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Synthesis of 2-[5-amino-2,3-dihydro-4*H*-imidazol-4-ylidene]malononitriles

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Abstract—Using the system of tetracyanoethylene, ammonium acetate and a carbonyl compound, the preparation of 2-[5-amino-2,3-dihydro-4*H*-imidazol-4-ylidene]malononitriles was carried out. The structures of these new dihydroimidazoles were determined by NMR experiments and by X-ray crystallography.

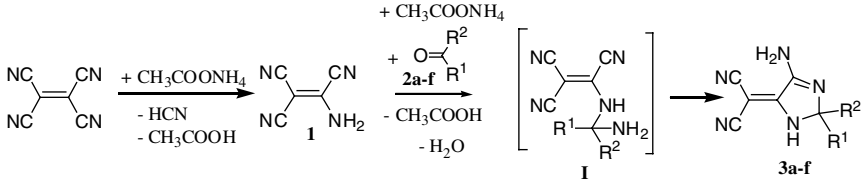
Various imidazoline-containing compounds are known to be the ligands of imidazoline-receptors and reveal pharmacological activity towards metabolism, secretion, ion exchange, intraocular pressure and to the cardiovascular system.[1]

Several synthetic methods have been utilized for the preparation of the imidazole ring.[2] Cyano-derivatives of imidazoles have been synthesized using diaminoethylenedicarbonitrile,[3] which is used in heterocyclization reactions with formation of the 1,2- and 2,3-bonds. We have developed a new method for the preparation of imidazoles through the formation of 1,2- and 3,4-C–N bonds on utilizing 2-amino-1,1,2-tricyanoethylene (Scheme 1 and Table 1).[4]

Reaction of tetracyanoethylene with amines gives *N*-alkyl-aminotricyanoethylenes[5] whereas reaction with ammonia leads to 2-[(1,2,2-tricyanovinyl)amino]-1,1,2-ethylenetricarbonitrile and its salts.[6] In the presence of ammonium acetate as ammonia donor we succeeded in isolating aminotricyanoethylene (**1**).[4] To prevent salt formation ammonium acetate was added in large excess. The structure of compound **1** was confirmed by X-ray crystallography.[4]

The 2-amino-1,1,2-tricyanoethylene obtained was used as a bifunctional H_2N–C–C≡N fragment in the [3+2]heterocyclization reaction with the imine formed in situ from the carbonyl compound and ammonium acetate. As a result 2-[5-amino-2,3-dihydro-4*H*-imidazol-4-ylidene]malononitriles **3a**–**f** were isolated (Table 1).[7]

Compounds **3a**–**f** were identified by IR, ^{1}H NMR and mass spectroscopy.[8] The structure of **3a** was confirmed by X-ray analysis (Fig. 1).[9]



Scheme 1. Synthesis of **3a**–**f**.

Keywords: Heterocyclic compounds; Cyano compounds; Imidazoles; Carbonyl compounds.
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Table 1. Preparation of 2-[5-amino-2,3-dihydro-4*H*-imidazol-4-ylidene]malononitriles (**3a–f**)

Carbonyl compound	R^1, R^2	Product	Yield[a] (%)	
			Method A	Method B
2a	$R^1+R^2=(CH_2)_5$	**3a**	72	62
2b	$R^1+R^2=(CH_2)_2CH(C_6H_5)(CH_2)_2$	**3b**	66	54
2c	$R^1+R^2=(CH_2)_2CH(CH_3)(CH_2)_2$	**3c**	80	65
2d	$R^1+R^2=(CH_2)_{11}$	**3d**	52	49
2e	$R^1=CH(CH_3)_2$, $R^2=H$	**3e**	56	42
2f	$R^1=CH(C_2H_5)_2$, $R^2=H$	**3f**	49	40

[a] Isolated yields.

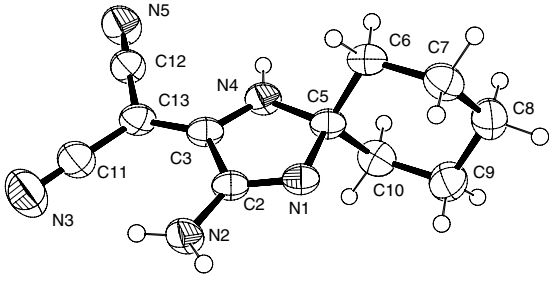

Figure 1. X-ray structure of compound **3a**.

Using the three-component system of tetracyanoethylene, ammonium acetate and a carbonyl compound, the preparation of 2-[5-amino-2,3-dihydro-4*H*-imidazol-4-ylidene]malononitriles was also carried out as a one-pot synthesis.[10]

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4. Tafeenko, V. A.; Paseshnichenko, K. A.; Ershov, O. V.; Eremkin, A. V.; Aslanov, L. A. *Acta Crystallogr.* **2005**, *C61*, o434–o437. Procedure for the preparation of 2-amino-1,1,2-tricyanoethylene (**1**). Tetracyanoethylene 0.64 g (0.005 mol) was added to a suspension of 0.97 g ammonium acetate in dioxane. After 20 min the solution was filtered, mixed with 0.02 ml of methyl iodide and then evaporated in vacuum. The residue was triturated in hexane and filtered, yielding 0.55 g (94%) of a solid compound.
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7. *Typical procedure* for the preparation of 2-[5-amino-2,3-dihydro-4*H*-imidazol-4-ylidene]malononitriles **3a–f**: *Method A.* To 0.29 g (0.0025 mol) of 2-amino-1,1,2-ethylenetricarbonitrile in dioxane, 0.6 g of ammonium acetate and 0.0025 mol of the carbonyl compound were added. After 6 h, the reaction mixture was diluted with water and the resulting precipitate was isolated by filtration.
8. Analytical data for compounds **3a–f**. Compound **3a**: mp 199 °C. IR 3440, 3100–3280 (NH, NH_2), 2225 (C≡N), 2210 (C≡N), 1645 (C=N), 1600 (C=C) cm^{-1}. ^1H NMR (500.13 MHz, DMSO-d_6): δ 11.41 (1H, s, NH), 6.25 (2H, s, N=C–NH_2), 1.8–1.2 (10H, m, CH_2). MS: m/z 215 (M^+). Anal. Calcd for $C_{11}H_{13}N_5$: C, 61.38; H, 6.09; N, 32.54. Found: C, 61.23; H, 5.93; N, 32.47. Compound **3b**: mp 208 °C. IR 3500, 3400, 3100–3280 (NH, NH_2), 2225 (C≡N), 2200 (C≡N), 1650 (C=N), 1600 (C=C) cm^{-1}. ^1H NMR (500.13 MHz, DMSO-d_6): δ 11.53 (1H, s, NH), 7.30 (2H, t, $J=7.4$, *m*-Ph), 7.24 (2H, d, $J=7.4$, *o*-Ph), 7.19 (1H, t, $J=7.4$, *p*-Ph), 6.43 (2H, s, N=C–NH_2), 2.63 (1H, m, $(CH_2)_2CH$–Ph), 2.1–1.35 (8H, m, CH_2). MS: m/z 291 (M^+). Anal. Calcd for $C_{17}H_{17}N_5$: C, 70.08; H, 5.88; N, 24.04. Found: C, 69.95; H, 5.93; N, 23.90. Compound **3c**: mp 200 °C. IR 3460, 3100–3280 (NH, NH_2), 2235 (C≡N), 2200 (C≡N), 1665 (C=N), 1610 (C=C) cm^{-1}. ^1H NMR (500.13 MHz, DMSO-d_6): δ 11.45 (1H, s, NH), 6.34 (2H, s, N=C–NH_2), 1.9–1.2 (8H, m, CH_2), 0.90 (3H, d, $J=6.8$, CH_3). MS: m/z 229 (M^+). Anal. Calcd for $C_{12}H_{15}N_5$: C, 62.86; H, 6.59; N, 30.54. Found: C, 62.86; H, 6.69; N, 30.43. Compound **3d**: mp 205 °C. IR 3500, 3400, 3100–3280 (NH, NH_2), 2225 (C≡N), 2220 (C≡N), 1645 (C=N), 1600 (C=C) cm^{-1}. ^1H NMR (500.13 MHz, DMSO-d_6): δ 11.51 (1H, s, NH), 6.25 (2H, s, N=C–NH_2), 1.7–1.25 (22H, m, CH_2). MS: m/z 299 (M^+). Anal. Calcd for $C_{17}H_{25}N_5$: C, 68.19; H, 8.42; N, 23.39. Found: C, 68.02; H, 8.50; N, 23.30. Compound **3e**: mp 202 °C. IR 3460, 3100–3280 (NH, NH_2), 2225 (C≡N), 2220 (C≡N), 1645 (C=N), 1590 (C=C) cm^{-1}. ^1H (500.13 MHz, DMSO-d_6): δ 11.40 (1H, s, NH), 6.43 (2H, s, N=C–NH_2), 5.21 (1H, s, N–C*H*–NH), 2.04 (1H, m, CH–C*H*$(CH_3)_2$), 0.95 (3H, d, $J=6.7$, CH_3), 0.72 (3H, d, $J=6.7$, CH_3). MS: m/z 189 (M^+). Anal. Calcd for $C_9H_{11}N_5$: C, 57.13; H, 5.86; N, 37.01. Found: C, 57.02; H, 5.75; N, 37.03. Compound **3f**: mp 209 °C. IR 3430, 3100–3280 (NH, NH_2), 2225 (C≡N), 2200 (C≡N), 1650 (C=N), 1600 (C=C) cm^{-1}. ^1H NMR (500.13 MHz,

DMSO-d_6): δ 11.42 (1H, s, NH), 6.38 (2H, s, N=C–NH_2) 5.41 (1H, s, N–C*H*–NH), 1.62 (1H, m, CH–C*H*$(CH_2)_2$) 1.35 (2H, m, –CH–CH_2–CH_3), 1.10 (2H, m, –CH–CH_2–CH_3), 0.95 (3H, t, $J = 7.3$, CH_3), 0.85 (3H, t, $J = 7.3$, CH_3). MS: m/z 217 (M^+). Anal. Calcd for $C_{11}H_{15}N_5$: C, 60.81; H, 6.96; N, 32.23. Found: C, 60.71; H, 6.85; N, 32.03.

9. Crystallographic data (excluding structure factors) for the structure in this paper (**3a**) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 285846. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: http://deposit@ccdc.cam.ac.uk].
10. *One-pot procedure* for preparation of 2-[5-amino-2,3-dihydro-4*H*-imidazol-4-ylidene]malononitriles **3a**–**f**: *Method B*. To 0.64 g (0.005 mol) of tetracyanoethylene in 5 ml of dioxane, 0.97 g of ammonium acetate and 0.005 mol of the carbonyl compound **2a**–**f** were added. After 6 h, the reaction mixture was diluted with water and the resulting precipitate was isolated by filtration.