PHOTOCHEMICAL SYNTHESIS OF 4-ETHOXYCARBONYL-5--HYDROXYPYRAZOLES

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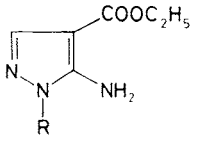
The photochemical decomposition of 4-ethoxycarbonyl-5-diazopyrazoles in tetrafluoroboric acid results in corresponding 4-ethoxycarbonyl-5-hydroxypyrazoles (*V*– *VII*). The irradiation of the diazocompound in dioxane, toluene or tetrahydrofurane proceeds with a reductive decomposition producing corresponding 4-ethoxycarbonylpyrazole (*VIII*) as the main photoproduct.

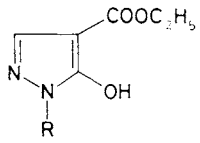
Cohen and Kirk reported a photochemical modification of the Schiemann method for synthesis of fluoroimidazoles[1]. The method involves a diazotization of aminoimidazole carboxylate with sodium nitrite in 50% tetrafluoroboric acid followed by photodecomposition of the obtained diazonium salt and results in fluoroimidazole formation in 40% yield.

We tried to apply the same procedure for preparation of 4-ethoxycarbonyl-5--fluoropyrazoles as analogs of 1-phosphoribosyl-5-aminoimidazole-4-carboxamide (AICAR) aglycone. The diazotization of the starting 5-amino-4-ethoxycarbonylpyrazoles *I*–*IV* was performed as described[1] in tetrafluoroboric acid with a solution of sodium nitrite at 0–3°C. A 80 W mercury-vapour lamp and a quartz cell placed 2 cm from the source were used in the irradiation procedure. The solutions were irradiated under argon blanket until nitrogen evolution ceased (15–30 h). However, photodecomposition of the diazonium salts of compounds *I*–*III* gave instead of expected fluoropyrazoles the corresponding hydroxy derivatives *V*– *VII* in 40–60% yield. The structure of the obtained compounds was determined by ^{1}H NMR spectra and confirmed by elemental analysis. The hydroxy protons of compounds *V*– *VII* and the imine proton of compound *V* were exchanged with deuterium by adding several drops of tetradeuterioacetic acid. The proton spectrum of *V* exhibits H-3 singlet (see Experimental), quartet of methylene protons and triplet of methyl protons, both from the ethoxycarbonyl group. The hydroxy- and imine protons occur as a broad singlet which disappear after deuterium exchange. Compounds *VI* and *VII* have similar singlets for H-3, quartets and triplets for methylene and methyl protons of ethoxycarbonyl group, as well as broad singlets for hydroxy protons.

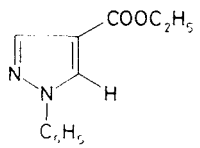
The irradiation of the diazonium salts of compounds *I*–*III* was repeated with 400 W mercury-vapour lamp with all other parameters unchanged and the only products isolated after photodecomposition were corresponding hydroxypyrazoles *V*–*VII*.



I, R = H
II, R = CH_3
III, R = CH_2CH_2OH
IV, R = C_6H_5



V, R = H
VI, R = CH_3
VII, R = CH_2CH_2OH



VIII

Similar photodecompositions were described for 4-diazo-3-cyanopyrazoles irradiated in aqueous acetone[2] as well as for 5-diazoimidazole-4-carboxamide[3]. The photodecomposition of the latter compound in spectroscopic-scale at the pH range 1–7·4 was reported to give 4-carbamoylimidazolium-5-olate, while at the same conditions the preparative-scale photolysis resulted in a product formed by coupling of 4-carbamoylimidazolium-5-olate with diazoimidazolecarboxamide, i.e. imidazolylazaimidazolium olate[3].

The failure to obtain hydroxypyrazoles *V*–*VII* via classic conversion of the diazonium salts of *I*–*III* in the presence of copper catalyst at 100°C suggests that the hydrolysis of the diazonium group is predominantly a photochemical process as far as pyrazoles and imidazoles are involved.

The diazotization of 5-amino-4-ethoxycarbonyl-1-phenylpyrazole (*IV*) resulted in a product insoluble in 30% tetrafluoroboric acid. The diazocompound was isolated and dissolved in dioxane (or some other solvent as toluene, tetrahydrofurane) and the solution irradiated under conditions described above to give 4-ethoxycarbonyl-1-phenylpyrazole (*VII*). Similar reductive decomposition was reported for diazoindazoles[4] and for 3(5)-cyano-4-diazo-5(3)-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)pyrazole[5].

Finally, we studied the diazotization of adenine and the photolysis of the resulting diazonium compound. 6-Hydroxypurine (hypoxanthine) was the main photoproduct in this case.

EXPERIMENTAL

The melting points were determined on a Kofler block and were uncorrected. Photodecomposition was followed by TLC. ^{1}H NMR spectra were recorded on Perkin–Elmer 90 MHz spectrometer in deuteriochloroform or hexadeuteriodimethylsulfoxide with tetramethylsilane as internal standard.

5-Hydroxy-4-ethoxycarbonylpyrazoles *V*—*VII*

5-Amino-4-ethoxycarbonylpyrazoles *I*—*III* (32 mmol) were dissolved in 32% tetrafluoroboric acid (125 ml), cooled to 0—3°C and treated dropwise (during 20 min) with solution of sodium nitrite (2·8 g, 41 mmol) in water (5 ml). The solution was irradiated until evolution of nitrogen ceased (18—20 h). The mixture was cooled in ice and neutralized with cold sodium hydroxide to pH 6. The solution was extracted with ethylacetate (3 × 80 ml), the combined extracts were dried over Na_2SO_4 and evaporated to dryness.

5-Hydroxy-4-ethoxycarbonylpyrazole (V), yield 50%, m.p. 181—183°C (H_2O), ref.[6] m.p. 180—181°C. ^{1}H NMR: 8·75 br, 2 H (OH, NH); 7·72 s, 1 H (H-3); 4·28 q, 2 H (CH_2); 1·33 t, 3 H (CH_3).

1-Methyl-4-ethoxycarbonyl-5-hydroxypyrazole (VI), yield 49%, m.p. 138—139°C (ethanol–ether), ref.[7] m.p. 137·5°C. ^{1}H NMR: 8·6 br, 1 H (OH); 7·58 s, 1 H (H-3); 4·35 q, 2 H (CH_2); 3·62 s, 3 H (NCH_3); 1·33 t, (CH_3).

1-Hydroxyethyl-4-ethoxycarbonyl-5-hydroxypyrazole (VII), yield 64%, m.p. 93—95°C. For $C_8H_{12}N_2O_4$ (200·2) calculated: 47·99% C, 6·04% H, 13·99% N; found: 47·85% C, 6·01% H, 13·42% N. ^{1}H NMR: 7·68 s, 1 H (H-3); 5·23 t, 2 H (CH_2N); 4·25 q, 2 H (CH_2); 3·9 br, 1 H (OH); 1·32 t, 3 H (CH_3).

1-Phenyl-4-ethoxycarbonylpyrazole (*VIII*)

1-Phenyl-4-ethoxycarbonyl-5-aminopyrazole (*IV*) (7·85 g, 34 mmol) was dissolved in 32% tetrafluoroboric acid (130 ml), cooled to 0—3°C and treated dropwise (30 min) with sodium nitrite (2·8 g, 41 mmol) in water (5 ml). The precipitate obtained was isolated and dissolved in dioxane and the resulting solution was irradiated for 20 h. The reaction mixture was cooled in ice and neutralized with sodium hydroxide to pH 5·5 and extracted with ethyl acetate (3 × × 100 ml). The combined extracts were dried over Na_2SO_4 and evaporated to dryness to give 3·0 g (40%) of *VIII*, m.p. 96—98°C, ref.[8] 99—100°C. ^{1}H NMR: 8·41 s, 1 H (H-5); 8·1 s, 1 H (H-3); 7·5 m, 5 H (C_6H_5); 4·38 q, 2 H (CH_2); 1·38 t, 3 H (CH_3).

6-Hydroxypurine (*X*)

Adenine (*IX*, 3·38 g, 25 mmol) was dissolved in 32% tetrafluoroboric acid (100 ml), cooled to 0—3°C and treated dropwise during 20 min with solution of sodium nitrite (2·07 g, 30 mmol) in water (4 ml). The resulting solution was irradiated for 15 h. The mixture was cooled and neutralized with cold sodium hydroxide to pH 6. The precipitate was filtered and sublimed to give 42% of *X*, m.p. >305°C, ref. >300°C. For $C_5H_4N_4O$ (136·1) calculated: 44·12% C, 2·96% H, 41·16% N; found: 44·13% C, 2·84% H, 40·78% N. ^{1}H NMR: 8·5 br, 1 H (OH); 8·39 s, 1 H (H-2); 8·29 s, 1 H (H-8); 5·9 br, 1 H (NH).

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