The Preparation of 4-Substituted 1-Methoxycarbonylbicyclo[2.2.2]octanes, Substituted 1-Phenylbicyclo[2.2.2]octanes, 4-Substituted 1-*p*-Nitrophenylbicyclo[2.2.2]octanes, and 1,4-Disubstituted Bicyclo[2.2.2]octanes

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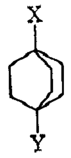
The preparation of several 1,4-disubstituted and 1-substituted bicyclo[2.2.2]octanes is described, including the following new compounds: 4-X-1-methoxycarbonylbicyclo[2.2.2]octane (X = H, Me, Et, Ph, Br, OH, or CO_2H), 4-X-1-phenylbicyclo[2.2.2]octane (X = H, Me, Et, *i*-Pr, or Ph), 4-X-1-*p*-nitrophenylbicyclo[2.2.2]octane (X = Et, *i*-Pr, Br, OMe, CN, or CO_2Me), 1-X-bicyclo[2.2.2]octane (X = *o*-, *m*-, *p*-nitrophenyl, *p*-aminophenyl, *p*-acetamidophenyl, 4-acetamido-3-nitrophenyl, 4-amino-3-nitrophenyl, 2,4-dinitrophenyl, or 4-amino-2-nitrophenyl), 1-X-4-Y-bicyclo[2.2.2]octane (X = OH, Y = *i*-Pr or isopropenyl; X = OMe, Y = isopropenyl; X = Br, Y = isopropenyl). An efficient preparation of dimethyl cyclohexa-1,3-diene-1,4-dicarboxylate is also reported.

In a 1,4-disubstituted bicyclo[2.2.2]octane (**1**) there will be a steric effect at a reaction site, Y, arising from



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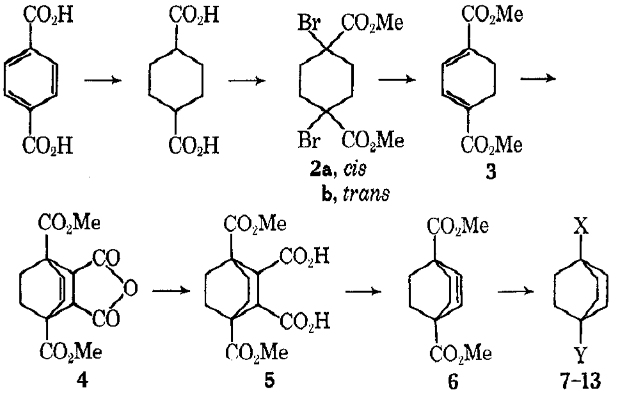
the bulk of the bicyclic system but, apart from any ponderal effect, independent of X, and so changing the substituent X will allow the nonconjugative polar effect of X to be studied in suitable reactions. Roberts, *et al.*,[2,3] Holtz and Stock,[4,5] Ritchie, *et al.*,[6,7] and Wilcox, *et al.*,[8,9] have used this system in investigations of polar and solvent effects. We wished to extend previous work on the kinetics of alkaline ester hydrolysis to 4-substituted 1-methoxycarbonylbicyclo[2.2.2]octanes, and to study electrophilic aromatic substitution in 4-substituted 1-phenylbicyclo[2.2.2]octanes, so that the nonconjugative polar effect of the substituent on the *ortho*, *meta*, and *para* positions of the benzene ring could be examined, steric effects being constant. We now describe the preparation of the compounds required for this investigation.

The reaction plan outlined in Scheme I was followed, despite reports that attempts to synthesise **6** by this sequence had failed.[10] The mixed *cis*- and *trans*-cyclohexane-1,4-dicarboxylic acid chlorides were brominated and were then converted into the mixed esters (**2**). The *cis* and the *trans* isomer can easily be separated at this stage, since the *cis* isomer is more soluble in methanol. Various conditions for the dehydrobromination of **2** were tried, but, as reported by Smith, *et al.*,[10] and Kauer, *et al.*,[11] the yields of **3** were variable. By using pyridine as solvent and as base for the dehydrobromination, the diene **3** was obtained from the mixed esters **2** in 80% yield; also hydrolysis of the esters was avoided and hence the need to reesterify the product. Ainbinder[12] recently reported a convenient six-stage synthesis of **3** from hydroquinone, and although this synthesis may be better than those described by Kauer, *et al.*,[11] Guha and Hazra,[13] von Baeyer,[14] Smith, *et al.*,[10] and Baker and Stock,[15] even better methods are that reported by Prinzbach, *et al.*,[16] and the method described here.

SCHEME I



7, X = Y = CO_2Me
8, X = CO_2Me; Y = CO_2H
9, X = CO_2Me; Y = Br
10, X = CO_2Me; Y = Ph
11, X = CO_2H; Y = OH
12, X = CO_2Me; Y = OH
13, X = CO_2Me; Y = H

Oxidative bisdecarboxylation of **5** with lead tetraacetate had been reported to fail by Humber, *et al.*,[17] and by Smith, *et al.*,[10] but we found that the reaction occurs smoothly in dimethyl sulfoxide or dioxane as solvent at room temperature.[18] Kauer, *et al.*,[11] have since found that **5** can be decarboxylated with lead tetraacetate in refluxing benzene. The Cristol–Firth method of brominative decarboxylation[19,20] was applied to **8** with 1,2-dibromoethane as solvent and gave

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[1] S. Sotheeswaran, Ph.D. Thesis, University of Hull, England, 1967. Department of Chemistry, University of Ceylon, Peradeniya, Ceylon.

[2] J. D. Roberts, W. T. Moreland, and W. Frazer, *J. Amer. Chem. Soc.*, **75**, 637 (1953).

[3] J. D. Roberts and W. T. Moreland, *ibid.*, **75**, 2167 (1953).

[4] H. D. Holtz and L. M. Stock, *ibid.*, **86**, 5183 (1964).

[5] H. D. Holtz and L. M. Stock, *ibid.*, **86**, 5188 (1964).

[6] C. D. Ritchie and E. S. Lewis, *ibid.*, **84**, 591 (1962).

[7] C. D. Ritchie and G. H. Megerle, *ibid.*, **89**, 1452 (1967).

[8] C. F. Wilcox and J. S. McIntyre, *J. Org. Chem.*, **30**, 777 (1965).

[9] C. F. Wilcox and C. Leung, *J. Amer. Chem. Soc.*, **90**, 336 (1968).

[10] G. Smith, C. L. Warren, and W. R. Vaughan, *J. Org. Chem.*, **28**, 3323 (1963).

[11] J. C. Kauer, R. E. Benson, and G. W. Parshall, *ibid.*, **30**, 1431 (1965).

[12] Z. Ainbinder, *ibid.*, **33**, 2564 (1968).

[13] P. C. Guha and G. D. Hazra, *J. Indian Inst. Sci.*, **22A**, 263 (1939); *Chem. Abstr.*, **34**, 2822 (1940).

[14] A. von Baeyer, *Ann. Chem.*, **251**, 280, 301 (1889).

[15] F. W. Baker and L. M. Stock, *J. Org. Chem.*, **32**, 3344 (1967).

[16] H. Prinzbach, H. Hagemann, J. H. Hartenstein, and R. Kitzing, *Chem. Ber.*, **98**, 2201 (1965).

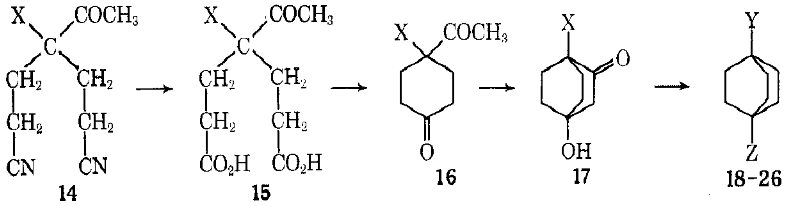
[17] L. G. Humber, G. Myers, L. Hawkins, and M. Boulerice, *Can. J. Chem.*, **42**, 2852 (1964).

[18] N. B. Chapman, S. Sotheeswaran, and K. J. Toyne, *Chem. Commun.*, 214 (1965).

[19] S. J. Cristol and W. C. Firth, *J. Org. Chem.*, **26**, 280 (1961).

[20] F. W. Baker, H. D. Holtz, and L. M. Stock, *ibid.*, **28**, 514 (1963).

SCHEME II



14-17a, X = Me
b, X = Et
c, X = Ph
d, X = *i*-Pr
e, X = isopropenyl

18, Y = OH; Z = X
19, Y = OMe; Z = X
20, Y = Br; Z = X
21, Y = Ph; Z = H
22, Y = Z = Ph

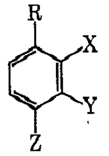
23, Y = CN; Z = Ph
24, Y = CO_2H; Z = X
25, Y = CO_2Me; Z = X
26, Y = Ph; Z = X

X as above

yields of **9** comparable with those obtained by the Hunsdiecker reaction,[21] but in the latter method unreacted acid was recovered; the Cristol–Firth reaction in petroleum ether (bp 60–70°) as solvent failed.

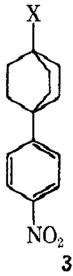
The synthesis of **13** we employed is essentially a modification of the method of Grob, *et al.*[22] In the preparation of 1-diethylaminobutadiene we used a solvent (ether) of lower boiling point than that used by Grob, *et al.*, so that the solvent could be removed more quickly before the final distillation, and consistent yields (60–65%) were obtained, without polymerization of the product.

By modifications of the methods of Bruson and Riener,[23,24] Colonge and Vuillemey,[25] and Holtz and Stock,[4] several 1,4-disubstituted bicyclo[2.2.2]octanes were prepared *via* the 4-substituted 1-hydroxybicyclo[2.2.2]-octan-3-ones (**17**) (Scheme II). Holtz and Stock[4] reduced the ketones **17a**–**17c** in 30–40% yields; we studied the reduction of the carbonyl group of **17c** in more detail and we used improved methods to reduce the carbonyl groups in **17a**–**17e**. The Huang-Minlon[26] modification of the Wolff–Kishner reduction of **17c** give a 20% yield of **18c**, but by using Grob's[27] modification of the Wolff–Kishner reduction a 40% yield was obtained. The yield was further improved by increasing the time taken for the formation of the hydrazone and by maintaining a slow distillation of hydrazine hydrate during 2 hr. The compound **18c** was consistently obtained in 65–70% yield by using these conditions, and 70–75% yields of **18a** or **18b** were obtained. However, only 10 and 25% yields of **18d** and **18e**, respectively were obtained, and the use of acidic conditions,[27] in the hope of increasing the yield of the hydrazone, gave no improvement. Further work with **17e** revealed that the reduction gave satisfactory yields if the hydrazone was isolated, anhydrous conditions were maintained in the decomposition of the hydrazone, and redistilled hydrazine hydrate was added to the mixture of pure hydrazone, potassium hydroxide and diethylene glycol to ensure a gradual rise in temperature as the hydrazine hydrate distilled off. In this way a 55% yield of **18e** was obtained. Another method tried for the reduction of **17e** was *via* the tosylhydrazone according to Caglioti and Grasselli;[28] a 27% overall yield was obtained.



27-35a, R = 1-bicyclo[2.2.2]octyl
b, R = *t*-butyl

27, X = Y = H; Z = NO_2
28, X = Y = H; Z = NH_2
29, X = Y = H; Z = $NHCOCH_3$
30, X = H; Y = NO_2; Z = $NHCOCH_3$
31, X = H; Y = NO_2; Z = NH_2
32, X = Z = H; Y = NO_2
33, X = Z = NO_2; Y = H
34, X = NO_2; Y = H; Z = NH_2
35, X = NO_2; Y = Z = H



36, X = Br
37, X = CO_2Me
38, X = OMe
39, X = Et
40, X = *i*-Pr
41, X = CN

The compound **23** was prepared from **20c** as described previously.[4] However, it proved difficult to isolate the product from the complex reaction mixture, and therefore Friedmann and Schechter's[29] extraction procedure was used.

The method we describe for the Koch–Haaf carboxylation[30] of **20a** or **20b** is an improvement on the one reported by Holtz and Stock.[4] The reaction involves the formation of a bridgehead carbonium ion, and although the formation of the 1-bicyclo[2.2.2]octyl carbonium ion is more difficult than, for example, the formation of the 1-adamantyl or *t*-butyl carbonium ion,[31,32] the formation of a 1-bicyclo[2.2.2]octyl carbonium ion is still conveniently easy.

The Friedel–Crafts alkylation of benzene with 1-bromoadamantane gave a high yield under mild conditions.[33,34] Likewise, we found that alkylations of benzene with **20a**–**20d** or **9** proceed easily and in good

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(21) R. G. Johnson and R. K. Ingham, *Chem. Rev.*, **56**, 219 (1956).

(22) C. A. Grob, M. Ohta, E. Renk, and A. Weiss, *Helv. Chim. Acta*, **41**, 1191 (1958).

(23) H. A. Bruson and T. W. Riener, *J. Amer. Chem. Soc.*, **64**, 2850 (1942).

(24) H. A. Bruson and T. W. Riener, *ibid.*, **65**, 18 (1943).

(25) J. Colonge and R. Vuillemey, *Bull. Soc. Chim. Fr.*, 2235 (1961).

(26) Huang-Minlon, *J. Amer. Chem. Soc.*, **71**, 3301 (1949).

(27) W. Nagata and H. Itazaki, *Chem. Ind.* (London), 1194 (1964).

(28) L. Caglioti and P. Grasselli, *ibid.*, 153 (1964).

(29) L. Friedman and H. Schechter, *J. Org. Chem.*, **26**, 2522 (1961).

(30) H. Koch and W. Haaf, *Angew. Chem.*, **72**, 628 (1960).

(31) R. C. Fort and P. von R. Schleyer, *Advan. Alicycl. Chem.*, 283 (1966).

(32) G. J. Gleicher and P. von R. Schleyer, *J. Amer. Chem. Soc.*, **89**, 582 (1967).

(33) R. C. Fort and P. von R. Schleyer, *Chem. Rev.*, **64**, 277 (1964).

(34) H. Stetter, M. Schwarz, and A. Hirschhorn, *Chem. Ber.*, **92**, 1629 (1959).

yield. For **20a** or **20b** the reaction with anhydrous ferric chloride as catalyst gave almost pure **26a** or **26b**. The compounds were purified by crystallization (**26a**) or by column chromatography (**26b**). For **20d** the crude product was less pure and purification proved difficult. With anhydrous aluminium chloride as catalyst the reaction was faster, and the impurities (*ca.* 15%) were removed by one crystallization from ethanol. The alkylation of benzene by using **9** or **20c** and anhydrous aluminium chloride gave **10** or **22** in 83 or 78% yield, respectively, and no by-products were formed in the reaction.

The nitration of **21** to obtain **27a** in different media and under different conditions was studied to find the optimum conditions for the mononitration. In glacial acetic acid a considerable excess of fuming nitric acid was necessary to achieve nitration (see method 2); the use of longer reaction times or greater amounts of nitric acid gave lower yields of **27a**. Addition of **21** in glacial acetic acid to fuming nitric acid in concentrated sulfuric acid gave variable results, probably because of the difficulty in controlling the temperature. With a mixture of glacial acetic acid and acetic anhydride as solvent and a threefold excess of nitric acid in sulfuric acid, a reasonable yield of **27a** was obtained (see method 1). In the most convenient preparation we used acetic anhydride as solvent and fuming nitric acid as nitrating agent, at room temperature (see method 3).

The compounds **32a** and **35a** were prepared by a modification of the method described by Wepster, *et al.*,[35] for the preparation of *o*- and *m*-*t*-butylnitrobenzene.

Experimental Section

Melting points and boiling points are uncorrected. Ir spectra were recorded with a Unicam SP200 instrument. Uv spectra were recorded at 25° with a Unicam SP700 spectrophotometer; the wavelength values quoted refer to maxima and the molecular extinction coefficients are given in parentheses. Nmr spectra were recorded with a Varian HA-100 spectrometer, with tetramethylsilane as internal standard and deuteriochloroform as solvent.

Cyclohexane-1,4-dicarboxylic Acids.—The mixture of acids was obtained by hydrogenating terephthalic acid in aqueous alkali, with a Raney nickel catalyst.[36]

Dimethyl 1,4-Dibromocyclohexane-1,4-dicarboxylate (2).—The above acids (172 g, 1 mol) in redistilled thionyl chloride (450 ml) were heated under reflux with stirring until the solution became clear (3–4 hr). Bromine (341.0 g, 2.135 mol) was added dropwise during 4–6 hr. The mixture was heated under reflux for 2 days in a dry atmosphere and for the last 24 hr the mixture was irradiated with a 100-W tungsten lamp. The excess of bromine and thionyl chloride was distilled off, anhydrous methanol (400 ml) was added to the residue cooled in ice, and the mixture was heated under reflux for a further 3 hr. Methanol (200 ml) was added to dissolve the dimethyl *cis*-1,4-dibromocyclohexane-*cis*-1,4-dicarboxylate. The residual solid was filtered off and recrystallized from 1:1 methanol–acetone to give dimethyl *trans*-1,4-dibromocyclohexane-*trans*-1,4-dicarboxylate (**2b**), yield 155 g, mp 148–150° (lit.[13] mp 150°).

The methanol was evaporated from the filtrate and the residue was distilled under reduced pressure [bp 120–128° (2 mm)] to give the *cis,cis* ester **2a**, yield 143.9 g, mp 61–63° (lit.[13] mp 68°). The overall yield of mixed esters was 83%.

Dimethyl Cyclohexa-1,3-diene-1,4-dicarboxylate (3). Method 1. Dehydrobromination with Cold Methanolic Potassium Hydroxide.—Compound **2** was dehydrobrominated with ice-cold potassium hydroxide in 95% aqueous methanol (1:2 w/w) for 48–50 hr. The mixture was then acidified with dilute hydrochloric acid, and the precipitated acid was reesterified. The product was crystallized from petroleum ether (bp 60–80°) to give **3**, mp 73–76°. Starting from **2a** the yield was 8.96 g (32%); and from **2b**, 0.924 g (3.3%).

Method 2. Dehydrobromination with Methanolic Potassium Hydroxide at 50–60°.—The method was the same as that just described except that the mixture was heated at 50–60° for 3–4 hr; compound **3** was produced, mp 75–77°. Starting from **2a** the yield was 5.60 g (20%); from **2b**, 5.32 g (19%).

Method 3. Dehydrobromination with Pyridine.—The diester **2** (118 g, 0.33 mol) was heated under reflux with an excess of pure, dry pyridine (150 ml) for 12–15 hr. The mixture was cooled and diluted with water (1 l.). The precipitate was filtered off, dried ($CaCl_2$) *in vacuo*, and recrystallized from petroleum ether to give **3**: mp 81–83° (lit.[13,14] mp 83–85°,[10] 84–85°,[16] 83–84°,[37] 81°); nmr τ 2.93 (s, 2 H), 6.21 (s, 6 H), and 7.46 (s, 4 H); λ_{max} (EtOH) 309 nm (ϵ 10,950). Starting from **2a** the yield was 43 g (66.5%); from **2b**, 59 g (91%).

1,4-Dimethoxycarbonylbicyclo[2.2.2]oct-2-ene-5,6-dicarboxylic Anhydride (4).—The ester **3** (19.6 g, 0.1 mol) was heated with maleic anhydride (29.4 g, 0.3 mol) at 100° for 1 hr and then at 170° for 1 hr. The mixture was cooled and the gummy solid was recrystallized four times from petroleum ether (bp 100–120°)–xylene (3:1) to give **4** (16.2 g, 55%), mp 181–183° (lit.[10] mp 191.5°,[17] 183–185°,[11] 188–188.6°).

1,4-Dimethoxycarbonylbicyclo[2.2.2]octane-2,3-dicarboxylic Acid (5).—The anhydride **4** (29.4 g, 0.1 mol) was treated with a solution of potassium bicarbonate (20 g, 0.2 mol) in deionized water (100 ml) and the mixture was heated on a steam bath for 20 min. 10% palladium on carbon (2–3 g) was added to the cold product, and the mixture was hydrogenated at atmospheric pressure. The catalyst was filtered off and the filtrate was acidified and cooled. The precipitated solid was recrystallized from water to give **5** (30 g, 95%), mp 166–168° (lit.[10] mp 177–178°,[17] 190–192°,[11] 210° dec).

1,4-Dimethoxycarbonylbicyclo[2.2.2]oct-2-ene (6).—This compound was prepared as described previously.[18] On a larger scale **6** was prepared[38] by heating **3** at 165° with ethylene under 1000 atm pressure in a silver-lined autoclave as reported by Kauer.[39] The crude product was recrystallized from hexane to give **6** (67%), mp 73–75° (lit.[39] mp 75–76°).

1,4-Dimethoxycarbonylbicyclo[2.2.2]octane (7).—The diester **6** was hydrogenated in methanol with a 10% palladium on carbon catalyst. The product was recrystallized from hexane to give **7** (90%), mp 98–100° (lit.[11] mp 100–101°).

4-Carboxy-1-methoxycarbonylbicyclo[2.2.2]octane (8).—The diester **7** (9.04 g, 0.04 mol), potassium hydroxide (2.24 g, 0.04 mol) in methanol (42.5 ml), and water (4.25 ml) were heated under reflux for 5–7 hr. The mixture was cooled and poured into water, and the product was shaken with ether. The organic phase was washed with water and dried ($MgSO_4$); evaporation of the solvent gave the recovered diester **7** (2.6 g). The aqueous phase was heated to drive off dissolved ether and was then acidified. The precipitated acids were washed with chloroform (3 × 50 ml) and the aqueous phase was filtered to remove any insoluble dicarboxylic acid. The chloroform layer was chilled, and any dicarboxylic acid which separated was filtered off. The filtrate was dried ($MgSO_4$) and the solvent was evaporated. The residue was crystallised from benzene to give the acid **8** (4.0 g, 66% allowing for the recovered diester): mp 180–182°; ir (KCl) 3000 (OH), 2950, 2875 (CH_3, CH_2), 1720, 1680 (C=O), 1240, and 1080 cm^{-1} (CO).

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.09; H, 7.59.

1,4-Dicarboxybicyclo[2.2.2]octane (1.4 g) had a melting point of 360–370° (lit.[2] mp >360°).

4-Bromo-1-methoxycarbonylbicyclo[2.2.2]octane (9).—The acid **8** (4 g, 0.0189 mol) was dissolved in acetone (30 ml) and neutralized (phenolphthalein) with aqueous 1 *N* sodium hydroxide. Silver nitrate (3.4 g, 0.020 mol) in water (5 ml) was added dropwise with stirring, and the gray-white precipitate was filtered off and washed with water, acetone, and ether. The residue was dried ($CaCl_2$) *in vacuo* for 24 hr and then at 100° under high vacuum for 2 days. The yield of silver salt was 4.3 g (71%) and of recovered acid was 0.13 g (3%).

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(35) H. J. B. Biekart, H. B. Dessens, P. E. Verkade, and B. M. Wepster, *Rec. Trav. Chim. Pays-Bas*, **71**, 321 (1952).

(36) R. G. Cooke and A. K. MacBeth, *J. Chem. Soc.*, 1245 (1939).

(37) R. H. Burnell and W. I. Taylor, *ibid.*, 3636 (1954).

(38) We thank I. C. I., Mond Division, England, for carrying out this reaction.

(39) J. C. Kauer, *Chem. Abstr.*, **59**, 6276*g* (1963).

The dry silver salt (4.3 g, 0.0135 mol) was made into a paste with dry petroleum ether (bp 40–60°, 50 ml). Pure, dry bromine (2.16 g, 0.0135 mol) was added dropwise to the vigorously stirred suspension under dry nitrogen. The mixture was stirred for a further 30 min and was then heated under reflux for 30 min. The product was filtered off and the residue was washed with ether. The filtrate and the ethereal washings were repeatedly washed with aqueous 1 *N* sodium carbonate and dried ($MgSO_4$). The solvent was evaporated and the residue was crystallized from methanol–water (10:1) to give the ester **9** (2.0 g, 60% based on the silver salt): mp 75–76°; ir (KCl) 2920, 2850 (CH_3, CH_2), 1719 (C=O), 1252, and 1080 cm^{-1} (CO).

Anal. Calcd for $C_{10}H_{15}O_2Br$: C, 48.60; H, 6.12; Br, 32.33. Found: C, 48.40; H, 6.06; Br, 32.65.

The yield of **8** recovered was 0.45 g (11%).

1-Methoxycarbonyl-4-phenylbicyclo[2.2.2]octane (10).—The bromo compound **9** (0.65 g, 0.00263 mol) in dry benzene (25 ml) was added during 15 min to a stirred solution of sublimed anhydrous aluminium chloride (1.3 g, 0.00975 mol) in benzene (20 ml) at −10° under dry nitrogen. For 1 hr the temperature was kept below 10° and the mixture was stirred vigorously. The temperature was then allowed to rise to room temperature during 1 hr. Stirring was continued overnight and the mixture was heated at 50–60° for 4 hr. The reaction mixture was cooled and poured into ice–hydrochloric acid, and the product was washed with ether. The ethereal layer was washed with aqueous sodium carbonate and water and dried ($MgSO_4$). The solvent was evaporated to give a brownish solid (0.6 g). The crude solid was dissolved in petroleum ether (bp <40°) and the solution was passed down a column (50 × 2 cm) of alumina. The solute was eluted with petroleum ether–acetone (99:1), and was crystallized from methanol to give the ester **10** (0.53 g, 83%): mp 89–91°; ir (KCl) 3020, 1590, 1490 (aromatic) 2900, 2800 (CH_3, CH_2), 1705 (C=O), 1240, 1070 (CO), 750, and 695 cm^{-1} (monosubstituted benzene); nmr τ 2.65–2.90 (complex, 5 H), 6.34 (s, 3 H), 8.11 (narrow peak, 12 H, $W_{1/2}$ = 1.5 cps).

Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.74; H, 8.00.

1-Carboxy-4-hydroxybicyclo[2.2.2]octane (11).—Compound **9** was hydrolyzed with sodium hydroxide by using a method similar to that described by Roberts, *et al.*,[2] for the hydrolysis of the ethyl ester. The yield of **11** was 68%, mp 221–223° (lit.[2] mp 222.9–225°).

4-Hydroxy-1-methoxycarbonylbicyclo[2.2.2]octane (12).—The acid **11** (1.7 g) in ether was treated with an ethereal solution of diazomethane until the yellow colour persisted. The ethereal solution was dried ($MgSO_4$) and the ether was evaporated. The residue was crystallized three times from hexane to give the ester **12** (51%): mp 61–63°; ir (KCl) 3300 (OH) 2975, 2875 (CH_3, CH_2), 1720 (C=O), 1240, and 1065 cm^{-1} (CO).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.25; H, 8.97.

1-Diethylaminobutadiene.—This compound was prepared (62%) by a modification of the method of Hünig and Kahanek,[40] by using ether instead of benzene as solvent; with benzene as solvent we frequently obtained yields of 20–30%. The diolefin had a boiling point of 70–80° (11 mm) [lit.[40] bp 60–70° (12 mm)].

1-Ethoxycarbonyl-2-diethylaminocyclohex-3-ene.—This compound was prepared (88%) as described by Hünig and Kahanek:[40] bp 85–95° (4.5 mm) [lit.[40] bp 80–83° (0.2 mm)].

1-Ethoxycarbonylcyclohexa-1,3-diene {52%, bp 68–78° (4 mm) [lit.[22] bp 90–92° (11 mm)]} and **1-ethoxycarbonylbicyclo[2.2.2]oct-2-ene-5,6-dicarboxylic anhydride** [91%, recrystallized three times from petroleum ether (bp 60–80°)-benzene (3:1), mp 84–85° (lit.[22] mp 86.5–87°)], were prepared as described by Grob, Ohta, Renk, and Weiss.[22]

1-Ethoxycarbonylbicyclo[2.2.2]octane-2,3-dicarboxylic Acid.—This compound was prepared from the above anhydride by the method described for the preparation of **5** (92%, from water), mp 143–146° (lit.[22] mp 135–147°).

1-Ethoxycarbonylbicyclo[2.2.2]oct-2-ene.—This compound was prepared as described previously,[18] bp 95–99° (10 mm) [lit.[22] bp 95–96° (10 mm)].

1-Ethoxycarbonylbicyclo[2.2.2]octane.—The above olefin was hydrogenated in ethanol with a 10% palladium on carbon catalyst and the residue was distilled (90%), bp 88–90° (4.5 mm) [lit.[22] bp 75–76° (3 mm)].

1-Carboxybicyclo[2.2.2]octane.—The above ester was hydrolyzed with ethanolic potassium hydroxide solution. The acidified solution gave the acid (89%, from acetone), mp 139–140° (lit.[2] mp 140.8–141.3°).

1-Methoxycarbonylbicyclo[2.2.2]octane (13).—The above acid in ether was treated with ethereal diazomethane until the yellow color persisted. The solvent was evaporated and the residue was chromatographed on an alumina column (20 × 1.3 cm); elution with petroleum ether (bp <40°) gave the pure ester. Evaporation of the solvent from the light petroleum eluates and distillation of the residue gave the ester **13** (57%): bp 54–56° (4 mm); mp 37–39°; ir (CCl_4) 2940, 2860, 1460, 1438 (CH_3, CH_2), 1720 (C=O), 1240, and 1065 cm^{-1} (CO).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.25; H, 9.25.

3-Acetyl-1,5-dicyano-3-X-pentanes (14a–14e).—These compounds were prepared by modification of the methods of Bruson and Riener.[23,24] Acrylonitrile (1 mol) was added slowly to a vigorously stirred solution of a ketone (0.5 mol) in *t*-butyl alcohol (100 g) containing a suitable base. The base, stirring time, and temperature used are given, respectively, after the ketone. Butan-2-one (30% methanolic potassium hydroxide, 3 g, 4–6 hr, 0–5°) gave **14a** (67%), mp 66–67° from benzene (lit.[23] mp 67°); pentan-2-one (Triton "B," 2 g, 4–6 hr, 10–15°) gave **14b** (42%), mp 107–109° from ethanol [lit.[23] mp 109°]; 3-phenylpropan-2-one (Triton "B," 5 g, 3 hr, 20–25°) gave **14c** (87%), mp 109° from ethanol (lit.[23] mp 109–110°); 4-methylpentan-2-one (10% methanolic potassium hydroxide, 2.5 g, 4–6 hr, 0–5°) gave **14d** (10.7%), bp 202–210° (2 mm) [lit.[23] bp 200–205° (2 mm)], mp 98–100° from ethanol (lit.[23] mp 101°); mesityl oxide (10% methanolic potassium hydroxide to give pH 10–10.5, 18–20 hr, 20–25°) gave **14e** (61%), mp 115–116° from methanol (lit.[24] mp 116–117°).

3-Acetyl-3-X-pentane-1,5-dicarboxylic Acids (15a–15e).—The compounds **14a–14e** were each hydrolyzed with aqueous sodium hydroxide, heated with decolorizing charcoal, and then acidified. The acid precipitated from the cold mixture was filtered off and crystallized from 1,2-dichloroethane to give **15a** (71%), mp 122–123° (lit.[23] mp 125°), or from water to give **15b** (76%), mp 112–113° (lit.[23] mp 112–113°); **15c** (90%), mp 168–170° (lit.[23] mp 171–172°); **15d** (85%), mp 146–148° (lit.[23] mp 148°); and **15e** (80%), mp 128–131° (lit.[24] mp 136–137°).

4-Acetyl-4-X-cyclohexanones (16a–16e).—These compounds were prepared by a modification of the method described by Colonge and Vuillemey:[25] **16a** (58%), bp 133–136° (15 mm) [lit.[25] bp 133° (15 mm)]; **16b** (72%), bp 140–147° (17 mm) [lit.[25] bp 144° (18 mm)]; **16c** (55%), mp 76–77° (lit.[25] mp 78°), bp 163–166° (2 mm) [lit.[25] bp 163–165° (2 mm)]. The reaction using **15d** produced two fractions. The first fraction was 4-acetyl-4-isopropylcyclohexanone (**16d**, 40%): bp 108–118° (2 mm); ir (KCl) 2950, 2880 (CH_3, CH_2), 1705, and 1690 cm^{-1} (C=O); nmr τ 9.10 (d, 6 H, J = 6.6 cps) and 7.5–8.5 (m, 12 H).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 71.99; H, 10.10.

The second fraction was 3-acetyl-3-isopropylpentane-1,5-dicarboxylic anhydride (2%), bp 194–204° (2 mm).

Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 64.01; H, 7.99.

Potassium bicarbonate solution hydrolyzed this product to give **15d**.

The reaction using **15e** produced an unidentified fraction, bp 120–180° (1 mm), and 4-acetyl-4-isopropenylcyclohexanone (**16e**, 45%): bp 80–83° (1 mm); ir (KCl) 2930, 2900 (CH_3, CH_2), 1705, 1695 (C=O), 1630, and 910 cm^{-1} (C=CH_2).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 72.85; H, 8.85.

When potassium acetate (0.30 mol/1 mol of **15e**) was added to the reaction mixture, the yield of **16e** was 58%.

1-Hydroxy-4-X-bicyclo[2.2.2]octan-3-ones (17a–17e).—These compounds were prepared as described by Colonge and Vuillemey:[25] **17a** (85%), bp 143–147° (15 mm) [lit.[25] bp 147° (18 mm)], mp 58–59° (lit.[25] mp 60°); **17b** (80%), bp 158–160° (15 mm) [lit.[25] bp 157° (16 mm)], mp 49–51° (lit.[25] mp 50°); **17c** (72%), crystallized from ethanol–water (2:1), mp 180–183° (lit.[25] mp 183°). 1-Hydroxy-4-isopropylbicyclo[2.2.2]octan-3-one (**17d**, 85%) had a melting point of 69–71° from cyclohexane, ir (KBr) 3300 (OH), 2950, 2850 (CH_3, CH_2), and 1710 cm^{-1} (C=O).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.88; H, 9.67.

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(40) S. Hünig and M. Kahanek, *Chem. Ber.*, **90**, 238 (1957).

1-Hydroxy-4-isopropenylbicyclo[2.2.2]octan-3-one (**17e**, 80%) had a melting point of 96–98° from cyclohexane; ir (KCl) 3200 (OH), 2910, 2840 (CH_3, CH_2), 1700 (C═O), 1630, and 895 cm^{-1} (C═CH_2).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.58; H, 9.21.

1-Hydroxy-4-X-bicyclo[2.2.2]octanes (18a–18e). Method 1.—The ketones **17a–17e** (0.02 mol) were each heated under reflux with hydrazine hydrate (25 ml of 98–100% w/w) for 5 hr; the mixture was cooled and potassium hydroxide (0.1 mol) and diethylene glycol (35 ml) were added. The apparatus was then arranged for distillation and the bath temperature was maintained at 160° for 1 hr and then raised to 220°. Nitrogen was evolved and the temperature was kept at 220° until the nitrogen evolution ceased (2 hr). The reaction mixture was cooled, poured into water, and washed with ether; the apparatus was washed out with ether, and the distillate was neutralized with 2 *N* hydrochloric acid and shaken with ether. The combined ethereal solutions were washed with 2 *N* hydrochloric acid and water and dried ($MgSO_4$). Evaporation of the ether left either a solid, **18a–18c** or **18e**, or a liquid, **18d**. Compound **18a** (70%) was sublimed at 70–80° (20 mm) [lit.[4] 70° (25 mm)], mp 98–101° (lit.[4] mp 103–104°); **18b** (75%) was sublimed at 80–90° (2 mm) [lit.[4] 70° (25 mm)], mp 101–103° (lit.[4] mp 104.5–106°); **18c** (69%) was crystallized from cyclohexane, mp 115–117° (lit.[4] mp 122–123°). The liquid from **17d** on distillation at 100–110° (1 mm) gave a solid, which was crystallized from cyclohexane to give 1-hydroxy-4-isopropylbicyclo[2.2.2]octane (**18d**, 10%): mp 124–127°; ir (KCl) 3250 (OH), 2900, and 2820 cm^{-1} (CH_3, CH_2).

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.34; H, 11.62.

Compound **18d** was also prepared by hydrogenating **18e** in methanol with a 10% palladium-on-carbon catalyst.

The solid from **17e** gave 1-hydroxy-4-isopropenylbicyclo[2.2.2]octane (**18e**, 25%): mp 110.9–112° from cyclohexane; ir (KCl) 3280 (OH), 2905, 2810 (CH_3, CH_2), 1625, and 892 cm^{-1} (C═CH_2).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.31; H, 10.88.

Method 2 for 18e.—The ketone **17e** (1.8 g, 0.01 mol) was heated under reflux with hydrazine hydrate (4 ml of 98–100% w/w) for 3 hr. The crude hydrazone, mp 128–145°, was precipitated by cooling the reaction product, and showed no carbonyl absorption in its infrared spectrum. This hydrazone (1.55 g, 0.008 mol), potassium hydroxide (3 g, 0.0535 mol), diethylene glycol (17 ml), and hydrazine hydrate (7 ml) were slowly heated and the procedure was then as given in method 1: yield 0.73 g, 55%.

Method 3 for 18e.—Compound **17e** (0.9 g, 0.005 mol), toluene-*p*-sulfonhydrazide (1.4 g, 0.0075 mol), and dry ethanol (40 ml) were heated under reflux for 4 hr and then cooled. The solid was filtered off and recrystallized from ethanol to give 1-hydroxy-4-isopropenylbicyclo[2.2.2]octan-3-one toluene-*p*-sulfonylhydrazone (1 g, 57%): mp 198–200° dec; ir (KCl) 3450 (NH, OH), 2925, 2850 (CH_3, CH_2), 1635, 885 (C═CH_2), 1590 (C═N), 1330, 1155 (S═O), and 820 cm^{-1} (1,4-disubstituted benzene).

Anal. Calcd for $C_{18}H_{24}N_2O_3S$: C, 62.04; H, 6.94; N, 8.04. Found: C, 62.18; H, 7.07; N, 8.50.

The tosyl hydrazone (0.664 g, 0.002 mol) was dissolved in freshly distilled dioxane (25–30 ml), sodium borohydride (2.22 g, 0.0587 mol) was added, and the mixture was heated under reflux for 8 hr. The mixture was cooled, poured into water, and shaken with ether and the solution was dried ($MgSO_4$). The solid left after evaporation of the ether was crystallized from cyclohexane to give **18e** (0.15 g, 47%); the overall yield from **17e** was 27%.

1-Methoxy-4-X-bicyclo[2.2.2]octanes (19c or 19e).—The alcohols **18c** or **18e** were methylated by using the method described by Holtz and Stock.[4] The product in either case was about 90% pure as indicated by glpc analysis. From **18c** chromatographic separation on an alumina column (30 × 1.3 cm) and elution with petroleum ether followed by petroleum ether–ether (92:8) gave **19c** (61%), bp 138–142° (5 mm) [lit.[41] bp 121° (0.8 mm)], mp 44–46° (lit.[41] mp 44°). From **18e** elution with petroleum ether gave 4-isopropenyl-1-methoxybicyclo[2.2.2]octane (**19e** 62.5%): bp 108–110° (8 mm); ir (liquid film) 2950, 2875, 2825 (CH_3, CH_2) 1635, 895 (C═CH_2), and 1110 cm^{-1} (CO).

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 80.28; H, 11.24.

1-Bromo-4-X-bicyclo[2.2.2]octanes (20a–20d).—These compounds were prepared as described by Holtz and Stock.[4] The bromide **20a** (85%) was sublimed at 80–90° (12 mm) [lit.[4] 70° (1 mm)], mp 90–93° (lit.[4] mp 92–94°); **20b** (85%) was sublimed at 50–60° (12 mm) [lit.[4] 70° (1 mm)], mp 34–36° (lit.[4] mp 34–35°); **20c** (90%) was crystallized from ethanol, mp 107–108° (lit.[4] mp 109–110°). The product from **18d** was sublimed at 75–80° (5 mm) to give 1-bromo-4-isopropylbicyclo[2.2.2]octane (**20d**, 87%): mp 36–38°; ir (liquid film) 2925, 2850 (CH_3, CH_2), and 685 cm^{-1} (CBr).

Anal. Calcd for $C_{11}H_{19}Br$: C, 57.14; H, 8.30; Br, 34.55. Found: C, 57.19; H, 8.31; Br, 34.10.

1-Phenylbicyclo[2.2.2]octane (21). Method 1.—The compound **20c** (13.2 g, 0.05 mol) in ethanol (500 ml) was added to a suspension of Raney nickel (15 g) in ethanolic sodium ethoxide (12 g of sodium in 100 ml of ethanol). The mixture was stirred at room temperature in an atmosphere of hydrogen until the calculated volume was absorbed (9–12 hr). The catalyst was filtered off, water was added, and the mixture was shaken with ether. The ethereal solutions were washed with water and dried ($MgSO_4$). The ether was evaporated and the residue was crystallized from ethanol–water (2:1) to give **21** (8 g, 86%): mp 78–80°; ir (KCl) 2910, 2825 (CH_3, CH_2), 1590, 1490 (aromatic), 755, and 695 cm^{-1} (monosubstituted benzene); nmr τ 2.65–2.97 (complex, 5 H) and 8.28–8.47 (br, 13 H).

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.23; H, 9.81.

Method 2.[42]—The compound **20c** (5.3 g, 0.02 mol) in dry tetrahydrofuran (30 ml) and *t*-butyl alcohol (2.96 g, 0.04 mol) was vigorously stirred under nitrogen, small pieces of lithium (0.694 g, 0.1 g-atom) were added, and the mixture was heated at 98° for 5–6 hr. Water was added to the cold product and the mixture was kept overnight at room temperature and then poured into water. The precipitated solid was crystallized as in method 1 to give **21** (3.27 g, 88%).

1,4-Diphenylbicyclo[2.2.2]octane (22).[43]—This compound was prepared from **20c** by the alkylation of benzene following the method described for the preparation of compound **10**. The hydrocarbon **22** (78% from ethanol) had a melting point of 210–211°; ir (KCl) 2950, 2915, 2862 (CH_2), 3090, 3060, 3022, 1598, 1498 (aromatic), 1005, 755, and 695 cm^{-1} (monosubstituted benzene); nmr τ 2.51–2.97 (complex, 10 H) and 8.05 (s, 12 H).

Anal. Calcd for $C_{20}H_{22}$: C, 91.55; H, 8.45. Found: C, 91.34; H, 8.47.

1-Cyano-4-phenylbicyclo[2.2.2]octane (23).—This compound was prepared as described by Holtz and Stock.[4] The crude reaction product (from 3.97 g of **20c**) was shaken with dimethylformamide and then poured into a solution of hydrated ferric chloride (20 g) in concentrated hydrochloric acid (5 ml) and water (30 ml). The mixture was heated at 60–70° to decompose the copper complex and then shaken successively with ether and benzene. The organic layers were washed with dilute hydrochloric acid and dried ($MgSO_4$), and the solvents were evaporated to give the crude cyanide, mp 120–135°. Glpc analysis showed the presence of the bromide **20c**. Chromatography on an acid-washed alumina column (60 × 2 cm) and elution with carbon tetrachloride removed the bromide; elution with methanol and crystallization of the product from ethanol gave **23** (0.85 g, 26.8%), mp 142–143° (lit.[4] mp 142–143.5°).

1-Carboxy-4-phenylbicyclo[2.2.2]octane (24c).—This compound was prepared as described by Holtz and Stock,[4] mp 289–291° (lit.[4] mp 293–294°).

1-Carboxy-4-X-bicyclo[2.2.2]octanes (24a or 24b).—The compound **20a** or **20b** (0.05 mol) and concentrated sulfuric acid (350 ml) were vigorously stirred at room temperature in an atmosphere of dry nitrogen. Formic acid ("AnalaR," 25 ml, 30.5 g, 0.663 mol) was added dropwise during 3–4 hr followed by silver sulfate (15.59 g, 0.05 mol) added portionwise. The mixture was stirred for a further 1 hr, silver bromide was filtered off, and the filtrate was poured onto ice. The precipitate was filtered off and washed with ether. The ethereal solution was washed with 4 *N* sodium hydroxide. The alkaline washings were heated

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[41] J. Colonge, P. Francois, and R. Vuillemey, *Bull. Soc. Chim. Fr.*, 1028 (1966).

[42] P. Bruck, *Tetrahedron Lett.*, 449 (1962).

[43] Prepared in the Department of Chemistry, University of Ceylon, Peradeniya, Ceylon.

to remove dissolved ether and acidified. The precipitated acid was filtered off, heated in methanol with decolorizing charcoal, and crystallized from methanol–water. The acid **24a** (70%) had a melting point of 186–188° (lit.[4] mp 187–188°,[44] 184.2–186.0°,[45] 194–195°); **24b** (75%) had a melting point of 167–169° (lit.[4] mp 170.5–171°,[45] 178.5–179.5°).

1-Methoxycarbonyl-4-X-bicyclo[2.2.2]octanes (25a or 25b).—The acid **24a** or **24b** was esterified with ethereal diazomethane as described for **13** and the residue was distilled under reduced pressure. 1-Methoxycarbonyl-4-methylbicyclo[2.2.2]octane (**25a**, 90%) was obtained: mp 19.5–20°; bp 62–64° (3 mm); ir (liquid film) 2925, 2860, 1460, 1438 (CH_3, CH_2), 1720 (C═O), 1240, and 1065 cm^{-1} (CO).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.58; H, 10.00.

4-Ethyl-1-methoxycarbonylbicyclo[2.2.2]octane (**25b**, 95%) was also obtained: bp 119–120° (16 mm); ir (liquid film) 2925, 2850, 1460, 1438 (CH_3, CH_2), 1719 (C═O), 1240, and 1065 cm^{-1} (CO).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.73; H, 10.13.

1-Phenyl-4-X-bicyclo[2.2.2]octanes (26a, 26b, or 26d). Method 1.[34]—Compound **20a**, **20b**, or **20d** (0.01 mol) in pure, dry benzene (30 ml) was added during 30 min to anhydrous ferric chloride (0.004 mol) in pure, dry benzene (20 ml) at room temperature and the mixture was stirred vigorously under dry nitrogen. The bath temperature was slowly raised during the addition and kept at 90–95° for 5–6 hr, and the mixture was then kept at room temperature overnight. The product was poured onto ice and hydrochloric acid and washed with ether. The organic layer was washed free of acid and dried ($MgSO_4$), and the solvent was evaporated. The purities of the residues (**26a**, **26b**, or **26d**) were shown by glpc to be 98, 95, and 85%, respectively, and the yields were 80, 78, and 74%, respectively. The crude residues were chromatographed on an alumina column (23 × 2 cm), and elution with petroleum ether removed contaminating starting material.

The material from **20a** was crystallized five times from ethanol to give 4-methyl-1-phenylbicyclo[2.2.2]octane (**26a**, 21%): mp 50–52°; ir (KCl) 2900, 2825 (CH_3, CH_2), 1375 (CH_3), 3040, 3005, 1598, 1492, 1458 (aromatic), 758, and 698 cm^{-1} (monosubstituted benzene); nmr τ 2.63–2.97 (complex, 5 H), 8.11–8.60 (symmetrical m, 12 H), and 9.17 (s, 3 H).

Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.67; H, 10.02.

The ethyl compound (**26b**) could not be purified by repeated crystallization and the remaining impurities were removed by chromatography on a silicic acid (100 mesh) column (18 × 1.5 cm). Elution with petroleum ether gave 4-ethyl-1-phenylbicyclo[2.2.2]octane (**26b**, 23%): mp 36–38°; ir (KCl) 2900, 2825 (CH_3, CH_2), 1380 (CH_3), 3035, 3000, 1595, 1495, 1450 (aromatic), 758, and 698 cm^{-1} (monosubstituted benzene); nmr τ 2.62–2.97 (complex, 5 H), 8.10–8.61 (symmetrical m, 12 H), 8.81 (q, 2 H), and 9.20 (t, 3 H).

Anal. Calcd for $C_{16}H_{22}$: C, 89.65; H, 10.35. Found: C, 89.44; H, 10.51.

The isopropyl compound **26d** was obtained by chromatography on a silicic acid column (20 × 1.3 cm) and elution with petroleum ether followed by crystallization three times from ethanol. 4-Isopropyl-1-phenylbicyclo[2.2.2]octane (**26d**, 1.3%) was obtained: mp 60–62°; ir (KCl) 2925, 2850 (CH_3, CH_2), 3038, 3010, 1598, 1495, 1445 (aromatic), 750, and 690 cm^{-1} (monosubstituted benzene); nmr τ 2.61–2.93 (complex, 5 H), 8.12–8.59 (symmetrical m, partially overlapping the methine resonance, 13 H), and 9.09 (d, 6 H).

Anal. Calcd for $C_{17}H_{24}$: C, 89.41; H, 10.59. Found: C, 89.59; H, 10.40.

The compound **26d** (31%, from ethanol) was also prepared by using aluminium chloride as catalyst.

1-(*p*-Nitrophenyl)bicyclo[2.2.2]octane (27a). Method 1.—The hydrocarbon **21** (2.5 g, 0.013 mol) was dissolved in glacial acetic acid (50 ml) and acetic anhydride (25 ml), and the solution was cooled to 0–5°. A mixture of fuming nitric acid (1.7 ml, *d* 1.5, 0.0384 mol) and sulfuric acid (15 ml, 98%) was added with stirring, keeping the temperature below 5°. The temperature was then allowed to rise slowly and the mixture was kept at room temperature for 45 min and then poured onto ice. The solid was filtered off, washed free of acid, and crystallized from ethanol to give **27a** (1.46 g, 47%): mp 104–106°; ir (KCl) 2898, 2825 (CH_2), 1510, 1345, 850, 750 (NO_2), 3098, 1590 (aromatic), 1100, and 850 cm^{-1} (1,4-disubstituted benzene); nmr τ 1.89 (d, 2 H, J = 9 cps), 2.56 (d, 2 H, J = 9 cps), 8.25 (br peak, 13 H, $W_{1/2}$ = 4 cps); λ_{max} (isooctane) 269.3 nm (ϵ 11,930).

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.36; H, 7.50; N, 6.23.

Method 2.[46]—The hydrocarbon **21** (2.5 g, 0.013 mol) was dissolved in glacial acetic acid (60 ml), and fuming nitric acid (10 ml, 0.23 mol) was added. The mixture was stirred vigorously and heated in an oil bath at 110–115° for 4 hr. The product was cooled and poured onto ice to give **27a** (1.0 g, 32%), which was purified as described in method 1.

Method 3.—The hydrocarbon **21** (0.232 g, 0.00125 mol) was dissolved in acetic anhydride (7.0 ml) and the solution was stirred at 25°. Fuming nitric acid (175 μl, *d* 1.5, 0.00396 mol) was slowly added from a micrometer syringe during 15–30 min. The mixture was stirred for 3 hr, poured into water, and shaken with ether. The ethereal layer was washed with dilute sodium carbonate and water and dried ($MgSO_4$). The ether was evaporated and the solid was crystallized from ethanol to give **27a** (0.15 g, 52%).

The following 4-substituted 1-(*p*-nitrophenyl)bicyclo[2.2.2]octanes were prepared from the corresponding 4-substituted 1-phenylbicyclo[2.2.2]octanes by using method 3 described above and were crystallized at least four times from ethanol to give the pure *para* isomer. 4-Bromo-1-(*p*-nitrophenyl)bicyclo[2.2.2]octane (**36**, 52%) was obtained: mp 153–155°; ir (KCl) 2950, 2875 (CH_2), 1518, 1350, 855, 755 (NO_2), 3090, 1600 (aromatic), 825 (1,4-disubstituted benzene), and 695 cm^{-1} (CBr).

Anal. Calcd for $C_{14}H_{16}BrNO_2$: C, 54.19; H, 5.20; Br, 25.75; N, 4.52. Found: C, 54.25; H, 5.06; Br, 25.91; N, 4.54.

4-Methoxycarbonyl-1-(*p*-nitrophenyl)bicyclo[2.2.2]octane (**37**, 48%) was obtained: mp 142–144°; ir (KCl) 2945, 2850 (CH_3, CH_2), 1518, 1350, 858, 745 (NO_2), 1718 (C═O), 1240, 1070 (CO), 1595 (aromatic), and 858 cm^{-1} (1,4-disubstituted benzene).

Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.26; H, 6.66; N, 5.01.

4-Methoxy-1-(*p*-nitrophenyl)bicyclo[2.2.2]octane (**38**, 40%) was obtained: mp 51–53°; ir (KCl) 2950, 2860 (CH_3, CH_2), 1518, 1350, 850, 750 (NO_2), 1098 (CO), 3090, 1595 (aromatic), and 850 cm^{-1} (1,4-disubstituted benzene).

Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.73; H, 7.50; N, 5.32.

4-Ethyl-1-(*p*-nitrophenyl)bicyclo[2.2.2]octane (**39**, 51%) was obtained: mp 53–55°; ir (KCl) 2925, 2875 (CH_3,CH_2), 1518, 1350, 850, 750 (NO_2), 1598 (aromatic), and 850 cm^{-1} (1,4-disubstituted benzene).

Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.35; H, 8.15; N, 5.42.

4-Isopropyl-1-(*p*-nitrophenyl)bicyclo[2.2.2]octane (**40**, 55%) was obtained: mp 111–113°; ir (KCl) 2930, 2850 (CH_3, CH_2), 1518, 1345, 850, 750 (NO_2), 1598 (aromatic), and 850 cm^{-1} (1,4-disubstituted benzene).

Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.83; H, 8.41; N, 5.16.

4-Cyano-1-(*p*-nitrophenyl)bicyclo[2.2.2]octane (**41**, 47%) was obtained: mp 158–160°; ir (KCl) 2950, 2875 (CH_2), 2225 (CN), 1520, 1342, 850, 748 (NO_2), 1595 (aromatic), and 850 cm^{-1} (1,4-disubstituted benzene).

Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.17; H, 6.20; N, 11.00.

***p*-*t*-Butylnitrobenzene (27b).**—This compound was prepared by nitrating *t*-butylbenzene:[35,47] mp 28.0° (lit.[47] mp 28.4°); bp 130–132° (14 mm) [lit.[47] bp 135° (10 mm)]; nmr τ 1.89 (d, 2 H, J = 9 cps) 2.47 (d, 2 H, J = 9 cps), and 8.64 (s, 9 H); λ_{max} (isooctane) 266.5 nm (ϵ 10,650).

1-(*p*-Aminophenyl)bicyclo[2.2.2]octane (28a) and ***p*-Amino-*t*-butylbenzene (28b).**—10% palladium on carbon (50 mg) was suspended in water (5 ml), sodium borohydride (0.38 g, 0.01 mol) in water (10 ml) was added,[48] and the mixture was kept under an atmosphere of nitrogen. A solution of the nitro compound **27a** or **27b** (0.005 mol) in methanol (75 ml) was added dropwise with cooling. Stirring was continued for 1–2 hr after the addition was

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[44] *Chem. Abstr.*, **62**, 14529*e* (1965).

[45] *Ibid.*, **64**, 15772*c* (1966).

[46] G. W. Gray and D. Lewis, *J. Chem. Soc.*, 5156 (1961).

[47] K. L. Nelson and H. C. Brown, *J. Amer. Chem. Soc.*, **73**, 5605 (1951).

[48] T. Neilson, H. C. S. Wood, and A. G. Wylie, *J. Chem. Soc.*, 371 (1962).

complete. The catalyst was filtered off and washed with ether. The filtrate was poured into water and shaken with ether and the combined ethereal layers were washed with 2 *N* hydrochloric acid. The aqueous phase was basified with 2 *N* sodium hydroxide to give either a solid (**28a**) or an oil (**28b**). The solid was filtered off and washed free of alkali to give **28a** (90%): mp 128–132°; ir (KCl) 2900, 2825 (CH_2), 3375, 3300, 1620, 1250 (NH_2), 3025, 1519 (aromatic), and 844 cm^{-1} (1,4-disubstituted benzene). Compound **28b** was isolated by shaking the final aqueous phase with ether. The ethereal layer was washed with water; the solvent was evaporated and the residue was distilled to give **28b** (95%), bp 132–138° (28 mm) [lit.[35] bp 120–123° (15 mm)].

1-(*p*-Acetamidophenyl)bicyclo[2.2.2]octane (29a) and *p*-Acetamido-*t*-butylbenzene (29b).—The amine **28a** or **28b** (0.010 mol) was treated with acetic anhydride (0.011 mol) and acetic acid (0.011 mol) and the mixture was heated in an oil bath at 160° for 30 min. The hot solution was poured into water and the brownish-white solid was filtered off and crystallized from ethanol–water (10:1). Compound **29a** (95%) was obtained: mp 175–177°; ir (KCl) 2900, 2850 (CH_3, CH_2), 3275, 1545, 1280 (NH), 1665 (C=O), 1605 (aromatic), and 838 cm^{-1} (1,4-disubstituted benzene).

Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.66; H, 8.71; N, 6.07.

Compound **29b** (81%) was obtained, mp 168–171° (lit.[35] mp 171–172°).

1-(4-Acetamido-3-nitrophenyl)bicyclo[2.2.2]octane (30a) and 4-Acetamido-3-nitro-*t*-butylbenzene (30b).—The compound **29a** or **29b** was nitrated by using the method of Wepster, *et al.*,[35] for the preparation of **30b**, and the product was crystallized from ethanol. Compound **30a** (95%) was obtained: mp 130–132°; ir (KCl) 2925, 2850 (CH_3, CH_2), 3350 (NH), 1515, 1345, 765 (NO_2), 1700 (C=O), 1620, 1580 (aromatic), and 850 cm^{-1} (1,3,4-trisubstituted benzene).

Anal. Calcd for $C_{16}H_{20}N_2O_3$: C, 66.64; H, 6.99; N, 9.72. Found: C, 66.70; H, 6.87; N, 9.79.

Compound **30b** (95%) was obtained, mp 104–106° (lit.[34] mp 107–107.5°).

1-(4-Amino-3-nitrophenyl)bicyclo[2.2.2]octane (31a) and 4-Amino-3-nitro-*t*-butylbenzene (31b).—The compound **30a** or **30b** (0.02 mol) and sodium methoxide (0.0324 g, 0.0006 mol) in methanol (20 ml) were heated under reflux for 2.5 hr.[49] The mixture was then cooled in the refrigerator and the reddish orange crystals which formed were filtered off and recrystallized from ethanol. Compound **31a** (95%) was obtained: mp 132–135°; ir (KCl) 2900, 2825 (CH_3, CH_2), 3450, 3325, 1635, 1245 (NH_2), 1518, 1345, 775 (NO_2), 1590, 1458 (aromatic), and 840 cm^{-1} (1,3,4-trisubstituted benzene).

Anal. Calcd for $C_{14}H_{18}N_2O_2$. C, 68.27; H, 7.37; N, 11.37. Found: C, 68.16; H, 7.42; N, 11.65.

Compound **31b** (93%) was obtained, mp 104–107° (lit.[35] mp 106–107°).

1-(*m*-Nitrophenyl)bicyclo[2.2.2]octane (32a) and *m*-*t*-Butylnitrobenzene (32b).—The amine **31a** or **31b** was deaminated by using Hodgson and Walker's method.[50] The amine **31a** or **31b** (0.005 mol) in glacial acetic acid (30–40 ml for **31a**, and 15–20 ml for **31b**) was added slowly to a solution of sodium nitrite (0.006 mol) in sulfuric acid (3.2 ml, 98%). The mixture was kept below 20° during the addition, and ethanol (10–15 ml) was added with cooling. The mixture was then heated under reflux for 4 hr, cooled, and poured into water. The mixture was shaken with ether and the ethereal layers were washed with 10% aqueous sodium hydroxide and water and dried ($MgSO_4$). The ether was evaporated, and for **32a** the residue was sublimed at 120–130° (1.0 mm) to give a solid which was crystallized from ethanol to give yellow crystals of **32a** (53%): mp 73–76°; ir (KCl) 2900, 2825 (CH_2), 1520, 1345, 738 (NO_2), 3050 (aromatic), 842, 802, and 685 cm^{-1} (1,3-disubstituted benzene); nmr τ 1.81–2.67 (4 H) and 8.23 (br peak, 13 H, $W_{1/2}$ = 5 cps); λ_{max} (isooctane) 259.2 nm (ϵ 7760).

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.69; H, 7.47; N, 6.10.

For **32b**, the residue was distilled to give **32b** (70%): bp 106–110° (3 mm) [lit.[35] bp 136–137° (16 mm)]; nmr τ 1.73–2.81 (4 H) and 8.62 (s, 9 H); λ_{max} (isooctane) 257.9 nm (ϵ 8870).

1-(2,4-Dinitrophenyl)bicyclo[2.2.2]octane (33a). Method 1.—The compound **21** (2.5 g, 0.013 mol) was added to a vigorously stirred mixture of sulfuric (4 ml, 98%) and nitric acid (4 ml, *d* 1.5, 0.0905 mol) at 20–30°. The mixture was then kept at 55–60° for 2 hr, cooled, and poured onto ice. The solid was filtered off and crystallized from ethanol to give **33a** (2.9 g, 78%): mp 154–156°; ir (KCl) 2900, 2850 (CH_2), 1530, 1350, 741 (NO_2), 3075, 1595 (aromatic), and 840 cm^{-1} (1,2,4-trisubstituted benzene).

Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.64; H, 5.84; N, 10.48.

Method 2.—The hydrocarbon **21** (2.5 g, 0.013 mol) in glacial acetic acid (65 ml) was added cautiously to a mixture of fuming nitric acid (10 ml, *d* 1.5, 0.23 mol) in sulfuric acid (15 ml, 98%) below 15°. The mixture was stirred for 2 hr below 30° and worked up as described in method 1 to give **33a** (3.1 g, 83%).

1-(4-Amino-2-nitrophenyl)bicyclo[2.2.2]octane (34a).—The compound **33a** (0.55 g, 0.00199 mol), water (5 ml), and ethanol (5 ml) were stirred vigorously at 60–70°. A solution of sodium sulfide nonahydrate (0.96 g, 0.0040 mol) and sulfur (0.128 g, 0.0040 mol) in water (1.5 ml) was added during 20 min. The mixture was heated under reflux for 2 hr and then poured into water. The solid was filtered off and boiled (five or six times) with an excess of 2 *N* hydrochloric acid, and the hot solution was filtered. The combined filtrates were basified with 2 *N* aqueous sodium hydroxide and the precipitated solid was filtered off, dried, and crystallized from petroleum ether (bp 100–120°) to give pale yellow needles of **34a** (0.32 g, 65%): mp 129–132°; ir (KCl) 2900, 2850 (CH_2), 3450, 3375, 3225, 1638, 1300 (NH_2), 1530, 1370 (NO_2), 1610, 1505 (aromatic), 860, and 820 cm^{-1} (1,2,4-trisubstituted benzene).

Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.10; H, 7.17; N, 11.02.

1-(*o*-Nitrophenyl)bicyclo[2.2.2]octane (35a).—The compound **34a** (1.23 g, 0.005 mol) was dissolved in dry ethanol (4.6 ml) and 98% sulfuric acid (1.47 g, 0.015 mol), and the cooled solution was diazotised at 5–10° with a solution of sodium nitrite (0.53 g, 0.00768 mol) in water (1.0 ml). The mixture was kept for 30 min at −10°, then heated under reflux for 4–5 hr. The product was cooled, poured into water, and shaken with ether. The ethereal layer was washed with 10% aqueous sodium hydroxide and water and dried ($MgSO_4$). The ether was evaporated and the residue was sublimed at 140–150° (2 mm) and crystallized from ethanol–water (5:1) to give **35a** (0.38 g, 33%): mp 58–61°; ir (KCl) 2900, 2850 (CH_2), 1530, 1375, 843, 745 (NO_2), 3050 (aromatic), and 775 cm^{-1} (1,2-disubstituted benzene); nmr τ 2.43–2.90 (4 H) and 8.04–8.44 (symmetrical m, 13 H); λ_{max} (isooctane) 287.8 nm (ϵ 5150).

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.59; H, 7.58; N, 6.11.

***o*-*t*-Butylnitrobenzene (35b).**—This compound was prepared by Mr. J. B. Woods following the procedure of Wepster, *et al.*,[35] bp 128–132° (16 mm) [lit.[35] bp 249–250° (761 mm)], nmr τ 2.40–2.85 (4 H) and 8.65 (s, 9 H). The uv spectrum (isooctane) did not show a maximum from 249.2 to 288.7 nm.

Registry No.—**3**, 1659-95-6; **8**, 18720-35-9; **9**, 23062-51-3; **10**, 23062-52-4; **12**, 23062-53-5; **13**, 2064-04-2; **16d**, 23102-72-9; **16e**, 23062-55-7; **17d**, 23062-56-8; **17e**, 23062-57-9; **17e**, toluene-*p*-sulfonylhydrazone, 23042-25-3; **18d**, 23062-58-0; **18e**, 23062-59-1; **19e**, 23062-60-4; **20d**, 23062-61-5; **21**, 23062-62-6; **22**, 23062-63-7; **25a**, 23062-64-8; **25b**, 23062-65-9; **26a**, 23062-66-0; **26b**, 23062-67-1; **26d**, 23102-73-0; **27a**, 23062-68-2; **28a**, 23062-69-3; **29a**, 23042-12-8; **30a**, 23102-74-1; **31a**, 23042-13-9; **32a**, 23042-14-0; **33a**, 23042-15-1; **34a**, 23042-16-2; **35a**, 23042-17-3; **36**, 23042-18-4; **37**, 23042-19-5; **38**, 23042-20-8; **39**, 23042-21-9; **40**, 23042-22-0; **41**, 23042-23-1; 3-acetyl-3-isopropylpentane-1,5-dicarboxylic anhydride, 23042-24-2.

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[49] P. E. Verkade and P. H. Witjens, *Rec. Trav. Chim. Pays-Bas*, **62**, 201 (1943).

[50] H. H. Hodgson and J. Walker, *J. Chem. Soc.*, 1620 (1933).