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Gas-Phase Pyrolysis of 2-Heteroaromatic-1-dimethylaminoethylenes: Kinetic and Mechanistic Study

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ABSTRACT: *Gas-phase pyrolysis reactions of 4(2′-dimethylaminoethenyl)-2-oxo-2H-benzo[b]pyran-3-carbonitrile (***1***), 4(2′-dimethylaminoethenyl)-2-oxo-2H-naphtho[1,2-b]pyran-3-carbonitrile (***2***), 1,6-dihydro-4-(2′-dimethylaminoethenyl)-6-oxo-1-phenylpyridazine-3,5-dicarbonitrile (***3***), 2-cyano-5-dimethylamino-3-phenyl-2,4-pentadienonitrile (***4***), 2-cyano-5-dimethylamino-3-(2-thienyl)-2,4-pentadienonitrile (***5***), 1,2-dihydro-4-(2′-dimethylaminoethenyl)-oxoquinoline-4-carbonitrile (***6***), 6-(ethylthio)-4-(2′-dimethylaminoethenyl)-2-phenylpyrimidine-5-carbonitrile (***7***) (Scheme 1) have been carried out. The rates of gas-phase pyrolytic reactions of compounds* **3, 4, 5,** *and* **7** *have been measured and found to correspond to unimolecular first-order reactions. Product analyses together with kinetic data were used to outline a feasible pathway for the pyrolytic reactions of the compounds under study.* © 2001 John Wiley & Sons, Inc. Heteroatom Chem 12:47–51, 2001

INTRODUCTION

Functionally substituted heteroaromatics are interesting as potential pharmaceuticals [1], agrochemicals [2], and as dye intermediates [3], and their chemistry is now receiving considerable attention [4,5]. In conjunction with our recent interest in adopting the environmentally friendly gas-phase technique in synthetic organic chemistry, we have previously reported on the utility of this technique for synthesis of substituted nitriles [6,7], ketones [8], and functionally substituted heteroaromatics. In the present article we report results of our efforts aimed at utilizing the same technique for syntheses of condensed pyridines utilizing the readily obtainable compounds (**1**–**6**) as starting materials [9] (See Scheme 1 for compound structures).

RESULTS AND DISCUSSION

Characterization of the products of the pyrolysis reaction of each substrate was based on the IR, NMR, and GC-MS data as follows:

1. IR: ν_{max} 2198–2219 ($C\equiv N$) in each substrate has disappeared from the IR spectra of the products.
2. ^1H NMR (DMSO-d_6): $6H^+$ corresponding to $N(Me)_2$ in each substrate has been reduced to $3H^+$, and the disappearance of the two doublets at δ values of 5.7 and 8.4 ppm that corresponds to α and β vinylic protons due to the aromatization of the product of pyrolysis.
3. GC-MS: Molecular mass of the products of each substrate corresponds to the molecular mass of the substrate − 15 units.

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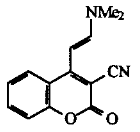
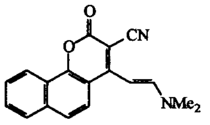
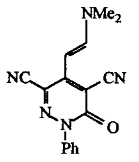
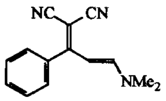
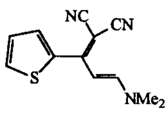
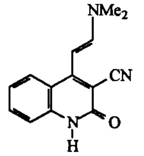
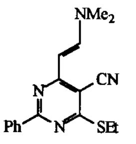
These data suggest the pathway shown in Scheme 2 for the pyrolytic reactions of compounds **1–6**.

For compound **7**, we have observed the following:

1. IR: ν_{max} 2219 (C≡N) in the substrate is shown in the IR spectra of the pyrolysis product.
2. NMR: ^1H (DMSO-d_6) of 1.4 (3H, t, CH_3) and 3.4 (2H, q, CH_2) of the S-C_2H_5 group in the substrate has disappeared from the H^+ (DMSO-d_6) of the product, and the disappearance of the two doublets at δ values of 5.35 and 8.4 ppm that correspond to α and β vinylic protons due to the aromatization of the product of pyrolysis.

No.	Compound	Name
1		4(2'-dimethylaminoethenyl)-2-oxo-2H-benzo[b]pyran-3-carbonitrile
2		4(2'-dimethylaminoethenyl)-2-oxo-2H-naphtho[1,2-b]pyran-3-carbonitrile
3		1,6-Dihydro-4-(2'-dimethylaminoethenyl)-oxo-1-phenylpyridazine-3,5-dicarbonitrile
4		2-Cyano-5-dimethylamino-3-phenyl-2,4-penta-dienonitrile
5		2-Cyano-5-dimethylamino-3-(2-thienyl) 2,4-penta-dienonitrile
6		1,2-Dihydro-4-(2-dimethylaminoethylene) 2-oxoquinoline-4-carbonitrile
7		6(ethylthio)-4-(2'-dimethylaminoethenyl)-phenyl pyrimidine-5-carbonitrile

SCHEME 1

3. GC/MS: The molecular mass of the product is less by a (29.2) unit from that of the substrate.

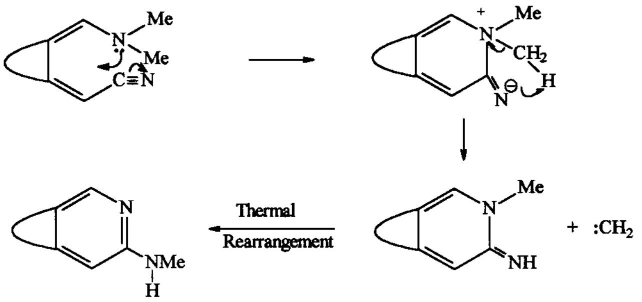
These data suggest loss of the C_2H_4 group through the pathway shown in Scheme 3.

The kinetic data and Arrhenius log A/s^{-1} and E_a/kJ mol^{-1} for the substrates (**3**,**4**,**5**, and **7**) are given in Table 1. Each of the substrates gave excellent and reproducible first-order kinetics, with strict linearity up to >95% reaction. The homogeneity of each reaction was tested by comparing the rate using an empty reaction tube with that of a similar vessel packed with glass helices. The results show that the change in the rate of reaction was within experimental error. Thus an increase in surface area of more than 50% caused a negligible change in reaction rate. It is noteworthy that the values obtained for the Arrhenius parameters are typical of polar homogeneous pyrolytic gas-phase reactions [10]. The kinetic data together with the results of analysis of the products of reaction support the mechanisms shown in Schemes 2 and 3.

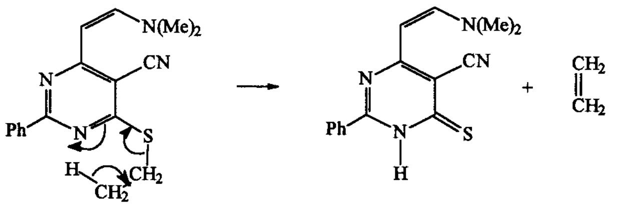
EXPERIMENTAL

Kinetic Studies

Reaction Setup. Preliminary kinetic results were obtained on a system featuring a Eurotherm 093 pyrolysis unit coupled to a Perkin Elmer Sigma 115 gas chromatograph. The kinetic data reported are from a reactor setup including an HPLC (BioRad



SCHEME 2 Pyrolysis Pathway of (1–6)



SCHEME 3 Pyrolysis Pathway for (7)

TABLE 1 Kinetic Data and Arrhenius Parameters for Pyrolysis of Substrates **3, 4, 5,** and **7**

Compound	*T* (K)	10^4 k(s^{-1})	E_a (kJ mol^{-1})	logA(s^{-1})	Correlation Coefficient (R^2)
3	622.5	1.12	165.16 ± 0.64	9.92 ± 0.05	0.9998
	636.3	2.25			
	644.2	3.14			
	653.4	5.13			
	662.3	7.75			
	669.7	10.83			
4	674.5	3.47	197.53 ± 0.03	11.84 ± 0.01	0.9999
	684.0	5.66			
	693.5	9.10			
	698.5	11.64			
	703.5	14.82			
	708.1	18.45			
5	653.1	1.56	236.62 ± 0.02	15.12 ± 0.01	0.9997
	663.0	2.99			
	673.1	5.69			
	683.1	10.57			
	688.0	14.22			
	693.0	19.17			
	698.1	25.88			
7	638.3	1.06	217.21 ± 0.89	13.80 ± 0.07	0.9989
	647.1	1.85			
	658.9	3.81			
	667.3	6.28			
	679.6	12.76			

Model 2700) fitted with a UV-vis detector (BioRad Model 1740) adjusted at 254 nm; HPLC Column LC-8, 25 cm, 4.6 mm, 5 μm (Supelco); and CDS custom-made pyrolysis unit for the thermolysis reactions. The pyrolysis tube is jacketed by an insulating aluminium block fitted with a platinum resistance thermometer and a thermocouple connected to a Comark microprocessor thermometer.

Kinetic Runs and Data Analysis. Aliquots (0.2 mL) of very dilute solutions (ppm) of neat substrates in acetonitrile as solvent and chlorobenzene as internal standard were pipetted into the reaction tube, which was then sealed under vacuum (0.28 mbar). The tube was then placed inside the pyrolyzer for 600 seconds at a temperature at which 10–20% pyrolysis is deemed to occur. The contents of the tube were analyzed using the HPLC probe. $CH_3CN–H_2O$ mixtures were used as the mobile phase in a ratio of 55:45 for compound **3** and in a ratio of 70:30 for compounds **4**,**5**, and **7**.

At least three kinetic runs were repeated for each 5–10°C rise in temperature of the pyrolyzer and for the same time interval until 90–95% pyrolysis was achieved. The rates were followed over a temperature range exceeding 55 K, and the rate coefficients were calculated using the expression for a first-order reaction: $kt = \ln(a_0/a)$. The Arrhenius parameters were obtained from a plot of log k vs. $1/T$(K).

Product Analysis

Flow Technique. Solutions of substrates in chlorobenzene were passed down a 1 m reactor column packed with helices [11]. The column was heated to temperatures comparable to those used in the kinetic investigations. The products of pyrolysis were swept through the column using a stream of nitrogen gas, and the effluents were trapped in a glass coil surrounded by a jacket of dry ice. The material collected on the walls of the trap (glass coil) was crystallized and analyzed by NMR, GC-MS, and IR spectroscopy.

Synthesis

*4(2'-Dimethylaminoethenyl)-2-oxo-2H-benzo[b]-pyran-3-carbonitrile (*1*).* A mixture of ethyl cyanoacetate and ammonium acetate was treated with *o*-hydroxyacetophenone. The reaction mixture was heated at 220°C for 15 minutes, left to cool, and then triturated with ethanol. The solid product so formed was collected by filtration and crystallized from dioxane to give yellow crystals, 80% yield, and m.p. = 197°C, and proved to be 4-methyl-2-oxobenzo[*b*]pyran-3-carbonitrile. The latter was then condensed with dimethylformamide dimethylacetal in refluxing xylene for 15 minutes, then allowed to cool. The solid product so formed was collected by filtration, and crystallized as green crystals from acetic acid, 86% yield, and m.p. 210°C, which corresponded to **1**.

IR $\nu_{\max}$: 2185 (CN) and 1671 cm^{-1} (ring CO). ^1H NMR (DMSO-d_6) δ_H: 3.26 [6H, s, $N(CH_3)_2$], 5.74 (1H, d, α-vinylic H; J = 13 Hz); 7.22–8.22 (4H, m, arom-H) and 8.51 ppm (1H, d, β-vinylic H; J = 13 Hz). Found: C, 69.86; H, 5.03; N, 11.62. $C_{14}H_{12}N_2O_2$ requires C, 69.99; H, 5.03; N, 11.66%.

*4(2′-Dimethylaminoethenyl)-2-oxo-2H-naphtho-[1,2-b]pyran-3-carbonitrile (***2***).* A mixture of ethyl cyanocetate and ammonium acetate was treated with 2-acetyl-1-naphthol. The reaction mixture was heated at 220°C for 15 minutes, left to cool, and then triturated with ethanol. The solid product, so formed, was collected and crystallized from dimethylformamide as green crystals, 70% yield, and m.p. 280°C, and proved to be 4-methyl-2-oxo-naphtho[1,2-*b*]pyran-3-carbonitrile. The latter was then condensed with dimethylformamide dimethylacetal in refluxing xylene for 15 minutes and allowed to cool. The solid product, so formed, was collected by filtration and crystallized as green crystals from acetic acid, 84% yield, and m.p. 240°C, and was proved to be **2**.

IR $\nu_{\max}$: 2165 (CN) and 1679 cm^{-1} (ring CO). ^1H NMR (DMSO-d_6) δ_H: 3.22 [6H, s, $N(CH_3)_2$], 5.75 (1H, d, α-vinylic H; J = 13 Hz); 7.59–8.22 (6H, m, arom-H) and 8.49 ppm (1H, d, β-vinylic H; J = 13 Hz). Found: C, 74.14; H, 4.79; N, 9.50. $C_{18}H_{14}N_2O_2$ requires C, 74.47; H, 4.86; N, 9.65%.

*1,6-Dihydro-4-(2-dimethylaminoethenyl)-6-oxo-1-phenylpyridazine-3,5-dicarbonitrile (***3***).* Compound **3** was prepared by condensing 4,6-dicyano-5-methyl-2-phenyl-3(2H)-pyridazinone with dimethylformamide dimethylacetal in refluxing xylene for 15 minutes. The mixture was allowed to cool, and the solid product, so formed, was filtered off and crystallized from dioxane as red crystals, 84% yield, and m.p. 198°C, and proved to be **3**.

IR $\nu_{\max}$: 2203 (CN) and 1656 cm^{-1} (ring CO). ^1H NMR (DMSO-d_6) δ_H: 3.10 (6H, s, $N(CH_3)_2$), 5.15 (1H, d, α-vinylic H; J = 13 Hz); 7.50 (5H, m, arom-H) and 8.50 ppm (1H, d, β-vinylic H; J = 13 Hz). Found: C, 65.97; H, 4.60; N, 23.80. $C_{16}H_{13}ON_5$ requires C, 65.97; H, 4.50; N, 24.04%.

*2-Cyano-5-dimethylamino-3-phenyl-2,4-pentadienonitrile (***4***).* From a condensation reaction of 2-phenylethylidenemalononitrile and dimethylformamide dimethylacetal, following the experimental procedure described earlier [12], the product was obtained in 75% yield as violet crystals from ethanol, m.p. 149°C.

IR $\nu_{\max}$: 2220 (CN) cm^{-1}. ^1H NMR ($CDCl_3$) δ_H: 3.00 (6H, s, $N(CH_3)_2$), 5.8 (1H, d, H-4; J = 13 Hz); 6.60 (1H, d, H-5, J = 13 Hz) and 7.20–7.50 (5H, m, arom-H). Found: C, 75.29; H, 5.82; N, 18.90. $C_{14}H_{13}N_3$ requires C, 75.31; H, 5.83; N, 18.82%.

*2-Cyano-5-dimethylamino-3-(2-thienyl)-2,4-pentadienonitrile (***5***).* From a condensation reaction of 2(2′-thienyl)ethylidenemalononitrile and dimethylformamide dimethylacetal, following the experimental procedure described earlier [12], the product was obtained in 80% yield as yellow crystals from ethanol, m.p. 160°C.

IR $\nu_{\max}$: 2220 (CN) cm^{-1}. ^1H NMR ($CDCl_3$) δ_H: 3.00 [6H, s, $N(CH)_3)_2$], 5.8 (1H, d, H-4; J = 13 Hz) and 7.06–7.60 (4H, m, H-5 and thienyl H). Found: C, 62.81; H, 4.80; N, 18.36; S, 13.99. $C_{12}H_{11}N_3S$ requires C, 62.85; H, 4.83; N, 18.32; S, 13.96%.

*1,2-Dihydro-4-(2′-dimethylaminoethylene)-2-oxoquinoline-4-carbonitrile (***6***).* From a condensation reaction of 1,2-dihydro-2-oxo-4-methylquinoline-3-carbonitrile and dimethylformamide dimethylacetal, following the experimental procedure described earlier [13], the product was obtained in 65% yield as yellow crystals from ethanol, m.p. 308°C.

IR $\nu_{\max}$: 3420 (NH), 2190 (CN) and 1649 (ring CO) cm^{-1}. ^1H NMR (DMSO-d_6) δ_H: 2.93 (6H, s, $N(CH_3)_2$), 5.56 (1H, d, α-vinylic H; J = 13 Hz); 7.04–8.07 (5H, m, arom-H and β-vinylic H); 11.35 (1H, s, NH). Found: C, 70.29; H, 5.50; N, 17.59. $C_{14}H_{13}N_3O$ requires C, 70.27; H, 5.48; N, 17.56%.

*6-(Ethylthio)-4-(2′-dimethylaminoethenyl)-2-phenylpyrimidine-5-carbonitrile (***7***).* A mixture of 5-cyano-6-methyl-2-phenyl(3H)-pyrimidine-4-thione (0.01 mol; 2.27 g) and ethyl iodide (0.01 mol) was treated in acetone (10 ml) and (0.01 mol; 1.38 g) K_2CO_3. The reaction mixture was refluxed for one hour and poured into water. The solid product, so formed, was collected by filtration and crystallized from ethanol to give 5-cyano-4-ethylthio-6-methyl-2-phenyl pyrimidine, m.p. 235°C, 75% yield.

A mixture of the latter and dimethylformamide dimethylacetal in xylene was refluxed for six hours. The reaction mixture was left to cool, and the solid product, so formed, was filtered off and crystallized from dioxane, 78% yield, m.p. 119.1°C, and was proved to be **7**.

IR $\nu_{\max}$: 2201 (CN) cm^{-1}. ^1H NMR (DMSO-d_6) δ_H:

2.40 (3H, s, CH_3)), 3.29 (6H, s, $N(CH_3)_2$), 3.38 (2H, q, CH_2), 5.35 (1H, d, α-vinylic H; $J = 13$ Hz); 7.55–8.40 (6H, m, arom-H and β-vinylic H). Found: C, 65.37; H, 5.67; N, 17.930; S, 10.46. $C_{17}H_{18}SN_4$ requires C, 65.79; H, 5.85; N, 18.05; S, 10.31%.

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