6 h, quenched with 8 mL of a 2 N solution of NaOH, and stirred at room temperature for 15 min. The resulting solution was diluted with ether and extracted with 2 N NaOH (3 × 10 mL). The base phases were combined, acidified with a 6 N solution of HCl (pH ~ 2) at 0 °C, and extracted with ether (4 × 15 mL). The etheral extracts were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated to afford 261 mg (60%) of 2(*S*)-[2-methyl-5(*S*)-(2-propenyl)-2-cyclohexen-1(*R*)-yl]propionic acid (10): ^{13}C NMR δ 182.4, 150.2, 134.7, 125.2, 109.1, 44.0, 42.1, 41.3, 32.2, 31.4, 21.9, 21.2, 13.2. For additional data, see ref 48. Neither the ^{13}C NMR nor the ^1H NMR spectra indicated the presence of the C(2) isomer, which was the major isomer in the absence of dipolar solvents in the enolization mixture.[50]

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Reaction of Aminopropanedinitrile 4-Methylbenzenesulfonate [Aminomalononitrile *p*-Toluenesulfonate (Tosylate)] with Aromatic Aldehydes

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Aminopropanedinitrile 4-methylbenzenesulfonate (ammoniopropanedinitrile *p*-toluenesulfonate, aminomalononitrile *p*-toluenesulfonate (tosylate), 1) reacts with aromatic aldehydes in methanolic sodium ethanoate to give diastereoselectively (*E,E*)-4-amino-1-aryl-3-cyano-4-methoxy-2-aza-1,3-butadienes (3) and *trans*-3,6-diaryl-2,2,5,5-tetracyanopiperazines (4). The product distribution (3:4) depends on the ratio of reactants and the structures of the substrates. Electron-releasing groups on the 4-position of the phenyl ring favor piperazine (4) formation (method B.) The formation of piperazines (4) may involve synthetically useful N-protonated aryl- and cyano-stabilized azomethine ylide (prototropic 1,3-dipoles) intermediates which could have resulted from an imine–azomethine ylide tautomerism of prior formed 1-aryl-3,3-dicyano-2-aza-1-propenes. 1,3-Dipolar cycloaddition [4 + 2] reactions of the highly reactive azomethine ylides with dimethyl 1,2-ethynedicarboxylate (DMAD) give 3,4-dicarbomethoxy-2-cyano-5-aryl-3-pyrrolines, which undergo facile dehydrocyanation to 3,4-dicarbomethoxy-2-cyano-5-arylpyrroles. The possible intermediacy of ketenimines and of aryl- and cyano-stabilized 2-azaallyl anionic intermediates in equilibrium with azomethine ylides is also considered.

Aminopropanedinitrile 4-methylbenzenesulfonate (ammoniopropanedinitrile *p*-toluenesulfonate, aminomalononitrile *p*-toluenesulfonate (tosylate), AMNT, 1)[1-6] reacts with aromatic aldehydes to give a wide variety of products, depending on experimental conditions and the structures of the substrates.[7,8] 1-Aryl-3,3-dicyano-2-aza-1-propenes (2) have been reported[8] as the products from the reaction of aminopropanedinitrile (aminomalononitrile)[2,3,9-11] and aromatic aldehydes. Aminomalononitrile tosylate (AMNT, 1) reacts with aromatic aldehydes in methanolic sodium ethanoate to give diastereoselectively (*E,E*)-4-amino-1-aryl-3-cyano-4-methoxy-2-aza-1,3-butadienes (3) in good to excellent yields.[7] This report describes experimental conditions for the concurrent formation of 2-aza-1,3-butadienes (3) and *trans*-3,6-diaryl-2,2,5,5-tetracyanopiperazines (4) from the reaction of AMNT (1) and aromatic aldehydes (Table I).[7,8] Some products precipitate during the reaction, and other product mixtures are easily separated by column chromatography. Highly functionalized 2-aza-1,3-butadienes are important in the Diels–Alder reactions of heterodienes and in mechanistic studies of cycloaddition reactions[7] and piperazine and its derivatives are well known for their bioactivity[12] and for their roles in the preparation of pharmaceuticals such as β-adrenergic blocking agents,[13a] medicinally important amino steroids,[13b] and antibiotics.[13c]

Table I shows that the yields of piperazines (4) increase on going from a mol ratio of sodium ethanoate:aldehyde = 1.0 (method A) to a molar ratio of 1.5 (method B) with phenylmethanal. It was also observed that the reaction of AMNT (1) with phenylmethanal did not proceed at a measurable rate in the absence of sodium ethanoate. Using a molar ratio of 2.0 (sodium ethanoate:aldehyde) with phenylmethanal gave a lower overall yield while a molar ratio of 0.5 led to a sluggish reaction that afforded a complex product mixture. An increase in methanol concentration from 494 to 741 mmol in method A (11 h) with

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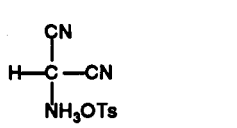

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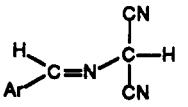
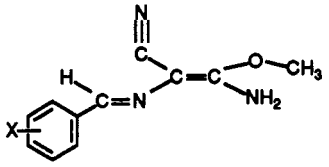
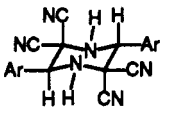


2a: Ar = C_6H_5
b: Ar = 2-HOC_6H_4
c: Ar = 4-$CH_3OC_6H_4$



3a: X = 4-OCH_3
b: X = 4-OC_2H_5
c: X = 4-$OC(O)CH_3$
d: X = H
e: X = 4-Br
f: X = 4-NO_2
g: X = 4-$C(O)OCH_3$
h: Ar = 3-pyridyl
i: X = 3-thienyl



4a: Ar = 4-$CH_3OC_6H_4$
b: Ar = 4-$C_2H_5OC_6H_4$
c: Ar = 4-$CH_3C(O)OC_6H_4$
d: Ar = C_6H_5
e: Ar = 4-BrC_6H_4
f: Ar = 4-$CH_3OC(O)C_6H_4$
g: Ar = 3-pyridyl
h: Ar = 3-thienyl

phenylmethanal led to an increase in the yield of (*E,E*)-4-amino-3-cyano-4-methoxy-1-phenyl-2-aza-1,3-butadiene (**3d**) from 22% to 43% and a decrease in yield of the 2,2,5,5-tetracyano-*trans*-3,6-diphenylpiperazine (**4d**) from 26% to 0%.

It is of interest to note that (2-bromophenyl)- and (2-chlorophenyl)methanal react rapidly with AMNT (**1**) in method A to give almost exclusively the corresponding 2-aza-1,3-butadiene (**3**, Table I).[7] (2-Nitrophenyl)- and (4-nitrophenyl)methanal and 2-naphthaldehyde also give good to excellent yields of 2-aza-1,3-butadienes (**3**) in method A.

It is also seen (Table I) that electron-attracting substituents on the 4-position of the aldehyde favor 2-aza-1,3-butadiene (**3**) formation (method A). (4-Nitrophenyl)methanal and AMNT (**1**) give 2-aza-1,3-butadiene **3f** (99%) in method A and afford a low yield of **3f** and no isolated piperazine (**4**) in method B. Similarily, (4-carbomethoxyphenyl)methanal and AMNT (**1**) give 2-aza-1,3-butadiene (**3g**, 72%) in method A and give low yields of **3g** (20%) and piperazine (**4f**, 32%) in method B. 3-Pyridylmethanal and AMNT (**1**) also yield 2-aza-1,3-butadiene (**3h**) as the major product in method A.

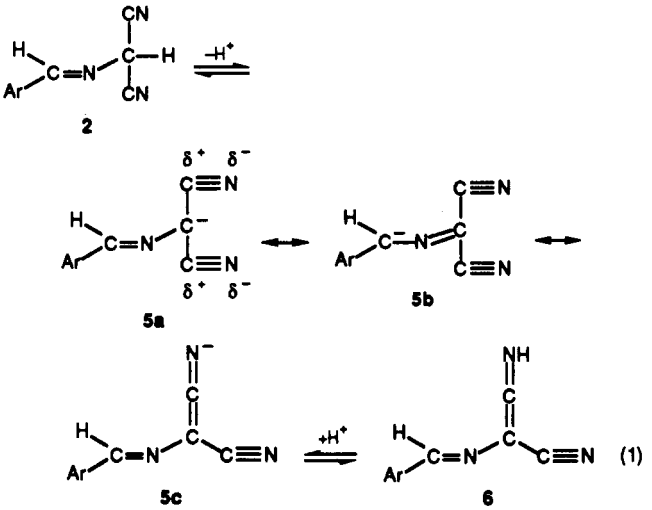
Electron-releasing substituents at the 4-position of phenylmethanal afford comparable yields of 2-aza-1,3-butadienes (**3**) and piperazines (**4**) in method A while piperazine (**4**) formation is favored with these substrates and with 3-thienylmethanal in method B (Table I).

Table II shows the ^{13}C NMR and ^{1}H NMR spectra of 2-aza-1,3-butadienes (**3**). It is of interest to note that the protons of the methoxy groups and the protons of the imine carbon atoms in **3** are more deshielded with electron-releasing and with electron-withdrawing substituents relative to the parent compound (**3d**, X = H). The protons of the amino group in azadienes **3** are more shielded with electron-releasing groups and more deshielded with electron-attracting groups relative to the parent compound (**3d**, X = H).

The crystal structure of (*E,E*)-4-amino-3-cyano-1-(4-hydroxyphenyl)-4-methoxy-2-aza-1,3-butadiene has been reported,[14] and the molecular structure of (*E,E*)-4-amino-3-cyano-1-(4-methoxyphenyl)-4-methoxy-2-aza-1,3-butadiene (**3a**) is shown in Figures 1 and 2. Figure 1 shows that the aryl ring is essentially coplanar with the imine (C=N) double bonds and that there is a cis (*Z*) relationship between the cyano and methoxy groups. The stereodiagram (Figure 2) shows the intermolecular interactions of the protons on the amino group of **3a** with the nitrogen of the cyano group of another molecule of **3a** and with the oxygen of methoxy group of a different molecule of **3a**.

The stereochemistry and structure of piperazines (**4**) were inferred from the X-ray single-crystal structure analysis of 2,2,5,5-tetracyano-*trans*-3,6-diphenylpiperazine (**4d**),[14,20] which crystallized with 2 equiv of solvent (propanone), and from their infrared, ^{1}H NMR, and ^{13}C NMR spectra. Although the infrared spectra of the piperazines (**4**) did not show a nitrile stretch in the 2250-cm^{-1} region, the ^{13}C NMR spectra showed two nitrile resonances in the 113–117 ppm region owing to the presence of axial and equatorial cyano groups.

The proton in the cyanocarbon acid **2**, which could be formed from **1** and aldehyde, is expected to be very acidic owing to conjugative and polar effects.[21-23] A reasonable mechanism for formation of the highly functionalized 2-aza-1,3-butadienes (**3**) could involve ketenimine intermediates **6** (eq 1). Nucleophilic attack by methanol at the α-carbon in ketenimine **6** leads to diastereoselective formation of 2-aza-1,3-butadiene (**3**).[23-27] Alternatively, methanolysis of the nitrile function in the 2-aza-1-propene **2** would also lead to the 2-aza-1,3-butadiene **3**.



2 **5a** **5b** **5c** **6** (1)

Cyclodimerization of 1-aryl-3,3-dicyano-2-aza-1-propene (**2**) to piperazine **4** is possible via an aryl and cyano stabilized 2-azaallyl anion system (**5**)[28-30] or a N-protonated

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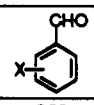
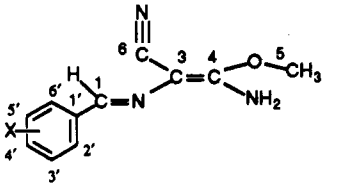
Table I. Product Distributions from the Reaction of Aminomalononitrile *p*-Toluenesulfonate (AMNT, 1) and Aromatic Aldehydes

	method[a]	reaction time, h	yield, % 2-aza-1,3-butadiene 3	mp, °C	yield, % piperazine 4	mp, °C	yield, % overall
4-OH	A[b]	24	23	165–167			23
4-OCH_3	A	20	26	155–156	38	246–247	54
	B	20	10		63		73
4-OC_2H_5	A	24	35	100–102	23	247–248	58
	B	20	11		51		62
4-$OC(O)CH_3$	A	24	43	141–144	30	246–247	73
	B	20	13		61		74
4-$C(O)OCH_3$	A	20	72	200–201	0		72
	B	20	20		32	253–254	52
H	A[b]	24	50	134–135			50
	A	11	22		26	238–240	48
	B	20	5		48		53
2-Cl	A[b]	6	99	214–215			99
2-Br	A[b]	3	92	205–206			92
4-Br	A	21	16	172–174	47	228–229	63
	B	20	11		47		58
2-NO_2	A[b]	72	80	210–212			80
4-NO_2	A	13	99	178–183	0		99
	B	20	*c*		0		*c*
2-naphthyl	A[b]	24	69	202–203			69
3-pyridyl	A	20	20	141–143	54	231–232	74
	B	20	5		14		19
3-thienyl	A	20	27	132–134	24	234–236	51
	B	20	11		55		66

[a] Experimental conditions (in 20 mL of absolute methanol) same except for equivalents of anhydrous sodium ethanoate used. Method A: equimolar amounts of aldehyde, AMNT (1), and CH_3CO_2Na. Method B: 1.0 equiv of aldehyde and of AMNT (1) and 1.5 equiv of CH_3CO_2Na. Reaction temperature is 22–24 °C. [b] From ref 7. [c] Complex product mixture that includes a low yield of 2-aza-1,3-butadiene **3g**.

Table II. NMR Spectral Data of (*E*,*E*)-4-Amino-1-aryl-3-cyano-4-methoxy-2-aza-1,3-butanedienes (3)



3

	^1H NMR (300 MHz, (DMSO-d_6/TMS) δ				^{13}C NMR (DMSO-d_6/TMS) δ										
X	OCH_3	HC=N	NH_2	ArH	C-1	C-3	C-4	C-5	C-6	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′
4-OH	4.01	7.88	7.55	6.86–7.77	147.30	84.01	170.62	60.50	120.69	132.90	132.60	119.40	162.35	119.40	132.60
4-OCH_3[a]	4.02	7.91	7.63	7.01–7.89	146.65	83.98	170.75	60.47	120.54	134.36	132.37	117.90	163.82	117.90	132.37
4-OC_2H_5[b]	4.01	7.88	7.62	6.99–7.86	146.61	83.86	170.61	60.46	120.46	134.18	132.35	118.29	163.07	118.29	132.35
4-$OC(O)CH_3$[c]	4.03	7.92	7.79	7.20–7.88	145.33	83.93	171.07	60.52	120.25	139.10	131.77	125.85	154.54	125.85	131.77
	4.05		{7.94–8.10}		144.29	84.60	171.51	60.59	119.90	132.58	133.23	130.66	145.76	130.66	133.23
4-$C(O)OCH_3$[d]															
H	3.94	7.66	7.85	7.35–7.82	146.41	84.09	171.11	60.51	120.32	141.37	132.39	130.84	132.48	130.84	132.39
2-Cl	4.05	8.25	7.99	7.37–8.34	141.02	84.88	171.46	60.59	120.08	137.90	135.91	131.65	133.49	131.02	133.55
2-Br	4.05	8.20	7.99	7.30–8.42	143.56	84.78	171.46	60.59	120.05	139.18	126.52	132.08	136.80	131.52	133.80
4-Br	4.03	7.87	7.87	7.61–7.88	144.76	84.11	171.24	60.53	120.15	140.66	135.27	132.61	125.39	132.61	135.27
2-NO_2	4.07	8.25	8.11	7.57–8.61	139.38	85.23	171.72	60.66	119.56	134.83	151.22	128.07	132.31	132.31	136.58
4-NO_2	4.07	7.93	8.18	8.14–8.26	142.67	85.26	171.79	60.69	119.54	147.63	131.08	127.59	150.20	127.59	131.08
2-naphthyl	3.97	7.86	7.76	7.50–8.24		84.50	171.20	60.60	120.33				127–140		
3-pyridyl	4.04	9.08	7.94	7.47–8.55	142.91	84.33	171.42	60.57	120.09	*e*	152.44	137.01	127.56	137.29	152.86
3-thienyl	4.01	7.86	7.65	7.61–7.99	142.11	83.52	170.82	60.48	120.38	*e*	130.43	145.75	130.10	128.87	

[a] δ_H = 3.87 ppm and δ_C = 59.17 ppm for OCH_3. [b] δ_H = 1.42 and 4.14 ppm and δ_C = 18.64 and 67.09 ppm or OCH_2CH_3. [c] δ_H = 2.36 ppm and δ_C = 24.89 ppm for $OCOCH_3$. [d] δ_H = 3.94 ppm and δ_H = 56.05 ppm for CO_2CH_3. The δ_H = 7.94–8.10 ppm range represents seven protons. [e] Heteroatom is position 1′.

aryl and cyano stabilized azomethine ylide (7, eqs 1, 2).[31-45] The dimerization of nonstabilized azomethine ylides to a mixture of isomeric piperazines has been observed.[38a,45b,f] Among other possible dimeric product structures from the

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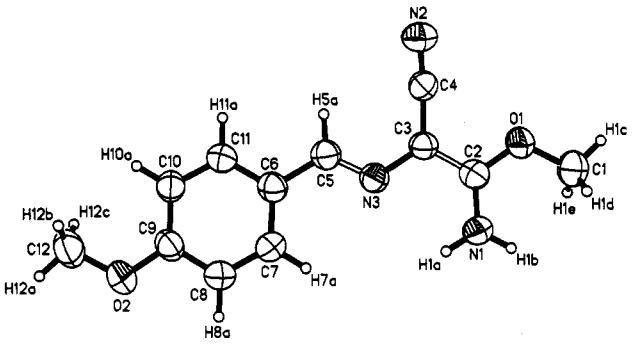
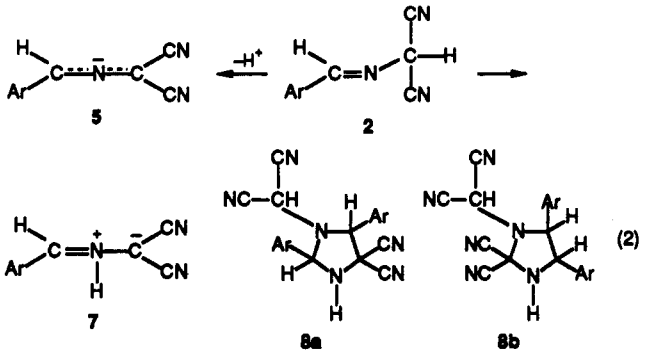


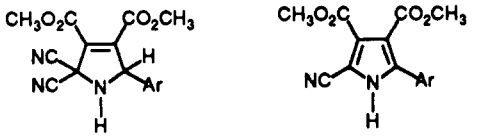
Figure 1. ORTEP view of the molecular structure and atom numbering of (*E*,*E*)-4-amino-3-cyano-1-(4-methoxyphenyl)-4-methoxy-2-aza-1,3-butadiene (**3a**). Thermal elipsoids are drawn at the 40% probability level.

2-azaallyl anion **5** and/or the azomethine ylide **7** are **8a** and **8b**, which were eliminated on the basis of spectral data.



The 2-azaallyl anions resemble 1,3-dipolar substances in their molecular orbital schemes[42-44] and undergo 1,3-anionic cycloaddition reactions. Although the resonance-stabilized 2-azaallyl anion system **5** is expected to have the negative charge less concentrated on the nitrogen atom than in the simple parent 2-azaallyl anion, it is likely that if **5** is formed it would be protonated under the acidic experimental conditions to afford the ketenimine **6** and/or the N-protonated stabilized azomethine ylide **7**, which is an example of a prototropic 1,3-dipole.[34] 1,2-Prototropy in **2** also affords the useful azomethine ylide **7**.[46]

A trapping experiment with AMNT (**1**) and phenylmethanal in the presence of bicyclo[2.2.1]hept-2-ene (method A) did not afford a cycloadduct of ylide **7**.[46] However, use of the electron-deficient dipolarophile dimethyl 1,2-ethynedicarboxylate (DMAD, method A) led to the formation of two products (**9a** and **9b**), the cycloadduct 3,4-dicarbomethoxy-2,2-dicyano-5-phenyl-3-pyrroline (**9a**, 14%), which underwent dehydrocyanation to 3,4-dicarbomethoxy-2-cyano-5-phenylpyrrole (**9b**, 50%). Neither 2-aza-1,3-butadiene (**3d**) nor piperazine (**4d**) was isolated from the trapping experiment owing to the rapid 1,3-dipolar cycloaddition reaction of DMAD and ylide **7**.[46] Similar results (method A, 3,4-dicarbomethoxy-2,2-dicyano-5-(4-methoxyphenyl)-3-pyrroline, **10a**, 12%; 3,4-dicarbomethoxy-2-cyano-5-(4-methoxyphenyl)pyrrole, **10b**, 33%)[46] were obtained with (4-methoxyphenyl)methanal in the presence of DMAD. Although (4-bromophenyl)-methanal did not afford 3,4-dicarbomethoxy-2,2-dicyano-5-(4-bromophenyl)-3-pyrroline (**11a**) in the presence of DMAD, 3,4-dicarbomethoxy-2-cyano-5-(4-bromophenyl)-pyrrole (**11b**, 55%) was isolated. These cycloaddition trapping experiments provide evidence for the intermediacy of azomethine ylide **7**, a 1,3-dipole of the allyl anion type with four electrons in three parallel π orbitals, which undergoes [π4s + π2s] cycloaddition with DMAD.[47,48]



9a: Ar = C_6H_5 **9b**: Ar = C_6H_5
10a: Ar = 4-$CH_3OC_6H_4$ **10b**: Ar = 4-$CH_3OC_6H_4$
11a: Ar = 4-BrC_6H_4 **11b**: Ar = 4-BrC_6H_4

This facile diastereoselective synthesis of (*E*,*E*)-2-aza-1,3-butadienes (**3**)[7] and *trans*-3,6-diaryl-2,2,5,5-tetra-

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(46) 3,4-Dicarbomethoxy-2,2-dicyano-5-(4-methoxyphenyl)-3-pyrroline (**10a**) showed only 11 ^{13}C NMR resonances while 3,4-dicarbomethoxy-2-cyano-5-(4-methoxyphenyl)pyrrole (**10b**) showed the expected 13 ^{13}C NMR peaks (see the Experimental Section). 3-Pyrroline **10a** in a solution of DMSO-d_6 is converted to pyrrole **10b**.

(47) (a) The adduct formed to DMAD does not provide *direct* evidence for the intermediacy of an azomethine ylide (**7**), which undergoes a cycloaddition reaction. 3-Pyrroline products **9a** and **10a** are not stereochemically unique so that the observation of these cycloadducts does not eliminate the possibility of the stepwise addition of the 2-azallyl anion (**5**) to DMAD.[47f] The concerted pathway of 1,3-dipolar cycloaddition is replaced by a two-step mechanism via a zwitterionic intermediate if there is a large difference of HOMO–LUMO energies of the dipolarophile and the 1,3-dipole, and large steric hindrance at one terminus of the 1,3-dipole.[47c] Stepwise addition of **5** to DMAD is also a very possible occurrence since 2-aza-1-propene (**2**) is a very strong acid which dissociates in methanol solution.[21,22] Thus, is seems probable that both the 2-azaallyl anion (**5**) and the azomethine ylide (**7**) are present (in equilibrium) in the reaction mixture with, perchance, both participating in the cycloaddition. (b) Huisgen, R.; Scheer, W.; Huber, H. *J. Am. Chem. Soc.* **1967**, *89*, 1753. (c) Hall, J. H.; Huisgen, R.; Ross, C. H.; Scheer, W. *J. Chem. Soc., Chem. Commun.* **1981**, 1188. (e) Kahn, S. D.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1987**, *109*, 1871. (f) Huisgen, R.; Langhals, E.; Mloston, G.; Oshima, T. *Heterocycles* **1989**, *29*, 2069. (g) Houk, K. N.; Yamaguchi, K. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1985; Vol. 2, p 407. (h) Yamaguchi, K. *THEOCHEM* **1983**, *12*, 101.

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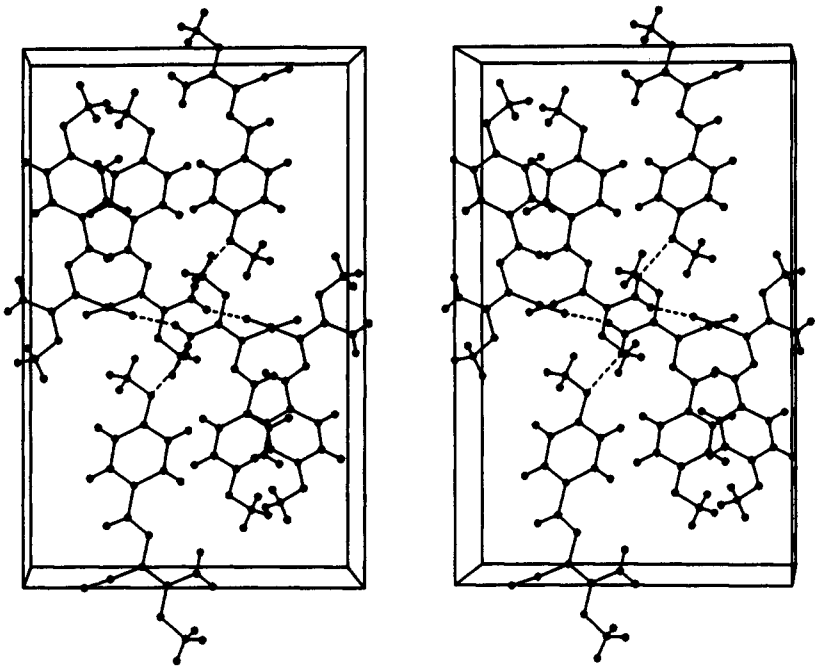

Figure 2. Stereodiagram illustrating the close intermolecular contacts for (*E,E*)-4-amino-3-cyano-1-(4-methoxyphenyl)-4-methoxy-2-aza-1,3-butadiene (**3a**). The N2–H1b, O2–H1a, and N2–N1 bond distances are 2.091, 2.281, and 2.948 Å, respectively.

cyanopiperazines (**4**) from AMNT (**1**) and aromatic aldehydes are unique and useful reactions.[48] The ease of formation of azomethine ylides (**7**) from AMNT (**1**) and aromatic aldehydes has advantages over other procedures for generating this class of 1,3-dipoles which has been previously prepared by desilylation of *N*-(silylmethyl)-amidines,[35,36] *N*-(silylmethyl)thioamides,[35,36] and benzyl-[[(trimethylsilyl)methyl]amino]malononitrile,[37c] by photolysis of carbene precursors in nitrile solvents,[49,51] by photolysis or thermolysis of aziridines,[38-42,52-54] and by treatment of imidoyl halides with bases.[55] Thus, the procedures described above are easily modified in order to perform cycloaddition reactions with in situ generated azomethine ylides (**7**).

Experimental Section

Melting points were determined in open capillary tubes with a Thomas-Hoover apparatus and are uncorrected. Elemental analyses were performed by Robertson Laboratory, Inc., Florham Park, NJ.

High-resolution mass spectra (HREIMS, HRCIMS) were obtained with a VG 7070-HF mass spectrometer (70 eV). Chemical ionization mass spectra (CIMS, 2-methylpropane) and electron impact mass spectra (EIMS) were obtained with a Finnigan 9610 GC-EI-CI mass spectrometer with a Nova 3 data system operating at an ionization potential of 70 or 100 eV.

Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a General Electric Model QE 300 (300 MHz), or on a General Electric Model GN 500 (500 MHz) spectrometer and chemical shifts (δ) are reported in parts per million relative to internal tetramethylsilane (0.00 ppm). Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded on a General Electric Model QE 300 (75.5 MHz) spectrometer, and chemical shifts are reported in parts per million relative to the central solvent (DMSO-d_6) resonance at 43.5 ppm.

IR spectra were obtained with a Perkin-Elmer 283 spectrophotometer, calibrated with the 1601-cm^{-1} absorption of polyphenylethene.

Analytical TLC was performed on Analtech Uniplate 10 × 20 cm (250 μm thick) silica gel GF prescored glass plates which were developed in a solvent mixture of 1:2 ethyl ethanoate/hexanes. After the solvent had risen to the top, the plates were checked under ultraviolet light and developed in a diiodine chamber to visualize the compounds.

Flash column chromatography was performed on 100–200-mesh silica gel.[56,57]

The aromatic aldehydes were distilled or recrystallized from aqueous ethanol immediately before use. Their boiling points, melting points, and their IR, ^{1}H NMR, and ^{13}C NMR spectra agreed with literature values.

(*E,E*)-4-Amino-1-aryl-3-cyano-4-methoxy-2-aza-1,3-butadienes (2): Method A. To an aluminum foil covered 50-mL round-bottomed flask containing a solution of aminomalononitrile tosylate (**1**, 1.17 g, 4.6 mmol), absolute methanol (20 mL, 15.82 g, 494 mmol), and anhydrous sodium ethanoate (0.38 g, 4.6 mmol) were added, dropwise, with stirring at 22–24 °C, 4.6 mmol of aromatic aldehyde. The reaction mixture was stirred at 22–24 °C, until no aminomalononitrile tosylate (**1**) was detectable on a TLC plate developed in 1:2 ethyl ethanoate/hexanes. The reaction mixture was diluted with 1:1 ethyl ethanoate/diethyl ether (100 mL), washed with water (2 × 100 mL), and transferred to a separatory funnel, and the layers were separated. The organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residue was chromatographed on silica gel (1:2 ethyl ethanoate/hexanes) to afford pure 2-aza-1,3-butadiene (**3**).

The purity of compounds **3a–c,e,g–i,4a,f,9a,b,10a,b,** and **11b** was judged to be ≥98% by high-resolution mass spectrometry and/or ^{13}C and ^{1}H NMR spectral determinations.

Method B is the same as method A except a mol ratio of CH_3CO_2Na:aldehyde = 1.5 was used.

(*E,E*)-4-Amino-3-cyano-4-methoxy-1-(4-methoxyphenyl)-2-aza-1,3-butadiene (3a): HREIMS *m/z* 231.1000

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(calcd for $C_{12}H_{13}N_3O_2$ 231.1008).

(*E*,*E*)-4-Amino-3-cyano-1-(4-ethoxyphenyl)-4-methoxy-2-aza-1,3-butadiene (3b): HREIMS *m/z* 245.1167 (calcd for $C_{13}H_{15}N_3O_2$ 245.1164).

(*E*,*E*)-1-(4-Acetoxyphenyl)-4-amino-3-cyano-4-methoxy-2-aza-1,3-butadiene (3c): HREIMS *m/z* 259.0953 (calcd for $C_{13}H_{13}N_3O_3$ 259.0957.

(*E*,*E*)-4-Amino-3-cyano-4-methoxy-1-phenyl-2-aza-1,3-butadiene (3d):[7] HREIMS *m/z* 201.0908 (calcd for $C_{11}H_{11}N_3O$ 201.0902). Anal. Calcd for $C_{11}H_{11}N_3O$: C, 65.67; H, 5.47; N, 20.89. Found: C, 65.44; H, 5.47; N, 20.89.

(*E*,*E*)-4-Amino-1-(4-bromophenyl)-3-cyano-4-methoxy-2-aza-1,3-butadiene (3e): HREIMS *m/z* 278.9984 (calcd for $C_{11}BrH_{10}N_3O$ 279.0007).

(*E*,*E*)-4-Amino-3-cyano-4-methoxy-1-(4-nitrophenyl)-2-aza-1,3-butadiene (3f):[7] HREIMS *m/z* 246.0753 (calcd for $C_{11}H_{10}N_4O_3$ 246.0753). Anal. Calcd for $C_{11}H_{10}N_4O_3$: C, 53.66; H, 4.07; N, 22.76. Found: C, 53.59; H, 4.01; N, 22.76.

(*E*,*E*)-4-Amino-1-(4-carbomethoxyphenyl)-3-cyano-4-methoxy-2-aza-1,3-butadiene (3g): HREIMS *m/z* 259.0000 (calcd for $C_{13}H_{13}N_3O_3$ 259.0957).

(*E*,*E*)-4-Amino-3-cyano-4-methoxy-1-(3-pyridyl)-2-aza-1,3-butadiene (3h): HREIMS *m/z* 202.0836 (calcd for $C_{10}H_{10}N_4O$ 202.0854).

(*E*,*E*)-4-Amino-3-cyano-4-methoxy-1-(3-thienyl)-2-aza-1,3-butadiene (3i): HREIMS *m/z* 207.0441 (calcd for $C_9H_9N_3OS$ 207.0466).

2,2,5,5-Tetracyano-*trans*-3,6-bis(4-methoxyphenyl)-piperazine (4a): mp 246–247 °C; IR (Nujol) 3310, 1600 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 3.87 (s, 3 H, OCH_3), 4.46 (s, 1 H, CH), 6.09 (s, 1 H, NH), 7.07–8.67 (m, 4 H, ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 60.39, 64.43, 67.26 (OCH_3), 116.36 (CN), 117.12 (CN), 118.14, 128.57, 134.11, 164.75; HRCIMS *m/z* 372.1440 (calcd for $C_{22}H_{18}N_6O_2$ MH^+ – HCN 327.1446).

2,2,5,5-Tetracyano-*trans*-3,6-bis(4-ethoxyphenyl)-piperazine (4b): mp 247–248 °C; IR (Nujol), 3320, 1610 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 1.44 (t, 3 H, CH_3), 4.18 (q, 2 H, CH_2), 4.55 (s, 1 H, CH), 6.19 (s, 1 H, NH), 7.14–7.73 (m, 4 H, ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 18.58 (CH_3), 60.31, 64.40, 87.26 (OCH_2), 116.26 (CN), 117.01 (CN), 118.44, 128.23, 128.33, 163.98. Anal. Calcd for $C_{12}H_{11}N_3O$: C, 67.61; H, 5.16; N, 19.72. Found: C, 67.44; H, 5.15, N, 19.92.

2,2,5,5-Tetracyano-*trans*-3,6-bis(4-acetoxyphenyl)-piperazine (4c): mp 246–247 °C; IR (Nujol) 3320, 1750, 1610, cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6), δ 2.40 (s, 3 H, CH_3CO), 4.71 (s, 1 H, CH), 6.37 (s, 1 H, NH), 7.41–7.91 (m, 4 H, ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6), δ 24.87 (CH_3), 59.88, 64.16, 116.02 (CN), 116.80 (CN), 126.28, 134.00, 134.09, 155.92, 173.03 (C=O). Anal. Calcd for $C_{12}H_9N_3O_2$: C, 63.44; H, 3.96; N, 18.50. Found: C, 63.34; H, 3.91; N, 18.22.

2,2,5,5-Tetracyano-*trans*-3,6-diphenylpiperazine (4d): mp 238–240 °C; IR (Nujol) 3320, 1600 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 4.56 (s, 1 H, CH), 6.24 (s, 1 H, NH), 7.58–7.74 (m, 5 H, ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 57.33, 62.46, 116.09 (CN), 116.79 (CN), 131.53, 132.81, 133.50, 138.48; HRCIMS *m/z* 339.1383 (calcd for $C_{20}H_{15}N_6$ 339.1358). Anal. Calcd for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.85. Found: C, 70.72; H, 4.53; N, 24.54.

2,2,5,5-Tetracyano-*trans*-3,6-bis(4-bromophenyl)piperazine (4e): mp 228–229 °C; IR (Nujol) 3310, 1600 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 4.62 (s, 1 H, CH), 6.27 (s, 1 H, NH), 7.70–7.78 (m, 4 H, ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 59.56, 63.93, 115.82 (CN), 116.14 (CN), 127.83, 134.72, 135.69, 136.00. Anal. Calcd for $C_{10}BrH_6N_3$: C, 48.58; H, 2.43; N, 17.00. Found: C, 48.30; H, 2.37; N, 16.96.

2,2,5,5-Tetracyano-*trans*-3,6-bis(4-carbomethoxyphenyl)piperazine (4f): mp 253–254 °C; IR (Nujol) 3280, 1610 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 3.99 (s, 3 H, CH_3O), 4.83 (s, 1 H, CH), 6.49 (s, 1 H, NH), 8.00–8.23 (m, 4 H, ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 56.40 (CH_3O), 59.45, 64.24, 115.80 (CN), 116.61 (CN), 133.25, 133.44, 135.52, 141.40; HRCIMS *m/z* 455.1465 (calcd for $C_{24}H_{19}N_6O_4$ 455.1468).

2,2,5,5-Tetracyano-*trans*-3,6-di-3-pyridylpiperazine (4g): mp 231–232 °C; IR (Nujol) 3160, 1600, 1580 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 4.83 (s, 1 H, CH), 6.27 (s, 1 H, NH), 7.62–8.75 (m, 3 H, ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 62.31, 62.42, 115.91 (CN), 118.54 (CN), 127.88, 132.65, 140.41, 153.80, 155.65; HRCIMS 341.1269 (calcd for $C_{18}H_{13}N_8$ 341.1262). Anal. Calcd for $C_9H_6N_4$: C, 63.53; H, 3.53; N, 32.94. Found: C, 63.41; H, 3.42; N, 33.08.

2,2,5,5-Tetracyano-*trans*-3,6-di-3-thienylpiperazine (4h): mp 234–236 °C; IR (Nujol) 3100 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 4.79 (s, 1 H, CH), 6.30 (s, 1 H, NH), 7.50–8.07 (m, 3 H, ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 56.69, 61.16, 116.30 (CN), 116.98 (CN), 131.01, 131.28, 137.80. Anal. Calcd for $C_8H_5N_3S$: C, 54.86; H, 2.86: N, 23.98. Found: C, 54.71; H, 2.83; N, 24.31.

Preparation of 3,4-Dicarbomethoxy-2,2-dicyano-5-phenyl-3-pyrroline (9a) and 3,4-Dicarbomethoxy-2-cyano-5-phenylpyrrole (9b). To an aluminum foil covered 50-mL round-bottom flask containing a solution of aminomalononitrile tosylate (1, 1.17 g, 4.6 mmol), absolute methanol (20 mL), and anhydrous sodium ethanoate (0.38 g, 4.6 mmol) were added, dropwise, with stirring at 22–24 °C, 4.6 mmol of phenylmethanal and then dimethyl ethynedicarboxylate (0.98 g, 6.9 mmol). The reaction mixture was stirred at 22–24 °C until no aminomalononitrile tosylate (1) was visible on a TLC plate developed in 1:2 ethyl ethanoate/hexanes. The reaction mixture was filtered, and the precipitate (3-pyrroline, **9a**) was washed with absolute methanol (5 mL) and air dried. Recrystallization of the white solid from aqueous methanol gave 195 mg (14%) of the 3-pyrroline **9a**, mp 198–198.5 °C; IR (Nujol) 1750, 1640 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 3.78 (6 H, s), 4.78 (1 H, s), 7.58–8.00 (5 H, m), 8.88 (1 H, s); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 53.74, 56.79, 62.87, 113.30, 115.80, 116.63, 132.71, 133.80, 136.28, 137.10, 137.23, 165.70, 170.77, 172.33; HREIMS *m/z* 311.0986 (calcd for $C_{16}H_{13}N_3O_4$ 311.0906).

The filtrate was diluted with a 1:1 solution of diethyl ether and ethyl ethanoate (100 mL) and transferred to a separatory funnel, washed with water (2 × 100 mL), and the layers were separated. The organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residue was chromatographed on silica gel with ethyl ethanoate/hexanes (1:2) to afford the pyrrole **9b** (645 mg, 50%): mp 140–141 °C; IR (Nujol) 3200, 2230, 1690 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 3.89 (6 H, q, J = 23.54 Hz), 7.56–7.67 (6 H, m); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 56.05, 56.14, 115.96, 119.08, 130.49, 131.50, 131.68, 132.91, 133.17, 140.54, 165.41, 168.43; HREIMS *m/z* 284.0799 (calcd for $C_{15}H_{12}N_2O_4$ 284.0797).

3,4-Dicarbomethoxy-2,2-dicyano-5-(4-methoxyphenyl)-3-pyrroline (10a) and 3,4-dicarbomethoxy-2-cyano-5-(4-methoxyphenyl)pyrrole (10b) were prepared using (4-methoxyphenyl)methanal as described above with phenylmethanal as the substrate.

3-Pyrroline 10a: 150 mg, 10%; mp 203–204 °C; IR (Nujol) 1750 (C=O), 1645, 1600 (C=C) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 3.43 (s, 3 H, ester OCH_3), 3.76 (s, 3 H, $ArOCH_3$), 3.94 (s, 3 H, ester OCH_3) 4.72 (s, 1 H), 7.11–7.95 (q, 4 H, ArH), 8.77 (s, 1 H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 56.93, 59.57, 108.61, 111.84, 116.44, 116.98, 118.34, 130.01, 136.09, 167.39, 171.16; HREIMS *m/z* 341.1005 (calcd for $C_{17}H_{15}N_3O_5$ 341.1011).

Pyrrole 10b: 465 mg, 32%; mp 139–140 °C; IR (Nujol) 3200 (NH), 2240 (CN), 1690 (C=O), 1620 (C=C); ^1H NMR (300 MHz, DMSO-d_6) δ 3.83 (s, 3 H, ester OCH_3), 3.90 (s, 3 H, ester OCH_3), 3.91 (s, 3 H, $ArOCH_3$), 7.13–7.60 (q, 4 H, ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 56.18, 56.28, 59.30, 107.19, 116.25, 118.34, 125.26, 126.84, 133.06, 140.75, 164.01, 168.71; HREIMS *m/z* 314.0913 (calcd for $C_{16}H_{14}N_2O_5$ 314.0903).

3,4-Dicarbomethoxy-2-cyano-5-(4-bromophenyl)pyrrole (11b) was prepared using (4-bromophenyl)methanal as described above with phenylmethanal as the substrate. Pyrrole **11b**: 540 mg, 35%; mp 163–164 °C; IR (Nujol) 3600, 3500 (NH), 2240 (CN), 1715 (C=O), 1590 (C=C) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 3.83 (s, 3 H, ester OCH_3), 3.91 (s, 3 H, ester OCH_3), 7.55–7.81 (q, 4 H, ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 56.28, 56.44, 108.06, 116.01, 119.26, 126.85, 126.94, 132.10, 133.65, 135.83, 139.53, 165.41, 168.36; HREIMS *m/z* 361.9894 (calcd for $C_{15}BrH_{11}N_2O_4$ 361.9902).

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Supplementary Material Available: ^{13}C NMR (75.5 MHz) and ^1H NMR (300 or 500 MHz) spectra of 2-aza-1,3-butadienes **3a–c,e,g–i**, piperazines **4a** and **4f**, 3-pyrrolines **9a** and **10a**, and pyrroles **9b**, **10b**, and **11b** and the X-ray crystallographic results for (*E,E*)-4-methoxy-2-aza-1,3-butadiene (**3a**) (52 pages). Ordering information is given on any current masthead page.

Addition, Substitution, and Deoxygenation Reactions of α-Phenyl-β-nitrostyrenes with the Anions of Thiols and Diethyl Phosphite: Formation of Indoles by Reaction with Ethyl Phosphites

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Reactions of excess RS^- (R = Ph, *t*-Bu) with $Ph_2C{=}C(SPh)NO_2$ in Me_2SO form $Ph_2C{=}CHSR$ via conversion of the initial Michael-type adducts into $Ph_2C(SR)CH{=}NO_2^-$ and $Ph_2C{=}CHNO_2$. In a similar fashion, reaction of $(EtO)_2PO^-$ with $Ph_2C{=}C(SPh)NO_2$ forms initially mainly $PhSP(O)(OEt)_2$ and $PH_2C[P(O)(OEt)_2]CH{=}NO_2^-$, which upon acidic workup will yield the nitroalkane or the Nef reaction product, $Ph_2C[P(O)(OEt)_2]CHO$. The reaction of $(EtO)_2PO^-$ with $Ph_2C{=}C(SPh)NO_2$ also produces $Ph_2C[P(O)(OEt)_2]C{\equiv}N$ via a Perkow-type reaction of the Michael adduct to yield $Ph_2C[P(O)(OEt)_2]CH{=}N(O)OP(O)(OEt)_2$ as an intermediate. The nitrile is also formed from $Ph_2C[P(O)(OEt)_2]CH(NO_2)_2$ with $(EtO)_2PO^-$ in $(EtO)_2P(O)H$ or Me_2SO at 30 °C and in >95% yield by the reaction of $(EtO)_3P$ with $Ph_2C[P(O)(OEt)_2CH(NO_2)_2$ at 150 °C. Reaction of $Ph_2C{=}CHNO_2$ or Ph_2C-$[P(O)(OEt)_2]CH_2NO_2$ with excess $(EtO)_2PO^-$ in Me_2SO or $(EtO)_2P(O)H$ forms 3-(diethoxyphosphinyl)-2,2-diphenylaziridine by a process postulated to involve $Ph_2C{=}CHN(O^-)OP(O)(OEt)_2$, $Ph_2C{=}CHNOP(O)(OEt)_2^-$, and 2,2-diphenyl-2*H*-azirine. Similarly, $Ph_2C{=}C(SBu\text{-}t)NO_2$ and $(EtO)_2PO^-$ give 3-(*tert*-butylthio)-2,2-diphenyl-2*H*-azirine in Me_2SO or 2-(*tert*-butylthio)-3-phenylindole in $(EtO)_2P(O)H$ solution. Deoxygenation of $Ph_2C{=}C(X)NO_2$ to form the 2-X-3-phenylindoles occurs in high yield at 150 °C in $(EtO)_3P$ with X = H, PhS, or *t*-BuS while 2-nitro-3-phenylindole is formed from $Ph_2C{=}C(NO_2)_2$ in $(EtO)_2P(O)H$ at 150 °C.

Introduction

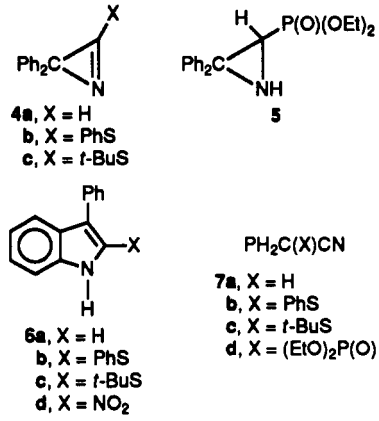
Reaction of 1,1-dinitro-2,2-diphenylethylene (**1d**) with 1 equiv of $(EtO)_2PO^-$ (P^-) in Me_2SO gives upon acidification a quantitative yield of the adduct **2d**.[1] The adduct **2a** is also formed from 2-nitro-1,1-diphenylethylene with P^- in the presence of $(EtO)_2P(O)H$ (PH). However, reactions of 1 equiv of PhS^- or *t*-BuS^- with **1d** in Me_2SO lead to the displacement of a nitro group forming **1b** or **1c** in high yield[1] while **1a** is converted to $Ph_2C{=}CHSR$.

$Ph_2C{=}C(X)NO_2$
1a, X = H
b, X = PhS
c, X = *t*-BuS
d, X = NO_2

$Ph_2C[P(O)(OEt)_2]CH(X)NO_2$
2a, X = H
b, X = PhS
c, X = *t*-BuS
d, X = NO_2

$Ph_2C(SR)CH(SPh)NO_2$
3a, R = Ph
b, R = *t*-Bu

We were initially drawn to a further study of these systems by the observation that excess PhS^- reacted slowly but essentially quantitatively with **1b** to form $Ph_2C{=}$ CHSPh and PhSSPh. Further work supported the premise that this denitrofication proceeded by the formation of the adduct **3a** followed by nucleophilic attack at the thiophenyl substituent to form the nitronate anion (Scheme I).[2,3] In a similar fashion the reaction of P^- with **1b** initially forms mainly **2a** and $PhSP(O)(OEt)_2$ via nucleophilic attack upon the sulfur atom in the adduct **2b**. However, we found that the reactions of excess P^- with the β-nitro-α-phenylstyrene derivatives **1** were complex and could yield heterocyclic products such as **4–6** or the nitriles **7**. This prompted us to examine the deoxygenations of



1 with $(EtO)_3P$ under conditions where nitroaromatics are converted to nitrenes.[4] At 150 °C the indoles **6a–c** are formed in high yield from **1a–c**, possibly via the azirines

Scheme I

$$3 + RS^- \rightarrow RSSPh + Ph_2C(SR)CH{=}NO_2^- \rightleftharpoons$$
$$RS^- + \mathbf{1a} \rightarrow Ph_2C{=}CHSR + NO_2^-$$

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