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ScienceDirect Mendeleev Commun., 2016, 26, 172–173

Mendeleev Communications

New stable form of nitroacetonitrile

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DOI: 10.1016/j.mencom.2016.03.031

Oxidation of ethyl cyanoglyoxylate 2-oxime followed by KOH treatment affords stable potassium salt of nitroacetonitrile which is a reliable substitute of hazardous free nitroacetonitrile in organic synthesis.



Reactivity of nitroacetonitrile (NAN) is poorly studied due to its very low thermodynamic stability.¹ Most of the reports is limited to azo coupling,² Knoevenagel condensation^{3–7} and similar processes.^{8–10} At the same time, possibilities of using NAN in the synthesis of 3-amino-4-nitropyrazoles,¹¹ chromenes,¹² azolo-[5,1-*c*][1,2,4]triazines, 6-azauracils^{14,15} and 2,4,6-tricyano-pyridine-*N*-oxide¹⁶ are documented. This brings a challenge to create a stable form of NAN, which can open new possibilities of its application. One of successful approaches is the decomposition of pyridinium salt of nitroisoxazolone.^{1,17,18}

Herein, we propose an easy method of obtaining stable potassium salt of NAN from more available reactants (*cf.* refs. 1,17,18) and its subjecting to some reactions reported earlier for free NAN. Previously, cesium,¹⁹ arylammonium and ammonium salts²⁰ were prepared directly from NAN. Obviously, these methods suffer explosion hazards when preparing NAN from methazonic acid.

In this work, ethyl nitrocyanoacetate potassium salt 1 was used as the starting compound for the synthesis of potassium salt of NAN 2 (Scheme 1). Oxidation of ethyl cyanoglyoxylate 2-oxime 3 at 35-40 °C gives compound 1 in 63-67% yield. According to the reaction equation it is necessary to add 1/3 equiv. of alkali to fully transfer compound 3 into aqueous phase.



Scheme 1

Salt 1 is a stable available easy-to-handle compound convenient for further preparation of potassium salt of NAN 2 (see Scheme 1). We have found that when stirring compound 1 in the equivalent of 5-10% KOH solution at room temperature, the pH of the solution decreases to 9 within several hours. Apparently, the process starts with the ester hydrolysis to form the unstable

dipotassium salt of nitrocyanoacetic acid which is then readily converted into the final NAN salt 2 in 45% yield. This salt is stable under normal conditions for a long time.[†]

The structure of compound **2** was proved on the basis of IR, ¹H, ¹³C NMR and 2D HMBC ¹H-¹⁵N NMR spectra and elemental analysis. The ultimate confirmation was established by a single crystal X-ray analysis (Figure 1).[‡]

[†] *Ethyl nitrocyanoacetate potassium salt* **1**. A solution of KMnO₄ (23.7 g, 0.15 mol) in water (400 ml) was prepared. The solution of KOH (1.848 g, 0.033 mol) in water (35 ml) was added to ethyl cyanoglyoxylate-2-oxime **3** (14.2 g, 0.1 mol) in warm water (240 ml). The solution of KMnO₄ was added dropwise to compound **3** for 30 min maintaining the temperature not higher than 40 °C. The mixture was stirred at room temperature until the permanganate was consumed (a sample on the filter paper does not give purple color). The precipitate was filtered off, the filtrate was concentrated on a rotary evaporator at *T* < 40 °C, the dry residue was washed with ethanol and filtered. The precipitate was recrystallized from ethanol and dried. Yield 12.4 g (63%), white crystals, mp 245 °C. ¹H NMR, δ : 1.22 (t, 3H, Me, *J* 7.10 Hz), 4.05 (q, 2H, CH₂, *J* 7.10 Hz). IR (ν /cm⁻¹): 772, 1015, 1089, 1222, 1292, 1337, 1367, 1700, 2211. Found (%): C, 30.41, H, 2.76, N, 14.17. Calc. for C₅H₅N₂O₄K (%): C, 30.61, H, 2.57, N, 14.28.

Nitroacetonitrile potassium salt **2**. Salt **1** (9.8 g, 0.05 mol) was added to a solution of KOH (2.8 g, 0.05 mol) in water (40 ml) and the mixture was stirred overnight. Next day the pH of the solution was reduced from 14 to 9. The solvent was removed *in vacuo* at T < 40 °C, the dry residue was washed with ethanol, filtered and dried in air. This material was extracted with methanol (3×50 ml) at room temperature and then 50 ml on refluxing. The methanol extract was concentrated on a rotary evaporator at T < 30 °C, the residue was washed with ethanol and filtered. Yield 2.8 g (45%), pale-yellow crystals, mp 137 °C. ¹H NMR (DMSO-*d*₆) δ : 5.62 (s, 1H, CH). ¹H NMR (D₂O) δ : 4.68 (s, 1H, CH). ¹³C NMR (GATE) δ : 81.10 (d, CH, *J* 197.30 Hz), 119.68 (d, CN, *J* 9.00 Hz). ¹⁵N NMR, δ : 267.4 (CN), 367.7 (NO₂). IR (ν /cm⁻¹): 973, 1240, 1339, 1454, 1631, 1695, 2198, 3083, 3436. Found (%): C, 19.23, H, 0.49, N, 22.17. Calc. for C₂HN₂O₂K (%): C, 19.35, H, 0.81, N, 22.57.

[‡] *Crystal data for* **2**. The fragment of crystal (colorless rhombus, $0.25 \times 0.20 \times 0.15$ mm) of compound **2** ($C_2HO_2N_2K$, M = 124.14) was used for X-ray analysis. Analysis was performed at 295(2) K on an Xcalibur 3 diffractometer by standard procedure (graphite monochromated, MoK α radiation, ω -scanning). Space group *Fdd2*, a = 14.447(3), b = 11.1109(4) and c = 12.003(3) Å, V = 1926.8(7) Å³, Z = 16. 6208 reflections were measured, 2.87 < θ < 33.57°, among them 956 unique ($R_{int} = 0.0343$), 741 reflections with $I > 2\sigma(I)$. The structure was solved and refined using



Figure 1 Molecular structure of nitroacetonitrile potassium salt **2**. Bond lengths (Å) and angles (°): N(1)–C(2) 1.142, C(2)–C(1) 1.388, C(1)–H(1) 0.995, C(1)–N(2) 1.323, N(2)–O(1) 1.273, N(2)–O(2) 1.266, O(1)–K(1) 2.903, O(2)–K(2) 2.797; N(1)–C(2)–C(1) 178.27, C(2)–C(1)–N(2) 117.75, C(2)–C(1)–H(1) 123.82, C(1)–N(2)–O(2) 120.83, O(2)–N(2)–O(1) 118.26.

Nitroacetonitrile potassium salt **2** as the very NAN readily reacts with aromatic and heterocyclic aldehydes **4a–e** to form 3-(het)aryl-2-nitroacrylonitriles **5** (Scheme 2).[§]



Scheme 2

Salt 2 turned out to be a suitable water-soluble azo coupling reagent. In this way, 2-nitro-2-phenylhydrazonoacetonitrile **6** was obtained by reacting phenyldiazonium salt with the potassium salt of NAN instead of NAN² (Scheme 3).



The procedure can be simplified if one does not isolate salt **2** from the reaction mixture after hydrolysis of ester **1**. For this purpose the required amount of sodium acetate solution is added to the crude mixture containing salt **2**. The resulting solution is used directly for the azo coupling.[¶]

In summary, we have developed a new safe and easy method for the synthesis of the potassium salt of nitroacetonitrile, and

the SHELX97 program package. All non-hydrogen atoms were refined anisotropically, the positions of the hydrogen atoms were calculated as a riding model in isotropic approximation. The correction of the absorption was taken into account using MultiScan technique ($\mu = 0.978 \text{ mm}^{-1}$). Goodness of fit at F^2 is 1.003; final *R* values [$I > 2\sigma(I)$], $R_1 = 0.0236$, $wR_2 = 0.0487$; *R* values (all reflections), $R_1 = 0.0331$, $wR_2 = 0.0496$. Residual electronic density $e_{\text{max}}/e_{\text{min}}$ was 0.169/-0.223 eÅ⁻³.

CCDC 1453318 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

[§] 2-*Nitro-3-phenylacrylonitrile* **5a**. Ethanol (1 ml), nitroacetonitrile potassium salt **2** (0.248 g, 0.002 mol) and benzaldehyde **4a** (0.212 g, 0.002 mol) were added sequentially to trifluoracetic acid (0.456 g, 0.004 mol) on stirring. The mixture was stirred for 3 h at room temperature and evaporated to dryness. Product **5a** was extracted with boiling CCl₄ and crystallized under cooling in ice bath. The precipitate was filtered, washed with CCl₄ and dried. Yield 0.216 g (62%), yellow crystals, mp 101 °C (lit, ⁴ 101 °C). ¹H NMR, δ: 7.60–7.74 (m, 3H, 3CH), 8.11 (m, 2H, 2CH), 9.01 (s, 1H, CH). IR (ν /cm⁻¹): 1183, 1210, 1294, 1320, 1537, 1587, 1615, 2229, 3044. Found (%): C, 61.85; H, 3.46; N, 16.04. Calc. for C₉H₆N₂O₂ (%): C, 62.07; H, 3.47; N, 16.08.

For synthesis and characteristics of compounds **5b–e**, see Online Supplementary Materials.

shown that this salt can be a promising substitute for the free nitroacetonitrile in a variety of organic reactions.

The work was supported by the Russian Science Foundation (grant no. 14-13-01301).

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2016.03.031.

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Received: 5th October 2015; Com. 15/4743

[¶] Nitro(phenylhydrazono)acetonitrile 6. Salt 1 (0.353 g, 0.0018 mol) was added to a solution of KOH (0.1 g, 0.0018 mol) in water (5 ml) and the mixture was stirred overnight. Next day the pH of the solution was reduced from 14 to 9 and aqueous AcONa solution (1.4 ml, 3.9 M, 0.0054 mol) was added and the mixture was cooled to 5 °C. In another vessel, cold solution of sodium nitrite (0.138 g, 0.002 mol) in water (3 ml) was added to a solution of aniline (0.167 g, 0.0018 mol) in water (3 ml) and 12 M HCl (0.45 ml, 0.0054 mol) at -5 °C maintaining the temperature of the reaction mixture not higher than 0°C. This mixture was stirred for 10 min and transferred to the above cooled solution of nitroacetonitrile with sodium acetate. The resulting suspension was stirred at room temperature for 1 h, filtered, washed with an aqueous alcohol solution and dried in air. Yield 0.14 g (41%), orange powder, mp 152 °C (lit.,²¹ 146 °C). ¹H NMR, δ: 7.15–7.79 (m, 5H, 5CH), 13.38 (br.s, 1H, NH). IR (v/cm⁻¹): 686, 731, 747, 761, 828, 890, 1150, 1231, 1247, 1318, 1412, 1487, 1532, 2232, 3191. Found (%): C, 50.33; H, 3.39; N, 29.07. Calc. for C₈H₆N₄O₂ (%): C, 50.53; H, 3.18; N, 29.46.