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 -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 $C_{20}H_{26}O$: 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 reproducible 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 titurated 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 reagent[12] (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 mμ (ε 77,800), 277 (sh) (5590), 282 (6000), 291 (sh) (4840), 308 (sh) (698) and 323 (652); ir (Nujol) 1708 cm^{-1} (C=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 $C_{20}H_{24}O$: 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-napthoate, 25097-55-6.

(12) J. Meinwald, J. Crandall and W. E. Hymans, *Org. Syn.*, **45**, 77 (1965).

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-tosyloxycyclohexane-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-

(1) (a) For paper VIII in this series, see R. N. McDonald and G. E. Davis, *J. Org. Chem.*, **34**, 1916 (1969). (b) National Defense Education Act Trainee, 1968–1970.

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

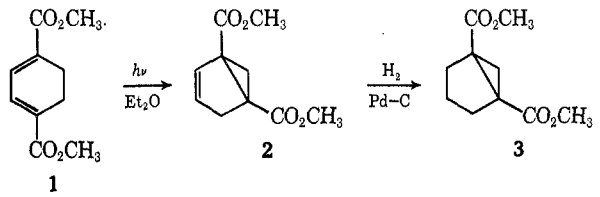
(3) F. W. Baker and L. M. Stock, *J. Org. Chem.*, **32**, 3344 (1967).

(4) C. F. Wilcox and J. S. McIntyre, *ibid.*, **30**, 777 (1965).

(5) C. F. Wilcox and C. Leung, *ibid.*, **33**, 877 (1968).

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

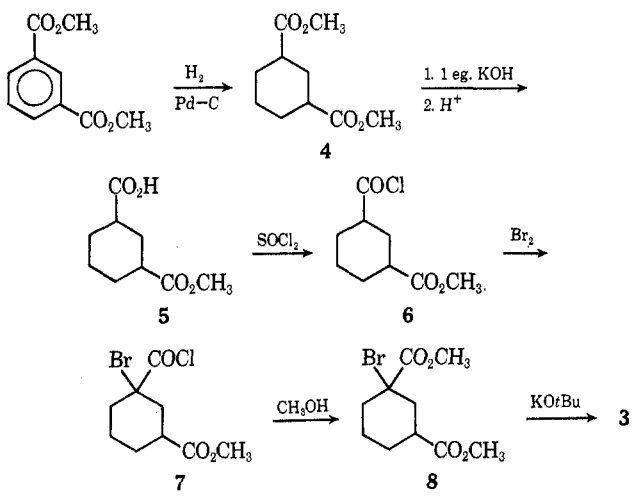
methyl cyclohexa-1,3-diene-1,4-dicarboxylate (1) with a Hanovia Type L, 450-W lamp in ether for 5 hr pro-



duced crude photo diester 2 in 40% yield after distillation. Hydrogenation of 2 over 5% Pd–C produced 3. Analysis of crude 3 by glpc showed the presence of several minor components.

Although 3 was available by this route, considerations of the time involved and small quantities of 3 produced per run suggested that an alternate synthesis of 3 be developed. Using the analogies of Nelson and Mortimer[7] and Wiberg[8] of using an intramolecular anionic displacement reaction in the preparation of [*n*.1.0] systems, a new synthetic route to 3 was devised according to the reaction sequence in Scheme I. Re-

SCHEME I



duction of dimethyl isophthalate produced 4 in a *cis*/*trans* ratio of 69:31, as analyzed by glpc. Partial saponification of diester 4, formation of the half-acid chloride 6, α-bromination of 6, and esterification of the product acid chloride 7 produced dimethyl 1-bromocyclohexane-1,3-dicarboxylate (8).

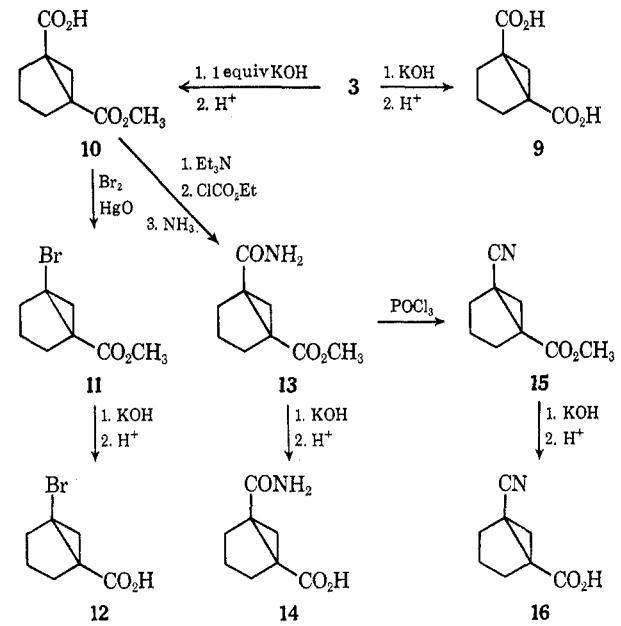
Treatment of 8 with a strong base led to formation of 3 by an intramolecular anionic displacement reaction. Reaction of 8 with sodium hydride in refluxing glyme for 6 hr produced 3 and a mixture of other ester products. Using sodium hydride and refluxing benzene for 24 hr, 3 was produced in crude yield of 50–55%. The nmr spectrum of the distillate also showed small amounts of other ester impurities. However, addition of 1 equiv of potassium *t*-butoxide in *t*-butyl alcohol to 8 in *t*-butyl alcohol produced 3 (85%) in high purity. Diester 3 so obtained was identical in all respects with the diester produced by Prinzbach[6] and represents an independent synthesis and structure proof of this bicyclic diester.

(7) N. A. Nelson and G. A. Mortimer, *J. Org. Chem.*, **22**, 1146 (1957).

(8) K. Wiberg, G. Lampman, R. Ciula, D. Connor, P. Schertler, and J. Lavanish, *Tetrahedron*, **21**, 2749 (1965).

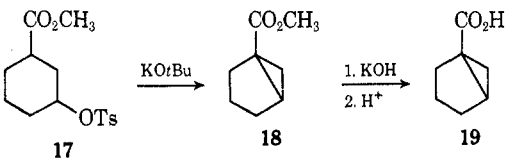
From 3 were produced 5-bromo- (12), 5-cyano- (16), 5-carbomethoxy- (10), 5-carboxamido- (14), and bicyclo[3.1.0]hexane-1,5-dicarboxylic acid (9) by standard routes[2-5] as outlined in Scheme II.

SCHEME II



Diester 3 could be saponified completely to diacid 9 or partially to half-ester 10. By a Hundsdiecker reaction 10 was converted to 11 which was hydrolyzed to bromo-acid 12. Half-ester 10 was converted to amide 13 which was then dehydrated to cyano ester 15. Esters 13 and 15 were hydrolyzed to their respective acids, 14 and 16.

Methyl bicyclo[3.1.0]hexane-1-carboxylate (18) was prepared by the method of Nelson and Mortimer[7] with the minor modification of using the *cis* and *trans* tosylate 17 in the 1,3-elimination reaction. Basic hydrolysis of 18 gave bicyclo[3.1.0]hexane-1-carboxylic acid (19).



Experimental Section[9]

Dimethyl Bicyclo[3.1.0]hex-2-ene-1,5-dicarboxylate (2).—The title compound was prepared by a modification of the procedure given by Prinzbach and coworkers.[6] In a usual irradiation apparatus, a solution (degassed with oxygen free nitrogen) of 4.0 g (20.4 mmol) of dimethyl 1,3-cyclohexadiene-1,4-dicarboxylate (1)[10] in 600 ml of anhydrous ether was irradiated for 5 hr. with a Hanovia 450-W lamp (Type L) in a quartz immersion well. The temperature of the solution was kept between −10 and 5° during the irradiation by means of an isopropyl alcohol–Dry Ice bath. It was necessary to wipe the irradiation well clean of polymer

(9) All melting points were determined on a Kofler hot stage and are corrected. Boiling points are uncorrected. Infrared and nmr spectra were obtained on a P-E 137 spectrophotometer and on a Varian A-60 spectrometer. Gas chromatographic analyses were performed using a F & M Model 500, temperature programmed, gas chromatograph. Microanalyses were done by Galbraith Laboratories. Mass spectra were determined on an MS-9 mass spectrometer.

(10) J. Kauer, R. Benson, and G. Parshall, *J. Org. Chem.*, **30**, 1431 (1965).

every 1.5 hr. Concentration of the irradiation solution and subsequent short-path distillation [90–100° (0.005 mm)] of the remaining viscous, yellow oil produced 1.60 g (40%) of crude diester **2**. The ir and nmr spectra were identical with those reported by Prinzbach.[6]

Dimethyl Bicyclo[3.1.0]hexane-1,5-dicarboxylate (3).—In a semimicrohydrogenation apparatus, 3.16 g (16.1 mmol) of crude **2** was hydrogenated in 15 ml of ethanol with 0.3 g of 5% Pd–C and one atmosphere of hydrogen. The reduction product was short-path distilled [65–70° (0.01 mm)] yielding 2.99 g (94%) of a light, colorless liquid. Glpc analysis of the crude mixture on a 10% Carbowax on Chromosorb P column showed at least eight components. The major component (>80%) was collected. Its ir and nmr spectra were identical with those reported for **3**.[6]

Reduction of Dimethyl Isophthalate.—To a solution of 10.0 g (51.6 mmol) of dimethyl isophthalate (Baker Chemical Co.) in 85 ml of dry methanol in a glass liner contained in a 150 ml capacity Magna Dash autoclave was added three spatula tips full of 5% Pd–C catalyst. Hydrogen was pressured into the autoclave to 1600 psi and it was heated to 100° for 48 hr. Pressure loss after cooling was approximately 400 psi. The catalyst was removed by filtration through a thin layer of filter cell and the solvent was removed by flash evaporation. The product from four 10.0-g runs was combined and short-path distilled [85° (0.01 mm)] producing 41.3 g (99.2%) of colorless diester **4**. The ir and nmr spectra agreed with the assigned structures, and the nmr spectrum indicated two different methyl ester singlets corresponding to the *cis* and *trans* isomers.

Separation of the *cis* and *trans* Isomers of Dimethyl Cyclohexane-1,3-dicarboxylate (4).—Glpc analysis of the *cis/trans* mixture reported above on a 8 ft × 0.25 in. 10% Carbowax on Chromosorb P (conditions: column temperature, 215°; helium gas flow, 60 ml/min) gave two peaks with retention times of 3.7 and 4.5 min. Integrations of the peak areas gave relative amounts of approximately 31 and 69%, respectively. Samples of both peaks were collected at a lower column temperature. The product with a retention time of 3.7 min gave an nmr spectrum (CCl_4, TMS internal) exhibiting absorption at τ 6.38 (s, 3, OCH_3), 7.2–7.6 (m, 2), and 7.9–8.5 [m (with characteristic sharp peaks at τ 8.03, 8.13, and 8.93), 8]. The product with a retention time of 4.5 min gave an nmr spectrum (CCl_4, TMS internal) exhibiting absorption at τ 6.40 (s, 3, OCH_3) and 7.6–8.9 [broad multiplet (with characteristic sharp peaks at τ 7.22, 7.92, 8.13, and 8.70), 10]. On the basis of the greater complexity of the multiplet from the ring hydrogens in the nmr spectrum of the second peak relative to the first peak, we have assigned the *trans* configuration to the first peak and the *cis* configuration to the second peak.

Methyl Hydrogen Cyclohexane-1,3-dicarboxylate (5).—To a solution of 39.0 g (0.195 mol) of *cis*- and *trans*-**4** in 50 ml of absolute methanol, 144 ml of a 1.36 *N* potassium hydroxide (0.196 mol) solution in absolute methanol was added dropwise over a 4 hr period. The mixture was heated under reflux for 24 hr and the methanol removed by flash evaporation. The residue was diluted with 100 ml of water and extracted with ether to remove unreacted starting material. The aqueous layer was acidified to pH 2–3 and extracted continuously with ether for 20 hr. The extract was dried ($MgSO_4$), filtered, and concentrated by rotary evaporation leaving a viscous, colorless liquid, crude monoester **5**. Diacid impurity was removed by dissolving crude **5** in carbon tetrachloride and filtering off the insoluble diacid. Monoester **5** was usually not purified further: ir (liquid film) 1720 (broad C=O) and 2500–3400 cm^{-1} (acid OH); nmr (CCl_4, TMS external) τ −1.0 (s, 1, CO_2H), 6.39 (s, 3, OCH_3), and 7.5–8.8 (m, 10, ring protons).

3-Carbomethoxycyclohexane-1-carbonyl Chloride (6).—Crude monoester **5** was dissolved in 30 ml of dry benzene. To this solution was added 40 ml of thionyl chloride and 4 drops of DMF. The mixture was stirred at room temperature for 2 hr and then at 50° for one hr until the evolution of gas had ceased. Solvent and excess thionyl chloride were removed by flash evaporation leaving a yellow liquid which was short-path distilled [80° (0.01 mm)] yielding 28.0 g (70% from 39.0 g of **4**) of colorless acid chloride-ester **6**: ir (thin film) 1730 and 1790 cm^{-1} (C=O); nmr (CCl_4, TMS internal): τ 6.35 (s, 3, OCH_3) and 7.2–8.3 [m (with a characteristic sharp peak at τ 8.31), 10].

Dimethyl 1-Bromocyclohexane-1,3-dicarboxylate (8).—To a solution of 31.0 g (0.152 mol) of acid chloride ester **6** in 30 ml of CCl_4 was added 9.0 ml (0.16 mol) of bromine. The mixture was heated under reflux for 8 hr until evolution of gas had ceased. Solvent and excess bromine were removed by flash evaporation and the yellowish residue was short-path distilled [100° (0.1 mm)] producing 43.0 g of a colorless liquid, crude **7**: ir (thin film) 1810 and 1740 cm^{-1} (C=O); nmr (CCl_4, TMS internal) τ 6.33 (s, 3, OCH_3) and 6.9–8.6 [m, (with characteristic sharp peaks at 7.89, 8.14, and 8.33), 9].

The crude bromination product, **7**, was then added dropwise to 100 ml of dry methanol with stirring at 0°. The solvent was removed after stirring for 1 hr and crystals formed upon standing. After two recrystallizations from methanol–water and sublimation [80° (0.01 mm)], 23.0 g (54% from 31.0 g of **6**) of bromo diester **8** was obtained: mp 73.5–74.5°; ir (KBr) 1725 cm^{-1} (C=O); nmr (CCl_4, TMS internal) τ 6.36 (s, 3, OCH_3), 6.22 (s, 3, OCH_3) and 6.9–8.9 [m (characteristic sharp peaks at 8.05, 8.13, and 8.28), 9]; mass spectrum (70 eV, direct insert) M^+ at *m/e* 278 and 280; mol wt 282 ± 2% (calcd 279.2).[11]

Anal. Calcd for $C_{10}H_{15}O_4Br$: C, 43.03; H, 5.42. Found: C, 42.82; H, 5.38.

Dimethyl Bicyclo[3.1.0]hexane-1,5-dicarboxylate (3) Produced by the 1,3-Elimination Reaction.—To 47.2 g (0.169 mol) of bromo diester **8** dissolved in 200 ml of dry *t*-butyl alcohol was added dropwise a solution of potassium *t*-butoxide in *t*-butyl alcohol [prepared from 7.0 g (0.179 g-atom) of potassium in 200 ml of dry *t*-butyl alcohol] over a 30-min period. During the addition a white precipitate formed and the mixture became thicker as the addition of base was continued. The mixture was allowed to stir 20 min after the addition of base was complete. The precipitate was removed by suction filtration and the filtrate concentrated to a volume of about 60 ml by flash evaporation. More precipitate formed when 200 ml of ether was added to the residue. After removal of precipitate and solvent, the liquid residue was short-path distilled [100° (0.1 mm)] yielding 27.8 g (85.6%) of **3**. Glpc analysis using the same column and conditions used for the analysis of **3** formed by the photochemical route showed only one peak with a retention time the same as that of **3** isolated previously. The ir and nmr spectra of these samples were identical. The mass spectrum (70 eV, heated inlet) showed M^+ at *m/e* 198.

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.72; H, 7.15.

Bicyclo[3.1.0]hexane-1,5-dicarboxylic Acid (9).—The title compound was prepared by the procedure given by Prinzbach.[6] Diacid **9** was isolated in 33% yield, sublimed in a sealed melting point tube at 220–225° and decomposed at 236–237° (lit.[6] sublimed 220–230°). The ir and nmr spectra agreed with those reported.[6]

Anal. Calcd for $C_8H_{10}O_4$: C, 56.47; H, 5.92. Found: C, 56.74; H, 6.02.

Methyl Hydrogen Bicyclo[3.1.0]hexane-1,5-dicarboxylate (10).—To 39.81 g (0.207 mol) of diester **3** in 100 ml of dry methanol was added dropwise a solution of 12.7 g (0.207 mol) of potassium hydroxide dissolved in 100 ml of dry methanol over a 2-hr period. A slight yellow color formed immediately and remained throughout the reaction. After stirring at room temperature for 24 hr and heating under reflux for an additional 3 hr, the solvent was removed by flash evaporation and crystallization occurred upon standing. To the crystals was added 150 ml of water and unreacted starting material was extracted with three 75-ml portions of ether (6.3 g of **3**). The aqueous layer was acidified to pH 2 and continuously extracted with ether for 24 hr. The extract was dried ($MgSO_4$), concentrated, and the residue was short-path distilled [130–145° (0.005 mm)] yielding 25.0 g (67.8%) of a viscous liquid, crude **10**, which solidified upon standing. From the distillation pot, 1.15 g of diacid was obtained after recrystallizing the residue from ethyl acetate. An analytical sample of **10** was obtained after several recrystallizations from cyclohexane and sublimation: mp 76.0–77.5°; ir (CCl_4) 2500–3500 (acid OH), and 1700 and 1730 (C=O) cm^{-1}; nmr (CCl_4, TMS internal) τ 6.35 (s, 3, OCH_3), 7.3–9.0 [m (with characteristic sharp peaks at τ 7.93, 8.05, 8.75, and 8.84), 8], and −1.1 (s, 1, acid proton); mass spectra (70 eV, heated inlet) M^+ at *m/e* 184.

Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.67; H, 6.75.

Methyl 5-Bromobicyclo[3.1.0]hexane-1-carboxylate (11).—The procedure for a similar Hunsdiecker reaction was followed.[12]

(11) Molecular weight determined on Mechrolab osmometer, Model 301 A.

(12) J. S. Meek and D. T. Osuga, *Org. Syn.*, **43**, 9 (1963).

A solution of 2.0 g (11 mmol) of half-acid **10** and 1.0 ml (19 mmol) of bromine in 20 ml of bromotrichloromethane (distilled from P_2O_5) was added dropwise over a 2 hr period to a stirred suspension of 1.5 g (7 mmol) of red mercuric oxide in 10 ml of bromotrichloromethane in a flask maintained at 35–40°. Stirring was continued until evolution of gas had ceased. Tlc (silica gel, $CHCl_3$) of the reaction mixture showed two spots, starting material and product. An additional 1.0 g (4.6 mmol) of mercuric oxide was added and evolution of gas increased until the bromine color had disappeared. Tlc showed the reaction to be essentially complete. The mixture was filtered, concentrated by flash evaporation of solvent, diluted with ether, and filtered again. The final filtrate was concentrated and the residue was short-path distilled [70° (0.1 mm)] producing 1.15 g (48%) of **11**: ir (thin film) 1730 (C=O), 1144 (C—O), and 1020 cm^{-1} (cyclopropyl-CH_2); nmr (CCl_4, TMS internal) τ 6.29 (s, 3, OCH_3) and 7.4–8.8 [m (with characteristic sharp peaks at 7.75, 8.07, 8.18, 8.63, and 8.75), 8]; mass spectrum (70 eV, heated inlet) M^+ at *m/e* 218 and 220.

Anal. Calcd for $C_8H_{11}O_2Br$: C, 43.86; H, 5.06. Found: C, 43.75; H, 5.18.

5-Bromobicyclo[3.1.0]hexane 1-carboxylic Acid (12).—A sample of bromoester **11** (1.15 g; 5.25 mmol) was saponified by a similar procedure to that described in the preparation of **9** except that 6.30 meq of base was employed. The crystalline residue from solvent evaporation was recrystallized twice from cyclohexane and sublimed at [80° (0.01 mm)] yielding 0.56 g (52%) of bromo acid **12**: mp 144.5–145.5°; ir (Fluorolube mull) 1700 (C=O), 2500–3200 (acid O—H), and 1048 cm^{-1} (cyclopropyl-CH_2); nmr (CCl_4, TMS internal) τ −2.3 (s, 1, acid proton) and 7.3–8.8 [m (characteristic sharp peaks 7.58, 7.72, 8.03, 8.58, and 8.68), 8].

Anal. Calcd for $C_7H_9O_2Br$: C, 41.00; H, 4.42. Found: C, 41.16; H, 4.42.

Methyl 5-Carboxamidobicyclo[3.1.0]hexane-1-carboxylate (13).—A solution of 5.00 g (27.4 mmol) of half-ester **10** and 2.7 g (28 mmol) of triethylamine in 50 ml of chloroform was cooled in an ice bath and 2.98 g (28 mmol) of ethylchloroformate was added rapidly with stirring. After 15 min anhydrous ammonia was bubbled through the mixture for 1.5 hr. The mixture was allowed to stand for 2 hr, filtered, and removal of the solvent left a yellowish oil. The residue was eluted fairly rapidly through 60 g of alumina (neutral, activity II) with chloroform until tlc (silica gel) showed that the product had ceased coming off the column. The eluant was concentrated and the residue crystallized upon standing. The crude amide ester **13** was recrystallized from a mixture of benzene–hexane yielding 4.1 g (82%) of white, crystalline **13**: mp 85.0–86.5°; ir (Fluorolube mull) 3300 and 3120 (N—H), 1720 (ester C=O), and 1660 cm^{-1} (amide C=O); nmr (CCl_4, TMS internal) τ 3.4–3.7 (m, 2, NH_2), 6.35 (s, 3, OCH_3), and 7.5–8.9 [m (characteristic sharp peaks at 7.95, 8.12, 8.22, 8.78, and 8.87), 8]; mass spectrum (70 eV, direct insert) M^+ at *m/e* 183.

Anal. Calcd for $C_9H_{13}O_3N$: C, 59.00; H, 7.15. Found: C, 59.15; H, 7.08.

5-Carboxamidobicyclo[3.1.0]hexane-1-carboxylic Acid (14).—The ester function of **13** was hydrolyzed in the usual manner as described in the preparation of **12**. Crude **14** was recrystallized from 1-propanol–ether yielding 0.49 g (53% from 1.0 g of **13**) of white, crystalline **14**. Amide acid **14** was further purified by sublimation [160° (0.1 mm)], another recrystallization, and resublimation: mp 189.0–190.5°; ir (Fluorolube mull) 3200 and 3300 (N—H), 2200–3000 (acid O—H), 1725 (acid C=O), 1640 (amide C=O), and 1045 cm^{-1} (cyclopropyl CH_2).

Anal. Calcd for $C_8H_{11}O_3N$: C, 56.80; H, 6.55; N, 8.28. Found: C, 56.70; H, 6.48; N, 8.23.

Methyl 5-Cyanobicyclo[3.1.0]hexane-1-carboxylate (15).—A solution of 1.0 g (5.52 mmol) of amide ester **13**, 1.5 ml (16 mmol) of freshly distilled phosphorus oxychloride, and 20 ml of ethylene dichloride was heated to 70° for 20 min with evolution of gas subsiding during that time. The mixture was diluted with chloroform and eluted rapidly through an alumina column (40 g of neutral, activity III) with chloroform. Heat was given off as the solution passed down the column. Two 70-ml fractions were collected, combined, and concentrated by evaporation of solvent. The liquid residue was short-path distilled [75° (0.1 mm)] producing 0.64 g (71%) of cyano ester **15**: ir (thin film) 2200 (C≡N), 1725 (C=O), and 1048 cm^{-1} (cyclopropyl CH_2); nmr (CCl_4, TMS internal) τ 6.27 (s, 3, OCH_3) and 7.4–8.9 [m (characteristic sharp peaks at 7.75, 8.08, 8.17, 8.66, and 8.75), 8]; mass spectrum (70 eV, heated inlet) M^+ at *m/e* 165.

Anal. Calcd for $C_9H_{11}O_2N$: C, 65.44; H, 6.71. Found: C, 65.54; H, 6.74.

5-Cyanobicyclo[3.1.0]hexane-1-carboxylic Acid (16).—Cyano-ester **15** was hydrolyzed in the usual manner as described in the preparation of **12**. The product was recrystallized from a mixture of ether-hexane giving 0.49 g (84%) of white crystalline **16**. The acid was further purified by recrystallization and sublimation [80° (0.01 mm)]: mp 117.0–118.5°; ir (Fluorolube mull) 2300–3300 (acid O—H), 2250 (C≡N), 1700 (C=O) and 1040 cm^{-1} (cyclopropyl CH_2); nmr (CCl_4, TMS internal) τ −2.2 (s, 1, acid proton) and 7.3–8.8 [m (characteristic sharp peaks at τ 7.93, 7.97, 8.61, and 8.70), 8].

Anal. Calcd for $C_8H_9O_2N$: C, 63.57; H, 6.00; N, 9.27. Found: C, 63.51; H, 5.99; N, 9.17.

Methyl Bicyclo[3.1.0]hexane-1-carboxylate (18).—To a solution of 4.03 g (24.5 mmol) of methyl 3-hydroxycyclohexane-1-carboxylate[7] in 40 ml of pyridine (freshly distilled from BaO) was added 5.2 g (26.5 mmol) of sublimed *p*-toluenesulfonyl chloride. The mixture was stirred for 15 hr at room temperature after which time a large amount of white pyridine hydrochloride had formed. Ice-cold 2 *N* sulfuric acid (50 ml) was added and the aqueous solution was then extracted with two 100-ml portions of ether. The combined ether extracts were washed with cold acid solution until the aqueous wash was acid to litmus paper. The ether extract was dried ($MgSO_4$) and concentrated to yield a slightly yellow, viscous liquid from which excess *p*-toluenesulfonyl chloride was removed by sublimation at 40° (0.1 mm). The product, **17**, remained as a viscous liquid (7.05 g, 90%): ir (thin film) 2900 (C—H), 1725 (C=O), 1190 and 1178 cm^{-1} (OTs); nmr (CCl_4, TMS internal) τ 2.26, 2.39, 2.70, and 2.84 (aromatic A_2B_2 pattern, 4), 5.1–5.9 (m, 1), 6.42 (s, 3, OCH_3), 7.56 (s, 3, CH_3), and 7.6–8.8 (m, 9).

To a solution of 7.05 g (22.8 mmol) of **17** in 30 ml of *t*-butyl alcohol was added dropwise 40 ml of a *t*-butyl alcohol solution of potassium *t*-butoxide [prepared from 1.0 g (25 mg-atoms) of potassium metal in 40 ml of *t*-butyl alcohol]. A white precipitate formed immediately upon addition. The mixture was stirred for 15 min after addition was complete. The mixture was filtered after addition of 50 ml of benzene. The filtrate was diluted with 150 ml of ether and washed with three 70-ml portions of distilled water. The organic layer was dried ($MgSO_4$) and concentrated to a low volume by flash evaporation. The residue was short-path distilled [60° (0.5 mm)] producing 2.275 g (71%) of colorless ester **18**: ir (thin film) 2900 (C—H), 1728 (C=O), 1145 (C—O), and 1040 cm^{-1} (cyclopropyl CH_2); nmr spectrum (CCl_4, TMS internal) τ 6.43 (s, 3, OCH_3), 7.7–8.5 (m, 6), 8.6–9.0 (m, 2), and 9.15–9.40 (m, 1); mass spectrum (70 eV, heated inlet) M^+ at *m/e* 140.

Bicyclo[3.1.0]hexane-1-carboxylic Acid (19).—The saponification of **18** was carried out in a similar manner to that described for the preparation of **12**. From 1.0 g (7.14 mmol) of **18**, there was obtained 0.785 g (87%) of **19** as a colorless liquid after short-path distillation [100° (0.01 mm)]: ir (thin film) 2600–3300 (acid O—H), 1680 (C=O), and 1045 cm^{-1} (cyclopropyl CH_2); nmr (CCl_4, TMS internal) τ −2.8 (s, 1, acid proton), 7.7–8.8 [m, (characteristic sharp peak at τ 8.16), 8], and 9.05–9.30 (m, 1).

Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.59; H, 7.91.

Registry No.—**5**, 25090-39-5; **6**, 25090-40-8; **7**, 25090-41-9; **8**, 25090-42-0; **10**, 25090-43-1; **11**, 25090-44-2; **12**, 25090-45-3; **13**, 25090-46-4; **14**, 25090-47-5; **15**, 25090-48-6; **16**, 25090-49-7; **17**, 25090-50-0; **18**, 25090-51-1; **19**, 25090-52-2.

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