A PHOTO-REARRANGEMENT OF 5-DIAZOURACIL. A CONVENIENT SYNTHESIS OF 2-OXO-4-IMIDAZOLINE-4-CARBOXYLIC ACID DERIVATIVES.[1]

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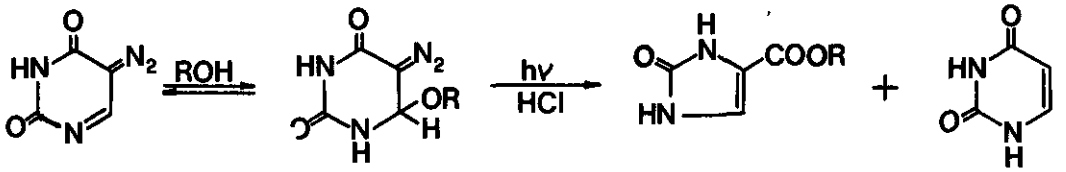
Abstract - A photochemical transformation of 5-diazouracil alcohol adducts into 2-oxo-4-imidazoline-4-carboxylates under strongly acidic conditions is described.

In the past, 2-oxo-4-imidazoline-4-carboxylic acid derivatives have been synthesized by the condensation of urea and urea derivatives with tartaric acid in fuming sulphuric acid[2] and by conversion of 5-fluorouracil derivatives in aqueous alkaline solutions[3].

On the other hand, 5-diazouracil has attracted a considerable interest because of its bactericidal[4-6] and cancerostatic activity[7,8]. Recently, the structures of 5-diazouracil, 5-diazouracil hydrate and 5-diazouracil methanol adduct and related derivatives have been reinvestigated[9-12] and some of them confirmed by X-ray analysis[13]. Conversions of 5-diazouracil into 1,2,3-triazole-4-carboxylic acid derivatives have been reported[12,14]. However, the transformation of 5-diazouracil into 2-oxo-4-imidazoline-4-carboxylic acid derivatives has not been reported so far, in spite of the fact that several other, less attractive, heterocyclic α-diazo ketones have been converted into the corresponding carboxylic acid derivatives since the Süss's first report[15,16], most probably because of the great stability of 5-diazouracil alcohol adducts under photochemical reaction conditions in neutral solutions.

In continuation of our studies on the transformation of heterocyclic α-diazo ketones[17,18] we wish to report a ring contraction of 5-diazouracil into 2-oxo-4-imidazoline-4-carboxylates under photochemical conditions in strongly acidic solutions, according to the Scheme.



I II III IV

R=H, alkyl

Scheme

When a suspension of 5-diazouracil (I) (200 mg) or 5-diazouracil hydrate (II, R=H) (200 mg) in an alcohol (20 ml) was irradiated at 254 nm in a Rayonet photochemical reactor RPR 100, the corresponding 5-diazouracil alcohol adducts (II, R=alkyl) were formed within one hour. This transformation is a thermal one, and can be followed by observing the shifting of the diazo peak in IR spectrum from ν_{N_2} = 2150 cm^{-1} for I or ν_{N_2} = 2120 cm^{-1} for II (R=H) to ν_{N_2} = 2100 cm^{-1} for II (R=alkyl). Since these adducts are insoluble in alcohol, they were isolated by filtration and characterized. The details are summarized in Table I.

Table I. 5-Diazouracil alcohol adducts (II,R=alkyl)

R	Yield[a] (%)	m.p.	Molecular formula[b]	I.R. ν_{N_2} /cm^{-1}/	^{1}H-NMR (d_6-DMSO) τ (ppm)			
					H_6	R	NH	J/Hz/
CH_3	86	195[c]	$C_5H_6N_4O_3$		4,20 (d)	6,75 (s)	1,20 (d) 0,3 (broad)	J_{H_6NH}=3,5
i-C_3H_7	85	169	$C_7H_{10}N_4O_3$	2100	4,15 (d)	6,1 /m,C<u>H</u>$(CH_3)_2$/ 8,9 /d,CH$(C\underline{H}_3)_2$/	1,3 (d) 0,3 (broad)	J_{H_6NH}=3,5 J_{CHCH_3}=6,0
n-Bu	64	136	$C_8H_{12}N_4O_3$	2100	4,20 (d)	6,5 /t,C<u>H</u>$_2(CH_2)_2CH_3$/ 8,6 /m,$CH_2(C\underline{H}_2)_2CH_3$/ 9,1 /t,$(CH_2)C\underline{H}_3$/	1,3 (d) 0,1 (broad)	J_{H_6NH}=3,5 $J_{CH_2CH_2}$=6,0 $J_{CH_2CH_3}$=6,0

a) yields of purified products are given

b) satisfactory analyses (C,H,N) were obtained for all compounds

c) Lit.[9] 198°;

By further irradiation of 5-diazouracil alcohol adducts (II,R=alkyl) elimination of nitrogen was taking place and 2-oxo-4-imidazoline-4-carboxylates (III,R=alkyl) were formed. This transformation was slow in neutral solutions. After 20 hours of irradiation only about 10-15% of the starting material was converted, yielding a mixture of the corresponding ester III and uracil (IV). On the other hand, the conversion proceeds smoothly to completion in 4-5 hours in a solution saturated with dry hydrogen chloride. The reactions were followed and the products separated by T.L.C. (Merck DC-Fertigplatten Kieselgel 60 F254 and a mixture of chloroform and methanol 6:1 as solvent was used). Besides the rearranged products (III, R=alkyl), 1-3 % of uracil (IV) as the protodediazonization product was also isolated.[19] An analogous irradiation of 5-diazouracil hydrate (II, R=H) in concentrated aqueous hydrochloric acid afforded 2-oxo-4-imidazoline-4-carboxylic acid (III,R=H). The experimental details are summarized in Table II.

Table II. 2-Oxo-4-imidazoline-4-carboxylic acid derivatives(III)

R	Yield[a] /%/	m.p.	Molecular formula[b] m/e M^+	I.R. $\nu_{C=O}$ /cm^{-1}/	^{1}H-NMR (d_6-DMSO) τ (ppm) H_5	R	NH	J/Hz/
H	65	270[c]	$C_4H_4N_2O_3$ 128					
CH_3	53	280	$C_5H_6N_2O_3$ 142	1740 1670	(d)			
CH_2CH_3	48	258[e]	$C_6H_8N_2O_3$ 156	1750 1670	2,95(d)	6,20(q,C$\underline{H}_2$CH$_3$) 8,75(t,CH$_2$C$\underline{H}_3$)	-0,5 -1,2	J_{H_5NH}=5,0 $J_{CH_2CH_3}$=6,0
n-C_3H_7	40	256	$C_7H_{10}N_2O_3$ 170	1750 1670	2,9(d)	6,20(t,C$\underline{H}_2$CH$_2$CH$_3$) 8,35(m,CH$_2$C$\underline{H}_2$CH$_3$) 9.05(t,CH$_2$CH$_2$C$\underline{H}_3$)	-1,5 -2,3	J_{H_5NH}=5,0 $J_{CH_2CH_2}$=6,0 $J_{CH_2CH_3}$=6,0
i-C_3H_7	45	248	$C_7H_{10}N_2O_3$ 170	1740 1670	2,85(s)	5,7/m,C$\underline{H}$(CH$_3$)$_2$/ 8,85/d,CH(C$\underline{H}_3$)$_2$/	-0,45 -1,1	J_{CHCH_3}=6,0
n-C_4H_9	35	236	$C_8H_{12}N_2O_3$ 184	1740	2,95(s)	6,20/t,C$\underline{H}_2$(CH$_2$)$_2$CH$_3$/ 8,50/m,CH$_2$(C$\underline{H}_2$)$_2$CH$_3$/ 9,07/t,(CH$_2$)$_3$C$\underline{H}_3$/	-0,4 -1,0	J_{H_5NH}=5,0 $J_{CH_2CH_2}$=6,0 $J_{CH_2CH_3}$=6,0

a) Yields of purified products are given

b) satisfactory analyses (C,H,N) were obtained for all compounds

c) Lit.[2] 261; d) NMR spectrum is identical with that reported in the Lit.[3]

e) Lit.[2] 255°;

The transformation is supposed to be a photo Wolff rearrangement[20] and represents a convenient one step synthesis of 2-oxo-4-imidazoline-4-carboxylates.

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19 When an aqueous solution of hydrochloric acid was used instead of dry hydrogen chloride in these experiments,a mixture of the corresponding ester (III,R=alkyl),acid (III,R=H) and traces of uracil (IV) was isolated. The ratio between the ester (III,R=alkyl) and the acid (III,R=H) was dependent on the amount of water present in the irradiated solution.

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