hydrazone, 2074-04-6; 2-phenyl[1-^{13}C]acetic acid, 57825-33-9; 2-phenyl[1-^{13}C]ethanol, 35462-98-7; 2-phenyl[1-^{13}C]ethene, 61415-37-0; 2-phenyl[3-^{13}C]oxirane, 78064-69-4; 2-phenyl[3,3-$^{2}H_2$]oxirane, 66255-92-3; phenylethanal-^{13}C, 78064-70-7.

Novel Condensation of 2,3-Epoxybutanal with 2-Aminopyridine and 2-Aminopyrazine. Synthesis and Stability of 3-(1-Hydroxyethyl)imidazo[1,2-*a*]azines

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In this study, we report a novel condensation of 2,3-epoxybutanal with 2-aminopyridine and 2-aminopyrazine. This unprecedented mode of reaction of an α,β-epoxy carbonyl compound is applied to synthesis of 3-(1-hydroxyethyl)imidazo[1,2-*a*]azines, which are not readily accessible by functionalization of the parent heterocycles due to their facile decomposition to the latter. The X-ray structure of a derived ketone is also reported as a characterization of the geometry of the imidazo[1,2-*a*]pyrazine ring system. The NMR signal and coupling constant assignments for the ring system are corrected.

Base-catalyzed hydrogen–deuterium exchange of imidazo[1,2-*a*]azines **1a,b** occurs at positions 3 (faster) and 5 (slower).[1a,b] This result suggests that kinetic deprotonation should afford anions **2a,b** which might be functionalized with aldehydes or ketones (Scheme I). Thermal reactions of methyl analogues of **1a** with acetaldehyde have been reported to result in inefficient condensation to give analogues of **4a**.[2] Condensation of **2a** with cyclohexanone gave a low yield of the 3-(1-hydroxycyclohexyl) analogue of **4a**.[3] These results suggest that 3-(1-hydroxyalkyl)-imidazo[1,2-*a*]azines **4** may be unstable with respect to **1** and **2**.

We investigated the condensation of **5a,b** with a mixture of cis and trans epoxy aldehyde **6** with the intent of developing a regioselective synthesis of compounds **4**, using the mechanistic hypothesis of Scheme II.

Reaction of **5b** with 1 equiv of **6** in ether–CH_2Cl_2 resulted in vigorously exothermic reaction giving a multitude of products including a trace of the desired **4b**. In spite of the negative result, we were encouraged by the report of Posner and Rogers that adsorption of nucleophiles, including amines, on activity I alumina catalyzed their reaction with epoxides.[4]

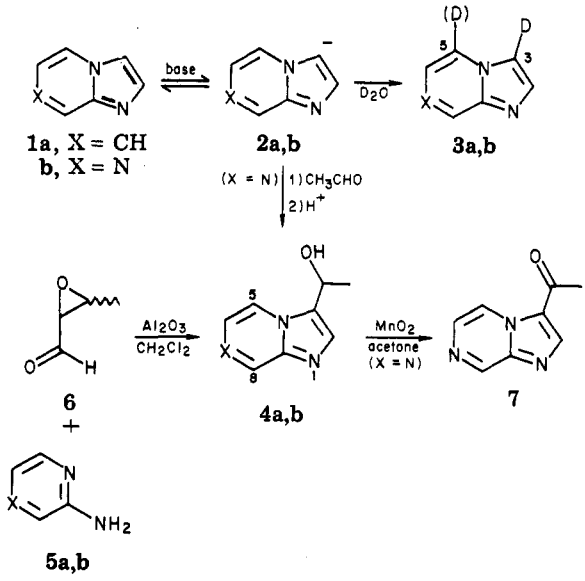
A suspension of **5b** adsorbed on alumina in CH_2Cl_2 reacted with 1 equiv of aldehyde **6** at room temperature to give a 26% yield of **4b**, after extraction of the alumina with methanol–CH_2Cl_2 and sublimation of the extracted products. When the alumina was extracted with hot methanol, a mixture of **4b** and imidazo[1,2-*a*]pyrazine was isolated.

Comparable reaction of **5a** with **6** gave **4a** in 53% yield. Attempted sublimation of **4a** gave a mixture of **4a** and imidazo[1,2-*a*]pyridine. These results confirm the instability of alcohols **4** with respect to **1**.

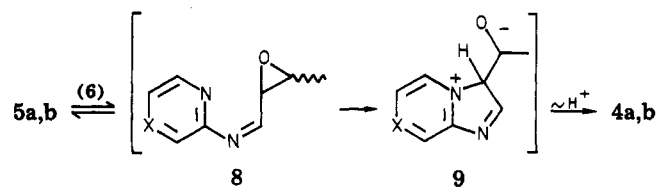
Oxidation of **4b** with excess MnO_2 in acetone for 6 days at room temperature gave ketone **7** in 81% yield. The structure of **7** was confirmed by its infrared and NMR spectra and unambiguously by single-crystal X-ray analysis (see Experimental Section).

The NMR of **7** shows a characteristic H_5 signal at δ 9.40, indicative of strong deshielding by the 3-acetyl function. From present NMR data and data on other substituted imidazo[1,2-*a*]pyrazines (W. C. Lumma, Jr., unpublished),

Scheme I



Scheme II



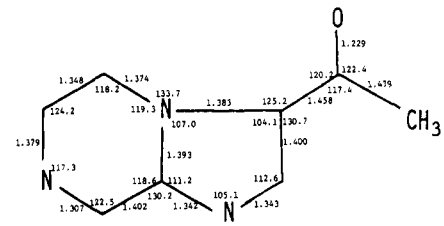


Figure 1. Bond distances (Å) and bond angles (deg) for **7**. The estimated standard deviations are 0.007 Å and 0.4°, respectively.

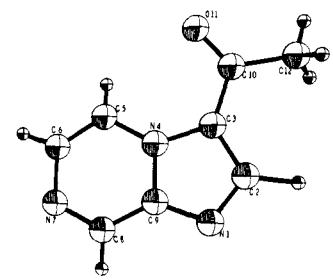


Figure 2. Drawing of **7** viewed perpendicular to the molecular plane.

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it is clear that $J_{5-8} \approx 1$ Hz, while $J_{6-8} \approx 0$. This fact apparently eluded Paudler and co-workers,[1b] who reversed H_5, H_6 chemical shift assignments even though their own data on 3,5-dideuterioimidazo[1,2-*a*]pyrazine (**3b**) showed no 6-8 coupling constant. The imidazo[1,2-*a*]pyridine analogue of **7** was previously synthesized in low yield from 2-bromoacetoacetaldehyde.[5]

To our knowledge the structure solution of **7** represents the first crystal structure of an imidazo[1,2-*a*]pyrazine.[6] Bond distances and angles are given in Figure 1 and Figure 2 is a two-dimensional representation of **7**. The nine atoms of the fused-ring system form a least-squares plane with a maximum deviation of 0.01 Å, while the maximum deviation from a plane for the four atoms of the keto group is also 0.01 Å. The angle between the two planes in the solid state is 6.7°.

Experimental Section

All melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. NMR spectra were recorded on Varian T-60 or EM-390 spectrometers in $CDCl_3$ (unless otherwise specified) relative to Me_4Si internal standard. Infrared spectra were recorded on a Perkin-Elmer 621 grating spectrophotometer. Microanalyses were within ±0.4% of calculated values. The X-ray structure was determined on a Syntex Model P-2_1 four-circle automatic diffractometer.

X-ray Structure of 3-(1-Oxoethyl)imidazo[1,2-*a*]pyrazine (7). Crystallization of **7** from dilute solution in toluene gave suitable crystals having symmetry *Pbca* with $a = 6.686$ (1) Å, $b = 9.37$ (2), and $c = 23.906$ (7). The structure was solved by using standard direct methods and refined by using the full-matrix least-squares method. The final R factor calculated from the 730 observed reflections measured with Cu Kα radiation was 0.048. Table I contains the final fractional coordinates and temperature parameters (see supplementary material available paragraph).

The following library of crystallographic programs was used: MULTAN 78, University of York, York, England (1978); X-RAY 72, University of Maryland, College Park, MD (1972); ORTEP-II, Oak Ridge National Laboratory, Oak Ridge, TN (1970).

3-(1-Hydroxyethyl)imidazo[1,2-*a*]pyrazine (4b). A solution of 2.85 g (30.0 mmol) of aminopyrazine in 100 mL of CH_2Cl_2 was added to 28.5 g alumina (E. Merck, Darmstadt; activity I). The resulting stirred suspension was treated with a solution of 2,3-epoxypropanal (cis and trans; 2.58 g, 30.0 mmol) in 10 mL of CH_2Cl_2 and the suspension was stirred overnight at room temperature under N_2. The mixture was vacuum filtered, and the cake was washed with 100 mL of CH_2Cl_2 and two, 100-mL portions of 2% MeOH-CH_2Cl_2. The combined filtrate was concentrated under vacuum at 25 °C to give 3.6 g of orange solid, which was chromatographed on activity III alumina. Elution with CH_2Cl_2 gave fractions containing 1.25 g of pure 3-(1-hydroxyethyl)-imidazo[1,2-*a*]pyrazine (26%): mp 152-153 °C; ^{1}H NMR (Me_2SO-d_6) δ 9.00 (1 H, d, $J = 1$ Hz), 8.50 (1 H, dd, $J = 1, 4$ Hz), 7.93 (1 H, d, $J = 4$ Hz), 7.75 (1 H, br s), 5.55 (1 H, d, $J = 6$ Hz), 5.27 (1 H, m), 1.62 (3 H, d, $J = 6$ Hz).

Anal. Calcd for $C_8H_9N_3O$: C, 58.88; H, 5.56; N, 25.75. Found: C, 58.63; H, 5.80; N, 26.03.

Extraction of the alumina in a Soxhlet thimble with boiling methanol caused partial decomposition of **4b** to imidazo[1,2-*a*]-pyrazine, mp 83-85 °C (mixture melting point with authentic sample[1b] undepressed; isolated from the column chromatography).

3-(1-Oxoethyl)imidazo[1,2-*a*]pyrazine (7). 3-(1-Hydroxyethyl)imidazo[1,2-*a*]pyrazine (1.47 g, 900 mmol) and manganese dioxide (7.2 g) were stirred in 50 mL of acetone for 1 week at room temperature. The mixture was filtered through Celite and the filtrate was concentrated to give 1.5 g of crude product. Chromatography on silica gel (MeOH-CH_2Cl_2) gave fractions containing 1.3 g (81%) of pure ketone **7**: mp 160-161.5 °C; ^{1}H NMR δ 9.40 (1 H, dd, $J = 1, 4.5$ Hz), 9.23 (1 H, d, $J = 1$ Hz), 8.42 (1 H, s), 8.18 (1 H, d, $J = 4.5$ Hz), 2.68 (3 H, s); IR (KBr) 1650, 1190 cm^{-1}.

Anal. Calcd for $C_8H_7N_3O$: C, 59.62; H, 4.38; N, 26.07. Found: C, 59.21; H, 4.33; N, 26.20.

3-(1-Hydroxyethyl)imidazo[1,2-*a*]pyridine (4a). By a procedure similar to that for synthesis of **4b**, reaction of 2-aminopyridine (2.82 g, 30.0 mM) and 2,3-epoxypropanal (2.58 g, 30.0 mM) in CH_2Cl_2 on alumina gave, after chromatography on alumina, 2.6 g (53%) of 3-(1-hydroxyethyl)imidazo[1,2-*a*]pyridine: mp 141-142.5 °C (CH_3CN) [lit.[5] mp 148-150 °C ($PhCH_3$; corr.)]; ^{1}H NMR δ 8.43 (1 H, d, $J = 6.5$ Hz), 7.47 (1 H, d, $J = 9$ Hz), 7.17 (1 H, s), 7.17 (1 H, t), 6.77 (1 H, t), 5.14 (1 H, q, $J = 6$ Hz) 1.7 (3 H, d, $J = 6$ Hz).

Attempted sublimation of the product at 140 °C (0.2 torr) gave a mixture of **4a** and imidazo[1,2-*a*]pyridine identical by mixture TLC (R_f 0.57 on silica gel; 5% 2-propanol in $CHCl_3$ saturated with aqueous NH_3) and ^{1}H NMR.[7]

Registry No. 4a, 30489-50-0; **4b**, 78109-24-7; **5a**, 504-29-0; **5b**, 5049-61-6; *cis*-**6**, 78109-25-8; *trans*-**6**, 71403-93-5; **7**, 78109-26-9; imidazo[1,2-*a*]pyrazine, 274-79-3; imidazo[1,2-*a*]pyridine, 274-76-0.

Supplementary Material Available: The positional and thermal parameters from the X-ray structure of **7** (1 page). Ordering information is given on any current masthead page.

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Spin Trapping of Radicals Generated in the UV Photolysis of Alkyl Disulfides

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Disulfide (S-S) linkages, their formation as well as bond scission, play a vital role in the areas of biochemistry[1] and food science.[2] It has been frequently observed that photolysis of disulfides yielded thiyl radicals.[3,4] Callear and Dickson[5] concluded that both S-S and C-S bond scission occurred during the flash photolysis of dimethyl disulfide. Byers et al.[6] showed by product analysis that C-S bond cleavage is predominant in the photodecomposition of *tert*-butyl disulfide and benzyl disulfide. Shortly thereafter, Rosenfeld et al.[7] presented photo-CIDNP evidence for C-S bond rupture in the photolysis of *tert*-butyl disulfide in benzene solution. Recently Ito et al.[4] reported that flash photolysis of di-*tert*-butyl disulfide resulted in a transient absorption band at 370 nm and they attributed this absorption to the thiyl radicals generated by S-S bond cleavage. The S-S bond cleavage has also been achieved by vapor pyrolysis,[8] enzymatic,[9] and other chemical means. Rosenthal and Oster[10] observed that successive alkylation causes shift in the UV absorption maximum and they proposed that the acidity of the C-H bond situated α to the S-S linkage plays a vital role in the alkali cleavage.

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