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Interaction of tetracyanoethylene with α,β-unsaturated aldehydes. Synthesis of 2,4-dialkyl-7-imino-6-oxabicyclo-[3.2.1]oct-3-ene-1,8,8-tricarbonitriles

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Abstract—The reaction of tetracyanoethylene with α,β-unsaturated aldehydes under hydrochloric acid catalysis leads to 2,4-dialkyl-7-imino-6-oxabicyclo[3.2.1]oct-3-ene-1,8,8-tricarbonitriles. The structures of these new cyclohexene derivatives were determined by NMR experiments and X-ray crystallography.

The reaction of tetracyanoethylene with a large number of ketones has been widely investigated to date.[1] It was shown that the product 4-oxoalkane-1,1,2,2-tetracarbonitriles are highly reactive substances that give different products with a number of reagents under mild conditions.[2] Some of the tetracyanoalkanone derivatives were found to be promising anticancer drugs,[3] charge transition complexes[4] and salts with planar organic anions have been obtained.[5] Curiously the reaction of tetracyanoethylene with aldehydes has not been studied. Hence, we decided to investigate this reaction in the case of α,β-unsaturated aldehydes.[6]

In our earlier publications, we reported that the interaction of tetracyanoethylene with α,β-unsaturated ketones under acidic catalysis led to two types of compounds: 3-acetonylcyclobutan-1,1,2,2-tetracarbonitriles[7] and 4-oxocyclohexane-1,1,2,2-tetracarbonitriles.[8] It has now been established that under similar conditions the reaction of tetracyanoethylene with α,β-unsaturated aldehydes gave 2,4-dialkyl-7-imino-6-oxabicyclo[3.2.1]oct-3-ene-1,8,8-tricarbonitriles in 38–72% yields (Scheme 1).[9]

We assume that the reaction proceeds through protonation of the carbonyl group followed by 1,4-elimination of a proton, with the formation of diene **A**. It is well known that being an active dienophile, tetracyanoethylene gives 4-cyclohexene-1,1,2,2-tetracarbonitriles in quantitative yields.[10] Therefore, diene **A** reacts with tetracyanoethylene leading to zwitterion **B**. As we reported earlier, stabilization of intermediate **B** in the case of α,β-unsaturated ketones proceeds with the formation of cyclobutanes,[7] that is leads to the 3,4-addition product. In the present case, the reaction gives products of 1,4-addition, resulting in cyclohexene **C**. The product is obtained finally via cyclization involving the hydroxy and cyano groups (Table 1).

Enolization of α,β-unsaturated carbonyl compounds involves hyperconjugation of the γ-hydrogen atom. Hyperconjugation is the reason why cyclobutanes are obtained from α,β-unsaturated ketones[7] and 2,4-dialkyl-7-imino-6-oxabicyclo[3.2.1]oct-3-ene-1,8,8-tricarbonitriles are obtained from the corresponding aldehydes.

The structures of compounds **2a**–**c** were confirmed by IR, ^{1}H NMR and mass spectrometry.[11] In the IR spectra of compounds **2a**–**c** intense N–H imino absorptions between 3200 and 3300 cm^{-1} as well as valence vibration bands of the C=N group at 1690 cm^{-1} were observed. Vibrations of the unconjugated cyano groups were registered as weak intensity bands at 2260–2270 cm^{-1}. In

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Keywords: Alicyclic compounds; Cyano compounds; Cyclohexenes; α,β-Unsaturated aldehydes.

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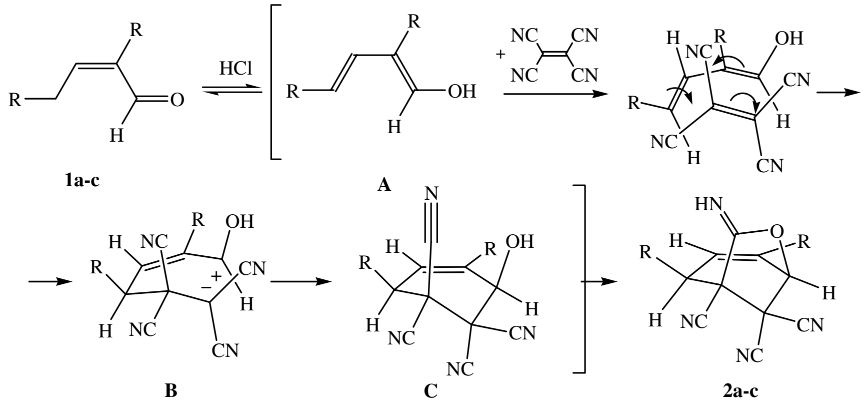

Scheme 1. Synthesis of tricarbonitriles **2a**–**c**.

Table 1. Preparation of 2,4-dialkyl-7-imino-6-oxabicyclo[3.2.1]oct-3-ene-1,8,8-tricarbonitriles (**2a**–**c**)

Carbonyl compound	R	Product	Yield[a] (%)
1a	R = CH_3	**2a**	50
1b	R = C_2H_5	**2b**	72
1c	R = C_3H_7	**2c**	63

[a] Isolated yields.

the ^{1}H NMR spectra, the characteristic signal for the proton of the imino group occurred as singlet at 9.7 ppm. The signals of the =C–C*H*O and C*H*=CR protons were observed as singlets at 5.9–5.8 and 5.6 ppm. The splitting of the signal of the double bond proton had a small spin–spin constant. This fact was explained by the proximity to 90° of the angle between the double bond proton and the proton of the cyclic carbon atom bearing the alkyl substituent.

The structure of compound **2b** was confirmed by X-ray diffraction analysis of single crystals.[12] The unit cell contained three independent molecules (Fig. 1). Figures 2, 2a and 2b show that the molecule with atoms numbered by index **b** (Fig. 2b) is enantiomeric to the molecule shown in Figure 2 and is conformationally isomeric to the structure depicted in Figure 2a. The difference between the structures in Figures 2a and 2b lies in the spatial arrangement of the ethyl substituent on the double bond. The torsion angle C^{14}–C^{11}–C^3–C^2 in the molecule in Figure 2 is 63.4°, while the corresponding values in the molecules in Figures 2a and 2b are 175.3° and −66.8°. In other respects the geometrical parameters of all the molecules were equal within standard specific tolerance for angles and distances and did not exceed the bounds for the values of appropriate bond types.[13]

In conclusion, we have reported a synthesis of 2,4-dialkyl-7-imino-6-oxabicyclo[3.2.1]oct-3-en-1,8,8-tricarbonitriles in dioxane under acid catalysis, demonstrating the 4+2 cycloaddition of tetracyanoethylene to three (enolized) α,β-unsaturated aldehydes. The cycloadducts undergo further cyclization in situ (intramolecular hydration of one of the cyano groups) to produce the title compounds.

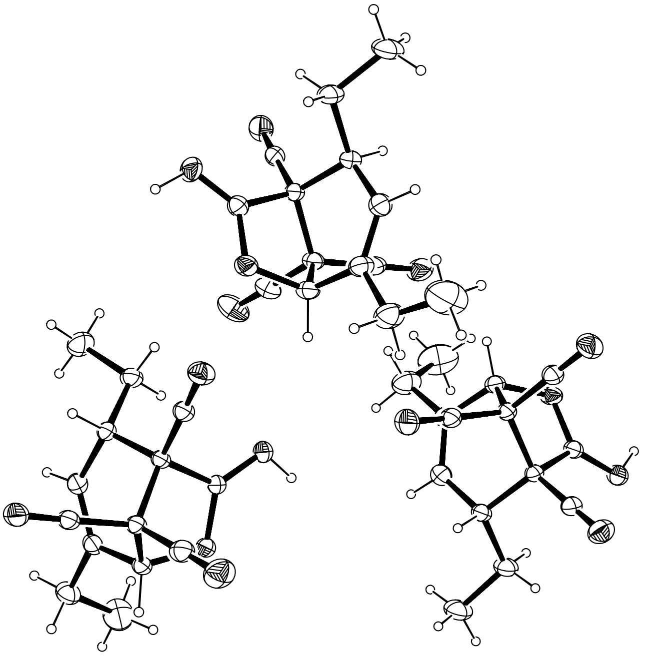

Figure 1.

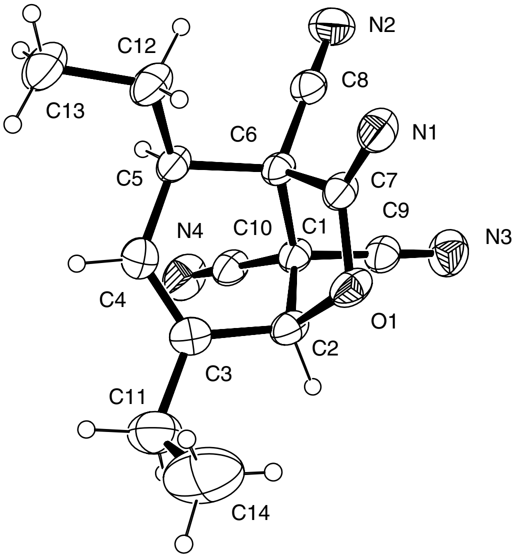

Figure 2.

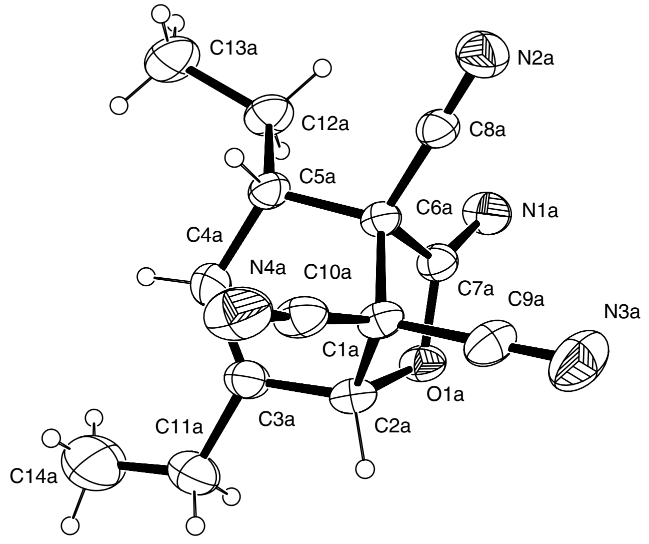

Figure 2a.

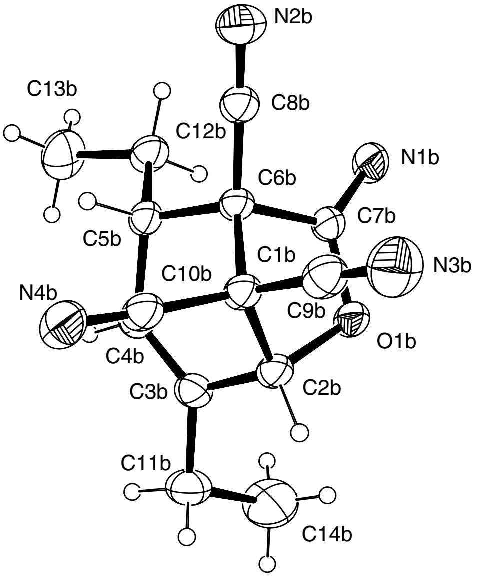

Figure 2b.

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9. *Typical procedure* for the preparation of 2,4-dialkyl-7-imino-6-oxabicyclo[3.2.1]oct-3-en-1,8,8-tricarbonitriles **2a**–**c**: a solution of tetracyanoethylene (0.64 g, 5 mmol) in dioxane (10 ml) was mixed with aldehyde **1a**–**c** (10 mmol) and several drops of concentrated hydrochloric acid were added. On completion of the reaction (TLC and hydroquinone test) the mixture was diluted with water, and the resulting precipitate was filtered and washed with water.
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11. Analytical data for compounds **2a**–**c**. Compound **2a**: mp: 110 °C. IR 3300, 3200 (NH), 2265 ($C{\equiv}N$), 1690 ($C{=}N$) cm^{-1}. ^{1}H NMR (500.13 MHz, DMSO-d_6): δ 9.64 (1H, s, NH), 5.78 (1H, s, =C*H*–CH), 5.62 (1H, s, –O–CH–), 3.36 (1H, m, –C*H*–CH$_3$), 1.85 (3H, s, CH$_3$–C=), 1.25 (3H,

d, $J = 6.8$ Hz, $\mathrm{C}H_3$–CH). MS: m/z 226 (M^+). Anal. Calcd for $\mathrm{C_{12}H_{10}N_4O}$: C, 63.71; H, 4.46; N, 24.76. Found: C, 63.66; H, 4.49; N, 24.72. Compound **2b**: mp 196 °C. IR 3300, 3275, 3245 (N–H), 2265 (C≡N), 1690 (C=N) $\mathrm{cm^{-1}}$. ^{1}H NMR (500.13 MHz, DMSO-d_6): δ 9.71 (1H, s, NH), 5.90 (1H, s, *H*–CH), 5.68 (1H, s, –O–CH–), 3.13 (1H, m, C*H*–$\mathrm{CH_2}$), 2.18 (2H, q, $J = 7.3$ Hz, =C–$\mathrm{C}H_2$–$\mathrm{CH_3}$), 1.77 (1H, m, $\mathrm{CH_3}$–HC*H*–CH), 1.42 (1H, m, $\mathrm{CH_3}$–*H*CH–CH), 1.12 (3H, t, $J = 7.3$ Hz, $\mathrm{C}H_3$–$\mathrm{CH_2}$), 1.01 (3H, t, $J = 7.9$ Hz, $\mathrm{C}H_3$-$\mathrm{CH_2}$). MS: m/z 254 (M^+). Anal. Calcd for $\mathrm{C_{14}H_{14}N_4O}$: C, 66.13; H, 5.55; N, 22.03. Found: C, 66.08; H, 5.57; N, 21.96. Compound **2c**: mp: 184 °C. IR 3290 (NH), 2265 (C≡N), 1690 (C=N) $\mathrm{cm^{-1}}$. ^{1}H NMR (500.13 MHz, DMSO-d_6): δ 9.72 (1H, s, NH), 5.90 (1H, s, =C*H*–CH), 5.67 (1H, s, –O–CH–), 3.17 (1H, dd, $J = 2.4$, 5.9 Hz, –C*H*–$\mathrm{CH_2}$), 2.12 (2H, t, $J = 7.3$ Hz, =C–$\mathrm{C}H_2$–$\mathrm{CH_3}$), 1.77–1.33 (6H, m, 3 × $\mathrm{CH_2}$), 0.93 (3H, t, $J = 7.3$ Hz, $\mathrm{C}H_3$–$\mathrm{CH_2}$), 0.86 (3H, t, $J = 7.3$ Hz, $\mathrm{C}H_3$–$\mathrm{CH_2}$). MS: m/z 282 (M^+). Anal. Calcd for $\mathrm{C_{16}H_{18}N_4O}$: C, 68.06; H, 6.43; N, 19.84. Found: C, 68.02; H, 6.47; N, 19.79.

12. Crystallographic data (excluding structure factors) for the structure in this letter (**2b**) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 625979. Copies of these 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].
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