XII) was allowed to stand at room temperature for 60 days or at 50 °C for 3 days. To the semicrystalline mixture of starting amine and isomeric cycloaddition product was added 1–2 mL of ethanol; the crystalline crop was filtered off and washed with small portions of ethanol. Recrystallization from ethanol gave colorless crystals of XIII–XV (Table II). A typical example is *N*-(*m*-chlorophenyl)-5,7a-epoxy-4H-isoindoline (*XV*): UV λ_{max} (log ϵ) 213 nm (4.31), 259 (4.34), and 308 (3.45). ^{1}H NMR (90 Hz, $CDCl_3$) δ 6.69–6.36 (m, 4 H) for meta-substituted phenyl; 7.24 (d, J = 7.6 Hz, 1 H) and 7.07 (d, J = 7.6 Hz, 1 H) for 6-CH and 7-CH but not specifically one or the other; 5.09 (d, J = 4.4 Hz, 1 H) for bridgehead proton 5-CH; 3.84 and 3.63 (q_{AB}, J = 11.7 Hz, 2 H) for 1-CH_2; 3.74 (t, J = 9.1, 1 H), 2.95 (t, J = 9.1, 1 H), and 2.44–1.37 (m, 3 H) for protons 4-CH_2, 3-CH_2, and 3a-CH but not necessarily respectively.

Picrates XIIIa–XVa. These compounds were prepared by the addition of picric acid in ethanol, followed by recrystallization from appropriate solvent.

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Registry No. I, 95124-20-2; II, 95124-21-3; III, 95124-24-6; IIIa, 95124-60-0; IIIb, 95124-61-1; IIIc, 95124-25-7; IV, 51597-76-3; IVa, 95124-26-8; IVb, 95124-27-9; IVc, 95124-28-0; V, 33829-87-7; Va, 95124-29-1; Vb, 95124-30-4; Vc, 95124-31-5; VI, 95124-32-6; VIa, 95124-33-7; VIb, 95124-34-8; VIc, 95124-35-9; VII, 95124-36-0; VIIa, 95124-37-1; VIIb, 95124-38-2; VIIc, 95155-93-4; VIII, 95124-39-3; VIIIa, 95124-40-6; VIIIb, 95124-41-7; VIIIc, 95124-42-8; IX, 51305-71-6; IXa, 95124-43-9; IXb, 95124-44-0; IXc, 95155-94-5; X, 95124-48-4; X·HI, 95124-45-1; Xa, 95124-51-9; XI, 95124-49-5; XI·HI, 95124-46-2; XIa, 95124-52-0; XII·HI, 95124-47-3; XII, 95124-50-8; XIIa, 95124-53-1; XIII, 95124-54-2; XIIIa, 95124-55-3; XIV, 95124-56-4; XIVa, 95124-57-5; XV, 95124-58-6; XVa, 95124-59-7; *N*-furfurylidene-*p*-chloroaniline, 13533-22-7; *N*-furfurylideneaniline, 61973-96-4; *N*-(5-methylfurfurylidene)-*p*-methylaniline, 95124-22-4; *N*-(5-methylfurfurylidene)-*p*-anisidine, 95124-23-5; *N*-(5-methylfurfurylidene)-*p*-chloroaniline, 51305-59-0; *N*-(*p*-methylphenyl)furfurylamine, 3139-27-3; furfural, 98-01-1; 5-methyl-2-furfural, 620-02-0; *m*-anisidine, 536-90-3; 3-chlorobenzeneamine, 108-42-9; 4-chlorobenzenamine, 106-47-8; benzenamine, 62-53-3; 4-methylbenzenamine, 106-49-0; 4-methoxybenzenamine, 104-94-9; allyl iodide, 556-56-9; phenyl isothiocyanate, 103-72-0.

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Preparation and Properties of *N*-Methyl- and *N*-(4-Chlorophenyl)-Substituted Hydroxamic Acids

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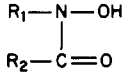
The preparation and properties of several new *N*-methyl- and *N*-(4-chlorophenyl)-substituted hydroxamic acids are described. The proton magnetic resonance and mass spectra of a typical *N*-methyl-substituted hydroxamic acid have also been recorded for characterization.

Hydroxamic acids exhibit biological activity and are used as antitubercular agents (*1*), fungicides (*2*), drugs reducing the cholesterol level (*3*), and antipyretics or analgetics (*4*). In this communication, a number of *N*-(4-chlorophenyl)- and *N*-methyl-substituted hydroxamic acids of the general formula



R_1 = methyl or 4-chlorophenyl

were prepared and characteristized by melting point, elemental analysis, and ultraviolet and infrared spectra. One *N*-methyl-substituted hydroxamic acid was also characterized by ^{1}H NMR and mass-spectral data.

The data on the ^{1}H NMR and mass spectra of a typical compound, *N*-methyl-cinnamohydroxamic acid, are presented in Table I and its ^{1}H NMR spectrum is shown in Figure 1.

Experimental Section

Ultraviolet spectra of hydroxamic acids in 95% ethanol were recorded on a Carl-Zeiss Jena, SPECORD recording spectrophotometer using two 10-mm matched silica cells. Fixed-wavelength measurements for the calculation of molar absorptivity, ϵ, were made with an Electronic Corp. of India, Model GS-865, spectrophotometer. Molar absorptivity is expressed in units of L mol^{-1} cm^{-1}.

Infrared absorption spectra were recorded on a Perkin-Elmer Model 377 spectrophotometer as Nujol mulls. The spectrophotometer was calibrated with polystyrene film.

The ^{1}H NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as internal standard. These were obtained with thanks from Central Drug Research Institute, Lucknow, and their instrument was operated at 90 Hz. Mass spectra were

† This work is part of the Ph.D. Thesis of T.R.C.

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Table I. ^{1}H NMR and Mass-Spectral Data of *N*-Methylcinnamohydroxamic Acid

^{1}H NMR spectra					mass spectra[a]		
chemical shift							
δ	τ	multiplicity	int	assignment	m/e	rel int	σ, %
3.21–3.25	6.79–6.75	doublet	3	*N*-methyl protons	77	319.5	11.77
5.31	4.69	singlet	2	—CH=CH— protons	103	618.1	22.77
6.75–7.60	3.25–2.40	multiplate	5	phenyl ring, protons	131	1000.0	36.83
					161	61.9	2.28
					177	46.3	1.70

[a] Base peak: m/e 131.0.

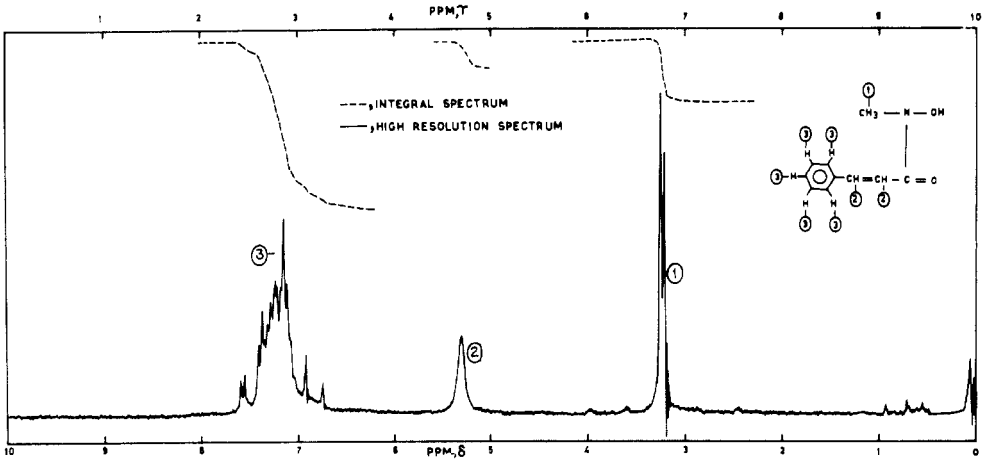


Figure 1. ^{1}H NMR spectrum of *N*-methylcinnamohydroxamic acid in $CDCl_3$.

also recorded at the Central Drug Research Institute, Lucknow.

Acid chlorides were obtained commercially from M/s BDH, M/s Aldrich, and M/s Schuchardt & Co. and were used without further purification. Some of the acid chlorides were prepared by the reaction of thionyl chloride on the corresponding carboxylic acids and were purified by distillation under reduced pressure (*5*).

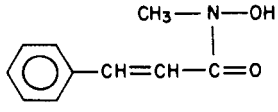
(4-Chlorophenyl)hydroxylamine (*6*, *7*) was freshly prepared and crystallized at least 2 times from a mixture of benzene and petroleum ether before used. The purer the hydroxylamine, the better are the desired hydroxamic acids.

Methylhydroxylamine was prepared by the reported (*8*, *9*) methods. Methylhydroxylamine is a low-melting solid and was used in situ for acylation reaction (*10*).

All *N*-(4-chlorophenyl)-substituted hydroxamic acids were prepared following basically the procedure developed in this laboratory (*11*).

Percentage yields are calculated for once-crystallized products. All of the hydroxamic acids are white and are stable to heat, light, and air.

A typical preparation of *N*-methylcinnamohydroxamic acid is described.



A freshly prepared aqueous solution of methylhydroxylamine, obtained from reducing 8.8 mL (10 g) of nitromethane with zinc dust, and 50 mL of diethyl ether were placed in a 250-mL reaction vessel. Sodium bicarbonate (15 g, 180 mmol) was added and the mixture was kept in an ice bath at 0 °C and stirred vigorously with a magnetic stirrer. A solution of cinnamoyl chloride dissolved in a 50-mL (1:1) mixture of diethyl ether and petroleum ether was added dropwise over 1 h. The absence of free hydroxylamine in the reaction mixture was tested with Tollen's reagent; 11.6 g (70 mmol) of cinnamoyl chloride was consumed in the acylation reaction. Most of the desired hydroxamic acid was precipitated as a faintly yellowish white product and was separated. The product obtained in distillation of the ethereal layer was combined with precipitated product and triturated in a glass mortar with an aqueous saturated solution of sodium bicarbonate for 15 min to remove acidic impurities. After filtration the product was washed with petroleum ether (60–80 °C) to remove the colored impurities and then purified from a mixture of hot benzene and petroleum ether (60–80 °C), yielding 11.7 g (94.8%) of white needles, mp 121 °C.

Melting points and percentage yields of nine other reported hydroxamic acids are as follows: *N*-(4-chlorophenyl)benzohydroxamic acid, 155 °C (reported (*12*) mp 155 °C), 68%; *N*-(4-chlorophenyl)-*o*-fluorobenzohydroxamic acid, 146 °C, 65%; *N*-(4-chlorophenyl)-*m*-fluorobenzohydroxamic acid, 117 °C, 80%; *N*-(4-chlorophenyl)-2,4-dichlorobenzohydroxamic acid, 179 °C, 59%; *N*-(4-chlorophenyl)-3,5-dimethoxybenzohydroxamic acid, 124 °C, 61%; *N*-(4-chlorophenyl)hydrocinnamohydroxamic acid, 134 °C (reported (*13*) mp 137 °C), 55%; *N*-(4-chlorophenyl)-*n*-hexanohydroxamic acid, 102 °C, 71%; *N*-(4-chlorophenyl)palmitohydroxamic acid, 97 °C, 56%; *N*-methyl-*o*-methoxybenzohydroxamic acid, 132 °C (reported (*14*) mp 138.5–139.2 °C), 33%. UV and IR spectral data of a typical compound, *N*-methylcinnamohydroxamic acid, are as follows:

UV spectra		IR spectra, cm^{-1}	
λ_{max}, nm	$10^{-3}\epsilon$	ν(O—H)	ν(C=O)
207	15.3	3120	1633
218	15.0		
224	12.2		
279	21.8		

Lower and longer wavelength ultraviolet absorption bands of the other nine reported compounds vary between 206–210 and 259–276 nm, respectively. Similarly, the infrared stretching frequencies due to O—H and c=O groups of the other nine reported compounds lie in the range of 3120–3230 and 1600–1632 cm^{-1}, respectively. Two additional ultraviolet absorption bands (218 and 224 nm) which appeared in *N*-

methylcinnamohydroxamic acid are absent in the other reported compounds.

Registry No. $C_6H_5CH{=}CHCON(CH_3)OH$, 69227-95-8; $C_6H_5CON(OH)C_6H_4$-4-Cl, 1528-82-1; 2-$FC_6H_4CON(OH)C_6H_4$-4-Cl, 94370-35-1; 3-$FC_6H_4CON(OH)C_6H_4$-4-Cl, 94370-36-2; 2,4-$Cl_2C_6H_3CON(OH)C_6H_4$-4-Cl, 94370-37-3; 3,5-$(CH_3O)_2C_6H_3CON(OH)C_6H_4$-4-Cl, 94370-38-4; $C_6H_5(CH_2)_2CON(OH)C_6H_4$-4-Cl, 94370-39-5; $CH_3(CH_2)_4CON(OH)C_6H_4$-4-Cl, 94370-40-8; $CH_3(CH_2)_{14}CON(OH)C_6H_4$-4-Cl, 94370-41-9; 2-$CH_3OC_6H_4CON(CH_3)OH$, 63977-15-1; CH_3NHOH, 593-77-1; 4-ClC_6H_4NHOH, 823-86-9; $C_6H_5CH{=}CHCOCl$, 102-92-1; C_6H_5COCl, 98-88-4; 2-FC_6H_4COCl, 393-52-2; 3-FC_6H_4COCl, 1711-07-5; 2,4-$Cl_2C_6H_3COCl$, 89-75-8; 3,5-$(CH_3O)_2C_6H_3COCl$, 17213-57-9; $C_6H_5(CH_2)_2COCl$, 645-45-4; $CH_3(CH_2)_4COCl$, 142-61-0; $CH_3(CH_2)_{14}COCl$, 112-67-4; 2-$CH_3OC_6H_4COCl$, 21615-34-9; CH_3NO_2, 75-52-5.

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Synthesis and Spectral Characteristics of *N*-Aryl-Substituted Glycines and Alanines

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A series of *N*-aryl ortho-substituted glycines and alanines, which serve as useful intermediates for the synthesis of N^1-aryl-substituted imidazolidine-2,4-diones and their 2-thioxo analogues, have been prepared and characterized by their infrared and carbon-13 and proton NMR spectra. Except for the naphthyl derivatives, all carbon resonances associated with the aryl moieties have been identified by employing relatively simple procedures. Various substituent effects operative in these compounds have been noted. A suitable procedure for the synthesis of *N*-aryl-substituted alanines is described.

Introduction

In connection with our interest in aryl ortho-substituted heterocyclic ring compounds which could exhibit biphenyl-like isomerism (*1-3*), we recently had need of some α-*N*-aryl ortho-substituted glycines and alanines. These amino acids serve as intermediates for the synthesis of N^1-arylimidazolidine-2,4-diones and their 2-thioxo analogues. In this report we describe the synthesis and the carbon-13 and proton NMR and infrared spectra of *N*-aryl ortho-substituted glycines (Ia-h) and alanines (IIa-g). The method of Eckstein et al. (*4*) was found to be a suitable procedure to produce the requisite glycines in adequate yields. However, the procedure described by Miller and Sharp (*5*) for synthesis of *N*-aryl ortho-substituted alanines was found to be unsatisfactory. A suitable procedure for this purpose is described in the Experimental Section.

$$\mathrm{R\text{-}NH\text{-}\overset{2}{C}H(R')\text{-}\overset{1}{C}OOH}$$

I, R′ = H	II, R′ = CH_3
Ia, R = phenyl	IIa, R = phenyl
Ib, R = 2′-tolyl	IIb, R = 2′-tolyl
Ic, R = 2′-methoxyphenyl	IIc, R = 2′-fluorophenyl
Id, R = 2′-fluorophenyl	IId, R = 2′-chlorophenyl
Ie, R = 2′-chlorophenyl	IIe, R = 2′-bromophenyl
If, R = 2′-bromophenyl	IIf, R = 2′,3′-dimethylphenyl
Ig, R = 2′,3′-dimethylphenyl	IIg, R = 1′-naphthyl
Ih, R = 1′-naphthyl	

Except in the case of 1′-naphthyl derivatives, Ih and IIg, all of the carbon-13 resonances have been identified in their NMR spectra. The assignments to various protons and carbon-13 signals in their proton and carbon spectra, respectively, from glycines and alanines were carried out by comparison of their spectra with those of the corresponding primary amines, by estimation of substituent effects (*6*), and, in a few cases, by off-resonance proton decoupling. Various signals of interest in the proton NMR and IR spectra have also been noted. The chemical shift values for given carbon or proton positions in carbon-13 and proton NMR spectra, respectively, for I and II vary over quite a narrow region, and the ranges for different positions of interest are well separated. There is, thus, no ambiguity in the assignment of signals in the carbon-13 and proton NMR spectra. These spectral data should prove very valuable in identification and characterization of compounds of these types.

Carbon-13 chemical shifts for *N*-aryl-substituted glycines, Ia-h, and alanines, IIa-g, are presented in Tables I and II, respectively. Proton NMR spectral data for these compounds are given in Table III. In the case of 2′-fluorophenyl derivatives, Id and IIc, the ^{13}C-^{19}F spin doublets are observable; the magnitude of the coupling constant, *J*, is useful (*7*) in assignment of various carbon signals in these two compounds. NMR signals associated with C-1′ and C-2′ carbons in the 2′-chlorophenyl derivative, Ie, could not be observed, whereas those in the corresponding alanine derivative, IId, showed resonance signals in the expected regions. The carbon signals in the 1′-naphthyl derivatives, Ih and IIg, have only partially been assigned. C-2 carbons experience a significant (6.6 ± 0.3 ppm) but below normal downfield α-effect upon substitution of a hydrogen atom by a methyl group, whereas the downfield β-substitution effect on the carboxyl carbons (C-1) is less pro-

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