Synthesis of Some Brominated Cage Molecules as Possible Precursors to Pentaprismane

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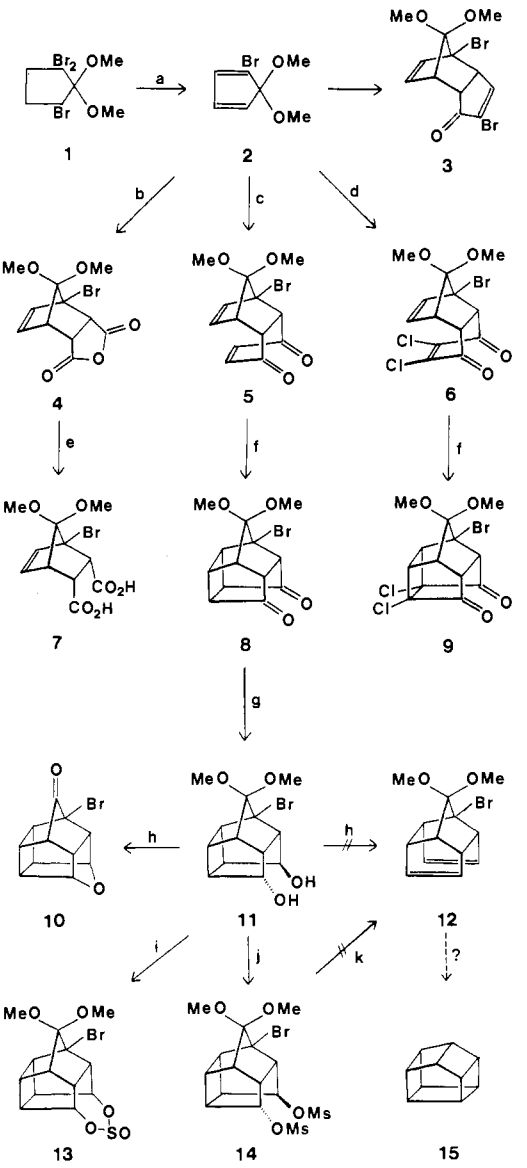
The bromo compounds 3–11, 13, and 14 have been prepared and characterized by analysis, IR and NMR.

Eaton and co-workers (*1*) have recently described a synthesis of pentaprismane (**15**) via homopentaprismanone, obtained by photocyclization and hydrolysis of a diene ketal identical with **12** except that it lacks the bromine. Consequently, the synthesis of this last compound would furnish a very simple alternative route to pentaprismane. Our attempts to thus obtain pentaprismane foundered on the steps **11** or **14** → **12** but afforded a variety of bromoketals shown in Scheme I, some of which may prove to be useful intermediates in the synthesis of other cage or half-cage compounds.

The preparation of the bromocyclopentadienone ketal **2** by bromination of 1,1-dimethoxycyclopentane to **1**, followed by dehydrobromination, was described by Eaton and Hudson in a preliminary communication without experimental details (*2*). If left in solution, the diene **2** dimerizes, and the product **3** (from partial hydrolysis during workup) is obtained. However, the diene **2** can be intercepted by strong dieneophiles such as maleic anhydride, benzoquinone, or 2,3-dichloro-*p*-benzoquinone to give the adducts **4–6**, respectively. (Adduct **5** was reported by Eaton and Hudson (*2*)). The endo–endo stereochemistry of compounds **5** and **6** was proved by their photocyclization to the cage products **6** and **9**. The anhydride **4** probably has similar stereochemistry; it was hydrolyzed by dilute potassium hydroxide to the dicarboxylic acid **7**.

Reduction of the diketone **8** with sodium borohydride gave the endo–endo diol **11**, the stereochemistry being established by formation of the cyclic sulfite **13** (cf. ref *3*). The diol reacted with *p*-toluenesulfonic acid in refluxing xylene to give the keto ether **10** (cf. ref *4*) and with methanesulfonyl chloride in pyridine to give the dimesylate **14**. Attempts to convert the dimesylate **14** to the diene **12** by treatment with iodide under conditions favorable in other reactions (*3*, *5*) gave intractable tars.

Scheme I



Experimental Section

Chemical reagents were of commercial grade and were used without prior purification unless otherwise stated. Melting points were taken in capillary tubes by using a Gallenkamp apparatus and are uncorrected. NMR spectra were recorded on a Varian T-60A spectrometer in $CDCl_3$ containing tetramethylsilane (Me_4Si) as internal standard unless otherwise stated. IR spectra were recorded in KBr pellets on a Perkin-Elmer 297 spectrophotometer. Mass spectra were recorded at 70 eV on a LKB 9000 or a Hewlett-Packard mass spectrometer. Elemental analyses, performed by Dr. C. Daessle of Montreal and Galbraith Laboratories, Inc., Knoxville, TN, were in agreement with theoretical values and have been submitted for review. (See paragraph at end of text regarding supplementary material.) Petroleum ether refers to the fraction with bp 30–60 °C. *tert*-Butyl alcohol was used without purification (Fisher spectrograde).

***1,1,3-Tribromo-2,2-dimethoxycyclopentane* (1).** 1,1-Dimethoxycyclopentane (*6*) (6.5 g, 0.05 mol) in methanol (20 mL) was added dropwise to a cooled, stirred solution of technical pyridinium bromide perbromide (Aldrich, technical 80%) (66 g, 0.165 mol) in methanol (80 mL). The solution was stirred at room temperature for 14–18 h, and then the product was extracted with petroleum ether (8 × 100 mL). The combined extracts were evaporated in vacuo to give a dense colorless oil (13.7 g, 74%) of the desired tribromo derivative **1**: NMR (CCl_4) δ 4.0–4.7 (m, 1 H, CHBr), 3.80 (s, 3 H, OCH_3), 3.65 (s, 3 H, OCH_3), 2.2–2.9 (m, 4 H, CH_2CH_2); IR (neat) 2920 (m), 2967 (w), 1448 (m), 1320 (s), 1295 (m), 1055 (s) cm^{-1}.

***2,4-Dibromodicyclopentadiene-1,8-dione 8,8-Dimethylacetal* (3).** To a cooled solution of potassium *tert*-butoxide (36 g, 0.30 mol) in *tert*-butyl alcohol (100 mL), the temperature being kept below 20 °C, was added dropwise the tribromo derivative **1** (27.4 g, 74 mmol). The mixture was stirred for 4–6 h and then poured into ice water (100 g). The product was extracted with petroleum ether (3 × 400 mL), and the combined extracts were washed with water (3 × 200 mL) and dried

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(Na_2SO_4). After standing at room temperature for 24 h, the solution was concentrated in vacuo to give **3** as colorless needles, mp 165–167 °C (15.0 g). Recrystallization from ethyl ether raised the mp to 170–171 °C: NMR ($CDCl_3$) δ 7.53 (d, $J \simeq 3$ Hz, 1 H), 5.80 (d, $J \simeq 2$ Hz, 2 H), 3.6–3.8 (m, 1 H), 3.45 (s, 3 H, OCH_3), 3.35 (s, 3 H, OCH_3), 3.0–3.3 (m, 2 H).

***1-Bromo-7,7-dimethoxybicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic Anhydride* (4).** The petroleum ether solution of **2** (from 27.4 g of **1**) was added to a solution of maleic anhydride (5.0 g, 50 mmol) in ethyl acetate (100 mL), and the mixture was stirred at room temperature for 24 h. After removal of solvent the crude product was triturated with ethyl ether to give the anhydride **4** (9.5 g), mp 90–95 °C. Recrystallization from ethyl ether–petroleum ether gave tiny colorless needles (8.9 g, 39% from **1**): mp 110–111 °C; IR (KBr) 3070 (w), 2980 (w), 2940 (w), 2820 (w), 1860 (m), 1780 (s), 1730 (m), 1240 (s), 1100 (s), 920 (s), 785 (m) cm^{-1}; NMR ($CDCl_3$) δ 6.37 (d, $J \simeq 2.5$ Hz, CH=CH), 3.8–3.9 (m, 2 H), 3.53 (s, 4 H, OCH_3 and H_4), 3.40 (s, 3 H, OCH_3); mass spectrum, *m/e* (relative intensity) 302, 304 (molecular ion, with respective intensities close to 1:1), 231 (88), 229 (90), 223 (55), 151 (46), 77 (82), 59 (100).

***1-Bromo-7,7-dimethoxybicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic Acid* (7).** A mixture of the anhydride **4** (3.03 g, 10 mmol) in water (140 mL) containing potassium hydroxide (3.0 g, 56 mmol) was heated on a steam bath for 10 min. The homogeneous solution was cooled, acidified with dilute hydrochloric acid, and extracted with ethyl acetate (3 × 150 mL). The combined extracts were dried (Na_2SO_4) and evaporated in vacuo. The residue was crystallized from ethyl ether–petroleum ether to give the diacid **7** as tiny colorless needles (2.70 g, 87%): mp 183.5–185 °C; NMR ($CDCl_3$) δ 6.18 (m, 2 H, olefinic protons), 4.8 (broad, 2 H, OH), 3.77 (m, 2 H), 3.50 (s, 3 H, OCH_3), 3.33 (s, 3 H, OCH_3), 3.2 (m, 1 H); IR (KBr) 3150 (broad), 2950 (s), 2830 (m), 1725 (s), 1400 (s), 1320 (m), 1250 (s), 1200 (s), 1120 (s), 1010 (m), 960 (m), 870 (m) cm^{-1}.

***1-Bromo-1,4,4a,8a-tetrahydro-9,9-dimethoxy-endo-1,4-methanonaphthalene-5,8-dione* (5).** The petroleum ether solution of **2** (from 13.7 g of **1**) was added to a solution of *p*-benzoquinone (2.64 g, 24 mmol) in ethyl acetate (50 mL). The mixture was stirred at room temperature for 24 h. After removal of solvent, the crude products were separated on a column of silica gel (400 g). Elution with carbon tetrachloride gave recovered benzoquinone (0.47 g, 4 mmol). Elution with benzene gave a 3:1 mixture of benzoquinone and dimer **3**. Finally, elution with methylene chloride gave the crude adduct **5** as a red oil (4.0 g), which crystallized on standing at room temperature to give yellowish needles (3.43 g, 30% from **1**): mp 115–116 °C (lit. 112–113.5 °C (*2*)); IR (KBr) 1675 (s), 1615 (m) cm^{-1}; NMR ($CDCl_3$ + acetone-d_6) δ 6.63 (s, 2 H), 6.00 (d, $J \simeq 2$ Hz, 2 H), 3.5–3.6 (m, 3 H), 3.50 (s, 3 H, OCH_3, overlap with the m), 3.33 (s, 3 H, OCH_3).

***1-Bromo-1,4,4a,8a-tetrahydro-6,7-dichloro-9,9-dimethoxy-endo-1,4-methanonaphthalene-5,8-dione* (6).** The petroleum ether solution (0.7 L) of **2** (from 7.3 g of **1**) was added to a solution of 2,3-dichloro-*p*-benzoquinone (*7*) (0.8 g) in ethyl acetate (10 mL). The mixture was stirred at room temperature for 30 h. The solution was concentrated to about 0.3 L and a fine yellowish powder was filtered off (0.8 g, 10% from **1**): mp 202–203 °C; NMR ($CDCl_3$) δ 6.30 (d, 2 H), 3.90 (m, 2 H), 3.63 (s, 4 H, OCH_3 and H_4), 3.43 (s, 3 H, OCH_3).

***3-Bromo-4,4-dimethoxypentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione* (8).** Compound **5** (0.936 g, 3 mmol) in ethyl acetate (150 mL) was irradiated by 16 low-pressure mercury lamps. The reaction was followed by NMR spectra of small samples; the end of the reaction was indicated by the disappearance of olefinic proton peaks at δ 6.63 and 6.00.

The solution was then decolorized with charcoal, filtered, and evaporated in vacuo to give a dense yellow oil (0.845 g). This crystallized from ethyl ether as tiny colorless needles (0.66 g, 70%): mp 134–135.5 °C; NMR ($CDCl_3$) δ 3.63 (s, 3 H, OCH_3), 3.60 (s, 3 H, OCH_3), 2.80–3.60 (complex m, 7 H); IR (KBr) 1770 (s), 1755 (s); mass spectrum, *m/e* (relative intensity) 312 (23.9), 314 (23.7) (molecular ion), 233 (32), 206 (14), 205 (97), 201 (6), 131 (60), 128 (64), 119 (100), 117 (90), 103 (48), 77 (67), 59 (50), 51 (62).

***3-Bromo-1,7-dichloro-4,4-dimethoxypentacyclo-[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione* (9).** Compound **6** (100 mg) in ethyl acetate (50 mL) was irradiated by 16 low-pressure mercury lamps for 3 h. Evaporation in vacuo gave a colorless solid (70 mg, 70%), mp 154–156 °C. An analytical sample was obtained by sublimation at 120 °C (8 mmHg): mp 171–172 °C; NMR δ 3.7 (m, 1 H), 3.57 (s, 6 H, OCH_3), 3.47 (m, 1 H), 2.8–3.4 (complex m, 3 H); mass spectrum, *m/e* (relative intensity) 380, 382, 384 (molecular ion with the intensity profile characteristic of Cl_2Br multiplet (*8*)), 305 (14), 303 (66), 301 (100), 300 (18), 275 (51), 273 (79), 265 (22), 187 (33), 136 (38).

***3-Bromo-4,4-dimethoxypentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-diol* (11).** Sodium borohydride (3.2 g, 84 mmol) in water (80 mL) was added dropwise during 0.5 h to dione **8** (2.19 g, 7 mmol) in ethanol (140 mL) cooled in an ice bath. The solution was then stirred at room temperature for 18 h and heated to 60 °C for 7 h. After being cooled in an ice bath, the solution was neutralized by aqueous HCl (4%) to pH ~5. The product was extracted with chloroform (3 × 250 mL), and the combined extracts were washed with water (2 × 200 mL), dried (Na_2SO_4), and filtered. Removal of chloroform in vacuo gave the crude diol **11** as a dense yellowish oil (2.0 g), which crystallized from ether as tiny colorless needles (1.32 g, 60%): mp 170–171 °C; IR (KBr) 3340 (br), 2970 (m), 2815 (w), 1370 (w), 1300 (m), 1270 (m), 1260 (m), 1145 (m), 1070 (s), 1040 (s), 970 (m), 955 (m), 910 (m) cm^{-1}; mass spectrum, *m/e* (relative intensity) 316 (27.6), 318 (27.4) (molecular ion), 298 (9), 300 (8.9), 237 (13), 219 (100), 91 (64). The low solubility in organic solvents precluded an NMR spectrum.

***3-Bromo-4,4-dimethoxypentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-8,11-diyl Sulfite* (13).** Thionyl chloride (150 mg, 1.25 mmol) in dry benzene (20 mL) was added at room temperature to a solution of the diol **11** (158 mg, 0.5 mmol) and dry pyridine (120 mg, 1.5 mmol) in dry benzene (30 mL). An immediate colorless precipitate was observed. The mixture was stirred and refluxed for 4 h. The cooled yellowish solution was washed with saturated salt solution (2 × 40 mL) and water (40 mL) and dried (Na_2SO_4). Removal of solvent gave the crude product as a yellowish oil (155 mg, 87%) which was purified by chromatography on a column of silica gel (30 g). Elution with CH_2Cl_2 gave an unidentified yellow oil (20 mg). Elution with $CHCl_3$ gave the sulfite **13** as a colorless oil (121 mg, 67%) which crystallized with difficulty from diethyl ether–petroleum ether: mp 124–126 °C; IR (neat) 2940, 2908, 2800, 1275, 1140, 1082, 1060, 1007, 783, 740, 705 cm^{-1}; NMR ($CDCl_3$) δ 4.90 (m, 1 H), 4.40 (m, 1 H), 3.56 (s, 3 H, OCH_3), 3.47 (s, 3 H, OCH_3), 2.90–3.47 (m, 6 H), 2.35 (m, 1 H); mass spectrum, *m/e* (relative intensity) 362 (52), 364 (54) (molecular ion), 298 (3), 300 (3), 283 (43), 219 (100), 191 (56), 91 (34), 77 (32), 59 (52).

***12-Oxa-3-bromohexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecan-4-one* (10).** *p*-Toluenesulfonic acid monohydrate (0.80 g, 4.2 mmol) was added to a refluxing solution of diol **11** (1.10 g, 3.5 mmol) in dry toluene (80 mL). The solution was refluxed for 3 h, and then the crude product was purified by chromatography on a column of Florisil (25 g). Elution with methylene chloride gave **10** as a colorless solid which crystallized from ethyl ether as tiny colorless needles (0.62 g, 67%): mp 89–90 °C; IR (KBr) 3000 (s), 1795 (s), 1780 (s) cm^{-1}; NMR ($CDCl_3$) δ 5.30 (m, 1 H), 5.10 (m, 1 H), 2.7–3.2 (unresolved m, 6 H), 2.40 (m, 1 H); mass spectrum, *m/e* (relative intensity) 252 (17.8), 254 (17.6), 173 (100), 145 (38), 129 (31), 116 (44), 115 (54).

***3-Bromo-4,4-dimethoxypentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-8,11-diyl Bismesylate* (14).** To a solution of diol **11** (1.0 g, 3.1 mmol) in dry methylene chloride (100 mL) containing 1.27 g (12.6 mmol) of triethylamine at 0 to −10 °C was added to 1.5 g (7.9 mmol) of methanesulfonyl chloride over a period of 10 min. The solution was stirred for 2 h. The mixture was first extracted with ice water, followed by cold 10% hydrochloric acid, saturated sodium bicarbonate solution, and brine. The methylene chloride solution was dried (Na_2SO_4) and the solvent removed in vacuo to give the crude product as a yellowish oil which crystallized from ethyl ether to give colorless needles of the dimesylate **14** (1.1 g, 70%): mp 131–132 °C; NMR ($CDCl_3$) δ 5.20 (m, 1 H), 4.80 (m, 1 H), 3.57 (s, 3 H, OCH_3), 3.45 (s, 3 H, OH), 3.0–3.3 (m, 6 H, overlaps with the singlet at 3.10), 3.10 (s, 6 H, SO_2CH_3), 2.40 (m, 1 H); mass spectrum, *m/e* (relative intensity) 472 (4.1), 474 (4.5) (molecular ion), 393 (3), 377 (2), 201 (27), 115 (11), 85 (33), 83 (38), 57 (29), 45 (100).

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Supplementary Material Available: Elemental analyses (C, H, N) for the compounds **3–11**, **13**, and **14** (1 page). Ordering information is given on any current masthead page.

Acetylenic Ketones. 8. Synthesis and Spectroscopic Studies of Some Hydrazones

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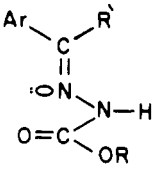
Aroylphenylacetylenes, benzaldehydes, and acetophenones reacted with ethyl and phenyl hydrazinecarboxylates to give the corresponding hydrazone *N*-carboxylic esters of ω-aroylacetophenone (IIIa–f), benzaldehyde (IXa–f), and acetophenone (IXg–l). UV, IR, and NMR spectra of these compounds are presented.

The reaction of some aroylphenylacetylenes with ethyl and phenyl hydrazinecarboxylates has been reported (*1*, *2*). The present work was intended to study the spectral and chemical properties of compounds III and IX in order to establish their structure and configuration. Thus, when phenyl- (Ia), *p*-(chlorophenyl)- (Ib), and *p*-(methoxyphenyl)benzoylacetylenes (Ic) were refluxed with an alcoholic solution of ethyl and phenyl hydrazinecarboxylates, they gave ω-benzoylacetophenone *N*-(ethoxycarbonyl)- (IIIa–c) and *N*-(phenoxycarbonyl)-hydrazone derivatives (IIId–f), respectively (cf. Figure 1). The structures of the products were established chemically and spectroscopically.

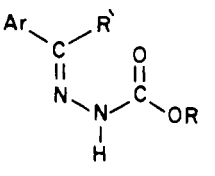
Chemical Evidence. Compounds IIIa–f were easily cyclized by refluxing with acetic anhydride to the corresponding 5-phenyl-1-(ethoxycarbonyl)- (Va–c) and -1-(phenoxycarbonyl)pyrazoles (Vd–f). The structures of the latter compounds were rigidly established by the fact that, when refluxed with 3% methanolic potassium hydroxide, they gave the corresponding 5(3)-aryl-3(5)-phenylpyrazoles (VI), identical with authentic samples prepared by reacting the acetylenic ketones I with hydrazine hydrate. Pyrazoles VI were also directly obtained from hydrazones III by refluxing with 3% methanolic potassium hydroxide. The IR spectra of pyrazoles V show a strong absorption band in the region 1780–1716 cm^{-1} ($\nu_{C=O}$) (*1*, *2*), and their NMR spectra gave a sharp signal in the range δ 6.80–6.69 (cf. Table I) attributable to the olefinic proton. Acetylation of pyrazoles VI by heating with acetic anhydride gave an inseparable mixture (A and B) of acetylpyrazoles VII (cf. Figure 1) (detected by TLC and NMR spectra) (*1*).

Spectroscopic Evidence. The IR and NMR spectra of IIIb,c,e,f are identical with those reported previously (*1*, *2*). Thus, their IR spectra (cf. Table II) show a sharp band in the region 3400–3380 cm^{-1} (ν_{NH}) and a strong band in the region 1722–1690 cm^{-1} with a shoulder at 1715–1680 cm^{-1}. This indicates that these compounds contain two different carbonyl groups and have either structure III, IVA, or IVB (cf. Figure 1). However, the fact that the mass spectrum of IIIa showed a base peak at *m/e* 105, $[C_6H_5CO]^+$, and that the electronic spectra of IIIa–f were similar to those of IX support structure III rather than IVA or IVB. Their NMR spectra (cf. Table II) (*3*) show a broad signal in the region δ 4.57–4.53 (NH) and a quartet (2 H), representing an AB system. The fact that these methylene protons behave as an AB system can be tentatively interpreted by assuming that III exists in solution as the ring tautomer IVB which possesses a chiral carbon atom.

The condensation of benzaldehydes VIIIa,b and acetophenones VIIIc,d with ethyl and phenyl hydrazinecarboxylates II led to the formation of benzaldehyde and acetophenone (*N*-phenoxycarbonyl)hydrazones IXa–h (cf. Figure 2). Their structures were established from their spectral data. The IR spectra (KBr) of compounds IXa–h (cf. Table III) show a broad band at 3300–3195 cm^{-1} (ν_{NH}) and two strong bands in the regions 1748–1710 and 1720–1690 cm^{-1} ($\nu_{C=O}$). Their NMR spectra and TLC, however, indicated that these compounds are pure and are not mixtures of two geometrical isomers. Accordingly, the two bands in the carbonyl region may be attributed to the presence of these compounds as a mixture of the two conformers IX, A and B. The higher stretching frequency



(IXA)



(IXB)

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