Properties and Reactions of Ylidenemalononitriles

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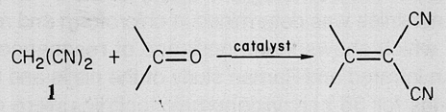
I. Introduction

Ylidenemalononitriles [**2**–**9**; alkylidenemalononitriles (**3**, **4**), cycloalkylidenemalononitriles (**5**), arylidenemalononitriles (**6**, **7**)] are usually the products of the Knoevenagel condensation between malononitrile (**1**) and carbonyl compounds.[1-16] Various



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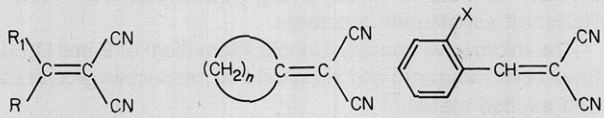
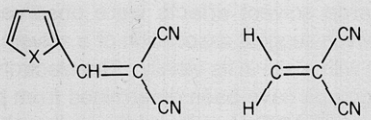


3, R = H; R_1 = alkyl
4, R = alkyl; R_1 = alkyl

5

6, X = H
7, X = Cl



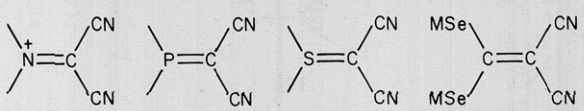
8, X = O or S 9

procedures for the preparation of ylidenemalononitriles have been described.[1,3,5]

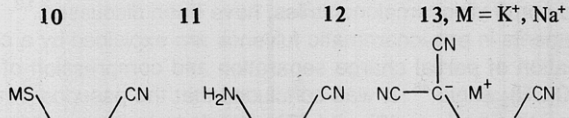
The simplest ylidenemalononitrile, 1,1-dicyanoethene (vinylidene dicyanide, **9**) may be prepared from the pyrolysis of tetracyanoethylene (TCNE),[17] 1-acetoxy-1,1-dicyanoethane,[18,19] 4,4-dicyanohexene,[20] 1,1,3,3-tetracyanopropane,[21] or dicyanoethyl acetate.[21]

This review, which covers the literature to 1979, will discuss the properties, reactions, and applications of ylidenemalononitriles. Particular attention will be given to 1,1-dicyanoethene (**9**) and to simple benzylidenemalononitriles (benzalmalononitriles, BMN) owing to their extensive chemical literature and their real and potential biomedical and industrial applications.[9] (2-Chlorobenzylidene)malononitrile (CS, **7**) is also of special interest because of its chemical properties and its role in antipersonnel (chemical warfare) and riot control devices.[9] Although a few cyclization reactions are discussed in this review, the annelation reactions of **2** have been described.[5] An excellent general review of benzylidenemalononitriles by Jones[9] and comprehensive reviews of the chemistry of malononitrile (**1**) by Freeman[1] and by Fatiadi[3] have been published.

The properties and reactions of *N*-dicyanomethylides (**10**), *P*-dicyanomethylides (**11**), *S*-dicyanomethylides (**12**), 1,1-di-

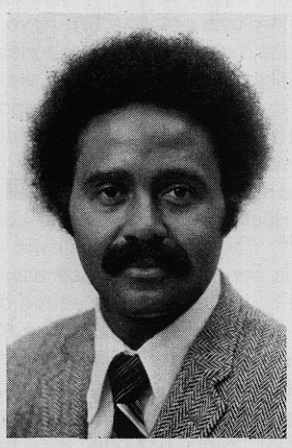


10 11 12 13, M = K^+, Na^+



14, M = K^+, Na^+ 15a 15b

selenoates (**13**) and their derivatives, 1,1-dithiolates (**14**), malononitrile dimer (2-amino-1-propene-1,1,3-tricarbonitrile, **15a**), and malononitrile trimer II (2-(cyanomethyl)-1,1,3,3-tetra-



Fillmore Freeman received his B.S. (1957) from Central State University, Wilberforce, Ohio, and his Ph.D. (1962, Professor H. Hart) from Michigan State University. After 2 years at the California Research Corporation he was an NIH Postdoctoral Fellow (1964–1965, Professor K. B. Wiberg) at Yale University. He joined the faculty at the University of California, Irvine, in 1973 after 8 years at California State University, Long Beach. He has been a Visiting Professor at the Université de Paris VII (Professor J. E. Dubois), at the University of Illinois, Chicago Circle (Professor J. Roček), and at the Max-Planck-Institut für Biophysikalische Chemie, Göttingen (Professor M. Eigen), a Fulbright-Hays Senior Research Scholar, and a Fellow of the Alexander von Humboldt-Stiftung. In addition to heterocyclic chemistry, Dr. Freeman's research interests include oxidation mechanisms, organosulfur chemistry, chemistry, and electrophilic addition reactions.

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cyanopropenide, **15b**) and other malononitrile trimers are not discussed.[1,3]

II. Properties

A. Molecular Structures and Spectral Properties

The crystal and molecular structures of several benzylidenemalononitriles have been reported.[22-27] Steric hindrance occurs between ortho substituents on the aromatic ring and the cyano groups.[22,25]

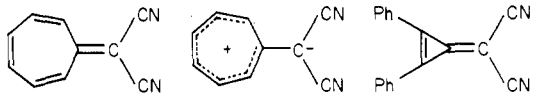
The π-electron structures for ylidenemalononitriles, and particularly for 1,1-dicyanoethene (**9**), have been calculated according to various molecular orbital theories.[28-45] The LCAO (Hückel)[28-34] modifications of the Pariser–Parr–Pople theory[34-37] and CNDO/2[38,39] calculations have been reported. LCAO molecular orbital methods were used to calculate the radical activity,[40] ionic polymerizability,[41] and polarographic reduction[42] of **9**. The relative pK values of **9** and other Lewis acids were estimated using Hückel MO method and compared with experimental data.[30] The tendency of Lewis acids to undergo Michael addition is correlated with their estimated pK values.

The relation of bond orders and electron densities, in ylidenemalononitriles, on the alteration of the π-electron energy in perturbed systems has been formalized by combining the Eyring theory of the activated condition with the equation of Coulson and Longuet-Higgins.[43] The linear combination of fragment configuration (LCFC) method has been used to predict the most stable structural isomer of the empirical formula $C_4H_2N_2$ (**9**).[44] The theoretical prediction that a 1,1-homodisubstituted molecule is more stable than the corresponding 1,2-isomer does not apply to **9** and its isomers owing to substituent overlap repulsion of the two cyano groups.

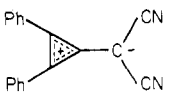
The effect of electrochemical behavior and electronic charge distribution on mono-, di-, and tricyano aromatic compounds was determined.[45] Molecular dipole moments were obtained and trends in half-wave potentials caused by variation in structure were correlated by means of the Hammett–Zeeman and molecular orbital approaches. Solution electrochemical techniques provide convenient means to study the effect of structural variations on molecular energy levels since it is known that polarographic reduction and oxidation potentials may be related to the corresponding gas-phase affinities and ionization potentials, respectively.[45]

The photoelectron spectrum of **9** and its assignment using various molecular orbital methods have been reported.[34]

The dipole moments (D) of substituted fulvenes, e.g., **16**, **17**,

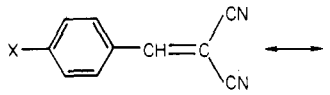


16a 16b 17a

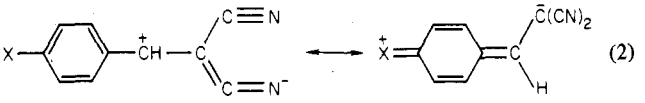


17b

and some ylidenemalononitriles, have been discussed.[1,3] The moments in pseudoaromatic fulvenes are explained by a combination of partial charge separation and compression of the $=C(CN)_2$ angle.[46] It was concluded that the pseudoaromatic structures such as **16b** and **17b** contribute to the ground state of the molecules. The dipole moments for a wide variety of ylidenemalononitriles were measured and found to agree with the values calculated by the LCAO method.[47] The dipole moments (D) for 5-, 7-, and 4-(dimethylamino)benzylidenemalononitrile are 3.5, 5.3, and 8.4, respectively.[38,47,48] Thus, polarity in the side chain[49,50] and conjugated resonance structures (**18**,



18a



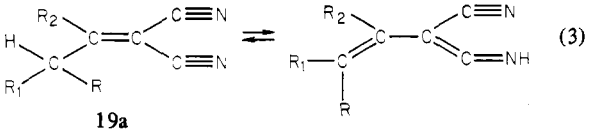
18b 18c (2)

eq 2) are important (cf. **16b**, **17b**).

The conjugated resonance structures are also supported by the observations that **6** does not react with ozone[51] or bromine, nitrous acid tends to substitute in the aromatic ring instead of reacting with the α,β carbon–carbon double bond,[52] and by the high extinction coefficients for ylidenemalononitriles in the ultraviolet.[47,48,50,53-63] Ylidenemalononitriles have λ_{max} values in the 282–313-nm region with the corresponding ϵ values systematically decreasing as the β-alkyl group increases in size.[57,64] However, in the 224–237-nm region, ϵ increases as the steric hindrance increases.

The dependence of the ultraviolet spectra of ylidenemalononitriles on hydrogen ion concentration indicated that ionization of the alkenyl carbon hydrogen bond α to the ring occurred.[59] pK_a's were determined and linearly related to Hammett σ values.[30,59] The charge-transfer peaks were also linearly related with σ.

The long-wavelength ultraviolet absorption band present in the spectra of some alkylidenemalononitriles has been shown[61] to be a result of anion formation and not of nitrile–ketenimine (**19a–19b**) tautomerism (eq 2, 3).[58,59,62]



19a 19b (3)

The infrared spectra of many ylidenemalononitriles have been obtained.[2,11,16,57,64-76] The effects of inductive, mesomeric, and steric factors are discussed for C≡N and C=C infrared band frequencies of α,β-unsaturated dinitriles.[69] Transfer of substituent polar effects to the infrared integral intensity of the C≡N group in ylidenemalononitriles was determined in chloroform and related to σ^+ values, which shows the importance of resonance contributions.[68] An infrared and Raman study of the nitrile and C=C stretching bands for 35 benzylidenemalononitriles were determined,[70] and the nitrile stretching frequencies were related to Hammett substituent constants.

The microwave spectra (Coriolis interaction) of **9** and $D_2C(CN)_2$ have been measured and assigned their respective ground states and excited states.[71]

The nuclear magnetic resonance spectra of a series of substituted benzalmalononitriles were determined in various solvents.[77-79] Large solvent effects were observed for the olefinic protons, which suggest association of a solvent molecule with the proton or with a site in its vicinity. The electronic effects of cyanocarbon groups have been determined from pK_a measurements and from ^{19}F NMR chemical shifts on fluorobenzene.[80] The ^{1}H and ^{13}C NMR spectra of substituted benzylidenemalononitriles have been reported in detail.[81-86] The ^{1}H chemical shift of the vinylic hydrogen may be correlated with σ or σ^+ substituent constants, and the ^{13}C chemical shift of the β-vinylic carbon correlates best with σ^+. Previously unreported σ^+ values are derived from these data.[81,86,87] Another implication of these data is that substituents on the phenyl rings serve to stabilize or destabilize the positive charge on the α-carbon atom (eq 2, 3).

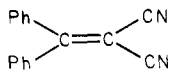
It appears that nitriles have not received much attention in

mass spectrometric studies owing to the complications generated by the presence of isobaric carbon–hydrogen and carbon–nitrogen ions and by complex fragmentation processes.[88–90] Nevertheless, mass spectrometry is a useful tool for identification of some ylidenemalononitriles.[16,91–96] The mass spectra of 8,8-dicyanoheptafulvene (**16**) and its derivatives have been obtained.[96] Bond-forming reactions occurring in the fragmentation of some α,β-unsaturated nitriles upon electron impact have been described.[93] A large number of common fragmentation and rearrangement reactions have been observed by the electron impact of **5**, **7**, and (3-nitrobenzylidene)malononitrile.[89,90,94,95]

The magnetic susceptibility of some ylidenemalononitriles has been determined.[97] Dorfman's theory gives a better correlation with experimental results than Pascals'. The paramagnetic susceptibility is related to dipole moment.

As expected, potentiometric titration of benzylidenemalononitriles demonstrates they are essentially neutral compounds.[98,99]

Substituted benzylidenemalononitrile anion radicals have been studied via electron spin resonance spectroscopy.[100–102] Two different anion radicals are observed for **6** in 1,2-dimethoxyethane by the successive additions of sodium–potassium alloy.[100] The hyperfine coupling constants for (α-phenylbenzylidene)malononitrile (**20**) are in good agreement with those calculated



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by McLachlan HMO theory.[101] In another study,[102] ESR coupling constants for the anion radicals of several substituted benzylidenemalononitriles correlated well with the corresponding substituted benzaldehyde anion radicals. However, there was only a poor correlation with the INDO calculated coupling constants. The observed ability of these para-substituted anion radicals to resist anionic polymerization and the ability of these compounds to deactive the growth of transplanted tumors in mice vary identically with the para substituent (NO_2 > CN > H > OCH_3 > CH_3).[102]

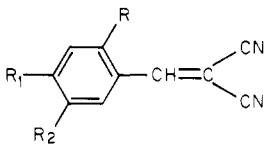
B. Toxicity and Analysis

The toxicity of benzylidenemalononitriles has been reviewed.[9,103] The effects of benzylidenemalononitriles on animals are fairly well documented, but their effects on humans are difficult to obtain, and some remain classified.[9] However, owing to the continuing interest of benzylidenemalononitriles as cytotoxic agents against tumors, as riot control agents,[104] and as chemical warfare agents,[2,9,103] more recent investigations are concerned with human exposure to these compounds. A few of the numerous more recent studies concerning animal exposure, human exposure, metabolism, and pharmacology of (2-chlorobenzylidene)malononitrile (CS, **7**) include toxicology,[105] toxicity,[106] pharmacology,[107] eye and skin toxicity,[108–113] effect of aerosol inhalation on human lungs,[114] effect on embryonic development,[115] possible relationship between CS and diarrhea,[116] toxicity in tobacco smoke,[117] irritant potential of dilute solutions,[118] acute effects of exposure and tolerance,[119] and the formation of cyanide from CS.[120]

In humans, CS produces erythema of the eyes, severe conjunctivitis, and an intense burning of the skin. The effects are manifested in the respiratory tract by coughing, burning of the throat, and feelings of chest congestion.[121,122] Another study[123] reported a differential racial response resulting from exposure to thermally generated aerosols of CS at high humidity and 37 °C.[9]

A detailed discussion of animal exposure to benzylidenemalononitriles, including values for LD_{50}, has been reported by Jones.[9] The inhalation toxicology and pathology of animals exposed to CS[124] and the effect of CS upon rabbit and rat development[125] have been reported. The effect of CS aerosols in monkeys has been described.[126]

Other 2-substituted benzylidenemalononitriles, especially the 2-nitro derivative **21**, are relatively effective irritants.[127] The



21, $R_1 = R_2 = H$; $R = NO_2$
22, $R = R_2 = H$; $R_1 = OH$
23, $R_1 = H$; $R = Cl$; $R_2 = NO_2$

strong effects of (4-hydroxybenzylidene)malononitrile (**22**) and (2-chloro-5-nitrobenzylidene)malononitrile (**23**) in uncoupling oxidative phosphorylation have been described in animal and plant systems. There do not appear to be any published reports concerning the use of benzylidenemalononitrile other than CS against humans.[9,103]

Gas–liquid chromatography is useful for detecting CS and other irritants.[128–131] Both malononitrile (**1**) and CS give intensely colored compounds with chloroanil, with maximum absorbance at 680–700 nm.[132] The sensitivity of this method of analysis is 2 μg/mL for CS and 1 μg/mL for **1** with a maximum error of 11%. CS may also be determined photometrically after its reaction with quinones.[133] The quinones [(optimum pH, λ (nm), sensitivity (μg/mL)] are chloroanil (6.4–6.8, 690, 2), *p*-benzoquinone (8, 600, 2), 1,4-naphthoquinone (6, 580, 1), and 1,2-naphthoquinone (8, 550, 1). Another spectrophotometric method for the quantitative analysis of CS has been reported.[134] This procedure is based on the formation of a yellow reaction product which results from the treatment of CS with methanal and sulfuric acid.

Arylidene (cinnamylidene or R-substituted benzylidene, where R = H, 2- or 4-OMe, 2- or 4-NO_2, 2- or 4-Cl, or 2-OH) derivatives of malononitrile are determined spectrophotometrically by measuring the absorbance at 408–432 nm of the orange-yellow products of their reactions with 1,3-dinitrobenzene in alkaline alcoholic solution.[135] Beer's law is obeyed in the parts per million region.

Malononitrile (**1**) and ylidenemalononitriles may be detected and quantitatively determined by reaction with benzofuran oxide in alkaline medium. The products give an intense violet color (580 nm).[136]

A modified Draize test is a useful predictive patch test procedure on human subjects to evaluate the skin sensitivization potential of CS and other compounds frequently found in commercial drug and cosmetic preparations.[137]

1,1-Dicyanoethene (**9**), which can be stabilized with organic sulfonic acids, sulfonyl halides, chlorosulfonic acid, and other compounds,[138,139] may be determined spectrophotometrically in solution via its cycloaddition reaction with anthracene.[140,141]

III. Reactions

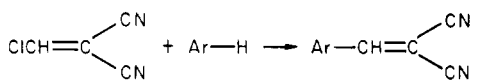
The dicyanomethylene functionality may also serve as a protecting group.[142] It appears to be very stable to a variety of electrophilic reaction conditions such as Friedel–Crafts acylation, chlorination with sulfuryl chloride, and hot mineral acids.[143] However, it may be cleaved by rather drastic treatment with concentrated alkali.[144] The dicyanomethylene group has been especially useful in protecting formylpyrroles.[143,144] Although the dicyanomethylene group is relatively stable, ylidenemalononitriles are reactive compounds which are valuable synthetic intermediates in the preparation of a wide variety of unique organic compounds.

A. Hydrolysis

Malononitrile (**1**) or the dicyanomethyl carbanion is usually one of the products from the mild hydrolysis of benzylidenemalononitriles (BMN).[145-153] The mechanisms for some of these hydrolyses have been discussed.[1,3,5] The hydrolysis (20% (v/v) EtOH) of benzylidenemalononitriles (BMN) in phosphate buffers in the absence or presence of cyanide ion has been reported to correlate with Hammett σ constants.[152]

$$\frac{-d[BMN]}{dt} = k_{H_2O} + k_{CN^-}[BMN][CN^-] \quad (4)$$

A new synthesis of aromatic aldehydes which involves hydrolysis of ylidenemalononitriles has been reported.[154] The procedure involves the reaction of a (chloromethylene)malonic acid derivative (**24**) with aromatic compounds in the presence



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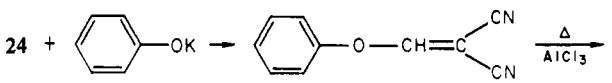

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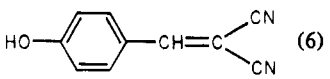

(6)

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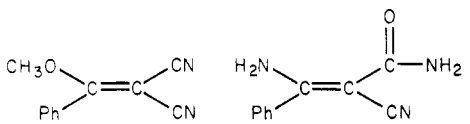
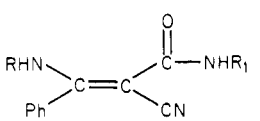
of $AlCl_3$ to give ylidenemalononitriles (eq 5) which are hydrolyzed to the corresponding aldehydes. Equation 6 shows the similar reaction of **24** and phenoxide ion.

Treatment of (α-methoxybenzylidene)malononitrile (**27**) with ammonium hydroxide gives **28**, which reacts with carbonyl compounds to give **29**.[155]



27 **28**



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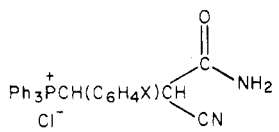
Although ylidenemalononitriles (**2**) are generally stable in dilute acid solution, various acid systems can hydrolyze one or both cyano groups.[5,156-160]

Ylidenemalononitriles are hydrolyzed in aqueous hydrochloric acid, in the presence of triphenylphosphine, to (1-aryl-2-carbamyl-2-cyanoethyl)phosphonium chlorides (**30**).[161] The rate of reaction and yields are enhanced with electron-attracting groups. Heating the phosphonium salts under reflux in ethanol



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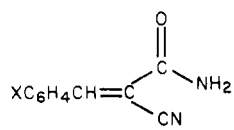

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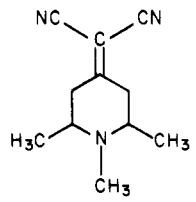
regenerates triphenylphosphine and the corresponding α-cyanocinnamide (**31**). Possible mechanisms for the formation of **30** could involve betaine and ketene imine intermediates.[161]

The acidic hydrolytic decarboxylation esterification of **32** to **33** is an intermediate step in the synthesis of 1,2,6-trimethylquinuclidine, which is a precursor of azabicyclic alkaloids.[162]



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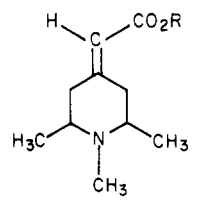

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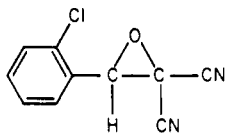
B. Oxidation and Reduction

Benzylidenemalononitriles do not react with ozone.[51]

Permanganate ion in acetone oxidizes benzylidenemalononitriles to the corresponding benzoic acids.[145]

2-Chlorobenzylidenemalononitrile (CS, **7**) reacts with hypochlorite ion to give the corresponding epoxide (**34**).[163] Presumably the epoxide (**34**) is the agent which augments the irritant effect of a mixture of **7** and hypochlorite bleaches.[164]



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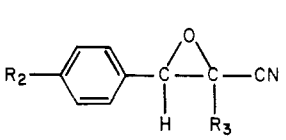
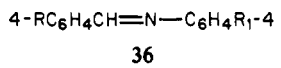


35, R_3 = CN, OEt

Oxazolidines (**37**) are obtained from the regiospecific addition of the epoxide-derived ylide from **35** to the imine **36**.[165] The



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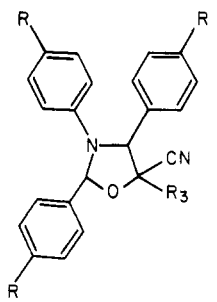
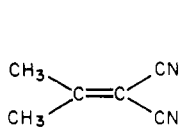


37

influence of ylide substituents and imine substituents on the reaction may be interpreted by interactions of the frontier molecular orbitals.

Isopropylidenemalononitrile (**38**) reacts readily with hydrogen peroxide under controlled pH conditions to produce the epoxide **39** (9%) and the epoxy amide **40** (69%). Hydrolysis of **39** or



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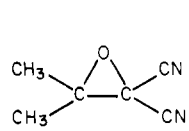

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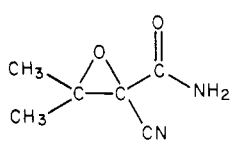
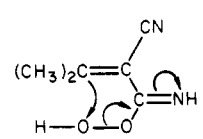
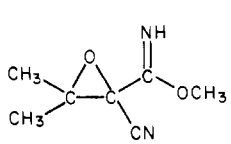


40

rearrangement of **41** could lead to **40**.[166] The epoxide **39** can be prepared in 45% yield from the alkaline *tert*-butyl hydroperoxide reaction with **38** in benzene. In methanol, the reaction gives methyl 3-methyl-2,3-epoxy-2-cyanobutyrimidate (**42**, 59%). The base-catalyzed hydrolysis of **39** also gives the imino ester **42**.[166]



41

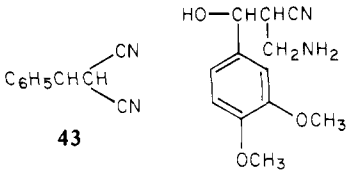


42

The reaction of superoxide anion radical with ylidenemalononitriles in 18-crown-6 ether gives atropic and benzoic acids.[167]

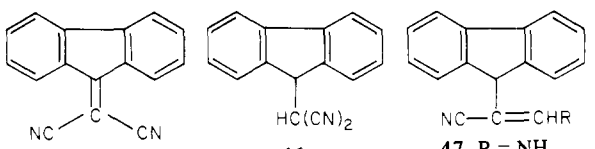
The selective reduction of carbon–carbon double bonds conjugated with cyano, nitro, or sulfonyl groups is achieved by heating the substrate with an azeotrope of formic acid with triethylamine in DMF.[168,169] Benzylidenemalononitrile (**6**) has also been selectively reduced to benzylmalononitrile (**43**) with potassium zinc borohydride in ether–THF,[170] with trialkyltin hydrides via protolysis of the organotin compound with ethanol,[171,172] and with lithium aluminum hydride at low temperatures.[173]

An excess of sodium borohydride reduces one cyano group in 3,4-dimethoxybenzylidenemalononitrile, and water adds across the α,β-double bond to give α-(aminomethyl)-3,4-dimethoxyhydroxyhydrocinnamonitrile (**44**).[174]



43 44

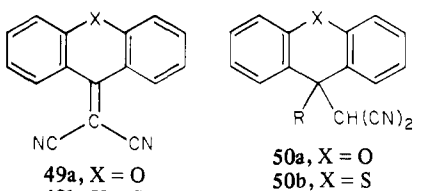
The reduction of fluoren-9-ylidenemalononitrile (**45**), which possesses well-defined cytostatic activity, with $LiAlH_4$ in THF at −10 to −15 °C under nitrogen gives fluoren-9-ylmalononitrile (**46**),



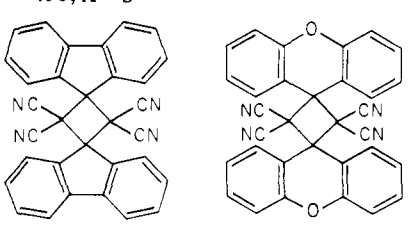
45 46 47, R = NH_2; 48, R = OH

via the deep red anion.[173] This process appears to be more efficacious than the isobutylmagnesium iodide reduction of **45**.[175–182] Treatment of **45** with $LiAlH_4$ in THF for 5 min at room temperature followed by addition of 20% potassium sodium tartrate solution gives 3-amino-2-(9-fluorenyl)acrylonitrile (**47**).[173] A similar reaction worked up with dilute sulfuric acid gave the enolic aldehyde **48** in high yield.

Although alkylmagnesium halides add to ylidenemalononitriles (**49**) to give the expected 1,4-adducts (**50**),[175,182] arylmagnesium



49a, X = O; 49b, X = S 50a, X = O; 50b, X = S



51 52

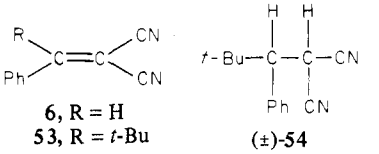
halides react with certain ylidenemalononitriles (**45**, **49a**) to give dimeric cyclobutane derivatives (**51**, **52**).[175–182] The nature of the products is dependent on the structure of the organometallic reagent and the ylidenemalononitrile. Ylidenemalononitriles which have a secondary β-carbon atom, e.g., the benzylidene and furfurylidene compounds, all behave alike and give 1,4-adducts regardless of the nature of the Grignard reagent. This is mainly because the steric requirements of these unsaturated nitriles, in contrast to the ylidene compounds which have a tertiary β-carbon atom, are not large.

In contrast to the analogous ylidenemalononitriles, xanthen-, thioxanthen-, and fluoren-9-ylidenecyanoacetates react with organomagnesium halides to give 1,4-adducts regardless of the nature of the Grignard reagent and its steric requirements.[183]

A noncyclic mechanism with polar orientation of reactants in the activated complex has been proposed for the reduction of cyclohexylidenemalononitriles and cyclohexylidenecyanoacetates with several alkylmagnesium chlorides.[179,180]

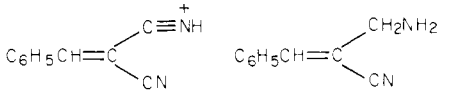
Benzylidenemalononitriles are active poisons of Raney nickel in the catalytic reduction of cyclohexene.[189]

Ylidenemalononitriles undergo smooth, efficient, and specific cathodic hydrogenation of the carbon–carbon double bond in the presence of added proton donors in aprotic solvents.[185] Cathodic reduction of α-*tert*-butylbenzylidenemalononitrile (**53**) in the presence of chiral proton donors ((−)-ephedrine or (+)-quinidine) gives a racemic product (**54**), which implies protonation is not the stereochemistry-determining step.



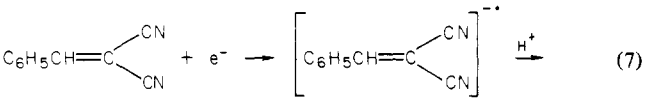
6, R = H; 53, R = *t*-Bu (±)-54

The reduction of benzylidenemalononitriles has been studied polarographically.[186–192] The half-wave potentials of phenyl-substituted derivatives for a series of conjugated heteroenoid compounds follow a Hammett relationship.[191] The mechanism of the reduction of benzylidenemalononitrile (**6**) at the dropping mercury electrode in 50% aqueous methanol changes with pH.[192] In acidic solutions the reduction proceeds via a four-electron transfer to a monoprotonated species (**55**) to give **56**.



55 56

Although hydrolysis of **6** to form benzaldehyde occurs at high pH values (6.8–11.4), in alkaline solutions two one-electron steps involving vinyl double bond reduction of the unprotonated species are observed (eq 7). Interestingly, at pH 5–6 the unprotonated



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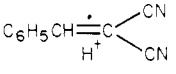
6 57



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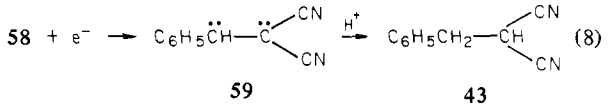
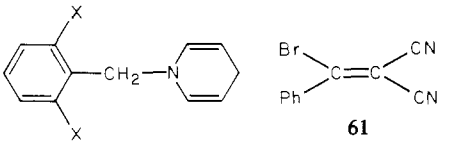


(8)

59 43

form of **6** is reduced at more positive potentials than the protonated form, which implies a change in the mechanism of the reduction process. It is generally thought that the protonated form of an electropositive species is reduced more easily than the unprotonated form.[192]

Benzylidenemalononitrile (**6**) is asymmetrically reduced with a chiral NAD(P)H model compound in the presence of magnesium perchlorate, which represses a base-catalyzed side reaction.[193] The double bond in ylidenemalononitriles is reduced by the dihydropyridines (**60**).[194] The direct transfer of hydrogen



60, X = H or Cl 61

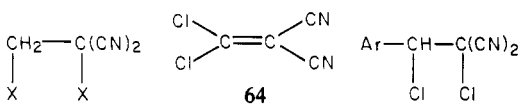
from position 4 of **60** to the carbon atom in the β position to the cyano group was demonstrated with tritium-labeled **60**. Debromination to **6**, instead of reduction of the double bond, occurred with **61**.[194]

C. Unsaturated Compounds, Cyclizations, and Dimerizations

The discussion in this section will be concerned with the reactions of ylidenemalononitriles with unsaturated carbon compounds and with the chemical reactivity of the olefinic linkage in ylidenemalononitriles. Photochemical and thermal reactions are described in Section H. Dimerization in the Grignard reaction is described above.

Although ylidenemaloninitriles have been reported not to add ozone,[51] bromine, nitrous acid,[52] Br^-, I^-, or SCN^-,[195] they do react with HCN and hydrazoic acid in the presence of acetic acid.[145,151,162,195]

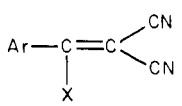
Bromine or chlorine adds to the carbon–carbon double bond of **9** to give **62** or **63**. Successive dehydrochlorination, chlo-



62, X = Br
63, X = Cl

64

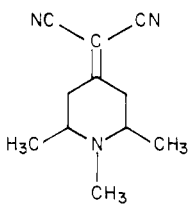
65



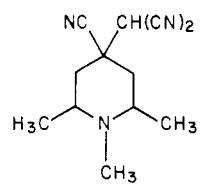
66, X = Cl
67, X = F

rination, and dehydrochlorination of **63** gives **64**.[51,52,196,197] Chlorination of benzylidenemalononitriles affords the corresponding α,β-dichloro compounds (**65**), which, on reaction with tertiary amines, leads to (β-chlorobenzylidene)malononitriles (**66**) after dehydrochlorination.[198] Halogen exchange with **66** gives the corresponding (β-fluorobenzylidene)malononitriles (**67**) in good yields.

The terminal α,β-unsaturated dicyanomethylene group adds hydrogen cyanide with formation of polycyano derivatives.[145,162] For example, compound **62** is converted into the new cyanocarbon acid (**68**), which can be isolated as its hydrochloride or its resonance-stabilized salt.[162]



62



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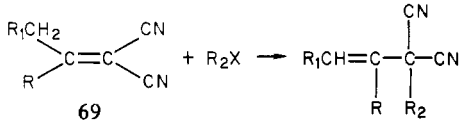
Ylidenemalononitriles (**69**) may be alkylated (**70**) with alkyl halides in the presence of sodium alkoxides[13] (eq 9). The

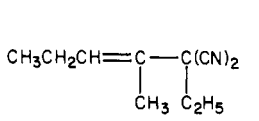


(9)

69 **70**

alkylation of the sodium derivative obtained from (1-methylbutylidene)malononitrile with ethyl iodide, ethyl bromide, or ethyl sulfate gave a mixture of (1-methyl-1-butenylethyl)malononitrile (**71**) and the corresponding imino ether (**72**).[13,199,200]

Cyclic dicyano and tetracyano compounds of the general formula $R[CH_2CH(CN)_2]_n$, where n = 1 or 2 and R is a mono-



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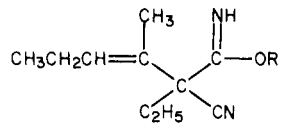
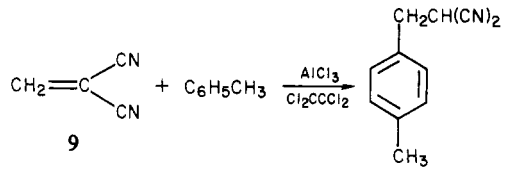


72

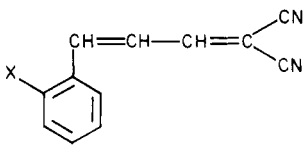
or disubstituted radical or a substituted or unsubstituted polynuclear radical, are prepared from ylidenemalononitriles.[201,202] An example (**73**), involving **9**, is shown in eq 10.



(10)

9 **73**

Conjugated ylidenemalononitriles (**74**) undergo Michael addition (**75**) with the dicyanomethyl anion (eq 11).[13,15,203,204]



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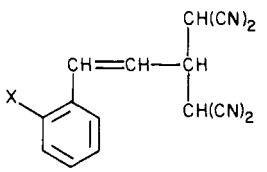

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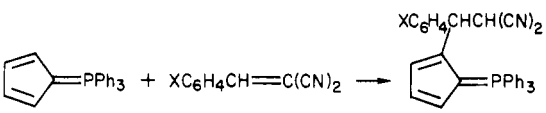
75

Third-order rate constants (k_3) for the acid-catalyzed nucleophilic addition of cyclopentadienyltriphenylphosphorane (**76**) to a series of benzylidenemalononitriles (eq 12) in benzene

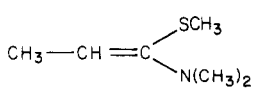


(12)

76 **77**

solvent have been obtained.[205] Thermodynamic parameters ($E^‡$ = 5.0 to 5.2 kcal mol^{-1}, $\Delta S^‡$ = −36 to −55 eu, $\Delta F^‡$ = 10.9 to 15.6 kcal mol^{-1}) were also obtained. A possible mechanism, which involves π complex formation, has been discussed. The λ_{max} and equilibrium constant (K_π) values for π complexes of benzylidenemalononitriles with *N,N,N′,N′*-tetramethyl-*p*-phenylenediamine have been reported. A linear free energy relationship between k_3 and K_π has been demonstrated.

Stable 1,4-dipolar compounds are possible from ketene acetals and ylidenemalononitriles.[206] Treatment of **78** with **79**



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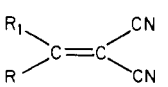
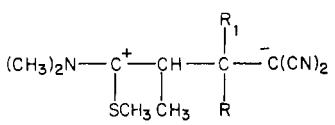
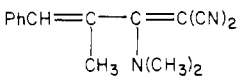


6, R = H; R_1 = Ph
38, R = R_1 = CH_3
79, R = H; R_1 = 4-$O_2NC_6H_4$
80, R = R_1 = CF_3
81, RR_1 = $(CH_2)_5$



82, R = H, R_1 = 4-$O_2NC_6H_4$
83, R = R_1 = CF_3

or **80** gives stable red-orange (**82**) or yellow (**83**) compounds, respectively. The product from **6** and **78** is unstable, and reacts further to give **84**. Compound **38** reacts with **78** to give **85** while cyclohexylidenemalononitrile (**81**) and **78** react to give 1-methyl-5-amino-6-cyano-1,2,3,4,7,8,9,10-octahydrobenzo[*h*]-quinoline (**86**).



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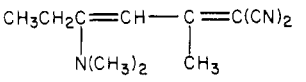

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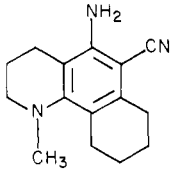
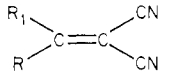
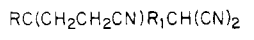


86

Cross-cathodic dimerization of 1,1-dicyano-2-methyl-1-propene (**38**) and its analogues (**87**, **88**) with acrylonitrile and methyl



38, R = R_1 = CH_3
87, R = CH_3; R_1 = alkyl
88, RCR_1 = cyclopentylidene



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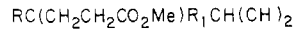
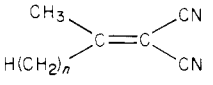


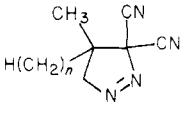
90

acrylate was carried out in a diaphragm electrolyzer to give the reduction addition products **89** and **90**, respectively. Current yields, which were correlated with the Taft equation, decreased with increasing length and branching in the alkylidene group.[207]

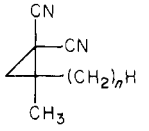
At −15 °C isopropylidenemalononitrile (**38**) reacts with an equimolar amount of diazomethane (CH_2N_2, **91**) to yield the pyrazoline **92**, which loses nitrogen upon heating to give 2,2-



38, *n* = 1
94, *n* = 2



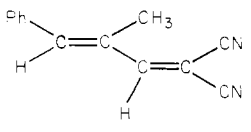
92



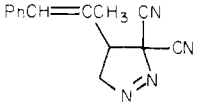
93, *n* = 1
95-99, *n* = 2-5

dimethyl-1,1-dicyanocyclopropane (**93**) and 2-butylidenemalononitrile (**94**). At room temperature, with an excess of **91**, **38** gives a number of homologous 2-methyl-2-*n*-alkyl-1,1-dicyanocyclopropanes (**95–99**) via the corresponding homologous alkylidenemalononitrile.[208]

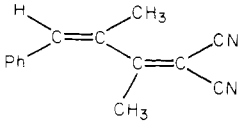
Diazomethane (**91**) adds regiospecifically and stereospecifically to **100** and **101** to give the thermally labile pyrazolines **102** and **103**, respectively. Thermolysis of **102** and **103** gives the corresponding ylidenemalononitriles **104** and **105**.[209]



100, *E*
101, *Z*

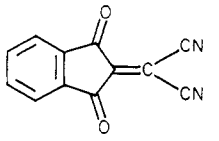


102, *E*
103, *Z*



104, *E*
105, *Z*

2-(Dicyanomethylene)-1,3-indandione (**106**) can be epoxidized on treatment with diphenyldiazomethane and 9-diazofluorene to produce the interesting spirocyclopropane derivatives **107** and **108**, respectively.[211] 9-Diazofluorene also reacts with other



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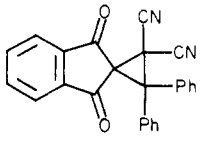

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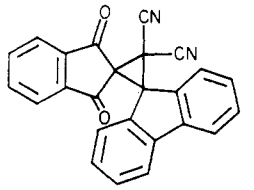
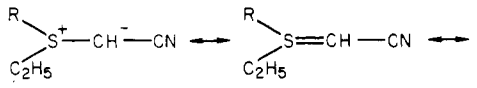


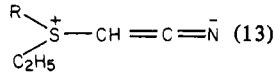
108

ylidenemalononitriles to afford cyclopropane derivatives[212a] and unstable pyrazolines.[212b]

The nitrile-stabilized sulfur methylides (**109**) react with **6** to give tricyanocyclopropane (**111**)[213] (eq 13, 14).

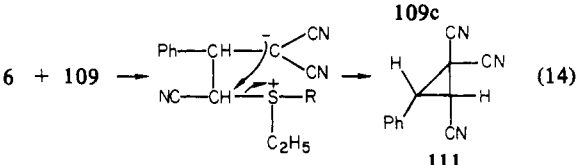


109a 109b



(13)

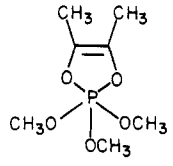
109c



(14)

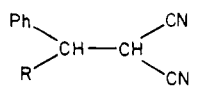
110 111

Dicyanocyclopropanes are formed by the reaction of ylidenemalononitriles and 1,3,2-dioxaphospholene (**112**), which is available from the reaction of $P(OCH_3)_3$ and 2,3-butanedione.[214]

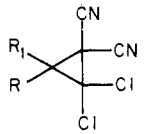


112

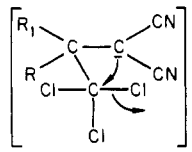
Benzylidenemalononitrile (**6**) reacts with 3-oxopropanoic acid[215a] and trichloroacetic acid[215b] to give the decarboxylated addition products **113** and **114**, respectively. Ylidenemalono-



113, R = CH_2OCCH_3
114, R = CCl_3



115



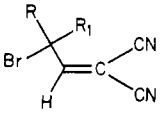
116

nitriles and trichloroacetic acid give a wide variety of substituted 1,1-dichloro-2,2-dicyanocyclopropanes (**115**). Presumably, cyclopropanation does not involve dichlorocarbene, but the trichloromethylated derivative **116**.[215a]

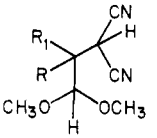
A novel, simple cyclopropane synthesis involves the reaction of ylidenemalononitriles, e.g., **28**, **81**, with nitromethane in the presence of base.[216]

(2-Bromo-2-methylpropylidene)malononitrile (**117**) and [(1-

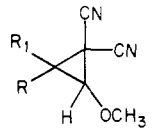
bromocyclohexyl)methylidene]malononitrile (**118**) react with pyridine in methanol to give 1,1-dicyano-2,2-dimethyl-3,3-dimethoxypropane (**119**, 80%) and (1-(dimethoxymethyl)cyclohexyl)malononitrile (**120**, 75%), respectively.[217] The mechanism,



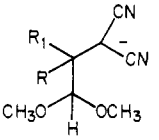
117, $R = R_1 = CH_3$
118, $R\text{-}R_1 = (CH_2)_5$



119, $R = R_1 = CH_3$
120, $R\text{-}R_1 = (CH_2)_5$



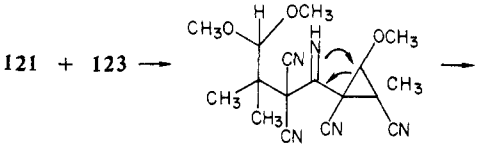
121, $R = R_1 = CH_3$
122, $R\text{-}R_1 = (CH_2)_5$



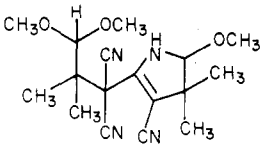
123, $R = R_1 = CH_3$
124, $R\text{-}R_1 = (CH_2)_5$

which is similar to the Favorskii rearrangement, involves an unstable cyclopropane intermediate (**121**, **122**). Nucleophilic attack at the 2-position of cyclopropane (**121**, **122**) produces an anion (**123**, **124**) which leads to the open acetal (**119**, **120**).

Changing the weak nucleophilic and basic medium of pyridine/methanol to sodium methoxide in methanol leads to a significantly different reaction outcome. For example, the active allylic bromide **117** gives **119** (20%) and the Δ^2-pyrroline dimer (**126**, 65%) in strong base. The mechanism probably involves a Thorpe reaction between the acetal anion (**123**) and the cyano



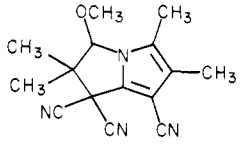
125



(15)

126

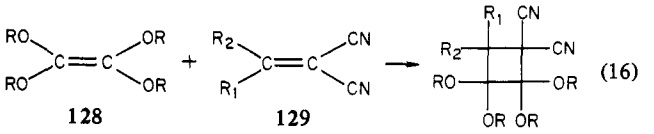
group of the cyclopropane (**121**) to give the α-cyano imine adduct (**125**) which subsequently yields **126**. Δ^2-Pyrrolines, e.g., **125**, are aromatized to 1,2-dihydro-3*H*-pyrrolizines, e.g., **127**, via a concerted 1,2-alkyl shift and expulsion of methanol and elimination of a proton, in strong acid.[217]



127

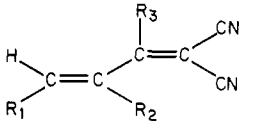
Electrophilic ylidenemalononitriles undergo [2 + 2] cycloadditions with electron-rich (nucleophilic) alkenes to give substituted cyclobutanes (eq 16),[218-223] which may be converted to cyanocyclobutene or 1,2-cyclobutenedione derivatives.[219,221] The conjugated ylidenemalononitriles (**131**) undergo [2 + 2] cycloaddition with **128**, instead of [4 + 2] cycloaddition, to give **132**, which are easily converted to **133**[220,221] (eq 16). Bulky or electron-releasing substituents at the 2-position in ylidenemalononitriles retard cyclobutane formation.[218]

Benzylidenemalononitrile (**6**) reacts with the enamine **134** to give a 2:1 adduct (**135**) which can be hydrolyzed to **136**.[224] The 1:1 adduct (**137**) of **6** and **134** is unstable. However, **6** reacts with **138** to give the stable 1:1 adduct **139**. 1,1-Dicyano-3-

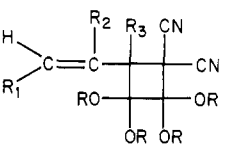


(16)

128 **129** **130**



131



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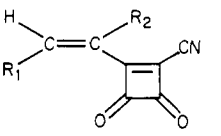

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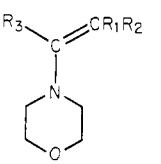
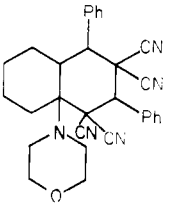


134, $R_1 = H$, $R_2\text{-}R_3 = (CH_2)_4$
138, $R_1 = R_2 = CH_3$; $R_3 = H$



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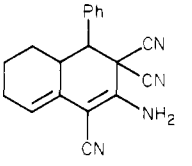

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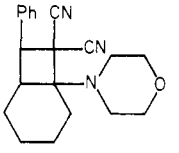

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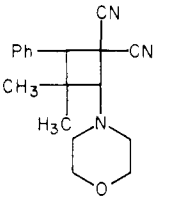
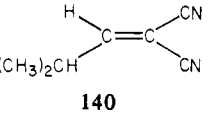
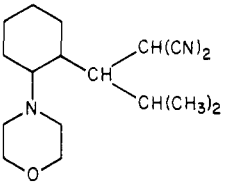


139

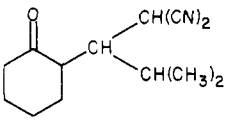


140

methyl-1-butene (**140**) reacts with **134** to produce **141**, which is hydrolyzed to **142**.

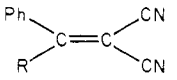


141



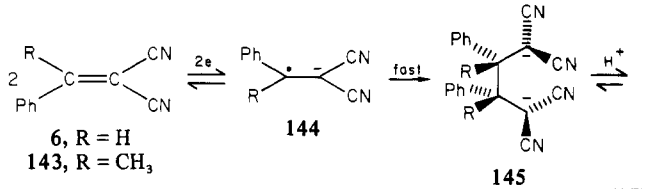
142

The data above and below[185,207] and theoretical considerations suggest that electrochemistry could be a convenient and useful technique for the preparation of new monomers and dimers of malononitrile (**1**).[225-232] A comparison[185] of the cathodic reduction of the carbon–carbon double bond in **20** vs. catalytic hydrogenation of sodium borohydride[253] suggests electrochemistry is the preferred method of reduction when dimerization is precluded. Although compounds **23** and **54** undergo simple reduction of the carbon–carbon double bond (vide supra), mixtures of stereoisomeric cyclic hydrodimers (**147**) are the only products of similar reduction of **6** and **143**.[185]



6, R = H
20, R = Ph
54, R = *t*-Bu
143, R = CH_3

A cyclic voltammetric study[185,232] led to the conclusion that rapid combination of radicals took place after electron transfer (eq 17). This conclusion is consistent with the mechanism

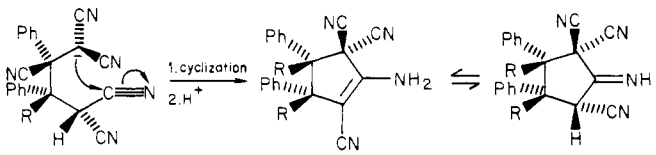


6, R = H
143, R = CH_3

144

145

(17)

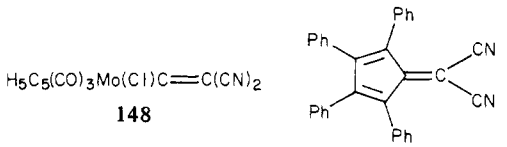


146 **147a** + isomer **147b**

established for the hydrodimerization of other activated olefins at low concentrations.[234]

The mechanism of the electrodimerization of (4-methylbenzylidene)malononitrile was studied by convolution potential sweep voltammetry (CPSV), which is a more powerful tool than linear sweep voltammetry for discriminating among numerous mechanistic possibilities.[231] The rate constant was determined and the mechanism involves coupling of the radical–radical type.[230,231]

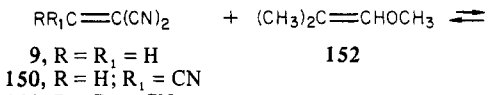
Reaction of **148** with diphenylacetylene in boiling benzene results in a novel cyclization of 1,1-dicyanoethene (**9**) with two diphenylacetylene units to give 6,6-dicyano-1,2,3,4-tetraphenylfulvene (**149**).[235]



148 **149**

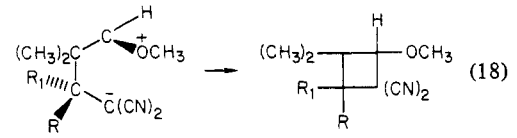
The [2 + 2] (vide supra) and [4 + 2] (Diels–Alder) reactions of polycyanoolefins [acrylonitrile, fumaronitrile, maleonitrile, **9**, 1,2-dicyanoethene, tricyanoethene, tetracyanoethene (TCNE)] are of considerable synthetic and theoretical interest.[236-247] The kinetics and mechanisms of the reactions of various polycyano olefins with phencyclone,[236] isoprene,[237] 1,3-butadiene,[237] 2-(trifluoromethyl)butadiene,[237] 1,3-diphenylisobenzofuran,[238] cyclopentadiene,[239,242-244] 9,10-dimethylanthracene,[239,242,243] 9-methylanthracene,[240] anthracene,[240] and 9,10-dimethoxyanthracene[241] have been reported. A dienophilic scale, D_i, was derived from the rate constants of the Diels–Alder reaction of cyclopentadiene with various dienophiles, including **9**, in dioxane at 30 °C.[244]

An interesting comparison of the possible activated complexes for [2 + 2] and [4 + 2] cycloaddition reactions involving polycyanoolefins has been reported.[239] On going from acrylonitrile to TCNE, one observes a (4×10^7)-fold increase of the rate constant toward cyclopentadiene and a (1.5×10^{10})-fold increase vs. 9,10-dimethylanthracene.[242-244] In contrast, the rate constants of [2 + 2] cycloadditions of polycyano olefins to isobutenyl methyl ether (**152**), in the sequence 1,1-dicyano- (**9**) < tricyano- (**150**) < tetracyanoethene (**151**), decrease by a factor of 16. Moreover, acrylonitrile and fumaronitrile did not react with **152**,



9, R = R_1 = H
150, R = H; R_1 = CN
151, R = R_1 = CN

152



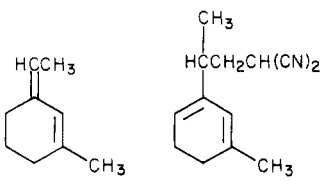
(18)

153 **154**

and **150** afforded *E*–*Z* isomeric cyclobutanes.

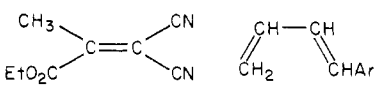
The reasons for these divergent substituent effects are explicable in terms of an early transition state (reactant-like) for the [4 + 2] reaction and a late transition state for the [2 + 2] cycloaddition.[239] The addition of polycyano olefins to cyclopentadiene and 9,10-dimethylanthracene belongs to the "normal" Diels–Alder reactions, which are HO(diene)–LU(dienophile) controlled. The successive introduction of cyano groups lowers the HO and LU energies of ethene. Thus, the diminishing frontier orbital separation corresponds to a greater energy gain in the activated complex. In contrast, the slow step of the [2 + 2] cycloaddition bears a structural similarity to the zwitterion rather than to reactants. Consequently, the MO energies of the reactants suffer gross changes before the activated complex is reached.

1,1-Dicyanoethene (**9**) undergoes the ene reaction with **155** to give the cyclo-hexadiene **156**, which can give a Diels–Alder adduct with a second mole of **9**.[239]

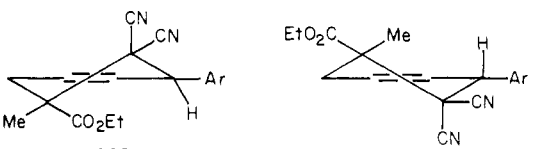


155 **156**

Ethyl(2-dicyanomethylene)propanoate (**157**)[249] is a useful dienophile in the in the Diels–Alder reaction.[250] Reluxing **157**



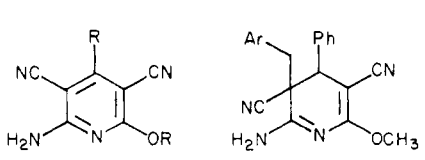
157 **158**



159 **160**

with **158** in benzene gives a mixture of isomers (**159**, **160**) in a ratio of 2.2:1. These compounds (**159**, **160**) are valuable precursors in the total synthesis of natural products.[250]

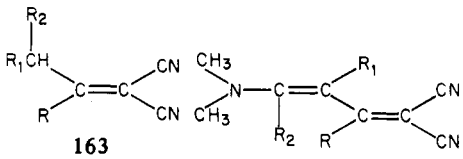
Many of the reactions of ylidenemalononitriles and malononitrile or the dicyanomethyl anion have been described.[1,3,13,15,203,204] The reaction of malononitrile with benzylidenemalononitriles in the presence of an alcohol–alkoxide system provides a convenient route to 2-amino-3,5-dicyano-4-substituted-6-alkoxypyridines (**161**).[1,3,251-253] The mechanism involves Michael addition of the dicyanomethyl anion to the ylidenemalononitrile. The reaction does not proceed with iso-



161 **162**

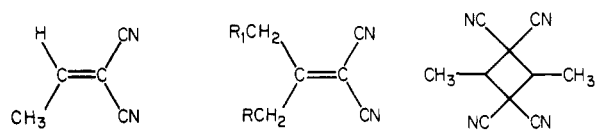
propyl or *tert*-butyl alcohol. Benzylmalononitrile (**43**) and **6** react in methanol–sodium methoxide to give 2-amino-3-benzyl-3,5-dicyano-6-methoxy-4-phenyl-3,4-dihydro-pyridine (**162**).[253]

4-(Dimethylamino)-1,3-butadiene-1,1-dicarbonitriles of the type **164**, which are precursors for the synthesis of heterocyclic compounds,[254] are readily available from the reaction of ylidenemalononitriles (**163**), lithium diisopropylamide, and dimethylformamide dichloride ($ClCH{=}N^{+}(CH_3)_2Cl^{-}$).[255,256] Ring closure, with loss of dimethylamine in aqueous or methanolic ammonia, gives 2-amino-3-cyanopyridines (**165**).[255,257-259] Thio-substituted pyridines are also available via this method.[255,260]



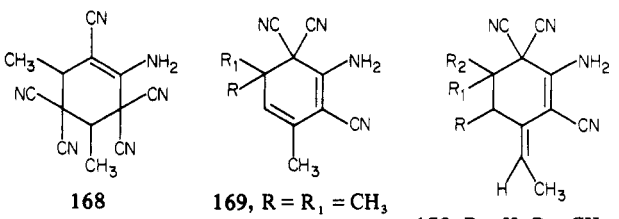
163 164 165

The mechanisms for the chemical dimerization of several ylidenemalononitriles have been discussed (ref 1, 3, 11, 15, 145, 148, 252, 260–269). The base-catalyzed dimerization[145,148] of ethylidene- (**143**),[266,269] isopropylidene-, (**38**),[263,264] 2-butylidene-



38, R = R_1 = H
81, RR_1 = $(CH_2)_3$
94, R = H; R_1 = CH_3
166, R = R_1 = CH_3

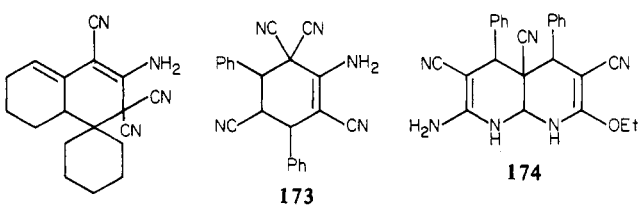
167



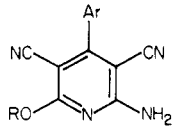
168 169, R = R_1 = CH_3 170, R = H; R = CH_3; R_1 = CH_3CH_2 171, R_1 = R_2 = CH_3CH_2

(**94**),[264] and 3-pentylidenemalononitrile (**166**)[264] gives **167** or **168**, **169**, and **170**, respectively. Cyclohexylidenemalononitrile (**81**)[11,264,265] and benzylidenemalononitrile (**6**)[266] give the dimers **172** and **173** or **174**, respectively.

Under slightly different experimental conditions, benzylidenemalononitriles give 2-amino-3,5-dicyano-4-aryl-6-alkoxypyridines (**161**, **175**).[252,267] Dimers have also been obtained from cyclopentylidene-[11] and (β-methylbenzal)malononitrile.[264]

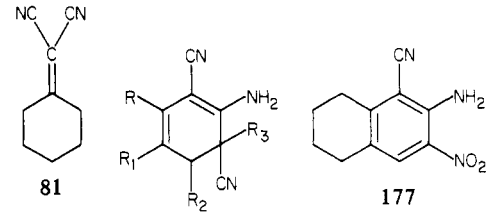


172 173 174

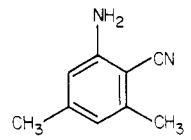


175

The base-catalyzed reaction of ylidenemalononitriles with ylidenemalononitriles or with the monoethyl esters of monocyano malonic acid gives the cyclohexadiene **176**, which loses either



81 176 177



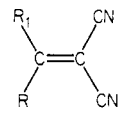
178

HCN or CO and ethyl alcohol to produce 2,6-dicyanoaniline. Compound **176** (RR_1 = $(CH_2)_4$; R_2 = Ph; R_3 = CN) is formed directly from the reaction of malononitrile, benzaldehyde, and cyclohexanone. The addition product of **81** and β-nitrostyrene undergoes immediate dehydration to 2-amino-1-cyano-3-nitro-4-phenyl-5,6,7,8-tetrahydronaphthalene (**177**).[268a]

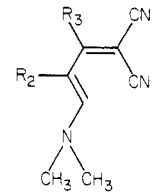
The condensation product of mesityl oxide and malononitrile cyclized to the benzonitrile (**178**) and refluxing pulegone with malononitrile gives 2-amino-4,7-dimethyl-5,6,7,8-tetrahydro-1-naphthalenecarbonitrile.[268b]

D. Oxygen Compounds

A convenient synthetic method has been described for the preparation of 4- and 5-substituted 2-halonicotinic acid derivatives.[270] The condensation of ylidenemalononitriles (**6**, **92**, **143**, **179**, **180**) with either DMF acetal (method A) or ethyl orthor-

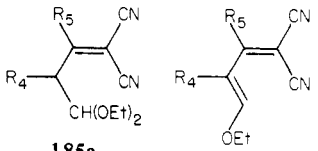


6, R = H, R_1 = C_6H_5
38, R = R_1 = CH_3
81, RCR_1 = cyclohexylidene
88, RCR_1 = cyclopentylidene
92, R = CH_3; R_1 = C_2H_5
143, R = CH_3; R_1 = C_6H_5
179, R = H; R_1 = C_2H_5
180, R = C_2H_5; R_1 = C_6H_5



181, R_2 = CH_3; R_3 = H
182, R_2 = H; R_3 = C_6H_5
183, R_2 = H; R_3 = C_6H_5
184, R_2 = CH_3; R_3 = C_6H_5

formate and zinc chloride in acetic anhydride (method B) yields the equivalent of a β,γ-unsaturated aldehyde (**181–184**) or **185**,

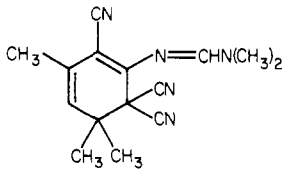


185a 185b

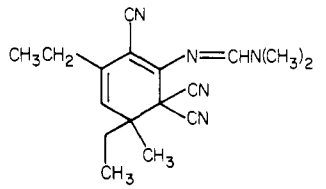
respectively, which undergoes cyclization with acid to provide polysubstituted pyridines. No products are obtained with **38**, **81**, and **88** via method A. Method A is severely limited by the formation of dimeric type derivatives **186**, **187**, **188**, and **189** from **38**, **92**, **81**, and **88**, respectively.

Method B, which yields the corresponding β,γ-unsaturated acetals (**185a**) as the major products, has more utility and versatility than method A. The unsymmetrical olefin **143** reacts via method A and method B, in a regiospecific manner, to yield two different β,γ-unsaturated aldehyde equivalents, **183** and **190**, respectively.

The product resulting from heating 1-cyano-1-pentenenitrile (**179**) with ethyl orthoformate in acetic anhydride is refluxed with



186



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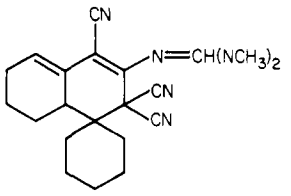

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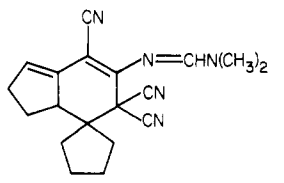

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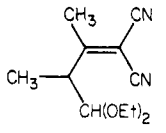

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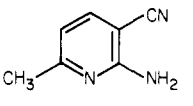
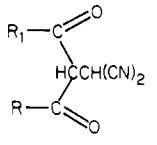


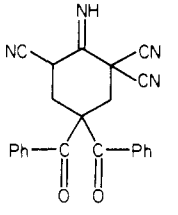
191

ammonia in order to produce **191**. Compound **191** is an intermediate for the manufacture of pyridopyrimidines which are useful herbicides.[271-274]

Treatment of **9** with 2,4-pentanedione and ethyl acetoacetate, at 100–120 °C without catalyst, gives **192** (64%) and **193** (70%), respectively. Similarly, dibenzoylmethane gives **194** and **195**.[275,276] Other 1,3-dicarbonyl compounds react with **9** or its



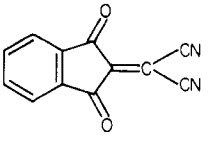
192, $R = R_1 = CH_3$
193, $R = CH_3$; $R_1 = OC_2H_5$
194, $R = R_1 = C_6H_5$



195

homopolymer without catalyst or with P_2O_5 (polymerization inhibitor) in chloroform.

2-Dicyanomethylene-1,3-indandione (**106**) reacts with phenols to give (hydroxyphenyl)-1,3-dioxo-2-indanylmalononitriles which lose HCN to yield oxonole-type polymethines [(hydroxyphenyl)(1,3-dioxo-2-indanylidene)acetonitriles (**196**)] with the



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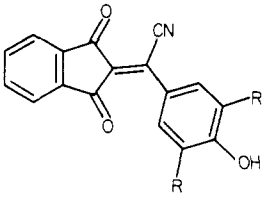

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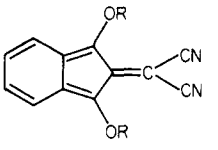
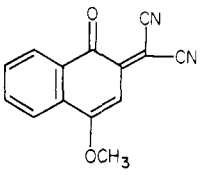


197, R = H
198, $R = CH_3$

properties of pH indicators.[275] With 2,6-dialkylphenols, **197** becomes the major product. Treatment of **197** with diazomethane (**91**) gives (1,3-dimethoxy-2*H*-inden-2-ylidene)malononitrile (**198**). In contrast to the cyclopropanation reactions described above, **106** reacts with **91** to yield 2-dicyanomethylene-4-methoxy-1,2-dihydro-1-naphthalenone (**199**; cf. **107**, **108**). Similarly, the 3-(dicyanomethylene)oxindoles (**200a–d**) react with **91** to give *O*-methyl derivatives of 2-hydroxy-1,4-dihydroquinoline (**201**).[276] Phenyldiazomethane reacts with **200a**



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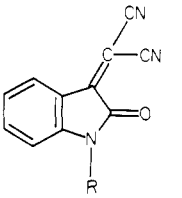
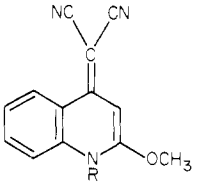
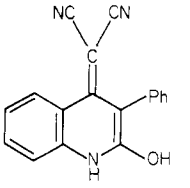


200a, R = H
200b, R = OH
200c, $R = CH_3$
200d, $R = OCOCH_3$



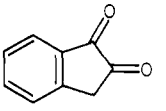
201a, R = H
201b, $R = OCH_3$
201c, $R = OCOCH_3$



202

to afford the 2-hydroxy-1,4-dihydroquinoline derivative **202**, which exists almost entirely in the enol form. The acid hydrolysis of **200** has been described.[276]

Compound **204** undergoes a novel coupling reaction with 1,2-indandione (**203**) to give **205**.[3] Similarly, 1,1,3,3-tetra-



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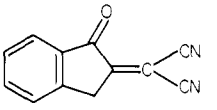

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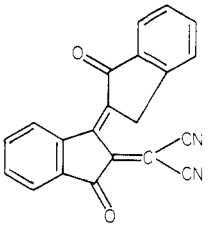
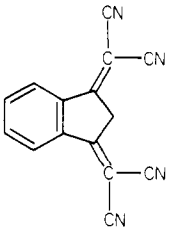


205

cyanoindandimethane (tetracyanoindan, **206**)[277] condenses with benzaldehydes to give benzylideneindans (**207**, 70–94%).[278]



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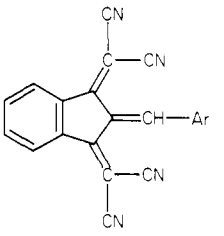
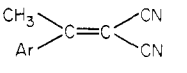


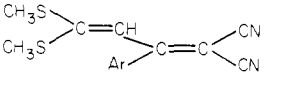
207

The kinetically controlled nucleophilic attack of methoxide ion on conjugated ylidenemalononitriles takes place at the β-carbon atom, and the negative charge is delocalized over the cyanomethide fragment. The initially formed 1,2-carbanionic adducts isomerize spontaneously to the thermodynamically more stable 1,4- or 1,6-adducts.[279]

Push–pull butadienes (**209**) are prepared in 36–50% yields by adding **208** to sodium ethoxide and then adding a mixture of



208



209

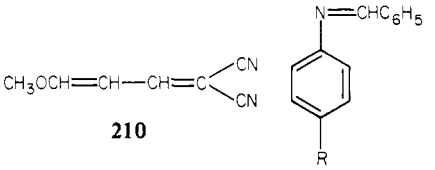
carbon disulfide and methyl iodide.

It has been observed that benzylidenemalononitrile (**6**) decreases the rate of the self-etherification of benzhydrol in benzene.[281]

E. Nitrogen Compounds

The ylidenemalononitrile **210** reacts with ammonia to give a nicotinic acid derivative which is a precursor for the preparation of herbicides.[272-274]

The reactions of amines and ylidenemalononitriles are of considerable biological interest.[9] Amines have been used as catalysts in the cyclodimerization of ylidenemalononitriles,[252,264-267] and the reactions of amines and ylidenemalononitriles have received some study.[50,282-292] Rate constants for the addition of butylamine to ylidenemalononitriles have been derived.[282,283] Malononitrile (**1**) and benzylideneaniline (**211**) in

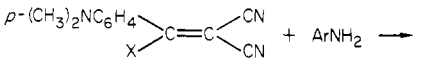


210

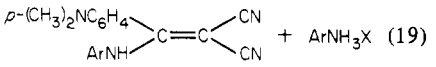
211, R = H
212, R = CH_3

ethanol give **6**, whereas aniline or 4-methylaniline fails to react with **6**. *N*-Benzylidene-4-methylaniline (**212**) in benzene reacts with malononitrile (**1**) to give a 30% yield of unidentified $C_{18}H_{18}N_4$.[285]

The substitution of 1,1-dicyano-2-[*p*-(dimethylamino)-phenyl]-2-chloro- and -2-fluoroethenes (**213**, **214**) by substituted



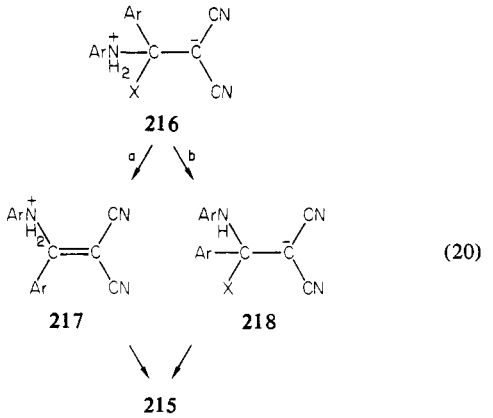
213, X = Cl
214, X = F



(19)

215

anilines in acetonitrile is second order in the amine for the fluoro compound and of increasing first order in the amine for the chloro compound. The rates are slower with sterically hindered amines, have high negative $\Delta S^{\ddagger}$, low $\Delta H^{\ddagger}$, and large negative Hammett ρ values.[284] A possible mechanism involves initial nucleophilic attack to form the zwitterion **216** which may (a) expel the halide ion followed by N–H bond cleavage and/or (b) undergo amine-catalyzed N–H bond cleavage followed by C–X bond fission. Presumably process a is the major route with **214** (eq 20).



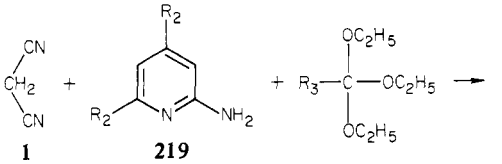
216

217 **218**

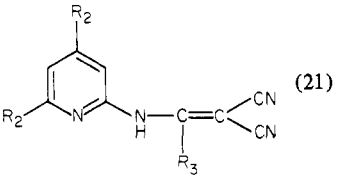
215

(20)

A simple three component synthesis of [[(2-pyridyl)amino]-methylene]malononitriles (**220**) has been reported[293,294] (eq 21). Good yields of **220** are obtained by heating malononitrile (**1**) with 2-aminopyridines (**219**) in the presence of orthoformates. It is not necessary to isolate the intermediate (ethoxymethylene)-malononitrile.[295,296] Acid hydrolysis of **220** leads to pyrido-



1 **219**

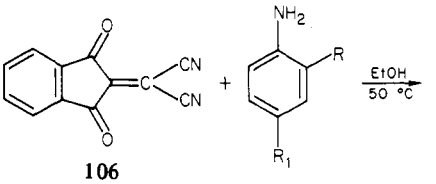


(21)

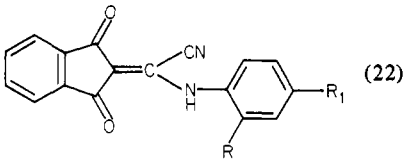
220

[1,2-*a*]pyrimidines.[293]

The potential electron acceptor 2-(dicyanomethylene)-1,3-indandione (**106**) reacts with anilines, and other aromatic amines, to give anilino-(1,3-dioxo-2-indanylidene)acetonitriles (**221**) as crystalline, orange to dark-red dyes[289,297] (eq 22). The reaction,



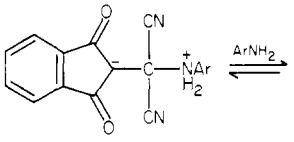
106



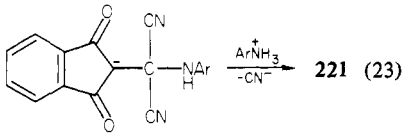
(22)

221

in acetonitrile, is nearly second order in the amine, is catalyzed by pyridines, and has a Hammett ρ value of −6.9 at 30 °C. A possible mechanism involves the initial formation of a zwitterion (**222**) which is reversibly deprotonated by a second amine molecule (eq 23). A subsequent anilinium ion assisted expulsion



222



(23)

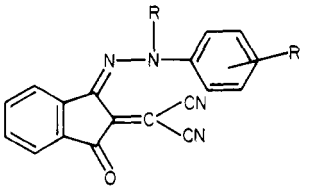
223

of cyanide ion gives the product (**221**).[292]

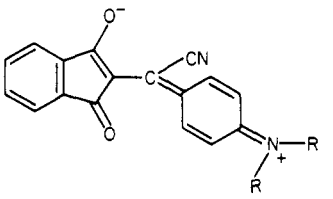
Although a crystalline adduct was not obtained with hydrazine and **106**, unsymmetrical hydrazines (e.g., 1,1-dimethylhydrazine) and benzidine, via involvement of both amino groups, gave similar crystalline dyes (**221**).[289]

Other interesting reactions of **106** and amines have been reported. Compound **224** is formed from the reaction of **106** and phenylhydrazine.[298] *N*,*N*-Disubstituted anilines and **106** produce **225**,[299] and compound **226**, which also results from the reaction of **106** and aminopyrazoles, is formed by elimination of HCN and condensation.[275,300] Further examples of the amine–HCN exchange reaction (eq 22) of **106** with aminonaphthoquinones and aminoanthraquinones have also been observed.[300]

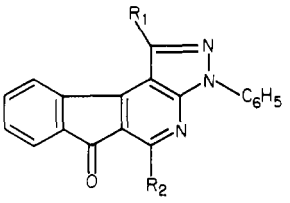
Azacyanine-type polymethine dyes with the aminodicyanoallylidenimide chromophore **230** have been prepared from the



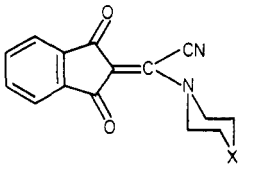
224



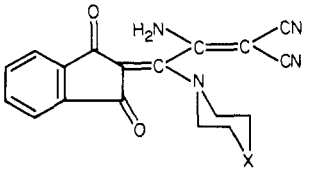
225



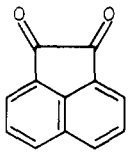
226



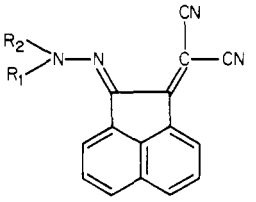
227a, X = N
227b, X = O



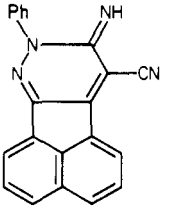
228a, X = N
228b, X = O



229



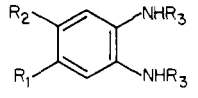
230



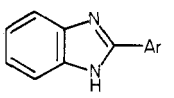
231

reaction of acenaphthenequinene (**229**) with malononitrile (**1**) and unsymmetrically substituted hydrazines.[301] Monosubstituted **230** cyclizes to the orange-red acenaphtho[1,2-*c*]pyridazine (**231**) on heating.

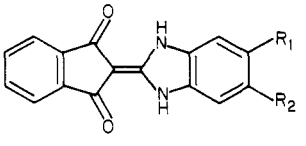
An interesting reaction occurs between *o*-phenylenediamine (**232a**) and ylidenemalononitriles to give 2-arylbenzimidazoles (**233**).[302,303] The reaction of **106** with **232** gives 2-(1,3-dioxo-



232a, $R_1 = R_2 = R_3 = H$



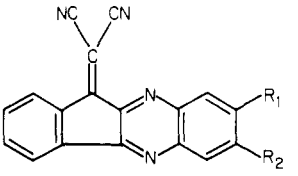
233



234

2-indanylidene)benzimidazoline (**234**) and (11*H*-indeno[1,2-*b*]-quinoxalin-1-ylidene)malononitrile (**235**). The intermediate **236** was also isolated, and alternate syntheses for **234** and **235** were described.[297,304,305] Compounds **234** may be classified as isomers of indigo with respect to the C=O and NH functions.

Malononitrile (**1**) reacts with *N*-monoaryl-substituted amidines (**237**) to give ylidenemalononitriles (**238**, 31–50%).[306,307] Acid-catalyzed cyclization of **238a** at elevated temperatures affords the quinoline **239**. Treatment of **238a** with hydrazine hydrate or guanidine gives the pyrazole **240** (70%) and the



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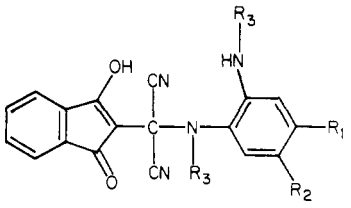

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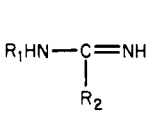
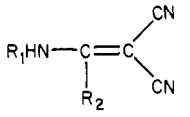
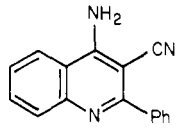


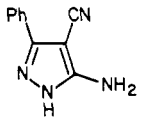
237



238a, $R_1 = R_2 = Ph$



240



240

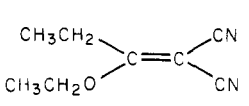
241

pyrimidine **241** (55%), respectively.

CS (**7**) reacts with substituted *N*-arylbenzimidoyl chlorides (**246**) in the presence of $AlCl_3$ to give quinazolines (**247**).[310]

Heterocyclic onium betaines (**248**) of **106** are prepared by treating **106** with a heterocyclic nitrogen base, e.g., pyridine, in dioxane solvent.[311]

The pyrazoles **243** (R = H, F, Cl) were prepared by cyclization of 3-substituted phenylhydrazines with **242**, followed by hydrolysis



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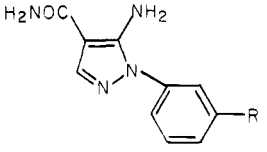
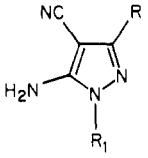


243



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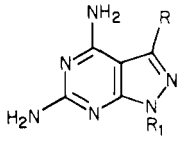

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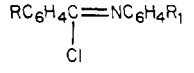
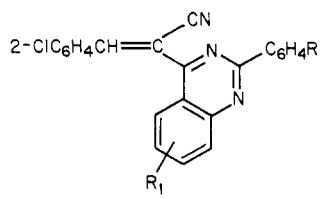


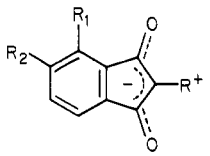
246

of the resulting nitrile.[308] Compounds **243** controlled carrageenin-induced edema in rat paws and were analgesic in the writhing test. Ylidenemalononitriles react with hydrazine to give the 5-amino-4-cyanopyrazoles **244** (cf. **240**) which react with guanidine carbonate or formamide to afford 4,6-diaminopyrazolo[3,4-*d*]pyrimidines (**245**).[309]

4-(Dicyanomethylene)-2,6-dimethyl-4*H*-pyran (**249**) reacts with branched-chain primary amines or cyclic amines to give different dihydropyridine derivatives, depending on reaction conditions. Heating **249** and isopropylamine in an autoclave at 150 °C gives **250** and **251**. However, treatment of **249** with cyclohexylamine

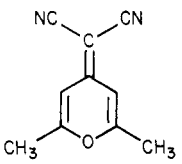


247

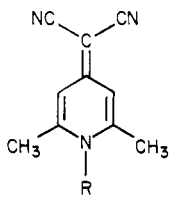


248

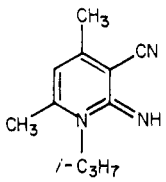
or isopropylamine in refluxing ethanol gives a high yield of the acetonylidenedihydropyridines **252** and **253**, which on prolonged refluxing rearrange to **250** and **254**.[288]



249

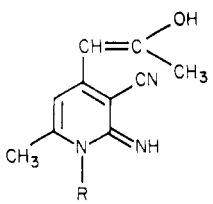


250, R = i-C_3H_7
254, R = C_6H_{11}

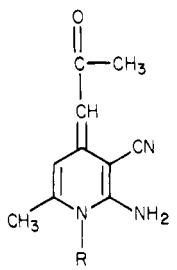


251

4-(Dicyanomethylene)-2,6-diphenyl-4*H*-pyran (**255**) reacts with alkylamines below 100 °C to give a mixture of 1-alkyl-4-(cyanomethylene)-2,6-diphenyl-1,4-dihydropyridine and 1-alkyl-2-amino-3-cyano-4-phenacylidene-6-phenyl-1,4-dihydropyridine.[287]

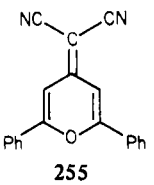


252a, R = i-C_3H_7
252b, R = C_6H_{11}

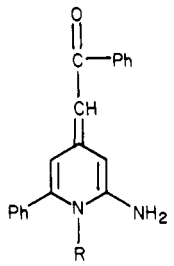


253a, R = i-C_3H_7
253b, R = C_6H_{11}

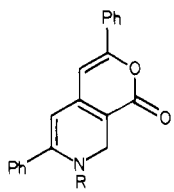
The exclusive formation of the respective phenacylidenedihydropyridine derivatives is observed from the reaction of **255** and cyclohexylamine, isopropylamine, or dimethylamine (**256**, **257**, **258**). Compounds **256–258** on treatment with hydrochloric acid in alcohol undergo cyclization to the lactones **259–261**.



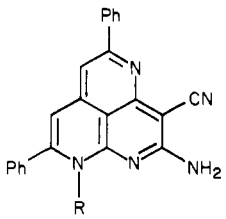
255



256, R = C_6H_{11}
257, R = i-C_3H_7
258, R = $N(CH_3)_2$



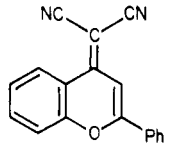
259-261



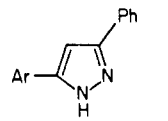
262-264

Polynuclear hydrocarbons (**262–264**) are obtained from the reaction of **256–258** with malononitrile (**1**) in alkaline medium.[312,313]

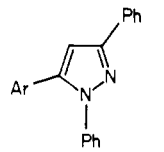
Compound **265** and hydrazine hydrate give 5-(2-hydroxyphenyl)-3-phenylpyrazole (**266**), while **265** and phenylhydrazine give 5-(2-hydroxyphenyl)-1,3-diphenylpyrazole (**267**).[312]



265

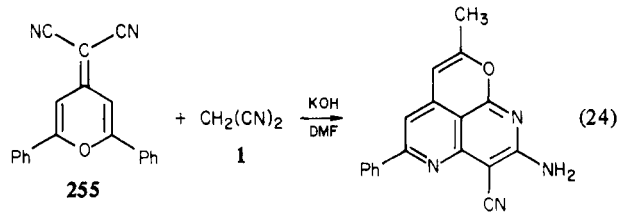


266, Ar = 2-HOC_6H_4



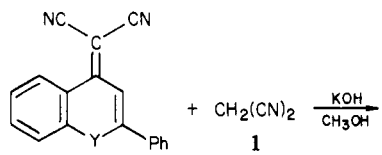
267, Ar = 2-HOC_6H_4

Some 4-dicyanomethylene derivatives of pyran, benzo[*b*]-pyran, and thiapyran react with **1** or malonitrile dimer (**15a**) to give polynuclear heterocyclic compounds (eq 24–26).[311]

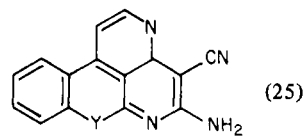


(24)

255 + 1 → 268

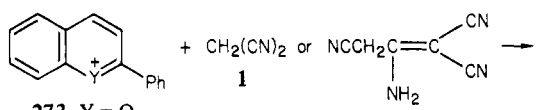


269, Y = O
270, Y = S



(25)

271, Y = O
272, Y = S

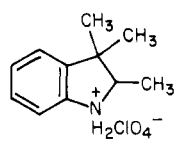


273, Y = O
274, Y = S

15a

271 or 272 (26)

Benzylidenemalononitrile (**6**) reacts with 1 mol of 2,3,3-trimethyl-3*H*-indole·$HClO_4$ (**275**) to give the heterocyclic quaternary



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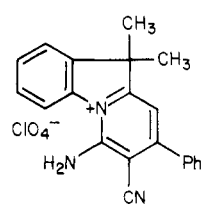
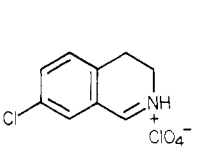


276

salt **276** via cyclization and aromatization. Treatment with triethylamine converts **276** to the corresponding imine.[286] Reaction of 7-chloro-3,4-dihydroisoquinoline·$HClO_4$ (**277**) with isopropylidenemalononitrile at 150 °C gives 8,9-diamino-2,15-dichloro-5,6,11,12,16b,17-hexahydrodiisoquino[2,1-*b*:1′,2′-*g*]-[2,7]naphthyridine-7,10-dilum diperchlorate, which on refluxing with triethyl formate in DMF-NEt_3 and treatment with anion exchanger affords **278**. These salts are useful as intermediates in the preparation of azamethine dyes or rigidized carbocyanines.[286]



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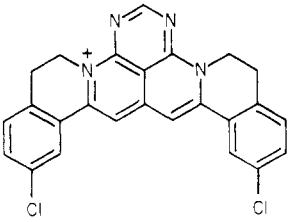
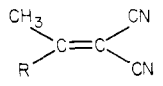
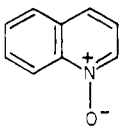


278

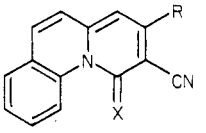
2,1-Annelations on the quinoline nucleus, leading to α-quinolizones (**282**), via **281**, can be achieved by means of con-



143, R = C_6H_5
279, R = *t*-Bu

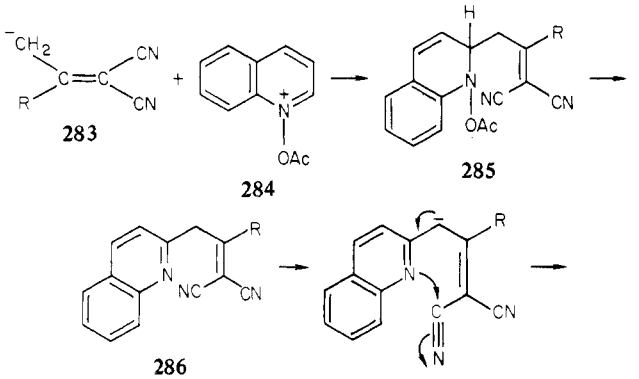


280



281, X = NH
282, X = O

densation of quinoline 1-oxide (**280**) with suitably substituted ylidenemalononitriles (**143, 279**) in the presence of acetic anhydride and triethylamine.[314] A reasonable mechanism for the annelation is shown in eq 27. Attempts to isolate the imine

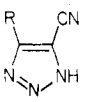


283 284 285 286

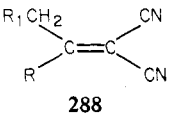
$$\mathbf{281} \xrightarrow{H_3O^+} \mathbf{282} \quad (27)$$

281 were unsuccessful, and complex product mixtures were obtained if the R group contained α hydrogen atoms.

Ylidenemalononitriles react slowly with HCN and hydrazoic acid in the presence of acetic acid.[145,150,162,195,315] Triazoles (**287**) are obtained by cyclization of ylidenemalononitriles with sodium azide.[315]

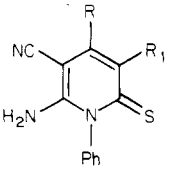


287



288

Ylidenemalononitriles (**288**) add phenyl isothiocyanate (PhNCS) in the presence of a basic catalyst to give 6-amino-1-phenyl-3-cyanopyridinethiones (**289**).[316] The reactions of **289** with dimethyl sulfate, amines, and hydroxide ion have been described.



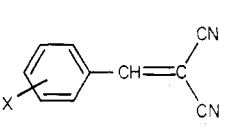
289a, R = Ph; R_1 = H
b, R = Et; R_1 = Me
c, R = Ph; R_1 = Me
d, RR_1 = $(CH_2)_4$

290, R = H
291, R = Ph

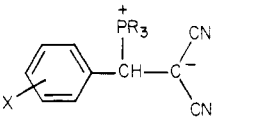
Phenyl isocyanate (PhNCO) reacts with ylidenemalononitriles to give derivatives (**290**) which, on reaction with another unit of PhNCO and loss of HOCN, give **291**.

F. Phosphorus Compounds

Ylidenemalononitriles, including **292–294**, react reversibly with trialkyl- or triarylphosphines to give resonance-stabilized phos-



292, X = 4-Cl
293, X = 4-NO_2
294, X = 2,4-Cl_2
295, X = 3,4-$(OCH_3)_2$



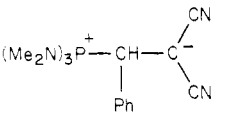
296a, X = 4-Cl; R = *n*-C_4H_9
b, X = 4-NO_2; R = *n*-C_4H_9
c, X = 2,4-Cl_2; R = *n*-C_4H_9

phinemethylene ylides (phosphonium dicyanomethylides, **296**).[49,317,318] Electron-withdrawing groups in the benzene ring enhance the reaction while electron-releasing substituents decrease or eliminate adduct formation. Thus, no adduct is formed with **295**.[318] Infrared spectra are consistent with a zwitterionic structure for these 1:1 adducts (**296**).[318-320] Treatment of **296** with hydrogen chloride gives phosphonium salts, and attempted C-alkylation with methyl iodide in methanol unexpectedly leads to cleavage of the adducts to methyltributylphosphonium iodide and the original benzylidenemalononitrile.[318]

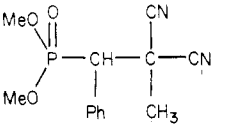
The thermodynamic parameters for the formation of the adducts from tributylphosphine and seven ylidenemalononitriles in methanol were spectrophotometrically measured.[320] The equilibrium constant varied from 17.4 × 10^3 to 37 L mol^{-1} and decreased when the dielectric constant of the solvent was lowered. Enthalpy of activation values ranged from −13.4 to −21.4 kcal mol^{-1} and $\Delta S^{\ddagger}$ values ranged from −27.4 to −50 eu. ρ values of 1.27, 1.12, and 0.85 were obtained at 34, 44, and 54 °C, respectively. It was suggested that the first step in the mechanism involves a nucleophilic attack of neutral phosphine on the β carbon atom to form the zwitterion.[320-322]

The crystal and molecular structure of the 1:1 adduct formed by the reaction of tributylphosphine and CS (**7**) has been determined with diffractometer data by direct methods.[323] The zwitterionic adduct has the positive charge localized on the phosphorus atom and the negative charge mainly on the terminal dicyanomethyl group.

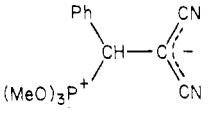
The moderately exothermic reaction of **6** with tris(dimethylamino)phosphine [$P(NMe_2)_3$] in methylene chloride gives **297**,



297



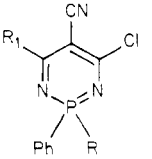
298a



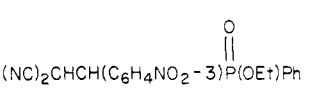
298b

which could not be recrystallized. The same reaction in dioxane gives the adduct $C_{16}H_{24}N_5P{\cdot}C_3H_8O$.[324a] Excess trimethyl phosphite [$P(OCH_3)_3$] reacts with **6** to give **298a**, in 4 days.[324] Under different experimental conditions, the zwitterion **298b** is formed.[324b]

Dimethyl phosphonate [$(MeO)_2PHO$] reacts with **6** in the presence of sodium methoxide to give **298b**.[324a]



299a



299b

Phenyltetrachlorophosphorane reacts with ylidenemalononitriles to give **299a** (R_1 = Ph, Cl_3C, H, Et, Pr), which react with a variety of nucleophilic agents.[325a]

The reaction of $PhPCl_2$ and $3\text{-}O_2NC_6H_4CH{=}C(CN)_2$, followed by hydrolysis and esterification gives **299b**, which is a plant growth regulating agent.[325b]

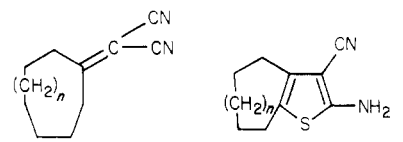
G. Sulfur Compounds

Although the mechanism of the rapid reaction of thiols with ylidenemalononitriles has not been elucidated, equilibrium constants have been determined for the interaction between butanethiol and ylidenemalononitriles in aqueous phosphate-buffered ethanol.[326] The formation of adducts between CS and various thiols, mostly of biological origin, has been reported.[327] Thus far, it appears that none of these adducts have been isolated.

The distribution of glutathione *S*-alkenetransferases in the livers of nine vertebrates suggested that different enzymes may catalyze the reactions of glutathione with CS and other α,β-unsaturated compounds.[328]

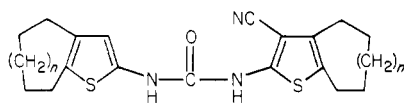
A rapid scan polarograph with a trielectrode system has been used to study the mechanism and rate of reaction of CS and 2-(diethylamino)ethyl mercaptan.[329]

Ylidenemalononitriles (**300**) undergo facile cyclization with sulfur,[330,331] in the presence of diethylamine, to give cycloalka[*b*]thiophenes (**301**).[332] Carbon disulfide and **300** give the

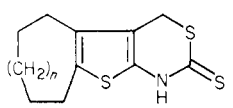


300

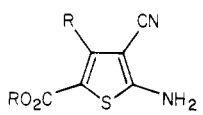
301



302



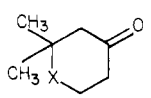
303



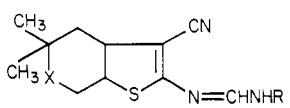
304

dimeric ureas **302** instead of the 1,3-thiazine ring system (**303**).[332,333] Thiaphenecarboxylates (**304**) are prepared by the reactions of an alkanoylacetate with malononitrile (**1**), sulfur, and triethylamine, followed by cyclization of the reaction product.[334]

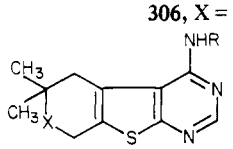
Antispasmodic pyrano- and thiopyranothienopyrimidines (**307**) are obtained in 41–86% yield in five steps from **305** by con-



305, X = O, S

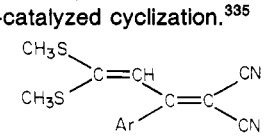


306, X = O, S



307, X = O, S

densation with **1**, cyclization with sulfur, condensation with ethyl orthoformate, amination with RNH_2 to give **306**, and subsequent base-catalyzed cyclization.[335]



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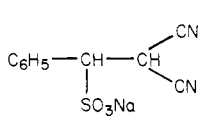


308

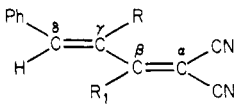
Presumably, **6** dissolves slowly in sodium hydrogen sulfite solution to give **308**, which could not be isolated.[145]

Preparation of the push–pull butadienes (**209**) is described above.[280]

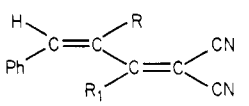
H. Photochemistry and Thermolysis

The potential-energy surface for isomerization of **9** in strongly polar solvents was shown to possess a double-well form, which was accompanied by an inverted double-well potential on the lowest excited singlet surface.[336]

The dienes **309** (cf. **100**, **101**) are photoisomerized to the corresponding **310** (cf. **104**, **105**) via a process which involves only the γ,δ-double bond.

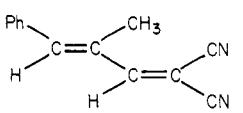


309, R = Me, Ph; R_1 = H, Me

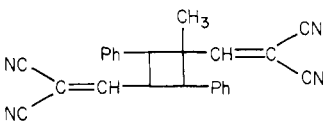


310, R = Me, Ph; R_1 = H, Me

The photodimerization of **100** gives **311**.[209]

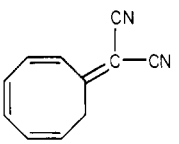


100



311

The photochemical valence isomerization of 1-(dicyanomethylene)cyclooctatriene (**312**)[337] and related methylene-



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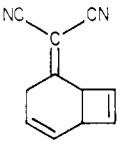

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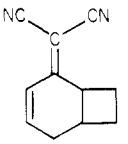
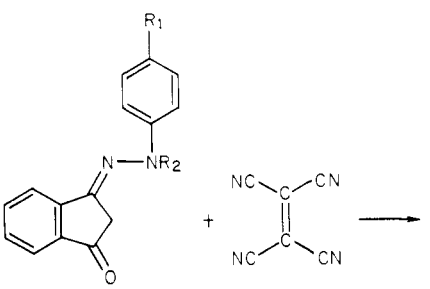
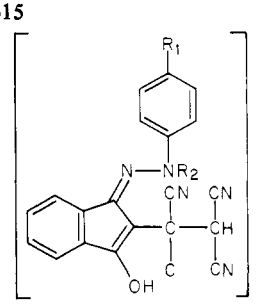


314

2,4,5-cyclooctatrienes has been studied.[338] Irradiation of **312** in cyclohexane at 242 nm gives the valence tautomer (dicyanomethylene)bicyclo[4.2.0]octadiene (**313**, 100%). Isomerization of **313** to **314** is accomplished with dilute mineral acid. Photochemical transformation and thermolysis show promise as useful procedures for the preparation of unique malononitrile



315



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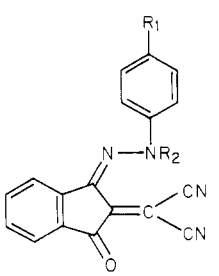
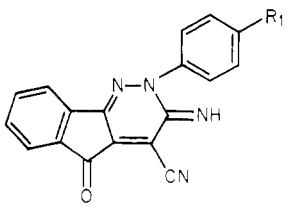


317a, R_1 = H; R_2 = H
317b, R_1 = NO_2; R_2 = H
317c, R_1 = H; R_2 = C_6H_5
317d, R_1 = H; R_2 = CH_3

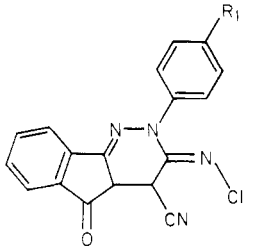
derivatives.

Junek and co-workers[298,339] prepared a series of very intensely colored dyes (**317**, 62–82%) via the retro-Michael reaction of the corresponding 1,3-indandione monophenylhydrazone (**315**) with tetracycloethylene (TCNE). Use of TCNE in the retro-Michael reaction is a useful procedure for indirect insertion of the malononitrile group into an organic molecule.[340–342]

The dyes **317** are thermally unstable and cyclize readily in aprotic and in polar solvents at 50 °C to the pyridazine derivatives **318**. Photolysis of **317** in dichloromethane at 220–250



318a, R = H

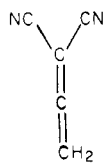


319

nm leads to the discharge of the violet color and formation of the pyridazine *N*-chloroimine **319**.[339a]

The rearrangement of 2-(dicyanomethylene)-1,3-indandione monophenylhydrazone (**317c**) to 3-imino-5-oxo-2-phenyl-2,3-dihydro-5*H*-indeno[1,2-*c*]pyridazine-4-carbonitrile (**318a**) has been observed upon irradiation or interaction with Lewis bases.[319b] Deprotonation of **317a** and the corresponding anionic intermediate has been detected by stopped-flow experiments and flash photolysis. Kinetic data for deprotonation and for thermal and photochemical rearrangements have been compared.

The valence isomerization of the homoheptafulvene derivative **312** at 185 °C gives benzene and the propadienyl compound **320**.[343] The intermediacy of the valence tautomer **321** was



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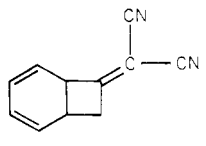

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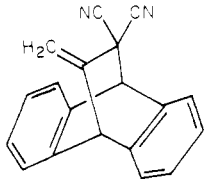

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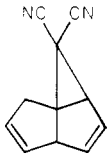
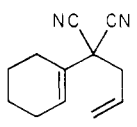


323

demonstrated in a trapping experiment with anthracene, which gave **322**. Refluxing **313** in xylene gives the highly strained valence tautomer **323**.

(1-Cyclohexenylallyl)malononitrile (**324**) and [1-(ethylpropenyl)-2-allyl]malononitrile (**325**), which are prepared by alkylating the ylidenemalononitriles,[13] undergo the Cope rearrangement to (2-allylcyclohexylidene)malononitrile (**326**) and (1-ethyl-2-methyl-4-pentylidene)malononitrile (**327**), respectively.[344] The variable activated complex structure in the Cope rearrangement has been discussed.[345]



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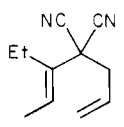

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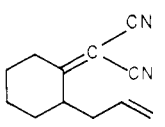

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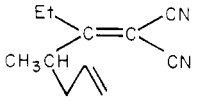
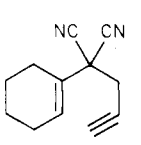


327

Cyclohex-1-enyl(prop-2-ynyl)malononitrile (**328**)[337] undergoes the Cope rearrangement in xylene to give the expected propadienyl compound **329** ([2-(propa-1,2-dien-1yl)cyclohexylidene]malononitrile.[338] When neat liquid **328** is heated to 250 °C, 5,6,7,8-tetrahydronaphthalene-1,3-dicarbonitrile (**330**) and much polymer are formed. The aromatic dinitrile **330** is also obtained from heating **329**. Heating **328** in diethylamine gives a crystalline homoannular diene (1,2,5,6,7,8-hexahydronaphthalene-1,1-dicarbonitrile, **331**), which is also converted to **330** on heating. Although other intermediates may be involved, a speculative mechanistic scheme has been proposed for the conversion of **328** to **330**.[338]



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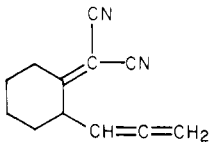

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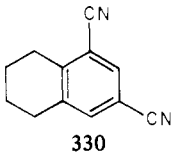

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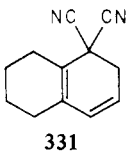
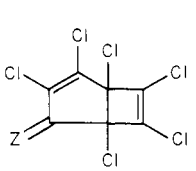
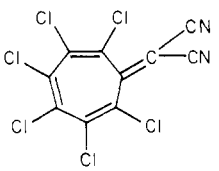


331

The heptafulvene (2,3,4,5,6,7-hexachloro-8,8 dicyanoheptafulvene) **333** was prepared by fusing bicyclic **332a** with malononitrile (**1**) and $AlCl_3$ at 150 °C to give **332b**, which rearranged photochemically or thermally to **333**. An alternate synthesis of **333** and its spectroscopic properties have been discussed.[346]

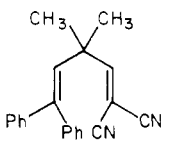


332a, Z = Cl_2
332b, Z = $C(CN)_2$

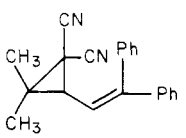


333

Direct irradiation of the dicyanodiene **334a** in benzene leads to regioselective formation of a single vinylcyclopropane (**334b**) via diphenylvinyl migration rather than dicyanovinyl. Sensitized irradiation of **334a** does not lead to **334b**, which suggests **334a** undergoes di-π-methane rearrangement from its singlet excited state.[347]



334a



334b

The dimer and excimer fluorescence spectra of several benzylidenemalononitriles have been reported.[349–351] A sandwich-type dimer with a center of symmetry has been proposed for several (dialkyl-4-methoxybenzylidene)malononitriles.[349]

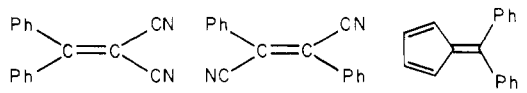
I. Miscellaneous Reactions

Owing to their large number and their versatile chemical reactivity, it is not possible to adequately categorize all of the reactions of ylidenemalononitriles. In this section a wide variety of representative chemical reactions will be discussed. It is not possible to include the extensive polymer chemistry and of the

metal complexes of ylidenemalononitriles.

The possibility of electron-transfer (ET) biradical formation in the ground state has been investigated in relation to the one-electron-transfer mechanism in ionic reaction of the addition of methyl carbanion to **9**.[353]

Homogeneous electron transfer from cyclooctatetraene dianion to **20** and **335** yields the dianions, and to **336** yields only

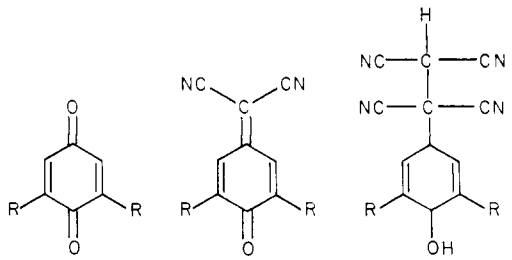


20 335 336

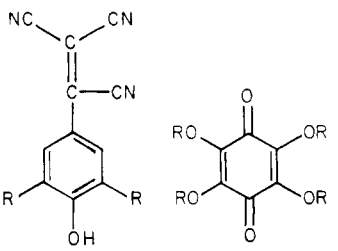
the radical anion. Electron affinity, which is strongly dependent on steric as well as electronic factors, increased in the order **336** < **20** < **335** according to MO calculations of the energies of the LUMO in the neutral molecules and the HOMO in the dianions.[354]

Infrared data are given for **20** and for (1) the anionic adduct formed by the reaction of **20** with sodium methoxide in Me_2SO, (2) the anion radicals and dimeric dianions formed by electrochemical reduction of **20**, and (3) the monomeric dianion formed by the reaction of **20** with dipotassium naphthalenide.[355]

Treatment of 2,6-dialkyl-*p*-benzoquinone (**337**) with an excess of malononitrile in ethanol–pyridine gives an 80% yield of 2,6-dialkyl-4-(tricyanovinyl)phenol (**340**). A reasonable mechanism



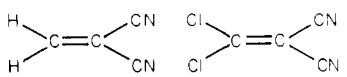
337 338 339



340 341

could involve the quinomethide intermediate (2,6-tri-*tert*-butyl-4-(dicyanomethylene)-1-oxo-2,5-cyclohexadiene, **338**), and the 1,6-malononitrile adduct (**339**) which loses HCN to yield **340**.[356] A similar reaction has been observed with **341**.[357]

Rotational barriers and conformational preferences in **9**– and **342**–$PtCl_3^-$ and **9**– and **342**–$Ni(PH_3)_2$ complexes have been analyzed in terms of differential interactions between the orbitals of the ML_n fragment and the ethene π and π^*.[358]

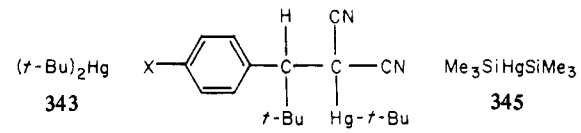


9 342

Complexes, in which the cuprous ion is associated with the double bond, have been prepared from ylidenemalononitriles and cuprous bromide or chloride.[359] Copper acetylacetonate reacts with ylidenemalononitriles to form polychelates.[360]

Ylidenemalononitriles react with nickel carbonyl to form charge-transfer complexes, which are similar to the copper(I) complexes described above.[361] These complexes have been discussed in terms of LCAO–MO and their radical character.

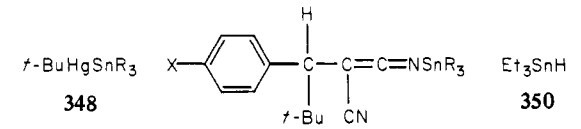
Although nonpolar olefins react very slowly or not at all with di-*tert*-butylmercury (**343**), the strong polar double bond in ylidenemalononitriles reacts at 20–25 °C to produce 1,2-adducts



343 344 345

(**344**) instead of the 1,4-addition product (ketenimines).[362] A four-center activated complex is assumed, although radicals may also be involved. The reactivity of **343** is greater than that of Et_2Hg and comparable to that of **345**. The reaction of *tert*-butyl(trimethylsilyl)mercury (**346**) with ylidenemalononitriles gives *N*-(trimethylsilyl)ketenimines (**347**).[363] Other alkyl derivatives of **346** (R = *t*-Bu) do not react.

N-(Trialkylsilyl)ketenimines (**349**) may be prepared from *t*-$BuHgSnR_3$ (**348**) and ylidenemalononitriles, from trialkyltin hydride

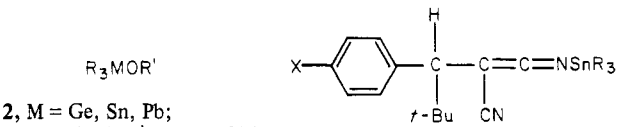


348 349 350

351, R = Et

and **344**, or by transmetalation, from *N*-silylketenimine. Other alkyl derivatives ($R'HgSnR_3$) of [*tert*-butyl(trialkylstannyl)mercury (**348**) did not react.[363,364] The adduct **344** reacts with triethyltin hydride (**350**) to give **351**.

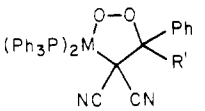
The *N*-(trimethylsilyl)keteneimine (**347**) and *N*-stannylketenimine (**349**) can be transmetalated with alkoxides or acetates (**352**) to give **353**.[363]



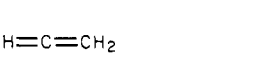
352, M = Ge, Sn, Pb; R = alkyl; R′ = Me, COMe

353, M = Ge, Sn, Pb; R = alkyl

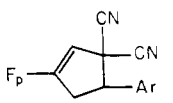
Niobium complexes are formed with ylidenemalononitriles.[365] Acetonitrile (AN) is substituted under very mild conditions in AN–phosphine–molybdenum dicarbonyls by ylidenemalononitriles.[366] The dioxygen complexes ($Ph_3PPd_3PtO_2$) readily add to ylidenemalononitriles at 20–25 °C to give cyclic peroxy adducts (**354**) in high yields.[367] The metal-assisted cycloaddition reaction of dicarbonyl (η^5-cyclopentadienyl)(allenyl)iron (**355**) and CS gives **356** as the exclusive product.[369]



354, M = Pd_3Pt



355, $F_p = (\eta^5\text{-}C_5H_5)Fe(CO)_2$



356

Cyanocarbon derivatives of transition metals have received considerable recent attention.[369,370] In 1972 reactions of metal carbonyl anions with poly(cyanovinyl) halides were reported[371] to give good yields of stable poly(cyanovinyl) transition-metal derivatives.[372] Reactions of these poly(cyanovinyl) transition-metal derivatives[373,374] give a variety of unusual and interesting cyanocarbon transition-metal complexes including compounds containing terminal[375,376] and bridging[371,372] dicyanovinylidene ligands, dicyanoketenimmonium derivatives,[377–380] novel types of chelates,[377] and new (poly(cyano olefin) complexes.[369,370]

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