v-Triazolines; X[1]. The Permanganate Oxidation of 1-Aryl-5-(tertiary)-amino-*v*-triazolines

Luisa Maria Rossi, Pasqualina Trimarco*

Istituto di Chimica Organica della Facoltà di Farmacia, Università di Milano, Viale Abruzzi 42, I-20131 Milano, Italy

Several examples of aromatization of 4,5-dihydro-*v*-triazoles by potassium permanganate have been reported[2,3]. However, only examples with aryl and acyl substituents on the triazoline ring are known.

Owing to our interest in the synthesis of 1-aryl-5-(tertiary)-amino-*v*-triazoles[4], we attempted their preparation by permanganate aromatization of the readily available 1-aryl-5-morpholino- and -dimethylamino-4,5-dihydro-*v*-triazoles, **1a–f**.

We wish to report that this oxidation did not afford aromatization products. Instead, the corresponding 4,5-dihydro-*v*-triazoles substituted in position 5 with a 2-oxomorpholino or *N*-methyl-*N*-formylamino group, respectively, were formed in fair yield.

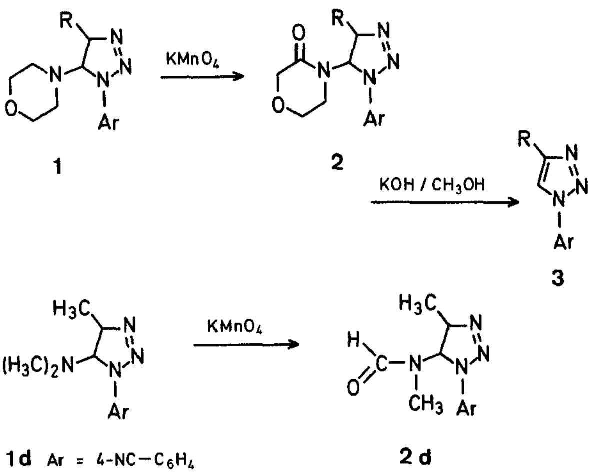

Table. *v*-Triazolines **2**

Product	R	Ar	Method	Yield [%]	m.p.[a] (solvent)	Molecular formula[b]	I.R. (nujol) ν_{max} [cm^{-1}]	^{1}H-N.M.R. (solvent) δ [ppm]	M.S.: *m/e* (relative intensity %)
2a	CH_3	4-O_2N—C_6H_4	A B	40 25	133° (ethanol)	$C_{13}H_{15}N_5O_4$ (305.3)	1640 (C=O)	C_6D_6: 0.80 (d, 3H, *J* = 7 Hz, CH_3); 1.84–2.15 (m, 2H, —CH_2—N); 2.72–3.01 (m, 2H, CH_2CH_2O); 3.64–3.98 (m, 3H, $COCH_2$ and H-4); 6.20 (d, 1H, *J* = 3 Hz, H-5)	277 (9); 249 (1); 219 (10); 177 (100); 149 (11); 131 (57); 82 (58)
2b	CH_3	4-NC—C_6H_4	A	45	121–123° (ethanol)	$C_{14}H_{15}N_5O_2$ (285.3)	2220 (C≡N), 1655 (C=O)	$CDCl_3$: 1.42 (d, 3H, *J* = 7 Hz, CH_3); 2.35–3.12 (m, 2H, —CH_2—N); 7.34–4.02 (m, 2H, CH_2CH_2O); 4.15 (s, 2H, $COCH_2$); 4.54 (2q, 1H, *J* = 7 Hz, *J'* = 3 Hz, H-4); 6.41 (d, 1H, *J* = 3 Hz, H-5)	257 (14); 229 (3.5); 199 (11.5); 157 (97); 156 (100); 129 (43); 102 (87); 82 (50)
2c	CH_3	4-F—C_6H_4	B	45	128° (benzene/pentane)	$C_{13}H_{15}FN_4O_2$ (278.3)	1640 (C=O)	C_6D_6: 0.95 (d, 3H, *J* = 7 Hz, CH_3); 2.05–2.35 (m, 2H, —CH_2—N); 2.83–3.15 (m, 2H, CH_2CH_2O); 3.76–4.07 (m, 3H, $COCH_2$ and H-4); 6.33 (d, 1H, *J* = 3 Hz, H-5)	250 (6); 222 (2); 192 (18); 150 (100); 149 (100); 122 (63); 95 (98); 82 (50)
2d	CH_3	4-NC—C_6H_4	B	20	144° (ethanol)	$C_{12}H_{13}N_5O$ (243.3)	2210 (C≡N), 1640 (C=O)	$CDCl_3$: 1.40 (d, 3H, *J* = 7 Hz, CH_3); 2.43 (s, 3H, CH_3N); 4.52 (2q, 1H, *J* = 7 Hz, *J'* = 3 Hz, H-4); 6.29 (d, 1H, *J* = 3 Hz, H-5); 7.88 (s, 1H, CHO)	215 (6); 186 (17); 157 (64); 156 (78); 129 (40); 102 (78); 70 (100)
2e	H	C_6H_5	B	10	143° (dec.) (ethanol)	$C_{12}H_{13}N_5O_4$ (291.3)	1640 (C=O)	DMSO-d_6: 2.39–2.70 (m, 2H, —CH_2—N); 3.47–3.90 (m, 2H, CH_2CH_2O); 4.08 (s, 2H, $COCH_2$); 4.59–4.82 (m, 2H, H-4); 6.84 (2d, *J* = 4.5 Hz, *J'* = 9 Hz, H-5)	263 (1.7); 205 (2.2); 162 (42); 138 (100); 109 (70); 101 (52); 92 (46)

[a] Uncorrected.

[b] All products gave satisfactory microanalyses (C ± 0.25 %, H ± 0.16 %, N ± 0.20 %).

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The starting triazolines **1** were easily prepared by cycloaddition of aryl azides to enamines according to a known procedure[5].

A first series of experiments was carried out employing potassium permanganate in acetone (Procedure A). The reaction was slow at room temperature and heating was necessary. However, this led to a very high consumption of permanganate owing to extensive oxidation of the solvent. Satisfactory results were also obtained when the oxidation was carried out in benzene or chlorobenzene with aqueous permanganate in the presence of a phase-transfer catalyst[6–9] (Procedure B). This made it possible to operate at room temperature or slightly above. About 1.5 mol of potassium permanganate were consumed for 1 mol of triazoline.

The structures of **2a–f** were confirmed by their analytical and spectroscopic data as shown in the Table. Moreover, **2a** underwent an easy deamination on refluxing with potassium hydroxide in methanol yielding 1-(4-nitrophenyl)-4-methyl-*v*-triazole (**3a**).

As a by-product of all oxidations a small amount of triazole **3** was obtained. Only the 4-nitro derivative (from **1a**, Method A) was isolated. In all other cases the compound was identified by T.L.C. (comparison with an authentic sample). Clearly, triazoles **3** are formed through base-induced elimination of amine[10,11,12] or of amide from the starting compounds or from the oxidation products, respectively.

Triazolines 1a–e:
Compounds **1a**[5] and **1e**[13] are obtained according to literature methods. The triazolines **1b** (R = CH_3, Ar = 4-NC—C_6H_4, m.p. 113–115°), **1c** (R = CH_3, Ar = 4-F—C_6H_4, m.p. 79°) and **1d** (m.p. 94°) are prepared in the same way.

Preparation of 4-Methyl-1-(4-nitrophenyl)-5-(2-oxomorpholino)-4,5-dihydro-*v*-triazole (2a); General Procedure A:
In a 100 ml round-bottomed flask with stirrer and reflux condenser triazoline **1a** (0.728 g; 2.5 mmol) is dissolved in acetone (40 ml). Potassium permanganate (1.58 g, 10 mmol) is added in small amounts over 4–6 h. The reaction mixture is stirred for 18 h at 50° until disappearance of the starting compound. The excess of permanganate is then reduced with sodium metabisulphite and the manganese dioxide filtered off. The acetone solution is evaporated and the residue, on chromatography over silica gel with benzene/ethyl acetate (4 : 1) as eluent, affords the product which is recrystallized from ethanol. Yields and physical properties are listed in the Table.

Preparation of 1-(4-Fluorophenyl)-4-methyl-5-(2-oxomorpholino)-4,5-dihydro-*v*-triazole (2c); General Procedure B:
To a 250 ml round-bottomed flask fitted with a dropping funnel and an efficient mechanical stirrer is added cetyltrimethylammonium bromide (36.4 mg, 0.1 mmol), benzene (25 ml), and a solution of potassium permanganate (0.553 g, 3.5 mmol) in water (40 ml). Under stirring a solution of the triazoline **1c** (0.53 g, 2 mmol) in benzene (40 ml) is dropped and stirring is continued until no more starting compound is detectable by T.L.C. The reaction mixture is filtered and the organic layer separated. After concentration, the product is precipitated by adding pentane to the benzene solution and purified by chromatography over silica gel with benzene/ethyl acetate (4 : 1). The product is recrystallized from benzene/pentane. Yields and physical properties are given in the Table.

Preparation of 4-Methyl-1-(4-nitrophenyl)-*v*-triazole 3a from 2a:
Triazoline **2a** (0.1 g, 3.24 mmol) is dissolved in methanol (10 ml). A solution of sodium hydroxide (0.25 g, 6.25 mmol) in methanol (10 ml) is added and the mixture is heated under reflux for 2 h. The reaction solution is evaporated and the residue washed with water. After recrystallization from ethanol triazole **3a** is obtained; yield: 0.053 g (80 %); m.p. 235°[14].

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[1] Part IX, L. M. Rossi, P. Trimarco, *Synthesis* **1978**, 465.

[2] R. Huisgen, G. Szeimies, L. Möbius, *Chem. Ber.* **99**, 475 (1966).

[3] R. Huisgen, G. Szeimies, unpublished results in S. Patai Ed., *The Chemistry of Alkenes*, 1964, p. 839.

[4] G. Bolis, D. Pocar, R. Stradi, P. Trimarco, *J. Chem. Soc. Perkin Trans. 1* **1977**, 2365.

[5] R. Stradi, D. Pocar, *Gazz. Chim. Ital.* **99**, 1131 (1969).

[6] C. M. Starks, *J. Am. Chem. Soc.* **93**, 195 (1972).

[7] W. P. Weber, J. P. Shepherd, *Tetrahedron Lett.* **1972**, 4907.

[8] M. Fieser, L. Fieser, *Reagents for Organic Synthesis*, Vol. 4, p. 30.

[9] F. Montanari, *Chim. Ind. (Milan)* **1975**, 17.

[10] N. E. Munk, Y. K. Kim, *J. Am. Chem. Soc.* **88**, 2213 (1964).

[11] P. Ferruti, D. Pocar, G. Bianchetti, *Gazz. Chim. Ital.* **97**, 109 (1967).

[12] D. Pocar, R. Stradi, L. M. Rossi, *J. Chem. Soc. Perkin Trans. 1* **1972**, 769.

[13] R. Stradi, D. Pocar, G. Bianchetti, *Org. Magn. Reson.* **4**, 247 (1972).

[14] H. El Khadem, H. A. R. Mansour, M. H. Meshereki, *J. Chem. Soc.* **1968**, 1329.