Preparation and Properties of Some Analogues of *N*-Benzylbenzohydroxamic Acid

Usha Tandon*

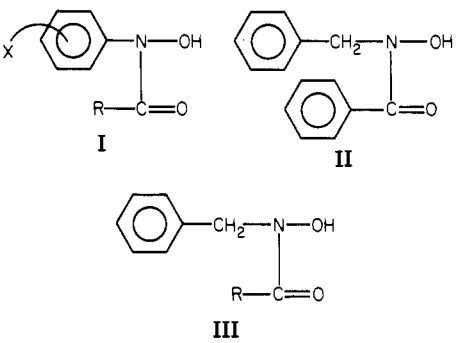
Department of Chemistry, Govt. Science College, Raipur, 492.002 India

Basant R. Sahu

Department of Chemistry, Ravishankar University, Raipur, 492.010 India

Eleven new analogues of *N*-benzylbenzohydroxamic acid (BBHA) have been prepared by the acylation of *N*-benzylhydroxylamine with suitable acid chlorides at low temperature in mixed diethyl ether and petroleum ether media containing an aqueous suspension of sodium bicarbonate. The yield ranges from 48% to 80%. These compounds, prepared with a view to investigating their possible analytical and biological applications, were characterized by elemental analysis, melting point, and infrared, ultraviolet, and in some cases proton nuclear magnetic resonance spectra.

The *N*-benzyl-substituted parent compound, *N*-benzylbenzohydroxamic acid (BBHA) was prepared and reported earlier (*1*). Unlike *N*-aryl-substituted hydroxamic acids, I, the nitrogen atom of the hydroxamic acid functional grouping, —N(OH)C=O, is attached to the side chain of the aromatic ring in BBHA, II, and its analogues of the general structure III. X is variously substituted and R is an alkyl or aryl radical. BBHA has been reported to be a highly selective reagent for the determination of vanadium in biological materials, viz., blood, tissues, and urine (*2*). In an attempt to study the substituent effect on the selectivity, the analogues were prepared.



Experimental Section

Apparatus. Infrared spectra, in Nujol, were recorded on a

Table I. Physical and Spectral Characteristics of *N*-Benzylhydroxamic Acids

compd no.	compd	molecular formula (mol wt)	MP, °C	yield, %	UV spectra in 95% ethanol: λ_{max}, nm	$10^{-3}\epsilon$, L mol^{-1} cm^{-1}	λ_{11}/λ_1	IR spectra frequency, cm^{-1}: ν(O—H)	ν(C=O)
1	*N*-benzylbenzohydroxamic acid	$C_{14}H_{13}NO_2$ (227.26)	108	80	205	22.5		3270 vs	1625 vs
2	*N*-benzyl-*o*-chlorobenzohydroxamic acid	$C_{14}H_{12}NO_2Cl$ (261.71)	159	65	205	30.0		3140 vsb	1630 vs 1610 vs
3	*N*-benzyl-*o*-nitrobenzohydroxamic acid	$C_{14}H_{12}N_2O_4$ (272.26)	145	55	207 257	27.2 7.3	1.24	3240 vs	1625 vs
4	*N*-benzyl-*o*-methoxybenzohydroxamic acid	$C_{15}H_{15}NO_3$ (257.29)	175	52	207 281	26.0 2.8	1.35	3140 s 3070 s	1620 sh 1608 s
5	*N*-benzyl-*p*-bromobenzohydroxamic acid	$C_{14}H_{12}NO_2Br$ (306.17)	137	66	205 238	30.0 13.7	1.16	3205 s	1615 vs
6	*N*-benzyl-*p*-fluorobenzohydroxamic acid	$C_{14}H_{12}NO_2F$ (245.26)	123	60	207	17.7		3120 s	1600 vs
7	*N*-benzyl-*m*-nitrobenzohydroxamic acid	$C_{14}H_{12}N_2O_4$ (272.26)	98	60	209 253	26.0 11.5	1.21	3180 sb 3080 s	1600 vs
8	*N*-benzyl-2-naphthohydroxamic acid	$C_{18}H_{15}NO_2$ (277.32)	130	67	226 270 (inf) 280	56.0 8.4 8.2	1.23	3120 sb	1628 m 1590 vs
9	*N*-benzyl-1,2-dibromocinnamohydroxamic acid	$C_{16}H_{13}NO_2Br_2$ (413.13)	165	48	208 244	22.2 10.8	1.17	3160 m	1620 s
10	*N*-benzyl-*n*-valerohydroxamic acid	$C_{12}H_{17}NO_2$ (207.27)	55	70	209	12.0		3180 sb	1630 s 1610 s
11	*N*-benzylpelargonohydroxamic acid	$C_{16}H_{25}NO_2$ (263.38)	68	80	209	15.7		3170 vs	1620 sh
12	*N*-benzylstearohydroxamic acid	$C_{25}H_{43}NO_2$ (389.63)	91	65	209	14.5		3160 s	1600 vs

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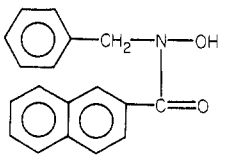
Table II. Proton NMR Absorptions of *N*-Benzylhydroxamic Acids

compd no.	compd	δ (τ)	multiplicity (intensity)	assignment
1	C_6H_5—CH_2—N(OH)—C(=O)—C_6H_5	4.85 (5.15)	singlet (2)	—CH_2—
		7.34 (2.66)	singlet (5)	C_6H_5—CH_2—
		7.45 (2.55)	singlet (2)	meta protons to C=O
		7.51-7.60 (2.49-2.4)	multiplet (3)	ortho and para protons to C=O
6	C_6H_5—CH_2—N(OH)—C(=O)—*p*-FC_6H_4	4.85 (5.15)	singlet (2)	—CH_2—
		7.33 (2.67)	singlet (5)	C_6H_5—CH_2—
		7.0-7.18 (3.0-2.82)	triplet (2)	meta protons to C=O
		7.55-7.66 (2.5-2.34)	multiplet (2)	ortho protons to C=O
		8.38 (1.62)	singlet (1), broad hump	—O*H*
11	C_6H_5—CH_2—N(OH)—C(=O)—CH_2—CH_2—$(CH_2)_5$—CH_3	4.81 (5.19)	singlet (2)	C_6H_5—CH_2—
		7.32 (2.68)	singlet (5)	C_6H_5—CH_2—
		0.8-0.94 (9.2-9.06)	distorted triplet (3)	CH_3—
		1.25 (8.75)	singlet (10)	CH_3—$(CH_2)_5$
		1.56-1.70 (8.44-8.30)	broad multiplet (2)	—$(CH_2)_5$—CH_2—
		2.34-2.48 (7.66-7.52)	distorted triplet (2)	—CH_2—C=O

Perkin-Elmer 377 spectrophotometer and ultraviolet spectra in 95% ethanol on a Carl-Zeiss Jena SPECORD spectrophotometer with matched silica cells of 1-cm light path. Proton NMR spectra were recorded on a Varian XL-100A high-resolution NMR spectrometer using tetramethylsilane (Me_4Si) as the internal reference and deuteriochloroform as the solvent.

Preparation. *N*-Benzylhydroxylamine was prepared bascially by the method of Jones and Sneed (*3*) and acylated with appropriate acid chlorides at 0 °C or lower temperatures following the modified procedure of Priyadarshini and Tandon (*4*). Resulting hydroxamic acids were generally crystallized 2 or 3 times from benzene or a mixture of benzene and petroleum ether (boiling range 60–80 °C).

A typical preparation of *N*-benzyl-2-naphthohydroxamic acid, IV, is described here.



IV

In a 500-mL narrow-mouth flask freshly crystallized *N*-benzylhydroxylamine (0.034 mol) in 60 mL of diethyl ether and petroleum ether (3:1) and a slurry of sodium bicarbonate (0.113 mol) in 10–15 mL of water were added, stirred thoroughly with a magnetic stirrer, and cooled at 0 °C.

A solution of 2-naphthoyl chloride (0.034 mol) in 50 mL of diethyl ether was added dropwise over a period of 1 h with constant stirring and keeping the temperature near 0 °C. The reaction mixture was stirred further for 15–20 min. A major amount of the product was separated as a granular white mass during the acylation process. This was separated and reserved. The ethereal mother liquor was concentrated under vacuum at room temperature. An additional 1.2 g of product was obtained. This was combined with the reserved product and triturated with an aqueous suspension of sodium bicarbonate to remove the acidic impurities. The separated solid was filtered off and washed with a little cold water and petroleum ether. Two crystallizations from a mixture of benzene and petroleum ether gave a white crystalline product suitable for analytical work: yield, 5.10 g (67%).

The synthesized hydroxamic acids along with their physical, IR, and UV characteristics are presented in Table I. All the compounds are white except **3** (*N*-benzyl-*o*-nitrobenzohydroxamic acid), which is light yellow. These hydroxamic acids give reddish violet chloroform-extractable complexes with vanadium(V) from hydrochloric acid solutions (2–11 M) and offer potentialities of use for developing spectrophotometric methods of determining vanadium(V). The shifting of ν(O—H) and ν(C=O) bands to the lower frequency region is due to strong intramolecular hydrogen bonding (*5*).

Proton NMR absorptions are summarized in Table II. Infrared bands are marked as follows: vs, very strong; s, strong; m, medium; sb, strong broad; sh, shoulder. Elemental analyses (C, H, N), in agreement with theoretical values, have been obtained.

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Registry No. **1**, 7339-99-3; **2**, 85407-73-4; **3**, 85407-74-5; **4**, 85407-75-6; **5**, 85407-76-7; **6**, 85407-77-8; **7**, 85407-78-9; **8**, 85407-79-0; **9**, 85407-80-3; **10**, 85407-81-4; **11**, 85407-82-5; **12**, 85407-83-6; *o*-chlorobenzoyl chloride, 609-65-4; *o*-nitrobenzyl chloride, 610-14-0; *o*-methoxybenzoyl chloride, 21615-34-9; *p*-bromobenzoyl chloride, 586-75-4; *p*-fluorobenzoyl chloride, 403-43-0; *m*-nitrobenzoyl chloride, 121-90-4; 2-naphthoyl chloride, 2243-83-6; 1,2-dibromocinnamoyl chloride, 85407-84-7; *n*-valeroyl chloride, 638-29-9; pelargonoyl chloride, 764-85-2; stearoyl chloride, 112-76-5; *N*-benzylhydroxylamine, 622-30-0.

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