

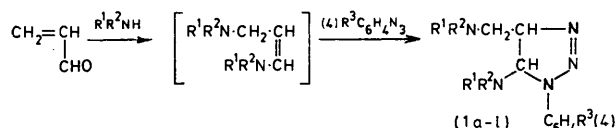
v-Triazolines. Part II.¹ Synthesis and Reactions of 5-Amino-4-amino-methyl-1-aryl-*v*-triazolines

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5-Amino-4-aminomethyl-1-aryl-*v*-triazolines are synthesized by treating aryl azides with acrylaldehyde and secondary amines. The triazolines readily react with strong bases yielding the corresponding triazoles. Acids act differently, depending on the kind of the amine residues. When these are strongly basic (aliphatic) the triazoline ring is cleaved with nitrogen evolution. Among the degradation products propane-1,2-dione is identified. When the amine residues are less basic (aromatic) the ring is not cleaved and both the corresponding 1-aryl-*v*-triazoles and 4-aminomethyl-1-aryl-*v*-triazoles are obtained. The mechanisms of these reactions are discussed.

THE synthesis of 5-amino-4-(α -aminoethyl)-1-aryl-*v*-triazolines from aromatic azides and but-1-ene-1,3-diamines has been described. It is known that by reacting acrylaldehyde with a secondary amine propene-1,3-diamines are formed,² these compounds exhibit behaviour typical of enamines.^{3,4} Here we describe the synthesis, by a previously described procedure,^{1,5} of the triazolines (1a—l) from acrylaldehyde, a secondary amine, and an aryl azide (see Scheme 1). The data for the triazolines are summarized in Table 1. The structure of the products has been confirmed by n.m.r.

Reaction with Bases.—Triazoles were obtained upon treatment of the triazolines with ethanolic sodium



SCHEME 1

hydroxide^{1,8,9} (see Scheme 2); their properties are listed in Table 2.

TABLE 1

| Compd. | R ¹ | R ² | R ³ | N.m.r. data * | | | React. time (h) | M.p. (°C) | Preparation | | Yield (%) |
|--------|----------------|---|-----------------|----------------------|----------------------|-----------|-----------------|-----------|--------------------------------|----|-----------|
| | | | | $\delta(4\text{-H})$ | $\delta(5\text{-H})$ | $J_{4,5}$ | | | Cryst. solvent | | |
| (1a) | Me | Me | NO ₂ | 4.62 | 4.81 | 3 | 6 | 96 | EtOH | 80 | |
| (1b) | Et | Et | NO ₂ | 4.59 | 4.93 | 3 | 6 | 98 | EtOH | 85 | |
| (1c) | | —[CH ₂] ₄ — | NO ₂ | 4.68 | 5.22 | 3 | 4 | 103 | EtOH | 70 | |
| (1d) | | —[CH ₂] ₅ — | NO ₂ | 4.76 | 4.87 | 3 | 4 | 148 | EtOH | 50 | |
| (1e) | | —[CH ₂] ₅ — | Cl | 4.58 | 4.69 | 3 | 36 | 84 | Pr ¹ ₂ O | 50 | |
| (1f) | | —[CH ₂] ₂ NCH ₂ [CH ₂] ₂ — | NO ₂ | 4.76 | 4.84 | 3 | 24 | 139 | EtOH | 90 | |
| (1g) | | —[CH ₂] ₂ O[CH ₂] ₂ — | NO ₂ | 4.87 | 4.90 | 3 | 6 | 184 | EtOH | 60 | |
| (1h) | | —[CH ₂] ₂ O[CH ₂] ₂ — | Cl | 4.60 | 4.70 | 3 | 36 | 131 | Pr ¹ ₂ O | 70 | |
| (1i) | Me | C ₆ H ₁₁ | NO ₂ | 4.65 | 5.04 | 3 | 1 | 161 | AcOEt | 85 | |
| (1j) | Me | Ph | NO ₂ | 4.84 | 5.71 | 3 | 12 | 173 | EtOH | 55 | |
| (1k) | Me | Ph | Cl | 4.74 | 5.65 | 3 | 6 † | 129 | Pr ¹ ₂ O | 20 | |
| (1l) | Me | PhCH ₃ (2) | NO ₂ | 4.92 | 5.36 | 3 | 24 | 141 | EtOH/AcOEt | 65 | |

* In CDCl₃ with Me₄Si as internal standard. † Backflux.

spectroscopy. As expected, the configuration of the triazoline ring is *trans*, as reflected in the $J_{4,5}$ value of ca. 3 Hz which is characteristic of *trans*-triazolines^{1,6} and -isoxazolines.⁷

¹ Part I, D. Pocar, R. Stradi, and L. M. Rossi, *J.C.S. Perkin I*, 1972, 919.

² C. Mannich, K. Handke, and K. Roth, *Chem. Ber.*, 1936, **69**, 2112; R. Tschesche and G. Snatzke, *ibid.*, 1957, **90**, 597; U.S.P. 2,800,509/1957 (*Chem. Abs.*, 1957, **51**, 17,979).

³ L. A. Paquette and M. Rosen, *Tetrahedron Letters*, 1967, 703; *J. Amer. Chem. Soc.*, 1967, **89**, 4102.

⁴ R. H. Hasek, P. G. Gott, and J. C. Martin, *J. Org. Chem.*, 1966, **31**, 1931.

Reaction with Acids.—Treatment of the triazolines (1a, d, f, i) with dilute acid gave cleavage of the ring and evolution of nitrogen (1 molar equiv.). Propane-1,2-dione (15–35%), 4-nitroaniline, and secondary

⁵ R. Stradi and D. Pocar, *Gazzetta*, 1969, **99**, 1131.

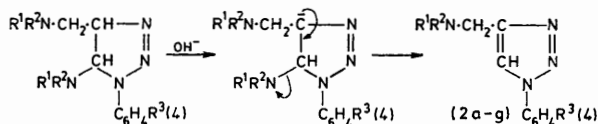
⁶ R. Sustmann, R. Huisgen, and H. Huber, *Chem. Ber.*, 1967, **100**, 1802.

⁷ P. Caramella and P. Bianchessi, *Tetrahedron*, 1970, **26**, 5773.

⁸ N. E. Munk and Y. K. Kim, *J. Amer. Chem. Soc.*, 1964, **86**, 2213.

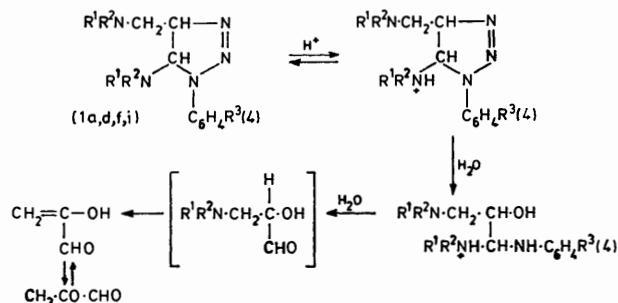
⁹ P. Ferruti, D. Pocar, and G. Bianchetti, *Gazzetta*, 1967, **97**, 109.

amine were obtained as products (see Scheme 3). The formation of the diketone is not unexpected.¹⁰⁻¹²



SCHEME 2

In contrast, under similar conditions, the triazolines (1j) and (1k) resisted ring cleavage and gave rise to the triazoles (2f) and (3a) and (2g) and (3b) respectively.



SCHEME 3

From compound (1l) only (3a) was isolated (see Scheme 4). Yields of triazoles were 60–80%; no carbonyl compounds were formed.

acid reduction product of *N*-hydroxymethyl-*N*-methyl-aniline). If the reaction is carried out with dilute HCl formaldehyde is evolved.

This difference in behaviour of the two classes of triazolines depends on their different basicity. Strongly basic triazolines are readily protonated and thus undergo ring cleavage. In contrast triazolines (1j–l) are less readily protonated and thus tend to undergo elimination reactions rather than ring cleavage.

EXPERIMENTAL

The n.m.r. spectra were recorded on a Jeol JNM-C-60 HL spectrometer at 60 MHz. Satisfactory analytical values were obtained for all the products described.

General Method for the Preparation of the Triazolines (1a–l).—Acrylaldehyde (10 mmol) was added to the aryl azide (10 mmol) dissolved in chloroform (10 mmol). The secondary amine (20 mmol) was then added dropwise. External cooling was sometimes necessary for moderately exothermic reactions. After several hours at room temperature (see Table 1), the product was precipitated by dilution with light petroleum. Some triazolines crystallize only with difficulty and with these the product was dissolved in a little di-isopropyl ether and the solution set aside for 12 h at ca. -10°C . The experimental data for the products are quoted in Table 1.

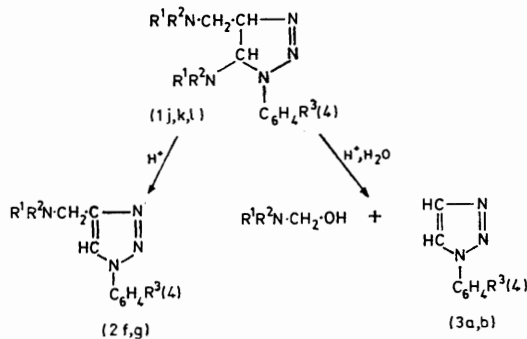
General Method for the Preparation of the Triazoles (2a–g).—The triazoline (5 mmol) dissolved in a boiling solution of

TABLE 2

| Compd. | R ¹ | R ² | R ³ | N.m.r. data † | | M.p. (°C) | Preparation | |
|--------|---|----------------|-----------------|------------------------|----------------------------|-----------|-------------------|-----------|
| | | | | δ_{CH_2} | δ_{H_α} | | Cryst. solvent | Yield (%) |
| (2a) | Et | Et | NO ₂ | 3.89 | 8.01 | 212 | AcOEt | 60 |
| (2b) | —[CH ₂] ₄ — | | NO ₂ | 4.68 * | 9.25 * | 128 | EtOH | 30 |
| (2c) | —[CH ₂] ₅ — | | Cl | 3.72 | 7.97 | 121 | Pr ¹ O | 75 |
| (2d) | —[CH ₂] ₃ O[CH ₂] ₂ — | | NO ₂ | 3.81 | 8.16 | 195 | EtOH | 45 |
| | | | | 3.70 * | 8.91 * | | | |
| (2e) | —[CH ₂] ₂ O[CH ₂] ₃ — | | Cl | 3.75 | 7.91 | 123 | Pr ¹ O | 65 |
| (2f) | Me | Ph | NO ₂ | 4.72 | 7.82 | 146–147 | EtOH | 75 |
| (2g) | Me | Ph | Cl | 4.65 | 7.62 | 90 | Pr ¹ O | 80 |

* In (CD₃)₂SO. † In CDCl₃ with Me₄Si as internal standard.

The retro-Mannich mechanism of the formation of the 4-unsubstituted triazoles is confirmed by the identi-



SCHEME 4

fication of *NN*-dimethylaniline as a product (the formic

¹⁰ G. Bianchetti, P. Dalla Croce, D. Pocar, and G. G. Gallo, *Rend. Ist. Lombardo Sci. Lettere*, 1965, **A**, **99**, 296; G. Bianchetti, D. Pocar, and P. Dalla Croce, *ibid.*, 1965, **A**, **99**, 316.

sodium hydroxide (10 mmol) in 95% ethanol (50 ml) was heated until no more triazoline was detectable by t.l.c. (after ca. 30–60 min). The solution was then evaporated under reduced pressure and the residue was treated with a little water. The precipitate was filtered off and recrystallized. The data for the products are collected in Table 2.

Acid Degradation of Compounds (1a, d, f, i).—The triazoline (1 mmol) was dissolved in 95% ethanol (15 ml). Acetic or formic acid (0.5 ml) was then added to the mixture which was then refluxed until no more N₂ was evolved (10–60 min).

(a) The reaction mixture was diluted with water (50 ml) and concentrated to a small volume by distillation. Phenylhydrazine (2 mmol) dissolved in 50% acetic acid (5 ml) was then added to the distillate. The propane-1,2-dione phenylosazone was filtered after 1 h and recrystallized from dilute ethanol or cyclohexane; it had m.p. 144–148° (lit.,¹³

¹¹ C. Mannich and M. Bauroth, *Chem. Ber.*, 1922, **55**, 3504.

¹² H. O. L. Fischer, C. Taube, and E. Baer, *Chem. Ber.*, 1927, **60**, 480.

¹³ Beilstein, XV, 156; II 65.

145—154°). The product was identical (mixed m.p., n.m.r., and i.r.) with an authentic sample.

(b) After being heated under reflux, the reaction mixture was treated with phenylhydrazine (2 mmol) dissolved in 50% acetic acid (5 ml). The mixture was set aside for several hours; the phenylosazone was precipitated by dilution with water. After recrystallization, the products had m.p. 144—147°.

(c) Substituting 4-nitrophenylhydrazine for phenylhydrazine in the above procedures (a) and (b), the corresponding 4-nitrophenylosazone was obtained as a red precipitate. After recrystallization from pyridine, the product decomposed above 270° and analysed correctly.

Acid Degradation of Compound (1j).—(a) The triazoline (2 mmol), formic acid (0.5 ml), and 95% ethanol (25 ml), were refluxed for 4 h. Water (50 ml) was then added to the mixture and the precipitate was filtered and chromatographed (silica gel—Celite; benzene—AcOEt, 4 : 1) to yield the triazoles (2f) (m.p. 145—146°, 20% yield) and (3a) (m.p. 199—200°, lit.,^{9,14} 202—204°, 45% yield). The filtrate was made alkaline and extracted with ether. In the extract *N*-methylaniline and *NN*-dimethylaniline were identified by gas chromatography.

(b) A similar result was obtained by employing 2% HCl

(15 ml) instead of the formic acid. In this case the reaction was accompanied by formaldehyde evolution.

Acid Degradation of Compound (1k).—The reaction was performed essentially in the same way as indicated for (1j). After being heated under reflux the mixture was diluted with water (50 ml) and extracted with chloroform. The extracted product was chromatographed (silica gel—Celite; benzene) to yield (2g) (m.p. 89—90°, 15% yield) and (3b) (m.p. 119°, 35% yield from ethanol). The products were identified by n.m.r. spectroscopy and by their analytical data.

Acid Degradation of Compound (1l).—The reaction was performed as indicated for (1j). After 3 h under reflux, the 1-(4-nitrophenyl)-*v*-triazole (3a) was identified in the reaction mixture by t.l.c. (silica gel; benzene—AcOEt, 4 : 1) by comparison with an authentic sample. Water (50 ml) was added to the mixture and the precipitate was recrystallized from ethanol to yield (3a), m.p. 199° (50% yield).

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¹⁴ A. Michael, F. Luehn, and H. H. Higbee, *Amer. Chem. J.*, 1898, **20**, 377.