chloride and 0.010 mol of sodium acetate dissolved in aqueous ethanol. The resulting solution was refluxed until evolution of hydrogen sulfide had ceased (1–2 h). In some cases (indicated in Table VII), sodium methoxide was used instead of sodium acetate. Then the reaction was carried out in 10 ml of methanol and the mixture was stirred magnetically (22–24 h).

Acknowledgments. Financial support by the Research Corporation, the Research Allocations Committee of the University of New Mexico, and the Department of Chemistry of the University of New Mexico is gratefully acknowledged.

Registry No.—**1** (R = 3-indolyl), 59812-11-2; **1** (R = Et), 59812-12-3; **1** (r , ph), 5499-31-0; **11** (R = 4-ClC_6H_4), 59812-13-4; indole, 120-72-9; ethoxycarbonyl isothiocyanate, 16182-04-0; ethyl bromide, 74-96-4; benzyl chloride, 100-44-7; methylhydrazine, 60-34-4; phenylhydrazine, 100-63-0; *N*-ethoxycarbonyl-4-chlorothiobenzamide, 57774-74-0; semicarbazide HCl, 563-41-7; 1,2-dimethylhydrazine 2HCl, 306-37-6; hydroxylamine HCl, 7803-49-8; *N*-methylhydroxylamine HCl, 4229-44-1.

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(8) Melting points lower than 300 °C were determined in a Thomas-Hoover apparatus, and those higher than 300 °C by use of a heated metal block; all are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 337 spectrophotometer using mineral oil mulls. NMR spectra were obtained on a Varian EM360 spectrophotometer using solutions in Me_2SO-d_6 or in Me_2SO-d_6 + CF_3COOD with tetramethylsilane as internal standard. Ultraviolet spectra were recorded in a Perkin-Elmer 402 spectrophotometer using solutions in 95% ethanol.
(9) E. P. Papadopoulos, *J. Org. Chem.*, **41**, 962 (1976).
(10) Originally prepared and characterized by S. A. Brueggemann, Department of Chemistry, University of New Mexico.

Nitrones and Nitroxides Derived from Oxazolines and Dihydrooxazines[1]

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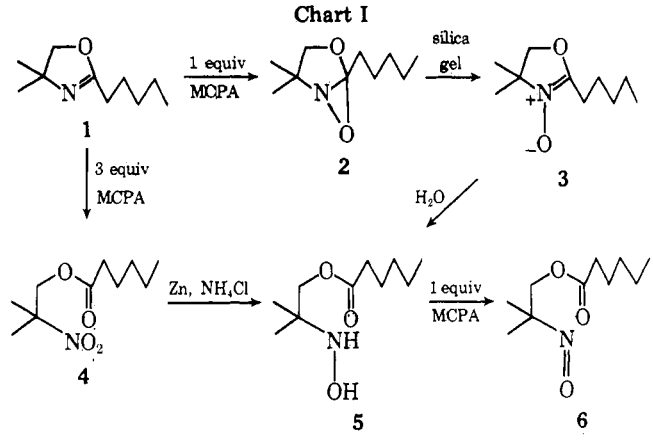
A new synthetic route to several doxyl nitroxides **14** and two tetrahydro-1,3-oxazine nitroxides **26** and **27** is described. Oxidation of the representative oxazoline **1** with 1 equiv of MCPA gave oxaziridine **2**. Excess MCPA led to nitro ester **4** and nitroso ester **6**. Isomerization of **2** on silica gel afforded nitrone **3**, reaction of which with moisture produced ester **5**. Analogous reactions applied to dihydrooxazine **7** led to oxaziridine **8**, nitroso ester **10**, nitro ester **11**, nitrone **9**, and ester **12**. Treatment of **3** with a series of organometallic reagents followed by Cu^{2+}-catalyzed air oxidation of the intermediate **13** led to doxyl nitroxides. In contrast, reaction of **3** with vinylmagnesium bromide or vinyllithium at 25 °C gave dienes **19** and **21**. With excess 1-lithio-1-hexyne at −15 °C, nitrone **3** gave open-chain nitrone **22**. Allylmagnesium bromide and **3** at 25 °C followed by oxidation gave nitroxide **23**. Analogous reactions at 25 °C of nitrone **9** with methyllithium and butyllithium afforded the nitroxides **26** and **27**.

Doxyl (4,4-dimethyloxazolidine-*N*-oxyl) nitroxide spin labels[3] have played an important role in studies of biological systems using the spin labeling technique.[4] Alternative, flexible synthetic entries to new stable nitroxides are central to continued progress in the spin labeling field. We recently communicated a new procedure for assembling doxyl nitroxides which bypasses the usual ketone precursors and which permits the synthesis of doxyl nitroxides having unsaturation in the doxyl chains (**1** → **3** → **14**).[1] This procedure takes advantage of the wide variety of oxazolines made available through the elegant work of Meyers.[5,6,7] We now present experimental details relating to our new doxyl synthesis, starting with the representative oxazoline **1**. We also describe for the first time analogous reactions of dihydrooxazine **7** and its conversion into a second series of stable nitroxide free radicals.[17]

Results and Discussion

The addition of an organometallic reagent to the requisite nitrone constitutes the key step in the new doxyl synthesis.[8] Since the nitrones are derived from the corresponding oxazoline or dihydrooxazine, we have investigated the oxidation of these latter substances in some detail.[9] Thus, oxidation of oxazoline **1** with 1 equiv of *m*-chloroperoxybenzoic acid (MCPA) in ether at −10 °C produced oxaziridine **2** (~95%) (Chart I). Small amounts of blue nitroso ester **6** could be observed visually and by NMR in samples of crude **2**, although

Chart I

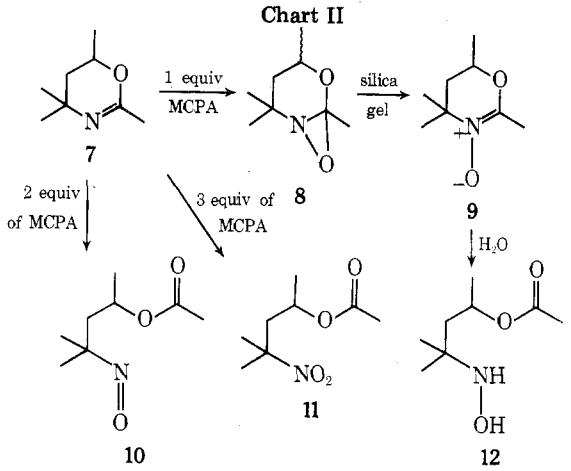


reaction of **1** with 2 equiv of MCPA still gave mostly **2** with minor amounts of **6** and nitro ester **4**. Prolonged reaction of **1** with 3 equiv of MCPA gave a good yield of nitro ester **4**. In order to confirm the identity of compounds **4** and **6**, nitro ester **4** was synthesized by acylation of the corresponding alcohol with hexanoic acid and then reduced with zinc and NH_4Cl to *N*-hydroxy ester **5**. Reaction of **5** with 1 equiv of MCPA gave blue nitroso ester **6** in good yield. Structure assignments throughout this paper are based on the highly characteristic NMR spectra together with other analytical data found in the Experimental Section.

Initial attempts to prepare nitrone 3 were patterned after Padwa's isomerization of certain oxaziridines into nitrones in acetonitrile at 80 °C.[10] Under these conditions, oxaziridine 2 afforded a mixture which was shown by its NMR spectrum to consist of nitrone 3 (8%), nitro ester 6 (31%), nitro ester 4 (11%), oxazoline 1 (48%), and *N*-hydroxy ester 5 (3%). Fortunately, during an attempted purification of oxaziridine 2, it was discovered that chromatography over silica gel effected smooth isomerization of 2 to the desired nitrone 3.

The oxidation of dihydrooxazine 7 (Chart II) with 1 equiv of MCPA in ether afforded oxaziridine 8 in good yield. When 2 equiv of MCPA was used, nitroso ester 10 was the major

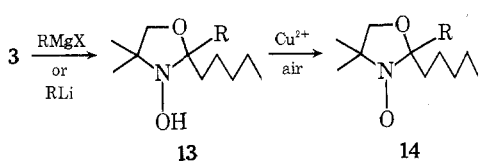
Chart II



product while 3 equiv of MCPA led in good yield to nitro ester 11. Oxaziridine 8, like its five-membered ring counterpart 2, also underwent smooth isomerization to its corresponding nitrone 9.

Nitrones 3 and 9 were quite hygroscopic. Nitrone 9 was obtained from the silica gel column as a white, crystalline solid which quickly melted on exposure to air. The NMR spectrum invariably contained peaks attributed to *N*-hydroxy ester 12. When samples were carefully protected from moisture, nitrones 3 and 9 could be isolated with only trace amounts of the corresponding *N*-hydroxy ester derivatives 5 and 12. Oxaziridines 2 and 8, however, may be conveniently stored at −20 °C for months without evidence of decomposition. Thus, the starting nitrones for the reactions described below were always freshly prepared from the oxaziridine immediately prior to use.

The reaction of nitrone 3 with a two- to threefold excess of organometallic reagent in ether solution at reduced temperatures afforded, after cold aqueous workup, the corresponding *N*-hydroxyoxazolidine 13 (eq 1). The crude mixture was immediately taken up in methanol containing a trace of $Cu(OAc)_2 \cdot H_2O$[11] and stirred under air in order to form the corresponding doxyl nitroxides 14. Several doxyl nitroxides



(1)

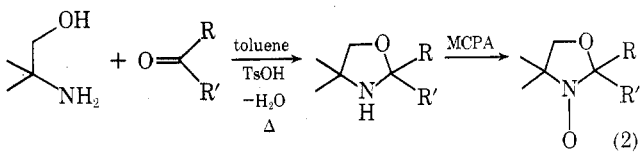
prepared in this way are summarized in Table I. In those instances where the doxyl nitroxide may also be prepared from the requisite ketone utilizing our earlier method (eq 2),[3] the yields by this present nitrone procedure are comparable. The nitrone procedure can afford at times two major advantages, however: (a) the synthesis does not depend on the availability of the requisite ketone and (b) addition to the nitrone produces the easily oxidized *N*-hydroxy amine intermediate.

Table I. Doxyl Nitroxides Prepared from Nitrone 3

Doxyl derivative 14	Organometallic reagent	Temp, °C	Rxn time	Yield,[c] %
R = CH_3[a]	CH_3Li	25	1 h	43
R = CH_3CH_2[b]	CH_3CH_2MgBr	−15	5 min	27[d]
R = $CH_3(CH_2)_6$[b]	$CH_3(CH_2)_6MgBr$	−15	5 min	27[d]
R = CH_2=CH	CH_2=CHLi	−78	2 h	29[d]

[a] Identical by ir with a sample prepared by our earlier method.[3] [b] All doxyl derivatives showed the expected mass spectral fragmentation patterns[12] and each showed the typical three-line nitroxide ESR spectrum. [c] Isolated yield, based on starting nitrone. [d] Analytical sample obtained by preparative VPC on a 2-ft 5% SE-30/Firebrick column.

Thus doxyls may be prepared which contain functional groups sensitive to MCPA (e.g., entry 4, Table I).



Interestingly, the course of the reaction between the nitrones and the organometallic reagents depended markedly on the reaction temperature and on the structure of the organometallic reagent. In general, when the organometallic reagent was added to the nitrone at −78 °C and then the mixture was allowed to warm to 25 °C, workup afforded significant quantities of recovered nitrone and its hydrolysis product. Thus, at lower temperatures the organometallic reagents tended to act as bases, generating the inert (to addition) anion of the nitrone. Quite possibly, this side reaction could be used to advantage through alkylation reactions, for example.

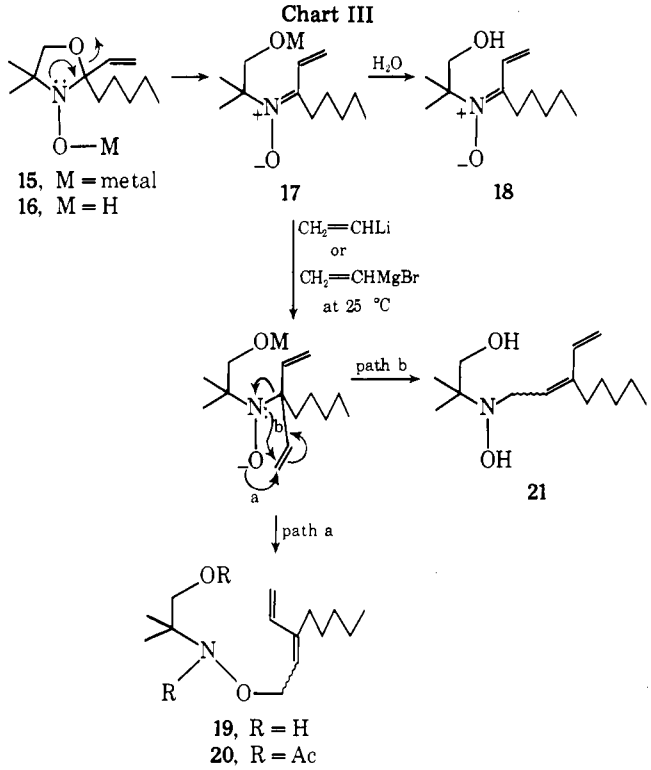
A second pronounced effect of temperature was observed in reactions between nitrone 3 and organometallic reagents containing unsaturation near the metal atom. With temperatures in excess of −15 °C, the intermediate *N*-hydroxyoxazolidine (as the metal salt) apparently was capable of undergoing a ring-opening isomerization reaction in the reaction medium to give the corresponding open-chain nitrone (15 → 17). This latter substance in certain instances suffered addition of a second equivalent of organometallic reagent, leading to a new branched chain nitroxide after oxidation (3 → 23). These reactions are illustrated by the following examples.

Reaction (Chart III) of nitrone 3 with vinyllithium at −78 °C followed by a cold aqueous workup afforded *N*-hydroxyoxazolidine 16, uncontaminated by its ring-opened isomer 18 (by NMR). While a quite pure sample of 16 could be obtained by rapid chromatography over alumina, chromatography over silica gel invariably afforded a mixture of 16 and 18, in which the latter predominated. It was also not possible to prepare a sample of 18, free of 16.

The addition of vinyllithium or vinylmagnesium bromide to 3 at 25 °C gave two stable products which were isolated by column chromatography and were tentatively assigned the interesting structures 19 and 21 based on their spectral properties and the observation that the predominant product 19 afforded an *O,N*-diacetyl derivative 20 upon treatment with acetic anhydride in pyridine. Alcohols 19 and 21 were likely formed by the route outlined in Chart III.

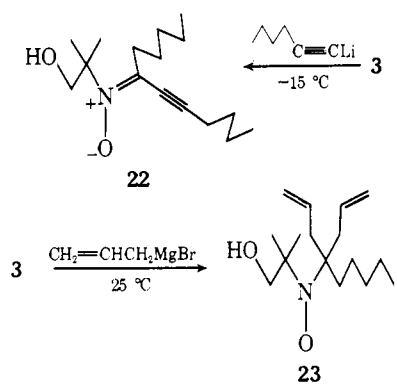
The reaction of two other unsaturated organometallic reagents with nitrone 3 with briefly investigated. Treatment of nitrone 3 with excess 1-lithio-1-hexyne at −15 °C gave open-chain nitrone 22 in 13% yield, while at −78 °C, starting 3 was recovered unchanged. The reaction of excess allylmagnesium

Chart III



15, M = metal
16, M = H
17
18
21
19, R = H
20, R = Ac

bromide with 3 at 25 °C followed by air oxidation gave nitroxide **23** in 20% yield.



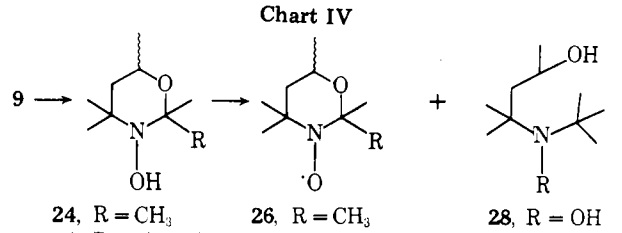
22

23

In general, the *N*-hydroxyoxazolidines produced by the addition (>−15 °C) of saturated alkyl groups to nitrone **2** showed much less tendency toward isomerization to the corresponding open-chain nitrones. Indeed, the best yield (43%) of **14** (R = CH_3) was obtained when the reaction was done at 25 °C. The product resulting from the addition of 2 mol of methyllithium was not detected. Even so, with the higher homologues, minor absorptions attributed to the open-chain nitrones could be observed in the NMR spectra of the crude *N*-hydroxyoxazolidines obtained from reactions done at 25 °C.

Several reactions of the six-membered ring nitrone **9** with organometallic reagents have also been examined. Reactions involving Grignard reagents gave complex mixtures of products. The reaction (Chart IV) of **9** with methyllithium at 25

Chart IV



24, R = CH_3
25, R = $(CH_2)_3CH_3$
26, R = CH_3
27, R = $(CH_2)_3CH_3$
28, R = OH
29, R = O

°C for 1 h followed by $Cu(OAc)_2 \cdot H_2O$-catalyzed air oxidation gave, in addition to nitroxide **26**, some nitroxide **29** resulting from the addition of 2 mol of methyllithium. Comparison of the NMR spectrum of the crude product mixture after workup of the methyllithium addition with the NMR spectra of *N*-hydroxy compounds **24** and **28** obtained via reduction of the corresponding nitroxides with phenylhydrazine[13] indicated a relatively clean mixture of **24** and **28**. Much **26** was lost during isolation owing to its volatility. Nitroxide **27** was similarly prepared in 18% yield using butyllithium. As in earlier experiments, the objective was the preparation of the nitroxide and while several minor products were formed they were not isolated or characterized. None of the nitroxide resulting from the addition of 2 mol of the reagent was detected in the butyllithium reaction.

Nitroxides **26** and **27** are members of a recently described[17] class of stable nitroxides which possess a tetrahydrooxazine ring system. Such nitroxides may prove useful in spin labeling studies though at present their overall synthesis starting from dihydrooxazine **7** is not as convenient as the five-membered ring doxyl synthesis herein described, and the presence of the ring methyl group leads to pesky isomer possibilities.

Experimental Section[14]

2-Pentyl-4,4-dimethyloxazoline 2,3-Oxide (2). To a solution of 1.69 g (10.0 mmol) of oxazoline **1**[15] in 20 ml of dry ether at −10 °C was added dropwise with stirring under N_2 a solution of 2.03 g (10.0 mmol) of 85% MCPA dissolved in 30 ml of ether. After standing at 8 °C for 48 h the solution was washed well with aqueous 10% Na_2CO_3 and dried over K_2CO_3. Evaporation of the solvent gave 1.67 g (99%) of crude (94% by NMR) oxaziridine **2** as a pale blue oil: NMR δ 1.13 (3 H, s, *gem*-Me), 1.36 (3 H, s, *gem*-Me), 2.1 (2 H, m, α-CH_2), 3.46 [1 H, d (J = 8 Hz), CH_2O], 3.61 [1 H, d (J = 8 Hz), CH_2O]; mass spectrum *m/e* (rel intensity) 185 (3), 184 (7), 170 (3), 156 (11), 142 (31), 129 (100), 114 (10), 99 (20), 71 (12), 56 (36), 43 (38), 41 (18). Crude **2** was used for subsequent reactions.

2-Nitro-2-methylpropyl Hexanoate (4). A. From 1. To a solution of 169 mg (1.00 mmol) of **1** in 5 ml of ether at 0 °C was added a solution of 608 mg (3.00 mmol) of 85% MCPA dissolved in 3 ml of ether. After standing for 6 days at 8 °C the colorless solution was washed well with aqueous 10% Na_2CO_3 and brine and then dried over K_2CO_3. Evaporation of the solvent gave 206 mg (95%) of a yellow oil which was ~78% nitro ester **4** by NMR. The analytical specimen was obtained as an oil by preparative VPC: NMR δ 1.61 (6 H, s, *gem*-Me), 2.33 [2 H, t (J = 7 Hz), α-CH_2], 4.41 (2 H, s, CH_2O); ir 1745, 1550 cm^{-1}. Anal. Calcd for $C_{10}H_{19}NO_4$: C, 55.28; H, 8.81; N, 6.45. Found: C, 55.56; H, 8.82; N, 6.18.

B. From 2-Nitro-2-methylpropanol. A mixture of 2.38 g (20 mmol) of 2-nitro-2-methylpropanol, 1.162 g (10 mmol) of hexanoic acid, and 50 mg of $TsOH \cdot H_2O$ in 50 ml of benzene was brought to reflux for 24 h, water being collected in a Dean-Stark trap containing K_2CO_3. The benzene solution was washed with water, aqueous saturated $NaHCO_3$, and brine and then dried over K_2CO_3. Evaporation of the solvent and distillation of the yellow residue gave 1.215 g (61%) of **4**, bp 85–87 °C (0.06 mm).

2-(Hydroxyamino)-2-methylpropyl Hexanoate (5). A solution of 464 mg (2.14 mmol) of **4** and 114 mg (2.14 mmol) of NH_4Cl in 20 ml of H_2O was cooled to <10 °C in an ice bath. To the stirred solution was added 688 mg (10.7 mmol) of powdered zinc. After stirring for 4 h at <15 °C, the mixture was filtered and the zinc cake was washed with methanol. The solution was concentrated and extracted with several portions of ether. The ether solution was dried over K_2CO_3 and evaporated to yield a blue oil, chromatography of which gave 120 mg (28%) of *N*-hydroxy ester **5** as a colorless oil: NMR δ 1.10 (6 H, s, *gem*-Me), 2.37 [2 H, t (J = 7 Hz), α-CH_2], 4.07 (2 H, s, CH_2O); ir 3280 (OH), 1735 cm^{-1} (ester); mass spectrum *m/e* (rel intensity) 203.153 (2) (calcd for $C_{10}H_{21}NO_3$, 203.152), 172 (27), 99 (26), 74 (100), 71 (19), 58 (39), 56 (26), 55 (12), 43 (22), 42 (18), 41 (16).

2-Nitroso-2-methylpropyl Hexanoate (6). To a solution of 17.2 mg (0.085 mmol) of *N*-hydroxy ester **5** in 3 ml of ether at 0 °C was added dropwise with stirring under N_2 a solution of 17.2 mg (0.085 mmol) of 85% MCPA dissolved in 1.0 ml of ether. After 10 min, the solution was diluted with ether and washed several times with aqueous 10% Na_2CO_3 and brine. Evaporation of the solvent gave a blue oil which was chromatographed on a silica gel column to yield 13.1 mg (77%) of purified **6**. An analytical sample of **6** as a dark blue oil was

prepared by preparative VPC: NMR δ 1.13 (6 H, s, *gem*-Me), 2.22 [2 H, t (J = 7 Hz), α-CH_2], 4.80 (2 H, s, CH_2O); ir 1745 (ester), 1567 cm^{-1} (N–O). Anal. Calcd for $C_{10}H_{19}NO_3$: C, 59.68; H, 9.52; N, 6.96. Found: C, 59.85; H, 9.66; N, 6.69.

2,4,4,6-Tetramethyl-5,6-dihydro-1,3-oxazine 2,3-Oxide (8). To a solution of 821 mg (5.82 mmol) of 7[16] in 20 ml of dry ether at −23 °C under N_2 was added with stirring dropwise over 20 min a solution of 1.18 g (5.82 mmol) of 85% MCPA dissolved in 20 ml of ether. The bath was allowed to warm to −10 °C and then aqueous 10% Na_2CO_3 was added. The ether layer was separated, washed with chilled aqueous 10% Na_2CO_3, and dried over K_2CO_3. Evaporation of the solvent gave 570 mg (64%) of the crude (84% by NMR) oxaziridine 8 as a blue oil (some loss due to volatility): NMR δ 1.26 (6 H, s, *gem*-Me), 1.17 [3 H, d (J = 6 Hz), Me at C_6], 1.65 (3 H, s, Me at C_2), 4.05 (1 H, m, H at C_6). Crude 8 was used for subsequent reactions.

2-Nitroso-2-methyl-4-acetoxypentane (10) and Dimer. To a solution of 119 mg (0.84 mmol) of 7 in 2 ml of dry ether at 0 °C was added dropwise over 15 min with stirring under N_2 a solution of 341.2 mg (1.68 mmol) of 85% MCPA dissolved in 3 ml of ether. The solution was allowed to warm to 25 °C and was stirred for 5 h, after which the ether solution was washed with four portions of aqueous 10% Na_2CO_3 and then with brine. Evaporation of the solvent and chromatography on silica gel yielded 115 mg (79%) of nitroso ester **10** as a dark blue oil. Upon standing at −20 °C, colorless crystals of the dimer separated out. These were washed with cold CCl_4 and sublimed (50 °C, 0.025 mm) to obtain the analytical specimen: mp 65–67 °C; NMR δ 1.57 (6 H, s, *gem*-Me), 1.22 [3 H, d (J = 6 Hz)], 2.02 (3 H, s, acetyl), 4.95 (1 H, m, methine H). Anal. Calcd for $C_{16}H_{30}N_2O_6$: C, 55.47; H, 8.73; N, 8.09. Found: 55.26; H, 8.76; N, 7.93.

Complete dissociation to the blue monomer occurred in $CDCl_3$ in 1 h: NMR (monomer) δ 1.06 (3 H, s, *gem*-Me), 1.13 (3 H, s, *gem*-Me), 1.21 [3 H, d (J = 6 Hz)], 1.87 (3 H, s, acetyl), 4.94 (1 H, m, methine H); ir (CCl_4) 1745 (ester), 1565 cm^{-1} (N–O).

2-Nitro-2-methyl-4-acetoxypentane (11). To a solution of 238 mg (1.68 mmol) of 7 in 10 ml of ether was added at 25 °C a solution of 1.01 mg (5.00 mmol) of 85% MCPA dissolved in 10 ml of ether. After standing for 12 h the ether solution was washed well with aqueous 10% Na_2CO_3 and dried over K_2CO_3. Evaporation gave 200 mg (64%) of **11** as a pale yellow oil. The analytical specimen was obtained by preparative VPC: NMR δ 1.58 (6 H, s, *gem*-Me), 1.23 [3 H, d (J = 6 Hz)], 1.96 (3 H, s, acetyl), 5.09 (1 H, m, methine H); ir (CCl_4) 1750 (ester), 1555 cm^{-1} (nitro); mass spectrum (30 eV) *m/e* (rel intensity) 189.102 (0.02) (calcd for $C_8H_{15}NO_4$, 189.100), 174 (1), 143 (3), 129 (4), 118 (4), 99 (5), 83 (53), 56 (11), 55 (24), 43 (100), 41 (29).

General Procedure for Isomerization of Oxaziridines 2 and 8. A solution of ~150 mg of crude oxaziridine in 2 ml of $CHCl_3$ was placed on top of a dry silica gel column (1.5 × 10 cm). After standing for 30 min, the column was successively eluted with 20 ml of $CHCl_3$, 20 ml of acetone, and finally 15 ml of methanol. Evaporation of the methanol at 20 °C afforded the nitrone (>85%).

2-Pentyl-4,4-dimethyloxazoline *N*-oxide (**3**) was obtained as a pale yellow oil: NMR δ 1.50 (6 H, s, *gem*-Me), 2.62 [2 H, t (J = 7 Hz), α-CH_2], 4.29 (1 H, s, CH_2O); uv (EtOH) 244 nm (ε 4540); mass spectrum *m/e* (rel intensity) 185.139 (3) (calcd for $C_{10}H_{19}NO_2$, 185.142), 172 (9), 154 (25), 126 (29), 113 (100), 99 (35), 74 (45), 58 (62), 43 (43).

2,4,4,6-Tetramethyl-5,6-dihydro-1,3-oxazine *N*-oxide (**9**) was obtained as low-melting white crystals: NMR δ 1.51 (6 H, s, *gem*-Me), 1.38 [3 H, d (J = 6 Hz)], 2.25 (3 H, s, Me at C_2), 4.63 (1 H, m, methine H); mass spectrum *m/e* (rel intensity) 157.111 (13) (calcd for $C_8H_{15}NO_2$, 157.110), 141 (9), 115 (40), 100 (81), 83 (53), 74 (52), 73 (34), 58 (23), 56 (20), 55 (16), 43 (100).

Usually evident in samples of **9** by NMR was a small contaminant of *N*-hydroxy ester **12**: NMR δ 1.09 (6 H, s, *gem*-Me), 1.25 [3 H, d (J = 6 Hz)], 2.03 (3 H, s, Me at C_2); 5.12 (1 H, m, methine H); ir (CCl_4) 3280 (OH), 1740 cm^{-1} (ester).

2-Pentyl-2,4,4-trimethyloxazolidine-*N*-oxyl (14, R = CH_3). To a solution of 150 mg (0.800 mmol) of freshly prepared nitrone **3** in 5 ml of dry ether at 25 °C with stirring under N_2 was added 3 equiv of 2 M methylmagnesium iodide in ether. After 1 h, aqueous saturated NH_4Cl was added, the ether layer was separated, and the residue was washed thoroughly with fresh ether. Evaporation of the combined ether solutions afforded crude *N*-hydroxyoxazolidine **13** (R = CH_3), which was taken up in 10 ml of methanol containing ~2 mg of $Cu(OAc)_2 \cdot H_2O$ and stirred under air for 30 min at 25 °C. Evaporation of the solvent and column chromatography on silica gel afforded the nitroxide (**14** R = CH_3). The pure specimen was obtained by preparative VPC and its infrared spectrum was identical with that of **14** (R = CH_3) prepared by our earlier method.[3]

2-Pentyl-2-ethyl-4,4-dimethyloxazolidine-*N*-oxyl (14, R = CH_2CH_3). Similarly prepared using ethylmagnesium bromide at −15 °C was **14** (R = CH_2CH_3): mass spectrum *m/e* (rel intensity) 214 (7), 186 (5), 158 (16), 143 (21), 129 (100), 72 (22), 56 (33). Anal. Calcd for $C_{12}H_{24}NO_2$: C, 67.25; H, 11.29; N, 6.54. Found: C, 67.38; H, 11.69; N, 6.34.

2-Pentyl-2-heptyl-4,4-dimethyloxazolidine-*N*-oxyl [14, R = $(CH_2)_6CH_3$]. Similarly prepared using heptylmagnesium iodide at −15 °C was **14** [R = $(CH_2)_6CH_3$]: mass spectrum *m/e* (rel intensity) 284 (3), 228 (11), 210 (41), 199 (81), 198 (62), 186 (45), 170 (46), 99 (40), 85 (32), 71 (73), 57 (100), 43 (90). Anal. Calcd for $C_{17}H_{34}NO_2$: C, 71.78; H, 12.05; N, 4.92. Found: C, 71.99; H, 12.54; N, 4.69.

2-Pentyl-2-vinyl-4,4-dimethyloxazolidine-*N*-oxyl (14, R = Vinyl). To a solution of 100 mg (0.540 mmol) of freshly prepared **3** in 10 ml of dry ether at −78 °C was added with stirring dropwise under N_2 a twofold excess of vinyllithium (2 M in THF). After 2 h, some ether saturated with water was added and then the mixture was allowed to warm to 25 °C. Water was added and the ether phase separated. The aqueous phase was extracted with ether and the combined ether solutions were dried (K_2CO_3) and evaporated, affording crude *N*-hydroxyoxazolidine **13** (R = vinyl) along with some mineral oil from the vinyllithium reagent. The crude product was dissolved in 10 ml of MeOH containing ~2 mg of $Cu(OAc)_2 \cdot H_2O$ and stirred under air at 25 °C for 2 h. The solvent was evaporated to yield a yellow oil. Column chromatography over silica gel followed by preparative TLC over silica gel afforded 33 mg (29%) of pure title nitroxide. The analytical specimen was obtained as an orange oil by preparative VPC: mass spectrum *m/e* (rel intensity) 212 (8), 156 (12), 142 (16), 127 (100), 70 (17), 56 (36), 55 (32). Anal. Calcd for $C_{12}H_{22}NO_2$: C, 67.89; H, 10.44; N, 6.60. Found: C, 67.33; H, 10.81; N, 6.41.

Reaction of Nitrone 3 with Vinylmagnesium Bromide at 25 °C. To a solution of 85 mg of freshly prepared **3** in 10 ml of dry ether at 0 °C was added with stirring under N_2 2 equiv of vinylmagnesium bromide (2 M in THF). After the mixture was allowed to warm to 25 °C, the usual workup with aqueous saturated NH_4Cl gave a yellow oil which consisted of two major components by TLC. Chromatography over silica gel using $CHCl_3$ as the eluent gave 41 mg (37%) of diene **19** as a colorless oil which crystallized upon standing at −20 °C: mp 30–31 °C; NMR δ 1.04 (6 H, s, *gem*-Me), 2.25 (2 H, m, allylics), 3.46 (2 H, s, CH_2O), 4.33 [2 H, d (J = 7 Hz), C=C–CH_2O], 5.60 [1 H, t (J_{trans} = 18 Hz), terminal vinyl], 6.30 (1 H, dd, terminal vinyl); mass spectrum *m/e* (rel intensity) 241.201 (4) (calcd for $C_{14}H_{27}NO_2$, 241.204), 210 (2), 137 (35), 95 (38), 81 (71), 74 (37), 67 (100), 55 (17), 41 (18); ir ($CHCl_3$) 3300–3600 (NH and OH), 1600 cm^{-1} (C=C); uv (EtOH) 232 nm (ε 18 200).

Further elution with ether gave 14 mg (12%) of diene **21** as a colorless oil: NMR δ 1.20 (6 H, s, *gem*-Me), 2.27 (2 H, m, allylics), 3.54 (2 H, s, CH_2O), 3.44 [2 H, d (J = 7 Hz), CH_2N], 5.64 (1 H, t (J = 7 Hz), vinyl], 5.02 [1 H, d (J_{cis} = 11 Hz), terminal vinyl], 5.21 [1 H, d (J_{trans} = 18 Hz), terminal vinyl], 6.32 (dd, terminal vinyl); mass spectrum *m/e* (rel intensity) 241.202 (1) (calcd for $C_{14}H_{27}NO_2$, 241.204), 210 (32), 194 (13), 137 (18), 95 (38), 81 (67), 67 (100), 55 (43), 41 (40).

When the reaction and workup for the vinyl Grignard addition were done at 0 °C rather than 25 °C, the major component by NMR was the open-chain nitrone **18**: NMR δ 1.60 (6 H, s, *gem*-Me), 2.65 (2 H, m, N=C–CH_2), 3.73 (2 H, s, CH_2O, 5.54 [1 H, d (J_{cis} = 11 Hz), terminal vinyl], 5.52 [1 H, d (J_{trans} = 17 Hz), terminal vinyl], 5.99 (1 H, dd, terminal vinyl). It was not possible to obtain a sample of **18** free from **16**.

Acetylation of Diene 19. To a solution of 8.5 mg (0.036 mmol) of **19** in 1 ml of acetic anhydride was added 1 drop of pyridine. The solution was left standing at 25 °C for 5 days and then the solvent was evaporated. Preparative TLC on silica gel gave 5.0 mg (44%) of diacetate **20** as a light yellow oil: NMR δ 1.44 (6 H, s, *gem*-Me), 2.06 (3 H, s, acetyl), 2.16 (3 H, s, acetyl), 4.47 (2 H, s, OCH_2), 4.51 (2 H, m, C=C–CH_2O), 5.16 [1 H, d (J_{cis} = 11 Hz), terminal vinyl], 5.32 [1 H, d (J_{trans} = 18 Hz), terminal vinyl], 5.56 (1 H, t (J = 7 Hz), vinyl], 6.32 (1 H, dd, terminal vinyl); ir 1745 (ester), 1670 cm^{-1} (amide).

Reaction of Nitrone 3 with 1-Lithio-1-hexyne. To a solution of 41 mg (0.50 mmol) of 1-hexyne in 5 ml of dry ether at 0 °C under N_2 was added 1 equiv of methyllithium (1.7 M in ether). After 30 min at 25 °C, the solution was cooled to −15 °C and treated with 65 mg (0.35 mmol) of freshly prepared nitrone **3** in 2 ml of ether. After 5 min, the reaction mixture was worked up in the usual manner. Column chromatography of the crude product followed by preparative TLC produced 12 mg (13%) of oily nitrone **22**: NMR δ 1.69 (6 H, s, *gem*-Me), 2.52 [4 H, t (J = 7 Hz), α-CH_2], 3.73 (2 H, s, CH_2O); ir (CCl_4) 3350 (OH), 1580 cm^{-1} (N–O); mass spectrum *m/e* (rel intensity) 267.220 (8) (calcd for $C_{16}H_{29}NO_2$, 267.220), 220 (34), 196 (41), 180 (66), 139 (26), 99 (100), 87 (32), 79 (90), 74 (50), 59 (95), 58 (66), 43 (63).

3-Aza-4,4-diallyl-2,2-dimethyl-1-hydroxynonane-*N*-oxyl (23). To a solution of 50 mg (0.27 mmol) of nitrone **3** in 4 ml of ether at 25 °C with stirring under N_2 was added 3 equiv of 1 M allylmagnesium bromide in ether. After 30 min, aqueous saturated NH_4Cl was added,

the ether layer was separated, and the residue was washed thoroughly with fresh ether. Evaporation of the combined ether portions gave a yellow oil which after Cu^{2+}-catalyzed air oxidation and TLC on silica gel gave 15 mg (20%) of **23:** ir 3360 (OH), 1640 cm^{-1} (C=C); mass spectrum *m/e* (rel intensity) 268.229 (6) (calcd for $C_{16}H_{30}NO_2$, 268.228), 228 (18), 212 (19), 196 (27), 180 (30), 164 (41), 156 (43), 123 (42), 109 (56), 95 (85), 93 (84), 81 (100), 67 (84), 55 (74), 41 (73).

2,2,4,4,6-Pentamethyltetrahydrooxazine-*N*-oxyl (26) and 3-Aza-6-hydroxy-2,2,4,4-tetramethylheptane-*N*-oxyl (29). To a solution of 76 mg (0.48 mmol) of **9** in 5 ml of dry ether with stirring at 25 °C was added 4 equiv of 2 M methyllithium in ether. After 1 h, aqueous 20% K_2CO_3 was added and the ether phase was separated and combined with several ether washings of the aqueous residue. Evaporation of the solvent gave a nearly colorless oil (79.5 mg) which was taken up in 5 ml of CH_3OH and stirred under air with 2 mg of $Cu(OAc)_2 \cdot H_2O$ for 30 min. Evaporation of the solvent and preparative tlc on silica gel gave 15 mg (18%) of nitroxide **26** (considerable loss due to volatility), mass spectrum *m/e* (rel intensity) 172.133 (5) (calcd for $C_9H_{18}NO_2$, 172.134), 157 (5), 142 (5), 114 (20), 84 (49), 69 (100), 59 (35), 43 (55), 41 (47); and 22 mg (24%) of nitroxide **29,** ir 3430 cm^{-1} (OH), mass spectrum 188.163 (12) (calcd for $C_{10}H_{22}NO_2$, 188.165), 158 (6), 132 (13), 114 (23), 88 (40), 84 (30), 83 (36), 74 (33), 56 (22), 57 (100), 45 (41), 43 (20), 41 (38).

Treatment of **26** with phenylhydrazine in $CDCl_3$[13] gave the corresponding *N*-hydroxylamine **24:** NMR δ 1.18 [3 H, d (*J* = 6 Hz)], 1.28 (6 H, s, *gem*-Me), 2.45 (3 H, s, *gem*-Me), 2.47 (3 H, s, *gem*-Me), 5.04 (1 H, m, CHO).

Treatment of **29** with phenylhydrazine in $CDCl_3$ gave the corresponding *N*-hydroxylamine **28:** NMR δ 1.28 [3 H, d (*J* = 6 Hz)], 1.30 (3 H, s, *gem*-Me), 1.34 (9 H, s, *tert*-butyl), 4.20 (1 H, m, CHO).

2-Butyl-2,4,4,6-tetramethyltetrahydrooxazine-*N*-oxyl (27). Similarly prepared by the method above was nitroxide **27** in 18% yield: mass spectrum *m/e* (rel intensity) 214.183 (12) (calcd for $C_{12}H_{24}NO_2$, 214.181), 199 (3), 157 (25), 114 (43), 101 (32), 84 (84), 69 (83), 55 (29), 43 (93), 41 (100).

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Registry No.—**1,** 55011-28-4; **2,** 55011-29-5; **3,** 55011-30-8; **4,** 59813-15-9; **5,** 59813-16-0; **6,** 59813-17-1; **7,** 26939-18-4; **8,** 59813-18-2; **9,** 59813-19-3; **10,** 59813-13-7; **10** dimer, 59813-14-8; **11,** 59813-20-6; **12,** 59813-21-7; **13** (R = CH_2CH_3), 55011-32-0; **13** [R = $(CH_2)_6CH_3$], 55011-33-1; **13** (R = vinyl), 55011-34-2; **14** (R = CH_2CH_3), 55011-35-3; **14** [R = $(CH_2)_6CH_3$], 55011-36-4; **14** (R = vinyl, 55011-37-5; **18,** 56348-28-8; **19,** 59813-22-8; **20,** 59813-23-9; **21,** 59813-24-0; **22,** 59813-25-1; **23,** 59813-26-2; **24,** 59813-27-3; **26,** 55179-45-8; **27,** 59813-28-4; **28,** 59813-29-5; **29,** 59813-30-8; 2-nitro-2-methylpropanol, 76-39-1; hexanoic acid, 142-62-1; oxaziridine, 6827-26-5; 1-hexyne, 693-02-7; phenylhydrazine, 100-63-0.

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Mobile Activated Allyl Systems. 19.[1] Reactions of Amines with α-(Bromomethyl)cinnamonitrile

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The reactions of a variety of amines with α-(bromomethyl)cinnamonitrile (1) in solvents of different polarities are reported. The ratio of the two products formed, namely the substitution–rearrangement (S–R) product **2** and the substitution product **3,** was found to vary with the polarity of the solvent as well as with the basicity and the steric effectiveness of the amine used. Except for the *tert*-butylamine reaction product **2a** and the diisopropylamine reaction product **2e,** all S–R products **2** isomerized to the thermodynamically more stable substitution products **3** in a polar solvent. Product **2a** was found to be susceptible to the attack of free amines to give the appropriate amine exchange product **3.** Product **2e,** however, was inert even to the highly reactive nucleophile piperidine.

Although primary allyl halides react with amines to give normal substitutions, Cromwell and Rebman[2] observed substitution–rearrangement (S–R) products upon treatment of *trans*-α-(bromomethyl)chalcone (Ia) with *tert*-butylamine and piperidine in hydrocarbon solvents. The amine reaction has been extended to other mobile allyl systems, namely, α-(bromomethyl)benzalacetone (Ib)[3] and methyl α-(bromomethyl)cinnamate (Ic).[4] In hydrocarbon solvents, morpholine and piperidine react with the above-mentioned mobile allyl systems to give both substitution and S–R products. With *tert*-butylamine, only the S–R products were isolated. It has been shown that the amine molecule attacks the mobile keto allyl system in an S_N2' manner, giving initially the S–R product (II). The substitution product (III) is a result of either