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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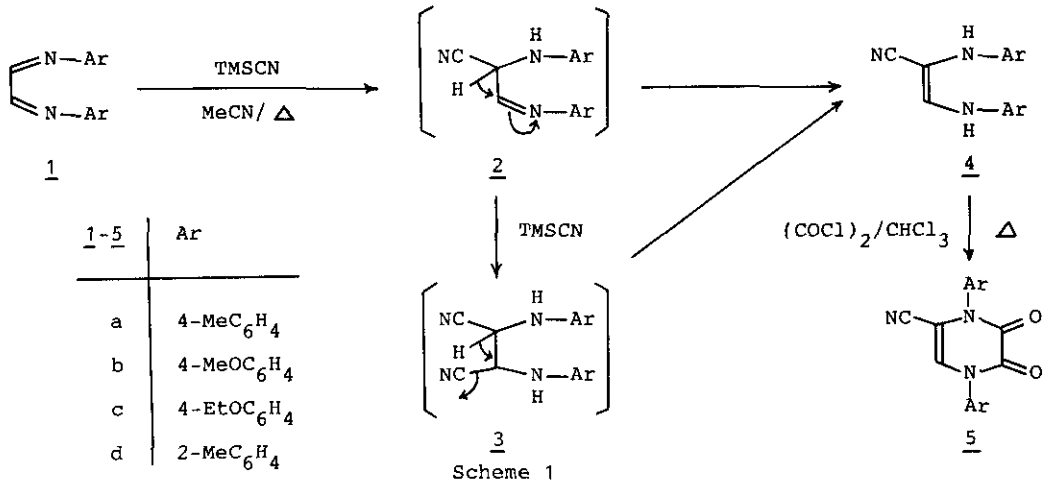
Abstract——Reaction of 1,4-diaza-1,3-butadienes (1) with cyanotrimethylsilane gave 2,3-bis(arylamino)propenenitriles (4), which were cyclized to 1,4-diaryl-2,3-dioxo-5-pyrazinecarbonitriles (5) on treatment with oxalyl chloride. The propenenitriles (4) were oxidized by oxygen to 2,3-bis(arylimino)-propanenitriles (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 TMSCN[2] 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-oxides[4] were α-cyanated by TMSCN, whereas nitrones[5] 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-tetrazines[8] 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 arylamines[10] were treated with 2.4 equivalent of TMSCN in acetonitrile under reflux to yield

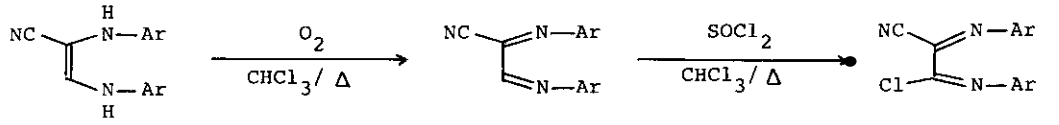


Scheme 1

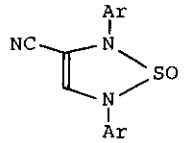
2,3-bis(arylamino)propenenitriles (4a-d) in 36-48% yields (Scheme 1). The structure 4 was confirmed on the basis of the analytical and spectral data (Table 1 and 2). The ir spectra of 4a-d showed absorptions due to amino and cyano groups at 3380-3260 and 2180-2160 cm^{-1}, respectively, and in the nmr 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 scarecely 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.



4 7 9



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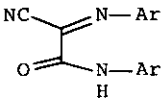

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Scheme 2

4-9	Ar
a	4-MeC_6H_4
b	4-$MeOC_6H_4$
c	4-$EtOC_6H_4$
d	2-MeC_6H_4

EXPERIMENTAL

Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. ^{1}H-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. (%) C	Calcd. (%) H	Found (%) C	Found (%) H
4a	48	163-164 (MeOH)	$C_{17}H_{17}N_3$	77.53	6.51	77.60	6.36
4b	48	152-153 (C_6H_6)	$C_{17}H_{17}N_3O_2$	69.13	5.80	69.28	5.64
4c	36	138-141 (C_6H_6)	$C_{19}H_{21}N_3O_2$	70.56	6.55	70.51	6.78
4d	39	137-139 (MeOH)	$C_{17}H_{17}N_3$	77.53	6.51	77.78	6.72
5a	65	>300 (MeCN)	$C_{19}H_{15}N_3O_2$	71.91	4.76	72.16	4.73
5b	58	>300 (MeCN)	$C_{19}H_{15}N_3O_4$	65.32	4.33	65.44	4.51
5c	51	260-262 (MeCN)	$C_{21}H_{19}N_3O_4$	66.83	5.07	66.85	5.22
5d	28	180-182 (PhMe)	$C_{19}H_{15}N_3O_2$	71.91	4.76	72.07	4.90
7a	46	107-110 (MeOH)	$C_{17}H_{15}N_3$	78.13	5.79	78.10	5.84
7b	34	144-145 (C_6H_6)	$C_{17}H_{15}N_3O_2$	69.61	5.15	69.85	4.84
7c	50	113-115 (C_6H_6)	$C_{19}H_{19}N_3O_2$	71.01	5.96	70.82	6.00
7d	29	100-102 (C_6H_6)	$C_{17}H_{15}N_3$	78.13	5.79	78.30	5.97
8a	10	161-162 (C_6H_6)	$C_{17}H_{15}N_3O$	73.63	5.45	73.47	5.50
9a	12	160-162 (C_6H_6)	$C_{17}H_{14}ClN_3$	69.04	4.77	68.74	4.77
9b	21	156-158 (C_6H_6)	$C_{17}H_{14}ClN_3O_2$	62.30	4.31	62.39	4.35
9c	44	159-160 (C_6H_6)	$C_{19}H_{18}ClN_3O_2$	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 $CHCl_3$ (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 $CHCl_3$ 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 $CHCl_3$ (5 ml) was refluxed for 2-3 h. After evaporation of the solvent, the residue was purified by column chromatography on silica gel with $CHCl_3$ 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)
4a	263	3350 3260 2170 1640	2.28 (s, 6H) 4.40 (s, 1H) 6.60-7.50 (m, 10H)[a]
4b	295	3320 2180 1640 1500	3.72 (s, 3H) 3.69 (s, 3H) 5.62 (s, 1H) 6.73-7.61 (m, 10H)[b]
4c	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]
4d	263	3380 3330 2160 1640	2.05 (s, 3H) 2.25 (s, 3H) 4.47 (s, 1H) 6.63-7.50 (m, 10H)[a]
5a	---	2220 1680 1640 1505	2.06 (s, 6H) 6.97-7.13 (m, 9H)[c]
5b	---	2220 1680 1595 1500	3.59 (s, 6H) 6.71-7.12 (m, 9H)[c]
5c	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]
5d	317	2230 1690 1635 1485	2.27 (s, 6H) 7.05 (s, 1H) 7.39 (s, 8H)[a]
7a	261	2210 1600 1580 1500	2.38 (s, 6H) 7.23 (s, 4H) 7.28 (s, 4H) 8.35 (s, 1H)[a]
7b	293	2200 1580 1485 1450	3.87 (s, 6H) 6.88-7.65 (m, 8H) 8.40 (s, 1H)[a]
7c	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]
7d	261	2200 1615 1480 1455	2.30 (s, 3H) 2.47 (s, 3H) 7.23 (s, 8H) 8.33 (s, 1H)[a]
8a	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]
9a	295	2210 1630 1590 1560	2.39 (s, 3H) 2.42 (s, 3H) 7.25 (s, 4H) 7.35 (s, 4H)[a]
9b	327	2200 1570 1480 1445	3.87 (s, 6H) 6.90-7.72 (m, 8H)[a]
9c	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]

[a] In $CDCl_3$. [b] In acetone-d_6. [c] In CF_3COOH.

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