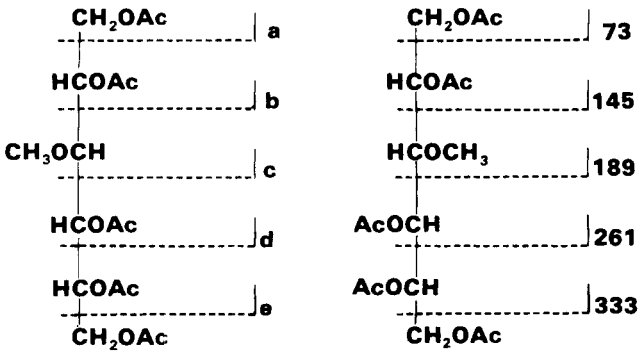
Table II. Selected Ion Abundances from the EI Spectra of 8 and 9

8[a]	9[b]	assignment
73 (5.2)	73 (4.2)	a
129 (100.0)	129 (100.0)	c-CH_3COOH)
145 (5.0)	145 (5.0)	b
189 (77.0)	189 (71.8)	c
261 (80.5)	261 (31.5)	d
333 (0.2)	333 (0.2)	e
347 (1.8)	347 (2.7)	(M − $CH_3COO\cdot$)

[a] Registry no., 20250-53-7. [b] Registry no., 68679-97-0.

a structure containing a substituted C-3 hydroxyl.

The variation in reactivities of the C-2 and C-3 hydroxyl groups of L-ascorbic acid may be rationalized in terms of the equilibra (5 ⇄ 6 ⇄ 7). Diazomethane methylation of 5 involves



the more acidic 3-hydroxyl. Conversely, under the basic conditions used to prepare 1 and 4, the dianion 7 predominates and substitution occurs preferentially at the C-2 hydroxyl in accord with its greater basicity.

Experimental Section

The ^{13}C NMR spectra were recorded in D_2O with a Varian CFT-20 spectrometer. Dioxan was used as the internal reference. The mass spectra were obtained at 70 eV using a Dupont 490 spectrometer.

Reduction of 3-*O*-Methylascorbic Acid (2). 2 (0.1 g) in ethanol (50 mL) was hydrogenated in the presence of Pd–C. Uptake of the theoretical volume of hydrogen (13.5 mL) and disappearance of the characteristic UV band of 2 (245 nm) were consistent with complete saturation of the olefinic bond. Workup gave a syrup which was reduced with sodium borohydride[16] and acetylated to give 9.

1,2,4,5,6-Penta-*O*-acetyl-3-*O*-methyl-D-glucitol (8). 8 was prepared from 3-*O*-methyl-D-glucose (Aldrich) by reduction with sodium borohydride and acetylation.

Registry No.—3, 68582-37-6; 7, 63983-50-6; 3-*O*-methyl-D-glucose, 146-72-5.

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Peracid Oxidation of Aliphatic Amines: General Synthesis of Nitroalkanes

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Nitroalkanes are versatile synthetic intermediates[1] which have recently proved useful in the preparation of alkenes[2] and diazetines.[3] In connection with our work on the synthesis of pyramidalized[4] and torsionally strained[5] alkenes, we required a method for preparing nitroalkanes from amines. Several literature procedures[6] were tried without success before we found that *m*-chloroperbenzoic acid oxidation of amino groups can be made to yield primary and secondary nitroalkanes.[7] Our results are consistent with the intermediacy of nitrosoalkanes in this reaction.

In the early 1950's, Emmons reported that aliphatic amines (cyclohexyl, 2-butyl, and *n*-hexyl) can be oxidized to the corresponding nitroalkanes in good to poor yields (70, 65, and 32%, respectively) with anhydrous peracetic acid.[8] This reagent is not commercially available and was prepared from 90% hydrogen peroxide, which is a hazardous material with which to work. Moreover, as Emmons pointed out, his reaction conditions may facilitate prototropic rearrangement of nitrosoalkane intermediates into oximes, thus leading to reduced yields of nitroalkanes.[8]

Emmons has also reported that oxidation of amines at 0 °C provides a general synthesis of azo dioxides (nitrosoalkane dimers).[9] Since azo dioxides are in equilibrium with nitrosoalkanes, which can be trapped at elevated temperatures with *m*-chloroperbenzoic acid (*m*-CPBA),[3,10] we felt that it should be possible to develop a general, high yield synthesis of nitroalkanes from amines, using *m*-CPBA as the oxidant. In fact, Robinson and co-workers discovered that *m*-CPBA was capable of oxidizing steroidal amines to nitrosteroids,[11] but we have found that their reaction conditions are not generally useful (vide infra).

Results and Discussion

Attempts to effect direct oxidation of aliphatic amines with 4 equiv of *m*-CPBA in halocarbon solvents gave mixtures of

Scheme I

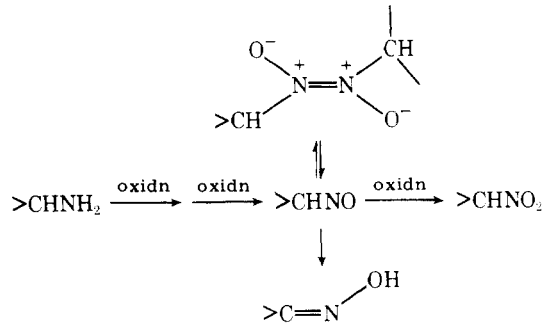

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Table I. *m*-CPBA Oxidations of Aliphatic Amines

amine	registry no.	solvent, temp. (°C), time (h)	ratio[c] RNO	registry no.	RNO_2	registry no.	yield %
cyclohexylamine	108-91-81	CH_2Cl_2, 23, 18	100	2696-95-9	0	1122-60-7	43[a]
		$CHCl_3$, 61, 0.5	27		73		100[b]
		$CHCl_3$, 61, 3	12		88		100[b]
		1,2-$(CH_2Cl)_2$, 83, 0.5	0		100		86[b]
		1,2-$(CH_2Cl)_2$, 83, 3	0		100		75[a]
2-butylamine	13952-84-6	CH_2Cl_2, 23, 18	85	44377-25-5	15	600-24-8	100[b]
		$CHCl_3$, 61, 0.5	81		19		95[b]
		$CHCl_3$, 61, 3	45		55		90[b]
		1,2-$(CH_2Cl)_2$, 83, 0.5	13		87		83[b]
		1,2-$(CH_2Cl)_2$, 83, 3	0		100		63[a]
1-hexylamine	111-26-2	CH_2Cl_2, 23, 18	100	68582-32-1	0	646-14-0	79[b]
		$CHCl_3$, 61, 0.5	72		28		66[a]
		$CHCl_3$, 61, 3	58		42		54[a]
		1,2-$(CH_2Cl)_2$, 83, 0.5	45		55		65[a]
		1,2-$(CH_2Cl)_2$, 83, 3	10		90		85[a]
2-phenylethylamine	64-04-0	CH_2Cl_2, 23, 18	100	68582-33-2	0	6125-24-2	91[a]
		$CHCl_3$, 61, 0.5	100		0		95[b]
		$CHCl_3$, 61, 3	59		41		100[b]
		1,2-$(CH_2Cl)_2$, 83, 0.5	34		66		81[b]
		1,2-$(CH_2Cl)_2$, 83, 3	0		100		73[a]
propylamine	107-108	CH_2Cl_2, 23, 18	100	927-78-6	0	108-03-02	95[b]
		$CHCl_3$, 61, 0.5	67		33		52[a]
		$CHCl_3$, 61, 3	60		40		55[a]
		1,2-$(CH_2Cl)_2$, 83, 0.5	40		60		62[a]
		1,2-$(CH_2Cl)_2$, 83, 3	0		100		59[a]

[a] Isolated yield; see Experimental Section. [b] Crude yield. [c] Ratio determined by NMR integration of protons on nitrogen-bearing carbon except for 1-hexyl and 1-propyl cases. In these cases the crude product was distilled, which converts RNO into oximes, which could then be analyzed by NMR.

nitroalkanes and azo dioxides. The proportions of the two products were temperature dependent. Thus, cyclohexylamine in CH_2Cl_2 at room temperature gave only *N,N'*-dicyclohexyldiazene *N,N'*-dioxide,[9] while in refluxing $CHCl_3$, Robinson's reaction conditions,[11] mixtures of the azo dioxide and nitrocyclohexane were obtained. Finally, in 1,2-dichloroethane at reflux, only nitrocyclohexane was isolated. The results for the other amines studied were similar and are given in Table I.

In all cases studied, formation of nitroalkane was favored over azo dioxide by higher temperatures and increased reaction times. The changes in the azo dioxide–nitroalkane ratio with temperature can probably be attributed to both a more favorable equilibrium constant for azo dioxide dissociation[3,12] and an increased rate of oxidation of nitrosoalkane (Scheme I). With our method, the prototropic shift of nitrosoalkanes to oximes is not observed. Thus, 1-nitrohexane is obtained in 66% yield, while the yield in the peracetic acid oxidation is only 32%.[8] The azo dioxides are, however, converted to oximes on attempted distillation at 80–100 °C.

This paper reports a general, one-step synthesis of primary and secondary nitroalkanes, using a commercially available reagent. Since amines are readily available from ketones by oxime reduction,[13] this method allows the facile transformation of a carbonyl into a nitro group.[14]

Experimental Section

General. Melting points and boiling points are uncorrected. NMR spectra were taken on a Varian EM-360L 60-MHz spectrometer as $CDCl_3$ solutions, and chemical shifts are reported as downfield shifts (ppm) from tetramethylsilane. High-resolution mass spectra were obtained on an AEI MS-9 double-focusing instrument. The amines employed in this study were commercial samples and were used without further purification. *m*-Chloroperbenzoic acid was obtained as technical grade material (85%) (Aldrich Chemical Co.) and was used as received.

General Procedure for Amine Oxidations. *m*-Chloroperbenzoic acid (4.1 g, 0.020 mol, 85% pure) was dissolved in 30 mL of solvent in a three-neck flask equipped with a condenser and a pressure-equalizing dropping funnel. Amine (0.0050 mol) in 3–5 mL of solvent was added dropwise to the refluxing peracid solution. Reflux was continued for the specified time after the addition; then, the reaction mixture was cooled, filtered, washed with 3 × 50 mL of 1 N NaOH, and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave the crude mixtures which were weighed and analyzed by NMR (see Table I). When the NMR analysis indicated only one component, this was isolated by crystallization or distillation.

***N,N'*-Dicyclohexyldiazene *N,N'*-dioxide** was recrystallized from hexane: mp 112–113 °C (lit.[9] mp 120 °C); NMR δ 1.1–2.1 (broad, 10 H), 4.7–5.3 (broad, 1 H).

Nitrocyclohexane: bp 112–113 °C (45 mm) [lit.[6b] bp 106–108 °C (40 mm)]; NMR δ 1.0–2.5 (broad multiplet, 10 H), 4.28 (sextet, 1 H).

***N,N'*-Bis(1-methylpropyl)diazene *N,N'*-Dioxide:** oil; NMR δ 0.88 (t, 3 H), 1.32 (d, 3 H), 1.70 (nonet., 2 H), 5.27 (sextet, 1 H). Exact mass calcd for $C_8H_{18}N_2O_2$: 174.1368. Found: 174.1352.

2-Nitrobutane: bp 65–66 °C (70 mm) [lit.[6b] bp 64–66 °C (70 mm)]; NMR spectrum was identical with the literature.[15]

***N,N'*-(Di-1-hexyl)diazene *N,N'*-Dioxide:** oil; NMR δ 0.87 (m, 3 H), 1.32 (br s, 6 H), 1.85 (br t, 2 H), 4.23 (t, 2 H). Exact mass calcd for $C_{12}H_{26}N_2O_2$: 230.1994. Found: 230.1992.

1-Nitrohexane: bp 103–108 °C (35 mm) [lit.[16] bp 84 °C (21 mm)]; NMR[17] δ 0.9 (t, 3 H), 1.32 (br s, 5 H), 1.97 (t, 3 H), 4.28 (t, 2 H).

***N,N'*-Bis(2-phenylethyl)diazene *N,N'*-Dioxide:** mp 94–95 °C; NMR δ 3.08 (t, 2 H), 4.45 (t, 2 H), 7.24 (s, 5 H). Exact mass calcd for $C_{16}H_{18}N_2O_2$: 270.1368. Found: 270.1414.

1-Nitro-2-phenylethane: bp 88–90 °C (1.2 mm) [lit.[18] bp 73–74 °C 0.5 mm)]; NMR[19] δ 3.19 (t, 2 H), 4.47 (t, 2 H), 7.20 (s, 5 H).

***N,N'*-(Di-1-propyl)diazene *N,N'*-Dioxide:** oil; NMR δ 0.97 (t, 3 H), 1.88 (sextet, 2 H), 4.20 (t, 2 H). Exact mass calcd for $C_6H_{14}N_2O_2$: 146.1055. Found: 146.1058.

1-Nitropropane: bp 79–81 °C (140 mm) [lit.[20] bp 130–131.5 °C (760 mm)]; NMR δ 0.95 (t, 3 H), 1.97 (sextet, 2 H), 4.30 (t, 2 H).

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Registry No.—*N,N'*-Dicyclohexyldiazene *N,N'*-dioxide, 3378-45-8; *N,N'*-bis(1-methylpropyl)diazene *N,N'*-dioxide, 3378-41-4; *N,N'*-(di-1-hexyl)diazene N,N'-dioxide, 68582-34-3; *N,N'*-bis(2-phenylethyl)diazene *N,N'*-dioxide, 3378-37-8; *N,N'*-(di-1-propyl)-diazene *N,N'*-dioxide, 3600-99-5.

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Formation of *N,N*-Dialkylhydroxylamines in the Oximation of Some Mannich Bases

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Several years ago Kyi and Wilson reported that the Mannich base **1a** undergoes an "abnormal oximation" in aqueous sodium acetate. They suggested the product might be either an unsaturated oxime or an isomeric 2-isoxazoline,[1] and later a third structure, a 4-isoxazoline, was proposed.[2] On the basis of new evidence we now report that the product is actually the *N,N*-dialkyhydroxylamine **2a.** We also wish to propose a mechanism for the formation of **2a** and have examined the behavior of some other Mannich bases under these conditions.

$R_1COCHR_2CH_2NMe_2$ (1) $(R_1COCHR_2CH_2)_2NOH$ (2)

a, $R_1 = PhCH_2$; $R_2 = Ph$
b, $R_1 = R_2 = Ph$
c, $R_1 = Ph$; $R_2 = Me$
d, $R_1 = Ph$; $R_2 = H$
e, $R_1 = Me$; $R_2 = Ph$

The reaction of **1a** with hydroxylamine hydrochloride was carried out as reported. The product appeared homogeneous by TLC, but the melting point varied from 100–125 °C for different runs (Kyi and Wilson report mp 101–02 °C), and fractional crystallization gave two compounds, mp 105–06 and 128–29.5 °C. These substances were not merely dimorphic crystal forms, since they were unchanged by further crystallization. The evidence suggests that the compounds are stereoisomeric and represent the racemic modification and meso forms of **2a,** but the exact configurational assignment was not attempted.

The two diastereomers of **2a** gave satisfactory analyses for C, H, and N. The infrared spectra of the two isomers in solution ($CHCl_3$) were virtually identical, with absorptions at 3580 and 1712 cm^{-1} for the hydroxyl and carbonyl groups. However, the spectra run as Nujol mulls showed significant differences for the two compounds, undoubtedly due to inter- or intramolecular interactions in the solid phase. The compounds gave similar ^1H NMR spectra, with all signals, save for the phenyl hydrogens, appearing as an unresolved multiplet at δ 2.5–4.5. An *O*-acetyl derivative of the low-melting isomer confirmed that four phenyl groups were present by integration relative to the acetyl methyl signal in the ^1H NMR.

The formation of **2a** in the reaction is undoubtedly analogous to the reported conversion of **1d** to **2d** under other oximation conditions[3] and the synthesis of **3** from **1d** by reaction with *N*-phenylhydroxylamine.[4]

$PhCOCH_2CH_2NPhOH$ (3)

Formation of **2a** is consistent with a process involving the elimination of dimethylamine from **1a** to give the unsaturated ketone **4a,** not an uncommon reaction for Mannich bases.

$R_1COCR_2{=}CH_2$ (4)

Evidence for this process was obtained by heating **1a** in aqueous sodium acetate in the absence of hydroxylamine, giving **4a** in high yield, along with some dibenzyl ketone.[5] The subsequent conversion of **4a** to **2a** is reasonable, since acrylophenone **4d,**[6,7] or its precursors,[8–10] are known to react with hydroxylamine to give **2d,** and a similar conjugate addition has been reported for chalcone.[11] Indeed, a sample of **4a** was found to react readily with hydroxylamine to give a mixture of the isomeric forms of **2a** in good yield.

The Mannich bases **1b–d** were prepared, and their behavior under the reaction conditions was investigated. Of these compounds only **1b** underwent an abnormal oximation to **2b,** the remaining compounds giving normal oximation products. The phenyl substituents at R_2 in **1a** and **1b** might be expected to facilitate the abnormal reaction by promoting elimination to **4a** and **4b.** However, **1e** failed to give **2e,** in spite of the presence of the phenyl group at R_2, suggesting that the bulky groups at R_1 in **1a** and **1b** help promote the abnormal oximation by hindering the formation of the normal ketoximes.

The unsaturated ketones **4a–c** were prepared by elimination from the methiodide derivatives of **1a–c,** and their reaction with hydroxylamine at room temperature gave **2a–c.** There is some indication that **2b** and **2c** are formed as diastereomeric mixtures like **2a,** but only a single sharp-melting isomer was isolated and characterized in each case. Although the ketone **4e** was also readily prepared, its reaction with hydroxylamine gave complex mixtures, and attempts to isolate pure **2e** were unsuccessful. Competition between conjugate addition and attack at the carbonyl group may be responsible for the complications in this case.

The compounds **2a–c** seem to be the first reported examples of such β-acylethylhydroxylamines having substituents at the position adjacent to the carbonyl group. This abnormal oximation of Mannich bases only seems to occur in cases where structural features favor elimination and where the reactivity of the carbonyl group is relatively low. Even then, special re-

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