

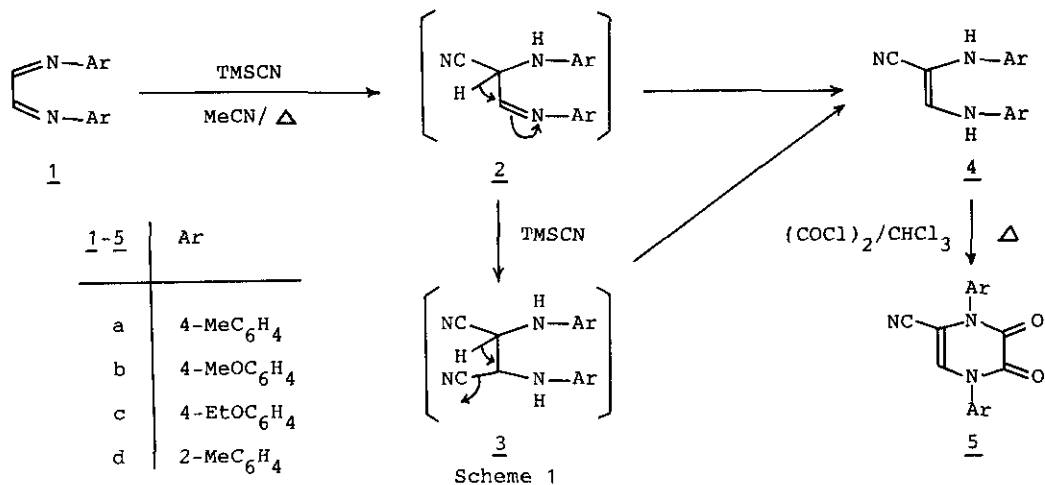
REACTION OF 1,4-DIAZA-1,3-BUTADIENES WITH CYANOTRIMETHYLSILANE.
 SYNTHESIS OF 2,3-BIS(ARYLAMINO)PROPENENITRILES AND THEIR
 CYCLIZATION TO 1,4-DIARYL-2,3-DIOXO-5-PYRAZINECARBONITRILES

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Abstract—Reaction of 1,4-diaza-1,3-butadienes (1) with cyanotrimethylsilane gave 2,3-bis(arylamino)propenenitriles (4), which were cyclized to 1,4-diaryl-2,3-dioxo-5-pyrazinecarbonitriles (5) on treatment with oxalyl chloride. The propenenitriles (4) were oxidized by oxygen to 2,3-bis(arylimino)propanenitriles (7), which were chlorinated with thionyl chloride to yield 2,3-bis(arylimino)-3-chloropropanenitriles (9).

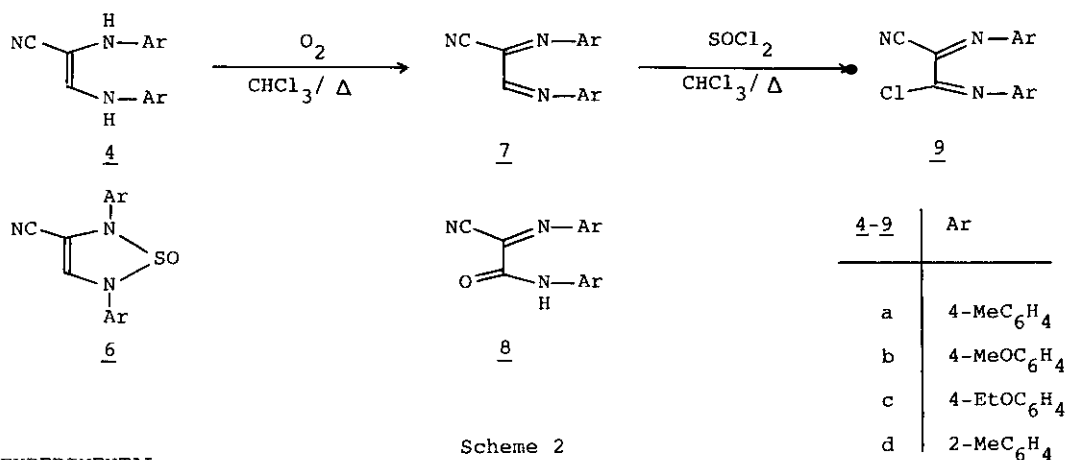
Cyanotrimethylsilane (TMSCN) has been extensively used in organic synthesis.¹ However, the reaction of carbon-nitrogen double bonds with TMSCN² and their synthetic applications remain comparatively unexplored. Reissert compounds became easy to prepare by the use of TMSCN in stead of potassium cyanide.³ Heterocyclic amine N-oxides⁴ were α -cyanated by TMSCN, whereas nitrones⁵ gave cyano-O-silyl-hydroxylamines or α -iminonitriles. Treatment of 1-aza-1,3-butadienes with TMSCN followed by hydrolysis afforded β,γ -unsaturated amino acids.⁶ On the other hand, 2-F-alkylated 1-aza-1,3-butadienes underwent cyanation in the presence of palladium (II) salts at the 2- and/or 4-positions.⁷ Recently, we have shown that the carbon-nitrogen double bonds of 1,2,4,5-tetrazines⁸ reacted with TMSCN to give 4-aminopyrazoles.⁹ In continuation of our studies on the use of TMSCN in heterocyclic synthesis, we have found that 2,3-bis(arylamino)propenenitriles obtained from 1,4-diaza-1,3-butadienes and TMSCN are useful starting materials for the synthesis of 2,3-dioxo-5-pyrazinecarbonitriles.

1,4-Diaza-1,3-butadienes (1a-d) readily available from glyoxal and arylamines¹⁰ were treated with 2.4 equivalent of TMSCN in acetonitrile under reflux to yield



2,3-bis(arylamino)propenenitriles (4a-d) in 36-48% yields (Scheme 1). The structure 4 was confirmed on the basis of the analytical and spectral data (Table 1 and 2). The ir spectra of 4a-d showed absorptions due to amino and cyano groups at 3380-3260 and 2180-2160 cm^{-1} , respectively, and in the nmr spectra no proton resonance was observed in the region of methine protons. This indicates that the initial addition product 2 would undergo 1,3-hydrogen shift to form more resonance-stabilized propenenitriles (4) or the second addition product 3 would eliminate hydrogen cyanide to give 4. This class of compounds 4 seems to be rare in the literature; 2,3-dianilinopropenenitrile was prepared from 1,2-dichloro-1,2-diethoxyethene.¹¹ Since these polyfunctional ethenes 4 appear to be useful starting materials for the synthesis of heterocyclic compounds, we studied the reactivities of 4 and found a facile preparation of 1,4-diaryl-2,3-dioxo-5-pyrazinecarbonitriles (5). The propenenitriles (4) reacted with oxalyl chloride in chloroform under reflux to yield cyclized products in 28-65% yields, which were assigned to be 5. The ir spectra of 5a-d showed cyano and carbonyl absorptions at 2230-2210 and 1695-1680 cm^{-1} , respectively. Although the resonances of the proton at the C-5 position of 5a-c in the nmr spectra were overlapped with those of aromatic protons, that of 5d was observed at δ 7.05 as a singlet. Pyrazine-2,3-diones which have cyano groups at the position of C-5 and/or C-6 are scarcely known.¹² Recently, Mitsuhashi et al. have reported a synthesis of 2,3-dioxo-5,6-pyrazinedicarbonitrile and its condensed heterocycles.¹³ Synthesis of other heterocycles was further attempted. Reaction of 4 with thionyl chloride was expected to give 1,2,5-thiadiazole S-oxide (6) (Scheme 2). However,

the product obtained in a low yield on treatment with thionyl chloride in chloroform under reflux was revealed to be 2,3-bis(arylimino)-3-chloropropanenitrile (9a) on the basis of the spectral and analytical data. The results suggest that 4a was at first oxidized by oxygen to 2,3-bis(arylimino)propanenitrile (7a), which was then chlorinated with thionyl chloride. In fact, when a solution of 4a in chloroform was heated in a stream of oxygen, 7a was obtained in 46% yield after separation on column chromatography, accompanied by a by-product amide 8a. This tendency to autoxidation is in accord with the case from 2,3,3-tris(alkylamino)propenenitrile to 3-alkylamino-2,3-bis(alkylimino)propanenitrile.¹⁴ Chlorination of 7a with thionyl chloride in chloroform under reflux gave, as expected, 9a in 12% yield. The propanenitrile derivatives 7b-d and 9b-c were also obtained in a similar manner and are shown in Table 1 and 2.



EXPERIMENTAL

Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. ¹H-Nmr, ir, and mass spectra were measured with a JEOL JNM-PMX 60, a JASCO A-102, and a JEOL JMS-DX 300 spectrometer, respectively. Microanalysis was performed with a Shimadzu UM-3B microanalyzer.

General Procedure for 2,3-Bis(arylamino)propenenitriles (4a-d).

A mixture of 1,4-diaryl-1,4-diaza-1,3-butadienes (1)¹⁰ (1.0 mmol) and TMSCN (2.4 mmol) in acetonitrile (10 ml) was refluxed for 4-12 h under nitrogen atmosphere. After evaporation of the solvent the residue was recrystallized to give 4.

Cyclization of 4a-d to 1,4-Diaryl-2,3-dioxo-5-pyrazinecarbonitriles (5a-d).

To a stirred solution of 4 (1.0 mmol) in anhydrous $CHCl_3$ (5 ml) was added oxalyl chloride (1 ml) dropwise at room temperature. The mixture turned green or black immediately. After refluxing for 2-5 h the precipitates formed were collected by

Table 1. Physical and Analytical Data of Compounds 4, 5, 7, 8, and 9

Compound	Yield (%)	M. p. (°C)	Molecular Formula	Calcd. (%)		Found (%)	
				C	H	C	H
<u>4a</u>	48	163-164 (MeOH)	C ₁₇ H ₁₇ N ₃	77.53	6.51	77.60	6.36
<u>4b</u>	48	152-153 (C ₆ H ₆)	C ₁₇ H ₁₇ N ₃ O ₂	69.13	5.80	69.28	5.64
<u>4c</u>	36	138-141 (C ₆ H ₆)	C ₁₉ H ₂₁ N ₃ O ₂	70.56	6.55	70.51	6.78
<u>4d</u>	39	137-139 (MeOH)	C ₁₇ H ₁₇ N ₃	77.53	6.51	77.78	6.72
<u>5a</u>	65	>300 (MeCN)	C ₁₉ H ₁₅ N ₃ O ₂	71.91	4.76	72.16	4.73
<u>5b</u>	58	>300 (MeCN)	C ₁₉ H ₁₅ N ₃ O ₄	65.32	4.33	65.44	4.51
<u>5c</u>	51	260-262 (MeCN)	C ₂₁ H ₁₉ N ₃ O ₄	66.83	5.07	66.85	5.22
<u>5d</u>	28	180-182 (PhMe)	C ₁₉ H ₁₅ N ₃ O ₂	71.91	4.76	72.07	4.90
<u>7a</u>	46	107-110 (MeOH)	C ₁₇ H ₁₅ N ₃	78.13	5.79	78.10	5.84
<u>7b</u>	34	144-145 (C ₆ H ₆)	C ₁₇ H ₁₅ N ₃ O ₂	69.61	5.15	69.85	4.84
<u>7c</u>	50	113-115 (C ₆ H ₆)	C ₁₉ H ₁₉ N ₃ O ₂	71.01	5.96	70.82	6.00
<u>7d</u>	29	100-102 (C ₆ H ₆)	C ₁₇ H ₁₅ N ₃	78.13	5.79	78.30	5.97
<u>8a</u>	10	161-162 (C ₆ H ₆)	C ₁₇ H ₁₅ N ₃ O	73.63	5.45	73.47	5.50
<u>9a</u>	12	160-162 (C ₆ H ₆)	C ₁₇ H ₁₄ ClN ₃	69.04	4.77	68.74	4.77
<u>9b</u>	21	156-158 (C ₆ H ₆)	C ₁₇ H ₁₄ ClN ₃ O ₂	62.30	4.31	62.39	4.35
<u>9c</u>	44	159-160 (C ₆ H ₆)	C ₁₉ H ₁₈ ClN ₃ O ₂	64.14	5.10	64.34	5.13

filtration, washed with a small amount of MeOH, and were recrystallized to give 5.

Oxidation of 4a-d to 2,3-Bis(arylimino)propanenitriles (7a-d).

A solution of 4a-c (1.0 mmol) in CHCl₃ (20 ml) or 4d (1.0 mmol) in acetonitrile (20 ml) was refluxed for 5-17 h in a stream of oxygen. After evaporation of the solvent the residue was purified by recrystallization to give 7b and c, or column chromatography on silica gel with CHCl₃ to give 7a and d. In the case of 4a, 8a was also separated from the silica gel column in addition to 7a.

Chlorination of 7a-c to 2,3-Bis(arylimino)-3-chloropropanenitriles (9a-c).

A mixture of 7 (1.0 mmol) and thionyl chloride (1 ml) in anhydrous CHCl₃ (5 ml) was refluxed for 2-3 h. After evaporation of the solvent, the residue was purified by column chromatography on silica gel with CHCl₃ to give 9.

Table 2. Spectral Data of Compounds 4, 5, 7, 8, and 9

Compound	Ms (M ⁺) (m/z)	Ir (KBr) (cm ⁻¹)				¹ H-Nmr (δ, ppm)		
<u>4a</u>	263	3350	3260	2170	1640	2.28 (s, 6H)	4.40 (s, 1H)	6.60-7.50 (m, 10H) ^a
<u>4b</u>	295	3320	2180	1640	1500	3.72 (s, 3H)	3.69 (s, 3H)	5.62 (s, 1H) 6.73-7.61 (m, 10H) ^b
<u>4c</u>	323	3320	2170	1635	1510	1.40 (t, J=7 Hz, 6H)	4.00 (q, J=7 Hz, 4H)	4.30 (s, 1H) 6.60-7.45 (m, 10H) ^a
<u>4d</u>	263	3380	3330	2160	1640	2.05 (s, 3H)	2.25 (s, 3H)	4.47 (s, 1H) 6.63-7.50 (m, 10H) ^a
<u>5a</u>	---	2220	1680	1640	1505	2.06 (s, 6H)	6.97-7.13 (m, 9H) ^c	
<u>5b</u>	---	2220	1680	1595	1500	3.59 (s, 6H)	6.71-7.12 (m, 9H) ^c	
<u>5c</u>	377	2210	1695	1640	1505	1.11 (t, J=7 Hz, 6H)	3.92 (q, J=7 Hz, 4H)	6.76-7.17 (m, 9H) ^c
<u>5d</u>	317	2230	1690	1635	1485	2.27 (s, 6H)	7.05 (s, 1H)	7.39 (s, 8H) ^a
<u>7a</u>	261	2210	1600	1580	1500	2.38 (s, 6H)	7.23 (s, 4H)	7.28 (s, 4H) 8.35 (s, 1H) ^a
<u>7b</u>	293	2200	1580	1485	1450	3.87 (s, 6H)	6.88-7.65 (m, 8H)	8.40 (s, 1H) ^a
<u>7c</u>	321	2200	1595	1560	1495	1.45 (t, J=7 Hz, 6H)	4.13 (q, J=7 Hz, 4H)	6.88-7.67 (m, 8H) 8.42 (s, 1H) ^a
<u>7d</u>	261	2200	1615	1480	1455	2.30 (s, 3H)	2.47 (s, 3H)	7.23 (s, 8H) 8.33 (s, 1H) ^a
<u>8a</u>	277	3330	2200	1670	1510	2.35 (s, 3H)	2.45 (s, 3H)	7.07-7.62 (m, 8H) 8.95 (br s, 1H) ^a
<u>9a</u>	295	2210	1630	1590	1560	2.39 (s, 3H)	2.42 (s, 3H)	7.25 (s, 4H) 7.35 (s, 4H) ^a
<u>9b</u>	327	2200	1570	1480	1445	3.87 (s, 6H)	6.90-7.72 (m, 8H) ^a	
<u>9c</u>	355	2100	1580	1490	1465	1.43 (t, J=7 Hz, 6H)	4.08 (q, J=7 Hz, 4H)	6.83-7.63 (m, 8H) ^a

^aIn CDCl₃. ^bIn acetone-d₆. ^cIn CF₃COOH.

REFERENCES

1. (a) W. P. Weber, "Silicon Reagents for Organic Synthesis," Springer-Verlag, New York (1983). (b) W. C. Groutas and D. Felker, Synthesis, 1980, 861.
2. (a) I. Ojima, S. Inaba, and K. Nakatsugawa, Chem. Lett., 1975, 331. (b) I. Ojima and S. Inaba, Chem. Lett., 1975, 737.
3. (a) B. C. Uff, S. L. A. A. Chen, Y. Ho, F. D. Popp, and J. Kant, J. Chem. Soc., Chem. Commun., 1984, 1245. (b) W. Dostal and G. Heinisch, Heterocycles, 24, 793 (1986). (c) S. Ruchirawat, N. Phadungkul, M. Chuankammerdkarn, C. Thebtaranonth, Heterocycles, 6, 43 (1977).
4. (a) W. K. Fife, Heterocycles, 22, 93 (1984). (b) T. Sakamoto, S. Kaneda, S. Nishimura, and H. Yamanaka, Chem. Pharm. Bull., 33, 565 (1985).
5. (a) A. Padwa and K. F. Koehler, J. Chem. Soc., Chem. Commun., 1986, 789. (b) D. K. Dutta, D. Prajapati, J. S. Sandhu, and J. N. Baruah, Synth. Commun., 15, 335 (1985).
6. W. J. Greenlee, J. Org. Chem., 49, 2632 (1984).
7. Y. Yamasaki, T. Maekawa, T. Ishihara, and T. Ando, Chem. Lett., 1985, 1387.
8. M. Takahashi and H. Kikuchi, Tetrahedron Lett., 28, 2139 (1987).
9. P. Imming, R. Mohr, E. Muller, W. Overheu, and G. Seitz, Angew. Chem. Int. Ed. Engl., 21, 284 (1982).
10. J. M. Kliegman and R. K. Barnes, J. Org. Chem., 35, 3140 (1970).
11. H. Baganz and J. Pelug, Chem. Ber., 90, 386 (1957).
12. G. W. H. Cheeseman and E. S. G. Werstiuk, "Advances in Heterocyclic Chemistry," Vol. 14, p 99, ed. by A. R. Katritzky and A. J. Boulton, Academic Press, New York (1972).
13. (a) T. Suzuki, Y. Nagae, and K. Mitsuhashi, J. Heterocycl. Chem., 23, 1419 (1986). (b) K. Mitsuhashi, Y. Nagae, and T. Suzuki, J. Heterocycl. Chem., 23, 1741 (1986).
14. L. De Vries, J. Org. Chem., 36, 3442 (1971).

Received, 6th August, 1987