# Transformation of 1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole derivatives into isoxazoles*

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The reactions of 1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole derivatives with electrophilic reagents, such as protic acids, benzoyl chloride, $BF_3$, and bromine, produce isoxazole, 2,2,3,3-tetramethylaziridine, and 2,3,3-trimethylpropen-2-ylamine derivatives.

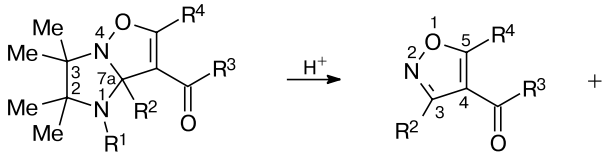
**Key words:** isoxazole, 4-isoxazoline, 1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole, electrophile, 1,3-dipolar cycloaddition.

The synthetic scope of the 1,3-dipolar cycloaddition reaction of nitrones with dipolarophiles is determined by its high regio- and stereoselectivity and the possibility of subsequent transformations of the resulting cycloadducts. 1,2,3,7a-Tetrahydroimidazo[1,2-*b*]isoxazole derivatives **1**,[1] which are produced by the cycloaddition of nitrones of the 2-imidazoline series with alkynes, contain a heteroatomic substituent at position 3 of the isoxazoline ring. As a result, untypical and previously unknown transformations of these cycloadducts can be performed, including those with retention of the isoxazoline ring. In the present study, we investigated the transformations of cycloadducts **1** in the presence of electrophilic reagents.

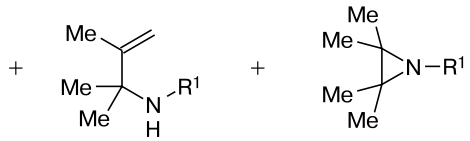
The reactions of *p*-toluenesulfonic acid with cycloadducts **1** were demonstrated to be accompanied by the imidazolidine ring opening to form isoxazoles **2** and a mixture of amine **3** and aziridine **4** (Scheme 1). Structurally similar isoxazoles were detected in the reaction in trifluoroacetic acid. The yields of compounds **2a—f** in the small-batch reactions were 47—90%.

The formation of isoxazoles **2** has been observed earlier[2] in the 1,3-dipolar cycloaddition reaction of nitrone **5** with alkynes **6** in the presence of dimethylammonium chloride. In the study,[2] it was hypothesized that isoxazoles **2** are generated in the independent process competitive with the 1,3-dipolar cycloaddition (Scheme 2) rather than in the acid-initiated transformation of cycloadduct **7**.

**Scheme 1**



**1a—h** **2a—f**



**3a,b** **4a,b**

| **1** | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **a** | H | Ph | OMe | Ph |
| **b** | H | Ph | OMe | $CO_2Me$ |
| **c** | Me | Ph | OMe | $CO_2Me$ |
| **d** | H | Me | OMe | $CO_2Me$ |

| **1** | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **e** | H | 4-$Me_2NC_6H_4$ | OMe | $CO_2Me$ |
| **f** | H | Me | Me | Ph |
| **g** | H | 4-$MeOC_6H_4$ | Me | Ph |
| **h** | Me | Ph | OMe | Ph |

| **2** | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|
| **a** | Ph | OMe | Ph |
| **b** | Ph | OMe | $CO_2Me$ |
| **c** | Me | OMe | $CO_2Me$ |

| **2** | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|
| **d** | 4-$Me_2NC_6H_4$ | OMe | $CO_2Me$ |
| **e** | Me | Me | Ph |
| **f** | 4-$MeOC_6H_4$ | Me | Ph |

**3, 4:** $R^1$ = H (**a**), Me (**b**)

We did not observe the formation of cycloadducts of sterically hindered nitrone **8** and alkynes **9** at room temperature (under the conditions typical of this process[1]).

* Dedicated to the memory of Academician N. N. Vorozhtsov on the 100th anniversary of his birth.

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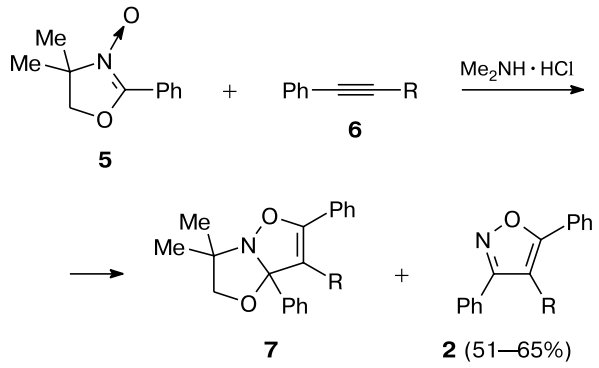
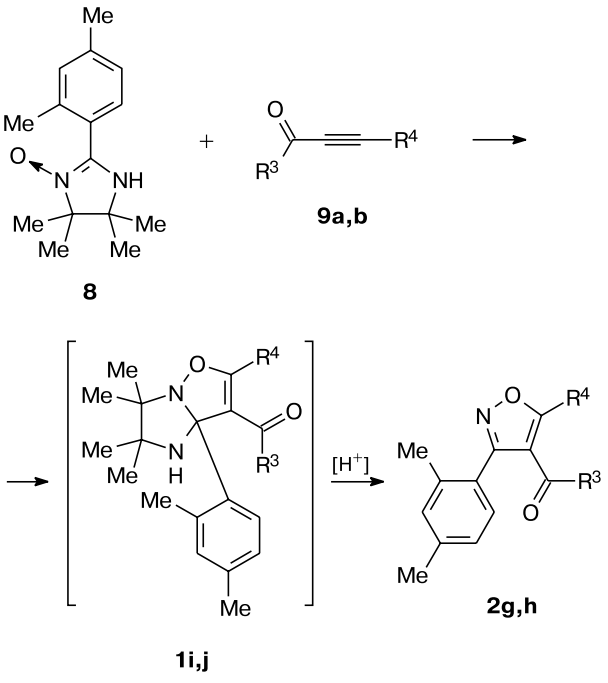
**Scheme 2**




R = $CO_2Me$, CN

After heating or prolonged storage, isoxazoles **2g,h** (Scheme 3) were isolated from the reaction mixtures. This reaction in the presence of excess triethylamine afforded the corresponding cycloadducts **1i,j** (the $^1H$ NMR spectroscopic data), which were transformed into isoxazoles **2g,h** after alumina or silica gel chromatography. Apparently, this is attributed to the successive formation of the cycloadduct and its acid-catalyzed cleavage. In this case, the starting imidazoline **8** can serve as the proton source because it exists partially (45%) in the *N*-hydroxyaminoimine tautomeric form in a solution in $CHCl_3$.[3] It should be noted that we isolated isoxazole **2a** as a by-product

**Scheme 3**




$R^3$ = OMe, $R^4$ = $CO_2Me$ (**1i**, **2g**, **9a**);
$R^3$ = Ph, $R^4$ = COMe (**1j**, **2h**, **9b**)

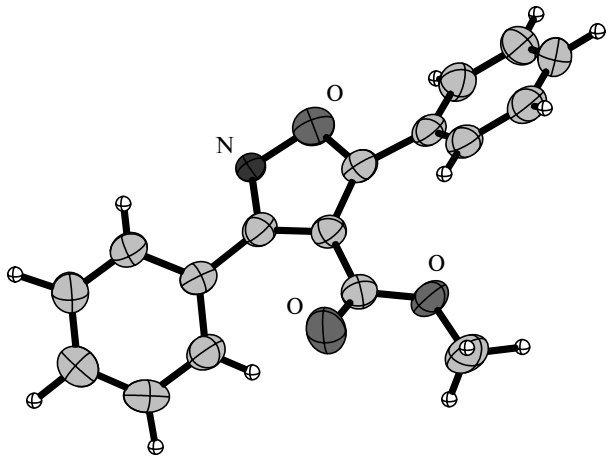


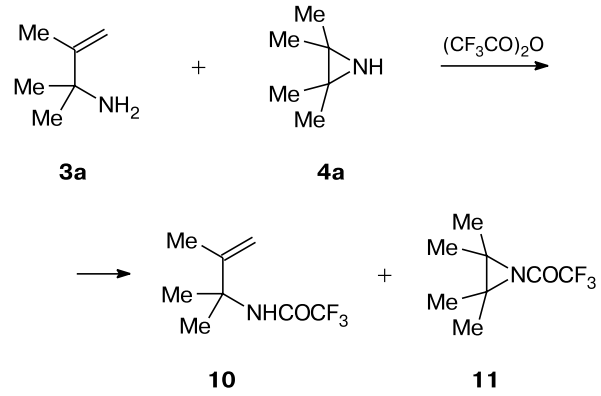

**Fig. 1.** X-ray three-dimensional structure of methyl 3,5-diphenylisoxazole-4-carboxylate (**2a**).

when synthesizing cycloadduct **1a**. This can be accounted for by the presence of acidic impurities in the reaction mixture.

The structures of the reaction products were confirmed by IR, $^1H$ NMR, and $^{13}C$ NMR spectroscopy. The structure of isoxazole **2a** was established by X-ray diffraction (Fig. 1). The bond lengths in molecule **2a** are typical of the isoxazole ring.

A mixture of *N*-methyl-substituted derivatives **3b** and **4b** was isolated from the reaction mixture, and the structures of the products were confirmed by $^1H$ and $^{13}C$ NMR spectroscopy. Volatile amines **3a** and **4a** were identified as trifluoroacetamides **10** and **11**, respectively (Scheme 4). The structures and compositions of the latter were established by $^1H$ and $^{19}F$ NMR spectroscopy and mass spectrometry.

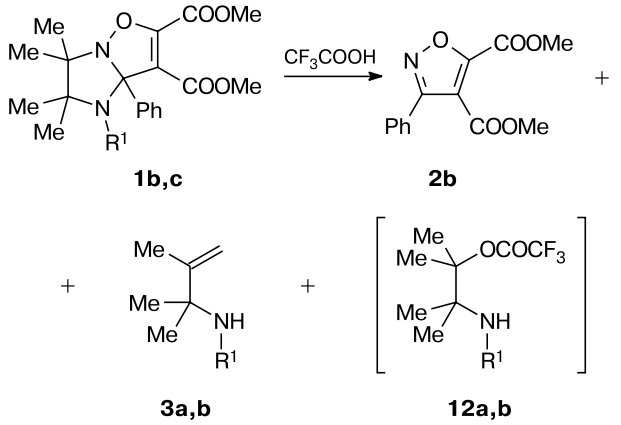
**Scheme 4**




According to the $^1H$ NMR spectroscopic data for the reaction mixtures, the ratio between aziridine **4** and amine **3** remained unchanged with time. It should be noted that this ratio does not correspond to the position

of the thermodynamic equilibrium because it depends on the structures of the starting cycloadducts **1**, all other factors being the same. The reaction of cycloadducts **1b,c** in trifluoroacetic acid affords isoxazole along with amines **3** and, apparently, **12** (Scheme 5), whereas aziridine **4** is not generated. These data provide evidence that amines **3** and **4** are not transformed into each other under the reaction conditions.

**Scheme 5**



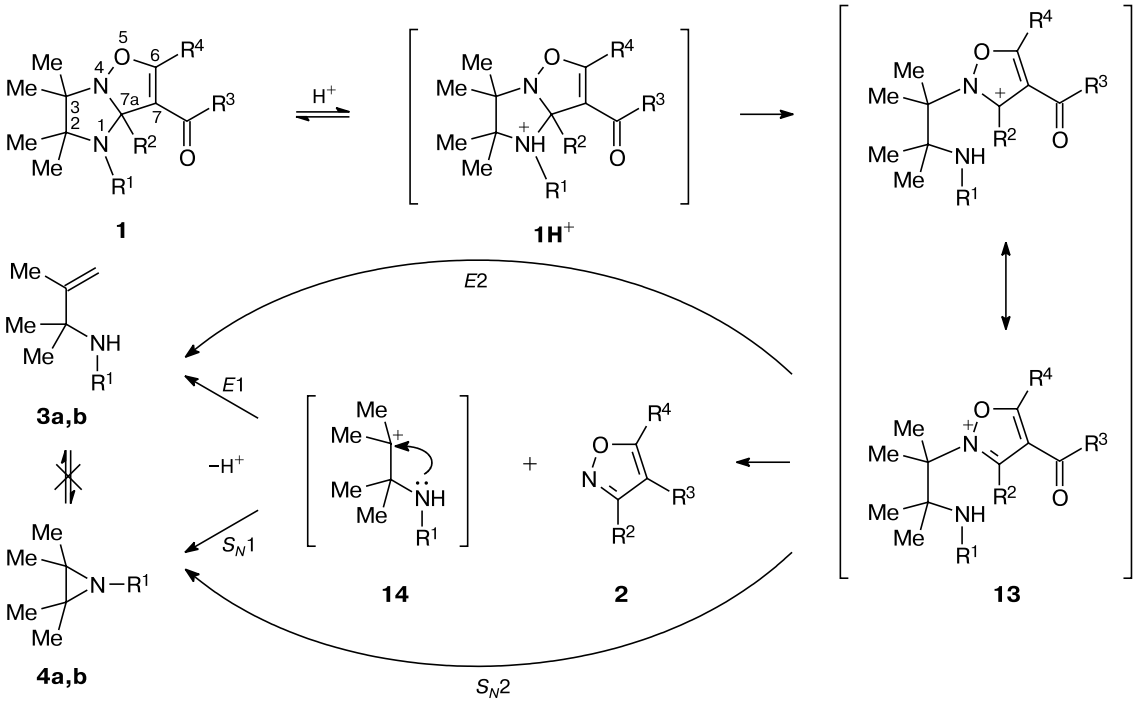

**3, 12:** $R^1$ = H (**a**), Me (**b**)

Presumably, the first step of the reaction under consideration involves the protonation of the starting compound **1** at the N(1) atom, resulting in the C(7a)—N(1) bond cleavage to form aromatic cation **13**, which is rather stable under the reaction conditions (Scheme 6). For example, the $^1$H NMR spectrum of a solution of compound **1d** and *p*-toluenesulfonic acid in deuteromethanol shows a signal for the protons of the methyl group at the C(7a) atom (δ 1.76) along with a signal for the protons of the methyl group at δ 2.62, which does not disappear within several tens of hours and belongs, apparently, to intermediate **13**. This low-field signal cannot be attributed to the formation of the protonated form **1H**$^+$ (see Scheme 6); otherwise, only one exchange-narrowed signal of two forms would be observed.

Then elimination of isoxazole **2** occurs (the chemical shift of the methyl group at the C(3) atom at δ 2.46) to give amines **3** and **4**. This step can follow three pathways. The first pathway produces tertiary carbocation **14**, which can undergo cyclization to form aziridine **4** ($S_N1$) or produce amine **3** (*E*1). The second pathway involves the concerted elimination *E*2 giving rise to amine **3**. The third pathway involves the intramolecular nucleophilic substitution $S_N2$ with the amino group yielding exclusively aziridine **4** (see Scheme 6).

The relatively high percentage of amine **3** in going from a methanolic solution of *p*-toluenesulfonic acid to trifluoroacetic acid, which is a substantially less alkaline medium, is evidence against the *E*2 mechanism (see the determination of the percentage of amines **3** and **12** and aziridines **4** in the above-mentioned mixtures from the $^1$H NMR spectroscopic data).

**Scheme 6**



| Reagent | $R^1$ | Percentage | | | |
|---|---|---|---|---|---|
| | | $CD_3OD$—TsOH | | $CF_3COOH$ | |
| **1b** | H | 70 (**3a**) | 30 (**4a**) | 45 (**3a**) | 55 (**12a**) |
| **1c** | Me | 17 (**3b**) | 83 (**4b**) | 32 (**3b**) | 68 (**12b**) |

At the same time, the absence of aziridine **4** resistant against acids in the reaction performed in trifluoroacetic acid can be evidence against the intramolecular nucleophilic substitution in cation **13** ($S_N2$). The introduction of the substituent $R^1$ at the nitrogen atom should decrease its nucleophilicity in the $S_N2$ process, thus decreasing the percentage of product **4**. In the real situation, the introduction of the methyl group, on the contrary, leads to an increase in the percentage of aziridine **4** in the reaction mixture by a factor of ~11, which is also evidence against the $S_N2$ mechanism. Therefore, the pathway involving the formation of cation **14** seems to be most probable.

The reactions of cycloadducts **1** with other electrophiles also lead to the imidazolidine ring cleavage giving rise to isoxazoles **2**. For example, the reaction of compound **1c** with a small excess of boron trifluoride etherate or benzoyl chloride in anhydrous DMSO at room temperature produces isoxazole **2b** ($^1$H NMR spectroscopic data). Under the same conditions, the reaction with benzyl chloride or iodomethane does not proceed. The corresponding isoxazole **2a** is generated also in the reaction of cycloadduct **1h** with bromine in chloroform at 0 °C.

To summarize, cycloadducts **1** are transformed into isoxazoles **2** in high yield in the reactions with such electrophiles as protic acids, PhCOCl, $Br_2$, or $BF_3$. Amines **3** and **4** can be isolated along with isoxazoles from the reaction mixtures obtained in the acid-catalyzed reactions. The reaction proceeds through the formation of isoxazolinium cation **13**, which undergoes cleavage to give isoxazole **2** and cation **14**.

## Experimental

The $^1$H NMR spectra were recorded on Bruker AM-400, Bruker AV-300, Bruker AC-200, and Bruker WP-200 spectrometers using the signal of the solvent as the standard. The fully $J_{C,H}$-decoupled $^{13}$C NMR spectra were measured. The IR spectra were recorded on a Vector-22 spectrometer (Bruker) in KBr pellets. The UV spectra were measured on a Specord M-40 spectrometer in EtOH. The melting points were determined on a Boetius hot-stage microscope. The high-resolution mass spectra were obtained on a Finnigan MAT 8200 instrument at an ionizing voltage of 70 eV. The elemental analysis was carried out in the Laboratory of Microanalysis of the N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry of the Siberian Branch of the Russian Academy of Sciences. The GC-mass spectra were recorded on a Hewlett Packard G1800A instrument consisting of an HP5890 Series II gas chromatograph and an HP5971 mass-selective detector. The course of the reactions was monitored by TLC on Silufol UV-254 plates and aluminum oxide TLC cards (Fluka) using chloroform, ethyl acetate, or the mixture of the latter with hexane as the eluent. The compounds were isolated by silica gel (Silica gel 60, Merk) or alumina (analytical grade, neutral, for chromatography) column chromatography. Chloroform (technical) was dried with $CaCl_2$ and distilled; DMSO was dried with NaOH and distilled *in vacuo* over BaO. Hexane, ethyl acetate, and diethyl ether (high-purity grade) were used without additional purification. In all cases, solutions were concentrated using a vacuum aspirator pump.

1,2,3,7a-Tetrahydroimidazo[1,2-*b*]isoxazole derivatives **1a—d,f—h** were synthesized according to a known procedure.[1]

**Dimethyl 7a-(4-dimethylaminophenyl)-2,2,3,3-tetramethyl-1,2,3,7a-tetrahydroimidazo[1,2-*b*]isoxazole-6,7-dicarboxylate (1e).** 1) 2,3-Bis(hydroxyamino)-2,3-dimethylbutane sulfate (3.6 g, 13.6 mmol) and 4-(dimethylamino)benzaldehyde (2.0 g, 13.6 mmol) were dissolved in MeOH and refluxed under argon until the starting aldehyde was completely consumed (TLC monitoring). The reaction mixture was neutralized with a saturated $NaHCO_3$ solution, MeOH was removed by evaporation, and the precipitate was filtered off, washed with water, and dried. The resulting **2-(4-dimethylaminophenyl)-4,4,5,5-tetramethylimidazolidine-1,3-diol** was used without additional purification.

2) A solution of 2-(4-dimethylaminophenyl)-4,4,5,5-tetramethylimidazolidine-1,3-diol (1.87 g, 6.7 mmol) in $CHCl_3$ (30 mL) was stirred with a solution of $NaIO_4$ (2 g) in water (20 mL) for 20 min. The organic phase was separated, and the aqueous phase was extracted with $CHCl_3$ (2×20 mL). The combined solutions in $CHCl_3$ were dried with $MgSO_4$ and then concentrated to ~20 mL. A solution of $NaNO_2$ (0.5 g) in water (15 mL) was added to the resulting solution. Then 5% HCl (0.6 mL) was added dropwise with vigorous stirring. The organic phase was separated, and the aqueous phase was extracted with $CHCl_3$ (20 mL). The combined solutions in $CHCl_3$ were dried with $MgSO_4$ and concentrated. The reaction product, **2-(4-dimethylaminophenyl)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazole 1-oxyl**, was isolated by alumina chromatography using $CHCl_3$ as the eluent.

3) The product was reduced with hydrogen in MeOH in the presence of Pd/C as the catalyst. The catalyst was filtered off and the solution was concentrated. The residue, *viz.*, **2-(4-dimethylaminophenyl)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazole 3-oxide**, crystallized out upon the addition of hexane. The product was filtered off and washed on a filter with a 1 : 1 hexane—AcOEt mixture. The yield was 0.59 g (34%), m.p. 157.5—159 °C (hexane—AcOEt). $^1$H NMR ($CDCl_3$), δ: 1.21 and 1.27 (both s, 6 H each, C(4)Me, C(5)Me); 2.92 (s, 6 H, $NMe_2$); 6.57 and 8.17 (both d, 2 H each, H arom., $^3J$ = 8.1 Hz). $^{13}$C NMR ($CDCl_3$), δ: 19.3, 24.2 (C(4)$\underline{C}H_3$, C(5)$\underline{C}H_3$); 39.8 ($NMe_2$); 60.7 (C(4)); 73.2 (C(5)); 110.9 (C(3′)); 113.1 (C(1′)); 128.5 (C(2′)); 144.2 (C(2)); 151.4 (C(4′)). High-resolution mass spectrum, found: *m/z* 261.1838 $[M]^+$. $C_{15}H_{23}N_3O$. Calculated: M = 261.1841. IR (KBr), ν/cm$^{-1}$: 2977, 1612, 1525, 1366, 1203.

4) A solution of dimethyl acetylenedicarboxylate (0.09 mL, 0.74 mmol) in $CHCl_3$ cooled to 0 °C was added with stirring to a suspension of 2-(4-dimethylaminophenyl)-4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazole 3-oxide (0.16 g, 0.62 mmol) in $CHCl_3$ (10 mL). Within 20 min after dissolution of the precipitate, the solvent was evaporated without heating, and hexane (10 mL) was added to the residue. The precipitate of compound **1e** was filtered off and washed on a filter with a cold 5 : 1 hexane—AcOEt mixture. The yield was 105 mg (42%), m.p. 174.5—176.5 °C

(hexane). Found (%): C, 62.35; H, 7.27; N, 10.35. $C_{21}H_{29}N_3O_5$. Calculated (%): C, 62.51; H, 7.24; N, 10.41. $^1$H NMR ($CDCl_3$), δ: 0.92, 1.08, 1.21, and 1.33 (all s, 3 H each, C(2)Me, C(3)Me); 2.92 (s, 6 H, $NMe_2$); 3.59 and 3.85 (both s, 3 H each, $CO_2Me$); 6.65 and 7.49 (both d, 2 H each, H arom., $^3J$ = 8.7 Hz). UV (EtOH), $\lambda_{max}$/nm (logε): 247 (3.99), 268 (4.09), 349 (3.40). IR (KBr), ν/cm$^{-1}$: 3350, 2981, 2951, 1740, 1719, 1648, 1611, 1521, 1434, 1341, 1308, 1211, 1074.

**Methyl 3,5-diphenylisoxazole-4-carboxylate (2a).**[4] A solution of compound **1a** (0.015 g, 0.04 mmol) and TsOH (0.008 g, 0.05 mmol) in MeOH (1.5 mL) was kept at ~20 °C for 2 days. The solution was concentrated, the residue was made alkaline to pH 9 with an aqueous $Na_2CO_3$ solution, the product was extracted with $CHCl_3$ (3×10 mL), and the extract was dried with $MgSO_4$ and concentrated. Compound **2a** was purified by silica gel chromatography using $CHCl_3$ as the eluent. The yield was 0.010 g (90%), m.p. 99—100 °C (hexane). $^1$H NMR ($CDCl_3$), δ: 3.70 (s, 3 H, OMe); 7.45—7.53 (m, 6 H, H arom.); 7.62—7.67 and 7.88—7.93 (both m, 2 H each, H arom.). High-resolution mass spectrum, found: *m/z* 279.09019 $[M]^+$. $C_{17}H_{13}NO_3$. Calculated: M = 279.08954. UV (EtOH), $\lambda_{max}$/nm (logε): 238 (4.19), 264 (4.26). IR (KBr), ν/cm$^{-1}$: 3061, 2957, 1727, 1613, 1593, 1572, 1448, 1408, 1326, 1237, 1121.

**Reaction of compound 1h with bromine.** A solution of bromine (0.31 mL) in $CHCl_3$ (0.064 mL of $Br_2$ in 3 mL of $CHCl_3$) was added dropwise with stirring to a solution of compound **1h** (50 mg, 0.12 mmol) cooled to 0 °C. The reaction mixture was kept at 0 °C for 30 min. Then the solution was concentrated and the reaction mixture was analyzed by $^1$H NMR spectroscopy. The transformation **1h** → **2a** was brought to completion.

**Dimethyl 3-phenylisoxazole-4,5-dicarboxylate (2b).**[5] ***A.* Catalysis with *p*-toluenesulfonic acid.** A solution of compound **1c** (0.103 g, 0.29 mmol) and TsOH (0.060 g, 0.34 mmol) in MeOH (2 mL) was kept at ~20 °C for 2 day. Then the reaction solution was concentrated, and the residue was analyzed by $^1$H NMR spectroscopy. The residue was made alkaline to pH 8 with an aqueous $NaHCO_3$ solution, the product was extracted with $CHCl_3$ (3×10 mL), and the extract was dried with $MgSO_4$ and concentrated. Compound **2b** was purified by silica gel chromatography using a 4 : 1 hexane—AcOEt mixture as the eluent and recrystallized from hexane at −10 °C. The yield was 0.056 g (75%), m.p. 62—63 °C (hexane). $^1$H NMR ($CDCl_3$), δ: 3.87 and 3.98 (both s, 3 H each, OMe); 7.43—7.47 (m, 3 H, H arom.); 7.64—7.69 (m, 2 H, H arom.). $^{13}$C NMR ($CDCl_3$), δ: 52.9, 53.2 ($CO_2\underline{C}H_3$); 115.8 (C(4)); 126.7 (C(1′)); 127.9, 128.7 (C(2′), C(3′)); 130.5 (C(4′)); 156.3 (C(3)); 159.2 (C(5)); 161.1, 161.6 ($\underline{C}O_2CH_3$). High-resolution mass spectrum, found: *m/z* 261.06474 $[M]^+$. $C_{13}H_{11}NO_5$. Calculated: M = 261.06371. UV (EtOH), $\lambda_{max}$/nm (logε): 227 (4.25). IR (KBr), ν/cm$^{-1}$: 3077, 2958, 1733, 1627, 1463, 1443, 1426, 1320, 1302, 1283, 1229, 1186, 1138, 1067.

***B.* Catalysis by PhCOCl or $BF_3$.** A 1.5-fold molar excess of boron trifluoride etherate or benzoyl chloride was added to a solution of compound **1c** in anhydrous DMSO-$d_6$ (0.5 mL), and the reaction mixture was kept for 1 day. According to the $^1$H NMR spectroscopic data, the reaction mixture contained isoxazole **2b**, whereas the starting compound **1c** was absent.

**Dimethyl 3-methylisoxazole-4,5-dicarboxylate (2c).**[5] A solution of compound **1d** (0.032 g, 0.09 mmol) and a twofold molar excess of TsOH in MeOH (1 mL) was kept at ~20 °C for 20 h. Then the reaction solution was concentrated, $CHCl_3$ (10 mL) was added to the residue, and the solution was washed with an aqueous $NaHCO_3$ solution, dried with $MgSO_4$, and concentrated. The residue, *viz.*, compound **2c**, was recrystallized from hexane. The yield was 0.010 g (47%). $^1$H NMR ($CDCl_3$), δ: 2.45 (s, 3 H, C(3)Me); 3.88 and 3.98 (both s, 3 H each, $CO_2Me$). High-resolution mass spectrum, found: *m/z* 199.04802 $[M]^+$. $C_8H_9NO_5$. Calculated: M = 199.04807. IR (KBr), ν/cm$^{-1}$: 2958, 1734, 1611, 1438, 1308, 1213, 1109.

**Dimethyl 3-(4-dimethylaminophenyl)isoxazole-4,5-dicarboxylate (2d).** A solution of dimethyl acetylenedicarboxylate (0.01 mL, 0.07 mmol) in $CHCl_3$ (1 mL) was added to a solution of 2-(4-dimethylaminophenyl)-4,4,5,5-tetramethyl-2-imidazoline 1-oxide (16 mg, 0.06 mmol) in $CHCl_3$ (2 mL). After 1 min, the reaction solution was concentrated, and the residue was dissolved in $CF_3COOH$ (1 mL). After 5 h, the reaction mixture was made alkaline to pH 8.5 with an aqueous $NaHCO_3$ solution and extracted with $CHCl_3$ (3×10 mL). The extract was dried with $MgSO_4$ and concentrated. Compound **2d** was isolated by silica gel chromatography using a 4 : 1 hexane—AcOEt mixture as the eluent. The yield was 10 mg (55%), oil. $^1$H NMR ($CDCl_3$), δ: 3.00 (s, 6 H, $NMe_2$); 3.90 and 3.97 (both s, 3 H each, $CO_2Me$); 6.70 and 7.54 (both dt, 2 H each, H arom., $^3J$ = 9.0 Hz, $^4J$ = 1.5 Hz). $^{13}$C NMR ($CDCl_3$), δ: 40.0 ($NCH_3$); 53.0, 53.1 ($CO_2\underline{C}H_3$); 111.7 (C(3′)); 113.7 (C(1′)); 115.8 (C(4)); 128.8 (C(2′)); 151.7 (C(4′)); 156.5, 158.4 (C(3), C(5)); 160.9, 162.4 ($\underline{C}O_2CH_3$). High-resolution mass spectrum, found: *m/z* 304.10720 $[M]^+$. $C_{15}H_{16}N_2O_5$. Calculated: M = 304.10591. IR ($CCl_4$), ν/cm$^{-1}$: 2956, 2927, 2854, 1744, 1615, 1457, 1444, 1431, 1313, 1279, 1223, 1203, 1137, 1072.

**1-(3-Methyl-5-phenylisoxazol-4-yl)ethanone (2e).**[6] A solution of compound **1f** (120 mg, 0.4 mmol) and TsOH (200 mg, 1.2 mmol) in MeOH (10 mL) was kept at 50 °C for 15 h. Then the reaction solution was concentrated, the residue was made alkaline to pH 8 with an aqueous $NaHCO_3$ solution, and the solution was extracted with $CHCl_3$ (3×10 mL). The combined extracts were dried with $MgSO_4$ and concentrated. Compound **2e** was isolated by silica gel chromatography using a 4 : 1 hexane—AcOEt mixture as the eluent. The yield was 64 mg (80%), colorless oil. $^1$H NMR ($CDCl_3$), δ: 2.17 (s, 3 H, COMe); 2.43 (s, 3 H, C(3)Me); 7.48—7.55 (m, 5 H, H arom.). $^{13}$C NMR ($CDCl_3$), δ: 11.8 (C(3)$\underline{C}H_3$); 30.0 (CO$\underline{C}H_3$); 117.0 (C(4)); 127.3 (C(1′)); 128.6, 128.9 (C(2′), C(3′)); 131.1 (C(4′)); 159.8 (C(3)); 172.2 (C(5)). High-resolution mass spectrum, found: *m/z* 201.07923 $[M]^+$. $C_{12}H_{11}NO_2$. Calculated: M = 201.07897. UV (EtOH), $\lambda_{max}$/nm (logε): 262 (3.66). IR ($CCl_4$), ν/cm$^{-1}$: 2929, 1679, 1584, 1448, 1414, 1378, 1134, 696.

**1-[3-(4-Methoxyphenyl)-5-phenylisoxazol-4-yl]ethanone (2f).** A solution of compound **1g** (165 mg, 0.42 mmol) and TsOH (220 mg, 1.3 mmol) in MeOH (10 mL) was kept at 50 °C for 5 h. Then the reaction solution was concentrated, and the residue was made alkaline to pH 8 with an aqueous $NaHCO_3$ solution and extracted with $CHCl_3$ (3×10 mL). The combined extracts were dried with $MgSO_4$ and concentrated. The residue was recrystallized from hexane (20 mL). The yield was 95 mg (77%), m.p. 105—106 °C (hexane). Found (%): C, 73.24; H, 5.12; N, 4.77. $C_{18}H_{15}NO_3$. Calculated (%): C, 73.71; H, 5.15; N, 4.78. $^1$H NMR ($CDCl_3$), δ: 2.19 (s, 3 H, COMe); 3.84 (s, 3 H, OMe); 7.00 (dt, 2 H, H arom., $^3J$ = 8.8 Hz, $^4J$ = 1.5 Hz); 7.49—7.51 (m, 3 H, H arom.); 7.56 (dt, 2 H, H arom., $^3J$ = 8.8 Hz, $^4J$ = 8.8 Hz); 7.81—7.83 (m, 2 H, H arom.). $^{13}$C NMR ($CDCl_3$), δ: 31.4 (CO$\underline{C}H_3$); 55.2 ($OCH_3$); 117.0 (C(4)); 114.2,

120.5, 126.9, 128.3, 128.7, 130.0, 131.2, 161.0 (C arom.); 161.6 (C(3)); 170.0 (C(5)); 195.5 (CO). UV (EtOH), $\lambda_{max}$/nm (log$\varepsilon$): 263 (4.08). IR (KBr), $\nu$/cm$^{-1}$: 2946, 1693, 1608, 1527, 1495, 1427, 1395, 1365, 1305, 1249, 1179, 1028, 838, 780.

**Dimethyl 3-(2,4-dimethylphenyl)isoxazole-4,5-dicarboxylate (2g).** A solution of 2-(2,4-dimethylphenyl)-4,4,5,5-tetramethyl-2-imidazoline 1-oxide (**8**) (0.055 g, 0.19 mmol) and dimethyl acetylenedicarboxylate (0.038 mL, 0.31 mmol) in $CHCl_3$ (5 mL) was kept at ~20 °C for 20 days. Then the reaction solution was concentrated, and the product was isolated by alumina chromatography using $CHCl_3$ as the eluent. The yield was 0.015 g (24%), m.p. 67—68 °C (hexane). Found (%): C, 62.72; H, 5.49; N, 4.90. $C_{15}H_{15}NO_5$. Calculated (%): C, 62.28; H, 5.23; N, 4.84. $^1$H NMR ($CDCl_3$), δ: 2.23 and 2.34 (both s, 3 H each, C(2′)Me, C(4′)Me); 3.75 and 4.01 (both s, 3 H each, $CO_2Me$); 7.03—7.10 (m, 2 H, H arom.); 7.15—7.19 (m, 1 H, H arom.). $^{13}$C NMR ($CDCl_3$), δ: 19.8, 21.2 (C(2′)$\underline{C}H_3$, C(4′)$\underline{C}H_3$); 52.6, 53.3 ($CO_2\underline{C}H_3$); 116.4 (C(4)); 123.4, 126.4, 129.5, 131.2 (C(1′), C(3′), C(5′), C(6′)); 137.0 (C(2′)); 140.1 (C(4′)); 156.7, 159.5, 160.9, 162.1 (C(3), C(5), $\underline{C}O_2CH_3$). UV (EtOH), $\lambda_{max}$/nm (log$\varepsilon$): 227 (4.15). IR (KBr), $\nu$/cm$^{-1}$: 3001, 2951, 1753, 1732, 1635, 1615, 1462, 1439, 1391, 1314, 1277, 1221, 1192, 1156, 1120, 1067, 988, 949, 905.

**1-[3-(2,4-Dimethylphenyl)-5-phenylisoxazol-4-yl]ethanone (2h).** A solution of 2-(2,4-dimethylphenyl)-4,4,5,5-tetramethyl-2-imidazoline 1-oxide (**8**) (0.139 g, 0.56 mmol) and 4-phenylbut-3-yn-2-one (0.196 mL, 1.35 mmol) in $CHCl_3$ (3 mL) was refluxed for 6 h. Then the reaction solution was concentrated, and the product was isolated by alumina chromatography using $CHCl_3$ as the eluent. The yield was 0.044 g (27%), m.p. 82.5—83.5 °C (hexane). Found (%): C, 78.48; H, 6.02; N, 4.92. $C_{19}H_{17}NO_2$. Calculated (%): C, 78.33; H, 5.88; N, 4.81. $^1$H NMR ($CDCl_3$), δ: 2.00 (s, 3 H, COMe); 2.26 and 2.38 (both s, 3 H each, C(2′)Me, C(4′)Me); 7.09—7.14 (m, 2 H, H arom.); 7.22 (m, 1 H, H arom.); 7.49—7.52 (m, 3 H, H arom.); 7.91—7.94 (m, 2 H, H arom.). $^{13}$C NMR ($CDCl_3$), δ: 19.7, 21.2 (C(2′)$\underline{C}H_3$, C(4′)$\underline{C}H_3$); 30.6 (CO$\underline{C}H_3$); 117.6 (C(4)); 125.3, 126.7, 126.8, 128.5, 128.7, 129.5, 131.3, 131.3, 136.7, 139.9 (C arom.); 162.3 (C(3)); 170.9 (C(5)); 193.8 (CO). UV (EtOH), $\lambda_{max}$/nm (log$\varepsilon$): 269 (4.22). IR (KBr), $\nu$/cm$^{-1}$: 2988, 2952, 1681, 1614, 1585, 1561, 1490, 1411, 1385, 1094, 939, 825.

**Isolation of amines formed under acid catalysis (general procedure).** A solution of compound **1b** or **1h** and a 1.5—2-fold molar excess of TsOH in MeOH (2—5 mL) was kept at ~20 °C for 24 h and then concentrated. Acetic acid was added to the residue to bring the solution to pH 1—2. The solution was washed three times with diethyl ether, made alkaline to pH 8—9 with a sodium carbonate solution, and extracted with diethyl ether. The extract was dried with $MgSO_4$.

**1,1,2-Trimethylprop-2-enylamine (3a).** A solution of compound **1b** (0.10 g, 0.29 mmol) and TsOH (0.06 g, 0.34 mmol) in $CD_3OD$ (0.5 mL) was kept at ~20 °C for 24 h. The reaction mixture was analyzed by $^1$H NMR spectroscopy. The ratio **3a** : **4a** = 70 : 30. $^1$H NMR ($CD_3OD$), δ: 1.48 (s, 6 H, C(1)Me); 1.86 (dd, 3 H, C(2)Me, $^4J$ = 1.5 Hz, $^4J$ = 0.7 Hz); 5.01 and 5.03 (both m, 1 H each, H(3)). $^{13}$C NMR ($CD_3OD$), δ: 19.9 (C(1)$\underline{C}H_3$); 26.7 (C(2)$\underline{C}H_3$); 56.4 (C(1)); 111.2 (C(3)); 149.2 (C(2)).

**(1,1,2-Trimethylprop-2-enyl)methylamine (3b)** was synthesized according to the general procedure from compound **1c** (0.237 g, 0.73 mmol). The ether was distilled off from the extract using a reflux condenser to ~2 mL. For further evaporation, the residue was sublimed at 70 °C (450 Torr). The ratio **3b** : **4b** = 33 : 67. $^1$H NMR ($CDCl_3$), δ: 1.16 (s, 6 H, C(1)Me); 1.68 (dd, 3 H, C(2)Me, $^4J$ = 1.5 Hz, $^4J$ = 0.7 Hz); 2.15 (s, 3 H, NMe); 4.79 (dq, 1 H, H(3), $^2J$ = 1.5 Hz, $^4J$ = 0.7 Hz); 4.86 (dq, 1 H, H(3), $^2J$ = 1.5 Hz, $^4J$ = 1.5 Hz). $^{13}$C NMR ($CDCl_3$), δ: 18.9 (C(1)$\underline{C}H_3$); 26.5 (C(2)$\underline{C}H_3$); 29.3 ($NCH_3$); 58.2 (C(1)); 112.9 (C(3)); 148.3 (C(2)).

**2,2,3,3-Tetramethylaziridine (4a).**[7] A solution of compound **1b** (0.10 g, 0.29 mmol) and TsOH (0.06 g, 0.34 mmol) in $CD_3OD$ (0.5 mL) was kept at ~20 °C for 24 h. Then the reaction mixture was analyzed by $^1$H NMR spectroscopy. The ratio **3a** : **4a** = 70 : 30. $^1$H NMR ($CD_3OD$), δ: 1.52 (s, 12 H, C(2)Me, C(3)Me). $^{13}$C NMR ($CD_3OD$), δ: 19.76 (C(2)$\underline{C}H_3$, C(3)$\underline{C}H_3$); 51.94 (C(2), C(3)).

**1,2,2,3,3-Pentamethylaziridine (4b)**[8] was synthesized according to the general procedure from compound **1c** (0.237 g, 0.73 mmol). The ether was distilled off from the extract to the volume of ~2 mL using a reflux condenser. For further evaporation, the residue was sublimed at 70 °C (450 Torr). The ratio **3b** : **4b** = 33 : 67. $^1$H NMR ($CDCl_3$), δ: 1.12 and 1.04 (both s, 6 H each, C(2)Me, C(3)Me); 2.19 (s, 3 H, NMe). $^{13}$C NMR ($CDCl_3$), δ: 14.2 (C(2)$\underline{C}H_3$); 23.4 (C(3)$\underline{C}H_3$); 31.4 ($NCH_3$); 40.9 (C(2), C(3)).

***N*-(1,1,2-Trimethylprop-2-enyl)-2,2,2-trifluoroacetamide (10)** and **2,2,3,3-tetramethyl-1-(trifluoroacetyl)aziridine (11)** were synthesized from a mixture of amines **3a** and **4a**, which was prepared according to the general procedure from compound **1b** (0.26 g, 0.72 mmol). Trifluoroacetic anhydride (0.20 mL, 1.44 mmol) was added to the resulting ethereal solution, and the reaction mixture was kept at ~20 °C for 40 min. Then the ether was distilled off to the volume of ~0.5 mL using reflux condenser. The residue was dissolved in $CH_2Cl_2$ (4 mL) and washed with an aqueous sodium carbonate solution to steady weakly alkaline pH of the washing liquor. The solution was dried with $MgSO_4$, the solvent was evaporated by distillation to the volume of ~0.5 mL using a reflux condenser. According to the $^1$H NMR spectroscopic data, the resulting mixture contained 88.5% of compound **10** and 11.5% of compound **11**. Compound **10**. $^1$H NMR ($CDCl_3$), δ: 1.48 (s, 6 H, C(1)Me); 1.72 (dd, 3 H, C(2)Me, $^4J$ = 1.4 Hz, $^4J$ = 0.7 Hz); 4.88 and 4.90 (both m, 1 H each, H(3)); 6.37 (br.s, 1 H, NH). $^{19}$F NMR ($CDCl_3$), δ: 85.8 ($CF_3$). Compound **11a**. $^1$H NMR ($CDCl_3$), δ: 1.11 and 1.38 (both s, 6 H each, C(2)Me, C(3)Me). $^{19}$F NMR ($CDCl_3$), δ: 85.5 ($CF_3$). High-resolution mass spectrum, found: *m/z* 195.08737 $[M]^+$. $C_8H_{12}F_3NO$. Calculated: M = 195.08709.

**X-ray diffraction study.** Single crystals of compound **2a** suitable for X-ray diffraction were grown by recrystallization from hexane. X-ray diffraction data were collected on a Smart Apex diffractometer (graphite monochromator, Mo-K$\alpha$ radiation). Crystals are triclinic: $a$ = 8.205(4) Å, $b$ = 9.153(4) Å, $c$ = 9.786(4) Å, $\alpha$ = 82.882(8)°, $\beta$ = 78.285(8)°, $\gamma$ = 70.745(7)°, $V$ = 678.0(5) Å$^3$, space group $P\bar{1}$, $C_{17}H_{13}NO_3$, $Z$ = 2, $M_r$ = 279.09, $d_{calc}$ = 1.368 g cm$^{-3}$, $\mu$ = 0.095 mm$^{-1}$. The intensities of 2799 reflections (1912 independent reflections, $R_{int}$ = 0.0290) were measured in the range of 2.96° < $\theta$ < 23.31° ($-9 \le h \le 9$, $-8 \le k \le 10$, $-7 \le l \le 10$), $R_1$ = 0.0663, $wR_2$ = 0.1746 ($I > 2\sigma(I)$), $R_1$ = 0.0782, $wR_2$ = 0.1839 (based on all data), GOOF 1.036, the residual electron density ($\rho_{max}/\rho_{min}$) 0.286/−0.268 e Å$^{-3}$. The structure of compound **2a** was solved by direct methods. All nonhydrogen atoms were refined by the full-matrix least-squares method with

anisotropic displacement parameters (H atoms were located in difference electron density maps and refined isotropically). All calculations were carried out using the Bruker SHELXTL software (Version 6.14). The atomic coordinates, equivalent displacement parameters, and geometric characteristics for the structure of compound **2a** were deposited at the Cambridge Crystallographic Data Centre (CCDC 633036).

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