-0.34 ppm and yielded 4 on hydrolysis. A dimer, 5, with a longer retention time was also identified on the basis of its spectra.

By comparison of proton and ^{13}C NMR spectra from three different Grignard reagent samples, the reagent prepared from 3, and the reagent prepared from 6 before and after heating, it was possible to make assignments of methyl proton resonance signals and to assign all of the significant ^{13}C resonances. The methyl proton resonances are reproduced in Figure 1. In the Grignard reagent prepared from 3, the sharp resonance at 0.84 ppm is the hydrocarbon dimer; Grignard reagent 1 and monomeric hydrocarbon 4 overlap to give the broadened peak at about 0.90 ppm. The Grignard reagent from 6 *after heating* also has the signal from 1 at 0.90 ppm. At lower field are two strong signals which appear to result from overlap of the *gem*-dimethyl groups of monomer and dimer hydrocarbons 7 and 8. The methyl doublet from 7 is also observed. Before the reagent from 6 was heated, the two methyl singlets of Grignard reagent 2 were present at 1.02 and 0.97 ppm. In a sample which had been hydrolyzed, only the signals from 7 and 8 are observed, with the doublet from monomer 7 being more prominent.

In the ^{13}C NMR spectrum of the Grignard reagent from 3, all six resonances of dimer hydrocarbon 5 appear prominently. The methyl and methylene resonances of the monomeric hydrocarbon 4, which differ from those of 5, are present but are weak, indicating that dimerization is the principal side reaction in Grignard reagent formation. The remaining prominent resonances fall approximately in the location predicted from the parameters of Leibfritz, Wagner, and Roberts[24] for Grignard reagent 1. It is probable that the methylene carbon adjacent to the magnesium is buried in the solvent signal. The same five signals from 1 are present in the Grignard reagent prepared from 6, after heating. In the Grignard reagent from 6, several signals are prominent in the spectra both before and after heating. Most of these probably result from the dimeric hydrocarbon 8, since the resonances observed most clearly for the isolated monomer 7 in $CDCl_3$ appear rather weakly in the Grignard reagent. There remain six significant signals which disappear on heating and follow the general pattern observed for the other substituted (3,3-dimethylcyclobutyl)methyl derivatives. These may therefore be assigned to Grignard reagent 2. Table I includes NMR assignments which have been discussed above.

A sample of the open-chain Grignard reagent 1 prepared from 3 was heated for 48 h at 100 °C. The tube was opened in a drybag and connected to an adapter which permitted the solvent and other volatiles to be distilled to a trap under high vacuum. After evacuation for 1 h at about 5-μm pressure, the vacuum was broken with nitrogen, a small amount of THF was added, and the reagent was hydrolyzed by addition of an excess of water. Volatile materials were again distilled to a trap under vacuum and analyzed by GC on column B. Peak areas were assumed to be proportional to the amount of material for isomeric hydrocarbons 4 and 7. The peak corresponding in retention time to cyclized hydrocarbon 7 was trapped in a tube with liquid nitrogen cooling and analyzed by mass spectrometry.

Registry No. 1, 34164-52-8; 2, 76207-19-7; 3, 76207-20-0; 4, 76262-9; 5, 76207-21-1; 6, 76207-22-2; 7, 75017-20-8; 8, 76207-23-3; 3,3-dimethylcyclobutylmethanol, 75017-17-3; 3,3-dimethylcyclobutanecarboxylic acid, 34970-18-8; 3,3-dimethylcyclobutanemethanol tosylate, 76207-24-4; 2,2-dimethyl-4-pentenoic acid, 16386-93-9; allyl α-bromoisobutyrate, 40630-82-8; 2,2-dimethyl-4-penten-1-ol, 3420-42-6.

(24) Leibfritz, D.; Wagner, B. O.; Roberts, J. D. *Justus Liebigs Ann. Chem.* **1972**, *763*, 173.

Rates of Formation of Some Phenazines by Cyclization of Di- and Monoimines of *N*-(2-Aminophenyl)-*p*-benzoquinone[1]

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The spectrophotometrically determined rates for cyclization of *N*-(2-aminophenyl)-*p*-benzoquinonediimine and its 5-methyl and 5-chloro derivatives in buffered aqueous media are reported in Table I for the pH range 6–9. The first-order rate equation involves protonated diimine. At higher pH these diimines hydrolyze to the corresponding monoimines which then undergo cyclization. The first-order rate expression for cyclization for monoimine 3 (k_L) involves the neutral monoimine and under the conditions used for the reaction is faster than the second-order hydrolysis (k_h) of diimine 1a. Around pH 1 the diimines hydrolyze at the nonterminal imine nitrogen to the corresponding *p*-benzoquinone monoimine and *o*-phenylenediamine, which react further. Monoimine 3 undergoes a similar hydrolysis.

Mechanisms have been proposed for cyclization reactions which result in phenazines by formation of a nitrogen–carbon bond.[2] However, more data are needed to reduce the speculative nature of the proposed mechanisms and to eliminate possible alternatives. Rate-limiting steps have been observed that involve cationic, neutral (or zwitterionic), and/or anionic species. Presented here are the results of some rate studies of the cyclization of *N*-(2-aminophenyl)-*p*-benzoquinonimine (3) and -diimine and the 5-methyl and 5-chloro derivatives of the diimine (1a–c).

Diimines. Diphenylamines were synthesized by condensing *o*-fluoronitrobenzene with the appropriately substituted *p*-phenylenediamine followed by reduction of the nitro group with hydrogen and palladium. The resulting amines were recovered as the dihydrochlorides.

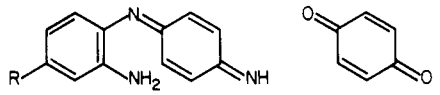
The diimines 1 (see Chart I) are prepared in dilute solution by potassium ferricyanide oxidation of the corresponding diphenylamines (6a–c). Within the pH range

(1) Taken in part from the M.S. Thesis of N. P. Loveless, University of Bridgeport, 1977, and presented in part at the 175th National Meeting of the American Chemical Society, Anaheim, CA, Mar 1978, Abstract No. ORGN 71.

(2) Brown, K. C.; Corbett, J. F. *J. Chem. Soc., Perkin Trans. 2* **1979**, 304.

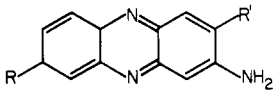
0022-3263/81/1946-1182$01.25/0

Chart I

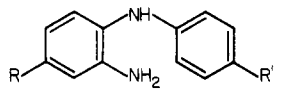


1a, R = H
b, R = CH_3
c, R = Cl

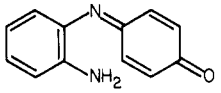
5



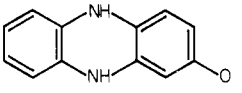
2a, R = H; R′ = H
b, R = CH_3; R′ = H
c, R = Cl; R′ = H
d, R = H; R′ = NH_2



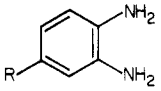
6a, R = H; R′ = NH_2
b, R = CH_3; R′ = NH_2
c, R = Cl; R′ = NH_2
d, R = H; R′ = OH



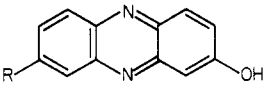
3



7

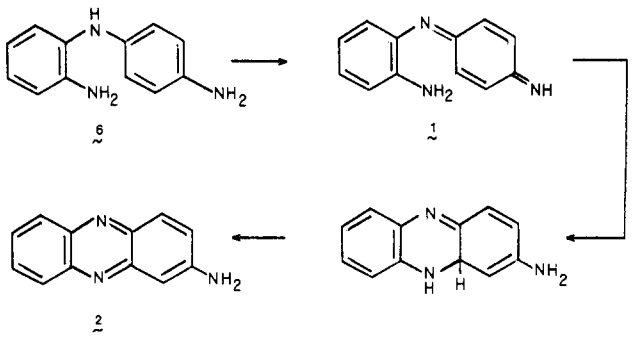


4a, R = H
b, R = CH_3
c, R = Cl



8a, R = H
b, R = CH_3
c, R = Cl

Scheme I. Proposed Mechanism of Cyclization of N-(2-Aminophenyl)-p-benzoquinonediimine



examined, this oxidation can be considered as being instantaneous.

Because protonation of the diimines is also a rapid reversible reaction, their pK_a's could be determined spectrophotometrically. Table II includes spectral data for protonated and neutral diimines as well as the calculated pK_a's.

In aqueous solution the diimines exhibited three types of characteristics depending on solution pH. Around pH 1 the diimine absorptions disappeared, but no immediate products with a spectral absorption between 360 and 700 nm could be detected. Between pH 6 and 9 highly colored products were formed which proved to be the corresponding phenazines. Above pH 10 products formed which were also highly colored but were different from those formed at lower pH.

At low pH the apparent reaction is hydrolysis at the azomethine bridge to form a p-benzoquinonimine and an o-phenylenediamine. A more detailed discussion of that reaction is presented later.

As demonstrated by the visible spectra, which exhibited sharp isosbestic points, the cyclizations proceeded smoothly between pH 6 and 9, quantitatively producing the corresponding phenazine as the exclusive organic product (Scheme I). Additionally, it was found that the observed rate increased with diimine concentration but

Table I. Rate Constants for Cyclization at 30 °C[a]

compd	k_c	compd	k_c
6a	27.6	6c	433.0
6b	13.1		

[a] See eq 1.

Table II. Maximum Visible Absorption, Molar Absorptivity, and pK_a's of Various Species

	cation		neutral species		anion, λ, nm (log ε)
compd	λ, nm (log ε)	pK_a	λ, nm (log ε)	pK_a	
1a	520 (3.93)	4.3	480 (3.51)		
1b	530 (3.75)	4.2	470 (3.51)		
1c	510 (3.61)	4.2	480 (3.58)		
2a	517 (3.99)	4.3	448 (3.80)		
2b	514 (3.98)	4.8	450 (3.75)		
2c	518 (3.99)	2.9	450 (3.73)		
8a	450 (3.81)	2.2	510 (2.98), 400 (3.81)	7.4	474 (3.84)
8b	446 (3.71)	2.4	510 (3.24), 410 (3.68)	7.2	472 (3.83)
8c	470 (3.51)	1.0	530 (3.24), 410 (3.60)	5.9	475 (3.70)

decreased by a factor of 10 for each unit increase in pH. Such behavior is to be expected where protonated diimine initiates the rate-limiting step in the cyclization. The appropriate rate expression is given by eq 1, where k_c is

$$-d[D_T]/dt = d[P]/dt = k_c[HD^+] = k_c\alpha[D_T] \quad (1)$$

the rate constant for cyclization, D_T is total diimine, i.e., in all its ionic and neutral forms, HD^+ is singly protonated diimine, α is the fraction of D_T present as singly protonated diimine, P is phenazine, and t is time. Values for k_c are reported in Table I.

When the reaction was run at pH 10.5 and above, the products were no longer the expected 2-aminophenazines but were instead the corresponding 2-hydroxyphenazines (8). While it is apparent that hydrolysis of the terminal imine occurred, it conceivably could happen either before or after cyclization. By studying the monoimines, we made a choice between these two possibilities.

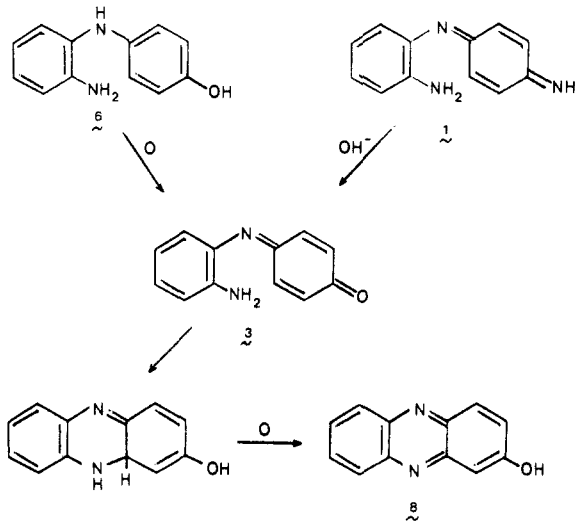
Role of Monoimines. Separate rate studies on the cyclization of hydrolyzed diimine, i.e., monoimine 3, showed that above pH 5 cyclization occurs quantitatively, even at pH 12. The rate obtained by following the loss of neutral monoimine at 550 nm fits first-order kinetics with the rate constant, k_L, equal to 1.3×10^{-3} s^{-1} at 30 °C. However, starting from diimine 1a, the observed rate constants for formation of 2-hydroxyphenazine at high pH (>10) were independent of pH and had a value of 2.0×10^{-4} s^{-1}. This suggests that the rate-controlling step for high pH reaction of diimine 1a is alkaline hydrolysis rather than monoimine cyclization. That hydrolysis preceded cyclization was established by allowing the conversion of diimine to phenazine to take place at a pH sufficiently low as to preclude hydrolysis of the diimine and then, after 10 half-lives, injecting hydroxide base into the reaction mixture until the pH exceeded 10.5. No hydrolysis of the phenazine was observed (Scheme II).

In an analogous system[3] it has been shown that hydrolysis of the diimine is second order: first order in diimine cation and first order in hydroxide ion concentration. The rate expression for hydrolysis based on this mechanism is shown in eq 2 with k_h, the second-order rate con-

$$-d[D_T]/dt = k_h\alpha[D_T][OH^-] \quad (2)$$

(3) Tong, L. K. J. J. Phys. Chem. 1954, 58, 1090.

Scheme II. Proposed Mechanism of Cyclization of *N*-(2-Aminophenyl)-*p*-benzoquinonimine



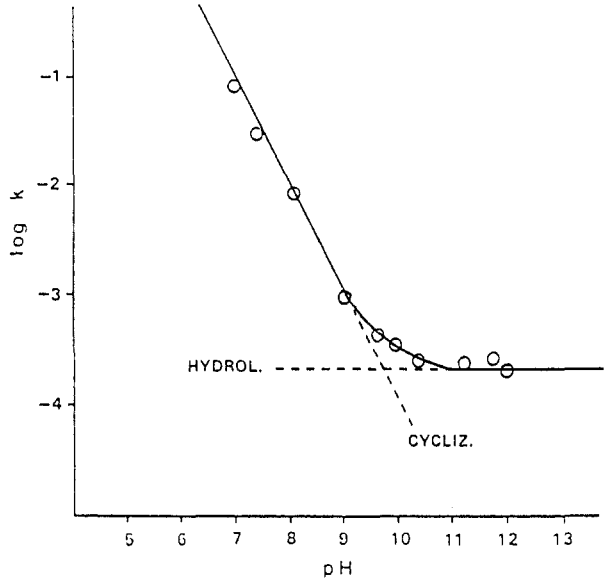


Figure 1. Logarithmic plot of the observed rate constant, $k = (d[D_T]/dt)[D_T]^{-1}$, as a function of pH at 30 °C for competing cyclization and for hydrolysis and then cyclization for **1a**. The curve is from eq 3 and uses k_c from Table I and $k_h = 1.02 \times 10^6$ L mol^{-1} s^{-1}. Experimental data are plotted independently.

stant for hydrolysis, equal to 1.02×10^6 L mol^{-1} s^{-1} at 30 °C. This expression may be combined with eq 1 to give eq 3. When eq 3 is compared to the experimental data,

$$-d[D_T]/dt = k_c\alpha[D_T] + k_h\alpha[D_T][OH^-] \quad (3)$$

as shown in Figure 1 for **1a**, the agreement for all three compounds is satisfactory even in the range where cyclization and hydrolysis of the terminal imine compete effectively. (The possibility of hydrolysis occurring by reaction of neutral diimine with a water molecule is discussed in ref 8 and 9.) The latter observation confirms that this type of hydrolysis of the diimines precedes cyclization to produce 8.

Above pH 7, rate constants calculated by following the loss of monoimine **3** (k_L) are less than those for formation of hydroxyphenazine **8a** (k_F). The largest discrepancy occurs about pH 9 where $k_L \approx 4k_F$. The sharp isosbestic point observed in the pH range 5–7 becomes blurred at higher pH. These observations indicate the formation of an intermediate.

Scheme III. Low pH Reaction of Monoimine 3

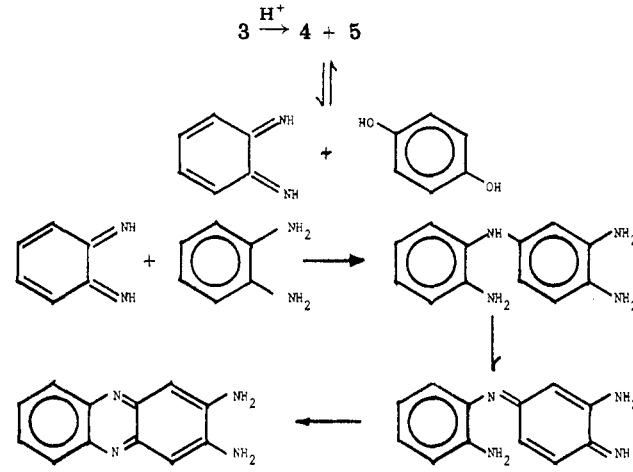


Table III. Yield of 2,3-Diaminophenazine (2d) as a Function of the Relative Concentrations of *o*-Phenylenediamine (4a) and *p*-Benzoquinone (5)

[5][a]	[4a][a]	[2d][a]
1.0	1.0	0.49
1.0	2.0	0.99
2.0	1.0	0.57
2.0	2.0	1.00

[a] Values are in moles per liter and are $\times 10^4$.

It has been previously reported[4] that some dihydrophenazines are slowly oxidized to phenazines by dissolved oxygen, and the oxidation is kinetically significant when cyclizations occur with first-order rate constants in excess of 10^{-3} s^{-1} at 30 °C. Apparently, the cyclization of monoimine **3** involves such a dihydrophenazine intermediate whose oxidation is rate limiting. In any event, cyclization is no longer rate limiting.

Like the diimines, monoimine **3** also cleaves at the imine bridge at low pH. Complicating this reaction is the observation that over a period of 1–2 h a new product is formed. It is suggested that the reaction proceeds by oxidation of *o*-phenylenediamine (**4a**) from the cleavage reaction, followed by coupling and cyclization as suggested by Hishida et al.[5] (Scheme III). Chromatographic evidence for **4a**, **5**, and hydroquinone was noted.

Separate experiments were run by starting with **4a** and **5** and no potassium ferricyanide and using various molar ratios of the reactants. These data, reported in Table III, implicate **5** as the oxidizing agent for **4a**. The second-order rate constant for the overall reaction was 3.86 L mol^{-1} s^{-1} at 30 °C. This contrasts with 0.91 L mol^{-1} s^{-1} for formation of **2d** by starting from monoimine **3**. It is therefore reasonable to assume that cleavage of the imine bridge is the rate-limiting step at low pH. In the case of the diimine, the hydrolysis appears to go by a similar process, although potassium ferricyanide may also act as an oxidizing agent. The rate of hydrolysis of the diimines did not fit a simple kinetic expression and was not studied further. Hishida et al. also studied oxidation of **4a** to the diimine which then coupled.[5]

Comments on Mechanism. Mechanisms for cyclizations to phenazines by formation of a carbon–nitrogen bond have been proposed previously.[2] Because these cyclization mechanisms and the results obtained here are

(4) Brown, K. C.; Corbett, J. F. *J. Org. Chem.* **1979**, *44*, 25.
(5) Hishida, T.; Nogami, T.; Yamada, M.; Mikawa, H.; Shirota, Y. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 3709.

Table IV. Analytical Data for Imines and Phenazines

compd	mp, °C	calcd, %			found, %		
		C	H	N	C	H	N
6a	293–298	52.9	5.6	15.5	52.9	5.7	15.2
6b	260–263	54.6	6.0	14.7	53.8	5.9	14.6
6c	281–284	47.0	4.6	13.7	46.5	4.8	13.4
7	190–192	60.8	5.5	11.8	60.1	5.6	11.6
2b		74.6	5.3	20.1	74.7	5.3	19.7
2c		62.8	3.5	18.3	62.9	3.8	18.6
2d		54.5	4.9	21.2	54.4	5.1	21.4

compatible with the previously suggested mechanism, they give it support. The suggested mechanisms rely strongly on kinetic evidence and therefore are exposed to the limitations thereof. Objectivity prompts the recognition of possible alternative or modified mechanisms, and it is suggested that future work take an approach which is capable of distinguishing between these alternatives and the proposed mechanism.

An argument for such an alternative mechanism may be suggested by the following question. Why does the rate of cyclization for these diimines vary with *protonated* diimine only, while for the corresponding monoimine it is the *neutral* species only that varies with the rate? Similar disparities occur in previous work also. For example, it has been reported that for *N'*-(*p*-hydroxyphenyl)-2-(methylamino)-*p*-benzoquinonediimine cyclization involves only the zwitterion even when the anion is the major species in solution; however, some of the same authors report evidence that the 2-phenylamino analogue cyclizes by involvement of both the zwitterion and the anion at pH's above 10.[4] These curious contrasts among the systems carry with them the implicit suggestion that there may be a common type of intermediate in these reactions and that perhaps electron-transfer reactions coupled with acid–base reactions may account for the differences among them. Some supporting evidence can be found in the susceptibility of these systems to electron transfer under the reaction conditions as revealed by the role of oxygen in the oxidizing of, for example, *p*-aminophenol, the oxidative cyclization of *N'*-(*p*-hydroxyphenyl)-2-(phenylamino)-5-methyl-*p*-benzoquinonediimine, and the effect of potassium ferricyanide. However, a radical ion mechanism is not proposed here for two reasons. It is not clear which of the array of specific possibilities should be considered, and it is a more involved mechanism than the one proposed.

Experimental Section

Melting points and analytical data for the imines and phenazines are given in Table IV.

2,4'-Diaminodiphenylamines 6. This was prepared from the corresponding 2-nitro-4'-aminodiphenylamines (or 2-nitro-4'-hydroxydiphenylamine for **6d**) by catalytic reduction in a Parr apparatus using a 5% Pd/C catalyst in ethyl acetate. After reduction, the mixture was filtered into ethyl acetate which had been saturated with gaseous HCl. The diphenylamine immediately precipitated as the hydrochloride salt.

2-Aminophenazines 2. 2,4'-Diaminodiphenylamine was refluxed for 8 h in nitrobenzene containing $MgSO_4$. After solvent removal, the phenazine [mp 280 °C (lit.[6] mp 279 °C)] was recrystallized from xylene. Substituted 2-aminophenazines were prepared by silver oxide oxidation of the corresponding 2,4'-diaminodiphenylamine in dry ether for 48 h and evaporation of the solvent.

2-Hydroxyphenazines 8 (mp 254–256 °C) were prepared according to ref 7.

2,3-Diaminophenazine Hydrochloride. Stoichiometric amounts of *o*-phenylenediamine and *p*-benzoquinone were mixed in 0.1 N HCl, precipitating the phenazine as fine red needles, mp 250 °C. The free base was isolated by neutralizing the salt with ammonium hydroxide. Anal. Calcd: C, 54.5; H, 4.9; N, 21.2. Found: C, 54.4; H, 5.1; N, 21.4.

Kinetics. Reaction rates were determined spectrophotometrically in buffered aqueous solutions with a Unicam SP 800 A recording spectrophotometer equipped with a thermostated cell compartment. For slow reactions the visible spectrum was scanned periodically. For reactions with first-order half-lives of less than 1 min, the optical density was recorded at a fixed wavelength. Spectra and pK_a's were determined by standard techniques.

Reactions were initiated by addition of the stoichiometric amount of potassium ferricyanide solution to thermally equilibrated diphenylamine solution (1.6×10^{-4}–5.0×10^{-4} M).

Acknowledgment. We express our deep gratitude to Clairol Research Laboratories for their generous support, both financial and otherwise, and for allowing N.P.L. to perform most experiments at their facilities. More specifically many thanks are due to Dr. John F. Corbett for suggesting the project as one of mutual interest.

Registry No. 1a, 76190-26-6; **1b**, 76190-27-7; **1c**, 76190-28-8; **2a**, 2876-23-5; **2b**, 76190-29-9; **2c**, 23677-11-4; **2d**, 655-86-7; **4a**, 95-54-5; **5**, 106-51-4; **6a**·HCl, 76190-30-2; **6b**·HCl, 76190-31-3; **6c**·HCl, 76190-32-4; **7**·HCl, 76190-33-5; **8a**, 4190-95-8; **8b**, 76190-34-6; **8c**, 4190-96-9; **2d**·HCl, 76190-35-7.

(6) Kehrmann, F.; Chirpillod, C. *Helv. Chim. Acta* **1924**, *7*, 975.
(7) Halasz, A.; Cohen, D. U.S. Patent 3 950 127.
(8) Tong, L. K. J.; Glesmann, M. C. *J. Am. Chem. Soc.* **1956**, *78*, 5827.
(9) Corbett, J. F.; Pohl, S.; Rodriguez, I. *J. Chem. Soc., Perkin Trans. 2* **1975**, 728.