Ring-Degenerate Rearrangement of 5-Amino-4-iminomethyl-1,2,3-triazoles Gerrit L'abbé* and Anna Vandendriessche

Department of Chemistry, University of Leuven, Celestijnenlaan 200F, 3030 Heverlee, Belgium Received September 20, 1988

5-Amino-4-(substituted)iminomethyl-1-phenyl-1,2,3-triazoles 5 rearrange thermally to 4-amidino-substituted triazoles 6 instead of undergoing the Dimroth rearrangement to 5-anilinotriazoles 3.

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5-Amino-1-aryltriazoles 1 are known to equilibrate thermally with 5-anilinotriazoles 3 via diazoamidines 2 as intermediates [1]. This interconversion, known as the Dimroth rearrangement [2], has been studied in detail for R^4 = phenyl and ester substituents [2-4]. We now report a different cyclization pathway of the intermediate 2 when R^4 is an imine function [5].

5-Amino-4-formyl-1-phenyl-1,2,3-triazole (4), the key intermediate of the title compounds, is readily available by a three-step sequence from methyl cyanoacetate [6]. When 4 was heated with a series of amines (1-2 equivalents) in ethanol for 2 hours, the rearranged triazoles 6a-h were obtained in high yields. Their precursors were isolated in the cases of 5d,f,g when equimolar amounts of 4 and the respective amines were allowed to react at room temperature. Under similar conditions, ethylamine, isopropylamine, t-butylamine, benzylamine and p-chloroaniline gave mixtures of 5a,b,c,e,h and 6a,b,c,e,h.

The rate of isomerization of 5d was determined in dimethyl sulfoxide- d_6 solution at 40° by integration of the methylene singlets at δ 4.76 and 5.97, for 5d and 6d respectively, in the nmr spectra at several time intervals. The first-order rate constant, $k_1 = 12.3 \ 10^{-5} \ s^{-1}$ (half-life 94 minutes), is a magnitude larger than that for the Dimroth rearrangement of 4 in the same solvent [7], thus explaining the exclusive formation of 6 rather than 3.

The structures **5** and **6** were differentiated on the basis of the 13 C nmr spectra as shown in Scheme I. The most diagnostic features are the resonance positions of the *ipso*-phenyl, *para*-phenyl and triazole C-4 and C-5 carbon atoms. A useful criterion to distinguish between the two structures is also the 1 J_{CH} coupling constant of the CH = N in **5** (ca 160 Hz) [8] versus that of C₅-H in **6** (ca 200 Hz) [9]. Finally, in the 1 H nmr spectra the N-1 phenyl protons of **5** resonate in a narrow range (0.1 ppm) at δ 7.6, whereas those of **6** are split into two multiplets at δ 6.9-7.6.

Scheme I

EXPERIMENTAL

Synthesis of 5-Amino-4-(*N*-isopropyl)iminomethyl-1-phenyl-1,2,3-triazole (**5b**).

Compound 4 (0.5 g, 2.6 mmoles) was allowed to react with 2 equivalents of isopropylamine (0.35 g) in ethanol (20 ml) at room temperature for 15 minutes. After removal of the solvent at room temperature, the residue was shown by ¹H nmr to consist of a mixture of **5b** and **6b** in a ratio of 95:5 and was not further purified. Spectral data of **5b**; ir (potassium bromide): 3380 and 3285 (m), 1640 and 1620 cm⁻¹ (s); ¹H nmr (deuteriochloroform): δ 1.2 (d, 6H, two Me), 3.5 (septet, 1H, CH), 5.2 (br, 2H, NH₂), 7.7 (s, 5H, Ph), 8.7 (s, 1H, CH = N).

Synthesis of 5-Amino-4-(N-cyanomethyl)iminomethyl-1-phenyl-1.2.3-triazole (5d).

Aminoacetonitrile hydrochloride (0.24 g, 2.6 mmoles) was first neutralized with sodium ethoxide (from 0.06 g of sodium) in ethanol (20 ml). Then, one equivalent of 4 (0.5 g) was added and the solution was stirred at room temperature for 2 hours. The solvent was removed without heating and the residue was crystallized from methanol (also without heating!) to give 5d in 76-83%,

mp 161°; ir (potassium bromide): 3400 and 3300 (m), 1630 and 1605 cm⁻¹ (s); ¹H nmr (dimethyl sulfoxide-d₆): δ 4.76 (s, 2H, CH₂), 6.7 (br, 2H, NH₂), 7.6 (s, 5H, Ph), 8.66 (s, 1H, CH = N); ¹³C nmr (dimethyl sulfoxide-d₆): δ 45.2 (CH₂), 117.7 (CN), 125.3 (C-4), 143.3 (C-5), 123.9, 129.0, 129.7 and 134.6 (Ph), 158.8 (CH = N, ¹J_{CH} = 160 Hz).

Anal. Calcd. for $C_{11}H_{10}N_6$ (mol wt 226): C, 58.40; H, 4.46. Found: C, 58.33; H, 4.52.

Synthesis of the 5-Aminotriazoles 5f,g.

Equimolar amounts (2.6 mmoles) of 1 (0.5 g) and amine were allowed to react in ethanol (20 ml) at room temperature for 15 minutes. After removal of the solvent at room temperature, the residue was crystallized (without heating!) from chloroform/ether.

5-Amino-1-phenyl-4-(N-phenyl)iminomethyl-1,2,3-triazole (5f).

This compound was obtained in 18% yield, mp 124°; ir (potassium bromide): 3460 and 3300 (m), 1630 cm⁻¹ (br, s); ¹H nmr (deuteriochloroform): δ 5.9 (br, 2H, NH₂), 7.0-7.5 (m, 5H, = NPh), 7.6 (s, 5H, Ph), 8.8 (s, 1H, CH = N); ¹³C nmr (deuteriochloroform): δ 120.8, 123.6, 129.4 and 151.2 (= NPh), 123.8, 130.2, 130.0 and 134.4 (Ph), 127.6 (C-4), 142.4 (C-5), 153.4 (CH = N, ¹J_{CH} = 162 Hz).

Anal. Calcd. for $C_{15}H_{15}N_5$ (mol wt 263): C: 68.43; H, 4.98. Found: C, 68.26; H, 4.93.

5-Amino-4-(N-p-methoxyphenyl)iminomethyl-1-phenyl-1,2,3-triazole (5g).

This compound was obtained in 39% yield, mp 191°; ir (potassium bromide): 3460 and 3320 (m), 1630 cm⁻¹ (br, s); ¹H nmr (deuteriochloroform): δ 3.8 (s, 3H, OCH₃), 6.9 and 7.2 (two d, 4H, anisyl), 7.5 (s, 5H, Ph), 8.8 (s, 1H, CH = N); ¹³C nmr (deuteriochloroform): δ 55.0 (OCH₃), 113.9, 121.5, 143.8 and 158.0 (anisyl), 123.3, 128.5, 129.4 and 134.7 (Ph), 126.7 (C-4), 142.8 (C-5), 150.0 (CH = N, ¹J_{CH} = 161 Hz).

Anal. Calcd. for $C_{16}H_{15}N_5O$ (mol wt 293): C, 65.52; H, 5.15. Found: C, 65.48; H, 5.06.

Synthesis of the 4-Amidinotriazoles 6a-h.

A solution of 4 (0.5 g, 2.6 mmoles) and amine (two equivalents of ethylamine, isopropylamine, t-butylamine, benzylamine and aniline, and one equivalent of aminoacetonitrile, p-methoxy-aniline and p-chloroaniline) in ethanol (20 ml) was refluxed for 2 hours. Compounds 6d,e,g,h precipitated from the solutions and were filtered off, washed with n-hexane and crystallized from alcohol. In the other cases, 6a,b,c,f, the solvent was removed and the residue was crystallized from the appropriate solvent.

1-Ethyl-4-(N-phenyl)amidino-1,2,3-triazole (6a).

This compound was obtained in 90% yield, mp 143° (benzene); ir (potassium bromide): 3365 and 3180/3140 (m), 1635/1615 cm⁻¹ (s); ¹H nmr (deuteriochloroform): δ 1.6 (t, 3H, CH₃), 4.5 (q, 2H, CH₂), 5.5 (br, 2H, NH₂), 7.0-7.4 (two m, 5H, Ph), 8.2 (s, 1H, triazole H); ¹³C nmr (deuteriochloroform): δ 15.4 and 45.6 (Et), 121.7, 123.2, 129.5 and 148.6 (Ph), 122.9 (C-5), 144.5 (C-4), 147.8 (C = N). Anal. Calcd. for C₁₁H₁₃N₅ (mol wt 215): C, 61.38; H, 6.09. Found: C, 61.26; H, 6.00.

1-Isopropyl-4-(N-phenyl)amidino-1,2,3-triazole (6b).

This compound was obtained in 76% yield, mp 120° (chloroform/ether); ir (potassium bromide): 3470 and 3320 (m), 1630 cm⁻¹ (s); ¹H nmr (deuteriochloroform): δ 1.6 (d, 6H, two Me), 4.9

(septet, 1H, CH), 5.5 (br, 2H, NH₂), 6.9-7.5 (two m, 5H, Ph), 8.2 (s, 1H, triazole H); 13 C nmr (deuteriochloroform): δ 22.9 and 53.3 (*i*-Pr), 121.7, 123.2, 129.4 and 148.5 (Ph), 121.1 (C-5), 144.1 (C-4), 147.9 (C = N).

Anal. Calcd. for $C_{12}H_{15}N_5$ (mol wt 229): C, 62.86; H, 6.59. Found: C, 62.79; H, 6.48.

1-t-Butyl-4-(N-phenyl)amidino-1,2,3-triazole (6c).

This compound was obtained in 93% yield, mp 157° (ether); ir (potassium bromide): 3480 and 3340 (m), 1630 cm⁻¹ (s); ¹H nmr (deuteriochloroform): δ 1.7 (s, 9H, t-Bu), 5.4 (br, 2H, NH₂), 6.9-7.5 (two m, 5H, Ph), 8.2 (s, 1H, triazole H); ¹³C nmr (deuteriochloroform): δ 30.0 and 59.9 (t-Bu), 121.8, 123.2, 129.5 and 148.5 (Ph), 121.0 (C-5), 143.6 (C-4), 148.2 (C=N).

Anal. Calcd. for $C_{13}H_{17}N_s$ (mol wt 243): C, 64.17; H, 7.04. Found: C, 64.00; H, 7.00.

1-(Cyanomethyl)-4-(N-phenyl)amidino-1,2,3-triazole (6d).

This compound was obtained in 66% yield, mp 136° (methanol); ir (potassium bromide): 3450 and 3300 (m), 2210 (m), 1640 cm⁻¹ (s); ¹H nmr (dimethyl sulfoxide-d₆): δ 5.97 (s, 2H, CH₂), 6.4 (br, 2H, NH₂), 6.9-7.5 (two m, 5H, Ph), 8.77 (s, 1H, triazole H); ¹³C nmr (dimethyl sulfoxide-d₆): δ 37.6 (CH₂), 114.8 (C = N), 121.5, 122.1, 129.0 and 148.8 (Ph), 125.7 (C-5, ¹J_{CH} = 203.4 Hz), 144.6 (C-4), 146.9 (C = N).

Anal. Calcd. for $C_{11}H_{10}N_6$ (mol wt 226): C, 58.40; H, 4.46. Found: C, 58.26; H, 4.54.

1-Benzyl-4-(N-phenyl)amidino-1,2,3-triazole (6e).

This compound was obtained in 95% yield, mp 216° (ethanol); ir (potassium bromide): 3470 and 3320 (m), 1630 cm⁻¹ (s); 'H nmr (deuteriochloroform): δ 5.45 (br, 2H, NH₂), 5.54 (s, 2H, CH₂), 6.9-7.45 (three m, 10 H, two Ph), 8.05 (s, 1H, triazole H); ¹³C nmr (deuteriochloroform): δ 54.6 (CH₂), 121.6, 123.3, 129.5 and 148.5 (= NPh), 128.4, 129.0, 129.2 and 133.8 (Ph), 123.5 (C-5), 144.8 (C-4), 147.7 (C = N).

Anal. Calcd. for $C_{16}H_{15}N_5$ (mol wt 277): C, 69.30; H, 5.45. Found: C, 69.28; H, 5.54.

1-Phenyl-4-(N-phenyl)amidino-1,2,3-triazole (6f).

This compound was obtained in 91% yield, mp 151° (benzene); ir (potassium bromide): 3480 and 3340 (m), 1630 cm⁻¹ (s); ¹H nmr (deuteriochloroform): δ 5.6 (br, 2H, NH₂), 7.0-7.8 (four m, 10 H, two Ph), 8.65 (s, 1H, triazole H); ¹³C nmr (deuteriochloroform): δ 121.6, 123.3, 129.5 and 148.4 (= NPh), 120.5, 129.1, 129.8 and 136.6 (Ph), 121.7 (C-5, ¹J_{CH} = 198 Hz), 145.0 (C-4), 147.5 (C = N). Anal Calcd. for M*: 263.1171. Found: 263.1167. **Note**: No sat-

Anal Calcd. for M*: 263.1171. Found: 263.1167. Note: No satisfactory elemental analysis could be obtained (Calcd. C, 68.43; H, 4.98. Found: C, 67.42; H, 5.09).

1-(p-Methoxyphenyl)-4-(N-phenyl)amidino-1,2,3-triazole (6g).

This compound was obtained in 83% yield, mp 183° (ethanol); ir (potassium bromide): 3480 and 3345 (m), 1625 cm⁻¹ (s); ¹H nmr (deuteriochloroform): δ 3.9 (s, 3H, OMe), 5.5 (br, 2H, NH₂), 7.0-7.7 (three m, 9 aromatic H), 8.55 (s, 1H, triazole H); ¹³C nmr (deuteriochloroform): δ 55.0 (OMe), 121.7, 123.3, 129.5 and 148.6 (Ph), 114.9, 122.2, 130.1 and 160.1 (anisyl), 121.8 (C-5, ¹J_{CH} = 198 Hz), 144.9 (C-4), 147.5 (C = N).

Anal. Calcd. for $C_{16}H_{15}N_5O$ (mol wt 293): C, 65.52; H, 5.15. Found: C, 65.42; H, 5.17.

1-(p-Chlorophenyl)-4-(N-phenyl)amidino-1,2,3-triazole (6h).

This compound was obtained in 87% yield, mp 206° (ethanol); ir (potassium bromide): 3480 and 3340 (m), 1642 cm⁻¹ (s); 'H nmr (dimethyl sulfoxide-d₆): δ 3.5 (br, 2H, NH₂), 6.9-8.0 (four m, 9 aromatic H), 9.2 (s, 1H, triazole H); ¹³C nmr (dimethyl sulfoxide-d₆): δ 121.5, 122.4, 129.5 and 148.7 (Ph), 121.3, 128.9, 133.3 and 135.0 (p-ClC₆H₄), 122.0 (C-5), 145.0 (C-4), 147.0 (C = N).

Anal. Calcd. for $C_{15}H_{12}ClN_s$ (mol wt 297): C, 60.51; H, 4.06. Found: C, 60.45; H, 4.07.

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