

SHORT
COMMUNICATIONS

Amidines Synthesis by Reaction of 4-Amino-1,2,4-triazole with Nitriles

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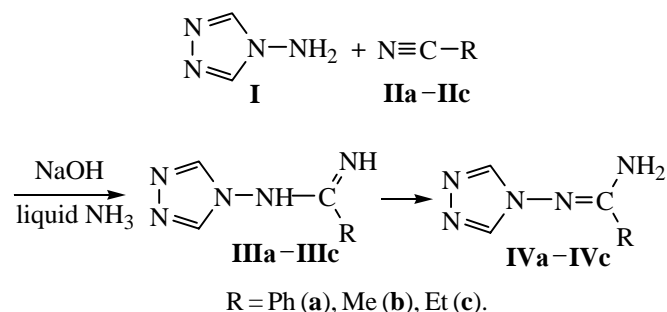
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Amidine chemistry attracts attention of researchers for this class compounds are extensively used in organic synthesis [1]. Amidines with a 1,2,4-triazole ring are capable of complex formation with transition metals and are of interest as low-temperature molecular ferromagnetics [2]. Amidines are commonly prepared by amines addition to nitriles in the presence of acids or bases [3]. For instance, a number of *N*-triazolyl-4-amidines was obtained from nitriles and 4-amino-1,2,4-triazoles in the presence of equimolar amount of sodium ethylate in up to 75% yield [4].

In this study the comparative activity of aromatic and aliphatic nitriles in reaction with 4-amino-1,2,4-triazole was investigated in various solvents (liquid ammonia, methanol, and acetonitrile) in the presence of alkali (KOH, NaOH). The reaction of 4-amino-1,2,4-triazole (**I**) with nitriles **II** in liquid ammonia or methanol proceeded along the following scheme:



Reaction of amine **I** with benzonitrile (**IIa**) in liquid ammonia (-33°C , KOH or NaOH, 7 h) proceeded presumably through the formation of *N*²-substituted triazol-4-ylamidine **IIIa** that via prototropic “amidine” tautomerism converted into amidine **IVa** (yield 96%).

Since the triazole ring is an electron-withdrawing substituent, the nitrogen atom of amidine $\text{N}=\text{C}$ group possesses a positive charge favoring the equilibrium shift in the direction of structure **IVa** [5]. This effect is reinforced by the presence of a phenyl substituent. The structure of compound **IVa** was elucidated by IR and ^1H , ^{13}C , ^{15}N NMR spectroscopy. The IR spectrum contained absorption bands of $\text{HC}=\text{N}$ bond in the ring at 1640 cm^{-1} and of stretching vibrations of $\text{C}=\text{N}$ bond in the side chain at 1590 cm^{-1} with an overtone at 3180 cm^{-1} . In the ^1H NMR spectrum of compound **IVa** in DMSO the following signals were observed (δ , ppm): 8.46 s ($\text{HC}=\text{N}$, ring), 7.46–7.91 (Ph), and 7.36 s (NH_2). ^{15}N NMR spectrum contained at 294.99 ppm the signal of NH_2 group. The reaction of triazole **I** with nitrile **IIa** occurred successfully also in methanol (KOH or NaOH, 65°C , 7 h), yield up to 92%.

Under comparable conditions (liquid NH_3 , -33°C , KOH, 10 h) reaction of triazole **I** with acetonitrile **IIb** gave rise to a mixture of amidines **IIIb** and **IVb** in a ratio 1:6 in overall yield 89%. The best yield of the mixture **IIIb** and **IVb** (91%) was obtained in excess acetonitrile at prolonged keeping of the reaction mixture at 20°C (KOH, 72 h). The presence of two isomers **IIIb** and **IVb** is apparently due to the electron-donor property of the methyl group favoring to a certain extent stabilization of amidine structure **IIIb**. The assignment of structures **IIIb** and **IVb** was done basing on the ^1H and ^{13}C NMR spectra registered in DMSO. In the ^1H NMR spectrum of amidines **IIIb** and **IVb** were observed the following signals (δ , ppm): 8.39 s and 8.31 s ($\text{HC}=\text{N}$, ring), 1.73 s and 1.97 s (CH_3) respectively.

The reaction of triazole **I** with propionitrile **IIc** in liquid NH_3 (KOH, -33°C , 14 h) provided a mixture of com-

pounds **IIIc** and **IVc** in a ratio 1:20 in overall yield 92%. By recrystallization from ethanol amidine **IVc** was isolated, mp 213–214°C. In methanol (NaOH, 65–67°C, 18 h) formed amidine **IVc** in 79% yield. In the ¹H NMR spectrum appeared the following signals (δ, ppm): 1.13 t (CH₃), 2.20 q (CH₂), 8.27 s (HC=N, ring); weak signals corresponding to amidine **IIIc** were also present.

N¹-(1,2,4-Triazol-4-yl)benzamidine (IVa). *a.* To a solution of 3 g (0.025 mol) of benzonitrile (**IIa**) and 2.79 g (0.033 mol) of aminotriazole **I** in 200 ml of liquid NH₃ was added 0.3 g of NaOH, and the reaction mixture was stirred for 7 h at –33°C, ammonia was evaporated, the residue was washed with water and ethyl ether. Yield 5.22 g (96%), mp 245–247°C. IR spectrum, cm⁻¹: 3350 br, 3180 br, 3110, 3050, 1640, 1590, 1550, 1490, 1440, 1310, 1305, 1300, 1170, 1090, 1030, 970, 930, 920, 840, 830, 770, 700, 610, 570. ¹H NMR spectrum, δ, ppm: 8.46 s (2H, HC=N, ring), 7.91 d (2H^o), 7.53 t (1Hⁱ), 7.46 t (2H^m), 7.36 s (2H, NH₂). ¹³C NMR spectrum, δ, ppm: 163.22 (C=N), 141.25 (HC=N, ring), 132.93 (C¹, Ph), 131.65 (C⁴, Ph), 128.78 (C^{2,6}, Ph), 127.71 (C^{3,5}, Ph). ¹⁵N, δ, ppm: 64.92 (N–N), 163.75 (N⁴, ring), 177.62 (N^{1,2}, ring), 294.99 (NH₂). Found, %: C 57.88; H 4.68; N 37.38. C₉H₉N₅. Calculated, %: C 57.74; H 4.85; N 37.41.

b. A solution of 20 g (0.19 mol) of benzonitrile (**IIa**), 10 g (0.12 mol) of aminotriazole **I**, and 2 g of KOH in 25 ml of CH₃OH was stirred for 7 h at 65–67°C, then ~30 ml of water was added, the precipitated crystals were filtered off and washed with ethyl ether. Yield 20.5 g (92%), mp 245–247°C (262°C [4]).

N¹-(1,2,4-Triazol-4-yl)acetamidine (IVb). *a.* A solution of 1 g (0.012 mol) of aminotriazole **I** in 40 ml of acetonitrile in the presence of 0.97 g of KOH was maintained for 72 h at 20°C. The precipitated crystals were filtered off, washed with water, and recrystallized from acetonitrile. Yield of the mixture of compounds **IIIb** and **IVb** in a ratio 1:6 1.36 g (91%), mp 212–215°C. IR spectrum, cm⁻¹: 3380, 3320, 3150, 3110 sh, 3090, 1640, 1600, 1500, 1410, 1405, 1350, 1320, 1190, 1180, 1110, 1040, 1000, 980, 940, 890, 840, 770, 700, 680, 560. ¹H NMR spectrum, δ, ppm: 8.34 s (2H, HC=N, ring), 1.67 s (3H, CH₃) in **IIIb**; 8.29 s (2H, HC=N, ring), 6.99 (2H, NH₂), 1.92 s (3H, CH₃) in **IVb**. ¹³C NMR spectrum, δ, ppm: 168.89 (C=N), 141.47 (CH=N, ring), 14.98 (CH₃) in **IIIb**; 164.16 (C=N), 140.82 (CH=N, ring), 19.12 (CH₃) in **IVb**.

b. A solution of 3 g (0.036 mol) of aminotriazole **I**, 2.91 g (0.071 mol) of acetonitrile (**IIb**), and 0.3 g of NaOH in 200 ml of liquid NH₃ was stirred for 10 h at –33°C, NH₃ was evaporated, the residue was washed with water and ethyl ether. Yield 2.73 g (89%), mp 210–215°C. The ratio **IIIb**:**IVb** = 1:6. Found, %: C 38.29; H 5.36; N 55.77. C₄H₇N₅. Calculated, %: C 38.39; H 5.64; N 55.97.

N¹-(1,2,4-Triazol-4-yl)propioamidine (IVc). *a.* From 5 g (0.059 mol) of aminotriazole **I**, 7.86 g (0.143 mol) of propionitrile (**IIc**), 1.5 g of NaOH in 150 ml of liquid NH₃ (–33°C, 14 h) we obtained 11.56 g (92%) of a mixture of compounds **IIIc** and **IVc** in a ratio 1:20, mp 213–214°C. IR spectrum, cm⁻¹: 3290 sh, 3210 br, 3110 sh, 3070, 2970, 1680, 1590, 1495, 1460, 1440, 1315, 1245, 1200, 1110, 1045, 980, 950, 880, 830, 740, 700, 620. ¹H NMR spectrum, δ, ppm: 1.13 t (3H, CH₃), 2.20 q (2H, CH₂), 6.80 s (2H, NH₂), 8.27 s (2H, CH=N, ring) in **IVc**; 0.96 t (3H, CH₃), 1.87 q (2H, CH₂), 8.36 s (2H, CH=N, ring) in **IIIc**. ¹³C NMR spectrum, δ, ppm: 11.64 (CH₃), 26.51 (CH₂), 140.94 (CH=N, ring), 168.83 (C=N) in **IVc**.

b. A solution of 5 g (0.059 mol) of aminotriazole **I**, 7.86 g (0.143 mol) of propionitrile (**IIc**) in 25 ml of CH₃OH in the presence of 1.5 g NaOH was stirred for 18 h at 65–67°C. After usual workup we isolated 6.6 g (79%) of a mixture, mp 213–214°C. ¹H NMR spectrum, δ, ppm: 0.96 t (3H, CH₃), 1.85 q (2H, CH₂), 6.21 s (2H, NH), 8.36 s (2H, CH=N, ring) in **IIIc**; 1.14 t (3H, CH₃), 2.23 q (2H, CH₂), 8.28 s (2H, CH=N, ring) in **IVc**. Found, %: C 43.02; H 6.45; N 50.07. C₅H₉N₅. Calculated, %: C 43.15; H 6.52; N 50.38.

IR spectra of compounds were recorded on a spectrophotometer Specord 75IR from KBr pellets. NMR spectra were recorded from solutions in DMSO-*d*₆ with internal reference HMDS on spectrometers Bruker DPX-400 (¹H, 400 MHz) and Bruker DPX-250 (¹³C, 62.5 MHz).

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