20.5 mmol, 1 equiv), and DMF (50 mL) were mixed and stirred at 0 °C. After 48 h at 0 °C, the DMF was removed in vacuo and the residue flash chromatographed in 9:1 pentane/ethyl acetate to yield 4.84 g (85%) of a white solid: mp 106.5–107.0 °C; NMR ($CDCl_3$) δ 7.45–7.20 (m, 10 H), 5.94 (m, 1 H), 3.47 (t of d, 2 H, J = 7, 7 Hz), 2.62 (t, 2 H, J = 7 Hz), 2.00 (s, 3 H). Anal. ($C_{18}H_{18}N_2O$) C, H, N.

The following compounds were prepared by the procedures used in the synthesis of 8 (method A in Table I).

***N*-(2-Cyanoethyl)butanamide (20a)**: mp 72.5–74.0 °C; NMR (DMSO-d_6) δ 8.17 (s, 1 H), 3.27 (dt, 2 H, J = 7, 7 Hz), 2.63 (t, 2 H, J = 7 Hz), 2.07 (t, 2 H, J = 7 Hz), 1.52 (tq, 2 H, J = 7, 7 Hz), 0.85 (t, 3 H, J = 7 Hz). Anal. ($C_7H_{12}N_2O$) C, H, N.

***N*-(2-Cyanoethyl)-4-methylbenzamide (20d)**: mp 108.0–108.5 °C; NMR (DMSO-d_6) δ 8.78 (t, 1 H, J = 7 Hz), 7.77 (d, 2 H, J = 8 Hz), 7.29 (d, 2 H, J = 8 Hz), 3.49 (dt, 2 H, J = 7, 7 Hz), 2.78 (t, 2 H, J = 7 Hz), 2.36 (s, 3 H). Anal. ($C_{11}H_{12}N_2O$) C, H, N.

***N*-(2-Cyanoethyl)-2,6-dimethylbenzamide (20e)**: mp 148.5–149.5 °C; NMR (DMSO-d_6) δ 8.66 (m, 1 H); 7.16 (t, 1 H, J = 7 Hz), 7.04 (d, 2 H, J = 7 Hz), 3.46 (dt, 2 H, J = 7, 7 Hz), 2.77 (t, 2 H, J = 7 Hz); 2.23 (s, 6 H). Anal. ($C_{12}H_{14}N_2O$) C, H, N.

***N*-(2-Cyanoethyl)-2-[4-(2-methylpropyl)phenyl]propanamide (20f)**: wax; NMR (DMSO-d_6) δ 8.30 (m, 1 H), 7.21 (d, 2 H, J = 8 Hz), 7.06 (d, 2 H, J = 8 Hz), 3.58 (m, 1 H), 3.50–3.10 (m, 2 H), 2.61 (t, 2 H, J = 7 Hz), 2.40 (d, 2 H, J = 7 Hz), 1.95–1.70 (m, 1 H), 1.33 (d, 3 H, J = 7 Hz), 0.86 (d, 6 H, J = 7 Hz). Anal. ($C_{16}H_{22}N_2O$) C, H, N.

The following compound was prepared by procedures used in the preparation of **20c** (method B in Table I).

(*S*)-[2-[(2-Cyanoethyl)amino]-2-oxo-1-(phenylmethyl)-ethyl]carbamic acid, 1,1-dimethylethyl ester (20b): mp 83.5–85.5 °C; NMR (DMSO-d_6) δ 8.31 (t, 1 H, J = 7 Hz), 7.40–7.00 (m, 5 H), 6.96 (d, 1 H, J = 8 Hz), 4.13 (m, 1 H), 3.50–3.15 (m, 2 H), 2.96 (dd, 1 H, J = 7, 7 Hz), 3.00–2.67 (m, 1 H), 2.60 (t, 2 H, J = 7 Hz), 1.40–1.10 (m, 9 H). Anal. ($C_{17}H_{23}N_3O_3$) C, H, N.

The following compounds were prepared by the method described for making tetrazole 6 from amide 8 via the chromatographic purification of intermediate 12.

5-*n*-Propyl-1*H*-tetrazole (21a):[15] wax; NMR (DMSO-d_6) δ 2.86 (t, 2 H, J = 7 Hz), 1.71 (tq, 2 H, J = 7, 7 Hz), 0.91 (t, 3 H, J = 7 Hz). Anal. ($C_4H_8N_4$) C, H, N.

(*S*)-[2-Phenyl-1-(1*H*-tetrazol-5-yl)ethyl]carbamic acid, 1,1-dimethylethyl ester (21b): mp 140.0–144.0 °C; NMR (DMSO-d_6) δ 7.61 (d, 1 H, J = 8 Hz), 7.35–7.10 (m, 5 H), 5.06 (dd, 1 H, J = 7, 7 Hz), 3.40–3.00 (m, 2 H), 1.40–1.00 (m, 9H); $[\alpha]^{25}_D$ (c = 1.02, MeOH) = −15.9 ± 0.8°. Anal. ($C_{14}H_{19}N_5O_2$) C, H, N.

5-[1,1-Diphenylethyl]-1*H*-tetrazole (21c): mp 131.5–134.0 °C; NMR ($CDCl_3$) δ 7.40–7.20 (m, 6 H), 7.20–7.00 (m, 4 H), 2.27 (s, 3 H). Anal. ($C_{15}H_{14}N_4$) C, H, N.

5-[4-Methylphenyl]-1*H*-tetrazole (21d): mp 249.0–250.5 °C; NMR (DMSO-d_6) δ 7.93 (d, 2 H, J = 8 Hz), 7.41 (d, 2 H, J = 8 Hz), 2.40 (s, 3 H). Anal. ($C_8H_8N_4$) C, H, N.

5-[2,6-Dimethylphenyl]-1*H*-tetrazole (21e): mp 168.0–169.5 °C; NMR (DMSO-d_6) δ 7.38 (t, 1 H, J = 8 Hz), 7.23 (d, 2 H, J = 8 Hz), 2.02 (s, 6 H). Anal. ($C_9H_{10}N_4$) C, H, N.

The following compound was made by the same procedure described for making tetrazole 6 from amide 8 in one pot without the isolation of intermediate 12.

(*R,S*)-5-[1-[4-(2-Methylpropyl)phenyl]ethyl]-1*H*-tetrazole (21f):[16] mp 101.0–102.0 °C; NMR (DMSO-d_6) δ 7.30–7.00 (m, 4 H), 4.50 (q, 1 H, J = 7 Hz), 2.38 (d, 2 H, J = 7 Hz), 1.79 (m, 1 H), 1.66 (d, 3 H, J = 7 Hz), 0.86 (d, 6 H, J = 7 Hz). Anal. ($C_{13}H_{18}N_4$) C, H, N.

(*S*)-5-(1-Amino-2-phenylethyl)-1*H*-tetrazole (22). (*S*)-2-phenyl-1-(1*H*-tetrazol-5-yl)ethylcarbamic acid, 1,1-dimethylethyl ester (21b) (500 mg, 1.7 mmol, 1 equiv), 4 N HCl (2.16 mL, 8.6 mmol, 5 equiv), and THF were mixed and stirred at room temperature. After 4 h, another 5 equiv of 4 N HCl was added. After 20 h, the THF was removed in vacuo, water (10 mL) was added, and the pH of the aqueous mixture was adjusted to 4–5 with 10 N NaOH. Solids precipitated. These were filtered and dried under high vacuum to yield 218 mg (66%) of a white powder: mp 273.5–277.0 °C (slow decomposition); NMR (DMSO-d_6) δ 7.30–7.00 (m, 5 H), 4.66 (dd, 1 H, J = 7, 7 Hz), 3.34 (dd, 1 H, J = 7, 7 Hz), 3.16 (dd, 1 H, J = 7, 7 Hz); $[\alpha]^{27}_D$ (c = 0.74, DMSO) = +46.4 ± 1.1°. Anal. ($C_9H_{11}N_5$) C, H, N.

Acknowledgment. We thank Alfred J. Mical for the chiral HPLC analysis of compound 22. M.E.P. is grateful to Dean S. Irino for technical assistance.

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(17) Both the L enantiomer and the D,L-mixture of 22 were synthesized. Chiral resolution of D,L-22 was achieved on a Crownpak CR column at 40 °C at pH = 3 in 10% ethanol and 90% aqueous perchloric acid. Elution of L-22 under identical conditions showed the presence of only one enantiomer, thereby signifying that the sample is at least 98% the L-isomer.

Formation of Imidazopyridines by the Phase Transfer Catalyzed Reaction of α-(Aminomethyl)pyridines with $CHCl_3$ and Alkaline Hydroxide

Kevin C. Langry

Environmental Sciences Division, Lawrence Livermore National Laboratory, P.O. Box 808, Livermore, California 94550

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The reaction of chloroform with 2-(aminomethyl)pyridine (1) under basic phase-transfer catalysis affords the highly fluorescent imidazo[1,5-*a*]pyridine (2) in 25% isolated yield. Despite the formation of considerable tarry residue, GC–MS indicates that the volatile fraction of the reaction is simple and consists of 2 and two minor components identified as *N*-(2-pyridylmethyl)formamide (6) and (2-pyridylmethyl)isonitrile (7). The basic phase transfer catalyzed reaction of chloroform with a series of α-(aminomethyl)azanaphthalenes was found to be general and yield the corresponding annulated imidazo derivatives in comparable yields. Despite product yields in the 25% range, GC of the reaction mixtures indicates that the volatile fractions generally consist of residual starting aminomethyl compound, the imidazo product, and a minor amount of the (α-azanaphthylmethyl)formamide. However, 3-(aminomethyl)isoquinoline (18) failed to provide any of the expected imidazo[1,5-*b*]isoquinoline (19). The failure to detect 19 was investigated.

Groundwater contaminated with $CHCl_3$ has become an important public health issue, and considerable effort is being directed toward development of low-cost, on-site analytical methods for monitoring contamination levels. We sought to apply remote fiber fluorometry to groundwater analysis by development of a method capable of

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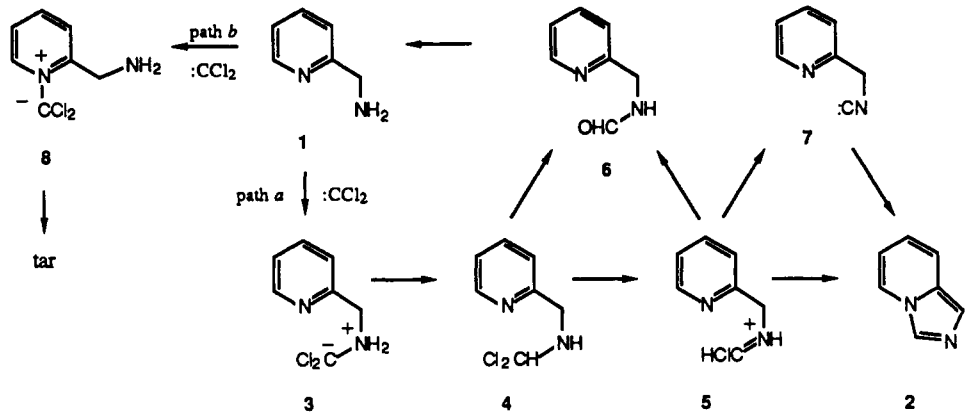
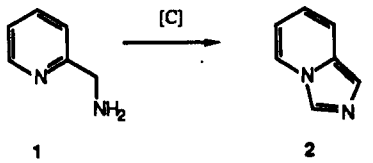
Scheme I



measuring 10^{-6}–10^{-9} M $CHCl_3$ dissolved in water.[1] In this report, we describe the reaction of $CHCl_3$ under basic phase-transfer catalysis (PTC) with 2-(aminomethyl)-pyridyl derivatives to form intensely fluorescent imidazopyridines.

Our goal was to develop a "one-pot" reaction that would generate fluorescent products from $CHCl_3$ and nonfluorescent precursors. The most direct approach was to exploit the carbene chemistry of $CHCl_3$ and attempt to trap the base-derived $:CCl_2$ with a compound that would ultimately yield a luminescent product. The nonfluorescent 2-(aminomethyl)pyridine (2-AMP, **1**) was selected as the precursor because the α-aminomethyl group of this substrate, with the addition of $:CCl_2$, could potentially be converted into the highly fluorescent imidazo[1,5-*a*]-pyridine (**2**, eq 1)[2] by way of a chloromethylenimine intermediate.[3]



Results and Discussion

The reaction of 2-AMP in 1,2-dimethoxyethane (DME) with $CHCl_3$ and tetrapropylammonium bromide stirred over 40% aqueous NaOH at 50 °C provided, along with considerable tarlike residue, the expected imidazo[1,5-*a*]pyridine (**2**) in 25% isolated yield. Despite the condition of the final reaction mixture and the relatively poor yield, the intense fluorescence of **2** (ex. at 254 or 366 nm, em. λ_{max} 447 nm) allowed the progress of the reaction to be easily monitored by analytical TLC.

Clearly, the low product yield suggests that the reaction of $:CCl_2$ with **1** does not follow a single pathway. In addition to the aminomethyl group, the pyridyl ring nitrogen is also a potential site for reaction with $:CCl_2$. Presented in Scheme I are the most probable paths available to the reaction of 2-AMP with $CHCl_3$ under basic PTC.

Path a of Scheme I is consistent with the generally accepted sequence for the reaction of $:CCl_2$ with primary amines; however, this progression of intermediates avails itself to a variety of potentially isolable reaction products.[4] In this sequence and subsequent to the formation of zwitterion **3**, hydrolysis of either the (dichloromethyl)amine **4** or the ensuing chloromethyliminium ion **5** would yield *N*-(2-pyridylmethyl)formamide (**6**).[5] In addition, **5** can undergo ring closure and form the imidazopyridine or it can suffer α-dehydrochlorination to provide the corresponding isonitrile (**7**).

Analysis by GC–MS of the organic phase from the reaction indicated that the volatile fraction was not very complex. In addition to **1** and **2**, the only other principal components were a minor fraction (<3%) that exhibited a molecular ion of m/z 136 and a fourth fraction that provided a molecular ion of m/z 118. The GC retention time and MS fragmentation pattern of the compound with m/z 136 were consistent with data obtained from an authentic sample of formamide **6**.[3] However, the quantity of **6** detected is probably not representative of the actual amount produced during the course of the reaction because control experiments show that under the basic PTC conditions the formamide is cleanly and rapidly hydrolyzed to **1**.

The existence of a second component with m/z 118 suggested that (2-pyridylmethyl)isonitrile (**7**) was also formed. Although **7** could not be isolated in appreciable yields and its fate remains unknown, FTIR spectra of aliquots of the reaction mixture show a moderate absorbance at 2153 cm^{-1}, further supporting the presence of the isonitrile. The GC retention times for **2** and **7** were distinct, with the isonitrile fraction eluting the column first. The MS fragmentation patterns for the two compounds were similar except for a consistent difference in the ratios of the fragment ion intensities: **2** m/z (%) 118 (100), 92 (22), 78 (17), 64 (40); **7** m/z (%) 118 (100), 92 (20), 78 (94), 64 (26). The isonitrile **7** was present throughout the course of the reaction and was equal to ~10% of the amount of **2** produced. It has been suggested that **7** can cyclize to **2**, and we hope to investigate this possibility.[6]

The reactivity of $:CCl_2$ is such that it probably cannot discriminate between the nitrogen of the primary amino moiety and the pyridyl ring nitrogen of 2-AMP. This assumption is supported by calculations that estimate the enthalpy of activation for the reaction of $:CCl_2$ with ethylene to be almost zero and indicate that the transition-state free energy is determined by entropy consider-

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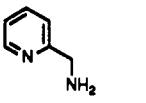
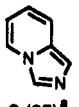
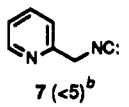
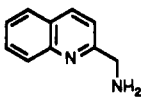
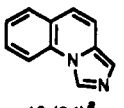
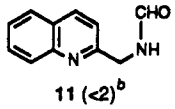
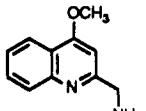
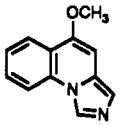
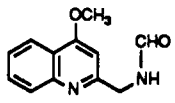
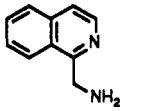
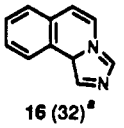
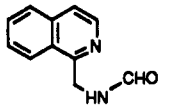
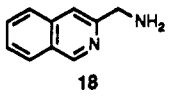
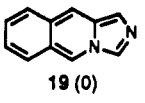
Table I. Products from the PTC Reaction of $CHCl_3$ with α-(Aminomethyl)pyridyl Derivatives over Aqueous NaOH

substrate	principal product	major byproduct
 1	 2 (25)[a]	 7 (<5)[b]
 9	 10 (24)[a]	 11 (<2)[b]
 12	 13 (20)[a]	 14 (3)[a]
 15	 16 (32)[a]	 17 (<5)[b]
 18	 19 (0)	

[a] Isolated yield. [b] GC yield.

ations.[7] In addition, the bimolecular rate constant for the reaction of dichlorocarbene, generated by laser flash photolysis, with pyridine has been measured to be $\sim 8 \times 10^9$ M^{-1} s^{-1}.[8] Consequently, it is reasonable to assume that the reaction of hydroxide-generated $:CCl_2$ with 2-AMP will approach diffusion-controlled conditions and that the carbene will not exhibit much selectivity and will react with the first nitrogen-based unshared electron pair that it encounters. In this case, path b of Scheme I represents an important competing reaction sequence that leads to the production of unwanted products and reduced yields of **2**.

Path b is similar to the Fujiwara reaction in which $CHCl_3$ reacts with pyridine in a solution of alkaline hydroxide.[9] The major products of the Fujiwara reaction are aldehydic imines and amidines derived from cleavage of the *N*-alkylated pyridine ring.[10] There are other reports of basic phase transfer catalyzed reactions of $CHCl_3$ with substituted pyridines that invoke mechanisms involving the reaction of $:CCl_2$ with the pyridyl ring nitrogen.[11] Moreover, stabilized carbenes (e.g., $:C(CN)_2$ and $:C(CO_2Et)_2$) form isolable ylides with pyridine and azanaphthalenes,[12] and recently it was reported that ylide intermediates are formed by the reaction of pyridine with laser flash generated phenylchlorocarbene[13] and dichlorocarbene.[8] In the case of 2-AMP, an analogous reaction is proposed in which the pyridyl ring nitrogen competes with the aminomethyl group for $:CCl_2$ to generate a $^-CCl_2$–pyridinium species (**8**). Assuming that the initial ylide survives to be protonated, such electron-deficient *N*-alkylated and *N*-acylated rings are extremely susceptible to reactions with nucleophiles at the ortho and para positions.[14,15] The carbene-activated pyridyl ring undoubtedly suffers attack by ambient nucleophiles (OH^-, 2-AMP, H_2O) to form numerous byproducts and tar.

The reaction of chloroform under basic PTC with the 2-(aminomethyl)pyridyl moiety is general and can be applied to other systems. As shown in Table I, the α-aminomethyl derivatives of both quinoline and isoquinoline are converted into their corresponding imidazo analogues. Unfortunately, the yields of the annulated products are in the 25% range, despite nearly complete consumption of the starting amines. Nevertheless, the reaction mixtures of the azanaphthalenes provided relatively simple gas chromatograms that were analogous to the results obtained for **1**.[16] 2-(Aminomethyl)quinoline (**9**) was converted into the imidazoquinoline **10** in 24% yield, and the only other significant component (<2%) detected by GC was a compound whose GC and MS data corresponded to that of *N*-(2-quinolylmethyl)formamide (**11**). Treatment of **15** produced the imidazo[5,1-*a*]isoquinoline (**16**) in 32% yield along with a minor amount of formamide **17**. The reaction of the 4-methoxyquinoline derivative **12** with $CHCl_3$ gave, in addition to the expected imidazo compound **13**, the N-formylated derivative **14**.

3-(Aminomethyl)isoquinoline (**18**) did not provide any imidazo[1,5-*b*]isoquinoline (**19**). Analysis of the early stages of the reaction by GC–MS indicated the presence of a single component with a molecular ion of *m/z* 168, and the reaction mixture exhibited an absorbance in the IR at 2152 cm^{-1}. These spectral features vanished long before **18** was completely consumed and are more consistent with formation of an isonitrile than a ring closure reaction to form **19**. In fact, **19** is a rather elusive compound and presumably has not been reported.

In order to evaluate the stability of **19** under the conditions of basic PTC, an attempt was made to prepare **19** by treatment of *N*-(3-isoquinolylmethyl)formamide (**20**) with 1 molar equiv of $POCl_3$ in CH_2Cl_2 and excess Et_3N. The use of this method is significant because the intermediates formed in the reaction of $POCl_3$ with formamides are the same as those postulated for the reaction of $:CCl_2$ with primary amines.[4,17] Despite mild reaction conditions (25 °C, 3 min), no **19** was formed. However, the reaction did provide as the major product an unstable compound with an intense IR absorbance at 2152 cm^{-1}, indicating the presence of an isonitrile group. A 200-MHz ^1H NMR ($CDCl_3$) spectrum of material rapidly purified on silica gel

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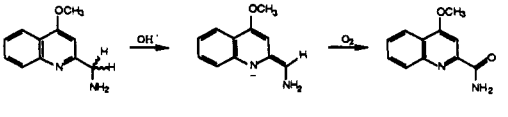
(16) It was noticed that if the base-catalyzed reactions were performed in the presence of air the α-aminomethyl derivatives were oxidized at the α-pyridyl methylene carbon to give small amounts (10%) of the corresponding amides. This occurs through a reaction of O_2 with the base-formed carbanion:



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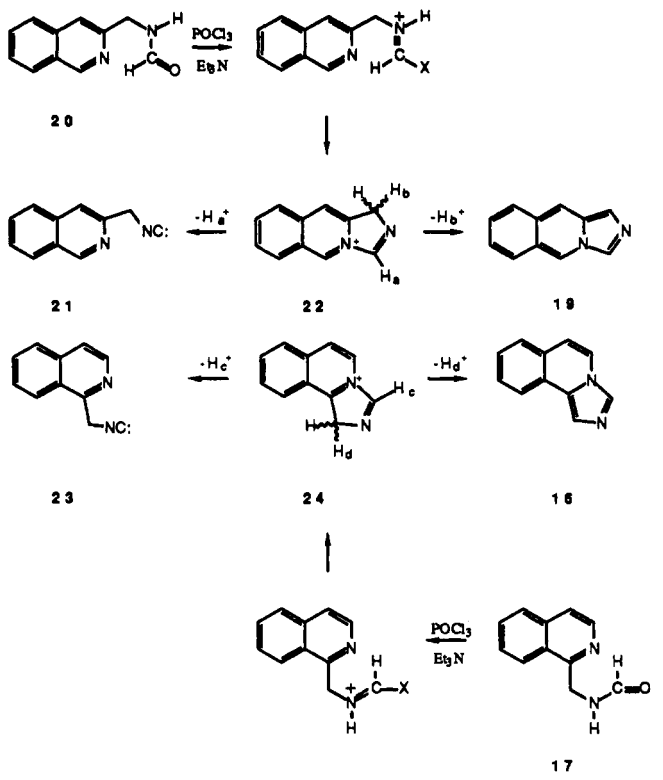
Scheme II



(1:4 heptane/EtOAc) exhibited all the normal isoquinoline ring resonances found in **20**, except that the formamide C*H*O (δ 8.34) and N*H*CHO (δ 6.89) protons were absent and the α-methylene doublet ArCH_2NHCHO (δ 4.68) had collapsed into a singlet and was shifted downfield (ArCH_2NC:, δ 4.92). Clearly, an activated imine (–N=CHX, X = Cl or $OPOCl_2$) is being formed, but apparently rapid α-elimination of HX to give isonitrile **21** is a more favorable course for the reaction than is cyclization to **19**.

These results with **20** are in contrast to those obtained for the reaction of *N*-(1-isoquinolylmethyl)formamide (**17**) with $POCl_3/Et_3N$, whereby **17** is efficiently and quantitatively cyclized to **16** without formation of any of the corresponding isonitrile **23**. Because the formamidomethyl groups of **17** and **20** are both located adjacent to the isoquinolyl nitrogen, these two compounds probably react with $POCl_3/Et_3N$ such that both reactions progress toward transition states that are preceded by intermediates of similar structure, as shown in Scheme II. For the case of the 1-substituted isoquinoline **17**, loss of the methylene proton H_d of **24** results in the elimination of charge on the isoquinolyl nitrogen and occurs simultaneously with aromatization of the imidazo ring. This process undoubtedly has a low activation energy and occurs more rapidly than loss of H_c, a step that would otherwise generate isonitrile **23**. The empirical resonance energies (RE) of compounds **16** and **17** are not known, but the sum of the RE for the isolated rings suggests that formation of the imidazo ring in **16** leads to a net gain of resonance stabilization relative to **17** or **23**.[18] In comparison, the inability to generate **19** from **18** or **20** most likely resides in the high activation energy that is associated with the forfeiture of resonance stabilization that would occur upon formation of **19**. Loss of H_b in **22** eliminates the charge on the isoquinolyl nitrogen, but this can occur only at the expense of considerable RE due to partial bond fixation.[19] Elimination of H_a apparently is a less energetic process that maintains the aromatic character of the isoquinolyl system and leads to formation of isonitrile **21**.

The instability of isonitriles **7** and **21** is apparently related to the position of the isonitrilomethyl group being adjacent to the heterocyclic nitrogen. We have prepared (3-pyridylmethyl)isonitrile from the corresponding 3-(aminomethyl)pyridine by the PTC reaction of $CHCl_3$ with NaOH solution and found that the purified isonitrile (25% yield) was stable for months, indicating that the reactivity of **7** and **21** is an intramolecular phenomenon and not simply related to the reactivity of ring-based nitrogens toward the isonitrile group.

The PTC reactions of $CHCl_3$ with the aminomethyl compounds were monitored by GC, and the concentration of the imidazo compounds increased linearly with time; however, before the starting material was completely consumed (~10–20% remaining), the rate of product formation changed and the concentration of the imidazo compound began to decline. In the absence of $CHCl_3$, the purified imidazo heterocycles were unaffected by the basic phase-transfer reaction conditions. However, the addition of $CHCl_3$ to these control reactions resulted in a measurable time-dependent reduction in the concentration of lumophore. Exhaustion of the imidazo compounds did not result in the commensurate production of any identifiable compounds, but rather lead to a menagerie of very minor products inseparable by TLC. The GC traces of these reactions were typified by a reduction in the intensity of the imidazo peak, and no additional compounds were present. Jones and Rees have described some reactions of $:CCl_2$ with pyrroles[20] and imidazoles[21] and have shown that the carbene insertion into the double bond of $-C_\beta=C_\alpha NH-$ is the primary reaction that leads to isolable products with these ring systems. Similar reactions may be important to the $CHCl_3$-dependent decomposition of the imidazo products reported here.

Experimental Section

Melting points were obtained from samples in open capillary tubes and are uncorrected. IR spectra were obtained on an Mattson Polaris FTIR spectrometer. NMR spectra were recorded on a Varian EM-390, a Bruker MSL-300, or a Nicolet 200-MHz spectrometer with tetramethylsilane as an internal standard. Low-resolution electron-impact mass spectra were recorded on a Hewlett-Packard Model 5987 mass spectrometer with direct sample insertion or by GC separation on a 0.32 mm × 30 m DB1 capillary column. High-resolution mass spectra were recorded at the Facility for Advanced Instrumentation at the University of California, Davis on a VG ZAB-2H. All thin-layer chromatography (TLC) was performed on Analtech (Newark, DE) precoated glass plates of silica gel GF. Analytical TLC to monitor reactions was accomplished with 0.25-mm thick silica gel plates briefly exposed to anhydrous ammonia. Preparative TLC was performed on 20 cm × 20 cm plates coated to a thickness of either 0.50 mm or 1.0 mm of silica gel. Chromatograms were visualized by illumination with a hand-held lamp emitting 254-nm or 366-nm light. Routine capillary gas chromatography was done on a Hewlett-Packard Model 5880 gas chromatograph using a 0.25 mm × 30 m DB1 column with an injector temperature of 250 °C and an FID detector at 325 °C. GC chromatograms were displayed and integrated by a Hewlett-Packard Level Two 5880A Series terminal. $CHCl_3$ was passed through neutral aluminum oxide

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(Brockmann activity I) to remove ethanol. 1,2-Dimethoxyethane (DME) was refluxed over calcium hydride and distilled under nitrogen. 2-(Aminomethyl)pyridine was obtained from Aldrich Chemical Co. and distilled at reduced pressure prior to use. The quinoline and isoquinoline aminomethyl dihydrochlorides were synthesized, and their preparations will be reported elsewhere.

Imidazo[1,5-*a*]pyridine (2). To a solution of 2-(aminomethyl)pyridine (1.0 mL, 9.7 mmol), $CHCl_3$ (2.0 mL, 25 mmol), and tetrapropylammonium bromide (53 mg, 0.2 mmol) in DME (15 mL) was added 20 mL of a 40% w/v solution of aqueous NaOH. The two-phase reaction mixture was rapidly stirred under N_2 at 50 °C and monitored periodically by TLC and GC. After 4.5 h, the dark brown organic phase was collected, diluted with CH_2Cl_2 (50 mL), and washed with water (2 × 30 mL). The aqueous phases were back-extracted with CH_2Cl_2 (3 × 30 mL). The organic fractions were combined, dried over anhydrous Na_2SO_4 and filtered and the solvents removed with a rotary evaporator. The thick brown residue was chromatographed on a 2.0 × 18 cm column of silica gel eluted first with EtOAc and then with 5% CH_3CN in EtOAc. The fractions containing product were collected, and the solvent was removed under reduced pressure, leaving a brown residue that crystallized upon cooling. This material was condensed onto a cold finger (80 °C (1–2 mmHg)), giving 293 mg (25% yield) of white solid **2**: mp 53–54 °C (lit.[3] mp 54–55 °C); IR (KBr, cm^{-1}) 3085, 1633, 1443, 1437, 1329, 1245, 1116, 996, 921, 795, 739, 657; ^1H NMR (90 MHz, DMSO-d_6) δ 6.44–6.81 (m, 2 H), 7.41–7.54 (m, 2 H), 8.13–8.20 (d, 1 H), 8.29 (s, 1 H); EIMS *m/z* (relative intensity) 118 (100), 91 (24), 78 (18), 64 (42); HRMS for $C_7H_6N_2$ calcd 118.0531, found 118.0519.

Imidazo[1,5-*a*]quinoline (10). To a mixture of 2-(aminomethyl)quinoline dihydrochloride (520 mg, 2.25 mmol) and tetrapropylammonium bromide (53 mg, 0.2 mmol) in DME (10 mL) was added 10 mL of a 40% w/v solution of aqueous NaOH. The mixture was rapidly stirred under N_2, and when the solids had dissolved, the two-phase solution was heated to 50 °C and $CHCl_3$ (800 μL, 10 mmol) was added in one portion. The reaction mixture was monitored periodically by TLC (silica gel, 5% CH_3CN in EtOAc) and GC. After 16 h, the organic phase was collected, diluted with CH_2Cl_2 (30 mL), and washed with saturated aqueous KCl (2 × 30 mL). The organic fraction was dried over anhydrous Na_2SO_4 and filtered, and the solvents were removed with a rotary evaporator. The residue was chromatographed on two preparative 1-mm thick thin-layer silica gel plates eluted with 7% CH_3CN in EtOAc. The major fluorescent fraction (R_f 0.4) was washed from the silica with 5% MeOH in CH_2Cl_2, the solvent removed, and the residue condensed onto a cold finger (90–95 °C (0.3 mmHg)), giving 92 mg (24% yield) of white solid **10**: mp 75–76 °C (lit.[22] mp 73–75 °C); ^1H NMR (200 MHz, acetone-d_6) δ 7.13–7.18 (d, 1 H), 7.42–7.51 (m, 3 H), 7.58–7.68 (m 1 H), 7.77–7.83 (dd, 1 H), 8.27–8.33 (dm, 1 H), 8.91 (s, 1 H); IR (KBr, cm^{-1}) 3100, 1610, 1485, 1454, 1405, 1332, 1263, 1219, 1118, 926, 810, 758, 655; EIMS *m/z* (relative intensity) 168 (100), 140 (30), 129 (21); HRMS for $C_{11}H_8N_2$ calcd 168.0687, found 168.0690.

Imidazo[5,1-*a*]isoquinoline (16). To a suspension of 1-(aminomethyl)isoquinoline dihydrochloride (231 mg, 1.0 mmol) and tetrapropylammonium bromide (27 mg, 0.1 mmol) in DME (5 mL) was added 5 mL of a 40% w/v solution of aqueous NaOH. $CHCl_3$ (400 μL, 5 mmol) was added in one portion, and the reaction was performed as for **10**. After 3.25 h, the concentration of **16** had reached its maximum value and the reaction mixture was worked up as for **10**. The residue was chromatographed on two preparative thin-layer silica gel plates eluted with 5% MeOH in CH_2Cl_2. The major fluorescent fraction (R_f 0.4) was collected, the solvent removed, and the residue sublimed onto a cold finger (90–95 °C (0.3 mmHg)), giving a white solid that was crystallized from heptane (54 mg, 32% yield): mp 115–116 °C (lit.[22-24] mp 116–117 °C); IR (KBr, cm^{-1}) 3122, 3072, 1489, 1459, 1445, 1369, 1239, 1114, 912, 821, 793, 762, 656; ^1H NMR (200 MHz, acetone-d_6) δ 6.92–6.96 (d, 1 H), 7.41–7.60 (m, 12 lines, 2 H), 7.68–7.73 (dm, 1 H), 7.86 (s, 1 H), 8.11–8.17 (dm, 2 H), 8.25 (s, 1 H); EIMS *m/z* (relative intensity) 168 (100), 140 (33), 128 (8); HRMS for $C_{11}H_8N_2$ calcd 168.0687, found 168.0691.

5-Methoxyimidazo[1,5-*a*]quinoline (13). To a suspension of 2-(aminomethyl)-4-methoxyquinoline dihydrochloride (522 mg, 2.0 mmol) and tetrapropylammonium bromide (53 mg, 0.2 mmol) in DME (10 mL) was added 10 mL of a 40% w/v solution of aqueous NaOH. $CHCl_3$ (800 μL, 10 mmol) was added in one portion, and the reaction was performed as for **10**. After 4.4 h, the concentration of **13** had reached its maximum value and the reaction mixture was worked up as for **10**. The residue was chromatographed on two preparative thin-layer silica gel plates eluted with a solution of 3% MeOH in CH_2Cl_2. The major fluorescent fraction (R_f 0.4) was collected, the solvent removed, and the brown residue sublimed onto a cold finger at reduced pressure (150 °C (0.3 mmHg)), giving 95 mg of white solid. Recrystallization from heptane gave 79 mg (20% yield) of pure **13**: mp 131.5–132.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 4.01 (s, 3 H), 6.80 (s, 1 H), 7.18 (s, 1 H), 7.44–7.54 (m, 1 H), 7.62–7.72 (m, 1 H), 8.08–8.08 (dd, 1 H), 8.24–8.30 (dm, 1 H), 8.73 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.43, 131.17, 129.07, 128.71, 126.52, 124.91, 123.71, 120.11, 119.75, 114.17, 91.03, 55.29; IR (KBr, cm^{-1}) 3098, 2967, 1631, 1565, 1486, 1460, 1400, 1359, 1277, 1211, 1139, 1103, 926, 820, 761, 652; EIMS *m/z* (%) 198 (100), 183 (43), 155 (68); HRMS for $C_{12}H_{10}N_2O$ calcd 198.0793, found 198.0766. Anal. Calcd for $C_{12}H_{10}H_2O$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.77; H, 5.27; N, 13.81.

The band of silica from the base line to R_f 0.2 was collected, stirred with 40 mL of 5% MeOH in CH_2Cl_2, and then filtered. The solvent was removed from the filtrate and the residue chromatographed on a 0.5-mm thick silica gel plate that was eluted with 5% MeOH in CH_2Cl_2. The band with R_f 0.5 was collected and crystallized from CH_2Cl_2/heptane, giving 13 mg (3% yield) of ((4-methoxy-2-quinolyl)methyl)formamide (**14**) as white needles: mp 147–148 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 4.06 (s, 3 H), 4.72 (d, 2 H), 6.66 (s, 1 H), 7.34 (br s, 1 H), 7.53–7.48 (m, 1 H), 7.73–7.68 (m, 1 H), 7.91 (d, J = 8.25 Hz, 1 H), 8.18 (d, J = 8.85 Hz, 1 H), 8.41 (s, 1 H); IR (KBr, cm^{-1}) 3295, 3059, 2878, 1657, 1595, 1570, 1546, 1511, 1464, 1445, 1420, 1386, 1361, 1242, 1234, 1188, 1112, 989, 761; EIMS *m/z* (%) 216 (29), 187 (83), 173 (100), 159 (31). Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.60; N, 12.96. Found: C, 66.73; H, 5.82; N, 12.81.

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