Table IV. Observed and Computed Q_{hkl} Values for $Ni(L-H)_2$[a]

powder pattern lines	Q_{obsd}	Q_{comp}	hkl
1	0.0146	0.0140	101
2	0.0325	0.0340	112
3	0.0440	0.0440	400
4	0.0480	0.0480	004
5	0.0624	0.0590	104
6	0.0824	0.0820	212
7	0.0966	0.0967	115
8	0.1185	0.1190	205
9	0.1915	0.1920	008
		0.1900	411
10	0.2000	0.1990	412

[a] Lattice parameters: a = 19.08 Å, c = 18.24 Å, ρ = 0.8 g cm^{-3}, ρ(calcd) = 0.78 g cm^{-3}, z = 4.

Table V. Antifungal Activity[a] for Ligand and Complexes

compd	concn 50 ppm	concn 100 ppm
ligand	13.3	31.1
VOL_2SO_4	6.9	19.3
CuL_2Cl_2	0.0	0.0
CdL_2Cl_2	88.3	100.0
HgL_2Cl_2	37.7	42.4
$Co(L-H)_2$	12.5	13.3
$Ni(L-H)_2$	0.0	0.0

[a] Percent inhibition.

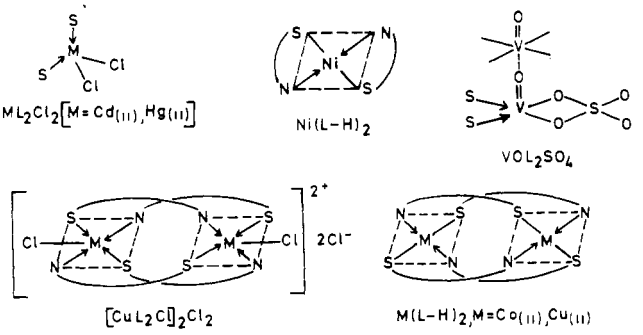

Figure 1.

zation and subsequent removal of the proton by the metal ion. The presence of four bands at 1245, 1150, 1025, and 975 cm^{-1} is indicative of the bidentate chelating (*27*) nature of SO_4^{2-} in VOL_2SO_4. Fungitoxicity increases at 100 ppm in the following order: $Co(L-H)_2 < VOL_2SO_4 < HgL_2Cl_2 < CdL_2Cl_2$.

Chemical compositions and physicochemical data suggest the structures in Figure 1 for the complexes.

Acknowledgment

Sincere thanks are also due to RSIC, IIT Madras, for running ESR spectra of the complexes.

Registry No. VOL_2SO_4, 89909-15-9; CuL_2Cl_2, 89922-01-0; CdL_2Cl_2, 89909-16-0; HgL_2Cl_2, 89909-17-1; $Cu(L-H)_2$, 89909-19-3; $Co(L-H)_2$, 89909-18-2; $Ni(L-H)_2$, 89909-20-6.

Literature Cited

(1) Satpathy, K. C.; Mishra, H. P. *J. Indian Chem. Soc.* **1981**, *58*, 844.
(2) Johnson, C. W.; Joyner, J. W.; Perry, R. P. *Antibiot. Chemother. (Washington, D.C.)* **1952**, *2*, 636.
(3) Gansman, H. W.; Rhykerd, C. I.; Hinderliter, H. R.; Scott, E. S.; Andrieth, L. F. *Bot. Gaz. (Chicago)* **1953**, *114*, 292.
(4) Benos, B. G.; Gingras, B. A.; Bayley, C. H. *Appl. Microbiol.* **1961**, *8*, 353.
(5) Das, B. C.; Mahapatra, G. N. *J. Indian Chem. Soc.* **1967**, *44*, 939.
(6) Rai Rameshwar; Verma, V. K. *Indian J. Chem., Sect. B* **1979**, *18*, 284.
(7) Vogel, A. I. "A Text Book of Quantitative Inorganic Analysis", 3rd ed.; ELBS and Longmans: London, 1973.
(8) Figgis, B. N.; Lewis, J. In "Modern Coordination Chemistry"; Lewis, J., Wilkins, R. G., Eds.; Interscience: New York, 1960; p 403.
(9) Azaroff, L. V.; Burger, M. J. "The Powder Method in X-ray Crystallography"; McGraw-Hill: New York, 1958; p 119.
(10) Schmitz, H. *Ind. Eng. Chem. Anal.* **1930**, *4*, 361.
(11) Geary, W. J. *Coord. Chem. Rev.* **1971**, *7*, 81.
(12) Stocklosa, H. J.; Wasson, J. R.; McCormic, B. J. *Inorg. Chem.* **1974**, *13*, 592.
(13) Farmer, R. L.; Urbach, F. L. *Inorg. Chem.* **1974**, *13*, 587.
(14) Nishida, Y.; Kida, S. *Inorg. Nucl. Chem. Lett.* **1971**, *7*, 325.
(15) Singh, P. P.; Shukla, U. P.; Makhija, R.; Rivest, R. *J. Inorg. Nucl. Chem.* **1975**, *37*, 679.
(16) Lever, A. B. P. "Inorganic Electron Spectroscopy"; Elsevier: Amsterdam, 1964; p 343.
(17) Sacconi, L.; Ciampolini, M. *J. Chem. Soc.* **1964**, 276.
(18) Yamada, S.; Nishikava, H.; Tsuchida, T. *Bull. Chem. Soc. Jpn.* **1960**, *33*, 1278.
(19) Hathaway, B. J. *Coord. Chem. Rev.* **1981**, *35*, 231.
(20) Syamal, A. *Coord. Chem. Rev.* **1975**, *16*, 309.
(21) Nyholm, R. S. *Proc. Chem. Soc.* **1961**, 273.
(22) Pignedoli, A.; Peyronel, G. *Gazz. Chim. Ital.* **1962**, *92*, 745.
(23) Khuller, I. P.; Agarwala, U. *Can. J. Chem.* **1975**, *53*, 1165.
(24) Harris, C. M.; Hoskens, B. F.; Martin, R. L. *J. Chem. Soc.* **1959**, 3728.
(25) Churchill, M. R.; Davies, G.; El-Sayed, M. A.; Shazly, M.; Hutchinson, J. P.; Rupich, M. W. *Inorg. Chem.* **1980**, *19*, 201.
(26) Peyronel, G.; Pellacani, G. C.; Pignedoli, A. *Inorg. Chim. Acta* **1981**, *58*, 1149.
(27) Nakamoto, K. "Infrared and Raman Spectra of Inorganic and Coordination Compounds", 3rd ed.; Wiley-Interscience: New York, 1978.

Received for review April 25, 1983. Accepted January 9, 1984. B.P.Y. is thankful to the UGC, New Delhi, for the award of a Teacher Fellowship.

Synthesis of Some Dihydroxamic Acid Siderophores

M. K. Das,* P. Bose, and N. Roy

Department of Chemistry, Jadavpur University, Calcutta—700 032, India

Twenty-two new dihydroxamic acids having the general formula $(CH_2)_n[CON(R)OH]_2$ (n = 2, 3, 4, 6, 8; R = H, aryl) have been synthesized either by condensation of the acid chlorides with suitable arylhydroxylamines or by the reaction of the esters with hydroxylamine and characterized by elemental analyses and infrared, UV, and proton NMR spectra.

The importance of hydroxamic acids, RCON(R')OH, in both biology and medicine is now well recognized (*1*–*4*), and much of their biological activity seems to be related to their ability to chelate iron specifically (*1*, *2*, *4*). The trihydroxamic acid desferrioxamine B is currently being used for the treatment of iron overload disease (*5*, *6*) and is usually given as the methanesulfonate salt under the trademark Desferal of the Ciba-Geigy Corp. Rhodotorulic acid, a dihydroxamic acid, has also

0021-9568/84/1729-0345$01.50/0

Table I. Physical Properties of the Dihydroxamic Acids[a,b]

compd no.	n	R	mp, °C	solvent of crystallization	ν(OH), cm^{-1}	ν(C=O), cm^{-1}	λ_{max}, nm	log ϵ_{max}
1	3	H	143	abs alcohol	3180 vs, br	1670–1635 vs, br	208	3.95
2	6	H	135–140	abs alcohol	3340 sh	1700–1650 vs, br	<200	
					3280 sh			
3	2	C_6H_5	158	rectified spirit	3330 sh	1615 vs, br	210	4.26
					3160 s, br		240	4.29
4	2	2-$CH_3C_6H_4$	148	rectified spirit	3220 s, br	1655 s, sh	214	4.30
						1610 s	228	4.23
5	2	4-$CH_3C_6H_4$	165	rectified spirit	3320 sh	1640 s, sh	205	4.47
					3160 s, br	1620 s	216	4.40
						1605 s, sh	240	4.28
6	2	4-ClC_6H_4	155	rectified spirit	3600–3100 vbr, s	1600 m	202	4.19
						1580 m	234	4.03
							330	4.24
7	3	C_6H_5	130	rectified spirit	3200 s, br	1655 sh	212	4.31
						1630 s	230	4.24
8	3	2-$CH_3C_6H_4$	145	rectified spirit	3280 s	1640 s	210	4.52
					3130 s, br	1610 s, sh	228	4.37
9	3	4-$CH_3C_6H_4$	172	rectified spirit	3180 s, br	1635 s	218	4.53
						1615 s, sh	250	4.35
10	3	4-ClC_6H_4	174	rectified spirit	3600–3100 vbr, s	1595 m	204	4.50
						1580 s	222	4.45
							244	4.33
11	4	C_6H_5	183	rectified spirit	3160 vs, br	1620 vs	218	4.15
							248	4.14
12	4	2-$CH_3C_6H_4$	156	alcohol/water	3100 vs, br	1642 s	262	3.90
					3065 vs	1618 vs	222	4.19
					3010 vs			
13	4	4-$CH_3C_6H_4$	206	rectified spirit	3235 s	1638 vs	220	4.26
							250	4.31
14	4	4-ClC_6H_4	196	rectified spirit	3180 s, br	1628 vs	222	4.25
							246	4.21
15	6	C_6H_5	168	rectified spirit	3340 w	1625 vs	218	4.42
					3160 vs, br		258	4.10
					3070 sh			
16	6	2-$CH_3C_6H_4$	118	benzene/petroleum ether	3280 m	1685 s	210	4.33
						1650 s	224	4.05
17	6	4-$CH_3C_6H_4$	168	rectified spirit	3160 m, br	1622 s	220	4.53
							258	4.12
18	6	4-ClC_6H_4	130	rectified spirit	3310 m	1690 vs	210	4.28
					3180 s	1655 vs	226	4.29
					3100 m	1645 vs	246	4.41
						1620 vs		
19	8	C_6H_5	158	rectified spirit	3170 s	1630 vs	219	4.38
							270	4.02
20[c]	8	2-$CH_3C_6H_4$	120	benzene/petroleum ether	3600–3100 vbr, s	1682 vs	219	3.99
							262	3.26
21	8	4-$CH_3C_6H_4$	135	rectified spirit	3400 w	1655 m	220	4.41
					3190 s	1620 s	256	3.97
22	8	4-ClC_6H_4	130	rectified spirit	3400 m	1725 m	226	4.29
					3200 s	1630 s	238	4.30
							330	4.21

[a] All the compounds are colorless or off-white, except 15, which is green. [b] Elemental analytical data were submitted for review. [c] LH·$2H_2O$ (LH = hydroxamic acid).

undergone preliminary clinical trials for the same (*7*). We therefore report here the synthesis of a series of dihydroxamic acids, $(CH_2)_n[CON(R)OH]_2$, with increasing chain length and different substituents on nitrogen in order to investigate their influence, if any, on the iron chelation (*8*).

Experimental Section

All solvents and chemicals used were of reagent-grade quality. Ethanol was distilled over CaO and methanol was dried by refluxing over Mg turnings and distilled prior to use. Elemental analyses were done by the microanalytical service of Jadavpur University. IR spectra were recorded as Nujol mulls in NaCl cells on a Perkin-Elmer 297 spectrometer over the range 4000–600 cm^{-1} and were calibrated with respect to the 1601-cm^{-1} band of a polystyrene film. Electronic spectra were recorded in the region 200–400 nm in matched silica cells on a Unicam SP8-300 UV–vis spectrophotometer in methanol, except for compounds **1** and **2**, whose spectra were recorded in doubly distilled water (the second distillation being carried over $KMnO_4$). The ^1H NMR spectra were recorded on a Jeol-FX 90Q or a Varian EM 360L in $CDCl_3$ or D_2O solvent with Me_4Si or *tert*-butyl alcohol (in the case of D_2O) as internal standard at ambient temperatures.

Preparation of N-Substituted Dihydroxamic Acids, $(CH_2)_n[CON(R)OH]_2$ (n = 2, 3, 4, 6, 8; R = C_6H_5, 2-$CH_3C_6H_4$, 4-$CH_3C_6H_4$, 4-ClC_6H_4). Substituted phenylhydroxylamines, X–C_6H_4NHOH (X = H, 2-CH_3, 4-CH_3, 4-Cl) (I), have been prepared by reduction of the corresponding nitro compounds X–$C_6H_4NO_2$, with Zn/NH_4Cl in alcohol/water. The various acid chlorides were prepared from the corresponding acids with thionyl chloride. Appropriate freshly prepared arylhydroxylamine (I) (0.1 mol) was mixed with pyridine (7.9 g, 0.1 mol) in ether (100 mL) and acid chloride (0.05 mol) was added dropwise to the ice-cold ethereal solution with constant stirring. After filtration the product was washed successively with ether, dilute HCl, and water to remove excess pyridine and pyridine

Table II. Infrared Absorptions in the Range 1800–600 cm^{-1}

compd no.	infrared absorptions,[a] cm^{-1}
1	1670–1635 vs br, 1575 s, 1555 s sh, 1400 s, 1360 vs, 1338 vs, 1240 s, 1230 s, 1145 m, 1095 s, 1050 s, 1030 s, 1025 m, 1010 s, 965 s, 795 m br, 765 m, 725 s, 640 s
2	1700–1650 v br, vs, 1620 s, 1560 s, 1400 vs, 1322 vs, 1285 s, 1270 s, 1250 vs, 1185 vs, 1125 s, 1095–1085 m, 1070 s, 1035 m, 1005 m, 995 m, 970 s, 920 vs, 790 m, 720 s, 675 s
3	1615 vs, 1595 s, 1530 m, 1480 s sh, 1435 s, 1400 s, 1320 m, 1305 m, 1250 m, 1180 m, 1150 m, 1090 m, 1065 m, 1030 m, 965 m, 915 m, 898 m, 790 m, 745 vs, 680 s
4	1655 s, 1610 vs, 1598 s, 1530 s, 1490 s, 1450 s, 1400 m, 1390 m, 1310 m, 1195 m, 1155 m, 1115 m, 1080 s, 1035 m, 995 m, 938 m, 915 m, 900 m, 895 m, 775 m, 755 s, 745 s sh, 715 m
5	1640 s sh, 1620 s, 1605 s sh, 1505 s, 1450 s br, 1308 m, 1260 m, 1180 m, 1085 m, 965 m, 920 m, 820 s, 798 m, 660 m br
6	1600 m, 1580 m, 1450 s br, 1400 s, 1160 s sh, 1090 s br, 1010 s sh, 915 m, 832 s, 720 m, 710 m, 665 m, 618 s
7	1655 s sh, 1630 s, 1590 m, 1525 m, 1480 m, 1450 s, 1440 s sh, 1390 s, 1340 m, 1300 m, 1290 s sh, 1240 m, 1175 m, 1092 m, 1065 vs, 1030 m, 910 s, 755 vs, 695 m, 682 m
8	1640 s, 1610 s sh, 1605 s, 1595 s, 1580 s, 1525 s, 1485 m, 1340 m, 1280 m, 1252 m, 1190 m, 1115 m, 1075 m, 1055 m, 1035 m, 965 m, 940 m, 910 m, 760 m, 745 s, 720 s
9	1635 s, 1615 s sh, 1500 s, 1335 s, 1300 m, 1240 m, 1088 m, 1075 m, 1060 m, 1015 m, 890 m, 825 m, 805 s, 742 m, 640 m
10	1595 m, 1580 s, 1460 s, 1400 m, 1280 m, 1160 m, 1090 s, 1010 s, 915 s, 830 s, 660 m, 612 m
11	1620 vs, 1580 s, 1520 m, 1322 vs, 1312 s, 1295 vs, 1280 vs, 1220 s, 1190 m, 1175 s, 1145 m, 1128 m, 1085 s, 1065 s, 1020 m, 890 m, 885 m, 750 s, 743 s, 730 s, 680 s, 645 s, 630 m
12	1642 s, 1618 vs, 1600 vs, 1590 vs, 1570 vs, 1520 vs, 1478 vs, 1410 vs, 1335 m, 1282 s, 1270 m, 1230 m, 1218 m, 1190 s, 1150 m, 1115 s, 1070 vs, 1030 m, 995 m, 935 m, 925 m, 902 m, 775 s sh, 760 s, 740 vs, 718 vs, 611 m
13	1638 vs, 1515 s, 1418 m, 1325 m, 1285 m, 1255 m, 1220 m, 1175 m, 1110 m, 1050 m, 1006 m, 975 m, 905 m, 850 m, 830 s, 738 m, 722 m
14	1628 vs, 1485 vs, 1418 s sh, 1405 vs, 1328 s, 1292 s, 1280 m, 1242 m, 1180 s, 1098 s, 1083 s, 1008 m, 910 m, 898 m, 835 m, 822 vs, 735 m, 656 m, 618 m
15	1625 vs, 1592 s, 1532 m, 1352 vs, 1286 vs, 1226 s, 1185 s, 1152 m, 1125 m, 1095 s, 1071 vs, 1033 m, 1015 m, 970 m, 905 s, 791 m, 756 s sh, 750 s, 725 s, 689 s, 650 s, 611 m
16	1685 s, 1650 s, 1580 m, 1517 m, 1400 m, 1280 m, 1250 m, 1231 m, 1178 m, 1035 m, 960 m, 930 m, 742 m, 708 m, 692 m
17	1622 s, 1508 m, 1352 m, 1291 m, 1282 m, 1181 m, 1081 s, 1070 m, 910 m, 815 s, 725 m
18	1690 vs, 1655 vs, 1645 vs, 1620 vs, 1592 s, 1525 s, 1486 vs, 1405 vs, 1340 vs, 1287 s, 1270 vs, 1245 s sh, 1207 s, 1190 s, 1175 s, 1095 s, 1075 s, 1005 s, 960 m br, 930 m, 905 m, 840 s, 825 s, 722 m
19	1630 vs, 1592 s, 1335 s, 1330 s, 1306 s, 1287 s, 1270 vs, 1220 s, 1177 m, 1150 m, 1115 m, 1093 s, 1047 m, 1030 s, 1023 s, 1000 m, 905 m, 850 m, 756 s, 750 s, 720 m, 650 m, 647 s, 615 m
20	1682 vs, 1510 m, 1485 m, 1450 m, 1420 s, 1405 s, 1345 m, 1295 s, 1235 s, 1182 s, 922 s, 750 m, 720 m, 670 m
21	1655 m, 1620 s, 1505 m, 1330 m, 1305 m, 1268 m, 1075 m, 815 m
22	1725 m, 1630 s, 1490 s, 1418 s, 1318 m, 1295 m, 1270 m, 1250 m, 1180 s, 1120 m, 1110 m, 1080 s, 1048 m, 1030 m, 1010 m, 832 s, 815 m, 720 m

[a] v = very, br = broad, s = strong, m = medium, sh = shoulder.

Table III. Chemical Shifts (δ) of $HORNOC(CH_2)_nCONROH$[a,b]

compd no.	n	R	$-(CH_2)_n-$	aryl	$ArCH_3$
4	2	2-$CH_3C_6H_4$	2.0–2.4 m, 2.6–2.8 br	7.15 m	2.48 s
5		4-$CH_3C_6H_4$	2.2–2.4 m, 2.7 s, br	7.16 m	2.3 s[c]
1	3	H	2.19 m		
8		2-$CH_3C_6H_4$	1.85–2.25 m, 2.35–2.6 m, br	7.15 m	2.28 s
9		4-$CH_3C_6H_4$	1.8–2.08 br, 2.4–2.6 m	7.17 m	2.32 s
12	4	2-$CH_3C_6H_4$	1.5–1.8 br, 2.0–2.2 br	7.25 m	2.28 s
13		4-$CH_3C_6H_4$	1.43–1.75 br, 1.95 br	7.13 m	2.28 s
2	6	H	2.23 m		
16		2-$CH_3C_6H_4$	1.05–1.45 br, 1.5–1.85 br	7.16 m	2.21 s
17		4-$CH_3C_6H_4$	1.05–1.35 br, 1.4–1.8 br	7.16 m	2.31 s
18		4-ClC_6H_4	1.1–1.3 br, 1.35–1.8 br	7.18 m	
20	8	2-$CH_3C_6H_4$	1.0–1.35 br, 1.4–1.8 br	7.18 m	2.33 s
21		4-$CH_3C_6H_4$	0.95–1.3 br, 1.3–1.7 br	7.06 m	2.22 s
22		4-ClC_6H_4	1.15–1.35 m, 1.4–1.8 br	7.26 m	

[a] Taken in $CDCl_3$ except 1 and 2, which are taken in D_2O. [b] s = singlet, m = multiplet, br = broad. [c] Overlapping partially with one portion of $-(CH_2)_2-$ absorption.

hydrochloride. The resulting solid/oily mass was extracted with liquor ammonia and the extract was poured into ice-cold H_2SO_4 (1:1) when the crude products were precipitated. In the case of **3**, the crude product precipitated from the ethereal solution. The products were then recrystallized from rectified spirit or benzene/petroleum ether (40–60 °C) mixture; the yields were in the range of 40–50% (Table I).

Preparation of N-Unsubstituted Dihydroxamic Acids, $(CH_2)_n(CONHOH)_2$ (n = 3, 6). Two new N-unsubstituted dihydroxamic acids, glutarohydroxamic acid (n = 3) and suberohydroxamic acid (n = 6), have been prepared by treating the corresponding esters (0.1 mol) with NaOEt and free hydroxylamine (0.2 mol) (*9*), which was obtained from the reaction of $NH_2OH{\cdot}HCl$ and NaOEt (0.2 mol each). The products were recrystallized from absolute alcohol, yield ca. 45% for n = 3 and ca. 80% for n = 6 (Table I).

Results and Discussion

The N-unsubstituted and N-aryl-substituted dihydroxamic acids, respectively, are obtained according to reactions 1 and 2.

The physical properties and spectral data are given in Table I, whereas in Table II are given the major IR absorption bands from 1800 to 600 cm^{-1}. The ^1H NMR spectral data of those hydroxamic acids which are soluble in either $CDCl_3$ or D_2O are

$$(CH_2)_n(COOEt)_2 + 2NH_2OH + 2NaOEt \longrightarrow$$

$$(CH_2)_n(CONHONa)_2 + 4EtOH \xrightarrow{2HCl} (CH_2)_n(CONHOH)_2 + 2NaCl \quad (1)$$

$$(CH_2)_n(COCl)_2 + 2RNHOH + 2C_5H_5N \longrightarrow (CH_2)_n(CON(R)OH)_2 + 2C_5H_5N{\cdot}HCl \quad (2)$$

(R = C_6H_5, 2-$CH_3C_6H_4$, 4-$CH_3C_6H_4$, 4-ClC_6H_4)

given in Table III, showing the effect of variation of n on the nature of the spectra.

Acknowledgment

Thanks are due to Dr. B. K. Nath of the Indian Institute of Chemical Biology for recording the UV spectra and B. Bhattacharya and S. Bose for performing the microanalysis and recording the IR spectra. The ^1H NMR spectra were recorded at Duke University (courtesy of J. M. Garrison) and the Regional Sophisticated Instrumentation Centre, Central Drug Research Institute, Lucknow, India.

Registry No. 1, 7068-55-5; 2, 38937-66-5; 3, 20533-09-9; 4, 89959-30-8; 5, 89959-31-9; 6, 89959-32-0; 7, 28484-24-4; 8, 89959-33-1; 9, 89959-34-2; 10, 89959-35-3; 11, 20654-65-3; 12, 89959-36-4; 13, 89959-37-5; 14, 89959-38-6; 15, 89959-39-7; 16, 89959-40-0; 17, 89959-41-1; 18, 89959-42-2; 19, 89959-43-3; 20, 89959-44-4; 21, 89959-45-5; 22, 89959-46-6; $(CH_2)_3(COOEt)_2$, 818-38-2; $(CH_2)_8(COOEt)_2$, 2050-23-9; $(CH_2)_2(COCl)_2$, 543-20-4; $(CH_2)_3(COCl)_2$, 2873-74-7; $(CH_2)_4(COCl)_2$, 111-50-2; $(CH_2)_6(COCl)_2$, 10027-07-3; $(CH_2)_8(COCl)_2$, 111-19-3; NH_2OH, 7803-49-8; C_6H_5NHOH, 100-65-2; 2-$CH_3C_6H_4NHOH$, 611-22-3; 4-$CH_3C_6H_4NHOH$, 623-10-9; 4-ClC_6H_4NHOH, 823-86-9.

Literature Cited

(1) Neilands, J. B. *Struct. Bonding (Berlin)* **1966**, *1*, 59.
(2) Feeney, R. E.; Komatsu, St. K. *Struct. Bonding (Berlin)* **1966**, *1*, 149.
(3) Brown, D. A.; McKeith, D.; Glass, W. K. *Inorg. Chim. Acta* **1979**, *35*, 5.
(4) Malstrom, B. G. "Biochemical Functions of Iron in Iron Deficiency"; Academic Press: New York, 1970.
(5) Anderson, W. F., Hiller, M. C., Eds. "Development of Iron Chelators for Clinical Use"; Department of Health, Education, and Welfare, U.S. Government Printing Office: Washington, DC, 1977; No. (N/H) 76-994.
(6) Zaino, E. C., Roberts, R. H., Eds. "Chelation Therapy in Chronic Iron Overload"; Stratton International Medical Book Corp.: New York, 1977.
(7) *Chem. Eng. News* **1977**, *55* (18), 24.
(8) Das, M. K., Bose, P.; Roy, N., in preparation.
(9) Hurd, C. D.; Botheron, D. G. *J. Org. Chem.* **1946**, *11*, 207.

Received for review April 28, 1983. Accepted December 8, 1983. M.K.D. expresses his sincere thanks to the CSIR, India, for a research grant [1-(894)/80/EMR-II] incorporating two JRFs.

Thermal Stability of Nitrobenzyl Halogenides

Paolo Cardillo and Alberto Girelli*

Stazione sperimentale per I Combustibili, 20097 San Donato Milanese, Italy

After a violent explosion occurred during the drying of *o*-nitrobenzyl bromide in a chemical factory, the thermal stability of nitrobenzyl halogenide isomers (X = Cl, Br) was studied by conventional thermoanalytical techniques (TGA, DSC) and by adiabatic calorimetry (ARC). All the nitrobenzyl halogenides tested decompose exothermally with abundant gas evolution. Bromide derivatives are less stable than chlorides; ortho isomers are less stable than meta and para isomers; *m*-nitrobenzyl bromide is slightly less stable than its para isomer, while *p*-nitrobenzyl chloride is slightly less stable than its meta isomer.

Introduction

Nitrobenzyl halogenides are an important group of intermediates for organic syntheses. Specific information on their thermal stability is almost nonexistent in the literature (*1*, *2*). Two papers refer to the possible explosive decomposition of *o*-nitrobenzyl bromide when heated above 125–130 °C (*3*, *4*). A violent explosion during the drying of this compound in a fine-chemicals factory (*5*) suggested that tests of the thermal stability be run on the nitrobenzyl halogenides (X = Cl, Br). The presence of NO_2 groups in organic molecules is generally an index of possible thermal instability. However, nitrobenzene is stable up to 300 °C (*6*).

To evaluate the influence of the substituents CH_2Cl and CH_2Br, and of their position on the thermal stability of nitrobenzene, the series of compounds listed in Table I was studied by conventional thermoanalytical techniques (TGA, DSC) and by adiabatic calorimetry (ARC).

Table I. Nitrobenzyl Halogenides Tested by Thermoanalytical Techniques and by Adiabatic Calorimetry

	purity, mol %
o-nitrobenzyl bromide	97
m-nitrobenzyl bromide	99
p-nitrobenzyl bromide	99
o-nitrobenzyl chloride	99
m-nitrobenzyl chloride	97
p-nitrobenzyl chloride	99

Experimental Section

Commercial-grade products (Aldrich, Beerse, Belgium) with purities between 97% and 99% were used without further treatment.

Instruments and Procedures. A Mettler TA 2000 C thermoanalyzer was used for the simultaneous recording on the same sample of TGA and DSC curves from room temperature to 1200 °C (*7*). An added module allows one to record the derivative of the TGA curve (DTG). Runs were performed at a heating rate of 10 °C min^{-1} on 5-mg samples, in air and in inert (nitrogen) atmosphere, with 40 mL min^{-1} gas flow. Platinum crucibles (0.15 mL) without caps were used.

A Mettler TA 3000 differential scanning calorimeter was used for testing in a sealed crucible (*8*). Runs were performed at a heating rate of 5 °C min^{-1} on 7–10-mg samples in Nimonic crucibles (0.5 mL), with gold safety disks resistant up to 10 000-kPa pressure.

In both experiments, aluminum oxide was used as an inert reference. The recorded temperature of the exotherm being an "instrumental temperature", depending mainly on the heating

0021-9568/84/1729-0348$01.50/0