# Gold-Catalyzed Cyclization of *N*-Alkynyl Carbamates

A. Stephen K. Hashmi,*[1] Ralph Salathé, Wolfgang Frey

Institut für Organische Chemie, Universität Stuttgart, Pfaffenwaldring 55, 70569 Stuttgart, Germany
Fax +49(711)68564330; E-mail: hashmi@hashmi.de

*Received 1 March 2007*

**Abstract:** Six different *N*-alkynyl carbamates containing Boc groups were prepared. Their gold(I)-catalyzed cyclization to oxazolinones proceeded radily at room temperature or even lower temperatures.

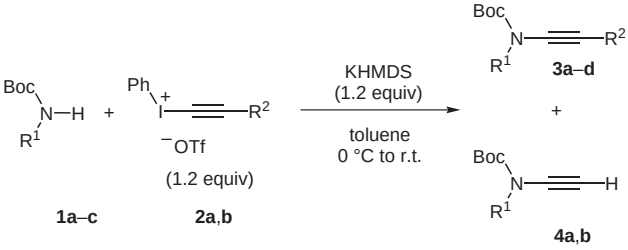
**Key words :** alkynes, carbamates, gold catalysis, iodonium salts, oxazolinones

Among gold-catalyzed reactions[2] the intramolecular oxyauration of C–C multiple bonds is an excellent tool for the formation of oxygen-containing heterocycles. The first example was the cycloisomerization of allenyl ketones or propargyl ketones,[3] similar results were obtained with 2-alkynyl-2-alken-1-ones.[4] Subsequently, the isomerization of *N*-propargylcarboxamides to oxazoles or even the rare alkylidene oxazolines was investigated.[5] Propargylic and homopropargylic trichloroacetimidates react analogously.[6] Carboxylates and *tert*-butyl carboxylates also react.[7] A study of the cyclization of *tert*-butyl allenoates showed that the *tert*-butyl group is eliminated and a butenolide is formed.[8] This principle was then extended to *tert*-butyl carbonates,[9] where for example a propargylic carbonate was shown to cyclize faster than a homopropargylic one.[9a] A similar behavior was reported for propargylic and homopropargylic *tert*-butyl carbamates.[9c,d]

We now wanted to investigate *N*-alkynylcarbamates as substrates, where instead of a 5-*exo*-*dig* or 6-*exo*-*dig*, a 5-*endo*-*dig* cyclization would lead to oxazolinones. To the best of our knowledge, so far only one reference has described the use of derivatives of alkynylamines in gold-catalyzed reactions.[10]

The synthesis of the substrates started from the Boc-protected amines **1**, using the phenyliodonium salts **2**,[11] the *tert*-butyl *N*-alkynylcarbamates **3** and **4** were obtained (Table 1). For the ynamine synthesis two acceptors are needed on the amine, the Boc group is either accompanied by a second Boc group, a Ts group, or a pivaloyl group. When the terminal position of the alkyne was occupied by the TMS group, partial desilylation was observed. Changing to the more robust TBDMS group avoided this problem. Overall, the yields of these substrates were not high, but still allowed the investigation of the cyclization of **3** and **4**.

**Table 1** Alkynyl Carbamates

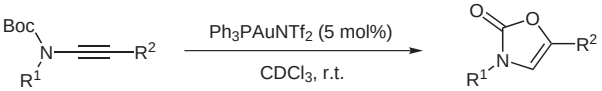



| Entry | Carbamate | Iodonium salt | Product | Yield (%) |
|---|---|---|---|---|
| 1 | **1a**; $R^1$ = Ts | **2a**; $R^2$ = TMS | **3a**/**4a** | 24/46 |
| 2 | **1b**; $R^1$ = Boc | **2a** | **4b** | 23[a] |
| 3 | **1b** | **2a** | **3b** | 51 |
| 4 | **1b** | **2b**; $R^2$ = TBDMS | **3c** | 27 |
| 5 | **1c**; $R^1$ = Piv | **2a** | **3d** | 27 |

[a] $Cs_2CO_3$ (1.3 equiv) instead of KHMDS; DMF instead of toluene.

Gold catalysis with Gagosz's catalyst[12] $[Ph_3PAu]NTf_2$ readily delivered the corresponding oxazolinones **5** in 65–93% yield. As shown in Table 2, the terminal (entries 1 and 3), the TMS (entries 2, 4, and 6), and the TBDMS (entry 5) carbamates all react well. With the combination Ts/Boc it was very clear that the Boc carbonyl oxygen atom is the more nucleophilic partner (entries 1 and 2), but in the combination Piv/Boc also a high selectivity towards

**Table 2** Gold-Catalyzed Oxazolinone Synthesis



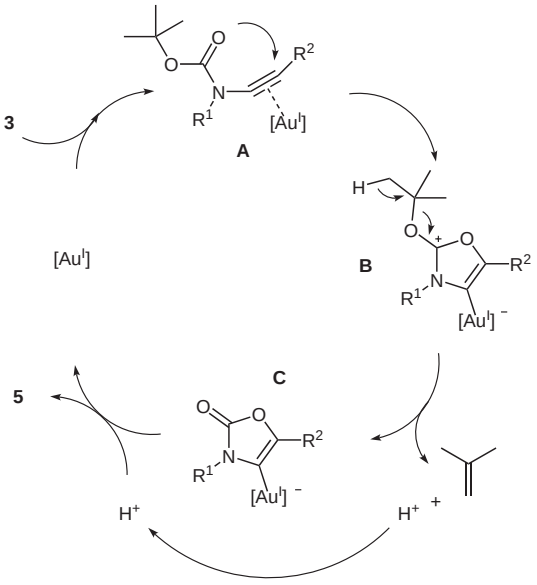

| Entry | Alkynyl carbamate | Product | Yield (%) |
|---|---|---|---|
| 1 | **4a**; $R^1$ = Ts,[a] $R^2$ = H | **5a** | 71 |
| 2 | **3a**; $R^1$ = Ts,[a] $R^2$ = TMS | **5b** | 67 |
| 3 | **4b**; $R^1$ = Boc, $R^2$ = H | **5c** | 65 |
| 4 | **3b**; $R^1$ = Boc, $R^2$ = TMS | **5d** | 90 |
| 5 | **3c**; $R^1$ = Boc, $R^2$ = TBDMS | **5e** | 93 |
| 6 | **3d**; $R^1$ = Piv, $R^2$ = TMS | **5f** | 87 |

[a] $C_2H_4Cl_2$ instead of $CDCl_3$, 0 °C.

***SYNLETT*** 2007, No. 11, pp 1763–1766
Advanced online publication: 25.06.2007
DOI: 10.1055/s-2007-982562; Art ID: Y00507ST

cyclization via the Boc carbonyl oxygen atom was observed, the less nucleophilic Piv carbonyl oxygen atom did not compete (entry 6).

Mechanistically, it is interesting to note that the nucleophilic oxygen atom reaches the distal position of the alkyne. A mechanistic proposal basing on the knowledge from the mechanistic investigation of reactions mentioned in the introduction is shown in Scheme 1. While in **3** the distance between the carbonyl oxygen atom and the distal alkyne carbon atom is relatively large, the coordination of the catalyst on the alkyne[13] should bend[14] the latter in the sense shown by both donation and back donation and thus reduce this distance (intermediate **A**).




**Scheme 1**

After the nucleophilc attack, intermediate **B** fragments and delivers **C**, isobutene and the proton, which is necessary for the final protodeauration step to set free the catalyst and produced product **5**.

**{[*tert*-Butyl(dimethyl)silyl]ethynyl}(phenyl)iodonium Trifluoromethanesulfonate (2b)**

Compound **2b** was synthesized in analogy to the corresponding TMS derivative.[15] A crystal structure analysis of the TBDMS derivative **2b** could be obtained (Figure 1).[16]

Yield 63%.

Mp 138 °C.

IR (neat): 2929, 2859, 1285, 1213, 1168, 985 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 0.17 (s, 6 H), 0.91 (s, 9 H), 7.51–7.56 (m, 2 H), 7.64–7.69 (m, 1 H), 8.06–8.09 (m, 2 H).

$^{13}$C NMR (126 MHz, $CDCl_3$): δ = 5.08 (q, 3 C), 16.93 (s), 26.00 (q, 2 C), 44.46 (s), 117.36 (s), 119.01 (s), 119.91 (q, *J* = 320 Hz, 1 C), 132.68 (d, 2 C), 132.79 (d), 133.95 (d, 2 C).

Anal. Calcd for $C_{15}H_{20}F_3IO_3SSi$: C, 36.59; H, 4.09. Found: C, 36.71; H, 4.12.

MS (ESI): *m*/*z* = 343 [M – OTf]$^+$.

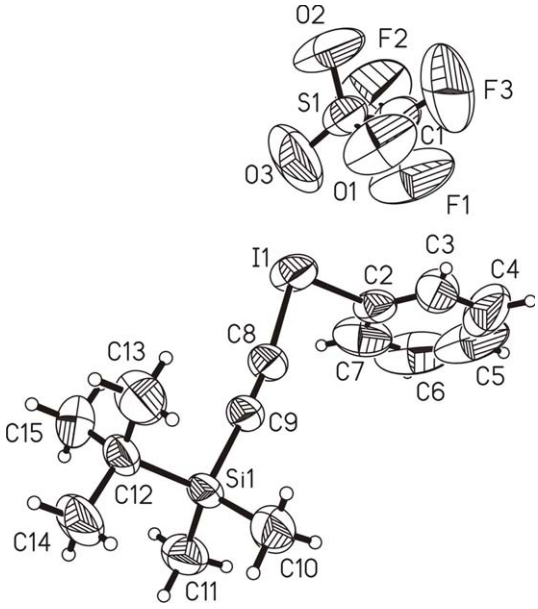



**Figure 1** Solid state structure of **2b**

**Representative Experimental Procedure for the Synthesis of Alkynyl Carbamates**

KHMDS (4.44 mL, 2.22 mmol) was added to a solution of carbamate **1b** (402 mg, 1.85 mmol) in 8 mL toluene under argon at 0 °C. The reaction mixture was allowed to warm to r.t. and trimethylsilylethynyl(phenyl)iodonium triflate (**2a**, 1.00 g, 2.22 mmol) was added. The mixture was stirred for 12 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (hexane–EtOAc–$Et_3N$) to yield the desired product **3b** (300 mg, 51%) as a white solid.

***tert*-Butyl (4-Methylphenyl)sulfonyl[(trimethylsilyl)ethynyl]carbamate (3a)**

Mp 60 °C.

IR (neat): 2959, 2172, 1744, 1381, 1244, 1143 cm$^{-1}$.

$^1$H NMR (300 MHz, $CD_2Cl_2$): δ = 0.20 (s, 9 H), 1.39 (s, 9 H), 2.44 (s, 3 H), 7.36 (d, *J* = 8.2 Hz, 2 H), 7.84 (d, *J* = 8.2 Hz, 2 H).

$^{13}$C NMR (126 MHz, $CD_2Cl_2$): δ = 0.00 (q, 3 C), 21.98 (q), 27.89 (q, 3 C), 79.82 (s), 86.78 (s), 88.78 (s), 128.97 (d, 2 C), 130.09 (d, 2 C), 135.40 (s), 146.50 (s), 149.49 (s).

MS (EI, 70 eV): *m*/*z* = 367 (2) [M$^+$], 267 (23), 155 (94), 91 (48), 57 (100).

Anal. Calcd for $C_{17}H_{25}NO_4SSi$: C, 55.55; H, 6.86; N, 3.81. Found: C, 55.77; H, 6.87; N, 3.68.

***tert*-Butyl Ethynyl[(4-methylphenyl)sulfonyl]carbamate (4a)**

IR (neat): 3281, 2934, 1751, 1371, 1142 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.41 (s, 9 H), 2.45 (s, 3 H), 3.19 (s, 1 H), 7.35 (d, *J* = 8.3 Hz, 2 H), 7.89 (d, *J* = 8.3 Hz, 2 H).

$^{13}$C NMR (126 MHz, $CDCl_3$): δ = 21.86 (q), 27.76 (q, 3 C), 65.19 (d), 69.84 (s), 86.75 (s), 128.65 (d, 2 C), 129.74 (d, 2 C), 134.99 (s), 145.93 (s), 149.12 (s).

MS (ESI): *m*/*z* = 318 [M + Na]$^+$ (100), 262 [M + Na – *t*-Bu]$^+$ (23).

HRMS (ESI): calcd for $C_{14}H_{17}NO_4S$: 318.0770 [M + Na]$^+$; found 318.0768 [M + Na]$^+$.

**Di-*tert*-butyl Ethynylimidodicarbonate (4b)**
IR (neat): 3276, 2981, 2360, 1808, 1768, 1347, 1242 $cm^{-1}$.

$^1H$ NMR (500 MHz, $C_6D_6$): δ = 1.33 (s, 18 H), 2.78 (s, 1 H).

$^{13}C$ NMR (126 MHz, $C_6D_6$): δ = 27.54 (q, 6 C), 62.86 (d), 72.42 (s), 84.17 (s, 2 C), 149.97 (s, 2 C).

MS (CI, 70 eV): *m*/*z* = 242 (10) [M + $NH_4^+$], 186 (35), 103 (32), 57 (100).

HRMS (CI): *m*/*z* calcd: 242.1392; found: 242.1391.

**Di-*tert*-butyl (Trimethylsilyl)ethynylimidodicarbonate (3b)**
Mp 30 °C.

IR (neat): 2981, 2195, 1811, 1774, 1370, 1248, 1137 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CD_2Cl_2$): δ = 0.16 (s, 9 H), 1.49 (s, 18 H).

$^{13}C$ NMR (126 MHz, $CD_2Cl_2$): δ = 0.00 (q, 3 C), 27.89 (q, 6 C), 76.61 (s), 84.93 (s, 2 C), 91.21 (s), 149.90 (s, 2 C).

MS (ESI): *m*/*z* = 336 [M + Na]$^+$, 236 [M + Na – Boc]$^+$.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{27}NO_4Si$: 336.1602 [M + Na]$^+$; found 336.1592 [M + Na]$^+$.

**Di-*tert*-butyl [*tert*-butyl(dimethyl)silyl]ethynylimidodicarbonate (3c)**
Mp 27 °C.

IR (neat): 2931, 2193, 1810, 1773, 1245, 1137 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CD_2Cl_2$): δ = 0.10 (s, 6 H), 0.93 (s, 9 H), 1.48 (s, 18 H).

$^{13}C$ NMR (126 MHz, $CD_2Cl_2$): δ = –4.38 (q, 2 C), 17.06 (s), 26.37 (q, 3 C), 28.05 (q, 6 C), 75.15 (s), 84.98 (s, 2 C), 91.58 (s), 149.95 (s, 2 C).

MS (ESI): *m*/*z* = 378 [M + Na]$^+$ (100), 278 [M + Na – Boc]$^+$ (21).

Anal. Calcd for $C_{18}H_{33}NO_4Si$: C, 60.81; H, 9.36; N, 3.89. Found: C, 60.73; H, 9.26; N, 3.84.

***tert*-Butyl 2,2-Dimethylpropanoyl[(trimethylsilyl)ethynyl]carbamate (3d)**
IR (neat): 2962, 2179, 1748, 1297, 1115 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CD_2Cl_2$): δ = 0.17 (s, 9 H), 1.36 (s, 9 H), 1.48 (s, 9 H).

$^{13}C$ NMR (62.9 MHz, $CD_2Cl_2$): δ = 0.00 (q, 3 C), 27.68 (q, 3 C), 28.01 (q, 3 C), 43.61 (s), 79.52 (s), 85.09 (s), 92.74 (s), 151.56 (s), 179.09 (s).

MS (ESI): *m*/*z* = 320 [M + Na]$^+$ (100), 224 [M + Na – TMSacetylene] (12).

HRMS (ESI): calcd for $C_{15}H_{27}NaNO_3Si$: 320.1652 [M + Na]$^+$; found 320.1643 [M + Na]$^+$.

**Representative Experimental Procedure for the Synthesis of Oxazolinones**
[$Ph_3PAuNTf_2$] (3.50 mg, 4.79 μmol) was added to **3d** (28.5 mg, 95.8 μmol) in 700 μL $CDCl_3$. The reaction was monitored by $^1H$ NMR spectroscopy. After the reaction was finished the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (hexane–EtOAc) to yield the desired product **5f** (20.0 mg, 87%) as a white solid.

**3-[(4-Methylphenyl)sulfonyl]-1,3-oxazol-2(3*H*)-one (5a)**
IR (neat): 3154, 2361, 1788, 1381, 1178 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CD_2Cl_2$): δ = 2.44 (s, 3 H), 6.76 (d, *J* = 2.3 Hz, 1 H), 7.05 (d, *J* = 2.3 Hz, 1 H), 7.39 (d, *J* = 8.7 Hz, 2 H), 7.91 (d, *J* = 8.7 Hz, 2 H).

$^{13}C$ NMR (126 MHz, $CD_2Cl_2$): δ = 21.93 (q), 113.86 (d), 128.80 (d, 2 C), 129.42 (d), 130.50 (d, 2 C), 133.45 (s), 147.37 (s), 150.24 (s).

MS (ESI): *m*/*z* = 262 [M + Na]$^+$ (100), 166 (2), 155 (2).

HRMS (ESI): calcd for $C_{10}H_9NO_4S$: [M + Na]$^+$ 262.0144; found [M + Na]$^+$ 262.0142 .

**3-[(4-Methylphenyl)sulfonyl]-5-(trimethylsilyl)-1,3-oxazol-2(3*H*)-one (5b)**
IR (neat): 2960, 2360, 1776, 1381, 1177 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CD_2Cl_2$): δ = 0.20 (s, 9 H), 2.44 (s, 3 H), 7.06 (s, 1 H), 7.39 (d, *J* = 8.3 Hz, 2 H), 7.91 (d, *J* = 8.3 Hz, 2 H).

$^{13}C$ NMR (126 MHz, $CDCl_3$): δ = –2.68 (q, 3 C), 21.84 (q), 120.06 (d), 128.62 (d, 2 C), 128.91 (s), 130.09 (d, 2 C), 133.29 (s), 146.50 (s), 152.19 (s).

MS (ESI): *m*/*z* = 334 [M + Na]$^+$, 262 [M + Na – TMS]$^+$.

HRMS (ESI): calcd for $C_{13}H_{17}NO_4SSi$: [M + Na]$^+$ 334.0540; found [M + Na]$^+$ 334.0533.

***tert*-Butyl 2-Oxo-1,3-oxazole-3(2*H*)-carboxylate (5c)**
Mp 84 °C.

IR (neat): 3162, 2980, 2359, 1807, 1371, 1254 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CD_2Cl_2$): δ = 1.55 (s, 9 H), 6.72 (d, *J* = 2.3 Hz, 1 H), 6.95 (d, *J* = 2.3 Hz, 1 H).

$^{13}C$ NMR (126 MHz, $CD_2Cl_2$): δ = 27.96 (q, 3 C), 85.91 (s), 113.50 (d), 128.46 (d), 146.98 (s), 150.53 (s).

MS (ESI): *m*/*z* = 208 [M + Na]$^+$, 152 [M + Na – *t*-Bu]$^+$.

HRMS (ESI): *m*/*z* calcd for $C_8H_{11}NO_4$: 208.0580 [M + Na]$^+$; found: 208.0586 [M + Na]$^+$.

***tert*-Butyl 2-Oxo-5-(trimethylsilyl)-1,3-oxazole-3(2*H*)-carboxylate (5d)**
Mp 80 °C.

IR (neat): 3126, 2957, 1772, 1747, 1337, 1252, 1100 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 0.24 (s, 9 H), 1.59 (s, 9 H), 6.96 (s, 1 H).

$^{13}C$ NMR (126 MHz, $CDCl_3$): δ = –2.66 (q, 3 C), 27.90 (q, 3 C), 85.44 (s), 120.22 (d), 144.04 (s), 146.84 (s), 152.62 (s).

MS (ESI): *m*/*z* = 280 [M + Na]$^+$ (100), 224 [M + Na – *t*-Bu]$^+$ (22), 180 [M + Na – Boc]$^+$ (32).

HRMS (ESI): calcd for $C_{11}H_{19}NO_4Si$: 280.0976 [M + Na]$^+$; found 280.0970 [M + Na]$^+$.

***tert*-Butyl 5-[*tert*-Butyl(dimethyl)silyl]-2-oxo-1,3-oxazole-3(2*H*)-carboxylate (5e)**
Mp 71 °C.

IR (neat): 3121, 2929, 1794, 1335, 1282, 1094 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 0.19 (s, 6 H), 0.94 (s, 9 H), 1.59 (s, 9 H), 6.98 (s, 1 H).

$^{13}C$ NMR (126 MHz, $CDCl_3$): δ = –7.03 (q, 2 C), 16.59 (s), 26.28 (q, 3 C), 28.02 (q, 3 C), 85.63 (s), 121.41 (d), 142.94 (s), 146.97 (s), 152.71 (s).

MS (ESI): *m*/*z* = 322 [M + Na]$^+$ (58), 266 [M + Na – *t*-Bu]$^+$ (44), 222 [M + Na – Boc]$^+$ (100).

HRMS (ESI): calcd for $C_{14}H_{25}NO_4Si$: 322.1445 [M + Na]$^+$; found 322.1443 [M + Na]$^+$.

**3-(2,2-Dimethylpropanoyl)-5-(trimethylsilyl)-1,3-oxazol-2(3*H*)-one (5f)**
IR (neat): 3281, 2982, 2144, 1751, 1371, 1252, 1142 $cm^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 0.27 (s, 9 H), 1.38 (s, 9 H), 7.07 (s, 1 H).

$^{13}$C NMR (126 MHz, $CDCl_3$): δ = –1.64 (q, 3 C), 28.80 (q, 3 C), 33.92 (s), 135.73 (d), 135.73 (s), 154.33 (s), 175.15 (s).

MS (EI, 70 eV): *m*/*z* = 242 (25) [M – $H^+$], 157 (11), 57 (100) [M – $H^+$ – *t*-Bu].

## Acknowledgment

We are grateful to the DFG and Umicore AG & Co. KG for their steady support of our research.

## References and Notes

(1) New address: A. S. K. Hashmi, Organisch-Chemisches Institut, Ruprecht-Karls-Universität Heidelberg, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany.
(2) Hashmi, A. S. K.; Hutchings, G. *Angew. Chem. Int. Ed.* **2006**, *45*, 7896; *Angew. Chem.* **2006**, *118*, 8064.
(3) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem. Int. Ed.* **2000**, *39*, 2285; *Angew. Chem.* **2000**, *112*, 2382.
(4) (a) Yao, T.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 11164. (b) Yao, T.; Zhang, X.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 7679.
(5) (a) Milton, M. D.; Inada, Y.; Nishibayashi, Y.; Uemura, S. *Chem. Commun.* **2004**, 2712. (b) Hashmi, A. S. K.; Weyrauch, J. P.; Frey, W.; Bats, J. W. *Org. Lett.* **2004**, *6*, 4391. (c) Dorsch, D.; Burgdorf, L. T.; Gericke, R.; Beier, N.; Mederski, W. WO 2005123688 A2, **2005**; *Chem. Abstr.* **2005**, *144*, 69837. (d) Hashmi, A. S. K.; Rudolph, M.; Schymura, S.; Visus, J.; Frey, W. *Eur. J. Org. Chem.* **2006**, 4905.
(6) (a) Kang, J.-E.; Kim, H.-B.; Lee, J.-W.; Shin, S. *Org. Lett.* **2006**, *8*, 3537. (b) Hashmi, A. S. K.; Rudolph, M.; Schymura, S.; Visus, J.; Frey, W. *Eur. J. Org. Chem.* **2006**, 4905.
(7) (a) Genin, E.; Tullec, P. Y.; Antoniotti, S.; Brancour, C.; Genêt, J.-P.; Michelet, V. *J. Am. Chem. Soc.* **2006**, *128*, 3112. (b) Shin, S. *Bull. Korean Chem. Soc.* **2005**, *26*, 1925. (c) Kang, J.-E.; Shin, S. *Synlett* **2006**, 717.
(8) Kang, J.-E.; Lee, E.-S.; Park, S.-I.; Shin, S. *Tetrahedron Lett.* **2005**, *46*, 7431.
(9) (a) Buzas, A.; Gagosz, F. *Org. Lett.* **2006**, *8*, 515. (b) Kang, J.-E.; Shin, S. *Synlett* **2006**, 717. (c) Buzas, A.; Gagosz, F. *Synlett* **2006**, 2727. (d) Robles-Machin, R.; Adrio, J.; Carretero, J. C. *J. Org. Chem.* **2006**, *71*, 5023.
(10) Couty, S.; Meyer, C.; Cossy, J. *Angew. Chem. Int. Ed.* **2006**, *118*, 6878.
(11) (a) Stengel, T.; Witulski, B. *Angew. Chem. Int. Ed.* **1998**, *37*, 489; *Angew. Chem.* **1998**, *110*, 495. (b) Alayrac, C.; Witulski, B. *Angew. Chem. Int. Ed.* **2002**, *41*, 3281; *Angew. Chem.* **2002**, *114*, 3415.
(12) Mezailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133.
(13) Hashmi, A. S. K. *Gold Bull.* **2004**, *37*, 51.
(14) (a) Dávila, R. M.; Staples, R. J.; Fackler, J. P. Jr. *Organometallics* **1994**, *13*, 418. (b) Schulte, P.; Behrens, U. *Chem. Commun.* **1998**, 1633.
(15) Kitamura, T.; Kotani, M.; Fujiwara, Y. *Synthesis* **1998**, 1416.
(16) CCDC 638182 (**2b**) contains the supplementary crystallographic data for this paper. These data can be obtained online free of charge [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336033; or deposit@ccdc.cam.ac.uk].