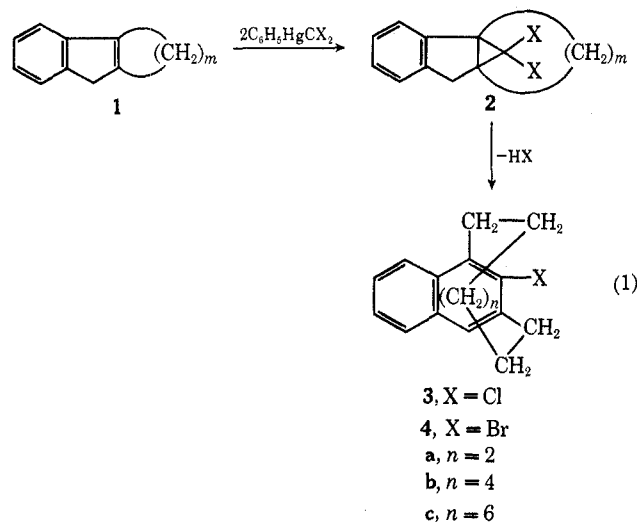


1,3-Bridged Aromatic Systems. VI.^{1,2} 12,13-Benzo-16-bromo[10]metacyclophaneWILLIAM E. PARHAM, RICHARD W. DAVENPORT,³ AND J. KENT RINEHART*School of Chemistry of the University of Minnesota, Minneapolis, Minnesota 55455*

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12,13-Benzo-10-bromo[10]metacyclophane (**4c**) has been prepared and chemical transformations of the derived Grignard reagent (**5a**) and the corresponding aryllithium reagent (**5b**) are described. The Grignard function in **5a** is quite hindered, but reacts normally with mineral acids, deuterium oxide, and benzaldehyde; however, reduction occurs with acetone-*d*₆, acetaldehyde, and presumably with other enolizable ketones. Reaction of the Grignard reagent **5a** with carbon dioxide is quite slow, and, with oxygen, transannular reactions occur. The ultraviolet spectrum of ketones **8** and **9** suggests that lack of coplanarity of carbonyl group with the aromatic ring results in considerable change in wavelength of absorption.

We have recently^{2,4} described synthesis of the 1,3-bridged naphthalenes **3a–3c** and **4a** by procedures summarized in eq 1. The lower practical limit of *m* (in 1)

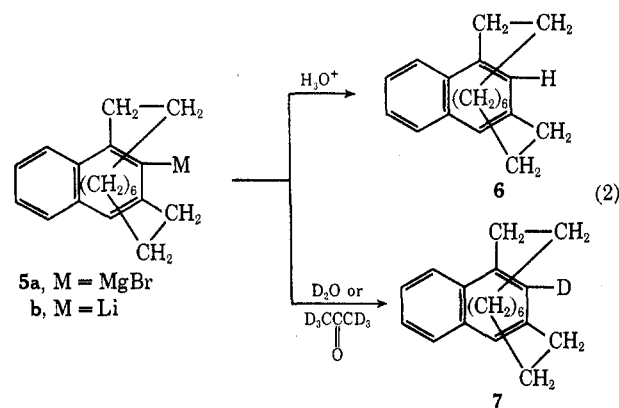


in this synthesis was found to be six, and the aromatic ring containing the methylene bridge in **3a** and **4a** was observed to be highly strained and reactive. The present work was directed to a study of the chemical behavior of the analogous 1,3-bridged aromatic system, 12,13-benzo-16-bromo[10]metacyclophane (**4c**).

Preparation of 4c.—12,13-Benzo-16-bromo[10]metacyclophane (**4c**) was prepared in 80% yield by reaction of **1** (*m* = 10) with two equivalents of potassium *t*-butoxide and bromoform, essentially as previously described for the preparation of **3c**.² The nmr spectrum of **4c**, which showed characteristic broad and complex methylene absorption at τ 6.00–10.27 and which was analogous to that reported for **3c**, established the fact that the methylene bridge is tightly packed over the face of the aromatic system to which it is attached and that the methylene bridge cannot pass over the halogen to the other face of the aromatic system (*i.e.*, the molecule is asymmetric and exists as a *dl* pair).² The very high field absorption of **4c** near τ 10.27 was expected by analogy with **3a**² (near τ 11.0) since the 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 metacyclophane **4c** reacted readily with magnesium in tetrahydrofuran to give the corresponding Grignard reagent **5a** or with *n*-butyllithium in hexane to give the corresponding aryllithium derivative **5b**. By contrast, the analog **3c** did not react⁴ with magnesium even when an entrainment agent was added.

Reactions of 5. A. With Acids.—The Grignard reagent **5a** reacted in a normal manner with dilute hydrochloric acid to give **6** in quantitative yield and with D₂O to give **7** in 74% yield (75% deuterium incorpora-



tion by nmr). When the Grignard reagent **5a** reacted with acetone-*d*₆ the metacyclophane **7** was obtained (85% yield, 70% deuterium incorporation) together with only trace amounts of other materials which could have been addition products. Similarly, the reaction of **5b** with mineral acid gave **6** in 99% yield.

The nmr spectrum of **6** is in sharp contrast to that of the bromo derivative **4c**. The rather simple spectrum for the former (see Experimental Section) shows that conformational averaging is occurring and that the bridge methylenes pass rapidly to the opposite face of the aromatic ring.

The position of deuterium in **7** was evident by its nmr spectrum, which showed almost complete disappearance of hydrogen in the aromatic region at τ 2.76. This absorption for the hydrogen at position 16 in **6** corresponds to absorption at τ 3.06 for the 2-hydrogen in 1,3-dimethylnaphthalene⁴ which is also upfield, and which similarly exhibits no *ortho* coupling as predicted for the 1,3-dialkylnaphthalene structure.

B. With Benzaldehyde and with Acetaldehyde.—It was of interest to note that reaction of **5a** with excess benzaldehyde proceeded directly to the ketone **8** (63% yield). Although oxidation of magnesium salts of alcohols by hydride transfer with aldehydes is well

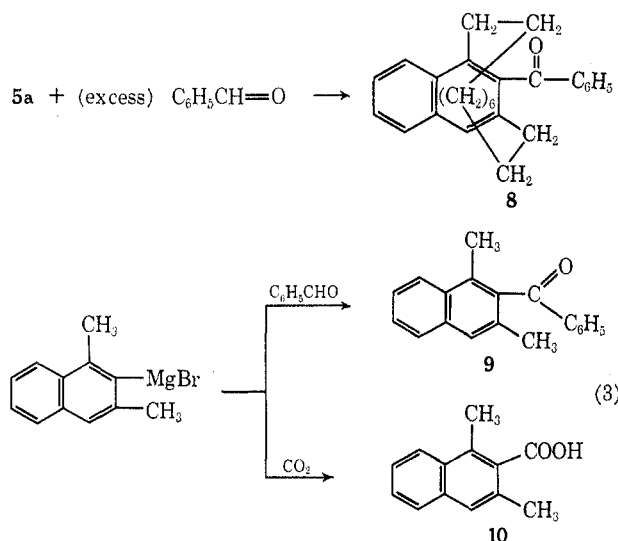
(1) Supported by the National Science Foundation, Grants GP-6169X and GP-11918.

(2) For the preceding article in this series, see W. E. Parham, D. R. Johnson, C. T. Hughes, M. K. Meilahn, and J. K. Rinehart, *J. Org. Chem.*, **35**, 1048 (1970).

(3) Taken in large part from the thesis of Richard W. Davenport, The University of Minnesota, 1969.

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

known, the ketone **8** rather than the corresponding alcohol was unexpected in view of the steric demands in this system.



Rekker and Nauta⁵ have investigated steric effects in the ultraviolet spectrum of substituted benzophenones, and have shown that *ortho* substituents prevent coplanarity of the carbonyl group with the benzene nuclei. These steric effects cause only small changes in the wavelength and somewhat larger decreases in the absorption intensity. By analogy, the uv spectrum of **8** [λ_{\max} 232 $m\mu$ (ϵ 66,100), 250 (sh) (22,600), 276 (sh) (8240) and 320 (sh) (595)] was expected to be similar to that of 2-benzoylnaphthalene⁶ [λ_{\max} 254 $m\mu$ (31,600), 285 (11,500), and 335 (2400)]. In view of the great difference noted, 2-benzoyl-1,3-dimethylnaphthalene (**9**) was prepared (eq 3) as a model. The uv spectrum of **9** (see Experimental Section) was in good agreement with that of **8**. The *ortho* substituents in both of these ketones undoubtedly prevent coplanarity of the naphthalene ring and the carbonyl groups, and unlike previous reports for related hindered benzophenones, lack of coplanarity of the carbonyl group with the aromatic ring results in considerable change in wavelength of absorption.

There was no evidence for the formation of addition products when **5a** was treated with acetaldehyde; extensive enolization occurred, as evidenced by the isolation of **6** (64% yield).

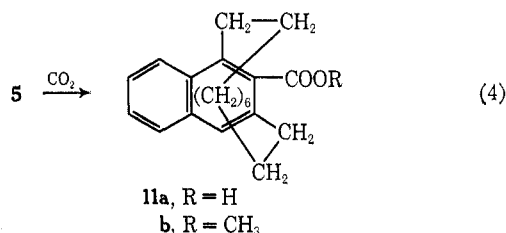
These results, coupled with those described for reaction of **5a** with acetone-*d*₆, established that functionality at C-16 in **5** could be introduced by organometallic addition reactions to carbonyl groups provided that no enolizable hydrogen was present in the carbonyl function.

C. With Carbon Dioxide.—Reaction of **5a** with crushed Dry Ice, under conditions which gave excellent yields (73%) of the model compound **10**, gave only the metacyclophane **6** (96%). While the result was surprising, the Grignard reagent is highly hindered and prefers to react with water, inevitably present on Dry Ice, rather than carbon dioxide, even though the latter is present in large excess.

(5) R. F. Rekker and W. Th. Nauta, *Recl. Trav. Chim. Pays-Bas*, **73**, 969 (1954); *Spectrochim. Acta*, **8**, 348 (1957).

(6) L. Láng, "Absorption Spectra in the Ultraviolet and Visible Region," Academic Press, New York, N. Y., 1961.

In one experiment the acid **11a** was obtained from **5a** in 48% yield, together with **6** (20%) and an unidentified

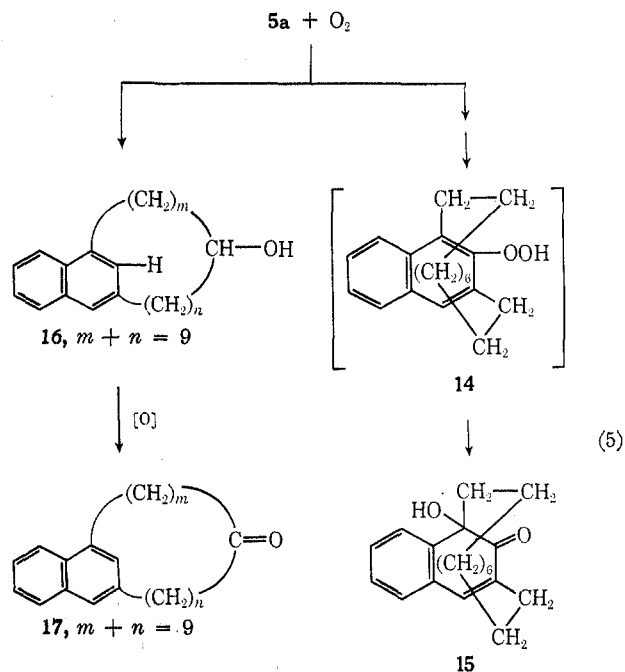


hydrocarbon (see Experimental Section), by bubbling dry carbon dioxide (generated from Dry Ice) through the Grignard reagent for 6 hr. The ester **11b** was prepared from the acid **11a**; however, preparation of the acid by this procedure could not be repeated. The major products from such reactions were subsequently shown to be **6** (~22%), **15** (~18%), and **16** (~42%). Attempts to prepare the acid **11a** from **5a** using >99% pure commercial carbon dioxide were generally unsuccessful.

Reaction of the lithium reagent **5b** with solid Dry Ice also gave **6** (89% yield); however, reaction of **5b** with carbon dioxide generated from Dry Ice gave the acid **11a** in 18% yield, or with high purity commercial carbon dioxide the acid **11a** in 38% yield. These results were reproducible.

D. With Oxygen.—In a number of reactions of the type described in section C, the Grignard reagent was completely reacted but only small quantities of **6** or acid **11a** were formed. It was concluded that the Grignard reagent **5a** was reacting selectively with small concentrations of oxygen present as an impurity in the carbon dioxide. This conclusion was confirmed by a study of the reaction of **5a** with oxygen.

Oxygen was bubbled through a solution of the Grignard reagent in tetrahydrofuran for 2 hr (tlc analysis indicated the reaction was complete within 30 min). The products isolated and characterized were the metacyclophane **6** (42%), the α -hydroxy ketone **15** (16%), and a mixture of isomeric alcohols **16** (34%) formed by transannular reaction (eq 5). These results compare



with yield of 22%, 18%, and 42% **6**, **15**, and **16**, respectively, when the Grignard reagent **5a** was treated with carbon dioxide generated from Dry Ice.

The structure of the hydroxy ketone **15** was not established unequivocally, but was assigned on the basis of its composition; comparison of its ultraviolet spectrum with that of **18**;⁷ its infrared spectrum which showed strongly hydrogen bonded OH at 3520 cm⁻¹



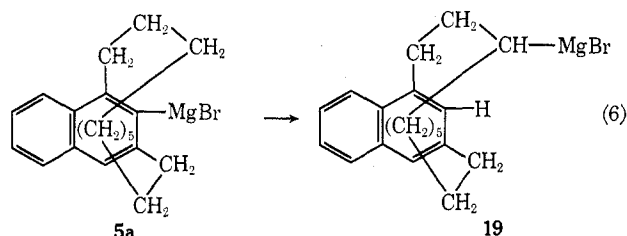
characteristic of α -hydroxy ketones;⁸ and its nmr spectrum.⁹ The hydroxy ketone **15** is assumed to be derived from the expected hydroperoxide **14** (eq 5) and, while arylhydroperoxides do not normally lead to such products, the effective rearrangement of **14** to **15** is logical for such a strained system.¹⁰

The mixture of alcohols **16** was obtained as an oil that was partially crystallized to give one pure isomer of **16** (11% overall yield from **5a**). The ir and nmr spectra of the mixture of alcohols were essentially identical with those of the pure isomer, which suggested that the mixture contained only isomers of **16**. The alcohols could not be resolved by tlc; however, oxidation of the mixture with Jones reagent gave a mixture of ketones in 79% yield which showed four spots on tlc. The ir and nmr spectra of this mixture suggested that only isomers of the ketone **17** (eq 5) were present. The principal isomeric ketone was isolated in 26% yield from the isomeric alcohols and in 89% yield from the pure isomer of **16**. From these data it was concluded that the alcohols **16** consisted of at least four isomers (the OH groups at different positions on the methylene bridge) one of which comprised a minimum of 55% of the mixture.

The uv spectrum of the major ketone **17** derived from the major alcohol **16** showed typical naphthalene absorption similar to the metacyclophane **6**. The nmr spectrum of this ketone showed for the methylene protons τ 6.42–6.68 (2 protons), 6.88–7.38 (4 protons), and 7.88–9.55 (12 protons). Using the data of Tiers¹¹ and standard chemical shifts it was concluded that only when the carbonyl group is at C₃ or C₈ (C₁, C₂, C₉, and C₁₀ being eliminated by the nmr spectrum of the major alcohol **16**) on the chain will there be six protons absorbing in the region of τ 6.4–7.6 as experimentally observed. Thus, it was concluded that the major transannular alcohol derived by reaction of **5a** with oxygen has the hydroxyl function at either C₃ or C₈ of the meth-

ylene chain. This conclusion is consistent with examination of models which show hydrogen at C-3 and C-8 in close proximity to functionality at C-16.

The mechanism of the transannular reaction of **5a** leading to **16** is not known. It does not appear that the Grignard reagent undergoes appreciable exchange in the absence of oxygen as shown in **5a** \rightarrow **19** (eq 6), since the Grignard reagent behaves normally in its reactions with acids and acetone-*d*₆. The details of the mechanism are under further examination and will be reported subsequently.



Experimental Section

Glpc separations were performed on a Beckman Model GC-4 or Varian-Aerograph Model 90-P instrument. All ultraviolet spectra were determined in 95% ethanol. Petroleum ether used, unless otherwise specified, had bp 60–70°.

12,13-Benzo-16-bromo[10]metacyclophane (4).—Decahydro-cyclododec[b]indene (0.0532 mol) was treated with bromoform (0.106 mol) and potassium *t*-butoxide (0.256 mol) in anhydrous benzene (200 ml, 20 min at 0°) by a procedure similar to that described^{2,4} for related syntheses with chloroform. Chromatography (alumina, petroleum ether as eluent) of the oil gave 0.0426 mol (80.1% yield) of **4c** (mp 57–63.5°) which was purified (from ethanol) to give pure **4c**: mp 63–64.5°; uv max 232 m μ (sh) (ϵ 68,800), 237 (77,300), 268 (sh) (3960), 278 (5280), 287 (5650), 298 (sh) (3960), and 320 (339); nmr (CCl₄) τ 1.90–2.76 (m, 4.8, aromatic H) and 6.00–10.27 (very complex, 20.2, CH₂); mass spectrum *m/e* 344 (calcd 344).

Anal. Calcd for C₂₀H₂₂Br: C, 69.56; H, 7.30. Found: C, 69.56; H, 7.33.

12,13-Benzo[10]metacyclophane (6). 1. From **5a**.—A mixture of **4c** (0.273 g, 0.792 mol) and magnesium (0.108 g, 0.00444 g-atom) was heated at the reflux temperature under nitrogen for 4 hr after which time glpc analysis (6 ft, 1/8 in., 20% SE-30 on AW-DMCS, 200°) showed that all **4c** was consumed. The cooled mixture was hydrolyzed with aqueous hydrochloric acid (10%, 10 ml), the resulting mixture was extracted with ether, and the ether was dried (MgSO₄). The oil (0.202 g, 96% yield) obtained by concentration of the ether was shown to be ~100% pure **6** by glpc analysis using *n*-docosane as an internal standard. Pure **6** was obtained as a solid, mp 38–39°, by recrystallization of the oil from petroleum ether, bp 30–60°, at –78°, and showed uv max 225 m μ (sh) (ϵ 60,600), 231 (85,200), 278 (sh) (5290), 285 (5650), 293 (sh) (4440), and 322 (363); nmr (CCl₄) τ 1.96–2.72 (m, 5.0, aromatic H), 2.76 (d, 0.9, *J* = 2 Hz, H at C₁₆), 6.91 (t, 2.0, *J* = 7.0 Hz, benzylic CH₂), 7.20 (t, 1.9, *J* = 7.0 Hz, benzylic CH₂), and 7.97–9.33 (m, 16.2, CH₂); mass spectrum *m/e* 266 (calcd 266).

Anal. Calcd for C₂₀H₂₆: C, 90.16; H, 9.84. Found: C, 90.29; H, 9.96.

2. From **5b**.—A solution of **4c** (0.565 g, 1.64 mmol) in anhydrous hexane (10 ml) was added over a period of 10 min to a solution of *n*-butyllithium (3.3 ml of 1.5 *m* *n*-butyllithium in hexane, 4.9 mmol, threefold excess) in anhydrous hexane (5 ml) maintained under a nitrogen atmosphere. The mixture was heated at reflux for 5.5 hr when glpc (see 1, above) showed complete absence of **4c**. The mixture was treated as in 1, above, to give 0.396 g (91%, 98% corrected for amount used for analysis) of pure **6**.

12,13-Benzo[10]metacyclophane-16-d (7). 1. From **4c**.—The procedure was essential as described for **6** from **4c** except that 3 drops of 1,2-dibromoethane was added as a carrier and an 8-hr reflux period was required for complete reaction of **4c**. The mixture was treated with deuterium oxide (1 ml) stirred over-

(7) R. D. Campbell and N. H. Cromwell, *J. Amer. Chem. Soc.*, **79**, 3456 (1957).

(8) L. Joris and P. von R. Schleyer, *ibid.*, **90**, 4599 (1968).

(9) The nmr spectrum is summarized in the Experimental Section. The allylic protons in **15** are nonequivalent owing to the asymmetric center at C₅; one of the allylic protons is deshielded by the adjacent carbonyl group; consequently, the allylic protons have widely different chemical shifts.

(10) The conversion of one aromatic ring carbon atom from sp² to sp³ relieves strain. The enhanced reactivity of strained systems of this type toward electrophilic reagents has already been noted and discussed in ref 2. Rather obvious reaction paths from the conversion of **14** to **15** can be formulated.

(11) G. V. D. Tiers, "Characteristic Nuclear Magnetic Resonance (NMR) 'Shielding Values' (Spectral Positions) for Hydrogen in Organic Structures," Minnesota Mining and Manufacturing Company, St. Paul, Minnesota, 1958. This assignment is tentative since the data of Tiers are gathered from saturated acyclic systems and may not be applicable to **17**. For example, this treatment ignores possible transannular shielding or deshielding effects which possibly could be important in this system.

night and then treated with aqueous acid and processed as above. The oil was chromatographed on alumina (Woelm neutral, activity I, 20 g, petroleum ether was used as eluent). The cyclophane **7** was obtained pure (by glpc) as an oil (74% yield) that was recrystallized to mp 38.5–39.5°. The infrared spectrum of **7** was essentially identical with that of **6** but absorption at 772 cm^{-1} was considerably less intense. Pure **7** showed uv max 225 $\text{m}\mu$ (sh) (ϵ 61,700), 231 (93,400), 276 (sh) (5410), 286 (5630), 292 (sh) (4720), and 323 (412); nmr (CCl_4) τ 1.96–2.79 (m, 5.25, indicating 75% deuterium incorporation, aromatic H), 6.91 (t, 2.0, $J = 7.0$ Hz, benzylic CH_2), 7.20 (t, 2.0, $J = 7.0$ Hz, benzylic CH_2), and 7.97–9.33 (m, 17.3, CH_2).

2. From Acetone- d_6 .—The procedure was essentially the same as that described above. Acetone- d_6 (1 g, Stohler Isotope Chemical Co.) was added and the mixture was stirred at room temperature overnight prior to processing. The resulting oil was purified by preparative tlc (alumina PF 254, petroleum ether). Two bands (R_f 0.8 and 0.0) were separated and eluted with chloroform. The deuterated cyclophane **7** ($R_f = 0.8$) solidified (mp 36–38.5°, 84.5% yield) and was further purified by recrystallization (petroleum ether, bp 30–60°, at -78°) to mp 38.5–39.5° and was identical with **7** prepared above, mass spectrum analyses indicated 70% deuterium incorporation.

The other band (R_f 0.0) was shown by tlc (silica gel HF 254, benzene) to contain at least six components and was not further processed.

12,13-Benzo-16-benzoyl[10]metacyclophane (8).—A mixture containing **4c** (0.620 g, 1.80 mmol), magnesium (0.120 g, 0.00494 g-atom), and 1,2-dibromoethane (4 drops) in tetrahydrofuran was heated at reflux for 6 hr [until **4c** completely reacted (by tlc)] and freshly distilled benzaldehyde (0.912 g, 8.6 mmol) was added all at once. The resulting stirred mixture was allowed to cool to room temperature and was then stirred overnight and finally for 2 hr at the reflux temperature. The dry oil obtained by processing the mixture in a conventional manner was chromatographed on alumina (40 g, petroleum ether). There was obtained cyclophane **6** (25.2% yield) and the ketone **8** as an oil (0.422 g, 64% yield) which melted at 78.5–84° after crystallization from ethanol-water. The solid ketone was rechromatographed and the product was recrystallized from acetone-water to give pure **8**: mp 85.5–88.5°; uv max 232 $\text{m}\mu$ (ϵ 66,100), 250 (sh) (22600), 276 (sh) (8240), and 320 (sh) (595); ir (KBr) 1665 cm^{-1} (C=O), 743 and 698 (*ortho* and monosubstituted benzene); ir (CCl_4) 1678 cm^{-1} (C=O); nmr (CCl_4) τ 1.88–3.00 (m, 9.9, aromatic H) and 6.38–10.47 (complex, 20.1, CH_2).

Anal. Calcd for $\text{C}_{27}\text{H}_{20}\text{O}$: C, 87.52; H, 8.16. Found: C, 87.43; H, 8.18.

2-Bromo-1,3-dimethylnaphthalene was prepared from 2,3-dimethylindene⁴ essentially as described for **4c**. The crude material was chromatographed on alumina (petroleum ether) and was obtained as a liquid: bp 92–93° (0.10 mm); 75% yield; n_D^{25} 1.6494; uv max 232 $\text{m}\mu$ ($\log \epsilon$ 4.93), 245 (sh) (3.44), 266 (sh) (3.60), 275 (3.73), 285 (3.76), 296 (3.58), 319 (sh) (2.37), 324 (sh) (2.37); nmr (CCl_4) τ 2.18–2.93 (m, 5, aromatic H), 7.42 (s, 3, CH_3), 7.61 (s, 3, CH_3).

Anal. Calcd for $\text{C}_{12}\text{H}_{11}\text{Br}$: C, 61.30; H, 4.72, Br, 33.99. Found: C, 61.52; H, 4.75; Br, 33.78.

2-Benzoyl-1,3-dimethylnaphthalene (9) was prepared from the Grignard reagent obtained from 2-bromo-1,3-dimethylnaphthalene and benzaldehyde by a procedure similar to that described above for **8**. The crude ketone was obtained by chromatography as a yellow oil (13.2% yield) that solidified, mp 101.5–106.5° (one spot by tlc on alumina HF 254, petroleum ether, R_f 0.15). Recrystallization of the crude ketone from ethanol gave pure **9**: mp 109.5–110.5°; uv max 227 $\text{m}\mu$ (ϵ 74,700), 250 (21,000), 280 (sh) (7800), 292 (sh) (5380), and 320 (sh) (742); ir (CCl_4) 1774 cm^{-1} (C=O); nmr (CDCl_3) τ 1.67–2.87 (m, 10.3, aromatic H), 7.53 (s, 2.9, CH_3), and 7.73 (s, 2.8, CH_3).

Anal. Calcd for $\text{C}_{19}\text{H}_{16}\text{O}$: C, 87.68; H, 6.17. Found: C, 87.86; H, 6.05.

1,3-Dimethyl-2-naphthoic Acid (10).—The Grignard reagent was prepared under a nitrogen atmosphere from 2-bromo-1,3-dimethylnaphthalene (10.6 g, 0.045 mol) in anhydrous ether, magnesium (1.20 g, 0.0494 g-atom) and 1,2-dibromoethane (5 drops). The reagent was added to a slurry of Dry Ice in ether. The resulting mixture was treated with 20% sulfuric acid (20 ml), and the resulting mixture was extracted with ether. The crude acid **10** (7.23 g, 72.6% yield) was obtained from the dry ether (MgSO_4) extract. The pure acid (5.62 g, 62.3% yield, mp 147.5–148.5° from toluene), showed uv max 227 $\text{m}\mu$ (ϵ 66,400),

274 (sh) (5230), 280 (5610), 290 (sh) (4250), 307 (sh) (697), 315 (sh) (557), and 321 (583); ir (Nujol) 3250–2200 cm^{-1} (OH) and 1700 (C=O); nmr (CDCl_3) τ -0.20 (broad s, 1.2, -OH), 1.83–2.81 (m, 5.1, aromatic H), 7.23 (s, 2.8, 1 CH_3) and 7.43 (s, 3.0, 3- CH_3).

Anal. Calcd for $\text{C}_{18}\text{H}_{12}\text{O}_2$: C, 77.98; H, 6.04. Found: C, 77.98; H, 6.15.

Methyl 1,3-dimethyl-2-naphthoate (from **10** and diazomethane) showed mp 51–52° (from methanol-water); uv max 227 $\text{m}\mu$ (ϵ 69,600), 272 (5020), 281 (5540), 293 (sh) (4060), and 323 (753); ir (Nujol) 1732 cm^{-1} (C=O).

Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_2$: C, 78.48; H, 6.59. Found: C, 78.26; H, 6.81.

12,13-Benzo-16-carboxy[10]metacyclophane (11a).—The Grignard reagent was prepared as described for the preparation of **6** [1,2-dibromoethane was used as a carrier and about 6 hr was generally required for complete conversion (glpc) of **4c**]. The Grignard reagent was treated as follows.

(a) **With Crushed Dry Ice.**—Such reaction gave only the reduced cyclophane **6** (~96% yield).

(b) **With Carbon Dioxide Generated from Dry Ice.**—In these experiments the carbon dioxide was dried by passing successively through columns (2 ft \times 1.5 in.) of calcium chloride Tel-Tale $\text{\textcircled{R}}$ (a silica gel desiccant, Davison Chemical Co.) and molecular sieves (Linde 13X) and then bubbled through the Grignard mixture for 6 hr. Chromatography of the mixture of products obtained by conventional means on silica gel using petroleum ether-acetone as eluent gave (1) reduced metacyclophane **6** (0.092 g, 19.8% yield), (2) a hydrocarbon (0.07 g crude, mp 113–140°, petroleum ether-2% acetone), and (3) the acid **11a** (0.26 g, 48% yield, mp 213–214°, petroleum ether-10% acetone). Attempts to repeat this experiment failed.

The unknown hydrocarbon showed mp 147–149° (from acetone); uv max 231 $\text{m}\mu$ ($\epsilon_{\text{cm}}^{1\%}$ 2620), 237 (sh) (1550), 276 (sh) (173), 287 (205), 298 (sh) (153), and 322 (12.8); nmr (CCl_4) τ 2.00–3.00 (m, aromatic H), and 6.07–9.76 (complex, CH_2), $\text{CH}_2/\text{aromatic} = 3.96$; mass spectrum m/e (rel intensity) 264 (16), 282 (100), 566 (1.8).

Anal. Found: C, 89.98; H, 9.90.

Acid **11a** showed mp 213.5–215.5° (from ethanol-water); uv max 234 $\text{m}\mu$ (ϵ 81,300), 286 (5210), and 325 (511); ir (KBr) 3600–2150 cm^{-1} (OH), 1678 (C=O), 1455 and 1440 (CH_2), 1286 and 1262 (aryl C=O stretch), and 750 (*ortho* substituted benzene); nmr (CDCl_3) τ 0.47 (broad s, 0.9-COOH), 1.67–2.67 (m, 5.0, aromatic H) and 6.06–10.50 (very complex, 21.0 CH_2).

Anal. Calcd for $\text{C}_{21}\text{H}_{20}\text{O}_2$: C, 81.25; H, 8.44. Found: C, 81.43; H, 8.55.

The methyl ester **11b** (from **11a** and diazomethane) showed mp 112.0–113.0° (from methanol-water); uv max 233 $\text{m}\mu$ (ϵ 67,300), 283 (5210), and 325 (635); ir (KBr) 1730 cm^{-1} (C=O).

Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{O}_2$: C, 81.44; H, 8.70. Found: C, 81.49; H, 8.99.

(c) **Isolation of 15 and 16.**—An experiment using **4c** (2.00 g, 5.80 mmol) was conducted essentially as described in (b), above, except the carbon dioxide was pretreated through columns of only calcium chloride and molecular sieves (Linde 4A). The crude product obtained subsequent to neutralization with sulfuric acid and extraction with chloroform, was chromatographed over silica gel (50 g). Elution of the column with petroleum ether gave **6** (0.334 g, 21.6% yield). The next fraction (0.112 g), eluted with petroleum ether-2% acetone, contained at least four components (tlc) and was not processed further.

The α -hydroxy ketone **15** (0.303 g, 17.5%, eluted with petroleum ether-4% acetone) showed one spot (R_f 0.50) on tlc (silica gel HF 254, petroleum ether-10% acetone-1% acetic acid) and showed the following: mp 143–144.5° (from ethanol-water); uv max 242 $\text{m}\mu$ (ϵ 15,900) and 317 (9500); ir (CCl_4) 3520 cm^{-1} (OH), 1671 cm^{-1} (C=O); nmr (CDCl_3) τ 2.27–3.07 (m, 5.2, aromatic H and C=C-H), 6.23 (s, 0.9, OH), 6.80–7.30 (m, 1.1, allylic H), 7.63–9.67 (m, 18.8, allylic H and CH_2); mass spectrum m/e 298 (calcd mol wt 298).

Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{O}_2$: C, 80.50; H, 8.78. Found: C, 80.44; H, 8.96.

The alcohols **16** (0.690 g, 42.4% yield, eluted with petroleum ether-6% acetone) showed only one spot on tlc (silica gel HF 254, petroleum ether (bp 60–70°)-20% acetone-1% acetic acid, $R_f = 0.35$). The isomeric alcohols **16** were dissolved in petroleum ether and allowed to stand at -20° for several days. The principal isomeric alcohol **16** crystallized and showed mp 114–115°; uv max 225 $\text{m}\mu$ (sh) (ϵ 64,600), 231 (96,100), 278 (sh) (5570),

285 (4890), 292 (sh) (4820), 308 (sh) (751), and 322 (455); ir (Nujol) 3415 cm^{-1} (broad OH) and 735 (*ortho* substituted benzene); nmr (CDCl_3) τ 1.93–2.96 (m, 5.8, aromatic H), 6.36–7.43 (m, 4.9, benzylic CH_2 and $-\text{CHOH}$), and 7.77–9.53 (m, 15.3, CH_2 and OH); mass spectrum m/e 282 (calcd mol wt 282).

Anal. Calcd for $\text{C}_{20}\text{H}_{26}\text{O}$: C, 85.06; H, 9.28. Found: C, 85.03; H, 9.37.

The spectra of the crude alcohol and the isolated pure isomeric alcohol were essentially identical and suggested that the former contained only isomers of 16.

The hydroxy ketone 15, the alcohols 16 and acid 11a (~10%) were obtained when commercial carbon dioxide (99.8%, J. T. Baker Chemical Co.) was employed.

Preferred Procedure for 11a.—The acid 11a (mp 202–208°, 38% yield) was prepared reproducibly from the aryl lithium derivative prepared from 4c (1.00 g, 2.90 mmol), *n*-butyllithium (10 ml, 1.5 *M* in hexane, ~15 mmol) in anhydrous hexane (50 ml) at reflux (~6 hr until tlc confirmed the absence of 4c). The solution was cooled to -78° and carbon dioxide (99.8%, J. T. Baker Chemical Co.) was passed over the surface for 3.5 hr. The mixture was allowed to warm to room temperature and carbon dioxide was passed through the solution for 41 hr. The acid 11a is not soluble in alkali. Water was added to the mixture which was then extracted with chloroform (white solid that separated was kept in solution by addition of more chloroform). The combined organic layer was washed with water. The oil obtained from the dried (MgSO_4) extract partially solidified. The mixture was titrated with cold (0°) petroleum ether to give acid 11a (0.340 g, 38% yield; mp 202–208°, mp 213.5–214° from ethanol-water).

Reactions of 5a with Oxygen.—The Grignard reagent 5a, prepared from 4c (0.500 g, 1.45 mmol) as described above, in tetrahydrofuran (50 ml) was cooled to room temperature and oxygen (Air Reduction Co.), dried by passing through a column of CaCl_2 , was bubbled through the mixture for 2 hr. Analysis (tlc, silica gel HF 254, petroleum ether–10% acetone) showed alcohol 16 (R_f 0.16), hydroxy ketone 15 (R_f 0.44), and reduced cyclophane (R_f 0.78). The crude mixture obtained subsequent to hydrolysis (H_2SO_4 , 15%, 10 ml, 20 min), extraction (ether, 15 ml), washing (H_2O), and drying (MgSO_4) was purified by preparative tlc (silica gel PF 254, petroleum ether–10% acetone). The products (yields) were reduced cyclophane 6 (~42% yield), unchanged 4c (~18%), unidentified mixture (0.04 g), hydroxyketone 15 (0.06 g, 15% yield; mp 125–131°, mp 142–143° from ethanol-water), and alcohols 16 (0.130 g, 34.4%).

In a duplicate experiment the yield of 15 was 9% and the yield of 16 was 37%.

Oxidation of 16. (a)—The pure isomer of 16 (0.180 g, 0.639 mmol, mp 111.5–113.0°) in reagent grade acetone was oxidized with Jones reagent¹² (0.7 ml of 1 *M* solution prepared from 35 g of chromic acid, 250 ml of water and 30.5 ml of concentrated sulfuric acid) added dropwise over a period of 5 min. Analysis of the crude white ketone (mp 122–125°, 0.160 g, 89.5% yield) by tlc (silica gel HF 254, petroleum ether–5% ethyl acetate) indicated that a single product (R_f 0.38) was present. The pure ketone showed mp 125–126° (from ethanol); uv max 230 $\text{m}\mu$ (ϵ 77,800), 277 (sh) (5590), 282 (6000), 291 (sh) (4840), 308 (sh) (698) and 323 (652); ir (Nujol) 1708 cm^{-1} ($\text{C}=\text{O}$); nmr (CDCl_3) τ 1.77–3.15 (m, 5.9, aromatic H) and 6.42–9.55 (m, 18.1, CH_2); the methylene protons (τ 6.42–9.55) consisted of a series of multiplets with principal absorption as follows, 6.42–6.68 (1.8), 6.88–7.38 (3.7), and 7.88–9.55 (11.7); mass spectrum m/e 280 (calcd mol wt 280).

Anal. Calcd for $\text{C}_{20}\text{H}_{24}\text{O}$: C, 85.67; H, 8.63. Found: C, 85.82; H, 8.76.

(b)—The oxidation was repeated as described above but using the mixture of isomeric alcohols of 16. The ir spectrum of the product was essentially identical with the product described in (a), above; the nmr spectrum was quite similar with the exception of a multiplet at τ 6.68–6.88 and a multiplet at 7.90 that are absent in the spectrum of the ketone described above. Recrystallization of this mixture (petroleum ether, bp 30–68° at -20°) gave the principal product (mp 122–123.5°, mixture melting point with ketone in (a), mp 125–126°, was 122–125°). The mother liquor gave a mixture of ketone (mp 64–82°); analysis by tlc (silica gel HF 254, petroleum ether–5% ethyl acetate) suggested that four isomeric ketones were formed by oxidation of 16.

Registry No.—4c, 25097-45-4; 6, 25097-46-5; 7, 25097-47-6; 8, 25097-48-7; 9, 25097-49-8; 10, 25097-50-1; 11a, 25097-51-2; 11b, 25097-52-3; 15, 25097-53-4; bromo-1,3-dimethylnaphthalene, 25097-54-5; methyl 1,3-dimethyl-2-naphthoate, 25097-55-6.

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Strained-Ring Systems. IX.^{1a} The Preparation of Some 5-Substituted Bicyclo[3.1.0]hexane-1-carboxylic Acids

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Several 5-substituted bicyclo[3.1.0]hexane-1-carboxylic acids have been prepared and characterized. Dimethyl bicyclo[3.1.0]hexane-1,5-dicarboxylate (3) was prepared by a 1,3 elimination of hydrogen bromide from dimethyl 1-bromocyclohexane-1,3-dicarboxylate (8) in 85% yield. From bicyclic diester 3, by standard reaction sequences, bicyclo[3.1.0]hexane-1,5-dicarboxylic acid (9) and 5-carbomethoxy- (10), 5-bromo- (12), 5-carboxamido- (14), and 5-cyanobicyclo[3.1.0]hexane-1-carboxylic acid (16) were prepared. Bicyclo[3.1.0]hexane-1-carboxylic acid (19) was prepared by a 1,3 elimination of the elements of *p*-toluenesulfonic acid from methyl 3-tosyloxy-cyclohexane-1-carboxylate (17) and subsequent hydrolysis.

Useful methods have been reported for the preparation of bicyclic, bridgehead substituted carboxylic acids.^{2–5} This paper presents the syntheses of certain 5-substituted bicyclo[3.1.0]hexane-1-carboxylic acids

which were required for pK_a studies as well as solvolytic studies on derivatives of the 1-carbinols.

The key to the synthesis of the bicyclohexanecarboxylic acids was the preparation of dimethyl bicyclo[3.1.0]hexane-1,5-dicarboxylate (3). Prinzbach, *et al.*,⁶ have reported the synthesis of 3 by a photochemical route. We employed some slight modifications to Prinzbach's procedure to allow preparation of larger quantities of material. Irradiation of a sample of di-

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