3-Methylpyrazolo[1,2-*a*]pyridazin-1-one. Selenium Derivatives of 5,8-Dihydropyrazolo[1,2-*a*]pyridazine.

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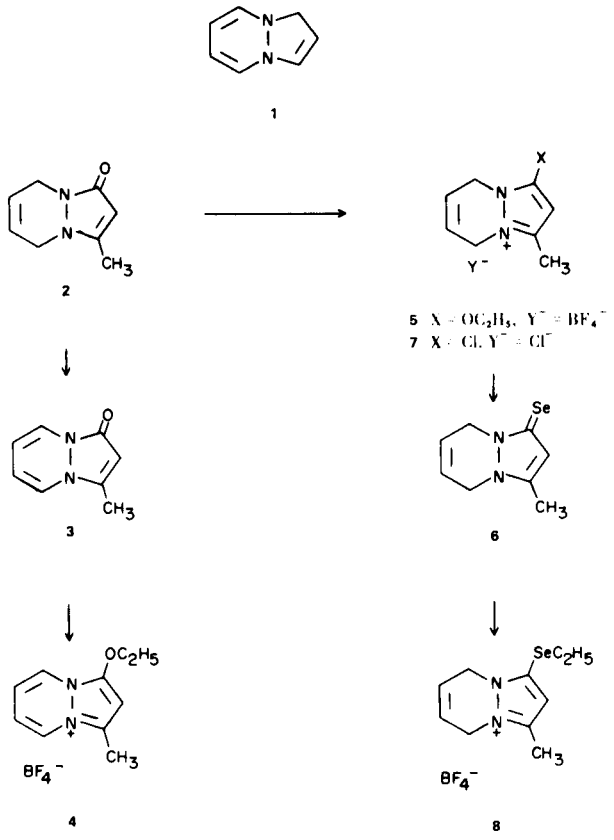
The dehydrogenation of the known 3-methyl-5,8-dihydropyrazolo[1,2-*a*]pyridazin-1-one (**2**) to the ten π electron heteroaromatic 3-methylpyrazolo[1,2-*a*]pyridazin-1-one (**3**) is reported. Conversions of the pyrazolone **2** to the pyrazoloselenone **6** *via* the chloropyrazolium chloride **7**, and of pyrazolones **2** and **3** and pyrazoloselenone **6** into the corresponding O or Se ethyl pyrazolium fluoroborates **5**, **4**, and **8** by triethyloxonium fluoroborate are also described.

Our continuing interest in the pyrazolo[1,2-*a*]pyridazine system (**1**) (1) led us to consider the known 3-methyl-5,8-dihydropyrazolo[1,2-*a*]pyridazin-1-one (**2**) (2) as a possible precursor. Although the desired conversion was not accomplished, we report here some interesting reactions of the pyrazolone **2** and its novel ten π electron heteroaromatic dehydrogenation product, 3-methylpyrazolo[1,2-*a*]pyridazin-1-one (**3**).



Several attempts were made to dehydrogenate pyrazolone **2** to dehydropyrazolone **3**. Selenium dioxide in a variety of solvents was without effect, while chloranil led to intractable material. However, palladium on charcoal in boiling chlorobenzene afforded dehydropyrazolone **3** as light yellow needles, m.p. 115-118° in modest yield.

The ir and nmr spectra of the product (see Experimental) confirmed its structure, but provided no help in determining the extent of aromaticity as compared with **2**. The compound was rather unstable, although it could be stored in the refrigerator for one month before decomposition became appreciable. Numerous attempts to reduce the carbonyl group of dehydropyrazolone **3** to a methylene group by metal hydrides led to overreduction as evidenced by the disappearance of the vinyl hydrogens in the nmr. Similar results were obtained for the *O*-ethylpyrazolium tetrafluoroborate **4**, obtained from **3** by treatment with Meerwein's reagent (3). Reduction of the double bonds also occurred when pyrazolone **2** or its *O*-ethyl derivative **5** were used as model compounds to explore possible methods for the reduction of the carbonyl function to a methylene group, so this approach was finally abandoned.

During our efforts to reduce the carbonyl group of **2** to a methylene group, an unexpected sequence of reactions resulting in the formation of the selenium derivative **6** was encountered. Pyrazolone **2** could be converted to the chloropyrazolium chloride **7** easily with phosphorus oxychloride. It was our intent to dehydrogenate **7**, then reduce the halogen function to a methylene group. In an effort to realize this intent, **7** was treated with selenium dioxide in water, then with sodium borohydride without isolation of intermediates. The product obtained was a selenium containing substance whose ir, nmr, and mass spectra were in accord with the proposed pyrazoloselenone structure **6**. This product obviously had arisen by reaction

of the chloropyrazolium chloride **7** with selenide or hydroselenide ion generated by borohydride reduction of the selenium dioxide, and could be prepared more directly using sodium hydroselenide in water.

Selenium derivatives of pyrazoles and other heterocycles have been commonly described in the early literature (4). Only recently, however, has there appeared to be a revival of interest in selenium derivatives of carbonyl compounds (5). Our pyrazoloselenone **6** could be converted smoothly to the Se-ethylpyrazolium tetrafluoroborate **8** with Meerwein's reagent. An attempt to carry out a similar sequence of reactions with the dehydropyrazolone **3** aborted with the failure to obtain a characterized chloropyrazolium chloride from **3** with phosphorus oxychloride.

EXPERIMENTAL

Melting points were determined in open capillaries on a Thomas-Hoover melting point bath or a Fisher-Johns block and are uncorrected. Infrared spectra were recorded using a Perkin-Elmer Infracord Model 137. Nmr spectra were obtained on a Varian A-60 or JEOLCO C-60H spectrometer with TMS as an internal standard. Mass spectra were determined on a Perkin-Elmer Hitachi RMU-6 spectrometer. Ultraviolet data were recorded on a Beckman DK spectrophotometer. Analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Michigan.

3-Methyl-5,8-dihydropyrazolo[1,2-*a*]pyridazin-1-one (**2**).

The title compound was prepared by a procedure similar to that described by Gillis and Weinkam (2). Methylpyrazolin-5-one (19.6 g., 0.20 mole) was added to a methylene chloride solution saturated with butadiene at $-10°$. Lead tetraacetate (92 g., 0.21 mole) was added in portions with stirring over a period of 20 minutes. The reaction mixture was stirred at $-10°$ until it gave a negative potassium iodide paper test (>4 hours). The insoluble lead diacetate was filtered and washed several times with methylene chloride. The methylene chloride was washed with a saturated solution of sodium bicarbonate until the washings were basic. After drying over anhydrous sodium sulfate, the solvent was removed. The dark red viscous residue crystallized on cooling. Recrystallization from ether gave 8.4 g. of light-brown crystals (28%), m.p. 51-53°; ir (chloroform) 1625 cm^{-1}; nmr (deuteriochloroform) τ 3.8 (broad s, 2H, $H_{6,7}$), 4.6 (s, 1H, H_2), 5.9 (broad m, 4H, $H_{5,8}$), 7.9 (s, 3H) (6); uv λ max (methanol) 207 (ϵ = 4070), 257 mμ (ϵ = 7780).

Anal. Calcd. for $C_8H_{10}N_2O$: C, 63.98; H, 6.71; N, 18.65; MW 150. Found: C, 63.88; H, 6.65; N, 18.61; MW 150 (parent peak, mass spectrum).

1-Chloro-3-methyl-5,8-dihydropyrazolo[1,2-*a*]pyridazinium Chloride (**7**).

In a procedure analogous to that described by Clemo and Holmes (7), 3-methyl-5,8-dihydropyrazolo[1,2-*a*]pyridazin-1-one (1.0 g., 6.7 mmoles) and phosphorus oxychloride (8 ml.) were heated in a sealed tube at 170° for 6 hours. Excess phosphorus oxychloride was removed by washing several times with carbon tetrachloride. Treatment of the residual dark oil with hexamethylphosphoramide yielded a grey solid which was recrystallized from dry nitromethane to give 0.62 g. of an off-white solid (42%), m.p. 227-229°; ir (Nujol) 3335, 1667, 1535 cm^{-1}; nmr (formic acid) τ 3.3 (s, 1H, H_2), 3.9 (broad s, 2H, $H_{6,7}$), 5.2 (broad s, 4H, $H_{5,8}$), 7.6 (s, 3H). Analysis indicated the presence of variable amounts of water which was difficult to control.

Anal. Calcd. for $C_8H_{10}Cl_2N_2 \cdot H_2O$: C, 43.07; H, 5.42; N, 12.55; Cl, 31.78. For $C_8H_{10}Cl_2N_2$: C, 46.85; H, 4.91; N, 13.66; Cl, 34.57. Found: C, 43.92, 45.84; H, 4.98, 5.44; N, 12.89, 13.14; Cl, 31.89, 32.72.

3-Methyl-5,8-dihydropyrazolo[1,2-*a*]pyridazin-1-selenone (**6**).

(a) Selenium dioxide (0.10 g., 0.94 mmole) was added to a solution of the pyrazolium chloride (**7**) (0.16 g., 0.8 mmole) in 4 ml. of water and the mixture was heated at 75-80° for 30 hours. After cooling to room temperature, ether (10 ml.) was added and sodium borohydride (0.061 g., 1.6 mmoles) was added in small portions with stirring. After the mixture was stirred overnight, the ether layer was separated and the aqueous part extracted with ether. Removal of the ether gave 0.095 g. of the selenone (57%), m.p. 170-172°. Recrystallization from ethyl acetate gave the selenone as straw-colored needles, m.p. 170-172°; ir (chloroform) 1535 cm^{-1}; nmr (deuteriochloroform) τ 3.7 (s, 1H, H_2), 4.0 (broad s, 2H, $H_{6,7}$), 5.5 (broad d, 4H, $H_{5,8}$), 7.8 (s, 3H); uv λ max (methanol) 300 mμ (ϵ = 7990), 213 mμ (ϵ = 7990).

Anal. Calcd. for $C_8H_{10}N_2Se$: C, 45.08; H, 4.73; N, 13.14; Se, 37.05; MW, 214. Found: C, 45.34; H, 4.89; N, 12.94; Se, 36.81; MW, 223 (osmometric in chloroform); mass spectrum: 214 (parent peak), 216, 212, 211 and 210 with relative intensities 3.4:1:2:1.2:1.1.

(b) Sodium borohydride (61 mg., 1.6 mmoles) was added in portions to a stirred solution of selenium dioxide (100 mg., 0.94 mmole) in 3 ml. of water. An instantaneous reaction occurred with gas evolution. The pyrazolium chloride (160 mg., 0.8 mmole) was added to the brown-red solution after 20 minutes. After three hours at room temperature, the greyish insoluble material was filtered and the aqueous solution was extracted six times with chloroform. After washing with water and drying over anhydrous sodium sulfate, the solvent was removed. The crystalline residue was recrystallized from ethyl acetate to give 25 mg. (15%) of straw-colored needles, m.p. 167-170°. The mixed melting point with the selenone obtained in (a) was undepressed.

The aqueous solution on removal of water *in vacuo* yielded 120 mg. of a white powder, m.p. >300°. An nmr spectrum of the sample in deuterium oxide showed absorptions at τ 3.1, 3.7, 5.05 and 7.4 identical with those for the starting material.

(c) Hydrogen selenide was generated by dropwise addition of dilute sulfuric acid to 1.0 g. of powdered aluminum selenide in an atmosphere of nitrogen and bubbled into a solution of sodium bicarbonate (380 mg., 4.5 mmoles) in 15 ml. of deoxygenated water at 0°. The pyrazolium chloride (500 mg., 2.5 mmoles) in 5 ml. of water was added to the solution of sodium hydrogen selenide and stirred overnight. After filtration from selenium metal, the aqueous solution was extracted with four 10 ml. portions of chloroform. The organic extract was washed with water and dried over anhydrous sodium sulfate. Removal of the solvent and drying of the residue in a vacuum desiccator yielded 375 mg. (70%) of product, m.p. 165-170°. Recrystallization from ethyl acetate gave 339 mg. of the pure selenone, m.p. 168-170°. The mixed melting point with material obtained in (a) was undepressed.

1-Ethylseleno-3-methyl-5,8-dihydropyrazolo[1,2-*a*]pyridazinium Tetrafluoroborate (**8**).

Meerwein's reagent (7) (0.15 g., 0.8 mmole) was added to a stirred solution of pyrazoloselenone **6** (213 mg., 1 mmole) in 5 ml. of dry methylene chloride. After it was stirred for four hours, the methylene chloride was removed and the crude solid was recrystallized from ethyl acetate-ethanol. A mixture of colorless needles and yellow crystals was obtained. A mixed melting point of the two crystal forms gave no depression and their ir and nmr spectra were identical. An analytical sample obtained after four recrystallizations had m.p. 81-82°; nmr (deuteriochloroform) τ 3.35 (s, 1H, H_2), 3.84 (s, 2H, $H_{6,7}$), 5.2 (m, 4H, $H_{5,8}$), 6.9 (q, 2H, $-SeCH_2-$), 7.55 (s, 3H), 8.55 (t, 3H, CH_3 on ethyl); ir (chloroform) 1540, 1449, 1408, 1087-1030 cm^{-1}.

Anal. Calcd. for $C_{10}H_{15}N_2Se\cdot BF_4$: C, 36.50; H, 4.60; N, 8.51. Found: C, 36.59; H, 4.50; N, 8.37.

3-Methylpyrazolo[1,2-a]pyridazin-1-one (**3**). Dehydrogenation of Pyrazolone **2**.

Many attempts to dehydrogenate pyrazolone **2** were made. Reactions were monitored by looking for the change in the vinyl proton region of the nmr spectrum of the mixtures. Selenium dioxide in boiling chloroform or acetic acid, and chloranil in boiling xylene gave no change. Palladium on charcoal in boiling decalin gave an insoluble resinous product. The following procedure using palladium on charcoal in boiling chlorobenzene proved moderately satisfactory.

A mixture of the pyrazolone **2** (2.0 g., 0.013 mole) and 10% palladium on charcoal (1.5 g.) in chlorobenzene (40 ml.) was boiled under reflux for 40 hours, then filtered free from the catalysts while still hot. After removal of the chlorobenzene *in vacuo*, the residue was recrystallized from dry ether to give yellow needles (0.35 g., 17%). An analytical sample was prepared by three recrystallizations from acetone-hexane, m.p. 115-117°; ir (chloroform) 1630, 1600, 1440 cm^{-1}; nmr (acetone-d_6) τ 2.4 (m, 2H, $H_{5,8}$), 4.1 (m, 2H, $H_{6,7}$), 4.5 (s, 1H, H_2), 7.7 (s, 3H); uv λ max (methanol) 238 (ϵ = 10,350), 297 (ϵ = 7030), 350 (ϵ = 874).

Anal. Calcd. for $C_8H_8N_2O\cdot\frac{1}{2}H_2O$: C, 61.13; H, 5.77; N, 17.83; MW 148 (anhydrous material). Found: C, 60.92; H, 5.77; N, 17.79; MW 148 (mass spectrum, parent peak. A weak peak at 150 was often found from contamination by starting material which was difficult to remove completely.)

1-Ethoxy-3-methylpyrazolo[1,2-a]pyridazinium Tetrafluoroborate (**4**).

A solution of triethyloxonium tetrafluoroborate (2.2 g., 12 mmoles) and pyrazolone **3** (1.2 g., 8.1 mmoles) in methylene chloride (10 ml.) was stirred at *ca.* 25° for 10 hours. The methylene chloride was removed *in vacuo* and the crude brown residue was recrystallized twice from absolute ethanol-ethyl acetate to give 1.6 g. (75%). A sample for analysis was obtained by recrystallization from absolute ethanol-ethyl acetate, m.p. 129-131°; ir (chloroform) 1590, 1560, 1070 cm^{-1}; nmr (acetone-d_6) τ 1.84 (m, 2H, $H_{5,8}$), 2.98 (s, 1H, H_2), 3.20 (m, 2H, $H_{6,7}$), 5.35 (q, 2H, $-OCH_2-$), 7.26 (s, 3H), 8.49 (t, 3H, CH_3 on ethyl).

Anal. Calcd. for $C_{10}H_{13}N_2O\cdot BF_4$: C, 45.49; H, 4.96; N, 10.61. Found: C, 45.58; H, 4.96; N, 10.42.

Attempted Reduction of 1-Ethoxy-3-methyl-5,8-dihydropyrazolo-[1,2-a]pyridazinium Tetrafluoroborate (**5**).

The pyrazolium tetrafluoroborate **5** was not purified, but was only characterized by its spectroscopic properties and used directly for reduction attempts with sodium borohydride in ethanol or diglyme, or lithium aluminum hydride in diglyme. In all cases reduction of the double bond occurred as evidenced by the nmr and ir spectra of the crude reaction products. The nmr spectrum was incompatible with the presence of a useful yield of the desired product. The following is a representative experiment.

A solution of Meerwein's reagent (2.8 g., 0.015 mole) and pyrazolone **2** (2.0 g., 0.013 mole) in methylene chloride (*ca.* 10 ml.) was refluxed for 3 hours. The nmr spectrum showed peaks at τ 3.8 (m), 5.2 (broad m), 5.6 (q), 7.5 (s), and 8.5 (t) compatible with the structure **5**. The solvent was removed *in vacuo* and a small sample of the residue was recrystallized from absolute ethanol-ethyl acetate to give crystals, m.p. 101-102°; ir (chloroform) 1575, 1520, 1460, 1075 cm^{-1} (broad, strong); nmr (deuteriochloroform) τ 3.8 (broad m, 3H, $H_{2,6,7}$), 5.2 (m, 4H, $H_{5,8}$), 5.6 (q, 2H, $-OCH_2-$), 7.5 (s, 3H), 8.5 (t, 3H, CH_3 on ethyl).

The remainder of the residue was dissolved in absolute ethanol (10 ml.), brought to 0°, and sodium borohydride (1.3 g.) was carefully added in small portions. The mixture was stirred 16 hours at room temperature, then poured into 40 ml. of water and extracted with chloroform. The chloroform solution was evaporated to dryness on a rotary evaporator and the residue (*ca.* 0.5 g.) (ir (chloroform) 1650, 1625 cm^{-1}; nmr (chloroform) τ 4.6, 6.3-8.5 (many peaks), 8.8 (d) as well as peaks characteristic of pyrazolone **2**) was taken up in 5 ml. of 95% ethanol and treated with 5 ml. of ethanol saturated with picric acid. The yellow, crystalline precipitate was recrystallized three times from ethanol to give yellow needles, m.p. 147-149°.

Anal. Calcd. for $C_{14}H_{17}N_5O_7$: C, 45.77; H, 4.67; N, 19.07. Found: C, 45.51; H, 4.12; N, 19.10.

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