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# Hydration and Hydrogenation of Acetylenic Side-Chains at the 4- or 5-Position of Isoxazoles

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Hydration of 5-isoxazolyl-phenyl(or -butyl)acetylenes (**1a, b**) in dilute sulfuric acid in the presence of mercuric sulfate afforded 5-isoxazolylmethyl phenyl (or butyl) ketones (**3a, b**), predominantly. In contrast, the hydration of 4-isoxazolyl-phenyl(or -butyl)-acetylenes (**2a—d**) under identical conditions gave 4-isoxazolyl benzyl (or pentyl) ketones (**5a—d**) as the main products. The structure of one of these products, 3,5-dimethyl-4-isoxazolyl benzyl ketone (**5a**), was determined by Beckmann rearrangement.

Isoxazoles containing a *cis*-alkene or alkane chain were obtained by the catalytic reduction of the above acetylenes without cleaving the isoxazole nucleus.

**Keywords**——4-isoxazolylacetylene; 5-isoxazolylacetylene; hydration; isoxazolyl-ketone; Beckmann rearrangement; hydrogenation of ethynyl bond

Based on the electron-withdrawing effect of a ring nitrogen atom, the 5-position of isoxazole is considered to correspond to the 4-position of pyridine, whereas the 4-position has a strong resemblance to the 3-position of furan because of the electron-donating effect of a ring oxygen atom. On the other hand, we reported in the preceding paper[1] that isoxazole derivatives having an ethynyl group were easily prepared by the cross-coupling reaction of 4- and 5-haloisoxazoles with acetylene compounds. Since the orientation of hydration on an acetylene linkage is well known to be affected by the nature of substituents in the neighborhood of the linkage, our interest was focussed on a comparison of the hydration of 4-ethynylisoxazoles with that of 5-ethynylisoxazoles.

When 3-phenyl-5-phenylethynylisoxazole (**1a**) was heated in dilute sulfuric acid in the presence of mercuric sulfate until the starting material (**1a**) had completely disappeared, phenyl 3-phenyl-5-isoxazolylmethyl ketone (**3a**), mp 84—85°C, was obtained in 75% yield. The hydration of 5-(1-hexynyl)-3-phenylisoxazole (**1b**) under the same conditions also resulted in a selective formation of butyl 3-phenyl-5-isoxazolylmethyl ketone (**3b**). bp 148—150°C (1 mmHg), in 85% yield. In both cases, the presence of benzyl (or pentyl) 3-phenyl-5-isoxazolyl ketones (**4a, b**) in the reaction mixture was not recognized.

In contrast with the results described above, the addition of water to the 4-ethynyl groups gave the reversely hydrated products with excellent selectivity. Namely, 3,5-dimethyl-4-isoxazolyl pentyl ketone (**5b**), bp 100—103°C (4 mmHg), or 3-methyl-5-phenyl-4-isoxazolyl pentyl ketone (**5d**), bp 165—168°C (3 mmHg), was obtained as a sole product when 3,5-dimethyl-4-(1-hexynyl)-(**2b**) or 4-(1-hexynyl)-3-methyl-5-phenylisoxazole (**2d**), respectively was treated under the hydration conditions. The hydration of 3,5-dimethyl-4-phenylethynyl-isoxazole (**2a**) gave a mixture of benzyl 3,5-dimethyl-4-isoxazolyl ketone (**5a**), mp 67—68°C, and 3,5-dimethyl-4-isoxazolylmethyl phenyl ketone (**6a**), mp 123—124°C, but an overwhelming predominance of **5a** (**5a**: **6a**=89: 11) was proved by gas-chromatographic analysis of the product. Similarly, 3-methyl-5-phenyl-4-phenylethynyl-isoxazole (**2c**) was converted into benzyl 3-methyl-5-phenyl-4-isoxazolyl ketone (**5c**) and 3-methyl-5-phenyl-4-isoxazolylmethyl phenyl ketone (**6c**) in a ratio of 87: 13. Four ketones (**5a—d**) thus obtained could be purified by column chromatography, and their structures were determined as described later.

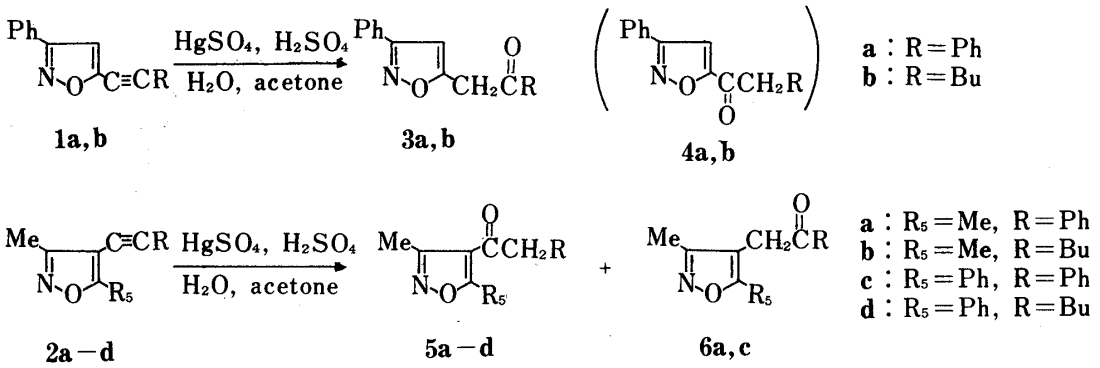



Chart 1

On the basis of the results described above, the orientation of the hydration appears to reflect well the electron density in the isoxazole ring. Furthermore, the site-selectivity is so remarkable that the hydration seems to be applicable for the synthesis of isoxazoles with a carbonyl group.

The structures of the hydration products (**3a**, **b**, **5a**—**d**, and **6a**, **c**) were determined as follows. The proton magnetic resonance ($^1$H-NMR) spectrum of **3b** shows a singlet due to an isolated methylene group at 3.88 ppm (2H), which is evidence for the pentanoylmethylisoxazole structure. On the contrary, in the $^1$H-NMR spectra of **5b** and **5d**, no signal due to an isolated methylene group was observed. This strongly supported the 4-acylisoxazole structure of these products.

The compounds **3a**, **5a**, and **5c** could not be discriminated from the compounds **4a**, **6a**, and **6c**, respectively by $^1$H-NMR spectroscopy, because all the above compounds have an isolated methylene group on their side chain. However, in the mass spectra of **3a**, **5a**, and **5c**, peaks corresponding to $PhCH_2^+$ (tropylium cation) ($m/e$=91) and $(M-91)^+$ ions were observed whereas peaks corresponding or $Ph^+$ ($m/e$=77) and $(M-77)^+$ ions appeared in the mass spectra of **6a** and **6c**. Although this is helpful evidence for the structural elucidation, the structure **5a** was determined by Beckmann rearrangement as follows. After **5a** had been converted into the corresponding ketone oxime (**7**), the oxime was treated with phosphorus pentachloride in ether to give two kinds of amide, mp 133—134°C (**8**) and mp 124—125°C (**9**). Reaction of 3,5-dimethylisoxazole-4-carboxylic acid[2] with thionyl chloride followed by treatment with benzylamine gave N-benzyl-3,5-dimethylisoxazole-4-carboxamide, which was identical with the former amide (**8**). The latter amide (**9**) is also identical with N-(3,5-dimethyl-4-isoxazolyl)-phenylacetamide, which was prepared from 4-amino-3,5-dimethylisoxazole[3] and phenylacetyl chloride in the presence of potassium carbonate. These results clearly demonstrated the

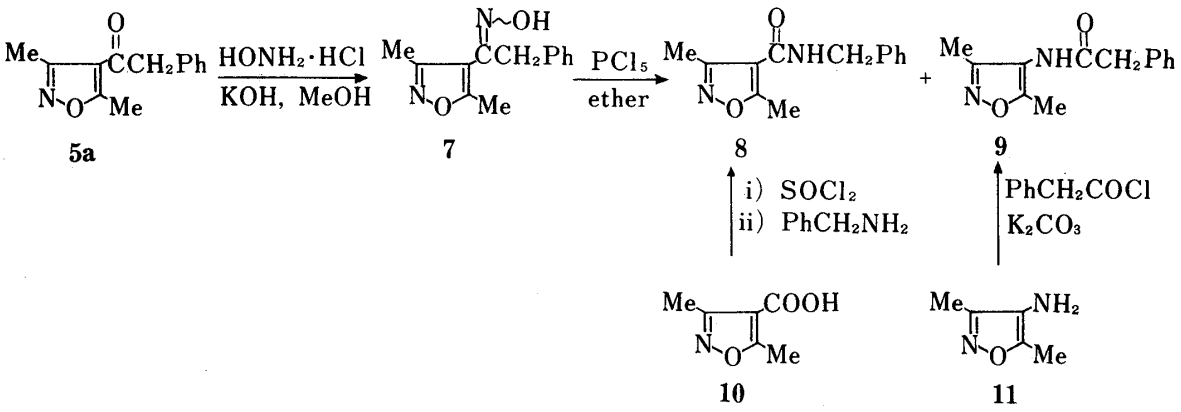
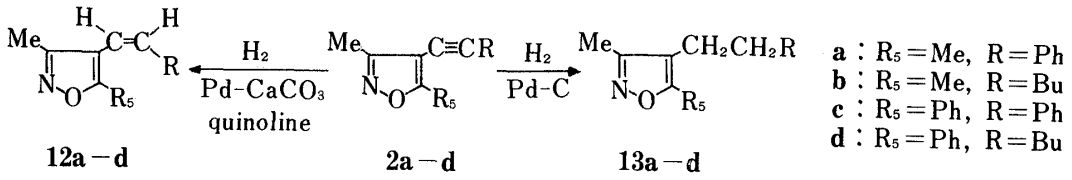


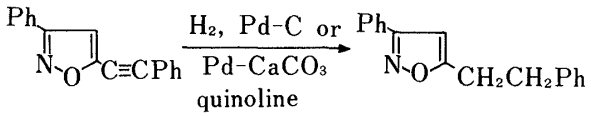

Chart 2

compound **5a** to contain a benzyl ketone structure in spite of the uncertainty of geometry of the ketone oxime (**7**).

Finally, the stepwise catalytic reduction of the ethynyl compounds (**2a—d** and **1a**) was examined, because we were also interested in the competition between reductive cleavage of the isoxazole ring and saturation of the acetylenic side chains. Catalytic hydrogenation of **2a—d** over palladium calcium carbonate catalyst in the presence of quinoline stopped at the stage of one equivalent volume of hydrogen absorption, and the corresponding olefins (**12a—d**) were obtained in good yields. The $^1$H-NMR spectra of these olefins suggested the *cis* configuration of their side chains showing (the coupling constants of signals due to olefinic protons were less than 12 Hz). However, the hydrogenation of **1a** under the same conditions failed to give the expected olefinic isoxazole, when the hydrogenation was stopped halfway.




**12a—d** **2a—d** **13a—d**




**1a** **14**

Chart 3

The exhaustive hydrogenation of these ethynyl compounds (**2a—d** and **1a**) over palladium charcoal gave the isoxazole derivatives with saturated carbon chains (**13a—d** and **14**). In every case, no product formed by the reductive ring cleavage of isoxazole moiety was isolated, so the catalytic reduction of ethynylisoxazoles seems to be practical for the preparation of derivatives.

## Experimental

All melting points and boiling points are uncorrected. Infrared (IR) spectra were measured with a JASCO IRA-1 spectrometer. $^1$H-NMR spectra were taken at 60 MHz with a Hitachi-Perkin-Elmer R-20 spectrometer. Chemical shifts are expressed as ppm downfield from tetramethylsilane (TMS) as an internal standard. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, and m=multiplet. Mass spectra (MS) were taken on a Hitachi M-52G spectrometer.

**General Procedure for Hydration of Alkynylisoxazoles**——Conc. $H_2SO_4$ (1.0 g) was slowly added with stirring to an aq. acetone solution (20 ml) of an alkynylisoxazole (0.005 mol) and $HgSO_4$ (0.005 mol). After the mixture had been refluxed for a suitable time, it was concentrated to dryness under reduced pressure. An appropriate quantity of $H_2O$ (40—50 ml) was added to the residue. The aqueous layer was made alkaline with $K_2CO_3$ and extracted with $CHCl_3$. The $CHCl_3$ extract was passed through a short $Al_2O_3$ column. Removal of the $CHCl_3$ gave the crude products, which were purified by distillation under reduced pressure, recrystallization or (and) $SiO_2$ column chromatography.

The analytical data and the physical constants of all products obtained by this procedure are listed in Table I.

Phenyl 3-Phenyl-5-isoxazolylmethyl Ketone (**3a**): A mixture of 3-phenyl-5-phenylethynylisoxazole (**1a**) (0.4 g, 0.0016 mol), $HgSO_4$ (1.20 g, 0.042 mol), conc. $H_2SO_4$ (1.2 g), and 90% aq. acetone (20 ml) was refluxed for 23 h. The crude product was distilled under reduced pressure to give a colorless liquid, bp 175—178°C (1 mmHg), which was purified by $SiO_2$ column chromatography using $C_6H_6$. Recrystallization from ether–hexane gave colorless needles. Yield 0.32 g. $^1$H-NMR ($CDCl_3$): 4.48 (2H, s), 6.62 (1H, s), 7.10—8.10 (10H, m).

Table I. Isoxazolyl Ketones (**5a—d**) and Isoxazolylmethyl Ketones (**6a,c** and **3a,b**)

| No. | Yield (%) | mp (°C) | bp (mmHg) (°C) | IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$ | Formula | Analysis (%) Calcd (Found) C | H | N |
|---|---|---|---|---|---|---|---|---|
| **5a** | 69 | 67—68 | — | 1688 | $C_{13}H_{13}NO_2$ | 72.54 (72.72 | 6.09 6.15 | 6.51 6.47) |
| **5b** | 78 | — | 100—103(4) | 1680 | $C_{11}H_{17}NO_2$ | 67.66 (67.44 | 8.87 8.81 | 7.17 6.86) |
| **5c** | 66 | 96—97 | — | 1680 | $C_{18}H_{15}NO_2$ | 77.96 (78.03 | 5.45 5.42 | 5.05 4.82) |
| **5d** | 66 | — | 165—168(3) | 1680 | $C_{16}H_{19}NO_2$ | 74.68 (74.50 | 7.44 7.28 | 5.44 5.19) |
| **6a** | 7 | 123—124 | — | 1700 | $C_{13}H_{13}NO_2$ | 72.54 (72.38 | 6.09 6.06 | 6.51 6.51) |
| **6c** | 14 | 107—108 | — | 1695 | $C_{18}H_{15}NO_2$ | 77.96 (78.21 | 5.45 5.70 | 5.05 4.85) |
| **3a** | 75 | 84—85 | — | 1695 | $C_{17}H_{13}NO_2$ | 77.55 (77.77 | 4.98 4.96 | 5.32 5.13) |
| **3b** | 85 | — | 148—150(1) | 1720 | $C_{15}H_{17}NO_2$ | 74.05 (73.80 | 7.04 7.02 | 5.76 5.67) |

Butyl 3-Phenyl-5-isoxazolylmethyl Ketone (**3b**): A mixture of 5-(1-hexynyl)-3-phenylisoxazole (**1b**) (0.6 g, 0.0027 mol), $HgSO_4$ (1.0 g, 0.0035 mol), conc. $H_2SO_4$ (1.0 g), and 80% aq. acetone (10 ml) was refluxed for 24 h to give a pale yellow liquid. Yield 0.55 g. $^1$H-NMR ($CDCl_3$): 0.70—2.06 (7H, m), 2.56 (2H, t, $J$=7.0 Hz), 3.88 (2H, s), 6.53 (1H, s), 7.20—7.58 (3H, m), 7.58—7.98 (2H, m).

Benzyl 3,5-Dimethyl-4-isoxazolyl Ketone (**5a**) and 3,5-Dimethyl-4-isoxazolylmethyl Phenyl Ketone (**6a**): A mixture of 3,5-dimethyl-4-phenylethynylisoxazole (**2a**) (2.0 g, 0.01 mol), $HgSO_4$ (2.50 g, 0.01 mol), conc. $H_2SO_4$ (2.50 g), and 70% acetone (40 ml) was refluxed for 27.5 h. The crude product was purified by $SiO_2$ column chromatography using $C_6H_6$ as an eluent. The first fraction gave colorless needles (**5a**) which were recrystallized from acetone–hexane. Yield 1.50 g. $^1$H-NMR ($CDCl_3$): 2.41 (3H, s), 2.64 (3H, s), 4.03 (2H, s), 7.28 (5H, broad s). MS *m/e*: 215 ($M^+$), 124, 91.

The second fraction gave colorless needles (**6a**) which were recrystallized from acetone–hexane. Yield 0.15 g. $^1$H-NMR ($CDCl_3$): 2.13 (3H, s), 2.26 (3H, s), 3.97 (2H, s), 7.28—7.74 (3H, m), 7.90—8.22 (2H, m). MS *m/e*: 215 ($M^+$), 110, 77.

3,5-Dimethyl-4-isoxazolyl Pentyl Ketone (**5b**): A mixture of 3,5-dimethyl-4-(1-hexynyl)isoxazole (**2b**) (0.85 g, 0.005 mol), $HgSO_4$ (1.50 g, 0.005 mol), conc. $H_2SO_4$ (1.5 g), and 70% aq. acetone (20 ml) was refluxed for 20 h to give a pale yellow liquid. Yield 0.74 g. $^1$H-NMR ($CDCl_3$): 0.91 (3H, t, $J$=7.0 Hz), 1.10—2.05 (6H, m), 2.05—2.94 (2H, m), 2.43 (3H, s), 2.65 (3H, s).

Benzyl 3-Methyl-5-phenyl-4-isoxazolyl Ketone (**5c**) and 3-Methyl-5-phenyl-4-isoxazolylmethyl Phenyl Ketone (**6c**): A mixture of 3-methyl-5-phenyl-4-phenylethynylisoxazole (**2c**) (1.0 g, 0.004 mol), $HgSO_4$ (1.20 g, 0.004 mol), conc. $H_2SO_4$ (1.50 g), and 80% aq. acetone (15 ml) was refluxed for 70 h. The crude product was purified by $SiO_2$ column chromatography using $C_6H_6$ as an eluent. The first fraction gave colorless prisms (**5c**) which were recrystallized from acetone–hexane. Yield 0.70 g. $^1$H-NMR ($CDCl_3$): 2.38 (3H, s), 3.80 (2H, s), 6.70—7.40 (5H, m), 7.55 (5H, s). MS *m/e*: 277 ($M^+$), 186, 91.

The second fraction gave colorless needles (**6c**) which were recrystallized from acetone–hexane. Yield 0.15 g. $^1$H-NMR ($CDCl_3$): 2.21 (3H, s), 4.24 (2H, s), 7.20—7.80 (8H, m), 7.90—8.20 (2H, m). MS *m/e*: 277 ($M^+$), 172, 105, 77.

3-Methyl-5-phenyl-4-isoxazolyl Pentyl Ketone (**5d**): A mixture of 4-(1-hexynyl)-3-methyl-5-phenylisoxazole (**2d**) (1.2 g, 0.005 mol), $HgSO_4$ (1.50 g, 0.005 mol), conc. $H_2SO_4$ (1.5 g), and 70% aq. acetone (20 ml) was refluxed for 19 h to give a pale yellow liquid. Yield 0.85 g. $^1$H-NMR ($CDCl_3$): 0.81 (3H, t, $J$=5.5 Hz), 1.00—2.02 (6H, m), 2.05—2.76 (2H, m), 2.48 (3H, s), 7.50—7.80 (5H, m).

Beckmann Rearrangement of Benzyl 3,5-Dimethyl-4-isoxazolyl Ketone Oxime (**7**): An MeOH (150 ml) solution of KOH (13 g, 0.023 mol) was added to an aq. solution (17 ml) of $HONH_2 \cdot HCl$ (16 g, 0.023 mol). After removal of the precipitated KCl by filtration, **5a** (4.0 g, 0.018 mol) was added to the filtrate and the mixture was refluxed for 42 h. The mixture was concentrated to dryness under reduced pressure and the residue was dissolved in $H_2O$ (50 ml). The aqueous layer was extracted with $CHCl_3$ and the removal of the $CHCl_3$ gave the crude ketone oxime (**7**) as a viscous liquid. Yield 4.0 g (94%).

Phosphorus pentachloride (11.6 g, 0.056 mol) was slowly added with stirring at 0—5°C to an ethereal solution (60 ml) of **7** (4.0 g, 0.016 mol). After the mixture had been stirred at room temperature for 20 h,

a small amount of ice was added. The aqueous layer was made alkaline and extracted with $CHCl_3$. Removal of the $CHCl_3$ gave the crude product, which was purified by $SiO_2$ column chromatography. The $C_6H_6$ eluate gave colorless needles, N-benzyl-3,5-dimethylisoxazole-4-carboxamide (**8**), which were recrystallized from acetone–hexane. Yield 0.75 g (19%). mp 134—135°C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3260, 1640. $^1$H-NMR ($CDCl_3$): 2.27 (3H, s), 2.46 (3H, s), 4.50 (2H, d, $J$=6.0 Hz), 6.20—6.70 (1H, broad), 7.25 (5H, s). *Anal.* Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.60; H, 6.00; N, 12.30.

The $C_6H_6$–AcOEt (2: 1) eluate gave colorless needles, N-(3,5-dimethyl-4-isoxazolyl)phenylacetamide (**9**), which were recrystallized from acetone–hexane. Yield 0.25 g (6%). mp 124—125.5°C. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3270, 1670. $^1$H-NMR ($CDCl_3$): 1.93 (3H, s), 2.06 (3H, s), 2.52 (2H, s), 7.23 (5H, s), 8.20 (1H, broad). *Anal.* Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 68.04; H, 6.22; N, 12.16.

N-Benzyl-3,5-dimethylisoxazole-4-carboxamide (**8**): A mixture of 3,5-dimethylisoxazole-4-carboxylic acid (**10**)[2] (1.0 g, 0.007 mol) and $SOCl_2$ (24.5 g, 0.2 mol) was refluxed for 2 h. The reaction mixture was concentrated to dryness under reduced pressure and the residue was dissolved in $CHCl_3$ (40 ml). Benzylamine (1.80 g, 0.017 mol) was added to the $CHCl_3$ solution with stirring at 0—5°C. After refluxing for 3 h, the mixture was washed with 3 N HCl, 3 N NaOH, and $H_2O$. The $CHCl_3$ layer was passed through a short $Al_2O_3$ column. Removal of the $CHCl_3$ gave colorless needles, which were recrystallized from acetone–hexane. Yield 1.2 g (74%). mp 133—134.5°C.

N-(3,5-Dimethyl-4-isoxazolyl)phenylacetamide (**9**): 4-Amino-3,5-dimethylisoxazole (**11**)[3] (1.5 g, 0.013 mol) was slowly added at 0—5°C to a $CHCl_3$ solution (30 ml) of phenylacetyl chloride (2.50 g, 0.016 mol) and the mixture was refluxed for 1.5 h. After the mixture had been washed with 15% $K_2CO_3$ and $H_2O$, the $CHCl_3$ layer was passed through a short $Al_2O_3$ column. Removal of the $CHCl_3$ gave colorless needles, which were recrystallized from acetone–hexane. Yield 1.85 g (60%). mp 124—125°C.

**General Procedure for Hydrogenation of Alkynylisoxazoles with 5% Pd-$CaCO_3$ in the Presence of Quinoline**——A mixture of an alkynylisoxazole (0.005 mol), 5% Pd-$CaCO_3$ (0.1 g), and quinoline (0.1 g) in MeOH (30 ml) was shaken under an $H_2$ stream (1 atm) at room temperature. After $H_2$ absorption had ceased, the catalyst was removed by filtration. The filtrate was concentrated to dryness under reduced pressure and the residue was passed through a short $SiO_2$ column using $C_6H_6$ as an eluent. Removal of the $C_6H_6$ gave the crude products, which were purified by distillation under reduced pressure or (and) recrystallization.

3,5-Dimethyl-4-*cis*-styrylisoxazole (**12a**): Hydrogenation of **2a** (1.10 g, 0.005 mol) according to the general procedure gave a colorless liquid. Yield 0.9 g. $^1$H-NMR ($CDCl_3$): 1.98 (6H, s), 6.15 (1H, d, $J$= 12.0 Hz), 6.68 (1H, d, $J$=12.0 Hz), 7.18 (5H, s).

3,5-Dimethyl-4-(*cis*-1-hexenyl)isoxazole (**12b**): Hydrogenation of **2b** (0.9 g, 0.005 mol) according to the general procedure gave a colorless liquid. Yield 0.65 g. $^1$H-NMR ($CDCl_3$): 0.55—1.08 (3H, m), 1.08—1.65 (4H, m), 1.65—2.46 (2H, m), 2.14 (3H, s), 2.25 (3H, s), 5.51—6.10 (2H, m).

3-Methyl-5-phenyl-4-*cis*-styrylisoxazole (**12c**): Hydrogenation of **2c** (1.3 g, 0.005 mol) according to the general procedure gave colorless needles, which were recrystallized from ether–hexane. Yield 1.15 g. $^1$H-NMR ($CDCl_3$): 1.80 (3H, s), 6.39 (1H, d, $J$=11.0 Hz), 6.80 (1H, d, $J$=11.0 Hz), 7.17 (5H, s), 7.30—7.55 (3H, m), 7.68—8.07 (2H, m).

4-(*cis*-1-Hexenyl)-3-methyl-5-phenylisoxazole (**12d**): Hydrogenation of **2a** (1.2 g, 0.005 mol) according to the general procedure gave a colorless liquid. Yield 0.9 g. $^1$H-NMR ($CDCl_3$): 0.50—1.00 (3H, m), 1.00—1.60 (4H, m), 1.60—2.20 (2H, m), 2.20 (3H, s), 5.65—6.20 (1H, m), 6.15 (1H, d, $J$=11.0 Hz), 7.20—7.65 (3H, m), 7.65—8.05 (2H, m).

**General Procedure for Hydrogenation of Alkynylisoxazoles with 10% Pd-Charcoal**——A mixture of an alkynylisoxazole (0.005 mol) and 10% Pd-charcoal (1.0 g) in MeOH (30 ml) was shaken under an $H_2$ stream (1 atm) at room temperature. After $H_2$ absorption had ceased, the catalyst was filtered off. The filtrate was concentrated to dryness under reduced pressure and the residual oil was distilled under reduced pressure.

The analytical data and boiling points of all 4-alkylisoxazoles are listed in Table II together with those of 4-alkenylisoxazoles obtained by the preceding procedure.

3,5-Dimethyl-4-phenethylisoxazole (**13a**): Hydrogenation of **2a** (0.6 g, 0.003 mol) according to the general procedure gave a colorless liquid. Yield 0.5 g. $^1$H-NMR ($CDCl_3$): 1.97 (3H, s), 2.05 (3H, s), 2.31—2.95 (4H, m), 6.90—7.44 (5H, m).

3,5-Dimethyl-4-hexylisoxazole (**13b**): Hydrogenation of **2b** (1.0 g, 0.056 mol) according to the general procedure gave a colorless liquid. Yield 0.75 g. $^1$H-NMR ($CDCl_3$): 0.67—1.10 (3H, m), 1.10—1.90 (8H, m), 2.15—2.55 (2H, m), 2.18 (3H, s), 2.27 (3H, s).

3-Methyl-4-phenethyl-5-phenylisoxazole (**13c**): Hydrogenation of **2c** (0.52 g, 0.002 mol) according to the general procedure gave a colorless liquid. Yield 0.43 g. $^1$H-NMR ($CDCl_3$): 2.07 (3H, s), 2.82 (4H, s), 6.90—7.83 (10H, m).

4-Hexyl-3-methyl-5-phenylisoxazole (**13d**): Hydrogenation of **2d** (1.0 g, 0.004 mol) according to the general procedure gave a pale yellow liquid. Yield 0.86 g. $^1$H-NMR ($CDCl_3$): 0.61—1.04 (3H, m), 1.04—1.83 (8H, m), 2.10—2.85 (2H, m), 2.25 (3H, s), 7.30—7.90 (5H, m).

5-Phenethyl-3-phenylisoxazole (**14**): i) A mixture of **1a** (0.2 g, 0.0008 mol) and 10% Pd-charcoal in MeOH (10 ml) was hydrogenated under an $H_2$ stream (1 atm) at room temperature. Usual treatment of the reaction mixture gave colorless needles, mp 93—94°C, which were recrystallized from ether–hexane.

Table II. 4-Olefinic (**12a—d**) and 4-Alkyl Isoxazoles (**13a—d**)

| No. | Yield (%) | bp (mmHg) or [mp] (°C) | Formula | Analysis (%) Calcd (Found) C | H | N |
|---|---|---|---|---|---|---|
| **12a** | 81 | 111—115(5) | $C_{13}H_{13}NO$ | 78.36 (78.04 | 6.58 6.74 | 7.03 6.87) |
| **12b** | 71 | 112—114(16) | $C_{11}H_{17}NO$ | 73.70 (73.67 | 9.56 9.52 | 7.81 7.66) |
| **12c** | 88 | [104—105] | $C_{18}H_{15}NO$ | 82.73 (83.01 | 5.79 5.93 | 5.36 5.32) |
| **12d** | 67 | 127—129(5) | $C_{16}H_{19}NO$ | 79.63 (79.66 | 7.94 8.09 | 5.80 5.82) |
| **13a** | 82 | 116—120(3) | $C_{13}H_{15}NO$ | 77.58 (77.86 | 7.51 7.52 | 6.96 6.72) |
| **13b** | 73 | 84(3) | $C_{11}H_{19}NO$ | 72.88 (72.74 | 10.57 10.74 | 7.73 7.69) |
| **13c** | 81 | 160(4) | $C_{18}H_{17}NO$ | 82.10 (82.34 | 6.51 6.71 | 5.32 5.02) |
| **13d** | 85 | 145—146(3) | $C_{16}H_{21}NO$ | 78.97 (78.80 | 8.70 8.77 | 5.76 5.66) |

Yield 0.16 g (79%). *Anal.* Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.77; H, 6.30; N, 5.63. $^1$H-NMR ($CDCl_3$): 3.06 (4H, s), 6.23 (1H, s), 7.25 (5H, s), 7.08—7.60 (3H, m), 7.60—7.95 (2H, m).

ii) A mixture of **1a** (0.25 g, 0.001 mol), 5% Pd-$CaCO_3$ (70 mg), and quinoline (70 mg) in MeOH (40 ml) was hydrogenated under an $H_2$ stream (1 atm) at room temperature. In this case, the hydrogen absorption curve showed no inflexion point until the reduction was over. Usual treatment of the reaction mixture gave colorless needles, mp 93—94°C, which were identical with the compound obtained in the above experiment. Yield 0.19 g (75%).

## References and Notes

1) H. Yamanaka, M. Shiraiwa, E. Yamamoto, and T. Sakamoto, *Chem. Pharm. Bull.*, **29**, 3543 (1981).
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