those nmr peaks most essential to the structure proof. Dimer **11** had a molecular ion at *m/e* 320 in its mass spectrum.

Registry No.—Lithium, 7439-93-2; **1b**, 2521-13-3; **3b**, 17052-38-9; **5a**, 120-72-9; **6a**, 26686-10-2; **6b**, 17052-39-0; **6c**, 26686-12-4; **6d**, 26573-83-1; **6d** acetate, 26686-14-6; **7a**, 5263-87-6; **7b**, 91-22-5; **8a**, 17052-40-3; **8b**, 26686-17-9; **8b** picrate, 17052-42-5; **9** picrate, 17052-41-4; **11**, 18995-96-5.

Acknowledgment.—We wish to thank Mr. L. Brancone and staff for microanalyses and Mr. W. Fulmor and staff for spectra.

Alkylation of Benzohydroxamic Acid[1]

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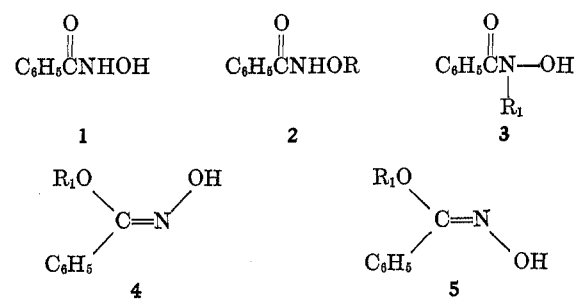
The alkylation behavior of the potassium and silver salts of alkyl benzohydroxamates **2** has been investigated. The structures of the alkylation products were determined by comparison of their nmr spectra and vpc retention times with independently synthesized compounds: ethyl *N*-ethylbenzohydroxamate (**6a**), the *Z* and *E* isomers of ethyl *O*-ethylbenzohydroximate (**7a** and **8a**), *n*-propyl *N*-*n*-propylbenzohydroxamate (**6b**), the *Z* and *E* isomers of ethyl *O*-*n*-propylbenzohydroximate (**7e** and **8e**), the *Z* and *E* isomers of *n*-propyl *O*-isopropylbenzohydroximate (**7f** and **8f**), *n*-propyl *N*-benzylbenzohydroxamate (**6h**), and the *Z* and *E* isomers of benzyl *O*-*n*-propylbenzohydroximate (**7h** and **8h**). Alkylation of the potassium salts of **2** with primary alkyl halides in methanol–water solutions gives mixtures of **6** (major product) and **7** (minor product). Isopropyl halides lead to mixtures of **6** and **7** in which **7** predominates. Oxygen alkylation of the potassium salts is increased considerably in dimethyl sulfoxide or dimethylformamide. Alkylation of potassium benzohydroxamate with 1,2-dibromoethane, 1,3-dibromopropane, and 1,4-dibromobutane gives cyclized products **16**, **17**, and **18**, respectively. Heterogeneous reactions of the silver salts of **2** with alkyl halides in anhydrous ether give mixtures of **7** and **8**. Alkyl iodides give mainly (*Z*)-hydroximates (**7**), whereas alkyl bromides favor hydroximates with the *E* configuration (**8**). The amount of the *Z* isomer increases when dimethylformamide is used as the solvent. The configuration of the products from the reactions of alkylbenzohydroximoyl chlorides (**19**) with sodium alkoxides were determined. In all of the reactions investigated only the *Z* isomers (**7**) of the hydroximates are formed. The alkylbenzohydroximoyl chlorides are prepared by the reaction of **2** with phosphorus pentachloride. Mechanisms for the alkylation reactions are discussed.

In connection with another study currently being carried out in our laboratory we have found it necessary to investigate methods of synthesizing and identifying the geometrical isomers of alkyl *O*-alkylbenzohydroximates[3] (**7** and **8**). The most direct route to these compounds appeared to be alkylation of alkyl benzohydroxamates **2**. Recent reports[4-6] on the alkylation of benzohydroxamates prompts us to describe our observations concerning alkylations of the ambident anions derived from this class of compounds.

Benzohydroxamic acid **1** offers three sites for alkylation: the hydroxylamine oxygen, the nitrogen, and the carbonyl oxygen. The four possible monoalkylation products are an alkyl benzohydroxamate **2**, an *N*-alkylbenzohydroxamic acid **3**, and the *Z* and *E* isomers of an alkyl benzohydroximate (**4** and **5**, respectively).[7]

Extensive study has shown that the monoalkylation of the potassium salt of benzohydroxamic acid results in the exclusive or preferential formation of a hydroxamate **2**.[8,9]



a, R or R_1 = C_2H_5
b, R = *n*-C_3H_7
c, R_1 = *i*-C_3H_7
d, R = *n*-C_4H_9
e, R_1 = $CH_2C_6H_5$

The dialkylation of **1** or the monoalkylation of **2** could give rise to an alkyl *N*-alkylbenzohydroxamate (**6**), an alkyl (*Z*)-*O*-alkylbenzohydroximate (**7**), or an alkyl (*E*)-*O*-alkylbenzohydroximate (**8**). In all of the earlier investigations the alkylation of either **1** or **2** has been reported to give exclusively an alkyl *O*-alkylbenzohy-

(1) A preliminary communication of this work, was presented at the Southwest Regional Meeting of the American Chemical Society, Little Rock, Ark., Dec 7, 1967, Abstracts p 61A.

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(3) We have named the compounds described in this paper as derivatives of benzohydroxamic acid, $C_6H_5C(=O)NHOH$, and its tautomer benzohydroximic acid, $C_6H_5C(OH)=N—OH$. Compounds substituted with alkyl or acyl groups on the hydroxylamine oxygen of benzohydroxamic acid are named alkyl or acyl benzohydroxamates. Substitution on the nitrogen is denoted with the prefix *N*-alkyl. A compound with alkyl substitution on the C–OH of benzohydroximic acid is named an alkyl benzohydroximate and substitution on the oxime oxygen is designated with the prefix *O*-alkyl.

(4) M. Chehata, F. Bocabeille, G. Thuillier, and P. Rumpf, *C. R. Acad. Sci., Ser. C*, **268**, 445 (1969).

(5) R. Blaser, P. Imfeld, and O. Schindler, *Helv. Chim. Acta*, **52**, 569 (1969).

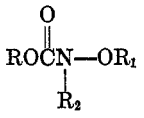
(6) O. Exner and O. Schindler, *ibid.*, **52**, 577 (1969).

(7) In the past the configurational descriptors syn and anti have been used to designate the two geometrical isomers of alkyl benzohydroximates and their derivatives. However, in the older reports[10,21,22] a different convention was used than that proposed more recently by Exner.[19] To avoid confusion we will designate these isomers using the configurational descriptors *Z* and *E*. The rules which permit unambiguous description of double bond stereoisomerism in terms of the descriptors *Z* and *E* have been reported by J. E. Blackwood, G. L. Gladys, K. L. Loening, A. E. Petrarca, and J. E. Rush, *J. Amer. Chem. Soc.*, **90**, 509 (1968).

(8) P. A. S. Smith, "The Chemistry of Open-Chain Organic Nitrogen Compounds," Vol. II, W. A. Benjamin, New York, N. Y., 1966, pp 68–98.

(9) J. H. Cooley, W. D. Bills, and J. R. Throckmorton, *J. Org. Chem.*, **25**, 1734 (1960).

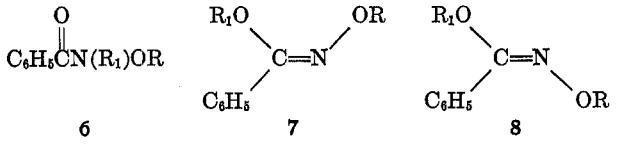
droximate (7 or 8).[8,10-17] No experimental evidence was presented in these reports for the existence of the two geometrical isomers of the alkyl *O*-alkylbenzohydroximates.[18] In contrast, alkyl alkoxyformohydroxamates (9, R_2 = H) have been reported to alkylate primarily on nitrogen.[8]



9a, R = C_2H_5; R_1 = R_2 = H
b, R = R_1 = R_2 = C_2H_5
c, R = C_2H_5; R_1 = R_2 = *n*-C_3H_7

Results

In order to study the alkylation reactions of benzohydroxamic acid, it was desirable to synthesize model compounds so that correlations of nmr spectra and vpc retention times with the structures of the alkylation products could be established. Since a considerable



6 **7** **8**

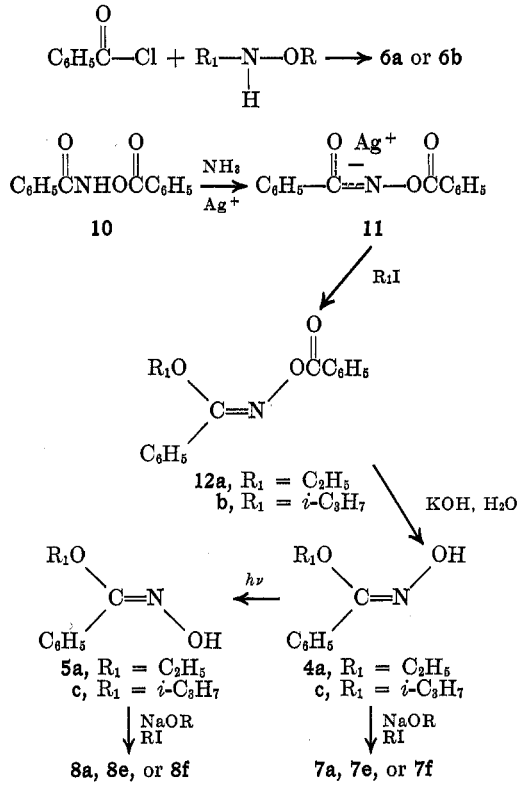
a, R = R_1 = C_2H_5
b, R = R_1 = *n*-C_3H_7
c, R = R_1 = *n*-C_4H_9
d, R = *n*-C_3H_7; R_1 = CH_3
e, R = *n*-C_3H_7; R_1 = C_2H_5
f, R = *n*-C_3H_7; R_1 = *i*-C_3H_7
g, R = *n*-C_3H_7; R_1 = allyl
h, R = *n*-C_3H_7, R_1 = $CH_2C_6H_5$
i, R = R_1 = $CH_2C_6H_5$

amount of work has been published concerning the geometrical isomers of ethyl benzohydroximate (**4a** and **5a**), the first compounds to be independently synthesized in this study were the three diethylated isomers of benzohydroxamic acid (**6a**, **7a**, and **8a**).

The synthesis of ethyl *N*-ethylbenzohydroxamate (**6a**) was accomplished by reacting benzoyl chloride with *O*,*N*-diethylhydroxylamine (Scheme I). The *O*,*N*-diethylhydroxylamine was prepared by diethylation of ethoxyformohydroxamic acid (**9a**) followed by acid hydrolysis.

The *Z* and *E* isomers of ethyl *O*-ethylbenzohydroximate (**7a** and **8a**) were synthesized according to the procedure outlined in Scheme I. Exner, Jehlička, and Reiser[19] have reported the preparation and separation of the ethyl benzohydroximates **4a** and **5a**, but we have found it more convenient to synthesize these isomers by a modification of the older procedure reported by

SCHEME I



Gurke.[20] Benzoyl benzohydroxamate (**10**) was converted into its silver salt **11** and then alkylated with ethyl iodide to produce the *Z* isomer of ethyl benzoylbenzohydroximate (**12a**) along with a small amount of the *E* isomer. Basic hydrolysis of the crude alkylation product gave mainly ethyl (*Z*)-benzohydroximate (**4a**). Alkylation of **4a** with ethyl iodide and sodium ethoxide resulted in the formation of ethyl (*Z*)-*O*-ethylbenzohydroximate (**7a**).

Since **5a** was produced in the hydrolysis of crude **12a** in low yield, isolation of **5a** was not attempted on this sample. Instead the crude hydrolysis product was enriched in the *E* isomer by uv irradiation before attempting the separation. Column chromatography of the irradiated sample afforded pure ethyl (*E*)-benzohydroximate (**5a**) which was alkylated to give ethyl (*E*)-*O*-ethylbenzohydroximate (**8a**).

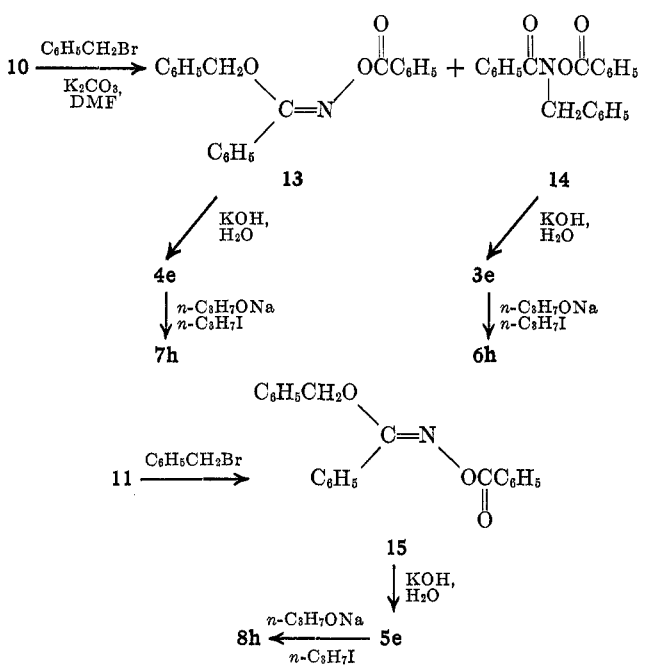
The unambiguity of the syntheses of the authentic samples of the *Z* and *E* isomers of ethyl *O*-ethylbenzohydroximate depends on accurate knowledge of the stereochemistry of their precursors, **4a** and **5a**. Werner[21,22] first reported evidence concerning the stereochemistry of these compounds. He subjected the two isomers to Beckmann rearrangement conditions (phosphorus pentachloride in ether) and found that the isomer with mp 53.5° gave, after hydrolysis, *N*-phenylurethane, whereas the other isomer with mp 67.5–68° did not rearrange and afforded only a phosphate ester after hydrolysis. Werner drew the wrong conclusion concerning the configurations of these compounds since at the time of his work the Beckmann rearrangement was thought to involve migration of the group syn to the

(10) "Beilsteins Handbuch der Organischen Chemie," Vol. IX, Verlag von Julius Springer, Berlin, 1926, pp 309–313.
(11) H. L. Yale, *Chem. Rev.*, **33**, 209 (1944).
(12) A. T. Fuller and H. King, *J. Chem. Soc.*, 963 (1947).
(13) W. Lossen, *Justus Liebigs Ann. Chem.*, **252**, 170 (1889).
(14) W. Lossen, *Ber.*, **24**, 4059 (1891).
(15) M. E. Waldstein, *Justus Liebigs Ann. Chem.*, **181**, 384 (1876).
(16) There have also been several reports of alkylations of the salts of acyl benzohydroxamates to give alkyl *O*-acylbenzohydroximates: (a) W. Lossen, *ibid.*, **281**, 169 (1894); (b) A. Werner and J. Subak, *Ber.*, **29**, 1153 (1896); (c) see also ref 13, 20, and 39.
(17) Cooley, Bill, and Throckmorton[9] have reported a few dialkylated hydroxamic acids but did not assign structures to the compounds.
(18) In the recent literature[5] the synthesis of the *Z* and *E* isomers of methyl *O*-carbethoxymethylbenzohydroximate and some of its derivatives have been reported.
(19) O. Exner, V. Jehlička, and A. Reiser, *Collect. Czech. Chem. Commun.*, **24**, 3207 (1959).
(20) O. Gurke, *Justus Liebigs Ann. Chem.*, **205**, 273 (1880).
(21) A. Werner, *Ber.*, **25**, 27 (1892).
(22) A. Werner, *ibid.*, **26**, 1561 (1893).

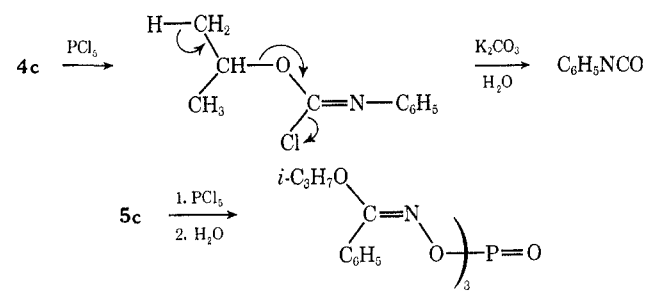
hydroxyl groups. It is now known,[23] of course, that the group anti to the hydroxyl group migrates to nitrogen. One would now conclude that the ethyl benzohydroximate with mp 53.5° has the *Z* configuration (**4a**) and the isomer with mp 67.5–68° has the *E* configuration (**5a**). This conclusion has been substantiated by cyroscopic[24] and dipole moment[19,25] measurements of these two isomers.

Eight additional model compounds were synthesized according to the methods outlined in Scheme I (**6b**, **7e**, **8e**, **7f**, and **8f**) and Scheme II (**6h**, **7h**, and **8h**). The procedures used for the synthesis (Scheme II) of the three isomers **13**, **14**, and **15** depend on the variations of product distribution with changes in the alkylation reaction conditions of benzoyl benzohydroxamate (**10**). Admittedly these procedures were developed in the later stages of this study and were based on the results obtained with alkyl benzohydroxamates.

SCHEME II



The *Z* and *E* isomers of isopropyl benzohydroximate (**4c** and **5c**) have not been previously reported. In order to establish the configurations of these compounds, they were reacted with phosphorus pentachloride in ether. One isomer (**5c**, assigned the *E* configuration) did not undergo a Beckmann rearrangement and was converted into a phosphate ester. The other isomer (**4c**, assigned the *Z* configuration) gave phenyl isocyanate which probably arose by elimination of the isopropyl group from the Beckmann rearrangement product.



The stereochemical assignments[26] for the isomers of benzyl benzohydroximate (**4e** and **5e**) are based on their melting points by comparison to the melting points of the isomeric pairs **4a**–**5a** and **4c**–**5c** and other hydroximates of known configuration.[27] It is assumed that the *Z* isomer **4e** has a lower melting point than the corresponding *E* isomer **5e**. This difference in melting point behavior presumably is due to intramolecular hydrogen bonding in the (*Z*)-hydroximates *vs.* intermolecular hydrogen bonding in the *E* isomers.

The nmr spectra of the isomers **6**, **7**, and **8** differ mainly in the chemical shifts of the methylene hydrogens attached to the nitrogen and oxygen atoms of these molecules. From the nmr spectra of the model compounds the following generalizations have been made. (1) The chemical shift of the $NOCH_2$ hydrogens of the *Z* isomer of an alkyl *O*-alkylbenzohydroximate occurs further downfield than the chemical shift for the $NOCH_2$ hydrogens of the *E* isomer. Similarly, the chemical shift of the $COCH_2$ hydrogens of the *Z* isomer occurs further downfield than the $COCH_2$ hydrogens of the *E* isomer. (2) The chemical shift of the $NOCH_2$ and $COCH_2$ hydrogens of the *E* isomer of an alky *O*-alkylbenzohydroximate occurs further downfield than the $NOCH_2$ and NCH_2 hydrogens of an alkyl *N*-alkylbenzohydroxamate.

In addition, on the basis of the results obtained with the model compounds, it has been concluded that the alkylated isomers elute from a vpc column of 20% SE-30 in the following order: alkyl (*E*)-*O*-alkylbenzohydroximate (shortest retention time), alkyl (*Z*)-*O*-alkylbenzohydroximate, and alkyl *N*-alkylbenzohydroxamate (longest retention time).

Chemical shift data for the methylene hydrogens attached to nitrogen or oxygen atoms in the dialkylated hydroxamic acids prepared in this investigation are located in Tables I and II.

Having established methods for determining the product distributions, a systematic study of the alkylation of the salts of alkyl benzohydroxamates was undertaken. The first alkylation reactions investigated were carried out on the potassium salts of alkyl benzohydroxamates. These salts were not isolated but generated *in situ* by adding potassium carbonate to aqueous-methanol solutions of the hydroxamates. The results of this study are summarized in Tables III and IV. The most obvious consequence of this study is that the reaction of the potassium salts of alkyl benzohydroxamates with primary alkyl bromides gives primarily products resulting from alkylation on nitrogen rather than oxygen as previously reported. This is in accord with the recent findings of Chehata, *et al.*[4,28] Furthermore, we have found that the minor product in the reac-

(23) N. V. Sidgwick, I. T. Millar, and H. D. Springall, "The Organic Chemistry of Nitrogen," 3rd ed, Clarendon Press, Oxford, 1966, pp 316–333.

(24) H.-C. Yuan and K.-C. Hua, *J. Chin. Chem. Soc.* (*Taipei*), **7**, 76 (1940).

(25) O. Exner, *Collect. Czech. Chem. Commun.*, **30**, 652 (1965).

(26) Both stereoisomers of benzyl benzohydroximate gave the same major product (by tlc and nmr) when reacted with phosphorus pentachloride. No attempt was made to identify this product.

(27) The configurations of three other pairs of hydroximate isomers have been determined: methyl benzohydroximate[5] (*Z* mp 44°, *E* mp 52–53°), ethyl *p*-nitrobenzohydroximate[19] (*Z* mp 95°, *E* mp 141°), and ethyl *p*-methylbenzohydroximate[24] (*Z* mp 35.5–36°, *E* mp 101.5–102°).

(28) The reaction conditions employed by Chehata, Bocabeille, Thuillier, and Rumpf[4] are somewhat different from ours. They reacted benzyl benzohydroxamate with alkyl iodides in a solution of sodium ethoxide in absolute ethanol.

TABLE I
NMR SPECTRAL DATA FOR BENZOHYDROXIMATES[a]

Compd	Chemical shift, δ, ppm (multiplicity, J in Hz) =NOCH₂–	=COCH₂
7a[b]	4.11 (q, 7)	4.35 (q, 7)
8a[b]	4.05 (q, 7)	4.18 (q, 7)
7b	4.05 (t, 6.5)	4.24 (t, 6.5)
8b	3.92 (t, 6.5)	4.08 (t, 6.5)
7c	4.08 (t, 6)	4.26 (t, 6)
8c	3.97 (t, 6)	4.13 (t, 6)
7d	4.05 (t, 6.5)	3.96 (CH_3, s)
8d	3.93 (t, 6.5)	3.81 (CH_3, s)
7e	4.05 (t, 6.5)	4.33 (q, 7)
8e	3.93 (t, 6.5)	4.17 (q, 7)
7f	4.05 (t, 6.5)	4.98 (CH, septet, 6)
8f	3.92 (t, 6.5)	5.00 (CH, septet, 6)
8g	3.96 (t, 6.5)	*ca.* 4.69 (m)
7h	4.07 (t, 6.5)	5.31 (s)
8h	3.96 (t, 6.5)	5.17 (s)

[a] Unless otherwise noted all spectra were determined in $CDCl_3$ with tetramethylsilane as an internal standard. [b] Determined on the neat liquid.

TABLE II
NMR SPECTRAL DATA FOR BENZOHYDROXAMATES[a]

Compd	Chemical shift, δ, ppm (multiplicity, J in Hz) NCH_2–	OCH_2–
6a[b]	3.71 (q, 7)	3.68 (q, 7)
6b	3.72 (t, 7)	3.63 (t, 6.5)
6c	3.75 (t, 6.5)	3.67 (t, 6)
6d	3.34 (CH_3, s)	3.65 (t, 6)
6e	3.76 (q, 7)	3.65 (t, 6.5)
6f	*ca.* 4.52 (CH, m)	3.70 (t, 6)
6g	*ca.* 4.31 (m)	3.63 (t, 6)
6h	4.92 (s)	3.56 (t, 6)
6i	4.67 (s)	4.49 (s)

[a] Unless otherwise noted all spectra were determined in $CDCl_3$ with tetramethylsilane as an internal standard. [b] Determined on the neat liquid.

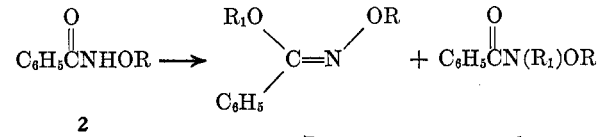
tions with primary alkyl bromides is in all cases studied the *Z* isomer of an alkyl *O*-alkylbenzohydroximate.

We have repeated the two potassium salt reactions described in the older literature. Lossen[13,14] reported that ethyl *O*-ethylbenzohydroximate was the only product from the reaction of ethyl benzohydroxamate with ethyl iodide in an aqueous ethanol solution of potassium hydroxide. We have found that this reaction actually results in the exclusive formation of the *N*-alkylated isomer, **6a**.

Fuller and King[12] have reported that the alkylation of potassium benzohydroxamate with *n*-butyl bromide in a mixture of ethanol and potassium carbonate forms *n*-butyl benzohydroxamate (**2d**) in 33% yield and *n*-butyl *O*-*n*-butylbenzohydroximate (**7c** or **8c**) in 24% yield. In our hands this alkylation gave 43% yield of the monoalkylated product, **2d**, along with an 8% yield of the (*Z*)-hydroximate, **7c**, and a 17% yield of the hydroxamate, **6c**. Fuller and King[29] based their structure assignment for the dialkylated product on a hydrolysis experiment from which they isolated *O*-*n*-butylhydroxylamine hydrochloride. Apparently they isolated only one of the hydrochlorides and overlooked the *O*,*N*-di-*n*-butylhydroxylamine hydrochloride which was probably present in their hydrolysis mixture.

(29) The per cent yields reported in this work are based on vpc analyses of the crude products whereas the yields reported by Fuller and King[12] were of distilled samples.

TABLE III
EFFECT OF THE ALKYLATING AGENT ON THE ALKYLATION PRODUCTS OF THE POTASSIUM SALTS OF ALKYL BENZOHYDROXAMATES[a]



2 7 6

Alkylating agent	R	Crude yield, %	Product distribution, % 7	6
Ethyl bromide	C_2H_5	48	23	77
n-Butyl bromide	*n*-C_4H_9	21	28	72
Methyl iodide	*n*-C_3H_7	91	3	97
Ethyl bromide	*n*-C_3H_7	56	25 (26)	75 (74)
Ethyl iodide	*n*-C_3H_7	78	20 (19)	80 (81)
Diethyl sulfate[b]	*n*-C_3H_7	83	49 (48)	51 (52)
n-Propyl bromide	*n*-C_3H_7	29	26 (28)	74 (72)
n-Propyl iodide	*n*-C_3H_7	31	20 (18)	80 (82)
Isopropyl bromide	*n*-C_3H_7	19	78	22
Isopropyl iodide	*n*-C_3H_7	22	63	37
Allyl chloride	*n*-C_3H_7	47	25	75
Allyl bromide	*n*-C_3H_7	62	19	81
Allyl iodide	*n*-C_3H_7	66	9	91
Benzyl bromide[d]	*n*-C_3H_7	51[c]	15	85

[a] These reactions were carried out using mole ratios of 1:2:1.6 of alkyl benzohydroxamate to alkyl halide to potassium carbonate. The reactions were all run at 38° for 15 hr using methanol–water (1.45:1) as the solvent. The crude yields and product distributions were determined by vpc analyses of the crude products. Numbers in parentheses represent product distributions obtained in duplicate runs. [b] This reaction was carried out in anhydrous ether and was heterogeneous. [c] Per cent yield based on distilled product. [d] Product distribution determined by integration of benzyl hydrogens in nmr spectrum of crude product.

The product distributions for the potassium salt reactions appear to be sensitive to the structure of the alkyl bromide. A small increase in the amount of oxygen alkylation was observed with increase in the length of the straight chain of the primary alkyl bromide, but, more dramatically, isopropyl halides gave more alkylation on oxygen than on nitrogen.

The leaving group may have an effect on the product distribution in the potassium salt reactions as evidenced by the large increase in oxygen alkylation when diethyl sulfate was used as the alkylating agent. However, this reaction cannot be compared to the other potassium salt reactions since it was a heterogeneous reaction carried out in anhydrous ether.

We have considered the possibility that the predominance of nitrogen alkylation in the reactions with primary alkyl halides is due to rearrangement of one or both of the oxygen alkylated isomers. This was of particular concern since rearrangements of this type are known, albeit at elevated temperature.[30] We have subjected mixtures of the oxygen alkylated isomers **7b** and **8b** to the potassium salt reaction conditions and have found no rearrangement to the nitrogen alkylated isomer, **6b**, or for that matter we observed no change in the ratio of the geometrical isomers. We therefore conclude that these isomers are formed irreversibly and that no interconversion between the isomers occurs during the alkylation reactions.

(30) J. W. Schulenberg and S. Archer, *Org. React.*, **14**, 24 (1965).

TABLE IV
EFFECT OF TEMPERATURE, REACTION TIME, SOLVENT, AND CONCENTRATION OF ALKYL BROMIDE ON THE PRODUCT DISTRIBUTIONS IN THE POTASSIUM SALT REACTIONS OF BENZOHYDROXAMIC ACID AND ALKYL BENZOHYDROXAMATES[a]

Hydroxamate	Alkyl bromide	Mole ratio of hydroxamate to alkyl bromide	Reaction time, hr	Temp, °C	Crude yield of dialkylated isomers, %	Product distribution, % 7	6
PhCONHOK	n-C_3H_7	1:3	15	38	29	28	72
PhCONHOK	n-C_3H_7	1:3	15	48	30	23	77
PhCONHOK	n-C_3H_7	1:3	15	58	63	27	73
2b	n-C_3H_7	1:2	15	38	29	28	72
2b	n-C_3H_7	1:2	15	48	58	31	69
2b	n-C_3H_7	1:2	15	58	76	34	66
2b	n-C_3H_7	1:1	15	58	47	34	66
2b	n-C_3H_7	1:3	15	58	77	33	67
2b	n-C_3H_7[b]	1:2	15	58	91	66	34
2b	n-C_3H_7[c]	1:2	15	58	88	63	37
2d	n-C_4H_9	1:2	10	58	62	34	66
2d	n-C_4H_9	1:2	15	58	68	33	67
2d	n-C_4H_9	1:2	20	58	5	33	67
2b	i-C_3H_7	1:2	15	38	19	78	22
2b	i-C_3H_7	1:2	15	58	45	73	27
2b	i-C_3H_7[c]	1:2	15	58	94	92	8

[a] These reactions were carried out using a mole ratio of 1:1.6 of alkyl benzohydroxamate to potassium carbonate or a mole ratio of 1:2 of potassium benzohydroxamate to potassium carbonate. Methanol–water (1.45:1) was used as a solvent except when otherwise noted. [b] In dimethyl sulfoxide solvent. [c] In dimethylformamide solvent.

The effects of temperature, concentration of alkylating agent, and reaction time on the product distributions in the potassium salt reactions (Table IV) have been studied. Although the product distributions changed only slightly with these variables the product yields underwent considerable change. Our data shows that optimum conditions for the potassium salt reactions are a temperature of 58°, a reaction time of 15 hr, and a 2:1 ratio of alkyl bromide to alkyl benzohydroxamate.

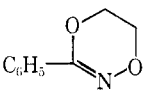
The synthesis of dialkylated hydroxamates, where both alkyl groups are the same, can be carried out starting with potassium benzohydroxamate and adding enough alkyl halide to achieve dialkylation. This method has the obvious advantage of eliminating an isolation step. The product distributions for these reactions are in Table V.

TABLE V
PRODUCTS OF THE REACTION OF POTASSIUM BENZOHYDROXAMATE WITH ALKYL BROMIDES[a]

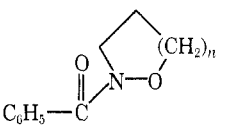
Alkyl bromide	Crude yield of alkyl benzohydroxamate **2**, %	Crude yield of dialkylated products **7** and **6**, %	Dialkylation product distribution, % **7**	**6**
C_2H_5	34	33	20	80
n-C_3H_7	62	23	21	79
n-C_4H_9	60	10	32	68
$C_6H_5CH_2$[b]	...[c]	47		100[d]

[a] These reactions were carried out using mole ratios of 1:3:2 of potassium benzohydroxamate to alkyl bromide to potassium carbonate. The reactions were run at 38° for 15 hr and methanol–water (1.45:1) was used as the solvent. The crude yields and distributions of the dialkylated products were determined by vpc analyses of the crude products. [b] This reaction was refluxed for 15 hr. [c] The amount of benzyl benzohydroxamate produced in this reaction was not determined. [d] Tlc analysis of the crude product showed that it contained only one isomer which was assumed to be **6i**.

When potassium benzohydroxamate was allowed to react with dibromides cyclized products were obtained. 1,4-Dibromobutane and 1,3-dibromopropane reacted at nitrogen and the hydroxylamine oxygen to give 2-benzoyltetrahydro-1,2-oxazine (**18**) and 2-benzoyloxazolidine (**17**), respectively. Cyclization with 1,2-dibromoethane led to the formation of 3-phenyl-5*H*-1,4,2-dioxazine (**16**). The structures of these compounds were determined by comparison of their nmr, uv, and ir spectra with the spectra of the model compounds described earlier.



16



17, $n = 1$
18, $n = 2$

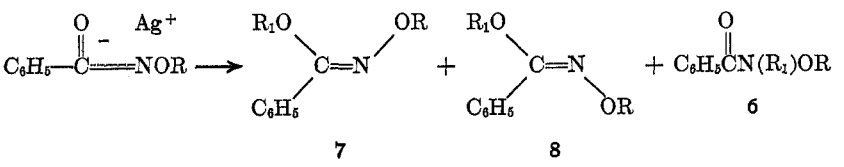
Table VI summarizes data on the product distributions observed for alkylations of the silver salts of alkyl benzohydroxamates. All reactions listed in this table were heterogeneous and conducted in anhydrous solvents under comparable reaction conditions. It is clear that alkylation occurs on oxygen in preference to nitrogen in these reactions. In addition, the halogen of the alkyl halide has a significant effect on the stereochemistry of the product. Whereas alkyl iodides afford mainly (*Z*)-hydroximates, alkyl bromides favor hydroximates with the *E* configuration. It should also be noted that there is a substantial difference in the rate of the silver salt alkylations depending on the kind of halogen of the alkyl halide. Alkylations with alkyl iodides are complete in about 3 days, but most of the alkyl bromide reactions require a reaction time of approximately 7 days. Several experiments were carried out to ensure that the observed product distributions did not result from isomerization.

The literature[31] contains another general method for the preparation of alkyl *O*-alkylbenzohydroximates. This procedure (Scheme III) involves the preparation of

(31) F. Tieman and P. Kruger, *Ber.*, **18**, 727 (1885).

TABLE VI

EFFECT OF THE ALKYLATING AGENT ON THE ALKYLATION PRODUCTS OF THE SILVER SALTS OF ALKYL BENZOHYDROXAMATES[a]



7 8

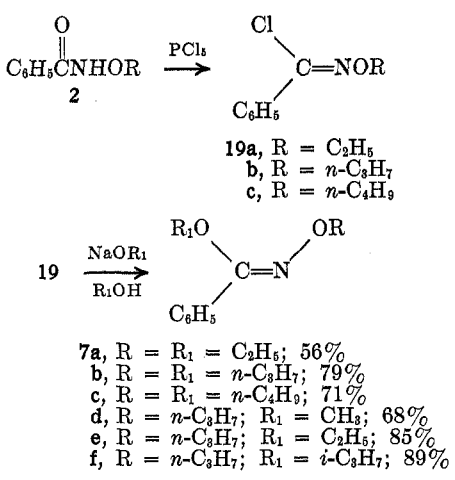
Alkyl halide	R	Crude yield, %	Product distribution, % 7	8	6
Methyl iodide[b]	n-C_3H_7	71	42 (41)	20 (21)	38 (38)
Ethyl bromide	n-C_3H_7	69	23 (23)	74 (74)	3 (3)
Ethyl iodide	n-C_3H_7	81	69 (71)	23 (21)	8 (8)
n-Propyl bromide	n-C_3H_7	22	30 (31)	67 (66)	3 (3)
n-Propyl iodide	n-C_3H_7	67	70	22	8
Isopropyl bromide	n-C_3H_7	72	22	76	2
Isopropyl iodide	n-C_3H_7	66	72	26	2
Allyl bromide	n-C_3H_7	83	9	75	16
Allyl iodide	n-C_3H_7	72	32	38	30
Benzyl bromide[c]	n-C_3H_7	63	20	71	9
Benzyl iodide[c]	n-C_3H_7	100	27	28	45
Ethyl bromide[d]	C_2H_5	49	32	61	7
Ethyl iodide[d]	C_2H_5	54	81	18	1
n-Butyl iodide[d]	n-C_4H_9	50	62	35	3
Ethyl iodide[e]	n-C_3H_7	60	83	8	9
Allyl bromide[e]	n-C_3H_7	68	38	40	22
Benzyl bromide[c,e]	n-C_3H_7	65	42	33	25
Benzyl iodide[c,e]	n-C_3H_7	73	55	13	32

[a] These reactions were carried out using a mole ratio of 1:1.9 of the silver salt of the alkyl benzohydroxamate to the alkyl halide. The reactions were run at room temperature for 7 days. Anhydrous ether was used as the solvent unless otherwise noted and all of the reactions were heterogeneous. The crude yields and product distributions were determined by vpc analyses of the crude products. Numbers in parentheses represent product distributions obtained in duplicate runs. [b] The distribution of isomers as determined from integration of the nmr spectrum of the crude product was 41% **7**, 22% **8**, and 37% **6**. [c] The relative amounts of the isomers were determined from the nmr spectra by integration of the benzyl hydrogens. [d] The silver salts used in these reactions were prepared by reaction of the alkyl benzohydroxamate with silver nitrate and sodium hydroxide rather than ammonium hydroxide. [e] Reaction solvent was dimethylformamide.

an alkylbenzohydroximoyl chloride (**19**)[32] by the reaction of an alkyl benzohydroxamate (**2**) with phosphorus pentachloride followed by the reaction of **19** with a sodium alkoxide.[33] In all of the reactions that we have carried out only the Z isomers (**4**)[34] of the hydroximates were formed.

During the course of this investigation it was necessary to isolate pure samples of **6** and **8** from mixtures containing two (**6** and **7**) or three (**6**, **7**, and **8**) of the isomers. Though pure samples of the (E)-hydroximates (**8**) had to be obtained from these mixtures by preparative vpc, a more convenient method has been developed for preparing pure samples of **6**. This procedure depends on the greater hydrolysis rate (acid catalyzed) of the hydroximates compared to the hydroxamates. Treatment of the mixtures of **6**, **7**, and **8** with warm concentrated hydrochloric acid for short periods caused hydrolysis of **7** and **8** leaving relatively pure **6** which could be further purified by distillation.

SCHEME III



19a, R = C_2H_5
b, R = n-C_3H_7
c, R = n-C_4H_9

7a, R = R_1 = C_2H_5; 56%
b, R = R_1 = n-C_3H_7; 79%
c, R = R_1 = n-C_4H_9; 71%
d, R = n-C_3H_7; R_1 = CH_3; 68%
e, R = n-C_3H_7; R_1 = C_2H_5; 85%
f, R = n-C_3H_7; R_1 = i-C_3H_7; 89%

Discussion

The most interesting result of our alkylation studies was the observation of changes in the distribution of the stereoisomeric benzohydroximates with changes in cation, solvent, and alkylating agent. We believe that two competing factors are important in determining the stereochemistry of the hydroximates. One factor we have considered is the relative stability of the two geometrical isomers. From examination of the structures of the stereoisomeric benzohydroximates it would appear that in all cases the Z isomer is more stable than

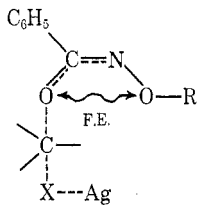
(32) The vapor phase chromatograms and nmr spectra of these compounds show that only one isomer is formed in the reaction of **2** with PCl_5. Work is currently in progress on the determination of the configurations of these compounds.

(33) The reaction to obtain **7d** from **19b** was carried out at 55° with dimethyl sulfoxide as a solvent.

(34) Less than 2% of the E isomer was formed in each of these reactions with the exception of the preparation of **7d** in which 4% E isomer was obtained.

the E isomer. This is based solely on the obvious difference in steric interactions between the E and Z isomers where the N-alkoxy group is interacting with either a phenyl group or the smaller alkoxy group. Clearly, the magnitude of this effect will depend upon the degree of carbon–nitrogen double bond character in the transition state.

A second factor that we have considered is a repulsive field effect (F.E) between the two oxygen atoms in the transition state. The importance of this effect should



change with variations in the magnitude of the negative charge on the carbonyl oxygen in the transition state.

It seems reasonable that bond formation between the silver ion and the halogen of the alkyl halide is further advanced in the case of an alkyl iodide transition state than a corresponding alkyl bromide reaction. This would be expected since silver ion is a soft Lewis acid and should react more readily with iodide which is a softer base than bromide.[35] As a consequence of more advanced silver–halogen bond formation, the incipient carbon–nitrogen double bond may also be further advanced in the alkyl iodide transition states as compared to the alkyl bromides. In addition, the developing bond between the carbonyl oxygen and the carbon atom of the alkylating agent should be formed to a greater extent in the iodide reactions. Accordingly, the carbonyl oxygen should carry a larger negative charge in the alkyl bromide reactions than in reactions with alkyl iodides.

In the alkyl bromide reactions, the repulsive field effect would become negligible if the hydroxylamine oxygen assumed a position opposite to the carbonyl oxygen in the transition state. Obviously, this transition state would lead to the E isomer. It is possible that the repulsive field effect in the alkyl bromide reactions outweighs the stability factor causing a predominance of the E isomer. In the alkyl iodide reactions the stability factor is more important resulting in the formation of the Z isomer.

The hydroximates formed in the potassium salt reactions[36] in all cases studied have the Z configuration. It is conceivable that the charge on the carbonyl oxygen in the transition state is dispersed by the solvent molecules thus diminishing the field effect. However, this explanation would lead to the conclusion that dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) are effective in dispersing the charge on the carbonyl oxygen since in these solvents only the Z isomers of the hydroximates are obtained. This does not seem to be a plausible conclusion because DMF and DMSO, while being very effective at solvating cations, are relatively ineffective at solvating anions.[37] We propose instead that the lack of a significant field effect in the potassium salt reactions is due to the inherent charge dispersal of a pure or nearly pure SN2 reaction. In other words the potassium salt reactions are typical SN2 reactions with considerable dispersal of the negative charge in the transition state. The field effect, therefore, is important only in those reactions where bond cleavage and bond formation are not completely synchronous. This would be the case in the silver salt reactions where cleavage of the carbon–halogen bond is ahead of carbon–oxygen bond formation.

When DMF was used as the solvent in the silver salt alkylations a significant decrease in the amount of the E isomer was observed. It seems likely that in DMF the silver ion is at least partially solvated. This should diminish the effect of the silver ion on the reaction and impart more SN2 character to the transition state. The decrease in the field effect in DMF is thus due to an increase in the SN2 character of the alkylation transition state.

(35) R. G. Pearson and J. Songstad, *J. Amer. Chem. Soc.*, **89**, 1827 (1967).

(36) The mechanisms of alkali metal–ambident anion alkylations have been reviewed: R. Gomper, *Angew. Chem., Int. Ed. Engl.*, **3**, 560 (1964).

(37) (a) N. Kornblum, R. Seltzer, and P. Haberfield, *J. Amer. Chem. Soc.*, **85**, 1148 (1963); (b) E. M. Kosower, "Physical Organic Chemistry," Wiley, New York, N. Y., 1968, pp 334–342.

Experimental Section

Melting points are corrected and were determined on a Thomas–Hoover capillary melting point apparatus. All the boiling points are uncorrected. Magnesium sulfate was employed as a drying agent for ether extracts. The petroleum ether used throughout this work had a boiling point of 30–60°. The thin layer chromatograms were carried out on Mallinckrodt's SilicAR TLC-7GF adsorbent using chloroform–petroleum ether (1:1) as the solvent. The infrared spectra were determined with a Beckman Model IR-20 infrared recording spectrophotometer. The ultraviolet spectra were determined with a Beckman recording spectrophotometer, Model DK-2A. The nmr spectra were determined at 60 Mc with a Varian Model A-60A nmr spectrometer. The chemical shifts are expressed in δ values relative to a tetramethylsilane internal standard. The vapor phase chromatograms were determined with a Beckman Model GC-5 fitted with a Disc Integrator. The chromatograms were obtained with a column (6 ft × 0.25 in.) consisting of 20% silicone gum rubber (SE-30) on 60–70 mesh diatomaceous earth (Anolabs' Anakrom SD) at a column temperature of 200° and a flow rate of 60 ml of He/min. The microanalyses were performed by John R. Springfield of this laboratory using an F & M Scientific Model 185 Carbon, Hydrogen, and Nitrogen Analyzer. The properties for most of the compounds prepared in this work are in Table VII. One example of each type of alkylation procedure is described in this section.

Silver Salt of Benzoyl Benzohydroxamate (11).—A procedure for the preparation of this salt has been reported previously by Lossen.[38] In Lossen's procedure sodium hydroxide was used as the base. A solution of silver nitrate (40.0 g) in distilled water (34 ml) was added to a warm (40°) solution of benzoyl benzohydroxamate (55.5 g) in methanol (860 ml). Concentrated ammonium hydroxide (16 ml) was then added to the vigorously stirred reaction mixture. The precipitate which formed was filtered, washed thoroughly with acetone, and dried in a vacuum desiccator to give 72.4 g (90%) of a white powder.

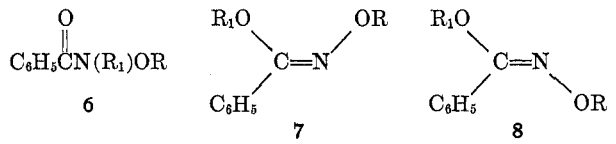
Anal. Calcd for $C_{14}H_{10}NO_3Ag$: C, 48.30; H, 2.90; N, 4.02. Found: C, 47.91; H, 2.80; N, 3.99.

Ethyl (*Z*)-*O*-Benzoylbenzohydroximate (12).—The reaction was carried out according to a procedure described by Eiseler.[39] A mixture of ethyl iodide (39.0 g), the silver salt of benzoyl benzohydroxamate (87.0 g), and anhydrous ether (500 ml) was stirred at room temperature for 3 days. The insoluble salts were removed by filtration and the ether was evaporated from the filtrate. The residual oil solidified upon standing to give 58.4 g (88%) of white crystals, mp 45–48°. The tlc of this crude product showed one major spot (Z isomer) along with one small spot (E isomer). Several recrystallizations of the crude product from large volumes of petroleum ether gave white needles, mp 58.5–59° (lit.[20,39] mp 58°). The tlc of the recrystallized product showed only one spot due to the Z isomer: ir (Nujol) 1750 (m,

(38) W. Lossen, *Justus Liebigs Ann. Chem.*, **161**, 347 (1880).

(39) E. Eisler, *ibid.*, **175**, 326 (1875).

TABLE VII
PROPERTIES OF DIALKYLATED BENZOHYDROXAMIC ACIDS[a]



6 7 8

R	R1	Compd no.	Bp (mm) or mp, °C	Method of preparation[b]
n-C_3H_7	n-C_3H_7	**8b**		G
n-C_4H_9	n-C_4H_9	**6c**		G
n-C_4H_9	n-C_4H_9	**7c**	129–134 (0.4)	A
n-C_4H_9	n-C_4H_9	**8c**		G
n-C_3H_7	CH_3	**6d**	108–109 (0.4)	E
n-C_3H_7	CH_3	**7d**	85–87 (0.5)	A
n-C_3H_7	CH_3	**8d**		G
n-C_3H_7	C_2H_5	**6e**	126–129 (1.2)	E
n-C_3H_7	C_2H_5	**7e**	86–87 (0.4)	A and B
n-C_3H_7	C_2H_5	**8e**	83–84 (0.5)	C
n-C_3H_7	i-C_3H_7	**7f**	78–79 (0.2)	A and B
n-C_3H_7	i-C_3H_7	**8f**	89–97 (0.5)	C
n-C_3H_7	Allyl	**6g**		G
n-C_3H_7	Allyl	**8g**		G
n-C_3H_7	Benzyl	**6h**	145–147 (0.13)	D
n-C_3H_7	Benzyl	**7h**	151–159 (0.5)	B
n-C_3H_7	Benzyl	**8h**	135–139 (0.15)	C
Benzyl	Benzyl	**6i**	66–67[c]	F

[a] Satisfactory analytical values (±0.30% for C, H, and N) were reported for all compounds in this table: Ed. [b] Pure samples (95% or better by vpc) prepared by distillation (or recrystallization) of samples obtained from reactions of the following types: A, benzohydroximoyl chloride with a sodium alkoxide; B, alkylation of alkyl (*Z*)-benzohydroximate; C, alkylation of alkyl (*E*)-benzohydroximate; D, alkylation of *N*-alkylbenzohydroxamic acid; E, selective hydrolysis of *Z* and *E* hydroximates in a mixture containing **6**, **7**, and **8** or **6** and **7**. Those samples labeled with a G were obtained by preparative vpc of an alkylation reaction mixture. [c] Reported: mp 66° [R. Behrend and K. Leuchs, *Justus Liebigs Ann. Chem.*, **257**, 203 (1890)], 65–66° [R. Kothe, *ibid.*, **266**, 310 (1891)], 65° (ref 4).

C=O), 1615 (m, C=N), 1610 (m, aromatic), 1580 cm^{-1} (w, aromatic).

Ethyl (*Z*)-Benzohydroximate (4a).—The procedure was that of Gurke,[20] with minor modifications. Crude ethyl (*Z*)-*O*-benzoylbenzohydroximate (58.4 g) was dissolved in a solution of potassium hydroxide (28 g) and water (300 ml) and the mixture was stirred and refluxed for 12 hr. Carbon dioxide was then bubbled through the solution until it became cloudy and an oil separated. The mixture was extracted with ether (four 75-ml portions) and the combined ether extracts were dried and evaporated to give an oil that crystallized upon standing at room temperature (27.5 g, 77%), mp 49–50°. The tlc of the crude product showed one major spot (*Z* isomer) along with one small spot (*E* isomer) with a higher R_f value. Three recrystallizations from petroleum ether followed by sublimation yielded white crystals that showed only one spot on tlc: mp 53–53.5° (lit. mp 53.5°,[20] 53°[19]); uv max (95% ethanol) 248 mμ (log ε 4.00); ir (Nujol) 3140 (s, broad, OH), 1630 cm^{-1} (s, C=N); nmr ($CDCl_3$) δ 1.33 (t, 3, J = 7 Hz, OCH_2CH_3), 4.31 (q, 2, J = 7 Hz, OCH_2CH_3), 7.2–8.0 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_9H_{11}NO_2$: C, 65.45; H, 6.71; N, 8.48. Found: C, 65.86; H, 6.70; N, 8.59.

Ethyl (*E*)-Benzohydroximdate (5a).—A solution of crude ethyl (*Z*)-benzohydroximate (89.5 g) in dry benzene (500 ml) was irradiated for 2 hr at 70° with a Hanovia 450-W high-pressure lamp contained in a quartz water-cooled immersion apparatus (Ace Glass Inc., Vineland, N. J.). Subsequent evaporation of the benzene at aspirator pressure yielded an oily residue that solidified upon cooling. This solid was dissolved in hot petroleum ether and the solution was allowed to cool slowly to room temperature. During the cooling, a dark viscous red oil separated and was removed by decantation. The decantation was repeated several times until the red oil no longer appeared. The solution was then kept at room temperature until crystals (79.2 g, 90%) were obtained, mp 32–36°. The tlc of this material showed two spots with the largest spot corresponding to the *E* isomer.

Column chromatography on silica gel (250 g, 100–200 mesh) of 8.10 g of product using chloroform–petroleum ether (25:75) as the eluting solvent gave **ethyl (*E*)-benzohydroximate** (6.15 g, 68%), mp 61–66°, and ethyl (*Z*)-benzohydroximate (1.75 g, 19%), mp 39–45°. The *E* isomer eluted from the column before the *Z* isomer. Recrystallization of the crude **5a** from petroleum ether gave colorless needles that showed only one spot on tlc: mp 67–67.5° (lit.[19,20] mp 67.5–68°); uv 248 mμ (log ε 3.72); ir (Nujol) 3160 (s, broad, OH), 1650 (s, C=N), 1600 cm^{-1} (w, aromatic); nmr ($CDCl_3$) δ 1.32 (t, 3, J = 7 Hz, OCH_2CH_3), 4.15 (q, 2, J = 7 Hz, OCH_2CH_3), 7.2–8.1 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_9H_{11}NO_2$: C, 65.45; H, 6.71; N, 8.48. Found: C, 65.73; H, 6.67; N, 8.47.

Ethyl (*E*)-*O*-Ethylbenzohydroximate (8a).—Ethyl (*E*)-benzohydroximate (5.00 g) and ethyl iodide (4.06 g) were added to a solution of sodium ethoxide that had been prepared by adding sodium (0.59 g-atom) to absolute ethanol (50 ml). The resulting solution was heated to 45° and stirred for 72 hr after which time it was found to be acidic to litmus. The ethanol was evaporated at reduced pressure and the residue was triturated with chloroform (100 ml) and filtered. The chloroform filtrate was evaporated at reduced pressure and the residue was distilled to yield a colorless oil, bp 79–80° (0.1 mm). Vpc analysis of the distilled product showed that it was mainly **ethyl (*E*)-*O*-ethylbenzohydroximate** (3.74 g, 75%) contaminated with ethyl benzoate (0.06 g, 2%), ethyl (*Z*)-*O*-ethylbenzohydroximate (0.06 g, 2%), and a mixture of the *E* and *Z* isomers of ethyl benzohydroximate (0.29 g, 7%). A pure sample of **8a** was obtained by preparative vpc:[40] uv max (95% ethanol) 256 mμ (log ε 3.70); ir (neat) 1620 cm^{-1} (m, C=N); nmr (neat) δ 1.22 (t, J = 7 Hz, $COCH_2CH_3$), 1.26 (t, J = 7 Hz, $NOCH_2CH_3$), the signals between 1.0 and 1.5 integrated for a total of 6 H, 4.05 (q, J = 7 Hz, $COCH_2CH_3$), 4.18 (q, J = 7 Hz, $NOCH_2CH_3$), the signals between 3.8 and 4.5 integrate for a total of 4 H, 7.1–8.2 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.59; H, 7.83; N, 7.32.

Ethyl (*Z*)-*O*-Ethylbenzohydroximate (7a).—Ethyl (*Z*)-benzohydroximate (5.00 g) and ethyl iodide (5.46 g) were added to a solution of sodium ethoxide prepared from 0.81 g of sodium and 50 ml of ethanol. The solution was heated to 45° and stirred for 48 hr after which time it was found to be acidic to litmus. Compound **7a** (4.27 g, 73%), bp 80–81° (0.1 mm), was isolated as described above: uv max (95% ethanol) 256 mμ (log ε 4.01); ir (neat) 1615 (s, C=N), 1580 cm^{-1} (m, aromatic); nmr (neat) δ 1.25 (t, 6, J = 7 Hz, $NOCH_2CH_3$ and $COCH_2CH_3$), 4.11 (t, J = 7 Hz, $COCH_2CH_3$), 4.35 (t, J = 7 Hz, $NOCH_2CH_3$), the signals between 3.9 and 4.6 integrate for a total of 4 H, 7.1–8.0 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.59; H, 7.89; N, 7.38.

Ethyl *N*-Ethylethoxyformohydroxamate (9b).—The procedure was similar to that reported by Major and Fleck.[41] A 20% solution of potassium hydroxide (300 ml) was slowly added to a vigorously stirred solution of ethoxyformohydroxamic acid[12] (50.0 g) and ethyl sulfate (164 g). The mixture was stirred for 3 hr and then acidified with dilute sulfuric acid using congo red paper as an indicator. The mixture was extracted with ether (four 100-ml portions) and the combined ether extracts were washed with 3 *N* sodium hydroxide solution (five 50-ml portions), dried, and evaporated at aspirator pressure. The residue was distilled to yield a colorless oil (48.4 g, 75%), bp 91–98° (34 mm) [lit.[41] 56%, bp 107–112° (70 mm)].

Ethyl *N*-Ethylbenzohydroxamate (6a).—Ethyl *N*-ethylethoxyformohydroxamate (48.4 g) was added to a cold solution (10°) of potassium hydroxide (50.5 g) in 50% ethanol (117 ml). The solution was allowed to warm to room temperature, refluxed for 1 hr, and then distilled at atmospheric pressure. All of the distillate up to 83° was cooled in an ice bath and acidified with cold 12 *N* hydrochloric acid. After the acidified solution had warmed

(40) The preparative vpc was carried out using a Varian Aerograph Autoprep Model 705 with a column (20 ft × 3/8 in.) consisting of 30% silicone gum rubber (SE-30) on 45–60 mesh diatomaceous earth. The column temperature for the chromatography was 200° with nitrogen flow of approximately 300 ml/min.

(41) R. T. Major and E. E. Fleck, *J. Amer. Chem. Soc.*, **50**, 147 (1928).

to room temperature, it was concentrated on a hot plate, cooled in an ice bath, and then made basic to litmus with a concd. solution of potassium hydroxide.

One-half of the above solution (which was assumed to contain 13.4 g of *O,N*-diethylhydroxylamine) was added to benzoyl chloride that had been cooled in an ice bath. During the addition, the reaction was stirred and cooled in an ice bath so that the reaction temperature did not rise above 10°. Potassium carbonate was added during the course of the addition in order to maintain a solution that was basic to litmus. After all the *O,N*-diethylhydroxylamine solution had been added, the reaction mixture was allowed to warm to room temperature and then stirred for 6 hr. After acidification with 12 *N* hydrochloric acid, the material was extracted with ether (six 50-ml portions), the combined extracts were dried, and the solvent was removed at aspirator pressure. Distillation of the residue gave **6a** (12.6 g, 100%) as a colorless oil, bp 75–87° (0.1 mm) (lit.[18] bp 267°); the uv spectrum did not show a maximum but rather an increasing end absorption which had a log ϵ of 3.52 at 256 mμ; ir (neat) δ 0.90 (t, J = 7 Hz, NCH_2CH_3), 1.17 (t, J = 7 Hz, OCH_2CH_3), the signals between 0.70 and 1.40 integrate for a total of 6 H, 3.68 (q, J = 7 Hz, NCH_2CH_3), 3.71 (q, J = 7 Hz, OCH_2CH_3), the signals between 3.3 and 4.0 integrate for a total of 4 H, 7.1–7.9 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.14; H, 7.65; N, 7.33.

***n*-Propyl *N*-*n*-Propylethoxyformohydroxamate (9c).**—The reaction was carried out by the procedure described for **9b** except that *n*-propyl bromide was used as the alkylating agent. A 37% yield of **6c** was obtained: bp 75–83° (0.2 mm); ir (neat) 1700 cm^{-1} (s, C=O); nmr ($CDCl_3$) δ 0.7–1.9 (m, 13, $OCH_2CH_2CH_3$, $NCH_2CH_2CH_3$ and OCH_2CH_3), 3.40 (t, J = 7 Hz, 2, $NCH_2CH_2CH_3$), 3.78 (t, J = 6 Hz, 2, $OCH_2CH_2CH_3$), 4.11 (q, J = 7 Hz, 2, OCH_2CH_3).

Anal. Calcd for $C_9H_{19}NO_3$: C, 57.12; H, 10.11. Found:[42] C, 56.86; H, 10.15.

***n*-Propyl *N*-*n*-Propylbenzohydroxamate (6b).**—A solution of *O,N*-di-*n*-propylhydroxylamine was prepared by the procedure described above for **3a**. The reaction of the *O,N*-di-*n*-propylhydroxylamine solution with benzoyl chloride gave **6b** in 100% yield: bp 93–97° (0.2 mm); ir (neat) 1645 cm^{-1} (s, C=O); nmr $CDCl_3$ δ 0.5–2.1 (m, 10, $OCH_2CH_2CH_3$ and $NCH_2CH_2CH_3$), 3.63 (t, J = 6.5 Hz, $OCH_2CH_2CH_3$), 3.72 (t, J = 7 Hz, $NCH_2CH_2CH_3$), the signals between 3.4 and 3.9 integrate for a total 4 H, 7.1–7.8 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.55; H, 8.65; N, 6.33. Found: C, 70.62; H, 8.43; N, 6.24.

Benzyl (*E*)-*O*-Benzoylbenzohydroximate (15).—A mixture of benzyl bromide (35.0 g), the silver salt of benzoyl benzohydroxamate (65.0 g), and anhydrous ether (140 ml) was stirred at room temperature for 3 days. When the ether was evaporated from the filtrate of this mixture, an oil (44.7 g) was obtained. The nmr spectrum of this oil indicated that it was a mixture of the isomers **15** (56%), **13** (17%), and **14** (27%). The oil was dissolved in ether–petroleum ether and kept in a freezer for 1 day. This resulted in the formation of an oil along with some crystalline solid. The crystals were collected and recrystallized from ether to yield 19.7 g (32%) of **15**, mp 83–86°. One recrystallization from methanol and two from ether–petroleum ether afforded an analytical sample: mp 86–88°; ir (Nujol) 1730 (s, C=O), 1620 (m, C=N), 1600 (m, aromatic), 1580 cm^{-1} (w, aromatic); nmr ($CDCl_3$) δ 5.48 (s, 2, CH_2), 7.1–8.1 (m, 15, aromatic **H**).

Anal. Calcd for $C_{21}H_{17}NO_3$: C, 76.12; H, 5.17; N, 4.23. Found: C, 75.87; H, 5.05; N, 4.14.

In several other similar reactions crystallization of the crude oil from ether–petroleum ether did not give pure **15**, but rather a mixture of **15** and **14**. However, it has been found that it is possible to hydrolyze a mixture of **15** and **14** and obtain pure **5e** (see next experiment).

Benzyl (*E*)-Benzohydroximate (5e).—A crystalline mixture (33.4 g) of **15** and **14** in a 73:27 ratio (by nmr) was added to a solution of potassium hydroxide (16.7 g) and water (25 ml) and the mixture was stirred and refluxed for 10 min. Water (40 ml) was added and the solution was extracted with ether (two 100-ml portions). The ether extracts were dried and evaporated to give **4e** (14.3 g, 85% based on the amount of **15** in the starting mixture), mp 127–133°. One recrystallization from methanol and one from benzene yielded a microcrystalline powder: mp 132–134°; ir (Nujol) 3270 (m, broad, OH), 1650 (m, C=N), 1600 cm^{-1} (w, aromatic); nmr ($CDCl_3$) δ 5.19 (s, 2 H, CH_2), 7.1–8.1 (m, 11 H, aromatic **H** and **OH**).

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.97; H, 5.62; N, 6.28.

Benzyl (*Z*)-*O*-Benzoylbenzohydroximate (13) and Benzoyl *N*-Benzoylbenzohydroxamate (14).—A mixture of benzoyl benzohydroxamate (58.0 g), benzyl bromide (60.0 g), anhydrous potassium carbonate (48 g), and dimethylformamide (250 ml) was stirred at 42° for 1 day (an initial exothermic reaction was controlled by cooling with an ice bath). The mixture was diluted with water (1 l.) and then extracted with chloroform (two 100-ml portions). The chloroform extracts were washed with water (three 500-ml portions), dried, and evaporated. An nmr spectrum of the oil residue (70.1 g) indicated that it consisted of **13** (23%) and **14** (77%). The oil was dissolved in ether (100 ml) and placed in a freezer overnight which resulted in the formation of 55.3 g (69%) of **14**, mp 83–89°. Two recrystallizations from chloroform–petroleum ether gave white prisms: mp 95–96° (lit.[43] mp 96–97°); ir (Nujol) 1745 (s, ester C=O), 1615 (s, amide C=O), 1590 and 1560 cm^{-1} (m, aromatic); nmr ($CDCl_3$) δ 5.11 (s, 2, CH_2), 7.1–8.1 (m, 15, aromatic **H**).

Anal. Calcd for $C_{21}H_{17}NO_3$: C, 76.12; H, 5.17; N, 4.23. Found: C, 76.23; H, 5.11; N, 4.22.

Petroleum ether was added to the ether filtrate from the above crystallization and after 3 hr in a freezer crystals of **13** (6.40 g, 8%) were obtained, mp 64–66°. Recrystallization from ether–petroleum ether gave white needles: mp 68–70°; ir 1740 (s, C=O), 1610 (s, C=N), 1570 cm^{-1} (w, aromatic); nmr ($CDCl_3$) δ 5.30 (s, 2, CH_2), 7.1–8.2 (m, 15, aromatic **H**).

Anal. Calcd for $C_{21}H_{17}NO_3$: C, 76.12; H, 5.17; N, 4.23. Found: C, 75.85; H, 5.15; N, 4.23.

Benzyl (*Z*)-Benzohydroximate (4e).—Benzyl (*Z*)-*O*-benzoylbenzohydroximate (6.40 g) was added to a solution of potassium hydroxide (3.3 g) and water (5 ml) and the mixture was heated (steam bath) and stirred until the reaction was homogeneous (*ca.* 5 min). Water (50 ml) was added and carbon dioxide was bubbled through the solution until it became cloudy and an oil separated. The mixture was extracted with ether (two 20-ml portions), the ether extracts were dried and evaporated, and the oil residue was crystallized from benzene–petroleum ether to yield 3.67 g (85%) of **4e**, mp 55–58°. Recrystallization from benzene–petroleum ether provided an analytical sample: mp 58–60°; ir (Nujol) 3120 (m, broad, OH), 1660 (m, C=N), 1580 cm^{-1} (w, aromatic) δ 5.31 (s, 2, CH_2), 7.1–7.8 (m, 10, aromatic **H**).

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.50; H, 5.73; N, 5.95.

***N*-Benzylbenzohydroxamic Acid (3e).**—The hydrolysis of **14** (15.7 g) was carried out by the procedure described in the preceding experiment except that chloroform was used as the extraction solvent. Evaporation of the chloroform extracts gave crystalline **3e** (9.61 g, 89%), mp 100–104°. Two recrystallizations from chloroform–petroleum ether afforded white microcrystals, mp 104–106° (lit.[43] mp 106°) that gave a magenta color with an ethanolic solution of ferric chloride: ir (Nujol) 3250 (m, broad, OH), 1620 (s, C=O), 1600 (m, aromatic), 1570 cm^{-1} (w, aromatic); nmr ($CDCl_3$) δ 4.77 (s, 2, CH_2), 7.0–7.7 (m, 10, aromatic **H**).

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.13; H, 5.58; N, 6.15.

Isopropyl (*Z*)-*O*-Benzoylbenzohydroximate (12b).—A mixture of isopropyl iodide (30.0 g), the silver salt of benzoyl benzohydroxamate (50.0 g), and anhydrous ether (200 ml) was stirred at room temperature for 3 days. The insoluble salts were removed by filtration and washed with ether. Evaporation of the ether filtrate gave a solid (35.0 g) that was recrystallized from ether–petroleum ether to yield 22.3 g (55%) of **12b**, mp 101–104°. Two more recrystallizations gave white needles: mp 105–106°; ir (Nujol) 1740 (s, C=O), 1620 (s, C=N), 1600 cm^{-1} (m, aromatic).

Anal. Calcd for $C_{17}H_{17}NO_3$: 3, 72.07; H, 6.05; N, 4.94. Found: C, 72.28; H, 6.03; N, 4.99.

Isopropyl (*E*)-Benzohydroximate (5c).—Crude isopropyl (*Z*)-*O*-benzylbenzohydroximate (35.0 g) obtained in an experiment identical with the one described above was added to a solution of

(42) This analysis was carried out by M-H-W Laboratories, Garden City, Mich.

(43) E. Beckmann, *Ber.*, **26**, 2272, 2631 (1893).

potassium hydroxide (17.5 g) and water (25 ml) and the mixture was stirred and refluxed for 10 min. After the reaction mixture had cooled to room temperature, water (100 ml) was added to give a solid which was collected (the aqueous filtrate was kept for further work-up) and triturated with ether. Filtration of the insoluble salts, evaporation of the ether filtrate, and recrystallization of the residue from petroleum ether gave **5c** (3.62 g), mp 95–101°.

Carbon dioxide was bubbled through the aqueous filtrate until it became cloudy. The resulting mixture was extracted with ether (three 100-ml portions) and the ether extracts were dried and evaporated. An nmr spectrum of the oil residue (14.4 g) showed that it was a mixture of **5c** and **4c** in *ca.* 15:85 ratio. The oil was dissolved in benzene (80 ml) and irradiated in quartz tubes for 3 hr in a Rayonet RPR-100 Reactor (The Southern New England Ultraviolet Company, Middletown, Conn.) fitted with 2537-Å lamps. Subsequent evaporation of the benzene at aspirator pressure yielded an oil that was shown by its nmr spectrum to be a mixture of **5c** and **4c** in *ca.* 45:55 ratio. Column chromatography on silica gel (160 g, 100–200 mesh) of this oil using chloroform–petroleum ether (25:75) as the eluting solvent gave in the first fractions **isopropyl (*E*)-benzohydroximate** (3.50 g, mp 97–101° after recrystallization from petroleum ether). Later fractions gave the *Z* isomer (4.62 g, 21%, mp 51–55° after recrystallization from petroleum ether). The combined yield of the *E* isomer was 32%. Two more recrystallizations of the *E* isomer from petroleum ether gave colorless prisms: mp 101–102°; ir (Nujol) 3250 (s, broad, OH), 1555 (s, C=N), 1605 cm^{-1} (w, aromatic); nmr ($CDCl_3$) δ 1.35 (d, J = 6 Hz, 6, CH_3CHCH_3), 4.90 (septet, J = 6 Hz, 1, CH_3CHCH_3), 7.1–8.0 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.28; H, 7.21; N, 7.88.

Isopropyl (*Z*)-Benzohydroximate (4c).—Hydrolysis of isopropyl (*Z*)-*O*-benzoylbenzohydroximate (16.0 g, mp 101–104°) was carried out by the procedure described for the preparation of **4e**. The oil left after evaporation of the ether extracts was dissolved in petroleum ether and cooled in a Dry Ice–acetone bath. The crystals (5.46 g, 54%) thus obtained were recrystallized from petroleum ether to afford an analytical sample: mp 53.5–55.5°; ir (Nujol) 3210 (m, broad, OH), 1640 (m, C=N), 1575 cm^{-1} (w, aromatic); nmr ($CDCl_3$) δ 1.34 (d, J = 6 Hz, 6, CH_3CHCH_3), 4.87 (septet, J = 6 Hz, 1, CH_3CHCH_3), 7.2–7.8 (m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.92; H, 7.01; N, 7.81.

Beckmann Rearrangement of Isopropyl (*Z*)-Benzohydroximate (4c).—Solid phosphorus pentachloride (1.67 g) was added slowly, with stirring, to a solution of **4c** (1.08 g) in ether (10 ml) which was cooled in a water bath. After the addition was complete, the mixture was stirred for an additional 30 min. The reaction mixture was then cooled in an ice bath and water (5 ml) was added slowly with stirring. The ether layer was separated, washed with 10% potassium carbonate (10 ml), dried, and evaporated. An infrared spectrum of the orange colored residual oil (0.62 g) indicated that it contained phenyl isocyanate. To an ether solution of this oil was added a solution of aniline (0.56 g) in ether. The solid (0.40 g, 31%) thus produced was recrystallized from acetone–water to give white crystals, mp 239–241°. A mixture melting point of these crystals with *s*-diphenylurea showed no depression, mp 240–242°.

Attempted Beckmann Rearrangement of Isopropyl (*E*)-Benzohydroximate (5c).—The reaction of **5c** (0.50 g) with phosphorus pentachloride (0.45 g) was carried out by the procedure described in the preceding experiment. Evaporation of the ether gave an oil that partially crystallized upon standing. The crystals were separated and recrystallized from ethanol to give the phosphate ester of **5c** as white needles (0.25 g, 46%), mp 116–117°. One more recrystallization from ethanol gave white needles: mp 117–119°; ir (Nujol) 1620 (m, C=N), 1600 (m, aromatic), 1580 cm^{-1} (w, aromatic); nmr ($CDCl_3$) δ 1.29 (d, J = 6 Hz, 18, CH_3CHCH_3), 5.00 (*ca.* septet, J = 6 Hz, 3, $CH_3CH_3CH_3$), 7.1–7.9 (m, 15, aromatic **H**).

Anal. Calcd for $C_{30}H_{36}N_3O_7P$: C, 61.95; H, 6.24; N, 7.23. Found: C, 62.02; H, 6.19; N, 7.34.

Monalkylation of Potassium Benzohydroxamate with *n*-Propyl Bromide.—A solution of potassium benzohydroxamate (87.4 g), *n*-propyl bromide (69.7 g), and anhydrous potassium carbonate (25.0 g) in methanol (374 ml) and water (250 ml) was stirred at 45° for 3 days. After the methanol was removed by distillation at atmospheric pressure, the residue was cooled to below 10° and acidified with 12 *N* hydrochloric acid. The mixture was extracted with ether (four 100-ml portions) and the combined ether extracts were washed with 10% sodium bicarbonate solution (100 ml). The ether solution was then extracted with 6 *N* sodium hydroxide solution (six 50-ml portions) and the combined basic extracts were acidified with 12 *N* hydrochloric acid and extracted with ether (four 50-ml portions). These ether extracts were dried and the solvent was removed at aspirator pressure. After the residue solidified, it was recrystallized from ether–petroleum ether to yield 63.0 g (71%) of *n*-propyl benzohydroxamate, mp 52–58°. Several more recrystallizations from ether–petroleum ether gave the analytical sample, mp 58–59° (lit.[44] mp 58–59°).

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.81; H, 7.41; N, 8.04.

The Silver Salt of *n*-Propyl Benzohydroxamate.—A solution of silver nitrate (38.0 g) in distilled water (80 ml) was added slowly to a vigorously stirred solution of *n*-propyl benzohydroxamate (40.5 g) and concentrated ammonium hydroxide (15 ml) in 95% ethanol (160 ml). After approximately half of the silver nitrate solution had been added, a white precipitate began to form. When the addition was complete, the mixture was stirred for an additional 30 min. The precipitate was then filtered, washed thorougly with acetone, and dried at 60° in a vacuum desiccator for 24 hr to yield 48 g (76%) of a white powder.

Anal. Calcd for $C_{10}H_{12}NO_2Ag$: C, 41.96; H, 4.24; N, 4.90. Found: C, 41.30; H, 4.42; N, 4.99.

Alkylation of the Silver Salt of *n*-Propyl Benzohydroxamate with Methyl Iodide.—A mixture of methyl iodide (8.43 g), the silver salt of *n*-propyl benzohydroxamate (9.00 g), and anhydrous ether (10 ml) was stirred at room temperature (approximately 24°) for 7 days. Addition of more ether, filtration of the insoluble salts, and evaporation of the ether from the filtrate yielded an oil. Vpc analysis of this oil showed that it was a mixture of *n*-propyl benzoate (0.33 g, 6%), methyl (*E*)-*O*-*n*-propylbenzohydroximate (0.87 g, 14%), methyl (*Z*)-*O*-*n*-propylbenzohydroximate (1.87 g, 30%), and *n*-propyl *N*-methylbenzohydroxamate (1.66 g, 27%).

Alkylation of the Potassium Salt of *n*-Propyl Benzohydroxamate with Ethyl Bromide.—A solution of *n*-propyl benzohydroxamate (7.00 g), ethyl bromide (8.72 g), and potassium carbonate (8.45 g) in methanol (22 ml) and water (15 ml) was stirred at 38° in a constant temperature bath for 15 hr. After evaporation of the methanol at aspirator pressure, the residue was cooled to below 10° and acidified with 12 *N* hydrochloric acid. The mixture was then extracted with ether (four 20-ml portions) and the combined ether extracts were washed with 10% sodium bicarbonate solution (40 ml). The acidic material was extracted from the ether with 3 *N* sodium hydroxide solution (three 15-ml portions). The nonacidic material remained in the ether. The combined sodium hydroxide extracts were cooled to below 10°, acidified with 12 *N* hydrochloric acid, and extracted with ether (three 15-ml portions). The ether extracts were dried and the solvent was evaporated at aspirator pressure to yield *n*-propyl benzohydroxamate (2.60 g, 37%).

The ether was evaporated from the nonacidic material at aspirator pressure to yield a light yellow oil. Vpc analysis of this oil showed that it consisted of ethyl (*Z*)-*O*-*n*-propylbenzohydroximate (1.10 g, 14%) and *n*-propyl *N*-ethylbenzohydroxamate (3.40 g, 42%).

Dialkylation of Potassium Benzohydroxamate with *n*-Propyl Bromide.—A solution of potassium benzohydroxamate (10.0 g), *n*-propyl bromide (21.0 g), and anhydrous potassium carbonate (15.8 g) in methanol (42 ml) and water (29 ml) was stirred at 58° in a constant temperature bath for 15 hr. The following products were obtained as described above: *n*-propyl benzohydroxamate (2.07 g, 20%), *n*-propyl (*Z*)-*O*-*n*-propylbenzohydroximate 2.10 g, 17%), and *n*-propyl *N*-*n*-propylbenzohydroxamate (5.82 g, 46%).

***O*-*n*-Propylbenzohydroximoyl Chloride (19b).**—Solid phosphorus pentachloride (58.3 g) was added in small portions to *n*-propyl benzohydroxamate (50.2 g) that was cooled in an ice bath and magnetically stirred. After all the phosphorus pentachloride had been added, the oily reaction mixture was stirred for a few minutes, then dissolved in ether and washed with water. The ether was dried and evaporated and the residue was distilled

(44) Cooley, Bills, and Throckmorton[9] prepared this compound by the catalytic hydrogenation of allyl benzohydroxamate.

to yield **19b** (45.1 g, 82%) as a clear liquid: bp 82–83° (0.3 mm); ir (neat) 1590 (w, C=N), 1570 cm^{-1} (w, aromatic); nmr (neat) δ 0.92 (t, 3, J = 7 Hz, $OCH_2CH_2CH_3$), 1.4–2.1 (m, 2, $OCH_2CH_2CH_3$), 4.16 (t, 2, J = 6.5 Hz, $OCH_2CH_2CH_3$), 7.0–8.1 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_{10}H_{12}NOCl$: C, 60.76; H, 6.12; N, 7.09. Found: C, 60.64; H, 5.90; N, 7.01.

***O*-Ethylbenzohydroximoyl Chloride (19a).**—By the procedure described above phosphorus pentachloride (8.66 g) and ethyl benzohydroxamate[9] (6.87 g) yielded 6.08 g (80%) of **19a**: bp 85–86° (0.5 mm) [lit. bp 125° (45 mm),[31] bp 239°[18]]; ir (neat) 1585 (w, C=N), 1565 cm^{-1} (w, aromatic); nmr ($CDCl_3$) δ 1.33 (t, 3, J = 7 Hz, OCH_2CH_3), 4.27 (q, 2, J = 7 Hz, OCH_2CH_3) 7.2–7.9 (2 m, 3 and 2, aromatic **H**).

***O*-*n*-Butylbenzohydroximoyl Chloride (19c).**—Phosphorus pentachloride (5.26 g) and *n*-butyl benzohydroxamate (4.88 g) yielded 3.56 g (62%) of **19c**, bp 104–114° (0.7 mm); ir (neat) 1585 (w, C=N), 1560 cm^{-1} (w, aromatic).

Anal. Calcd for $C_{11}H_{14}NOCl$: C, 62.41; H, 6.66; N, 6.61. Found: C, 61.80; H, 6.47; N, 6.57.

***n*-Propyl (*Z*)-*O*-*n*-Propylbenzohydroximate (7b).**—*O*-*n*-Propylbenzohydroximoyl chloride (25.6 g) was added slowly with stirring to a cold solution of sodium propoxide prepared from sodium (6.0 g) and 1-propanol (250 ml). The mixture was refluxed for 3 hr and the 1-propanol was removed by evaporation at reduced pressure. Water (100 ml) was added to the residue and the mixture extracted with ether (four 50-ml portions). The combined ether extracts were washed with 3 N sodium hydroxide solution (three 50-ml portions), dried, and evaporated at aspirator pressure. The residue was distilled to yield **7b** (21 g, 79%): bp 84–86° (0.1 mm); ir (neat) 1610 (s, C=N), 1570 cm^{-1} (m, aromatic); nmr ($CDCl_3$) δ 0.7–2.1 (2 m, 6 and 4, $NOCH_2CH_2CH_3$, and $COCH_2CH_2CH_3$), 4.05 (t, J = 6.5 Hz, $NOCH_2$), 4.24 (t, J = 6.5 Hz, $COCH_2$), the signals between 3.8 and 4.5 integrate for a total of 4 H, 7.1–8.0 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.55; H, 8.65; N, 6.33. Found: C, 70.31; H, 8.65; N, 6.11.

2-Benzoyltetrahydro-1,2-oxazine (18).—A solution of potassium benzohydroxamate (7.35 g), 1,4-dibromobutane (10.0 g), and anhydrous potassium carbonate (11.6 g) in methanol (31 ml) and water (21 ml) was stirred at 35° in a constant temperature bath for 3 days. The methanol was then removed at reduced pressure, water (50 ml) was added to the residue, and the mixture was extracted with ether (two 50-ml portions). The combined ether extracts were dried and the ether was evaporated at aspirator pressure. The crude product was distilled to give a colorless, viscous liquid (4.33 g, 54%): bp 113–120° (0.1 mm) [lit.[45] bp 152–153° (2 mm)]; rising end absorption in uv with log ε of 3.66 at 256 mμ (95% ethanol); ir (neat) 1640 (s, C=O), 1580 cm^{-1} (w, aromatic); nmr (neat) δ 1.3–1.9 (m, 4, $CH_2CH_2CH_2CH_2$), 3.5–4.1 (m, 4, NCH_2 and OCH_2), 7.2–8.0 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.13; H, 6.80; H, 7.52.

2-Benzoyloxazolidine (17).—By the procedure described above (reaction temperature of 38°), potassium benzohydroxamate (7.35 g), 1,3-dibromopropane (9.35 g), and anhydrous potassium carbonate (11.6 g) in methanol (31 ml) and water (21 ml) yielded **2-benzoyloxazolidine** (2.13 g, 29%) as a colorless liquid: bp 124–126° (0.16 mm); rising end absorption in uv with log ε of 3.71 at 256 mμ (95% ethanol); ir (neat) 1630 (s, C=O), 1580 cm^{-1} (m, aromatic); nmr ($CDCl_3$) δ 2.17 (quintet, 2, J = 7 Hz, $CH_2CH_2CH_2$), 3.77 (t, J = 7 Hz, OCH_2), 3.82 (t, J = 7 Hz, NCH_2), the signals between 3.6 and 4.0 integrate for a total of 4 H, 7.1–8.0 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 6.90. Found: C, 67.58; H, 6.13; N, 6.92.

3-Phenyl-5*H*-1,4,2-dioxazine (16).—By the procedure described above (reaction temperature of 32°), potassium benzohydroxamate (14.7 g), 1,2-dibromoethane (17.5 g), and anhydrous potassium carbonate (23.2 g) in methanol (62 ml) and water (42 ml) yielded **3-phenyl-5*H*-1,4,2-dioxazine** (5.72 g, 42%) as a light yellow liquid: bp 103–107° (0.07 mm); uv max (95% ethanol) 252 mμ (log ε 3.95); ir (neat) 1610 (s, C=N), 1580 cm^{-1} (s, aromatic); nmr (neat) δ 3.9–4.5 (2 m, $A_2'X_2'$, 2 and 2, $=COCH_2$ and $=NOCH_2$), 7.1–8.1 (2 m, 3 and 2, aromatic **H**).

Anal. Calcd for $C_9H_9NO_2$: C, 66.25; H, 5.56; N, 8.58. Found: C, 66.10; H, 5.48; N, 8.70.

Alkylation of Potassium Benzohydroxamate with *n*-Butyl Bromide.—The reaction was carried out according to a procedure described by Fuller and King[12] except on a smaller scale. A solution of potassium benzohydroxamate (15.0 g), *n*-butyl bromide (13.2 g), and potassium carbonate (12.0 g) in 95% ethanol (72 ml) was stirred and refluxed for 15 hr. The ethanol was evaporated at aspirator pressure and after using the work-up procedure described above the following products were obtained (as determined by vpc analyses of the crude oil): *n*-butyl benzohydroxamate (7.03 g, 43%), *n*-butyl (*Z*)-*O*-*n*-butylbenzohydroximate (1.59 g, 8%), and *n*-butyl *N*-*n*-butylbenzohydroxamate (3.71 g, 17%).

Alkylation of Ethyl Benzohydroxamate with Ethyl Iodide.—The reaction was carried out according to a procedure described by Lossen.[13] A solution of ethyl benzohydroxamate (10.0 g), potassium hydroxide (3.4 g), ethyl iodide (25.8 g), and 70% ethanol (70 ml) was refluxed over a water bath for 2 hr. The reaction was worked up in the usual manner and the nonacidic fraction was distilled *in vacuo* yielding ethyl benzoate (1.27 g) and ethyl *N*-ethylbenzohydroxamate (4.12 g, 36%).

Isolation of *n*-Propyl *N*-Isopropylbenzohydroxamate (6f) by Selective Hydrolysis of Isopropyl *Z*-*O*-*n*-Propylbenzohydroximate (7f) in a Mixture Containing 6f and 7f.—An oil (7.26 g) consisting of **6f** and **7f** in a 27:73 ratio (by vpc) was dissolved in concentrated hydrochloric acid (72 ml) and the resulting solution was stirred at 50–54° for 30 min. After the solution had cooled to room temperature, it was neutralized with 6 N sodium hydroxide and extracted with ether (two 40-ml portions). The ether extracts were dried and evaporated and the residual oil was distilled to give pure **6f** (1.23 g, 63% based on the amount of **6f** in the starting material): bp 106–110° (0.45 mm); nmr ($CDCl_3$) δ 0.6–1.8 (m, $OCH_2CH_2CH_3$), 1.29 (d, J = 7 Hz, CH_3CHCH_3), the signals between 0.6 and 1.8 integrate for a total of 11 H, 3.7 (t, J = 6 Hz, 2, $OCH_2CH_2CH_3$), *ca.* 4.52 (*ca.* septet, J = 7 Hz, 1, CH_3CHCH_3), 7.2–7.7 (m, 5, aromatic **H**).

Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.55; H, 8.65; N, 6.33. Found: C, 70.67; H, 8.68; N, 6.28.

Registry No.—**1**, 495-18-1; **3e**, 7339-99-3; **4a**, 26198-44-7; **4c**, 26889-49-6; **4e**, 26889-50-9; **5a**, 26198-45-8; **5c**, 26889-52-1; **5c** phosphate ester, 26963-86-0; **5e**, 26889-53-2; **6a**, 26893-77-6; **6b**, 26893-52-7; **6c**, 26893-53-8; **6d**, 26893-54-9; **6e**, 26929-64-6; **6f**, 26893-55-0; **6g**, 26893-56-1; **6h**, 26893-57-2; **6i**, 5553-73-1; **7a**, 26889-10-1; **7b**, 26889-11-2; **7c**, 26889-12-3; **7d**, 26889-13-4; **7e**, 26889-14-5; **7f**, 26889-15-6; **7h**, 26893-59-4; **8a**, 26889-16-7; **8b**, 26889-17-8; **8c**, 26889-18-9; **8d**, 26889-19-0; **8e**, 26889-20-3; **8f**, 26889-21-4; **8g**, 26889-22-5; **8h**, 26889-23-6; **9c**, 26893-60-7; **11**, 26893-61-8; **12a**, 26198-46-9; **12b**, 26889-25-8; **13**, 26889-26-9; **14**, 19172-64-6; **15**, 26885-65-4; **16**, 26893-63-0; **17**, 26893-64-1; **18**, 26893-65-2; **19a**, 26893-66-3; **19b**, 26893-67-4; **19c**, 26929-66-8.

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(45) This compound has been prepared previously by the reaction of benzoyl chloride with tetrahydro-1,2-oxazine: O. Witchterele and J. Novak, *Collect. Czech. Chem. Commun.*, **15**, 309 (1950).