H, 6.91.

***cis*-1,6,7,8,9,9a-Hexahydro-2*H*-benzo[*cd*]azulenyl-6-acetic Acid (14).**—Diacid **24** (0.3 g) was treated with 4 g of polyphosphoric acid as described for the preparation of **15** from **13** except that the ethereal extracts of the diluted reaction mixture were washed with H_2O before extraction with 10% sodium bicarbonate, and acidification of the alkaline extracts gave 280 mg of light tan plates, mp 176–181°, presumed to be the crude tricyclic keto acid. This material was treated as described for the conversion of **17** to **19** except that 85% hydrazine hydrate was used, the mixture was heated to 165° after the addition of ethylene glycol, and the reflux period after the addition of KOH was 5 hr. Acidification of the ether-extracted alkaline solution gave 200 mg of impure acid, mp 112–135°. This product was treated with 1 g of amalgamated zinc, 3 ml of concentrated hydrochloric acid, 1 ml of H_2O, and 3 ml of toluene as described for the reduction of 5-phenyl-5-oxopentanoic acid to **21** except that five additions of concentrated hydrochloric acid (1 ml) were made at 12-hr intervals. The final mixture was extracted with ether and the extracts were extracted with 10% sodium bicarbonate. Acidification and recrystallization gave 120 mg (48%) of **14** as colorless plates, mp 117–119°.

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.11; H, 7.67.

Dicyclopenta[*ef,kl*]heptalene (Azupyrene) (25).—In a 50-ml, three-necked, pear-shaped flask equipped with a Hershberg dropping funnel, reflux condenser, and magnetic stirring bar was placed 2 g of **19** and the flask was heated (oil bath) to 140–150°.[40] To the stirred liquid was added 7 ml of ethyl diazoacetate over a period of 3 hr (N_2 evolution) and stirring and heating were continued at 150–160° for an additional 1.5 hr. The cooled, red-brown, viscous mixture was transferred onto a 5.5 × 15 cm column of acidic alumina with the aid of the minimal amount of dichloromethane. Unchanged **19** (1 g) was eluted with petroleum ether, and then dichloromethane–petroleum ether (1:3) removed pink and green product fractions. The pink solution (maroon when concentrated) became green on standing. Removal of the solvent from the combined product fractions gave 1.2 g of crude ester.

The combined ester products from four of the above reactions were treated with 4 g of KOH in 25 ml of methanol under reflux for 1.5 hr. The brown solution was added to 250 ml of H_2O and acidified with 2 *N* hydrochloric acid. The gelatinous precipitate was extracted into ether and removal of the solvent from the dried ($MgSO_4$) extracts gave 4.2 g of crude acid as a viscous brown oil.

A solution of the crude acid in 15 ml of methyl oleate was refluxed (*ca.* 350°) under an O_2-free N_2 atmosphere in the presence of 220 mg of 10% Pd/C catalyst[23] for 10 min, during which time the solution became dark green. The cooled mixture, diluted with a small quantity of petroleum ether, was chromatographed on a 5.5 × 20.5 cm column of neutral, activity II alumina. Petroleum ether eluted a blue band which was set aside and then a wide yellow-green band. The dark yellow-green oil residue from the latter fraction was chromatographed twice on Florisil (3.5 × 13 cm) with petroleum ether as the eluate to give 109 mg (2.5%) of **25** as a bronze solid, mp 249–254°. Subjecting the blue fraction to a second treatment with Pd/C afforded an additional 58 mg[41] for a total of 167 mg (3.8%). Recrystallization from methanol formed square, bronze platelets: mp 250–258° (sealed tube under N_2, uncorrected); uv and visible (cyclohexane) 252 nm ($\log \epsilon$ 4.73), 267 (5.03), 285 (4.49), 299 (4.32), 308 (4.27), 334 (4.07), 343 (4.13), 356 (3.62), 409 (2.92), 442 (3.17), 452 (3.28), 459 (3.17), 470 (3.49), and 483 (4.11) plus poorly defined maxima at *ca.* 550 (1.64), 600 (1.64), 645 (1.60), 663 (1.60), 720 (1.31), 738 (1.26), and 770 (0.96); ir ($HCCl_3$) 1377, 1538, 1588, and 3000 cm^{-1}; nmr ($DCCl_3$) 7.34 (t, 2), 8.40 (s, 4), and 8.68 ppm (d, 4); mol wt (mass spectrometry) 202.076 (calcd, 202.078); $\Lambda/\Lambda_{bz} = 3.9 \pm 0.3$.

Anal. Calcd for $C_{16}H_{10}$: C, 95.02; H, 4.98. Found: C, 94.75; H, 4.99.

Registry No.—**1,** 14528-87-1; **2,** 38434-48-9; **3,** 7235-16-7; **4,** 38434-50-3; **8,** 38434-51-4; **9,** 38434-52-5; **11,** 38434-53-6; **13,** 38434-54-7; **14,** 38434-55-8; **15,** 38434-56-9; **16,** 38434-57-0; **16** DNP, 38434-58-1; **17,** 38434-59-2; **18,** 38434-60-5; **19,** 38434-61-6; **20,** 38434-62-7; **21,** 2270-20-4; **21** acid chloride, 20371-41-9; **22,** 1075-16-7; **23,** 38434-66-1; **24,** 38434-67-2; **25,** 193-85-1; ethyl bromoacetate, 105-36-2; 6,7,8,9-tetrahydro-5*H*-cycloheptabenzen-5-one, 826-73-3; sodiomalonic ester, ethyl, 28290-06-4.

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[38] G. O. Aspinall and W. Baker, *J. Chem. Soc.*, 743 (1950).

[39] Pl. A. Plattner, *Helv. Chim. Acta*, **27**, 804 (1944).

[40] Temperatures of less than 140° or greater than 160° gave much poorer results.

[41] In practice the blue fractions from several runs were combined and the 58 mg represents the average yield per fraction.