Hapalindole O: $[\alpha]_D$ -106.0° ($CHCl_3$, c 2.4); high resolution EIMS, m/z 352.1609 (calcd for $C_{21}H_{24}N_2OS$, mmu error 0.0).

Hapalindole P: $[\alpha]_D$ -16.3° ($CHCl_3$, c 0.8); FDMS, m/z 354,356 (relative intensity 3:1).

Hapalindole Q: $[\alpha]_D$ +24.1° (CH_2Cl_2, c 1.1); high resolution EIMS, m/z 336.1659 (calcd for $C_{21}H_{24}N_2S$, mmu error -0.1).

Hapalindole T: $[\alpha]_D$ -137° (CH_2Cl_2, c 1.5); high resolution FABMS, m/z 387.1299 (calcd for $C_{21}H_{24}N_2SO^{35}Cl$, mmu error +0.1, MH ion); UV (MeOH) λ_{max} nm (ϵ) 222 (35 400), 283 (7100); IR ($CHCl_3$) ν_{max} 3473, 3400, 1679 cm^{-1}.

Hapalindole U: $[\alpha]_D$ +12° (CH_2Cl_2, c 0.6); high resolution FABMS, m/z 305.1996 (calcd for $C_{21}H_{25}N_2$, mmu error -2.0, MH ion).

Hapalindole V: high resolution FABMS, m/z 355.1599 (calcd for $C_{21}H_{24}N_2O^{35}Cl$, mmu error +2.2, MH ion); UV (MeOH) λ_{max} nm (ϵ) 220 (34 000), 273 (5700), 279 (5800), 290 (4500); IR ($CHCl_3$) ν_{max} 3600, 3480, 2140 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 117.3 (C-2), 116.8 (C-3), 133.9 (C-4), 115.0 (C-5), 123.9 (C-6), 108.4 (C-7), 139.7 (C-8), 123.5 (C-9), 72.4 (C-10), 67.8 (C-11), 44.8 (C-12), 63.8 (C-13), 29.3 (C-14), 47.4 (C-15), 37.7 (C-16), 26.6 (C-17), 28.0 (C-18), 17.9 (C-19), 143.9 (C-20), 116.0 (C-21), 159.4 (C-23).

X-ray Structure Analysis. Hapalindole A crystallized from CH_2Cl_2/heptane as yellow plates in the space group $P2.2.2.$, $Z = 4$, with unit cell dimensions $a = 7.926$ (2), $b = 10.118$ (4), and $c = 23.302$ (8) Å. The calculated density was found to be 1.200 g cm^{-3}. A total of 1515 unique reflections with $2[\theta]$ less than 116.0 were measured on an automated four-circle diffractometer using monochromatic copper radiation. The structure was solved by the direct methods routines of the SHELXTL program library (G. M. Sheldrick, 1981) and was refined by the least-squares method with anisotropic temperature factors for all atoms except hydrogen. Hydrogen atoms were included with isotropic temperature factors at calculated positions. The final R-factor was 0.0386 for 1393 observed reflections. Figure 1 shows an ORTEP plot of the molecule and tables in the supplementary material section give atom coordinates, anisotropic temperature factors, bond lengths, bond angles, and hydrogen coordinates.

Hapalindole D crystallized from CH_2Cl_2 as yellow-orange prisms in the space group $P222$, $Z = 4$, with unit cell dimensions $a = 9.847$ (4), $b = 9.990$ (3), and $c = 19.439$ (5) Å. The calculated density was 1.169 g cm^{-3}. A total of 1539 unique reflections with $2[\theta]$ less than 116.0 were measured and the structure was solved as described above. The final R-factor was 0.0610 for 1457 observed reflections. Figure 2 shows an ORTEP plot of the molecule and tables in the supplementary material section give atom coordinates, anisotropic temperature factors, bond lengths, bond angles, and hydrogen coordinates.

Hapalindole K crystallized from CH_2Cl_2/heptane as thick yellow plates in the space group $P222$, $Z = 4$, with unit cell dimensions $a = 8.447$ (4), $b = 13.487$ (7), and $c = 15.497$ (9) Å. The calculated density was 1.263 g cm^{-3}. A total of 1429 unique observed reflections with $2[\theta]$ less than 116.0 were measured and the structure was solved as described above. The final R-factor was 0.0559 for 1260 observed reflections. The absolute configuration was determined through use of the anomalous dispersion technique as suggested by Rogers.[5] Figure 3 shows an ORTEP plot of the molecule and tables in the supplementary material section give atom coordinates, anisotropic temperature factors, bond lengths, bond angles, and hydrogen coordinates.

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Supplementary Material Available: ORTEP stereodrawings showing hydrogens; tables for atom coordinates and temperature factors, bond lengths, bond angles, anisotropic temperature factors, and hydrogen coordinates and temperature factors for hapalindoles A, D, and K; tables for in vitro antibacterial and antifungal activity (13 pages). Ordering information is given on any current masthead page.

(5) Rogers, D. *Acta Crystallogr., Sect. A* **1981**, *A37*, 734.

Reduction of Heterocycles with Nickel-Aluminum Alloy†

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Pyrazines, pyridazines, isoxazoles, oxazole, 4-methylpyrimidine, and indole are reduced by nickel-aluminum alloy in potassium hydroxide solution. The reaction is simple to carry out and does not require special apparatus or hydrogen atmospheres. The products were the fully hydrogenated species although benzene rings were not attacked. 4-Methylpyrimidine gave 1,3-diaminobutane and oxazole gave 2-(methylamino)ethanol. It was found that the reaction frequently exhibited an induction period.

Introduction

We recently discussed[1] the use of nickel-aluminum alloy in dilute base to reduce pyridines to the corresponding piperidines. The reaction is particularly easy to perform and high temperatures, high pressures, and hydrogen atmosphere and special apparatus are not required. We now wish to report that this process may be used to reduce a variety of other heterocycles. Specifically, we have reduced pyrazines, pyridazines, isoxazoles, oxazole, 4-methylpyrimidine, and indole; these results are summarized in Table I. We also found that imidazole, 3,5-dimethylpyrazole, and 2,3,5,6-tetramethylpyrazine were essentially not reduced in 24 h under these conditions (lack of reduction was confirmed by comparing ^{13}C NMR spectra of the reaction mixtures before and after the reduction procedure). Pyrrole was reduced only slowly to pyrrolidine (24% after 24 h; 58% after 4 days). The compounds listed in Table I were completely reduced after an overnight reaction, with the longest reaction taking about 30 h. In a number of instances, much more rapid reaction was observed; in fact, in some cases it was not necessary to add the usual amount of nickel-aluminum alloy. It is useful to monitor the reaction by gas chromatography and thus

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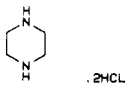
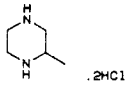
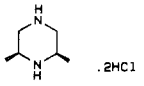
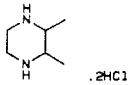
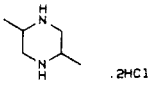
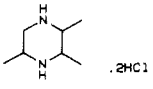
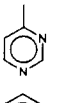
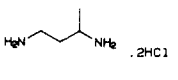
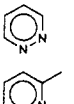
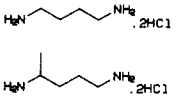
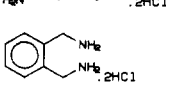
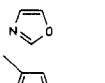
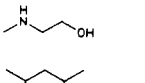
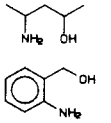
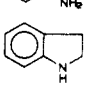
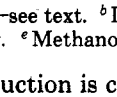
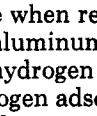
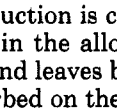
(1) Lunn, G.; Sansone, E. B. *J. Org. Chem.* **1986**, *51*, 513.

0022-3263/87/1952-1043$01.50/0

Table I. Reduction of Heterocycles

starting material	product	yield (%)	Ni/Al (g)	time (h)	mp/bp	lit. mp/bp	ref
		76	35	18.5	330-3	322-3	32
		68	45	21.5	255-7	245	33
		70	50	22.8	a		
		76	25	24.3	a		
		76	25	3.6	a		
		74	25	19.3	a		
		69	25	19.3	170-1[b]	177	30
		61	50[c]	2.5	b,d	280	34
		56	40[c]	2.8	168-9[b]		
		53	30[e]	21.7	306-8	>300	35
		28	9[f]	26.1	61-2/7	64-5/12	36
		75	16	1.2	49-53/2	72-7/15-20	37
		65	21[e]	0.7	82-3	83	38
		73	30[e]	30.1	100-4/6	70-5/2	39

[a] Mixture of isomers—see text. [b] Identical with an authentic sample. [c] Performed in a more dilute solution with more Ni-Al alloy. [d] Slowly decomposed on heating. [e] Methanol was the cosolvent. [f] Performed on a reduced scale (1.5 g of oxazole in 60 ml of 0.5 M KOH solution).

determine when reduction is complete. We hypothesize that the aluminum in the alloy reacts with the base to generate hydrogen and leaves behind highly active nickel with hydrogen adsorbed on the surface. The heterocycle is then hydrogenated on this surface. In contrast to Raney nickel, which has a short shelf-life,[2] the (less expensive) nickel–aluminum alloy appears to be quite stable.

In general, the standard conditions proved effective for all of the compounds in Table I (although with some variation in reaction times), but, for reasons that are not clear, the reduction of pyridazine and 3-methylpyridazine proceeded in better yield when the reactions were done in more dilute solution with a larger quantity of nickel–aluminum alloy. For example, the yield of 1,4-diaminobutane dihydrochloride from pyridazine increased from 28% to 61% when the dilution was increased.

The products are generally those that would be expected from full saturation of the ring combined with cleavage of N–N or N–O bonds. Thus, the pyrazines were converted to the corresponding piperazines. 2,6-Dimethylpyrazine gave only *cis*-2,6-dimethylpiperazine and 2,3-dimethylpyrazine yielded mostly *cis*-2,3-dimethylpiperazine, whereas 2,5-dimethylpyrazine gave a mixture of *cis*- and *trans*-2,5-dimethylpiperazine. Structure assignments were made by examination of the ^{13}C NMR spectra by analogy to the cyclohexanes.[3] 2,3,5-Trimethylpyrazine gave an isomeric mixture of 2,3,5-trimethylpiperazine dihydrochlorides. Examination by ^{13}C NMR showed that all four possible isomers appeared to be present.

Under the conditions of the reaction, the initial reduction product from 4-methylpyrimidine is presumably readily hydrolyzed to the observed product, 1,3-diaminobutane (identified by comparison with an authentic sample). The pyridazines were reduced to the corresponding diamines and the isoxazoles gave the corresponding hydroxy amines. These cases demonstrate N–N and N–O bond cleavage as well as hydrogenation of the ring.

Interestingly, 3,5-dimethylisoxazole gave the two diastereomeric amino alcohols which were easily separated by GC. Reduction of oxazole gave 2-(methylamino)ethanol as the only isolated product, demonstrating a C–O bond cleavage, which is rare under these conditions. Saavedra[4]

(2) Billica, H. R.; Adkins, H. In *Organic Syntheses*; Horning, H. C., Ed.; Wiley: New York, 1955; Collect. Vol. III, p 176.

(3) Dalling, D. K.; Grant, D. M. *J. Am. Chem. Soc.* **1967**, *89*, 6612.

(4) Saavedra, J. E. *Org. Prep. Proc. Int.* **1985**, *17*, 155.

has observed similar C–O bond cleavage with nickel–aluminum alloy reduction of the related *N*-nitrosooxazolidines. The low yield is probably due to the water-soluble nature of the product. This reaction is quite sluggish and we found that more highly substituted oxazoles (e.g., 2,3,5-trimethyloxazole) could not be successfully reduced. 1,3,5-Triazine gave a 53% yield of ammonium chloride as the only isolated product. This was not surprising in view of a report[5] of complete hydrolysis in distilled water in 10 min.

Previous reports in the literature indicate that furans[6] and thiophenes[7] may also be reduced using the nickel–aluminum alloy technique.

In the course of this work, we observed that the reaction exhibited an induction period. Using a thermocouple attached to a chart recorder, we observed that the initial addition of alloy caused an initial temperature rise but the temperature soon declined to ambient levels. Typically, about 3 h after the start of the reaction, a much larger temperature rise occurred, reaching a peak in about 20 min. The reaction mixture frequently boiled at this stage. As might be expected, monitoring by GC showed that most of the reduction occurred at this point. These results were fairly reproducible, and it was found that the induction time increased as the amount of base present decreased. In fact, we have observed the reduction of 2-methylpyridine to 2-methylpiperidine to proceed without any added base but only after an induction period of 70 h. This induction period presumably occurs because of the presence of an oxide layer on the aluminum particles. This effect was previously noted for the reaction of aluminum with water[8] and alkali.[9] The existence of this induction period emphasizes the importance of performing these reactions in flasks that are no more than half-full and of using a reflux condenser. We have found that an air condenser is generally sufficient.

Similar reductions have been reported using catalytic hydrogenation, but the procedure discussed here eliminates the need for special apparatus or hydrogen atmospheres. The catalysts generally used are platinum and palladium. For example, platinum oxide[10] and palladium on charcoal[11] have been used to reduce pyrazines to piperazines and also to reduce[12] pyrimidines to tetrahydropyrimidines. Further reduction produces hydrogenolysis of the ring,[13] as indeed we found in this work. Catalytic hydrogenation of indoles tends to proceed to the octahydroindole[14] rather than the 2,3-dihydroindole, which was the only product we observed. On nickel, isoxazoles have been reported[15] to be reduced to the corresponding imino ketone, although more rigorous conditions[16] gave the amino alcohol, the product which we observed. Oxazoles have been shown[17] to undergo C–O bond cleavage to yield the corresponding amide. In accordance with our results, pyrroles,[18] imidazoles,[19] and pyrazoles[20] have been reported to be difficult to hydrogenate. Sodium in ethanol has been reported to reduce pyridazines,[21] pyrimidines,[22] pyrazines,[23] oxazoles,[24] and isoxazoles,[25] although different products were generally obtained.

Experimental Section

Warning. These reductions generate hydrogen and should be performed in an efficient hood. The nickel that is removed by filtration is potentially pyrophoric and should not be sucked dry for extended periods. It should be allowed to dry on a metal tray in the absence of flammable solvents for 24 h before disposal.

General. Nickel–aluminum alloy and all other reagents were obtained from Aldrich Chemical Co., Milwaukee, WI. Melting points were determined on an Electrothermal melting point apparatus. NMR spectra were obtained on a Nicolet NT300 machine operating at 300 MHz for proton or 75.4 MHz for carbon. Mass spectra were obtained on a Finnigan 3300 mass spectrometer equipped with a Finnigan 6000 MS data system. The gas chromatograph was a Hewlett-Packard HP5830A fitted with a 1.8 m × 2 mm i.d. silanized glass column using flame ionization detection. Peak areas were integrated by means of a built-in electronic integrator. The column packings were 10% Carbowax 20 M + 2% KOH on 80/100 Chromosorb W AW and 2% Carbowax 20 M + 1% KOH on 80/100 Supelcoport, and column temperatures ranged from 100 to 200 °C. The carrier gas was nitrogen flowing at about 30 mL/min. Samples were injected directly onto a precolumn, which was changed periodically to protect the main column. Analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

Reaction Temperature Measurement. Internal reaction temperatures were measured by using a chromel–alumel thermocouple placed in a test tube that dipped into the reaction mixture. The thermocouple was attached to a 5-mV strip-chart recorder.

Typical Reduction Procedure. 4-Methylpyrimidine (4.92 g, 52.3 mmol) was dissolved in water (100 mL), and a potassium hydroxide solution (1 M, 100 mL) was added. This mixture was stirred in a 500-mL, round-bottomed flask fitted with a reflux condenser, and nickel–aluminum alloy (25 g) was added in portions over a period of 1 h. After another 18 h 21 min, GC showed that the reaction had gone to completion so the contents of the flask were filtered through Celite 545 (Fisher Scientific Co., Fairlawn, NJ). The mixture was washed through with a further portion of water (500 mL), and the entire filtrate was distilled under a stream of nitrogen to about 20 mL. The nitrogen entered at the still head and exited through a trap containing 80 mL of dilute hydrochloric acid.

The residue (20 mL) was extracted six times with dichloromethane and the extracts were dried over anhydrous sodium sulfate. The extracts, the distillate, and the contents of the trap were combined and the water and dichloromethane removed with a rotary evaporator to yield a colorless oil that was crystallized from EtOH to give 1,3-diaminobutane dihydrochloride as white crystals (6.35 g, 69%). This material exhibited spectroscopic characteristics identical with those of an authentic sample.

Other compounds were reduced as detailed above. In some cases, it was possible to simply extract the products from the filtrate (indole, anthranil, phthalazine). In other cases (e.g., oxazole) the filtrate was acidified and evaporated to dryness, the base was freed with a little potassium hydroxide solution (10 M), and the product was extracted into dichloromethane. Compounds were isolated either as the hydrochloride or the free base as

(5) Grundmann, C.; Kreutzberger, A. *J. Am. Chem. Soc.* **1954**, *76*, 5646.
(6) Schwenk, E.; Papa, D.; Hankin, H.; Ginsberg, H. In *Organic Syntheses*; Horning, E. C., Ed.; Wiley: New York, 1955; Collect. Vol. III, p 742.
(7) Papa, D.; Schwenk, E.; Ginsberg, H. F. *J. Org. Chem.* **1949**, *14*, 723.
(8) Bernard, W. J.; Randall, J. J., Jr. *J. Electrochem. Soc.* **1960**, *107*, 483; *Chem. Abstr.* **1960**, *54*, 18149a.
(9) Lur'e, B. A.; Chernyshov, A. N.; Perova, N. N.; Svetlov, B. S. *Kinet. Katal.* **1976**, *17*, 1453; *Chem. Abstr.* **1977**, *86*, 79370c.
(10) Kipping, F. B. *J. Chem. Soc.* **1929**, 2889.
(11) Behun, J. D.; Levine, R. *J. Org. Chem.* **1961**, *26*, 3379.
(12) Smith, V. H.; Christensen, R. E. *J. Org. Chem.* **1955**, *20*, 829.
(13) Rylander, P. *Catalytic Hydrogenation in Organic Synthesis*; Academic Press: New York, 1979; p 227.
(14) Robinson, B. *Chem. Rev.* **1969**, *69*, 785.
(15) D'Alcontres, G. S. *Gazz. Chim. Ital.* **1950**, *80*, 441; *Chem. Abstr.* **1951**, *45*, 3837g.
(16) Touster, O.; Carter, H. E. *J. Am. Chem. Soc.* **1951**, *73*, 54.
(17) Young, P. C.; Robinson, R. *J. Chem. Soc.* **1933**, 275.
(18) Adkins, H.; Coonradt, H. L. *J. Am. Chem. Soc.* **1941**, *63*, 1963.
(19) Freifelder, M. *Catalytic Hydrogenation in Organic Synthesis*; Wiley-InterScience: New York, 1978; p 159.
(20) Lipp, M.; Dallacker, F.; Munnes, S. *Justus Liebigs Ann. Chem.* **1958**, *618*, 110.
(21) Katzenellenbogen, A. *Ber. Dtsch. Chem. Ges.* **1902**, *34*, 3828.
(22) Byk, A. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 1915.
(23) Stoehr, C. *J. Prakt. Chem.* **1893**, *47*, 439.
(24) Oesterreich, M. *Ber. Dtsch. Chem. Ges.* **1897**, *30*, 2254.
(25) Claisen, L. *Ber. Dtsch. Chem. Ges.* **1891**, *24*, 3900.

indicated in Table I. All compounds exhibited the appropriate spectroscopic characteristics. Monitoring by GC showed that some reactions were complete before all of the nickel–aluminum alloy had been added; in other cases more alloy was needed to drive the reaction to completion. These items are detailed in Table I.

We found that the reduction of pyridazines proceeded best when the reaction was performed at fairly high dilution. The following procedure is typical. Pyridazine (4.59 g, 57.4 mmol) was dissolved in water (500 mL), and potassium hydroxide solution (500 mL, 1 M) was added. Nickel–aluminum alloy (50 g) was added over a period of 1 h and stirring was continued for 1.5 h. Workup as described above gave 1,4-diaminobutane dihydrochloride as colorless crystals (5.60 g, 61%) that were spectroscopically identical with an authentic sample.

Reduction of 2,3-Dimethylpyrazine. 2,3-Dimethylpyrazine (5.02 g, 46.5 mmol) was reduced to give, after crystallization from EtOH, *cis*-2,3-dimethylpiperazine dihydrochloride (6.00 g, 69%, mp 204–210 °C, 79% cis) and another crop (0.62 g, 7%, mp 257–273 °C, 57% cis). The isomers were assigned on the basis of ^{13}C NMR spectra (of the hydrochlorides in NaOD/D_2O); for cis the shifts were 11.64, 37.28, and 50.56 ppm and for trans the shifts were 14.98, 40.16, and 53.73 ppm. The lower values were assigned to the more crowded cis molecule (axial, equatorial) and the higher values to the less crowded trans molecule (diequatorial) by analogy to *cis*- and *trans*-1,2-dimethylcyclohexanes.[3,26]

Reduction of 2,5-Dimethylpyrazine. 2,5-Dimethylpyrazine (3.61 g, 33.4 mmol) was reduced to give, after crystallization from EtOH, *cis*-2,5-dimethylpiperazine dihydrochloride (3.03 g, 48%, mp 256–295 °C, 75% cis) and *trans*-2,5-dimethylpiperazine dihydrochloride (1.73 g, 28%, mp >350 °C, 89% trans). As before, ^{13}C NMR shifts were used to assign the structures; for cis the shifts were 13.98, 42.46, and 46.98 ppm and these values were assigned to the more crowded (axial, equatorial) molecule; for trans the shifts were 15.03, 45.42, and 48.44 ppm and these values were assigned to the less crowded (diequatorial) molecule.

Reduction of 2,6-Dimethylpyrazine. 2,6-Dimethylpyrazine (4.39 g, 40.6 mmol) was reduced to give, after crystallization from EtOH, *cis*-2,6-dimethylpiperazine dihydrochloride (5.30 g, 70%, mp >340 °C). Only one isomer was detected by ^{13}C NMR, and this was identified by comparison with commercially available material (Aldrich Chemical Co.) that was determined, by comparison with the literature,[27] to be mostly cis. ^{13}C NMR (D_2O): 15.11, 44.82, 49.08 ppm.

Reduction of 2,3,5-Trimethylpyrazine. 2,3,5-Trimethylpyrazine (5.03 g, 41.2 mmol) was reduced to give an isomeric mixture of 2,3,5-trimethylpiperazine dihydrochlorides which was crystallized from EtOH to give two batches (5.98 g, 72%, mp 265–270 °C, and 0.12 g, 1.4%, 340–342 °C dec), which were enriched in different isomers. Examination of the ^{13}C NMR spectra of these mixtures showed that all four possible isomers were present. MS of mixture *m/e* (relative intensity): 128 (10), 113 (38), 97 (6), 85 (12), 84 (13), 83 (5), 72 (99), 71 (46), 70 (79), 57 (15), 55 (57), 41 (35), 35 (100).

1,3-Diaminobutane Dihydrochloride. An authentic sample of 1,3-diaminobutane dihydrochloride was prepared by the method of Campbell and Urbach:[28] mp 172–173 °C (lit. mp 169–170 °C,[29] 176 °C,[28] 177 °C[30]); ^1H NMR (D_2O) δ 1.36 (d, J = 6.6 Hz, CH_3), 2.0 (m, $H_2NCH_2CH_2$), 3.14 (t, J = 8.2 Hz, H_2NCH_2), 3.5 (m, CH).

1,4-Diaminopentane Dihydrochloride. An authentic sample of 1,4-diaminopentane dihydrochloride was prepared in a manner exactly analogous to the previous procedure: mp 168–169 °C. Anal. Calcd for $C_5H_{16}Cl_2N_2$: C, 34.30; H, 9.21; N, 16.00. Found: C, 34.62; H, 9.41; N, 15.89; ^1H NMR (D_2O) δ 1.32 (d, J = 6.6 Hz, CH_3), 1.75 (m, $H_2NCH_2CH_2CH_2$), 3.05 (m, H_2NCH_2), 3.42 (m, CH).

***o*-Xylenediamine dihydrochloride:** ^1H NMR (D_2O) δ 4.4 (s, CH_2), 7.6 (s, Ar); ^{13}C NMR (D_2O) 39.55 (CH_2), 130.14 (CH), 131.20 ppm (C); MS, *m/e* (relative intensity) 136 (4), 117 (7), 45 (5), 34 (100). In accordance with a previous report[31] in the literature we found that this compound crystallized with half a water of crystallization. Anal. Calcd for $C_8H_{12}N_2 \cdot 2HCl \cdot {}^1/_2H_2O$: C, 44.05; H, 6.93; N, 12.85. Found: C, 43.48; H, 6.73; N, 12.59.

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(26) Stothers, J. B. *Carbon-13 NMR Spectroscopy*; Academic Press: New York, 1972; p 64.
(27) Cignarella, G.; Gallo, G. G. *J. Heterocycl. Chem.* **1974**, *11*, 985.
(28) Campbell, T. G.; Urbach, F. L. *Inorg. Chem.* **1973**, *12*, 1836.
(29) Kost, A. N.; Golubeva, G. A.; Stepanov, R. G. *J. Gen. Chem. USSR* **1962**, *32*, 2207.
(30) Strack, E.; Schwaneberg, H. *Ber. Dtsch. Chem. Ges.* **1934**, *67*, 39.
(31) Gabriel, S.; Pinkus, G. *Ber. Dtsch. Chem. Ges.* **1893**, *26*, 2210.
(32) Stone, P. J.; Cymerman Craig, J.; Thompson, H. W. *J. Chem. Soc.* **1958**, 52.
(33) Abderhalden, E.; Schwab, E. *Hoppe-Seyler's Z. Physiol. Chem.* **1924**, *139*, 68.
(34) Aldrich Catalog/Handbook of Fine Chemicals, Aldrich Chemical Co., Milwaukee, WI, 1984.
(35) CIBA Ltd. Brit. Pat. 1 183 135 (4 March 1970); *Chem. Abstr.* **1970**, *72*, 121598w.
(36) Schotte, H.; Priewe, H.; Roescheisen, H. *Hoppe-Seyler's Z. Physiol. Chem.* **1928**, *174*, 119.
(37) Sicher, J.; Pankova, M.; Jonas, J.; Svoboda, M. *Collect. Czech. Chem. Commun.* **1959**, *24*, 2727; *Chem. Abstr.* **1960**, *54*, 7689h.
(38) Lindemann, H.; Schultheis, W. *Justus Liebigs Ann. Chem.* **1928**, *464*, 237.
(39) Berger, J. G. *Synthesis* **1974**, 508.