IR and MS were similar to **49**; NMR δ 8.01 (1 H at 6, m), 7.94 (1 H, NH, br s), 6.79–7.06 (2 H, m), 2.25 (3 H, d, $^4J_{HF}$ = 2.6 Hz), 2.18 (3 H, s); ^{19}F NMR −135.7 ppm. Anal. Calcd for $C_9H_{10}FNO$: C, 64.67; H, 5.99. Found: C, 64.44; H, 6.18. Fraction II was found to be a mixture of two difluoro isomers. The less polar one was 2,4-difluoro-5-methylacetanilide (**51**) in 11% yield: mp 93 °C (from MeOH); MS, *m/e* 185 (M^+), 142 ($M - COCH_3)^+$; NMR δ 8.00 (1 H at 6, t, $^4J_{HF}$ = 8.4 Hz), 7.46 (1 H, NH, br s), 6.78 (1 H at 3, t, 9.3 Hz), 2.19 (6 H, br s), ^{19}F NMR −131.5 (1 F), 119.0 ppm (1 F). Anal. Calcd for $C_9H_9F_2NO$: C, 58.38; H, 4.86. Found: C, 58.47; H, 5.14. The more polar compound isolated proved to be 2,4-difluoro-3-methylacetanilide (**50**) in 10% yield: mp 104 °C (MeOH); MS, as for **51**; NMR δ 7.97 (1 H at 6, q, J_{HH} = $^4J_{HF}$ = 8.8 Hz), 7.42 (1 H, NH, br s), 6.80 (1 H, m), 2.19 (6 H, br s); ^{19}F NMR −131.4 (1 F), −120.5 (1 F).

Fluorination of Bromoacetanilides 55 and 62. Both starting materials were reacted with **1** by method A, using a 3-fold excess of the hypofluorite. Full conversion was achieved. After the usual workup of the reaction of **55** with **1**, the crude mixture was chromatographed on HPLC, using 50% EtOAc in cyclohexane. Two fractions were isolated, and the less polar one was found to be 2-fluoro-5-bromoacetanilide (**57**): mp 113 °C (from EtOH); yield 47%; IR 3460 and 1660 cm^{-1}; MS, *m/e* 231, 233 (M^+), 188, 190 ($M^+ - COCH_3$), 152 ($M - Br)^+$; NMR δ 8.52 (1 H at 6, dd, $^4J_{HF}$ = 7 Hz, $^4J_{HH}$ = 2 Hz), 7.58 (1 H, NH, br s), 7.24–6.93 (2 H, m), 2.22 (3 H, s); ^{19}F NMR −133.0 ppm. Anal. Calcd for C_8H_7BrFNO: C, 41.38; H, 3.02. Found: C, 41.28; H, 3.06. The more polar fraction **56** had IR and MS very similar to **57**. It was obtained in 25% yield: mp 74 °C (from CCl_4); NMR δ 8.25 (1 H at 6, dt J_{HH} = $^4J_{HF}$ = 7.3 Hz, $^4J_{HH}$ = 1.5 Hz), 7.30 (1 H, NH, br s), 6.84–7.36 (2 H, m), 2.23 (3 H, s); ^{19}F NMR −125.3 ppm. When compound **62** was reacted, only one fluorine-containing product was isolated in 65% yield and it proved to be 2-fluoro-4-bromoacetanilide (**65**). The conversion in this case was rather low (about 30%) because **62** is not very soluble in $CHCl_3$ and was added as a cold suspension to **1**. **65**: NMR δ 8.22 (1 H at 6, t, J_{HH} = $^4J_{HF}$ = 7.8 Hz), 7.78 (1 H, NH, br s), 7.19–7.41 (2 H, m), 2.21 (3 H, s); ^{19}F NMR −129.1 ppm. Anal. Calcd for C_8H_7BrFNO: C, 41.38; H, 3.02. Found: C, 42.30; H, 3.60.

Fluorination of 3,5-Dimethylacetanilide (58). Method A: full conversion. The purification of the crude was achieved by chromatography. Pure 2-fluoro-3,5-dimethylacetanilide (**59**) was eluted by $CHCl_3$ and crystallized from EtOH: mp 95 °C; yield 67%; IR 3460 and 1666 cm^{-1}; MS, *m/e* 181 (M^+), 138 ($M - Ac)^+$, 123 ($M - NHAc)^+$; NMR δ 7.91 (1 H at 6, br d, $^4J_{HF}$ = 6.8 Hz), 7.37 (1 H, NH, br s), 6.70 (1 H at 4, br d, $^4J_{HF}$ = 6.8 Hz), 2.19–2.25 (9 H, m); ^{19}F NMR −141.4 ppm. Anal. Calcd for $C_{10}H_{12}FNO$: C, 66.30; H, 6.63. Found: C, 66.00; H, 6.73.

Fluorination of 4-methylacetanilide (60) was carried according to method A with a full conversion. The solid crude was chromatographed in a short silica column with chloroform as eluent and thus the known 2-fluoro-4-methylacetanilide (**63**)[38] was obtained in 85% yield: ^{19}F NMR −131.6 ppm.

Fluorination of Triphenylamine (66). Method A. Molar excess of **1** over **66** was about 5 times; full conversion. After the usual workup the crude was chromatographed on silica, using 5% EtOAc in PE as eluent. A considerable amount of polymeric and quinonic materials was absorbed on the silica, but two products still could be isolated and purified. The less polar one proved to be the trifluoro compound **67**: mp 77 °C (from EtOH); yield 28%; MS, *m/e* 299 (M^+), 204 $[(FC_6H_4)_2N]^+$, 95 $(C_6H_4F)^+$; NMR δ 7.01–7.24 (m); ^{19}F NMR −122.1 ppm. Anal. Calcd for $C_{18}H_{12}F_3N$: C, 72.24; H, 3.01; F, 19.06; N, 4.68. Found: C, 72.43; H, 4.16; F, 18.86; N, 4.98. The more polar compound **68** was obtained in 11% yield: mp 76 °C (from EtOH); MS, *m/e* 317 (M^+), 204 $[(FC_6H_4)_2N]^+$, 95 $(C_6H_4F)^+$; NMR δ 6.90–7.16 (m); ^{19}F NMR −123.5 (3 F), −119.7 ppm (1 F). Anal. Calcd for $C_{18}H_{11}F_4N$: C, 68.14; H, 3.47; F, 23.97; N, 4.42. Found: C, 68.60; H, 3.60; F, 23.10; N, 4.51.

Registry No. **1**, 78948-09-1; **2**, 321-28-8; **3**, 459-60-9; **4**, 88288-00-0; **5**, 10471-09-7; **6**, 120-57-0; **7**, 88288-01-1; **8**, 274-09-9; **9**, 88288-02-2; **10**, 151-10-0; **11**, 17715-70-7; **12**, 79069-70-8; **13**, 88288-03-3; **14**, 27602-71-7; **15**, 5263-87-6; **16**, 88288-04-4; **17**, 1078-19-9; **18**, 88288-05-5; **19**, 88288-06-6; **20**, 103-73-1; **21**, 2741-16-4; **22**, 451-80-9; **23**, 459-26-7; **24**, 91-16-7; **25**, 613-70-7; **26**, 635-67-6; **27**, 31083-15-5; **28**, 2539-21-1; **29**, 91-23-6; **30**, 484-94-6; **31**, 100-17-4; **32**, 455-93-6; **33**, 100-02-7; **34**, 403-19-0; **35**, 119-36-8; **36**, 70163-98-3; **37**, 391-92-4; **38**, 103-84-4; **39**, 399-31-5; **40**, 351-83-7; **41**, 404-24-0; **42**, 6625-74-7; **43**, 61984-68-7; **44**, 88288-07-7; **45**, 344-62-7; **46**, 88288-08-8; **47**, 537-92-8; **48**, 704-37-0; **49**, 325-74-6; **50**, 76350-71-5; **51**, 88288-09-9; **52**, 351-36-0; **53**, 88288-10-2; **54**, 349-27-9; **55**, 621-38-5; **56**, 88288-11-3; **57**, 88288-12-4; **58**, 2050-45-5; **59**, 88288-13-5; **60**, 103-89-9; **61**, 349-97-3; **62**, 103-88-8; **63**, 326-67-0; **64**, 88288-14-6; **65**, 326-66-9; **66**, 603-34-9; **67**, 88288-15-7; **68**, 88288-16-8; F_2, 7782-41-4; ^{18}F, 13981-56-1; sodium acetate, 127-09-3; benzene, 71-43-2.

(38) Finger, G. C.; Grotatowski, M. J.; Shiley, R. H.; White, R. H. *J. Am. Chem. Soc.* **1959**, *81*, 94.

Hydrogen Cyanide Chemistry. 9. Cycloaddition Reactions and Nitrenium Ion Type Reactivity of Diiminosuccinonitrile†,[1]

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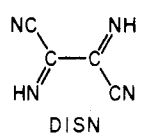
Received August 26, 1983

Cycloaddition reactions of diiminosuccinonitrile (DISN) with nucleophilic olefins yield a variety of products including [4 + 2] cycloadducts and aziridines. All of the products derived from 1,3-dienes, styrene, para-substituted styrenes, cycloheptatriene, norbornene, and norbornadiene can be accounted for by rearrangements of a common intermediate, zwitterionic aziridinium ion. We introduce the concept of reverse polarization and propose that DISN is a latent nitrenium ion source (isoelectronic with carbenes) and that reverse polarization of one of the >C=N bonds of DISN is responsible for the observed reactions. Comments are made on reverse polarization of other >C=X bonds, and facile 1,1-cycloreversion of aziridines is also reported.

Diiminosuccinonitrile (DISN) **1**, prepared by base-catalyzed addition of hydrogen cyanide to cyanogen, is a highly versatile polyfunctional reagent, from which a variety of heterocycles have been synthesized through condensation and displacement reactions.[2] In this paper, we focus our attention to the hetero diene unit HN=CC=NH



DISN

1

and describe its electrocyclic reactions.[1]

Because nitrogen is more electronegative than carbon,

† Contribution No. 3313.

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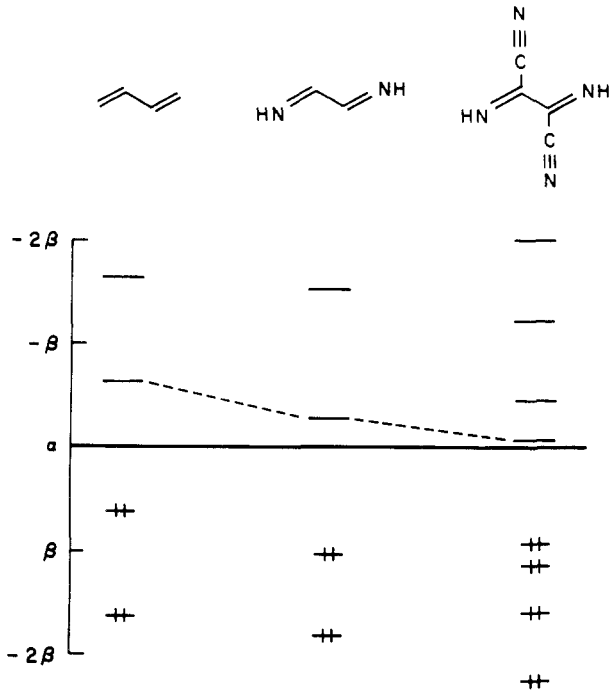
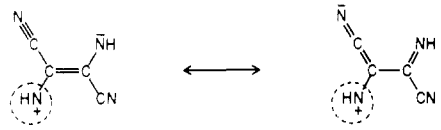


Figure 1. HMO energy levels for butadiene, 1,4-diazabutadiene, and DISN. HMO parameters are taken from Van-Catledge (Van-Catledge, F. A. *J. Org. Chem.* **1980**, *45*, 4801; QCEP, **1980**, *12*, 385).

1,4-diaza-1,3-butadienes are more electron demanding than simple 1,3-butadienes, and their π orbitals are more bonding. The two electron-withdrawing cyano groups in **1** make it even more electron deficient (Figure 1). Thus, one may anticipate that **1** will react as an electron-accepting 4π component in [4 + 2] cycloadditions.[2a,3] Furthermore, this cross-conjugated system presents an intriguing possibility that normal polarization of one of the azomethine groups will generate a resonance stabilized β-amidoacrylonitrile moiety, and more importantly, it will induce reverse polarization of the other azomethine group to generate a nitrenium center (see **1a** and **1b**). Since



1a **1b**

nitrenium ions are isoelectronic with carbenes, DISN may

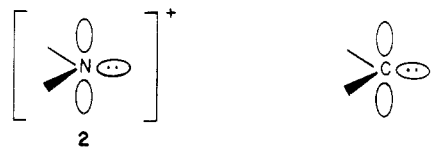


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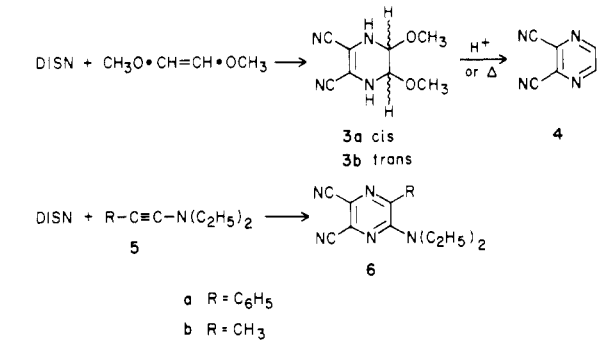
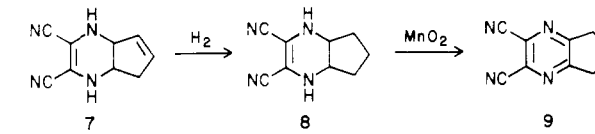
exhibit carbene-like behavior. Although there is no evidence for this polarization in the ground state, it may well be induced upon interaction with nucleophiles.

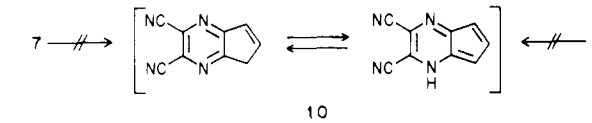
Cycloaddition Reactions of DISN. DISN undergoes [4 + 2] cycloadditions with electron-rich olefins; for example, 1,2-dimethoxyethylene reacts exothermically with DISN in acetonitrile to give tetrahydrodicyanopyrazine **3** in 76% yield.[2a] The adduct readily eliminates methanol to yield 2,3-dicyanopyrazine (**4**). Ynamines **5** directly gave pyrazine **6** in 50–60% yields.



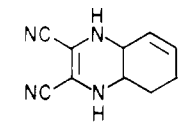
Cyclic 1,3-dienes are much less reactive than the electron-rich dienophiles, and the reactions often require more than several days in acetonitrile at ambient temperatures. Under these conditions, cyclopentadiene yields **7** in 50%



yield (24 h).[4] Adduct **7** can be further characterized by catalytic hydrogenation to **8**, which aromatizes readily to pyrazine **9**. However, attempts to oxidize **7** or **9** to diazaindene **10**, isoelectronic with azulene, have been unsuc-



cessful. The cyclohexa-1,3-diene adduct **11**, 78.5% yield (5 days),[4] is much less stable than **7**, and the solid samples darken considerably within a day at room temperature in the air. Attempted hydrogenation and aromatization



11

(MnO_2) have led to intractable tars.

In contrast to the [4 + 2] cycloadditions, styrene and *p*-halostyrenes (**12a–c**) yield aziridines **13** as the only isolable products (Chart I). More electron-rich *p*-methoxystyrene (**12d**) and 2-vinylfuran (**12e**) give [4 + 2] cycloadduct **14**, and no aziridine can be detected in the crude reaction products. The aziridine-forming reactions are much slower than the [4 + 2] cycloadditions, which are essentially complete within a day. The yield of **14d** is low

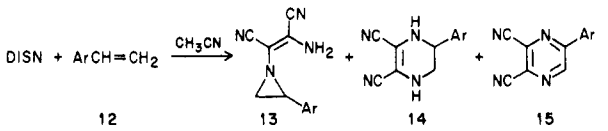
(1) (a) This work in part was reported in a preliminary communication: Fukunaga, T. *J. Am. Chem. Soc.* **1972**, *94*, 3242. (b) Begland, R. W.; Hartter, D. R.; Jones, F. N.; Sam, D. J.; Sheppard, W. A.; Webster, O. W.; Weigert, F. J. *J. Org. Chem.* **1974**, *39*, 2341.

(2) (a) Begland, R. W.; Cairncross, A.; Donald, D. S.; Hartter, D. R.; Sheppard, W. A.; Webster, O. W. *J. Am. Chem. Soc.* **1971**, *93*, 4953. (b) Begland, R. W.; Hartter, D. R. *J. Org. Chem.* **1972**, *37*, 4136. (c) Begland, R. W.; Hartter, D. R.; Donald, D. S.; Cairncross, A.; Sheppard, W. A. *Ibid.* **1974**, *39*, 1235.

(3) Cycloaddition reactions of 1,4-diazabutadiene derivatives have been recently reported: (a) Friedrichsen, W.; Oeser, H.-G.; Schmidt, R. *Tetrahedron Lett.* **1974**, 2827. (b) Kito, K.; Ohno, A. *J. Org. Chem.* **1974**, *39*, 3373. (c) Friedrichsen, W.; Schmidt, R. *Liebigs Ann. Chem.* **1978**, 1129. (d) Friedrichsen, W.; Oeser, H.-G. *Ibid.* **1978**, 1139. (e) Hammer, J. "1,4-Cycloaddition Reactions"; Academic Press: New York, 1967.

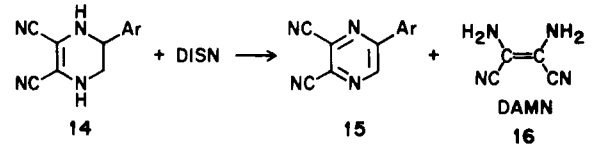
(4) All cycloaddition reactions of DISN were carried out in acetonitrile at ambient temperatures, unless noted otherwise, because the products often decomposed at higher temperatures. Some reactions were terminated before complete disappearance of DISN, and the yields were, therefore, unoptimized. In other solvents such as THF, ethyl acetate, and methylene chloride, the reactions proceeded sluggishly and gave more complex products.

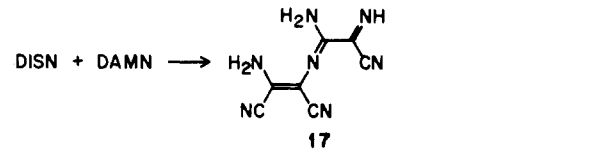
Chart I



ArCH=CH$_2$	Ar	REACTION TIME	YIELD %		
			13	14	15
12a	C_6H_5	2 d	58	-	-
12b	p-ClC_6H_4	6 d	51	-	-
12c	p-FC_6H_4	4 d	79	-	-
12d	p-$CH_3OC_6H_4$	24 h	-	46	17
12e	2-furyl	20 h	-	81	-
12f	p-$CH_3C_6H_4$	2 d	62	-	1.3

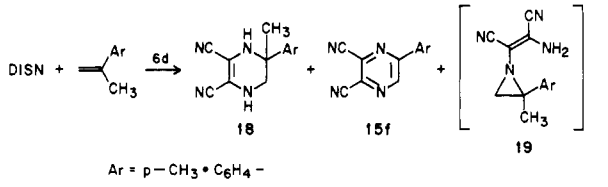
partly because it further consumes DISN under the reaction conditions to give pyrazine **15d** and diaminomaleonitrile (DAMN), **16**, which in turn reacts with DISN





to give 1,4-diamino-1,2,5-tricyano-3,6-diazahexatriene **17**.[2c] In fact, each of these products could be isolated from the reaction mixture. Similar complications may be responsible for the poor yield of **6**. Tetrahydropyrazines **14d** and **14e** can be cleanly aromatized (MnO_2 or SeO_2) to the corresponding pyrazine **15**.

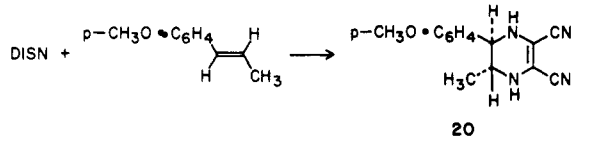
p-Methyl-substituted styrenes give both azirdine and [4 + 2] adduct. Thus, *p*-methylstyrene (**12f**) gives **13f** and **15f** in 62% and 1.3%, respectively. 2-(*p*-Tolyl)propene yields, however, [4 + 2] adduct **18** as the major product (19%) and traces of pyrazine **15f** and aziridine **19**.



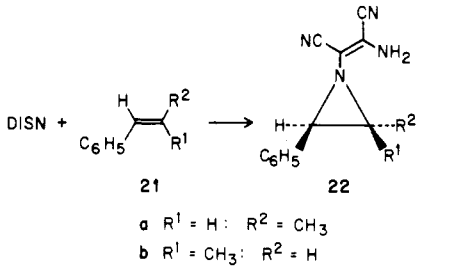
Ar = p-CH_3 • C_6H_4 -

Simple olefinic and acetylenic substrates such as cyclohexene, stilbene, phenanthrene, and phenylacetylene do not react with DISN. On the other hand, 2-vinylpyridine and indene yield uncharacterizable products.

Stereochemistry. The [4 + 2] cycloadditions of DISN with *cis*- and *trans*-1,2-dimethoxyethylene proceed with complete retention of stereochemistry to give **3a** and **3b**, respectively, and no crossover products could be detected in the NMR spectra.[5] Similarly, only trans adduct **20** is formed from *trans*-anethole.



The aziridine formation is also stereospecific with regard to phenylpropenes. The trans isomer **21a** is as reactive as



styrene (**12a**) and gives (*E*)-aziridine **22a** as the sole product recognizable by NMR spectra. However, chromatographic fractions of **22a** are invariably contaminated by **21a**, and pure crystalline **22a** could not be isolated. The cis propene **21b** is much less reactive than the trans isomer because of steric inhibition of resonance,[6a] and it does not react with DISN at room temperature. However, in refluxing acetonitrile **21b**[6b] reacts to give **22b** not contaminated with the *E* isomer **22a**. The *Z* isomer **22b** is thermally much more stable than **22a** and can be readily isolated in a pure form. Thus, in contrast to 2-phenylpropenes, 1-phenylpropenes give little or no pyrazines or their tetrahydro derivatives.

Mechanism. The results show that the ease of the DISN reactions qualitatively parallels the nucleophilicity of the substrates and suggest that the reactions are DISN LUMO controlled. DISN, like electron-deficient 1,3-dienes, has the LUMO that is low-lying[7] and possesses the largest and equal coefficients on the terminal atoms of the diene system. Thus, DISN is expected to undergo concerted [4 + 2] cycloaddition with electron-rich dienophiles, provided that the cis form, diiminomaleonitrile, is energetically accessible. However, unlike simple 1,3-dienes, the HOMO of DISN is the orthogonal and relatively high-lying, lone-pair orbital of the nitrogen: the lowest energy electronic transition of DISN is a $\pi^* \leftarrow$ n transition, λ_{max} 292 nm (ϵ 280).[7] The frontier MO structure then incorporates the essential feature of π-delocalized, σ^2 nitrenium ions (see **2**). We, therefore, propose that nucleophilic dienophiles interact initially with the DISN LUMO at the nitrogen terminus as depicted by **23** (Scheme I). It then follows a pathway similar to the familiar carbene addition reactions[8] to yield the zwitterionic aziridinium ion **24**.[9] Proton migration from the ring nitrogen to the terminal NH group leads to the formation of aziridine **25**, whereas a sigmatropic [σ2s + π4s] migration of the ring carbon to the anionic NH group could give rise to 2,3-dicyano-1,4,5,6-tetrahydropyrazine **26** with retention of olefin stereochemistry.

This mechanism is consistent with the observation that as the electron-donating power of group R increases, the reaction becomes more facile and the formation of the formal [4 + 2] adduct **26** becomes more favorable. This is expected because strong electron donors, such as alkoxy or *p*-methoxyphenyl, would increase contributions of the

(5) We thank Dr. D. R. Hartter for these experiments.

(6) (a) Mixer, R. Y.; Heck, R. F.; Winstein, S.; Young, W. G. *J. Am. Chem. Soc.* **1953**, *75*, 4094. (b) Traces of the trans isomer were removed by pretreatment of *cis*-phenylpropene with DISN at room temperature; see Experimental Section.

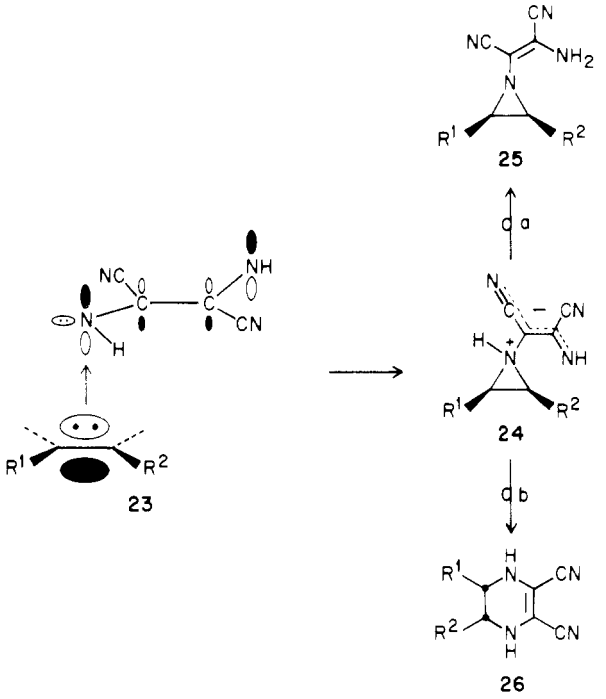
(7) Irreversible reduction of DISN occurs at −1.45 V (vs. hydrogen, dropping Hg electrode): Webster, O. W.; Hartter, D. R.; Begland, R. W.; Sheppard, W. A.; Cairncross, A. *J. Org. Chem.* **1972**, *37*, 4133.

(8) Hoffmann, R.; Hays, D. M.; Skell, P. S. *J. Phys. Chem.* **1972**, *76*, 664.

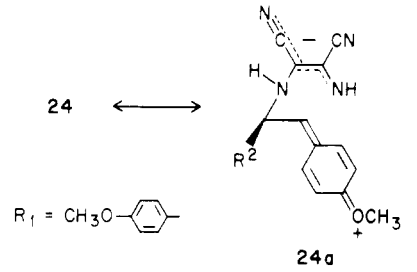
(9) The *cis*-maleonitrile structure is assumed for the side chain of **24**, although DISN is transoid. It is not clear how or when this isomerization occurs. However, DISN is readily converted to DAMN derivatives (ref 2 and 7), and DAMN is thermodynamically more stable than the trans isomer.[10]

(10) Yamada, Y.; Nagashima, N.; Nakamura, A.; Kumashiro, I. *Tetrahedron Lett.* **1968**, 4529.

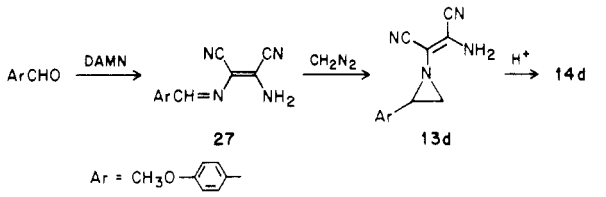
Scheme I



open-chain zwitterionic structure (e.g., **24a**) to the resonance hybrid, thus leading preferentially to aziridine ring opening to give **26**.



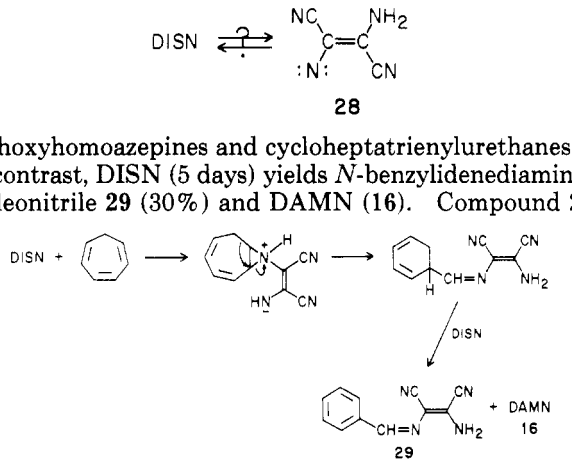
To further probe this two-step [4 + 2] cycloaddition, we have prepared **13d** by methylene addition to Schiff base **27**. Aziridine **13d** is a stable compound and does not



rearrange spontaneously. However, treatment with *p*-toluenesulfonic acid affords **14d** in up to 60% yield. By contrast, similar rearrangement of aziridine **13a** cannot be accomplished either with acid or with base. These results are consistent with but by no means prove the two-step [4 + 2] process involving the zwitterionic intermediate **24**. Nevertheless, the mechanism in Scheme I is attractive since a single intermediate can account for the formation of both types of products, and the participation of the cisoid form of DISN need not be invoked.

Reversely, polarizable azomethines that have a latent electrophilic nitrogen center are rare but have been invoked in special cases.[11,12] On the other hand, nitrenium ions are well-documented, useful reactive intermediates in a variety of solvolytic reactions and rearrangements.[13,14] However, the ability of nitrenium ions to form aziridinium ions has not been unequivocally demonstrated. It is interesting to note that *O*-(arylsulfonyl)hydroxylamines are capable of transforming typical olefins to their corresponding aziridines[15a,b] and that 1,1-dimethyldiazenium ion also yields aziridines.[15c] Oxidation of primary amines by various means is known to generate reactive intermediates that give to aziridines.[16-19] For these reactions, nitrene,[17] nitrenium ion,[14d,18] and olefin-assisted α-elimination mechanism[20] have been proposed.

Our postulate that DISN reacts as a latent nitrenium ion, but not as a nitrene such as **28**, is further supported by cationic-type rearrangements observed with certain substrates. For example, cycloheptatriene is reported to react with carbethoxynitrene to give a mixture of *N*-carbethoxyhomoazepines and cycloheptatrienylurethanes.[21] In contrast, DISN (5 days) yields *N*-benzylidenediaminomaleonitrile **29** (30%) and DAMN (**16**). Compound **29**

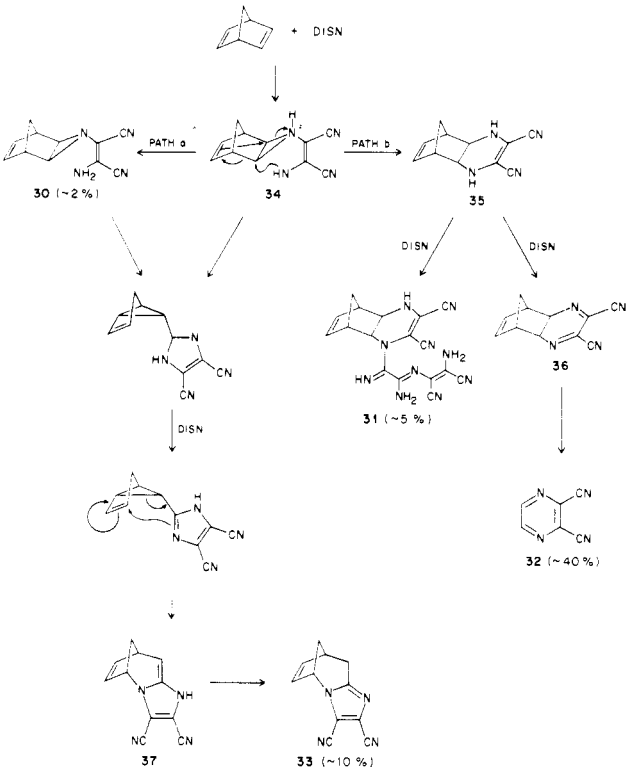


is identical with the Schiff base[22] obtained from benzaldehyde and DAMN. The reaction with norbornadiene (7 days) is rather complex, but the observed products, **30–33**, can be accounted for by the aziridinium ion mechanism (see Scheme II). The [4 + 2] cycloadduct **35** apparently further reacts with DISN either in a manner analogous to the formation of **17** to give **31** or oxidatively to yield **36**. The retro-Diels–Alder reaction of **36** affords the major product 2,3-dicyanopyrazine, **32**. Compound **33** probably arises from either **30** or **34** via a known rearrangement[23] of norbornadiene-*exo*-aziridines to give **37**, which then aromatizes.

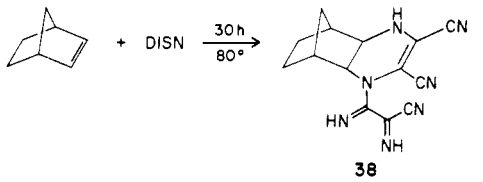
Norbornene (IP 8.97 eV)[24] is less reactive than nor-

(11) (a) Middleton, W. J.; Metzger, D. *J. Org. Chem.* **1970**, *35*, 3985. (b) Wiley, D. W.; Webster, O. W.; Blanchard, E. P. *Ibid.* **1976**, *41*, 1889.
(12) Bodforss, S. *Liebigs Ann. Chem.* **1971**, 99.
(13) (a) Gassman, P. G. *Acc. Chem. Res.* **1970**, *3*, 26. (b) Deyrup, J. A. In "Small Ring Heterocycles"; Hassner, A., Ed.; Wiley: New York, 1983; Part I, Chapter 1.
(14) (a) Hiyama, T.; Koide, H.; Nozaki, H. *Tetrahedron Lett.* **1973**, 2143. (b) De Rosa, M.; Haberfield, P. *J. Org. Chem.* **1981**, *46*, 2639. (c) Shell, F. M.; Ganguly, R. N. *Ibid.* **1980**, *45*, 4069. (d) Hoffman, R. V.; Cadena, R.; Poelker, D. J. *Tetrahedron Lett.* **1978**, 203. (e) Gutschke, D.; Heesing, A.; Heuschkel, U. *Ibid.* **1979**, 1363. (f) Ng, J. S.; Katzenellenbogen, J. A.; Kilbourn, M. R. *J. Org. Chem.* **1981**, *46*, 2520. (g) Margosian, D.; Speier, J.; Kovacic, P. *Ibid.* **1981**, *46*, 1346. (h) Margosian, D.; Kovacic, P. *Ibid.* **1981**, *46*, 877. (i) Boyer, J. H. *Chem. Rev.* **1980**, *80*, 495. (j) Takeuchi, H.; Ihara, R. *J. Chem. Soc., Chem. Commun.* **1983**, 175 and references therein.
(15) (a) Bottaro, J. C. *J. Chem. Soc., Chem. Commun.* **1980**, 560. (b) Shudo, K. *Synthesis* **1980**, 461. (c) Urry, W. H.; Gaibel, Z. L. F.; Duggan, J. C.; Teng, S. S. *J. Am. Chem. Soc.* **1973**, *95*, 4338.
(16) (a) Nagata, W.; Hirai, S.; Kawata, K.; Okumura, T. *J. Am. Chem. Soc.* **1967**, *89*, 5045.
(17) (a) Atkins, R. S.; Malpass, J. R. *J. Chem. Soc. Perkin Trans. 1* **1977**, 2242; *J. Chem. Soc., Chem. Commun.* **1975**, 555. (b) Atkins, R. S.; Malpass, J. R.; Skinner, K. L.; Woodthorpe, K. L. *J. Chem. Soc., Chem. Commun.* **1981**, 549. (c) Anderson, D. J.; Gilchrist, T. L.; Gymer, G. E.; Rees, C. W. *J. Chem. Soc. Perkin Trans. 1*, **1973**, 35.
(18) Cauquis, G.; Genies, M. *Tetrahedron Lett.* **1971**, 3959.
(19) Portoghese, P. S.; Sepp, D. T. *Tetrahedron* **1973**, *29*, 2253.
(20) See ref 14a, footnote 3.

Scheme II. DISN Reactions with Norbornadiene



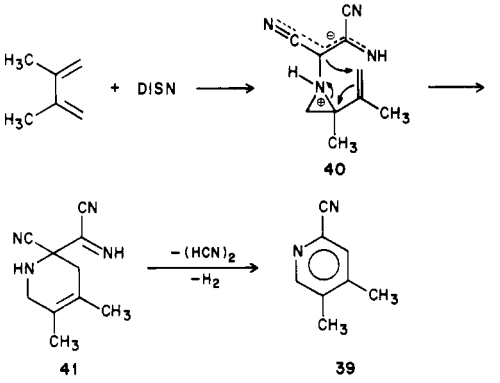
bornadiene (IP 8.69 eV)[24] and reacts with DISN only at reflux in acetonitrile to yield (30 h) the modified [4 + 2] cycloadduct **38** (20%) as the only identifiable product.



Although it is entirely possible that small amounts of other products are also formed, one might expect that, with norbornene, path b is favored over a in Scheme II, because anchimeric assistance is greater in norbornane than norbornene.[25]

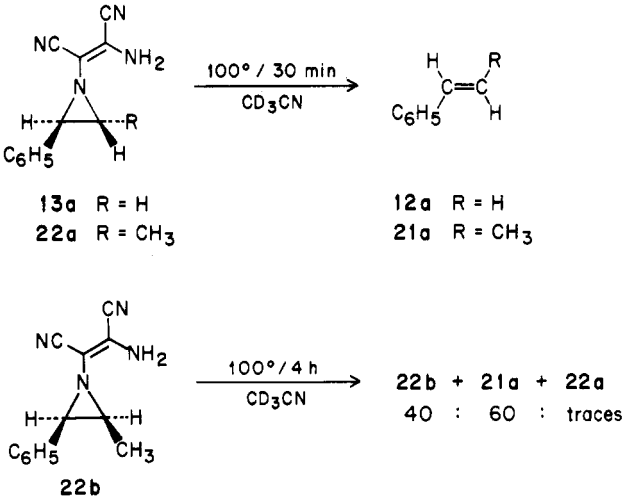
2,3-Dimethylbutadiene reveals yet another mode of DISN reactivity. In this case, DISN reacts formally as a dienophile to yield 2-cyano-4,5-lutidine **39** (20%). The initial adduct **41** that may arise from the zwitterionic aziridinium ion **40** loses a HCN dimer equivalent and is further dehydrogened by DISN.

Thus, DISN cycloadds to sufficiently nucleophilic but nonbasic olefins and acetylenes[26] to give three different types of products, i.e., aziridines and pyrazine and pyridine derivatives. Some reactions are complex and proceed sluggishly. All of the observed products can be accounted for by the proposed nitrenium ion mechanism involving a zwitterionic aziridinium ion as a common intermediate. Other alternative mechanisms such as nonconcerted



pathways to aziridines, however, cannot be rigorously excluded at this time.

Thermal Behavior of Aziridines. Because of the significant difference in the apparent thermal stability of the aziridines, we have examined the thermolyses of **13a**, **22a**, and **22b**. Heating (*E*)-aziridine **22a** in CD_3CN in a sealed NMR tubing at 100 °C results in complete cycloreversion to *trans*-propenylbenzene **21a** within 30 min. Neither **21b** nor **22b** can be detected by NMR. This cycloreversion occurs slowly even at room temperature and is apparently responsible for the unsuccessful isolation of **21a** in pure form. Aziridine **13a** also cycloreverts readily at 100 °C to give styrene, and its crystalline samples slowly decompose at room temperatures. The thermal instability of **22a** raises the possibility that the reaction of *cis*-propenylbenzene (**21b**) with DISN in refluxing acetonitrile might have generated (*E*)-aziridine **22a**, but it had subsequently decomposed. However, the propenylbenzene recovered from the reaction of DISN with **21b** (in a 1:2 ratio) had completely retained the cis stereochemistry judged by NMR. The *cis*-aziridine **22b** is surprisingly stable, and approximately 40% of **22b** remains after being heated at 100 °C in CD_3CN for 4 h. The mixture consists of the starting aziridine **22b** and *trans*-olefin **21a** in a 40:60 ratio. Traces of (*E*)-aziridine **22a** can be detected by



NMR but no *cis*-propenylbenzene (**21b**). The observed thermal instability of these aziridines is rather surprising because aziridines bearing an electron-withdrawing group on the nitrogen atom are ordinarily constitutionally and configurationally stable at ambient temperatures.[27]

(21) Okamura, W. H.; Snider, W. H.; Katz, T. J. *Tetrahedron Lett.* **1968**, 3367.
(22) (a) Hinkel, L. E.; Richards, G. O.; Thomas, O. *J. Chem. Soc.* **1937**, 1432. (b) Robertson, P. S.; Vaughan, J. *J. Am. Chem. Soc.* **1958**, *80*, 2691.
(23) (a) Anastassiou, A. G. *J. Org. Chem.* **1966**, *31*, 1131. (b) Oehlschlager, A. C.; Zalkow, L. H. *Ibid.* **1965**, *30*, 4205.
(24) Bischof, P.; Hashmall, J. A.; Heilbronner, E.; Hornung, V. *Helv. Chim. Acta* **1969**, *52*, 1745.
(25) Winstein, S.; Trifan, D. *J. Am. Chem. Soc.* **1952**, *74*, 1147, 1154.
(26) Basic reagents often displace the cyano groups; see ref 2b. 2-Vinylpyridine and enamines do not give cycloadducts.
(27) (a) Nadir, U. K., Koul, V. K. *J. Chem. Soc., Chem. Commun.* **1981**, 417. (b) Huisgen, R., Ross, C. H., Matsumoto, K. *Heterocycles* **1981**, *15*, 1131. (c) Analogous stereochemical results have been reported, however, in thermal decompositions of *N*-amino-*cis*- and *trans*-2,3-diphenylaziridine, see: Lahti, P. M. *Tetrahedron Lett.* **1983**, *24*, 2339 and references therein.

The significant difference between **22a** and **22b** in the ease of 1,1-cycloreversion is also unexpected, if only thermodynamic stabilities of the reactants and products are compared. The product olefins are of comparable energy; **21a** is 1.0 kcal/mol more stable than **21b**.[28,29] The aziridines are also expected to be thermodynamically nearly equivalent.[27b,30] As discussed earlier, however, (*Z*)-olefin **21b** is much less reactive than (*E*)-olefin **21a** toward DISN. If this kinetic bias is also to operate on the hypothetical 1,1-cycloaddition to the nitrene **28** (an expected fragment of the decomposition) to the olefins, the principle of microscopic reversibility suggests that the cycloreversion of (*Z*)-aziridine **22b** would require a greater activation energy than that of *E* isomer **22a**. We are further examining the thermal behavior and *E*–*Z* isomerization of these compounds.

Product Characterization. The aziridines exhibit characteristic ^{1}H NMR coupling constants (see Experimental Section) that are in good agreement with those reported for styrenimines;[31] J_{vic}(cis) ~ 6, J_{vic}(trans) ~ 3, J_{gem}(H,CH$_3$) ~5, and J_{gem}(H,H) < 0.6 Hz. The electron-withdrawing N substituent of the aziridines reported in this paper, however, causes deshielding[32] of the aziridine ring protons by 0.5–1.0 Hz relative to the corresponding protons in styrenimines.[31] As in the latter, the aziridine ring protons and methyl protons are shielded when cis to the phenyl ring, suggesting that the conjugative effect of the three-membered ring places the phenyl ring in a bisecting conformation. Assignment of diaminomaleonitrile rather than *trans* fumaronitrile structure follows from the known stability of the cis over the trans isomer[1b] and from comparison of the UV absorption data with those of DAMN (λ_{max} 295 nm, ϵ 12 000)[33] and its cis isomer (λ_{max} 310 nm, ϵ 8200).[34] Oligomeric side chains in **31** and **38** are assigned on the basis of elemental analyses and spectral comparison with related structures such as **17** and its homologues.[2c] Pertinent structural information for other compounds are included in the Experimental Section.

Concluding Remarks. DISN reacts with sufficiently electron-rich but nonbasic olefins to give [4 + 2] cycloadducts or aziridines with retention of olefin stereochemistry. Although the conventional concerted process cannot be rigorously excluded for the [4 + 2] cycloadditions, all of the products are accounted for by the reactions of a common intermediate, zwitterionic aziridinium ion, arising from the nitrenium ion type 1,1-addition of DISN to olefin. We postulate that azomethines exhibit nitrenium ion reactivity (isoelectronic with carbenes) if the C=N bond is polarizable in the direction opposite to the normal polarization. In other words, divalent nitrogen species such as azomethines are latent nitrenium ion sources[35a] if the system has the mutually orthogonal HOMO and LUMO, both of which are energetically reactive and sufficiently localized on the divalent atomic center. A similar consideration has been advanced recently to account for the nitrene-type reactivity of certain diazo compounds.[35b]

Finally, it should be mentioned that reverse polarization is well-known for thiocarbonyl compounds,[36] whereas understandably carbonyl compounds are not readily polarizable to give an oxenium ion terminus. However, α-diketones and *o*-benzoquinones react with nucleophiles such as phosphites at the oxygen terminus,[3e] suggesting contributions from the dipolar forms involving an oxenium ion center. In this sense, they may be regarded as the vinylogue and benzologue of singlet oxygen. Furthermore, it is not inconceivable that [4 + 2] cycloadditions of 1,2-dicarbonyl compounds to give dioxenes[3e] proceed also in two steps, as in the case of the DISN reactions, involving the formation of a zwitterionic vinylogous perepoxide.[37] New chemistry may be expected from reversely polarizable functional groups.

Experimental Section

DISN has an oral toxicity ALD 90 mg/kg in rats. It causes severe irritation on contact with rabbit eyes, and permanent damage is prevented only by immediate flushing with water. It causes mild skin and nose irritation. Also, since DISN produces hydrogen cyanide when wet or in contact with hydroxylic solvent, we strongly *caution that it be handled only in well-ventilated areas with adequate protection.*

All reactions were run under dry nitrogen atmosphere. Infrared spectra were determined on either Perkin-Elmer 21 (KBr pellet) or 137 (Nujol mull) spectrometers and are reported in reciprocal centimeters. ^{1}H NMR spectra were determined on either Varian A-60, EM-390CW, or FT-80A instruments. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. The UV spectra were recorded on a Cary 14 or 17 spectrometer. All melting points were taken on a Mel-Temp apparatus and are uncorrected. Unless indicated otherwise, all chemicals were reagent grades and were obtained from commercial sources.

Some reactions of DISN produce dark tarry materials that prevent ready isolation of products. We have found that a simple fractional filtration works satisfactorily for removing these by-products. Thus, the soluble product is preadsorbed on a quantity (3–5 g per 1 g of product) of silica gel, and the dry preadsorbed material is placed in a wide-diameter column on top of a 1–2 times quantity of fresh silica gel. Column diameter is such that the height to diameter ratio is nearly unity. The resulting column flows quite rapidly and usually gives sufficient separation by merely changing solvents. Mallinckrodt's SilicAR CC7 (100–200 mesh) works satisfactorily. Woelm neutral alumina was used without deactivation for chromatography on alumina. DISN was freshly purified[2] immediately before use.

2,3-Dimethoxy-5,6-dicyano-1,2,3,4-tetrahydropyrazine (3).[5] A solution of 4.40 g (50 mmol) of *cis*-dimethoxyethylene[38] [NMR (neat) δ 3.16 (s, 6 H) and 4.87 (s, 2 H)] in 25 mL of acetonitrile was added dropwise over a period of 30 min at 10 °C to a solution of 5.30 g (50 mmol) of DISN in 75 mL of acetonitrile. This solution

(28) Stull, D. R.; Westrum, E. F.; Sinke, G. C. "The Chemical Thermodynamics of Organic Compounds"; Wiley: New York, 1969.

(29) A substantial portion of this energy difference may reflect the activation energy difference between cycloreversion of **22a** and **22b**, since transition states of electrocyclic reactions are in general edduct-like; see for example: (a) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779. (b) Hoffman, R. *J. Am. Chem. Soc.* **1968**, *90*, 1475. (c) RajanBabu, T. V.; Eaton, D. F.; Fukunaga, T. *J. Org. Chem.* **1983**, *48*, 652.

(30) The NMR data discussed later show that the benzene ring is perpendicular to the aziridine ring, so that no significant steric destabilization of the (*Z*)-aziridine **22b** is expected.

(31) Brois, S. J. *J. Org. Chem.* **1962**, *27*, 3533.

(32) This deshielding and the absence of NMR signals from aziridine invertomers collectively suggest that the aziridines reported herein are essentially planar.

(33) Webb, R. L.; Frank, S.; Schneider, W. C. *J. Am. Chem. Soc.* **1955**, *77*, 3491.

(34) Yamada, Y.; Nagashima, N.; Nakamura, A.; Kumashiro, I. *Tetrahedron Lett.* **1968**, 4529.

(35) (a) Formation of zwitterionic aziridinium ions have been postulated for the addition reactions of triazolinedione and pentafluoronitrosobenzene to olefins: Seymour, C. A.; Greene, F. D. *J. Am. Chem. Soc.* **1980**, *102*, 6384; *J. Org. Chem.* **1982**, *47*, 5227. (b) Padwa, A.; Rodriguez, A.; Tohidi, M.; Fukunaga, T. *J. Am. Chem. Soc.* **1983**, *105*, 933.

(36) See, for example: Middleton, W. J.; Sharkey, W. H. *J. Org. Chem.* **1965**, *30*, 1384. Vedejs, E.; Perry, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 1683 and references therein.

(37) (a) Schaap, A. P.; Recher, S. G.; Faler, G. R.; Villasenor, S. R. *J. Am. Chem. Soc.* **1983**, *105*, 1691 and references therein. (b) Hotokka, M.; Roos, B.; Siegbahn, P. *Ibid.* **1983**, *105*, 5263. (c) For theoretical description of singlet oxygen, see; e.g.: Salem, L. "Electrons in Chemical Reactions: First Principles"; Wiley: New York, 1982.

(38) Waldron, J. T.; Snyder, W. H. *J. Org. Chem.* **1973**, *38*, 3059.

was stirred for 7 h at room temperature and evaporated to dryness. The crude product was crystallized from ethyl acetate, yielding 7.38 g (76%) of **3a** as white prisms: mp 157–158 °C; NMR (Me_2SO-d_6) δ 3.33 (s, 6 H), 4.45 (d, 2 H), 7.02 (d, 2 H); IR (Nujol) 3370, 3240, 2210, 1610, 1065, 980, 900, 780, 720 cm^{-1}.

Anal. Calcd for $C_8H_{10}N_4O_2$: C, 49.48; H, 5.19; N, 28.85. Found: C, 49.68, H, 5.41; N, 29.21.

In an identical manner, 4.40 g (50 mmol) of *trans*-dimethoxyethylene [NNR (neat) δ 3.02 (s, 6 H) and 5.90 (s, 2 H)] was reacted with 5.30 g (50 mmol) of DISN. The crude product was recrystallized from ethyl acetate to yield **3b**: white needles; mp 160–161 °C; NMR (Me_2SO-d_6) δ 3.20 (s, 6 H), 4.47 (d, 2 H), 7.54 (d, 2 H); IR (Nujol) 3280, 2210, 1610, 1090, 915, 855, 720 cm^{-1}.

NMR solutions prepared from 106 mg of DISN and 0.10 mL of *cis*- or *trans*-dimethoxyethylene in 1 mL of acetone-d_6 showed a half-life of about 15 min and distinctly different spectra. No crossover products could be detected in the spectra (NMR (acetone-d_6)) of **3a** [δ 3.43 (s, 6 H), 4.57 (d, 2 H), 5.98 (d, 2 H)] or **3b** [δ 3.30 (s, 6 H), 4.58 (m, 2 H), 6.65 (d, 2 H)]. Thus the cycloaddition is at least 98% stereospecific. Both **3a** and **3b** eliminated methanol readily either thermally or on silica gel, giving 2,3-dicyanopyrazine (**4**), mp 132–134 °C (lit.[22a] mp 132 °C).

2-(Diethylamino)-3-phenyl-5,6-dicyanopyrazine (6a). A solution of 5.3 g (50 mmol) of DISN in 50 mL of THF was cooled to −70 °C, and 8.56 g (50 mmol) of phenyl(diethylamino)acetylene was added dropwise. The solution was warmed to room temperature, preabsorbed, and chromatographed on SilicAR CC7. Benzene elution gave 3.3 g (48%)[39] of **6a** as yellow plates. An analytical sample was obtained by a recrystallization from cyclohexane: mp 107–108 °C; NMR ($CDCl_3$) δ 1.08 (t, 6 H, CH_3), 3.42 (q, 4 H, CH_2), 7.5 (m, 5 H, C_6H_5); UV (CH_3CN) 223 nm (ε 13 400), 247 (10 500), 325 (16 700), 380 (5800); IR (KBr) 2225, 1575, 1535, 1495, 767, 705 cm^{-1}.

Anal. Calcd for $C_{16}H_{15}N_5$: C, 69.30; H, 5.45; N, 25.25. Found: C, 69.63; H, 5.35; N, 25.29.

2-(Diethylamino)-3-methyl-5,6-dicyanopyrazine (6b). A solution of 10.6 g (0.10 mol) of DISN in 150 mL of THF was cooled to −70 °C, and 11.1 g (0.10 mol) of (diethylamino)-1-propyne was added dropwise. The resulting solution was allowed to warm to room temperature and was evaporated to give an oil. Chromatography (benzene–chloroform) gave 6.7 g (62%)[39] of **6b** as a yellow oil: NMR ($CDCl_3$) δ 1.33 (t, 6 H, CH_3), 2.71 (s, 3 H, CH_3), 3.70 (q, 4 H, CH_2); IR (neat) 2960, 2910, 2215, 1545, 1500 cm^{-1}.

Anal. Calcd for $C_{11}H_{13}N_5$: C, 61.38; H, 6.09; N, 32.53. Found: C, 61.35; H, 6.03; N, 32.72.

1,4,4a,7a-Tetrahydro-5*H*-cyclopentapyrazine-2,3-dicarbonitrile (7). To a solution of 5.0 g (47 mmol) of DISN in 50 mL of CH_3CN was added 18 mL of cyclopentadiene dropwise at 24–30 °C (moderately exothermic). The pale yellow solution was stirred at 24 °C overnight and worked up according to the general procedure. The residual solid was recrystallized from $CHCl_3$ to give 4.06 g (50.2%) of **7**, mp 115–118 °C. Another recrystallization from $CHCl_3$–CCl_4 afforded an analytical sample:[40] mp 119–120 °C; NMR (CD_3CN) δ 2.37 (q × d, 2 H, CH_2), 3.61 (m, 1 H, CH), 4.13 (t × m, 1 H, CH), 4.70 (br, 2 H, NH), 5.76 (m, 2 H, vinyl); UV (C_2H_5OH) 325 nm (ε 13 400); IR (KBr) 3330, 2220, 1620 cm^{-1}.

Anal. Calcd for $C_9H_8N_4$: C, 62.77; H, 4.68; N, 32.55. Found: C, 62.40; H, 4.56; N, 33.14.

6,7-Dihydro-5*H*-cyclopentapyrazine-2,3-dicarbonitrile (9). A solution of 1.72 g (10.0 mmol) of **7** was hydrogenated at atmospheric pressure by using 160 mg of 10% Pd/C. Absorption was complete in 70 min after uptake of 210 mL of H_2. The mixture was filtered through a Celite bed, evaporated, and recrystallized from benzene–hexane, yielding 1.68 g (96.5%) of **8** as tan crystals: NMR (CD_3CN) δ 1.70 (m, 6 H, CH_2), 3.42 (br, 2 H, CH), 4.60 (br, 2 H, NH). Compound **8** darkens considerably at room temperature within a day and is difficult to purify.

To a stirred suspension of 4.4 g of active manganese(IV) oxide in 50 mL of dichloromethane was added 1.00 g of **8** in portions at 15–20 °C (exothermic). The mixture was slowly warmed to room temperature during 1 h, filtered through Celite, and washed with ethyl acetate. Evaporation of the solvents followed by recrystallization gave 724 mg of an analytical sample of **9**: mp 138–139 °C; NMR ($CDCl_3$) δ 2.42 (qui, 2 H), 3.28 (t, 4 H); UV (C_2H_5OH) λ_{max} 310 (sh) nm (ε 3080), 291 (7900), 248 (8040); IR (KBr) 2250, 1565, 1550 cm^{-1}.

Anal. Calcd for $C_9H_6N_4$: C, 63.52; H, 3.55; N, 32.93. Found: C, 63.49; H, 3.57; N, 32.79.

1,4,4a,5,6,8a-Hexahydroquinoxaline-2,3-dicarbonitrile (11). A solution of 3.0 g (28.2 mmol) of DISN and 5.0 g (62.5 mmol) of 1,3-cyclohexadiene in 30 mL of acetonitrile was stirred at room temperature for 5 days. The clear, pale orange solution was stirred with charcoal, filtered, and evaporated. The residue was filtered and washed with ether to give 4.13 g (78.5%) of **11** as colorless crystals, mp 97–99 °C. The sample was analyzed without further purification because it darkened at room temperature within a day and decomposed into black tar after a few days: NMR ($CDCl_3$) δ 1.55 (m, 2 H, CH_2), 2.20 (m, 2 H, CH_2), 3.35 (m, 1 H, CH), 3.90 (m, 1 H, CH), 11.8 (br, 2 H, NH), 6.03 (t, 1 H, vinyl), 6.48 (t, 1 H, vinyl); IR (Nujol) 3380, 3160, 2240, 1610 cm^{-1}.

Anal. Calcd for $C_{10}H_{10}N_4$: C, 64.50; H, 5.41; N, 30.09. Found: C, 63.88; H, 5.38; N, 30.02.

Reactions of DISN with Styrenes. Styrene (12a). A solution of 3.0 g (28.2 mmol) of DISN and 16 mL of styrene in 30 mL of CH_3CN was stirred at room temperature for 2 days; some DISN was still present. Crude product, 3.93 g, was recrystallized from ether–hexane to give 3.42 g of colorless crystals, mp 91–93 °C, which were recrystallized from ether–hexane to give an analytical sample of **13a**: mp 92–93 °C dec; NMR δ 2.50 (d, J = 4 Hz, 1 H, trans-CH_2), 2.66 (d, J = 7 Hz, 1 H, cis-CH_2), 3.12 (d × d, J = 4 and 7 Hz, 1 H, CH), 4.55 (br, 2 H, NH_2), 7.33 (s, 5 H, Ar); UV (C_2H_5OH) 300 nm (ε 14 200); IR (KBr) 3380, 3290, 3200, 2220, 2200, 1635, 1600, 781, 730, 699 cm^{-1}.

Anal. Calcd for $C_{20}H_{10}N_4$: C, 68.55; H, 4.79; N, 26.65. Found: C, 68.54; H, 4.86; N, 26.96.

***p*-Chlorostyrene (12b).** A solution of 3.0 g of DISN and 8.5 g of *p*-chlorostyrene in 40 mL of CH_3CN was stirred at room temperature for 6 days; some DISN was still present. A recrystallization of crude product from benzene gave 3.48 g of tan crystals, mp 112–115 °C. Another recrystallization from benzene afforded an analytical sample of **13b**: mp 126–128 °C dec; NMR (CD_3CN) δ 2.49 (d, J = 4.1 Hz, trans-CH_2), 2.54 (d, J = 6.8 Hz, cis-CH_2, 2 H together with d at 2.49), 3.22 (d × d, J = 6.8 and 4.1 Hz, 1 H, CH), 5.25 (br, 2 H, NH_2), 7.38 A_2B_2, 4 H, Ar); IR (Nujol) 3460, 3320, 3150, 2250, 2190, 1620 cm^{-1}.

Anal. Calcd for $C_{12}H_9N_4Cl$: C, 58.90; H, 3.71; N, 22.89. Found: C, 59.10; H, 3.63; N, 22.90.

***p*-Fluorostyrene (12c).** A solution of 3.0 g of DISN, 7.5 g of **12c**, and 40 mL of CH_3CN was stirred for 4 days; some DISN was present. Crude product, 5.10 g, was recrystallized from benzene to give an analytical sample of **13c**: mp 108–110 °C dec; NMR (CD_3CN) δ 2.49 (d, J = 4 Hz, trans-CH_2), 2.51 (d, J = 7 Hz, cis-CH_2, 2 H together with d at 2.49), 3.25 (d × d, J = 4 and 7 Hz, 1 H, CH), 5.22 (br, 2 H, NH_2), 6.5–7.5 (m, 4 H, Ar); UV (C_2H_5OH) 299 nm (ε 14 400); IR (KBr) 3440, 3320, 3175, 2250, 2200, 1625 cm^{-1}.

Anal. Calcd for $C_{12}H_9N_4F$: C, 63.15; H, 3.98; N, 24.56; F, 8.32. Found: C, 63.10; H, 4.01; N, 24.91, F, 8.30.

***p*-Methoxystyrene (12d).** A solution of 3.0 g of DISN and 7.8 g (58 mmol) of **12d** in 40 mL of CH_3CN was stirred at room temperature. No DISN was detected by IR after a day. Crude product was chromatographed on silica. Benzene fractions, 560 mg (16.8%), afforded 281 mg of **15d** as yellow crystals. Methylene chloride fractions, 3.09 g (45.6%), afforded 2.02 g of analytically pure **14d** (benzene) as a colorless solid. Further elution with ether afforded **16**[7] and **17**.[2c] Oxidation of **14d** with SeO_2 in boiling benzene gave **15d** in 45% yield.

14d: mp 135–136 °C; NMR (CD_3CN) δ 3.18 (m, 2 H, CH_2), 4.11 (m, 1 H, CH), 4.8 (br, 2 H, NH), 3.81 (s, 3 H, CH_3), 6.96 (d, J = 9 Hz, 2 H, Ar), 7.27 (d, J = 9 H, 2 H, Ar); UV (C_2H_5OH) 324 nm (ε 10 300), 224 (21 800); IR (KBr) 3330, 2220 cm^{-1}.

Anal. Calcd for $C_{13}H_{12}N_4O$: C, 64.98; H, 5.03; N, 23.32. Found: C, 64.97; H, 4.89; N, 23.26.

(39) Calculated on the basis of DISN, 2 mol of which are consumed for the formation of the pyrazine.

(40) Because of thermal and oxidative instability, satisfactory elemental analyses were difficult to obtain.

15d: mp 178–180 °C; NMR ($CDCl_3$) δ 3.92 (s, 3 H, CH_3), 7.15 (d × m, J = 9 Hz, 2 H, Ar), 8.16 (d, J = 9 Hz, 2 H, Ar), 9.34 (s, 1 H, pyrazine); UV (C_2H_5OH) 351 nm (ε 23 400), 260 (sh) (5490), 229 (13 900); IR (KBr) 2235, 1605, 1550, 1515, 1505 cm^{-1}.

Anal. Calcd for $C_{13}H_8N_4O$: C, 66.09; H, 3.41; N, 23.72. Found: C, 65.92; H, 3.25; N, 23.75.

***p*-Methylstyrene (12f).** A solution of 6.0 g (56.5 mmol) of DISN and 17 g (144 mmol) of **12f** in 100 mL of CH_3CN was stirred at room temperature for 2 days. The solvent and excess **12f** were evaporated in vacuum to give 10.3 g of a brown solid, which was recrystallized from benzene to give 7.83 g (61.8%) of **13f**. An ether solution of **13f** was filtered through alumina, and a recrystallization from benzene afforded an analytical sample. The original benzene filtrate was chromatograhed on alumina, and 161 mg (1.3% of **15f**) was obtained as pale yellow crystals, which were sublimed to give an analytical sample of **15f**.

13f: mp 108–110 °C dec; NMR (CD_3CN) δ 2.48 (d, J = 4 Hz, trans-CH_2), 2.47 (d, J = 7 Hz, cis-CH_2, 2 H together with d at 2.48), 3.17 (d × d, J = 7 and 4 Hz, 1 H, CH), 5.11 (br, 2 H, NH_2), 7.17 (s, 4 H, Ar), 2.40 (s, 3 H, CH_3); UV (C_2H_5OH) 300 nm (ε 14 700); IR (KBr) 3440, 3310, 3155, 2240, 2195, 1620 cm^{-1}.

Anal. Calcd for $C_{13}H_{12}H_4$: C, 69.62; H, 5.39; N, 24.99. Found: C, 69.74; H, 5.44; N, 25.09.

15f: mp 183–184 °C; NMR (CD_3CN) δ 2.54 (s, 3 H, CH_3), 7.50 (d, 2 H, Ar), 8.19 (d, 2 H, Ar), 9.43 (s, 1 H, pyrazine); UV (C_2H_5OH) 335 (sh) nm (ε 18 300), 311 (20 300), 253 (4360), 222 (13 200); IR (KBr) 2240, 1610, 1560, 1520, 1505 cm^{-1}.

Anal. Calcd for $C_{13}H_8N_4$: C, 70.89; H, 3.66; N, 25.44. Found: C, 70.34, H, 3.57; N, 25.69.

2-(*p*-Tolyl)propene. A solution of 3.0 g of DISN and 8.0 g (60.5 mmol) of 2-(*p*-tolyl)propene in 40 mL of CH_3CN was stirred for 6 days; no DISN was detected by IR. The solvent was evaporated, and the residue was chromatographed on silica. After the olefin was eluted out with hexane, the first 200-mL benzene fraction was collected, giving 36 mg of yellow orange crystals, which was identified by IR and NMR to be **15f**. The next 400-mL benzene fraction gave a dark orange oil (150 mg); the IR and NMR spectra were suggestive of **19**, but no pure compound could be isolated. Methylene chloride fractions gave 1.28 g of a brown solid, a recrystallization of which from CH_2Cl_2–ether gave 880 mg of **18** as pale yellow crystals. Further elution with ether gave DAMN.[7] **18**: mp 190–192 °C dec; NMR (CD_3CN) δ 1.40 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3), 2.82 (d × d, J = 12.2 and 5 Hz, 1 H, CH_2), 3.45 (d × d, J = 12.2 and 5 Hz, 1 H, CH_2), 4.56 (br, 1 H, NH), 5.00 (br, 1 H, NH), 7.24 (s, 4 H, Ar); UV (C_2H_5OH) 323 nm (ε 9700); IR (KBr) 3380, 3330, 2210 cm^{-1}.

Anal. Calcd for $C_{14}H_{14}N_4$: C, 70.56; H, 5.92; N, 23.51. Found: C, 70.50; H, 6.19; N, 23.76.

***trans*-Anethole.** A solution of 5.3 g of DISN and 20 g of *trans*-anethole in 100 mL of CH_3CN was stirred for 3 days and worked up to give 9.28 g (73%) of **20** as a tan solid, which was recrystallized from $CHCl_3$ to give 8.13 g of analytically pure, colorless crystals: mp 179–181 °C dec; NMR (CD_3CN) δ 0.92 (d, J = 6.4 Hz, 3 H, CH_3), 3.05 (m, 1 H, CH), 3.58 (d × d, J = 6.4 and 2.4 Hz, 1 H, CH), 3.76 (s, 3 H, OCH_3), 4.60 (br, 1 H, NH), 4.80 (br, 1 H, NH), 7.05 (A_2B_2, 4 H, Ar).

Anal. Calcd for $C_{14}H_{14}N_4O$: C, 66.12; H, 5.55; N, 22.04. Found: C, 66.30; H, 5.63; N, 22.04.

Oxidation of **20** with active MnO_2 in CH_2Cl_2 gave, after recrystallization from benzene and vacuum sublimation at 150 °C, 5-methyl-6-*p*-anisylpyrazine-2,3-dicarbonitrile: mp 178–182 °C dec; NMR (CD_3CN) δ 2.71 (s, 3 H), 3.83 (s, 3 H), 7.00 (d, J = 8.5 Hz, 2 H), 7.60 (d, J = 8.5 Hz, 2 H).

Anal. Calcd for $C_{14}H_{10}N_4O$: C, 67.19; H, 4.03; N, 22.39. Found: C, 67.21; H, 3.89; N, 22.16.

***trans*-Propenylbenzene (21a).** A solution of 5.3 g (50 mmol) of DISN and 13 g (110 mmol) of **21a** in 30 mL of acetonitrile was stirred at room temperature for 4 days, filtered with charcoal, and evaporated in vacuum below 30 °C. The dark residue containing **21a** and **22a** in ca. 1:1.6 ratio (NMR) and DISN (IR) was chromatographed on 200 g of alumina. After three 200-mL toluene fractions, the first 200-mL CH_2Cl_2 fraction was collected and evaporated at room temperature to give 2.92 g of a pale yellow semisolid: NMR ($CDCl_3$) δ 1.29 (d, J = 5.5 Hz, 3 H, CH_3), 2.70 (d × q, J = 5.5 and 4 Hz, 1 H, CH-Me), 3.12 (d, J = 4 Hz, 1 H, CH-Ar), 4.48 (br, 2 H, NH_2), in addition to minor peaks due to **21a** at 180 (d, J = 5 Hz), 6.27 (m), 6.72 (m). Chromatographically purified samples darkened considerably within several hours, and an analytical sample could not be obtained.

A freshly chromatogramed sample of **22a** in CD_3CN in a sealed NMR tube was heated at 100 °C in an oil bath for 30 min; no **22a** remained and only **21a** was detected.

***cis*-1-Phenylpropene (21b).** A solution of 50 g of **21b** and 5 g of DISN in 200 mL of acetonitrile was stirred at room temperature for 5 days. After the solvent was evaporated below 28 °C, the residue was chromatographed on alumina. The hexane fractions were combined and fractionally distilled. The center cut, bp 165 °C, was used for the following run.

A solution of 2.1 g of DISN and 7.0 mL of **21b** in 30 mL of acetonitrile was refluxed for 2 days under nitrogen. The solvent was evaporated, and the residue was distilled in vacuum. The distillate collected in a trap at −78 °C was found by NMR to be **21b** uncontaminated by **21a**. The residue was chromatographed on silica, and benzene fractions were recrystallized twice from CCl_4 to give an analytical sample of **22b**: mp 119–120.5 °C; NMR ($CDCl_3$) δ 1.08 (s, 3 H, CH_3), 2.74 (d × d, J = 5.5 and 7 Hz, 1 H, CH-Me), 3.35 (d, J = 7 Hz, 1 H, CH-Ar), 4.45 (br, 2 H, NH_2), 7.34 (m, 5 H, Ar).

Anal. Calcd for $C_{13}H_{12}N_4$: C, 69.62; H, 5.39; N, 24.99. Found: C, 69.66; H, 5.51; N, 25.10.

A solution of **22b** in CD_3CN in a sealed NMR tube was heated at 100 °C in an oil bath; **22b**, **22a**, and **21a** were detected in ~18:1:~6.3 and ~9:1:~14 ratio after 1 and 4 h, respectively.

5-(2-Furyl)-1,4,5,6-tetrahydropyrazine-2,3-dicarbonitrile (14e). A solution of 3.0 g of DISN and 6.0 g (62.8 mmol) of 2-vinylfuran in 40 mL of CH_3CN was stirred for 20 h; no DISN remained. The mixture was evaporated, and 6.0 g of a dark orange viscous oil was chromatographed on 60 g of alumina. Four 200-mL CH_2Cl_2 fractions and a 200-mL ethyl acetate fraction gave, after recrystallization from ether–hexane, 4.64 g (81%) of **14e** as a tan solid, mp 78–82 °C. An analytical sample was prepared by recrystallization from benzene–hexane: mp 87–89 °C dec; NMR ($CDCl_3$) δ 2.32 (t, 2 H, CH_2), 4.41 (q, 1 H, CH), 4.7–4.9 (br, 2 H, NH), 6.36 (m, 2 H, furan), 7.46 (m, 1 H, furan); UV (C_2H_5OH) 320 nm (ε 10 400), 215 (18 800); IR (KBr) 3360, 2220 cm^{-1}.

Anal. Calcd for $C_{10}H_8N_4O$: C, 59.99; H, 4.03; N, 27.99. Found: C, 60.08; H, 4.05; N, 27.82.

5-(2-Furyl)pyrazine-2,3-dicarbonitrile (15e). A solution of 1.0 g of **14e** in 50 mL of CH_2Cl_2 was added to a stirred suspension of 4.4 g of active MnO_2 at 25 °C over a period of 1 h, stirred for 2 more h, filtered through Celite, and washed with ethyl acetate. Evaporation of the solvent gave 930 mg of yellow crystals, which were recrystallized from ethyl acetate to give an analytical sample of **15e**: mp 87–89 °C dec; NMR (CD_3CN) δ 6.75 (d × d, J = 3.7 and 1.7 Hz, 1 H), 7.54 (d × d, J = 3.7 and 0.7 Hz, 1 H), 7.89 (d × d, J = 1.7 and 0.7 Hz, 1 H), 9.20 (s, 1 H); UV (C_2H_5OH) 350 nm (ε 20 200), 325 (sh) (17 600), 253 (3940), 222 (11 700); IR (KBr) 2235, 1590, 1540, 1510 cm^{-1}.

Anal. Calcd for $C_{10}H_4N_4O$: C, 61.23; H, 2.06; N, 28.57. Found: C, 61.26; H, 1.97; N, 28.84.

2-Amino-3-[2-(*p*-methoxyphenyl)aziridin-1-yl]maleonitrile (13d). To a solution of 7.08 g (30 mmol) of Schiff base **27**[22a] in 200 mL of THF was added 60 mmol of diazomethane in 100 mL of ether. The resulting solution was stirred for 4 days and the solvent was removed, giving 6.6 g of a solid, which was refluxed with 200 mL of ether and filtered. Recrystallization of the ether soluble solid from ether–petroleum ether gave 1.7 g (24%) of **13d** as light yellow crystals: mp 98–100 °C dec; NMR ($CDCl_3$) δ 2.6 (m, 2 H, CH_2), 3.1 (m, 1 H, CH), 3.83 (s, 3 H, OCH_3), 4.5 (br, 2 H, NH), 6.92 (d, J = 8.5 Hz, 2 H, Ar), 7.25 (d, J = 8.5 Hz, 2 H, Ar); IR (Nujol) 3500, 3380, 3225, 2205, 1610, 1510 cm^{-1}.

A solution of 0.20 g of **13d** and 0.01 g of *p*-toluenesulfonic acid monohydrate in 30 mL of THF was stirred for 1 h. The solvent was removed, and the resulting dark oil was slurried with ether. Removal of the ether from the filtrate gave 0.12 g (60%) of **14d** identical by IR with a sample prepared directly from DISN and *p*-methoxystyrene.

***N*-Benzylidene-2,3-diaminomaleonitrile (29).** A solution of 3.0 g (28.2 mmol) of DISN and 5 g (54.3 mmol) of cycloheptatriene in 30 mL of CH_3CN was stirred for 5 days and evaporated. The black gummy residue was dissolved in 100 mL of CH_2Cl_2, and insoluble DAMN, 646 mg, was filtered. The filtrate

was evaporated and chromatographed on 40 g of alumina. Methylene chloride fractions (500 mL) gave 0.84 g (15%) of **29** as yellow solid: mp 202–204 °C (lit.[22] mp 191 °C); NMR (CD_3CN) δ 5.80 (br, 2 H, exchange with D_2O), 7.15 (m, 3 H, *m*- and *p*-H), 7.50 (m, 2 H, *o*-H), 8.01 (s, 1 H, NCH).

Reaction of DISN with Norbornadiene. A solution of 32 g (0.30 mol) of DISN and 50 g of freshly distilled norbornadiene in 320 mL of CH_3CN was stirred at 25 °C under nitrogen for 7 days and evaporated. The black gummy solid was extracted with four 150-mL portions of hot CH_2Cl_2. The insoluble gummy solid was recrystallized from CH_3CN and identified as 1,4-diamino-1,2,5-tricyano-3,6-diazahexatriene 17[2c] by IR.

The CH_2Cl_2 extracts gave upon concentration 3.23 g of a greenish yellow solid, which was recrystallized twice from ethyl acetate to give 1-substituted 1,4,4a,5,8,8a-hexahydro-5,8-methanoquinoxaline-2,3-dicarbonitrile **31**: UV (C_2H_5OH) 395 nm (ε 15 700), 320 (11 000), 240 sh (9750); IR (KBr) 3425, 3330, 3200, 2220, 2200, 1605, 1565 cm^{-1}; NMR (Me_2SO-d_6/D_2O) δ 1.40 (AB, 2 H, CH_2), 3.15 (m, 2 H), 4.02 (d, 1 H), 4.38 (d, 1 H), 6.41 (m, 2 H, olefinic).

Anal. Calcd for $C_{17}H_{14}N_{10}$: C, 56.97; H, 3.94; N, 39.09. Found: C, 57.23; H, 3.71; N, 39.14.

The above CH_2Cl_2 filtrate was evaporated, and ether-insoluble solid was filtered, 3.58 g, mp 134–135 °C (from CCl_4), identical with an authentic sample of 2,3-dicyanopyrazine (**32**).[2a]

The ether-soluble fraction, 6.5 g, was chromatographed on 60 g of silica. Benzene fractions (200 mL) gave 2.26 g of crude **32**, which gave 1.64 g of colorless crystals, mp 133–135 °C.

The column was further eluted with benzene (450 mL) and CH_2Cl_2 (700 mL). The combined material was rechromatographed on 50 g of alumina. Benzene fractions gave 422 mg of a solid, which was triturated with cold ether to give 214 mg of 2,5-diazatricyclo[6.2.1.$0^{2,6}$]undeca-3,5,9-triene-3,4-dicarbonitrile (**33**) as colorless crystals. An analytical sample was prepared by a recrystallization from CCl_4–ether: mp 120–122 °C; NMR ($CDCl_3$) δ 2.08 (d, J = 12 Hz, 1 H), 2.50 (d × t, J = 12 and 4 Hz, 1 H), 3.05 (m, 1 H), 3.30 (d, J = 14.5 Hz), 3.34 (m), together 2 H, 5.05 (m, 1 H), 6.40 (m, 2 H); UV (C_2H_5OH) 255 nm (ε 10 400); IR (KBr) 2235, 1504, 1415, 1304 cm^{-1}.

Anal. Calcd for $C_{11}H_8H_4$: C, 67.33; H, 4.11; N, 28.56. Found: C, 67.43; H, 4.01; N, 28.48.

Further elutin with CH_2Cl_2 gave 460 mg of a solid, which was triturated with cold ether to give 349 mg of 3-aza-3-(2-amino-1,2-dicyanovinyl)tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**30**). An analytical sample was prepared by a recrystallization from benzene–hexane: mp 122–124 °C; NMR ($CDCl_3$) δ 1.80 (m, 2 H, CH_2), 2.97 (m, 4 H, CH), 5.89 (t, 2 H, olefinic), 4.42 (br, 2 H, NH_2); UV (C_2H_5OH) 303 nm (ε 14 000); IR (KBr) 3400, 3310, 3205, 2227, 2217, 1635, 1597 cm^{-1}.

Anal. Calcd for $C_{11}H_{10}N_4$: C, 66.65; H, 5.09; N, 28.27. Found: C, 66.66; H, 5.10; N, 28.22.

1-(1,2-Diimino-2-cyanoethyl)-1,4,4a,5,6,7,8,8a-octahydro-5,8-methanoquinoxaline-2,3-dicarbonitrile (38). A solution of 3.0 g of DISN and 5 g of norbornene in 40 mL of CH_3CN was refluxed under nitrogen for 30 h, treated with charcoal, and evaporated. The gummy solid was recrystallized from ethyl acetate to give 657 mg of yellow crystals. A recrystallization from CH_3CN gave an analytical sample, which decomposed above 250 °C without melting: NMR (Me_2SO-d_6) δ 1.17 (m, 2 H, CH_2), 1.52 (m, 4 H, CH_2), 2.44 (m, 2 H, CH), 4.10, 4.36 (d, J = 7.6 Hz, 2 H, CH), 7.64 (s, 2 H, NH), 8.55 (s, 1 H, NH); UV (C_2H_5OH) 398 nm (ε 11 700), 317 (8560); IR (KBr) 3380, 3300, 3190, 2205, 1603, 1560 cm^{-1}.

Anal. Calcd for $C_{14}H_{13}N_7$: C, 60.20; H, 4.69; N, 35.11. Found: C, 60.57; H, 4.69; N, 35.37.

4,5-Dimethylpicolinonitrile (39). To a solution of 3.0 g of DISN in 30 mL of CH_3CN was added 16 mL of 2,3-dimethylbutadiene dropwise over a period of 20 min and stirred for 4 h at 22–33 °C; no DISN remained. The solvent was evaporated under vacuum. The yellow-orange oil turned black at room temperature within a few hours, and 840 mg of DAMN was isolated by filtration of $CHCl_3$ solution. The filtrate was chromatographed on alumina. A benzene fraction (270 mL) gave 1.21 g of colorless crystals contaminated with a yellow oil. Three recrystallizations from ether–hexane gave an analytical sample: 676 mg, of **39**, mp 76–78 °C; NMR ($CDCl_3$) δ 2.35 (s, 6 H), 7.49 (s, 1 H), 8.44 (s, 1 H); UV (C_2H_5OH) 328 nm (ε 15), 275 (2840), 267 (3300), 230 (11 400); IR (KBr) 2230, 1587, 1560 cm^{-1}.

Anal. Calcd for $C_8H_8N_2$: C, 72.70; H, 6.10; N, 21.19. Found: C, 72.41; H, 5.96; N, 21.32.

Registry No. **3a**, 88548-87-2; **3b**, 88548-88-3; **4**, 13481-25-9; **5a**, 4231-26-9; **5b**, 4231-35-0; **6a**, 72113-14-5; **6b**, 88548-89-4; **7**, 88548-90-7; **8**, 88548-91-8; **9**, 88548-92-9; **11**, 88548-93-0; **12a**, 100-42-5; **12b**, 1073-67-2; **12c**, 405-99-2; **12d**, 637-69-4; **12f**, 622-97-9; **13a**, 88548-94-1; **13b**, 88548-95-2; **13c**, 88548-96-3; **13d**, 88549-04-6; **13f**, 88548-98-5; **14d**, 37494-42-1; **14e**, 37494-43-2; **15d**, 67170-60-9; **15e**, 72545-80-3; **15f**, 67823-06-7; **16**, 1187-42-4; **17**, 88548-97-4; **18**, 88548-99-6; **19**, 88549-00-2; **20**, 88549-01-3; **21a**, 873-66-5; **21b**, 766-90-5; **22a**, 88549-03-5; **22b**, 88588-22-1; **27**, 59574-37-7; **29**, 56029-18-6; **30**, 88549-07-9; **31**, 88549-05-7; **32**, 13481-25-9; **33**, 88549-06-8; **38**, 88549-08-0; **39**, 24559-31-7; DISN, 28321-79-1; *cis*-dimethoxyethylene, 7062-96-6; cyclopentadiene, 542-92-7; 1,3-cyclohexadiene, 592-57-4; 2-(*p*-tolyl)propene, 1195-32-0; *trans*-anethole, 4180-23-8; 5-methyl-6-*p*-anisylpyrazine-2,3-dicarbonitrile, 88549-02-4; 2-vinylfuran, 1487-18-9; diazomethane, 334-88-3; cycloheptatriene, 544-25-2; norbornadiene, 121-46-0; norbornene, 498-66-8; 2,3-dimethylbutadiene, 513-81-5.

Retro-Inverso Isomerization of Peptides: Side Reactions in the Synthesis of *N,N'*-Diacyl-1,1-diamino-2-phenylethane Derivatives

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Received June 7, 1982

In general, the synthesis of retro-inverso peptides requires the formation of diacylated *gem*-diaminoalkyl structures. One way to prepare these *gem*-diaminoalkyl residues involves the Curtius rearrangement of the N-acylated amino acid hydrazides to the corresponding *N*-acyl-α-aminoalkyl isocyanates which are subsequently trapped by an alcohol. We have found that the side reactions associated with alcohol addition to the isocyanate vary with the nature of the N-acylating group on the α-amino function and the ratio of alcohol to isocyanate. These side reactions can be minimized by using only small excesses of alcohol over isocyanate or by performing the Curtius rearrangement on hydrazides derived from *N*-acetyl residues rather than on *N*-alkoxycarbonyl amino acids.

In the course of our studies on linear, retro-inverso peptide isomers, we have incorporated 1,1-diaminoalkyl and malonyl residues as basic structural units into the modified peptide backbone.[2] This modification, which

0022-3263/84/1949-0821$01.50/0 © 1984 American Chemical Society