HETEROCYCLES, Vol 22, No 8, 1984

PHOTOCHEMICAL WOLFF REARRANGEMENT OF 5-DIAZO-6-PHENYLURACIL IN NEUTRAL SOLUTIONS. THE SYNTHESIS OF ALKYL 5-PHENYL-2-OXO-4-IMIDAZOLINE-4-CARBOXYLIC ACID DERIVATIVES

Wilhelm Klötzer* and Gerhard Dörler
Institute of Organic and Pharmaceutical Chemistry,
University of Innsbruck, A-6020 Innsbruck, Austria

and

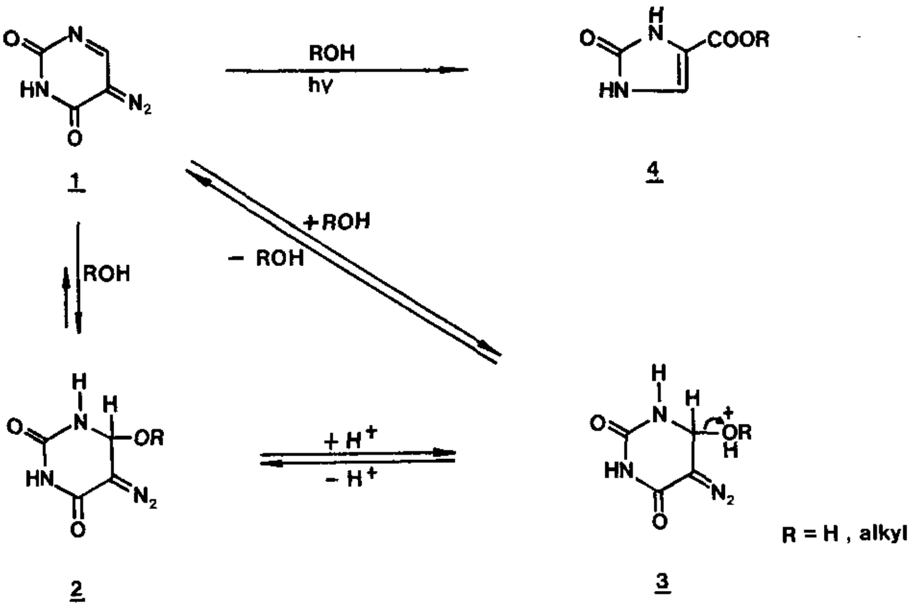
Branko Stanovnik* and Miha Tišler
Department of Chemistry, E.Kardelj University of Ljubljana
61000 Ljubljana, Yugoslavia

Abstract - A photochemical Wolff rearrangement of 5-diazo-6-phenyluracil (6), the compound which does not form the corresponding hydrate or alcohol adducts, into alkyl 5-phenyl-2-oxo-4-imidazoline-4-carboxylic acid derivatives 8a-h in neutral solutions is described.

Since the Süss's first report[1], a number of heterocyclic carboxylic acid derivatives has been prepared from heterocyclic α-diazo ketones[2] either by thermal or photochemical Wolff rearrangement[3]. Recently, indole-3-carboxylic acid derivatives[4-6], 6-substituted pyrazolo/3,2-c/-s-triazolo-7-carboxylates[7] and 5-hydroxy-1-phenylpyrazole carboxylates[8,9] in neutral solutions, and 2-oxo-4-imidazoline-4-carboxylic acid derivatives[10] and methyl 1,3-dimethyl-2-oxo-4-imidazoline-4-carboxylate[11] in strongly acidic solutions have been described[12].

As a continuation of our studies in this area we report a photochemical Wolff rearrangement of 5-diazo-6-phenyluracil (6) into 5-phenyl-2-oxo-4-imidazoline-4-carboxylic acid derivatives (8a-h).

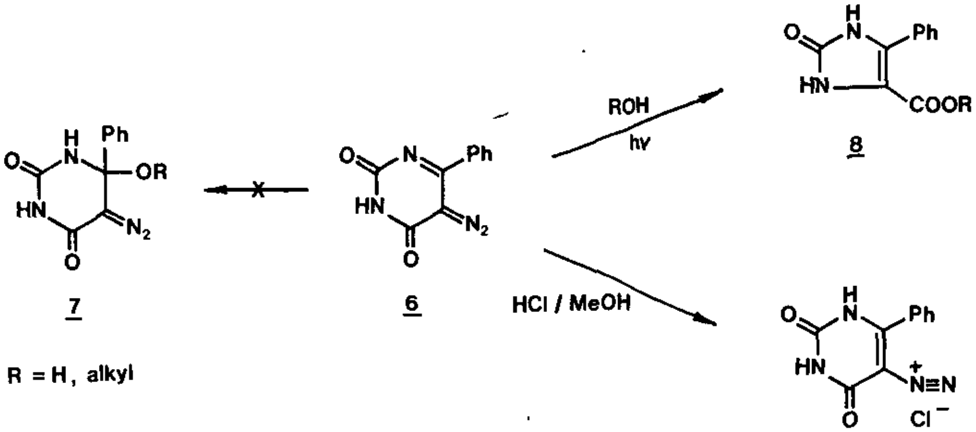
5-Diazouracil (1) and its adducts 2 have been thermally converted into 1,2,3-triazole-4-carboxylic acid derivatives[13,14]. On the other hand, the photochemical transformation into 2-oxo-4-imidazoline-4-carboxylic acid derivatives[4] in neutral solutions is not possible due to the great stability of 5-diazouracil-alcohol adducts 2. However, the photochemical Wolff rearrangement could be achieved in solutions saturated with dry hydrogen chloride[10]. The explanation for this phenomenon is that 5-diazouracil (1), which exists in neutral solutions entirely in the form of the hydrate or the corresponding alcohol adduct 2, is in strongly acidic solutions, due to protonation followed by elimination of water from the protonated form of the alcohol adduct 3, in equilibrium with the free diazo compound 1. This undergoes the photochemical Wolff rearrangement to give 2-oxo-4-imidazoline-4-carboxylic acid derivatives 4 (Scheme 1).



Scheme 1

In order to test this hypothesis, a search for a properly 6-substituted 5-diazouracil, which can not form the corresponding hydrate or alcohol adducts, has been carried out. In this connection, 5-diazo-6-phenyluracil 6 was found as an example, which fulfills this requirement. Indeed, the irradiation of 6 in aqueous acetic acid afforded the corresponding 5-phenyl-2-oxo-4-imidazoline-4-carboxylic acid 8a, while by irradiation of the compound 6 in alcohol in neutral solution the corresponding esters 8b-h were smoothly formed for a few hours in practically quantitative yields.

Unlike the unsubstituted 5-diazouracil the 6-phenyl derivative 6 is soluble in diluted aqueous hydrochloric acid and forms an isolable, though labile, hydrochloride. The ir spectrum of this salt displays a band at shorter wavelenght which is consistent with an $N\equiv N$ triple bond[15] in the diazonium salt 9. (Scheme 2).



Scheme 2

EXPERIMENTAL

Melting points were determined on a Kofler hot plate mp apparatus. ^{1}H nmr spectra recorded on a JEOL JNM C-60HL spectrometer (TMS as internal standard, δ-values in ppm), mass spectra on a Hitachi-Perkin-Elmer RMU-6L instrument, and ir spectra on a Perkin-Elmer 727B instrument. Elemental analyses (C, H, N) were obtained on a Perkin-Elmer CHN Analyser 240 C.

5-Diazo-6-phenyltetrahydropyrimidine-2,4-dione (5-Diazo-6-phenyluracil) (6)

Sodium nitrite (1.9 g, 0.0275 mole) dissolved in water (10 ml) was added during 15 min to a stirred solution of 5-amino-6-phenyluracil[16] (5.1 g, 0.025 mole) in hydrochloric acid (2N, 50 ml) at -3°C. After additional 15 min the solution was adjusted to pH 5-6 with solid sodium acetate. The resulting precipitate was isolated, washed with cold water (15 ml) and dried. Recrystallisation from methanol yielded 4.8 g (89%) of 6, mp 196-200°C, ir (KBr) 2140 ($C=\overset{+}{N}=\bar{N}$), 1750 cm^{-1} (C=O). ^{1}H nmr (DMSO-d_6) δ 7.3-7.9 (m, 5H, Ar-H), 11.56 (s, 1H exchangeable, 3-H). According to the ^{1}H nmr spectrum no trace of the methanol adducts 7 could be detected after repeated recrystallisation from methanol.
Anal.,Calcd. for $C_{10}H_6N_4O_2$: C, 56.08; H, 2.82 ; N 26.16. Found: C, 56.20; H, 3.12; N, 25.98.

Dissolving 6 in anhydrous methanolic hydrochloric acid followed by precipitation with anhydrous ether provided a colorless, water-soluble salt which slowly looses

Table I. Alkyl 5-Phenyl-2-oxo-4-imidazoline-4-carboxylic Acid Derivatives (8)

Product	R	Yield/%/a) (solvent for recrystallization)	m.p. /°C/	Molecular formula	Analysis			
						C	H	N
8a	H	79 (H_2O)	285-7	$C_{10}H_8N_2O_3$	Calcd	58.82	3.95	13.72
				(204,18)	Found	58.76	4.07	13.53
8b	CH_3	76 (MeOH:H_2O 1:1)	242-3	$C_{11}H_{10}N_2O_3$	Calcd	60.64	4.62	12.84
				(218.2)	Found	60.70	4.58	12.96
8c	C_2H_5	70 (EtOH:H_2O 2:1)	235-7	$C_{12}H_{12}N_2O_3$	Calcd	62.06	5.21	12.06
				(232.2)	Found	62.00	5.20	12.28
8d	n-C_3H_7	84 (MeOH)	222-3	$C_{13}H_{14}N_2O_3$	Calcd	63.40	5.73	11.38
				(246.3)	Found	63.21	5.44	11.63
8e	i-C_3H_7	80 (MeOH:H_2O 1:1)	218-20	$C_{13}H_{14}N_2O_3$	Calcd	63.40	5.73	11.38
				(246.3)	Found	63.49	5.72	11.68
8f	n-C_4H_9	68 (EtOH:H_2O 1:1)	185-7	$C_{14}H_{16}N_2O_3$	Calcd	64.60	6.20	10.76
				(260.3)	Found	64.53	5.83	10.72
8g	$(CH_3)_2CHCH_2$	64 (EtOH:H_2O 1:1)	228-30	$C_{14}H_{16}N_2O_3$	Calcd	64.60	6.20	10.76
				(260.3)	Found	64.53	6.42	10.72
8h	t-C_4H_9	92 (EtOH:H_2O 1:1)	266-7	$C_{14}H_{16}N_2O_3$	Calcd	64.60	6.20	10.76
				(160.3)	Found	64.24	6.39	10.73

a) Yields of purified products are given

Table II. Spectroscopic Data for Alkyl 5-Phenyl-2-oxo-4-imidazoline-4-carboxylic Acid Derivatives (**8**)

Product	IR $\nu_{C=o}$ /cm⁻1/	M. S. m/e M^+	^1H NMR(CD_3OD) δ |ppm|			
			R	Ph	NH	J|Hz|
8a	1715 1660	204	5.2(br.s)	7.45-7.65(m)	5.2(br.s)	
8b	1720 1650	218	3.50(s,CH_3)	7.45-7.55(m)	4.75(br.s)	
8c	1715 1650	232	1.0(t,$CH_2\underline{CH_3}$) 3.70(q,$\underline{CH_2}CH_3$)	7.25-7.60(m)	4.70(br.s)	$J_{CH_2CH_3}$=6.5
8d	1700 1650	246	0.90(t,CH_3) 1.80(deg tq $CH_2\underline{CH_2}CH_3$) 3.70(t,$\underline{CH_2}CH_2CH_3$)	7.40-7.60(m)	4.80(br.s)	$J_{CH_2CH_3}$=6.5 $J_{CH_2CH_2}$=6.0
8e	1700 1655	246	0.95(d,CH_3) 4.15|m,$C\underline{H}(CH_3)_2$|	7.40-7.60(m)	4.80(br.s)	$J_{CH_2CH_3}$=6.0
8f	1705 1655	260	0.90|t,$(CH_2)_3\underline{CH_3}$)| 1.90|m,$CH_2\underline{CH_2}\underline{CH_2}CH_3$| 4.20|t,$\underline{CH_2}CH_2CH_2CH_3$|	7.40-7.55(m)	4.80(br.s)	$J_{CH_2CH_3}$=6.5 $J_{CH_2CH_2}$=6.0
8g	1700 1660	260	0.75(s,CH_3) 1.90|m,$CH_2\underline{CH}(CH_3)_2$| 3.50|d,$CH_2CH(CH_3)_2$|	7.40-7.55(m)	4.75(br.s)	J_{CHCH_3} = =J_{CHCH_2}=6.0
8h	1700 1655	260	1.05(s,CH_3)	7.45-7.65(m)	4.75(br.s)	

HCl on storage in a vacuum desiccator to yield the free compound 6 again. The freshly prepared hydrochloride salt 9 showed a weak ir band (KBr) at 2140 cm^{-1} $(C=\overset{+}{N}=\overset{-}{N})$ for the already formed free compound 6 and a strong band at 2190 cm^{-1} $(C-\overset{+}{N}\equiv N)$ for the diazonium salt 9.

5-Phenyl-2-oxo-4-imidazoline-4-carboxylic acid (8a).- 5-Diazo-6-phenyluracil (6) (107 mg, 0.0005 mole) was dissolved in glacial acetic acid (2 ml) and diluted with water (18 ml). The resulting solution was irradiated in quarz tube at 300 nm in a Rayonet photochemical reactor RPR 100 until the evolution of nitrogen ceased (approx. 8 h). The mixture was evaporated in vacuo to give the crude acid 8a in practically quantitative yield. The experimental details and other data are given in the Tables I and II.

Preparation of alkyl 5-phenyl-2-oxo-4-imidazoline-4-carboxylates (8b-h). General procedure.

A solution of 5-diazo-6-phenyluracil (6) (107 mg, 0.0005 mole) in the corresponding alcohol (15 ml) in quarz tube was irradiated at 300 nm in a Rayonet photochemical reactor RPR 100 until the evolution of nitrogen ceased (8-12 h). The reaction mixture was evaporated in vacuo and the solid residue was recrystallized from an appropriate solvent to give esters 8b-h. The yields of crude products are practically quantitative. Analytical and spectroscopic data and other experimental details are given in the Tables I and II.

REFERENCES

1. O.Süss, Ann., 1953, **579**, 135.
2. For a review see: M.Tišler and B.Stanovnik, Heterocycles, 1976, **4**, 1115.
3. For reviews of the Wolff rearrangement see:
   a) Kirmse, "Carbene, Carbenoide und Carbenanaloge". Verlag Chemie, Weinheim, 1969, p. 166.
   b) M.Jones and R.A.Moss, "Carbenes",J.Wiley and Sons, New York, 1973, p. 117.

4. B.Stanovnik, M.Tišler, and J.T.Carlock, *Synthesis*, 1976, 755.

5. J.T.Carlock, J.S.Bradshaw, B.Stanovnik, and M.Tišler, *J.Org.Chem.*, 1972, **42** 1883.

6. J.T.Carlock, J.S.Bradshaw, B.Stanovnik, and M.Tišler, *J.Heterocyclic Chem.*, 1977, **14**, 519.

7. B.Stanovnik, M.Tišler, B.Kirn, and I.Kovač, *J.Heterocyclic Chem.*, 1979, **16**, 195.

8. Ger.pat. 1, 133, 386; *Chem.Abstr.*, 1962, **57**, P 13765e (1962).

9. B.Stanovnik, M.Tišler, J.Bradač, B.Budič, B.Koren, and B. Mozetič-Reščič, *Heterocycles*, 1979, **12**, 457.

10. B.Stanovnik, M.Tišler, and E.Vončina, *Heterocycles*, 1979, **12**, 761.

11. B.Stanovnik, M.Prhavc, B.Koren, and M.Tišler, *Vestn.Slov.Kem.Drus.*, 1983, **30**, 459.

12. For a review see: B.Stanovnik, *Rad Jugosl.akad.znan. i umet., kem.*, 1983, **2**, 163.

13. S.Romani and W.Klötzer, *J.Heterocyclic Chem.*, 1978, **15**, 1349.

14. T.C.Thurber and L.B.Townsend, *J.Org.Chem.*, 1976, **41**, 1041, and references cited therein.

15. M.Regitz, "Diazoalkane", Georg Thieme Verlag, Stuttgart 1977, p. 21.

16. P.Bamberg, P.Hemmerich, and H.Erlenmeyer, *Helv.Chim.Acta*, 1960, **43**, 395.

Received, 9th April, 1984