

Anal. Calcd for $C_{10}H_{11}BrO_2$ (243.1): OCH₃, 12.75. Found: OCH₃, 12.50.

When a sample of **12** was distilled from a short-neck bulb at 0.3 Torr and 95–100° (bath temperature), the distillate gave unchanged ir and nmr spectra. Distillation of a larger quantity of **12** from an ordinary flask at 0.8 Torr and 108–110° (bath, 140–160°) caused the distillate to contain a considerable amount of isochromanone as revealed by spectroscopy. After three such distillations a sample was found to be nearly free from bromine (Found: Br, 0.42. Calcd for **12**: Br, 32.87.) and to give C and H values corresponding to isochromanone (Found: C, 73.34; H, 5.90. Calcd: C, 72.97; H, 5.40.).

Phenyl 2-(2-Bromoethyl)benzoate (13).—The acid **11** (508 mg) was refluxed with thionyl chloride (2 ml) for 1 hr. The excess of the reagent was then distilled off, and the reaction product was dissolved in pyridine (5 ml). Phenol (209 mg) was added, and the mixture was magnetically stirred for 2 hr at ambient temperature. The crystalline precipitate was discarded and the solution was evaporated to dryness. Crystallization of the residue from ethanol afforded colorless, hexagonal plates (400 mg) of the phenyl ester, mp 84°, ν_{max} 1730 cm^{-1} .

Anal. Calcd for $C_{15}H_{13}BrO_2$ (305.2): C, 59.00; H, 4.29; Br, 26.17. Found: C, 59.23; H, 4.16; Br, 26.06.

Methyl 2-(2-Nitroethyl)benzoate (4).—The bromo ester **12** (710 mg), sodium nitrite (350 mg), and phloroglucinol (166 mg) were stirred in dimethyl sulfoxide (3 ml) at room temperature for 8 hr. The mixture was then triturated with crushed ice, and the solid precipitate was collected and dried (375 mg, mp 45–48°). Recrystallization from methanol afforded **4** as colorless rods, mp 55–56°, ν_{max} 1720 (C=O) and 1550 cm^{-1} (NO₂).

Anal. Calcd for $C_{10}H_{11}NO_4$ (209.2): C, 57.41; H, 5.29; N, 6.69. Found: C, 57.20; H, 4.99; N, 6.35.

Use of sodium nitrite in *N,N*-dimethylformamide or of silver nitrite in ether failed to afford **4**.

Phenyl 2-(2-Nitroethyl)benzoate (14).—The bromo ester **13** (305 mg) and sodium nitrite (110 mg) were stirred in dimethyl sulfoxide (5 ml) at room temperature for 4 hr. The mixture was poured into ice water which was immediately extracted with three portions of ether. The combined extracts were washed twice with water, dried (Na₂SO₄), and evaporated to give a colorless solid (155 mg). Recrystallization from ethanol furnished prisms, mp 71°, ν_{max} 1730 (C=O) and 1550 cm^{-1} (NO₂). This material showed two major spots in tlc on silica gel G with cyclohexane-chloroform (2:3, v/v). The nitrogen content (2.47%) was half of that expected, and the carbon content (63.35%) lay between the values calculated for **14** and **13**. Separation of the mixture by preparative tlc furnished unreacted **13** (77 mg) by chloroform extraction of the faster moving band, and pure **14** (60 mg, mp 81°) by extraction of the slow moving band.

Anal. Calcd for $C_{15}H_{13}NO_4$ (271.3): C, 66.40; H, 4.83; N, 5.16. Found: C, 66.20; H, 4.86; N, 5.33.

Extension of the reaction time to 24 hr yielded a product that was difficult to purify.

Registry No.—**4**, 25109-81-3; **6**, 25109-82-4; **8**, 25109-83-5; **9**, 25109-84-6; **10**, 25109-85-7; **12**, 25109-86-8; **13**, 25109-87-9; **14**, 25158-13-8.

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Synthesis of Bridgehead Functionalized Bicyclo[3.3.1]nonanes

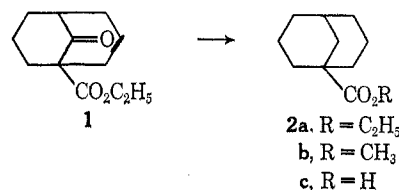
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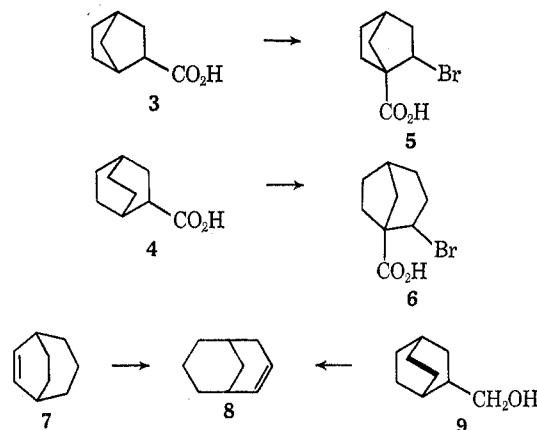
A wide variety of synthetic routes to the bicyclo[3.3.1]nonane ring system involves annelation of a three-membered bridge to the α positions of a cyclohexanone

derivative.¹ Some of these methods^{1c–f} have been applied to the synthesis of bicyclononanes functionalized at the bridgehead,² and our previous synthesis³ of 1-ethoxycarbonylbicyclo[3.3.1]nonane (**2a**) is typical, being based on previous work. As we desired a compound functionalized only at the bridgehead, the ester **1** (prepared from acrolein and 2-ethoxycarbonylcyclohexanone^{1c,d}) was converted to the ethylene dithioketal which was desulfurized with Raney nickel to give the ester **2a**. While the yields for this procedure are satis-



factory, the desulfurization step is cumbersome and somewhat dangerous because of the quantities of Raney nickel which must be handled on large runs. Thus we have sought an alternative method for the synthesis of **2**.

Our alternative synthesis is based on the reports that bicyclo[2.2.1]heptane-2-carboxylic acid⁴ (**3**) and bicyclo[2.2.2]octane-2-carboxylic acid⁵ (**4**) rearrange when brominated under Hell-Volhard-Zelinsky conditions to give acids **5** and **6**, respectively. Hartmann⁶ has shown



(1) For example, see (a) V. Prelog, P. Barman, and M. Zimmermann, *Helv. Chim. Acta*, **32**, 1284 (1949); (b) V. Prelog, P. Barman, and M. Zimmermann, *ibid.*, **33**, 356 (1950); (c) A. C. Cope and M. E. Synerholm, *J. Amer. Chem. Soc.*, **72**, 5228 (1950); (d) E. W. Colvin and W. Parker, *J. Chem. Soc.*, 5764 (1956); (e) R. P. Nelson and R. G. Lawton, *J. Org. Chem.*, **34**, 1225 (1969); (f) S. Danishevsky, G. Koppel, and R. Levine, *Tetrahedron Lett.*, 2257 (1969); (g) P. W. Hickmott and J. R. Hargreaves, *Tetrahedron*, **23**, 3151 (1967); (h) G. Stork and H. K. Landesman, *J. Amer. Chem. Soc.*, **78**, 5130 (1956); (i) A. C. Cope, D. L. Nealy, P. Scheiner, and G. Wood, *ibid.*, **87**, 3130 (1965).

(2) For other routes to bridgehead-substituted bicyclononanes, see (a) W. G. Dauben and C. D. Poulter, *J. Org. Chem.*, **33**, 1237 (1968); (b) P. von R. Schleyer and P. R. Isele, *ibid.*, **33**, 1239 (1968); (c) J. P. Ferris and N. C. Miller, *J. Amer. Chem. Soc.*, **85**, 1325 (1963); (d) H. Meerwein and W. Schurmann, *Justus Liebigs Ann. Chem.*, **398**, 196 (1913); (e) R. Rabe and M. Jahr, *ibid.*, **360**, 276 (1908).

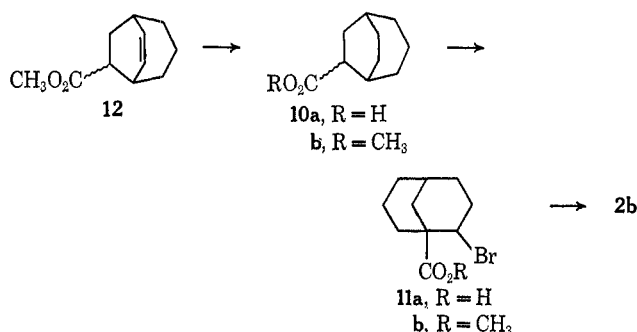
(3) (a) J. R. Wiseman and W. A. Pletcher, *J. Amer. Chem. Soc.*, **92**, 956 (1970); (b) J. R. Wiseman, *ibid.*, **89**, 5966 (1967).

(4) (a) W. R. Boehme, *ibid.*, **81**, 2762 (1959); (b) H. Kwart and G. Null, *ibid.*, **81**, 2765 (1959).

(5) A. W. Chow, D. R. Jakas, and J. R. E. Hoover, *Tetrahedron Lett.*, 5427 (1966).

(6) M. Hartmann, *Z. Chem.*, **7**, 101 (1967).

that bicyclo[3.2.2]non-6-ene (7) rearranges under acidic conditions to bicyclo[3.3.1]non-2-ene (8), and bicyclo[2.2.2]octane-2-methanol (9) has been converted to 8 by treatment with phosphoric acid.⁷ On the basis of these results we felt that bromination of bicyclo[3.2.2]nonane-6-carboxylic acid (10a) would produce 2-bromobicyclo[3.3.1]nonane-1-carboxylic acid (11a) as the major product.



Reaction of cycloheptadiene with methyl acrylate⁸ produced a 25:75 mixture of the *endo* and *exo* isomers of adduct 12.⁸ Esters 12 were hydrogenated to esters 10b, which were saponified to acids 10a. The mixture of acids 10a melted sharply, but reaction of the purified acids 10a with diazomethane produced a mixture of esters 10b close to the original mixture produced by hydrogenation of 12.

Bromination of acids 10a in the presence of a catalytic amount of phosphorous tribromide, followed by esterification with methanol, produced the bromo ester 11b in 58% yield. Debromination of 11b with zinc in acetic acid produced ester 2b, identical in all respects with the compound formed when acid 2c³ is treated with diazomethane. It is of interest that bromination of the acid chloride of 10a gave a mixture of at least six products, presumably isomers of both unrearranged bromo esters, and probably including bromo esters with the [4.2.1] skeleton as well. This is similar to the findings of other workers^{4a,b} and suggests that rearrangement is more rapid when the carboxylic acid is present. Apparently, slow rearrangement accompanies bromination of the acid chloride, but when the acid 10a is brominated with a catalytic quantity of phosphorous tribromide, more rapid rearrangement allows equilibration of the bromo acids with formation of the thermodynamically favored bicyclo[3.3.1]non-yl skeleton.

The sequence described above is comparable in yield to other methods of synthesis of bridgehead-functionalized bicyclo[3.3.1]nonanes, but is clearly superior in convenience and efficiency.

Experimental Section⁹

8-Methoxycarbonylbicyclo[3.2.2]non-6-ene (12).—A mixture of 1,3-cycloheptadiene (17.0 g, 0.185 mol) and methyl acrylate

(20 g, 0.232 mol) was heated in a sealed tube at 170° for 150 hr. Distillation of the reaction mixture (62–65°, 0.75 mm) gave 18.6 g (57%) of a 75:25 mixture of the *exo* and *endo* isomers of the unsaturated ester: ν_{max} 1740, 1645, 3060, 2020 cm^{-1} ; nmr τ 3.8–4.05 (complex, 2 H), 6.35, 6.43 (singlets, 3 H), 7.1–8.65 (complex, 11 H).

Anal. Calcd for $\text{C}_{11}\text{H}_{16}\text{O}_2$: C, 73.30; H, 8.95. Found: C, 73.31; H, 8.99.

6-Methoxycarbonylbicyclo[3.2.2]nonane (10b).—An *exo:endo* (75:25) mixture of 12 (18 g, 0.10 mol) in 200 ml of methanol was hydrogenated on a Parr shaker apparatus using palladium-on-carbon catalyst. Distillation (67–68°, 0.70 mm) gave 17.5 g (96.4%) of saturated ester 10b: ν_{max} 1740 cm^{-1} ; nmr τ 6.38, 6.40 (singlets, 3 H), 7.90–8.60 (complex, 15 H).

Anal. Calcd for $\text{C}_{11}\text{H}_{18}\text{O}_2$: C, 72.49; H, 9.96. Found: C, 72.53; H, 9.92.

Bicyclo[3.2.2]nonane-6-carboxylic Acid (10a).—Compound 10b (16.5 g, 0.091 mol) was stirred at reflux with 100 ml of 15% aqueous sodium hydroxide until complete solution was obtained (ca. 3 hr). The solution was cooled in an ice bath and acidified with 10% hydrochloric acid. The precipitate was filtered, washed with ice water, and dried in a vacuum desiccator (25°, 20 mm) overnight to yield 15.3 g (100%) of acid. Compound 10a sublimes (100°, 1 mm) to give white crystals: mp 63–64°; ν_{max} 1710, 3400–3000 (broad) cm^{-1} ; nmr τ 7.1–8.8 (complex, 15 H), –1.7 (singlet, 1 H).

Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_2$: C, 71.39; H, 9.59. Found: C, 71.31; H, 9.58.

2-Bromo-1-methoxycarbonylbicyclo[3.3.1]nonane (11b).—Acid 10a (5.0 g, 0.03 mol) was dissolved in bromine (10 g, 0.063 mol). Phosphorus tribromide (0.75 ml, 0.0079 mol) was then added slowly with stirring. The mixture was heated for 2 hr at 80°, and more bromine (5 g, 0.031 mol) was added. Heating was continued for 8 hr, then excess PBr_3 was added and heating was continued for 1 hr (ir showed complete conversion to acid halide). The cooled mixture was then poured into 65 ml of methanol. Some methanol was removed on the rotary evaporator, and the residue was taken up in ether, washed with 10% sodium bicarbonate (3 × 30 ml) and water (2 × 30 ml), and dried over sodium sulfate. Distillation (105–107°, 1.5 mm) gave 3.9 g (58%) of the bromo ester: ν_{max} 1740 cm^{-1} ; nmr τ 5.25 (broad singlet, 1 H, width at half height 8 Hz), 6.36, 6.35 (singlets, 3 H), 7.5–9.0 (complex, 13 H).

Anal. Calcd for $\text{C}_{11}\text{H}_{17}\text{O}_2\text{Br}$: C, 50.58; H, 6.56; Br, 30.60. Found: C, 50.37; H, 6.37; Br, 30.41.

1-Methoxycarbonylbicyclo[3.3.1]nonane (2b).—Bromo ester 11b (1.0 g, 0.0038 mol) was dissolved in 14 ml of glacial acetic acid. Zinc dust (2.4 g, 0.037 mol) was added slowly and stirred 1 hr. Water (25 ml) was then added and the mixture was let stand overnight. The suspension was extracted with ether (four 15-ml portions), washed with sodium bicarbonate (two 15-ml portions) and water (two 15-ml portions), and dried over sodium sulfate. The solvent was removed by a rotary evaporator and the product was distilled (66–68°, 0.50 mm) to give 0.51 g (74%) of ester 2b: ν_{max} 1740 cm^{-1} ; nmr τ 6.50 (singlet, 3 H), 7.7–8.65 (complex, 15 H).

Anal. Calcd for $\text{C}_{11}\text{H}_{18}\text{O}_2$: C, 72.49; H, 9.95. Found: C, 72.66; H, 9.96.

1-Methoxycarbonylbicyclo[3.3.1]nonane (2b).—Bicyclo[3.3.1]nonane-1-carboxylic acid (2c) (1.0 g, 0.006 mol) in 100 ml of ether was treated with an ether solution of diazomethane¹⁰ until the yellow color persisted. The solvent was distilled and the product was isolated by vpc. This ester was identical (ir, nmr, vpc retention time) with the ester prepared by debromination of the bromo ester 11b as described above.

Registry No.—2b, 24825-09-0; 10a, 19574-12-0; 10b, 24825-11-4; 11b, 24825-12-5; *exo*-12, 23217-55-2; *endo*-12, 23217-53-0.

(9) Infrared spectra were determined in carbon tetrachloride with a Perkin-Elmer Model 237 spectrophotometer. Nmr spectra were obtained in carbon tetrachloride solution with TMS as standard with a Varian A-60 spectrometer. Microanalyses were carried out by Spang Microanalytical Laboratory, Ann Arbor, Mich.

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(7) J. P. Schaefer, L. S. Endres, and M. D. Moran, *J. Org. Chem.*, **32**, 3963 (1967).

(8) The *exo* isomer in the [3.2.2] ring system is the favored isomer by Alder's rule: K. Alder and G. Stein, *Angew. Chem.*, **50**, 510 (1937).