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PALLADIUM-CATALYZED COUPLING REACTION OF HALOHETEROAROMATIC COMPOUNDS IN WATER

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Abstract - Palladium-catalyzed coupling reaction of π-deficient heteroaromatic halide in water was accomplished with excellent to good yields without any side reactions such as hydrolysis.

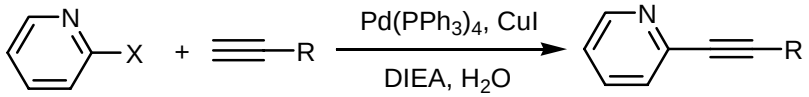
The use of water as a solvent in organic synthesis is helpful from the viewpoint of protection of the environment and reduction of chemical resources; water is a non-toxic and cheap material. Recently, organic reactions in aqueous media have been developed worldwide.[1,2]

The coupling reaction of aromatic compounds with alkenes or alkynes using a palladium complex as a catalyst has been reported from the middle of the 1970s, and the reaction is well known as an important method for introducing an alkenyl or alkynyl substituent into an aromatic moiety.[3-5] Similarly, ethynylheteroaromatics are prepared by the reaction of haloheteroaromatics with acetylene derivatives in the presence of a palladium complex in organic solvent. For example, the coupling reaction of bromopyridines with phenylacetylene proceed to give phenylethynylpyridines in toluene as a solvent.[6] Although the palladium-catalyzed reaction of haloaromatics (halobenzenes and halonaphthalenes) in water was already reported by Bhattacharya,[7] the reaction of π-deficient haloheteroaromatics has not been reported. It is well known that π-deficient nitrogen-containing heteroaromatics such as azines or diazines are reactive with nucleophiles. For example, π-deficient nitrogen-containing heteroaromatic halides react with carbanions, amines, or alkoxides to give the corresponding nucleophile-substituted π-deficient nitrogen-containing heteroaromatics by an addition-elimination mechanism.[8,9] Thus, in palladium-catalyzed alkynylation of π-deficient nitrogen-containing heteroaromatic halides in water, an undesired reaction such as hydrolysis may occur whereas the coupling reaction in organic solvents is reported.[10] In this paper we wish to report the palladium-catalyzed cross-coupling reaction of

iodoheteroaromatics in water.

At first, the reaction of 2-halopyridines with phenylacetylene in the presence of tetrakis(triphenylphosphine)palladium, copper iodide, and diisopropylethylamine (DIEA) in water under various conditions was carried out (Entries 1-5, Table 1). The desired product, 2-(phenylethynyl)pyridine, was obtained using 2-bromopyridine (Entries 2-3), or 2-iodopyridine (Entries 4-5) as a substrate, whereas the coupling reaction of 2-chloropyridine at 70 °C for 24 h afforded no product (Entry 1). The coupling reaction proceeded smoothly using 2-iodopyridine as a substrate to give excellent yields of the product. Some acetylene derivatives (1-hexyne, propargyl alcohol) were found to react to afford the corresponding product, but reactivity of propargyl alcohol was lower than that of phenylacetylene or 1-hexyne (Entries 7-8). Cross-coupling reaction proceeded at a temperature between rt and 70 °C to afford the corresponding 2-alkynylpyridines, and hydrolysis of 2-iodopyridine was not observed under these conditions.

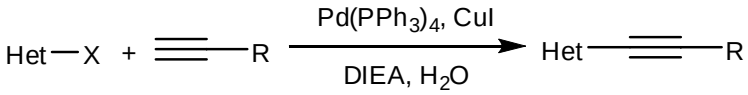
Table 1. Coupling reaction of 2-halopyridine with acetylene derivatives in water

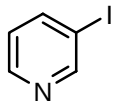
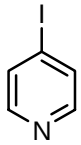
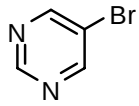
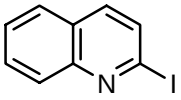
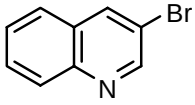
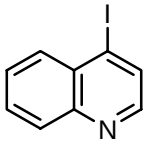
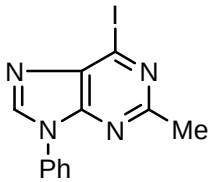
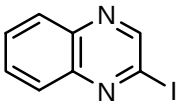


Entry	X	R	Condition	Yield (%)	Recovery (%)
1	Cl	Ph	70 °C, 24 h	0	
2	Br	Ph	rt, 72 h	52	
3	Br	Ph	70 °C, 6 h	91	
4	I	Ph	70 °C, 0.5 h	90	
5	I	Ph	rt, 72 h	89	
6	I	Bu	rt, 7 h	87	
7	I	CH_2OH	rt, 24 h	65	17
8	I	CH_2OH	70 °C, 6 h	60	15

Next, the cross-coupling reaction using some haloheteroaromatics and alkynes was carried out. As shown in Table 2, 3-iodopyridine (Entries 1-3), 4-iodopyridine (Entries 4-8), 5-bromopyrimidine (Entry 9), 2-iodoquinoline (Entries 10-12), 3-bromoquinoline (Entry 13), 4-iodoquinoline (Entries 14-16), 6-iodo-9-phenylpurine (Entries 17-19), and 2-iodoquinoxaline (Entries 20-22) were used as a substrate in this coupling reaction. It was found that the use of iodoheteroaromatics as a substrate is a desirable method for the coupling reaction in water since coupling reaction of bromoheteroaromatics (5-bromopyrimidine and 3-bromoquinoline) with phenylacetylene in water did not proceed smoothly.

Table 2. Coupling reaction of haloheteroaromatics with acetylene derivatives in water



Entry	Het-I	R	Condition	Yield (%)	Recovery (%)
1		Ph	rt, 30 h	98	
2		Bu	70 °C, 2 h	75	8
3		CH_2OH	70 °C, 6 h	76	
4		Ph	rt, 24 h	94	
5		Bu	70 °C, 1 h	9	53
6		Bu	70 °C, 6 h	83	
7		CH_2OH	rt, 6 h	0	27
8		CH_2OH	rt, 23 h, then 70 °C, 6 h	57	13
9		Ph	70 °C, 18 h	26	25
10		Ph	rt, 24 h	92	
11		Bu	70 °C, 6 h	91	
12		CH_2OH	70 °C, 24 h	89	
13		Ph	70 °C, 26 h	11	78
14		Ph	rt, 24 h	89	
15		Bu	70 °C, 15 h	47	33
16		CH_2OH	70 °C, 22 h	65	
17		Ph	rt, 25 h	86	
18		Bu	70 °C, 18 h	93	
19		CH_2OH	70 °C, 23 h	0	76
20		Ph	rt, 22 h	88	
21		Bu	70 °C, 6 h	88	
22		CH_2OH	70 °C, 15 h	57	17

In summary, the coupling reaction of π-deficient iodoheteroaromatics in aqueous media was accomplished without any undesired side reactions such as hydrolysis.

EXPERIMENTAL

All melting points were not corrected. ^{1}H-NMR spectra was measured with Hitachi R-90H spectrometer (90 MHz) and JEOL JNM-EX270 FT NMR system (270 MHz) using tetramethylsilane as an internal standard. Iodoheteroaromatics except iodopyridines (commercially available), 2-iodoquinoline and 6-iodo-2-methyl-9-phenylpurine (prepared from 2-chloroquinoline and 6-chloro-2-methyl-9-phenylpurine, respectively) were prepared from hydroxyheteroaromatics according to the procedure reported by us[11] with minor modifications.

Preparation of 6-iodo-2-methyl-9-phenylpurine : A mixture of 6-chloro-2-methyl-9-phenylpurine (4894 mg, 20.0 mmol), sodium iodide (8993 mg, 60.0 mmol), 2-butanone (100 mL), and hydroiodic acid (1 mL) was stirred at room temperature for 14 h and then heated to reflux for 5 h. After the reaction mixture was basified with triethylamine, the insoluble solids was filtered off. The filtrate was treated with silica gel column chromatography (eluted with hexane – EtOAc (3:2)) to give 6-iodo-2-methyl-9-phenylpurine.

Coupling reaction of iodoheteroaromatics with acetylene derivatives (general procedure) : Iodoheteroaromatics (2.00 mmol), acetylene derivatives (3.00 mmol), diisopropylethylamine (3.00 mmol), water (10 mL), copper iodide (0.02 mmol), and tetrakis(triphenylphosphine)palladium (0.01 mmol) was added to a round-bottom flask and stirred at the condition shown in Table 1. The reaction mixture was extracted with EtOAc and the organic layer was treated with silica gel column chromatography to give the corresponding ethynylheteroaromatics.

2-(Phenylethynyl)pyridine[12] : Pale yellow oil. MS 179 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 7.18-7.28 (1H, *m*, pyridine-H), 7.32-7.42 (3H, *m*, phenyl-H), 7.48-7.73 (4H, *m*, phenyl and pyridine-H), 8.63 (1H, *d*, J=4.6 Hz, pyridine-H).

2-(1-Hexynyl)pyridine[13] : Yellow oil. MS 159 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 0.94 (3H, *t*, J=7.3 Hz, $\underline{CH_3}CH_2CH_2CH_2$), 1.40-1.70 (4H, *m*, $CH_3\underline{CH_2}\underline{CH_2}CH_2$), 2.45 (2H, *t*, J=7.2 Hz, $CH_3CH_2CH_2\underline{CH_2}$), 7.12-7.22 (1H, *m*, pyridine-H), 7.36 (1H, *d*, J=7.8 Hz, pyridine-H), 7.61 (1H, *t*, J=7.8 Hz, pyridine-H), 8.54 (1H, *d*, J=4.6 Hz, pyridine-H).

3-(2-Pyridinyl)-2-propyn-1-ol[14] : Pale yellow solids. Mp 85 °C (lit.,[13] 81-83 °C). MS 133 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 2.58 (1H, *brs*, OH), 4.53 (2H, *d*, J=5.9 Hz, CH_2), 7.20-7.30 (1H, *m*, pyridine-H), 7.44 (1H, *d*, J=7.9 Hz, pyridine-H), 7.67 (1H, *td*, J=7.9 Hz, 2.0 Hz, pyridine-H), 8.57 (1H, *d*, J=2.0 Hz, pyridine-H).

3-(Phenylethynyl)pyridine[15] : Pale brown solids. Mp 50 °C (lit.,[14] 50-51 °C). MS 179 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 7.29 (1H, *dd*, J=7.8 Hz, 4.4 Hz, pyridine-H), 7.32-7.42 (3H, *m*, phenyl-H), 7.50-7.60 (2H, *m*, phenyl-H), 7.81 (1H, *dt*, J=7.8 Hz, 1.5 Hz, pyridine-H), 8.55 (1H, *dd*, J=4.4 Hz, 1.5 Hz, pyridine-H),

8.77 (1H, *d*, J=1.5 Hz, pyridine-H).

3-(1-Hexynyl)pyridine[16] : Yellow liquids. MS 159 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 0.96 (3H, *t*, J=7.3 Hz, $\underline{CH_3}CH_2CH_2CH_2$), 1.40-1.55 (2H, *m*, $CH_3\underline{CH_2}CH_2CH_2$), 1.55-1.65 (2H, *m*, $CH_3CH_2\underline{CH_2}CH_2$), 2.43 (2H, *t*, J=6.9 Hz, $CH_3CH_2CH_2\underline{CH_2}$), 7.22 (1H, *dd*, J=8.0 Hz, 4.6 Hz, pyridine-H), 7.67 (1H, *dt*, J=8.0 Hz, 1.6 Hz, pyridine-H), 8.48 (1H, *dd*, J=4.6 Hz, 1.6 Hz, pyridine-H), 8.62 (1H, *d*, J=1.6 Hz, pyridine-H).

3-(3-Pyridinyl)-2-propyn-1-ol[17] : White solids. Mp 101-102 °C (lit.,[16] 99-100 °C). MS 133 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 2.76 (1H, *brs*, OH), 4.52 (2H, *d*, J=4.6 Hz, CH_2), 7.20-7.32 (1H, *m*, pyridine-H), 7.74 (1H, *dt*, J=8.1 Hz, 2.0 Hz, pyridine-H), 8.53 (1H, *dd*, J=4.6 Hz, 2.0 Hz, pyridine-H), 8.73 (1H, *d*, J=2.0 Hz, pyridine-H).

4-(Phenylethynyl)pyridine[18] : Pale brown solids. Mp 94-94.5 °C (lit.,[17] 91-93 °C). MS 179 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 7.35-7.42 (5H, *m*, phenyl and pyridine-H), 7.53-7.59 (2H, *m*, phenyl-H), 8.61 (2H, *d*, J=5.9 Hz, pyridine-H).

4-(1-Hexynyl)pyridine[19] : Yellow liquids. MS 159 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 0.95 (3H, *t*, J=7.3 Hz, $\underline{CH_3}CH_2CH_2CH_2$), 1.40-1.70 (4H, *m*, $CH_3\underline{CH_2}\underline{CH_2}CH_2$), 2.43 (2H, *t*, J=6.9 Hz, $CH_3CH_2CH_2\underline{CH_2}$), 7.24 (2H, *d*, J=6.3 Hz, pyridine-H), 8.52 (2H, *d*, J=6.3 Hz, pyridine-H).

3-(4-Pyridinyl)-2-propyn-1-ol[20] : Milky white solids. Mp 119-120 °C. MS 133 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 2.31 (1H, *t*, J=5.2 Hz, OH), 4.52 (2H, *d*, J=5.2 Hz, CH_2), 7.29 (2H, *d*, J=5.8 Hz, pyridine-H), 8.57 (2H, *d*, J=5.8 Hz, pyridine-H).

5-(Phenylethynyl)pyrimidine[12] : Dark brown liquids. MS 180 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 7.28-7.69 (5H, *m*, phenyl-H), 8.85 (1H, *s*, pyrimidine-H), 9.13 (1H, *s*, pyrimidine-H).

2-(Phenylethynyl)quinoline[21] : Pale yellow solids. Mp 64-65 °C (lit.,[20] 66-67 °C). MS 229 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 7.35-7.43 (3H, *m*, phenyl-H), 7.56 (1H, *td*, J=7.8 Hz, 1.4 Hz, quinoline-H), 7.62 (1H, *d*, J=8.4 Hz, quinoline-H), 7.64-7.70 (2H, *m*, phenyl-H), 7.74 (1H, *td*, J=7.8 Hz, 1.4 Hz, quinoline-H), 7.81 (1H, *d*, J=7.8 Hz, quinoline-H), 8.14 (1H, *d*, J=7.8 Hz, quinoline-H), 8.15 (1H, *d*, J=8.4 Hz, quinoline-H).

2-(1-Hexynyl)quinoline[19,21] : Yellow liquids. MS 209 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 0.96 (3H, *t*, J=7.3 Hz, CH_3), 1.43-1.60 (2H, *m*, CH_2), 1.60-1.74 (2H, *m*, CH_2), 2.51 (2H, *t*, J=7.3 Hz, CH_2), 7.46 (1H, *d*, J=8.4 Hz, quinoline-H), 7.52 (1H, *t*, J=7.8 Hz, quinoline-H), 7.70 (1H, *dd*, J=8.4 Hz, 7.8 Hz, quinoline-H), 7.77 (1H, *d*, J=7.8 Hz, quinoline-H), 8.08 (2H, *d*, J=8.4 Hz, quinoline-H).

3-(2-Quinolinyl)-2-propyn-1-ol[21] : Brown solids. Mp 82-84 °C (lit.,[20] 86-87 °C). MS 183 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 2.97 (1H, *brs*, OH), 4.61 (2H, *s*, CH_2), 7.50 (1H, *d*, J=8.5 Hz, quinoline-H), 7.55 (1H, *t*, J=8.4 Hz, quinoline-H), 7.73 (1H, *t*, J=8.4 Hz, quinoline-H), 7.80 (1H, *d*, J=8.4 Hz, quinoline-H), 8.09 (1H, *d*, J=8.4 Hz, quinoline-H), 8.13 (1H, *d*, J=8.5 Hz, quinoline-H).

3-(Phenylethynyl)quinoline[12] : Pale brown liquids. MS 229 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 7.27-7.90 (8H, *m*, phenyl- and quinoline-H), 8.11 (1H, *d*, J=8.3 Hz, quinoline-H), 8.30 (1H, *d*, J=1.9 Hz, quinoline-H),

9.00 (1H, *d*, J=1.9 Hz, quinoline-H).

4-(Phenylethynyl)quinoline[21] : Yellow oil. MS 229 (M^+). ^{1}H-NMR (90 MHz, in $CDCl_3$) ppm : 7.30-7.90 (8H, *m*, phenyl- and quinolinyl-H), 8.13 (1H, *dd*, J=7.3 Hz, 2.2 Hz, quinolinyl-H), 8.36 (1H, *dd*, J=7.3 Hz, 2.2 Hz, quinolinyl-H), 8.89 (1H, *d*, J=4.6 Hz, quinolinyl-H).

4-(1-Hexynyl)quinoline[21] and 4-iodoquinoline (an inseparable mixture): Pale yellow solids with oil. MS 255 (M^+) and 209 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 1.00 (3H, *t*, J=7.3 Hz, $\underline{CH_3}CH_2CH_2CH_2$), 1.48-1.78 (4H, *m*, $CH_3\underline{CH_2}\underline{CH_2}CH_2$), 2.60 (2H, *t*, J=7.3 Hz, $CH_3CH_2CH_2\underline{CH_2}$), 7.43 (1H, *d*, J=4.6 Hz, product-H), 7.55-7.80 (*m*, product and substrate-H), 7.98-8.13 (*m*, product and substrate-H), 8.27 (1H, *d*, J=7.3 Hz, product-H), 8.46 (0.69H, *d*, J=4.6 Hz, substrate-H), 8.83 (1H, *d*, J=4.6 Hz, product-H).

3-(4-Quinolinyl)-2-propyn-1-ol[21] : Pale orange solids. Mp 142-143 °C (dec.) (lit.,[20] 142-144 °C). MS 183 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 2.66 (1H, *brs*, OH), 4.69 (2H, *s*, CH_2), 7.46 (1H, *d*, J=4.6 Hz, quinoline-H), 7.59 (1H, *t*, J=8.1 Hz, quinoline-H), 7.74 (1H, *t*, J=8.1 Hz, quinoline-H), 8.13 (1H, *d*, J=8.1 Hz, quinoline-H), 8.24 (1H, *d*, J=8.1 Hz, quinoline-H), 8.86 (1H, *d*, J=4.6 Hz, quinoline-H).

2-Methyl-9-phenyl-6-(phenylethynyl)purine : White needles (recryst. from benzene). Mp 207-208 °C. MS 310 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 2.86 (3H, *s*, CH_3), 7.36-7.46 (3H, *m*, phenyl-H), 7.48-7.54 (1H, *m*, phenyl-H), 7.56-7.66 (2H, *m*, phenyl-H), 7.72-7.82 (4H, *m*, phenyl-H), 8.35 (1H, *s*, C^8-H). *Anal*. Calcd for $C_{20}H_{14}N_4$: C, 77.40; H, 4.55; N, 18.05. Found: C, 77.23; H, 4.54; N, 18.03.

6-(1-Hexynyl)-2-methyl-9-phenylpurine : Pale brown needles (recryst. from petroleum benzin). Mp 107-108 °C. MS 290 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 0.96 (3H, *t*, J=7.3 Hz, $\underline{CH_3}CH_2CH_2CH_2$), 1.53 (2H, *sextet*, J=7.3 Hz, $CH_3\underline{CH_2}CH_2CH_2$), 1.73 (2H, *quintet*, J=7.3 Hz, $CH_3CH_2\underline{CH_2}CH_2$), 2.62 (2H, *t*, J=7.3 Hz, $CH_3CH_2CH_2\underline{CH_2}$), 2.81 (3H, *s*, CH_3), 7.48 (1H, *t*, J=7.8 Hz, phenyl-H), 7.59 (2H, *t*, J=7.8 Hz, phenyl-H), 7.73 (2H, *d*, J=7.8 Hz, phenyl-H), 8.30 (1H, *s*, purine-H). *Anal*. Calcd for $C_{18}H_{18}N_4$: C, 74.46; H, 6.25; N, 19.30. Found: C, 74.40; H, 6.28; N, 19.17.

2-(Phenylethynyl)quinoxaline[22] : Yellow solids. MS 230 (M^+). Mp 65 °C (lit.,[21] 64-65 °C). ^{1}H-NMR ($CDCl_3$) ppm : 7.32-7.48 (3H, *m*, phenyl-H), 7.63-7.73 (2H, *m*, phenyl-H), 7.73-7.85 (2H, *m*, quinoxaline-H), 8.05-8.15 (2H, *m*, quinoxaline-H), 8.99 (1H, *s*, quinoxaline-H).

2-(1-Hexynyl)quinoxaline[23] : Yellow oil. MS 210 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 0.98 (3H, *t*, J=7.3 Hz, $\underline{CH_3}CH_2CH_2CH_2$), 1.45-1.60 (2H, *m*, $CH_3\underline{CH_2}CH_2CH_2$), 1.60-1.76 (2H, *m*, $CH_3CH_2\underline{CH_2}CH_2$), 2.55 (2H, *t*, J=7.3 Hz, $CH_3CH_2CH_2\underline{CH_2}$), 7.69-7.82 (2H, *m*, quinoxaline-H), 8.02-8.11 (2H, *m*, quinoxaline-H), 8.83 (1H, *s*, quinoxaline-H).

3-(2-Quinoxalinyl)-2-propyn-1-ol[24] : Pale brown solids. Mp 142 °C (lit.,[23] 140-141 °C). MS 184 (M^+). ^{1}H-NMR ($CDCl_3$) ppm : 2.34 (1H, *q*, J=6.1 Hz, OH), 4.63 (2H, *d*, J=6.1 Hz, CH_2), 7.73-7.87 (2H, *m*, quinoxaline-H), 8.02-8.17 (2H, *m*, quinoxaline-H), 8.90 (1H, *s*, quinoxaline-H).

REFERENCES

1. For a review of organic synthesis in water, see: C.-H. Li and T.-H. Chan, *Organic Reactions in Aqueous Media*, John Wiley & Sons: New York, 1997.
2. For a review of organic synthesis in water, see: P. A. Grieco, *Organic Synthesis in Water*, Blackie Academic and Professional: London, 1998.
3. L. Cassar, *J. Organomet.Chem.*, 1975, **93**, 253.
4. H. D. Dieck and F. R. Heck, *J. Organomet. Chem.*, 1975, **93**, 259.
5. K. Sonogashira, Y. Tohda, and N. Hagihara, *Tetrahedron Lett.*, 1975, **50**, 4467.
6. C. J. Walsh and B. K. Mandal, *J. Org. Chem.*, 1999, **64**, 6102.
7. S. Bhattacharya and S. Sengupta, *Tetrahedron Lett.*, 2004, **45**, 8733.
8. For a review of the reaction of heterocyclic compounds, see: G. Illuminati, *Adv. Heterocycl. Chem.*, 1964, **3**, 285.
9. For a review on reaction of heterocyclic compounds, see: R. G. Shepherd and J. L. Fedrick, *Adv. Heterocycl. Chem.*, 1965, **4**, 145.
10. H. Yamanaka, M. Shiraiwa, K. Edo, and T. Sakamoto, *Chem. Pharm. Bull.*, 1979, **27**, 270.
11. O. Sugimoto, M. Mori, K. Moriya, and K. Tanji, *Helv. Chim. Acta*, 2001, **84**, 1112.
12. U. S. Sorensen and E. Pombo-Villar, *Tetrahedron*, 2005, **61**, 2697.
13. P. Pierrat, P. C. Gros, and Y. Fort, *J. Comb. Chem.*, 2005, **7**, 879.
14. T. Tsuchiya, H. Sashida, and A. Konoshita, *Chem. Pharm. Bull.*, 1983, **31**, 4568.
15. N. Morita and S. I. Miller, *J. Org. Chem.*, 1977, **42**, 4245.
16. Z. Novak, A. Szabo, J. Repasi, and A. Kotschy, *J. Org. Chem.*, 2003, **68**, 3327.
17. L. S. Bleicher, N. D. P. Cosford, A. Herbaut, J. S. McCallum, and I. A. McDonald, *J. Org. Chem.*, 1998, **63**, 1109.
18. A. Elangovan, Y. Wang, and T. Ho, *Org. Lett.*, 2003, **5**, 1841.
19. M. Lautens and M. Yoshida, *J. Org. Chem.*, 2003, **68**, 762.
20. N. Kim, K. S. Kim, A. K. Gupta, and C. H. Oh, *Chem. Commun.*, 2004, 618.
21. H. Yamanaka, M. Shiraiwa, K. Edo, and T. Sakamoto, *Chem. Pharm. Bull.*, 1979, **27**, 270.
22. C. Iijima and E. Hayashi, *Yakugaku Zasshi*, 1988, **108**, 586.
23. M. Armengol and J. A. Joule, *J. Chem. Soc., Perkin Trans. 1*, 2001, 154.
24. M. Armengol and J. A. Joule, *J. Chem. Soc., Perkin Trans. 1*, 2001, 978.