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THE CHEMISTRY OF MALONONITRILE

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Contents

I. Introduction

The weak cyanocarbon acid[1] malononitrile (**1**) is a versatile compound of exceptional reactivity. It is used extensively as a reactant or reaction intermediate since the methylene group and either one or both cyano groups can take part in condensation reactions to give a variety of addition products and heterocyclic compounds. This unique reactivity makes **1** an important chemical in research and in medical, industrial, and agricultural chemistry.

II. Scope of the Review

The chemistry of malononitrile (**1**), sodiomalononitrile (**2**), 1,1,3-tricyano-2-amino-1-propene (malononitrile dimer, **3**), malononitrile trimer (**4**), bromomalononitrile (**5**), dibromomalononitrile (**6**), dichloromalononitrile (**7**), difluoromalononitrile (**8**), and aminomalononitrile (**9**) will be discussed. Owing to space limitations and the extensive literature on the subject, the reactions of other substituted malononitriles will not be included in this review.

$CH_2(CN)_2$ (**1**) $NaCH(CN)_2$ (**2**) $NCCH_2C(NH_2)=C(CN)_2$ (**3**)

$NCCH_2C(NH_2)=C(CN)C(NH_2)=C(CN)_2$ (**4**) $BrCH(CN)_2$ (**5**) $Br_2C(CN)_2$ (**6**)

$Cl_2C(CN)_2$ (**7**) $F_2C(CN)_2$ (**8**) $H_2NCH(CN)_2$ (**9**)

Considering the current interest in polycyano com-

(1) Also known as malonic dinitrile, propiodinitrile, cyanoacetic nitrile, methylene cyanide, and dicyanomethane.

(2) H. Hart and F. Freeman, *J. Am. Chem. Soc.*, 85, 1161 (1963).

(3) H. Luther, *Arch. Pharm.*, 287, 361 (1954).

(4) T. L. Cairns, R. A. Carboni, D. D. Coffman, V. A. Engelhardt, R. E. Heckert, E. L. Little, E. G. McGeer, B. C. McKusick, W. J. Middleton, R. M. Scribner, C. W. Theobald, and H. E. Winberg, *J. Am. Chem. Soc.*, 80, 2775 (1958).

(5) R. E. Merrifield and W. D. Phillips, *ibid.*, 80, 2778 (1958).

(6) W. J. Middleton, R. E. Heckert, E. L. Little, and C. G. Krespan, *ibid.*, 80, 2783 (1958).

(7) W. J. Middleton and V. A. Engelhardt, *ibid.*, 80, 2788 (1958).

(8) W. J. Middleton, E. L. Little, D. D. Coffman, and V. A. Engelhardt, *ibid.*, 80, 2795 (1958).

(9) B. C. McKusick, R. E. Heckert, T. L. Cairns, D. D. Coffman, and H. F. Mower, *ibid.*, 80, 2806 (1958).

(10) G. N. Sausen, V. A. Engelhardt, and W. J. Middleton, *ibid.*, 80, 2815 (1958).

(11) W. J. Middleton, V. A. Engelhardt, and B. S. Fisher, *ibid.*, 80, 2822 (1958).

(12) W. J. Middleton and V. A. Engelhardt, *ibid.*, 80, 2829 (1958).

(13) E. L. Little, Jr., W. J. Middleton, D. D. Coffman, V. A. Engelhardt, and G. N. Sausen, *ibid.*, 80, 2832 (1958).

(14)(a) R. A. Carboni, D. D. Coffman, and E. G. Howard, *ibid.*, 80, 2838 (1958); (b) E. C. Taylor and K. H. Hartke, *ibid.*, 81, 2452 (1959).

(15) C. E. Looney and J. R. Downing, *ibid.*, 80, 2840 (1958).

(16) H. F. Mower and C. L. Dickenson, *ibid.*, 81, 4011 (1959).

(17) J. K. Williams, *ibid.*, 81, 4013 (1959).

(18) Y. C. Kim, Ph.D. Thesis, Michigan State University, E. Lansing, Mich., 1965.

(19) F. Freeman, Ph.D. Thesis, Michigan State University, E. Lansing, Mich., 1962.

pounds,[2-19] and the nucleophilicity of the dicyanomethyl anion, it is important to extend our discussion to include some of the useful reactions of **2** in cyanocarbon chemistry. Although alkyl- and arylidenemalononitriles will not be discussed, several examples of exceptional theoretical and synthetic interest are included. The review covers the literature to the end of 1967.

III. Methods of Preparation

1 can be prepared in 72–96% yield by the reaction of cyanoacetamide and phosphorus oxychloride or phosphorus pentachloride in the presence of inorganic salts.[20-23] The reaction

$$2NCCH_2CONH_2 + POCl_3 \longrightarrow \underset{\mathbf{1}}{2CH_2(CN)_2} + H_3PO_3 + 3HCl \quad (1)$$

$$NCCH_2CONH_2 + PCl_5 \longrightarrow \mathbf{1} + POCl_3 + 2HCl \quad (2)$$

of acetonitrile and cyanogen chloride in a Pyrex tube gives a near-quantitative yield of **1**.[24]

$$CH_3CN + CNCl \xrightarrow{658^\circ} \mathbf{1} + HCl \quad (3)$$

1 containing $^{13}_{6}C$, $^{14}_{6}C$, or $^{15}_{7}N$ has also been prepared.[25,26]

IV. Physical Properties

1 is a highly toxic[27] (LD_{50} = 18.6 mg/kg) solid with a melting point of 30–31°, a boiling range of 218–220° (760 mm), a refractive index ($n^{34.2}D$) of 1.41463, a specific gravity ($d^{34.2}_4$) of 1.0488, and a pK_a[28] of 11.2. The heat of formation of **1** is 63.5 kcal/mole.[29]

The relationship between acid strength and the heat and entropy of ionization of **1** in water has been investigated.[28] The values of ΔG, ΔH, and $-T\Delta S$, in kcal/mole, are 15.28, 13.4, and 1.9. $\Delta S°$ has a value of −6.4 eu. The π-electron bond orders and π-electron densities of **1** have been calculated by the application of a method of self-consistent charges to LCAO MO calculations.[30] Spectral studies (*vide infra*) have further elucidated the molecular structure of **1**.

V. Spectral Properties

The infrared spectra of gaseous, liquid, and solid **1** have been obtained with complete assignment of the 15 fundamental frequencies and a determination of the force constants and the thermodynamic functions.[31] In solution the nitrile stretching frequency[31,32] occurs at about 4.40 μ.

Jencks and Lienhard[33] reported that **1** shows a low end absorption in 0.01 *M* hydrochloric acid, but has maxima at *ca.* 225 mμ (ϵ 20,000) in 0.1 *M* sodium hydroxide, and at 234 mμ (ϵ 4530) in 0.1 *M* hydrochloric acid. The ultraviolet absorption spectra of **1** and its anion in sodium hydroxide, as a function of pH, have also been reported.[34]

Table I

Chemical Shifts of Malononitrile in Various Solvents[37] at 20°

Solvent	*Dielectric constant*	*δ, Hz*
Benzene	2.28	85.5
Carbon tetrachloride	2.24	209.2
Chloroform	4.81	215.5
Dioxane	2.21	228.1
Acetonitrile	38.8	226.7
Dimethyl sulfoxide	45	264.4
Acetone	21.4	253.8

Table II

Molecular Structure of Malononitrile[25,40]

C—C	1.468 ± 0.034 Å	∠CCC	109° 22′ ± 2° 54′
C≡N	1.167 ± 0.026 Å	∠HCH	108° 42′ ± 1° 22′
C—H	1.088 ± 0.010 Å	∠CCN (outside)	180° − (3° 40′ ± 2° 54′)

The pmr spectrum[35] of **1** contains a singlet at τ 6.44. The ^{13}C–H coupling constant is 145 Hz indicating the C–H bond has approximately 29% s character.[35,36]

The effects of various solvents on the chemical shifts of **1** have also been measured[37] (Table I). Although the dielectric constant is not necessarily a measure of solvent polarity,[38] the data show that the chemical shift is strongly dependent on solvation and/or the polarity of the solvent; *e.g.*, there is a difference of 55 Hz between carbon tetrachloride and dimethyl sulfoxide. A difference in solvation would be expected since the lone-pair electrons of dimethyl sulfoxide could be weakly associated with the partially positive carbon of **1**. This association introduces a new electric field and magnetic anisotropy due to the sulfinyl group. At the same time a change in polarization occurs in the cyano group, and the over-all effect is a low-field shift of the proton signal.

The solvent shifts in carbon tetrachloride, chloroform, and dioxane may be caused by weak intermolecular interactions of the easily polarizable lone-pair electrons of the solvents and **1**, while the large diamagnetic shift in benzene can be the result of complex formation between solute and solvent molecules.

The malononitrile molecule has a twofold symmetry axis, and the moment of inertia about this axis is of an intermediate magnitude. The selection rule allows only the *b*-type rotational transitions. The *a* axis lies on a plane made by the two cyano groups and the central carbon atom.[25,39] Microwave studies[25,40] of **1** are summarized in Table II.

Assuming a C–H radius of 1.09 Å and a C≡N radius of 1.15 Å, Pritchard and Muller[41] calculated ∠H–C–H = 105° 30′ and ∠C–C–C = 113° 39′ from their microwave studies.

^{14}N pure quadrupole resonance frequencies[42] for **1** at 77° K

(20) A. R. Surrey, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1944, p 535.
(21) B. B. Corson, R. W. Scott, and C. E. Vose, ref 20, Coll. Vol. II, 1943, p. 379.
(22) M. J. Fahrenbach, U. S. Patent 2,459,128 (1949); *Chem. Abstr.*, 43, 3470 (1949).
(23) Lonza Ltd., French Patent 1,365,202 (1962); *Chem. Abstr.*, 61, 13202 (1964).
(24) J. K. Dixon, U. S. Patent 2,553,406 (1951); *Chem. Abstr.*, 45, 9081 (1951).
(25) E. Hirota and Y. Morino, *Bull. Chem. Soc. Jap.*, 33, 705 (1960).
(26) L. F. Cavalieri, J. F. Tinker, and A. Bendich, *J. Am. Chem. Soc.*, 71, 533 (1949).
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(28) R. H. Boyd and C.-H. Wang, *J. Am. Chem. Soc.*, 87, 430 (1965).
(29) R. H. Boyd, K. R. Guha, and R. L. Wruthruk, *J. Phys. Chem.*, 71, 2187 (1967).
(30) J. B. Moffat, *Can. J. Chem.*, 42, 1323 (1964).
(31) F. Halverson and R. J. Francel, *J. Chem. Phys.*, 17, 694 (1949).
(32) G. P. Van der Kelen, *Bull. Soc. Chim. Belges*, 71, 421 (1962).
(33) W. P. Jencks and G. E. Llenhard, *J. Am. Chem. Soc.*, 87, 3863 (1965).
(34) F. Hashimoto, J. Tanaka, and S. Nazakura, *J. Mol. Spectry.*, 10, 401 (1963).
(35) G. P. Van der Kelen and Z. Eckhaut, *ibid.*, 10, 141 (1963).
(36) N. Muller and D. E. Pritchard, *J. Chem. Phys.*, 31, 1471 (1959).
(37) T. Matsuo and Y. Kodera, *J. Phys. Chem.*, 70, 4087 (1966).
(38) E. M. Kosower, *J. Am. Chem. Soc.*, 80, 3253 (1958).
(39) P. Trumel, *Ann. Chem.*, 12, 93 (1939).
(40) E. H. Hirota, *J. Mol. Spectrosc.*, 1, 242 (1961).
(41) N. Muller and D. E. Pritchard, *J. Am. Chem. Soc.*, 80, 3483 (1958).
(42) P. A. Casabella and P. V. Bray, *J. Chem. Phys.*, 29, 1105 (1958).

are 3.0154 ± 0.0002 and 2.8670 ± 0.0002 Mc/sec, and the ^{14}N quadrupole coupling constant is 3.9216 ± 0.0003 Mc/sec with an asymmetry parameter of 7.57%.

The electric moments of **1** at 25 and 75° are 3.56[35,43] and 3.61 D.[25,39,44] The calculated molar Kerr constant (mK) of -27 and -33×10^{-12} differ markedly from the observed mK of -72×10^{-12}. This anomaly could be attributed to the bending of the CCN group,[44] the large negative exaltation, or solute–solvent interactions in the benzene solution.

The infrared and Raman spectra of **1**, and its deuterium compounds, $CHD(CN)_2$ and $CD_2(CN)_2$, have been measured.[45] The normal modes and frequencies of the three compounds were calculated on the basis of the Urey–Bradley force field, and assignments of vibrational bands were made. A compilation of the infrared and Raman spectra of **1** and its deuterated compounds appears in ref 45.

VI. Chemical Reactions

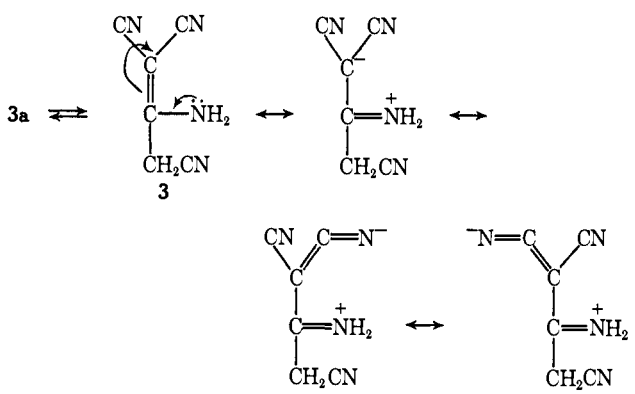
A. DIMERIZATION

A Thorpe-type reaction between two molecules of **1** yields the dimer 2-amino-1,1,3-tricyanopropene (**3**). The infrared spectrum[14] shows absorption bands at 2.98 and 2.10 μ ($-NH_2$) and at 4.22, 4.51, and 4.55 μ (conjugated –CN), which indicates that the enamine structure **3** predominates. Pmr also suggests

$$1 \xrightarrow[\text{base}]{\text{acid or}} (NC)_2HCC(NH)CH_2CN \rightleftharpoons (NC)_2C{=}C(NH)_2CH_2CN \quad (4)$$

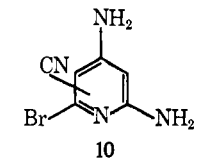
3a **3**

that **3** exists in one of several resonance-stabilized zwitterionic forms.[46]



3 can be prepared in several ways: (1) reaction of nitrous oxide and **2** in absolute alcohol[47] (a side reaction gives ethyl cyanoacetate); (2) reaction of **1**, aqueous alkali, and copper sulfate (42%);[14] (3) acid hydrolysis of the solid formed by treating a solution of **1** in an inert solvent with sodium (75%);[14] (4) passage of dry hydrogen chloride through a benzene solution of **1** (53%).[48] Use of dry hydrogen bromide gives a compound postulated to be cyano-2,4-diamino-6-bromopyridine (**10**).[13,14] Since the same product was obtained by using **3** instead of **1**, the reaction probably proceeds *via* eq 5. Although the position of the cyano group was not specified, it is probably located at

$$1 + NH{=}CBrCH_2CN \longrightarrow \mathbf{3a} \rightleftharpoons \mathbf{3} \xrightarrow{HBr}$$



(5)

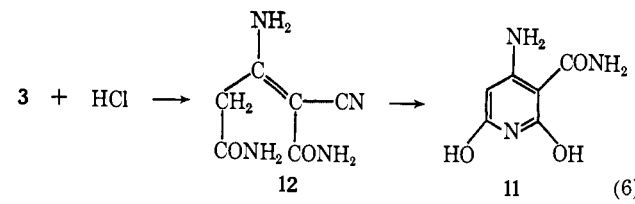
10

the 3 position since the hydrochloric acid hydrolysis of **3** gives 4-amino-3-carboxamido-2,6-dihydroxypyridine (**11**) in 77% yield[49] (*vide infra*).

1. Reactions of Malononitrile Dimer

a. Hydrolysis

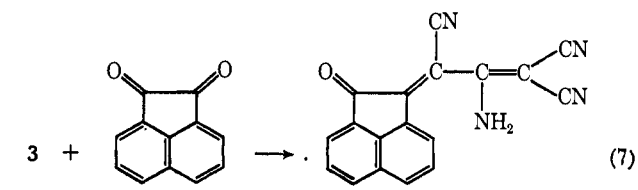
Hydrolysis of **3** with concentrated hydrochloric acid gives **11** in 77% yield.[49] Presumably, hydrolysis of two nitrile groups gives the intermediate **12** which cyclizes to **11**.



12 **11** (6)

b. 1,2-Diketones

The methylene group of **3** condenses with one of the carbonyl groups of acenaphthenequinone to give 1-(1,3,3-tricyano-2-aminopropene-2-yl)acenaphthen-2-one (**13**).[50]

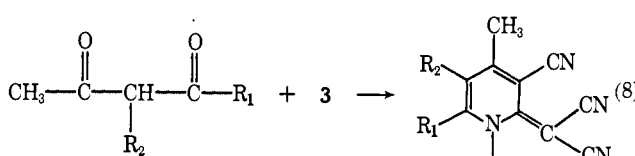


(7)

13

c. 2,4-Diketones

2,4-Diketones condense with **3** to give 4,6-disubstituted 1,2-dihydro-3-cyano-2-dicyanomethylenepyridines (**14**).[51] Similarly, 2-acetylcyclohexanone gives 3-cyano-2-dicyanomethylene-4-methyl-1,2,5,6,7,8-hexahydroquinoline (**15**). It is surprising that none of the corresponding hexahydroisoquinoline



(8)

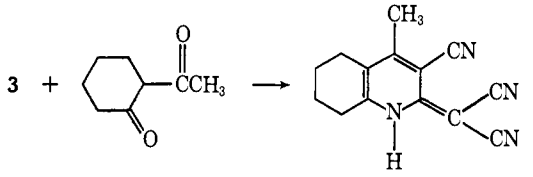
R_1 = *p*-tolyl; R_2 = H
R_1 = *n*-butyl; R_2 = H
R_1 = *sec*-butyl; R_2 = H
R_1 = isobutyl; R_2 = H
R_1 = *n*-amyl; R_2 = H

14

R_1 = methyl; R_2 = H
R_1 = ethyl; R_2 = H
R_1 = R_2 = methyl
R_1 = C_6H_5; R_2 = H

(43) Y. Urushibara, *Bull. Chem. Soc. Jap.*, 2, 306 (1928).
(44) R. J. W. Le Ferre, B. J. Orr, and G. L. D. Ritchie, *J. Chem. Soc.*, 2499 (1965).
(45) T. Fugiyama and T. Shimanouchi, *Spectrochim. Acta*, 20, 829 (1964).
(46) F. S. Eberts, Jr., G. Slomp, and J. L. Johnson, *Arch. Biochem. Biophys.*, 95, 305 (1961).
(47) R. Meir, *Chem. Ber.*, 86, 1491 (1953).
(48) J. Decombe and C. Verry, *Compt. Rend.*, 256, 5156 (1963).
(49) H. Junek and A. Schmidt, *Monatsh. Chem.*, 98, 70 (1967).
(50) H. Junek, H. Hambock, and B. Hornischer, *ibid.*, 98, 315 (1967).
(51) H. Junek, *ibid.*, 95, 1200 (1964).

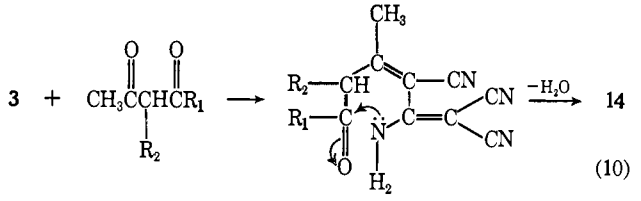
was formed since initial attack of the anion could also occur at the cyclic carbonyl carbon. Also, it is known[52] that alicyclic



(9)

15

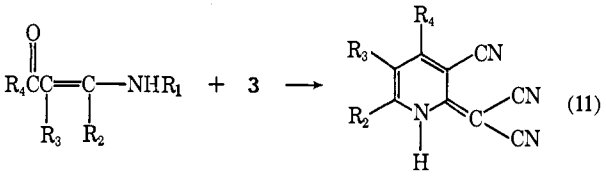
carbonyl carbons frequently undergo addition reactions faster than acyclic carbonyl carbons. The reaction presumably involves condensation of the active methylene group of **3**, a nucleophilic attack of the nitrogen unshared electron pair at the remaining carbonyl carbon, and loss of water to give **14** or **15**.



(10)

d. Enamino Ketones

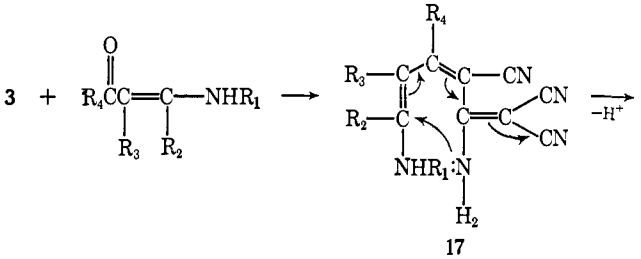
The reaction of β-amino ketones with **3** gives substituted dihydropyridines (**16**), whereas the corresponding reaction with N-substituted amino ketones is accompanied by elimination of the amino group (Table III).[53] The mechanism is similar to the one for 2,4-diketones. The combined electronegativity of the nitrile groups in **16** contributes to the driving force for the for-



(11)

16

mation of **18**. Loss of the amino group in the final stage is not without precedent.[54,55]



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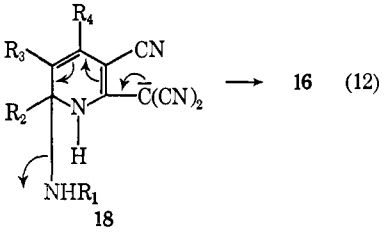
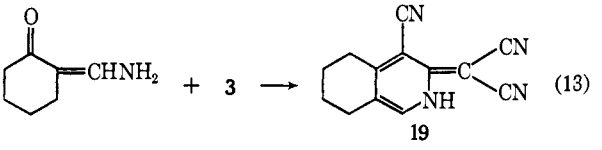


(12)

18

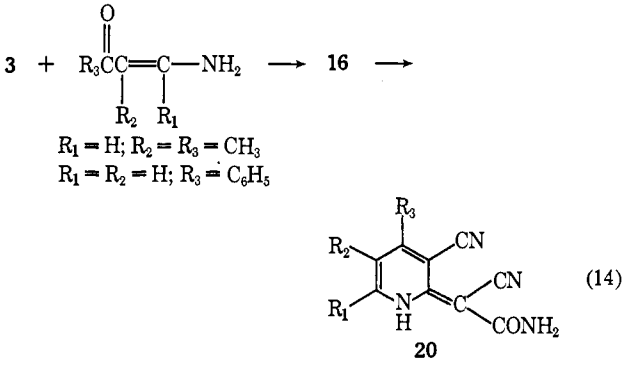
In contrast to the reaction of **3** and 2-acetylcyclohexanone which gives the hexahydroquinoline (**15**), 2-aminomethylenecyclohexanone yields the hexahydroisoquinoline (**19**). The structure of **19** was deduced from the isoquinoline infrared band at 6.47 μ and the absence of the characteristic quinoline bands[3] at 6.58 and 7.59 μ.



(13)

19

By varying the reaction conditions one may obtain amides **20** from the reaction of **3** and unsaturated amino ketones.[57] **20** is hydrolyzed under acidic conditions to 1,5,6,7-tetrahydropyrido[4,3-*b*]pyridine-5,7-diones (**21**).



(14)

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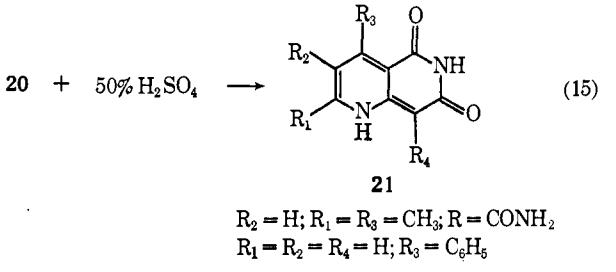
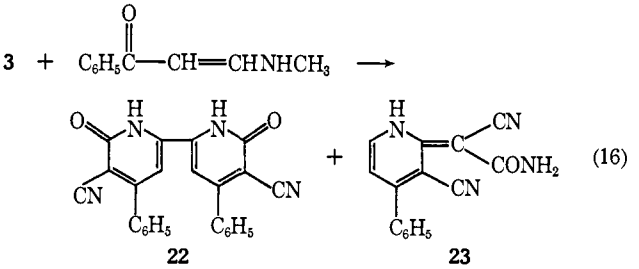


(15)

21

$R_2 = H; R_1 = R_3 = CH_3; R = CONH_2$
$R_1 = R_2 = R_4 = H; R_3 = C_6H_5$

An unusual reaction[58] occurs with **3** and 1-methylamino-3-phenyl-1-propen-3-one in boiling acetic acid to give 3,3′-dicyano-4,4′-diphenyl-6,6′-bipyridon-2,2′-yl (**22**) and **23**. The



(16)

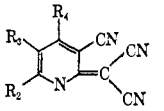
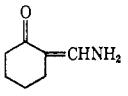
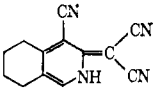
22 23

structure of **22** was established *via* infrared, pmr, and mass spectrometry. Although all the steps in this remarkable transformation have not been elucidated, the mechanism probably involves condensation of the methylene group of **3**, partial hydrolysis of the nitrile groups, ring closure, and elimination of the amino group.

(52) A. Lapworth and R. H. F. Manske. *J. Chem. Soc.*, 2533 (1928); 1976 (1930).
(53) H. Junek, *Monatsh. Chem.*, **95**, 1473 (1964).
(54) H. R. Snyder and J. H. Brewster, *J. Am. Chem. Soc.*, 70, 4230 (1948).
(55) D. Taber, J. Becker, and P. E. Spoerri, *ibid.*, **76**, 776 (1954).
(56) M. Coenen and M. Pestemer, *Z. Electrochem.*, **57**, 785 (1953).
(57) H. Junek, *Monatsh. Chem.*, **96**, 2046 (1965).
(58) H. Junek, H. Sterk, and A. Schmidt, *Z. Naturforsch.*, **21**, 1145 (1966).

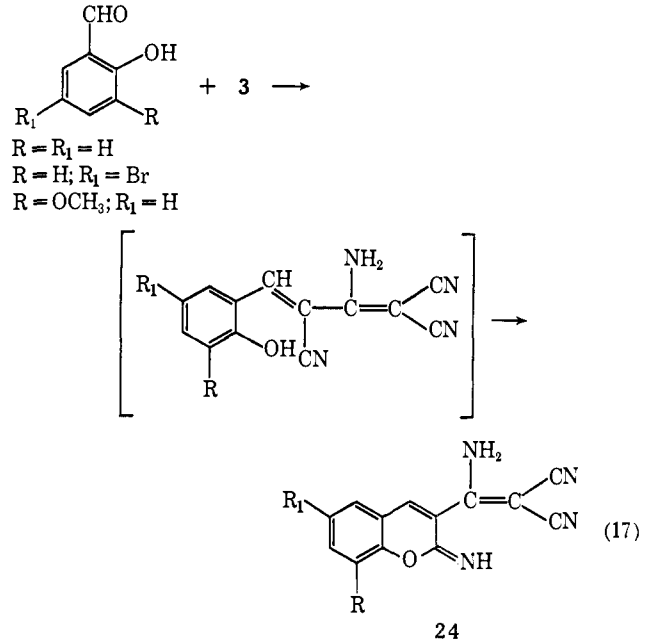
Table III

Dihydropyridines from Malononitrile Dimer and β-Amino Ketones[55,56]

Enamino ketone	*Exptl conditions*	
$CH_3C(=O)C(CH_3)=CHNH_2$	Acetic acid, heat	$R_2 = H; R_3 = R_4 = CH_3$
$CH_3C(=O)CH=CHNH_2$	Pyridine	$R_2 = R_3 = H; R_4 = CH_3$
$C_6H_5C(=O)CH=CHNH_2$	Pyridine	$R_2 = R_3 = H; R_4 = C_6H_5$
$C_6H_5C(=O)CH=C(CH_3)NH_2$	Pyridine	$R_2 = CH_3; R_3 = H; R_4 = C_6H_5$
$CH_3C(=O)CH=C(CH_3)NH_2$	Pyridine	$R_2 = R_4 = CH_3; R_3 = H$
$CH_3C(=O)CH=C(CH_3)NHC_6H_5$	Acetic acid, heat	$R_2 = R_4 = CH_3; R_3 = H$
$C_6H_5C(=O)CH=C(CH_3)NHC_6H_5$		$R_2 = CH_3; R_4 = C_6H_5; R_3 = H$
	Piperidine	

e. *o*-Hydroxybenzaldehydes

Substituted *o*-hydroxybenzaldehydes react[59] with **3** in the presence of piperidine to form the corresponding substituted iminocoumarins **24**. The iminocoumarin from *o*-hydroxybenz-

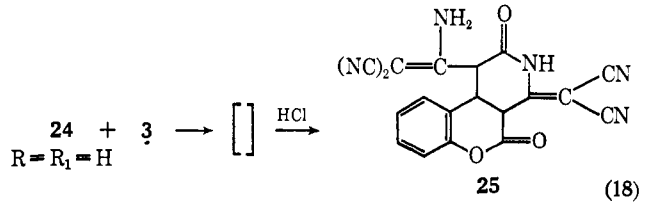


$R = R_1 = H$
$R = H; R_1 = Br$
$R = OCH_3; R_1 = H$

(17)

24

aldehyde ($R = R_1 = H$) adds a second mole of **3**, *via* a Michael-type addition, to give a cyclic imine which is hydrolyzed to **25**.



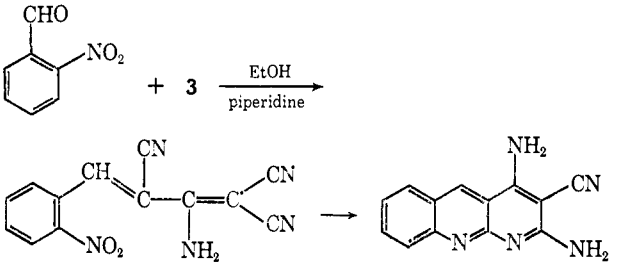
$R = R_1 = H$

(18)

25

f. *o*-Nitrobenzaldehyde

o-Nitrobenzaldehyde reacts with **3** to give 2-nitro-α-(1-amino-2,2-dicyano-β-ethylene)cinnamonitrile (**26**), in 70% yield, which is cyclized to 2,4-diamino-3-cyanobenzo[*b*]-1,8-naphthyridine (**27**) with iron and acetic acid.[60]

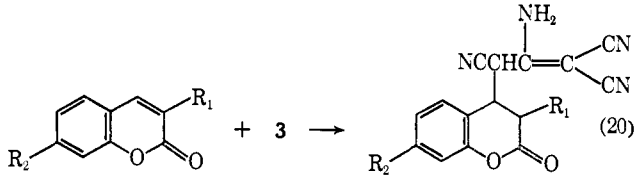


26 **27**

(19)

g. Coumarins

3 adds smoothly to position four of 4-unsubstituted coumarins, *via* a Michael addition, to form 3,4-dihydrocoumarin derivatives (**28**).[61,62]



$R_1 = CN; R_2 = H$
$R_1 = COCH_3; R_2 = H$
$R_1 = H; R_2 = Cl$

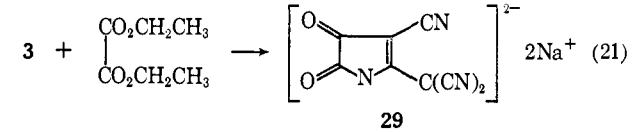
28

$R_1 = H; R_2 = CH_3$
$R_1 = H; R_2 = NO_2$

(20)

h. Miscellaneous Reactions

The interesting structural features of **3** have been used in a variety of unusual chemical transformations.[14] Diethyl oxalate, sodium ethoxide, and **3** give the highly acidic disodium dioxopyrrolidine (**29**). **3** reacts with 2 moles of bromine to give



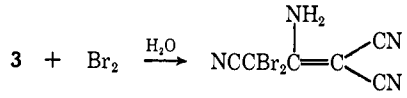
29

(21)

(59) H. Junek, *Monatsh. Chem.*, **94**, 192 (1963).

(60) H. Junek, *ibid.*, **94**, 890 (1963).
(61) H. Junek, *ibid.*, **95**, 235 (1964).
(62) H. Junek, *ibid.*, **93**, 684 (1962).

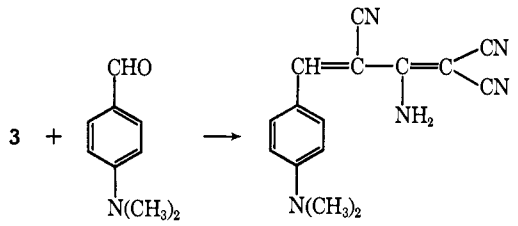
2-amino-1,1,3-tricyano-3,3-dibromopropene (**30**), and the



(22)

30

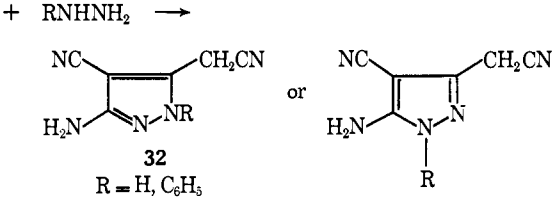
activated methylene group of **3** condenses with *p*-dimethylaminobenzaldehyde in the presence of an amine to give a yellow benzylidene dye (**31**).



(23)

31

It has been reported that phenylhydrazine or hydrazine hydrate reacts with **3** to give 3-amino-4-cyano-5-pyrazoleacetonitriles (**32**) or 5-amino-4-cyano-3-pyrazoleacetonitrile (**33**).[14] However, subsequent studies have shown that **33** is the correct structure.[14a]



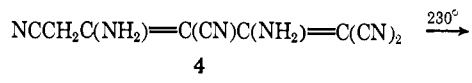
(24)

32
R = H, C_6H_5

33

B. TRIMERIZATION

It has been reported that treatment of **1** with ammonium hydroxide,[63] sodium ethoxide,[64] diethyl oxalate, and either ammonia or diethylamine gives a trimer of **1**.[64] Schenck and Finken[65] suggested three different structures for the trimer and Anderson, Bell, and Duncan[63] suggested structures **4** and **34**.



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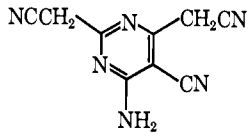
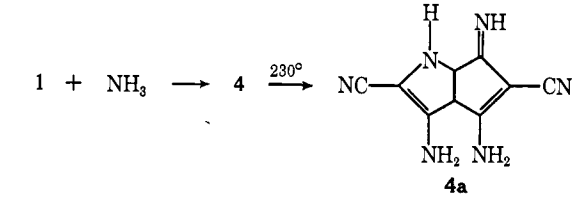


(25)

34

Junek and Sterk[66] showed the reaction product of **1** and ammonia to be 1,3,5,5-tetracyano-2,4-diaminopenta-2,4-diene (**4**) which is converted to **4a**, instead of **34**, on heating. When

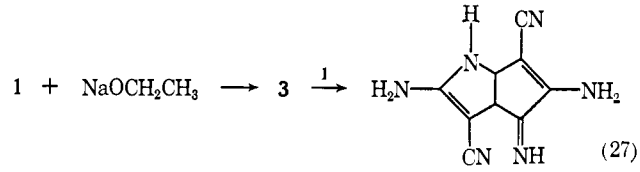


(26)

4a

(63) D. M. W. Anderson, F. Bell, and J. L. Duncan, *J. Chem. Soc.*, 405 (1961).
(64) H. Junek, *Monatsh. Chem.*, **93**, 44 (1962).
(65) R. Schenck and H. Finken, *Ann. Chem.*, **462**, 267 (1928).
(66) H. Junek and H. Sterk, *Z. Naturforsch.*, **22**, 732 (1967).

sodium ethoxide is used, the reaction proceeds *via* **3** to the bicyclic structure **4b**. The structures of all products were established *via* infrared, ultraviolet, and mass spectrometry.[66]



(27)

4b

C. HYDROLYSIS

1 can be hydrolyzed to malonic acid with dilute hydrochloric acid or with dilute sulfuric acid and mercuric sulfate.[67,68] Hydrolysis with alcoholic sulfuric acid gives diethyl malonate and ethyl cyanoacetate,[69] and treatment with sodium hydroxide and ammonia yields malonoamide.[70]

D. REDUCTION

In the presence of hydrochloric acid **1** is reduced electrolytically to 1,3-diaminopropane in 50% yield.[71]

E. ORTHOESTER FORMATION

Treatment of **1** with equivalent amounts of methanol or ethanol, and hydrogen chloride gives the monoimino salts (**35**) in 94 and 98% yields, respectively.[72] These salts are easily methanolyzed to the corresponding orthoesters in 62–65% yields.

(28)

F. COMPLEX FORMATION

1. Silver Fluoroborate

1 reacts with silver fluoroborate in nitromethane or 1,2-dichloroethane to give the stable complex (**36**) which decomposes at 200°.[73] **36** is also prepared from a suspension of silver oxide in **1** and boron trifluoride etherate.

(29)

36

2. Phenylmagnesium Bromide

1 does not form an addition product with phenylmagnesium bromide but gives an insoluble magnesium derivative which does not react with excess Grignard reagent. However, this complex may be hydrolyzed to give **1** quantitatively.[74]

(67) L. Henry, *Compt. Rend.*, 102, 1396; Bellstein II, 590.
(68) G. Travagli, *Ann. Univ. Studi. Ferrara*, **6**, (1947); *Chem. Abstr.*, **43**, 1248 (1949).
(69) L. Splegel and H. Szydlowsky, *Chem. Ber.*, **51**, 296 (1918).
(70) K. Takeda and K. Tokuyama, *J. Pharm. Soc. Jap.*, **76**, 77 (1956); *Chem. Abstr.*, 50, 13035 (1956).
(71) M. Ohta, *Bull. Chem. Soc. Jap.*, 17, 485 (1942).
(72) (a) S. M. McElvain and J. P. Schroeder, *J. Am. Chem. Soc.*, **71**, 40 (1949); (b) S. M. McElvain and R. E. Lyles, Jr., *ibid.*, 72, 384 (1950).
(73) H. Meerwein, V. Hederich, and K. Wunderlich, *Arch. Pharm.*, 291, 541 (1958).
(74) I. L. E. Erickson and M. M. Barrett, *J. Am. Chem. Soc.*, 57, 560 (1935).

3. Cuprous Complex

The cuprous complex of **1**, [bis(malononitrile)copper chloride], which is used for dyeing polyacrylonitrile fibers, is prepared by the reaction of **1**, copper sulfate, and hydroxylamine hydrochloride.[75]

4. Group IV Halides

1 reacts as a Lewis base with titanium tetrachloride or tetrabromide, zirconium tetrachloride, and stannic chloride to give coordination complexes.[76,77] Analytical results, structural considerations, and infrared spectral data indicate that, depending on experimental conditions, three types of compounds are obtained: $2TiCl_4 \cdot L\text{–}L$, $MX_4 \cdot L\text{–}L$, and $MX_4 \cdot 2L\text{–}L$ where MX_4 is a Lewis acid and L–L a bidentate ligand. $2TiCl_4 \cdot L\text{–}L$ is formed by halogen bridging between two metal atoms, $MX_4 \cdot L\text{–}L$'s are coordination polymers or chelates of variable ring size, and $MX_4 \cdot 2L\text{–}L$'s are addition compounds where no chelation takes place because of the mutual interaction of the two nitrile groups.

5. Platinum Group Metals Chelates

The chelate formed by the reaction of **1** and a platinum group metal is used to apply thin corrosion-resistant coatings to other metals.[78]

G. SALT FORMATION

1. Sodiomalononitrile

Sodiomalononitrile (**2**) can be prepared in a variety of ways.[79–81] Although it has been reported[79] that an ethereal solution of **1** reacts with sodium ethoxide to form a mixture of mono- and disodium malononitrile, it is doubtful if sodium ethoxide in ether is a strong enough base to remove both hydrogens from **1**. **2** can best be prepared by treating a 50% dispersion of sodium hydride in mineral oil with **1** in a dry solvent[80] or by the reaction of **1** with sodium hydride in dimethyl sulfoxide.[81]

$$\mathbf{1} + NaH \xrightarrow{DMSO} \mathbf{2} \qquad (30)$$

2. Reactions of Sodiomalononitrile

a. Alkyl Halides

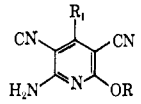
1, sodium methoxide, and methyl iodide in methyl alcohol have been reported to give 1-imino-2-methyl-2-cyanopropyl methyl ether (**37**).[79] Dimethylmalononitrile (30%) results from the reaction of **1**, sodium ethoxide, and methyl iodide. The

$$\mathbf{1} + NaOCH_3 + CH_3I + CH_3OH \longrightarrow [2] \longrightarrow (CH_3)_2\underset{\displaystyle OCH_3}{\overset{\displaystyle CN}{\underset{|}{\overset{|}{C}}}}\!-\!C\!=\!NH \qquad (31)$$

37

Table IV

2-Amino-3,5-dicyano-6-alkoxypyridines



R	R_1	Yield, %	Ref.
CH_3	H	65	80
C_2H_5	H	50	80
C_2H_5	H	96	13
$n\text{-}C_3H_7$	H	35	80
$i\text{-}C_3H_7$	H	50	80
$t\text{-}C_4H_9$	H	0	80
C_2H_5	CN	75	13
$i\text{-}C_3H_7$	CN	31	13
CH_3	C_6H_5	85.7	13
C_2H_5	C_6H_5	93.4	13

intermediates are methylmalononitrile and sodium dicyanomethanide.[79]

$$\mathbf{2} + CH_3I \longrightarrow CH_3CH(CN)_2 \longrightarrow CH_3\bar{C}(CN)_2 + CH_3I \longrightarrow (CH_3)_2C(CN)_2 \qquad (32)$$

A good method for alkylating **1** with methyl iodide, butyl bromide, benzyl chloride, and isopropyl bromide in 60, 75, 75, and 60% yields, respectively, has been reported by Bloomfield.[81] The success of this reaction is due to the nonnucleophilic nature of the base sodium hydride, and the ability of the solvent dimethyl sulfoxide to dissolve the reaction intermediates.

b. Cyanocarbon Chemistry

Chloroform and Ethoxymethylenemalononitrile. The reaction of **2** with chloroform and sodium ethoxide in ethyl alcohol has been reported[82] to give **38** or **39**. However, a rein-

$$(NC)_2C\!=\!\underset{\displaystyle CN}{\underset{|}{CH}}CONHCH_2CH_3 \cdot {}^1/_2H_2O$$

38

$$(NC)_2CH\underset{\displaystyle CN}{\underset{|}{CH}}\!=\!CCONHCH_2CH_3 \cdot {}^1/_2H_2O$$

39

vestigation has shown that the actual product is 2-amino-3,5-dicyano-6-ethoxypyridine (**40**) (Table IV).[80] The pyridine system is probably formed by the cyclization of the intermediate salt of 1,1,3,3-tetracyanopropene (**41**).[13] Support for this mechanism arises from the exothermic reaction of **2** and ethoxymethylenemalononitrile to give **40**. However, when the

$$\mathbf{2} \longrightarrow \underset{\displaystyle \mathbf{41}}{(NC)_2C\!=\!CH\bar{C}(CN)_2Na^+} \xrightarrow{ROH} \underset{\displaystyle \mathbf{40}}{\text{2-amino-3,5-dicyano-6-alkoxypyridine}} \qquad (33)$$

$R = CH_3CH_2$

reaction temperature is maintained at 0°, **41** is obtained in

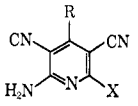
$$\mathbf{2} + (NC)_2C\!=\!CHOCH_2CH_3 \longrightarrow \mathbf{40} + \mathbf{41} \qquad (34)$$

90% yield. **41** is converted to **40** by reflux in ethyl alcohol in the presence of concentrated sulfuric acid.[13] A summary of substituted pyridines prepared by both methods[13,80] is given in Table IV.

(75) H. Roth and E. Specht, *Melliand Textilber.*, **39**, 281 (1958); *Chem. Abstr.*, **52**, 11427 (1958).
(76) M. Kubota and S. R. Schulze, *Inorg. Chem.*, **3**, 853 (1964).
(77) S. C. Jain and R. Rivest, *Can. J. Chem.*, **41**, 2130 (1963).
(78) Deutsche Gold and Silver-Scheideanstalt vorm. Roessler, British Patent 990,174 (1965); *Chem. Abstr.*, **63**, 9264 (1965).
(79) B. C. Hesse, *J. Am. Chem. Soc.*, 18, 723 (1896).
(80) A. P. Krapcho and P. S. Huyffler, *J. Org. Chem.*, 28, 2461 (1963).
(81) J. J. Bloomfield, *ibid.*, 26, 4112 (1961).
(82) A. Kotz and W. Zörnig, *J. Prakt. Chem.*, 182, 425 (1906).

Table V

2-Amino-6-halo-3,5-dicyanopyridines[13]

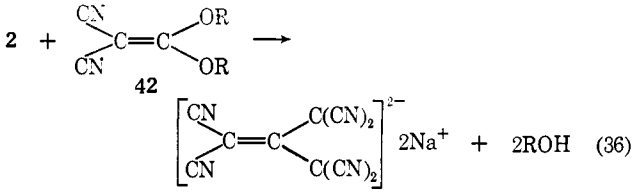


Salt	*X*	*R*	*Yield, %*
$Na[(NC)_2C{=}CHC(CN)_2]\cdot H_2O$	Cl	H	90
$Na[(NC)_2C{=}CHC(CN)_2]\cdot H_2O$	Br	H	93.5
$Na[(NC)_2C{=}C(OEt)C(CN)_2]$	Cl	OEt	77.7
$[(CH_3)_4N][(NC)_2C{=}C(C_6H_5)C(CN)_2]$	Cl	C_6H_5	87.6
$Na[(NC)_2C{=}C(N(CH_3)_2)C(CN)_2]$	Cl	$N(CH_3)_2$	10
$[(CH_3)_4N][(NC)_2C{=}C(CN)C(CN)_2]$	Br	CN	90

Cyanogen Chloride. **1** and cyanogen bromide or chloride in the presence of sodium ethoxide give cyanoform (tricyanomethane).[83-85] When the reaction is carried out with the sodium salts of substituted malononitriles, instead of **2**, the products are alkyl- and aryltricyanomethanes.[86-88] This route provides the first general synthesis of compounds containing the tricyanomethyl group.

$$R\bar{C}(CN)_2Na^+ + ClCN \longrightarrow RC(CN)_3 \qquad (35)$$

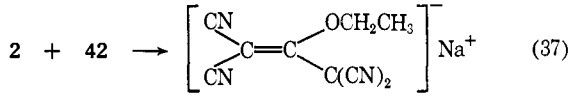
Dicyanoketene Acetals. **2** reacts with dicyanoketene acetals (**42**) to give salts of cyanocarbon acids.[8,89,90] The structures of these anions can be represented by a number of resonance forms in which the negative charge is on either nitrogen or carbon. For example,[8] sodium 2-dicyanomethylene-1,1,3,3-tetracyanopropanediide (**43**), which is prepared from **42** and **2**



42

43

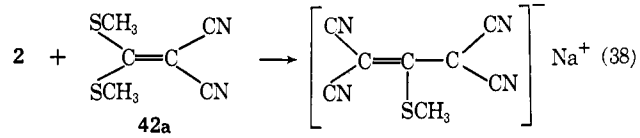
equiv of **2**, has 27 contributing resonance structures. When 1 equiv of **2** is used, sodium 2-ethoxy-1,1,3,3-tetracyanopropenide (**44**) is formed.[8] The reaction is also successful with the



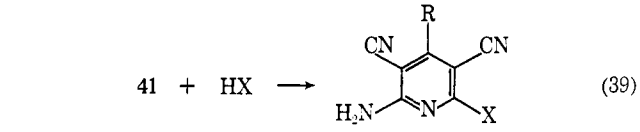
44

sulfur analog of **42**. For example, dicyanoketene dimethyl thioacetal (**42a**) reacts with **2** to give sodium 2-methylthio-1,1,3,3-tetracyanopropenide (**43a**).[8,91]

The salts of cyanocarbon acids react with hydrogen halides to yield 2-amino-6-halo-3,5-dicyanopyridines[13] (Table V; *cf.* Table IV).

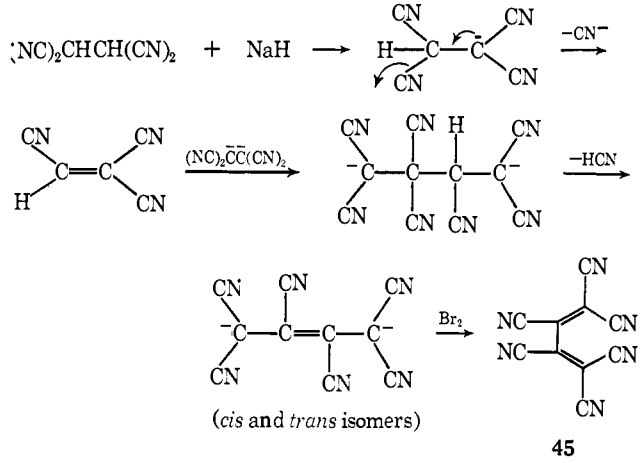


42a **43a**



Tetracyanoethane and Hexacyanobutadiene. The first percyanodiene,[92,93] hexacyanobutadiene (**45**), was prepared from sodium hydride and tetracyanoethane according to Scheme I.

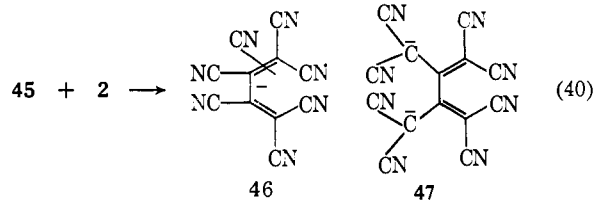
Scheme I



(*cis* and *trans* isomers)

45

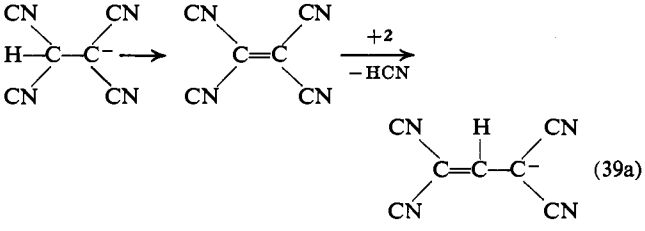
Excess **45** reacts with **2** to give a bright red cyanocarbon anion believed to be heptacyanopentadienide (**46**). When **2** is present



46 **47**

in excess, the product is the yellow cyanocarbon anion **47**. It appears that **47** results from substitution at the 2 position followed by a second substitution at the position of lowest electron density (position 3). The structure of **47** was assigned on the basis of infrared and visible spectra.[92]

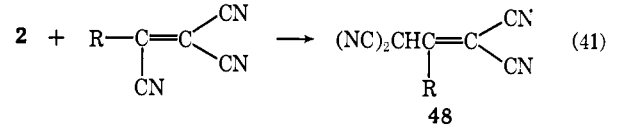
Tetracyanoethane reacts with **2** and sodium hydride in 1,2-dimethoxyethane to give a 67% yield of 1,1,3,3-tetracyanopropenide. This experiment established that sodium tetracyanoethanide could function as a tricyanoethylene source.[92]



Tricyanovinyl Compounds. Reaction of 1,2,2-tricyanovinyl compounds with nucleophilic reagents generally results

(83) L. Birckenbach and K. Huttner, *Chem. Ber.*, 62, 153 (1929).
(84) A. Hantzsch and G. Oswald, *ibid.*, 32, 643 (1899).
(85) H. Schmidtmann, *ibid.*, 29, 1168 (1896).
(86) J. K. Williams, U. S. Patent 2,995,597 (1961); *Chem. Abstr.*, 56, 423 (1962).
(87) E. L. Martin and J. K. Williams, U. S. Patent 3,166,583 (1965).
(88) J. K. Williams, E. L. Martin, and W. A. Sheppard, *J. Org. Chem.*, 31, 919 (1966).
(89) W. J. Middleton, U. S. Patent 2,766,246 (1956); *Chem. Abstr.*, 51, 11372 (1957).
(90) W. J. Middleton, U. S. Patent, 2,766,247 (1956); *Chem. Abstr.*, 51, 11372 (1957).
(91) H. D. Edwards and J. D. Kendall, U. S. Patent 2,533,233 (1950); *Chem. Abstr.*, 45, 2804 (1951).
(92) O. W. Webster, *J. Am. Chem. Soc.*, 86, 2898 (1964).
(93) Y. Urushibara, *Bull. Chem. Soc. Jap.*, 2, 278 (1927).

in replacement of the 1-cyano group. **2** reacts with tricyanovinyl compounds in ethanolic or inert media to give the corresponding 2-substituted 1,1,3,3-tetracyanopropenes (**48**).[10] **2** also converts the intermediate 1-alkoxy compounds to tetracyanopropenes.[94]

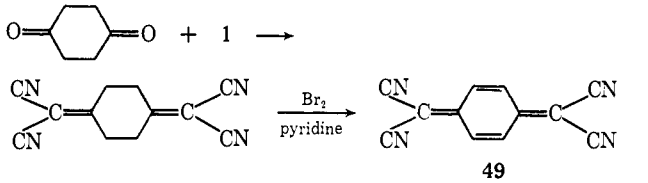


(41)

48

R = C_6H_5, $(CH_3)_2NC_6H_4$

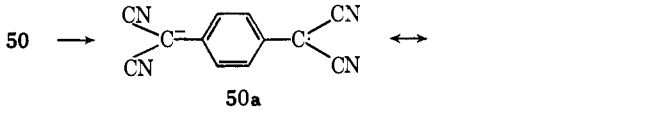
Substituted Quinodimethans. 7,7,8,8-Tetracyanoquinodimethan (TCNQ, **49**), one of the few stable quinodimethans, has been prepared from the condensation product of **1** and 1,4-cyclohexanedione.[95] **49** easily accepts one electron to form



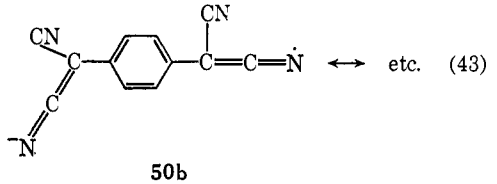
(42)

the isolable solid anion radical (**50**), which is the first example of a quinodimethan anion radical.[96] The complex anion-radical salts of **50** have the highest electrical conductivities known for any organic compound.

Because of the unusual stability of **49** and electrical properties of **50**, several alkyl derivatives were prepared for comparison according to eq 44.[97] A by-product in the preparation of methyl-TCNQ is the dimer **51**.

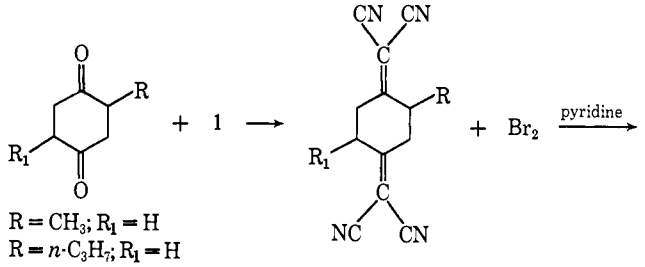


50a

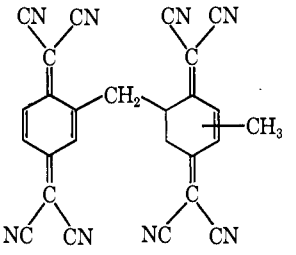


(43)

50b

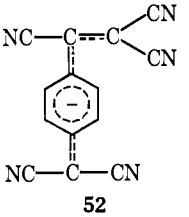


(44)

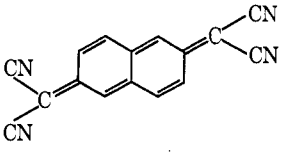


51

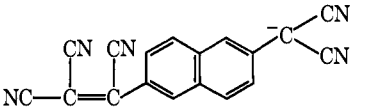
As expected, the alkyl substituents exerted a normal inductive effect which produced a decrease in the oxidation–reduction potentials relative to TCNQ. The solid-state properties of the parent paramagnetic TCNQ anion radical were not strongly influenced by alkyl substituents.[97] TCNQ reacts with **1** to give the blue anion **52** while the more conjugated 11,11,12,12-tetracyano-2,6-naphthoquinodimethan (TNAP, **53**) gives 6-(tricyanovinyl)-2-naphthyldicyanomethanide (**54**).[98]



52



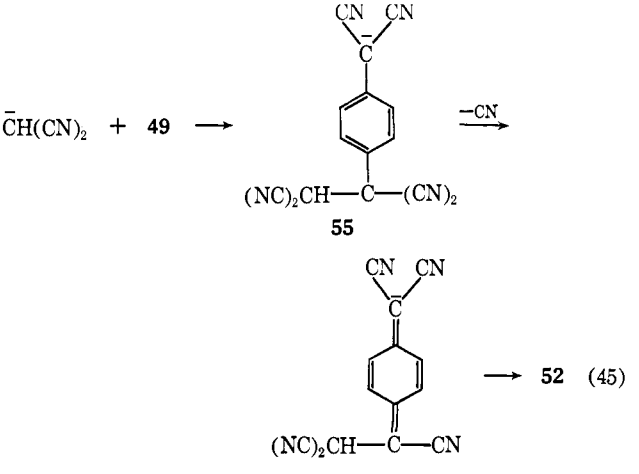
53



54

The mechanism for the formation of **52** probably involves the addition of the dicyanomethyl anion to **49** to form **55** which eliminates cyanide ion to give the conjugate acid of **52**. **52** can also be prepared from the reaction of **49** and tetracyanoethylene (**56**) in moist dimethylformamide or from the reaction of **49** and 1,1,3,3-tetracyanopropane in dimethylformamide.[98]

Condensation of **1** with *cis*-2,3,5,8,9,10-hexahydro-1,4-naphthaquinone yields 1,4-tetracyano-*cis*-2,3,5,8,9,10-hexa-



(45)

(94) Y. Urushibara and M. Takebayaski, *Bull. Chem. Soc. Jap.*, **11**, 557 (1936).

(95) D. S. Acker and W. R. Hertler, *J. Am. Chem. Soc.*, 84, 3370 (1962).

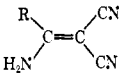
(96) L. R. Meby, R. J. Harder, W. R. Hertler, W. Mahler, R. E. Benson, and W. E. Mockel, *ibid.*, **84**, 3374 (1962).

(97) J. Diekmann, W. R. Hertler, and R. E. Benson, *J. Org. Chem.*, 28, 2719 (1963).

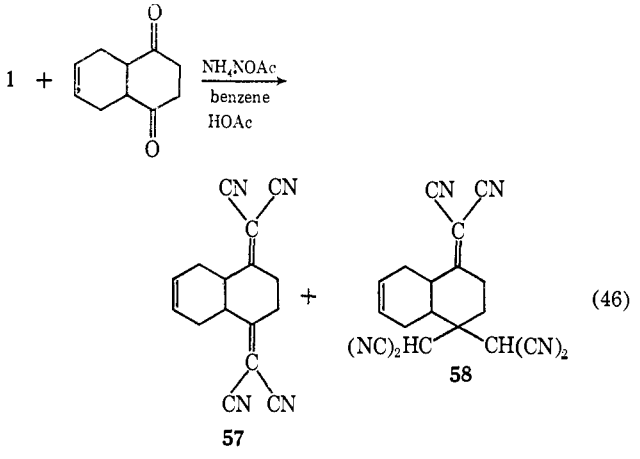
(98) J. K. Williams, *J. Am. Chem. Soc.*, 84, 3478 (1962).

Table VI

1-Amino-1-fluoroalkylethylenes[101]



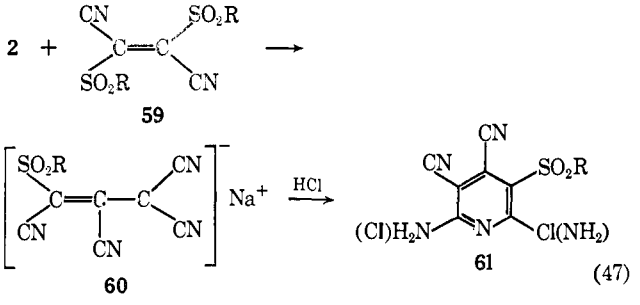
R	*Yield, %*	λ_{max}^{EtOH} · *mμ*
CF_3	98	283
CF_2CF_3	97	287
$CF_2CF_2CF_3$	87	289
$NCC{=}C(NH_2)CF_3$	100	240, 252, 301, 330
$NCCF(C_6H_5)$	55	285



(46)

hydronaphthaquinodimethan (**57**) and **58**.[99] The simple mono-addition product is formed when 3-aminopropionic acid is the catalyst.

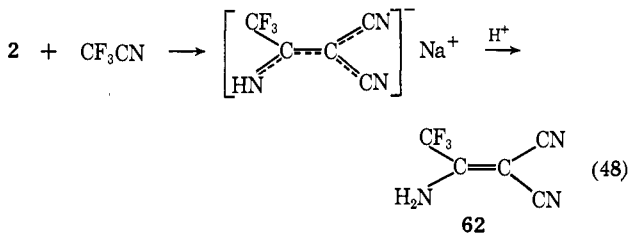
Dicyanodisulfonylethylenes. Recently, a new class of tetra-(negatively substituted)ethylenes, the 1,2-dicyano-1,2-disulfonylethylenes, has been prepared. **2** displaces one of the sulfonyl groups of the 1,2-dicyano-1,2-disulfonylethylenes (**59**) to give the tetrasubstituted propenes (**60**).[100] This is similar to



(47)

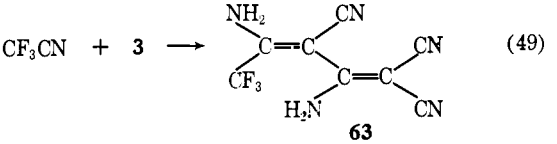
the reaction of **2** with tricyanovinyl compounds. The resulting tetrasubstituted propenes are strong acids[13] and are easily isolated as tetraalkylammonium salts. Treatment of **60** with hydrochloric acid gives 2(6)-amino-6(2)-chloro-4,5-dicyano-3-(4-tolysulfonyl)pyridine (**61**).

Fluoroalkyl Cyanides. Addition of **2** to the cyano group of fluoroalkyl cyanides gives 1-amino-1-fluoroalkylethylenes (**62**) in 55–100% yields[101] (Table VI). The enamine structures are supported by infrared spectra which show resonances for the amino group as well as the carbon–carbon double bond conjugated with the nitrile groups. The ultraviolet spectra contain a single characteristic absorption maximum which is predictably influenced by the nitrile groups.



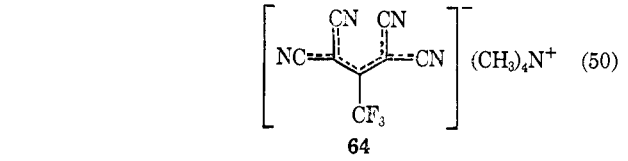
(48)

The reaction can also be extended to **3** which reacts with CF_3CN to give the highly substituted butadiene **63**.[101]



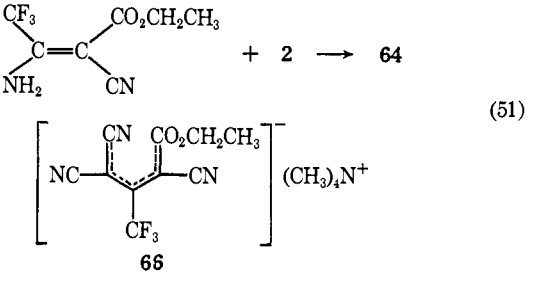
(49)

Although the enamine structure predominates, the 1-amino-1-perfluoralkylethylenes display none of the basic characteristics of the free amino group.[101] In fact, they are weakly acidic. **62** reacts with sodium hydroxide, in the presence of tetramethylammonium chloride, to give the hybrid 2-trifluoromethyl-1,-1,3,3-tetracyanopropenide salt (**64**), which is formed by the



(50)

addition of the dicyanomethyl anion to **62**, followed by elimination of ammonia. Surprisingly, when **65** is treated with **2**, the product is **64** instead of **66**.[101] Further study of this trans-

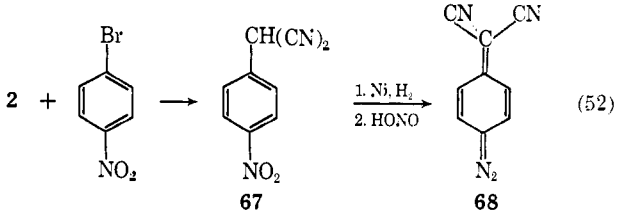


(51)

formation is necessary to decide which among the many reasonable mechanistic pathways is correct.

c. Halogen Substitution

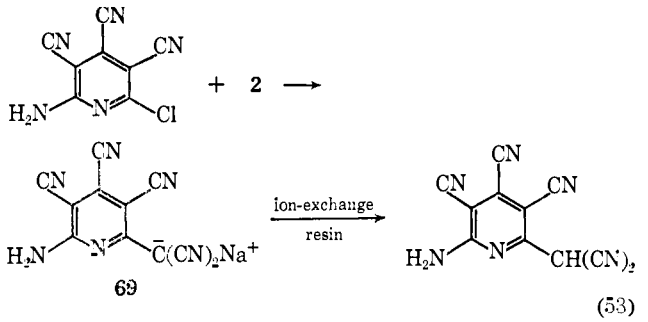
The nucleophilic character of **2** is again demonstrated in its reaction with 1-bromo-4-nitrobenzene, in diglyme at 120°, to give a 40% yield of the sodium salt of *p*-nitrophenylmalononitrile (**67**).[102] The interesting π acid 3-diaza-6-dicyanometh-



(52)

(99) S. Chatterjee, *J. Chem. Soc., B*, 1170 (1967).
(100) E. L. Martin, *J. Am. Chem. Soc.*, 85, 2449 (1963).
(101) A. D. Josey, *J. Org. Chem.*, 29, 707 (1964).
(102) H. D. Hartzler, *J. Am. Chem. Soc.*, 86, 2174 (1964).

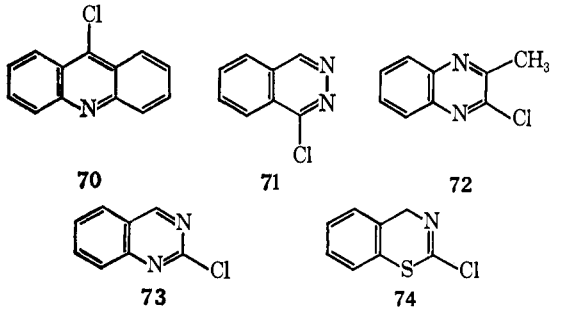
ylene-1,4-cyclohexadiene (**68**) is obtained by diazotizing the reduction product of **67**. **2** displaces chloride in 2-amino-6-chloro-3,4,5-tricyanopyridine to give the sodium salt **69**.[13] The



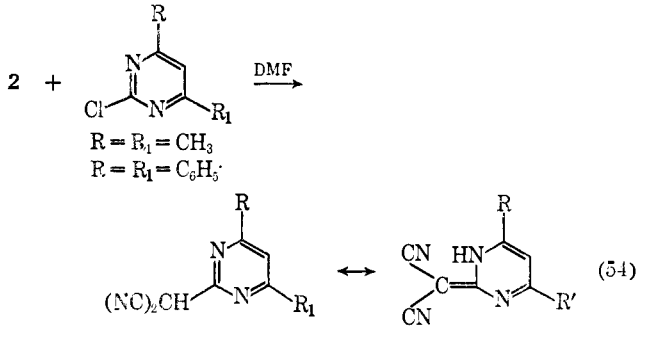
(53)

electron-attracting groups on the aromatic rings facilitate the substitution reactions.

The dicyanomethyl anion also displaces chloride ion in its reactions with 9-chloroacridine (**70**, 96%), 1-chlorophthalazine (**71**, 31.6%), 2-chloro-3-methylquinoxaline (**72**), 2-chloroquinozoline (**73**), and 2-chlorophthalazine (**74**),[103] in its reaction



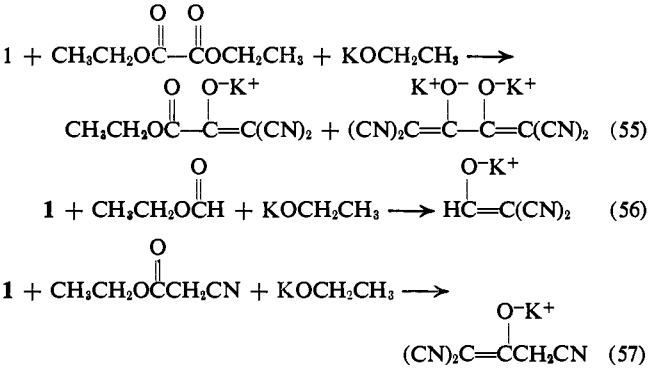
with 2-chloropyrimidines.[104] The tautomeric forms of the products were established *via* elemental analyses, pmr, and infrared and ultraviolet spectroscopy.[104]



(54)

d. Esters

Methyl or ethyl oxalate, ethyl formate, and ethyl cyanoacetate condense with **1**, *via* its potassium salt, to give the corresponding salts[105] in 76–89% yields. Webster[92] has prepared the sodium salt of **75**, disodium 1,1,4,4-tetracyanobuta-2,3-dionediide, in quantitative yield from **1**, sodium hydride, and diethyl oxalate in 1,2-dimethoxyethane solvent. Ethyl acetoacetate

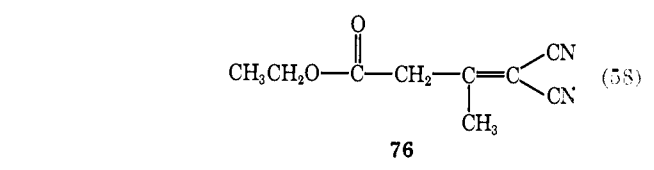


(55)

(56)

(57)

and **2** condense to give **76**.[43] Ethyl chloroformate and **1**, in the presence of sodium ethoxide, give sodium dicyanoacetate,[106]

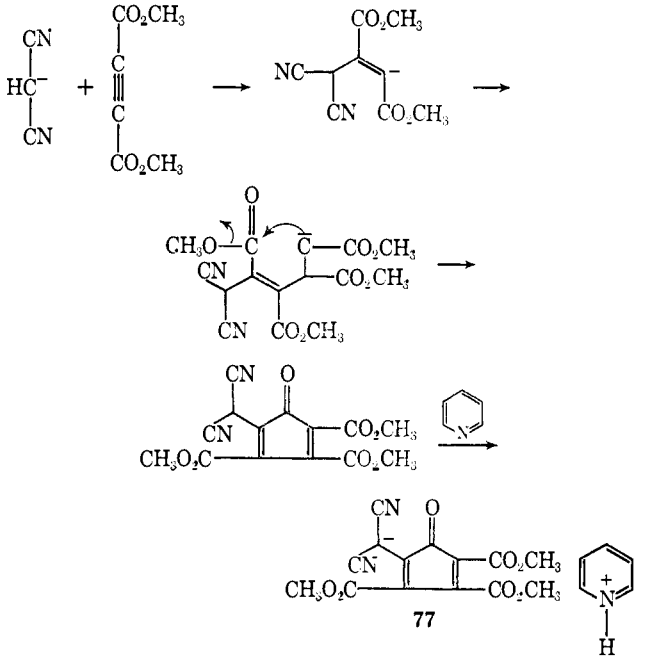


(58)

while sodium trichloroacetate and **2** do not react in refluxing dimethoxymethane.[80]

In the presence of a mixture of pyridine and acetic acid, dimethyl acetylenedicarboxylate condenses with **2** to give the pyridinium salt **77**.[107] A possible mechanism involving the dicyanomethyl anion may be envisaged as shown in Scheme II.

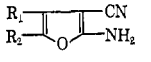
Scheme II



(103) Y. Mizuno, K. Adachi, and K. Ikeda, *Pharm. Bull.* (Tokyo), 2, 225 (1954); *Chem. Abstr.*, 50, 1034 (1956).
(104) O. A. Zagulyaeva and V. P. Mamaev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2087 (1965); *Chem. Abstr.*, 64, 6649 (1966).
(105) R. Schenck, H. Finken, P. Michaelis, and F. Pleuger, *Ann. Chem.*, 462, 158 (1928).
(106) F. Arndt, H. Scholz, and E. Frobel, *ibid.*, 521, 95 (1935).
(107) E. Le Goff and R. B. Le Count, *J. Org. Chem.*, 29, 423 (1964).

Table VII

4,5-Disubstituted 2-Amino-3-cyanofurans[108]

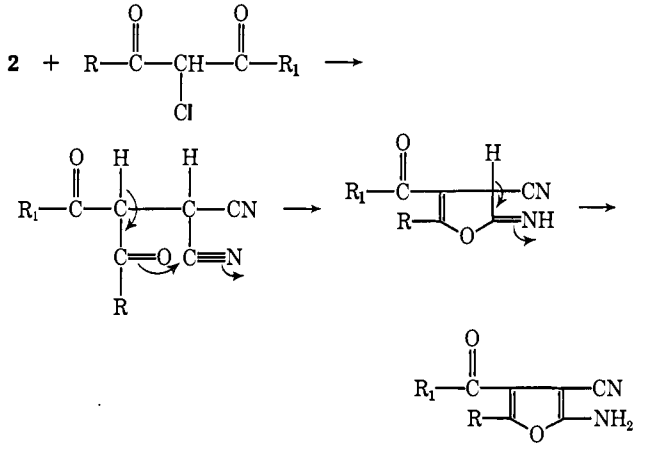


α-Halo ketone	R_1	R_2	Yield, %
α-Chlorodeoxybenzoin	C_6H_5	C_6H_5	73.6
Ethyl α-chloroacetoacetate	$CO_2CH_2CH_3$	CH_3	...
Ethyl α-chlorobenzoylacetate	H	C_6H_5	78.3
Ethyl α-chlorooxaloacetate	$CO_2CH_2CH_3$	$CO_2CH_2CH_3$	43.6
α-Chloro-α-benzoylacetone	$COCH_3$	C_6H_5	...
α-Chlorodibenzoylmethane	COC_6H_5	C_6H_5	71

e. α-Halo Ketones

2 reacts with α-halo ketones to give 4,5-disubstituted 2-amino-3-cyanofurans (Table VII).[108] The mechanism probably proceeds *via* Scheme III.

Scheme III



3. *Miscellaneous Salts*

Calcium dimalononitrile is the product reported from the reaction of **1** and calcium carbide.[109] It has been also reported that **1** forms an addition compound with cyclohexyldimethylamine.[110]

Silver malonitrile was first prepared[67] from an ammoniacal silver nitrate solution of **1**. The high reactivity of the silver salt of **1** is demonstrated in its reactions with ethyl and methyl iodide. A mixture of silver and **1**[79] reacted with ethyl iodide to give diethylmalononitrile, ethyl isocyanide, and an amorphous substance.[79] Similarly, the reaction with methyl iodide gave dimethylmalononitrile, methyl isocyanide, and polymers. Consequently, since the silver salt is more reactive than sodiomalononitrile, **3** is the preferred salt of **1** for chemical reactions.

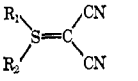
The potassium salt of **1** has been prepared,[65,111] and as expected, its reactivity is comparable with and similar to **2**.

H. YLIDE FORMATION

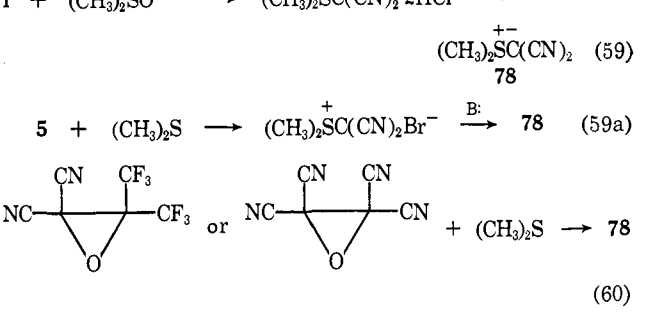
S,S-Disubstituted sulfonium dicyanomethylides (**78**) have been prepared by the condensation of dimethyl sulfoxide with **1** in the presence of hydrogen chloride or thionyl chloride (41%), by dehydrobromination of the dimethyl sulfide bromomalononitrile adduct (20%), and by the reaction of tetracyanoethylene oxide or 2,2-dicyano-3,3-bis(trifluoromethyl)-ethylene oxide with various sulfides (Table VIII).[112] The first two methods are specific for the dimethyl derivative whereas the third is general. However, the third method was unsuccessful with diphenyl sulfide.

Table VIII

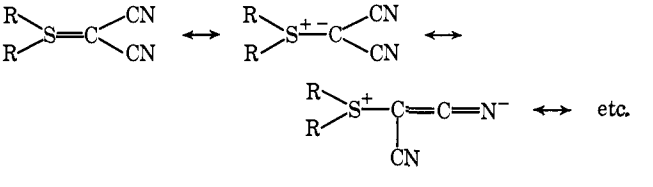
S,S-Disubstituted Dicyanomethylides[113]



R_1	R_2	Dipole moment, D	Yield, %	Mp, °C
CH_3	CH_3		77	100–101
C_2H_5	C_2H_5		74	85–86
C_4H_9	C_4H_9	7.7	62	29–30
$-(CH_2)_4-$			80	94–95
CH_3	$C_{12}H_{25}$		85	46–47
CH_3	C_6H_5		70	77–78
C_2H_5	C_6H_5	7.6	75	75–76
CH_3	$C_{10}H_7$	8.1	74	136–137
C_4H_9	C_6H_5		74	Oil
CH_3	p-$CH_3OC_6H_4$	8.0	67	92–93
CH_3	p-BrC_6H_4	7.0	45	124–125
CH_3	p-$CH_3SC_6H_4$		26	136–137



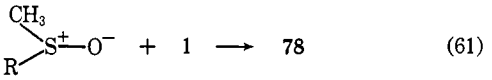
Ylides are frequently unstable intermediates in various elimination and rearrangement reactions. In contrast to other sulfonium ylides, the sulfonium dicyanomethylides are unique in their thermal and chemical stability. This new class of sulfonium ylides can be represented by the following structures.



Stable sulfur ylides have also been prepared[113] from **1** and sulfoxides by reflux in acetic anhydride for 24 hr, or by

(108) T. I. Temnikova and Y. A. Sharanin, *Zh. Org. Khim.*, 2, 2018 (1966); *Chem. Abstr.*, 66, 7061 (1967).
(109) K. Packendorff, *Chem. Ber.*, 64, 948 (1931).
(110) M. Pestemer and D. Lauerer, *Angew. Chem.*, 72, 612 (1960).
(111) A. D. Josey, C. L. Dickinson, K. C. Dewhurst, and B. C. McKusick, *J. Org. Chem.*, 32, 1941 (1967).
(112) W. J. Middleton, E. L. Buhle, I. G. McNally, Jr., and M. Zanger, *ibid.*, 30, 2384 (1965).
(113) H. Nozaki, Z. Morita, and K. Kondo, *Tetrahedron Letters*, 2913 (1966).

interaction with triethylamine and phosphorus pentoxide. This reaction was also unsuccessful with diphenyl sulfide.



$$\xrightarrow{} \mathbf{78} \qquad (61)$$

R = CH_3 (11%)
R = C_6H_5 (15%)

Trimethylammonium dicyanomethylide (**82**) is prepared in 30% over-all yield by the following reactions.[114] The stability of the ylide is probably due to the delocalization of the free electron pair on the carbon atom by the two nitrile groups.

$$(CH_3)_2NCHO + COCl_2 \longrightarrow \underset{\mathbf{79}}{[(CH_3)_2N{=}CHCl]^+Cl^-} \qquad (62)$$

$$\mathbf{79} + HCN \longrightarrow \underset{\mathbf{80}}{(CH_3)_2NCH(CN)_2} \qquad (63)$$

$$\mathbf{80} + p\text{-}CH_3C_6H_4SO_3CH_3 \longrightarrow \underset{\mathbf{81}}{[(CH_3)_3NCH(CN)_2]^+(p\text{-}CH_3C_6H_4SO_3)^-} \qquad (64)$$

$$\mathbf{81} + NaOH \longrightarrow \underset{\mathbf{82}}{(CH_3)_3\overset{+}{N}\overset{-}{C}(CN)_2} \qquad (65)$$

I. HALOGENATION

1 reacts with bromine to give the mono or dibromo derivatives, with chlorine to give dichloromalononitrile (**7**), and with fluorine to give difluoromalononitrile (**8**). The mono and diiodo derivatives have not been reported. An attempt to prepare diiodomalononitrile *via* the reaction of **6** and sodium iodide was unsuccessful.[115]

1 and bromine give **6** which reacts with **1** to give **5**.[116,117] **6** can also be prepared by treating α-aminopropionitrile with bromine in the presence of a base.[118] By using high bromine

$$\mathbf{1} + Br_2 \longrightarrow \underset{\mathbf{5}}{CBr_2(CN)_2} \xrightarrow{1} \underset{\mathbf{6}}{CHBr(CN)_2} \qquad (66)$$

concentrations, in the absence of initially added acid, Pearson and Dillon[119] obtained good first-order kinetics with a rate constant independent of bromine concentration and inversely proportional to hydrogen ion concentration for the bromination of **1**. The data suggest that the rate of combination of the anion with bromine is slower than the rate of recombination of the carbanion with a proton.

1. Reactions of Bromomalononitrile

5 is slightly acidic with a K_a of $<10^{-5}$, and its pmr[19] spectrum shows a singlet at τ 4.95.

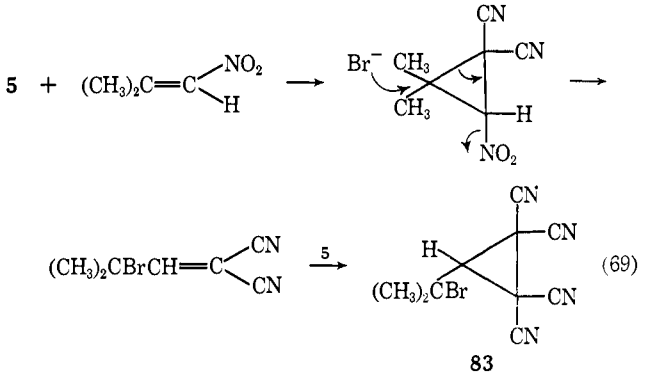
a. Alkenes

5 reacts *via* a free-radical mechanism with terminal olefins to yield primarily 1:1 adducts[120] (eq 67 and 68).

$$CH_3(CH_2)_5CH{=}CH_2 + \mathbf{5} \xrightarrow[\text{benzene}]{Cu} \underset{36\%}{CH_3(CH_2)_5CHBrCH_2CH(CN)_2} \qquad (67)$$

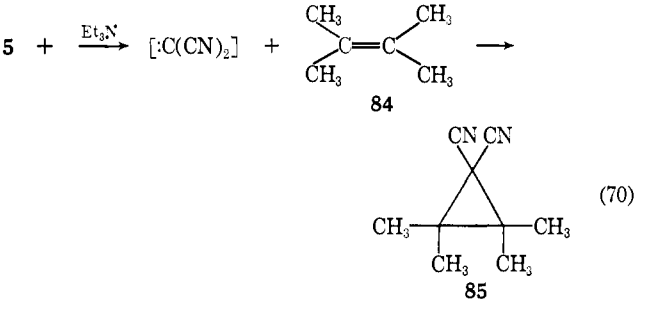
$$C_6H_5CH{=}CH_2 + \mathbf{5} \xrightarrow[CHCl_3]{Cu} \underset{61\%}{C_6H_5BrCH_2CH(CN)_2} \qquad (68)$$

An interesting reaction occurs[18] with 2-methyl-1-nitropropene and **5** in aqueous ethanol to give **83** and an unidentified product of empirical formula $C_7H_8N_4O_3$. A possible mechanism for the formation of **83** is shown in eq 69. **83** was transparent in the ultraviolet and visible, and the pmr spectrum was consistent with the proposed structure.



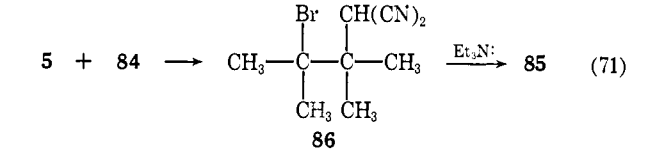
83 (69)

Dicyanocarbene, which can be generated from dicyanodiazomethane,[121] has been postulated[122] as an intermediate in the reaction of **5**, triethylamine, and tetramethylethylene (**84**) which gives 1,1-dicyano-2,2,3,3-tetramethylcyclopropane (**85**). Dicyanocarbene could be formed *via* an α elimination. However, Boldt and Schulz[123] have demonstrated that the formation of **85** does not require the intermediacy of dicyanocarbene since it is also prepared *via* eq 71.



84

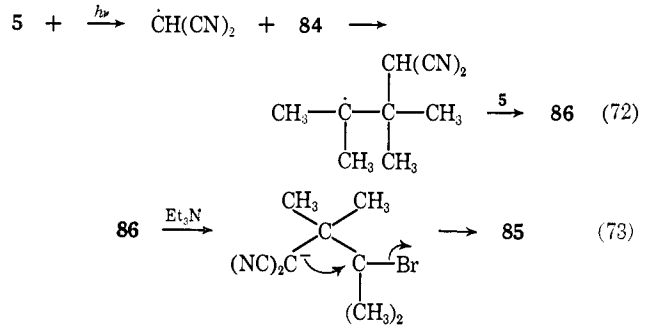
85 (70)



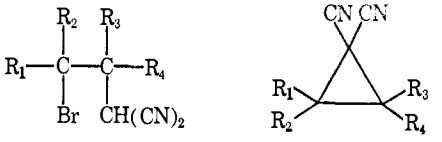
86

The free-radical addition reaction[124] proceeds according to eq 72, and cyclopropanization occurs according to eq 73.

(114) Z. Arnold, *Chem. Ind.* (London), 1478 (1960); *Collect. Czech. Chem. Commun.*, 26, 1113 (1961).
(115) E. Ott and B. Lapman, *Chem. Ber.*, 55, 1255 (1922).
(116) T. Hata, *Bull. Chem. Soc. Jap.*, 37, 547 (1964).
(117) W. Ramberg and S. Wideqvist, *Arkiv Kemi, Mineral. Geol.*, 12A, No. 22 (1937).
(118) E. I. Du Pont de Nemours & Co., British Patent 935,313 (1963); *Chem. Abstr.*, 60, 2794 (1964).
(119) R. G. Pearson and R. L. Dillon, *J. Am. Chem. Soc.*, 75, 2439 (1953).
(120) K. Torssel and E. Ruusa, *Arkiv Kemi*, 23, 479 (1965).
(121) E. Ciganek, *J. Am. Chem. Soc.*, 87, 652 (1965); 88, 1979 (1966).
(122) J. S. Swenson and D. J. Renaud, *ibid.*, 87, 1394 (1965).
(123) P. Boldt and L. Schulz, *Tetrahedron Letters*, 1415 (1966).
(124) P. Boldt, L. Schulz, and J. Etzemuller, *Chem. Ber.*, 100, 1281 (1967).



A number of 3-bromo-1,1-dicyanoalkanes and 1,1-dicyanocyclopropanes have been prepared *via* this route.[124]

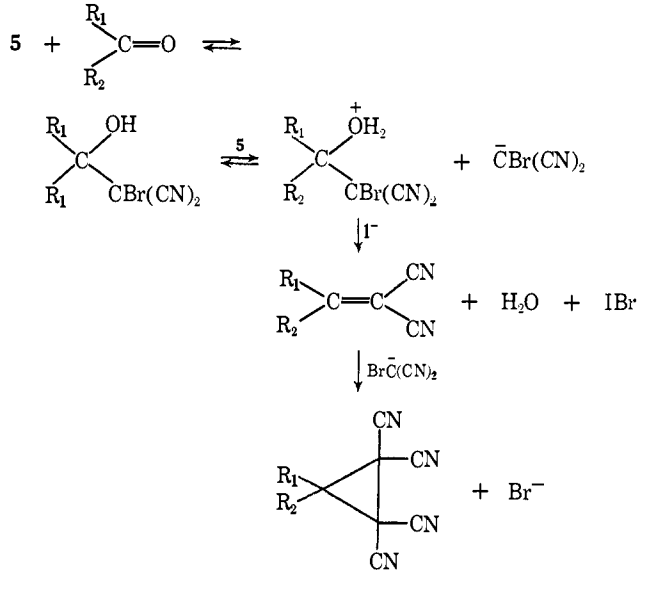


R_1	R_2	R_3	R_4
CH_3	CH_3	CH_3	CH_3
CH_3	CH_3	CH_3	H
CH_3	CH_3	H	H
n-C_4H_9	H	H	H
C_6H_5	H	H	H

b. Carbonyl Compounds

The synthesis of tetracyanocyclopropanes from carbonyl compounds, iodide ion, and **5** is known as the Wideqvist reaction.[2,125–127] The reaction probably involves a series of equilibria such as those shown in Scheme IV.[127] The

Scheme IV

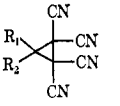


observation that equimolar amounts of isopropylidenemalononitrile and **5** in aqueous ethanol gave a high yield of the tetracyanocyclopropane[128] supports the above mechanism.[129]

(125) S. Wideqvist, *Arkiv Kemi, Mineral. Geol.*, **20B**, No. 4 (1945).
(126) R. M. Scribner, G. N. Sausen, and W. W. Pritchard, *J. Org. Chem.*, **25**, 1440 (1960).
(127) H. Hart and F. Freeman, *ibid.*, 28, 1220, 2063 (1963).
(128) H. Hart and Y. C. Kim, *ibid.*, **31**, 2784 (1966).
(129) R. P. Marlella and A. V. Roth, III, *ibid.*, 22, 1130 (1957).

Table IX

Tetracyanocyclopropanes *via* the Wideqvist Reaction

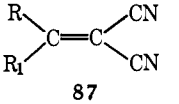


R_1	R_2	*Yield, %*	*Ref*
CH_3	CH_3	70	125
CH_3	CH_3CH_2	68	125
CH_3	$C_6H_5CH_2$	39	125
CH_3	n-C_6H_{13}	30	125
CH_3	C_6H_5	14	125
H	H	68	126
H	CH_3	70	125
H	C_6H_5	80	125
H	Furfuryl	59	125
H	CH_3CH_2	72	127
H	$CH_3CH_2CH_2$	76	127
H	$(CH_3)_2CH$	73	127
H	Cyclopropyl	93	127
H	p-ClC_6H_4	84	127
	$-(CH_2)_3-$	60	127
	$-(CH_2)_4-$	76	127
	$-(CH_2)_5-$	92	125

A summary of preparations of tetracyanocyclopropanes by the Wideqvist reaction is given in Table IX. Spiro systems are obtained from cyclic ketones, and several tetracyanocyclopropanes derived from ketones have been converted to substituted cyclopropanetetracarboxylic acids.[2,127] Methyl α-naphthyl ketone, mesityl oxide, acetol, benzophenone, quinone, and α-hydroxyacetophenone, glycidaldehyde, dicyclopropyl ketone, cyclodecanone, cyclododecanone, and cyclopentadecanone failed to give tetracyanocyclopropanes.[125,127,130]

c. Alkyl- and Arylidenemalononitriles

A new synthesis of tetracyanocyclopropanes has been reported by Hart and Kim.[128] This cyclopropanization procedure, which is similar to the Wideqvist reaction, uses alkyl- and arylidenemalononitriles and **5** in aqueous ethanol at room temperature. Although the reaction is sensitive to steric factors, it generally gives tetracyanocyclopropanes in better yields than the Wideqvist reaction (Table X). It also provides tetracyanocyclopropanes in some cases where the Wideqvist reaction fails. However, the following substituted 1,1-dicyanoethylenes (**87**) did not give tetracyanopropanes on reaction with **5**.[128]



87

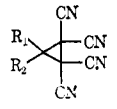
$R = R_1 = C_6H_5$ $R = R_1 = CN$
$R = CH_3$, $R_1 = OC_2H_5$ $R = R_1 =$ ethylenedioxy
$R = H$, $R_1 = OC_2H_5$

Cyclopropanization also occurs[18] when **5** adds to alkyl- and arylidenecyanoacetates to give 3,3-dialkyl- and 3-aryl-2-carbethoxy-1,1,2-tricyanocyclopropanes (**88**) (Table XI).

(130) G. Westoo, *Acta Chem. Scand.*, **13**, 692 (1959).

Table X

New Synthesis of Tetracyanocyclopropanes[128]

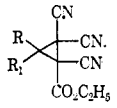


R_1	R_2	Yield, %	R_1	R_2	Yield, %
CH_3[a]	CH_3	86	C_6H_5[c]	CH_3	86.6
CH_3[a]	CH_3CH_2	91	C_6H_5[c]	CH_3CH_2	17.8
CH_3CH_2[a]	CH_3CH_{22}	88.5	2-$C_{10}H_7$[c]	CH_3	54.8
c-C_3H_5[b]	c-C_3H_5	62	n-C_5H_{11}[c]	CH_3	97.5
$-(CH_2)_4CH(CH_3)-$		39.3	$-(CH_2)_{11}-$[b]		94
$-(CH_2)_9-$[b]		34.8	$-(CH_2)_{14}-$[b]		36

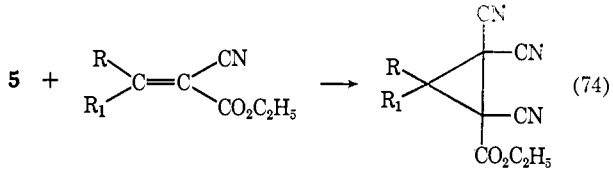
[a] Higher yield than Wideqvist reaction. [b] Not prepared *via* Wideqvist procedure. [c] New compound.

Table XI

3,3-Dialkyl- and 3-Aryl-2-carbethoxy-1,1,2-tricyanocyclopropanes[18]

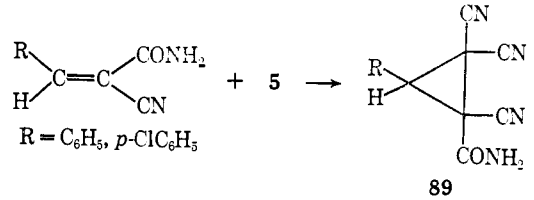


R	R_1	Yield, %	R	R_1	Yield, %
C_2H_5	C_2H_5	35.2	H	C_6H_5	76.7
CH_3	i-C_3H_7	6.5	H	p-$HCOC_6H_4$	36.2
CH_3	n-C_3H_7	37		$-(CH_2)_4-$	14.5
CH_3	C_2H_5	63.7		$-(CH_2)_5-$	97.5
CH_3	CH_3	73.5			

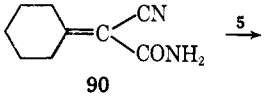


88

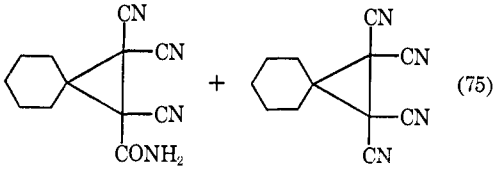
Arylidenecyanoacetamides react[18] with **5** to give 3-aryl-2-carboxamido-1,1,2-tricyanocyclopropanes (**89**). When cyclohexylidenecyanoacetamide (**90**) is allowed to react with **5**, **91** and **92** are formed in 10 and 60% yields, respectively.[18] The



89

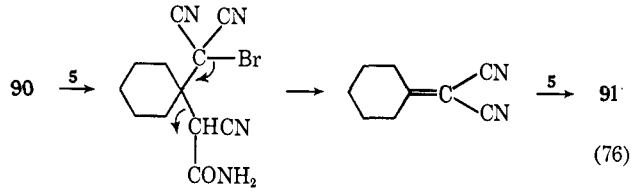


90

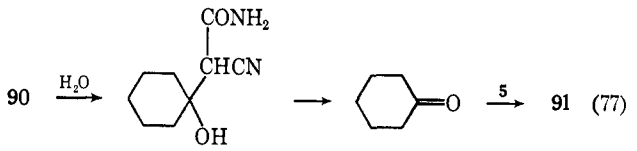


91 92

formation of **92** is surprising, and possible mechanisms are shown in eq 76 and 77. In eq 76, **90** adds **5**, *via* a Michael addition, to give a product which eliminates bromocyano-



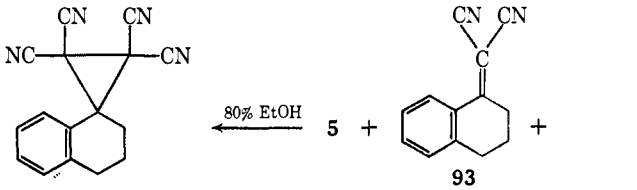
(76)



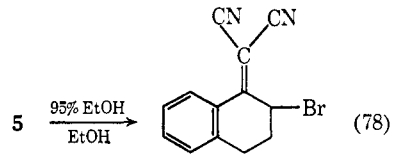
(77)

acetamide to yield cyclohexylidenemalononitrile, which reacts with **5** to give **91**. Alternately, hydrolysis of **90** affords cyclohexanone which reacts with **5** to yield **91**.

The unusual reaction of 2,3-benzocyclohexylidenemalononitrile (**93**) and **5** is noteworthy.[128] In 80% ethanol, cyclopropanization occurs in 54% yield. However, in 95% ethanol at room temperature or in 85% ethanol at reflux, the product, 6-bromo-2,3-benzocyclohexylidenemalononitrile (**94**), is formed in 40–50% yield. A similar bromination occurs with



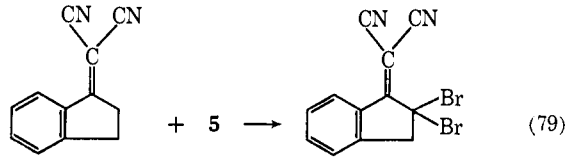
93



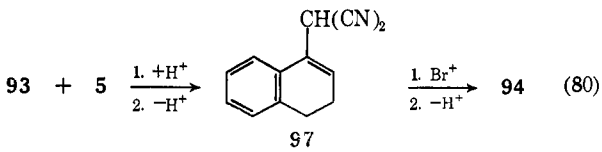
(78)

94

2,3-benzocyclopentylidenemalononitrile (**95**) to give 5,5-dibromo-2,3-benzocyclopentylidenemalononitrile (**96**).[127] A possible mechanism for bromination involves isomerization of **93** by acidic **5** to **97** which is then attacked by a positive bromine to give **94**.



95 96



97

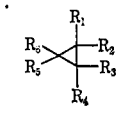
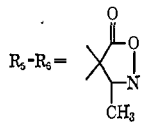
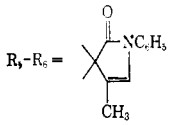
d. α,β-Unsaturated Carbonyl Compounds

5 undergoes a Michael addition with certain α,β-unsaturated carbonyl compounds to give hexasubstituted cyclopropanes[131]

(131) G. Westoo, *Acta Chem. Scand.*, 13, 683 (1959).

Table XII

Hexasubstituted Cyclopropanes from α,β-Unsaturated Carbonyl Compounds[131]

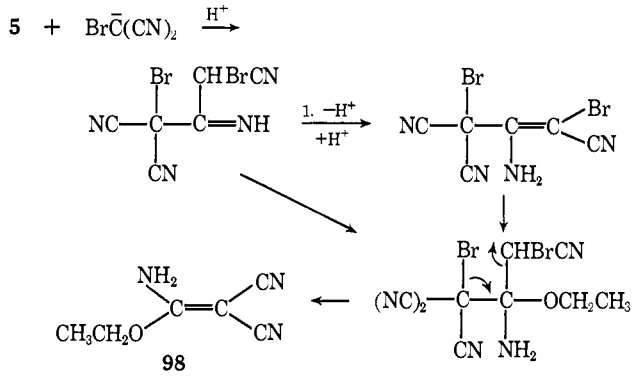
α,β-Unsaturated compound	
Ethyl isopropylidenecyanoacetate	$R_1 = R_2 = CH_3$; $R_3 = R_4 = R_5 = CN$; $R_6 = CO_2C_2H_5$
Ethyl *sec*-butylidenecyanoacetate	$R_2 = CH_3$; $R_2 = C_2H_5$; $R_3 = R_4 = R_5 = CN$; $R_6 = CO_2C_2H_5$
3-Methyl-4-isopropylidene-2-isoxazolin-5-one	$R_1 = R_2 = CH_3$; $R_3 = R_4 = CN$; 
1-Phenyl-3-methyl-4-isopropylidene-2-pyrazolin-5-one	$R_1 = R_2 = CH_3$; $R_3 = R_4 = CN$; 

(Table XII). The nucleophilic dicyanobromomethyl anion attacks the double bond and the resulting carbanion forms a cyclopropane by SN2-type displacement of the bromide ion. Attempts to prepare cyclopropanes with the substituents $R_1 = R_2 = CN$, $R_4 = CN$ or $CO_2C_2H_5$, and $R_5 = R_6 = COCH_3$ were unsuccessful.[131]

e. Ethyl Alcohol

5 reacts[128] with refluxing ethanol to give 1,1-dicyano-2-amino-2-ethoxyethane (**98**). Plausible mechanisms for the formation of **98** are shown in Scheme V.

Scheme V

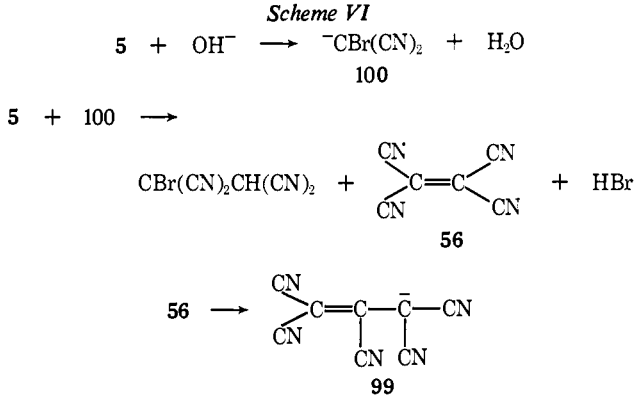


98

f. Bases

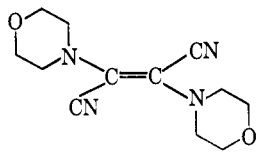
5 reacts[132] with potassium hydroxide, ammonia, triethylamine, and morpholine to give bromomalononitrile anion (**100**) and pentacyanopropenide anion (**99**). 1,1-Dimorpholino-2,2-dicyanoethylene (**102**), and not **101**,[133] is also formed in the reaction with morpholine. These products are explicable in terms of the reaction shown in Scheme VI. The intermediacy of **56** was demonstrated by its color reaction with dimethyl-

Scheme VI

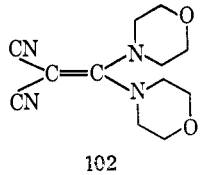


100 **56** **99**

aniline when the reaction mixture of **5** and ammonia was cooled to −80°.[132] Also, it is known[8,9] that **56** reacts with bases to give **99**. Under similar reaction conditions, Hart and



101



102

Kim have noted that **100** does not react with **56** to form hexacyanocyclopropane. However, since triethylamine reacts with **56** to form an anion radical[134] which is converted by oxygen to **99**, it is not possible to ascertain whether **99** is formed from the reaction of two tetracyanoethylene molecules or from condensation of **5** and **56**.[132]

The formation of the bromomalononitrile anion (**100**) in potassium hydroxide solution is noteworthy.[132] The existence of **100** was demonstrated when **5** was recovered unchanged on acidification of the alkaline solution. **100** has been postulated by Hart and Freeman[127] as an intermediate in the synthesis of tetracyanocyclopropanes *via* the Wideqvist reaction.

(132) J. P. Ferris and L. E. Orgel, *J. Org. Chem.*, 30, 2365 (1965).
(133) W. Ruske and E. Ruske, *Chem. Ber.*, **91**, 2496 (1958).
(134) O. W. Webster, W. Mahler, and R. E. Benson, *J. Am. Chem. Soc.*, 84, 3678 (1962).

Table XIII

Monobromo Derivatives from Dibromomalononitrile[116]

Monobromo deriv	*Yield, %*	*Monobromo deriv*	*Yield, %*
$CHBr(CN)_2$	60	$NCCHBrCONHC_6H_5$	79
$CHBr(CONH_2)_2$	75	$NCCHBrCONHCH_2C_6H_5$	79
$NCCHBrCONH_2$	57	$CH_3COCHBrCONHC_6H_5$	92
$NCCHBrCONC_6H_{11}$	59	$CH_3COCHBrCONHCH_2C_6H_5$	78
$CHBr(CO_2C_2H_5)_2$	52	$CH_3COCHBrCOCH_3$	0
$CH_3COCHBrCO_2C_2H_5$	43	$C_6H_5COCHBrCOCH_3$	0
$CHBr(CONHC_6H_5)_2$	85		

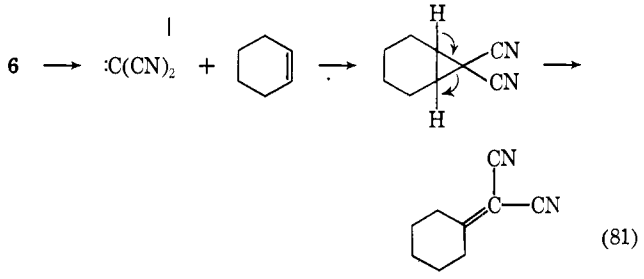
g. Hydrogen Iodide

Hydrogen iodide and **5** react to give **1**, hydrogen bromide, and iodine. This reaction has been used to determine the concentration of **5**.[117]

2. *Reactions of Dibromomalononitrile*

Debromination of the potassium bromide complex of **6** with copper powder in boiling benzene gives tetracyanoethylene (**56**) in 62% yield.[4,135,136] Pyrolysis at 325°, in the presence of copper powder, also gives **56**, in quantitative yield.[137]

When the pyrolysis is carried out in the presence of cyclohexene, the product is cyclohexylidenemalonitrile.[4] It was suggested that the pyrolysis proceeded through dicyanocarbene to give 7,7-dicyanobicyclo[4.1.0]heptane as the initial product which rearranged to cyclohexylidenemalononitrile. However, the alternate free-radical mechanism is greatly favored as a result of the studies on the free-radical-catalyzed addition of **6** to alkenes[138] (*vide infra*).

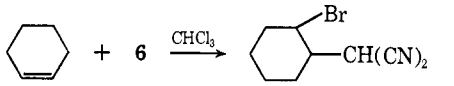


(81)

6 reacts with 1-alkenes to give 1:1 and 1:2 adducts.[119,138,139] The reaction proceeds *via* a free-radical mechanism and is catalyzed by free-radical initiators and some metal halides.[138] For example, the yields of 1-hexene adduct with copper and azonitrile initiator are 92 and 97.5%, respectively.[138] The reaction does not proceed in the absence of initiators. Since cyclohexylidenemalononitrile is probably formed in an initial radical chain addition of **6** to the double bond, it is likely that dicyanocarbene is not an intermediate in the pyrolytic reaction (eq 81).

6, with a catalytic amount of boron fluoride, is a selective monobrominating reagent for active methylene compounds (Table XIII).[116] **6** can be used to brominate the benzene ring[117] with such reactive compounds as aniline, phenol, and anthracene.[140]

$$CH_3(CH_2)_5CH{=}CH_2 + 6 \xrightarrow[\text{benzene}]{Cu} CH_3(CH_2)_5CHBrCH_2C(CN)_2CHBrR \quad (82)$$
$$R = n\text{-}C_6H_{13}$$



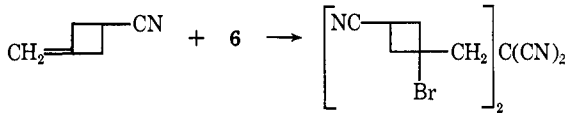
(83)

22%

$$CH_2{=}CH_2 + 6 \xrightarrow{150^\circ} (BrCH_2CH_2)_2C(CN)_2 \quad (84)$$
71%

$$CH_3(CH_2)_3CH{=}CH_2 + 6 \longrightarrow \text{1:2 adduct (isomers)} \quad (85)$$
38%

$$C_6H_5CH{=}CH_2 + 6 \longrightarrow (C_6H_5CHBrCH_2)_2C(CN)_2 \quad (86)$$



(87)

56%

$$2CH_2(CONH_2) + 6 \xrightarrow{BF_3} 2CHBr(CONH_2) + \mathbf{1} \quad (88)$$

$$C_6H_5N(CH_3)_2 + 6 \longrightarrow p\text{-}BrC_6H_4N(CN_3)_2 \quad (89)$$

6 reacts vigorously with iron pentacarbonyl[141] in inert solvents to give a complicated mixture of unresolved products, and in ethanol and methanol to give low yields of the ferrous salts of ethyl dicyanoacetate, $Fe[OC(OC_2H_5){=}C(CN)_2]_2$ and $Fe[OC(OCH_3){=}C(CN)_2]_2$.

Treatment of **6** with cold dilute sodium carbonate gives dibromocyanoacetamide,[142] which is a by-product in the bromination of **1**. **6** reacts with 2 moles of sodium azide to give $C(N_3)_2(CN)_2$ and with 3 moles to yield the bimolecular cyanazide C_2N_8 or sodioazidomalononitrile.[143]

6 reacts with alkali and alkaline earth salts to give complexes consisting of four molecules of **6** and one molecule of salt. Products were obtained with NaCl, NaI, NaBr, $NaClO_3$, KI, and KBr.[143] No complex was formed with $MgBr_2$ and $CuBr_2$.[117] Treatment of **6** or its potassium bromide complex with 2 moles of potassium cyanide gives potassium tricyanomethanide in excellent yields.[135]

Interaction of **6** with excess anhydrous hydrazine in tetra-

(135) R. A. Carboni, *Org. Syn.*, 39, 64 (1959).
(136) R. E. Heckert and E. L. Little, Jr., U. S. Patent 2,794,824 (1957); *Chem. Abstr.*, 51, 16515 (1957).
(137) E. L. Martin, U. S. Patent 3,076,836 (1963); *Chem. Abstr.*, 58, 13802 (1963).
(138) J. R. Roland, E. L. Little, Jr., and H. E. Winberg, *J. Org. Chem.*, 28, 2809 (1963).
(139) K. Torssell and K. Dahlquist, *Acta Chem. Scand.*, 16, 346 (1962).
(140) K. Torssell, *Arkiv Kemi*, 23, 537 (1965).
(141) E. Coffey, *J. Am. Chem. Soc.*, 83, 1623 (1961).
(142) E. Ott and H. Finken, *Chem. Ber.*, 58, 1703 (1925).
(143) E. Ott and H. Weissenburger, *ibid.*, 70, 1829 (1937).

hydrofuran, at −70°, gives carbonyl cyanide hydrazone (**103**) in 35–40% yield.[144] Oxidation of **103** with lead tetracetate gives the highly electrophilic diazoalkane dicyanodiazomethane (**104**), in nearly quantitative yield.

$$6 + 3NH_2NH_2 \rightarrow \underset{\mathbf{103}}{(NC)_2C{=}NNH_2} + \mathbf{1} + 2\dot{N}H_2NH_3Br^- \quad (90)$$

$$\mathbf{103} + Pb(OAc)_4 \xrightarrow{CH_3CN} \underset{\mathbf{104}}{(NC)_2C{=}N_2} \quad (91)$$

Formation of **103** from **6** and hydrazine is surprising in view of the highly positive character of the bromine atoms. Methylhydrazine does not give carbonyl cyanide N-methylhydrazone, but methyl hydrazinecarboxylate gives carbonyl cyanide N-methoxy-carbonylhydrazone in 13% yield.[144]

3. *Reactions of Dichloromalononitrile*

The reaction of **1** with aqueous chlorine[115,145] or aqueous sodium hypochlorite[146] gives dichloromalononitrile (**7**) in good yield. The rate of substitution of chlorine for the first hydrogen depends on the rate of proton dissociation from **1**

$$\mathbf{1} \xrightarrow[H_2O]{Cl_2} \underset{\mathbf{7}}{CCl_2(CN)_2} + C_3N_2Cl_4 + NH_4Cl \quad (92)$$

74% 8.5% 13%

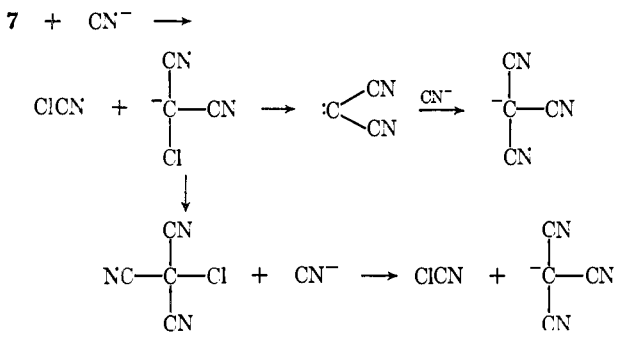
and the second chlorine enters more rapidly than the first owing to electronegativity effects.[119,147] The infrared spectrum of **7** shows cyano group absorption at 4.45 μ.[67]

Dichloroacetamide is also prepared from chlorine and **1** under basic conditions.[148]

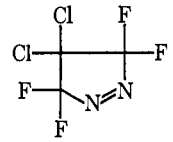
Salts of tricyanomethane have been prepared[149] from **5** and potassium cyanide, from **2** and cyanogen halides, and from **6** and potassium cyanide. The latter method gives the best yields and purest product.[150] If **7** is used in place of **6**, the reaction still proceeds in good yields.[150]

A probable mechanism for tricyanomethanide ion formation from **7** is shown in Scheme VII.[150] The reaction probably proceeds *via* the dicyanocarbene or the tricyanohalomethane since the central carbon atom in **7** is quite sterically hindered so that an SN2 mechanism is unlikely.

Scheme VII



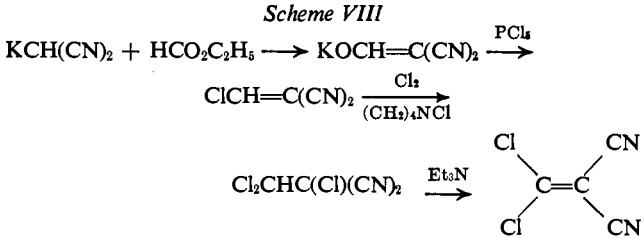
Argentic fluoride reacts with **7** to give 4,4-dichloro-3,3,5,5-tetrafluoro-1-pyrazoline (**105**) in addition to the cleavage and rearrangement products CF_4, C_2F_6, CF_3CN, CF_3NF, $CCIF_3$, and CCl_2F_2.[151]



105

The first monoperfluoroalkyl derivative of **1**, trifluoromethylmalononitrile (**106**), was reported[111] in 1967. **106** was prepared in 67% yield by the reaction of argentous fluoride with 1,1-dichloro-2,2-dicyanoethylene. The intermediate was demonstrated to be 1,1-difluoro-2,2-dicyanoethylene (**107**), which, due to the electrophilicity of the double bond, adds argentous fluoride to give the silver salt of **106**. **106** is a stable, strong acid and is hydrolyzed to 3,3,3-trifluoropropionic acid with hydrochloric acid.[111] Its precursor, 1,1-dichloro-2,2-dicyanoethylene, is conveniently prepared according to Scheme VIII.[111]

Scheme VIII

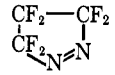


7 is hydrolyzed to dichlorocyanoacetamide by cold dilute sodium carbonate solution.[152]

4. *Reactions of Difluoromalononitrile*

Difluoromalononitrile (**8**) is prepared from **1** with perchloryl fluoride (ClO_3F) and sodium alkoxides[153] or by the dehydration of difluoromalonamide.[154] **8** shows an infrared spectrum absorption at 4.43 μ (–CN) and a ^{19}F resonance at τ 4.53 relative to CF_3COOH.[154]

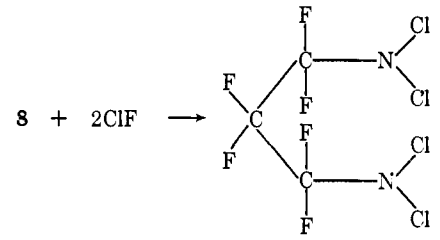
8 is readily hydrolyzed to the corresponding acid.[154] It undergoes cyclizations with argentic fluoride under autogenous pressure to give hexafluoro-1-pyrazoline (**108**) (15%), CF_4, C_2F_6, and $(CF_3)_2NF$.[154] With chlorine monofluoride, **8** gives **109**.[155] The reaction probably proceeds *via* the imine RCF=NCl which adds a second mole of chlorine monofluoride to give **109**. In an alternate mechanism, chlorine



108

(144) E. Ciganek, *J. Org. Chem.*, 30, 4198 (1965).
(145) W. R. Carpenter and P. Armstrong, *ibid.*, 29, 2772 (1964).
(146) D. H. Rosenblatt and G. H. Broome, *ibid.*, 26, 2116 (1961).
(147) R. G. Pearson and J. M. Mills, *J. Am. Chem. Soc.*, 72, 1692 (1950).
(148) D. H. Rosenblatt and G. H. Broome, U. S. Patent 3,092,661 (1963); *Chem. Abstr.*, 59, 12648 (1963).
(149) E. Cox and A. Fontaine, *Bull. Soc. Chim. Fr.*, 948 (1954).
(150) S. Trofimenko, E. L. Little, Jr., and H. F. Mower, *J. Org. Chem.*, 27, 433 (1962).
(151) J. B. Hynes, B. C. Bishop, and L. A. Bigelow, *ibid.*, 28, 2811 (1963).
(152) G. J. Östling, *Ofversicht Finska Vetenskaps Soc. Forhändl.*, 57A, No. 11, 13 (1915); *Chem. Abstr.*, 15, 2829 (1921).
(153) Pennsalt Chemicals Corp., British Patent 865,321 (1961); *Chem. Abstr.*, 56, 332 (1962).
(154) B. C. Bishop, J. B. Hynes, and L. A. Bigelow, *J. Am. Chem. Soc.*, 85, 1606 (1963).
(155) J. B. Hynes and T. E. Austin, *Inorg. Chem.*, 5, 488 (1966).

monofluoride could fluorinate the nitrile carbon of **8** and



(93)

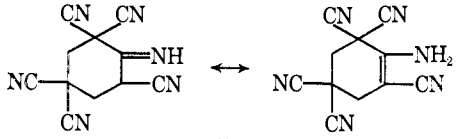
109

yield a nitrene intermediate. However, this pathway was excluded[155] since no azo compounds of the type $RCF_2N{=}NCF_2R$ were formed during the reaction.

J. CARBONYL CONDENSATION REACTIONS

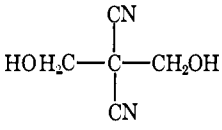
1. Alkylidene Bismalononitriles

The reaction of **1** with formaldehyde is unique and may give one of the following products depending on the reaction conditions: 2,2-dicyano-1,3-propanediol,[156] 1,1,3,3-tetracyanopropane,[157] 2,2,4,4-tetracyano-1,5-pentanediol,[158] 2,2,4,-



110

(94)



111

4,6-pentacyanocyclohexanonimine (**110**),[159] or dimethylol malononitrile (**111**).[160]

Acetaldehyde and **1** have been reported to give 1,1,3,3-tetracyano-2,4-dimethylcyclobutane[161] or 1,1,3,3-tetracyano-2-methylpropane.[137] Alkylidene bismalononitriles from several aliphatic aldehydes are shown in Table XIV.

Hart and Freeman[162] have shown, via pmr, that ethylidene and propylidene bismalononitriles undergo a facile reverse Michael equilibrium at room temperature. With methylene bismalononitrile the equilibrium apparently lies entirely to the left.[159]

$$RCH[CH(CN)_2]_2 \rightleftharpoons RCH{=}C(CN)_2 + \mathbf{1} \qquad (95)$$

$R = CH_3, CH_3CH_2$

Alkylidene bismalononitriles react with bromine to give tetracyanocyclopropanes which are hydrolyzed to substituted

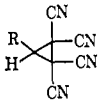
Table XIV

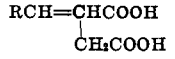
Alkylidene Bismalononitriles, $RCH[CH(CN)_2]_2$

R	*Yield, %*	*Ref*
H		157
CH_3	70	129
CH_3CH_2	80	129
$CH_3CH_2CH_2$	80	129

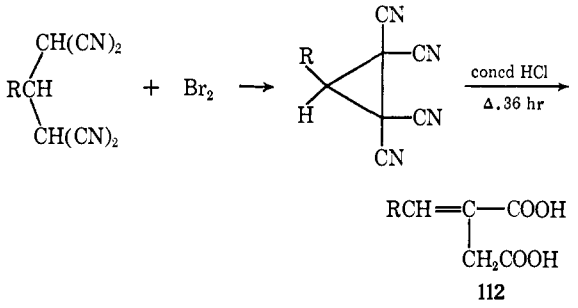
Table XV

Tetracyanocyclopropanes and Itaconic Acids from Alkylidene Bismalononitriles[129]





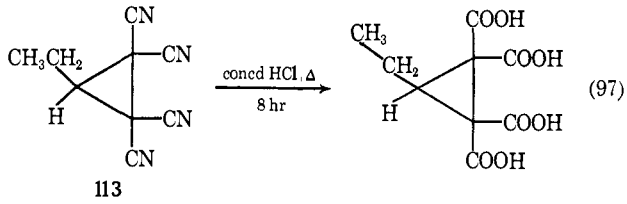
R	*Yield, %*	*Yield, %*
H[126,163]	28	..
CH_3	60	20
CH_3CH_2	90	35
$CH_3CH_2CH_2$	80	40



(96)

112

itaconic acids (**112**)[129] (Table XV[126,163]). The authors also reported the synthesis of 3-ethylcyclopropane-1,1,2,2-tetracarboxylic acid in 25% yield from the acid hydrolysis of **113**. This is surprising since the cyclopropane ring is very unstable in acid media and ring rupture generally occurs in strong acid.



(97)

113

2. Aryl- and Alkylidenemalononitriles

Aryl- and alkylidenemalononitriles are readily available by the reaction of aldehydes and ketones with **1** (Table XVI). The preferred procedures are modifications of the methods of Cope and Hoyle,[164] Mowry,[165] Schenck and Finken,[65] and Corson and Stoughton.[166]

(156) H. Gilbert, U. S. Patent 2,541,350 (1951); *Chem. Abstr.*, 45, 5716 (1951).
(157) O. Diels and B. Conn, *Chem. Ber.*, 56, 2076 (1923).
(158) H. Gilbert, U. S. Patent 2,541,351 (1951); *Chem. Abstr.*, 45, 5716 (1951).
(159) J. C. Westfahl and T. L. Gresham, *J. Org. Chem.*, 21, 319 (1956).
(160) A. E. Ardis, S. J. Averill, H. Gilbert, F. F. Miller, R. F. Schmidt, F. D. Stewart, and H. L. Trumbull, *J. Am. Chem. Soc.*, 72, 1305 (1950).
(161) O. Diels, H. Gartner, and R. Kaack, *Chem. Ber.*, 55, 3445 (1922).
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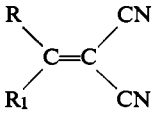
(163) F. I. Mikhailos and L. I. Bogomolova, USSR Patent 168,287 (1965); *Chem. Abstr.*, 62, 14508 (1965).
(164) A. C. Cope and K. E. Hoyle, *J. Am. Chem. Soc.*, 63, 733 (1941).
(165) D. T. Mowry, *ibid.*, 67, 1050 (1945).
(166) B. B. Corson and R. W. Stoughton, *ibid.*, 50, 2825 (1928).

Table XVI

Aryl- and Alkylidenemalononitriles



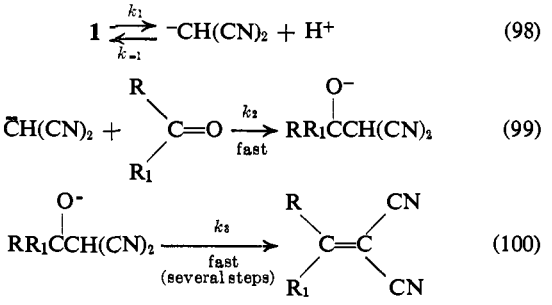
R_1	R_2	Yield, %	Ref	R_1	R_2	Yield, %	Ref
H	C_6H_5CHMe	75	167	H	2,3-$Cl_2C_6H_3$	...	168
H	*p*-$(Me)_2NC_6H_4$	...	168	H	3,4-$(MeO)_2C_6H_3$	100	168, 171
H	*p*-MeC_6H_4	85	167, 168	H	*m*-HOC_6H_4	59	168, 171
H	*p*-FC_6H_4	79	165	H	*p*-HOC_6H_4	77	168, 171
H	*p*-*t*-BuC_6H_4	67	165	H	*p*-NCC_6H_4	...	171
H	*p*-*i*-PrC_6H_4	63	165	H	5-O_2N-2-thenyl	93	172
H	*p*-EtC_6H_4	60	165	H	C_6H_5	90	166
H	2,5,$Me_2C_6H_3$	60	165	H	2-Thenyl	97	173, 174
H	*p*-$EtOC_6H_4$	78	165	H	*p*-$O_2NC_6H_4$	80	165
H	*m*-EtC_6H_4	61	165	H	*n*-C_5H_{11}	61	165
H	3,5-$Et_2C_6H_3$	60	165	H	α-Naphthyl	90	175
H	*p*-ClC_6H_4	80	165, 169	H	*p*-$(Me)_2NC_6H_4CHCH$	...	176
H	Xenyl	74	165	H	*p*-$O_2NC_6H_4CHCH$	...	176
H	*m*-$MeOC_6H_4$	90	166	H	*p*-$O_2NC_6H_4CH_2CHCH$	...	176
H	*p*-$MeOC_6H_4$	93	166, 168	H	*m*-ClC_6H_4	85	169
H	3,4-$(OCH_2O)C_6H_3$	96	166	H	*o*-BrC_6H_4	95	169
H	*o*-ClC_6H_4	85	166	H	*m*-BrC_6H_4	81	169
H	3-MeO-4-HOC_6H_3	85	166	H	*m*-IC_6H_4	85	169
H	2-Furyl	100	166, 170	H	*m*-IC_6H_4	85	169
H	*p*-$(Me)_2N$-*m*-BrC_6H_3	...	169	H	*o*-MeC_6H_4	51	169
H	*m*-$O_2NC_6H_4$	90	166, 169	H	2,4,6-Cl_3-3-HOC_6H	70	169
H	3,4,5-Tri-HOC_6H_2	100	167	H	*m*-MeC_6H_4	38	169
H	3,4-Di-HOC_6H_3	...	167	H	2,6-$Cl_2C_6H_3$	56	169
H	2,5-$(MeO)_2C_6H_3$	...	177	H	*p*-(2-ClEtS)C_6H_4	...	169
H	*o*-$H_2NC_6H_4$	...	168	H	*o*-HOC_6H_4	...	185
H	*p*-$MeCONHC_6H_4$	...	168	H	5-O_2N-2-furyl	53	186
H	*p*-$MeCOC_6H_4$	...	168	Me	*p*-$O_2NC_6H_4$	80	180
Me	Me	...	178	Me	α-Naphthyl	40	175
Me	Et	...	152	*i*-Pr	C_6H_5	93	181
Me	*n*-Pr	76	164	*n*-Pr	C_6H_5	70	165
Me	*t*-Bu	81.7	178	Et	*p*-$MeOC_6CHEt$	70	175
Me	C_6H_5	61	60, 179	Et	Et	85	56, 152
Me	*p*-$MeOC_6H_4$	80	180	C_6H_5	C_6H_5	68	181
Me	$C_6H_5CH_2$	78	175	C_6H_5	*p*-$MeOC_6H_4$	80	180
Me	$C_6H_5C(Me)_2$	...	175	C_6H_5	*p*-$O_2NC_6H_4$	80	180
t-Bu	C_6H_5	88	181	Et	C_6H_5	65	181
CF_3	CF_3	...	182	$C_6H_5CH_2$	$C_6H_5CH_2$	...	186
H_2N	CCl_3	...	182		$-(CH_2)_5-$	19.3	164, 178
H_2N	$CHCl_2$	...	183	α-Tetralyl		81	165, 181
H_2N	$MeCCl_2$	...	183	Anthronyl		88	187
Cinchoninaldehyde		98	184	2-Phenylcyclohexyl		74	175
1-Methyl-4-piperidone		98	72	Fluorenyl		87	10
Me	*n*-Amyl	60.9	128	Indanonyl		...	63
Et	*n*-Bu	78.3	128		$-CH(Me)CH_2CH_2CH(Me)-$	64.5	128
i-Pr	*i*-Pr	41.5	128		$-(CH_2)_4CH(Me)-$	71.6	128
i-Bu	*i*-Bu	55.7	128	H	*o*-$H_2NC_6H_4$	30	9
c-C_3H_5	*c*-C_3H_5	17.7	128	H	*p*-$(C_6H_5CH_2)_2NC_6H_4$	86	9
$-(CH_2)_4-$		22.1	128	H	*p*-$(NCCH_2CH_2$, -Et)NC_6H_4	79	9
$-(CH_2)_5-$		74.8	128	H	*p*-$H_2NC_6H_4$	78	9
$-(CH_2)_9-$		89.2	128	H	*p*-$AcHNC_6H_4$	67	9
$-(CH_2)_{11}-$		...	128	H	4-Et_2N-2-ClC_6H_3	89	9
$-(CH_2)_{14}-$		...	128				

Space limitation requires Table XVI to be general rather than exhaustive. However, the four most useful and general procedures are represented.[65,164–166] More esoteric aryl- and alkylidenemalononitriles, *e.g.*, heterocyclic, methine dye intermediates, bicyclic, etc., are included in references 10, 56, 73, 129, 168, and 188–199.

a. Kinetics and Mechanisms of Arylidenemalononitrile Formation

The kinetics of the reaction of **1** and aromatic aldehydes in water were measured spectrophotometrically.[200] The reactions were first order in **1** and zero in aldehyde (k_1, very slow) with a ρ of 0.55. The activation energies for benz-

aldehyde, *p*-methoxy-, and *p*-nitrobenzaldehydes were 7.2, 9.6, and 5.4 kcal/mole, respectively. The rate-determining step



(98)

(99)

(100)

is ionization of the carbon–hydrogen bond in **1**. Rates were retarded by hydrogen chloride and enhanced by lithium chloride and ethanol which is characteristic of a unimolecular reaction.

The kinetics were also studied in 95% ethanol.[201] The reaction is second order (eq 98 fast and eq 99 slow), reversible, catalyzed by bases, inhibited by acids, accelerated by salts, and has a ρ of +1.45. The activation energies for benzaldehyde and *p*-nitro-, *p*-chloro-, *p*-methoxy-, and *p*-hydroxybenzaldehyde were 6.4, 4.8, 6.1, 7.55, and 7.8 kcal/mole, respectively.

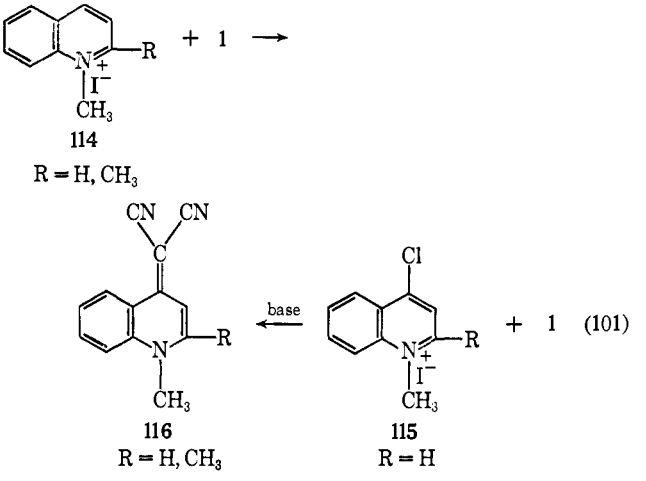
The kinetics of the reverse reaction, hydrolysis of arylidenemalononitriles to **1** and aldehydes, have also been studied.[202]

b. Aryl- and Alkylidenemalononitriles from Imines

Table XVII contains a number of aryl- and alkylidenemalononitriles prepared from ketimines.[203] The diarylketimines are generally more reactive than the corresponding ketones, and the hydrochloride and oxalate salts of diphenylketimine give benzophenone rather than benzhydrylidenemalononitrile.

c. Arylidenemalononitriles from Quinolinium Compounds

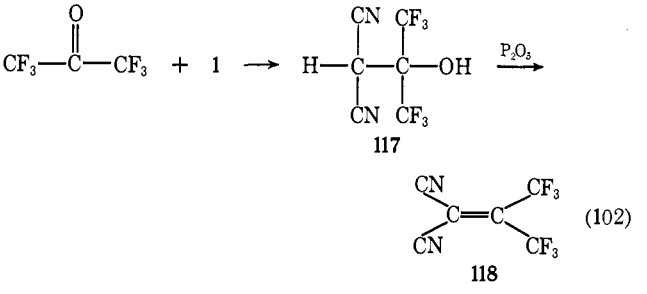
Sodium ethoxide and **1** react with 1-methylquinolinium iodide (**114**) or 1-methyl-4-chloroquinolinium iodide (**115**) and 1,2-dimethylquinolinium iodide to give 1-methyl-4-(α,α-dicyanomethylene)-1,4-dihydroquinoline (10%) and 1,2-dimethyl-4-(α,α-dicyanomethylene)-1,4-dihydroquinoline (**116**) (34%).[204] The reaction with **114** proceeds *via* condensation and dehydrogenation, whereas the reaction with **115** involves another example of a displacement by the dicyanomethyl anion.



(101)

d. Exceptional Cases

Perfluoro Carbonyl Compounds. **1** reacts with hexafluoroacetone in the presence of zinc chloride to yield the unstable alcohol **117** which can be dehydrated to 1,1-dicyano-2,2-bis(trifluoromethyl)ethylene (**118**).[182] Hexafluorocyclobutanone gives dicyanomethylenehexafluorocyclobutane (**119**) *via* the same procedure. **118** is of special interest because it is



(102)

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(168) L. Horner and K. Kluppel, *ibid.*, 591, 69 (1955).
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(170) T. Boehm and M. Grohnwald, *Arch. Pharm.*, 274, 318 (1936).
(171) H. Kauffmann, *Chem. Ber.*, 52, 1422 (1919).
(172) T. M. Patrick, Jr., and W. S. Emerson, *J., Am. Chem. Soc.*, 74, 1356 (1952).
(173) W. S. Emerson and T. M. Patrick, Jr., *J. Org. Chem.*, 14, 790 (1949).
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(185) W. Baker and C. S. Howes, *J. Chem. Soc.*, 119 (1953).
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(190) H. D. Edwards, F. P. Doyle, and S. J. Palling, U. S. Patent 2,721,799 (1955); *Chem. Abstr.*, 50, 1505 (1956).
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(192) D. J. Fry and B. A. Lea, British Patent 728,078 (1955); U. S. Patent 2,715,623 (1955); *Chem. Abstr.*, 50, 715 (1956).
(193) E. M. Gal, F.-H. Fung, and D. M. Greenberg, *Cancer Res.*, 12, 565 (1952); 13, 226 (1953).
(194) B. F. Goodrich Co., British Patent 795,107 (1958); *Chem. Abstr.*, 53, 1258 (1959).
(195) S. D. Gupte and S. V. Sunthankar, *J. Org. Chem.*, 24, 1334 (1959).
(196) M. W. Krell and F. E. Johnson, U. S. Patent 2,798,090 (1957); *Chem. Abstr.*, 52, 1230 (1958).
(197) W. J. Middleton, U. S. Patent 2,726,249 (1955); *Chem. Abstr.*, 50, 10775 (1956).
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(200) S. Patai and Y. Israeli, *J. Chem. Soc.*, 2020 (1960).
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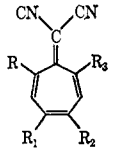
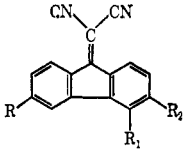
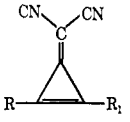
Table XVII

Aryl- and Alkylidenemalononitriles from Ketimines[203]

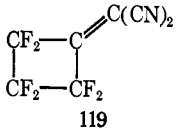
Ketimine	*Aryl- and Alkylidenemalononitrile*	*Yield, %*
p-$MeOC_6H_4CH{=}NBu$	*p*-$MeOC_6H_4CH{=}C(CN)_2$	96.3
$C_6H_5CH(N{=}CHC_6H_5)_2$	$C_6H_5CH{=}C(CN)_2$	82.5
$C_4H_3OCH(N{=}CH{-}C_4H_3O)_2$	$C_4H_3OCH{=}C(CN)_2$	...
$(C_6H_5)_2C{=}NH$	$(C_6H_5)_2C{=}C(CN)_2$	100
9-Iminofluorene	9-Fluorenylidenemalononitrile	100
$CH_3CH_2(C_6H_5)C{=}NBu$	$CH_3CH_2(C_6H_5)C{=}C(CN)_2$	45
$C_6H_5(Me_3C)C{=}NBu$	$C_6H_5(Me_3C)C{=}C(CN)_2$	53
$C_6H_5(p\text{-}MeC_6H_4)C{=}NH$	$C_6H_5(p\text{-}MeC_6H_4)C{=}C(CN)_2$	100
$(p\text{-}Me_2NC_6H_4)_2C{=}NH$	$(p\text{-}Me_2NC_6H_4)_2C{=}C(CN)_2$	100
$(C_6H_5)_2C{=}CHC(=NH)C_6H_5$	$(C_6H_5)_2C{=}CHC(C_6H_5){=}C(CN)_2$	100
$C_6H_5(m\text{-}ClC_6H_4)C{=}NH$	$C_6H_5(m\text{-}ClC_6H_4)C{=}C(CN)_2$	90
$(p\text{-}MeOC_6H_4)_2C{=}NC_6H_5$	$(p\text{-}MeOC_6H_4)_2C{=}C(CN)_2$	100
$(C_6H_5)_2C{=}NCH_2CH_2OH$	$(C_6H_5)_2C{=}C(CN)_2$	73
$(C_6H_5)_2C{=}NC_6H_5$	$(C_6H_5)_2C{=}C(CN)_2$	...
$(CH_3CH_2)C_6H_5C{=}NH$	$(CH_3CH_2)C_6H_5C{=}C(CN)_2$	65

Table XVIII

Preparation of Certain Fulvenes

Fulvene		*Ref*
	R = R_1 = R_2 = R_3 = H	206, 209, 210
	R = R_1 = OH; R_2 = R_3 = H	211
	R = R_1 = OH; R_2 = H; R_3 = *i*-C_2H_7	212
	R = R_1 = OH; R_3 = H; R_2 = *i*-C_3H_7	212
	R = R_1 = R_2 = H	213
	R = R_2 = NO_2; R_1 = H	214
	R = R_1 = R_3 = NO_2	215
	R = R_1 = C_6H_5	208
	R = R_1 = *n*-C_3H_7	216

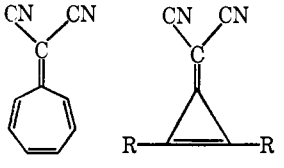
electron deficient owing to the four electronegative groups and is highly polarizable since the geminal cyano groups could stabilize a negative charge at only one end of the π bond in a transition state involving charge separation.[182]



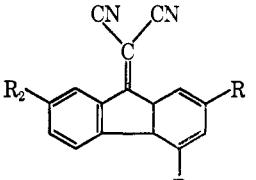
119

Fulvenes. Theoretical interests concerning the double-bond character and aromaticity of fulvene ring systems have attracted the attention of physical chemists as well as organic chemists.[205] **1** reacts with tropylium systems[206] to give heptafulvenes, (**120**), with the cyclopropenium[207,208] systems to give triafulvenes (**121**), and with the fluorenylidene systems to give substituted fulvenes (**122**) (Table XVIII[206,208,209–216]).

120 is also prepared from **1** and tropylium bromide (Scheme IX),[206] or **1** and ethoxytropylium fluoroborate (**123**).[209]



120 121



122a, R = R_1 = R_2 = H
b, R = R_1 = R_2 = NO_2
c, R = H; R = R_2 = NO_2

(205) E. D. Bergmann, *Chem. Rev.*, 68, 41 (1968).
(206) T. Nozoe, T. Mukai, K. Osaka, and N. Shishido, *Bull. Chem. Soc. Jap.*, **34**, 1384 (1961).
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(209) K. Hafner, H. W. Riedel, and M. Danielisz, *Angew. Chem. Intern. Ed. Engl.*, 2, 215 (1963).
(210) Y. Kitahara and K. Doi, Japanese Patent 13,071 (1962); *Chem. Abstr.*, **59**, 9914 (1963).
(211) Y. Katahara, K. Doi, and T. Kado, *Bull. Soc. Chem. Jap.*, **37**, 1747 (1964).
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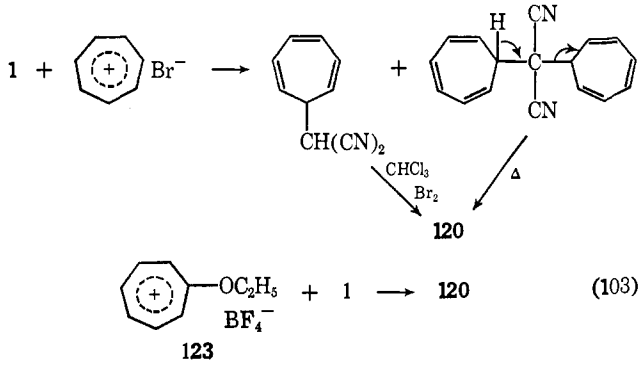
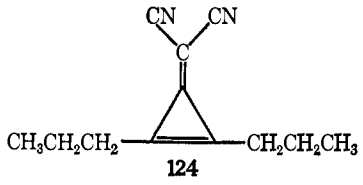
(213) N. Latif and N. Mishriky, *Can. J. Chem.*, **44**, 1271 (1966).
(214) T. K. Mukherjee, *J. Phys. Chem.*, 70, 3848 (1966).
(215) T. K. Mukherjee and L. A. Levasseur, *J. Org. Chem.*, **30**, 644 (1965).
(216) A. S. Kende and P. T. Izzo, *J. Am. Chem. Soc.*, 86, 3587 (1964).

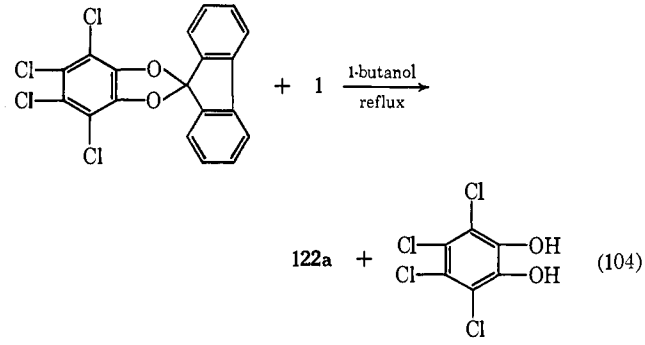
Scheme IX



The first fully aliphatic triafulvene (**124**) has been prepared by Kende and Izzo.[216]



Another preparation of α-(9-fluorenylidene)malononitrile (**122a**), which first involves hydrolysis of a ketal, has been reported.[213]



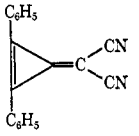
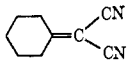
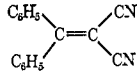
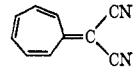
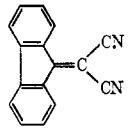
9-Dicyanomethylene-2,4,7-trinitrofluorene (**122b**) is obtained in 93% yield from **1** and 2,4,7-trinitrofluorenone.[215] **122b** is of interest because of its ability to form charge-transfer complexes and stable anion-radical salts of lithium and triethylammonium ions.

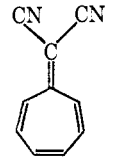
The phenomenon of photoconduction of the four dinitro isomers of fluorenmalononitrile and 2,4,5,7-tetranitrofluoren-$\Delta^{9\alpha}$-malononitrile has been investigated.[214] Although the experimental conditions were not very reliable, it was found that 2,7-dinitrofluoren-$\Delta^{9\alpha}$-malononitrile (**122c**) had the highest photoconductivity.

Dipole measurements[217] of **120** and **121** showed their pseudoaromatic character (Table XIX[208,218]). It is clear from the table that each of the highly strained molecules receives extra stabilization from the electron-withdrawing exocyclic substituents which produce appreciable positive character in the alicyclic ring. The contribution of the classical dipolar structures to the ground state has also been demonstrated *via* infrared and ultraviolet spectroscopy.[208]

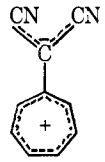
Table XIX

Dipole Moments of Substituted Fulvenes and Some Cycloalkylidenemalononitriles

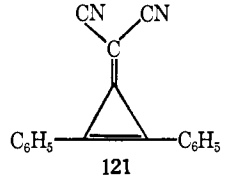
Compound	*Dipole moment, D*	*Ref*
	7.9 ± 0.1	208
	5.45 ± 0.02	208
	5.85 ± 0.05	208
	7.49	218
	5.53 ± 0.07	208



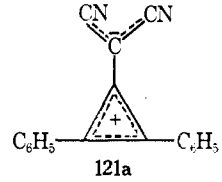
120



120a

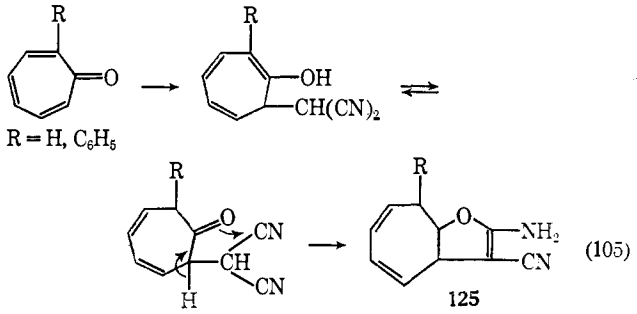


121



121a

It is of interest that the piperidine-catalyzed reaction of **1**, tropone, or 2-phenyltropone gives 1-oxoazulan-2-imine derivatives (**125**) in excellent yields,[219] *via* the following mechanism. The structures of the products were established by elemental analyses, chemical reactivity, and ultraviolet and pmr spectroscopy.[219]



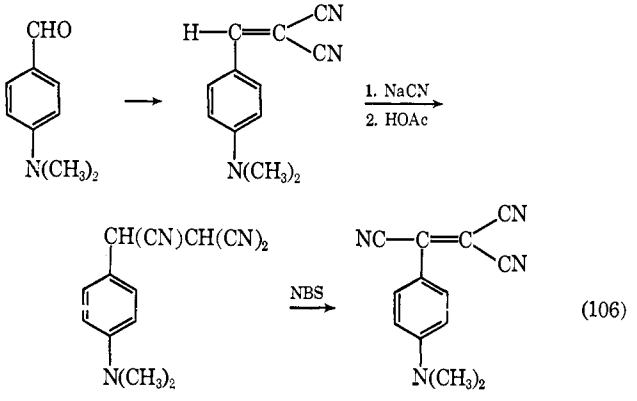
Tricyanovinylamines. One route to tricyanovinylarylamines involves the condensation of an aminobenzaldehyde with **1**, followed by addition of hydrogen cyanide to the product and oxidation.[9] Many of the 4-tricyanovinylarylamines give brilliant red dyes on hydrophobic fibers. These

(217) H. Weller-Fellchenfeld, I. Agranat, and E. D. Bergmann, *Trans. Faraday Soc.*, 62, 2084 (1966).

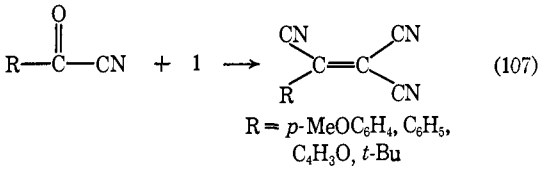
(218) M. Yamakawa, H. Watnabe, T. Mukai, T. Nozoe, and M. Kubo, *J. Am. Chem. Soc.*, 82, 5665 (1960).

(219) T. Nozoe, T. Mukai, and T. Suzuki, *Bull. Chem. Soc. Jap.*, 36, 38 (1963).

dyes generally are wash-fast, sublimation-fast, and light-fast. Over 50 of these compounds have been prepared. Alternatively, **1** condenses with acyl cyanides, in the presence of piperidine–acetic acid, β-alanine–acetic acid, or piperidine–acetic acid catalyst, to give the tricyanovinyl structure in one step.[220]



(106)

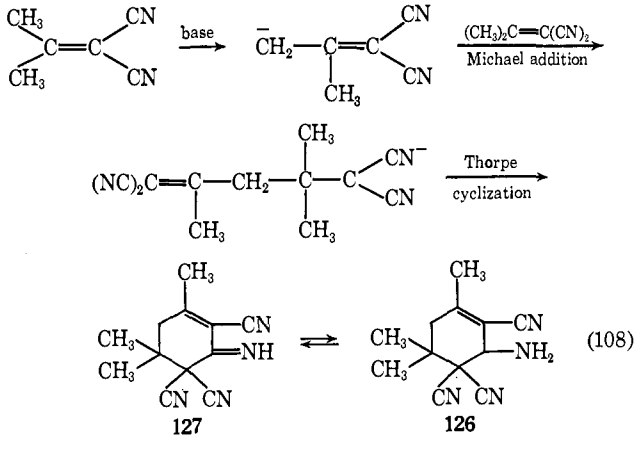


(107)

R = *p*-MeOC$_6$H$_4$, C$_6$H$_5$, C$_4$H$_3$O, *t*-Bu

e. Aryl- and Alkylidenemalononitrile Dimers

The preparation of α,β-unsaturated dinitriles is generally accompanied by dimerization of the initially formed dinitrile.[221] The formation of this dimeric product has previously led to confusion about the structures of the dinitriles. An example of this dimerization, and a probable mechanism, is shown with isopropylidenemalononitrile.[222] Spectral evidence shows that the dimer exists predominantly as the aminocyclohexadiene **126**, which is in equilibrium with its tautomer **127**.

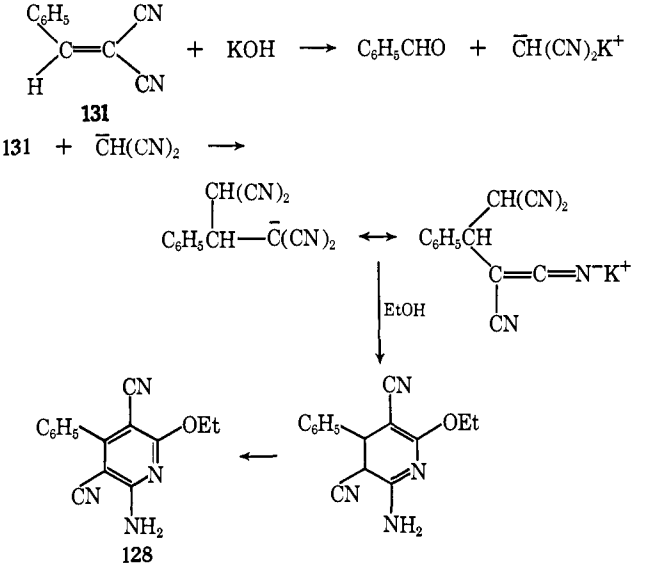


(108)

The dimers of 2-butylidene-, 3-pentylidene-, cyclohexylidene-, cyclopentylidene-,[18] and ethylidenemalononitriles have been prepared[221b] from **1** and carbonyl compounds or by dimerization of the respective alkylidenemalononitriles.

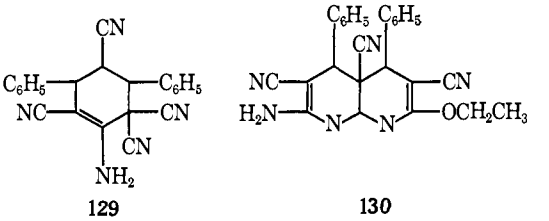
The base used in the base-catalyzed condensation has a marked influence on the reaction products. For example, benzalmalononitrile (**131**) reacts in ethanolic potassium hydroxide to give 2-amino-6-ethoxy-3,5-dicyano-4-phenylpyridine (**128**). A postulated mechanism[221] involves a reverse aldol cleavage of the dinitrile to benzaldehyde and dicyanomethyl anion, followed by an nucleophilic attack on the β carbon of a second dinitrile molecule by the dicyanomethyl anion, and subsequent ring closure (Scheme X). Support is given for this mechanism from the formation of pyridines by

Scheme X



refluxing 1,1,3,3-tetracyanopropenes with concentrated sulfuric acid and by refluxing ethoxymethylenemalononitrile and **2** in an alcoholic medium.[13]

In contrast to its behavior in ethanolic potassium hydroxide solution, benzalmalononitrile on treatment with *n*-butylamine in ethanolic solution gives two crystalline products, **129** and **130**.[221b] Again, the initial steps seem to be the same as described above for the reaction in ethanolic potassium hydroxide. Subsequent steps to the formation of **129** and **130** are shown in Schemes XI and XII.

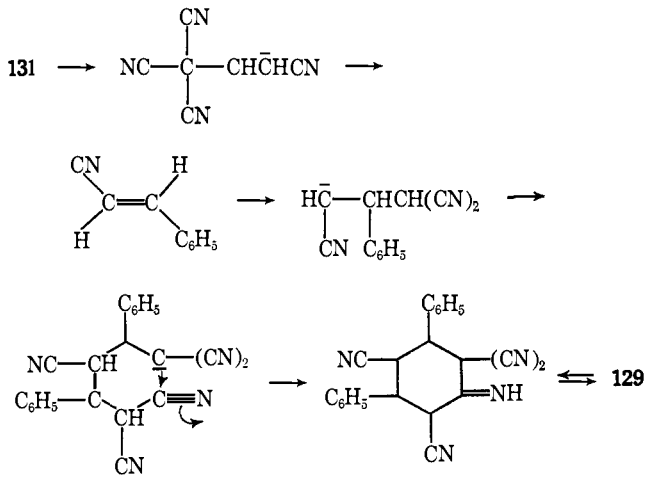


Dark polymeric products are obtained from the attempted base-catalyzed condensations of β-ethylbenzalmalononitrile, β-naphthylmethylenemalononitrile, and β-phenylbenzalmalononitrile.

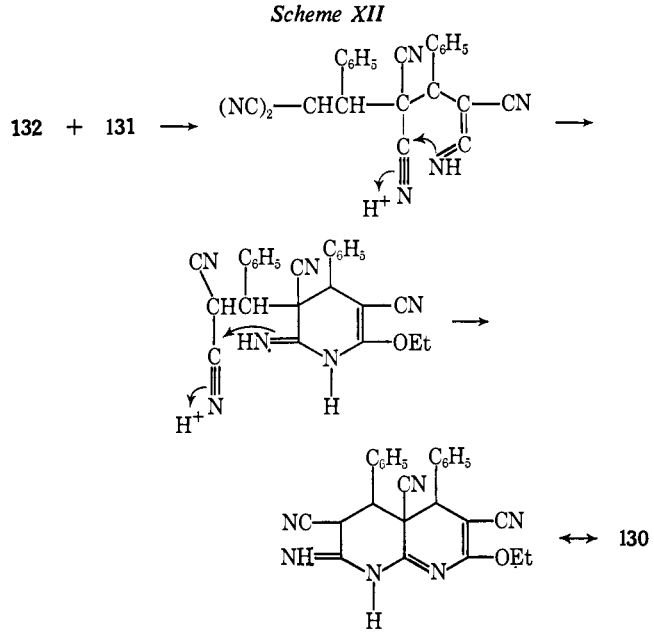
An unusual reaction occurs with the extremely sensitive-ethylidenemalononitrile to give **133** *via* the mechanism postulated in Scheme XIII.[223] In contrast to the reaction with isopropylidenemalononitrile where a proton is removed from a methyl group, attack by the dicyanomethyl anion occurs at the β carbon which is partially positive due to the electron-attracting ability of the two cyano groups.

(220) T. Sato, *J. Org. Chem.*, 24, 963 (1959).
(221) (a) M. R. S. Weir, K. E. Helmer, and J. B. Hyne, *Can. J. Chem.*, 41, 1042 (1963); (b) M. R. S. Weir and J. B. Hyne, *ibid.*, 43, 772 (1965).
(222) J. K. Williams, *J. Org. Chem.*, 28, 1054 (1963).
(223) M. R. S. Weir and J. B. Hyne, *Can. J. Chem.*, 42, 1440 (1964).

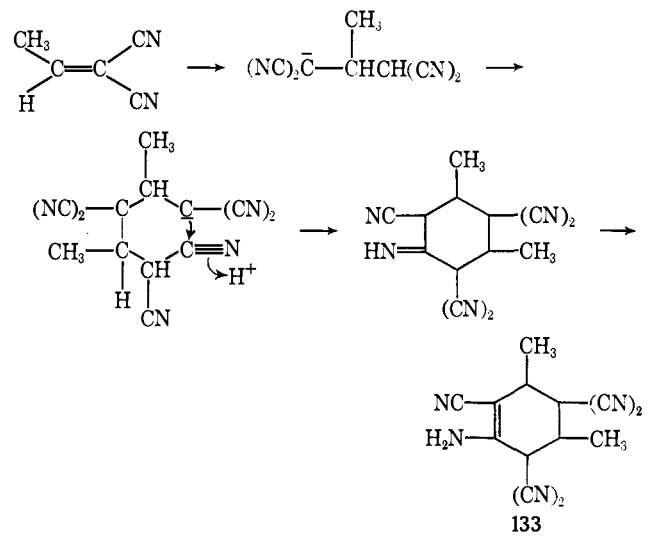
Scheme XI



Scheme XII



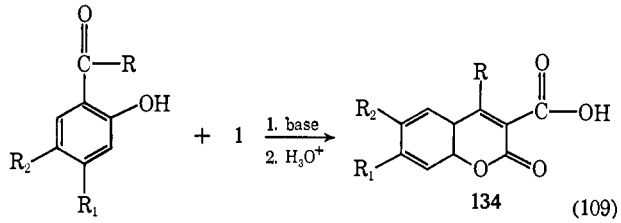
Scheme XIII



133

3. *Hydroxy Aldehydes and Hydroxy Ketones*

Salicylaldehyde, 5-chlorosalicylaldehyde, and 2,4-dihydroxybenzaldehyde condense with **1**, in the presence of piperidine, to give intermediate arylidenemalononitriles which are hydrolyzed to the corresponding coumarin-3-carboxylic acids (**134**) in 100, 100, and 85% yields, respectively.[224] 2-Hydroxyacetophenone gives 3-carboxy-4-methylcoumarin in 44% yield under the same conditions.[224] Schiemenz[225] reported that under milder conditions, **1** and salicylaldehyde give 3-coumarinimidenecarboxamide with pyridine catalyst. The importance of the nature of the base is demonstrated[61] in the variety of products obtained from different bases (Scheme XIV). Each reaction involves a Knoevenagel condensation followed by cyclization to the coumarin ring structure.

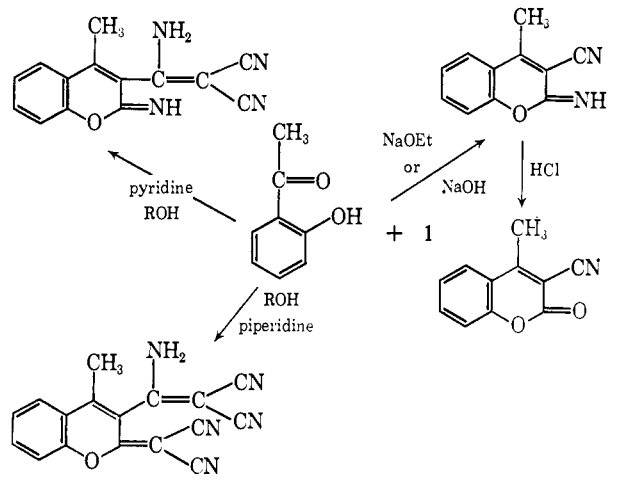


(109)

$R = R_1 = R_2 = H$
$R = R_1 = H; R_2 = Cl$
$R = R_2 = H; R_1 = OH$
$R = CH_3; R_1 = R_2 = H$

α-Hydroxy ketones react with **1** in the presence of base, at room temperature, to give 2-amino-3-cyanofurans (**135**). The reaction involves an initial Knoevenagel condensation followed by cyclization to the furan ring.[226]

Scheme XIV

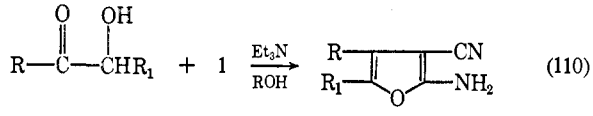


Previously, it has been erroneously reported that the condensation of benzoin and **1** gave **136**.[63] The structures of the products (**135**) were established *via* spectral analyses and chemical reactivity (eq 111).[226]

4. *Dicarbonyl Compounds*

1 and 2,4-pentanedione give 4,6-dimethyl-3-cyano-2-hydroxypyridine (**137**) *via* the mechanism in eq 112.[227,228] 1-

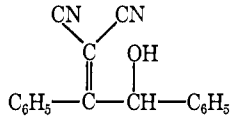
(224) L. L. Woods and J. Sapp, *J. Org. Chem.*, 30, 312 (1965).
(225) G. P. Schiemenz, *Chem. Ber.*, 95, 483 (1962).
(226) K. Gewald, *ibid.*, 99, 1002 (1966).
(227) C. Basu, *J. Indian Chem. Soc.*, 7, 815 (1930).
(228) A. Dornow and E. Neuse, *Arch. Pharm.*, 288, 174 (1955).



(110)

135

$R = CH_3$; $R_1 = H$ (67%)
$R = R_1 = CH_3$ (67%)
$R, R_1 = -(CH_2)_4-$ (51%)
$R = R_1 = C_6H_5$ (75%)



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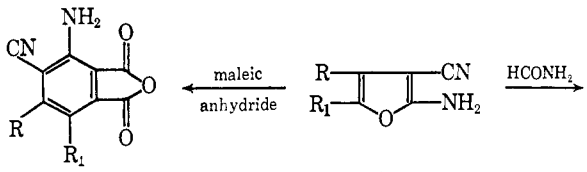

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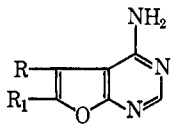
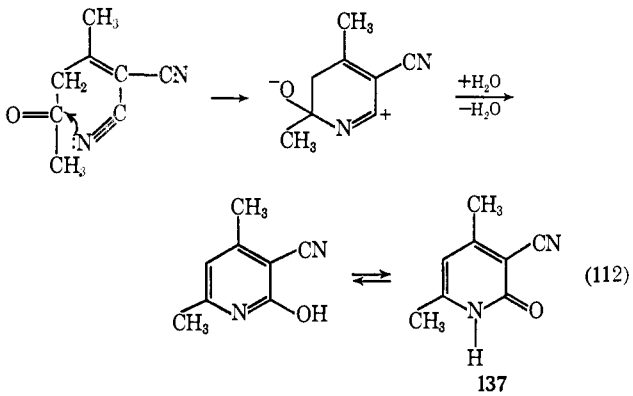


(111)

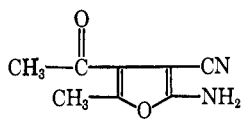
Phenyl-2,4-pentanedione yields the corresponding 5-phenyl derivative,[228] and 2-methyl-3-ketobutanal gives a substituted pyridinol.[228] Substituted furans and substituted pyridines are obtained when the sodium salts of 3-halo-2,4-pentanedione are used. For example, the sodium salt of 3-bromo- or 3-chloro-2,4-pentanedione reacts with **1**, in aqueous ethanol, to



(112)

137

give 2-amino-3-cyano-4-acetyl-5-methylfuran (**138**),[130] and the sodium salt of β-ketobutanal gives 2-methyl-5-cyano-6-hydroxypyridine (**139**).[229] The mechanisms for the formation of these products are similar to the ones described above.



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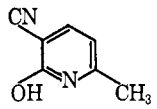
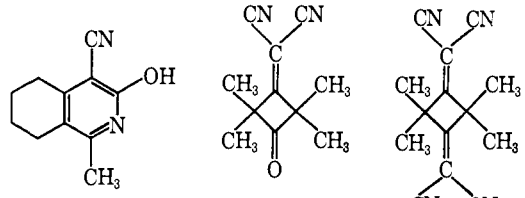


139

(229) T. Matsukaneau and T. Matsuno, *J. Pharm. Soc. Jap.*, **64**, 145 (1944): *Chem. Abstr.*, 45, 4724 (1951).

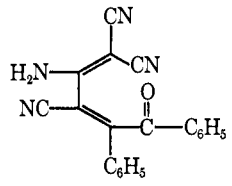
4-Methoxy-1,3-bis(dicyanomethylene)benzene has been prepared from the corresponding dialdehyde and **1**.[230] 2-Acetylcyclohexanone reacts to give 1-methyl-3-hydroxy-4-cyano-5,6,7,8-tetrahydroisoquinoline (**140**),[231] *via* the mechanism suggested for 2,4-pentanedione, whereas 2-acetylcyclopentanone gives a mixture of unidentified products.[232]

1 and 2,2,4,4-tetramethyl-1,3-cyclobutanedione in a 1:1.1 molar ratio give dicyanomethylene-2,2,4,4-tetramethylcyclobutanone (**141**) and bis(dicyanomethylene)-2,2,4,4-tetramethylcyclobutane (**142**) in 46 and 21% yields, respectively. By raising the molar ratio to 1:2.4, **142** is obtained in 97% yield.[223] 1,4-Cyclohexanedione in the presence of acetic acid and ammonium acetate yields 1,4-bis(dicyanomethylene)-cyclohexane.[95,234]



140 141 142

The diethylamine-catalyzed reaction of benzil and **1** gives 2-amino-4-benzoyl-1,1,3-tricyano-4-phenylbutadiene (**143**).[63] The dimer **3** is the reactive species. 2,3-Butanedione gives unidentified products with **1**.[235] 1,3-Indanone yields 1,1-dicyanomethylene-3-indanone (**144**),[78] whereas 5-methylisatin gives 5-methyl-3-dicyanomethyleneoxindole (**145**) or 3-(2-amino-1,3,5-tricyanoallylidene)5-methyloxindole (**146**), depending on reaction conditions.



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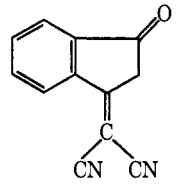

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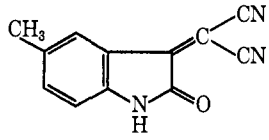

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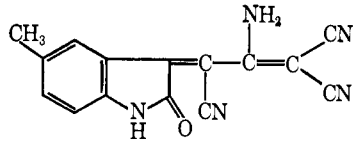
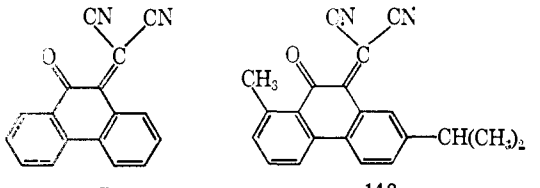


146

Acenaphthenequinone and phenananthraquinone have been reported to react with **1** to give unidentified colored products.[63,236,237] However, a reinvestigation[50] has shown that phenanthrenequinones and acenaphthenequinone react with **1** to give simple monocondensation products in excellent yields. The following products (**147–150**) have been obtained from the corresponding quinones. A novel cyclization occurs

(230) B. Relchert and W. Hoss, *Arch. Pharm.*, 280, 157 (1942).
(231) F. Freeman, D. K. Farquhar, and R. L. Walker, *J. Org. Chem.*, 33, 3648 (1968).
(232) F. Freeman and T. I. Ito, 1967, unpublished data.
(233) E. A. La Landette and R. E. Benson, *J. Am. Chem. Soc.*, 83, 4867 (1961).
(234) M. T. Jones and W. R. Hertler, *ibid.*, 86, 1881 (1964).
(235) F. Freeman, 1965, unpublished data.
(236) C. E. Gonter and J. J. Petty, *Anal. Chem.*, 35, 663 (1963).
(237) W. Kesting, *Chem. Ber.*, 62, 1422 (1929).



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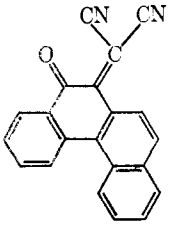

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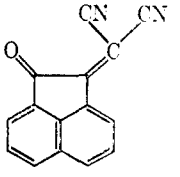

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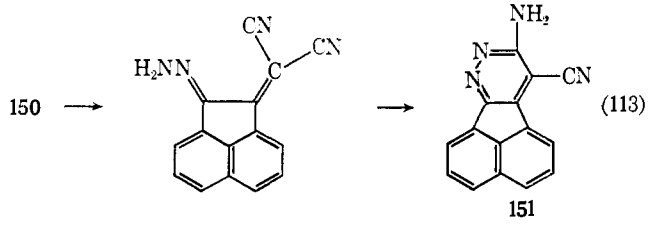


(113)

151

with the hydrazone of **150** to give acenaphthenepyridazine (**151**).[50]

1,4-Naphthoquinone (583 mμ), benzoquinone (517 mμ), and hydroquinone (480 mμ) react with **1** in aqueous alcoholic alkaline solution to give colored solutions which obey Beer's law.[236] 1,2-Naphthoquinone, methyl-*p*-benzoquinone, and 2,5-dimethyl-*p*-benzoquinone react with **1**, but the monethers of benzoquinone do not react under these conditions.[236] This method has been used to determine 1,4-naphthoquinone in concentrations as low as 0.5 ppm with a standard deviation of ±0.12.[236] Recently the color reaction for the detection of *o*-quinones in the naphthalene and phenanthrene series has been extended to 4-nitro-, 2-nitro-, 3-bromo-, and 3-benzoyl-9,10-anthraquinone, retenequinone, 3-acetylretenequinone, 1,2-chrysenequinone, and 1,2-naphthoquinone by Junek and Hamboeck.[238] The intense violet to blue shades are stable and can be formed from 0.5 to 10 μg of quinone.

5. Esters

Alkoxymethylenemalononitriles are prepared from **1** and orthoesters in the presence[239] or absence[240] of acetic anhydride. However, the yields are generally higher in the presence of acetic anhydride.[239,241] Orthoacetates, orthobenzoates, and orthoformates may be used.[242–244] Thioorthoesters also condense to give the nitrile ethers of α-cyano-β-mercaptoacrylic acids which are further condensed in anhydrous alcohol to pyrimidine compounds.[245]

$$\mathbf{1} + (CH_3CH_2O)_3CH \longrightarrow \underset{99\%}{CH_3CH_2OCH{=}C(CN)_2} \quad (114)$$

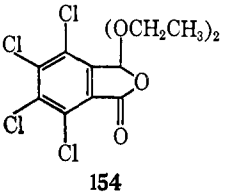
The mechanism for alkoxymethylenemalononitrile formation is not clear. It has been suggested[246,247] that the reaction involves condensation of ethyl orthoformate with acetic anhydride to form diethoxymethyl acetate (**152**). **152** alkylates the active methylene carbon or **1** to give the acetal, which then eliminates 1 mole of alcohol. This is not the only mechanism since the reaction proceeds in the absence of acetic anhydride.[239,240]

$$C_2H_5O)_3CH + (CH_3CO)_2O \longrightarrow \underset{\mathbf{152}}{(C_2H_5O)_2CHOCOCH_3} + C_2H_5OCOCH_3 \quad (115)$$

$$\mathbf{152} + \mathbf{1} \longrightarrow CH_3CO_2H + \underset{\mathbf{153}}{(NC)_2CHCH(OC_2H_5)_2} \quad (116)$$

$$\mathbf{153} \longrightarrow (NC)_2C{=}CHOC_2H_5 + C_2H_5OH \quad (117)$$

Although the pseudoesters[248,249] **154** and **155** do not react with **1**, ethyl 4-dimethylaminophenylglyoxylate condenses[9] to give **156**. Ethyl acetoacetate, phenoxyacetaldehyde, **1**, and



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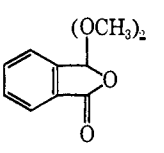
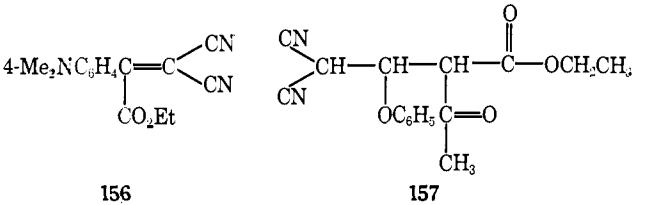


155

a secondary amine as catalyst give ethyl α-acetyl-β-phenoxymethyl-γ,γ-dicyanobutyrate (**157**)[250] which is useful in the preparation of medicinals. **157** is formed by the Michael addition of **1** to the aldol condensation product of ethyl acetoacetate and phenoxyacetaldehyde.

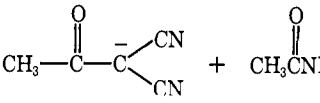


156 157

6. Amides

1 reacts with N,S-diacetylcysteamine (**158**) at 20° in aqueous solution of about pH 9 to form acetylmalononitrile and N-acetylcysteamine. The kinetics show that the dicyanomethyl anion is the reactive species.[33] Acetylmalononitrile is also formed from the condensation of **1** with acetic anhydride in the presence of anhydrous sodium or potassium carbonate.[251]

$$\mathbf{1} + \underset{\mathbf{158}}{CH_3CSCH_2CH_2NHCCH_3} \longrightarrow$$



+ $CH_3CNHCH_2CH_2SH$ (118)

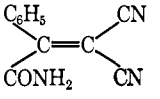
(238) H. Junek and H. Hamboeck, *Mikrochim. Acta*, 552 (1966).
(239) R. G. Jones, *J. Am. Chem. Soc.*, 74, 4889 (1952).
(240) J. P. Vila and M. Ballester, *Anales Real Soc. Espan. Fis. Quim.* (Madrid), 45B, 87 (1949); *Chem. Abstr.*, **44**, 3884 (1950).
(241) R. G. Jones, *J. Am. Chem. Soc.*, 73, 3684 (1951).
(242) W. Huber and H. A. Holscher, *Chem. Ber.*, 71, 87 (1938).
(243) A. Ishiwata, *Takamine Kenkyusho Nempo*, 9, 21 (1957); *Chem. Abstr.*, **55**, 1439 (1961).
(244) J. P. Vila and R. G. Jarque, *Anales Real Soc. Espan. Fis. Quim.* (Madrid), 40, 946 (1944); *Chem. Abstr.*, 39, 4329 (1945).
(245) Dr. Kereszty and Dr. Wolf, Hungarian Patent 128,404 (1941); *Chem. Abstr.*, 46, 2570 (1952).
(246) H. W. Post and E. R. Erickson, *J. Org. Chem.*, 2, 260 (1937).
(247) R. C. Fuson, W. E. Parham, and L. J. Reed, *ibid.*, 11, 194 (1946).
(248) J. P. Vila and M. Ballester, *Anales Real Espan. Fis. Quim.* (Madrid), 42, 1097 (1946); *Chem. Abstr.*, 41, 6549 (1947).
(249) J. P. Vila and M. Ballester, *Anales Real Espan. Fis. Quim.* (Madrid), *Chem. Ser. B*, 44, 593 (1948); *Abstr.*, 42, 8179 (1948).
(250) F. Hoffmann-La Roche & Co. A.G., Swiss Patent 221,164 (1942); *Chem. Abstr.*, 43, 689 (1949).
(251) I. Heri and Midorikawa, *Sci. Papers Inst. Phys. Chem. Res* 216 (1962); *Chem. Abstr.*, 58, 3311 (1963).

Table XX

Acyl- and Sulfonylmalononitriles[255]

$RCOCH(CN)_2$	$RSO_2CH(CN)_2$	*Method*	*Yield, %*	$(CH_3CH_2)_3N$ *salt*
	C_6H_5	B	20	
	p-MeC_6H_4	B	13	
	m-$O_2NC_6H_4$	C	67	+
	β-Naphthyl	B	65	
Me		B	30	
C_6H_5		A	79	+
p-$MeOC_6H_4$		C	65	+
p-ClC_6H_4		C	66	+
p-$O_2NC_6H_4$		A	85	+

Benzoylformamide and **1** give 1-phenyl-1-formanilido-2,2-dicyanoethylene (**159**) in 95% yield.[252] Formamide, **1**, and carbonyl chloride give aminomethylenemalononitrile (**160**), a useful intermediate for the synthesis of thiamine,[253] in 70% yield.



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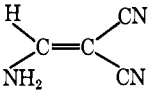
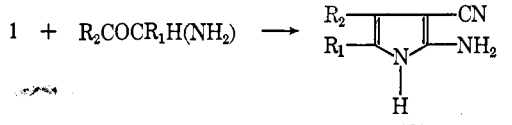


160

α-Amino ketones and **1** give 2-amino-3-cyanopyrroles (**161**) in 40–70% yields.[254] The reaction presumably involves condensation followed by cyclization with the amino group.



(119)

161

R_2	R_1	R_2	R_1
C_6H_5	H	CH_3	H
C_6H_5	CH_3	CH_3	CH_3

7. *Acid Chlorides*

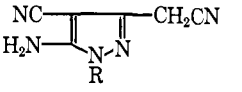
Acyl- and sulfonyl chlorides react with **1** in aqueous sodium hydroxide (A), or in benzene and triethylamine (B), to give acyl- and sulfonylmalononitriles. Reaction with **2** (C) yields the same products (see Table XX).[255]

$$RCOCl + \mathbf{1} \longrightarrow RCOCH(CN)_2 \quad (120)$$

$$RSO_2Cl + \mathbf{1} \longrightarrow RSO_2CH(CN)_2 \quad (121)$$

K. NITROGEN COMPOUNDS

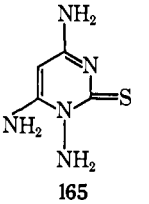
The reaction **1** with hydrazine was reported to yield 3,5-diaminopyrazoles.[256] However, more recent investigations[14,220,257] have shown that the product is 3-cyanomethyl-4-cyano-5-aminopyrazole (**162**). **1** is dimerized by the basic



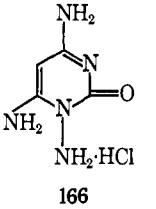
162, R = H
163, R = C_6H_5
164, R = CH_3

hydrazine to **3**, which is the reaction intermediate. The yield is higher when **3** is used instead of **1**.[257] Phenylhydrazine and methylhydrazine give 1-phenyl- and 1-methyl-3-cyanomethyl-4-cyano-5-aminopyrazole (**163** and **164**) in 58 and 59% yields, respectively.[257]

Condensation of a dibromomalononitrile–potassium bromide complex with thiosemicarbazide gave an unidentified product ($C_4H_5N_5S$). **1** condenses with thiosemicarbazide and semicarbazide hydrochloride to give 1,4,6-triamino-2-thioxo-1,2-dihydropyrimidine (**165**) and 1,4,6-triamino-2-oxo-1,2-dihydropyrimidine hydrochloride (**166**), respectively.[258]

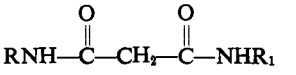


165



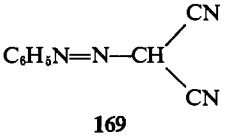
166

Ethyl orthoformate, **1**, and arylamines give condensation products which are useful dye intermediates. Aniline, tetrahydroquinoline, *p*-toluidine, and diphenylamine give $C_6H_5NHCH{=}C(CN)_2$, 1,1-dicyano-2-tetrahydroquinolylethylene, *p*-$CH_3C_6H_4NHCH{=}C(CN)_2$, and $(C_6H_5)_2NCH{=}C(CN)_2$, respectively.[259] N,N-Disubstituted amides have been prepared from **1** and aqueous methylamine (**167**) and benzylamine (**168**).[260] Side reactions include the base-catalyzed decomposition of **1**.



167, R = R_1 = CH_3 (31%)
168, R = R_1 = $C_6H_5CH_2$ (40%)

1 reacts with benzenediazonium chloride to give phenylazomalononitrile (**169**),[261] and **170** and **171** are the products obtained from the reaction of **1** and hydroxylamine.[85]



169

$$\mathbf{1} + NH_2OH \cdot HCl + KHCO_3 \longrightarrow CO_2 + H_2O + KCl + \underset{\mathbf{170}}{NCCH_2C(NH_2){=}NOH} \quad (122)$$

$$\mathbf{170} + NH_2OH \longrightarrow \underset{\mathbf{171}}{CH_2[C(NH_2){=}NOH]_2} \quad (123)$$

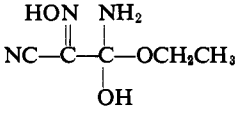
Sachs[262] reported that nitroso compounds condensed with **1** to give anils. *p*-Nitroso-N,N-dimethylaniline[199] yields the

(252) J. C. Scudi and H. G. Lindwall, *J. Am. Chem. Soc.*, 57, 1646 (1935).
(253) Takeda Chemical Industries Ltd., Japanese Patent 2414 (1965); *Chem. Abstr.*, 62, 14508 (1965).
(254) K. Gewald, *Z. Chem.*, 1, 349 (1961).
(255)(a) J. P. Fleury and B. Libes, *Compt. Rend.*, 256, 2419 (1963); (b) J. P. Fleury and B. Libes, *Bull. Soc. Chim. Fr.*, 413 (1964).
(256) R. von Rothenberg, *Chem. Ber.*, 27, 685 (1894).
(257) E. C. Taylor and K. S. Hartke, *J. Am. Chem. Soc.*, 81, 2456 (1959).
(258) R. W. Morrison, Jr., Ph.D. Thesis, Princeton University, Princeton, N. J., 1964.
(259) H. Fischer, German Patent 834,104 (1952); *Chem. Abstr.*, 50, 402 (1956).
(260) L. J. Exner, M. J. Hurwitz, and P. L. De Benneville, *J. Am. Chem. Soc.*, 77, 1103 (1955).
(261) E. L. Bennett, *ibid.*, 74, 2420 (1952).
(262) F. Sachs, *Chem. Ber.*, 33, 963 (1900).

anil (**172**). In contrast, from the interaction of various nitrosophenols with **1**, Anderson, Bell, and Duncan[63] only obtained black amorphous solids which resisted purification.

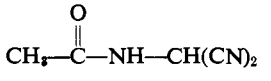
$$p\text{-}(CH_3)_2NC_6H_4NO + \mathbf{1} \longrightarrow \underset{\mathbf{172}}{p\text{-}(CH_3)_2NC_6H_4N{=}C(CN)_2} \quad (124)$$

1, amyl nitrite, and sodium ethoxide yield a compound provisionally assigned structure **173**.[263] The mechanism for the reaction has not been elucidated.

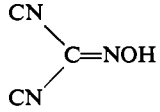


173

Zinc dust reduction of the product from the reaction of **1** and sodium nitrite in acetic acid gives acetaminomalononitrile (**174**) which is an intermediate for the manufacture of pyrimidines and purine derivatives,[253] or oximiomalononitrile (**175**) which is a precursor for aminomalononitrile (**9**).[264]

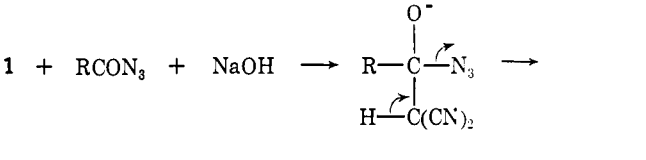


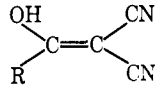
174



175

1 reacts with carbonyl azides[265] to give α-hydroxydinitriles (**176**) in excellent yields.



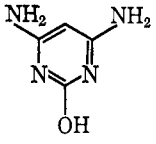


(125)

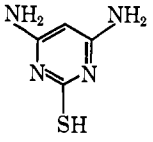
176

R = C_6H_5 (87%)
R = p-$O_2C_6H_4$ (84%)
R = p-$H_3COC_6H_4$ (81%)

The sodium ethoxide catalyzed reaction of **1** and urea yields 4,6-diamino-2-hydroxypyrimidine (6-aminocytosine) (**177**),[266] and the sodium ethoxide catalyzed reaction with thiourea gives the coreresponding 2-thiopyrimidine (**178**).[26]



177

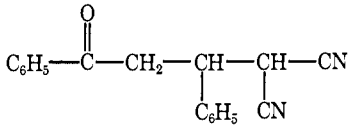


178

L. MISCELLANEOUS REACTIONS

1. Michael Addition

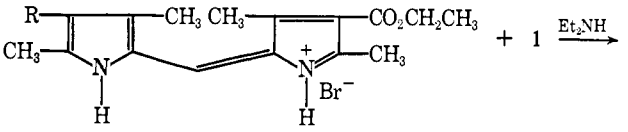
Benzalacetophenone, sodium methoxide, and **1** give **179**.[267] It is surprising that only the 1,4-addition product is obtained instead of some 1,2-addition product since the balance between the two possible modes of reaction is so delicate.



179

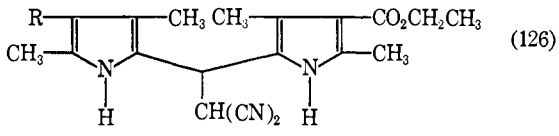
It has been reported[268] that the reaction of dibenzalacetone and **1**, in the presence or absence of basic and acidic catalysts, gave a cyclic addition product in 72% yield. Unfortunately, the structure and formula of the cyclic product were not given in the abstract.

Dipyrromethene hydrobromides (**180**) and **1** react in refluxing chloroform, *via* a 1,6-nucleophilic addition of the dicyanomethyl anion, to give **181**.[269]



R = CH_3CH_2O, CH_3CH_2

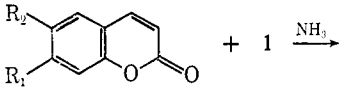
180



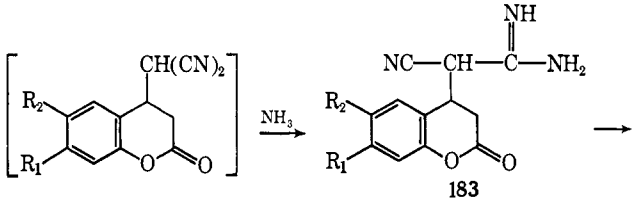
(126)

181

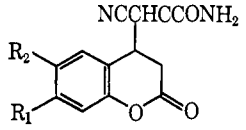
Aqueous ammonia catalyzes the Michael addition of **1** to coumarins (**182**) to give substituted coumarins (**183**) which can be hydrolyzed to amides (**184**).[62,270] When 10% sodium hydroxide is used, the rate of dimerization of **1** to **3** is faster than Michael addition and the product is **183a**. *m*-Nitro-



182

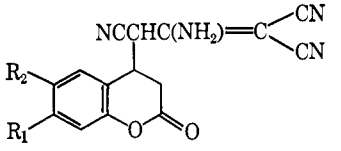


183



(127)

184



183a

(263) O. Diels and E. Borgwardt, *Chem. Ber.*, **54**, 1334 (1921).
(264) G. Ponzio, *Gazz. Chim. Ital.*, **61**, 561 (1931).
(265) R. Mertz and J. P. Fleury, *Compt. Rend., Ser. C.*, 262, 571 (1966); *Chem. Abstr.*, **64**, 14087 (1966).
(266) Merck &'Co., German Patent 166,448; Bellstein, II, 590.
(267) E. P. Kohler and B. L. Souther, *J. Am. Chem. Soc.*, 44, 2903 (1922).
(268) K. Takemoto, Y. Tanaka, and M. Imoto, *Kogo Kagaku Zasshi*, **69**, 524 (1966); *Chem. Abstr.*, **65**, 13835 (1966).
(269) P. Bamfield, A. W. Johnson, and J. Lenz, *J. Chem. Soc.*, 7001 (1965).
(270) H. Junek and H. Sterk, *Monatsh. Chem.*, **98**, 144 (1967).

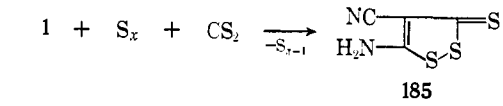
benzoylcoumarin[271] condenses with **1** to give $C_{19}H_9N_3O_4$, and *m*-nitrobenzoyl-2-thiocoumarin condenses with **1** to give $C_{29}H_{12}N_6O_5S$. Unfortunately the structures of the reactants and products were not carefully characterized.

2. Hydrogen Halides

At −78°, **1** and liquid hydrogen bromide and deuterium bromide give $[H_2N{=}CBrCH{=}CBrNH_2]Br$ and $[D_2N{=}CBr\text{-}CH{=}CBrND_2]Br$, respectively.[272] Hydrogen iodide yielded the corresponding product (unstable) while hydrogen chloride did not react at −85°.

3. Sulfur and Sulfur Compounds

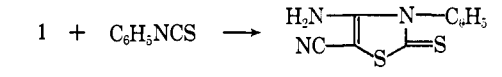
1 reacts with carbon disulfide and sulfur, in the presence of secondary or tertiary amines, to give 4-cyano-5-amino-1,2-dithio-3-thione (**185**) in 86% yield.[273,274] Another example of



(128)

185

this cycloaddition-type mechanism is found in the reaction of **1** and phenyl isothiocyanate to give 3-phenyl-4-amino-5-cyanothioazolinethi-2-one (**186**) in 80% yield.[275] Both **185** and **186** contain the relatively uncommon carbon–sulfur double



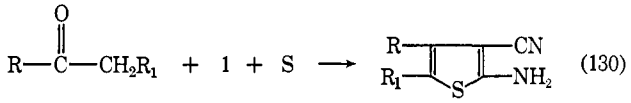
(129)

186

bond linkage.

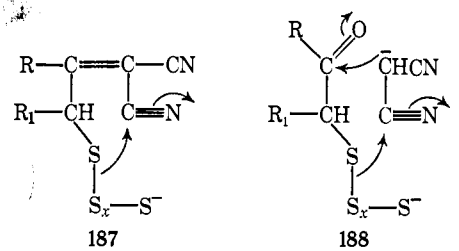
β,β-Dicyanoketene dialkyl mercaptoles, $(RS)_2C{=}C(CN)_2$, are prepared by the reaction of **2**, carbon disulfide, and an alkyl iodide or ester.[91] Many of these compounds are valuable as photographic sensitizers.

Substituted 2-aminothiophenes are prepared by the reaction of ketones and **1** in the presence of sulfur.[276] The reaction probably proceeds *via* intermediate **187** or **188**.



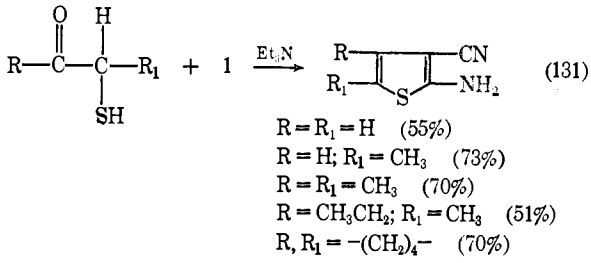
(130)

R = R₁ = CH₃ (42%)
R, R₁ = −(CH₂)₄− (90%)



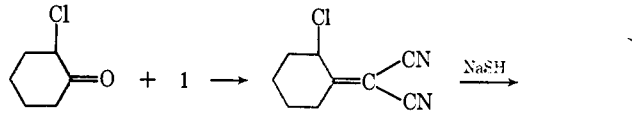
187 **188**

2-Aminothiophenes can also be prepared from α-oxomercaptans and **1** in alcohol or dimethylformamide solution.[277] The stepwise nature of this reaction is demonstrated in eq 131–133.



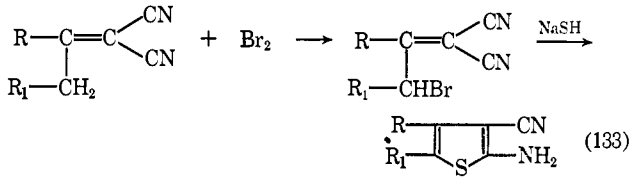
(131)

R = R₁ = H (55%)
R = H; R₁ = CH₃ (73%)
R = R₁ = CH₃ (70%)
R = CH₃CH₂; R₁ = CH₃ (51%)
R, R₁ = −(CH₂)₄− (70%)



(132)

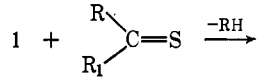
R, R₁ = −(CH₂)₄− (95%)



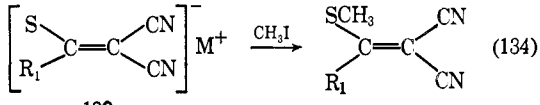
(133)

R = C₆H₅, R₁ = H (75%)
R = CH₃, R₁ = H (60%)

1 can be thioacylated[278] with esters of thiocarboxylic, dithiocarboxylic, trithiocarbonic, or xanthic acids in the presence of an alkali alkoxide catalyst. The salts are characterized by methylation to the sulfides **190**. The salts, **189**,



R = S-alkyl, O-alkyl
M = Na, K

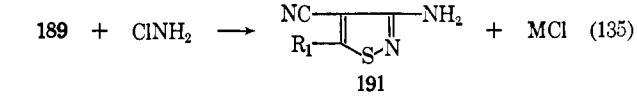


(134)

189 **190**

R₁ = CH₃ (60%)
R₁ = C₆H₅ (60%)
R₁ = C₆H₅CH₂ (95%)
R₁ = SCH₃ (50%)
R₁ = OCH₂CH₃ (60%)

are also alkylated to sulfides by α-chloro ketones and α-chloro carboxylic esters and nitriles. The sulfides are then cyclized to thiophenes by triethylamine catalyst.[278] Aqueous chloroamine solutions react with **189** to give isothiazoles (**191**). **191a** and **c** are also prepared using hydroxylamine-O-sulfonic acid.[279]



(135)

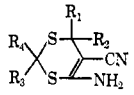
191

191a, R₁ = CH₃ (86%)
b, R₁ = OCH₂CH₃ (77%)
c, R₁ = SCH₃ (72%)
d, R₁ = C₆H₅CH₂ (93%)

(271) L. L. Woods and H. L. Williams, *Trans. Kansas Acad. Sci.*, 63, 165 (1960); *Chem. Abstr.*, 55, 13418 (1961).
(272) E. Allenstein and P. Quis, *Chem. Ber.*, 97, 1959 (1964).
(273) K. Gewald, *Z. Chem.*, 3, 26 (1963); *Chem. Abstr.*, 59, 10014 (1963).
(274) K. Gewald, *J. Prakt. Chem.*, 31, 214 (1966).
(275) K. Gewald, *ibid.*, 32, 26 (1966).
(276) K. Gewald, E. Schinke, and H. Bottcher, *Chem. Ber.*, 99, 94 (1966).
(277) K. Gewald, *ibid.*, 98, 3571 (1965).
(278) K. Hartke and L. Peshkar, *Angew. Chem. Intern. Ed. Engl.*, 6, 83 (1967).

Table XXI

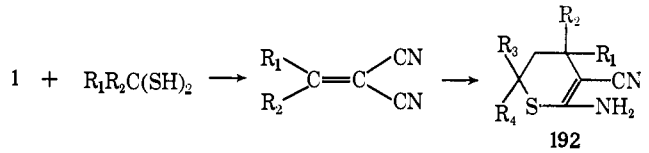
1,3-Dithiacyclohex-4-enes[279]



R_1	R_2	R_3	R_4	Yield, %	R_1	R_2	R_3	R_4	Yield, %
CH_3	CH_3	CH_3	CH_3	66	$-(CH_2)_5-$		$-(CH_2)_4-$		70
$-(CH_2)_5-$		$-(CH_2)_5-$		70	H	C_6H_5	$-(CH_2)_5-$		70
$-(CH_2)_4-$		$-(CH_2)_4-$		63					

The highly reactive unsaturated sulfides give pyrimidines with amidines or guanidines, pyrroles with 2-amino carboxylic esters, isoxazoles with hydroxylamines, and pyrazoles with hydrazines.[278]

1 reacts with *gem*-dithiols in methanolic potassium hydroxide to give 1,3-dithiacyclohex-4-enes (**192**)[279] (Table XXI). The same products are obtained from alkylidenemalononitriles.

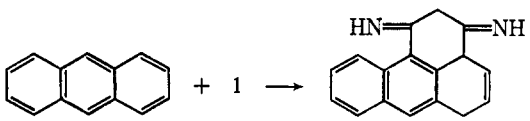


192 (136)

4. Oleic Acid and Aromatic Hydrocarbons

1 adds to the double bond of oleic acid, in sulfuric acid, to give α-cyanoacetamidostearic acid in 19% yield.[280]

1, in the presence of a metallic chloride, reacts with aromatic compounds, such as toluene, naphthalene, acenaphthene, α- or β-naphthol ether, 1-methylnaphthalene, and anthracene to give diketimides of type **193**.[281]



193 (137)

5. Tritylation

Four products are obtained from the reaction of triphenylcarbinol (**194**) and **1**.[282] These reactions are catalyzed by acids

(138)

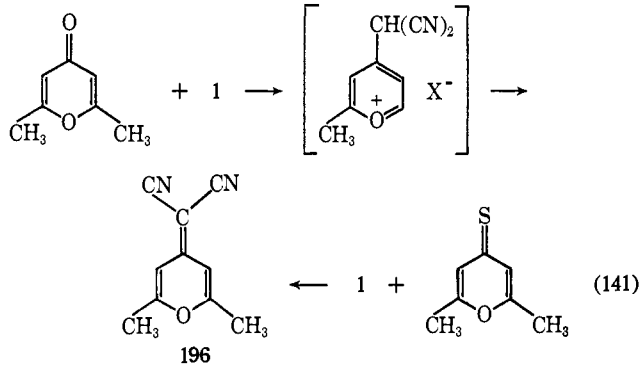
(139)

(140)

and inhibited by bases. With triphenylmethyl chloride, only the normal product (**195**) was isolated under a variety of conditions.[283]

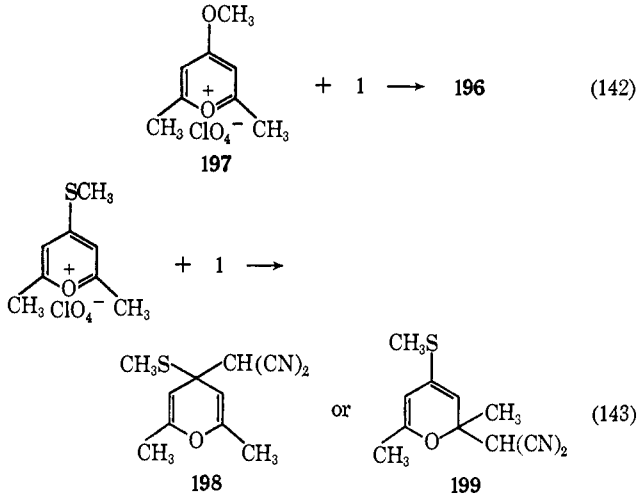
6. 4-Pyrones and Pyrylium Salts

2,6-Dimethylpyrone[284] and 2,6-dimethyl-4-thiopyrone[285–287] react with **1** in refluxing acetic anhydride to give the same product, 2,6-dimethylpyranylidenemalononitrile (**196**), in 90 and 33% yields, respectively. The condensation is not effected



196 (141)

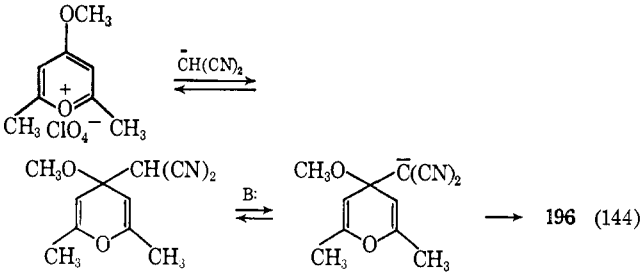
by the usual catalysts, *e.g.*, piperidine, sodium acetate, sodium ethoxide, or sodium *t*-butoxide.[287] If glacial acetic acid and acetic anhydride are used, one obtains the pyrylium salt with 2,6-dimethylpyrone.[284] 4-Methoxy-2,6-dimethylpyrylium perchlorate (**197**) can also be used for the preparation of **196**. Ohta and Kato[287] found that demethoxylation of **197** occurs in a refluxing mixture of *t*-butyl alcohol and **1** to give **196**. Surprisingly, with 4-methylmercapto-2,6-dimethylpyrylium perchlorate elimination of the methyl mercaptan does not occur, and compound **198** or **199** is obtained.



(142)

(143)

196 is probably formed by the following mechanism. Support for this mechanism is given by the formation of **198** and **199**.



(144)

(279) J. Jentzsch and R. Mayer, *J. Prakt. Chem.*, 18, 210 (1962).
(280) E. T. Roe and D. Swern, *J. Am. Chem. Soc.*, 75, 5479 (1953).
(281) I. G. Farbenindustrie, A.-G., French Patent 704,633 (1930); *Chem. Abstr.*, 25, 4717 (1931).
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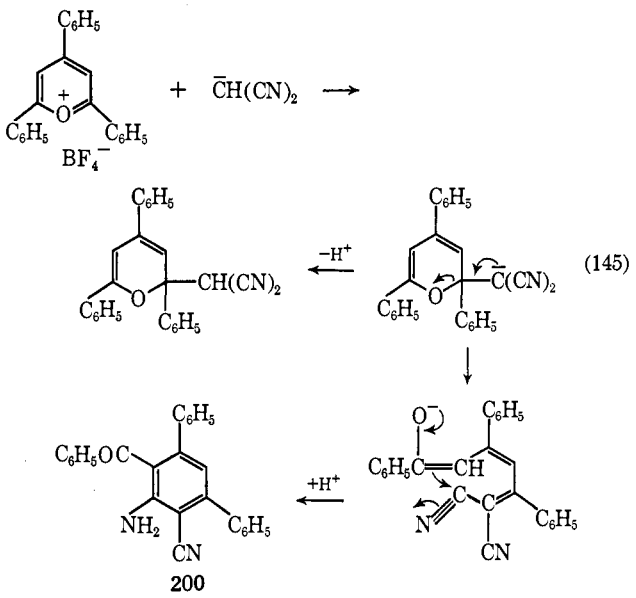
2,4,6-Triphenylpyrylium fluoroborate and **1** react to give 2-amino-3-cyano-4,6-diphenylbenzophenone (**200**) in 75% yield.[288] A possible mechanism is shown in eq 145. The scope of this interesting transformation has not been investigated.

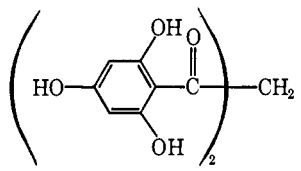


(145)

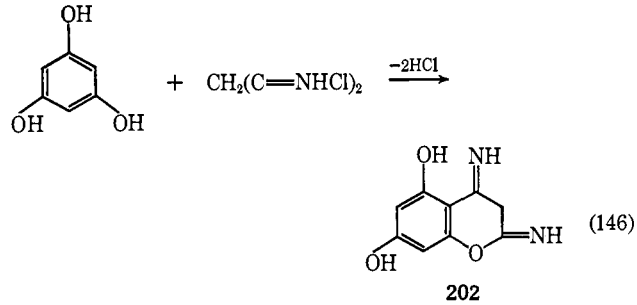
200

7. *Hoesch's Reaction*

Sonn[289] reported that hydrogen chloride, phloroglucinol, and I gave an intermediate imonium chloride which is hydrolyzed to *o*-cyanoacetylphloroglucinol, $NCCH_2COC_6H_2(OH)$. 2,2',-4,4',4,6',6'-Hexahydroxydibenzoylmethane (**101**) is the side product. A similar reaction was found to occur with resorcinol. In contrast, Shinoda[290] reported that the major product in the phloroglucinol reaction is 2,4-diimino-5,7-dihydroxycoumarin (**102**) which could be formed according to eq 146. These reactions should be reexamined under identical experimental conditions.



201



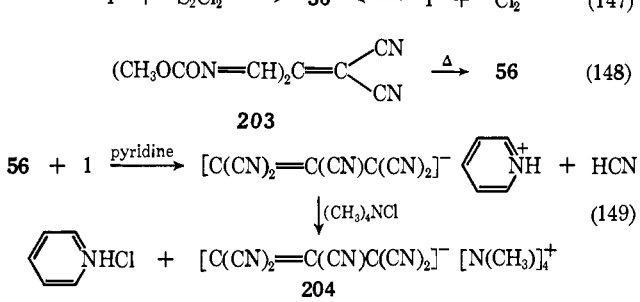
(146)

202

(288) K. Dimroth and G. Neubauer, *Chem. Ber.*, **92**, 2046 (1959).
(289) A. Sonn, *ibid.*, **50**, 1292 (1917).
(290) J. Shinoda, *J. Pharm. Soc. Jap.*, No. 548, 834 (1927); *Chem. Abstr.*, **22**, 768 (1928).

8. *Tetracyanoethylene*

Tetracyanoethylene (**56**) has been prepared from **1** and sulfur monochloride[4,291] or from the vapor-phase chlorination–dehydrochlorination of **1** at 450°.[292,293] Pyrolysis of the condensation product of **1** and 1,3-bis(acetoxyimino)-2-propanone (**203**) also gives **56**. However, the preferred synthetic preparation of **56** involves **6**. **1** reacts with **56** to give tetramethylammonium 1,1,2,3,3-pentacyanopropenide (**204**) according to eq 149.[294]



(147)

(148)

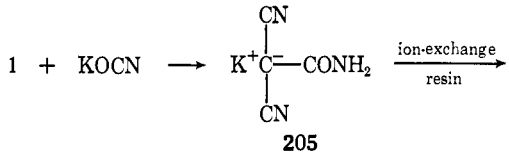
203

(149)

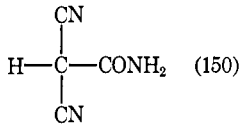
204

9. *Potassium Cyanate and Phosphorus Pentachloride*

Potassium carbamyldicyanomethanide (**205**) is obtained in 71% yield by the interaction of **1** and potassium cyanate in dimethylformamide.[150]

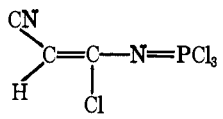


205

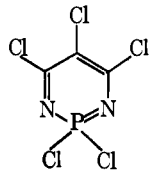


(150)

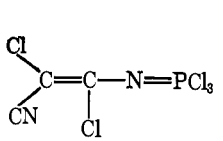
Heating (110–115°) an excess of **1** and phosphorus pentachloride[295] in benzene gives 40% **206** and 5–7% 1,1,3,4,5-pentachloro-1,2,6-phosphadiazine (**207**). When an excess of phosphorus pentachloride is used, **208** is formed in 85%



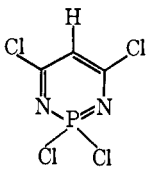
206



207



208



209

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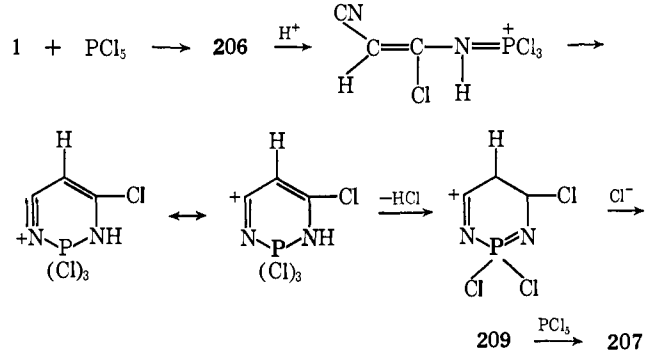
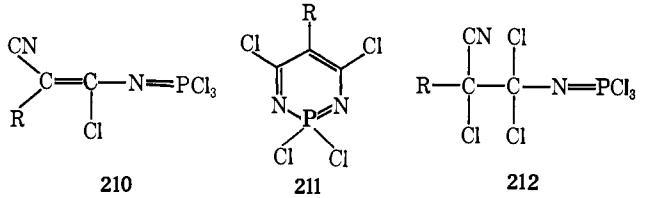
yield. An equimolar ratio of reactants at 20–25° gave a 75–80% yield of 1,1,3,5-tetrachloro-1,2,6-phosphadiazine (**209**). The cyclizations probably proceed *via* Scheme XV.

Scheme XV



Using a two molar excess of alkylmalononitriles[296] at 30–35° gave **210** and **211**, whereas a 25% excess of alkylmalononitriles at 20–25° gave **211** in 48–65% yields. If the



R	%
CH_3	17
CH_3CH_2	35
n-C_4H_9	32
n-C_3H_7	30
i-C_3H_7	48

211

212

R	%
Me	86
Et	57
Pr	53
i-Pr	61
Bu	84

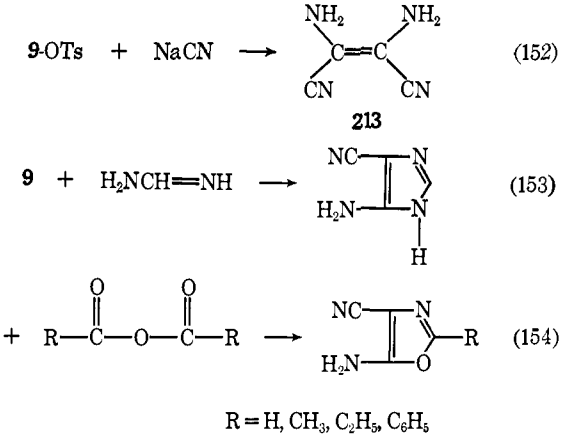
reaction mixture was saturated with dry HCl, **210** was obtained in 85–90% yield. Another product, **212**, was obtained by refluxing the dinitrile with an excess of phosphorus pentachloride.[296]

M. AMINOMALONONITRILE

Several incorrect reports have appeared concerning the synthesis of aminomalononitrile (**9**). Oro and Kimball[297] suggested that **9** was an intermediate in the synthesis of adenine from hydrogen cyanide and ammonia. Later, this low molecular weight intermediate was shown to be the hydrogen cyanide tetramer, diaminomaleonitrile. However, **9** is an intermediate in the polymerization of hydrogen cyanide.[298,299] The reported synthesis of **9** from **5** and ammonia by Ruske and Ruske[133] gives instead **56** and compounds derived from it (*vide infra*). **9** has been prepared[300] in 45–50% yields by the aluminum amalgam reduction of **175**.[264] The hydrogen

$$\mathbf{1} + NaNO_2 \xrightarrow{HOAc} \mathbf{175} \xrightarrow{Al(Hg)} \underset{\mathbf{9}}{H_2NCH(CN)_2} \qquad (151)$$

cyanide tetramer (diaminomaleonitrile, **213**) is obtained from the interaction of the tosylate salt of **9** and sodium cyanide. **9** is also a useful intermediate in the preparation of certain heterocyclic systems (eq 153, 154).[300]



(152)

(153)

(154)

R = H, CH_3, C_2H_5, C_6H_5

VII. Uses

1 is used widely in industrial and in biomedical applications. It is suggested that some of the studies of **1** on various biological systems be reinvestigated due to the inadvertent formation of **3** in alkaline solutions.[46]

A. INDUSTRIAL

Some of the industrial uses of **I** are: lubricating oil additive,[300] solvent for polyacrylonitriles,[301–303] polymerization,[304,305] herbicide,[306] defoliation–dessicant for broadleaf crops,[307] azomethine dyes,[308,309] resin with urea and an aliphatic aldehyde or furfural,[310] merocyanine-sensitizing dyes,[311] optical sensitizers,[312] washing and bleaching compositions,[313] polymers *via* a polyrecombination reaction,[314] reaction with polyacroleins,[315] dyeing polyacronitrile fibers,[75] ultraviolet filters,[316] polymers with 1-aziridinyl compounds,[317] stabili-

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Table XXII

Biomedical Uses of Malononitrile

Application or effect	*Ref*
Protection against toxic effect of X-ray and nitrogen mustard	322–325
Vitamin B_1 intermediate	326
Influence in neurotropic virus infections	327
Inhibitory effect on SH groups in bacteria	328
Lathyrogenic agent	329
Adrenolytic activity and adrenaline-blocking properties	330, 331
Effect on transfer of radioactive glycine to the brain	332
Synergy between sympathicolytic agents	333
Effect on spinal ganglion cells of *Rana pipiens*	334
Effect on metabolism	335, 336
Effect on growth of transplanted tumors in mice	193, 337
Regeneration of the nerves of the rabbit cornea	338, 339
Effects and fate in animal tissues	340
Restoration of nucleoproteins in central nervous system	341
Action on nerve cells in rabbits and guinea pigs	342, 343
Action on embryonic development of *Ambystoma mexicanum* and of *Rana temperaria*	344
Effect on cortical activity in rabbits	345
Lesions caused by poisoning rats	346
Lethal toxicity in mice	347
Effect on growth rate of flax seedlings	348
Effect on cerebral cortex in guinea pigs and rabbits	349, 350
Effects on incorporation of radioactive phosphates into the phospholipides of slices of cat brain	351
Influence on poliomyelitis in mice	352, 353

zation of methylchloroform,[310] extraction of aromatic compounds from mixtures of hydrocarbons,[318] cyanomethylidene quinoline dyes,[319] plant-growth inhibitors,[320] and elastomeric cross-linked copolymers of perfluorodiamidines and perfluoromonoamidines.[321]

B. BIOMEDICAL

Some of the many biomedical uses of **1** are shown in Table XXII.[193,322–353]

Acknowledgment. The author wishes to express his thanks to Dr. Penelope J. Cameron for her helpful comments and criticism during the preparation of the manuscript.

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