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Studies on Isoxazoles. XV.[1] Syntheses of 3-Aminoisoxazole Derivatives

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New versatile syntheses of 3-aminoisoxazoles and their derivatives are described. 3-(*N*,*N*-Disubstituted amino)isoxazoles **5** were synthesized by heating 3-chloro-2-methylisoxazolium chlorides **1** with secondary amines, or by the substitution reaction of **1** with primary amines, followed by the dehydrochlorination and the subsequent addition-elimination reaction of alkyl or acyl halides with the resulting imines **6**. Among the products **5**, 3-(*N*-substituted acetylamino)isoxazoles were hydrolyzed with base to give 3-(*N*-monosubstituted amino)isoxazoles **3**. 3-Aminoisoxazoles **7** were synthesized by the reaction of **1** with potassium phthalimide, followed by treatment with hydrazine.

Keywords——3-aminoisoxazole; 3-chloro-2-methylisoxazolium chloride; 3-imino-4-isoxazoline; *N*-(3-isoxazolyl)phthalimide; addition-elimination reaction

Various 3-aminoisoxazoles and their derivatives have been synthesized. Among them, sulfamethoxazole[2] (derived from 3-amino-5-methylisoxazole) is widely used as an antibacterial agent. Recently, a urea of 3-amino-5-*tert*-butylisoxazole has been reported[3] to possess strong herbicidal activity. Accordingly, several synthetic methods for 3-aminoisoxazoles and their derivatives have already been devised: the cyclization reactions of hydroxylamine with α,γ-diketoesters[2] (followed by Hofmann rearrangement), β-ketonitriles,[4] cyanoacetylenes,[5] acetylenethioamides,[6] or benzoylketene O,N-acetals.[7] Each method has limitations due to the lack of generality of available methods for the preparation of the respective starting materials. There is, in fact, no convenient method for the synthesis of 3-(*N*,*N*-disubstituted amino)isoxazoles. In the course of studies on the chemical properties of 3-chloroisoxazolium chlorides, which can be easily prepared[8] from 3-hydroxyisoxazoles, we found[9] that the chlorine at the 3-position was easily displaced by attack of a nucleophile, *i.e.*, thiophenol, and that the resulting 3-phenylthio-2-methylisoxazolium chlorides were transformed to 3-phenylthioisoxazoles on heating. On the basis of these findings, we planned new syntheses of 3-aminoisoxazoles and their derivatives using the substitution reaction of 3-chloro-2-methylisoxazolium chlorides with amines, followed by heating in an appropriate solvent.

In the presence of two equivalents of aniline, 3-chloro-5-phenyl-2-methylisoxazolium chloride **1a** afforded the 3-anilinoisoxazolium chloride **2a**, which was heated in *ortho*-dichlorobenzene (ODCB) to give 3-anilino-5-phenylisoxazole **3a** in 25% yield (Chart 1). The 5-methyl isomer was also obtained, but in only 15% yield, from the 3-chloroisoxazolium chloride **1b**. Under the same conditions the onium salts **1** reacted with secondary amines to give a series of 3-(*N*,*N*-disubstituted amino)isoxazoles **5a**—**f** (Table I) in moderate to excellent yields. However, no reaction occurred with acetanilide or ethyl *N*-phenylcarbamate.

We tried to improve this method. On treatment with one equivalent of sodium hydroxide, the 3-anilinoisoxazolium salt **2a** was transformed into the 3-phenylimino-4-isoxazoline **6a** (Chart 2, Table II). Quaternization of **6a** with methyl iodide proceeded smoothly at room

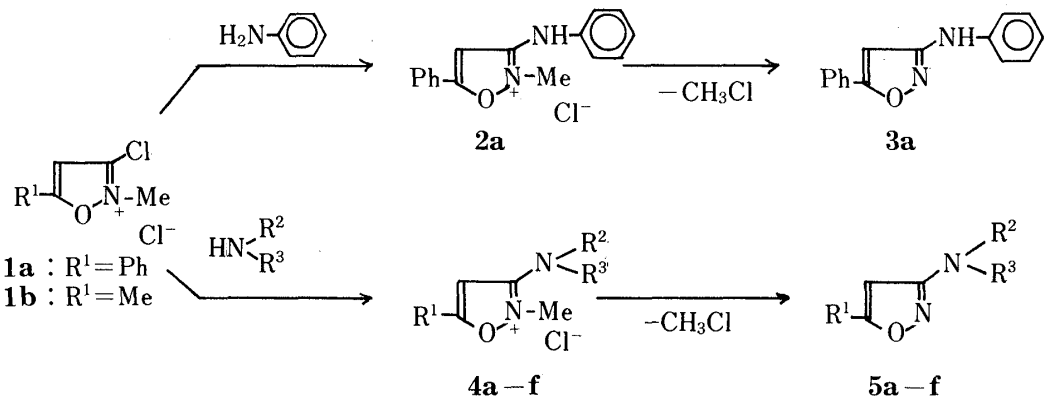


Chart 1

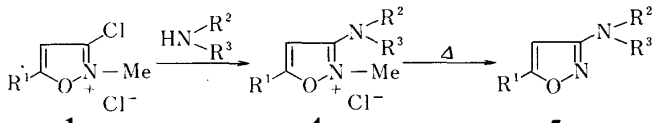
temperature to give an adduct **4g** in 89% yield, which afforded the 3-(*N*-methylanilino)-isoxazole **5g** quantitatively on heating. With increase of the bulkiness of the alkyl halides, the yields of the adducts **4** decreased in the following order: methyl iodide, allyl bromide, ethyl iodide, propyl iodide (Table III). Thermolysis of these salts **4g—j** gave the corresponding 3-(*N*-substituted anilino)isoxazoles **5g—j** along with the 3-anilinoisoxazole **3a**. The formation mechanism of **3a** has not yet been clarified.

On heating with acetyl chloride in place of methyl iodide (Chart 2), the 3-acetanilidoisoxazole **5l** was obtained in 75% yield without isolation of the intermediate quaternary salt. Accordingly, various 3-(*N*,*N*-disubstituted amino)isoxazoles **5g—s** (Table III), even those having an acyl group at the amino function, were synthesized by treatment of 3-imino-4-isoxazolines **6** with alkyl or acyl halides at 120—180 °C. Among them, the 3-acetanilidoisoxazole **5l** was hydrolyzed with base to produce the 3-anilinoisoxazole **3a** in quantitative yield. Base-catalyzed deacetylation of 3-(*N*-substituted acetylamino)isoxazoles consequently led to the synthesis of the 3-(*N*-monosubstituted amino)isoxazoles **3** (Table IV), starting from the 3-chloroisoxazolium chlorides **1**.

We tried to synthesize 3-amino-5-phenylisoxazole **7a** from 3-chloro-5-phenyl-2-methylisoxazolium chloride **1a**. The salt **1a** reacted with ammonia in methanol to produce the 3-aminoisoxazolium chloride **6a**. The thermolysis of **6a** resulted mainly in polymerization, though the 3-aminoisoxazole **7a** was isolated in only 16% yield. Next, the salt **6a** was transformed to the 3-imino compound **8** by treatment with one equivalent of sodium hydroxide. In view of the transformation from **6** to **5**, it was thought that it might be possible to synthesize 3-(*N*-monosubstituted amino)isoxazoles by treatment of **8** with an appropriate alkyl or acyl halide, with elimination of methyl halide; thus, the imine **8** was heated with *p*-acetylaminobenzenesulfonyl chloride. However, this did not give the expected product but resulted in the formation of the 3-sulfonylimino compound **9** together with the amino-isoxazolium salt **6a**. Furthermore, all attempts to eliminate the methyl group from **9** were unsuccessful. Finally, the reaction of **1a** with potassium phthalimide in boiling ODCB afforded the 3-phthalimidoisoxazole **10a** in considerable yield, and this product was successively transformed to the 3-aminoisoxazole **7a** by the action of hydrazine. The 5-methyl compound **7b** was similarly synthesized through the 3-phthalimidoisoxazole **10b**.

In conclusion, 3-(*N*-cyclic disubstituted amino)isoxazoles **5** were directly prepared by heating 3-chloro-2-methylisoxazolium chlorides **1** with cyclic secondary amines such as morpholine and piperidine. On the other hand, 3-(*N*-acyclic disubstituted amino)derivatives **5** were synthesized from **1** in a stepwise manner as follows: substitution reaction with primary amines, base-catalyzed imine formation, and thermal addition-elimination reaction with alkyl or acyl halides. Deacetylation of 3-(*N*-substituted acetylamino)isoxazoles gave 3-(*N*-

TABLE I. 3-(*N*,*N*-Disubstituted amino)isoxazoles **5**



1 **4** **5**

				4						5					
	R^1	R^2	R^3	Yield %	mp °C	Formula	Analysis (%) Calcd (Found) C	H	N	Yield	mp °C (n_D)	Formula	Analysis (%) Calcd (Found) C	H	N
a	Ph	Et	4-MeC_6H_4	61	175.5	$C_{19}H_{21}ClN_2O$	54.29 (53.91	5.04 4.83	6.67 6.85)	89.8	(n_D^{25} 1.6090)	$C_{18}H_{18}N_2O$	77.67 (77.32	6.52 6.69	10.06 10.05)
b	Ph			100	142—148	$C_{14}H_{17}ClN_2O_2 \cdot 2H_2O$	53.08 (52.79	6.68 6.79	8.84 8.68)	72.1	143—144	$C_{13}H_{14}N_2O_2$	67.81 (67.70	6.13 6.00	12.16 12.26)
c	Ph			75.3	151—154	$C_{16}H_{21}ClN_2O \cdot 1/2HCl \cdot 3/2H_2O$	56.83 (56.85	6.85 6.46	8.28 8.41)	65.9	59—63	$C_{15}H_{18}N_2O$	74.35 (74.74	7.49 7.49	11.56 11.32)
d	Me	Me	$PhCH_2$	—[a]						25.0[b]	(n_D^{23} 1.5270)	$C_{12}H_{14}N_2O$	71.26 (71.03	6.98 7.27	13.85 13.68)
e	Me	Me	*n*-Bu	—[a]						14.7[b]	(n_D^{22} 1.4760)	$C_9H_{16}N_2O$	64.25 (64.29	9.58 9.50	16.65 16.69)
f	Me			—[a]						20.0[b]	73—75	$C_8H_{12}N_2O_2$	57.13 (56.81	7.19 7.25	16.65 16.35)

a) The salt was not isolated.
b) The yield was based on 3-chloro-2,5-dimethylisoxazolium chloride **1b**.

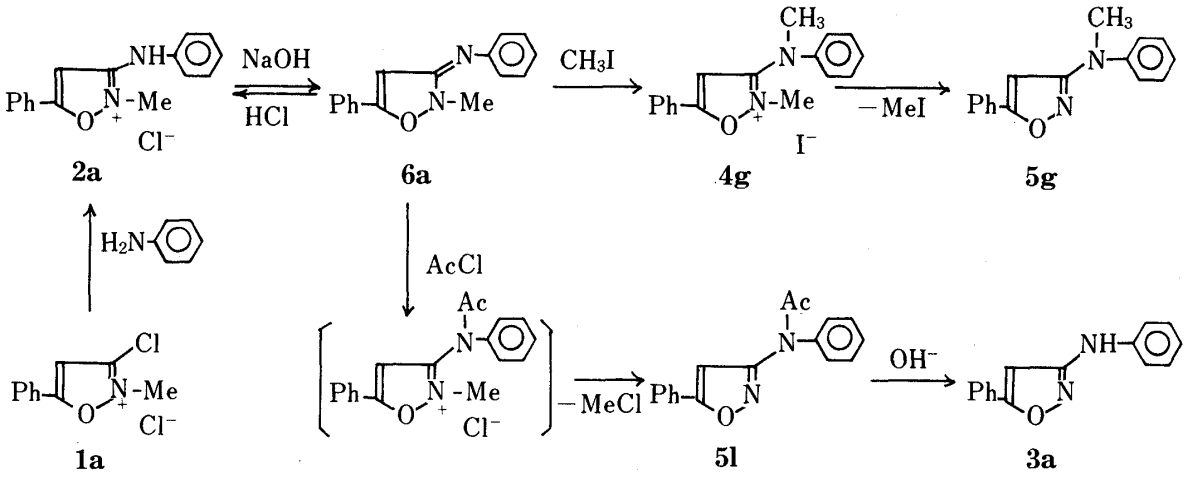
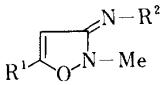


Chart 2

TABLE II. 3-Imino-2-methyl-4-isoxazolines **6**

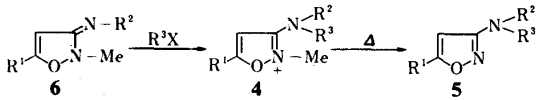


6

6	R^1	R^2	Yield %	mp °C (n_D)	Formula	Analysis (%) Calcd (Found)		
						C	H	N
a	Ph	Ph	87.1	73—74	$C_{16}H_{14}N_2O$	76.78	5.64	11.19
						(77.03	6.00	11.25)
b	Ph	4-MeC_6H_4	79.5	(n_D^{25} 1.5892)	$C_{17}H_{16}N_2O$	77.25	6.10	10.60
						(76.99	6.14	10.48)
c	Ph	4-ClC_6H_4	82.7	72—74	$C_{16}H_{13}ClN_2O$	67.49	4.60	9.84
						(67.52	4.56	10.12)
d	Ph	CH_2Ph	71.3	(n_D^{25} 1.6350)	$C_{17}H_{16}N_2O$	77.25	6.10	10.60
						(76.26	6.11	10.35)
e	Ph	*n*-Pr	72.3	(n_D^{25} 1.5905)	$C_{13}H_{16}N_2O$	72.19	7.46	12.95
						(72.15	7.77	12.65)
f	Me	Ph	75.8	(n_D^{24} 1.6038)	$C_{11}H_{12}N_2O$	70.19	6.43	14.88
						(70.06	6.37	14.94)
g	Me	2-FC_6H_4	94.3	(n_D^{25} 1.5852)	$C_{11}H_{11}FN_2O$	64.07	5.38	13.58
						(64.05	5.53	13.62)
h	Me	2-$MeOC_6H_4$	95.0	(n_D^{24} 1.5944)	$C_{12}H_{14}N_2O_2$	66.04	6.47	12.83
						(65.87	6.57	12.73)
i	Me	3,5-$Cl_2C_6H_3$	68.0	74—76	$C_{11}H_{10}Cl_2N_2O$	51.39	3.92	10.90
						(51.48	3.86	10.89)
j	Me	2,6-$Me_2C_6H_3$	89.3	(n_D^{25} 1.5693)	$C_{12}H_{16}N_2O$	70.56	7.89	13.71
						(70.90	7.52	13.42)

monosubstituted amino)isoxazoles **3**. 5-Substituted-3-aminoisoxazoles **7** were synthesized by heating **1** with potassium phthalimide, followed by treatment with hydrazine. The present method should be widely applicable to the synthesis of 3-aminoisoxazoles and should be especially useful for the synthesis of 3-(*N*,*N*-disubstituted amino)isoxazoles.

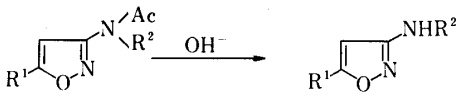
TABLE III. 3-(*N*,*N*-Disubstituted amino)isoxazoles **5**



	R¹	R²	R³X	4 Yield %	4 mp °C (n_D)	4 Formula	4 Analysis (%) Calcd (Found) C	H	N	5 Yield %	5 mp °C (n_D)	5 Formula	5 Analysis (%) Calcd (Found) C	H	N
g	Ph	Ph	MeI	88.5	154—156	$C_{17}H_{17}IN_2O$	52.06 (52.27	4.37 4.52	7.14 7.11)	100	(n_D^{31} 1.6268)	$C_{16}H_{14}N_2O$	76.78 (76.49	5.64 5.80	11.19 11.25)
h	Ph	Ph	EtI	33.8	152—154	$C_{18}H_{19}IN_2O$	53.22 (52.92	4.71 4.57	6.90 6.87)	59.5[b]	(n_D^{23} 1.6080)	$C_{17}H_{16}N_2O$	77.25 (76.93	6.10 6.16	10.60 10.49)
i	Ph	Ph	*n*-PrI	12.8	150—151	$C_{19}H_{21}IN_2O$	54.30 (54.08	5.04 4.73	6.67 6.66)	44.3[c]	(n_D^{23} 1.6050)	$C_{18}H_{18}N_2O$	77.67 (77.93	6.52 6.54	10.06 9.76)
j	Ph	Ph	AllylBr	34.9	143—145	$C_{19}H_{19}BrN_2O$	61.47 (61.19	5.16 4.92	7.54 7.67)	56.9[d]	(n_D^{25} 1.6223)	$C_{18}H_{16}N_2O$	78.24 (77.90	5.84 5.83	10.14 9.90)
k	Ph	Ph	PhCOCl	100	90—92	$C_{22}H_{19}ClN_2O_2$	69.55 (69.22	5.05 5.32	7.39 7.12)	90.9	123—126	$C_{21}H_{16}N_2O_2$	76.81 (76.93	4.91 4.82	8.53 8.45)
l	Ph	Ph	AcCl	—[a]						75.0[e]	111—113	$C_{17}H_{14}N_2O_2$	73.37 (73.23	5.07 5.18	10.07 9.84)
m	Ph	Ph	$ClCO_2Et$	90.2	104—106	$C_{19}H_{19}ClN_2O_3$	63.60 (63.40	5.34 5.40	7.81 8.05)	84.4	92—95	$C_{18}H_{16}N_2O_3$	70.12 (69.84	5.23 5.33	9.09 8.99)
n	Ph	Ph	TsCl	—[a]						33.3[e]	110—112	$C_{22}H_{18}N_2O_3S$	67.67 (67.68	4.65 4.92	7.17 7.06)
o	Ph	*n*-Pr	AcCl	—[a]						74.6[e]	(n_D^{24} 1.5644)	$C_{14}H_{16}N_2O_2$	68.83 (68.75	6.60 6.63	11.47 11.27)
p	Ph	CH_2Ph	AcCl	—[a]						88.6[e]	103—105	$C_{18}H_{16}N_2O_2$	73.96 (73.63	5.52 5.50	9.58 9.63)
q	Me	Ph	MeI	100	(n_D^{30} 1.6277)	$C_{12}H_{15}IN_2O$	43.65 (43.81	4.58 4.94	8.48 8.04)	68.2	(n_D^{26} 1.5681)	$C_{11}H_{12}N_2O$	70.19 (70.26	6.43 6.57	14.88 14.93)
r	Me	Ph	AcCl	—[a]						95.0[e]	(n_D^{29} 1.5413)	$C_{12}H_{12}N_2O_2$	66.67 (66.39	5.59 5.56	12.96 12.77)
s	Me	2,6-$Me_2C_6H_3$	AcCl	—[a]						61.3[e]	102—104	$C_{19}H_{18}N_2O_2$	74.49 (74.51	5.92 6.03	9.14 8.84)

a) The salt was not isolated. *b*) **3a** (26.0%) was isolated. *c*) **3a** (18.1%) was isolated.
d) **3a** (20.2%) was isolated. *e*) The yield was based on **6**.

TABLE IV. 3-(*N*-Monosubstituted amino)isoxazoles **3**



5 **3**

3	R^1	R^2	Yield %	mp °C (n_D)	Formula	Analysis (%) Calcd (Found)		
						C	H	N
a	Ph	Ph	100	147—149[a]	$C_{15}H_{12}N_2O$	76.25 (75.97	5.12 5.00	11.86 11.90)
b	Ph	*n*-Pr	96.0	41—43	$C_{12}H_{14}N_2O$	71.26 (71.27	6.98 6.99	13.85 13.72)
c	Ph	$PhCH_2$	85.1	140—141	$C_{16}H_{14}N_2O$	76.78 (76.67	5.64 5.61	11.19 11.12)
d	Me	Ph	97.1	138—140[b]	$C_{10}H_{10}N_2O$	68.95 (69.07	5.79 5.72	16.08 15.94)
e	Me	2,6-$Me_2C_6H_3$	100	150	$C_{12}H_{14}N_2O$	71.26 (71.50	6.98 7.06	13.85 13.86)

a) Lit.[7] mp 145—146 °C. *b*) Lit.[6b] mp 111—112 °C.

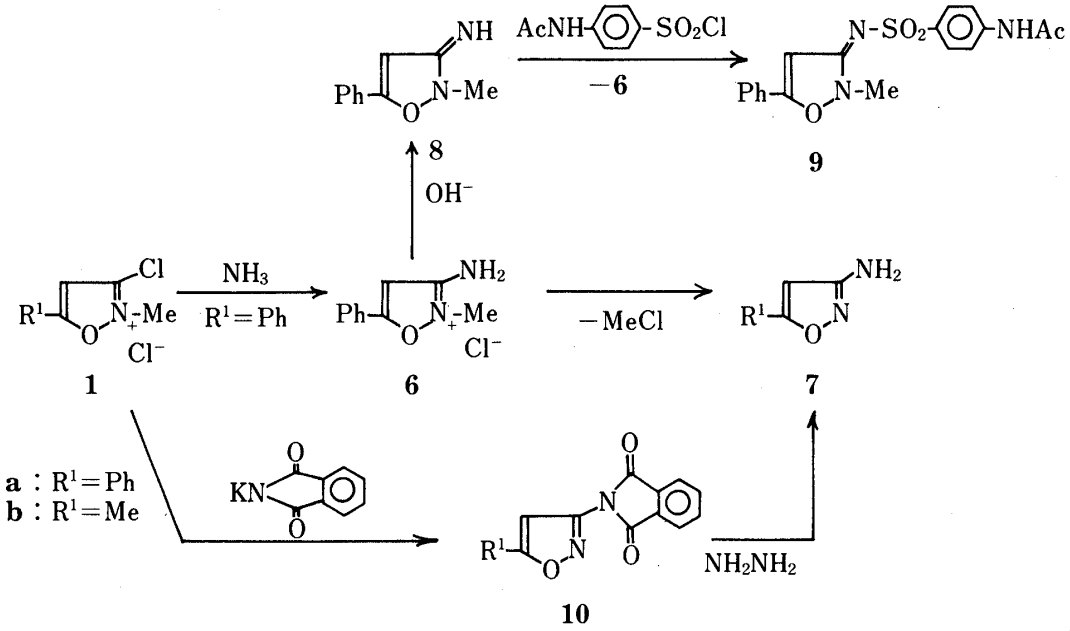


Chart 3

Experimental

Melting points are not corrected. Infrared (IR) spectra were recorded on a Jasco A-102 spectrometer. Nuclear magnetic resonance (NMR) spectra were taken on a Varian EM-360A spectrometer using tetramethylsilane as an internal standard. The following abbreviations are used: s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet).

3-Anilino-2-methyl-5-phenylisoxazolium Chloride 2a——Aniline (1.95) was added to a solution of 3-chloro-2-methyl-5-phenylisoxazolium chloride **1a** (2.3 g) in CH_3CN (30 ml) and $CHCl_3$ (30 ml). The mixture was stirred for 3 h, then concentrated. The residue was neutralized with 1 N NaOH, and washed with ether. The aqueous layer was

evaporated to dryness *in vacuo*, and the residue was washed with ether to give **2a** (2.96 g, 100%), mp 185 °C: *Anal.* Calcd for $C_{16}H_{15}ClN_2O \cdot 1/2H_2O$; C, 64.97; H, 5.45; N, 9.47. Found: C, 64.61; H, 5.47; N, 9.04. NMR (DMSO-d_6) δ: 4.40 (3H, s, C$\underline{H}_3$), 7.3—8.2 (11H, m, 2×C$_6\underline{H}_5$, N$\underline{H}$), 12.34 (1H, br s, 4-H). IR ν_{max}^{Nujol} cm^{-1}: 3330 (NH), 2750 (N^+), 1650 (C=N).

General Preparation of 3-(*N*-Substituted imino)-2-methyl-4-isoxazoline 6——A 3-chloro-2-methylisoxazolium chloride **1** (1 eq) was dissolved in a mixture of CH_3CN and $CHCl_3$ (1 : 1). A primary amine (2.1 eq) was added to this solution with stirring. The mixture was stirred for 2.5 h, then concentrated and neutralized with 1 N NaOH. After being washed with ether, the aqueous layer was basified with 1 N NaOH to pH 10, and extracted with ether. Evaporation of the solvents gave **6** (Table II).

General Preparation of 3-(*N*,*N*-Disubstituted amino)isoxazolium Halides 4——a) A mixture of a secondary amine (1 eq) and triethylamine (1.1 eq) was added to a suspension of a 3-chloro-2-methylisoxazolium chloride **1** (1 eq) in dry benzene, and the mixture was stirred for 2—6 h. After filtration, the filtrate was evaporated to dryness and the residue was recrystallized to give **4a**—**f** (Table I).

b) A mixture of an imine **6** (1 eq) and an alkyl halide or acyl halide (1.5—2.0 eq) in acetone was stirred for 5—24 h. The precipitated crystals were collected by filtration and washed with ether and hexane to give **4g**—**k**, **m**, **q** (Table III).

General Preparation of 3-(*N*,*N*-Disubstituted amino)isoxazoles 5——a) A suspension of **4** in ODCB was heated at 110—180 °C for 0.5—2.0 h. The reaction mixture was purified by column chromatography on silica gel to give **5** (Tables I and III).

b) A solution of **6** (1 eq) and an alkyl halide or acyl halide (R^3X) (1.0—2.0 eq) in ODCB was heated at 110—180 °C for 0.5—2.0 h. The reaction mixture was worked up as described in (a) to afford **5** (Tables I and III).

3-Anilino-5-phenylisoxazole 3a——a) A suspension of 3-anilino-2-methyl-5-phenylisoxazolium chloride **2a** (1.15 g) in ODCB (10 ml) was heated under reflux for 10 min. After cooling, the mixture was purified by column chromatography on silica gel with hexane–acetone (5 : 1) to afford **3a**, (0.24 g, 25.4%), mp 147—149 °C (lit.,[7] mp 145—146 °C).

b) A mixture of 3-*N*-acetanilido-5-phenylisoxazole **5l**, (93 mg) and NaOH (0.2 g) in EtOH (3 ml) and H_2O (2 ml) was heated at 80—85 °C for 4 h. The mixture was diluted with H_2O, acidified with dil. HCl, and extracted with ether. The solvents were evaporated off to give **3a** (79 mg, 100%). The *N*-acetyl compounds **5** (R^3=Ac) were hydrolyzed by method (b) to produce 3-(*N*-monosubstituted amino)isoxazoles **3** (Table IV).

3-Amino-2-methyl-5-phenylisoxazolium Chloride 6——Liq. NH_3 (2 ml) was added to a solution of **1a** (4.6 g) in MeOH (30 ml) with ice-water cooling. The mixture was stirred for 18 h, then concentrated to 1/4 of the original volume. After filtration, the filtrate was evaporated to dryness, and the residue was washed with acetone to give **6** (3.62 g, 86.0%), mp 213—214 °C (dec.): *Anal.* Calcd for $C_{10}H_{11}ClN_2O \cdot H_2O$; C, 52.52; H, 5.73; Cl, 15.50; N, 12.24. Found: C, 52.68; H, 5.48; Cl, 15.77; N, 12.63. NMR (DMSO-d_6) δ: 4.16 (3H, s, C$\underline{H}_3$), 7.10 (1H, s, 4-H), 7.40 (2H, s, N$\underline{H}_2$), 7.56—8.10 (5H, m, C$_6\underline{H}_5$). IR ν_{max}^{Nujol} cm^{-1}: 3300—3050 (NH_2), 1677 (C=N).

3-Imino-2-methyl-5-phenyl-4-isoxazoline 8——NaOH (0.34 g) was added to an aqueous solution of **6** (1.77 g). The mixture was stirred for 0.5 h, then extracted with CH_2Cl_2. The extract was dried over Na_2SO_4 and evaporated to give **8**, (1.35 g, 92.5%), mp 53—56 °C: *Anal.* Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08. Found: C, 69.28; H, 5.91; N, 16.23. NMR ($CDCl_3$) δ: 3.42 (3H, s, C$\underline{H}_3$), 5.88 (2H, s, 4-H, N$\underline{H}$), 7.3—7.8 (5H, m, C$_6\underline{H}_5$). IR ν_{max}^{Nujol} cm^{-1}: 3340 (NH), 1630 (C=N).

3-(4-Acetylaminobenzenesulfonyl)imino-2-methyl-5-phenyl-4-isoxazoline 9——A mixture of **8** (0.11 g) and *p*-acetylaminobenzenesulfonyl chloride (0.15 g) in THF (10 ml) was stirred for 20 h. The precipitated solid was collected, washed with H_2O, and dried in air to give **9** (0.11 g, 45.9%), mp 200—204 °C. The washing solution was evaporated to dryness, and the residue was washed with acetone to give 3-amino-2-methyl-5-phenylisoxazolium chloride **6**, 0.07 g (49.0%). **9**: *Anal.* Calcd for $C_{18}H_{17}N_3O_4S$: C, 58.21; H, 4.61; N, 11.31; S, 8.63. Found: C, 57.95; H, 4.80; N, 11.20; S, 8.41. NMR (CDSO-d_6) δ: 2.08 (3H, s, C$\underline{H}_3$CO), 3.78 (3H, s, N–C$\underline{H}_3$), 7.25 (1H, s, 4-H), 7.5—8.1 (5H, m, C$_6\underline{H}_5$), 10.35 (1H, s, N$\underline{H}$). IR ν_{max}^{Nujol} cm^{-1}: 3320 (NH), 1705 (CO), 1318, 1160, 1140 (SO_2N).

***N*-(5-Phenyl-3-isoxazolyl)phthalimide 10a**——A mixture of potassium phthalimide (2.7 g) and **1a** (2.0 g) in ODCB (20 ml) was heated at 100 °C for 5.5 h under an N_2 atmosphere. After filtration, the filtrate was purified by column chromatography on silica gel with hexane–acetone (30 : 1) to give **10a**, (1.13 g, 44.8%), mp 206—207 °C: *Anal.* Calcd for $C_{17}H_{10}N_2O_3$: C, 70.34; H, 3.47; N, 9.65. Found: C, 70.08; H, 3.50; N, 9.43. NMR ($CDCl_3$) δ: 7.07 (1H, s, 4-H), 7.42—8.13 (9H, m, C$_6\underline{H}_5$, C$_6\underline{H}_4$), IR ν_{max}^{Nujol} cm^{-1}: 1790, 1730, 1680 (CON).

***N*-(5-Methyl-3-isoxazolyl)phthalimide 10b**——20.6%, mp 203—204 °C. *Anal.* Calcd for $C_{12}H_8N_2O_3$: C, 63.16; H, 3.53; N, 12.28. Found: C, 63.11; H, 3.49; N, 12.35. NMR $(CD_3)_2CO$ δ: 2.54 (3H, s, C$\underline{H}_3$), 6.58 (1H, s, 4-H), 8.05 (4H, s, C$_6\underline{H}_4$). IR ν_{max}^{Nujol} cm^{-1}: 1790, 1740 (CON).

3-Amino-5-phenylisoxazole 7a——a) A suspention of **6** (0.8 g) in ODCB (5 ml) was heated at 180—190 °C for 1 h. After cooling, the mixture was purified by colum chromatography on silica gel with hexane–acetone (10 : 1) to give **7a** (0.10 g, 16.4%), mp 130—133 °C (lit.,[7] mp 135—137 °C).

b) A mixture of **10a** (146.5 mg) and $NH_2NH_2 \cdot H_2O$ (0.03 ml) in EtOH (2 ml) was refluxed for 2.5 h. After filtration, the filtrate was concentrated and the residue was purified by preparative thin layer chromatography

(TLC), developing with hexane–acetone (2/1) to give **7a** (75.1 mg, 92.9%), mp 135—138 °C.

3-Amino-5-methylisoxazole 7b——A mixture of **10b** (100 mg) and $NH_2NH_2 \cdot H_2O$ (100 mg) in EtOH (4 ml) was refluxed for 3 h. After filtration, the filtrate was concentrated. The residue was purified by preparative TLC, developing with hexane–acetone (2 : 1) to give **7b** (32.2 mg, 75.1%), mp 59—61 °C (lit.,[2] mp 61—62 °C).

References and Notes

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