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Isoxazoles. XXIII.[1] Synthesis of N-Substituted 4-Isoxazolines and Their Conversion into 2-Acylaziridines[2]

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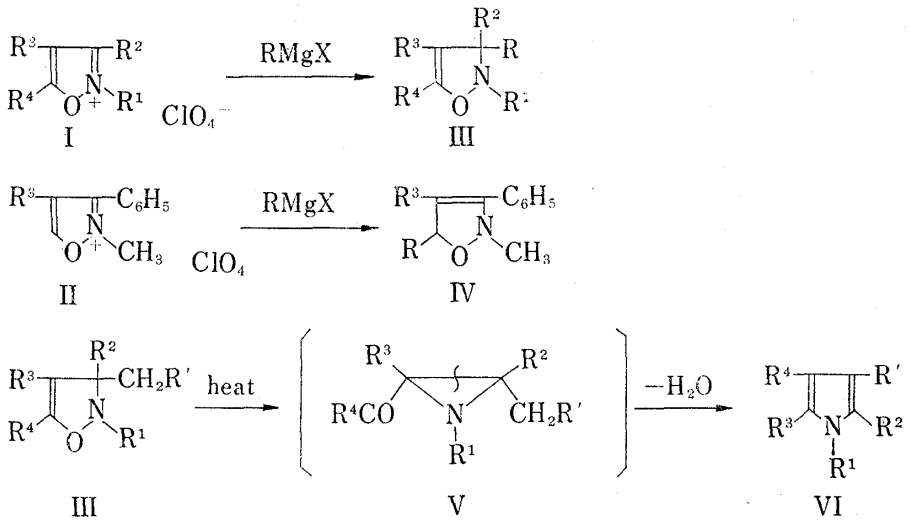
Synthesis and thermal-reaction of 4-isoxazolines were investigated. Reaction of 3-unsubstituted isoxazolium salts with sodium borohydride yielded the corresponding 4-isoxazolines and their borane complexes together with β-hydroxyaminopropiophenone derivatives. Analogous reaction of 5-unsubstituted isoxazolium salt yielded two isomeric products, 4- and 3-isoxazoline derivatives. The 3-isoxazoline derivative underwent further reduction to give isoxazolidine derivatives. Thermal-conversion of some 4-isoxazolines and their borane complexes into 2-acylaziridine derivatives is also reported.

A number of ring-cleavage reactions of 3- and 5-unsubstituted isoxazolium salts with base have been reported.[4,5] Recently, we have found that the reaction of isoxazolium salts (I and II) with Grignard reagents results in the formation of the corresponding 4- and 3-isoxazoline derivatives (III[1] and IV[6]); and that the 4-isoxazolines substituted with methyl or benzyl group at 3-position undergo thermal-conversion into pyrrole derivatives (VI) presumably *via* an acylaziridine intermediate (V). In continuation of work on this new isoxazoline synthesis, the present investigation deals with the reaction of N-substituted isoxazole



I II III IV V VI

Chart 1

1) Part XXII: I. Adachi, K. Harada, R. Miyazaki and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **22**, 61 (1974).
2) A part of this paper was presented at the 3rd International Congress of Heterocyclic Chemistry, Sendai, Japan, August, 1971.
3) Location: *Fukushima-ku, Osaka, 553, Japan.*
4) *a*) A. Kunst and O. Mumm, *Chem. Ber.*, **50**, 563 (1917); *b*) R.B. Woodward and R.A. Olofson, *Tetrahedron, Suppl.*, **7**, 415 (1966).
5) E.P. Kohler and A.R. Davis, *J. Am. Chem. Soc.*, **52**, 4520 (1930).
6) *a*) I. Adachi and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **17**, 2201 (1969); *b*) I. Adachi, *ibid.*, **17**, 2209 (1969).

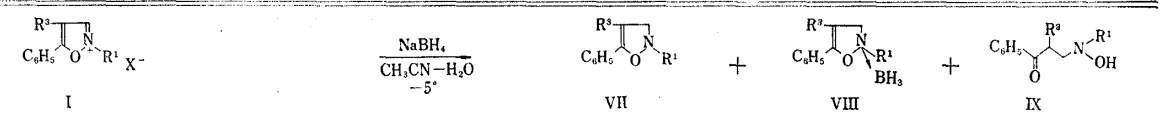
quaternary salts with sodium borohydride to give the corresponding 4-isoxazoline derivatives, and with the conversion of some 4-isoxazolines into 2-acylaziridine derivatives.

Reaction of 2-methyl-5-phenylisoxazolium perchlorate (Ia)[4b] with 1.5 molar equivalents of sodium borohydride in aqueous acetonitrile at −5° yielded an oily product, which was fractionated by chromatography through silica gel. An oil[7] of molecular formula $C_{10}H_{11}ON$ (VIIa) and two crystalline solids of formulae $C_{10}H_{14}ONB$ (VIIIa) and $C_{10}H_{13}O_2N$ (IXa) were isolated in 29.0, 55.5 and 3.6% yields, respectively. The structure of the oily product (VIIa) was assigned as 2-methyl-5-phenyl-4-isoxazoline from its infrared (IR) and nuclear magnetic resonance (NMR) spectra, shown in Table II. The structural assignment for VIIa was further supported by comparison of its ultraviolet (UV) spectrum, showing strong absorptions at 223 and 274 nm, with that of the known 2,3,4-trimethyl-5-phenyl-4-isoxazoline.[1] The crystalline product (VIIIa) was characterized as VIIa-borane by the IR spectrum, showing an absorption band assignable to borane at 2380 cm^{-1},[8] and by treatment of VIIIa with triethylamine to give VIIa and triethylamine-borane.[9] The structure of the other product (IXa) was assigned as β-(N-methylhydroxyamino)propiophenone from the spectral evidence given in the experimental part, and confirmed by comparison with an authentic sample obtained by the literature method.[10]

Standing a solution of VIIIa in ether saturated with water at room temperature yielded VIIa and IXa, besides the aziridine derivatives described later. However, no reaction occurred on treatment of VIIa with diborane in ether at room temperature. These results suggest that the reaction of Ia with sodium borohydride initially yields VIIIa, which liberates borane to give VIIa. The formation of IXa may occur from hydrolytic ring-cleavage of either VIIa or VIIIa.

Similarly, 2-ethyl-5-phenylisoxazolium fluoborate (Ib)[4b] and 2-*tert*-butyl-3-phenylisoxazolium perchlorate (Ic)[11] were allowed to react with sodium borohydride to yield the corresponding 4-isoxazolines (VIIb and VIIc) and their borane complexes (VIIIb and VIIIc), besides the ring-cleavage products (IXb and IXc). Reaction of 2,5-diphenyl-4-methylisoxazolium perchlorate (Id)[12] with sodium borohydride did not yield a borane complex, but gave free 4-methyl-2,5-diphenyl-4-isoxazoline (VIId) in good yield. The result may be attributed to the lower basicity of a 4-isoxazoline substituted with an N-aryl group. The analytical and spectral data of the products are all in accord with the structures assigned (see Table II).

Table I. Reaction of 3-Unsubstituted Isoxazolium Salts (I) with Sodium Borohydride in Aqueous Acetonitrile



I VII VIII IX

No.	X^-	R^1	R^3	Yield (%) VII	VIII	IX
a	ClO_4	CH_3	H	29.0	55.5	3.6
b	BF_4	C_2H_5	H	33.2	37.0	9.0
c	ClO_4	*tert*-C_4H_9	H	22.7	42.1	17.5
d	ClO_4	C_6H_5	CH_3	97.0	—	—

7) This oil gave satisfactory analytical data after chromatographic purification alone.
8) H. Watanabe and K. Nagasawa, *Inorg. Chem.*, **6**, 1068 (1967).
9) H. Noth and H. Beyer, *Chem. Ber.*, **93**, 928 (1960).
10) J. Thesing, H. Uhrig and A. Müller, *Angew. Chem.*, **67**, 31 (1955).
11) R.B. Woodward and D.J. Woodman, *J. Org. Chem.*, **31**, 2039 (1966).
12) D.J. Woodman and Z.L. Murphy, *J. Org. Chem.*, **34**, 1468 (1969).

Table II. Analytical and Spectral Data of 4-Isoxazolines (VII), Borane Complexes (VIII), and 2-Methyl-3-phenyl-3-isoxazoline (XIII)

No.	mp (°C)	Formula	Analysis(%) Calcd. C	H	N	Found C	H	N
VIIa	a)	$C_{10}H_{11}ON$	74.51	6.88	8.69	74.28	6.71	8.55
VIIb	a)	$C_{11}H_{13}ON$	75.40	7.48	7.99	75.18	7.31	7.58
VIIc	a)	$C_{13}H_{17}ON$	76.81	8.43	6.89	76.53	8.41	7.08
VIId	72—75	$C_{16}H_{15}ON$	80.98	6.37	5.90	81.06	6.60	6.03
VIIIa	55—57 b)	$C_{10}H_{14}ONB$	68.57	8.00	8.00	68.77	8.15	7.80
VIIIb	53—54 b)	$C_{11}H_{16}ONB$	69.88	8.53	7.41	69.52	8.34	7.11
VIIIc	65—66 b)	$C_{13}H_{20}ONB$	71.91	9.26	6.45	71.72	9.20	6.58
VIIe	a)	$C_{10}H_{11}ON$	74.51	6.88	8.69	75.00	7.01	8.34
XIII	c)	$C_{10}H_{11}ON$	74.51	6.88	8.65	74.28	7.03	8.51

No.	ν_{max}^{Neat} cm^{-1} C=C	BH	λ_{max}^{EtOH} nm (log ε)	N-R	τ (multiplicity,[d] J=Hz) in $CDCl_3$ (60 MHz) C_3-H or CH_3	C_4-R^3	C_5-R^4
VIIa	1651		223 (4.03), 274 (3.79)	7.19 (s)	5.95 (m)	4.82 (t, 2.5)	2.56 (m)
VIIc	1657		229 (4.09), 287 (3.67)	8.82 (s)	5.88 (d, 2.5)	4.85 (t, 2.5)	2.62 (m)
VIId	1651						
VIIIa	1671	2380	218 (3.93), 266(3.77)	6.75 (s)	5.28 (dd, 2.4, 13.4) 5.87 (dd, 2.4, 13.4)	4.73 (t, 2.4)	2.53 (m)
VIIIc	1669	2360	217 (4.09), 263 (3.88)	8.41 (s)	5.54 (d, 2.5)	4.81 (t, 2.5)	2.57 (m) 3.53 (m)
VIIe	1618			7.17 (s)	5.07 (t, 2.5)	5.36 (t, 2.5)	2.72 (m) 5.03 (d, 2.0)
XIII	1641			7.16 (s)	—	4.67 (t, 2.0)	2.62 (m)

a) unstable oily compounds, b) recryst. solvent=ether-hexane, c) bp 84° (0.2 mmHg)
d) abbreviation used: s=singlet, d=doublet, t=triplet, m=multiplet

The reaction of 5-unsubstituted isoxazolium salts with sodium borohydride proceeded somewhat differently. Reaction of 2-methyl-3-phenylisoxazolium perchlorate (II)[6] with sodium borohydride in aqueous acetonitrile at low temperature yielded 2-methyl-3-phenyl-4-isoxazoline (VIIe) in 12.4% yield together with two products, an oil of molecular formula $C_{10}H_{13}ON$ (X) and a crystalline solid of formula $C_{10}H_{16}ONB$ (XI), in 41.6 and 14.3% yields, respectively. When the reaction was carried out in ethanol instead of in aqueous acetonitrile, followed by treatment with acetic acid, a crystalline product (XII) of molecular formula $C_{10}H_{12}O_5NCl$ resulted in 33.4% yield, in addition to VIIe and X. Treatment of the product (XII) with alkali afforded an oil of molecular formula $C_{10}H_{11}ON$ (XIII). The structure of VIIe was evidenced by its analytical and spectral data (see Table II), and by catalytic reduction with platinum in the presence of hydrochloric acid, which gave cinnamic aldehyde (XIV). The products (X) and (XI) were characterized as 2-methyl-3-phenylisoxazolidine and its borane complex, respectively, on the basis of the following facts. The NMR spectrum of X exhibited a singlet at τ 7.41 (N-methyl hydrogens), a multiplet centered at τ 7.48 (two hydrogens at C-4), and triplets at τ 6.46 (a hydrogen at C-3) and at τ 5.95 (two hydrogens at C-5), besides the signal for aromatic hydrogens. The catalytic reduction of X with Raney

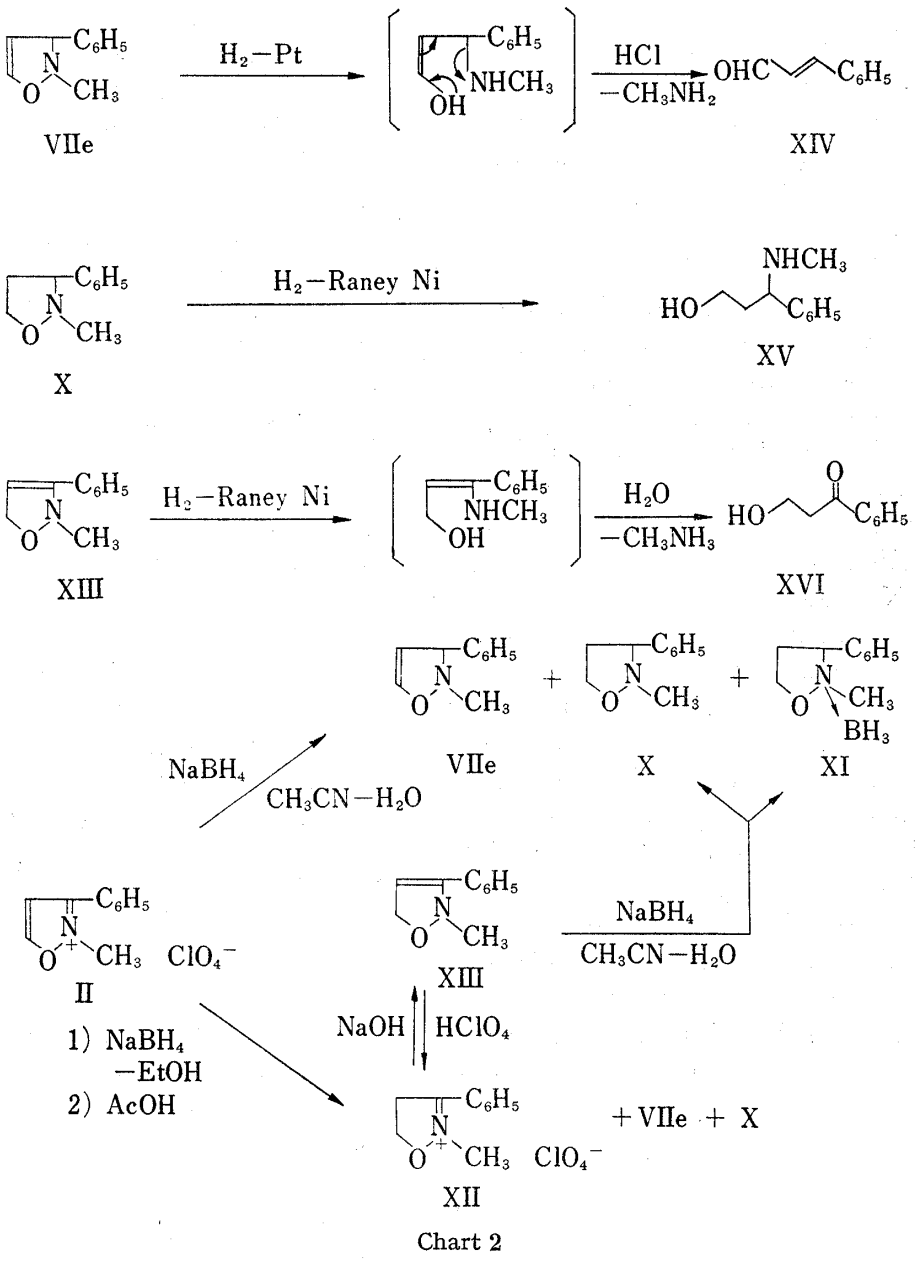


Chart 2

nickel yielded the known 3-methylamino-3-phenyl-1-propanol (XV).[13] The IR spectrum of XI showed an absorption assignable to borane at 2370 cm^{-1}, and treatment of XI with water gave X, along with boric acid. The product (XII) was assigned the structure 2-methyl-3-phenyl-2-isoxazolinium perchlorate from spectral and chemical evidence: the IR spectrum of XII showed a strong absorption band due to ClO_4^- ion, lying between 1000 and 1100 cm^{-1}; and the NMR spectrum exhibited multiplets centered at τ 5.95 (two hydrogens at C-4) and at τ 5.09 (two hydrogens at C-5), besides a N-methyl singlet at τ 6.15 and a phenyl multiplet centered at τ 2.27. Further, the product (XII) was identical with a sample obtained by the quaternization of XIII with perchloric acid. The product (XIII) was characterized as 2-methyl-3-phenyl-3-isoxazoline by the IR and NMR spectra (see Table II), and by catalytic reduction with Raney nickel giving β-hydroxypropiophenone (XVI).[14]

Furthermore, treatment of XIII with sodium borohydride in aqueous acetonitrile yielded X and XI, whereas no reaction occurred on analogous reduction of 4-isoxazoline (VIIe) with

13) E. Fourneau, E. Benoit and R. Firmnich, *Bull. Soc. Chim. Fr.*, **47**, 894 (1930).
14) M.G.J. Beets and L.G. Heeringa, *Rec. Trav. Chim.*, **74**, 1096 (1955).

sodium borohydride. In consequence, we believe that the reaction of II with sodium borohydride proceeds through a mechanism involving two competitive pathways: one by addition of hydride anion at the C_3-position of II to give the 4-isoxazoline (VIIe), and the other by addition at the C_5-position to give the 3-isoxazoline (XIII). The C_5-adduct (XIII) would undergo further reduction to give the isoxazolidines (X and XI).

The N-substituted 4-isoxazolines (VII) and their borane complexes (VIII) obtained were considerably unstable. Heating a solution of 2-methyl-5-phenyl-4-isoxazoline (VIIa) in xylene at 110° for 2 hr yielded an oil of molecular formula $C_{10}H_{11}ON$ (XVIIa) in 65.4% yield. The spectral data of XVIIa shown in Table III are consistent with 2-benzoyl-1-methylaziridine, and this was confirmed by an unequivocal synthesis of XVIIa from α,β-dibromopropiophenone with methylamine. Similarly, 2-*tert*-butyl-5-phenyl-4-isoxazoline (VIIc) yielded 2-benzoyl-1-*tert*-butylaziridine (XVIIc) in good yield, whose structure was confirmed by comparison with an authentic sample obtained by the literature method.[15] Similar conversion of 4-methyl-2,5-diphenyl-4-isoxazoline (VIId) into 2-benzoyl-2-methyl-1-phenylaziridine (XVIId) occurred merely on dissolving in ether at room temperature.

The coordination of the ring nitrogen atom of 4-isoxazoline with borane considerably weakens the N-O bond of ring, and facilitates the conversion of 4-isoxazoline into 2-acylaziridine. Thus, standing an ethereal solution of VIIa-borane (VIIIa) at 20° for a week yielded an oily product, from which two crystalline solids having molecular formulae $C_{10}H_{14}$-ONB (XVIIIa) and $C_{10}H_{16}$ONB (XIXa), besides XVIIa, were isolated in 12.5, 21.1 and 12.2% yields, respectively. The product (XVIIIa) was characterized as the borane complex of XVIIa by its spectral data (see Table III) and by comparison with a sample obtained from XVIIa with diborane. The product (XIXa) was assigned the structure 2-(α-hydroxybenzyl)-1-methylaziridine-borane from the spectral data given in the experimental part. This compound was also obtained by heating a solution of XVIIIa in benzene. Similarly, 2-benzoyl-1-ethylaziridine (XVIIb) and its borane complex (XVIIIb), together with 2-(α-hydroxybenzyl)-1-ethylaziridine (XIXb), were obtained from 2-ethyl-5-phenyl-4-isoxazoline-borane (VIIIb). The analytical and spectral data of these products are consistent with the structures assigned (see Table III). Similar treatment of an ethereal solution of 2-*tert*-butyl-5-phenyl-4-isoxazoline-borane (VIIIc) at 20°, however, did not yield the expected 2-acylaziridine derivative, but only liberated borane to give free 4-isoxazoline (VIIc).

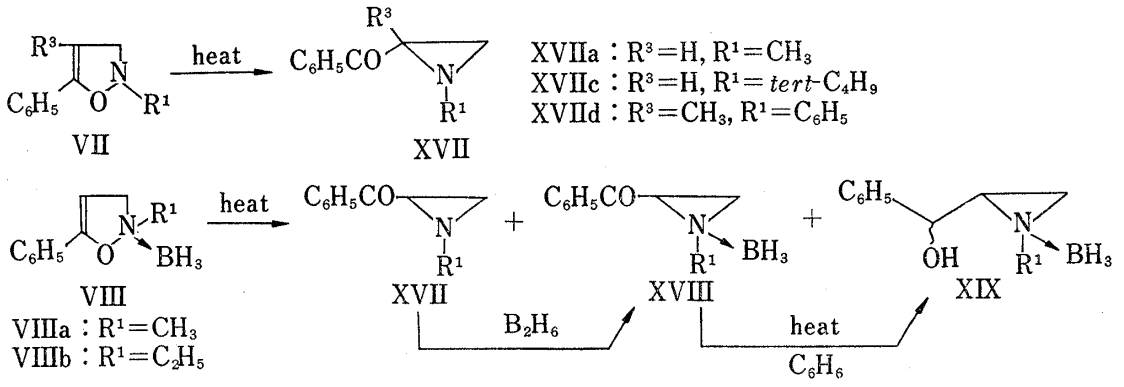


Chart 3

Although several examples[1,16] of conversion of 4-isoxazolines involving a possible 2-acylaziridine intermediate have been reported, in only one case has the intermediate been isolated, by Baldwin, *et al.*[16a] The reactions reported in this paper open up a new route to

15) J.A. Deyrup and C.L. Moyer, *J. Org. Chem.*, **35**, 3424 (1970).
16) *a*) J.E. Baldwin, R.G. Pudussery, A.K. Qureshi and B. Sklarz, *J. Am. Chem. Soc.*, **90**, 5325 (1968); *b*) S. Takahashi and H. Kanō, *J. Org. Chem.*, **30**, 1118 (1965); *c*) G. Schmidt, H. Stracke and E. Winterfeldt, *Chem. Ber.*, **103**, 3196 (1970).

TABLE III. Analytical and Spectral Data of 1-Substituted 2-Benzoylaziridines (XVII) and Their Borane Complexes (XVIII)

No.	Yield (%)	mp (°C)[a] or bp° (mmHg)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
XVIIa	65.3[b] 12.2[d]	—[c]	$C_{10}H_{11}ON$	74.51	6.88	8.69	74.40	7.00	8.45
XVIIb	18.2[d]	—[c]	$C_{11}H_{13}ON$	75.40	7.48	7.99	75.21	7.36	8.21
XVIIc	63.5[b]	bp 112 (0.5)	$C_{13}H_{17}ON$	76.81	8.43	6.89	76.81	8.40	6.78
XVIId	93.0[b]	mp74—75	$C_{16}H_{15}ON$	80.98	6.37	5.90	80.97	6.51	5.94
XVIIIa	12.5[d]	mp73—75	$C_{10}H_{14}ONB$	68.57	8.00	8.00	69.08	8.26	7.73
XVIIIb	13.7[d]	—[e]	$C_{11}H_{16}ONB$	69.88	8.53	7.41	69.46	8.62	7.01

No.	ν_{max}^{Neat} cm^{-1} C=O	BH	N-R^1	τ (multiplicity, J=Hz) in $CDCl_3$ (60 MHz) C_2-R^3	C_3-2H	C_6H_5
XVIIa	1678		7.46 (s)	7.16 (dd, 6.5, 3.0)	8.22 (dd, 6.5, 2.0) 7.72 (dd, 3.0, 2.0)	2.26 (m)
XVIIb	1679					
XVIIc	1679		8.93 (s)	6.90 (dd, 6.5, 3.0)	8.01 (dd, 6.5, 2.0) 7.88 (dd, 3.0, 2.0)	2.32 (m)
XVIId	1660		2.56 (m)	8.64 (s)	7.71 (d, 1.0) 7.22 (d, 1.0)	2.56 (m)
XVIIIa	1680	2360	7.43 (s)	6.07 (t, 5.5)	7.31 (m)	2.27 (m)
XVIIIb	1682	2360				

a) recryst. solvent=C_6H_6-hexane, *b*) Calcd. from VII, *c*) colorless oils purified by chromatography through alumina, *d*) Calcd. from VIII, *e*) colorless viscous

N-substituted 4-isoxazolines and 2-acylaziridines. A search for additional examples of similar synthetic methods, as well as chemical studies on the 4-isoxazolines mentioned in this paper, is now in progress.

Experimental

Melting points are uncorrected. The IR spectra were recorded for nujol mulls in the case of solids, or for thin films in the case of liquids, using a JASCO DS-402G spectrophotometer. The UV spectra were recorded in EtOH on a Hitachi EPS-2 spectrophotometer, and the NMR spectra were measured with a Varian A-60 analytical NMR spectrometer in $CDCl_3$ with TMS as an internal standard. Solvents and reagents were purified by conventional methods. All extracts were dried over anhydrous magnesium sulfate and evaporated under reduced pressure.

Quaternary Salts (Ia—d and II)——2-Methyl-5-phenylisoxazolium perchlorate (Ia),[4b] 2-ethyl-5-phenylisoxazolium fluoborate (Ib),[4b] 2-*tert*-butyl-5-phenylisoxazolium perchlorate (Ic)[11] and 4-methyl-2,5-diphenylisoxazolium perchlorate (Id)[12] were prepared by using the literature methods, respectively. 2-Methyl-3-phenylisoxazolium perchlorate (II) was prepared by the procedure reported in our preceding paper.[6a]

Reactions of Ia—c with $NaBH_4$——Reaction was carried out by using the following general procedure. To a solution of I (15 mmoles) in MeCN (10 ml) was added dropwise a solution of $NaBH_4$ (0.86 g) in H_2O (30 ml) with stirring at −5° and the mixture was stirred at below 0° for 1 hr. After addition of aqueous solution of NH_4Cl (2.0 g), the mixture was extracted with ether. Evaporation of the solvent under cooling *in vacuo* left an oil, which was chromatographed on silica gel with $CHCl_3$. The products (VIIa—c, VIIIa—c) listed in Table II were obtained, together with the following ring-cleavage products (IXa—c), respectively. β-(N-Methylhydroxyamino)propiophenone (IXa): colorless needles, mp 79—80° (from hexane); ν_{max}^{Nujol} 3200 (OH), 1683 cm^{-1} (C=O); τ: in $CDCl_3$ 7.32 (s, NCH_3), 6.25—6.71 [m, $-(CH_2)_2-$], 3.43 (OH), 2.35 (m, C_6H_5). *Anal.* Calcd. for $C_{10}H_{13}O_2N$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.22; H, 7.30; N, 7.93. β-(N-Ethylhydroxyamino)propiophenone (IXb): colorless needles, mp 37—39° (from hexane); ν_{max}^{Nujol} 3160 (OH), 1676 cm^{-1} (C=O). *Anal.* Calcd. for $C_{11}H_{15}O_2N$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.41; H, 7.90; N, 7.05.

β-(N-*tert*-Butylhydroxyamino)propiophenone (IXc): colorless needles, mp 86—88° (from hexane); ν_{max}^{Nujol} 3460 (OH), 1676 cm^{-1} (C=O). *Anal.* Calcd. for $C_{13}H_{19}O_2N$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.46; H, 8.65; N, 6.47.

Reaction of Id with $NaBH_4$——To a solution of Id (1.70 g) in MeCN (5 ml) was added dropwise a solution of $NaBH_4$ (0.23 g) in H_2O (15 ml) with stirring at −5°. After stirring for 1 hr, the precipitated crystalline solid was collected by filtration, washed with H_2O and dried *in vacuo* at room temperature. 4-Methyl-2,5-diphenyl-4-isoxazoline (VIId) listed in Table II was obtained.

Treatment of VIIIa with NEt_3——A mixture of VIIIa (0.51 g) and NEt_3 (1 ml) in ether (50 ml) was allowed to stand overnight at 20° and then evaporated. The residue was chromatographed on silica gel with $CHCl_3$. NEt_3–BH_3 (0.24 g) and VIIa (0.15 g) were obtained.

Reaction of II with $NaBH_4$——(A) To a solution of II (5.2 g) in MeCN (10 ml) was added a solution of $NaBH_4$ (1.14 g) in H_2O (20 ml) with stirring at 0°. After stirring at 5° for 1.5 hr, the mixture was extracted with ether. Evaporation of the solvent left an oil, which was chromatographed on silica gel with $CHCl_3$. The following products were obtained. 2-Methyl-3-phenylisoxazolidine-borane (XI) from the 1st fraction, 0.50 g (14.3%), colorless prisms, mp 80—82° (from 60% EtOH); ν_{max}^{Nujol} 2370 cm^{-1} (BH). *Anal.* Calcd. for $C_{10}H_{16}ONB$: C, 67.89; H, 9.05; N, 7.92. Found: C, 68.23; H, 9.32; N, 7.65. 2-Methyl-3-phenyl-4-isoxazoline (VIIe) from the 2nd fraction, 0.40 g (12.4%) (see Table II). 2-Methyl-3-phenylisoxazolidine (X) from the 3rd fraction, 1.356 g (41.6%), colorless oil, bp 87° (1.0 mmHg); τ 7.41 (s, NCH_3), 7.48 (m, C_4-2H), 6.46 (t, J=8.0 Hz, C_3-H), 5.95 (t, J=8.0 Hz, C_5-2H), 2.67 (m, C_6H_5). *Anal.* Calcd. for $C_{10}H_{13}ON$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.54; H, 7.96; N, 8.41. A solution of XI (0.20 g) in ether (10 ml), saturated with H_2O, was stirred at room temperature for 48 hr and then evaporated. The residue was chromatographed on silica gel with $CHCl_3$ to give X (0.15 g).

(B) To a suspension of II (5.80 g) in EtOH (30 ml) was added dropwise a solution of $NaBH_4$ (1.20 g) in EtOH (20 ml) with stirring at −5° and the mixture was stirred for 1 hr. After addition of AcOH (1.8 g), the mixture was stirred at 0° for 0.5 hr and the precipitated crystalline solid was collected by filtration. 3-Phenyl-2-isoxazolinium perchlorate (XII): 1.83 g (31.4%), colorless needles, mp 149—150° (from EtOH); τ 6.15 (s, NCH_3), 5.95 (m, C_4-2H), 5.09 (m, C_5-2H), 2.27 (m, C_6H_5); ν_{max}^{Nujol} 1000—1100 cm^{-1} (broad, ClO_4^-). *Anal.* Calcd. for $C_{10}H_{12}O_5NCl$: C, 45.90; H, 4.62; N, 5.35. Found: C, 45.91; H, 4.62; N, 5.41. The filtrate was evaporated and the residue was chromatographed on silica gel with $CHCl_3$ to give VIIe (0.96 g, 33.4%) and X (0.44 g, 12.1%). An aqueous solution of XII (1.74 g) was made alkali with dil. aq. NaOH and extracted with $CHCl_3$. Evaporation of the solvent left an oil, which was chromatographed on silica gel with $CHCl_3$ to give colorless oil. Distillation under reduced pressure gave 2-methyl-3-phenyl-3-isoxazoline (XIII) as colorless oil (0.92 g, 85.1%), bp 84° (0.2 mmHg) (see Table II).

Treatment of XIII with $NaBH_4$——A mixture of XIII (0.54 g) and $NaBH_4$ (0.2 g) in 30% aqueous MeCN (6 ml) was stirred at room temperature for 1 hr. After addition of AcOH, the mixture was extracted with ether. Evaporation of the solvent left an oil, which was chromatographed on silica gel with $CHCl_3$ to give XI (0.04 g, 6.9%) and X (0.21 g, 39.2%).

Catalytic Reduction of VIIe——A mixture of VIIe (0.59 g), PtO_2 (0.03 g) and 2N HCl (0.5 ml) in 70% EtOH (30 ml) was hydrogenated at room temperature under atmospheric pressure for 4 hr. Removal of the catalyst and solvent left an oil, which was chromatographed on silica gel with $CHCl_3$ to give colorless oil (XIV, 0.25 g). This was identical with an authentic sample of cinnamic aldehyde.

Catalytic reduction of X——A mixture of X (0.62 g) and Raney Ni(0.6 g) in EtOH (10 ml) was hydrogenated at room temperature under atmospheric pressure for 6 hr. Removal of the catalyst and solvent left an oil, which was chromatographed on alumina with $CHCl_3$–MeOH (19: 1) to give an oil (XV, 0.49 g). This was identical with 3-methylamino-3-phenylpropanol obtained by the literature method.[13]

Catalytic Reduction of XIII——A mixture of XIII (0.51 g) and Raney Ni (0.5 g) in EtOH (30 ml) was hydrogenated at room temperature under atmospheric pressure for 1 hr. Removal of the catalyst and solvent left an oil, which was dissolved in $CHCl_3$. After washing with dil. HCl and then H_2O, the solution was evaporated and the residue was chromatographed on alumina with C_6H_6 to give colorless oil (XVI, 0.18 g). This was identical with β-hydroxypropiophenone prepared by the literature method.[14]

2-Benzoyl-1-methylaziridine (XVIIa)——A solution of VIIa (0.5 g) in xylene (10 ml) was heated at 110° for 2 hr. Evaporation of the solvent left an oil, which was chromatographed on alumina with C_6H_6. XVIIa (0.33 g, 65.3%) listed in Table III was isolated. It was also prepared by the following procedure. To a solution of α,β-dibromopropiophenone[17] (4.3 g) in EtOH (10 ml) was added dropwise 30% $MeNH_2$–EtOH (30 ml) with stirring at 5° and the mixture was allowed to stand at room temperature for 3 days. Evaporation of the solvent left an oil, which was chromatographed on alumina with light petroleum to give XVIIa (0.22 g).

2-Benzoyl-1-*tert*-butylaziridine (XVIIc)——A solution of VIIc (0.50 g) in xylene (10 ml) was treated by the similar manner as the above. XVIIc (0.30 g) listed in Table III was obtained. It was identical with an authentic sample obtained by the literature method.[15]

17) E.P. Kohler, *Am. Chem. J.*, 42, 375 (1909).

2-Benzoyl-2-methyl-1-phenylaziridine (XVIId)——A solution of VIId (1.0 g) in ether (20 ml) was allowed to stand overnight at room temperature. Evaporation of the solvent left a crystalline solid, which was recrystallized from EtOH to give colorless prisms (XVIId, 0.93 g), listed in Table III.

Thermal-conversion of VIIIa into XVIIa, XVIIIa, and XIXa——A solution of VIIIa (0.56 g) in ether (20 ml) was allowed to stand at 20° for a week and then evaporated. The residue was chromatographed on alumina with C_6H_6. The following products were isolated. 2-Benzoyl-1-methylaziridine-borane (XVIIIa, 0.07 g) from the 1st fraction (see Table III). 2-(α-Hydroxybenzyl)-1-methylaziridine-borane (XIXa) from the 2nd fraction, 0.12 g (21.1%), colorless prisms, mp 86—87° (from C_6H_6–hexane); ν_{max}^{Nujol} 3290 (OH), 2350 cm^{-1} (BH); τ 7.30 (m, C_2-H), 7.66 (q, C_3-H), 7.94 (q, C_3-H), 7.14 (s, N-CH_3), 5.32 (d, benzyl-H), 2.57 (m, C_6H_5). *Anal.* Calcd. for $C_{10}H_{16}ONB$: C, 67.80; H, 9.04; N, 7.91. Found: C, 67.50; H, 9.57; N, 7.79. XVIIa from the 3rd fraction, 0.06 g (12.2%). To a solution of XVIIa (0.12 g) in ether (50 ml) was introduced B_2H_6, freshly prepared by the general procedure from $NaBH_4$ (0.12 g) and BF_3–ether (0.6 g), with stirring at room temperature. The mixture was stirred for 0.5 hr and then evaporated. The residue was chromatographed on alumina with C_6H_6 to give XVIIIa (0.05 g). A solution of XVIIIa (0.52 g) in C_6H_6 (10 ml) was refluxed for 1.5 hr and then evaporated. The residue was chromatographed on alumina with C_6H_6 to give XVIIa (0.10 g) and XIXa (0.19 g).

Thermal-conversion of VIIIb into XVIIb, XVIIIb, and XIXb——A solution of VIIIb (0.48 g) in ether (10 ml) was refluxed for 2 hr and then evaporated. The residue was chromatographed on alumina with C_6H_6. The following products were isolated. 2-Benzoyl-1-ethylaziridine-borane (XVIIIb) from the 1st fraction, 0.06 g (13.7%) (see Table III). 2-(α-Hydroxybenzyl)-1-ethylaziridine-borane (XIXb) from the 2nd fraction, 0.22 g (45.4%), colorless prisms, mp 109—110° (from ether–hexane); ν_{max}^{Nujol} 3430 (OH), 2310 cm^{-1} (BH). *Anal.* Calcd. for $C_{11}H_{18}ONB$: C, 69.14; H, 9.50; N, 7.33. Found: C, 68.93; H, 9.52; N, 7.32. 2-Benzoyl-1-ethylaziridine (XVIIb) from the 3rd fraction, 0.08 g (18.2%), colorless oil (see Table III).

Conversion of VIIIc into VIIc——A solution of VIIIc (1.20 g) in ether (60 ml), saturated with H_2O, was allowed to stand overnight at room temperature, then washed with H_2O and evaporated. The residue was chromatographed on alumina with C_6H_6 to give VIIc (0.93 g).

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