Anal. Calcd. for $C_{11}H_{14}BrN_3O_3S$: C, 37.94; H, 4.06; Br, 22.95; N, 12.07. Found: C, 38.04; H, 4.36; Br, 22.93; N, 12.08.

The yield in a second run using three times the above quantities was 74%. The reaction could also be run in dioxane solution, but the gummy product was difficult to crystallize and purify.

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[CONTRIBUTION FROM THE DEPARTMENT OF PHYSICAL SCIENCES, UNIVERSITY OF IDAHO]

Preparation of Some Alkyl-Substituted Monohydroxamic Acids, *N*-Acyl-*O*-alkylhydroxylamines. I

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In order to initiate a study of the reactions of the alkyl hydroxamates, the preparation of representative benzo-, aniso-, toluo-, aceto-, and propionhydroxamic esters has been carried out by the reaction of sodium and potassium salts of hydroxamic acid with alkyl halides. Several dialkyl hydroxamates were also obtained as by-products in these reactions. The infrared spectra of these compounds were studied and the bands attributed to N—H stretching, C=O stretching, amide II, and C—O stretching were observed.

The preparation of a number of hydroxamic acid esters has been carried out in order subsequently to study their reactions. The reaction of a hydroxamic acid salt with an alkyl halide was used to prepare the hydroxamic acid esters.[2,3]

Esters of aromatic hydroxamic acids were made using a procedure similar to that of Fuller and King,[4] who prepared *n*-butyl benzohydroxamate. Potassium salts of the hydroxamic acids were prepared by the reaction of ethyl esters with hydroxylamine and potassium hydroxide.[5] In this preparation the potassium salt precipitates from methanolic solution. Barium toluhydroxamate was also prepared by the reaction of the mother liquor from the potassium toluhydroxamate preparation with barium chloride. When the potassium or barium salt, sodium carbonate, and a primary alkyl halide in alcohol-water solution were stirred together and warmed, the alkyl hydroxamates were obtained in good yields. A ferric chloride spot test was used to follow the reaction. This color test changed from an initial dark purple to a final pale red during an interval that varied from two days, when the solutions were refluxed, to three weeks, when the solutions were stirred at room temperature.

The aceto- and propionhydroxamic acid esters were prepared in essentially the same manner. Ethyl acetate and ethyl propionate, respectively, were allowed to react with hydroxylamine and sodium methoxide in absolute methanol, and without isolation of the hydroxamic acid salt an alkyl halide, sodium carbonate, and water were added to prepare the hydroxamic ester.

Both the aromatic and aliphatic acid esters were worked up in the same way. The alcohol was removed by distillation from the reaction mixture, and the product was taken up in chloroform. Extraction of the chloroform with sodium bicarbonate removed all unchanged carboxylic acid formed by saponification of the starting material. The hydroxamic ester was extracted from the chloroform with sodium hydroxide. This alkaline solution was acidified and the hydroxamic ester was taken up in chloroform.

Dialkylhydroxamate esters were found in a number of the preparations in the chloroform solutions after they had been extracted with sodium hydroxide. In a few cases these were purified, and in some cases they were found to be intractable oils. We are uncertain of the structures of the dialkylhydroxamates. The several possible isomeric structures are *N*,*O*-dialkylhydroxamates(I) and syn- and anti- forms of the *O*,*O'*-dialkylhydroxamates (II). All of the dialkyl benzohydroxamates

I II

that have been reported in the literature have been assigned structure II.[2,4,6,7] On the other

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TABLE I

HYDROXAMIC ACID ESTERS PREPARED BY THE SAME PROCEDURE USED TO PREPARE ALLYL BENZOHYDROXAMATE

Name	M.P.[a]	Yield,[b] %	Analyses[c]		
Benzyl benzohydroxamate	103–105°	65	Previously reported,[d] m.p. 103°		
Methyl benzohydroxamate	63.5–64.5°	43	Previously reported,[e] m.p. 62°		
			C	H	N
Benzyl *p*-toluhydroxamate	127.5–129.5°	70	74.67	6.27	5.80
			74.86	6.40	5.77
n-Propyl *p*-toluhydroxamate[f]	47–48°	53	68.37	7.82	7.25
			68.53	7.82	7.23
n-Butyl *p*-toluhydroxamate[g]	50.5–51.5°	77	69.54	8.27	6.76
			69.41	8.52	6.96
Allyl anisohydroxamate	52.8–54°	82	63.75	6.32	6.76
			63.86	6.17	6.83
n-Propyl anisohydroxamate	83.5–84°	54	63.14	7.27	6.70
			63.02	6.98	6.95
Propargyl anisohydroxamate	116–116.7°	47	64.37	5.40	6.82
			64.48	5.62	6.60
n-Butyl anisohydroxamate[g]	67–67.8°	64	64.55	7.67	6.27
			64.71	7.72	6.19
Benzyl anisohydroxamate	113–114.5°	45	Previously reported,[h] m.p. 113°		

[a] All melting points are corrected and represent analytical samples. [b] The yields are based on the potassium salts of the hydroxamic acids. [c] The first line values represent calculated values, and the second line the analytical results. [d] See ref. 6. [e] W. Lossen, *Ann.*, **252**, 226 (1889). [f] Also isolated as a crystalline sodium salt during the extraction procedure. [g] These products were purified by vacuum sublimation. [h] W. Lossen, *Ann.*, **281**, 169 (1894).

hand the *N*-alkylation of ethyl ethoxycarbamate has been reported.[8–10]

The unsaturated hydroxamic acid esters, allyl benzohydroxamate and allyl anisohydroxamate, were hydrogenated using a platinum catalyst and low pressure. The resulting *n*-propyl benzohydroxamate and *n*-propyl anisohydroxamate were isolated directly in nearly quantitative yields. Similar results have been reported for the hydrogenation of *cis*-6-cyclopentena(e)tetrahydro-1,2-oxazin-3-one.[11]

EXPERIMENTAL

Allyl benzohydroxamate,[12] *(N-benzoyl-O-allylhydroxylamine), and diallyl benzohydroxamate.* A solution of 87.5 g. (0.50 mole) of potassium benzohydroxamate,[5] 72.5 g. (0.60 mole) of allyl bromide, 25 g. of anhydrous sodium carbonate in 375 ml. of methanol, and 250 ml. of water was stirred for 24 hr. The methanol was removed by distillation and the residue was acidified with 12*N* hydrochloric acid. The crude product was taken up in four 100-ml. portions of chloroform and was washed with 10% sodium bicarbonate. The allyl benzohydroxamate was extracted from the chloroform with six 50-ml. portions of 6*N* sodium hydroxide. Diallyl benzohydroxamate remained in the chloroform. The combined sodium hydroxide extracts were acidified with 12*N* hydrochloric acid and the aqueous solution was extracted with four 50-ml. portions of chloroform. The chloroform was removed by distillation and the residue which slowly solidified upon cooling to room temperature was recrystallized from ether and petroleum ether (b.p. 30–60°) mixture. The yield was 63.2 g. (68%), m.p. 62–63.5°. Two more recrystallizations gave 55.1 g. (59%) of pure allyl benzohydroxamate m.p. 62.5–63.5°,[13] reported[12] m.p. 58°. ν_{N-H} 3160 in Nujol, 3370, 3200 in chloroform, 3400, 3200 in potassium bromide; $\nu_{C=O}$ 1640 in Nujol, 1660 in chloroform, 1640 in potassium bromide; $\nu_{Amide\ II}$ 1500; ν_{C-O} 1300 cm^{-1}.

Anal. Calcd. for $C_{10}H_{11}NO_2$: C, 67.81; H, 6.26; N, 7.91. Found: C, 67.82; H, 6.22; N, 7.68.

A yield of 5 g. (5%) of diallyl benzohydroxamate, b.p. 101.5–102° at 0.6 mm., n_D^{20} 1.5312 was also obtained. ν_{C-H} 3120, 3040, 3010, 2950; $\nu_{C=O}$ 1660, ν_{C-O} 1270 $cm.^{-1}$ on pure liquid.

Anal. Calcd. for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.72; H, 6.85; N, 6.34.

Propargyl p-toluhydroxamate (N-p-methylbenzoyl-O-propargylhydroxylamine). When 110 g. (0.25 mole) of barium *p*-toluhydroxamate, 30 g. of sodium carbonate, 375 ml. of methanol, 250 ml. of water, and 68 ml. (104 g., 0.87 mole) of propargyl bromide were stirred together, 6 days were required for a ferric chloride test for hydroxamic acid to become very weak. The methanol was removed under reduced pressure, and the remaining mixture was acidified with 12*N* hydrochloric acid. A solid precipitated and was removed by filtration. Extraction of the organic material from this precipitate with acetone, and distillation of the acetone gave 69.0 g. of solid product. An additional 2 g. of product was obtained by extraction of the water solution with chloroform. The overall yield was 71 g. (75%). Two recrystallizations of 10 g. of this crude product from benzene gave 7.2 g. (55%) of pure ester, which was vacuum sublimed, m.p. 101.5–102.5°. ν_{N-H} 3450, 3350; ν_{C-H} 3300; $\nu_{C=O}$ 1675; $\nu_{Amide\ II}$ 1510; ν_{C-O} 1300 $cm.^{-1}$ in chloroform.

Anal. Calcd. for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 70.05; H, 6.07; N, 7.35.

Allyl *p*-toluhydroxamate (*N*-*p*-methylbenzoyl-*O*-allylhydroxylamine) was prepared from barium toluhydroxamate in 74% yield, b.p. 138° at 0.2 mm., $n_D^{21.5}$ 1.5531. ν_{N-H}

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(13) All melting points were determined in capillaries in an electrically heated aluminum block with a calibrated thermometer.

TABLE II

HYDROXAMIC ESTERS PREPARED BY THE SAME PROCEDURE USED TO PREPARE BENZYL ACETOHYDROXAMATE

Name	M.P., B.P.	n^t_D	Yield,[a] %	Analyses[b] C	H	N
Allyl acetohydroxamate	19–21°[c] 80/1 mm.	1.4619 (23°)	24	52.15	7.88	12.17
				51.49	7.70	12.05
Diallyl acetohydroxamate	93°/14 mm.	1.4586 (23°)	10	61.91	8.44	9.03
				61.66	8.39	8.97
n-Propyl acetohydroxamate	72°/0.5 mm.	1.4403 (24°)	34	51.26	9.47	11.96
				51.24	9.35	12.05
p-Nitrobenzyl acetohydroxamate	133.5–134°[d]		31	51.43	4.80	13.33
				51.88	4.93	13.41
Allyl propionhydroxamate[e]	11°[c] 74.5–76°/ 1 mm.	1.4618 (17.5°)	36	55.79	8.59	10.85
				55.54	8.37	10.95
Ethyl benzohydroxamate	63–64.2°		28.5	Previously reported,[f] m.p. 64–65°		

[a] The yields are based on hydroxylamine and the products were distilled once. [b] The first line values represent calculated values and the second line the analytical results. [c] These melting points are not exact. [d] This melting point is correct and represents an analytical sample. [e] A crude yield of diallyl propionhydroxamate of 11% was also obtained in this preparation. [f] W. Lossen, *Ber.*, **24**, 4059 (1891).

3220, $\nu_{C=O}$ 1650, $\nu_{Amide\ II}$ 1500, ν_{C-O} 1310 cm.$^{-1}$ on the pure liquid.

Anal. Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.28; H, 7.09; N, 7.12.

Benzyl acetohydroxamate (N-acetyl-O-benzylhydroxylamine) and dibenzyl acetohydroxamate. Sodium (23 g., 1 g.-atom) was dissolved in 600 ml. of absolute methanol, and a solution of 34.75 g. (0.50 mole) of hydroxylamine hydrochloride in 500 ml. of absolute methanol was added to the sodium methoxide solution during a half hour period. The mixture was stirred during the addition and then chilled for 15 min. in an ice bath. Ethyl acetate (44 g., 0.50 mole) was added and the sodium chloride was removed by pumping the solution under 2 p.s.i. of nitrogen through a sintered glass funnel. Three days later 750 ml. of methanol was removed by distillation, and 100 ml. of water, 20 g. of anhydrous sodium carbonate, and 75.5 g. (0.60 mole) of benzyl chloride were added. To obtain a negative ferric chloride test it was necessary to stir this mixture for 2 days, and then reflux it briefly. The remaining methanol was removed by distillation, and the residue was acidified with 12*N* hydrochloric acid. The aqueous solution was extracted with four 100-ml. portions of chloroform. The combined chloroform extracts were washed with two 100-ml. portions of 5% sodium bicarbonate. The weakly acidic hydroxamic acid ester was extracted into two 100-ml. portions of 20% sodium hydroxide while the neutral dialkyl hydroxamic acid ester remained in the chloroform solution. Removal of the chloroform and distillation of the product gave 10 g. (9%) of dibenzyl acetohydroxamate, b.p. 135–138° at 0.04 mm., m.p. 53–56°, which was recrystallized from ether-petroleum ether (b.p. 30–60°), m.p. 56–57°. $\nu_{C=O}$ 1670, ν_{C-O} 1260 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.26; H, 6.71; N, 5.49. Found: C, 74.92; H, 6.56; N, 5.72.

The combined sodium hydroxide extracts were acidified with 12*N* hydrochloric acid, and the monoalkyl hydroxamate was taken up in two 100-ml. portions of chloroform. Removal of the chloroform and distillation of the resulting oil gave 58.7 g. (71%) of benzyl acetohydroxamate b.p. 124° at 0.07 mm., m.p. 46–48°, n^{28}_D 1.5343 on the supercooled liquid. ν_{N-H} 3200, $\nu_{C=O}$ 1670, $\nu_{Amide\ II}$ 1500, ν_{C-O} 1290 cm.$^{-1}$ on the supercooled liquid.

Anal. Calcd. for $C_9H_{11}NO_2$: C, 65.43; H, 6.71; N, 8.48. Found: C, 65.59; H, 6.75; N, 8.19.

n-Propyl benzohydroxamate (N-benzoyl-O-n-propylhydroxylamine). Platinum oxide (0.1 g.) was added to 7.4 g. (0.041 mole) of allyl benzohydroxamate dissolved in 10 ml. of 95% ethanol and the mixture was shaken with 2 atm. of hydrogen in a Parr apparatus. Approximately 3.25 p.s.i. (0.038 mole) of hydrogen was taken up over a 6-hr. period. The catalyst was removed by filtration, and the ethanol was removed by distillation leaving 7.0 g. (93%) of a white solid. Recrystallization of this solid from ether–petroleum ether (b.p. 30–60°) gave a pure product m.p. 58–59°, mixed melting point with allyl benzohydroxamate 45–50°. Vacuum sublimation did not change the melting point. ν_{N-H} 3200, $\nu_{C=O}$ 1645, $\nu_{Amide\ II}$ 1520, ν_{C-O} 1300 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{10}H_{13}NO_2$: C, 67.01; H, 7.31; N, 7.82. Found: C, 67.11; H, 7.26; N, 7.65.

n-Propyl anisohydroxamate was also prepared by hydrogenation of allyl anisohydroxamate under these same conditions in 91% yield.

Infrared spectra. The following characteristic absorption peaks were observed in the infrared spectra of the *N*-acyl-*O*-alkylhydroxylamines reported here: In chloroform solution ν_{N-H} 3450–3400 and 3300–3230, $\nu_{C=O}$ 1675–1660 and with the solid in Nujol or KBr ν_{N-H} 3220–3160, $\nu_{C=O}$ 1655–1630 cm.$^{-1}$ were observed. A weak band at 1530–1500 cm.$^{-1}$ appeared in all spectra and was considered to be similar to the amide II band appearing in monosubstituted amides. The exact location of this absorption in the spectra of compounds which also contained an aromatic ring is uncertain. Four bands appeared in these spectra between 1600 and 1480 cm^{-1}. Three of these bands can be attributed to the aromatic ring and the other to Amide II. The band chosen as the amide II band most nearly resembled in shape, location, and intensity the single band which appeared in this region with the aliphatic analogues. A comparison of the alkyl hydroxamates reported here with *cis*-6-cyclopentena(e)-tetrahydro-1,2-oxazin-3-one[11] is interesting. The amide II absorption is absent from the latter compound and thus affords a parallel to the monosubstituted amide lactam case. A weak band at 1270–1310 cm.$^{-1}$ attributed to C—O stretching also appeared. In the spectra of the dialkyl hydroxamates as pure liquids $\nu_{C=O}$ 1660–1670 and ν_{C-O} 1270–1250 cm.$^{-1}$ both strong bands were observed.

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