α-Oxygenation of Aldehydes and Cyclic Ketones by Acylation–Rearrangement of Nitrones

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The reaction of *N-tert*-butylnitrones (**1a–e**) of aldehydes and *N*-methylnitrones (**2** and **3**) of cyclic ketones with acid chlorides in the presence of triethylamine afforded α-acyloxy imines by rearrangement of *N*-vinyl-*O*-acylhydroxylamine intermediates. Hydrolysis of the α-acyloxy imines gave α-acyloxy aldehydes and ketones. The acylation–rearrangement reaction offers a new method for α-oxygenation of carbonyl compounds.

The [3,3]-sigmatropic rearrangement of *N*-aryl-*N*,*O*-diacylhydroxylamines bearing enolizable substituents affords a new synthetic method for ortho alkylation of aromatic rings, giving rise to *o*-(acylamino)aryl ketones and esters.[1] A similar C–C bond-forming reaction could in principle be accomplished by enolization–rearrangement of *N*-vinyl-*O*-acylhydroxylamines, provided the requisite unsaturated hydroxylamines could be prepared. Since *N*-vinyl-*N*-alkylhydroxylamines should be accessible via tautomerization of nitrones (Scheme I), we undertook an investigation of the reaction of nitrones with acid chlorides in the presence of a basic catalyst. Although *N*-alkyl-*N*-vinyl-*O*-acylhydroxylamines were evidently formed as expected, all but one of the compounds underwent rapid rearrangement to α-acyloxy imines. The mild conditions of this reaction and the current interest in synthetic methods for α-oxygenation of carbonyl compounds[2] prompted us to investigate the scope of the process for the preparation of α-acyloxy aldehydes and α-acyloxy derivatives of cyclic ketones.

Considerable precedent for the rearrangement of nitrones and related compounds in the presence of acylating agents is available in the literature. The acylation–rearrangement of 2-alkylpyridine *N*-oxides to 2-(α-acetoxyalkyl)pyridines upon reaction with acetic anhydride is one well-known example.[3] The reaction of the cyclic nitrones, Δ^1-pyrroline *N*-oxides, with benzoyl chloride effects a similar intramolecular redox reaction to give α-benzoyloxy imines.[4] On the other hand, *N*-methylnitrones of steroidal ketones undergo a Beckman-type rearrangement to *N*-methyl lactams upon reaction with *p*-toluenesulfonyl chloride.[5] The facility of the former rearrangement is apparent from the observation that *N*-(1-cyclohexenyl)-*N*-methyl-*O*-acetylhydroxylamine isomerized rapidly to the *N*-methyl imine of α-acetoxycyclohexanone at 0 °C.[6] The *N*-vinyl-*O*-acylhydroxylamine was generated in this case as a transient intermediate by N-methylation of cyclohexanone oxime acetate and subsequent deprotonation with triethylamine.

Scheme I

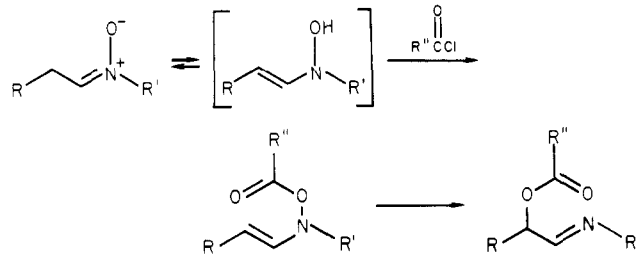
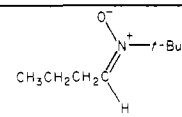
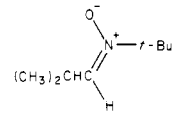
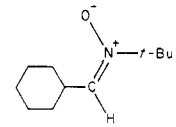
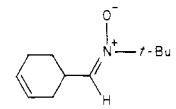
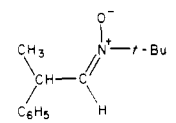


Table I. Preparation of Nitrones from Aldehydes and *N-tert*-Butylhydroxylamine

aldehyde	nitrone	no.	yield, %
n-butyraldehyde		1a	93
isobutyraldehyde		1b	72
cyclohexanecarboxladehyde		1c	80
3-cyclohexenecarboxaldehyde		1d	59
2-phenylpropionaldehyde		1e	88

Torssell and Zeuthen reported recently that the reaction of the *N-tert*-butylnitrone (**1a**) of *n*-butyraldehyde with benzoyl chloride and triethylamine in benzene afforded the *N*-vinyl-*O*-benzoylhydroxylamine **4**.[7] However, the thermal stability of the product [bp 86–106 °C (0.8 mm)]

(1) Coates, R. M.; Said, I. M. *J. Am. Chem. Soc.* **1977**, *99*, 2355–2357.
(2) Some leading references are the following: (a) Boar, R. B.; McGhie, J. F.; Robinson, M.; Barton, D. H. R. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1242–1244. (b) Wasserman, H. H.; Lipshutz, B. H. *Tetrahedron Lett.* **1975**, 1731–1734. (c) Hassner, A.; Reuss, R. H.; Pinnick, H. W. *J. Org. Chem.* **1975**, *40*, 3427–3429. (d) Konen, D. A.; Silbert, L. S.; Pfeffer, P. E. *Ibid.* **1975**, *40*, 3253–3258. (e) Rubottom, G. E.; Marrero, R. *Ibid.* **1975**, *40*, 3783–3784. (f) Rubottom, G. M.; Gruber, J. M.; Mong, G. M. *Ibid.* **1976**, *41*, 1673–1674. (g) Rubottom, G. E.; Gruber, J. M. *Ibid.* **1978**, *43*, 1599–1602. (h) Vedejs, E.; Engler, D. A.; Telschow, J. E. *Ibid.* **1978**, *43*, 188–196. (i) McCormick, J. P.; Tomasik, W.; Johnson, M. W. *Tetrahedron Lett.* **1981**, *22*, 607–610. (j) Moriarity, R. M.; Hu, H.; Gupta, S. C. *Ibid.* **1981**, *22*, 1283–1287. Moriarity, R. M.; Hu, H. *Ibid.* **1981**, *22*, 2747–2750. (k) Reddy, G. B.; Bhatt, M. V. *Synthesis* **1981**, 223–224.
(3) (a) Ochiai, E. "Aromatic *N*-Oxides"; Elsevier: Amsterdam, 1967; pp 173–302. (b) Tranelis, V. J. In "Mechanism of Molecular Migrations"; Thyagarajan, B. S., Ed.; Interscience: New York, 1969; Vol. 2, pp 1–42. (c) Katrizky, A. R.; Lagowski, J. M. "Chemistry of Heterocyclic N-Oxides"; Academic Press: New York, 1971; pp 1–50.
(4) (a) Gutterridge, N. J.; Dales, J. R. M. *J. Chem. Soc. C* **1971**, 122–125. (b) Alazard, J. P.; Khémis, B.; Lusinchi, X. *Tetrahedron Lett.* **1972**, 4795–4798. (c) Alazard, J. P.; Khémis, B.; Lusinchi, X. *Tetrahedron* **1975**, *31*, 1427–1436.
(5) Barton, D. H. R.; Day, M. J.; Hesse, R. H.; Pechet, M. M. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1764–1767
(6) House, H. O.; Richey, F. A., Jr. *J. Org. Chem.* **1969**, *34*, 1430–1439.
(7) Torssell, K.; Zeuthen, O. *Acta Chem. Scand., Ser. B* **1978**, *B32*, 118–124.

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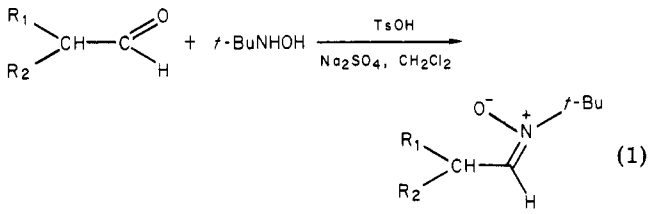
would seem to be at variance with the findings of House and Richey.[6] Furthermore, the NMR spectral data for the compound appear to be more appropriate for the isomeric α-benzoyloxy *N-tert*-butyl imine **5** which would result from a [3,3]-sigmatropic rearrangement of **4**.

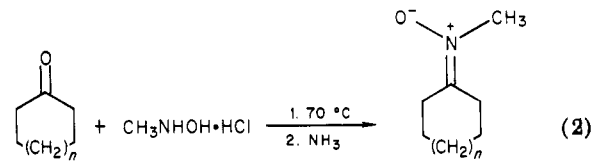
Results and Discussion

A series of five *N-tert*-butylnitrones (**1a–e**) was prepared by condensation of various aldehydes with *N-tert*-butylhydroxylamine[8] in dichloromethane containing *p*-toluenesulfonic acid and anhydrous sodium sulfate (eq 1)



(1)

1a–e



(2)

n = 0, 1

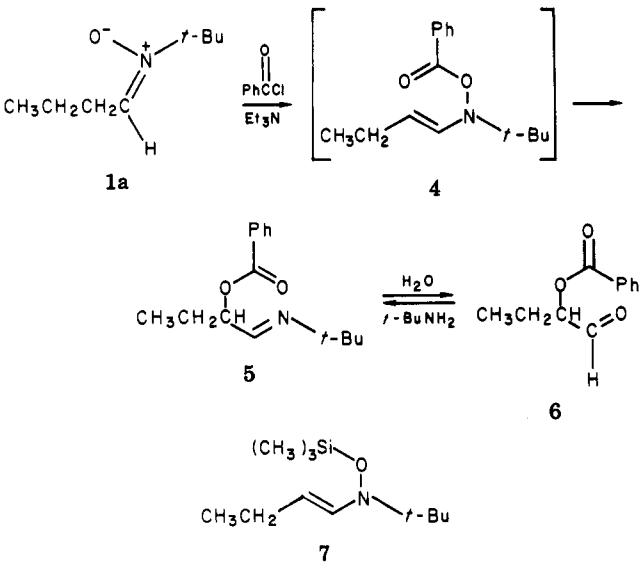
2, n = 0
3, n = 1

according to the procedure of Torssell and Zeuthen[7] (see Table I). Two of the five nitrones were obtained as colorless liquids after distillation under reduced pressure. Cyclohexanecarboxaldehyde, 3-cyclohexenecarboxaldehyde, and 2-phenylpropionaldehyde afforded crystalline *N-tert*-butylnitrones which had melting points of 59–61, 35–37, and 53–56 °C, respectively. Although the nitrones are somewhat hygroscopic in air, they could be stored under nitrogen at −20 °C for several weeks without appreciable decomposition or hydrolysis. The *N*-methylnitrones (**2** and **3**) of cyclopentanone and cyclohexanone were prepared according to the procedure of Exner[9] in which the ketones are condensed with *N*-methyhydroxylamine hydrochloride (eq 2). The nitrones are then liberated from their hydrochloride salts with ammonia.

The reaction of *n*-butyraldehyde nitrone **1a** with benzoyl chloride and triethylamine in benzene afforded a liquid product (36%) the boiling point and spectral properties of which agreed with those reported by Torssell and Zeuthen.[7] The structure of this compound had been assigned as the *N*-vinyl-*O*-acylhydroxylamine structure **4** (Scheme II) in analogy with the *N*-vinyl-*O*-(trimethylsilyl)-hydroxylamine **7** which was prepared from **1a** in a similar manner.[7] However, the NMR spectrum of the benzoylation product exhibits a doublet (J = 4 Hz) at δ 7.5 while the corresponding proton in the silylation product appears at δ 5.90 (d, J = 12 Hz). The large differences in the chemical shifts and coupling constants seemed to us to indicate that the initially formed O-benzoylation product had in fact undergone [3,3]-sigmatropic rearrangement to the α-benzoyloxy imine **5**.

The α-benzoyloxy imine structure was confirmed by hydrolysis to α-(benzoyloxy)butyraldehyde (**6**). Condensation of **6** with *tert*-butylamine regenerated the imine. The spectral properties of the crude benzoylation product

Scheme II



showed that the rearrangement occurred during the reaction and not during distillation.

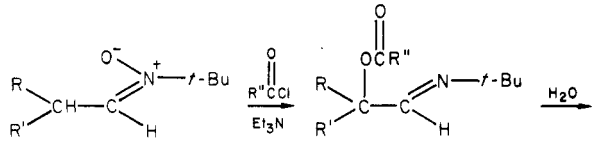
The scope of the nitrone acylation–rearrangement reaction was explored by using nitrones **1a–e** and pivaloyl and acetyl chlorides. The nitrones were added to solutions of the acid chlorides (1 equiv) and triethylamine (1 equiv) in ether at 0 °C. Precipitation of triethylamine hydrochloride began immediately, and the resulting suspensions were allowed to stir at room temperature for 2 h to complete the reaction. The progress of the reaction of nitrone **1b** with pivaloyl chloride was monitored by filtering aliquots into methanol and recording the NMR spectra. The formation of the α-pivaloyloxy imine **8** (R = R′ = CH_3, R″ = C $(CH_3)_3$) was complete after about 1 h at room temperature, and no intermediates were detected.

The α-pivaloyloxy imines from nitrones **1a–c** were purified by distillation and characterized by elemental analysis and/or spectral data. However, since the imines seemed to be hygroscopic and unstable, they were in most cases hydrolyzed immediately to the α-acyloxy aldehydes without purification. A number of methods for hydrolyzing the imines were tried. Trial reactions were done with aqueous hydrochloric acid and tetrahydrofuran, wet silica gel in dichloromethane,[10a] aqueous oxalic acid and benzene,[10b] and aqueous acetic acid/sodium acetate and benzene.[10c] The progress of the reactions was conveniently monitored by gas chromatographic analysis. Hydrolyses with the acetate buffer procedure were usually complete within 5 min at room temperature, and this method gave the best results. For example, yields from comparative runs with the wet silica gel method were consistently lower by 20–30%. The α-acyloxy aldehydes were purified by distillation or flash chromatography on silica gel. The yields of the α-pivaloyloxy imines, α-pivaloyloxy aldehydes, and α-acetoxy aldehydes are shown in Table II. Lower yields were obtained in some runs on using nitrones that had become impure after prolonged storage at −20 °C.

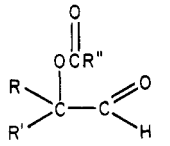
The scope of the acylation–rearrangement with respect to the acylating agent was tested by using the *N-tert*-butylnitrone (**1c**) of cyclohexanecarboxaldehyde and various acid chlorides. The overall isolated yields of α-(acyloxy)cyclohexanecarboxaldehydes **11a–e** are presented in Table III. Reaction of the *N*-methylnitrones **2** and **3** with

(8) Calder, A.; Forrester, A. R.; Hepburn, S. P. *Org. Synth.* **1972**, *52*, 77–82.
(9) Exner, G. *Collect. Czech. Chem. Comm.* **1951**, *16*, 258–267.
(10) (a) Huet, F.; Lechevallier, A.; Pellet, M.; Conia, J. M. *Synthesis* **1978**, 63–65. (b) Nagata, W.; Wakabayashi, T.; Hayase, Y. *Org. Synth.* **1973**, *53*, 104–107. (c) Stork, G.; Benaim, J. *Ibid.* **1977**, *57*, 69–72.

Table II. Preparation of α-Acyloxy Aldehydes from *N*-*tert*-Butylnitrones via α-Acyloxy Imines



1a-e 8



9-13a, R″ = CH_3
b, R″ = *t*-Bu

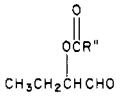
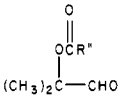
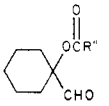
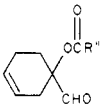
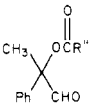
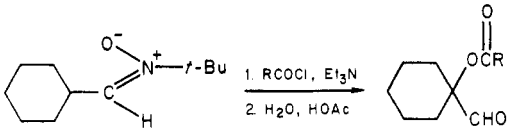
nitrone	imine yield, %	aldehyde	no.	overall yield, %
1a	69		9a 9b	22 70
1b	83		10a 10b	57 78
1c	78		11a 11b	80 95
1d			12a 12b	84 69
1e			13a 13b	81 74

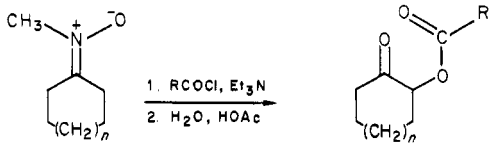
Table III. Preparation of α-(Acyloxy)cyclohexanecarboxaldehydes from Nitrone 1c and Various Acid Chlorides



1c 11a-e

acid chloride	α-acyloxy aldehyde no.	yield, %
CH_3COCl	11a	80
CH_3CH_2COCl	11c	86
$(CH_3)_2CHCOCl$	11d	91
$(CH_3)_3CCOCl$	11b	95
PhCOCl	11e	91

acetyl chloride and pivaloyl chloride (eq 3) gave the corresponding α-(acyloxy)cyclopentanones **14a** (47%) and **14b** (32%) and cyclohexanones **15a** (26%) and **15b** (59%).

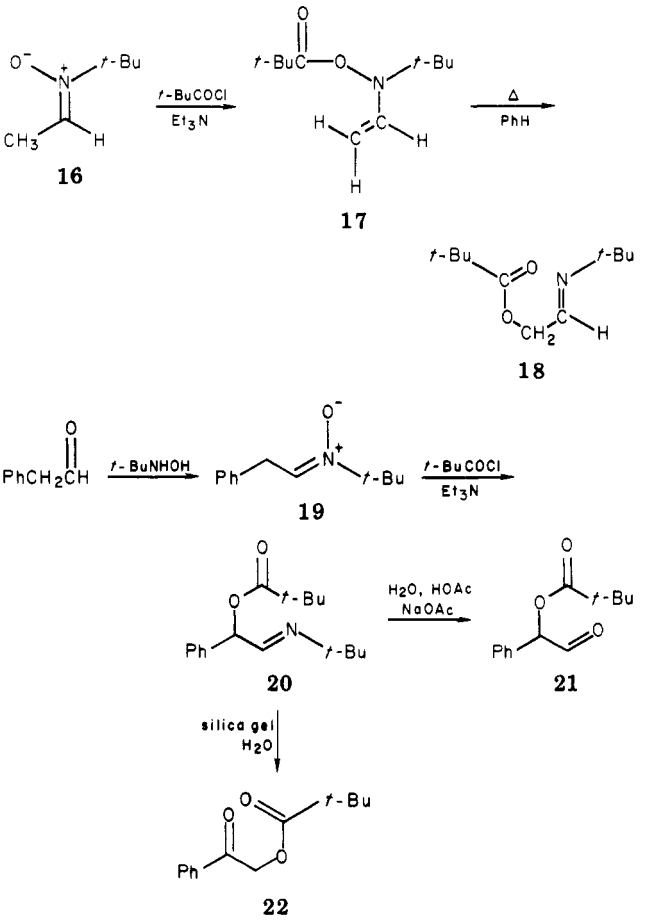


(3)

2, *n* = 0
3, *n* = 1

14a, *n* = 0; R = CH_3
b, *n* = 0; R = $C(CH_3)_3$
15a, *n* = 1; R = CH_3
b, *n* = 1; R = $C(CH_3)_3$

Scheme III



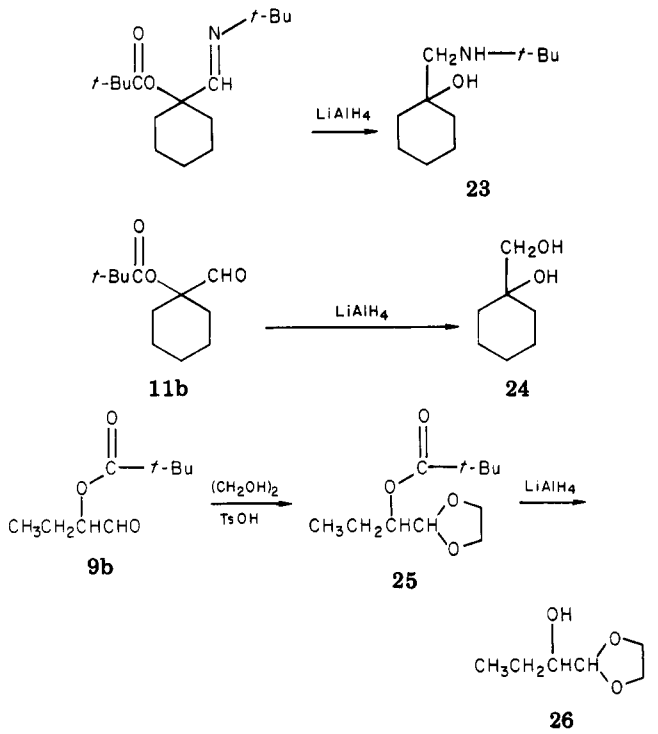
In contrast to the more highly substituted analogues, the *N*-*tert*-butylnitrone (**16**) of acetaldehyde afforded an isolable *N*-vinyl-*O*-pivaloylhydroxylamine, **17** (Scheme III), which underwent rearrangement to the α-pivaloyloxy imine in refluxing benzene. Treatment of the *N*-*tert*-butylnitrone (**19**) of phenylacetaldehyde with triethylamine and pivaloyl chloride gave α-pivaloyloxy imine **20**, judging from the spectral properties of the crude product. Hydrolysis by the acetate buffer procedure gave the expected α-(pivaloyloxy)phenylacetaledhyde (**21**). Hydrolysis of imine **20** with wet silica gel gave only α-(pivaloyloxy)acetophenone (**22**) in low yields, presumably via enolization of the aldehyde, intramolecular acyl transfer, and ketonization.[11] Exposure of aldehyde isomer **21** to the wet silica gel hydrolysis conditions showed no reaction, but the presence of 1 equiv of *tert*-butylamine with the wet silica gel effected partial equilibration to a 1:1 mixture of **21** and **22**.

In view of the isolation of **17**, it is reasonable to suppose that *N*-vinyl-*O*-acylhydroxylamines were formed as transient intermediates in the other acylation–rearrangement reactions. However, no evidence is presently available to distinguish between a concerted [3,3]-sigmatropic rearrangement and nonconcerted mechanisms involving short-lived radical or ionic intermediates.

Some further transformations of the α-acyloxy imines and aldehydes were carried out in order to demonstrate some synthetic applications of the compounds. Reduction of the α-pivaloyloxy imine and aldehyde derived from cyclohexanecarboxaldehyde with lithium aluminum hydride afforded the 1,2-amino alcohol **23** (60%) and 1,2-diol

(11) (a) Riehl, J. J.; Fougerousse, A. *Bull. Soc. Chim. Fr.* **1968**, 4083–4086 (b) Sakai, T.; Seko, K.; Tsuji, A.; Utaka, M.; Takeda, A. *J. Org. Chem.* **1982**, *47*, 1101–1106.

Scheme IV



24 (77%) (Scheme IV). The ethylene acetal (**26**) of α-hydroxybutyraldehyde was prepared from the α-pivaloyloxy aldehyde by acid-catalyzed acetalization with ethylene glycol (83%) and reductive cleavage of the ester with lithium aluminum hydride (58%).

The acylation–rearrangement of *N-tert*-butylnitrones affords a new method for effecting α-oxygenation of aldehydes and cyclic ketones via the respective α-acyloxy imines. The overall yields for the two- or three-step reaction sequence are good, the conditions are quite mild, and the use of electrophilic oxidizing reagents is obviated. The resulting α-acyloxy imines, aldehydes, and ketones may be employed for the preparation of 1,2-aminohydrins, 1,2-diols, and other vicinal difunctional compounds.

It is appropriate to cite some of the methods previously used to prepare α-hydroxy aldehydes or their derivatives by α-oxygenation. α-Acetoxy aldehydes have been obtained by oxidation of enol silanes with *m*-chloroperoxybenzoic acid and subsequent acetylation[2c] and by thermal rearrangement of epoxides of enol acetates.[12] Oxidation of enol silanes with lead tetrabenzoate affords α-benzoyloxy aldehydes.[2f] α-Acetoxyphenylacetaldehyde has been prepared by direct oxidation of phenylacetaldehyde with lead tetraacetate in the presence of boron trifluoride.[11] Solvolysis and displacement reactions of α-halo aldehydes or their derivatives have been employed to prepare α-hydroxy acetals,[13] α-acetoxy aldehydes,[11a] α-benzoyloxy aldehydes,[11b] and α,β-diacetoxy ethers.[14]

Experimental Section

Melting points were determined on a Büchi melting point apparatus and are uncorrected. IR spectra were determined on a Perkin-Elmer Model 137 spectrophotometer. Proton NMR spectra were obtained on a Varian EM-390 spectrometer. Microanalyses were performed by J. Nemeth and associates at the Microanalytical Laboratory, University of Illinois.

Silica gel chromatographic purifications were performed by flash chromatography[15] with Woelm 32–63-μm silica packed in glass columns. The weight of the silica was approximately 100 times the weight of the material. Thin-layer chromatography was used to determine the appropriate solvent system for elution, which was 20–30% ethyl acetate in hexane unless otherwise specified. Analytical gas chromatography was performed on a Varian Model 3700 gas chromatograph using 3% OV-17 on 100/120-mesh Chromosorb Q, packed in either 1.8 m × 6.4 mm or 3.6 m × 6.4 mm columns. Analyses were performed isothermally at temperatures between 90 and 150 °C as appropriate. The chromatography solvents were distilled, but all other solvents were reagent grade unless described otherwise. *N-tert*-Butylhydroxylamine was prepared according to the method of Calder, Forrester, and Hepburn[8] in similar yields. The hydroxylamine was dried under reduced pressure and stored under nitrogen in a freezer.

Preparation of *N-tert*-Butylnitrones. The nitrones were prepared by condensation of the appropriate aldehyde (71.0 mmol) with *N-tert*-butylhydroxylamine[8] (56.3 mmol) in 20 mL of dichloromethane containing suspended sodium sulfate, according to the procedure of Torssell and Zeuthen.[7] The solid nitrones were purified by recrystallization from hexane.

***N*-Butylidene-1,1-dimethylethanamine *N*-Oxide (1a)**: yield 7.43 g (93%); bp 50–53 °C (0.45 mm) [lit.[7] bp 87–90 °C (10 mm)]; IR (neat) 1095 (NO), 1575 cm^{-1} (C=N). The spectral data obtained for this compound are in agreement with the values reported in the literature.[7]

***N*-(2-Methylpropylidene)-1,1-dimethylethanamine *N*-oxide (1b)** was obtained as a colorless liquid which solidified on standing: yield 2.56 g (72%); bp 55–58 °C (0.9 mm); IR (neat) 1110 (NO), 1575 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 1.08 (d, 6 H, J = 7.5 Hz, $CH(CH_3)_2$, 1.47 (s, 9 H, $C(CH_3)_3$), 3.19 (d of septets, 1 H, J = 7.5, 7.5 Hz, $CH(CH_3)_2$), 6.58 (d, 1 H, J = 7.5 Hz, HC=N). Anal. Calcd for $C_8H_{17}NO$: C, 67.09; H, 11.96; N, 9.78. Found: C, 66.73; H, 12.01; N, 9.81.

***N*-(Cyclohexylmethylidene)-1,1-dimethylethanamine *N*-oxide (1c)** was obtained as a white, crystalline solid: yield 9.27 g (80%); mp 59–61 °C; ^1H NMR ($CDCl_3$) δ 0.93–1.97 (m, 10 H, $(CH_2)_5$), 1.48 (s, 9 H, $C(CH_3)_3$), 2.98 (m, 1 H, $CH(CH_2)_5$), 6.58 (d, 1 H, J = 7.5 Hz, HC=N). Anal. Calcd for $C_{11}H_{21}NO$: C, 72.08; H, 11.55; N, 7.64. Found: C, 71.95; H, 11.56; N, 7.63.

***N*-[(Cyclohex-3-enyl)methylidene]-1,1-dimethylethanamine *N*-oxide (1d)** was obtained as a white crystalline solid: yield 6.02 g (59%); mp 35–37 °C; ^1H NMR ($CDCl_3$) δ 1.47 (s, 9 H, $C(CH_3)_3$), 1.52–2.32 (m, 6 H, ring CH_2), 3.07–3.33 (m, 1 H, CH(CH=N)), 5.55–5.72 (m, 2 H, CH=CH), 6.64 (d, 1 H, J 7 Hz, HC=N). Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 72.65; H, 10.59; N, 7.67.

***N*-(2-Phenylpropylidene)-1,1-dimethylethanamine *N*-oxide (1e)** was obtained as a white crystalline solid: yield 10.11 g (88%); mp 53–56 °C; ^1H NMR ($CDCl_3$) δ 1.43 (d, 3 H, J = 5 Hz, CH_3), 1.47 (s, 9 H, $C(CH_3)_3$), 4.35 (dq, 1 H, J = 5, 7.5 Hz, $CH(CH_3)$), 6.86 (d, 1 H, J = 7.5 Hz, HC=N), 7.03–7.33 (m, 5 H, aromatic H). Anal. Calcd for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82. Found: C, 75.79; H, 9.14; N, 6.58.

***N*-Cyclopentylidenemethanamine *N*-oxide (2)** was prepared according to the method of Exner.[9] Purification by Kugelrohr distillation at 70 °C (0.1 mm) afforded 0.38 g (35%) of a pale yellow liquid: ^1H NMR ($CDCl_3$) δ 1.53–2.19 (m, 4 H, $CH_2(CH_2)_2CH_2$), 2.30–3.01 (m, 4 H, $CH_2(CH_2)_2CH_2$), 3.61 (s, 3 H, NCH_3).

***N*-Cyclohexylidenemethanamine *N*-oxide (3)** was prepared according to the method of Exner.[9] Purification by Kugelrohr distillation at 80 °C (0.1 mm) afforded 0.85 g (37%) of a pale yellow liquid: ^1H NMR ($CDCl_3$) δ 1.28–1.90 (m, 6 H, $CH_2(CH_2)_3CH_2$), 2.17–2.95 (m, 4 H, $CH_2(CH_2)_3CH_2$), 3.63 (s, 3 H, NCH_3).

General Procedure for the Preparation of α-Acyloxy Imines. A solution of the acid chloride (21 mmol) in 100 mL of

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anhydrous diethyl ether was stirred and cooled at 0 °C under nitrogen as 2.89 mL (21 mmol) of triethylamine was introduced via syringe. A solution of the *N-tert*-butylnitrone (21 mmol) in 20 mL of anhydrous ether was then added dropwise. The resulting suspension of precipitated triethylamine hydrochloride was allowed to warm to room temperature and stirred for an additional 2 h. Filtration of the precipitate and evaporation of the solvent at reduced pressure on a rotary evaporator afforded the crude α-acyloxy imines **8**, which were hydrolyzed directly to the α-acyloxy aldehydes in most cases. The imines from acylation–rearrangement of nitrones **1a–c** with pivaloyl chloride were purified by distillation under reduced pressure.

The *N*-methylnitrones of ketones were liberated from their hydrochloride salts (6.7 mmol) by treatment with ammonia in 50 mL of anhydrous diethyl ether, as described by Exner.[9] The ammonium chloride precipitate was filtered, and the filtrate was purged with dry nitrogen for 5 min. The nitrones were not isolated and purified as described in the preparation of compounds **2** and **3** since they are unstable but were maintained as ether solutions. The same acylation–rearrangement procedure described above was then followed, with the exception that more dilute solutions were employed. A solution of the acid chloride in 10 mL of anhydrous ether was used, and the 50-mL ethereal solution of the nitrone was added after injection of triethylamine.

***N*-[2-(Benzoyloxy)butanylidene]-1,1-dimethylethanamine (5)** was prepared by the method of Torssell and Zeuthen and purified by distillation: yield 1.25 g (36%); bp 84–88 °C (0.1 mm) [lit.[7] bp 96–106 °C (0.8 mm)]; IR (CCl_4) 1680 (C=N), 1735 cm^{-1} (CO_2R); ^1H NMR ($CDCl_3$) δ 1.02 (t, 3 H, J = 7.5 Hz, CH_2CH_3), 1.20 (s, 9 H, $C(CH_3)_3$), 1.94 (dq, 2 H, J = 5, 7.5 Hz, CH_2CH_3), 5.42 (m, 1 H, HCCH=N), 7.39–7.54 (m, 2 H, aromatic H), 7.61 (d, 1 H, J = 4.5 Hz, HC=N), 8.07–8.11 (m, 2 H, aromatic H).

α-Benzoyloxy imine 5 was also prepared by the preceding general method for preparation of α-acyloxy imines and by condensation of 0.18 g (2.4 mmol) of *tert*-butylamine and 0.47 g (2.4 mmol) of 2-(benzoyloxy)butanal in 5 mL of carbon tetrachloride for 30 min. The solution was dried with magnesium sulfate and evaporated at reduced pressure on a rotary evaporator. NMR analysis indicated that in both cases the purity of the imines was approximately 80%.

2-(Benzoyloxy)butanal (6) was prepared by benzoylation–rearrangement of 0.50 g of nitrone **1a** according to the preceding general procedure and subsequent hydrolysis with acetate buffer (see below for the details). Purification by flash chromatography with 8:1:1 hexane–ethyl acetate–methanol afforded 0.35 g (52%) of the α-benzoyloxy aldehyde **6**: IR (neat) 1735, 1750 (CO_2R, CHO), 3050 cm^{-1} (ArH); ^1H NMR ($CDCl_3$) δ 1.11 (t, 3 H, J = 9 Hz, CH_2CH_3), 1.98 (m, 2 H, CH_2CH_3), 5.16 (t, 1 H, J = 7.5 Hz, $HC(C_2H_5)$), 7.17–7.77 (m, 3 H, aromatic H), 7.88–8.20 (m, 2 H, aromatic H), 9.63 (s, 1 H, CHO). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74, H, 6.29. Found: C, 68.75; H, 6.32.

***N*-[2-[(2,2-Dimethylpropanoyl)oxy]butanylidene]-1,1-dimethylethanamine (8; R = H, R′ = CH_2CH_3, R″ = $C(CH_3)_3$)**: yield 0.55 g (69%); bp 45–47 °C (0.2 mm); IR (neat) 1365, 1380 ($CCH_3)_3$), 1675 (C=N), 1730 cm^{-1} (CO_2R); ^1H NMR ($CDCl_3$) δ 0.92 (t, 3 H, J = 6 Hz, CH_2CH_3), 1.15 (s, 9 H, $C(CH_3)_3$), 1.22 (s, 9 H, $C(CH_3)_3$), 1.77 (m, 2 H, CH_2CH_3), 5.09 (m, 1 H, HC(HC=N)), 7.43 (d, 1 H, J = 4.5 Hz, HC=N).

***N*-[2-[(2,2-Dimethylpropanoyl)oxy]-2-methylpropanylidene]-1,1-dimethylethanamine (8, R = R′ = CH_3, R″ = $C(CH_3)_3$)**: yield 5.27 g (83%); bp 39–40 °C (0.3 mm); IR (neat) 1700 (C=N), 1735 cm^{-1} (CO_2R); ^1H NMR ($CDCl_3$) δ 1.13 (s, 9 H, $C(CH_3)_3$), 1.17 (s, 9 H, $C(CH_3)_3$), 1.45 (s, 6 H, $C(CH_3)_2$), 7.12 (s, 1 H, HC=N). Anal. Calcd for $C_{13}H_{25}NO_2$: C, 68.68; H, 11.08; N, 6.16. Found: C, 68.59; H, 10.99; N, 6.01.

***N*-[[1-[(2,2-Dimethylpropanoyl)oxy]cyclohexyl]methylidene]-1,1-dimethylethanamine (8; R = R′ = $(CH_2)_5$, R″ = $C(CH_3)_3$)**: yield 6.91 g (78%); bp 84–90 °C (0.9 mm); IR (neat) 1375, 1400 ($C(CH_3)_3$), 1690 (C=N), 1740 cm^{-1} (CO_2R); ^1H NMR ($CDCl_3$) δ 1.13 (s, 9 H, $C(CH_3)_3$), 1.20 (s, 9 H, $C(CH_3)_3$), 1.40–2.30 (m, 10 H, $(CH_2)_5$, 7.59 (s, 1 H, HC=N).

General Procedure for the Hydrolysis of α-Acyloxy Imines. The acetate buffer solution was prepared by dissolving 5 g of sodium acetate in 10 mL of water and 10 mL of acetic acid. A heterogeneous mixture of 12 mL of acetate buffer and a solution of the unpurified α-acyloxy imine obtained from 0.5 g (2.4–3.5 mmol) of the nitrone in 25 mL of benzene was stirred rapidly at room temperature until the reaction was complete, generally within 5 min. The progress of the reaction was monitored by diluting a 15-μL aliquot of the organic layer with 10 drops of ether and analyzing a 1-μL portion of this solution by gas chromatography. The organic layer was separated, and the aqueous phase was extracted with four 20-mL portions of ether which were combined with the original organic layer. The solution was washed with three 20-mL portions of aqueous sodium bicarbonate and dried ($MgSO_4$). Filtration and evaporation of the solvent at reduced pressure on a rotary evaporator, followed by purification of the residue by distillation or flash chromatography,[15] afforded the α-acyloxy aldehydes **9–13** and the α-acyloxy ketones **14** and **15** as colorless liquids. Boiling points where given were obtained from previous runs on a larger scale. We found that the overall yields of the α-acyloxy aldehydes and ketones from the nitrones were not significantly improved by purification of the intermediate α-acyloxy imines; therefore, in the following procedures the crude imines were used in the hydrolysis step without purification.

2-(Acetyloxy)butanal (9a) was prepared from 0.25 g (1.7 mmol) of nitrone **1a** and was purified by Kugelrohr distillation: yield 0.05 g (22%); bp 25–27 °C (0.4 mm) [lit.[11] bp 65–66 °C (13 mm)]. The spectral data obtained for this compound are in agreement with the values reported in the literature.[11]

2-[(2,2-Dimethylpropanoyl)oxy]butanal (9b) was prepared from 0.5 g (3.5 mmol) of nitrone **1a**, and purified by Kugelrohr distillation: yield 0.42 g (70%); bp 35–37 °C (0.2 mm); IR (neat) 1375, 1400 ($C(CH_3)_3$), 1740 cm^{-1} (CHO), CO_2R); ^1H NMR ($CDCl_3$) δ 0.98 (t, 3 H, J = 7.5 Hz, CH_2CH_3), 1.25 (s, 9 H, $C(CH_3)_3$), 1.82 (m, 2 H, CH_2CH_3), 4.82 (dd, 1 H, J = 6, 7 Hz, $HC(C_2H_5)$), 9.39 (s, 1 H, CHO). Anal. Calcd for $C_9H_{16}O_3$: C, 62.79; H, 9.30. Found: C, 62.90; H, 9.46.

2-(Acetyloxy)-2-methylpropanal (10a) was prepared from 0.50 g (3.5 mmol) of nitrone **1b** and purified by Kugelrohr distillation at 90 °C (20 mm); yield 0.26 g (57%). The spectral data obtained for this compound are in agreement with the values reported in the literature.[11]

2-[(2,2-Dimethylpropanoyl)oxy]-2-methylpropanal (10b) was prepared from 1 g (7 mmol) of nitrone **1b** and purified by Kugelrohr distillation: yield 0.94 g (78%); bp 28–30 °C (0.3 mm); IR (neat) 1350, 1390 ($C(CH_3)_3$), 1735 (CO_2R), 1750 cm^{-1} (CHO); ^1H NMR ($CDCl_3$) δ 1.22 (s, 9 H, $C(CH_3)_3$), 1.38 (s, 6 H, $C(CH_3)_2$), 9.39 (s, 1 H, CHO). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 63.06; H, 9.30.

1-(Acetyloxy)cyclohexanecarboxaldehyde (11a) was prepared from 0.50 g (2.7 mmol) of nitrone **1c** and purified by Kugelrohr distillation: yield 0.37 g (80%); bp 77–79 °C (0.6 mm) [lit.[17] bp 140–145 °C (70 mm)]; IR (neat) 1735 (CO_2R), 1750 cm^{-1} (CHO); ^1H NMR ($CDCl_3$) δ 0.90–2.20 (m, 10 H, $(CH_2)_5$), 2.11 (s, 3 H, $OCOCH_3$), 9.44 (s, 1 H, CHO).

1-[(2,2-Dimethylpropanoyl)oxy]cyclohexanecarboxaldehyde (11b) was prepared from 1 g (5.5 mmol) of nitrone **1c** and purified by Kugelrohr distillation: 1.10 g (95%); bp 67–68 °C (0.3 mm); IR (neat) 1370, 1400 ($C(CH_3)_3$), 1730 (CO_2R), 1750 cm^{-1} (CHO); ^1H NMR ($CDCl_3$) δ 1.27 (s, 9 H, $C(CH_3)_3$), 1.10–2.50 (m, 10 H, $(CH_2)_5$), 9.34 (s, 1 H, CHO). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.94; H, 9.57.

1-(Propanoyloxy)cyclohexanecarboxaldehyde (11c) was prepared from 0.50 g (2.7 mmol) of nitrone **1c** and purified by Kugelrohr distillation: yield 0.43 g (86%); bp 67–68 °C (0.2 mm); IR (neat) 1745 cm^{-1} (CHO, CO_2R); ^1H NMR ($CDCl_3$) δ 1.18 (t, 3 H, J = 9 Hz, CH_2CH_3), 1.20–2.70 (m, 10 H, $(CH_2)_5$), 2.42 (q, 2 H, CH_2CH_3), 9.46 (s, 1 H, CHO). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.57; H, 8.96.

1-[(2-Methylpropanoyl)oxy]cyclohexanecarboxaldehyde (11d) was prepared from 0.50 g (2.7 mmol) of nitrone **1c** and purified by Kugelrohr distillation: yield 0.49 g (91%); bp 71–74 °C (1 mm); IR (neat) 1735 cm^{-1} (CHO, CO_2R); ^1H NMR ($CDCl_3$) δ 1.24 (d, 6 H, J = 6 Hz, $HC(CH_3)_2$), 1.10–2.40 (m, 10 H, $(CH_2)_5$), 2.63 (septet, J = 6 Hz, 1 H, $HC(CH_3)_2$), 9.42 (s, 1 H, CHO). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.76; H, 9.32.

1-(Benzoyloxy)cyclohexanecarboxaldehyde (11e) was prepared from 0.50 g (2.7 mmol) of nitrone **1c** and purified by

(17) Kulkarni, B. D.; Rao, A. S. *Synthesis* **1976**, 454–455.

flash chromatography: yield 0.57 g (91%); IR (neat) 1725 (CO_2R), 1745 (CHO), 3080 cm^{-1} (Ar H); ^1H NMR ($CDCl_3$) δ 1.07–2.39 (m, 10 H, $(CH_2)_5$), 7.20–7.50 (m, 3 H, aromatic H), 7.92–8.22 (m, 2 H, aromatic H), 9.59 (s, 1 H, CHO). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.13; H, 7.19.

1-(Acetyloxy)-3-cyclohexenecarboxaldehyde (12a) was prepared from 0.50 g (2.8 mmol) of nitrone **1d** and purified by Kugelrohr distillation at 105 °C (0.20 mm); yield 0.39 g (84%). The spectral data obtained for this compound are in agreement with the values reported in the literature.[2c]

1-[(2,2-Dimethylpropanoyl)oxy]-3-cyclohexenecarboxaldehyde (12b) was prepared from 0.50 g (2.8 mmol) of nitrone **1d** and purified by Kugelrohr distillation at 90 °C (0.3 mm): yield 0.4 g (69%); IR (neat) 1375, 1400 ($C(CH_3)_3$), 1740 (CO_2R and CHO), 3010 cm^{-1} (vinyl H); ^1H NMR ($CDCl_3$) δ 1.23 (s, 9 H, $C(CH_3)_3$), 1.60–2.60 (m, 6 H, ring CH_2), 5.49–5.69 (m, 2 H, CH=CH), 9.39 (s, 1 H, CHO). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.18; H, 8.64.

2-(Acetyloxy)-2-phenylpropanal (13a), a known compound,[17] was prepared from 0.50 g (2.4 mmol) of nitrone **1e** and purified by flash chromatography: yield 0.38 g (81%); IR (neat) 1740 (CO_2R, CHO), 3090 cm^{-1} (Ar H); ^1H NMR ($CDCl_3$) δ 1.85 (s, 3 H, CH_3), 2.25 (s, 3 H, $OCOCH_3$), 7.13–7.60 (m, 5 H, aromatic H), 9.43 (s, 1 H, CHO).

2-[(2,2-Dimethylpropanoyl)oxy]-2-phenylpropanal (13b) was prepared from 0.50 g (2.4 mmol) of nitrone **1e** and purified by Kugelrohr distillation at 100 °C (0.3 mm): yield 0.42 g (74%); IR (neat) 1740 (CO_2R, CHO), 3090 cm^{-1} (Ar H); ^1H NMR ($CDCl_3$) δ 1.34 (s, 9 H, $C(CH_3)_3$), 1.83 (s, 3 H, CH_3), 7.19–7.66 (m, 5 H, aromatic H), 9.35 (s, 1 H, CHO). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.65; H, 7.48.

2-(Acetyloxy)cyclopentanone (14a) was prepared from 1 g (6.7 mmol) of the hydrochloride salt of nitrone **2** and purified by Kugelrohr distillation at 75 °C (0.15 mm); yield 0.45 g (47%). The spectral data obtained for this compound are in agreement with the values reported in the literature.[18]

2-[(2,2-Dimethylpropanoyl)oxy]cyclopentanone (14b) was prepared from 1 g (6.7 mmol) of the hydrochloride salt of nitrone **2** and purified by flash chromatography: yield 0.46 g (37%); IR (neat) ^1H NMR ($CDCl_3$) δ 1.23 (s, 9 H, $C(CH_3)_3$), 1.63–2.60 (m, 6 H, $(CH_2)_3$), 4.89–5.18 (m, 1 H, HCOCOR). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.90; H, 8.93.

2-(Acetyloxy)cyclohexanone (15a) was prepared from 1 g (6.1 mmol) of the hydrochloride salt of nitrone **3** and purified by flash chromatography; yield 0.25 g (26%). The spectral data obtained for this compound are in agreement with the values reported in the literature.[18]

2-[(2,2-Dimethylpropanoyl)oxy]cyclohexanone (15b) was prepared from 1 g (6.1 mmol) of the hydrochloride salt of nitrone **3** and purified by flash chromatography: yield 0.71 g (59%); IR (neat) 1365, 1395 ($C(CH_3)_3$), 1745 cm^{-1} (CO, CO_2R); ^1H NMR ($CDCl_3$) δ 1.25 (s, 9 H, $C(CH_3)_3$), 1.53–2.60 (m, 8 H, $(CH_2)_4$), 4.93–5.27 (m, 1 H, HCOCOR). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.63; H, 9.15.

***N*-Ethylidene-1,1-dimethylethanamine *N*-oxide (16)** was prepared according to the method of Torssell and Zeuthen: yield 3.16 g (82%); bp 43–46 °C (0.5 mm) [lit.[7] bp 46 °C (1.4 mm)]. The spectral data obtained for this compound are in agreement with the values reported in the literature.[7]

***N*-[(2,2-Dimethylpropanoyl)oxy]-*N*-(1,1-dimethylethyl)-ethenamine (17)** was prepared as described in the procedure for preparation of α-acyloxy imines: yield 2.32 g (51%); bp 44–46 °C (0.4 mm); IR (neat) 1735 (CO_2R), 3100 cm^{-1} (vinyl H); ^1H NMR ($CDCl_3$) δ 1.20 (s, 9 H, $C(CH_3)_3$), 1.30 (s, 9 H, $C(CH_3)_3$), 4.20 (m, 2 H, CH=CH), 6.35 (dd, 1 H, J = 5, 15 Hz, CH_2=CH).

***N*-[2-[(2,2-Dimethylpropanoyl)oxy]ethanylidene]-1,1-dimethylethanamine (18).** A solution of 1 g (5 mmol) of hydroxylamine **17** in 50 mL of benzene was heated at reflux under nitrogen for 1 h. Evaporation of solvent on a rotary evaporator and distillation afforded 0.34 g (34%) of imine **18** as a colorless liquid: bp 35–37 °C (0.5 mm); IR (neat) 1365, 1395 ($C(CH_3)_3$), 1680 (CN), 1735 cm^{-1} (CO_2R); ^1H NMR ($CDCl_3$) δ 1.18 (s, 9 H, $C(CH_3)_3$), 1.25 (s, 9 H, $C(CH_3)_3$), 4.62 (d, 2 H, J = 4.5 Hz, CH_2), 7.52 (t, 1 H, J = 4.5 Hz, HC=N).

***N*-(2-Phenylethylidene)-1,1-dimethylethanamine *N*-oxide (19)** was prepared according to the procedure of Torssell and Zeuthen.[7] The crude nitrone (~100%) was obtained as a yellow oil the purity of which was judged to be greater than 90% on the basis of its ^1H NMR spectrum ($CDCl_3$): δ 1.50 (s, 9 H, $C(CH_3)_3$), 3.80 (d, 2 H, J = 4.5 Hz, CH_2), 6.92 (t, 1 H, J = 4.5 Hz, HC=N), 7.03–7.50 (m, 5 H, aromatic H).

2-[(2,2-Dimethylpropanoyl)oxy]-2-phenylethanone (21) was prepared from 1.08 g (5.6 mmol) of nitrone **19** and purified by flash chromatography: yield 0.61 g (49%); IR (neat) 1370, 1395 ($C(CH_3)_3$), 1735 (CHO and CO_2R), 3050 cm^{-1} (Ar H); ^1H NMR δ 1.33 (s, 9 H, $C(CH_3)_3$), 5.99 (s, 1 H, HCPh), 7.39 (s, 5 H, aromatic H), 9.52 (s, 1 H, CHO). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.01; H, 7.30.

2-[(2,2-Dimethylpropanoyl)oxy]-1-phenylethanone (22). Water (3.47 g) was added to a stirred suspension of 34.7 g of silica gel (Brinkmann, 0.05–0.20 mm) in 80 mL of dichloromethane.[10a] After 5 min, 3.47 g of the crude α-acyloxy imine **20**, prepared from 2.4 g (12.6 mmol) of nitrone **19**, was added. After 4 h the suspension was filtered, the silica gel was washed well with dichloromethane, and the filtrate was evaporated at reduced pressure on a rotary evaporator. Purification of the residue by flash chromatography on silica gel afforded ketone **21** as a white solid: yield 0.46 g (17%); mp 60–61.5 °C; ^1H NMR ($CDCl_3$) δ 1.29 (s, 9 H, $C(CH_3)_3$), 5.23 (s, 2 H, CH_2), 7.22–7.55 (m, 3 H, aromatic H), 7.66–7.93 (m, 2 H, aromatic H). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.97; H, 7.20.

1-[[(1,1-Dimethylethyl)amino]methyl]cyclohexanol (23). A suspension of 0.22 g (5.4 mmol) of lithium aluminum hydride (95% dispersion in mineral oil) in 15 mL of anhydrous diethyl ether was stirred under nitrogen at 0 °C. A solution of 0.25 g (0.9 mmol) of imine **8** [R = R′ = $(CH_2)_5$, R″ = $C(CH_3)_3$] in 3 mL of anhydrous diethyl ether was added dropwise. After the addition was complete, the suspension was allowed to warm to room temperature and stirred for an additional 1 h. After sequential addition of 0.25 mL of water, 0.25 mL of 15% aqueous sodium hydroxide, and 0.75 mL of water, the suspension was filtered, and the filter cake was washed well with ether. The ether portions were combined and dried ($MgSO_4$). Evaporation of solvent at reduced pressure on a rotary evaporator and Kugelrohr distillation of the residual liquid at 95 °C (0.75 mm) afforded 0.1 g (60%) of amino alcohol **23** as a colorless liquid: IR (neat) 3400 cm^{-1} (OH, NH); ^1H NMR ($CDCl_3$) δ 1.00–2.03 (m, 10 H, $(CH_2)_5$), 1.08 (s, 9 H, $C(CH_3)_3$), 2.43 (s, 2 H, CH_2). Anal. Calcd for $C_{11}H_{23}NO$: C, 71.30; H, 12.51; N, 7.56. Found: C, 71.44; H, 12.40; N, 7.69.

1-(Hydroxymethyl)cyclohexanol (24). A suspension of 0.24 g (6 mmol) of lithium aluminum hydride (95% dispersion in mineral oil) in 15 mL of anhydrous diethyl ether was stirred under nitrogen at 0 °C. A solution of 0.25 g (1 mmol) of aldehyde **11b** in 2 mL of anhydrous diethyl ether was added dropwise. The mixture was stirred for 30 min, the cooling bath was removed, and stirring was continued for another 30 min. After sequential addition of 0.25 mL of water, 0.25 mL of 15% aqueous sodium hydroxide, and 0.75 mL of water, the suspension was filtered, the solid was washed well with diethyl ether, and the ether portions were combined and dried ($MgSO_4$). Evaporation of the solvent at reduced pressure on a rotary evaporator and trituration of the resulting glass with diethyl ether, followed by filtration, afforded 0.10 g (77%) of diol **23** as a white solid: mp 75–76 °C (lit.[19] mp 73–75 °C); ^1H NMR ($CDCl_3$) δ 1.12–2.25 (m, 10 H, $(CH_2)_5$), 2.58 (s, 1 H, OH), 2.85–3.25 (br t, 1 H, J = 6 Hz, CH_2OH), 3.41 (d, 2 H, J = 6 Hz, CH_2OH).

2-[(2,2-Dimethylpropanoyl)oxy]butanal Ethylene Acetal (25). A solution of 0.50 g (2.9 mmol) of aldehyde **9b**, 0.35 g (6 mmol) of ethylene glycol, and a few milligrams of *p*-toluenesulfonic acid in 25 mL of benzene was heated at reflux under nitrogen for 5.5 h in an apparatus equipped with a Dean–Stark trap. The solution was diluted with 100 mL of diethyl ether and extracted with two 75-mL portions of saturated aqueous sodium bicarbonate. The bicarbonate extracts were combined and extracted with two 75-mL portions of ether. The ether extracts were combined with the original organic layer, and the solution was washed with two

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75-mL portions of brine and dried ($MgSO_4$). Filtration and evaporation of the solvent at reduced pressure on a rotary evaporator, followed by gravity chromatography of the residue on silica gel with 30% diethyl ether–hexane, afforded 0.52 g (83%) of acetal **25** as a pale yellow liquid: IR (neat) 1740 cm^{-1} (CO_2R); ^1H NMR ($CDCl_3$) δ 0.89 (t, 3 H, J = 7.5 Hz, CH_2CH_3), 1.20 (s, 9 H, $C(CH_3)_3$), 1.65 (m, 2 H, CH_2CH_3), 3.77–4.00 (m, 4 H, $(CH_2)_2$), 4.78–4.95 (m, 2 H, $HC(O(CH_2)_2O)$, $HC(C_2H_5)$). Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 61.41; H, 9.30.

2-Hydroxybutanal Ethylene Acetal (26). A suspension of 0.07 g (1.8 mmol) of lithium aluminum hydride (95% dispersion in mineral oil) in 5 mL of anhydrous diethyl ether was stirred under nitrogen at 0 °C. A solution of 0.20 g (0.9 mmol) of acetal **24** in 2 mL of anhydrous diethyl ether was added slowly. The mixture was stirred for 30 min, the cooling bath was removed, and stirring was continued for an additional 1 h. After sequential treatment with 0.5 mL water, 0.5 mL of 15% aqueous sodium hydroxide, and 1 mL of water, the suspension was filtered, and the solid washed well with diethyl ether. The ether portions were combined and dried ($MgSO_4$). Evaporation of solvent at reduced pressure on a rotary evaporator and Kugelrohr distillation of the residue afforded 0.07 g (58%) of alcohol **25** as a colorless liquid: IR (neat) 3500 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 0.98 (t, 3 H, J = 7 Hz, CH_2CH_3), 1.33–1.80 (m, 2 H, CH_2CH_3), 2.00 (d, J = 4.5 Hz, 1 H, OH), 3.40–3.73 (m, 1 H, HCOH), 3.77–4.07 (m, 4 H, $(CH_2)_2$), 4.68 (d, 1 H, J = 4.5 Hz, $HC(O(CH_2)_2O)$. Anal. Calcd for $C_6H_{12}O_3$: C, 54.53; H, 9.15. Found: C, 54.82; H, 8.98.

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Registry No. **1a**, 72552-75-1; **1b**, 85664-55-7; **1c**, 85664-56-8; **1d**, 85664-57-9; **1e**, 85664-58-0; **2**, 72552-74-0; **2**·HCl, 72552-79-5; **3**, 58751-78-3; **3**·HCl, 72552-80-8; **5**, 85664-59-1; **6**, 80387-13-9; **8** (R = H; R′ = CH_2CH_3; R″ = $C(CH_3)_3$), 85664-60-4; **8** (R = R′ = CH_3; R″ = $C(CH_3)_3$), 85664-61-5; **8** (R = R′ = $(CH_2)_5$; R″ = $C(CH_3)_3$), 85664-62-6; **9a**, 5921-90-4; **9b**, 85664-63-7; **10a**, 22094-24-2; **10b**, 85664-64-8; **11a**, 56037-77-5; **11b**, 85664-65-9; **11c**, 85664-66-0; **11d**, 85664-67-1; **11e**, 85664-68-2; **12a**, 55638-24-9; **12b**, 85664-69-3; **13a**, 60860-35-7; **13b**, 85664-70-6; **14a**, 52789-75-0; **14b**, 85664-71-7; **15a**, 17472-04-7; **15b**, 85664-72-8; **16**, 55830-07-4; **17**, 85664-73-9; **18**, 85664-74-0; **19**, 82937-45-9; **20**, 85664-75-1; **21**, 85664-76-2; **22**, 2522-81-8; **23**, 65055-38-1; **24**, 15753-47-6; **25**, 85664-77-3; **26**, 85664-78-4; CH_3COCl, 75-36-5; CH_3CH_2COCl, 79-03-8; $(CH_3)_2CHCOCl$, 79-30-1; $(CH_3)_3CCOCl$, 3282-30-2; PhCOCl, 98-88-4; *N-tert*-butylhydroxylamine, 16649-50-6; *tert*-butylamine, 75-64-9; *n*-butyraldehyde, 123-72-8; isobutyraldehyde, 78-84-2; cyclohexanecarboxaldehyde, 2043-61-0; 3-cyclohexene-carboxaldehyde, 100-50-5; 2-phenylpropionaldehyde, 93-53-8.

Electrophile-Initiated Ring-Opening Reactions of 2-Methylene-6,6-dimethylbicyclo[3.1.0]hexanes. New Methodology for the Synthesis of Highly Functionalized 1,2,3-Trisubstituted Cyclopentenes

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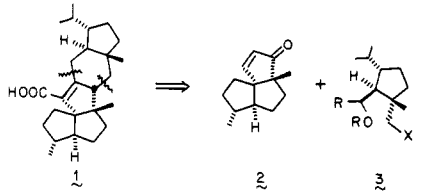
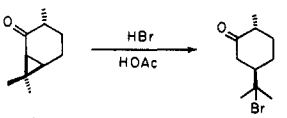
A pair of 1-substituted 2-methylene-6,6-dimethylbicyclo[3.1.0]hexanes has been determined to undergo smooth cyclopropane ring opening with formation of 1,2,3-trisubstituted cyclopentenes in the presence of electrophilic or free radical agents. High optical purity can be incorporated into these products, starting with the readily available *l*-menthyl 6,6-dimethyl-2-oxobicyclo[3.1.0]hexane-1-carboxylate, the two diastereomers of which are chromatographically separable. Through suitable chemical correlation, the absolute configurations of the various enantiomers have been made known. Finally, a scheme for transforming the cyclopentenes to 1,1,2,3-tetrasubstituted cyclopentanes as a necessary prelude to a synthesis of retigeranic acid is detailed.

Retigeranic acid (**1**), a pentacyclic sesterterpene having eight chiral centers and five quaternary carbon atoms,[2] is a topologically most unique polyquinane system.[3] At the outset of our consideration of **1** as a synthetic target, we set as our goal the development of a strategy that would yield optically active material by penultimate installation of the two indicated C–C σ bonds. Consequently, the success of this protocol rests rather specifically upon our ability to construct segments **2** and **3** in proper enantiomeric form. This requirement has proven to be more vexacious than originally expected in the case of the highly functionalized 1,1,2,3-tetrasubstituted cyclopentane **3**, a little-studied class of compounds whose members are virtually unknown in optically active condition. Herein, we describe a general and efficient method for the synthesis of heavily substituted precursor cyclopentenes which can be used for the preparation of racemates or either enantiomer with full knowledge of the relevant absolute configuration.



1 **2** **3**

Whereas cyclopropylcarbinyl cations have garnered considerable attention from physical organic chemists,[4] these strained and reactive intermediates have been much less used in directed synthesis. From the response of caranone **4** and related ketones to hydrogen bromide in



4 **5**

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