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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action conditions are required, since the normal ketoximes of **1a**[1] and **1b**[12] have been prepared using different oximation methods.

Experimental Section

Melting points were determined with a Thomas-Hoover Uni-melt apparatus and are corrected. Infrared spectra were recorded with a Perkin-Elmer 710B spectrometer. ^{1}H NMR spectra were obtained in $CDCl_3$ with a Hitachi Perkin-Elmer R-20 spectrometer, and values are reported as δ in ppm relative to Me_4Si as an internal standard. Elemental analyses were performed by Microanalysis, Inc., Wilmington, Del.

***N,N*-Bis[1-(2,4-diphenyl-3-oxo)butyl]hydroxylamine (2a). Method A.** A solution of 4.56 g (15 mmol) of the hydrochloride of 4-dimethylamino-1,3-diphenyl-2-butanone (**1a**), 6.15 g (45 mmol) of sodium acetate trihydrate, and 2.1 g (30 mmol) of hydroxylamine hydrochloride in 50 mL of H_2O was heated at 90–100 °C for 15 min and cooled in ice. The supernatant was decanted, and the residue was dissolved in 30 mL of 95% ethanol. After cooling at −20 °C overnight, the white solid was collected and dried to give 2.67 g (75%), mp 100–122 °C. Separation of the isomers is discussed below.

Method B. A mixture of 8.18 g (20 mmol) of the methiodide derivative of **1a** in 40 mL of H_2O and 75 mL of benzene was treated with 10 mL of 2 N NaOH and stirred at room temperature for 15 min. The organic layer was separated, and the aqueous layer was extracted with 15 mL of benzene. The organic solution was washed with 10% HCl and with H_2O, dried (K_2CO_3), and evaporated. The residual oil was dissolved in 20 mL of ethanol and was treated with a solution of hydroxylamine in aqueous ethanol (prepared by combining 0.7 g (10 mmol) of hydroxylamine hydrochloride in 3 mL of H_2O and 0.53 g (5 mmol) of Na_2CO_3 in 3 mL of H_2O, diluting with ethanol to 25 mL, and filtering). After standing at room temperature for 2 h the solvent was evaporated, and the residue was treated with 20 mL of H_2O and extracted with two 75-mL portions of ether. The ether solution was dried (K_2CO_3) and evaporated. The residue was dissolved in 30 mL of ethanol, and after standing at −20 °C for 4 h a first crop of 2.16 g (45%) of white solid was collected. Most of this material melted at 100–02 °C. Upon further standing and cooling a second crop of 0.99 g (21%) of white solid, mp 124–26 °C, was recovered.

The low-melting solid was recrystallized from CH_2Cl_2–hexane as fine needles: mp 105–06 °C; IR ($CHCl_3$) 3580 and 1712 cm^{-1} and (fluorolube mull) 3000 cm^{-1} (w, bd, OH) and 1722 (s, sh, CO); ^{1}H NMR 7.23 (s, bd, 20 H, ArH), 2.5–4.5 (complex, 11 H).

Anal. Calcd for $C_{32}H_{31}NO_3$: C, 80.47; H, 6.54, N, 2.93. Found: C, 80.28; H, 6.56; N, 2.92.

The high-melting compound was recrystallized from CH_2Cl_2–hexane as fine needles: mp 128–29.5 °C; IR (Nujol mull) 3490 cm^{-1} (s, OH), 1720, and 1690 cm^{-1} (s, CO); IR ($CHCl_3$) and ^{1}H NMR identical with low-melting isomer.

Anal. Found: C, 80.18; H, 6.56; N, 2.92.

***O*-Acetyl Derivative of 2a.** A solution of 0.5 g of the low-melting isomer of **2a** and 2 mL of acetic anhydride was heated on a steam bath for 15 min and cooled and diluted with 20 mL of H_2O. The solid was collected and recrystallized from 95% ethanol to give 0.45 g of fine white needles: mp 105–06 °C; IR (Nujol mull) 1747 cm^{-1} (s, ester CO), 1720 (s, ketone CO); ^{1}H NMR 7.15 (complex, 20 H, ArH), 2.6–4.2 (complex, 10 H), 1.46 (s, 3 H, Me).

Anal. Calcd for $C_{34}H_{33}NO_4$: C, 78.58; H, 6.40; N, 2.70. Found: C, 79.17; H, 6.65; N, 2.71.

***N,N*-Bis[1-(2,3-diphenyl-3-oxo)propyl]hydroxylamine (2b).** The product was obtained in 55% yield by method A and in 75% yield by method B. The compound was recrystallized as white needles from CH_2Cl_2–hexane, mp 158–59 °C.

Anal. Calcd for $C_{30}H_{27}NO_3$: C, 80.14; H, 6.06; N, 3.11. Found: C, 80.30; H, 6.01; N, 3.01.

***N,N*-Bis[1-(2-methyl-3-phenyl-3-oxo)propyl]hydroxylamine (2c).** The reaction by method A gave only the normal oxime of **1c** along with unreacted **1c**. The product was prepared by method B in 43% yield and was recrystallized as white needles, mp 114–15 °C, from CH_2Cl_2–hexane.

Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.64; H, 6.92; N, 4.22.

1,3-Diphenyl-3-buten-2-one (4a). A solution of 1.51 g (5 mmol) of the hydrochloride of **1a** and 2.05 g (15 mmol) of sodium acetate trihydrate in 15 mL of H_2O was heated at 90–100 °C for 15 min, cooled in ice, and extracted with two 20-mL portions of ether. The ether solution was dried (Na_2SO_4) and evaporated to give 1.16 g of faintly yellow liquid. Analysis by GLC (⅛ in. × 20 in. UCW-982) showed a mixture of **4a** (89%) and dibenzyl ketone (7%), identified by comparison with authentic samples. Further confirmation was obtained by TLC, IR, and ^{1}H NMR spectroscopy and by hydrogenation (10% Pd–C, 1 atm) to 1,3-diphenyl-2-butanone.

Registry No.—**1a**·HCl, 64824-53-9; **1b**, 22563-99-1; **1c**, 91-03-2; **1d**, 3506-36-3; **1e**, 25527-39-3; **1a**·MeI, 68646-44-6; **1b**·MeI, 31035-04-8; **1c**·MeI, 31035-03-7; **2a** (isomer 1), 68698-53-3; **2a** (isomer 2), 68646-45-7; **2a** (OAc derivative), 68646-46-8; **2b**, 68646-47-9; **2c**, 68646-48-0; **4a**, 68646-49-1; **4b**, 4452-11-3; **4c**, 769-60-8; **4e**, 32123-84-5.

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