Reaction of Acetaldehyde and Malononitrile.
2,2,4,4-Tetracyano-3,5-dimethylcyclohexylmalononitrile

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Received December 11, 1972[1]

JOHN J. KRAJEWSKI and JAMES W. MOYER. Can. J. Chem. **52**, 3626 (1974)

The condensation of acetaldehyde and malononitrile is reported to yield 1,1,3,3-tetracyano-2,4-dimethylcyclobutane. The n.m.r. spectrum of this material and several of its derivatives, however, was found to best fit the title compound. A reaction scheme for the formation of the title compound is suggested.

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Il a été rapporté que la condensation de l'acétaldéhyde avec le malononitrile conduit au tétracyano-1,1,3,3 diméthyl-2,4 cyclobutane. On trouve toutefois que le spectre r.m.n. de ce composé et plusieurs de ces dérivés correspond mieux à la structure tétracyano-2,2,4,4 diméthyl-3,5 cyclohexylemalononitrile. [Traduit par le journal]

The study of the condensation of simple aldehydes with malononitrile is historically old (1). The reaction of formaldehyde with malononitrile, which has been studied by a number of investigators (2–5), is unique and may, under the appropriate conditions, give several products.

1   **2**   **3**
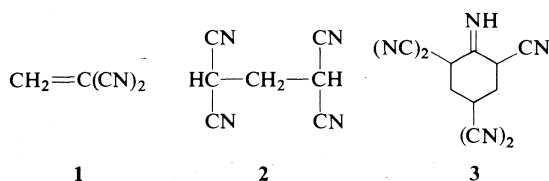
The simplest condensation product, vinylidene cyanide (**1**), was isolated, characterized, and found to be extremely reactive (2). Condensation of **1** with malononitrile in vapor or liquid phase occurs readily without base catalysis to form 1,1,3,3-tetracyanopropane (**2**) (2–4). Further condensation of **1** with **2** via Michael and Thorpe reactions yields 2,2,4,4,6-pentacyanocyclohexanonimine (**3**) (5).

The reaction of acetaldehyde with malononitrile follows a somewhat similar course. The simplest isolable product was found to be 1,1,3,3-tetracyano-2-methylpropane (**4**) (6). Although ethylidene malononitrile (**5**) has not been isolated and characterized, its existence in equilibrium with malononitrile and **4** has been demonstrated by n.m.r. spectroscopy (7).

4   **5**   **6**
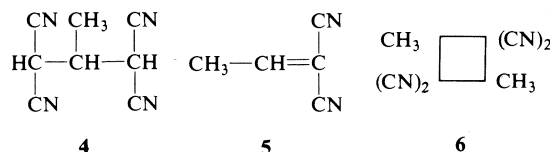
Primarily on the basis of elemental analysis and a cryoscopic molecular weight determination in acetic acid, a second equimolar condensation product of malononitrile and acetaldehyde was reported to be 1,1,3,3-tetracyano-2,4-dimethylcyclobutane (**6**), m.p. 184.5° (6).

In view of the similarity of the reaction of formaldehyde and acetaldehyde with malononitrile to produce unstable alkylidene malononitriles and subsequently 1,1,3,3-tetracyano-2-alkylpropanes, it was felt that the structure assigned to the acetaldehyde malononitrile condensation product, **6**, melting at 184° was incorrect. If the parallelism between the two aldehydes were to follow, one might anticipate instead the formation of 2,2,4,4,6-pentacyano-3,5-dimethylcyclohexanonimine (**7**). For this reason, the condensation of acetaldehyde and malononitrile was reexamined.

The condensation of 2 mol malononitrile with 1 mol acetaldehyde in ethanol, by a preparation slightly modified from that reported by Diels *et al.* (3), gave a product melting at 81–83°. Although melting points of 113–114° and 99–100° were reported (3, 7), the compound analyzed correctly for $C_8H_6N_4$ (7). The n.m.r. spectrum confirmed the findings of Hart and Freeman (7), that is, 1,1,3,3-tetracyano-3-methylpropane (**4**)

7

8

9 X = Br
10 X = Cl
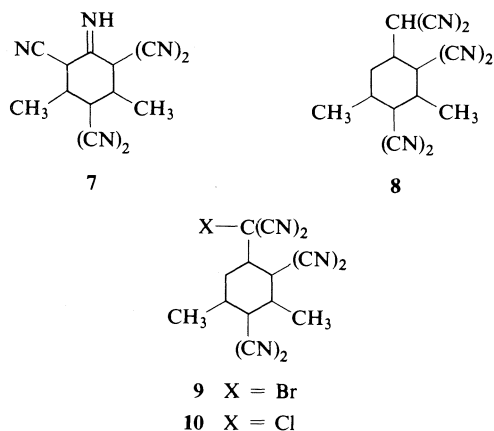
exists in equilibrium with malononitrile and ethylidene malononitrile (5). It is therefore clear that sharpness of melting point and accuracy of elemental analysis are insufficient criteria for the purity of 1,1,3,3-tetracyano-2-alkylpropanes. These results are brought about by shifts in the Michael-type equilibrium.

Condensation of equimolar quantities of acetaldehyde and malononitrile gave a compound having elemental analysis and melting point in agreement with those reported for **6** (6). Examination of the i.r. spectrum indicated the presence of nitrile groups but an absence of any N—H, C=C, or C=N bonds. Thus, the correct structure for this product cannot be 2,2,4,4,6-pentacyano-3,5-dimethylcyclohexanonimine (**7**) but instead some structure (**8**) which at this point was uncharacterized.

Several attempts to repeat the reported (6) cryoscopic molecular weight determination in glacial acetic acid failed because of severe supercooling. A determination of the ebullioscopic molecular weight in acetic acid gave a value of 287 (mol. wt. calcd. for $C_{15}H_{12}N_6$: 276).

The mass spectrum of **8** shows a molecular ion peak (M^+) at m/e 276 and an $(M + 1)^+$ ion peak at m/e 277. The presence of the $(M + 1)^+$ ion peak is consistent with a nitrile containing structure since peaks at mass $(M + 1)$ are characteristic of nitriles (8). The relatively large intensity of the $(M + 1)^+$ peak in comparison with the intensity of the molecular ion is attributed to a large number of nitrile groups in the structure. Significant fragment ion peaks support the proposed structure as follows: m/e 211, loss of $CH(CN)_2$; m/e 185 (base peak), loss of $CH(CN)_2$ and CN; m/e 66 and 65, $(CH_2(CN)_2)^+$ and

$(CH_2(CN)_2)^+$; m/e 41, $(CH_3CN)^+$; m/e 27 and 26, $(HCN)^+$ and $(CN)^+$. At lower electron ionization voltages, the relative intensities of the peaks at m/e 276 and 277 increase with respect to fragmentation ion peaks, thus supporting their assignment as M^+ and $(M + 1)^+$ ion peaks, respectively. The mass spectral data in general are consistent with the proposed structure for **8**. Consequently, the correct structure corresponds to a compound analyzing for $C_{15}H_{12}N_6$.

The n.m.r. spectrum of **8** was determined in deuterated nitromethane and deuterated pyridine. If one assigns a value of 1 proton for the integral of the smallest peak, the integration curves are then consistent with a total of 12 protons. This is in agreement with a $C_{15}H_{12}N_6$ (**8**) structure. Two doublets of three protons each correspond to two nonequivalent methyl groups attached to methine carbons. The methine proton coupled exclusively to one of the methyl groups appears as a quartet at δ 3.06 in deuterated nitromethane and at δ 3.66 in deuterated pyridine. The coupling of this methine proton to the methyl group at δ 1.90 in deuterated nitromethane was confirmed by double resonance experiments. One proton appearing as a doublet at δ 4.70 in deuterated nitromethane and as a singlet at δ 8.59 in deuterated pyridine is assigned to $CH(CN)_2$ and $C(CN)_2^- \cdot C_5D_5N^+H$, respectively. Further complex multiplets between δ 1.9–3.0 account for the methylene group and the remaining ring methine proton. These protons form the ABC part of an $ABCMX_3$ spin system whose chemical shifts and coupling constants cannot be readily determined. These spectral features are consistent with 2,2,4,4,-tetracyano-3,5-dimethylcyclohexylmalononitrile (**8**). Consequently, the structure **6** which was assigned to the compound melting at 184° is incorrect.

An examination of the proposed structure for **8** will show that it is stereochemically complex. 2,2,4,4-Tetracyano-3,5-dimethylcyclohexylmalononitrile (**8**) has three asymmetric carbons which give rise to four possible pairs of enantiomorphs. These enantiomorphic pairs are diasteriomeric with respect to each other. Attempts to separate these diasterioisomers by thin-layer or column chromatography on several supports with several solvents and their mixtures were unsuccessful.

The Michael and Knoevenagel condensation reactions leading to the formation of **8** are known

to be reversible and may, therefore, lead to the epimerization of **8**, particularly about the 1 position. Consequently, further attempts at a total structure proof including stereochemical and conformational analysis were abandoned in favor of a gross structure proof.

Bromination and chlorination of **8** resulted in the mono halogenation products, bromo-2,2,4,4-tetracyano-3,5-dimethylcyclohexylmalononitrile (**9**) and chloro-2,2,4,4-tetracyano-3,5-dimethylcyclohexylmalononitrile (**10**), respectively, as evidenced by elemental analysis and n.m.r. spectroscopy.

The n.m.r. spectra of **9** and **10** are much simplified in that the $CH(CN)_2$ proton is replaced by a halogen atom. The resonance of the proton at C-1 for **10** is thus reduced to a doublet of doublets with couplings of 11.8 and 3.0 Hz. These couplings very likely arise from an axial–axial interaction and an axial–equatorial interaction, respectively, with the two protons at C-6. This establishes axial conformation for the proton at C-1 (and equatorial conformation for the dicyanochloromethyl group).

The condensation of acetone with malononitrile or mesityl oxide with malononitrile is reported to yield 2,2,6-tricyano-3,3,5-trimethylcyclohex-5-eneonimine (**12**) via the same intermediate (9, 10).

The possibility that the noncyclic malononitrile adduct of crotonaldehyde (**14**) might similarly be an intermediate to **8** was investigated. The only solid material resulting from the condensation of crotonaldehyde and malononitrile was concluded to have an empirical formula $C_{10}H_8N_4$. The mass spectrum showed a molecular ion at m/e 184 and base peak at m/e 41 (CH_3CN^+) which is consistent with structures having nitrile groups in close steric proximity with a methyl group. The i.r. spectrum indicated the presence of nitrile (2260 cm^{-1}), N—H (ca. 3270 cm^{-1}), and C=C or C=N (1660 and 1620 cm^{-1}). These data are consistent with 2,2,6-tricyano-3-methylcyclohex-5-enonimine (**13a**) and its tautomer 2,2,6-tricyano-3-methylcyclohexa-4,6-dienamine (**13b**). These results preclude the possibility that a noncyclic crotonaldehyde–malononitrile adduct (**14**) is a common precursor to **8** and **13**. It is likely, however, on the basis of analogy to the reported mechanism for α,β-unsaturated ketone–malononitrile condensations (9, 10), that the noncyclic crotonaldehyde–malononitrile adduct (**14**) is the precursor to **13**.

Equimolar quantities of acetaldehyde and **4** upon refluxing in ethanol with a trace of piperidine was found to afford a 40.8% yield of **8**.

Upon mixing equimolar quantities of acetaldehyde and malononitrile in ethanol, with or without catalytic quantities of piperidine, a spontaneous exotherm occurs with the formation of a high yield of **4**. This reaction mixture contains 50 mol% **4** and 50 mol% acetaldehyde. Upon refluxing this reaction mixture, it may be assumed that the unreacted acetaldehyde undergoes aldol condensation to yield crotonaldehyde. After the reaction mixture has been refluxed for about 2 h, **8** appears as a precipitate in 84% yield. By refluxing a solution of $\frac{2}{3}$ mol **4** with $\frac{1}{3}$ mol crotonaldehyde in the presence of piperidine for about 2 h, a 37% yield of **8** (identified by i.r. and n.m.r. spectroscopy) resulted. When a solution of equimolar quantities of **4**, crotonaldehyde and malononitrile in ethanol containing one drop of piperidine is refluxed for 15–20 min, **8** (identified by i.r. and n.m.r. spectroscopy) precipitates from the reaction mixture in 52% yield. The above observations coupled with knowledge that the formation of **4** and **5** is reversible, leads the authors to suggest a reaction route for the formation of **8** outlined in Scheme 1.
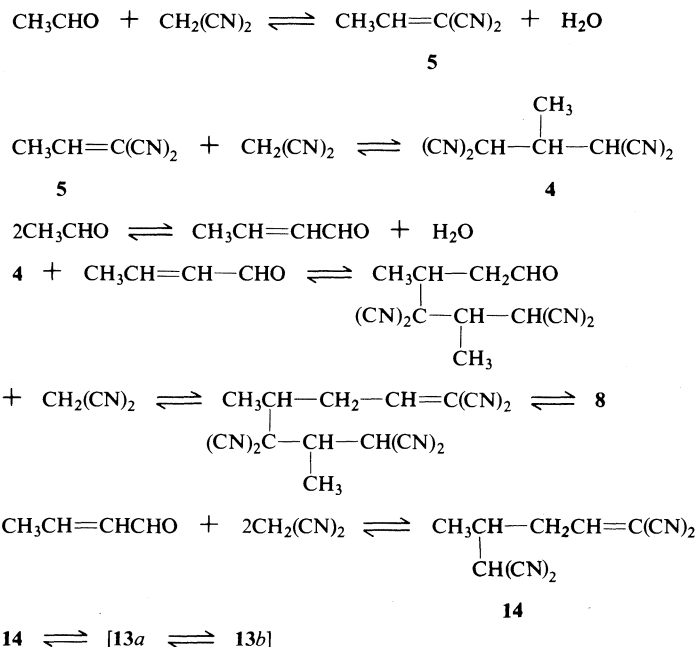
Experimental

1,1,3,3-Tetracyano-3-methylpropane (4)

The title compound was prepared by a method slightly modified from that reported by Diels *et al.* (3). A solution of malononitrile (54 g) and acetaldehyde (18 g) in ethanol (200 ml) was stirred overnight at room temperature. The resulting mixture was chilled, filtered, and the solids dried to yield crude **4** (53.4 g, 83%), m.p. 74–80°. Recrystallization twice from Skelly Solve C afforded an analytical sample, m.p. 81.2–83° (lit. (6) m.p. 113–114°). The n.m.r. spectrum of this material was in agreement with that published by Hart and Freeman (7), that is n.m.r. (CD_3SOCD_3): **4**, δ 1.60 (d, J = 7.0 Hz, 3H, $CHCH_3$ at C-2) δ 3.24 (m, 1H at C-2) δ 5.28 (d, J = 5.2 Hz, 2H at C-1 and C-3); malononitrile δ 4.47 (s, 2H); **5**, δ 2.25 (d, J = 7.2 Hz, 3H, $CHCH_3$) δ 7.98 (q, J = 7.2 Hz, 1H).

$$CH_3CHO + CH_2(CN)_2 \rightleftharpoons CH_3CH{=}C(CN)_2 + H_2O$$

5

$$CH_3CH{=}C(CN)_2 + CH_2(CN)_2 \rightleftharpoons (CN)_2CH{-}\underset{\overset{|}{CH_3}}{\overset{\overset{CH_3}{|}}{CH}}{-}CH(CN)_2$$

5   **4**

$$2CH_3CHO \rightleftharpoons CH_3CH{=}CHCHO + H_2O$$

$$\mathbf{4} + CH_3CH{=}CH{-}CHO \rightleftharpoons CH_3\underset{\underset{CH_3}{\overset{|}{(CN)_2C{-}CH{-}CH(CN)_2}}}{\overset{|}{CH}}{-}CH_2CHO$$

$$+ CH_2(CN)_2 \rightleftharpoons CH_3\underset{\underset{CH_3}{\overset{|}{(CN)_2C{-}CH{-}CH(CN)_2}}}{\overset{|}{CH}}{-}CH_2CH{=}C(CN)_2 \rightleftharpoons \mathbf{8}$$

$$CH_3CH{=}CHCHO + 2CH_2(CN)_2 \rightleftharpoons CH_3\underset{\overset{|}{CH(CN)_2}}{\overset{|}{CH}}{-}CH_2CH{=}C(CN)_2$$

14

$$\mathbf{14} \rightleftharpoons [\mathbf{13}a \rightleftharpoons \mathbf{13}b]$$

SCHEME 1

Anal. Calcd. for $C_8H_6N_4$: C, 60.8; H, 3.8; N, 35.4. Found: C, 60.7; H, 3.8; N, 35.2.

2,2,4,4-Tetracyano-3,5-dimethylcyclohexylmalononitrile (8)

A solution of malononitrile (66 g), acetaldehyde (45 g), and piperidine (2 drops) in ethanol (200 ml) was refluxed for 2 h. The resulting solid was filtered with suction, washed with water, and dried to yield crude **8** (77 g, 84%), m.p. 181–183°. An analytical sample was prepared by recrystallization from dimethyl sulfoxide–ethanol (1:10), m.p. 186–188° (lit. (6) m.p. 184–185°), mass spectrum (72 eV) m/e (relative intensity) 277(3.7), 276(0.7), 211(26), 185(100), 148(24), 147(24), 119(35), 93(33), 92(57), 66(30), 65(20), 52(34), 41(87), 27(38), 26(9). ν_{max} (KBr) 2230 cm^{-1} (saturated CN), no absorptions for C=C or C=NH; n.m.r. (CD$_3$NO$_2$): δ 1.51 (d, $J = 6.0$ Hz, 3H, CHCH$_3$ at C-5), δ 1.90 (d, $J = 7.0$ Hz, 3H, CHCH$_3$ at C-3), δ 1.9–3.0 (m, 1H, CHCH$_3$ at C-5) and m, 2H at C-6), δ 3.06 (q, $J = 7.0$ Hz, 1H, CHCH$_3$ at C-3), δ 3.1 (m, 1H at C-1), and δ 4.70 (d, $J = 4.4$ Hz, 1H, CH(CN)$_2$); n.m.r. (C$_5$D$_5$N): δ 1.23 (d, $J = 6.0$ Hz, 3H, CHCH$_3$ at C-5), δ 1.81 (d, $J = 7.0$ Hz, 3H, CHCH$_3$ at C-3), δ 3.66 (q, $J = 7.0$ Hz, 1H, CHCH$_3$ at C-3), δ 3.51 (d of d, $J = 10.3$ Hz, $J = 3.0$ Hz, 1H, at C-1), and δ 8.59 (s, 1H, C(CN)$_2^-$·C$_5$D$_5$NH$^+$).

Mol. Wt. Calcd. for $C_{15}H_{12}N_6$: 276. Found (ebullioscopic molecular weight in acetic acid): 287. (Blank, acetanilide, Calcd.: 135. Found: 133.4.)

Anal. Calcd. for $C_{15}H_{12}N_6$: C, 65.2; H, 4.3.; N, 30.4. Found: C, 65.3; H, 4.3; N, 30.4.

Bromo-2,2,4,4-tetracyano-3,5-dimethylcyclohexyl-malononitrile (9)

To a stirred solution of **8** (12 g) in glacial acetic acid (300 ml) was added bromine (11 g). The resulting solution

was treated with an equal volume of water, the solids filtered, washed with water and air dried to yield pure **9** (14.5 g, 94%), m.p. 168–169° (dec.), n.m.r. (CD$_3$SOCD$_3$): δ 1.40 (d, $J = 6.0$ Hz, 3H, CHCH$_3$ at C-5), δ 1.75 (d, $J = 7.0$ Hz, 3H, CHCH$_3$ at C-3), δ 1.9–2.9 (m, 1H, CHCH$_3$ at C-5 and m, 2H at C-6), δ 3.58 (q, $J = 7.0$ Hz, 1H, CHCH$_3$ at C-3), δ 3.92 (d of d, $J = 11.8$ Hz, $J = 3.0$ Hz, 1H at C-1).

Anal. Calcd. for $C_{15}H_{11}BrN_6$: C, 50.7; H, 3.1; N, 23.7; Br, 22.5. Found: C, 50.6; H, 3.2; N, 23.8; Br, 22.4.

Chloro-2,2,4,4-tetracyano-3,4-dimethylcyclohexyl-malononitrile (10)

Into a stirred solution of **8** (10 g) in glacial acetic acid (300 ml) and water (50 ml) was bubbled chlorine until no further change was noted. The reaction mixture was treated with an equal volume of water, the solids filtered, washed with water, and dried to yield crude **10** (9.8 g, 87%), m.p. 162–164° (dec.). An analytical sample was prepared by recrystallization three times from ethanol and water, m.p. 171° (dec.); n.m.r. (CD$_3$NO$_2$): δ 1.54 (d, $J = 6.0$ Hz, 3H, CHCH$_3$ at C-5), δ 1.97 (d, $J = 7.0$ Hz, 3H, CHCH$_3$ at C-3), δ 1.9–2.8 (m, 1H, CHCH$_3$ at C-5 and m, 2H at C-6), δ 3.14 (q, $J = 7.0$ Hz, 1H, CHCH$_3$ at C-3), and δ 3.52 (d of d, $J = 11.8$ Hz, $J = 3.0$ Hz, 1H, at C-1).

Anal. Calcd. for $C_{15}H_{11}ClN_6$: C, 58.0; H, 3.5; N, 27.1; Cl, 11.4. Found: C, 57.8; H, 3.6; N, 27.1; Cl, 11.2.

8 from Acetaldehyde and 4

A solution of 1,1,3,3-tetracyano-2-methylpropane (**4**) (15.8 g), acetaldehyde (4.5 g), piperidine (one drop) in ethanol (200 ml) was refluxed for 1 h. The resulting solid (7.5 g, 54%) was shown by its melting point (m.p. 182–183°) and i.r. spectrum to be **8**.

8 from Crotonaldehyde and 4

A solution of 4 (10.4 g), 2.33 g crotonaldehyde, one drop piperidine in 80 ml ethanol was refluxed for 2 h to yield a solid precipitate. This crude product was identified by i.r. and n.m.r. spectroscopy as 8. The yield was 4.5 g (49.5%).

8 from 4, Crotonaldehyde, and Malononitrile

A solution of 15.8 g 4 in 60 ml ethanol was treated with 7 g crotonaldehyde and 1 drop of piperidine. The reaction mixture was stirred at room temperature for 15 min, treated with 6.6 g malononitrile and refluxed for 15–20 min to yield 14.5 g (52%) 8. (Identified by i.r. and n.m.r. spectroscopy.)

2,2,6-Tricyano-3-methylcyclohex-5-enonimine (13)

A solution of malononitrile (33 g) and crotonaldehyde (17.5 g) in ethanol (200 ml) was treated with piperidine (one drop) and refluxed for 2 h. The resulting solution was chilled, filtered, and the solids dried to yield 13 (17 g, 37%) melting above 305°; v_{max} (KBr) 3270 (NH), 2260 (CN), 1660 and 1620 cm^{-1} (C=C or C=N); mass spectrum (78 eV) m/e (relative intensity) M$^+$ 184 (3), major fragment 41(100).

Anal. Calcd. for $C_{10}H_8N_4$: C, 65.2; H, 4.3; N, 30.4. Found: C, 65.3; H, 4.4; N, 29.3.

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