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# STRUCTURAL STUDIES ON A NOVEL REACTION PRODUCT OF MALONONITRILE WITH A β,γ-UNSATURATED ALLENE ALDEHYDE

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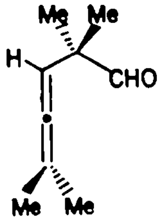
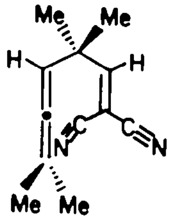
Abstract -- Condensation of 2,5,5-trimethylhexa-2,3-dien-6-al with malononitrile affords an unexpected product, $C_{15}H_{16}N_4$x, (3), the structure of which was partially characterized by spectral (infrared, ultraviolet, $^1H$, and $^{13}C$ nmr) methods and fully elucidated by single crystal X-ray analysis. 3 is 1-cyano-2-amino-3-(2-propenyl)-5,5-dimethy-6-dicyanomethycycohexa-1,3-diene in a half-chair conformation. Conjugation of the cis-aminocyanoethenyl moiety leads to intermolecular NH...N≡C hydrogen bonding in the crystal. A reaction sequence and its mechanistic implications are proposed.

In the course of our continuing study[1] of the di-π-methane rearrangement, we became interested in obtaining allenic di-π-methane substrates, which possessed strongly electron withdrawing substituents on the olefinic π-moiety. For this work it was necessary to prepare the dicyanoallene 2 from the allene aldehyde 1[2] and malononitrile.[3] The condensation of aldehydes or ketones with malononitrile via the Knoevenagel reaction[4] is known to yield alkylidene malononitriles. However when allene 1 was refluxed in benzene with malononitrile (aldehyde: malononitrile = 1:1) in the presence of ammonium acetate and acetic acid with concurrent removal of water (Dean Stark trap), a pale yellow solid (m.p. 167-8°C from 95% EtOH) was obtained. Preliminary analysis of the reaction product (combustion analysis and mass spectrometry)



1

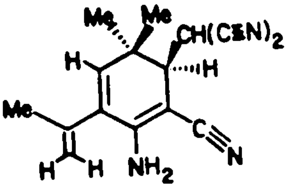


2

revealed that the product was not the anticipated 2 but rather a substance whose molecular formula ($C_{15}H_{16}N_4$) is consistent with the reaction stoichiometry shown below

$$1 + 2CH_2(CN)_2 \rightarrow C_{15}H_{16}N_4 + H_2O \qquad \text{(Eq. 1)}$$

The infrared spectrum of the product reveals the presence of a primary amino functionality, conjugated and non-conjugated nitriles, and the presence of a gem-dimethyl group. Notably absent from the infrared spectrum, however, was the expected allene absorption[5] at approximately 1950 $cm^{-1}$. This band would certainly be present if 2 had been obtained or if the allene functionality had been preserved during the reaction. The ultraviolet spectrum for the reaction product shows the presence of long wavelength absorption ($\lambda_{Max}$ 327 nm, ε 4500) suggesting the presence of extended conjugation. The proton nmr spectrum (acetone-$d_6$) confirms the presence of three different methyl groups, one of which is part of an isopropenyl moiety. The other two methyl signals, both of which are singlets, constitute the gem-dimethyl group (vida infra) as suggested by the infrared data. Additionally, there is a broad two-proton singlet and a one-proton doublet (both of which readily exchange with $D_2O$) as well as a vinyl proton doublet. A one-proton absorption appears as a doublet of doublets, and two one-proton multiplets can be attributed to the protons of the terminal isopropenyl double bond. These combined spectroscopic data indicate that the product obtained from the reaction of 1 with malononitrile under the reaction conditions cited is radically different from the usual and expected Knoevenagel condensation product. Thus, it was subjected to single crystal x-ray analysis and the isolated molecule was found to possess the novel structure 3.



3

## DISCUSSION

Crystal Structure. The crystal structure consists of descrete molecules of 3. The molecule (Figure 1) is a highly substituted 1,3-cyclohexadiene ring in the half-chair conformation ($\Delta C_2$ = 5.5°)[6]. This conformation is also found in a number of other 1,3-cyclohexadiene ring structures (Table 1). One of the endo-cyclic double bonds (C5 - C6) is of standard length. This π-system does not

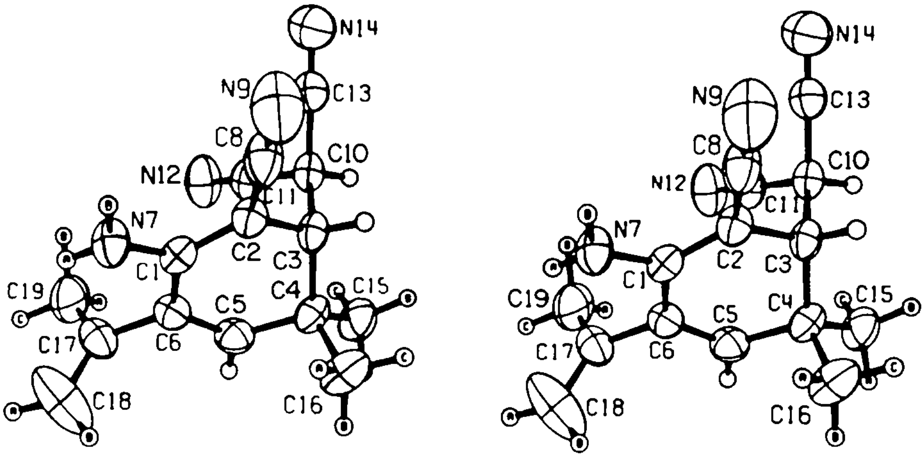
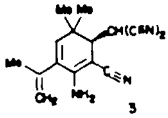
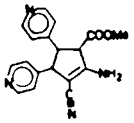
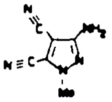
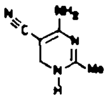
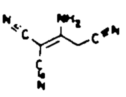
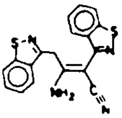
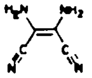
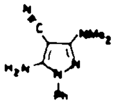


Figure 1. Stereoview of 3 showing 50% thermal ellipsoids.

TABLE 1

| Compound | $H_2N-C$ | $C=C$ | $C-C\equiv N$ | $\lvert\omega\rvert^a$ | Ref. |
|---|---|---|---|---|---|
|  3 | 1.351(4) | 1.365(4) | 1.421(4) | 3 | b |
|  | 1.342(10) | 1.341(10) | 1.385(10) | 2 | c |
|  | 1.387(9) | 1.391(9) | 1.419(9) | 4 | d |
|  | 1.350(6) | 1.368(6) | 1.404(6) | 1 | e |
|  FORM I | 1.312(5) | 1.381(5) | 1.422(5) | 3 | f |
| | | | 1.420(5) | 179 | |
| II | 1.308(6) | 1.377(6) | 1.424(6) | 2 | g |
| | | | 1.409(6) | 177 | |
|  | 1.318(11) | 1.387(11) | 1.424(11) | 174 | h |
|  | 1.365(8) | 1.363(8) | 1.421(8) | 175 | i |
| | | | 1.428(8) | 177 | |
|  | 1.360(9) | 1.390(9) | 1.410(9) | 3 | j |

[a] The torsion angle $H_2N-C=C-C\equiv N$. [b] This work. [c] I. Kompis and P. Schonholzer, Helv. Chim. Acta, 60, 618(1977). [d] P. Prusiner, M. Sundaralingam, T. Ito, and T. Sakuai, Acta Cryst., B32, 853(1976). [e] A. Edenhofer, H. Spiegelberg, and W. E. Oberhansli, Helv. Chim. Acta, 58, 1230(1975). [f] B. Klewe, Acta Chem. Scand., 25, 1999(1971). [g] B. Kleve, Acta Chem. Scand., 26, 317(1972). [h] E. Gaetari, T. Vitali, A. Mangia, M. Nardelli, and G. Pelizzi, J.C.S., PerkinII, 2125(1972). [i] B. R. Penfold, W. N. Lipscomb, Acta Cryst., 14, 589(1961). [j] J. P. Declerca, G. Germain, M. van Meerssche, A. Bettercourt, Z. Janousek, H. G. Viehe, Acta Cryst., B33, 413(1977).

Table III. Crystal Data.

| | |
|---|---|
| Space Group | $P\bar{1}$, triclinic |
| Cell Constants | a=9.043(7)Å |
| | b=9.095(7) |
| | c=9.934(6) |
| | $\alpha$=78.76(6)° |
| | $\beta$=73.86(6) |
| | $\gamma$=69.14(7) |
| | V=729.2Å$^3$ |
| Molecules per Cell | Z=2 |
| Molecular Formula | $C_{15}H_{16}N_4$ |
| Molecular Weight | MW=252.32 g-mole$^{-1}$ |
| Density (calc.) | d=1.149 g cm$^{-3}$ |
| Absorption Coefficient | $\mu$=0.62 cm$^{-1}$ |
| Radiation (Mo K$\alpha$) | $\lambda$=0.71073Å |
| Collection Range | $4° < 2\theta < 50°$ |
| Scan Width | $\Delta\theta=(1.10+0.35\tan\theta)°$ |
| Maximum Scan Time | 300 sec |
| Scan Speed Range | 0.33° to 3.35° min$^{-1}$ |
| Total Data Collected | 2596 |
| Independent Data with $I>\sigma(I)$ | 1447 |
| Total Variables | 236 |
| $R=\Sigma\|\,\|F_o\| - \|F_c\|\,\|/\Sigma\|F_o\|$ | 0.035 |
| $R_w=[\Sigma w(\|F_o\| - \|F_c\|)^2/\Sigma w\|F_o\|^2]^{1/2}$ | 0.030 |

Table IV. Fractional Atomic Coordinates of 3.

| ATOM | X/A | Y/B | Z/C |
|---|---|---|---|
| C1 | .2937(2) | .9598(3) | .2774(2) |
| C2 | .3446(2) | .8218(2) | .3603(2) |
| C3 | .3130(3) | .6745(2) | .3430(2) |
| C4 | .1485(3) | .7154(2) | .3053(2) |
| C5 | .1287(3) | .8555(3) | .1936(3) |
| C6 | .1931(2) | .9696(2) | .1794(2) |
| N7 | .3249(3) | 1.0932(2) | .2833(2) |
| C8 | .4281(3) | .8135(3) | .4641(2) |
| N9 | .4946(3) | .8048(3) | .5502(2) |
| C10 | .4593(3) | .5716(3) | .2377(2) |
| C11 | .4828(3) | .6428(2) | .0903(3) |
| N12 | .5097(3) | .6901(2) | -.0256(2) |
| C13 | .6125(3) | .5352(3) | .2796(2) |
| N14 | .7308(3) | .5095(3) | .3128(2) |
| C15 | .1313(4) | .5744(3) | .2557(3) |
| C16 | .0126(4) | .7634(4) | .4372(3) |
| C17 | .1647(3) | 1.1083(3) | .0685(3) |
| C18 | .0420(7) | 1.2432(4) | .1013(5) |
| C19 | .2714(4) | 1.0891(5) | -.0688(4) |

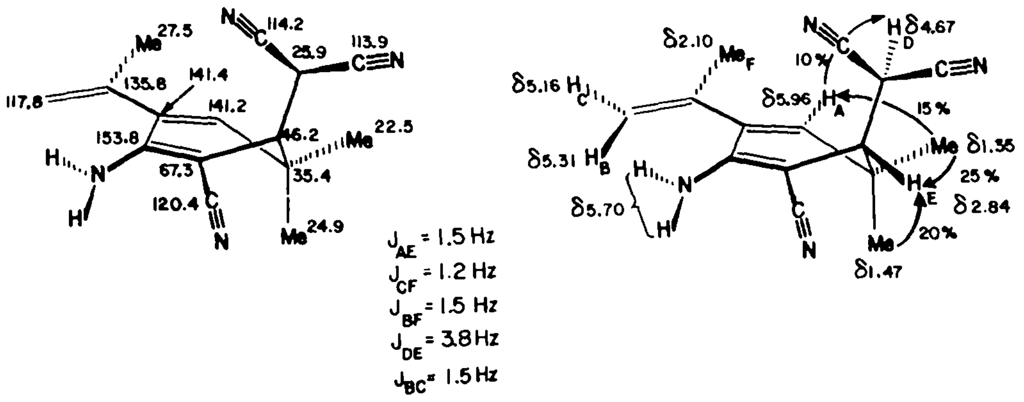
interact with either the adjacent vinyl substituent, which is orthogonally oriented, or with the other endocyclic π-system (C1 - C2). This latter double bond is significantly longer than C5 - C6 because the *cis*-aminocyanoethenyl moiety is highly conjugated ($H_2N\text{-}C\text{=}C\text{-}CN \leftrightarrow H_2N^+\text{=}C\text{-}C\text{=}N^-$), as has been observed in a number of previous cases (Table 1). All other bond lengths and bond angles are normal. Polarization of the *cis*-aminocyanoethenyl moiety gives rise to a strong dipolar attraction between adjacent molecules in the crystal; thus, molecules are joined in pairs by two N-H...N≡C bonds similar to the O-H...O=C bonding arrangement in carboxylic acid dimers. The extent of intermolecular hydrogen bonding can be judged by comparing the observed internuclear distance (H7B...N9' = 2.23 Å) with the distance expected from van der Waals contact alone. Assuming a van der Waals radius of 1.2 Å for hydrogen[7] and an oblate spheroidal nitrogen atom (major axis 1.69 Å, minor axis 1.42 Å)[8] the predicted contact distance is 2.67 Å.

**Structural Considerations and NMR Assignments.** The proton nmr data for **3** obtained in acetone-$d_6$ solution is summarized together with nuclear Overhauser effect data. The proton assignments are fairly straight forward with the exception of the proton signals of the *gem*-dimethyl group. Examination of Dreiding models of **3** indicates that one of the methyls occupies a pseudoequatorial position and the other methyl occupies a pseudoaxial position. The model shows that the pseudoequatorial methyl should be nearly coplanar with the vinyl proton attached to the cyclohexadiene moiety and should be spacially closer to the proton of the dicyanomethyl group than the pseudoaxial methyl. Application of the nuclear Overhauser effect permits assignment of the individual *gem*-dimethyl resonances. Interestingly, the pseudoequatorial methyl resonance is at a higher field than the pseudoaxial methyl and extends the trend which has been observed for equatorial and axial methyl resonances in six-membered carbocyclic rings.[9]

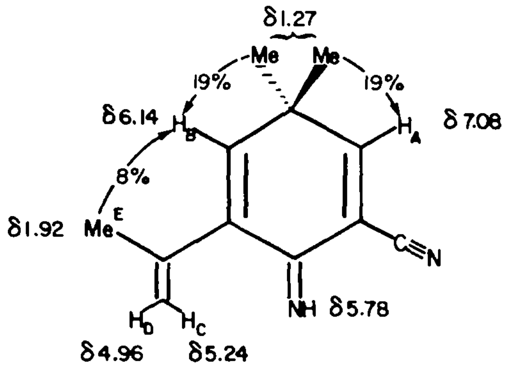
Structure **3** lacks symmetry and therefore requires that all carbons be chemically nonequivalent. The proton-noise-decoupled carbon-13 (PND) spectrum of **3** permits clear observation of all 15 carbon signals. The carbon-13 assignments (acetone-$d_6$) were obtained from a single-frequency-off-center-decoupling (SFOCD) experiment.

**Mechanistic Considerations.**

The formation of **3** represents a very unusual sequence of reactions although "abnormal" reaction chemistry involving malononitrile and carbonyl compounds is not without precedent.[10] The reaction pathway leading to the formation of **3** is shown in Scheme 1. In the initial step, malononitrile condenses with the allene aldehyde **1** to form the dicyanoalkylidene allene **2**. The dicyanoalkylidene allene **2** may then proceed potentially along two reaction pathways: (i)



thermal cyclization affords the imino-2,5-cyclohexadienone 4 which then reacts with a second equivalent of malononitrile to produce the final product 3; (ii) 2 may react with a second equivalent of malononitrile to afford 5 which then may cyclize thermally to produce the final 3. The treatment of 1 with one equivalent mole of malononitrile under fluoride ion catalysis[11] affords 2 (see experimental section). The subsequent reaction of 2 with another equivalent mole of malononitrile produces 3 in 69% yield. These reactions establish the intermediacy of 2 in the formation of 3 by either one of the two pathways.

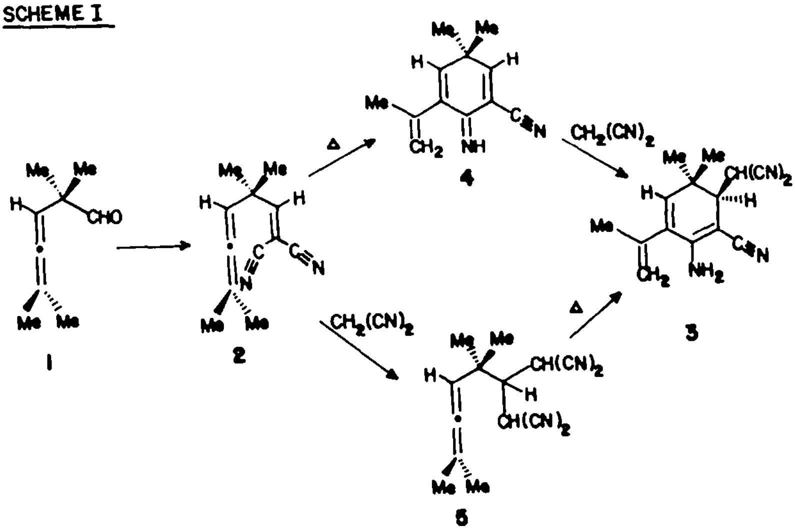


$J_{AB}$ = 2.6 Hz $J_{DE}$ = 0.6 Hz

$J_{CE}$ = 1.5 Hz $J_{CD}$ = 1.8 Hz

$$2 + CH_2(CN)_2 \xrightarrow{NH_4OAc} 3 \quad \text{(Eq.2)}$$

SCHEME I



The experimental evidence for the intermediacy of 4 during the conversion of 2 to 3 may be realized from the examination of the thermolyzed product of 2 in the absence of malononitrile. When 2 in $CDCl_3$ was heated at 50-55°C for 16 hours, a mixture consisting of 41% of 4 and 59% of unreacted 2 was obtained. Since this experiment was performed in an nmr sample tube, the results were derived from the $^1H$ nmr spectrum of the mixture. The $^1H$ nmr data for 4 are summarized below.

## Experimental Section

General. Infrared spectra were recorded on Perkin-Elmer 337 or 283 spectrophotometers and were calibrated against polystyrene. Ultraviolet spectra were recorded on a Cary Model 15 spectrophotometer. Proton magnetic resonance ($^1H$ nmr) spectra were obtained on Varian A-60, HA-100, or XL-100-15 nmr spectrometers. Proton noise decoupled (PND) carbon-13 nmr spectra were obtained on a Varian XL-100-15, spectrometer operating in the Fourier transform mode. Carbon assignments were confirmed by analysis of the single-frequency-off-center-decoupled (SFOCD) spectrum and by analysis of the undecoupled carbon-13 spectrum (gated with proton-carbon nOe). Electron impact mass spectra with an ionization voltage of 70eV were obtained on a Perkin Elmer-Hitachi RMU-6E spectrometer.

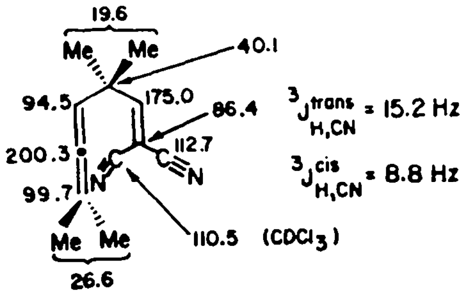
Condensation of malonitrile with 2,5,5-Trimethylhexa-2,3-dien-6-al (a) Ammonium Acetate Catalysis. - A solution of 13.8 g (0.10 mole) of 2,5,5-tri-methylhexa-2,3-dien-6-al, (1),[2] 6.6 g (0.10 mole) of malononitrile, 3 mL acetic acid, and 2.0 g of ammonium acetate in 30 mL of benzene was refluxed, using a Dean Stark trap, until the theoretical quantity of water (~ 3 mL) had been removed (18 hr). The benzene layer was cooled, washed with water (2 x 100 mL), dried (anhydrous $Na_2SO_4$), and evaporated to yield a brownish semisolid. The brown semisolid was recrystallized from 95% ethanol thus providing 3.75 g (30) of a pale yellow solid, m.p. 167-168°C which was identified as 3.

Anal. Calc. for $C_{15}H_{16}N_4$: C, 71.40; H, 6.38; N, 22.20.

Found: C, 71.23; H, 6.50; N, 22.29. Ir (Nujol), 3470(s), 3340(s) ($-NH_2$), 2250(w) (C≡N, non-conjugated), 2175(s) (C≡N, conjugated) 1375(m), 1365(m) (gem-$Me_2$); UV γMAX(MCOH), 228(ε 10,400), 327 (ε 4,500); mass spectrum, m/e (relative intensity), $M^+$ 252(6), 187(53), 171(100), 156(69), 147(56), 146(59), 131(15), 77(13), 66(83). (b) Potassium Fluoride Catalysis. - A solution of 2.8 g (0.02 mole) of 1, 1.3 g (0.02 mole) malononitrile, and 100 mg potassium fluoride in 25 mL of methanol was stirred overnight at room temperature. The methanol was evaporated, extracted with ether, and the product was distilled (110°C/2mm) affording 1.6 g (43%) of 2.

Anal. Calc. for $C_{12}H_{14}N_2$: C, 77.42; H, 7.53; N, 15.05.

Found: C, 77.31; H, 7.47; N, 15.10. $^1H$ NMR ($CDCl_3$), δ, 1.35 s (6H), (gem-$Me_2$); 1.73 d (J = 2.81 Hz) (6H), (allenic methyl groups); 5.04 septet, (J = 2.81 Hz) (1H), allenic proton; 7.22 s (1H), vinyl proton. The carbon-13 data together with assignments are given below:



Assignment of the two nitrile carbons is unequivocal based on the relative magnitude of the observed 3-bond proton-nitrile carbon coupling constants.[13]

Reaction of 2 with Malononitrile. A solution of 2 (900 mg, 4.84 x $10^{-3}$ mole), malononitrile (320 mg, 4.85 x $10^{-3}$ mole) and ammonium acetate (100 mg) in benzene (110 mL) was refluxed for 5 hrs. After cooling and washing the benzene with water (2 x 100 mL), drying (anhydrous $Na_2SO_4$), and evaporation of the benzene, there was obtained 840 mg (69%) of a crystalline solid which was shown (ir, nmr) to be identical to 3.

X-Ray Analysis. Data Collection. A nearly hexagonal plate-like crystal of approximate dimensions 0.4 x 0.3 x 0.2 mm was mounted on a glass fiber and aligned on an Enraf-Nonius CAD4 X-ray diffractometer. A preliminary survey of reflections indicated that the crystal is triclinic and precise lattice constants were obtained from least-squares refinement of 25 carefully centered reflections in the range 25° to 30° (2θ). Data collection was carried out as described elsewhere[14]. The crystal data are summarized in Table III.

Solution and Refinement. Statistical tests of the complete set of 2596 unitary structure factors indicated that the lattice is centrosymmetric. The E-map calculated with MULTAN[15] from the most probable phase set of 400 strongest refelections (E > 1.38) yielded all non-hydrogen atom positions. A Fourier difference map revealed the approximate hydrogen atom positions. The centrosymmetric refinement model in which all non-hydrogen atoms are assumed to undergo anisotropic thermal motion and all hydrogen atoms have isotropic thermal motion converged in several cycles of weighted ($w = \sigma(F)^{-2}$) full matrix least-squares to R(F) = 0.035 and Rw(F) = 0.030. The final values of the positional parameters are listed in Table IV. Table V lists observed and calculated structure factors.

Acknowledgements. We acknowledge the donors of the Petroleum Research Fund (Grant PRF 5471-AC1), administered by the American Chemical Society, and the Welsh Foundation (I.B.), for support of this work. We thank Division of Research Resources, National Institutes of Health, for support of the PROPHET system. The authors wish to thank Dr. George Gray (Varian Associates) for obtaining the carbon-13 nmr data described in this work.

Supplementary Material Available. Table II contains bond lengths, bond angles and torsion angles, table IVA contains refined positional and thermal parameters, and table V lists observed and calculated structure factors. Ordering information is given on any current masthead page.

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