Synthesis of Some Hydroxy and Methoxymethyl Derivatives of 1*H*-Pyrazolo[5,1-*c*]-1,2,4-triazoles

John D. Goddard

Research Division, Kodak Limited, Headstone Drive,
Harrow, Middlesex HA1 4TY, England

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Electrophilic hydroxylation of a pyrazolotriazole with a mixture of trifluoroacetic acid, hydrogen peroxide and boron trifluoride diethyl etherate gave a 7-hydroxypyrazolotriazole. Nucleophilic attack of methanolic hydroxide ion on a dichloropyrazolotriazole gave a 6-methoxymethylpyrazolotriazole by a mechanism involving a cyclopropane intermediate.

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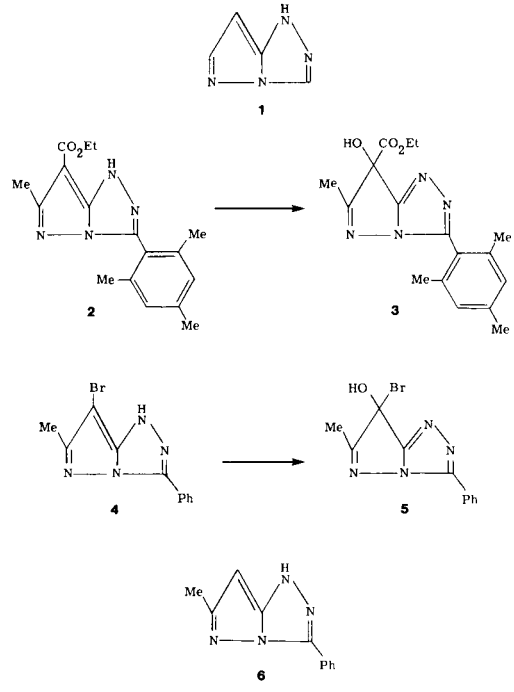
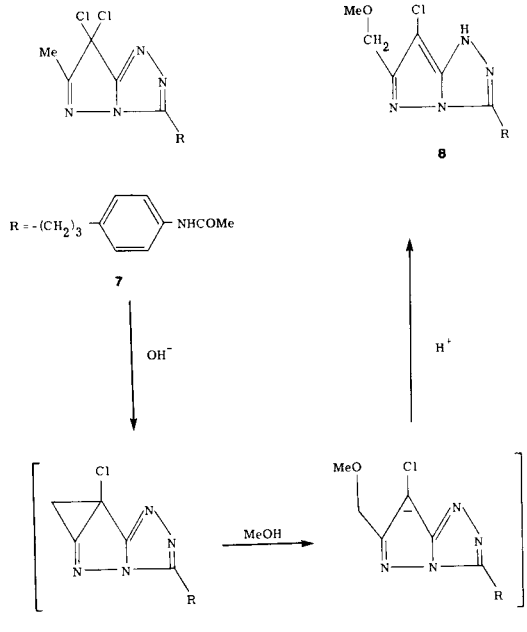
1*H*-Pyrazolo[5,1-*c*]-1,2,4-triazoles **1** are useful compounds for the preparation of colour photographic materials [1] since they can react with oxidized developers to give magenta image dyes which have low unwanted absorption [2] in the blue region of the visible spectrum.

In an effort to synthesize a variety of photographically active derivatives of the 1*H*-pyrazolo[5,1-*c*]-1,2,4-triazole nucleus, the previously unknown 7-hydroxy compounds were thought to be potentially useful intermediates. Access to these compounds has now been gained by electrophilic hydroxylation of ethyl 6-methyl-3-(2,4,6-trimethylphenyl)-1*H*-pyrazolo[5,1-*c*]-1,2,4-triazol-7-ylcarboxylate **2** using a mixture of trifluoroacetic acid, boron trifluoride diethyl etherate and hydrogen peroxide [3], whereupon the alcohol **3** was obtained in reasonable yield. 7-Bromo-6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*]-1,2,4-triazole **4** was also hydroxylated using this reagent mixture, however, the resulting bromo-alcohol **5** was very unstable. The heterocycle which is unsubstituted in the 7-position, 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*]-1,2,4-triazole **6**, gave an intractable mixture with the hydroxylating reagent. This might have been expected in view of the oxidizing power of the medium and the potential for oxidation of the resulting 7-hydroxypyrazolotriazole.

An attempt to prepare 7-hydroxypyrazolotriazoles by the nucleophilic attack of hydroxide ion on the dichloropyrazolotriazole **7** gave interesting results. In methanolic potassium hydroxide **7** gave the 6-methoxymethyl compound **8** in good yield. This unusual product may be rationalised by a sequence (Scheme 1) involving initial deprotonation of the acidic 6-methyl group in **7** followed by the formation of a fused cyclopropane ring. Opening of the unstable, intermediate cyclopropane ring by attack with methanol then ensues favourably due to the relief of



Scheme 1



ring strain and the stability of the resulting carbanion. The sequence is completed by reprotonation to give the observed product **8**.

EXPERIMENTAL

General Procedure.

All melting points are uncorrected. Proton magnetic resonance spectra were measured with a JEOL FX-100 spectrometer at 100 MHz using tetramethylsilane as an internal reference. Chemical shifts are given in the δ scale, relative to the internal reference.

Ethyl 7-Hydroxy-6-methyl-3-(2,4,6-trimethylphenyl)-1*H*-pyrazolo[5,1-*c*]-1,2,4-triazol-7-ylcarboxylate **3**.

Trifluoroacetic acid (30 ml), 100 volume hydrogen peroxide (30 ml) and boron trifluoride diethyl etherate (30 ml) were added in turn to a well stirred solution of ethyl 6-methyl-3-(2,4,6-trimethylphenyl)-1*H*-pyrazolo-[5,1-*c*]-1,2,4-triazol-7-ylcarboxylate **2** (3.4 g, 0.011 mole) in dichloromethane (120 ml). The mixture was stirred at room temperature for 2 hours then refrigerated at 4° for 48 hours. The organic layer was separated, washed with water and dried (magnesium sulfate). The solvent was removed under vacuum to give a yellow oil which solidified to form a buff coloured solid on trituration with diethyl ether. The product was purified by recrystallization from a mixture of cyclohexane and ethyl acetate yielding 2.6 g (73%), mp 190° dec; nmr (deuteriochloroform): 1.15 (t, 3H), 2.10 (s, 6H), 2.22 (s, 3H), 2.34 (s, 3H), 4.21 (q, 2H), 7.01 (s, 2H), 8.01 (s, 1H).

Anal. Calcd. for $C_{17}H_{20}N_4O_3$: C, 62.2; H, 6.1; N, 17.1. Found: C, 61.9; H, 6.1; N, 16.9.

N-{4-[3-(7,7-Dichloro-6-methyl-1*H*-pyrazolo[5,1-*c*]-1,2,4-triazol-3-yl)trimethylene]phenyl}acetamide **7**.

N-{4-[3-(1-Acetyl-6-methyl-1*H*-pyrazolo[5,1-*c*]-1,2,4-triazol-3-yl)trimethylene]phenyl}acetamide (10.0 g, 0.030 mole) was dissolved in dry dichloromethane and dry chlorine passed through the solution for 30 minutes with stirring. The buff coloured precipitate was filtered off, washed with dichloromethane and dried under vacuum. A near quantitative yield of the product was thus obtained as its hydrochloride salt. The product was recrystallized from acetonitrile yielding 9.8 g (91%) of the free base, mp 167° dec; nmr (perdeuteriomethanol): 2.26 (s, 3H), 2.39 (m, 2H), 2.76 (s, 3H), 2.91 (m, 2H), 3.28 (m, 2H), 7.22 (d, 2H), 7.52 (d, 2H).

Anal. Calcd. for $C_{16}H_{17}Cl_2N_5O$: C, 52.5; H, 4.7; Cl, 19.4; N, 19.1. Found: C, 52.4; H, 4.8; Cl, 18.9; N, 19.2.

N-{4-[3-(7-Chloro-6-methoxymethyl-1*H*-pyrazolo[5,1-*c*]-1,2,4-triazol-3-yl)-trimethylene]phenyl}acetamide **8**.

N-{4-[3-(7,7-Dichloro-6-methyl-1*H*-pyrazolo[5,1-*c*]-1,2,4-triazol-3-yl)trimethylene]phenyl}acetamide **7** (3.23 g, 0.009 mole) was dissolved in warm methanol and mixed with a solution of potassium hydroxide (10 g) in methanol (175 ml). The mixture was heated on a steam bath for 10 minutes then stirred at room temperature overnight. Excess methanol was evaporated off under reduced pressure and the residual solution poured onto ice. The solution was neutralized with acetic acid and the resulting precipitate filtered off, washed with water and dried under vacuum at 40°. The product was obtained as fluffy white needles by recrystallization from acetonitrile yielding 2.1 g (66%), mp 155-156°; nmr (deuteriochloroform): 2.13 (s, 1H), 2.18 (m, 2H), 2.62 (m, 2H), 2.92 (m, 2H), 3.44 (s, 3H), 4.45 (s, 2H), 7.00 (d, 2H), 7.24 (d, 2H).

Anal. Calcd. for $C_{17}H_{20}ClN_5O_2$: C, 56.4; H, 5.6; Cl, 9.8; N, 19.4. Found: C, 56.5; H, 5.6; Cl, 9.5; N, 19.5.

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