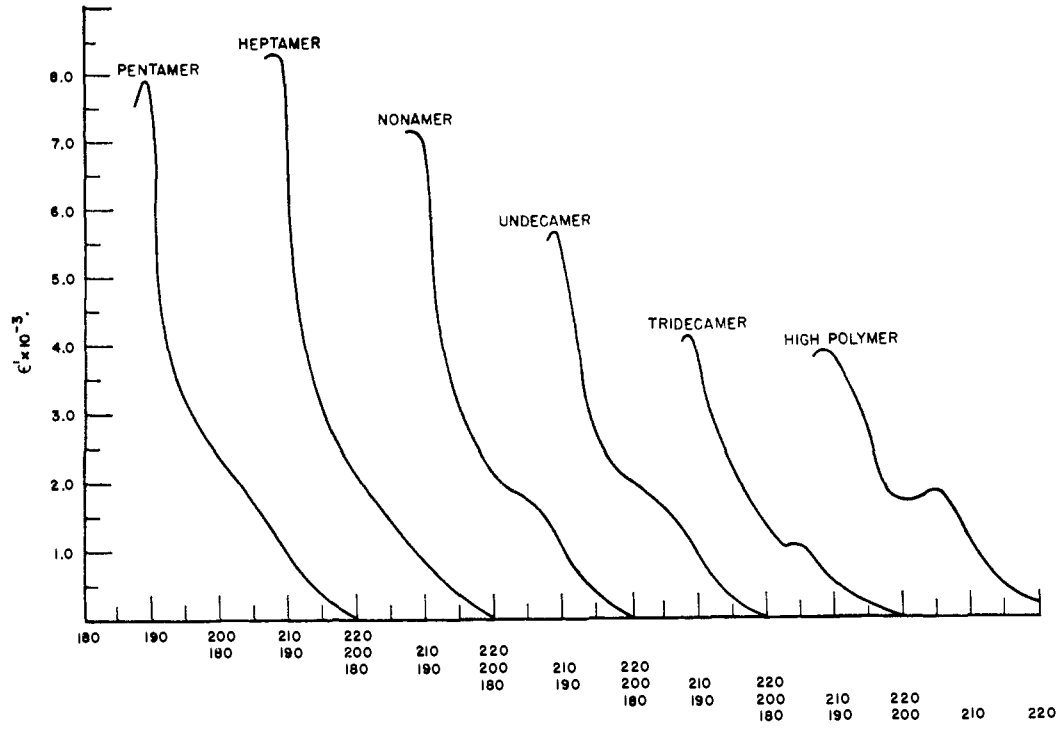

Fig. 1.—Molar extinction coefficients per residue of the oligomeric peptides and high polymer derived from γ-methyl-L-glutamate as a function of wave length in 2,2,2-trifluoroethanol at 25.0°.

189 mμ using the relationship[2]

$$(\epsilon_c' - \epsilon')/(\epsilon_c' - \epsilon_h') \times 100 = \%\ \text{helicity} \quad (1)$$

where ϵ' is the molar extinction coefficient per residue of the peptide, ϵ_c' is the molar extinction coefficient per residue of the random coil (based on the hepta and pentapeptides). ϵ_h' is the molar extinction coefficient per residue for the helical peptide (based on the polymer).

The data in Table I summarize the various absorption coefficients and the % helicity for the compounds using Equation 1.

TABLE I

ABSORPTION COEFFICIENTS, PERCENT HELICITY AND ROTATORY DISPERSION CONSTANTS FOR THE PEPTIDE SERIES IN TRIFLUOROETHANOL AT 25°

Compound	Molar extinction coefficients at 189 mμ ε(observed) × 10⁻³	ε'(corrected) × 10⁻³	% Helicity $(\epsilon_c' - \epsilon')/\epsilon_c' - \epsilon_h'$ × 100	Rotatory dispersion constants b_0
Dipeptide	17.3	7.1	(0)[a]	...
Tripeptide	..	..	...	+72
Tetrapeptide	..	..	...	+50
Pentapeptide	13.3	7.9	(0)[a]	0
Hexapeptide	..	..	...	0
Heptapeptide	12.3	8.2	(0)[a]	−42
Nonapeptide	10.4	7.1	26	−210
Undecapeptide	8.4	5.6	60	−277
Tridecapeptide	6.5	4.1	95	−337
Polymer	3.9	3.9	100	−816

[a] The helical content is zero or close to it.

The work of Tinoco, Halpern and Simpson[2] indicates that for very short chains the hypochromism calculated for the complete helix is somewhat lower than that calculated for the completely helical high polymers. Since this variation of hypochromism does not have much of an effect on our calculations of percentage helicity, we assume the hypochromism of the complete helix to be independent of the number of residues in the peptide chain.

These findings which we are reporting are in accordance with our studies using optical rotatory properties of the oligopeptides in other helical solvents.[1,7] Optical rotatory studies in 2,2,2-trifluoroethanol also were carried out. It is evident (Table I) that there is excellent agreement between the rotatory dispersion data and the results obtained from the ultraviolet spectra. The appearance of helical structures in trifluoroethanol at 25° commences at or about the monamer as can be seen by the abrupt change in b_0 and the extinction coefficients (Table I).

Acknowledgment.—We wish to thank Dr. I. Tinoco for his extremely helpful suggestions. We also wish to acknowledge gratefully the support given for this research by a grant from the National Institutes of Health RG 8974.

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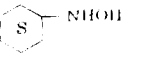
A CONVENIENT SYNTHESIS OF N-ALKYLHYDROXYLAMINES

Sir:

We wish to report a new synthesis of N-monosubstituted hydroxylamines by reduction of the

TABLE I

Oxime[a]	B_2H_6 (mmole) Added	Consumed	Product[b]	M.p., °C.	Yield, %
$H_3CCH_2C(CH_3)$=NOH	97.5	19.5	$H_3CCH_2CH(CH_3)NHOH$	67	91
	88.0	22.4		140	82
H_2C=NOH[c]	150.0	..	H_3CNHOH	129–130[d]	50
$H_3C(CH_2)_2CH$=NOH	90.0	25.7	$H_3C(CH_2)_2CH_2NHOH$	54	71
$H_3C(CH_2)_5CH$=NOH	95.0	25.5	$H_3C(CH_2)_5CH_2NHOH$	62	81
$H_3C(CH_2)_6CH$=NOH[c]	150.0	..	$H_3C(CH_2)_6CH_2NHOH$	73.5	87
C_6H_5CH=NOH	168.0	20.1	$C_6H_5CH_2NHOH$	57[e]	31

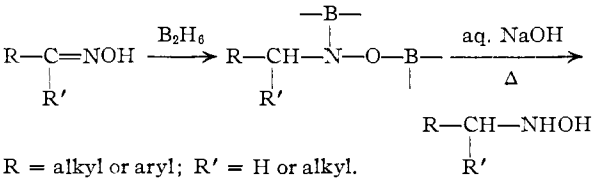
[a] 20 mmoles of each was employed. [b] The elemental analyses were satisfactory. [c] Expt. performed by R. S. Bartlett. [d] Isolated as the picrate [lit. value, m.p. 128–129°, C. Kjellin, *Ber.*, 2382 (1893)]. [e] R. Behrend and K. Leuchs, *Ann.*, 214 (1890), report m.p. 57°.

corresponding oxime with borane[1,2] in tetrahydrofuran (THF).

Hitherto, the only reported methods which have been available for the preparation of N-monosubstituted hydroxylamines were the catalytic reduction of ketoximes[3,4,5] or electrolytic reduction of primary nitroalkanes.[6] Only the latter procedure gave N-*n*-alkyl monosubstituted hydroxylamines such as *n*-propylhydroxylamine and ethylhydroxylamine in yields of 50 and 43%, respectively. On the other hand, the catalytic reduction of aldoximes afforded only N,N-disubstituted hydroxylamines.

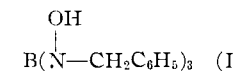
Our new synthesis provides a facile and convenient preparation of N-monosubstituted hydroxylamines by utilization of the readily available aldoximes and ketoximes. Moreover, it does not require expensive pressure equipment.

In Table I are listed the hydroxylamines prepared by the diborane reduction of oximes, the amount of hydride introduced and the amount of hydride consumed by the oximes. The consumption of hydride was determined by measuring the amount of unused hydrogen in both the reaction mixture and the acetone wash.[7] The results of these measurements indicate that one mole of oxime requires two equivalents of hydride.



R = alkyl or aryl; R′ = H or alkyl.

The low yield (31%) of N-benzylhydroxylamine may be explained by the difficult hydrolysis of the intermediate I. When hydrolysis was prolonged sufficiently (3 hr.) to cleave all of the boron–nitrogen bonds, the product was N,N-dibenzylhydroxylamine in 66% yield[4] and none of the desired benzylhydroxylamine was isolated. The latter was obtained when hydrolysis was limited to one hour. Similar difficulties have been observed in



(I)

protonolysis of organoboranes containing bulky groups.[8]

As shown in Table I the yields for the aliphatic compounds are good to excellent. The somewhat lower yield of N-*n*-butylhydroxylamine can be explained by its high volatility and by its facile reoxidation to the oxime.

The following procedure is typical. Into a magnetically stirred, nitrogen flushed, 50-ml. three-necked flask fitted with a thermometer, serum cap and reflux condenser to which is applied a small static pressure of nitrogen, is placed 2.28 g. (20 mmoles) of cyclohexanone oxime. The temperature of the flask is brought to 2° and 17 ml. of a 2 *M* solution of borane in tetrahydrofuran is introduced by means of a hypodermic syringe at such a rate that the temperature does not exceed 5°. When all of the reductant is added, the solution is allowed to attain ambient temperature slowly. After 4 hours the solvent is removed *in vacuo* and the vacuum broken with nitrogen. The temperature again is lowered to 2° and 10 ml. of 10% aqueous sodium hydroxide added through a syringe at such a rate that the temperature does not exceed 5°. (If the first few drops of base are added too rapidly, an exothermic decomposition occurs.) The mixture is then basified to pH 14 by the addition of concd. sodium hydroxide, and refluxed for one hour. Continuous extraction with pentane for 90 hours, and removing of the solvent by distillation through a short column afford 1.89 g. (82%) of N-cyclohexylhydroxylamine, m.p. 138–140° (lit. value,[3] 142°).

Since hydroxylamines are quite sensitive to oxidation and are hygroscopic, their exposure to air should be limited.

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