Chem. Pharm. Bull. 29(12)3543—3547(1981)

Cross-coupling Reactions of Haloisoxazoles with Olefins and Acetylenes

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(Received June 8, 1981)

3,5-Dimethyl-4-iodoisoxazole (**1a**) reacted with phenylacetylene with catalysis by palladium (II) chloride-triphenylphosphine complex to give 3,5-dimethyl-4-phenylethynylisoxazole (**2a**). When **1a** was treated with styrene under similar conditions, 3,5-dimethyl-4-*trans*-styrylisoxazole (**3a**) was obtained. In contrast, the palladium-catalyzed cross-coupling reaction of 3-phenyl-5-bromoisoxazole (**4**) with styrene afforded 3,3′-diphenyl-5,5′-biisoxazole (**6**) as the main product, instead of the desired styryl compound (**5a**). However, 3-phenyl-5-phenylethynylisoxazole (**7a**) was obtained, as in the case of **1a**, by the reaction of **4** with phenylacetylene. Some additional examples of these coupling reactions are also described.

Keywords——4-iodoisoxazole; 5-bromoisoxazole; 5-bromoisothiazole; palladium catalyzed cross-coupling; olefin; acetylene

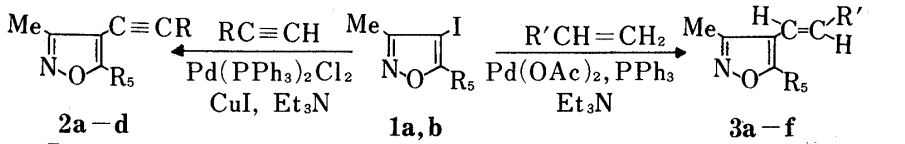
There are relatively few papers[1] dealing with the synthesis of isoxazole derivatives containing a functionalized carbon substituent, although many studies have appeared on the chemistry of isoxazoles. Meanwhile, it is reported that the cross-coupling reaction of aryl halides with ethynyl compounds in the presence of palladium-triphenylphosphine complex generally proceeds at α-, β-, and γ-positions of six-membered N-heteroaromatics without significant difference.[2] The cross-coupling reaction with a terminal vinyl compound,[3] on the contrary, is known to be subject to restrictions on the nature of the aryl halides employed. For example, 2-bromopyridine and 4-iodopyrimidines did not couple easily with styrene or ethyl acrylate, whereas 3-bromopyridine and 5-bromopyrimidines coupled with such olefins to give the corresponding olefin-substituted derivatives.

In the present paper, we describe the cross-coupling reaction of 4- and 5-haloisoxazoles with various unsaturated aliphatic compounds, which was investigated from the synthetic viewpoint.

As a result of the investigation, it became clear that the 4-position of isoxazole received olefins as well as acetylenes and that 5-haloisoxazoles did not undergo the cross-coupling reaction with olefins, but did with acetylenes.

First, the coupling reaction of 4-iodoisoxazoles with terminal acetylene compounds was investigated. When 4-iodo-3,5-dimethylisoxazole (**1a**) was heated with phenylacetylene in the presence of a catalytic quantity of palladium complex and cuprous iodide, 3,5-dimethyl-4-phenylethynylisoxazole (**2a**), mp 72—73°C, was obtained in 85% yield. Similarly, **1a** reacted with 1-hexyne under the same conditions to give 3,5-dimethyl-4-(1-hexynyl)-isoxazole (**2b**), bp 125—130°C (13 mmHg), in 76% yield. In addition, 4-iodo-3-methyl-5-phenylisoxazole (**1b**) was treated with phenylacetylene and 1-hexyne, and the corresponding acetyleneisoxazoles, 3-methyl-5-phenyl-4-phenylethynyl- (**2c**) and 4-(1-hexynyl)-3-methyl-5-phenylisoxazole (**2d**), respectively were obtained, although the yields were unsatisfactory.

The above isoxazoles (**1a, b**) readily coupled with olefins such as styrene, ethyl acrylate, and acrylonitrile in triethylamine in the presence of palladium (II) acetate and triphenylphosphine. Namely, the reaction of **1a** with ethyl acrylate gave ethyl 3,5-dimethylisoxazole-4-acrylate (**3b**), mp 72—73°C, in 78% yield. In the proton magnetic resonance (^{1}H-NMR) spectrum of **3b**, the coupling constant between two olefinic protons on the side chain was



2a–d
a : R_5=Me, R=Ph
b : R_5=Me, R=Bu
c : R_5=Ph, R=Ph
d : R_5=Ph, R=Bu

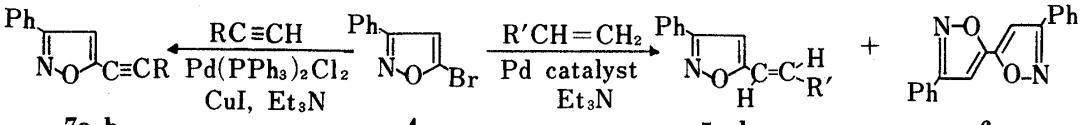
1a,b
a : R_5=Me
b : R_5=Ph

3a–f
a : R_5=Me, R'=Ph
b : R_5=Me, R'=COOEt
c : R_5=Me, R'=CN
d : R_5=Ph, R'=Ph
e : R_5=Ph, R'=COOEt
f : R_5=Ph, R'=CN

Chart 1

17.0 Hz, which demonstrates a *trans*-configuration of the double bond. Similarly, 3,5-dimethyl- (**3a**), 3-methyl-5-phenyl-4-styrylisoxazole (**3d**), 3,5-dimethyl- (**3c**), 3-methyl-5-phenyl-isoxazole-4-acrylonitrile (**3f**), and ethyl 3-methyl-5-phenylisoxazole-4-acrylate (**3e**) were obtained as shown in Chart 1.

Next, the above coupling reactions were examined at the 5-position, where the π-electron density is reduced by the electron-withdrawing nature of the nitrogen atom in the isoxazole ring. 3-Phenyl-5-bromoisoxazole (**4**) coupled smoothly with phenylacetylene and 1-hexyne, like 4-iodoisoxazoles (**1a**, **b**), and yielded 3-phenyl-5-phenylethynyl-(**7a**), mp 99—101°C, and 5-(1-hexynyl)-3-phenyl-isoxazole (**7b**), bp 110—115°C (2 mmHg), respectively. In contrast, the coupling reaction of **4** with the olefins resulted in the dimerization of the starting isoxazole (**4**). When **4** was treated with styrene under usual conditions of the olefin-coupling reaction, a compound, mp 211—212°C, was obtained as a main product together with a small amount of 3-phenyl-5-styrylisoxazole (**5a**). The molecular formula, $C_{18}H_{12}N_2O_2$, established by the elemental analysis and mass spectroscopy suggested the structure of the main product to be 3,3′-diphenyl-5,5′-biisoxazole (**6**). The ^{1}H-NMR spectral data of this compound supported the above assignment. The compound **6** was also obtained in 28% yield, when **4** was allowed to react with ethyl acrylate. In this case, the desired cross-coupling product, ethyl 3-phenylisoxazole-5-acrylate (**5b**), mp 93.5—94°C, was isolated as a minor product (13%).

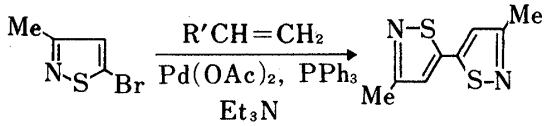


7a,b
a : R=Ph
b : R=Bu

4

5a,b
a : R'=Ph
b : R'=COOEt

6



8

9

R'=Ph, COOEt

Chart 2

Biaryl formation due to the homo-coupling reaction of aryl halides seems to be general at the position where the π-electron density is reduced by the ring nitrogen. For example, 4-iodopyrimidines were reported to undergo bipyrimidinyl formation predominantly,[3] and the reaction of 3-methyl-5-bromoisothiazole (**8**) under the same conditions gave 3,3′-dimethyl-5,5′-biisothiazole (**9**) in almost quantitative yield.

It has been reported[4,5] that the biaryl formation of the benzene series can be avoided by the use of palladium metal catalysts, such as palladium charcoal or palladium black,

instead of palladium (II)-triphenylphosphine complex. However, a trial with the azole series under the above conditions failed to retard the formation of dimeric products.

In conclusion, it should be mentioned that the cross-coupling reaction of 4-haloisoxazoles with olefins and acetylenes, and that of 5-haloisoxazoles with acetylenes are practical procedures for the preparation of isoxazole derivatives, but olefin coupling at the 5-position is rather difficult.

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.

General Procedure for Cross-Coupling Reaction of Haloisoxazoles with Acetylenic Compounds——A mixture of a haloisoxazole (0.01 mol), an acetylene (0.014 mol), $Pd(PPh_3)_2Cl_2$ (0.2 mmol), and CuI (0.4 mmol) in Et_3N (40 ml) was refluxed for a suitable time. After removal of the solvent, water (50—60 ml) was added to the residue. The aqueous layer was made alkaline with K_2CO_3 and extracted with C_6H_6. The C_6H_6 extract was passed through a short Al_2O_3 column and the crude products were purified by distillation under reduced pressure or (and) by recrystallization.

The analytical data and mp (or bp) of all the products obtained by this procedure are listed in Table I.

3,5-Dimethyl-4-phenylethynylisoxazole (**2a**): A mixture of 3,5-dimethyl-4-iodoisoxazole (**1a**)[6] (5.0 g, 0.022 mol), phenylacetylene (2.80 g, 0.026 mol), $Pd(PPh_3)_2Cl_2$ (400 mg), and CuI (200 mg) in Et_3N (80 ml) was refluxed for 10 h to give colorless needles which were recrystallized from hexane. Yield 3.85 g (85%). ^{1}H-NMR ($CDCl_3$): 2.30 (3H, s), 2.45 (3H, s), 7.10—7.60 (5H, m).

3,5-Dimethyl-4-(1-hexynyl)isoxazole (**2b**): A mixture of **1a** (4.40 g, 0.02 mol), 1-hexyne (2.50 g, 0.03 mol), $Pd(PPh_3)_2Cl_2$ (210 mg), and CuI (110 mg) in Et_3N (50 ml) was refluxed for 24 h to give a pale yellow liquid. Yield 2.55 g (76%). ^{1}H-NMR ($CDCl_3$): 0.80—1.20 (3H, m), 1.20—1.80 (4H, m), 2.20—2.70 (2H, m), 2.29 (3H, s), 2.45 (3H, s).

3-Methyl-5-phenyl-4-phenylethynylisoxazole (**2c**): A mixture of 4-iodo-3-methyl-5-phenylisoxazole (**1b**)[6] (2.80 g, 0.01 mol), phenylacetylene (1.40 g, 0.014 mol), $Pd(PPh_3)_2Cl_2$ (150 mg), and CuI (75 mg) in Et_3N (60 ml) was refluxed for 15.5 h to give colorless needles, which were recrystallized from ether–hexane. Yield 1.52 g (59%). ^{1}H-NMR ($CDCl_3$): 2.39 (3H, s), 7.16—7.76 (8H, m), 7.97—8.40 (2H, m).

4-(1-Hexynyl)-3-methyl-5-phenylisoxazole (**2d**): A mixture of **1b** (2.80 g, 0.01 mol), 1-hexyne (1.10 g, 0.014 mol), $Pd(PPh_3)_2Cl_2$ (200 mg), and CuI (100 mg) in Et_3N (60 ml) was refluxed for 23 h to give a pale yellow liquid. Yield 1.78 g (76%). ^{1}H-NMR ($CDCl_3$): 0.73—1.17 (3H, m), 1.17—1.95 (4H, m), 2.20—2.70 (2H, m), 2.30 (3H, s), 7.20—7.62 (3H, m), 7.90—8.33 (2H, m).

3-Phenyl-5-phenylethynylisoxazole (**7a**): A mixture of 5-bromo-3-phenylisoxazole (**4**)[7] (1.10 g, 0.005 mol), phenylacetylene (0.80 g, 0.008 mol), $Pd(PPh_3)_2Cl_2$ (80 mg), and CuI (40 mg) in Et_3N (40 ml) was refluxed for 18 h to give colorless needles, which were recrystallized from ether–hexane. Yield 0.75 g (62%). ^{1}H-NMR ($CDCl_3$): 6.80 (1H, s), 7.15—8.05 (10H, m).

Table I. Acetylenic Isoxazoles (**2a—d** and **7a,b**)

No.	mp (°C)	bp (mmHg) (°C)	IR $\nu_{max}^{CHCl_3}$ cm^{-1}	Formula	Analysis (%) Cacld (Found) C	N	H
2a	72—73	—	2220	$C_{13}H_{11}NO$	79.16 (79.27	5.61 5.72	7.10 7.10)
2b	—	125—130(13)	2220	$C_{11}H_{15}NO$	74.54 (74.51	8.53 8.59	7.90 7.82)
2c	61—62	175—178(2)	2220	$C_{18}H_{13}NO$	83.37 (83.44	5.05 4.88	5.40 5.31)
2d	—	140—142(2)	2220	$C_{16}H_{17}NO$	80.30 (80.20	7.16 7.31	5.85 5.62)
7a	99—101	145—149(1)	2220	$C_{17}H_{11}NO$	83.24 (83.23	4.52 4.51	5.71 5.57)
7b	—	110—115(2)	2220	$C_{15}H_{15}NO$	79.97 (80.01	6.71 6.61	6.22 5.77)

5-(1-Hexynyl)-3-phenylisoxazole (**7b**): A mixture of **4** (0.80 g, 0.0035 mol), 1-hexyne (0.60 g, 0.0075 mol), $Pd(PPh_3)_2Cl_2$ (80 mg), and CuI (40 mg) in Et_3N (25 ml) was refluxed for 16 h to give a pale yellow liquid. Yield 0.35 g (44%). ^{1}H-NMR ($CDCl_3$): 0.95 (3H, t, J=6.0 Hz), 1.16—1.95 (4H, m), 2.48 (2H, t, J=7.0 Hz), 6.56 (1H, s), 7.26—7.56 (3H, m), 7.56—7.93 (2H, m).

General Procedure for Cross-Coupling Reaction of Haloisoxazoles with Olefinic Compounds——A mixture of a haloisoxazole (0.01 mol), an olefinic compound (0.013 mol), $Pd(OAc)_2$ (30 mg), PPh_3 (60 mg), and Et_3N (0.012 mol) was heated in a sealed tube that had been flushed with nitrogen. The cooled reaction mixture was diluted with a suitable amount of H_2O, made alkaline with K_2CO_3, and extracted with $CHCl_3$. The $CHCl_3$ extract was passed through a short Al_2O_3 column using $CHCl_3$ as an eluent. Removal of the $CHCl_3$ gave the crude products, which were purified by distillation under reduced pressure or (and) by recrystallization.

The analytical data and mp (or bp) of all the products obtained by this procedure are listed in Table II.

3,5-Dimethyl-4-*trans*-styrylisoxazole (**3a**): A mixture of **1a** (2.20 g, 0.01 mol), styrene (1.30 g, 0.013 mol), $Pd(OAc)_2$ (30 mg), PPh_3 (60 mg), and Et_3N (1.20 g, 0.012 mol) was heated at 140°C for 15 h to give colorless needles which were recrystallized from hexane. Yield 0.85 g (43%). ^{1}H-NMR ($CDCl_3$): 2.30 (3H, s), 2.39 (3H, s), 6.71 (2H, s), 6.80—7.80 (5H, m).

Ethyl *trans*-3,5-Dimethyl-4-isoxazoleacrylate (**3b**): A mixture of **1a** (2.20 g, 0.01 mol), ethyl acrylate (1.30 g, 0.013 mol), $Pd(OAc)_2$ (30 mg), PPh_3 (60 mg), and Et_3N (1.20 g, 0.012 mol) was heated at 160°C for 4 h to give colorless needles, which were recrystallized from ether–acetone. Yield 1.50 g (78%). ^{1}H-NMR ($CDCl_3$): 1.33 (3H, t, J=7.5 Hz), 2.35 (3H, s), 2.47 (3H, s), 4.23 (2H, q, J=7.5 Hz), 6.07 (1H, d, J=17.0 Hz), 7.39 (1H, d, J=17.0 Hz).

trans-3,5-Dimethyl-4-isoxazoleacrylonitrile (**3c**): A mixture of **1a** (2.20 g, 0.01 mol), acrylonitrile (1.0 g, 0.019 mol), $Pd(OAc)_2$ (60 mg), PPh_3 (120 mg), and Et_3N (4.0 g, 0.04 mol) was heated at 120°C for 21 h to give colorless needles, which were recrystallized from acetone–hexane. Yield 0.75 g (51%). ^{1}H-NMR ($CDCl_3$): 2.35 (3H, s), 2.48 (3H, s), 5.61 (1H, d, J=17.0 Hz), 7.16 (1H, d, J=17.0 Hz).

3-Methyl-5-phenyl-4-*trans*-styrylisoxazole (**3d**): A mixture of **1b** (2.40 g, 0.0084 mol), styrene (1.30 g, 0.013 mol), $Pd(OAc)_2$ (930 mg), PPh_3 (60 mg), and Et_3N (1.20 g, 0.012 mol) was heated at 140°C for 5 h to give a colorless liquid. Yield 0.45 g (20%). ^{1}H-NMR ($CDCl_3$): 2.47 (3H, s), 6.96 (2H, s), 7.20—7.90 (10H, m).

Ethyl *trans*-3-Methyl-5-phenyl-4-isoxazoleacrylate (**3e**): A mixture of **1b** (1.40 g, 0.005 mol), ethyl acrylate (0.60 g, 0.006 mol), $Pd(OAc)_2$ (30 mg), PPh_3 (60 mg), and Et_3N (0.70 g, 0.007 mol) was heated at 120°C for 42.5 h to give colorless prisms, which were recrystallized from ether–hexane. Yield 0.95 g (78%). ^{1}H-NMR ($CDCl_3$): 1.31 (3H, t, J=7.5 Hz), 2.48 (3H, s), 4.25 (2H, q, J=7.5 Hz), 6.33 (1H, d, J=17.0 Hz), 7.30—8.00 (6H, m).

trans-3-Methyl-5-phenyl-4-isoxazoleacrylonitrile (**3f**): A mixture of **1b** (1.40 g, 0.005 mol), acrylonitrile (0.30 g, 0.006 mol), $Pd(OAc)_2$ (30 mg), PPh_3 (60 mg), and Et_3N (0.70 g, 0.007 mol) was heated at 120°C for 42.5 h to give colorless needles which were recrystallized from AcOEt. Yield 0.45 g (45%). ^{1}H-NMR ($CDCl_3$): 2.53 (3H, s), 5.85 (1H, d, J=17.0 Hz), 7.23—7.90 (6H, m).

Table II. Olefinic Isoxazoles (**3a—f** and **5a,b**)

No.	mp (°C)	bp (mmHg) (°C)	IR $\nu_{max}^{CHCl_3}$ cm^{-1}	Formula	Analysis (%) Calcd (Found) C	H	N
3a	65	160—165(2)	970	$C_{13}H_{13}NO$	78.36 (78.57	6.58 6.52	7.03 7.09)
3b	72—73	135—140(2)	1720 990	$C_{10}H_{13}NO_3$	61.52 (61.50	6.71 6.82	7.18 7.11)
3c	125—126	—	2200 960	$C_8H_8N_2O$	64.85 (65.04	5.44 5.63	18.91 18.89)
3d	—	180—185(2)	970	$C_{18}H_{15}NO$	82.73 (83.02	5.79 5.81	5.36 5.10)
3e	68—69	—	1720 985	$C_{15}H_{15}NO_3$	70.02 (69.85	5.88 5.78	5.44 5.30)
3f	149—150	—	2220 970	$C_{13}H_{10}N_2O$	74.27 (74.15	4.79 4.73	13.33 13.26)
5a	134—135	—	970	$C_{17}H_{13}NO$	82.57 (82.35	5.30 5.15	5.66 5.54)
5b	93.5—94	—	1720 970	$C_{14}H_{13}NO_3$	69.12 (68.90	5.39 5.39	5.76 5.62)

Cross-Coupling Reaction of 5-Bromo-3-phenylisoxazole (4) with Styrene——i) A mixture of **4** (1.10 g, 0.005 mol), styrene (0.80 g, 0.008 mol), $Pd(OAc)_2$ (30 mg), PPh_3 (60 mg), and Et_3N (1.20 g, 0.012 mol) was heated at 130°C for 15 h. The crude product was purified by Al_2O_3 column chromatography using hexane and $CHCl_3$ as eluents. The first fraction of the hexane eluate gave the starting material (0.20 g, 18%) and the second fraction afforded a trace of colorless needles, 3-phenyl-5-*trans*-styrylisoxazole (**5a**), which were recrystallized from ether–hexane. ^{1}H-NMR ($CDCl_3$): 6.55 (1H, s), 6.98 (1H, d, J=17.0 Hz), 7.20—7.70 (4H, m), 7.70—8.10 (2H, m).

The $CHCl_3$ eluate gave colorless needles, 3,3′-diphenyl-5,5′-biisoxazole (**6**), which were recrystallized from hexane–AcOEt. Yield 0.35 g (50%). mp 211—212°C. *Anal.* Calcd for $C_{18}H_{12}N_2O_2$: C, 74.99; H, 4.20; N, 9.72. Found: C, 75.02; H, 4.14; N, 9.42. ^{1}H-NMR ($CDCl_3$): 7.30 (2H, s), 7.40—7.70 (6H, m), 7.70—8.10 (4H, m). MS *m/e*: 288 (M^+).

ii) A mixture of **4** (1.20 g, 0.005 mol), styrene (1.60 g, 0.016 mol), $Pd(OAc)_2$ (40 mg), and Et_3N (3.0 g, 0.03 mol) was heated at 120°C for 19 h. The crude product was purified by Al_2O_3 column chromatography using hexane as an eluent. The first fraction gave the starting material (0.80 g, 67%) and the second fraction afforded **5a** (0.15 g, 11%).

Cross-Coupling Reaction of 4 with Ethyl Acrylate——i) A mixture of **4** (1.10 g, 0.005 mol), ethyl acrylate (0.80 g, 0.008 mol), $Pd(OAc)_2$ (30 mg), PPh_3 (60 mg), and Et_3N (1.20 g, 0.012 mol) was heated at 130°C for 22 h. The crude product was purified by Al_2O_3 column chromatography using hexane and $CHCl_3$ as eluents. The first fraction of hexane eluate gave the starting material (0.15 g, 14%) and the second fraction afforded colorless needles (0.15 g, 13%), ethyl *trans*-3-phenyl-5-isoxazoleacrylate (**5b**), which were recrystallized from ether–hexane. ^{1}H-NMR ($CDCl_3$): 1.34 (3H, t, J=7.5 Hz), 4.32 (2H, q, J=7.5 Hz), 6.75 (1H, d, J=17 Hz), 6.80 (1H, s), 7.30—7.70 (4H, m), 7.70—8.16 (2H, m). The $CHCl_3$ eluate gave **6** (0.20 g, 28%).

ii) A mixture of **4** (1.20 g, 0.005 mol), ethyl acrylate (1.60 g, 0.016 mol), $Pd(OAc)_2$ (40 mg), and Et_3N (3.0 g, 0.03 mol) was heated at 120°C for 19 h. The crude product was purified by Al_2O_3 column chromatography using hexane and C_6H_6 as eluents. The hexane eluate gave the starting material (0.90 g, 75%) and the C_6H_6 eluate afforded **5b** (0.13 g, 10%).

Cross-Coupling Reaction of 4 with Acrylonitrile——A mixture of **4** (1.20 g, 0.005 mol), acrylonitrile (1.0 g, 0.019 mol), $Pd(OAc)_2$ (40 mg), and Et_3N (3.0 g, 0.03 mol) was heated at 120°C for 19 h. Purification of the crude product by Al_2O_3 column chromatography using hexane as an eluent gave the starting material (1.0 g, 83%).

The analytical data and the physical constants of **5a, b** are also listed in Table II.

3,3′-Dimethyl-4,4′-biisothiazole (9)——i) A mixture of 5-bromo-3-methylisothiazole (**8**) (1.80 g, 0.01 mol), styrene (5.2 g, 0.05 mol), $Pd(OAc)_2$ (100 mg), PPh_3 (200 mg), and Et_3N (2.0 g, 0.02 mol) was heated at 120°C for 19 h to give colorless needles, which were recrystallized from ether. bp 125—130°C (2 mmHg). mp 121—122°C. Yield 0.85 g (86%). ^{1}H-NMR ($CDCl_3$): 2.51 (6H, s), 7.15 (2H, s). MS *m/e*: 196 (M^+). *Anal.* Calcd for $C_8H_8N_2S_2$: C, 48.98; H, 4.11; N, 14.28; S, 32.63. Found: C, 48.43; H, 4.09; N, 14.21; S, 32.63.

ii) A mixture of **8** (1.80 g, 0.01 mol), acrylonitrile (2.50 g, 0.05 mol), $Pd(OAc)_2$ (100 mg), PPh_3 (200 mg), and Et_3N (2.0 g, 0.02 mol) was heated at 120°C for 12 h to give colorless needles, which were identical with the product obtained in the above experiment.

References and Notes

1) A. Quilico, "Five- and Six-membered Compounds with Nitrogen and Oxygen: Part I, Isoxazoles and Related Compounds" ed. by A. Weissberger, Interscience Publishers, New York, 1962.
2) K. Edo, T. Sakamoto, and H. Yamanaka, *Chem. Pharm. Bull.*, **26**, 3843 (1978).
3) K. Edo, T. Sakamoto, and H. Yamanaka, *Chem. Pharm. Bull.*, **27**, 193 (1979).
4) F.R.S. Clark, R.O.C. Norman, and C.B. Thomas, *J. Chem. Soc. Perkin I*, **1957**, 1204.
5) T. Sakamoto, H. Arakida, K. Edo, and H. Yamanaka, *Heterocycles*, **16**, 965 (1981).
6) N.K. Kochetkov, S.D. Sokolov, and N.M. Vagurtova, *Zh. Obshch. Khim.*, **31**, 2326 (1961) [*Chem. Abstr.*, **56**, 3437*b* (1962)].
7) G. Adembri and P. Tedeschi, *Boll. Sci. Fac. Chim. Bologna*, **23**, 203 (1965) [*Chem. Abstr.*, **63**, 13235*a* (1965)].
8) A. Adams and R. Slack, *J. Chem. Soc.*, **1959**, 3061.