Registry No.—1b, 16709-60-7; 1c, 16709-61-8; 2a 2,4-dinitrophenylhydrazone, 16709-64-1; 2c, 16709-65-2.

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Synthesis of 6-Benzyl-3-oxo-6-azabicyclo[3.2.1]octane[1]

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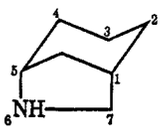
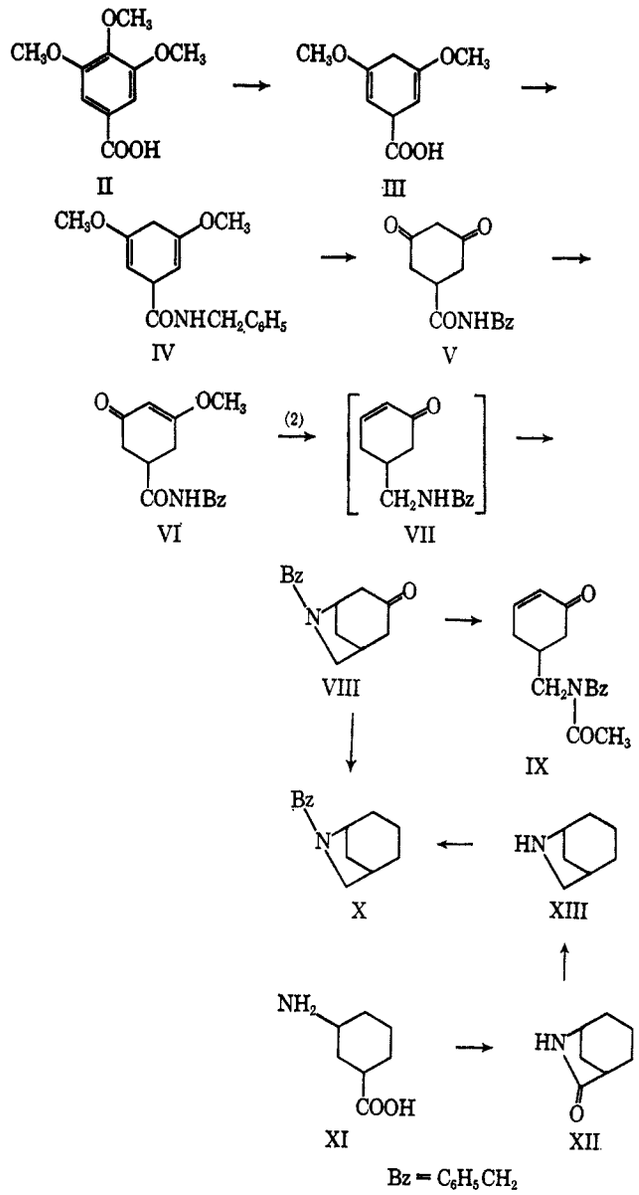
The literature reports only few syntheses of the 6-azabicyclo[3.2.1]octane system (I),[2-4] and only four syntheses of derivatives with a useful function on the three-membered bridge.[5,6] Our interest in this system as well as in other related azabicyclo compounds led us to investigate the sequence described below, which makes the 3-oxo derivative VIII readily available.



I

The starting point (see Scheme I) is trimethylgallic acid (II), which can be converted smoothly by Birch reduction into 3,5-dimethoxy-1,4-dihydrobenzoic acid (III).[7] Treatment of this acid with benzylamine and N,N-dicyclohexylcarbodiimide furnished the N-benzylamide IV. Acid hydrolysis of the enol ether groupings of IV gave diketo compound V which is probably largely enolic. With methanol in the presence of acid, diketo compound V was converted into the β-methoxy-α,β-unsaturated ketone VI. Reduction with lithium aluminum hydride followed by exposure to aqueous sulfuric acid gave rise to the α,β-unsaturated ketone VII,

SCHEME I



which cyclized spontaneously to the desired 6-benzyl-3-oxo-6-azabicyclo[3.2.1]octane (VIII). Interestingly, compound VII with hydroxyl in place of benzylamino appears not to cyclize to the corresponding 6-oxo-6-oxabicyclo[3.2.1]octane.[8] Although the α,β-unsaturated ketone VII could not be obtained, treatment of bicyclo compound VIII with acetic anhydride opened the ring by acyl cleavage to give the N-acetyl derivative IX of VII. The assigned structure for bicyclo ketone VIII was confirmed when its Wolff–Kishner reduction product X proved to be the same as the product obtained by benzylating the known 6-azabicyclo[3.2.1]-octane (XIII). The latter was prepared from 3-aminocyclohexanecarboxylic acid (XI) by cyclization to XII and reduction.[2,3]

Ethylenimine derivatives similar to XVIII have been found to react readily with nucleophiles to give both 6-azabicyclo[3.2.1]octanes (as in XVII) and 2-azabicyclo[2.2.2]octanes (*i.e.*, isoquinuclidines, as in XIX).[6] The possibility of reaching isoquinuclidine XIX was attractive, and the series of reactions V →

(1) This investigation was supported by Public Health Service Research Grant No. CA 08386 from the National Cancer Institute.

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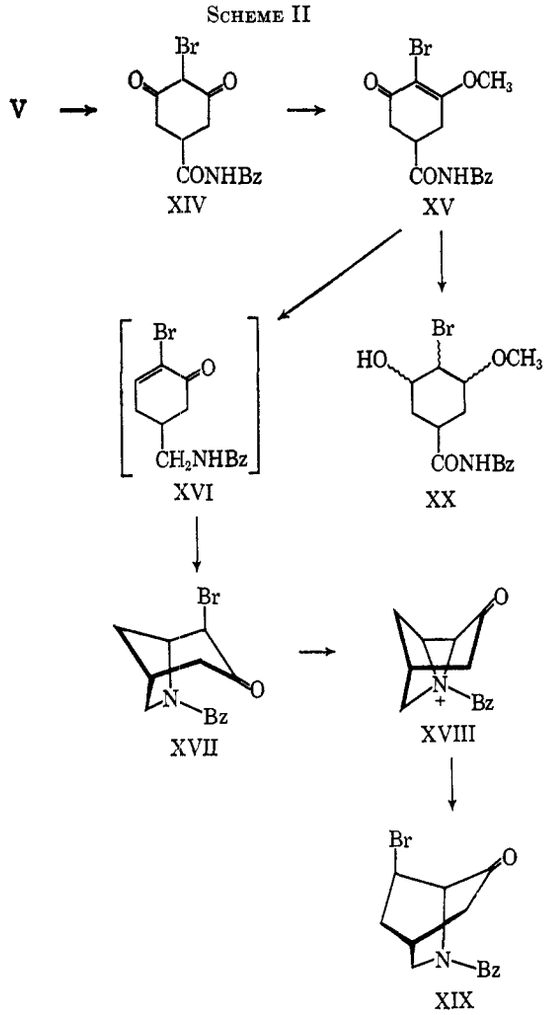
(8) E. E. van Tamelen and G. T. Hildahl, *ibid.*, **75**, 5451 (1953); **78**, 4405 (1956).

SCHEME II



Bz = $C_6H_5CH_2$

XIV →···→ XIX (Scheme II) appeared feasible as well as convenient and well worth exploring. Bromination of dioxo compound V gave the 4-bromo-3,5-dioxo derivative XIV, which could be converted smoothly into the enol ether XV. Here the plan broke down because lithium aluminum hydride reduction of XV gave oils that could not be identified with the key compounds XVI or XVII. Reduction of enol ether XV with sodium borohydride gave a crystalline product to which we have assigned structure XX. This approach was not pursued.

Experimental Section

General.—Melting points were taken in an apparatus calibrated against pure compounds. Infrared absorption curves were taken with the help of a recording spectrophotometer (Perkin-Elmer Model 237). Ultraviolet absorption curves were determined on a Cary Model 14 spectrophotometer. A Varian A-60 spectrometer was used for the nmr work.[9] The adsorbent in the thin layer chromatographic analyses was either silica or alumina. Exposing the developed chromatogram to iodine vapors made the spots visible. Analysis for elements were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich., and by Galbraith Laboratories, Inc., Knoxville, Tenn.

N-Benzyl-3,5-dimethoxy-1,4-dihydrobenzamide (IV).—N,N-Dicyclohexylcarbodiimide (7.3 g or 0.035 mol) followed by benzylamine (2.9 g or 0.027 mol) was added to a solution of 3,5-dimethoxy-1,4-dihydrobenzoic acid (III, 5.0 g or 0.027 mol)[7] in 250 ml of methylene chloride. After 2 days of stirring, the mixture was filtered. The slightly yellow filtrate was shaken with 3% hydrochloric acid, then 5% aqueous bicarbonate, and finally with two portions of water. The organic layer was taken to dryness *in vacuo* at room temperature. The residue, rubbed with a small amount of ether, produced a filterable white solid (6.0 g), mp 128–135° (rapid heating). Crystallization from methylene chloride–petroleum ether gave colorless needles (5.0 g or 68%), mp 128–132° (rapid heating). Further crystallization from ethyl acetate–petroleum ether and from benzene–pentane furnished analytically pure N-benzyl 3,5-dimethoxy-1,4-dihydrobenzamide (IV), homogeneous according to thin layer chromatography (chloroform solvent), with mp 127–129°.

Anal. Calcd for $C_{16}H_{19}O_3N$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.09; H, 7.39; N, 5.11.

The infrared absorption spectra taken in chloroform solution showed maxima at 3410 (NH), 1690 (enol ether), and 1660 cm^{-1} (amide carbonyl). A 10% solution in deuteriochloroform showed signals at 2.76 (2 H, d, J = 7 cps, with a suspicion of satellite signals at *ca.* 2.55 and 2.95, position 4), 3.50 (6 H, s, 2 OCH_3), 3.6–3.9 (1 H, complex, position 1), 4.36 (2 H, d, J = 6 cps, $ArCH_2$), 4.73 (2 H, d, J = 4 cps, positions 2 and 6), 6.5–6.7 (1 H, broad, NH), and 7.23 ppm (5 H, s, 5 ArH).

N-Benzyl-3,5-dioxocyclohexanecarboxamide (V).—N-Benzyl-3,5-dimethoxy-1,4-dihydrobenzamide (IV, 13.5 g or 0.051 mol) in 150 ml of warm tetrahydrofuran was treated with 100 ml of 5% hydrochloric acid. The homogeneous solution was kept at 50–65° for 2 hr and then concentrated *in vacuo* until much solid was evident. Distilled water (*ca.* 300 ml) was added and the precipitate was collected, rinsed with water, and dried at 120° *in vacuo* over phosphorus pentoxide. The N-benzyl-3,5-dioxocyclohexanecarboxamide (V) obtained in this way weighed 10.5 g and showed mp 183–185°. Two crystallizations from acetone gave white crystals, mp 199–201°, which as a mineral oil mull showed absorption peaks at 3333 (NH), 1642 (amide carbonyl), 1613 and 1550 cm^{-1} (1,3-diketone), and which as a 5.6×10^{-3} M solution in 95% ethanol showed an ultraviolet absorption maximum at 257 mμ (log ϵ 4.01).

Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.74; H, 6.22; N, 5.55.

N-Benzyl-3-methoxy-5-oxo-3-cyclohexenecarboxamide (VI).—To a warm solution of N-benzyl-3,5-dioxocyclohexanecarboxamide (V, 10.5 g or 0.043 mol) in 200 ml of methanol was added 0.3 g of *p*-toluenesulfonic acid. The solution was allowed to stand for a day at room temperature. Pyridine (four drops) was introduced, and more than half the solvent was removed under reduced pressures at room temperature. The precipitated solids were redissolved by warming and then brought out again by cooling the solution overnight. The collected dried crystals (8.1 g or 73%) melted at 162–164°. A second crystallization did not change the melting point of this N-benzyl-3-methoxy-5-oxocyclohexenecarboxamide (VI), which as a solution in chloroform showed infrared absorption bands at 3440 (NH), 1660 (amide carbonyl), 1650 and 1610 cm^{-1} (COC=$COCH_3$) and as a solution in methanol showed a band at λ_{max} 250 mμ (log ϵ 4.22).

Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.39; H, 6.52; N, 5.32, 5.37.

In deuteriochloroform solution, this compound showed nmr signals at 2.2–3.2 (5 H, complex, positions 1,2,6), 3.64 (3H, s, CH_3O), 4.40 (2 H, d, J = 6 cps, $ArCH_2$), 5.27 (1 H, s, C=C—H), 6.71 (1 H, broad s, NH), and 7.23 ppm (5 H, s, aromatic H's).

6-Benzyl-3-oxo-6-azabicyclo[3.2.1]octane (VIII).—A solution of N-benzyl-3-methoxy-5-oxo-3-cyclohexenecarboxamide (VI, 17.0 g or 0.065 mol) in 350 ml of dry tetrahydrofuran was slowly added to a stirred slurry of lithium aluminum hydride (9.88 g or 0.26 mol) in 150 ml of dry tetrahydrofuran. After a 14-hr period of refluxing and stirring, the cooled reaction mixture was treated with 50 ml of 10% sodium hydroxide solution. The organic layer was filtered, and the solids were washed with tetrahydrofuran. The combined filtrate and washings were dried, and all solvent was removed. The residual oil (15.0 g), cooled in an ice bath, was mixed with 20 ml of 25% sulfuric acid. After 1.5 hr of stirring, the mixture was filtered through glass wool, and the filtrate was made strongly basic with 10% aqueous sodium hydroxide (cooling). The alkaline mixture, containing a white precipitate, was extracted with ether, which was then washed twice with water and dried.

(9) We acknowledge the help of the National Science Foundation which, under Research Equipment Grant GP 3618, provided funds for the purchase of this instrument.

Removal of all ether left 14.0 g of an oil, which as a solution in 25 ml of warm benzene, was placed on a 3.3 × 9.8 cm column of neutral 200 mesh alumina. More benzene (200 ml) was passed through the column. Stripping all solvent from the combined eluates left a semisolid mass, which on crystallization from ether–petroleum ether (bp 38–51°) afforded 7.3 g (52% from enol ether VI) of 6-benzyl-3-oxo-6-azabicyclo[3.2.1]octane (VIII) as shiny white flakes, mp 81–82°. A chloroform solution of this material showed an infrared absorption peak at 1715 cm^{-1} (cyclohexanone carbonyl) but nothing attributable to NH or OH. No obvious absorption maxima were noted between 200 and 350 mμ in a 95% alcohol solution.

Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.17; H, 7.86; N, 6.41.

Bicyclo compound VIII in deuteriochloroform showed nmr signals at 1.80–2.10 (2 H, complex, CH_2 at position 8), 2.24 (1 H, d, J = 3 cps, position 1), 2.42 (4 H, complex, positions 2 and 4), 2.75 (2 H, s, position 7), 3.30 (1 H, broad, position 5), 3.72 (2 H, s, $ArCH_2$), and 7.22 ppm (5 H, s, ArH's).

Picrate of 6-Benzyl-3-oxo-6-azabicyclo[3.2.1]octane (VIII).—Mixing a hot solution of the azabicyclooctane VIII (0.5 g) in ether (30 ml) with picric acid (0.53 g) in ether (40 ml) produced an immediate separation of yellow crystals. Four crystallizations from methanol gave the shiny yellow, needlelike picrate, mp 157–158°.

Anal. Calcd for $C_{20}H_{20}N_4O_8$: C, 54.06; H, 4.54; N, 12.61. Found: C, 54.28; H, 4.80; N, 12.71.

Ring Opening of Bicyclic Compound VIII with Acetic Anhydride.—The bicyclic amino ketone VIII (5.0 g) was exposed for 10 min to boiling acetic anhydride (6 ml) under nitrogen. Distilled water (50 ml) was added to the cooled mixture, which was then extracted with chloroform. The chloroform solution was washed with water, dried, and warmed *in vacuo* to remove all volatile material. The gummy residue (5.1 g), largely a single product according to thin layer chromatography (two minor spots other than the main spot were evident), could not be induced to crystallize. Attempts at sublimation (175° at 0.05 mm) led only to decomposition.

All of the properties are consistent with acetyl derivative IX. The material did not dissolve in dilute hydrochloric acid. Its infrared absorption spectrum (chloroform solution) showed peaks at 1640 (acetyl carbonyl) and 1680 cm^{-1} (α,β-unsaturated carbonyl). The ultraviolet absorption spectrum, taken with a solution in 95% ethanol, indicated absorption maxima at 217 mμ (log ε 4.33) and 223 mμ (log ε 3.12). A 15% solution in carbon tetrachloride was prepared for the nmr spectrum: 2.02 (3 H, s, CH_3CO), 2.10–3.00 (5 H, complex, saturated ring CH's), 3.25 (2 H, complex, CH_2N), 4.53 (2 H, s, $ArCH_2$), 5.86 (1 H, J = 10 cps =CH—CO), 6.67–7.05 (1 H, complex, —CH=), and 7.21 ppm (5 H, s, ArH's).

The 2,4-dinitrophenylhydrazone of acetyl derivative IX was crystallized from ethyl acetate–ethanol to give shiny orange crystals, mp 178–179°.

Anal. Calcd for $C_{22}H_{23}N_5O_5$: C, 60.40; H, 5.30; N, 16.01. Found: C, 60.62; H, 5.25; N, 16.04.

Hydrochloride of 6-Benzyl-6-azabicyclo[3.2.1]octane (X).—A mixture of keto compound VIII (1.0 g or 4.7 mol) and 99–100% hydrazine hydrate (1.7 g) was boiled for 2 hr. Ethylene glycol (10 ml) plus potassium hydroxide (1.0 g) was added, and the mixture was slowly distilled until the inside temperature was *ca.* 200°. This solution was then boiled for 24 hr.

The cooled reaction mixture was poured into water, and the product was collected by ether extractions. The combined extracts were washed once with water, dried, and then warmed to remove all solvent. The orange residual gum (*ca.* 1.0 g) as a solution in 5 ml of benzene was placed on a 1.5 × 4.4 cm column of neutral alumina (200 mesh), which was then washed with more benzene until the emergent liquid was no longer yellow. The chromatography was repeated. Removal of solvent left a colorless gum (0.47 g), with no infrared absorption attributable to carbonyl or to NH. A 1% solution in deuteriochloroform gave the following nmr signals: 1.28 (10 H, s, cyclohexane H's), 2.47 (2 H, d, J = 4 cps CH_2N), 3.77 (2 H, s, $ArCH_2$), and 7.28 ppm (5 H, s, ArH's).

Treating a cold ethereal solution (1 ml) of the gum with hydrogen chloride produced a white precipitate, which was collected, washed with ether, and recrystallized from ethanol–ether (1:7). The hydrochloride of 6-benzyl-6-azabicyclo[3.2.1]octane (X) was obtained in 43% yield (0.47 g) as shiny, colorless leaflets, mp 217–218°. The mineral oil mull of this material revealed infrared absorption peaks at 2790, 2750, 2595, 2445, 2405, 750, and 695 cm^{-1}.

Anal. Calcd for $C_{14}H_{20}ClN$: C, 70.78; H, 8.43; Cl, 14.94; N, 5.89. Found: C, 71.06; H, 8.71; Cl, 14.85; N, 5.84.

Hydrochloride of 6-Benzyl-6-azabicyclo[3.2.1]octane (X) by Benzylation of 6-Azabicyclo[3.2.1]octane (XIII).—Catalytic hydrogenation of *m*-aminobenzoic acid gave a mixture of *cis*- and *trans*-3-aminocyclohexanecarboxylic acid, mp 270–282°. The melting point reported before was 264°.[10] Pyrolysis[2] at 305–312° produced a mixture, from which after extensive purification, 7-oxo-6-ababicyclo[3.2.1]octane (XII) could be obtained in low yield as waxy prisms, mp 197–199°. A chloroform solution showed infrared absorption maxima at 3460 and 1689 cm^{-1}. The melting point reported before for this lactam is 198–199°.[2] Reduction with lithium aluminum hydride[2] converted the lactam into 6-azabicyclo[3.2.1]octane (XIII) showing the expected NH absorption peak (3378 cm^{-1} in chloroform), but no absorption in the carbonyl region.

A solution of 6-azabicyclo[3.2.1]octane (XIII, 45 mg or 0.41 mmol) in 10 ml of ether to which benzyl chloride (133 mg or 0.41 mmol) in 10 ml of ether had been added was allowed to stand for 24 hr. A 15-min period of boiling produced a solid, which was discarded. Concentrating the pale green filtrate deposited a semisolid, which was dissolved in 4 ml of ethanol and treated with decolorizing charcoal. A white precipitate was obtained when the alcoholic solution was concentrated to *ca.* 1 ml and then flooded with 7 ml of ether. Two crystallizations from ethanol–ether (1:10) afforded the hydrochloride of 6-benzyl-6-azabicyclo[3.2.1]octane (X), which melted alone at 216–219° and, when mixed with the same material described above, at 217–219°. The infrared absorption spectra of the two samples mulled with mineral oil were superposable.

N-Benzyl-3,5-dioxo-4-bromocyclohexanecarboxamide (XIV).—A mixture of N-benzyl 3,5-dioxocyclohexanecarboxamide (V, 2.0 g or 8.0 mmol) and glacial acetic acid was held at 100° until a clear solution resulted. Sodium acetate trihydrate (1.08 g or 8.0 mmol) was added to the cooled solution. Then bromine (0.43 ml or 8.0 mmol) in 10 ml of acetic acid was added to the stirred mixture at 15° over a period of 5 min. A colorless solid precipitated. After stirring for an additional 0.5 hr, 100 ml of water was added, and the solid was collected on the funnel, washed with water, and dried *in vacuo*. This material, the desired product XIV, weighed 2.0 g (75%) and showed mp 175°. Crystallization from acetone–tetrahydrofuran gave mp 180–182°.

Anal. Calcd for $C_{14}H_{14}BrNO_3$: C, 51.88; H, 4.35; Br, 24.66; N, 4.32. Found: C, 52.00; H, 4.43; Br, 24.90; N, 4.11.

The infrared spectrum of compound XIV in mineral oil showed peaks at 3195, 1645, and 1610 cm^{-1}. In a 6.3 × 10^{-5} M ethanolic (95%) solution, the compound had an absorption maximum at 276 mμ (log ε 4.04). A 2% solution in deuterated dimethyl sulfoxide gave signals at 2.5–3.0 (5 H, complex, cyclohexane H's), 4.21 (2 H, d, J = 6 cps, $ArCH_2$), 6.4 (poor integration, broad, NH), 7.19 (5 H, s, ArH's), and 7.9 ppm (1 H, broad, enol OH).

N-Benzyl-3-methoxy-4-bromo-5-oxo-3-cyclohexenecarboxamide (XV).—This enol ether XV was formed from the corresponding dioxo compound XIV essentially according to the directions given for the bromine-free compound VI. The crystalline product, as it deposited from the reaction mixture (8.75 g or 65%), showed mp 199–203°. Recrystallization from methanol gave the analytically pure bromo enol ether XV as needles, mp 205–206°.

Anal. Calcd for $C_{15}H_{16}BrNO_3$: C, 53.25; H, 4.76; Br, 23.62; N, 4.14. Found: C, 53.12; H, 4.82; Br, 23.47; N, 3.95.

As a 6 × 10^{-5} M solution in 95% ethanol, the bromo enol ether XV had an absorption maximum at 277 mμ (log ε 4.08); as a mull with mineral oil, it showed peaks at 3333, 1642, 1565, and 1538 cm^{-1}. A 2–3% solution in deuterated dimethyl sulfoxide showed nmr signals at 2.1–3.2 (5 H, complex, cyclohexane H's), 3.55 (3 H, s, OCH_3), 4.20 (2 H, d, J = 6 cps, $ArCH_2$), 6.4 (poor integration, broad, NH), and 7.18 ppm (5 H, s, ArH's).

Reduction[7] of N-Benzyl-3-methoxy-4-bromo-5-oxo-3-cyclohexenecarboxamide (XV).—Sodium borohydride (2.85 g or 75 mmol) was added over a 10-min period to a stirred suspension of bromo enol ether XV (5.0 g or 15 mmol) in methanol (200 ml) cooled in an ice bath. Solution was complete in an hour. After 1 day of stirring, the reaction mixture was poured into 20 ml of sulfuric acid diluted with 40 ml of water and containing ice.

(10) J. P. Grunstein and J. Wyman, Jr., *J. Amer. Chem. Soc.*, **60**, 2341 (1938).

After 2 hr, solid sodium carbonate was added until all the acid was neutralized, and the mixture was then evaporated to dryness. The residue, treated with 100 ml of water, was extracted with three 50-ml portions of chloroform. The chloroform extracts were washed with water, dried, and warmed to remove all volatile material. The residue was a viscous oil (4.0 g), which could be resolved into two spots (R_f 0.54 and 0.83) on a thin-layer alumina chromatogram with benzene–chloroform (1:1) as the developing solvent. The oil was chromatographed through a 2.2 × 8.6-cm column of neutral alumina prepared from a slurry in benzene–chloroform (1:1). The elution solvents were 50 ml of benzene–chloroform (1:1), 25 ml of benzene–chloroform (1:4), 40 ml of ether–chloroform (1:1), 60 ml of chloroform, and 100 ml of chloroform–methanol. Fractions were monitored by thin-layer chromatography. A clean separation was effected, with the material with R_f 0.53 coming out in the earlier fractions and the material with R_f 0.83 coming out in the later fractions.

The R_f 0.53 material (0.4 g of crystals) was recrystallized three times from chloroform–petroleum ether to give white crystals, mp 124–126°. A mull with mineral oil gave infrared absorption maxima at 3279, 1634, 1538, 1269, and 1242 cm^{-1}. Ultraviolet absorption in the 200–350 mμ region was nil. The sample for analysis, recrystallized further from chloroform–petroleum ether, had mp 125–127°.

Anal. Found: C, 64.44, 64.60; H, 7.00, 7.13; Br, 5.94, 6.19; N, 4.84, 4.65.

The R_f 0.84 material (2.8 g of an oil) was brought out of benzene diluted with ether to give 2.2 g of white crystals XX. Three recrystallizations from acetone–ether furnished material with mp 135–136°.

Anal. Calcd for $C_{15}H_{20}BrNO_3$: C, 52.44; H, 5.97; Br, 23.35. Found: C, 52.38; H, 5.92; Br, 23.42.

A mull in mineral oil gave infrared absorption bands at 3344, 1631, and 1541 cm^{-1}. No ultraviolet absorption was detected between 200–350 mμ. A 3% solution of the borohydride reduction product XX in deuteriochloroform showed nmr signals at 1.7–2.7 (7 H, complex, cyclohexane ring H's), 3.13 (1 H, broad, OH), 3.37 (3 H, s, OCH_3), 4.42 (2 H, d, J = 4 cps, $ArCH_2$), 4.78 (1 H, complex, BrCH), 6.08 (1 H, broad, NH), and 7.27 ppm (5 s, H, ArH's).

Registry No.—IV, 16607-44-6; V, 16607-45-7; VI, 16607-46-8; VIII, 16607-47-9; VIII picrate, 16622-57-4; IX, 16607-48-0; IX 2,4-dinitrophenylhydrazone, 16607-49-1; X, 16607-51-5; X HCl, 16607-50-4; XIV, 16607-52-6; XV, 16607-53-7; XX, 16607-54-8.

Nuclear Magnetic Resonance of 1-Methylimidazole Methiodide. A Correction

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In the course of our studies in imidazoles, we reinvestigated the nmr spectrum of 1-methylimidazole methiodide (**1**), which had been reported in 1965.[1] In contrast to the earlier paper, we have now found that the aromatic protons at C-4 and C-5 absorb at a lower field (H-2, τ 1, 22 ppm, s, broad; H-4,5, τ 2.47 ppm, d, J = 1.7 Hz; in water, DSS = 10) than in 1-methylimidazole itself (2.59, 3.14, and 2.95 ppm; in $CDCl_3$, TMS = 10).[2] The chemical shifts of the corresponding protons in pilocarpine methiodide (τ 1.27 and 2.55 ppm in water) are of the same order. These data are in accord with a report of Mannschreck, *et al.*,[3] that the aromatic protons of imidazole are shifted downfield when the nitrogen is protonated in strong acids. Further we succeeded in splitting the N-methyl signal of **1** into a doublet with $J_{NCH_3,H\text{-}2}$ = 0.45 Hz as anticipated by Mannschreck.[3] The coupling between the N-methyl group and H-2 was confirmed by double resonance.

Registry No.—**1**, 16727-92-7.

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Ozonations of Olefinic Ferrocenes[1]

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The relative ease with which ferrocene may be oxidized presents serious difficulties in projected oxidative transformations of ferrocene derivatives. Thus, for example, in our laboratory we have tried a number of well-established procedures for carbon–carbon double-bond cleavage only to find that destruction of the ferrocene nucleus also occurred. In this Note, we report the results of our study on the ozonation of a series of model olefinic ferrocenes.

Our successful ozonation technique lay in the careful treatment of the olefinic ferrocene with the exact molar equivalent of ozone required for reaction with the alkenyl linkage. For this purpose preparation and use of standardized solutions of ozone in anhydrous ether was found to be satisfactory.

With the monosubstituted olefin, vinylferrocene (**1**), ozonization proceeded smoothly, giving hydroxymethylferrocene (**2**) in 74% yield upon reduction with lithium aluminum hydride. Hydrolysis in the presence of zinc dust provided ferrocenecarboxaldehyde (**3**) in 32% yield, while use of the trimethyl phosphite work-up procedure gave the aldehyde in 85% yield. Three examples of disubstituted olefinic ferrocenes were investigated. Lithium aluminum hydride treatment of the ozonization mixture obtained from 1-ferrocenyl-1-phenylethene (**4**) gave ferrocenylphenylcarbinol (**5**) in 51% yield. Benzoylferrocene (**6**) was produced by hydrolysis and by reaction with trimethyl phosphite in yields of 42 and 45%, respectively. Hydride reduction of the mixture obtained from ozonization of cinnamoylferrocene (**7**) gave the new glycol, 1-ferrocenyl-1,2-dihydroxyethane (**8**), in 36% yield, but no ferrocene compound could be detected after the zinc–water treatment

(1) (a) Taken in part from the dissertation submitted by W. D. L. to the Graduate School, University of South Carolina, May 1967, in partial fulfillment of the requirements for the Master of Science degree. (b) For a previous paper related to the present work, see S. I. Goldberg, W. D. Loeble, and T. T. Tidwell, *J. Org. Chem.*, **32**, 4070 (1967).