1,3-Bridged Aromatic Systems. V. Strained Aromatic Systems[1]

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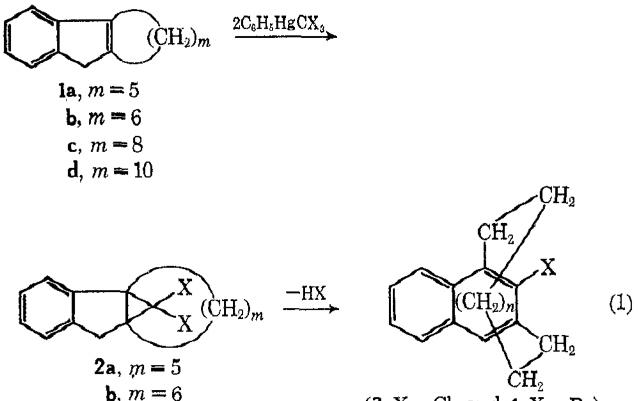
1,3-Bridged naphthalenes of type **3** and **4**, in which the minimum value of n is 2, have been prepared in high yield. Steric constraint in such metacyclophanes causes distortion or change in aromatic character of the aromatic ring to which the methylene bridge is attached, and this effect is noted by a variety of physical and chemical processes. Evidence is presented suggesting that **3** (with $n = 1$) can be prepared as a highly reactive, unstable intermediate; however, the principal product from the reaction of **1a** with dichlorocarbene is not a metacyclophane, but an isomer resulting from phenyl migration. The photochemistry of **3b** in ethanol is also discussed.

We have recently described[3] the preparation of 1,3-bridged naphthalenes **3c** and **3d** by the procedure summarized in eq 1. This synthesis is of particular interest since it involves an energetically favorable creation of an aromatic ring as the last step, in contrast to less favorable ring closures used traditionally for the preparation of related metacyclophanes.[4] This investigation was directed toward a study of the scope of this synthesis, with particular attention given to the lowest value of n in **3** and **4**, and the properties of the strained aromatic systems that resulted.[5]



1a, $m = 5$
b, $m = 6$
c, $m = 8$
d, $m = 10$

2a, $m = 5$
b, $m = 6$
c, $m = 8$
d, $m = 10$

(1)

(**3**, X = Cl, and **4**, X = Br)
a, $n = 1$
b, $n = 2$
c, $n = 4$
d, $n = 6$

A. 3b ($n = 2$, X = Cl).—Inspection of models revealed that the metacyclophanes **3b** or **4b** would probably result in distortion of the benzene ring to which the methylene chain is attached. This conclusion was supported by both the physical and chemical properties of **3b** and **4b**.

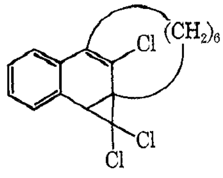
The metacyclophane **3b** was obtained as a white solid in high yield (74%) by reaction of **1b** with phenyl(trichloromethyl)mercury in hot benzene. The nmr spectrum showed characteristic broad and complex methylene absorption at τ 6.34–11.12. The methylene bridge cannot pass over the chlorine atom, thereby hindering mobility of the bridge and resulting in considerable nonequivalence of the ring methylene protons. The very high field absorption of **3b** near τ 11 was expected by analogy to **3c** and **3d**, since the central bridging atoms are held closely over the face of the benzene ring and, as a consequence, are held closely in the shielding cone of the aromatic ring.

The ultraviolet spectrum of **3b** was similar to those of **3c** and **3d** but showed complete loss of fine structures together with a slight bathochromic shift.

The distortion of the benzene ring in **3b** was also evidenced by a study of its oxidation with 40% nitric acid with subsequent methylation of the derived acids by action of diazomethane. The only products isolated, under conditions identical with those described for **3d**,[3] were dimethyl phthalate and dimethyl nitrophthalate. There was no evidence for the formation of tetramethyl 4-chloro-1,2,3,5-benzene tetracarboxylate, which was a major product from **3d**.

An impurity isolated (3–5% yield) from the synthesis of **3b** was assigned structure **5** on the basis of its composition and spectra and by its synthesis (eq 2) by addition of CCl_2 to **3b** (42% yield). Unactivated aromatic systems are generally resistant to reaction with dichlorocarbene; the facile addition of dichlorocarbene to **3b** is further evidence of the strain and distortion of the benzene ring to which the methylene bridge is attached.

$$\mathbf{3b} + C_6H_5HgCCl_3 \xrightarrow{\text{benzene}} \qquad (2)$$



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8,9-Benzo-12-chloro[6]metacyclophane (**3b**) decolorizes neutral potassium permanganate at room temperature and reacts readily with bromine in carbon tetrachloride at room temperature with evolution of hydrogen bromide. The product of the latter reaction was shown to be **6** by its composition, by its spectra, and by

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[1] Supported by the National Science Foundation Grant GP-6169X. For the preceding article in this series, see W. E. Parham, R. W. Davenport, and J. B. Biasotti, *Tetrahedron Lett.*, **7**, 557 (1969).

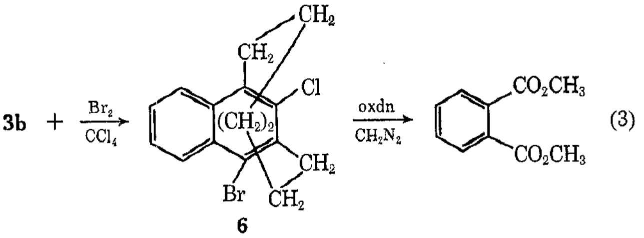
[2] Taken in large part from the Ph.D. Thesis of D. R. Johnson, University of Minnesota, 1969; National Aeronautics and Space Administration Fellow, 1966–1969.

[3] W. E. Parham and J. K. Rinehart, *J. Amer. Chem. Soc.*, **89**, 5668 (1967).

[4] For a review of methods used for cyclophane syntheses, see B. H. Smith, "Bridged Aromatic Compounds," Academic Press Inc., New York, N. Y., 1964, pp 24–185.

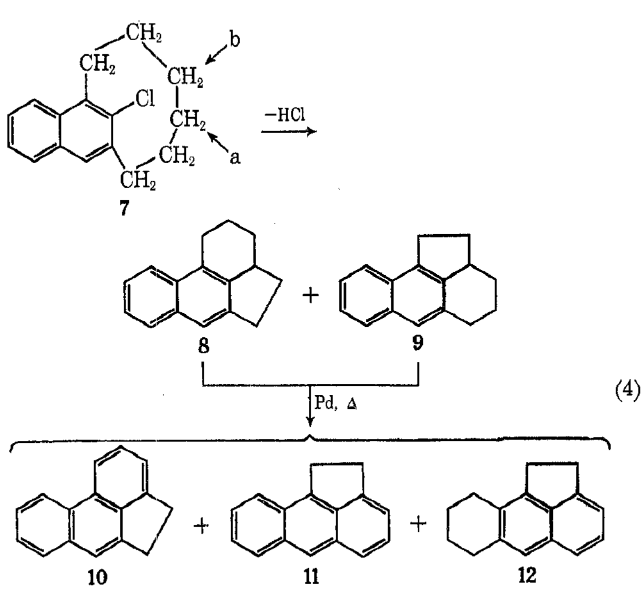
[5] For reviews of the chemical behavior of cyclophanes, see (a) R. W. Griffin, Jr., *Chem. Rev.*, **63**, 45 (1963); (b) R. B. Smith, "Bridged Aromatic Compounds," Academic Press Inc., New York, N. Y., 1964.

its conversion into dimethyl phthalate by oxidation and subsequent esterification of the derived acids (eq 3).



6

8,9-Benzo-12-chloro[6]metacyclophane (**3b**) was observed to undergo a rapid photochemical reaction in ethanol. The principal product (68–80% yield) was a mixture of two isomeric products ($C_{16}H_{16}$) shown to be 1,2,3,3′,4,5-hexahydroacephenanthrylene (**8**) and 1,2,2′,3,4,5-hexahydroaceanthrylene (**9**) (eq 4).

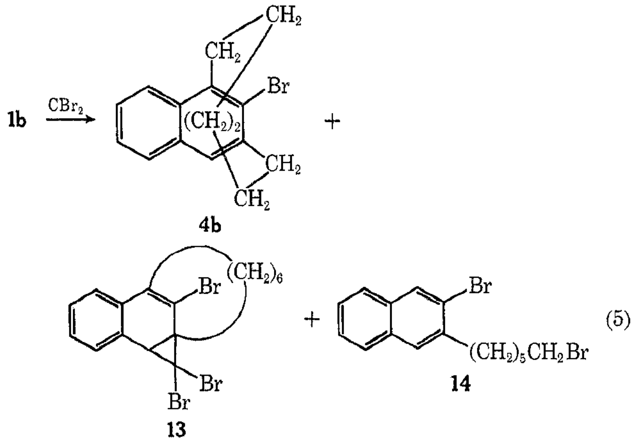


7 **8** **9** **10** **11** **12**

The composition, spectra, and analysis by glpc of the photoproduct was consistent for a mixture of **8** and **9** in the ratio of 70:30, respectively. These products are those expected by a photochemically catalyzed elimination of a chlorine atom followed by a series of events involving (a) naphthyl radical abstracting a proximate transannular hydrogen atom, and (b) subsequent reaction of the derived radical with the strained aromatic ring. Because of the unusual stereochemistry of the system one cannot rule out the alternate possibility that the departing chlorine atoms remove a proximate transannular hydrogen atom at a or b as shown in **7**, followed by coupling of the resulting caged diradical. The photoproduct was partially dehydrogenated by reaction with palladium on carbon to give a mixture of acephenanthrene (**10**) and aceanthrene (**11**). Both of these dehydrogenated products were known, and comparison of the ultraviolet spectrum of the mixture indicated the composition to be 65% **10** and 35% **11**, a value in close agreement to the ratio estimated for the hydrocarbon precursors by glpc. The mixture of **10** and **11** was not completely resolved by chromatography; however, a small amount of the principal product **10** was isolated pure and was shown to be identical with an authentic sample of **10**.

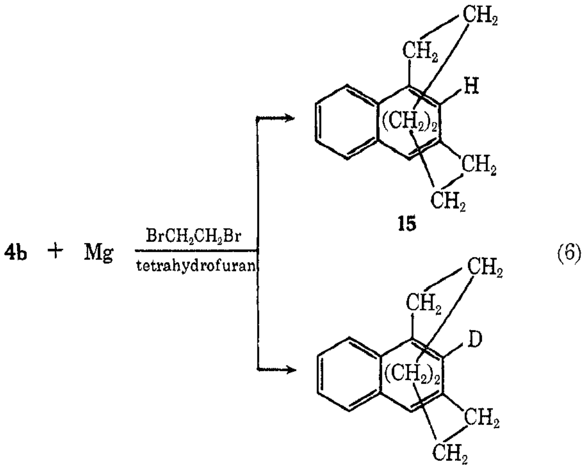
A third component isolated (20%) from the dehydrogenation of **8** and **9** was identified as **12** by its subsequent dehydrogenation to **11**. The product **12** was obviously formed by isomerization of **9** under conditions employed for dehydrogenation.

B. 4b ($n = 2$; $X = Br$).—The reaction of **1b** with phenyl(tribromomethyl)mercury in benzene was highly temperature dependent. Optimum yields (40%) of **4b** were obtained when the reaction was conducted in benzene at 50°. The cyclopropane **13** (mp 119–120°; spectral properties essentially identical with those described for **5**; not further analyzed) was a by-product (7.4%) in this reaction, together with unreacted starting material. At higher temperatures (60°, or reflux), 2-(6-bromohexyl)3-bromonaphthalene (**14**) was a significant by-product (14%). The dibromide **14** was identified by its composition, by its spectra, and by its synthesis from **4b**; the mechanism of its formation is discussed subsequently.



4b **13** **14**

8,9-Benzo-12-bromo[6]metacyclophane (**4b**) formed a Grignard reagent readily, which gave **15** (>80% yield) or **16** (93% yield, 97% deuterium incorporation), respectively, when hydrolyzed by action of water or deuterium oxide (eq 6).



15 **16**

The nmr spectrum of **15** was complex and showed methylene absorption at τ 6.33–10.40. These data establish the fact that there is a barrier to ring inversion (rotation to the opposite face of the aromatic ring) in **15** whether a hydrogen or a halogen atom occupies the 2 position of the naphthalene ring. These results are in contrast to similar studies involving **4d**[6a] in which ring

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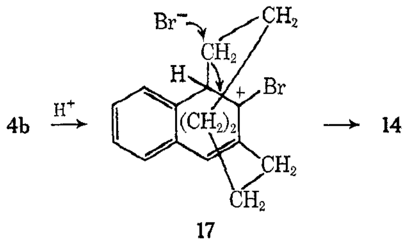
[6] (a) Private communication, R. W. Davenport, The University of Minnesota. The chemistry of **4d** will be presented in a subsequent communication. (b) Reference 5b, p 343.

inversion occurs when the 2 substituent is hydrogen, but not when it is halogen. The barrier to ring inversion in **15** is thus either a result of steric interference by hydrogen at the 2 position or, more likely, simply to the required stretching needed for the strained system to go through a planar transition state. Asymmetry in related cyclophanes has been noted.[6b]

That slow inversion is occurring at room temperature, which would constitute racemization if **15** could be resolved into its optical isomers, was evident from variable temperature nmr studies. At 92° the methylene absorption changed markedly and resembled that described for the dehalogenated derivative of **4d**[4] (rapid equilibration of the methylene bridge to the two faces of the naphthalene ring); at 1° the methylene absorption remained complex and broad, but showed marked sharpening of absorption, consistent with the conclusion that ring inversion is not occurring rapidly at this temperature.

It was observed that **4b** reacts readily with anhydrous hydrogen bromide in benzene at 60° or higher, but only slowly (not detected) at 50°. The product of the reaction (59.1% yield) was 2-(6-bromohexyl)-3-bromonaphthalene (**14**). Structure **14** was assigned to this product on the basis of its composition and spectra and by analogy to **19**, described in the next section. The dibromide **14** is assumed to be formed as shown in **17** (eq 7).

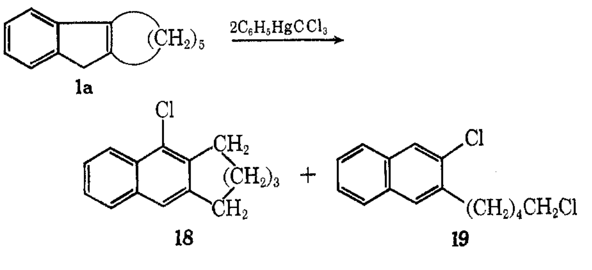


(7)

Reverse alkylations of aromatics are common when strong Lewis acids are employed (*i.e.*, isomerization of alkylbenzene with $AlCl_3$); however, cleavage of the type shown in eq 7 is exceptional.[7] In retrospect, such cleavage is not surprising in view of the demonstrated reactivity of the aromatic ring involved, and the relief of strain from such reaction.

Since the dihalocyclopropyl intermediates **2** are known[3] to decompose, with liberation of hydrogen halide, under conditions used for their formation, it is apparent that **14** could be formed as a by-product from the synthesis of **4b** by competitive reaction of the hydrogen bromide liberated with **4b** or with excess phenyl(tribromomethyl)mercury, used to remove hydrogen bromide.

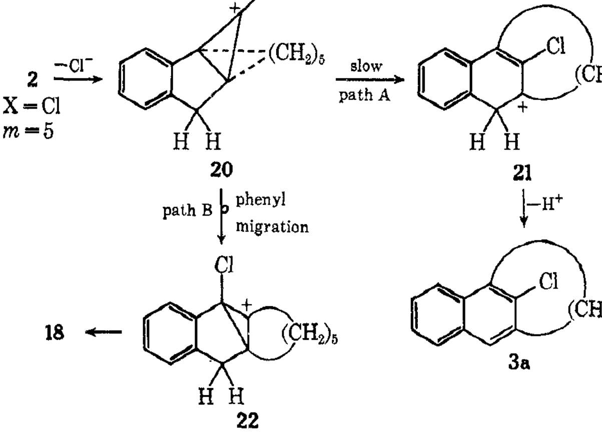
C. Reaction of 1a with Phenyl(trichloromethyl)mercury.—Two products (eq 8) were obtained from the reaction of pentahydrocyclohept[*b*]indene (**1a**) with 2 equiv of phenyl(trichloromethyl)mercury in boiling benzene.



(8)

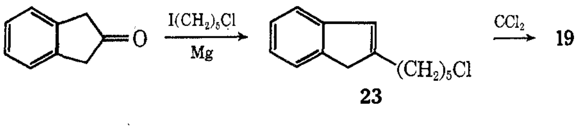
The major product **18** (66% yield) was identified by its composition and spectra and its structure was established by oxidation, with subsequent esterification of the derived acids with diazomethane, to tetramethyl-3-chloro-1,2,4,5-benzene tetracarboxylate. This ester was unknown and was prepared independently from monochlorodurene by a similar procedure; thus it was established that a molecular rearrangement had occurred in the carbene reaction.

Since it is known that the rate-determining step[8] in ring expansion of the type $2 \rightarrow 3$ involves ionization of halogen–carbon bond, a logical mechanism for the formation of **18**, shown as a stepwise process for clarity only, involves phenyl rearrangement of the neopentyl type, shown in eq 9 (path B). It is logical to assume that the collapse of the ion **20** by a concerted disrotatory process[9] to give **21** (path A), and subsequently **3a**, would be slow because of the high steric demands of **21** and/or **3a**. Consequently, path B, involving phenyl migration, dominates. With more than five methylene groups in the bridge, steric requirements for path A are less severe and metacyclophane formation dominates. It is interesting to note that no products analogous to **18** have been detected in reactions of indenes involving more than five methylene atoms in the bridge.



(9)

The second product shown in eq 8, isolated in 8.4% yield, was shown to be 2-(5-chloropentyl)-3-chloronaphthalene (**19**) by (a) its composition, (b) its spectra, and (c) by its independent synthesis as summarized in eq 10.



(10)

The formation of **19** probably occurs in a manner analogous to that described for **14** in section B, by cleavage of the derived metacyclophane **3a** by hydrogen

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(7) Dealkylation of aromatics substituted by *t*-alkyl groups by protonic acids is common: R. W. Frank and E. G. Laser, *J. Amer. Chem. Soc.*, **91**, 1577 (1969).

(8) W. E. Parham, H. E. Reiff, and P. Swartzentruber, *ibid.*, **78**, 1437 (1956).

(9) (a) R. B. Woodward and R. Hoffman, *ibid.*, **87**, 395 (1965); (b) C. H. DePuy, L. G. Swnack, J. W. Hausser, and W. W. Wiedman, *ibid.*, **87**, 4006 (1967).

chloride liberated during the decomposition of **2a**. Formation of this product suggests that it may be possible by careful choice of conditions to isolate metacyclophanes of type **3a**; however, this objective has not been realized.

Experimental Section

Hexahydrocyclooct[*b*]indene (1b).—The indene **1b** was prepared from cyclooctanone by a procedure similar to that described for **1c–1d**.[8,10]

1. ***o*-(1-Cyclooctenyl)benzonitrile.**—*o*-(1-Cyclooctenyl)chlorobenzene, obtained from *o*-bromochlorobenzene (100 g, 0.522 mol) and cyclooctanone (65.8 g, 0.522 mol), was not obtained pure [30.2% yield as determined by glpc; bp 82.5–87° (0.12 mm), n^{25}D 1.5597]. Impure material, obtained after removing the impurities boiling below 72° (0.1–0.2 mm), was heated with cuprous cyanide in N-methylpyrolidone and the product was purified by chromatography (alumina; eluent, petroleum ether, bp 60–70°) and distillation [bp 90–90.5° (0.015 mm)] to give pure nitrile: n^{25}D 1.5647; ir (neat) 2220 cm^{-1}; uv max (95% ethanol) 288 mμ (log ε 3.43), 250 (3.72), 221 (4.29); nmr ($CDCl_3$) τ 2.35–2.84 (m, 4.4, aromatic H), 4.13 (t, 0.9, *J* = 8 Hz, olefinic CH), 7.29–7.88 (m, 4.3, aliphatic CH_2), 8.39 (broad s, 7.5, aliphatic CH_2).

Anal. Calcd for $C_{15}H_{17}N$: C, 85.26; H, 8.11; N, 6.63. Found: C, 85.28; H, 8.22; N, 6.93.

2. ***o*-(1-Cyclooctenyl)benzylamine Hydrochloride.**—A 70–91% yield was obtained: mp 192.5–196° dec from ethanol, 193–197° dec by sublimation; ir (Nujol–halocarbon) 3150–2720, 2690, and 2590 cm^{-1} (NH_3^+); nmr (D_2O) τ 2.41–3.18 (m, 3.9, aromatic H), 4.56 (t, 1.0, *J* = 7 Hz, olefinic H), 5.92 (s, 2.0, benzylic CH_2), 7.43–8.02 (broad s, *ca.* 4, aliphatic CH_2), 8.20–8.80 (broad s, 8.1, aliphatic CH_2).

Anal. Calcd for $C_{15}H_{22}ClN$: C, 71.55; H, 8.81; N, 5.56. Found: C, 71.73; H, 8.86; N, 5.50.

3. **Hexahydrocyclooct[*b*]indene (1b).**—A 53–85% yield was obtained after chromatography (alumina; petroleum ether, bp 60–70): bp 83.0–83.3° (0.04 mm); n^{25}D 1.5784; ir (neat) 1628 cm^{-1} (C=C); uv max (95% ethanol) 282 mμ (sh) (log ε 3.21), 265 (sh), (4.04), 257 (4.14), 222 (sh) (3.90); nmr (CCl_4) τ 2.60–3.15 (m, 4.0, aromatic H), 6.83 (broad s, 2.0, benzylic CH_2), 7.23–7.60 (m, 4.0 allylic CH_2), 8.07–8.75 (m, 8.1, aliphatic CH_2).

Anal. Calcd for $C_{15}H_{18}$: C, 90.85; H, 9.19. Found: C, 91.05; H, 9.31.

Reaction of Hexahydrocyclooct[*b*]indene (1b) with Phenyl(trichloromethyl)mercury and with Phenyl(tribromomethyl)mercury.—The procedure used was essentially identical with that described for **1c–1d**[8] unless otherwise noted.

1. **8,9-Benzo-12-chloro[6]metacyclophane (3b).**—The crude product was obtained in 80–100% yield as a white mushy solid subsequent to column chromatography (alumina; petroleum ether, bp 60–70°): mp 43.5–45.3 (74% yield), 45.5–46.2° after chromatography on silica–petroleum ether followed by recrystallization from ethanol; white needles; uv max (95% ethanol) 321 mμ (sh) (log ε 2.49), 300 (sh) (3.59), 290 (3.70), 282 (sh) (3.67), 245 (4.74); nmr (CCl_4) τ 2.21–2.96 (m, 5.0, aromatic H), 6.34–6.82 (m, 3.0, benzylic CH_2), 7.36–9.58 (m, 8.2, aliphatic CH_2), 10.52–11.12 (broad s, 0.9, aliphatic CH_2).

Anal. Calcd for $C_{16}H_{17}Cl$: C, 78.51; H, 7.00. Found: C, 78.78; H, 7.01.

2. **Isolation of 5.**—Further elution of the column used to purify **3b**, above, with petroleum ether (bp 60–70°) gave **5** in 3–5% yield: white needles; mp 106.5–107.5° from petroleum ether and from ethanol; ir (KBr) 985 cm^{-1} (cyclopropyl); uv max (95% ethanol) 302 mμ (log ε 3.54), 244 (4.19), 237 (4.22); nmr ($CDCl_3$) τ 2.52–2.86 (m, 3.9, aromatic H), 6.63–7.36 (m, 4.2, allylic CH_2, benzylic CH), 7.88–9.15 (m, 9.0, aliphatic CH_2); mass spectrum (70 eV) *m/e* 326 molcular ion.

Anal. Calcd for $C_{17}H_{17}Cl_3$: C, 62.31; H, 5.23; Cl, 32.46; mol wt, 326. Found: C, 62.43; H, 5.26; Cl, 32.25; mol wt (mass spectroscopy), 326.

3. **8,9-Benzo-12-bromo[6]metacyclophane (4b).**—A mixture of **1b** (6.7 mmol) and phenyl(tribromomethyl)mercury (13.6 mmol) was heated in dry benzene, under nitrogen for 24 hr at 50°. The crude product (1.25 g), obtained subsequent to removal (by filtration and trituration) of phenylmercuric bromide, was chromatographed on alumina (eluent, petroleum ether, bp 60–70°) to give slightly impure (tlc) **4b** (yellow oil). The material was purified by recrystallization from pentane at Dry Ice–acetone temperature to give **4b** as a white powder (0.71 g, mp 51–52°, 40% yield). Pure **4b** was obtained by chromatography on silica gel with subsequent recrystallization of product from petroleum ether (bp 40–60°): mp 52–53°; uv max (95% ethanol) 238 mμ (log ε 4.71), 281 (sh) (3.72), 290 (3.74), 300 (sh) (3.64); nmr (CCl_4) τ 2.10–2.95 (m, 5.2, aromatic H), 6.30–6.76 (m, 3.0, benzylic CH_2), 7.26–9.53 (m, 8.2, aliphatic CH_2), 10.40–11.37 (broad s, *ca.* 0.6, aliphatic CH_2).

Anal. Calcd for $C_{16}H_{17}Br$: C, 66.44; H, 5.94; Br, 27.63. Found: C, 66.58; H, 6.01; Br, 27.38.

4. **Isolation of Compound Believed to Be 13.**—In a subsequent reaction conducted as described above (but for 40 hr at 50°), elution (petroleum ether, bp 60–70°) was continued after **4b** (65.4% yield) was removed. There was obtained 0.60 g of **13** (7.4% yield yellow needles: mp 119–120° from ethanol–water); ir (Nujol–halocarbon oil) 985 cm^{-1} (cyclopropyl); uv max (95% ethanol) 248 mμ (log ε 4.30), 321 (3.57); nmr (CCl_4) τ 2.68–2.94 (m, 3.9, aromatic H), 6.52–7.78 (m, 3.8, allylic CH_2, benzylic CH), 7.78–9.52 (m, 9.3, aliphatic CH_2). This compound was not analyzed owing to thermal instability, but assigned structure **13** by spectral analysis and by analogy to the isolation of **5** from the synthesis of **3b**.

5. **Isolation of 2-(6-Bromohexyl)-3-bromonaphthalene (14).**—When the reaction of **1b** with 2 equiv of phenyl(tribromomethyl)mercury was carried out at 60° for 20 hr (and at reflux for 3 hr) and the crude product was chromatographed as described in 3 above, there was obtained, subsequent to removal of **4b** (*ca.* 27% yield) and unchanged indene (small amount), 0.68 g (13.9% yield) of **14** (mp 59.5–64°). Pure **14**, obtained by preparative tlc (silica gel PF_{254}; eluent, 20% ether in petroleum ether) with subsequent recrystallization of the product from ethanol, was obtained as white needles: mp 66–67°; uv max (95% ethanol) 230 mμ (log ε 4.76), 253 (sh) (3.31), 262 (3.43), 271 (3.56), 281 (3.57), 292 (3.33), 307 (2.40), 321 (2.26); nmr (CCl_4) τ 2.01 (s, 1.1, aromatic H), 2.18–2.86 (m, 5.0, aromatic H), 6.70 (t, 1.8, *J* = 6.5 Hz, $-CH_2Br$), 6.86–7.35 (m, 2.0, benzylic CH_2), 7.83–8.79 (m, 8.1, aliphatic CH_2).

Anal. Calcd for $C_{16}H_{18}Br_2$: C, 51.91; H, 4.91; Br, 43.17. Found: C, 51.88; H, 4.91; Br, 42.88.

Reactions of 8,9-Benzo-12-chloro[6]metacyclophane (3b). 1. Oxidation with 40% Nitric Acid.—The procedure used was identical with that described[8,11] for oxidation of **3d**. The crude acid (soft yellow solid, 0.12 g, from 0.15 g of **3b**, mp 135–144° after digestion with benzene and showing no methylene absorption in the nmr) was esterified with excess diazomethane. Analysis of the product by glpc (identical conditions with those described[8]) showed it to be a 60:40 mixture of dimethyl phthalate and dimethyl nitrophthalate, respectively. There was no detectible amount of tetramethyl 4-chloro-1,2,3,5-benzene tetracarboxylate present.

2. **With Phenyl(trichloromethyl)mercury.**—A mixture of **3b** (1 equiv) and phenyl(trichloromethyl)mercury (1 equiv) was heated in dry benzene under nitrogen for 66 hr at the reflux temperature. Analysis of the crude product by glpc[12] showed it to contain unreacted **3b** (46.1%), unidentified material (12.1%), and dichlorocarbene adduct **5** (41.8%). The crude product was purified by preparative tlc (silica gel PF_{254}; eluent, petroleum ether, bp 60–70°); **5** was obtained as white needles (from petroleum ether), mp 108.5–109°, and caused no depression in melting point when admixed with **5** (mp 106.5–107.5°) obtained directly from **1b** as previously described.

3. **With Bromine.**—A mixture of **3b** (1 equiv) and bromine (1 equiv) was stirred at room temperature under nitrogen in carbon tetrachloride for 6 hr, during which time evolution of hydrogen bromide was evident. Isolated from the reaction was 0.30 g of slightly impure product (by tlc) which was purified by chromatography (alumina; eluent, petroleum ether, bp 60–70°) to give 0.18 g (90.6% yield, calculated as $C_{16}H_{16}BrCl$) of product, mp 72–82°, which was recrystallized from ethanol to give pure **6** as white needles: mp 83–84°; uv max (95% ethanol) 237 mμ

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[10] W. E. Parham, C. D. Wright, and D. A. Bolon, *J. Amer. Chem. Soc.*, **83**, 1751 (1961).

[11] H. Bamford and J. L. Simonsen, *J. Chem. Soc.*, **97**, 1904 (1910).

[12] Gas–liquid partition chromatography (glpc) was carried out on a Beckman GC-4 using dual flame detector with helium as a carrier (60 ml/min). The column used was 1/8 in. × 6 ft 5% DC-710 on Chromosorb W (80–100 mesh) at 200°.

(log ϵ 4.58), 254 (sh) (4.28), 290 (sh) (3.67), 299 (3.75), 308 (sh) (3.67), 350 (2.67); nmr (CCl_4) τ 1.78–3.16 (m, 3.6, aromatic H), 6.33–7.30 (m, 4.0, benzylic CH_2), 7.63–11.82 (m, 8.3, aliphatic CH_2).

Anal. Calcd for $C_{16}H_{16}BrCl$: C, 59.38; H, 4.98; Br, 24.69; Cl, 10.95. Found: C, 59.34; H, 4.94; Br, 24.42; Cl, 10.45.

The structure of 6 was established by oxidation with 40% nitric acid and subsequent esterification of the derived acids with diazomethane as described for **3d**.[3,11] Dimethyl phthalate, isolated by preparative glpc and characterized by ir, and dimethyl nitrophthalate were major products of the reaction, together with a material having a much higher retention time assumed to be tetramethyl 4-bromo-6-chloro-1,2,3,5-benzene tetracarboxylate.

4. **With Light.** a. A solution of **3b** (2.00 g, 8.18 mmol) in 95% ethanol was placed in a quartz tube and irradiated (Rayonet Srinivasan-Griffin photochemical reactor) under nitrogen atmosphere for 8.5 hr. The reaction progress was followed by glpc[12] which showed the disappearance of starting material to be complete after 8.5 hr. The orange oil obtained from the ethanol was chromatographed (150 g of silica gel eluent, petroleum ether, bp 60–70°) to give 1.17 g (68.7% yield, calcd as $C_{16}H_{16}$) of clear oil (containing an incompletely resolved mixture of two major components, a trace amount of starting material, and a very minor amount of another component, as determined by glpc[12]). Recrystallization of the oil from ethanol gave 0.58 g (34.1% yield) of white crystals, mp 36.0–37.0°. Analysis of the solid by glpc[12] (except at 150°) showed the photochemical product to be a mixture of 1,2,3,3′,4,5-hexahydroacephenanthrylene (**8**, *ca.* 70%) and isomeric ($C_{16}H_{16}$) 1,2,2′,3,4,5-hexahydroaceanthrylene (**9**, *ca.* 30%): uv max (95% ethanol) 320 mμ (sh) (log ϵ 2.93), 310 (sh) (3.18), 295 (sh) (3.72), 289 (sh) (3.76), 282 (3.80), 274 (sh) (3.73), 264 (sh) (3.59), 234 (5.04), 230 (sh) (4.96); nmr ($CDCl_3$) τ 2.13–2.86 (m, 5, aromatic H), 6.75–9.32 (m, 11, benzylic and aliphatic CH_2); mass spectrum (70 eV) *m/e* 208 molecular ion).

Anal. Calcd for $C_{16}H_{16}$: C, 92.26; H, 7.74. Found: C, 92.21; H, 7.76.

b.—The reaction was repeated as described above and the crude product was chromatographed on silica gel (130 g; eluent, petroleum ether, bp 60–70°) to give 1.02 g (79.8% yield) of a mixture of **8** and **9** as a clear oil (no other products visible by tlc).

Identification and Proof of Structure of 8 and 9.—A mixture (oil from b above, 0.20 g, 0.962 mmol) of the photoproducts **8** and **9** and 5% palladium on charcoal (50 mg) was heated under nitrogen at 180–210° for 50 min. Analysis of an aliquot by glpc[12] showed 53% unchanged starting material. Fresh catalyst (50 mg) was added and the heating continued for 1.5 hr. Analysis as described above showed a small amount of starting material and two principal components in a ratio of 60:40. The crude product was chromatographed (silica gel; 40 g; eluent, petroleum ether, bp 60–70°) to give (a) unreacted starting material (40 mg, 20% recovery, pure by glpc); (b) 1,2,7,8,9,10-hexahydroaceanthrylene (**12**) as a white solid, mp 74–78° (contaminated with a trace of starting material as detected by tlc); and (c) a mixture of acephenanthrene (**10**) and aceanthrene (**11**) as yellow crystals, mp 80–90° (indistinct).

The uv spectrum of the mixture, mp 80–90°, follows: uv max (95% ethanol) 212 mμ, 224, 236 (sh), 251 (sh), 257.5, 268 (sh), 279, 291, 302.5. 321, 336, 353 (instrument cut-off 360 mμ).

Pure acephenanthrene (**10**), mp 106–107° (lit.[13] mp 106°), identical with a sample of **10** (mp 105–107°, mixture melting point undepressed, mmp 106–107°) recovered from a sample of authentic picrate,[13] had the following uv spectrum: uv max (95% ethanol) 208 mμ (log ϵ 4.86), 224 (sh) (4.62), 238 (sh) (4.51), 250 (sh) (4.72), 257 (4.79), 267 (sh) (4.29), 278 (3.92), 290 (3.92), 302 (4.09), 319 (2.53), 334 (3.01), 350 (3.27).

The uv spectrum of aceanthrene (**11**), mp 113°, prepared by Bergman and Ikan,[14] is reported to be uv max (95% ethanol) 225 mμ (log ϵ 4.05), 256 (4.14), 258 (5.06), 355 (3.50), 375 (3.80), 395 (3.56).

Comparison of uv spectra of **10** and **11** revealed that acephenanthrene shows an absorption peak at 302 mμ, in which region the aceanthrene is essentially transparent. This information was used to calculate the composition of the mixture, mp 80–90°, to be 65% acephenanthrene and 35% aceanthrene. This value compares favorably with the ratio of 70:30 of **8** to **9**, respectively, observed for the mixture of the hexahydro precursors.

Chromatography of the mixture (mp 80–90°) on neutral Woelm aluminum, activity grade I, gave a small amount of the principal product, acephenanthrene (**10**, mp and mmp 106–107°), and an unresolved mixture of **10** and **11**: mp 95–102°; nmr (CCl_4) τ 2.18–3.78 (m, 8.0, aromatic H), 6.72 (s, 4.0, benzylic CH_2).

The white solid (mp 74–78°), isolated from the initial chromatography of the dehydrogenated photoproducts, was recrystallized from ethanol to give pure **12**: mp 80.5–81.0°; uv max (95% ethanol) 235 mμ (log ϵ 4.91), 260 (sh) (3.25), 276 (sh) (3.60), 286 (sh) (3.75), 297 (3.78), 305 (sh) (3.57), 309 (sh) (3.51), 320 (sh) (2.97), 324 (2.87); nmr τ 2.80–3.08 (m, 4.1, aromatic H), 6.50–7.53 (m, *ca.* 7.7, benzylic CH_2), 7.90–8.50 (m, *ca.* 4.1, aliphatic CH_2).

Anal. Calcd for $C_{16}H_{16}$: C, 92.26; H, 7.74. Found: C, 92.57; H, 7.98.

The structure of **13** was confirmed by its dehydrogenation, as described above, to **11**: mp 114.5–115.5° (yellow needles from ethanol) (lit.[14] mp 114–115°); uv max (95% ethanol) 224 mμ (log ϵ 4.15), 235 (4.31), 254 (sh) (5.00), 258 (5.20) (lit.[14] uv described above).

Reaction of 8,9-Benzo-12-bromo[6]metacyclophane (4b). 1. With HBr.—Gaseous hydrogen bromide was passed slowly through a solution of **4b** (0.20 g, 0.692 mmol) in dry benzene under nitrogen atmosphere. The reaction was followed by tlc (silica gel HF_{254}; eluent, 20% ether in petroleum ether, bp 60–70°). The reaction was very slow at 50° and after 2.5 hr the oil bath was raised to 80–90° and maintained at that temperature for 2.5 hr. Chromatography (silica gel; petroleum ether) of the mushy solid, obtained from the benzene solution, gave 0.15 g (59.1% yield) of **14** (mp 62–63.5°). A mixture melting point of the purified dibromo compound (mp 64.5–65.5° from ethanol) with **14** obtained from **1b** was undepressed.

2. **Conversion into 8,9-Benzo[6]metacyclophane (15).**—The reaction of **4b** (0.98 g, 3.50 mmol) with magnesium (0.24 g, 10.0 g-atoms) was carried out under nitrogen in tetrahydrofuran (20 ml, from lithium aluminum hydride) using 1,2-dibromoethane (0.66 g, 3.50 mmol) as a carrier.[15] The mixture, subsequent to formation of the Grignard reagent (>4-hr reflux), was decomposed with 5% hydrochloric acid (20 ml). The crude product was purified on alumina (150 g; eluent, petroleum ether, bp 60–70°) to give slightly impure **15** (82.7% yield) which was further purified by preparative glpc (5% SE-30 on Chromosorb W, 80–100 mesh, 4 ft × 1/4 in. column; 160°; helium flow, 60 ml/min): clear oil; uv max (95% ethanol) 236 mμ (log ϵ 3.88), 286 (2.79); nmr (CCl_4) τ 1.88–3.04 (m, 5.9, aromatic H), 6.31–10.43 (m, 13.3, aliphatic and benzylic CH_2); mass spectrum (70 eV) *m/e* 210 (molecular ion).

Anal. Calcd for $C_{16}H_{18}$: C, 91.37; H, 8.63. Found: C, 91.26; H, 8.73.

3. **Conversion into 8,9-Benzo[6]metacyclophane-12-^{2}H (16).**—The reaction was carried out essentially as described above except that special precautions to ensure dry equipment and reagents were taken. A small amount of methylmagnesium iodide in tetrahydrofuran was added to the reaction. The reaction mixture was heated at reflux for 5 hr, during which time a small amount of 1,2-dibromoethane in tetrahydrofuran was added. The Grignard reagent was decomposed with deuterium oxide (5 ml). The product was obtained in 92.5% yield (97% deuterium incorporation by nmr): uv max (95% ethanol) 236 mμ (log ϵ 3.86), 286 (2.78); nmr (CCl_4) τ CCl_4) τ 1.96–3.10 (m, 5.4, aromatic H), 6.33–10.40 (m, 12.7, benzylic and aliphatic CH_2); mass spectrum (70 eV) *m/e* 211 (molecular ion).

Anal. Calcd for $C_{16}H_{17}D$: C, 90.94; H, 9.06. Found: C, 91.21; H, 8.97.

Reaction of Pentahydrocyclohept[*b*]indene (1a) with Phenyl(trichloromethyl)mercury.—The reaction of **1a** (12.8 g, 0.0695 mol) was carried out essentially as described for **1b** (reflux temperature 41 hr). Chromatography of the product on alumina (600 g; eluent, petroleum ether, bp 60–70°) gave 10.69 g (66.5% yield, mp 89–93°) of **18** which was recrystallized with little loss of product to give pure **18**: mp 99–99.5°; white crystals; uv max (95% ethanol) 228 (sh) (log ϵ 4.90), 231 (5.07), 257 (sh) (3.42), 267 (sh) (3.62), 275 (3.77), 285 (3.80), 294 (3.64), 307 (sh) (2.75), 324 (2.49); nmr (CCl_4) τ 1.67–1.95 (m, 1.01, aromatic H), 2.27–2.83 (m, 4.0, aromatic H), 6.62–6.95 (m, 4.0, benzylic

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(13) L. F. Fieser and M. A. Peters, *J. Amer. Chem. Soc.*, **54**, 4373 (1932). A sample of the picrate of **10** was kindly supplied by Professor Louis L. Fieser.

(14) E. D. Bergman and R. Ikan, *J. Org. Chem.*, **23**, 907 (1958).

(15) H. Bamford and J. L. Simonsen, *J. Chem. Soc.*, **97**, 1904 (1910).

CH_2), 6.98–7.31 (m, 2.0, aliphatic CH_2), 8.02–8.63 (m, 6.0, aliphatic CH_2).

Anal. Calcd for $C_{15}H_{15}Cl$: C, 78.09; H, 6.55. Found: C, 78.33; H, 6.66.

Later fractions of the chromatograph, eluted with 75% petroleum ether (bp 60–70°) in benzene, gave 1.55 g (8.4% yield) of **19**, mp 46.5–48.5°. Pure **19** (mp 52–53° from ethanol) was obtained as white crystals: uv max (95% ethanol) 228 mμ (log ε 5.00), 252 (sh) (3.41), 262 (3.58), 270.5 (3.70), 281 (3.71), 290.5 (3.51), 302 (sh) (2.63), 317 (sh) (2.50), 323 (sh) (2.56); nmr (CCl_4) τ 2.12–2.80 (m, 6.0, aromatic **H**), 6.40–6.70 (t, 2.0, benzylic CH_2), 7.12–7.32 (t, 2.0, CH_2 Cl), 8.00–8.57 (m, 6.0, aliphatic CH_2).

Anal. Calcd for $C_{15}H_{16}Cl_2$: C, 67.42; H, 6.04. Found: C, 67.12; H, 5.91.

Tetramethyl 3-Chloro-1,2,4,5-benzene Tetracarboxylate. 1. From Chlorodurene.—Chlorodurene (0.20 g, 0.119 mol) was oxidzed as previously described for **3d**[3,11] The crude acid (white powder, mp 155–175°) was digested in benzene to give 0.50 g (72.8% yield) of acid melting at 248° dec. This acid (0.20 g) was esterified with excess diazomethane in ether to give, subsequent to recrystallization of the product from petroleum ether (bp 60–70°), 0.22 g (91.2% yield from the acid), mp 118–122°. The pure ester was obtained by preparative tlc (silica gel PF_{254}; eluent, 70% ether in petroleum ether) and recrystallization from petroleum ether (bp 60–70°): mp 122.6–123.1°; ir (Nujol-halocarbon oil) 1730, 1740, 1760 cm^{-1} (C═O); uv max (95% ethanol) 213 mμ (log ε 4.59), 243 (sh) (3.91), 291 (3.43), 300 (3.47); nmr ($CDCl_3$) τ 1.53 (s, 1, aromatic **H**), 6.05 (s, 6, OCH_3), 6.10 (s, 6, OCH_3).

Anal. Calcd for $C_{14}H_{13}ClO_8$: C, 48.78; H, 3.80; Cl, 10.29. Found: C, 48.74; H, 3.60; Cl, 10.39.

2. **From 18.**—The oxidation of **18** (0.25 g, 1.08 mmol) and esterification of the derived acid(s) were carried out essentially as described in 1 above. The crude ester (80 mg) was chromatographed on silica gel (30 g; eluent, petroleum ether, bp 60–70°), and the product was recrystallized from petroleum ether (bp 60–70°). The product (mp 122.6–123.4°) was identical (mixture melting point) with that described in 1 above.

Independent Synthesis of 2-(5-Chloropentyl)-3-chloronaphthalene (19). 1. 2-(5-Chloropentyl)indene (23).—The crude product, obtained by allowing 2-indanone (11.6 g, 0.80 mol) to react with the Grignard reagent [prepared from pentamethylenechloroiodide (25.0 g, 0.108 mol) and magnesium (2.7 g, 0.108 g-atom)] was chromatographed on alumina (100 g; eluent, petroleum ether, bp 60–70°), and the oil was distilled to give 1.2 g (4.6% yield) of **23** (67% pure by glpc). Pure **23** was obtained by preparative glpc (20% SE-30 on Chromosorb W, 80–100 mesh; 225°; helium flow, 60 ml/min): nmr (CCl_4) τ 2.63 (m, 5, aromatic **H**), 3.32 (broad s, 1, olefinic **H**), 6.42 (broad t, 2, CH_2Cl), 6.70 (broad s, 2, benzylic CH_2), 7.51 (broad t, 2, allylic CH_2), 8.41 (m, 6, aliphatic CH_2).

Anal. Calcd for $C_{14}H_{17}Cl$: C, 76.16; H, 7.78. Found: C, 76.32; H, 7.79.

2. **2-(5-Chloropentyl)-3-chloronaphthalene** (**19**).—The crude product obtained from **23** (0.34 mg, 0.155 mmol) and phenyl(trichloromethyl)mercury (2 equiv; see preparation of **3a**) was chromatographed on alumina (10 g; eluent, 20% benzene in petroleum ether, bp 60–70°). The product was recrystallized from petroleum ether (bp 60–70°) to give pure **19** (20 mg, 49%, mp 51–52.5°) which was identical (mixture melting point) with that obtained from **1a**.

Registry No.—*o*-(1-Cyclooctenyl)-benzonitrile, 23069-13-8; *o*-(1-cyclooctenyl)-benzylamine hydrochloride, 23115-92-6; **1b**, 23069-14-9; **3b**, 23069-15-0; **4b**, 23069-16-1; **5**, 23069-17-2; **6**, 23069-18-3; **8**, 23069-19-4; **9**, 23069-20-7; **12**, 23069-21-8; **14**, 23069-22-9; **15**, 23069-23-0; **16**, 23069-24-1; **18**, 23069-25-2; **19**, 23069-26-3; **23**, 23069-27-4; tetramethyl-3-chloro-1,2,4,5-benzene tetracarboxylate, 23069-28-5.

A Study on the Condensation of Mesityl Oxide with Acetoacetic Ester

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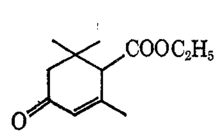
The zinc chloride catalyzed condensation of mesityl oxide with ethyl acetoacetate resulted in the formation of two structural isomers: 3,5,5-trimethyl-2-cyclohexen-1-one-4-carboxylic acid ethyl ester (**4**) and 3,5,5-trimethyl-2-cyclohexen-1-one-6-carboxylic acid ethyl ester (**5**). Isomer **5** was readily converted into isophorone by selective hydrolysis. The syntheses of two substituted β-ionones, 3-ethylenedioxy-β-ionone (**17**) and 3-ethoxy-3,4-dehydro-β-ionone (**20**), and a number of novel by-products are reported.

Merling and Welde[1] and Knoevenagel[2] reported the preparation of the cyclohexenone **4** from the condensation of acetoacetic ester with 2-isopropylidene acetoacetate. Rubinstein[3] obtained **4** in *ca.* 40% yield by condensing mesityl oxide and acetoacetic ester in the presence of boron trifluoride etherate. Since substituted intermediates which would find application for the preparation of the higher polyenes are not readily available, additional study of this interesting condensation was desirable.



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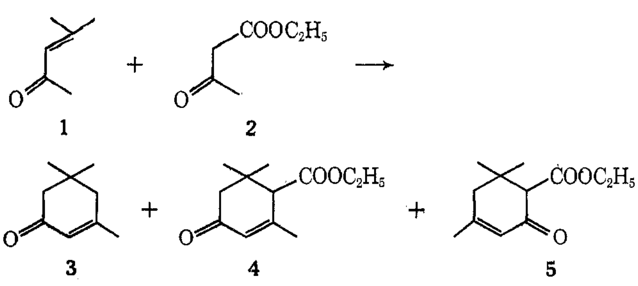
The zinc chloride catalyzed condensation of mesityl oxide (**1**) with ethyl acetoacetate (**2**) afforded 19% isophorone (**3**) and 40% a fraction distilling at 75–78° (0.2 mm). This was found to consist of two isomers, **4** and **5**, in a ratio of 4:1.



The isomeric ratio was measured by vpc, while analytical samples of **4** and **5** were prepared by column chromatography. The relative ease with which isophorone was formed by hydrolysis and decarboxylation of **5** made it convenient to prepare **4** by selectively hydrolyzing the mixture before fractionation.

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[1] G. Merling and R. Welde, *Ann.*, **366**, 141 (1909).

[2] E. Knoevenagel, *ibid.*, **297**, 185 (1897).

[3] H. Rubinstein, *J. Org. Chem.*, **27**, 3886 (1962).