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Mendeleev Commun., 2006, **16(4)**, 228–230

Mendeleev Communications

Transformations of cyanoacetylenic alcohols in the presence of the cyanide ion

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DOI: 10.1070/MC2006v016n04ABEH002250

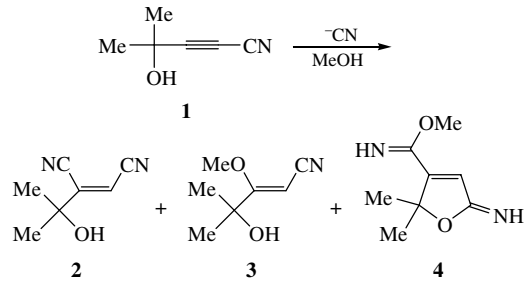
The transformation of 4-hydroxy-4-methylpent-2-ynenitrile in the presence of KCN in methanol (20–25 °C, 1 h) leads to (*Z*)-2-(1-hydroxy-1-methyl)but-2-enedinitrile, 4-hydroxy-3-methoxy-4-alkylalk-2-enenitrile and 2-imino-5,5-dimethyl-4-methoxycarbimide-2,5-dihydrofuran. In dioxane at room temperature, KCN catalyses the auto-transformation of cyanoacetylene to 2,2-dimethyl-3,4-di(cyanomethylene)oxetane and 2,5-di(cyanomethylene)-3,3,6,6-tetramethyl-1,4-dioxane; in aqueous dioxane (20–25 °C, 4 h), the reaction affords 5-amino-2,2-dimethyl-3(2*H*)-furanone.

Cyanoacetylenes belong to the organic compounds found in space, and they are likely involved in the origination of life.[1] In turn, the cyanide ion in water tends to form complex molecules, such as amino acids and purine bases,[2] which play a key role in the functioning of living organisms. The reactions of cyanoacetylenes with the cyanide ion in water may also be expected to give functionalised nitrogen-containing compounds, such as aspartic acid, asparagine, cytosine *etc*.[2] Therefore, a systematic study of cyanoacetylene transformation in the presence of cyanides under biomimetic conditions may extend our knowledge of the organonitrogen matter evolution under prebiotic conditions.

Cyanoacetylenic alcohols, $R^1R^2C(OH)C{\equiv}C–CN$, are simple Favorsky adducts of cyanoacetylene to aldehydes and ketones. They are the precursors of biologically important compounds related to ascorbic, penicillic, tetronic acids and their thiol analogues.[3,4]

Here, the transformations of cyanoacetylenic alcohols in the presence of the cyanide ion observed on the example of 4-hydroxy-4-methylpent-2-ynenitrile **1** are discussed.

In methanol (20–25 °C, 1 h), cyanoacetylene **1** reacts with the cyanide ion to afford (*Z*)-dinitrile **2**, (*Z*)-3-methoxypentenenitrile **3** and iminodihydrofuran **4** in a ratio of 2:2:1 (^{1}H NMR, GC/MS) (Scheme 1).†



Scheme 1

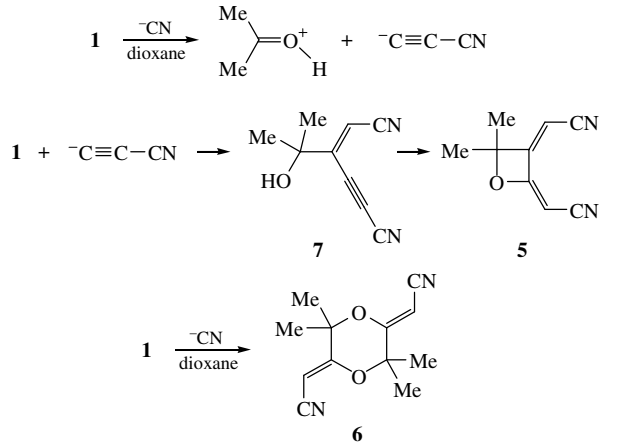
Dinitrile **2** is the expected adduct of $^-$CN to the triple bond of **1**, while nitrile **3** results from similar addition of the methoxide ion to cyanoacetylene **1**.[5] The ^{1}H NMR ($CDCl_3$) spectrum of dinitrile **2** shows one olefin proton at 6.42 ppm, which is indicative of the formation of a single isomer. The latter has probably (*Z*)-configuration, if the reaction proceeds as normal concerted nucleophilic addition.[6] Iminodihydrofuran **4** is a product

of further transformation of dinitrile **2** involving the methanol addition to a nilrile group and intramolecular cyclization of remaining nitrile function with the hydroxyl group.

In dioxane, cyanoacetylene **1** and the cyanide ion give 2,2-dimethyl-3,4-di(cyanomethylene)oxetane **5** as a major product with an admixture of 2,5-di(cyanomethylene)-3,3,6,6-tetramethyl-1,4-dioxane **6** (20:1, respectively), (^{1}H NMR, GC/MS) (Scheme 2).‡

The formation of oxetane **5** is seemingly preceded by the retro Favorsky reaction (the cleavage of cyanoacetylene **1** to protonated acetone and cyanoacetylene anion). The latter adds to the second molecule of cyanoacetylene **1** to give dicyanovinylacetylene **7**, which further cyclises to oxetane **5**.[7] 1,4-Dioxane **6** is a dimer of cyanoacetylene **1**.[8]

In aqueous dioxane (20–25 °C, 4 h), the same reaction leads to 5-amino-2,2-dimethyl-3(2*H*)-furanone **8**[9] in 17% yield (Scheme 3).§



Scheme 2

† Mass spectra were recorded on a Shimadzu GCMS-QP5050A spectrometer.

Chromatographic column parameters were as follows: SPB™-5, length of 60 m, internal diameter of 0.25 mm, stationary phase film thickness of 0.25 μm; injector temperature of 250 °C, carrier gas, helium, flow rate of 0.7 ml min^{-1}; detector temperature of 250 °C; mass analyzer: quadrupole, electron ionization, electron energy of 70 eV, ion source temperature of 200 °C; mass range of 34–650 Da. The reaction was controlled by thin-layer chromatography on neutral Al_2O_3 (chloroform–benzene–ethanol, 20:4:1, as an eluent). Potassium cyanide is a commercial reagent. 4-Hydroxy-4-methylpent-2-ynenitrile **1** was prepared according to a published method.[10]

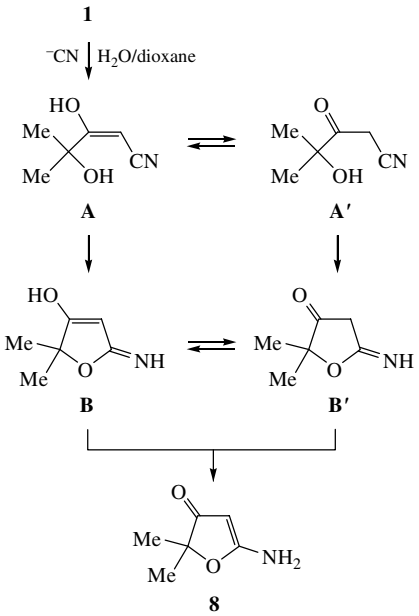
The reaction of 4-hydroxy-4-methylpent-2-ynenitrile with KCN in methanol. To a solution of KCN (0.25 g, 3.85 mmol) in methanol (4 ml) a solution of cyanoacetylene **1** (0.25 g, 2.29 mmol) in methanol (3 ml) was slowly added. The reaction mixture was stirred at room temperature for 1 h. Then, methanol was removed in a vacuum and the residue was distilled with water (2 ml). The distillate was extracted with diethyl ether (5×5 ml); the ether extracts were washed with water and dried over $MgSO_4$. The extractant was removed and the residue was evacuated to give 0.348 g of a faint-yellow oil-like product containing dinitrile **2**, 3-methoxypentenenitrile **3** and iminodihydrofuran **4**, 2:2:1, respectively (^{1}H NMR and GC/MS data).

1: MS, *m*/*z* (%): 94 [M – Me]$^+$ (100), 43 (74), 39 (24).

2: ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 6.42 (s, 1H, =CH), 2.63 (br. s, 1H, OH), 1.53 (s, 6H, Me). ^{13}C NMR (100.69 MHz, $CDCl_3$) δ: 144.26 (*C*=CH), 114.35, 114.23 (C≡N), 110.61 (=CH), 72.82 (Me–*C*), 28.71 (*Me*–C). IR (microlayer, ν/cm^{-1}): 3450 (OH), 3075, 1650 (HC=C, C=C), 2230, 2185 (CN). UV-Vis [EtOH, λ_{max}/nm (lg ε)]: 225 (4.24). MS, *m*/*z* (%): 136 [M]$^+$ (12), 121 [M – Me]$^+$ (34), 59 [Me(Me)C=OH]$^+$ (18), 43 (100). Found (%): C, 61.58; H, 5.73; N, 20.74. Calc. for $C_7H_8N_2O$ (%): C, 61.75; H, 5.92; N, 20.58.

3: ^{1}H NMR spectrum corresponds to the literature data.[5] MS, *m*/*z* (%): 141 [M]$^{+\cdot}$ (12), 126 [M – Me]$^+$ (26), 59 [Me(Me)C=OH]$^+$ (71), 43 (100).

4: ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 6.46 (s, 1H, =CH), 3.78 (s, 3H, OMe), 1.57 (s, 6H, Me). ^{13}C NMR (100.69 MHz, $CDCl_3$) δ: 168.45 (C=NH), 156.65 (*C*=CH), 124.67 (C=*C*H), 89.58 (*C*–Me), 53.19 (OMe), 26.05 (Me). IR (KBr, ν/cm^{-1}): 3438, 3216 (H–N=), 3101, 1627 (HC=C, C=C), 1673 (H–N=). UV-Vis [EtOH, λ_{max}/nm (lg ε)]: 213 (3.99), 246 (4.08). MS, *m*/*z* (%): 168 [M]$^+$ (2), 153 [M – Me]$^+$ (41), 125 [M – CHNO]$^+$ (100), 59 [Me(Me)C=OH]$^+$ (12), 43 (93). Found (%): C, 57.43; H, 7.40; N, 16.50. Calc. for $C_8H_{12}N_2O_2$ (%): C, 57.13; H, 7.19; N, 16.66.



Scheme 3

Apparently, the addition of the hydroxide ion to the triple bond of **1** gives intermediates **A** and **A′**, which undergo cyclization to hydroxyiminodihydrofuran **B** and iminodihydrofuran **B′**. The stabilization of intermediates **B** and **B′** affords aminofuranone **8**.

This work was supported by the Russian Foundation for Basic Research (grant no. 05-03-32290a) and the Presidium of the Russian Academy of Sciences (programme no. 25).

References

1 (*a*) S. Mitton, *New Sci.*, 1970, **47**, 369 (*Chem. Abstr.*, 1970, **73**, 92836); (*b*) B. E. Turner, *Astrophys. J.*, 1971, **163** (1), L35; (*c*) R. L. De Zafra, *Astrophys. J.*, 1971, **170** (1), 165; (*d*) D. F. Diskinson, *Astrophys. Lett.*, 1972, **12** (4), 235; (*e*) Ph. M. Solomon, *Phys. Today*, 1973, **26** (3), 32; (*f*) J. Tennyson, in *Handbook of Molecular Physics and Quantum Chemistry*, ed. S. Wilson, Wiley, Chichester, 2003, vol. 3, ch. 14, p. 356; (*g*) Y. Osamura and S. Petrie, *J. Phys. Chem. A.*, 2004, **108**, 3615; (*h*) S. Petrie and Y. Osamura, *J. Phys. Chem. A.*, 2004, **108**, 3623.

2 (*a*) R. A. Sanchez, J. P. Ferris and L. E. Orgel, *Science*, 1966, **154**, 784; (*b*) J. P. Ferris, R. A. Sanchez and L. E. Orgel, *J. Mol. Biol.*, 1968, **33**, 693.

‡ *The transformation of 4-hydroxy-4-methylpent-2-ynenitrile in the system KCN–dioxane*. The suspension containing cyanoacetylene **1** (0.25 g, 2.29 mmol), KCN (0.272 g, 4.18 mmol) and dioxane (6 ml) was stirred at room temperature for 24 h. The dark-brown reaction mixture was passed through a thin layer (3–4 cm) of Al_2O_3 (ether and chloroform as an eluent). The solvents were removed in a vacuum to give 0.212 g of a product consisting of cyanoacetylene **1**, 2,2-dimethyl-3,4-di(cyanomethylene)oxetane **5** and 2,5-di(cyanomethylene)-3,3,6,6-tetramethyl-1,4-dioxane **6**, 13:20:1, respectively (^{1}H NMR and GC/MS data).

5: ^{1}H and ^{13}C NMR spectra correspond to the literature data.[7] MS, *m*/*z* (%): 160 [M]$^+$ (59), 105 (61), 79 (91), 67 [M – $(Me)_2C_4NH$]$^+$ (42), 66 (100), 65 (54), 54 (41), 52 (47), 51 (44), 43 (79), 39 (99).

6: ^{1}H and ^{13}C NMR spectra correspond to the literature data.[8] MS, *m*/*z* (%): 218 [M]$^+$ (17), 110 [M – Me – C_6H_7N]$^+$ (90), 82 (51), 69 (45), 68 (44), 43 (49), 41 [C_2HO]$^+$ (100), 39 (59).

§ *The reaction of 4-hydroxy-4-methylpent-2-ynenitrile with KCN in aqueous dioxane.* A solution of cyanoacetylene **1** (0.255 g, 2.34 mmol) in dioxane (2 ml) and water (2 ml) was slowly added to a solution of KCN (0.31 g, 4.76 mmol) in dioxane (2 ml) and water (2 ml). Immediately, the reaction mixture became black. Then, the mixture was stirred at room temperature for 4 h. The mixture was extracted with diethyl ether (3×10 ml) and chloroform (3×10 ml), the extracts were combined, washed with water and dried over $MgSO_4$. The solvents were removed under reduced pressure, the residue was dried in a vacuum to afford 0.05 g of 5-amino-2,2-dimethyl-3(2*H*)-furanone **8** (17%) as a light-beige powder.

8: mp 228–230 °C. IR, ^{1}H and ^{13}C NMR spectra correspond to the literature data.[9] MS, *m*/*z* (%): 127 [M]$^+$ (33), 69 [M – $(Me)_2CO$]$^+$ (41), 41 [C_2HO]$^+$ (100).

3 G. Shenoy, P. Kim, M. Goodwin, Q. A. Nguyen, C. E. Barry and C. S. Dowd, *Heterocycles*, 2004, **63**, 519.
4 (*a*) B. A. Trofimov, A. G. Mal'kina and Yu. M. Skvortsov, *Zh. Org. Khim.*, 1993, **29**, 1268 (*Russ. J. Org. Chem.*, 1993, **29**, 1053); (*b*) B. A. Trofimov and A. G. Mal'kina, *Heterocycles*, 1999, **51**, 2485.
5 R. N. Kudyakova, Yu. M. Skvortsov, A. G. Mal'kina, E. I. Kositsyna and V. B. Modonov, *Zh. Org. Khim.*, 1991, **27**, 521 [*J. Org. Chem. USSR* (*Engl. Transl.*), 1991, **27**, 451].
6 H. G. Viehe, *Chemistry of Acetylenes*, Marcel Dekker, New York, 1969.
7 Yu. M. Skvortsov, A. G. Mal'kina, B. A. Trofimov, G. A. Kalabin, A. N. Volkov and V. B. Modonov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1980, 1349 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1980, **29**, 967).
8 Yu. M. Skvortsov, A. G. Mal'kina and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, 1983, 996 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1983, **19**, 806].
9 L. V. Andriyankova, N. D. Abramova, A. G. Mal'kina and Yu. M. Skvortsov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, 1421 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1989, **38**, 1301).
10 S. R. Landor, B. Demetriou, R. Grzeskowiak and D. Pavey, *J. Organomet. Chem.*, 1975, **93**, 129.

Received: 14th October 2005; Com. 05/2588