Reaction of 2,2,3,3-tetracyanocyclopropyl ketones with ammonia

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A single-step synthesis of 2,4-diamino-1,6-dicyano-3-azabicyclo[3.1.0]hex-2-en-6-carboxamides from 2,2,3,3-tetracyanocyclopropyl ketones and ammonia has been performed.

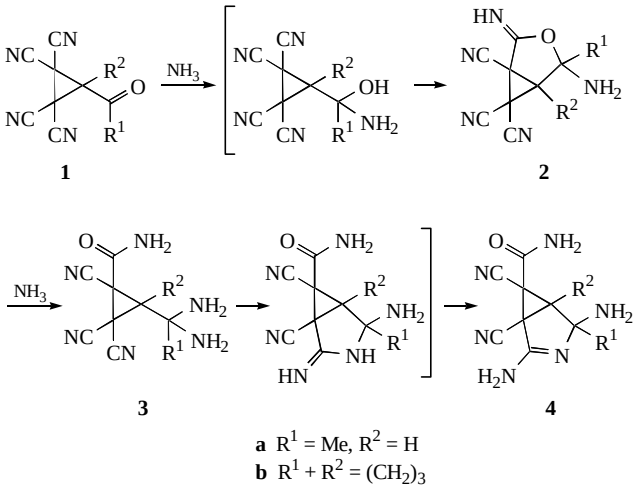
H. Hart and F. Freeman[1] were the first to use 3,3-dimethyl-1,1,2,2-tetracyanocyclopropane in the synthesis of nitrogen-containing heterocyclic compounds. The reaction time varied from 1 to 3 h. More recently, Yashkanova *et al.*[2,3] prepared oxygen-containing heterocycles from β-cyanocyclopropyl ketones. The reaction time varied from 1 h to a day, and the yields were 8–54%.

We have recently found that tetracyano-substituted alkanones exhibit high reactivity towards ammonia. We have synthesised 3-amino-1,2-dicyano-4,6-diazabicyclo[3.2.1]oct-2-en-7-ones[4] and 3-amidinio-2-aminopyridine-4-carboxylates[5] from β,β,γ,γ-tetracyanoalkanones and ammonia. Based on these data, we assumed that 2,2,3,3-tetracyanocyclopropyl ketones will also be highly reactive towards ammonia. As a result of the reaction of 2,2,3,3-tetracyanocyclopropyl ketones **1** with ammonia, we found a new property of tetracyanocyclopropanes, namely, the formation of a pyrroline ring, the transformation of only one of the cyano groups to a carboxamide group, and the addition of two ammonia molecules to a molecule of **1**. The mixing of compounds **1** with aqueous ammonia (at room temperature) gives bicyclic compounds **4a**,**b**.† The reaction proceeds very rapidly in 30–40 s with 72–82% yields. Moreover, complicated multistage processes correspond to this rapid reaction.

We synthesised compounds **1** from α-chloro ketones and tetracyanoethylene.[6]

The structure of compounds **4a**,**b** was determined by X-ray diffraction analysis using single crystals of **4b**‡ and by IR and ^{13}C NMR spectroscopy.†

The formation of a single carboxamide functional group in this reaction apparently occurs by an intramolecular process. Based on the fact that only the cyano groups disposed at the same side of the cyclopropane ring towards the C→O direction of the C=O bond[6] enter the reaction, we suppose that an ammonia molecule adds, and the HO···CN interaction leads to intermediate **2**. Analogous intramolecular processes of the formation of the carboxamide group were described earlier for the transformation of 6-hydroxy-3,3,4,4-tetracarbonitriles into 3,3,4-tricyano-2,3,4,5-tetrahydropyridine-4-carboxamides[7] and for the reaction of β-cyanoalkanones with ammonia.[8] Next, probably, the second ammonia molecule adds to form intermediate **3**. The formation of the pyrroline ring and compounds **4a**,**b** results from the interaction between amino and cyano groups in intermediate **3**.



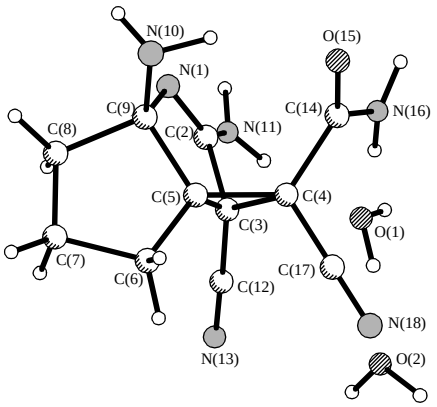


Figure 1 Molecular structure of **4b**. Bond lengths (Å): O(15)–C(14) 1.219(2), N(1)–C(9) 1.479(2), N(11)–C(2) 1.345, N(16)–C(14) 1.317(3), C(2)–C(3) 1.509(2), C(3)–C(5) 1.519(2), C(4)–C(17) 1.444(2), C(4)–C(14) 1.546(2), C(5)–C(9) 1.536(2), N(1)–C(2) 1.284(2), N(10)–C(9) 1.450(2), N(13)–C(12) 1.136(3), N(18)–C(17) 1.141(2), C(3)–C(12) 1.438(2), C(3)–C(12) 1.438(2), C(3)–C(4) 1.550(2), C(4)–C(5) 1.507(2), C(5)–C(6) 1.507(2), C(6)–C(7) 1.531(3), C(7)–C(8) 1.501(3), C(8)–C(9) 1.555(3).

† *Experimental procedure*: 0.01 mol of 2,2,3,3-tetracyanocyclopropyl ketones **1a**,**b** was mixed with 10 ml of aqueous ammonia (10–20%). The reaction was complete in 30–40 s. The formed precipitate was filtered off and washed with propan-2-ol.

^{13}C NMR spectra were recorded on a Geminee-300 (Varian) instrument in [$^2H_6$]DMSO.

For **4a**: yield 72%, mp 131–132 °C. ^{13}C NMR, δ: 31.83 [C(6)], 35.25 [C(1)], 53.75 [C(5)], 87.05 [C(4)], 112.88 (CN), 112.99 (CN), 154.66 [C(2)], 162.54 ($CONH_2$). IR (Vaseline oil, ν/cm^{-1}): 3500–3220 (ν_{NH}), 3085 (ν_{C-H}) 1640 (δ_{NH}), 2270 ($\nu_{C\equiv N}$), 1690 ($\nu_{C=O}$), 1580 ($\nu_{C=C}$).

For **4b**: yield 82%, mp 134–135 °C. ^{13}C NMR, δ: 34.72 [C(6)], 35.36 [C(1)], 54.26 [C(5)], 91.39 [C(4)], 113.51 (CN), 114.50 (CN), 151.65 [C(2)], 160.36 ($CONH_2$). IR (Vaseline oil, ν/cm^{-1}): 3490–3190 (ν_{NH}), 1650 (δ_{NH}), 2270 ($\nu_{C\equiv N}$), 1700 ($\nu_{C=O}$), 1590 ($\nu_{C=C}$).

The carbon atoms C(1)–C(6) are numbered in accordance with the name 2,4-diamino-1,6-dicyano-3-azabicyclo[3.1.0]hex-2-en-6-carboxamide.

‡ *Crystal data for* **4b**: $C_{11}H_{16}N_6O_3$, M = 280.30, triclinic crystals, at 25 °C a = 8.228(3), b = 8.682(3), c = 10.895(4) Å, α = 82.51(3)°, β = = 86.22(3)°, γ = 62.85(3)°, V = 687(1) Å^3, d_{calc} = 1.356 g cm^{-3}, Z = 2, space group $P1$. The cell parameters and intensities of 2796 independent reflections were measured on a Siemens P3/PC automatic four-circle diffractometer (λMoKα radiation, graphite monochromator, $\theta/2\theta$-scan to θ = 25°). The terminal discrepancy factors are $R_1(F)$ = 0.057, $wR_2(F^2)$ = = 0.150. The whole calculation was carried out according to the SHELXTL PLUS program. Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2000. Any request to the CCDC for data should quote the full literature citation and the reference number 1135/59.

The one-pot synthesis of compounds **4** is a new method for the annelation of a pyrroline ring to tetracyanocyclopropanes and for the preparation of new condensed compounds, in which a moiety contains several electron-acceptor substituents, and the other, several electron-donating substituents.

As compared with the heterocycle syntheses described in refs. 1–3, the method based on β-cyanocyclopropyl ketones is much easier to perform. The reaction proceeds more rapidly, and the yields are higher.

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