Polyamines from Cyanobutadienes[1a]

F. J. Weigert

Central Research and Development Department, E. I. du Pont de Nemours & Company, Wilmington, Delaware 19898

Received July 14, 1977

Hydrazine reacts with 1-cyanobutadiene to produce 3-(cyanomethyl)pyrazolidine (**2**), whose reduction gives 1,3,5-pentanetriamine (**4**). Pyrazolidine **2** reacts with a wide variety of compounds to give 1:1 and 1:2 open-chain and cyclic adducts. Amines react with 1- and 2-cyanobutadienes to give products ranging from 1:1 to 4:3 adducts depending on the nature of the amine and the reaction conditions.

The 1,4 addition of many HX such as amines, alcohols, and thiols to either 1- or 2-cyanobutadienes has been described.[1,2] Either acid or base catalysis can equilibrate 2- and 3-pentenenitriles. With some HX a second addition occurs to give 2:1 adducts.

$$CH_2{=}CHCH{=}CHCN \xrightarrow{HX} XCH_2CH{=}CHCH_2CN$$

$$\rightleftarrows XCH_2CH_2CH{=}CHCN \xrightarrow{HX} XCH_2CH_2CHXCH_2CN$$

$$CH_2{=}CHC(CN){=}CH_2 \xrightarrow{HX} XCH_2C(CN){=}CHCH_3$$

$$\xrightarrow{HX} XCH_2CH(CN)CHXCH_3$$

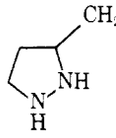
The reaction of hydrazine with 1-cyanobutadiene has been reported to give only hydrazinobutenenitrile **1**.[1]

We find that the general sequence is continued intramolecularly and 3-(cyanomethyl)pyrazolidine **2**, a reactive heterocycle, can be isolated in good yield.

$$N_2H_4 + CH_2{=}CHCH{=}CHCN \longrightarrow H_2NNHCH_2CH{=}CHCH_2CN$$

1

$$H_2NNHCH_2CH_2CH{=}CHCN \longrightarrow$$



2

In this paper, we describe the synthesis and chemistry of **2** and related compounds derived from the reactions of amines with cyanobutadienes.

Results

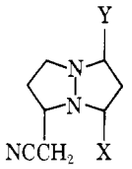
Combining methanol solutions of 1-cyanobutadiene and hydrazine at −25 °C and removing the solvent under vacuum at 0 °C gives 5-hydrazino-3-pentenenitrile **1**.[1] The infrared spectrum shows a primary amine and the NMR spectrum shows resonances for four allylic and two unconjugated vinyl protons.

The structure proof offered by Kurtz[1] for the *distilled* product does not distinguish between **1** or its cyclic isomer **2**. We find that any attempt to purify **1** involving temperature only slightly above ambient results in double-bond isomerization and subsequent ring closure.

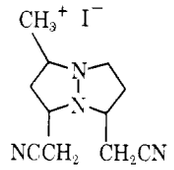
If the alcohol solution is refluxed before the solvent is removed, the NMR spectrum shows no vinyl absorptions. Distilling the viscous residue gives two fractions, the lower boiling being 3-(cyanomethyl)pyrazolidine **2**. Lower temperatures during the initial exothermic addition of hydrazine to 1-cyanobutadiene and excess hydrazine favor the formation of **2** over the higher boiling 2:1 adduct **3**. Either hydrazine hydrate or anhydrous hydrazine can be used.

The structure of **2** follows from its elemental analysis and NMR spectrum which shows no vinyl absorptions. At 220 MHz, all the ring protons are resolved and all the coupling constants can be obtained.

The gross structure of the higher boiling fraction **3a** or **3b** as an adduct of two cyanobutadienes to one hydrazine follows from its elemental analysis and proton NMR spectrum. Reacting pyrazolidine **2** with excess 1-cyanobutadiene also gives **3a, b.** There are several isomeric possibilities for **3a, b,** and the



3a, X = CH_2CN; Y = H
b, X = H; Y = CH_2CN



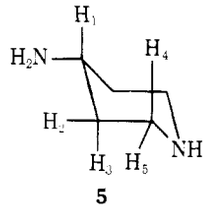
3c

carbon NMR spectrum shows that of the four plausible isomers two are present in the ratio of 2:1. Similar heterocycles have been isolated from hydrazine and 1,3-dibromopropane.[3] Reaction of the isomeric diazabicyclooctanes with methyl iodide in THF gives one crystalline product **3c** whose carbon NMR spectrum shows only six peaks in the ratio 2:2:2:2:2:1 which fixes the structure of its precursor as *cis*-**3a.** Any other isomer of **3** would have given a salt with 11 nonequivalent carbons. A logical assignment for the structure of the second isomer of **3** is *trans*-**3a** rather than a **3b** isomer. Only one of the four possible methiodides of *cis*-**3a** was isolated and the evidence is not sufficient to identify it.

Hydrogenations. Hydrogenating pyrazolidne **2** at room temperature and 40 psi with a Raney nickel catalyst gives 1,3,5-pentanetriamine **4**.[4] At higher temperatures loss of ammonia and intramolecular cyclization to 4-aminopiperidine **5**[5] becomes an important side reaction.

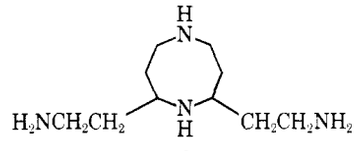
$H_2NCH_2CH_2CH(NH_2)CH_2CH_2NH_2$

4



5

Compound **3a** is reduced with a Raney nickel catalyst to tetramine **6**, but slightly more stringent conditions are required.

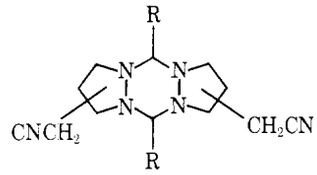


6

Chemistry of 3-(Cyanomethyl)pyrazolidine. Much of the chemistry of pyrazolidine **2** is typical of that of a dialkylhydrazine. It reacts with aldehydes such as formaldehyde or benzaldehyde to give 2:2 adducts **7**. Kurtz's benzaldehyde

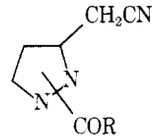
0022-3263/78/1943-0622$01.00/0

adduct of hydrazinopentenenitrile[1] may have been a slightly different isomer mix than our **7b.**



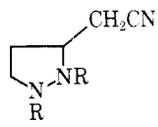
7a, R = H
b, R = C_6H_5

Phenyl isocyanate and isobutyl chloroformate give 1:1 adducts **8.**

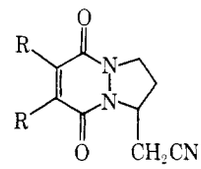


8a, R = NHC_6H_5
b, R = $OCH_2CH(CH_3)_2$

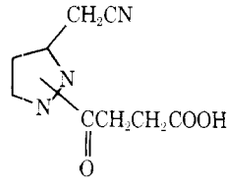
Benzoyl chloride and methyl isocyanate give 2:1 adducts **9.** Maleic and phthalic anhydrides give 1:1 adducts **10.** Succinic anhydride gives a 1:1 adduct **11,** where the ring isomer closure has not occurred. The site of acylation in **8** and **11** is unknown.



9a, R = COC_6H_5
b, R = $CONHCH_3$

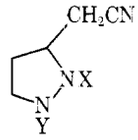


10a, R = H
b, R,R = benzo ring



11

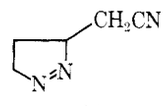
Pyrazolidine **2** gives a mixture of two 1:1 Michael adducts **12** with dimethyl acetylenedicarboxylate and a 2:1 adduct **13** with hexafluoro-2-butyne.



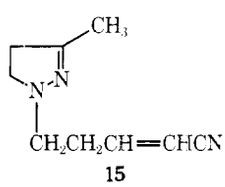
12, X = CR=CHR; Y = H
X = H; Y = CR=CHR
R = $COOCH_3$

13, X = Y = CR=CHR
R = CF_3

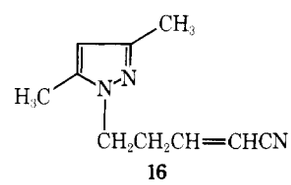
Mild oxidation with mercuric oxide gives the azo compound **14.** The products of the reaction of pyrazolidine **2** with methyl vinyl ketone and acetylacetone are pyrazoline **15** and pyrazole **16,** respectively. Both are formally derived from the open-chain hydrazinonitrile **1,** but the mechanism of these reactions is unknown and could involve either addition–elimination or elimination–addition.



14

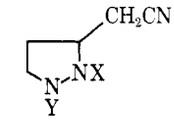


15



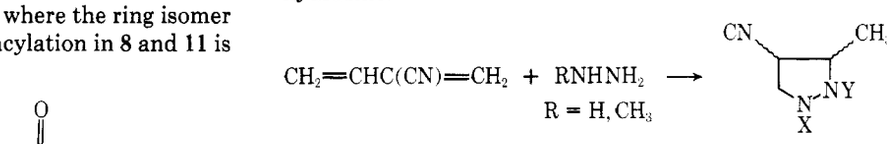
16

Other Hydrazines. The formation of cyanomethylpyrazolidines can be extended to monosubstituted hydrazines. Both phenyl- and methylhydrazines gives mixtures of 1(2)-substituted 3-(cyanomethyl)pyrazolidines **17.**



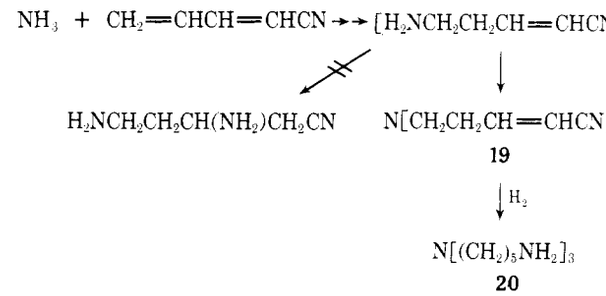
17a, X, Y = H, C_6H_5
17b, X, Y = H, CH_3

Reactions of Hydrazines with 2-Cyanobutadiene. Although the first addition of amines to 2-cyanobutadiene occurs easily, the second Michael addition is much more difficult than the corresponding reaction with 1-cyanobutadiene. Both hydrazine and methylhydrazine give a pyrazolidine from 2-cyanobutadiene, but strong base catalysis is required for the ring closure and the reaction proceeds poorly. Both *cis*- and *trans*-3-methyl-4-cyanopyrazolidine (**18a**) are formed from hydrazine.



18a, X = Y = H
b, X, Y = CH_3, H

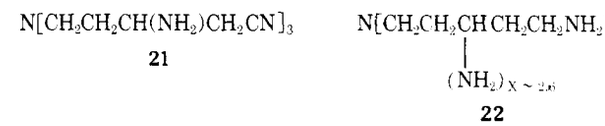
Reactions of Amines with Cyanobutadienes. An alternate route to pentanetriamine **4** might involve the addition of 2 mol of ammonia to 1-cyanobutadiene followed by reduction; however, the reaction follows a different course. Even in the presence of excess ammonia, the initial 1:1 adduct reacts with additional cyanobutadiene to form the adduct of three cyanobutadienes per ammonia **19.**[1] Even adding 1-cyanobutadiene slowly to hot ammonia did not produce 3,5-diaminopentanenitrile. Hydrogenation of amine **19** gives tetramine **20.** If **19** is heated with additional ammonia, the expected



19

20

Michael reaction occurs and the product isolated (**21**) consists of a mixture with an average of 2.6 primary amines. Reduction gave a septamine **22** with (nominally) six primary and one tertiary amine.



21 **22**

Ammonia reacts with 2-cyanobutadiene to give mixtures of 1:1 and 1:2 adducts **23.** The 1:1 adduct could not be pre-

23a, x = 1; y = 2
b, x = 2; y = 1

pared in analytically pure form because it rapidly lost NH_3 on standing. No 1:3 adduct was isolated, nor were any products found corresponding to a Michael addition to the initially formed materials.

No distinct products could be isolated from the reaction of methylamine with 1-cyanobutadiene because extensive cross-linking apparently occurs. Methylamine reacts smoothly with 2 mol of 2-cyanobutadiene to give adduct **24** which can be reduced to triamine **25.** Dimethylamine reacts smoothly with 1-cyanobutadiene to give 1:1 adducts which react with more dimethylamine to give 2:1 adduct **26.**[1] This compound can be reduced to a triamine **27** with two tertiary and one primary amines. Triamine **27** can be alkylated with formaldehyde and formic acid to give a tris(tertiary amine) **28** which can also be prepared from pentanetriamine **4.**

$CH_3N[CH_2C(CN)=CHCH_3]_2$

24

$CH_3N[CH_2CH(C_2H_5)CH_2NH_2]_2$

25

$XCH_2CH_2CHXCH_2Y$

26, X = $N(CH_3)_2$; Y = CN

27, X = $N(CH_3)_2$; Y = CH_2NH_2

28, X = $N(CH_3)_2$; Y = $CH_2N(CH_3)_2$

Experimental Section

Instrumentation. All melting and boiling points are uncorrected. NMR spectra were obtained on Varian A-60 and HR-220 spectrometers. Infrared spectra were measured on a Perkin-Elmer 21 instrument and mass spectra on a Du Pont CEC 21-103C instrument.

Materials. 1- and 2-cyanobutadienes were prepared by literature methods.[6]

Caution: Extensive outgassing during distillation of **2** and **3** can lead to loss of vacuum and rapid decomposition of the product. The distillation should be carried out at the lowest pressure and temperature possible.

5-Hydrazino-3-pentenenitrile (1).[1] To a solution of $N_2H_4 \cdot H_2O$ in CH_3OH at −25 °C was added dropwise 1-cyanobutadiene. The internal temperature was maintained at less than −20 °C. Solvent and starting materials were removed at 0 °C and 1 mm, leaving a colorless oil: IR 3.05, 3.44, 3.56, 4.46, 6.23, 10.32 μm; NMR δ 5.7 (m, 2 H, =CH), 3.1–3.4 (m, 7 H, CH_2 + NH).

The product cyclized to **2** during attempts at purification and on standing at room temperature.

3-(Cyanomethyl)pyrazolidine (2). To a solution of 30 g of hydrazine hydrate and 30 mL of methanol at 0 °C was added dropwise 30 g of 1-cyanobutadiene in 1 h. The exotherm was kept below 25 °C by ice-bath cooling. Solvent and excess hydrazine were removed on a rotary evaporator and the product was distilled: bp 88 °C (0.25 mm); yield 11 g; ^1H NMR ($CDCl_3/Me_4Si$), on HR220, δ 1.60 (d, d, t, J = 13, 6, 7 Hz, 1 H), 2.22 (d, d, t, J = 13, 3, 8, Hz, 1 H), 2.51 (d, d, J = 6, 1 Hz, CH_2), 2.72 (d, t, J = 12, 8 Hz, 1 H), 3.14 (d, d, d, J = 12, 8, 3 Hz, 1 H), 3.58 (q, J = 6 Hz, 1 H), 3.89, (s, 2 NH); IR 3.03, 3.38, 3.45, 4.44 μm. Anal. Calcd for $C_5H_9N_3$: C, 54.0; H, 8.2; N, 37.8. Found: C, 54.1; H, 8.0; N, 37.7.

1,7-Bis(cyanomethyl)tetrahydro-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole (3a). Continued distillation from the preparation of 3-(cyanomethyl)pyrazolidine gave 4.5 g of product as a light yellow liquid: bp 156 °C (0.2 mm); ^1H NMR ($CDCl_3/Me_4Si$) δ 1.78 (m, 1 H), 2.36–2.63 (m, 3 H), 2.85 (m, 1 H), 3.11 (m, 1 H), 3.34 (m, 1 H); ^{13}C NMR (neat/Me_4Si) major, δ 66.0, 72.7, 92.6, 100.8, 160.6; minor, 65.2, 76.0, 91.1, 97.9, 161.2. Anal. Calcd for $C_{10}H_{14}N_4$: C, 63.2; H, 7.4; N, 29.5; Found: C, 62.9; H, 7.6; N, 29.5.

1,7-Bis(cyanomethyl)tetrahydro-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole Methiodide (3c). A solution of cyclic hydrazine **3a** in THF was treated at room temperature with methyl iodide until no further exotherm occurred. A heavy phase separated. THF was decanted and the oil recrystallized (slowly) from ethanol, giving the salt as white needles: mp 200 °C (dec); IR 3.30, 3.38, 3.43, 4.45 μm; ^1H NMR (Me_2SO-d_6/Me_4Si) δ 3.4 (s, CH_3), remainder is an aliphatic multiplet; ^{13}C NMR (Me_2SO-d_6/Me_4Si) δ 118.1 (2 CN), 64.5 (2 C), 63.4 (2 C), 56.6 (CH_3), 29.8 (2 C), 22.1 (2 C). Only one of the four possible isomers is present in this particular sample. Anal. Calcd for $C_{11}H_{17}N_4I$: C, 39.8; H, 5.2; N 16.9. Found: C, 39.1; H, 5.1; N, 16.9.

1,3,5-Pentanetriamine (4). A slurry of 8.6 g of pyrazolidine **2,** 20 mL of EtOH, and 5 g of Raney nickel was shaken with 35 psi of H_2 at room temperature for 4 h. Catalyst was removed and the residue distilled, giving 6.1 g of pentanetriamine: bp 67 °C (0.12 mm);[4] NMR ($CDCl_3/Me_4Si$) δ 1.24 (s, 6 NH), 1.27–1.58 (m, 4 H, AB further split), 2.72 (t, J = 7 Hz, 4 H), 2.85 (t, J = 4 Hz, t, J = 8 Hz, 1 H). The IR spectrum was consistent with an aliphatic primary amine.

4-Aminopiperidine (5). If the Raney nickel catalyzed hydrogenation of pyrazolidine **2** is carried out above room temperature, some 4-aminopiperidine[5] is formed, bp 28–32 °C (0.4 mm). GC on any nonpolar column separates the diamine and the triamine conveniently. The diamine has the shorter retention time: ^1H NMR ($CDCl_3/Me_4Si$) δ 1.148 (d, J = 4 Hz, q, J = 12 Hz, H-3), 1.42 (s, NH), 1.75 (d, J = 12 Hz, br, H-2), 2.52 (d, J = 2 Hz, t, J = 12 Hz, H-4), 2.66 (t, J = 4 Hz, t, J = 10 Hz, H-1), 2.99 (t, J = 3 Hz, d, J = 12 Hz, H-5). The IR spectrum was consistent with a primary aliphatic amine.

2,8-Bis(2-aminoethyl)octahydro-1,5-diazocine (6). Ten grams of **3a,** 20 mL of CH_3OH, 10 g of NH_3, and 5 g of Raney nickel were pressured to 1000 psi of H_2 heated at 75 °C/6 h. The catalyst was filtered and the residue distilled, giving 3.9 g of light yellow liquid: bp 122–125 °C (0.18 mm); IR 3.04, 3.42, 3.49, 6.25 μm; ^1H NMR (CCl_4/Me_4Si) δ 1.07 (s, 6 NH), 1.42 (q, J = 6.5 Hz, 4 H), 1.0–2.1 (m, 4 H), 2.77 (t, J = 6.5 Hz, 4 H), 2.5–3.3 (m, 6 H). Anal. Calcd for $C_{10}H_{24}N_4$: C, 60.0; H, 12.1; N, 28.0. Found: C, 60.1; H, 11.6; N, 27.9.

1,7(9)-Bis(cyanomethyl)tetrahydro-1*H*,5*H*,7*H*,11*H*-dipyrazolo[1,2-*a*:1′,2′-*d*]-*S*-tetrazine (7a). To 5.5 g of pyrazolidine **2** in 25 mL of CH_3OH was added at room temperature 4 mL of formalin. The exothermic reaction was controlled by an ice bath. The solution became viscous and deposited a white solid which was filtered and recrystallized from $CHCl_3/C_6H_{12}$: yield 1.5 g; mp 154–158 °C; IR 3.37, 3.46, 3.52, 3.57, 4.45 μm; ^1H NMR ($CDCl_3/Me_4Si$) δ 4.02, 3.45 (2 AB, J = 9 Hz, 4 H), 2.57 (d, J = 5 Hz, 4 H), 1.7–3.4 (m, 10 H). Anal. Calcd for $C_{12}H_{18}N_6$: C, 58.5; H, 7.4; N, 34.1. Found: C, 58.5; H, 7.3; N, 34.3.

1,7(9)-Bis(cyanomethyl)-5,11-diphenyltetrahydro-1*H*,5*H*,7*H*,11*H*-dipyrazolo[1,2-*a*:1′,2′-*d*]-*S*-tetrazine (7b). A solution of 2.2 g of pyrazolidine **2** and 5 g of benzaldehyde in 25 mL of CH_3OH was stirred at room temperature. After 10 min a white precipitate formed. The suspension was stirred for 30 min and filtered, and the product was washed with CH_3OH and air-dried: yield 1.5 g; mp 165–185 °C; mol wt (mass spec) 398; IR 3.24, 3.27, 3.34, 3.46, 3.50, 4.44, 6.22, 6.28, 6.68, 13.28, 14.27 μm. Anal. Calcd for $(C_{12}H_{13}N_3)_n$: C, 72.3; H, 6.6; N, 21.1. Found: C, 72.2; H, 6.75; N, 21.4.

3-(Cyanomethyl)pyrazolidinecarboxanilide (8a). To 7.2 g of phenyl isocyanate in 20 ml of benzene was added dropwise at room temperature 3 g of pyrazolidine **2.** The initial exotherm was controlled by ice-bath cooling. The white precipitate which formed was filtered and washed with pentane, yield 6 g. The analytical sample was recrystallized from CH_3OH/H_2O: mp 140–141 °C; IR 2.97, 3.07, 3.37, 3.42, 4.44, 5.94, 6.26, 6.57, 13.26, 14.35 μm; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.5–2.45 (m, 2 H), 2.58 (d, J = 6 Hz, 2 H), 3.05–4.06 (m, 3 H), 5.69 (d, J = 7 Hz, 1 H), 6.85–7.81 (m, 5 H), 8.72 (s, NH). Anal. Calcd for $C_{12}H_{14}N_4O$: C, 62.6; H, 6.1; N, 24.3. Found: C, 62.6; H, 6.1; N, 24.0.

Isobutyl 3-(Cyanomethyl)pyrazolidinecarboxylate (8b). To pyrazolidine **2** (3.3 g) and triethylamine (3.1 g) in 50 mL of benzene was added at 0 °C with stirring 4.1 g of isobutyl chloroformate. An exothermic reaction deposited a white solid. After stirring at room temperature overnight, 50 mL of pentane was added and the solid was filtered. The liquid was stripped on a rotary evaporator and the residue distilled, giving 3 g of product as a light yellow liquid: bp 170 °C (0.25 mm); IR 3.07, 3.36, 3.43, 4.45, 5.87, 7.21 μm; ^1H NMR ($CDCl_3/Me_4Si$) δ 4.90 (s, NH), 3.4–4.1 (m, 5 H, CHN, CHO), 1.7–2.5 (m, 3 H), 2.58 (d, J = 6 Hz, CH_2CN), 0.92 [d, J = 7 Hz, $CH(CH_3)_2$]. Anal. Calcd for $C_{10}H_{17}N_3O_2$: C, 56.8; H, 8.1; N, 19.9. Found: C, 57.0; H, 8.1; N, 19.8.

1,2-Dibenzoyl-3-(cyanomethyl)pyrazolidine (9a). To 2 g of pyrazolidine **2** and 2 g of triethylamine in 50 mL of benzene was added at 0 °C with stirring 6 g of benzoyl chloride. After a vigorous exotherm, a white solid deposited. The slurry was stirred overnight at room temperature, filtered, washed with pentane and water, and air-dried, giving 2.3 g of product as white solid. The analytical sample was recrystallized from methanol/water, mp 151.5–152 °C; IR 3.24, 3.34, 4.44, 5.95, 6.05, 6.22, 6.31, 6.68, 13.42, 14.40 μm; ^1H NMR (Me_2SO-d_6) δ 7.35–7.88 (10 H, m, aromatic), 4.66 (br, NH), 3.84 (pentet, J = 7 Hz, 2 H), 3.09 (d, J = 6 Hz, 2 H), 1.78–2.64 (m, 2 H). Anal. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.5; H, 5.4; N, 13.2. Found: C, 71.4; H, 5.4; N, 13.5.

3-(Cyanomethyl)-1,2-bis(methylcarbamoyl)pyrazolidine (9b). To 3 g of pyrazolidine **2** in 20 mL of benzene was added dropwise 5 g of methyl isocyanate in 20 mL of benzene. The vigorous exotherm was

controlled by ice-bath cooling. The solution was stirred overnight at room temperature. Cooling deposited white needles which were filtered and washed with pentane, yield 1.8 g. The analytical sample was recrystallized from DMF: mp 238–240 °C; IR 3.01, 3.38, 4.44, 5.97, 6.42, 6.58 μm; ^{1}H NMR (Me_2SO) δ 6.9 (br m, 2 NH), 3.95–4.97 (m, 2 H), 1.5–3.2 (m, 9 H), 2.6 (d, J = 5 Hz, 2 H). Anal. Calcd for $C_9H_{15}N_5O_2$: C, 48.0; H, 6.7; N, 31.1. Found: C, 47.8; H, 6.4; N, 31.1.

1-Cyanomethyl-2,3-dihydro-1*H*-pyrazolo[1,2-*a*]pyridazine-5,8-dione (10a). To 5 g of maleic anhydride in 20 mL of THF was added in portions 5.5 g of pyrazolidine **2**. After a mild exotherm subsided, the product was deposited as a sticky yellow solid. Methanol recrystallization gave 5 g of product as a white crystalline solid: mp 139.5–143 °C (dec); IR 3.26, 3.31, 3.40, 4.44, 5.95, 6.15, 6.36 μm; ^{1}H NMR (Me_2SO/Me_4Si) δ 6.86 (s, 2 =CH), 4.87 (m, NCH), 4.16 (m, NCH_2), 3.13 (4 lines, CH_2CN), 1.97–2.90 (m, CCH_2C). Anal. Calcd for $C_9H_9N_3O_2$: C, 56.5; H, 4.7; N, 22.0. Found: C, 56.7; H, 4.9; N, 22.2.

1-(Cyanomethyl)-2,3-dihydro-1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione (10b). To 7.6 g of phthalic anhydride in 50 mL of THF was added in portions 5.5 g of pyrazolidine **2**. After a mild exotherm subsided, the solution was refluxed overnight. Solvent was removed on a rotary evaporator and the product recrystallized from water, giving 6.4 g of white crystalline solid: mp 140–143 °C; IR 3.24, 3.41, 3.49, 4.45, 6.14, 6.23, 6.78 μm; ^{1}H NMR ($CDCl_3/Me_4Si$) δ 8.20 (m, 2 H), 7.82 (m, 2 H), 5.00 (m, 1 H), 4.34 (m, 2 H), 2.95 (d, J = 6 Hz, 2 H), 1.50 (m, 2 H). Anal. Calcd for $C_{13}H_{11}N_3O_2$: C, 64.7; H, 4.6; N, 17.4. Found: C, 64.6; H, 4.6; N, 17.1.

3-(Cyanomethyl-γ-oxopyrazolidinebutyric Acid (11). To 5 g of succinic anhydride in 50 mL of THF was added 5.5 g of pyrazolidine **2**. After a slight exotherm subsided the solution was refluxed 4 h. Solvent was removed on the rotary evaporator and the residual oil was triturated with methanol to give 6 g of white crystalline solid; mp (CH_3OH) 110–112.5 °C; IR 3.05, 3.37, 3.5–4.0, 4.42, 5.83, 6.25 μm; NMR δ 1.7–3.8 with (2.50, d, J = 6 Hz, CH_2, 11 H), 5.4, 7.3 (br, NH + OH). Anal. Calcd for $C_9H_{13}N_3O_3$: C, 51.2; H, 6.2; N, 19.9. Found: C, 51.2; H, 6.2; N, 20.0.

Dimethyl 2-[3-(Cyanomethyl)pyrazolidinyl]fumarate (12). To 5.5 g of pyrazolidine **2** in 25 mL of CH_3OH was added dropwise 7.1 g of dimethyl acetylenedicarboxylate. After the initial exotherm at 50 °C subsided, the solution was heated at 50 °C/2 h. On standing overnight the bulk of the solvent evaporated, leaving a crystalline residue which was triturated with benzene, filtered, washed with pentane, and air-dried to give 5.7 g of light yellow solid: mp 100–102 °C; mol wt calcd for $C_{11}H_{15}N_3O_4$, 253; found (mass spec), 253; IR 3.11, 3.25, 3.39, 3.47, 4.46, 5.70, 5.97, 6.36, 8.65 μm; ^{1}H NMR ($CDCl_3/Me_4Si$) δ 3.62, 3.65, 3.72, 3.82 (s, OCH_3), 2.43, 2.68 (d, J = 6 Hz), the rest is broad. Anal. Calcd for $C_{11}H_{15}N_3O_4$: C, 52.2; H, 6.0; N, 16.6. Found: C, 51.8; H, 6.1; N, 16.8.

3-(Cyanomethyl)-1,2-bis[3,3,3-trifluoro-1-(trifluoromethyl)-1-propenyl]pyrazolidine (13). Pyrazolidine **2** (5.5 g), THF (10 mL), and hexafluorobutyne (20 g) were heated in an 80-cm^3 bomb at 50 °C/3 h. Distillation gave 14.3 g of product: bp 98–104 °C (0.6 mm); IR 3.36, 3.45, 4.43, 6.09, 8–9 μm; ^{1}H NMR ($CDCl_3/Me_4Si$) aliphatic absorption and 1 multiplet at δ 4.2; ^{19}F NMR ($CDCl_3/CFCl_3$) δ −70.4 (m), −61.0 (q, J = 10 Hz), −60.5 (m), −56.7 (pentet J = 10 Hz), ca. equal intensities. Anal. Calcd for $C_{13}H_9N_3F_{12}$: C, 35.9; H, 2.1; F, 52.4. Found: C, 36.2; H, 2.2; F, 52.0.

3-(Cyanomethyl)-Δ1-pyrazoline (14). To a refluxing solution of 5.5 g of pyrazolidine **2** in 100 mL of CH_3OH was added in portions 11 g of HgO (yellow). The yellow color was replaced by the dark gray of metallic mercury. After refluxing for 2 h, the solution was decanted from metallic residues, stripped on a rotary, and distilled, giving 4.4 g of product as a colorless liquid, bp 72–80 °C (0.25 mm); IR 3.36, 4.43, 6.42 μm; ^{1}H NMR ($CDCl_3/Me_4Si$) δ 0.9–2.2 (m, 2 H), 2.92 (d, d, J = 6, 2 Hz, 2 H), 3.8–5.0 (m, 3 H). Anal. Calcd for $C_5H_7N_3$: C, 55.0; H, 6.5. Found: C, 55.3; H, 6.3.

1-(4-Cyano-3-butenyl)-3-methyl-Δ2-pyrazoline (15). To 5.5 g of pyrazolidine **2** in 25 mL of CH_3OH was added in portions 3.5 g of methyl vinyl ketone. After a mild exotherm subsided, the yellow solution was refluxed 0.5 h, solvent was removed on a rotary evaporator, and the product was distilled to give 3.5 g of colorless liquid bp 90 °C (0.05 mm); IR 3.27, 3.42, 3.53, 4.51, 6.17, 7.22 μm; ^{1}H NMR δ 6.4–7.0 (m, 1 H), 5.2–5.6 (m, 1 H), 2.3–3.2 (m, 8 H), 1.92 (s, CH_3). Anal. Calcd for $C_9H_{13}N_3$: C, 66.2; H, 8.0; N, 25.7. Found: C, 65.2; H, 8.0; N, 26.3.

1-(4-Cyano-3-butenyl)-3,5-dimethylpyrazole (16). To 5.5 g of pyrazolidine **2** in 25 mL of CH_3OH was added in portions 5.0 g of acetylacetone. After the initial mild exotherm subsided, the yellow solution was heated at 50 °C/2 h. Solvent was removed on a rotary evaporator and the residue distilled, giving 6 g of colorless liquid; bp 89–92 °C (0.07 mm); IR 3.24, 3.37, 4.47, 6.08, 6.42 μm; ^{1}H NMR ($CDCl_3/Me_4Si$) δ 2.08 (s, CH_3), 2.18 (d, J = 2 Hz, CH_3), 2.71 (AA′), 3.93 (XX′), 5.08 (d, J = 14 Hz, m, 1 H), 5.60 (s, =CH), 6.44 (m, 1 H). Anal. Calcd for $C_{10}H_{13}N_3$: C, 68.5; H, 7.5; N, 24.0. Found: C, 68.3; H, 7.2; N, 24.3.

1(2)-Phenyl-3-(cyanomethyl)pyrazolidine (17a). A solution of 38 g of phenylhydrazine and 28 g of 1-cyanobutadiene in 100 mL of dioxane was refluxed for 3 h. Triton B (1 mL) and 25 mL of 1-cyanobutadiene were added and the solution was refluxed again. Distillation gave 20 g of yellow liquid, bp 140 °C (0.04 mm); IR 2255 cm^{-1}; NMR (CCl_4/Me_4Si) δ 6.5–7.3 (m, 5 H), 1.3–4.2 (m, 6 H), 2.43 (d, J = 6 Hz, CH_2). Anal. Calcd for $C_{11}H_{13}N_3$: C, 70.6; H, 7.0. Found: C, 70.7; H, 7.0.

1(2)-Methyl-3-(cyanomethyl)pyrazolidine (17b). Sixteen grams of 1-cyanobutadiene was added dropwise to 15 g of methylhydrazine in 20 mL of methanol. The internal temperature was kept below 15 °C by ice-bath cooling. The solution was stirred for 1 h at room temperature. Solvent was removed on a rotary evaporator and the residue distilled, giving 14.1 g of colorless liquid, bp up to 90 °C (0.06 mm).

A crude ^{1}H NMR spectrum showed that the product was not extensively cyclized. The product was added to 10 mL of triethylamine and the homogeneous solution refluxed for 2 h. Distillation gave 9.8 g of a light yellow liquid: bp 68–76 °C (0.25 mm); ^{1}H NMR ($CDCl_3/Me_4Si$) resembles 3-(cyanomethyl)pyrazolidine with sharp CH_3N singlets at δ 2.53 and 2.82. Anal. Calcd for $C_6H_{11}N_3$: C, 57.6; H, 8.9; N, 33.6. Found: C, 57.5; H, 8.5; N, 33.8.

4-Cyano-3-methylpyrazolidine (18a). A solution of 25 g of 95% N_2H_4, 25 g of 2-cyanobutadiene, and 200 mL of EtOH was refluxed for 3 h. A few grams of strong base ion-exchange resin was added and the solution refluxed overnight. The resin was filtered and the solution distilled. The bulk decomposed, but a 20% yield of product could be obtained from small-scale distillations; bp ~120 °C (2 mm); IR 3.1, 3.4, 4.5, 9.0, 9.2, 12.0 μm; NMR ($CDCl_3/Me_4Si$) δ 1.40, 1.32 (d, J = 6 Hz CH_3CH), 3.1–3.6 (m, 6 H). Two isomers are present in the ratio of ca. 2:1. Anal. Calcd for $C_5H_9N_3$: C, 54.0; H, 8.2; N, 37.8. Found: C, 53.7; H, 8.1; N, 37.8.

1(2),3-Dimethyl-4-cyanopyrazolidine (18b). A solution of 16 g of 2-cyanobutadiene, 10 g of methylhydrazine and 100 mL of EtOH was mixed at room temperature. After a mild exotherm subsided, 1 mL of Triton B was added and the dark solution was refluxed for 4 h. NMR examination of the crude product showed uncyclized material, so more Triton B was added and the solution again heated. Distillation gave 5 g of colorless liquid, bp 88–90 °C (2.5 mm), and other unidentified higher boiling fractions. IR 2.95, 3.05, 6.07, 3.36, 3.49, 3.57, 4.45, 7.21 μm; NMR δ 1.34 (several d, J = 7 Hz, CH_3CH), 2.48, 2.53 (s, s, NCH_3), 2.6–3.7 (m, 5 H). There are at least three isomers present in the ratio of 1:2:3. Anal. Calcd for $C_6H_{11}N_3$: C, 57.6; H, 8.9. Found: C, 57.2; H, 9.2.

Tris(5-aminopentyl)amine (20). A slurry of 38 g of crude adduct **19**,[1] 25 g of Raney nickel, and 25 g of NH_3 was heated at 100 °C/8 h under 2000 psi of H_2. Distillation at 180 °C (0.15 mm) gave 20 g of a colorless liquid. IR 2.96, 3.03, 3.39, 3.47, 6.23 μm; NMR (CCl_4/Me_4Si) δ 0.87 (s, 3 NH_2), 1.37 (m, 9 CH_2), 2.33 (t, J = 7 Hz, 6 H), 2.62 (t, J = 7 Hz, 6 H). Anal. Calcd for $C_{15}H_{36}N_4$: C, 66.1; H, 13.2; N, 20.6; mol wt 272. Found: C, 66.2; H, 13.2; N, 20.7; mol wt 262.

Tris(3-amino-4-cyanobutyl)amine (21). A 400-mL bomb was charged with 120 g of ammonia and heated to 90 °C. A solution of 1:1 1-cyanobutadiene in THF was injected at the rate of 10 mL/30 min. After the addition was complete (6 h), the solution was heated at 90 °C for an additional 2 h. Solvent was removed on a rotary evaporator leaving a yellow oil. ^{1}H NMR analysis gave a ratio of vinyl/aliphatic of 38:200, suggesting that the fourth ammonia had added ~60%. The sample was purified by falling film distillation, bp 160–165 °C/<5 μm. Anal. Calcd for $C_{15}H_{27}N_7$: C, 59.0; H, 8.9; N, 32.1. $C_{15}H_{24}N_6$: C, 62.4; H, 8.3; N, 29.2. Found: C, 60.9; H, 8.9; N, 30.0.

Tris(3,5-diaminopentyl)amine (22). A suspension of 75 g of Raney nickel, 150 g of amine **21**, and 500 mL of THF was loaded into a bomb, cooled, and evacuated. To this was added 100 g of NH_3 and 1000 psi of H_2. The mixture was heated at 100 °C/8 h. Catalyst was filtered and solvent removed on a rotary evaporator. The residue was passed through a falling film evaporator and the fraction, bp 135–140 °C/<2 μm, was analyzed: IR primary aliphatic amine; NMR ($CDCl_3/Me_4Si$) δ 1.28 (5, NH), 1.0–1.9 (m, CH_2CH_2C), 2.2–3.4 (m, CHN). Anal. Calcd for $C_{15}H_{39}N_7$ (average of five primary amines): C, 59.2; H, 13.1; N, 27.6. Found: C, 61.3; H, 11.5; N, 27.1.

Bis(2-cyano-2-butenyl)amine 23b. To a solution of 2.5 g of NH_3 in 25 mL of EtOH at 0 °C was added dropwise 34 g of 2-cyanobutadiene in 75 mL of EtOH. The solution was stirred at room temperature for 2 h and refluxed overnight. Solvent was removed on a rotary evaporator and the residual oil was distilled on a spinning-band col-

umn, giving, among others, 5 g of dinitrile as a colorless liquid; bp 138 °C (0.4 mm); IR 3.01, 3.28, 3.42, 3.49, 4.51, 6.09, 7.23 μm; NMR ($CDCl_3$/Me_4Si) δ 1.59 (s, NH), 1.88, 2.02 (d, J = 7 Hz, CH_3), 3.41 (s, CH_2), 6.48, 6.60 (q, J = 7 Hz, m, J = 1 Hz, =CH). Anal. Calcd for $C_{10}H_{13}N_3$: C, 68.5; H, 7.4; N, 24.0. Found: C, 68.0; H, 7.7; N, 24.8.

2-Cyano-2-butenylamine (23a). The fraction, bp 68–75 °C (2.1 mm) (17.5 g), showed: IR 3.0, 3.5, 3.6, 4.5, 6.1, 6.2, 6.9, 7.3 μm; ^1H NMR (CCl_4/Me_4Si) δ 1.21 (s, 2 NH), 2.00 (d, J = 7 Hz, t, J = 1.5 Hz, CH_3), 3.38 (m, J = 1.5 Hz, CH_2), 6.39 (q, J = 7 Hz, t, J = 1.5 Hz, =CH). Elemental analyses were unsatisfactory because the ammonia addition is apparently reversible.

Bis(2-cyano-2-butenyl)methylamine (24). To a solution of 5 g of methylamine in 25 mL of EtOH at 0 °C was added dropwise a solution of 28 g of 2-cyanobutadiene in 25 mL of EtOH over a 0.5-h period. The red solution was refluxed overnight and distilled, giving 20 g of colorless liquid: bp 113–120 °C (0.05 mm); IR 3.25, 3.37, 3.48, 3.55, 4.49, 6.07 μm; ^1H NMR δ 1.91, 2.05 (d, J = 6 Hz, CH_3CH), 2.30 (s, CH_3N), 3.20 (s, CH_2N), 6.48, 6.60 (q, J = 6 Hz, br, =CH). Anal. Calcd for $C_{11}H_{15}N_3$: C, 69.8; H, 8.0; N, 22.2. Found: C, 70.0; H, 8.0; N, 22.5.

Bis[2-(aminomethyl)butyl]methylamine (25). A slurry of 15 g of dinitrile **24**, 60 mL of THF, 25 g of NH_3, and 20 g of Raney nickel was shaken under 2000 psi of H_2 at 135 °C/8 h. The catalyst was separated, solvent was removed on a rotary evaporator, and the product was distilled through a small spinning-band column; bp 75–77 °C (0.02 mm); yield 9 g; IR 2.99, 3.06, 3.44, 3.49, 3.58, 6.26, 7.26 μm; ^1H NMR (CCl_4/Me_4Si) δ 2.13 (s, CH_3), 2.05–2.7 (m, CH_2N), 0.9 (t, J = 6 Hz, CH_3CH_2), 1.05–1.8 (m, CH_2). Anal. Calcd for $C_{11}H_{27}N_3$: C, 65.6; H, 13.5; N, 20.9. Found: C, 66.4; H, 13.2; N, 20.1.

3,5-Bis(dimethylamino)valeronitrile (26) was prepared by the addition of dimethylamine to 1-cyanobutadiene:[1] ^1H NMR (CCl_4/Me_4Si) δ 1.62 (q, J = 6.5 Hz, CH_2CN), 2.19, 2.30 (s, s, NCH_3), 2.42 (m, CH_2N), 2.90 (m, CHN).

1,3-Bis(dimethylamino)-5-aminopentane (27). A slurry of 18 g of nitrile **26**, 50 mL of THF, 20 g of NH_3, and 10 g of Raney cobalt was shaken under 1000 psi of H_2 at 135 °C/6 h. Distillation gave 7 g of triamine, bp 84–90 °C (2 mm); IR primary aliphatic amine; ^1H NMR δ 1.12 (s, NH_2), 1.2–1.8 (m, 4 H), 2.11, 2.17 (s, s, NCH_3), 2.27–2.79 (m, 5 H). Anal Calcd for $C_9H_{23}N_3$: C, 62.4; H, 13.4; N, 24.2. Found: C, 62.2; H, 13.4; N, 24.2.

1,3,5-Tris(dimethylamino)pentane (28). To 17 g of **27** at 0 °C was added 40 g of formic acid and then 40 g of formalin. The solution was refluxed, giving off 4.5 L of CO_2 in 2 h. After the addition of 5 mL of concentrated HCl, the solution was stripped on the rotary and poured onto ice. The solution was made basic with 50% NaOH, and the organic phase was extracted into ether, dried, and distilled, giving 12 g of colorless liquid: bp 68–70 °C (0.6 mm); IR saturated tertiary amine; NMR ($CDCl_3$/Me_4Si) δ 1.30 (m, $CH_2CH_AH_BCH$), 1.57 (m, $CH_2CH_AH_BCH$), 2.13 (s, 12 H, CH_3N), 2.19 (s, 6 H, CH_3N), 2.20 (m, J = 6 Hz, CH_2N), 2.40 (pentet, J = 6, CHN). Anal. Calcd for $C_{11}H_{27}N_3$: C, 65.6; H, 13.5; N, 20.9. Found: C, 66.1; H, 13.5; N, 21.0.

Registry No.—**1**, 64413-80-5; **2**, 64413-76-9; **3a**, 64413-74-7; **3c**, 64413-75-8; **4**, 59821-81-7; **5**, 13035-19-3; **6**, 64413-73-6; **7a**, 64414,07-9; **7b**, 64414-06-8; **8a**, 64414-05-7; **8b**, 64414-09-1; **9a**, 64413-85-0; **9b**, 64413-84-9; **10a**, 64413-83-8; **10b**, 64413-82-7; **11**, 64414-08-0; **12** isomer 1, 64413-81-6; **12** isomer 2, 64413-79-2; **13**, 64413-78-1; **14**, 64413-77-0; **15**, 64398-03-4; **16**, 64398-02-3; **17a** isomer 1, 64398-01-2; **17a** isomer 2, 64397-86-0; **17b** isomer 1, 64398-00-1; **17b** isomer 2, 64397-85-9; *cis*-**18a**, 64397-99-5; *trans*-**18a**, 64397-98-4; **18b** isomer 1, 64414-30-8; **18b** isomer 2, 64397-84-8; **19**, 64397,87-1; **20**, 64397-97-3; **21**, 64397-96-2; **22**, 64397-95-1; **23a**, 64397-94-0; **23b**, 64397,93-9; **24**, 64397-92-8; **25**, 64397-91-7; **26**, 64397-90-6; **27**, 64397-89-3; **28**, 64397-88-2; hydrazine, 302-01-2; 1-cyanobutadiene, 1615-70-9; benzaldehyde, 100-52-7; phenyl isocyanate, 103-71-9; isobutyl chloroformate, 17462-58-7; benzoyl chloride, 98-88-4; methyl isocyanate, 624-83-9; maleic anhydride, 108-31-6; phthalic anhydride, 85-44-9; succinic anhydride, 108-30-5; dimethyl acetylene dicarboxylate, 762-42-5; hexafluorobutyne, 692-50-2; methyl vinyl ketone, 78-94-4; acetylacetone, 123-54-6; phenylhydrazine, 100-63-0; methylhydrazine, 60-34-4; 2-cyanobutadiene, 5167-62-4; methylamine, 74-89-5; formalin, 50-00-0.

References and Notes

(1) (a) Contribution No. 2423. (b) P. Kurtz, *Justus Liebigs Ann. Chem.*, **572**, 23 (1951).
(2) M. Tanaka and M. Yubio, *Kogyo Kagaku Zasshi*, **61**, 714 (1958).
(3) E. L. Buhle, A. M. Moore, and F. Y. Wiselogle, *J. Am. Chem. Soc.*, **65**, 29 (1943).
(4) H. Russel, *Chem. Ber.*, **89**, 679 (1956).
(5) H. Taniyama and B. Yasui, *Yakugaku Zasshi*, **81**, 1497 (1961).
(6) Research Disclosure 11516, Nov., 1973.

Reactions of 1,1-Disubstituted Olefins Containing Electron-Attracting Substituents with Methylphenyldiazomethanes

Wakatu Nagai* and Yumiko Hirata

Department of Chemistry, Nagoya Institute of Technology, Showa-ku, Nagoya 466, Japan

Received June 3, 1977

Reactions of 1,1-disubstituted olefins **3** which carry cyano, carboalkoxy, halogen, etc. as a substituent with methyl-para-substituted-phenyldiazomethanes (**2**) in dichloromethane at −5–0 °C produce 1,1-disubstituted-3-phenyl-1-butene (**4**) and 1,1-disubstituted-2-methyl-2-phenylcyclopropane (**5**). Product ratios of **4** to **5** seem to depend upon the substituents on **3**. In the case of **3** with both cyano and carboalkoxy groups, product **4** is more favorable than **5**; on the other hand, when using **3** with both either a cyano or carboalkoxy group and either a halogen or hydrogen, product **5** is more favorable than **4**. The product ratios of **4** to **5** also depend upon the substituents of **2**; e.g., when the substituent is an electron-attracting group product **4** is more favorable than **5**, and when the substituent is an electron-donating group **5** is more likely than **4**.

It has been reported[1-3] that the reactions of 2-cyano-3-phenylacrylates with diazomethane give various products, including 2-cyano-3-methyl(or ethyl)-3-phenylacrylates, 2-cyano-3-methyl-3-benzylacrylates, and 1-cyano-2-methyl-2-phenylcyclopropanecarboxylates (**5a,b**). **5** (X = NO_2, R = H, Y = CN, Z = COOMe) has been isolated in pure form[4] but **5a** and **5b** have not.[5] We wished to obtain **5b** in its pure form and tried the following reactions.

Methylphenyldiazomethane (**2a**)[6,7] reacted with 2-cyanoacrylates **3a,b** in dichloromethane at −5–0 °C readily, and the crude products obtained were applied to a column of silicic acid (eluted with chloroform) and afforded 2-cyano-4-methyl-4-phenylcrotonates **4a,b**. In the case of **2a** with **3b**, **5b** was afforded, mp 105–106 °C, in 9.8% yield together with **6b** (X = H), mp 160–161 °C, in 2.7% yield. From its NMR, **6** was recognized as a geometrically simple compound.

0022-3263/78/1943-0626$01.00/0