  Bull. Chem. Soc. Jpn., 64, 375—380 (1991)

Synthesis of Substituted Pyridines by a Cycloaddition Route Using Nitrile Oxides and Homoallyl Alcohols

Shuji KANEMASA,* Yoshihiko ASAI,† and Junji TANAKA
Institute of Advanced Material Study, Kyushu University, Kasugakoen, Kasuga 816
†Department of Molecular Science and Technology, Interdisciplinary Graduate School of Engineering Sciences, Kyushu University, Kasugakoen, Kasuga 816
(Received August 13, 1990)

Cycloadditions of nitrile oxides with unprotected homoallyl alcohols, followed by Swern oxidations, lead to 5-(2-oxoalkyl)-2-isoxazolines. Subsequent Raney Ni reduction of the resulting heterocycles in ethanol in the presence of excess tetrafluoroboric acid affords substituted pyridine derivatives.

Cycloadditions of nitrile oxides with terminal olefins take place readily and regioselectively to produce 5-substituted 2-isoxazolines in high yields;[1] the nitrogen-oxygen bond of cycloadducts is reductively cleaved to lead to β-imino alcohol intermediates, which are further hydrolyzed into β-hydroxy ketones and related functionalities.[2] Since the synthetic application of β-imino alcohol functionality is quite limited, we planned to open a new entry to the synthesis of pyridine nuclei by utilizing this unusual functional group.

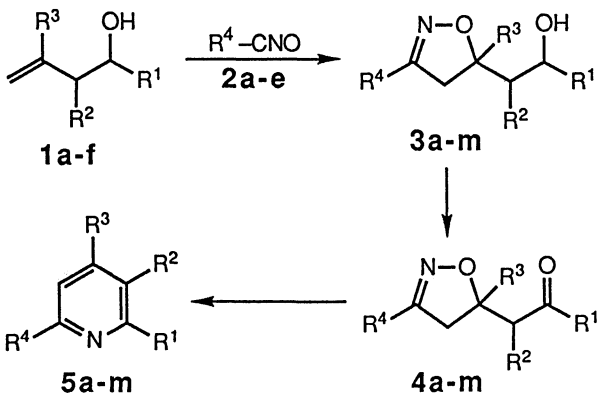
Our synthetic plan of pyridine synthesis consists of the combination of β-imino alcohol and carbonyl functionalities. Dehydrative cyclization of β-hydroxy-δ-imino ketones would offer a convenient construction route of pyridine skeletons, and the shortest access to the requisite β-hydroxy-δ-imino ketone functionality would be the nitrile oxide cycloaddition with β,γ-unsaturated ketones. However, the availability of β,γ-unsaturated ketones is quite narrow due to their susceptibility toward double bond migration.[3,4] Accordingly, we examined the nitrile oxide cycloadditions with homoallyl alcohols.

Nitrile oxides **2a—e** were found to react smoothly with a variety of homoallyl alcohols **1a—f** without protecting the hydroxyl group to give 5-(2-hydroxyalkyl)-2-isoxazolines **3a—m** in satisfactory yields (Scheme 1 and Table 1). These reactions make a striking contrast with the nitrile oxide cycloadditions with allyl alcohols where the use of unprotected dipolarophiles gave cycloadducts in poor yields.[5] Since homoallyl alcohols **1a—f** can be prepared in high yields by the reactions of readily available allyl bromides with aldehydes according to the Akiba's method,[6] this cycloaddition route is synthetically useful to construct pyridine skeletons.

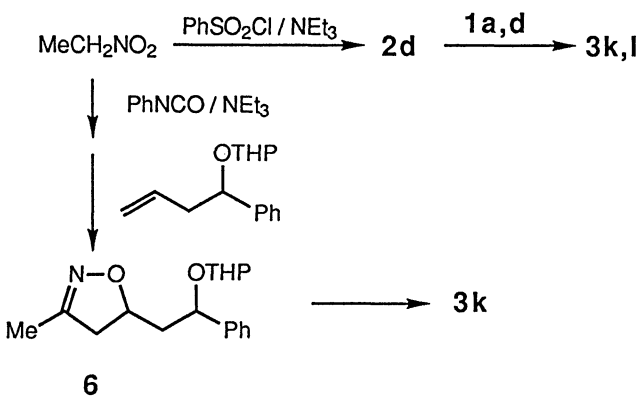
Nitrile oxides **2a—c** and **2e** were generated from the corresponding hydroximoyl halides by dehydrohalogenation with triethylamine, and ethanenitrile oxide (**2d**) was generated from nitroethane and benzenesulfonyl chloride/triethylamine (Scheme 2).[7] An effective generation method of **2d** by the Mukaiyama procedure[8] could not be successfully employed since phenyl isocyanate reacted with **1**.

Although the cycloaddition of **2d**, generated by the Mukaiyama's procedure, with the tetrahydropyranyl (THP) ether of **1a** produced the corresponding cycloadduct **6** in 76% yield, one further deprotection step (73%) was required; the overall yield of **3k** being 55%.

The secondary hydroxyl group of **3a—m** was oxidized according to the Swern oxidation procedure[9] to give ketones **4a—m** in almost quantitative yields (Table 1).

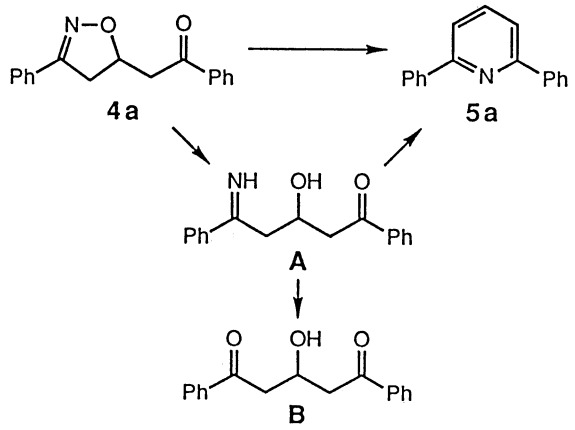


Scheme 1.



Scheme 2.

Reductive cleavage of the nitrogen-oxygen bond of 5-(2-oxoalkyl)-2-isoxazolines **4a—m** was carried out by use of Raney Ni (W-2). The Raney-Ni reduction of **4a** in the presence of boric acid in aqueous ethanol (ethanol/water=6 : 1 v/v)[10] gave the expected pyridine **5a** in only 19% yield (Scheme 3 and Table 2). In this case, a complex mixture of unidentified products was accompanied.[11]



Scheme 3.

It is likely that β-hydroxy-δ-imino ketone intermediate **A** undergoes either dehydrative cyclization to give pyridine **5a** or hydrolysis leading to 3-hydroxy-1,5-diphenyl-1,5-pentanedione (**B**) (Scheme 3). An acid would catalyze both the reactions, and presence of water is not favored for the pyridine formation. Several reaction conditions were examined on these basis, and we found that the Raney Ni reduction of **4a** in ethanol in the presence of tetrafluoroboric acid (42% aqueous solution) took place very cleanly to provide a satisfactory yield of **5a** (82%). Amount of tetrafluoroboric acid is not so important.

Under these reaction conditions, other 5-(2-oxoalkyl)-2-isoxazolines **4a—m** were reduced with Raney Ni to give pyridines **5a—m** (Scheme 1 and Table 1). The very poor yield of pyridine **5e** is in part due to its ready chelate formation with Raney Ni.[12]

In conclusion, substituted pyridines are synthesized by a sequence of the cycloaddition of nitrile oxides with homoallyl alcohols, Swern oxidation, and Raney Ni reduction. Since a variety of nitrile oxides and homoallyl alcohols are readily accessible, this method becomes a useful synthetic method of substituted pyridine derivatives.

Table 1. Pyridine Synthesis by Nitrile Oxide Cycloaddition Route

Entry	Cycloaddition reaction[a]									Swern oxidation[b]		Pyridine cyclization[c]	
	R^4CNO **2a—e**			Homoallyl alcohol **1a—f**				Product	Yield[d]/%	Product	Yield[d]/%	Product	Yield[d]/%
		R^4	Method		R^1	R^2	R^3						
1	**2a**	Ph	A	**1a**	Ph	H	H	**3a**	67	**4a**	98	**5a**	82
2	**2a**	Ph	A	**1b**	Ph	H	Me	**3b**	68	**4b**	100	**5b**	99
3	**2a**	Ph	A	**1c**	Ph	Me	H	**3c**	70	**4c**	97	**5c**	55
4	**2a**	Ph	A	**1d**	Et	H	H	**3d**	69	**4d**	100	**5d**	49
5	**2a**	Ph	A	**1e**	2-Py	H	H	**3e**	84	**4e**	98	**5e**	13
6	**2a**	Ph	A	**1f**	3-Py	H	H	**3f**	84	**4f**	81	**5f**	64
7	**2b**	*p*-$MeOC_6H_4$	A	**1a**	Ph	H	H	**3g**	91	**4g**	100	**5g**	60
8	**2b**	*p*-$MeOC_6H_4$	A	**1d**	Et	H	H	**3h**	72	**4h**	89	**5h**	72
9	**2c**	COOEt	B	**1a**	Ph	H	H	**3i**	87	**4i**	100	**5i**	53
10	**2c**	COOEt	B	**1d**	Et	H	H	**3j**	55	**4j**	100	**5j**	60
11	**2d**	Me	C	**1a**	Ph	H	H	**3k**	40	**4k**	100	**5k**	48
12	**2d**	Me	C	**1d**	Et	H	H	**3l**	30	**4l**	99	**5l**	40
13	**2e**	$(EtO)_2P(O)CH_2$	D	**1a**	Ph	H	H	**3m**	70	**4m**	84	**5m**	83

a) The reactions were carried out according to either of methods A to D (See the experimental section). b) The reaction conditions: $(COCl)_2$ (1.1 equiv), DMSO (2.2 equiv), and NEt_3 (5 equiv) in dichloromethane at −78 °C for 20 min and then at room temperature for 10 min. c) The reaction conditions: Raney Ni (W2) in ethanol containing aqueous HBF_4 (42%, 5 equiv) at room temperature under hydrogen (1 atm) for 14—16 h. d) Yield of isolated product.

Table 2. Reductive Cleavage of Nitrogen-Oxygen Bond of **4a**

Acid (equivalent)	Solvent	Reaction conditions	Yield of **5a**/%
$B(OH)_3$ (2)	$EtOH/H_2O$ (6 : 1 v/v)	Rt, 16 h	19
None	EtOH	Rt, 16 h	56
AcOH (2)	EtOH	Rt, 15 h	63
aq HBF_4 (5)	EtOH	Rt, 16 h	82
aq HBF_4 (10)	EtOH	Rt, 15 h	76

Experimental

Melting points were recorded on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with a JASCO IRA-1 or an A-702 spectrometer. ^{1}H and ^{13}C NMR spectra were measured on a Hitachi R-40 (^{1}H NMR: 90 MHz) or a JEOL GSX-270 (270 MHz for ^{1}H NMR and 67.94 MHz for ^{13}C NMR) instrument. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Mass spectra and high-resolution mass spectra (HRMS) were taken with a JEOL-01SG-2 spectrometer where the ionization energy of 70 eV was employed unless otherwise stated. Elemental analyses were performed on a Hitachi 026 CHN analyzer. For preparative column chromatography, Wakogel C-200, C-300 (Wako), and Silica gel 60 (Merck) were employed.

General Procedure for Cycloadditions of Homoallyl Alcohols 1a—f with Nitrile Oxides 2a—e Leading to 3a—m. Some typical procedures employing methods A—D for the nitrile oxide generation are described:

Method A: Triethylamine (0.404 g, 4 mmol) was added dropwise to a solution of benzohydroximoyl chloride (0.6 g, 3.85 mmol) and **1a** (0.57 g, 3.85 mmol) in dry diethyl ether (20 ml), and the mixture was stirred at room temperature for 15 h. The triethylammonium chloride was filtered off and the filtrate was evaporated in vacuo. The residue was chromatographed on silica gel by using hexane-ethyl acetate (4:1 v/v) to give **3a** (0.693 g, 67%).

Method B: Triethylamine (1.01 g, 10 mmol) in diethyl ether (14 ml) was added, at 0 °C in a period of 2 h, to a solution of ethyl chloro(hydroxyimino)acetate (1.212 g, 8 mmol) and **1a** (0.592 g, 4 mmol) in diethyl ether (20 ml), and the mixture was stirred at room temperature for 15 h. Similar workup mentioned above and subsequent column chromatography on silica gel using hexane-ethyl acetate (4:1 v/v) gave **3i** (0.92 g, 87%).

Method C: Benzenesulfonyl chloride (1.77 g, 10 mmol) was added dropwise to a solution of nitroethane (0.375 g, 5 mmol), **1a** (0.74 g, 5 mmol), and triethylamine (1.01 g, 10 mmol) in chloroform (25 ml), and the mixture was stirred at room temperature for 17 h. Water (30 ml) was added and the mixture was extracted with dichloromethane (30 ml×3). The combined extract was washed with water (20 ml×3), dried over magnesium sulfate, and the solvent was evaporated in vacuo. The residue was chromatographed on silica gel with hexane-ethyl acetate (2:1 v/v) to give **3k** (0.407 g, 40%).

Method D: To a solution of (diethoxyphosphinyl)acetaldehyde oxime (0.975 g, 5 mmol) in dry *N*,*N*-dimethylformamide (DMF, 10 ml) was added dropwise at −20 °C a DMF solution (10 ml) of *N*-bromosuccinimide (NBS, 2.1 g, 10 mmol). The mixture was stirred at −20 °C for 1 h and then at 0 °C for 30 min. Diethyl ether (10 ml), triethylamine (0.505 g, 5 mmol), and an ether solution (10 ml) of **1a** (1.48 g, 10 mmol) were added dropwise in this order, and the mixture was stirred overnight at room temperature. Water (50 ml) was added and the mixture was extracted with dichloromethane (30 ml×3). The combined extract was washed with water (30 ml×3), dried over magnesium sulfate, and the solvent was evaporated in vacuo. The residue was chromatographed on silica gel with ethyl acetate to give **3m** (1.2 g, 70%). Products **3a—m** were submitted to the Swern oxidation procedure. Spectral data for some of these compounds are given as follows and yields are summarized in Table 1:

3a: Solid (a 3:2 diastereomeric mixture (^{1}H NMR)); ^{13}C NMR ($CDCl_3$) δ=40.62, 40.64 (each C-4), 44.48, 44.62 (each 5-CH_2), 71.14, 72.47 (each C-5), 78.40, 79.67 (each CH(OH)Ph), 125.58, 125.96, 126.68, 126.71, 127.61, 128.58, 128.71, 128.74, 130.09, 130.16, 143.78, 144.36 (each Ph), 156.90, and 156.93 (each C-3). MS *m*/*z* (rel intensity) 267 (M^+, 12), 148 (9), 146 (10), 120 (9), 119 (28), 105 (18), and 104 (100).

3c: Solid (a roughly 1:1 diastereomeric mixture (^{1}H NMR)); IR (KBr) 3320, 1440, 1350, 750, and 690 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ=8.22, 9.16 (each Me), 38.10, 38.21 (each C-4), 44.58, 44.87 (each 5-CH), 73.32, 75.40 (each C-5), 83.24 (CH(OH)Ph), 125.96, 126.22, 126.62, 127.02, 127.31, 128.12, 128.25, 128.66, 129.57, 129.97, 130.05, 143.02, 143.26 (each Ph), 156.73, and 157.04 (each C-3).

3d: Solid (a 1:1 diastereomeric mixture (^{13}C NMR)); IR (KBr) 3380, 1440, 1350, 890, 755, and 690 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ=9.78, 9.85 (each Et), 30.34, 30.74 (each Et), 40.59, 40.65 (each C-4), 41.74, 42.26 (each 5-CH_2), 69.92, 71.24 (each each C-5), 78.77, 80.34 (each CH(OH)Ph), 126.65, 126.68, 128.68, 129.53, 129.67, 130.02, 130.10 (each Ph), 156.96, and 157.08 (each C-3). MS *m*/*z* (rel intensity) 219 (M^+, 27), 147 (10), 146 (100), 145 (23), 144 (13), and 118 (11).

3g: Solid (a 1:1 diastereomeric mixture (^{13}C NMR)); IR (KBr) 3280, 1600, 1240, 1010, 890, and 820 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ=40.81, 40.85 (each 5-CH_2), 44.43, 44.58 (each C-4), 55.32 (MeO), 71.06, 72.41 (each C-5), 78.10, 79.35 (each CH(OH)Ph), 114.11, 114.14, 122.04, 122.17, 125.58, 125.96, 127.50, 127.68, 128.19, 128.22, 128.51, 143.85, 144.44 (Ph and Ar), 156.50, 156.52 (each C-3), 161.03, and 161.09 (each Ar).

3h: Solid (a 1:1 diastereomeric mixture (^{13}C NMR)); IR (KBr) 3320, 1600, 1240, 1015, 890, and 820 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ=9.81, 9.88 (each Et), 30.35, 30.78 (each Et), 40.86, 40.89 (each 5-CH_2), 41.76, 42.27 (each C-4), 55.32 (MeO), 69.95, 71.26 (each C-5), 78.53, 80.08 (each CH(OH)Et), 114.11, 114.14, 122.11, 122.29, 128.17, 128.22 (each Ar), 156.54, 156.65 (each C-3), 161.00, and 161.07 (each Ar).

3i: Oil (a 1:1 diastereomeric mixture (^{13}C NMR)); IR (neat) 3400, 1715, 1250, 930, and 760 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ=14.11 (COOEt), 38.93, 39.08 (each 5-CH_2), 43.99, 44.62 (each C-4), 62.06 (COOEt), 70.73, 71.75 (each C-5), 81.02, 81.90 (each CH(OH)Ph), 125.53, 125.90, 127.79, 127.97, 128.64, 128.66, 143.48, 144.13 (Ph), 151.77, 151.80 (each C-3), and 160.76 (COOEt); MS *m*/*z* (rel intensity) 263 (M^+, 9), 190 (26), 172 (19), 157 (44), 129 (31), 115 (23), 111 (27), 108 (13), 107 (100), 105 (52), 104 (54), and 79 (26).

3j: Oil (a 1:1 diastereomeric mixture (^{13}C NMR)); IR (neat) 3420, 1720, 1590, 1250, 1130, and 930 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ=9.75 (Et), 14.13 (COOEt), 30.44, 30.81 (each Et), 38.96, 39.21 (each 5-CH_2), 41.58, 42.27 (each C-4), 62.06, 62.10 (each COOEt), 69.66, 70.68 (each C-5) , 81.44, 82.72 (each CH(OH)Et), 151.79, 151.92 (each C-3), 160.83, and 160.86 (each COOEt); MS *m*/*z* (rel intensity) 215 (M^+, 12), 186 (11), 183 (12), 157 (20), 142 (100), 129 (12), 124 (12), 114 (47), 111 (14), 96 (10), and 59 (11).

3k: Oil (a 1:1 diastereomeric mixture (^{13}C NMR)); IR (neat) 3380, 1435, 1325, 1040, 760, and 700 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ=13.12, 13.16 (each Me), 44.28, 44.35, 44.42, 44.52 (C-4 and 5-CH_2), 70.87, 72.31 (each C-5), 77.28, 78.60 (each CH(OH)Ph), 125.57, 125.93, 127.38, 127.58, 128.43, 143.94,

144.57 (each Ph), and 155.85 (C-3); MS *m/z* (rel intensity) 205 (M^+, 5), 120 (12), 107 (23), 105 (20), 104 (100), 99 (25), 79 (11), and 57 (29).

3l: Oil (a 1 : 1 diastereomeric mixture (^{13}C NMR)); IR (neat) 3420, 1440, 1335, and 870 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ=9.73, 9.86 (each Et), 13.22, 13.29 (each 3-Me), 30.32, 30.68 (each Et), 41.80, 41.97 (each 5-CH_2), 44.42, 44.65 (each C-4), 70.06, 71.66 (each C-5), 77.69, 79.67 (each CH(OH)Et), 155.79, and 155.91 (each C-3).

General Procedure for the Swern Oxidation of 3a—m Leading to 4a—m. The oxidation of **3a** is described as a typical example. To a solution of oxalyl dichloride (0.14 ml, 1.5 mmol) in dry dichloromethane (3.5 ml) was added dropwise, at −78 °C under nitrogen, a dichloromethane (3 ml) solution of dimethyl sulfoxide (0.24 ml, 3 mmol). After 5 min, a solution of **3a** (0.36 g, 1.35 mmol) in dichloromethane (3 ml) was added, and the stirring was continued for 20 min. Triethylamine (0.682 g, 6.8 mmol) was added. After 10 min, the mixture was warmed to room temperature, and poured into water (50 ml). The mixture was extracted with dichloromethane (30 ml×2). The combined extract was washed with saturated aqueous sodium chloride (30 ml×3), dried over magnesium sulfate, and the solvent was evaporated in vacuo. The residue was chromatographed on silica gel by using hexane-ethyl acetate (1 : 1 v/v) to give **4a** (0.351 g, 98%).

Results are summarized in Table 1.

5-(2-Oxo-2-phenylethyl)-3-phenyl-2-isoxazoline (4a): Colorless needles (ethyl acetate-hexane); mp 141—143 °C; IR (KBr) 1670, 1430, 1205, 910, 760, and 685 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.08 (1H, dd, J_{gem}=16.9 and $J_{4,5}$=7.7 Hz, one of H-4), 3.26 (1H, dd, J_{gem}=17.4 and $J_{CH,5}$=8.5 Hz, one of 5-CH_2), 3.66 (1H, dd, J_{gem}=17.4 and $J_{CH,5}$=4.6 Hz, the other of 5-CH_2), 3.67 (1H, dd, J_{gem}=16.9 and $J_{4,5}$=10.3 Hz, the other of H-4), 5.25 (1H, dddd, $J_{4,5}$=10.3, 7.7, $J_{5,CH}$=8.5, and 4.6 Hz, H-5), 7.4—7.7 (8H, m, Ph), and 7.9—8.0 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=40.73 (C-4), 43.87 (5-CH_2), 77.46 (C-5), 126.69, 128.09, 128.71, 128.74, 129.53, 130.10, 133.57, 136.51 (each Ph), 156.93 (C-3), and 197.36 (CO); MS *m/z* (rel intensity) 265 (M^+, 12), 160 (11), 147 (11), 146 (100), and 120 (26). Found: C, 77.01; H, 5.92; N, 5.34%. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28%.

5-(2-Oxo-2-phenylethyl)-5-methyl-3-phenyl-2-isoxazoline (4b): Pale yellow prisms (diethyl ether-hexane); mp 68—70 °C; IR (KBr) 1780, 1450, 1360, 920, 760, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.60 (3H, s, 5-Me), 3.32, 3.48 (each 1H, d, J_{gem}=17.2 Hz, H-4), 3.44, 3.59 (each 1H, J_{gem}=16.9 Hz, 5-CH_2), and 7.2—8.0 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=25.92 (5-Me), 45.44 (C-4), 47.69 (5-CH_2), 85.63 (C-5), 126.59, 128.16, 128.68, 128.71, 129.92, 129.97, 133.52, 136.99 (each Ph), 157.26 (C-3), and 197.46 (CO); MS *m/z* (rel intensity) 279 (M^+, 6), 161 (12), 160 (100), and 120 (9). Found: C, 77.77; H, 6.16; N, 4.88%. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01%.

5-(2-Oxo-1-methyl-2-phenylethyl)-3-phenyl-2-isoxazoline (4c): Obtained as a 1 : 1 mixture of diastereomers (^1H NMR); pale yellow liquid; IR (neat) 1670, 1440, 1215, 890, 760, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.23, 1.43 (each 1/2×3H, d, J=7.0 Hz, Me), 2.99, 3.26 (each 1/2H, dd, J_{gem}=17.2 and $J_{4,5}$=8.1 Hz, one of H-4), 3.42, 3.52 (each 1/2H, dd, J_{gem}=17.2 and $J_{4,5}$=11.3 Hz, the other of H-4), 3.77 (1/2H, dq, $J_{CH,Me}$=7.0 and $J_{CH,5}$=6.6 Hz, 5-CH), 3.95 (1/2H, quint, $J_{CH,Me}$=$J_{CH,5}$=7.0 Hz, 5-CH), 5.02 (1/2H, dt, $J_{5,4}$=11.3 and $J_{5,4}$=$J_{5,CH}$=8.1 Hz, H-5), 5.13 (1/2H, ddd, $J_{5,4}$=11.3, 8.1, and $J_{5,CH}$=6.6 Hz, H-5), 7.3—7.7 (8H, m, PH), and 7.9—8.0 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=12.30, 15.93 (each Me), 36.85, 39.42 (each C-4), 44.35, 46.09 (each 5-CH), 82.01, 82.89 (each C-5), 128.45, 128.56, 128.66, 128.71, 128.76, 128.79, 129.48, 130.05, 130.09, 133.37, 133.49, 136.08, 136.27 (each Ph), 156.64, 156.99 (each C-3), 201.43, and 202.46 (each CO); MS *m/z* (rel intensity) 279 (M^+, 5), 146 (47), and 134 (100). Found: C, 77.49; H, 5.95; N, 5.20%. Calcd for $C_{18}H_{17}NO_2$: C, 77.38; H, 6.14; N, 5.02%.

5-(2-Oxobutyl)-3-phenyl-2-isoxazoline (4d): Colorless needles (diethyl ether-hexane); mp 81—82.5 °C; IR (KBr) 1700, 1435, 910, 750, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.08 (3H, t, J=7.3 Hz, Et), 2.50, 2.52 (2H, each q, J=7.3 Hz, Et), 2.71 (1H, dd, J_{gem}=16.5 and $J_{CH,5}$=7.5 Hz, one of 5-CH_2), 2.99 (1H, dd, J_{gem}=16.7 and $J_{4,5}$=8.1 Hz, one of H-4), 3.04 (1H, dd, J_{gem}=16.5 and $J_{CH,5}$=5.7 Hz, the other of 5-CH_2), 3.56 (1H, dd, J_{gem}=16.7 and $J_{4,5}$=10.3 Hz, the other of H-4), 5.0—5.1 (1H, dddd, $J_{5,4}$=10.3, 8.1, $J_{5,CH}$=7.5, and 5.7 Hz, H-5), 7.3—7.4 (3H, m, Ph), and 7.6—7.7 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=7.56, 36.84 (each Et), 40.47 (C-4), 47.32 (5-CH_2), 77.07 (C-5), 126.69, 128.72, 129.50, 130.15 (each Ph), 156.78 (C-3), and 208.68 (CO); MS *m/z* (rel intensity) 217 (M^+, 11), 147 (10), 146 (100), and 57 (15). Found: C, 71.98; H, 7.10; N, 6.32%. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45%.

5-[2-Oxo-2-(2-pyridyl)ethyl]-3-phenyl-2-isoxazoline (4e): Colorless needles (diethyl ether-hexane); mp 81—83 °C; IR (KBr) 1690, 1435, 910, and 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.13 (1H, dd, J_{gem}=16.5 and $J_{4,5}$=7.3 Hz, one of H-4), 3.52 (1H, dd, J_{gem}=17.6 and $J_{CH,5}$=7.7 Hz, one of 5-CH_2), 3.62 (1H, dd, J_{gem}=16.5 and $J_{4,5}$=10.2 Hz, the other of H-4), 3.91 (1H, dd, J_{gem}=17.6 and $J_{CH,5}$=5.9 Hz, the other of 5-CH_2), 5.33 (1H, dddd, $J_{4,5}$=10.2, 7.3, $J_{5,CH}$=7.7, and 5.9 Hz, H-5), 7.3—7.4, 7.6—7.7 (3H and 2H, m, Ph), 7.55, 7.84, 8.05, and 8.68 (each 1H, m, Py); ^{13}C NMR ($CDCl_3$) δ=40.52 (C-4), 43.44 (5-CH_2), 77.41 (C-5), 121.78, 126.71, 127.48, 128.69, 129.69, 130.03, 136.97 (Ph and Py), 149.11, 152.95 (C-2 and C-6 of Py), 156.68 (C-3), and 198.97 (CO); MS *m/z* (rel intensity) 266 (M^+, 2), 163 (10), 122 (9), 121 (100), 93 (14), and 79 (11). Found: C, 72.31; H, 5.45; N, 10.44%. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.30; N, 10.52%.

5-[2-Oxo-2-(3-pyridyl)ethyl]-3-phenyl-2-isoxazoline (4f): Colorless needles (ethyl acetate-hexane); mp 138.5—139 °C; IR (KBr) 1675, 1570, 1210, 890, 790, and 755 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.12 (1H, dd, J_{gem}=17.2 and $J_{CH,5}$=7.7 Hz, one of 5-CH_2), 3.28 (1H, dd, J_{gem}=17.6 and $J_{4,5}$=8.1 Hz, one of H-4), 3.68 (1H, dd, J_{gem}=17.2 and $J_{CH,5}$=5.1 Hz, the other of 5-CH_2), 3.71 (1H, dd, J_{gem}=17.6 and $J_{4,5}$=9.9 Hz, the other of H-4), 5.29 (1H, dddd, $J_{5,4}$=9.9, 8.1, $J_{5,CH}$=7.7, and 5.1 Hz, H-5), 7.4—7.5, 7.6—7.7 (3H and 2H, m, Ph), 7.45, 8.25, 8.81, and 9.18 (each 1H, m, Py); ^{13}C NMR ($CDCl_3$) δ=40.72 (C-4), 44.12 (5-CH_2), 76.99 (C-5), 123.74, 126.73, 128.76, 129.31, 130.28, 131.77, 135.42 (Ph and Py), 149.69, 153.96 (C-2 and C-6 of Py), 156.93 (C-3), and 196.35 (CO); MS *m/z* (rel intensity) 266 (M^+, 18), 160 (9), 146 (54), 121 (100), and 106 (18). Found: C, 72.36; H, 5.49; N, 10.65%. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.30; N, 10.52%.

5-(2-Oxo-2-phenylethyl)-3-(4-methoxyphenyl)-2-isoxazoline (4g): Colorless needles (ethyl acetate-hexane); mp 146—147 °C; IR (KBr) 1670, 1600, 1255, and 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.05 (1H, dd, J_{gem}=16.8 and $J_{4,5}$=9.6 Hz, one of H-4), 3.25 (1H, dd, J_{gem}=17.6 and $J_{CH,5}$=8.5 Hz, one of 5-CH_2), 3.65 (1H, dd, J_{gem}=16.8 and $J_{4,5}$=10.3 Hz, the other of

H-4), 3.68 (1H, dd, J_{gem}=17.6 and $J_{CH,5}$=4.7 Hz, the other of 5-CH_2), 3.82 (3H, s, OMe), 5.23 (1H, dddd, $J_{5,4}$=10.3, 9.6, $J_{5,CH}$=8.5, and 4.7 Hz, H-5), and 6.9—7.9 (9H, m, Ph and Ar); ^{13}C NMR ($CDCl_3$) δ=41.02 (C-4), 43.93 (5-CH_2), 55.35 (MeO), 77.18 (C-5), 114.15, 122.10, 128.12, 128.25, 128.75, 133.57, 136.57 (Ph and Ar), 156.52 (C-3), 161.12 (Ar), and 197.50 (CO); MS *m/z* (rel intensity) 295 (M^+, 19), 177 (11), 176 (100), 175 (65), 147 (10), 120 (14), 105 (38), and 77 (29). Found: C, 73.48; H, 5.89; N, 4.42%. Calcd for $C_{18}H_{17}NO_3$: C, 73.19; H, 5.81; N, 4.74%.

5-(2-Oxobutyl)-3-(4-methoxyphenyl)-2-isoxazoline (4h): Colorless leaflets (diethyl ether-hexane); mp 111—112.5 °C; IR (KBr) 1690, 1595, 1380, 1240, 880, and 815 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.06 (3H, t, J=7.3 Hz, Et), 2.49 (2H, q, J=7.3 Hz, Et), 2.69 (1H, dd, J_{gem}=16.5 and $J_{4,5}$=8.0 Hz, one of H-4), 2.95 (1H, dd, J_{gem}=16.5 and $J_{CH,5}$=7.8 Hz, one of 5-CH_2), 3.02 (1H, dd, J_{gem}=16.5 and $J_{CH,5}$=6.5 Hz, the other of 5-CH_2), 3.51 (1H, dd, J_{gem}=16.5 and $J_{4,5}$=10.5 Hz, the other of H-4), 3.81 (3H, s, MeO), 5.03 (1H, dddd, $J_{5,4}$=10.5, 8.0, $J_{5,CH}$=7.8, and 6.5 Hz, H-5), 6.89, and 7.56 (each 2H, d, J=7.8 Hz, Ar); ^{13}C NMR ($CDCl_3$) δ=7.53, 36.74 (each Et), 40.63 (C-4), 47.31 (5-CH_2), 55.32 (MeO), 76.76 (C-5), 114.12, 122.06, 128.19 (each Ar), 156.32 (C-3), 161.09 (Ar), and 208.73 (CO); Found: C, 68.22; H, 6.95; N, 5.56%. Calcd for $C_{14}H_{17}NO_3$: C, 67.99; H, 6.93; N, 5.66%.

Ethyl 5-(2-Oxo-2-phenylethyl)-2-isoxazoline-3-carboxylate (4i): Colorless prisms (diethyl ether-hexane); mp 74—75.5 °C; IR (KBr) 1710, 1680, 1215, 935, and 755 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.36 (3H, t, J=7.3 Hz, EtO), 2.96 (1H, dd, J_{gem}=18.0 and $J_{4,5}$=8.4 Hz, one of H-4), 3.26 (1H, dd, J_{gem}=17.5 and $J_{CH,5}$=8.0 Hz, one of 5-CH_2), 3.53 (1H, dd, J_{gem}=18.0 and $J_{4,5}$=11.0 Hz, the other of H-4), 3.65 (1H, dd, J_{gem}=18.0 and $J_{CH,5}$=7.1 Hz, the other of 5-CH_2), 4.34 (2H, q, J=7.3 Hz, EtO), 5.33 (1H, dddd, $J_{5,4}$=11.0, 8.4, $J_{5,CH}$=8.0, and 7.1 Hz, H-5), and 7.4—8.0 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=14.11 (EtO), 39.32 (C-4), 43.57 (5-CH_2), 62.03 (EtO), 79.93 (C-5), 128.07, 128.79, 133.80, 136.32 (each Ar), 151.96 (C-3), 160.57 (COOEt), and 196.52 (CO); MS *m/z* (rel intensity) 262 (M^++1, 2), 188 (23), 162 (13), 120 (97), and 105 (100). Found: 64.57; H, 5.84; N, 5.02%. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36%.

Ethyl 5-(2-Oxobutyl)-2-isoxazoline-3-carboxylate (4j): Pale yellow liquid; IR (neat) 1710, 1250, 1115, and 925 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.07 (3H, t, J=7.3 Hz, Et), 1.36 (3H, t, J=7.1 Hz, EtO), 2.49 (2H, q, J=7.3 Hz, Et), 2.73 (1H, dd, J_{gem}=17.2 and $J_{CH,5}$=7.0 Hz, one of 5-CH_2), 2.88 (1H, dd, J_{gem}=17.6 and $J_{4,5}$=8.2 Hz, one of H-4), 3.03 (1H, dd, J_{gem}=17.2 and $J_{CH,5}$=5.9 Hz, the other of 5-CH_2), 3.43 (1H, dd, J_{gem}=17.6 and $J_{4,5}$=11.0 Hz, the other of H-4), 4.33 (2H, q, J=7.1 Hz, OEt), and 5.16 (1H, m, H-5); ^{13}C NMR ($CDCl_3$) δ=7.47 (Et), 14.11 (EtO), 36.69 (Et), 38.97 (C-4) , 46.91 (5-CH_2), 62.03 (EtO), 79.54 (C-5), 151.80 (C-3), 160.53 (COOEt), and 207.84 (CO); MS *m/z* (rel intensity) 214 (M^++1, 3), 205 (9), 184 (23), 169 (18), 168 (9), 157 (9), 142 (98), 140 (45), 114 (65), 96 (12), 84 (15), 72 (23), and 57 (100). Found: C, 56.20; H, 6.91; N, 6.48%. Calcd for $C_{10}H_{15}NO_4$: C, 56.32; H, 7.09; N, 6.57%.

5-(2-Oxo-2-phenylethyl)-3-methyl-2-isoxazoline (4k): Colorless needles (diethyl ether-hexane); mp 97—98 °C; IR (KBr) 1670, 1435, 1380, 1320, and 1210 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.00 (3H, s, 3-Me), 2.68 (1H, br dd, J_{gem}=17.2 and $J_{4,5}$=7.7 Hz, one of H-4), 3.17 (1H, dd, J_{gem}=17.2 and $J_{CH,5}$=8.0 Hz, one of 5-CH_2), 3.25 (1H, br dd, J_{gem}=17.2 and $J_{4,5}$=9.9 Hz, the other of H-4), 3.58 (1H, dd, J_{gem}=17.2 and $J_{CH,5}$=5.1 Hz, the other of 5-CH_2), 5.07 (1H, m, H-5), and 7.4—8.0 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=13.22 (3-Me), 43.86, 44.42 (C-4 and 5-CH_2), 76.40 (C-5), 128.09, 128.74, 133.55, 136.55 (each Ph), 155.82 (C-3), and 197.49 (CO); MS *m/z* (rel intensity) 203 (M^+, 1), 162 (7), 121 (9), 120 (100), 105 (84), and 84 (67). Found: C, 70.62; H, 6.51; N, 6.86%. Calcd for $C_{12}H_{13}NO_2$: C, 70.90; H, 6.45, N, 6.89%.

5-(2-Oxobutyl)-3-methyl-2-isoxazoline (4l): Colorless liquid; bp 115 °C/27 Pa (bulb-to-bulb); IR (neat) 1695, 1375, 1115, and 850 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.06 (3H, t, J=7.3 Hz, Et), 1.99 (3H, s, 3-Me), 2.49 (2H, q, J=7.3 Hz, Et), 2.60 (1H, dd, J_{gem}=17.2 and $J_{4,5}$=9.6 Hz, one of H-4), 2.63 (1H, dd, J_{gem}=16.9 and $J_{CH,5}$=7.0 Hz, one of 5-CH_2), 2.94 (1H, dd, J_{gem}=16.9 and $J_{CH,5}$=5.9 Hz, the other of 5-CH_2), 3.15 (1H, dd, J_{gem}=17.2 and $J_{4,5}$=10.2 Hz, the other of H-4), and 4.90 (1H, dddd, $J_{5,4}$=10.2, 9.6, $J_{5,CH}$=7.0, and 5.9 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ=7.53 (Et), 13.16 (3-Me), 36.86 (Et), 44.13 (C-4), 47.30 (5-CH_2), 76.05 (C-5), 155.61 (C-3), and 208.85 (CO); MS *m/z* (rel intensity) 155 (M^+, 5), 126 (12), 84 (100), 72 (11), 57 (34), and 43 (10). HRMS Found: *m/z* 155.0944. Calcd for $C_8H_{13}NO_2$: M, 155.0946.

3-[(Diethoxyphosphinyl)methyl]-5-(2-oxo-2-phenylethyl)-2-isoxazoline (4m): Pale yellow liquid; IR (neat) 1670, 1230, 1015, and 950 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.34 (6H, dd, J=7.2 and J_{HP}=4.0 Hz, OEt), 2.86 (1H, ddd, J_{gem}=17.6, $J_{4,5}$=7.3, and J_{HP}=3.7 Hz, one of H-4), 2.98 (2H, d, J_{HP}=22.4 Hz, CH_2P), 3.19 (1H, dd, J_{gem}=17.2 and $J_{CH,5}$=7.8 Hz, one of 5-CH_2), 3.40 (1H, ddd, J_{gem}=17.6, $J_{4,5}$=10.3, and J_{HP}=3.7 Hz, the other of H-4), 3.58 (1H, dd, J_{gem}=17.2 and $J_{CH,5}$=5.1 Hz, the other of 5-CH_2), 4.15 (4H, dq, J=7.2 and J_{HP}=7.0 Hz, OEt), 5.16 (1H, dddd, $J_{5,4}$=10.3, 7.3, $J_{5,CH}$=7.8, and 5.1 Hz, H-5), and 7.4—8.0 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=16.39 (d, J_{CP}=5.9 Hz, OEt), 26.31 d, J_{CP}=141.8 Hz, CH_2P), 42.97 (C-4), 43.64 (5-CH_2), 62.54 (d, J_{CP}=6.8 Hz, OEt), 77.22 (C-5), 128.06, 128.72, 133.56, 136.51 (each Ph), 151.93 (C-3), and 197.17 (CO); MS *m/z* (rel intensity) 339 (M^+, 1), 221 (9), 220 (100), and 192 (10). HRMS Found: *m/z* 339.1233. Calcd for $C_{16}H_{22}NO_5P$: M, 339.1235.

General Procedure for the Reductive N-O Bond Cleavage of 4a—m Leading to Pyridines 5a—m. The conversion of **4a** into **5a** is described as a typical example. To a solution of **4a** (0.068 g, 0.26 mmol) in ethanol (12 ml) were added tetrafluoroboric acid (42% aqueous solution, 0.269 g, 1.29 mmol) and Raney Ni (W-2 in ethanol, 0.8 ml). The mixture was stirred under a hydrogen atmosphere (1 atm) at room temperature for 16 h. The catalyst was removed by filteration and an aqueous solution of sodium hydroxide was added to the filtrate which was then extracted with dichloromethane (30 ml×3). The combined extract was dried over magnesium sulfate and the solvent was evaporated in vacuo. The residue was chromatographed on silica gel by using hexane-ethyl acetate (5 : 1 v/v) to give **5a** (0.049 g, 82%). Mp 82 °C (lit,[13] mp 81—82 °C).

In the case of **5e**, the filtrate from which the catalyst had been filtered off was evaporated in vacuo. The residue was treated with aqueous ethylenediaminetetraacetic acid, extracted with dichloromethane (30 ml×3), and the purification procedure was continued.

Yields of **5a—m** are summarized in Table 1. The following pyridines are all known: 2,6-diphenylpyridine (**5a**);[13,15] 4-methyl-2,6-diphenylpyridine (**5b**);[13] 3-methyl-2,6-diphenylpyridine (**5c**);[14] 2-phenyl-6-(2-pyridyl)pyridine (**5e**);[15] 2-(4-

methoxyphenyl)-6-phenylpyridine (**5g**);[16] 2-methyl-6-phenylpyridine (**5k**);[17] 2-ethyl-6-methylpyridine (**5l**).[18]

2-Ethyl-6-phenylpyridine (5d): Colorless liquid; IR (neat) 1565, 1440, and 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.36 (3H, t, J=7.7 Hz, 2-Et), 2.88 (2H, q, J=7.7 Hz, 2-Et), and 7.0—8.0 (8H, m, Ph and Py); ^{13}C NMR ($CDCl_3$) δ=13.85, 31.56 (each 2-Et), 117.65, 120.31, 126.98, 128.64, 136.90, 139.88, 156.73 (Ph and Py), and 163.36 (C-2 and C-6 of Py); MS m/z (rel intensity) 184 (M^++1, 12), 183 (M^+, 90), 182 (100), 155 (20), 154 (22), 127 (13), and 77 (18). HRMS Found: m/z 183.1047. Calcd for $C_{13}H_{13}N$: M, 183.1047.

2-Phenyl-6-(3-pyridyl)pyridine (5f): Pale yellow liquid; IR (neat) 3000, 1550, 1430, and 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.3—8.7 (11H, m, Ph and Py) and 9.30 (1H, br s, Py); ^{13}C NMR ($CDCl_3$) δ=118.66, 119.35, 123.57, 126.95, 128.76, 129.24, 134.41, 137.75, 139.03 (Ph and Py), 148.35, 149.87, 154.26, and 157.26 (Py); MS m/z (rel intensity) 232 (M^+, 100), 231 (42), 206 (8), 204 (8), and 77 (8). HRMS Found: m/z 232.1002. Calcd for $C_{16}H_{12}N_2$: M, 232.1000.

2-Ethyl-6-(4-methoxyphenyl)pyridine (5h): Colorless liquid; IR (neat) 1570, 1445, 1250, 1035, and 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.36 (3H, t, J=7.8 Hz, Et), 2.86 (2H, q, J=7.8 Hz, Et), 3.82 (3H, s, MeO), 6.93 (2H, d, J=9.2 Hz, Ar), 7.0—7.6 (3H, m, Py), and 7.95 (2H, d, J=9.2 Hz, Ar); ^{13}C NMR ($CDCl_3$) δ=13.82, 31.53 (each Et), 55.25 (MeO), 114.01, 116.83, 119.58, 128.48, 136.80, 156.31, 160.28, and 163.15 (Ar and Py); MS m/z (rel intensity) 214 (M^++1, 16), 213 (M^+, 100), 212 (84), 185 (10), and 170 (12). HRMS Found: m/z 213.1150. Calcd for $C_{14}H_{15}NO$: M, 213.1154.

Ethyl 6-Phenyl-2-pyridinecarboxylate (5i): Pale yellow needles; mp 44—45 °C; IR (KBr) 1720, 1580, 1435, 1280, 1225, 1160, and 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.46 (3H, t, J=7.2 Hz, COOEt), 4.47 (2H, q, J=7.2 Hz, COOEt), and 7.3—8.1 (8H, m, Ph and Py); ^{13}C NMR ($CDCl_3$) δ=14.31, 61.78 (each COOEt), 123.25, 123.42, 127.18, 128.79, 129.41, 137.62, 138.50, 148.36 (Ph and Py), 157.60 (C-5 of Py), and 165.47 (COOEt); MS m/z (rel intensity) 227 (M^+, 14), 156 (13), 155 (100), 154 (29), 127 (18), and 77 (10). Found: C, 74.25; H, 5.83; N, 6.18%. Calcd for $C_{14}H_{13}NO_2$: C, 73.98; H, 5.77; N, 6.17%.

Ethyl 6-Ethyl-2-pyridinecarboxylate (5j): Pale yellow liquid; IR (neat) 1715, 1460, 1300, 1175, and 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.34 (3H, t, J=7.7 Hz, 5-Et), 1.43 (3H, t, J=7.0 Hz, COOEt), 2.94 (2H, q, J=7.7 Hz, 5-Et), 4.47 (3H, q, J=7.0 Hz, COOEt), 7.36 (1H, br d, J=7.7 Hz, H-5 of Py), 7.74 (1H, t, J=7.7 Hz, H-4 of Py), and 7.94 (1H, br d, J=7.7 Hz, H-3 of Py); ^{13}C NMR ($CDCl_3$) δ=14.04 (5-Et), 14.33 (COOEt), 31.43 (5-Et), 61.78 (COOEt), 122.46, 125.31, 137.17, 147.79, 164.18 (each Py), and 165.52 (COOEt); MS m/z (rel intensity) 180 (M^++1, 15), 179 (M^+, 100), 178 (11), 133 (19), 107 (85), 106 (33), 105 (75), 104 (26), 79 (27), 78 (13), and 77 (25). HRMS Found: m/z 179.0946. Calcd for $C_{10}H_{13}NO_2$: M, 179.0946.

2-[(Diethoxyphosphinyl)methyl]-6-phenylpyridine (5m): Pale yellow liquid; IR (neat) 1570, 1450, 1240, and 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.26 (6H, t, J=7.2 Hz, EtO), 3.51 (2H, d, J_{HP}=21.6 Hz, CH_2P), 4.11 (4H, dq, J_{HP}=7.7 and J=7.2 Hz, EtO), and 7.3—8.0 (8H, m, Ph and Py); ^{13}C NMR ($CDCl_3$) δ=16.34 (d, J_{CP}=6.8 Hz, OEt), 36.68 (d, J_{CP}=134.0 Hz, CH_2P), 62.22 (d, J_{CP}=6.8 Hz, OEt), 118.50, 118.54, 122.56, 122.63, 126.86, 128.68, 128.97, 137.29, 139.12, 152.46, and 156.96 (Py and Ph); MS m/z (rel intensity) 306 (M^++1, 10), 305 (M^+, 48), 256 (12), 181 (11), 170 (14), and 169 (100). HRMS Found: m/z 305.1185. Calcd for $C_{16}H_{20}NO_3P$: M, 305.1181.

References

1) P. Caramella and P. Grünanger, "Nitrile Oxides and Imines in 1,3-Dipolar Cycloaddition Chemistry," ed by A. Padwa, John Wiley & Sons, New York (1984), Vol. 1, Chap. 3, pp. 291—392; D. P. Curran, "Advances in Cycloaddition," ed by D. P. Curran, JAI Press, Greenwich (1988), Vol. 1, pp. 129—189; S. Kanemasa and O. Tsuge, *Heterocycles*, **30**, 719 (1990).

2) G. Jones, "Pyridines and Their Benzo Derivatives: (V) Synthesis in Comprehensive Heterocyclic Chemistry," ed by A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford (1984), Vol. 2, pp. 395—510.

3) M. D'Auria, A. D. Mico, F. D'Onofrio, and A. Scettri, *Synthesis*, **1985**, 988.

4) Oxidation of 1-phenyl-3-buten-1-ol with pyridinium dichromate (PDC) gives a mixture of 1-phenyl-3-buten-1-one (34%) and 1-phenyl-2-buten-1-one (28%).

5) In the nitrile oxide cycloadditions with O-unprotected allyl alcohols, 1 : 2 cycloadducts are often formed. This would be responsible for the low yield formation of 1 : 1 cycloadducts. For the reaction examples with O-protected allyl alcohols, see O. Tsuge, S. Kanemasa, and H. Suga, *Bull. Chem. Soc. Jpn.*, **61**, 2133 (1988).

6) M. Wada, H. Ohki, and K. Akiba, *Tetrahedron Lett.*, **27**, 4771 (1986).

7) T. Shimizu, Y. Hayashi, H. Shibafuchi, and K. Teramura, *Bull. Chem. Soc. Jpn.*, **59**, 2827 (1986).

8) T. Mukaiyama and T. Hoshino, *J. Am. Chem. Soc.*, **82**, 5339 (1960).

9) A. J. Mancuso, S.-L. Huang, and D. Swern, *J. Org. Chem.*, **43**, 2480 (1978).

10) D. P. Curran, *J. Am. Chem. Soc.*, **104**, 4024 (1982); **105**, 5826 (1983).

11) This mixture shows strong and broad signals in the methylene region in ^1H NMR spectrum, indicating the formation of overreduction products.

12) It was necessary to treat the crude product with aqueous ethylenediaminetetraacetic acid in order to liberate **5e** from the complex.

13) E. Wenkert, J. M. Hanna, Jr., M. H. Leftin, E. L. Michelotti, K. T. Potts, and D. Usifer, *J. Org. Chem.*, **50**, 1125 (1985).

14) M. Scholtz, *Ber.*, **32**, 1935 (1899).

15) F. Kroehnke, *Synthesis*, **1976**, 1.

16) M. Scholtz and W. Meyer, *Ber.*, **43**, 1861 (1910).

17) J. Meisenheimer, E. Stratmann, and W. Theilacker, *Ber.*, **65**, 418 (1932).

18) K. Loeffler and F. Thiel, *Ber.*, **42**, 132 (1909).