Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Organometallic Chemistry 687 (2003) 322–326
Journal of Organometallic Chemistry
www.elsevier.com/locate/jorganchem

Palladium catalyzed thiol cross-coupling of cystein derivatives with aryl and alkenyl halides

Xavier Moreau, Jean-Marc Campagne *

Institut de Chimie des Substances Naturelles, CNRS, Avenue de la Terrasse, 91198 Gif sur Yvette, France

Received 26 May 2003; received in revised form 25 June 2003; accepted 30 June 2003

Dedicated to the Professor Jean-Pierre Genêt on the occasion of his 60th birthday

Abstract

Palladium catalyzed cystein thiol cross-coupling reactions with aryl and vinyl halides have been investigated: Pd_2dba_3-$CHCl_3$ and dppf are the key choice in these reactions. The role of the base in these reactions was also questioned: it has been shown that base can be replaced by an HX-scavenger such as propylene oxide.

Keywords: Palladium; Scavenger; Methodology; Thiol

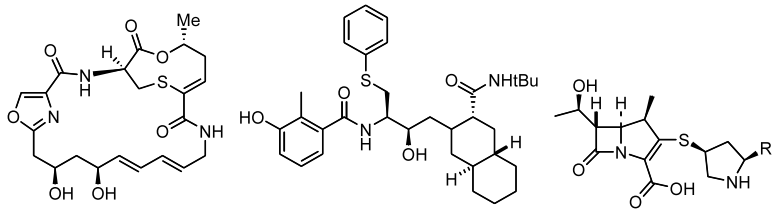
1. Introduction

Aryl and alkenyl sulfides are important building blocks present in a great number of natural and/or medicinal products (Scheme 1) and versatile reagents in organic synthesis [1]. However, in contrast to the corresponding amines or alcohols, the palladium catalyzed cross-coupling of thiols and aryl (vinyl) halides have received rather little attention in the literature [2–5]. During the course of an ongoing project towards the total synthesis of griseoviridin [6], we got interested in such methodology. In this paper, we would like to disclose and discuss the results of this study.

2. Results and discussion

The cross-coupling reaction of Boc-Cys-OEt with phenyl iodide was first investigated as a reaction model (Scheme 2).

The reaction proved to be tricky and highly sensitive to the choice of the catalytic system (Table 1, entries 1–



Scheme 1.

* Corresponding author. Tel.: +33-16-982-3091; fax: +33-16-907-7247.
E-mail address: jean-marc.campagne@icsn.cnrs-gif.fr (J.-M. Campagne).

0022-328X/03/$ - see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/S0022-328X(03)00635-1

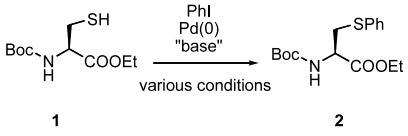
4). As previously noticed by Ortar and co-workers [3b] and Hartwig [2a], the combination of dppf with a preformed source of Pd(0) is crucial in these reactions. Other reaction conditions (Table 1, entries 1–3) lead to virtually no cross-coupling products. These conditions are however hampered by the need of the high boiling point solvent *N*-methylpyrrolidine (NMP) [3b]. Fortunately, this solvent could be efficiently replaced with acetone with no decrease (79%) in the reaction yield (Table 1, entry 5). When the same reaction conditions were applied to phenyl bromide, no cross-coupling product **2** could be isolated, highlighting the need of 'activated' substrates in these reactions.

While the precise mechanistic details of the thiol cross-coupling reaction are not firmly established [7], it is believed that the overall catalytic cycle is similar to those postulated for palladium catalyzed aminations and etherifications [2]. The role of triethylamine, crucial (see Table 1, entry 6) in these reactions, was thus questioned: Is it acting as a base (Scheme 3, path a) or as an HX-scavenger (Scheme 3, path b or c)?

In order to try to answer this question, the reaction was carried out in the presence of propylene oxide, a HX-scavenger (Table 1, entries 7–8). Indeed, the cross-coupling product **2** could be isolated in 47% yield (Table 1, entry 7). A larger excess (10 equivalents) of propylene oxide did not improve the yield of the reaction (Table 1, entry 8). Such a result highlights the possibility that path (b) or (c) could be relevant in the general mechanism of the palladium catalyzed thiol cross-coupling reactions.

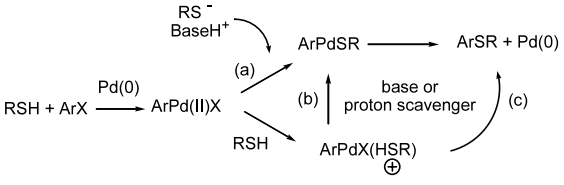
Gratifyingly, the optimized reaction conditions (acetone, Pd_2dba_3-$CHCl_3$, dppf and triethylamine) were successful in the cross-coupling reaction of protected cystein **1** with the protected *p*-iodo phenylalanine **3** leading to the pseudo-dipeptide **4** in 67% yield (Scheme 4).

In the light of the total synthesis of griseoviridin (Scheme 1), we then turned our attention to the cross-coupling reaction of Boc-Cys-OEt with various vinyl and alkynyl halides **5a**–**e** (Scheme 5).



1 2

Scheme 2.



Scheme 3.

Starting with model vinyl iodide **5a** (Table 2, entries 1–3), the reaction proved to be more demanding. Only reaction conditions using Pd_2dba_3-$CHCl_3$, dppf and triethylamine in NMP successfully led to the corresponding vinyl sulfide **6a**. Low yields, respectively 20 and 30%, were obtained when reactions were carried out in acetone or in the presence of propylene oxide (Table 2, entries 2–3). These reactions could then be used successfully (60% yield) with vinyl iodide **5b** (Table 2, entry 4), leading to **6b** a precursor of the macrocyclic thiolactone core of griseoviridin (Scheme 1). This methodology proved also to be efficient with β-bromo methyl methacrylate **5c**, leading to the cross-coupling vinyl sulfide **6c** in 74% yield. These reaction conditions seem to be however restricted to 'activated' vinyl halides. As previously observed with bromobenzene, when 'non-activated' vinyl iodide **5d** was used, a modest yield of 25% was obtained and no cross-coupling product was observed using alkynyl iodide **5e**.

In conclusion, we have shown that cystein thiol cross-coupling reactions with activated aryl and alkenylhalides are efficient processes to construct vinyl and aryl sulfides. The application of this methodology to the synthesis of macrocyclic aryl sulfide pseudo-peptides and griseoviridin are currently under intensive study in our laboratory.

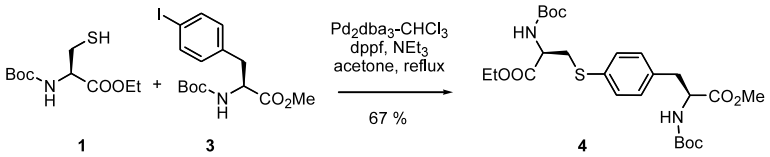
3. Experimental

Unless otherwise specified, the reactions were carried out in oven-dried glassware under an argon atmosphere. ^{1}H- and ^{13}C-NMR spectra were recorded at 300 and 75

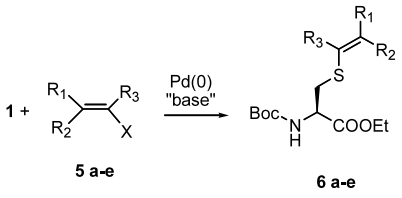
Table 1
Palladium catalyzed reactions of Boc-Cys-OEt with phenyl iodide

Entry	Pd catalyst	Base or additive	Solvent	Yield
1	$PdCl_2$dppf	NEt_3	NMP	NR
2	$PdCl_2$dppf	NEt_3	DMF	NR
3	Pd_2dba_3-$CHCl_3$ 	NEt_3	NMP	< 10%
4	Pd_2dba_3-$CHCl_3$ dppf	NEt_3	NMP	80%
5	Pd_2dba_3-$CHCl_3$ dppf	NEt_3	Acetone	79%
6	Pd_2dba_3-$CHCl_3$ dppf	--	Acetone	< 5%
7	Pd_2dba_3-$CHCl_3$ dppf	Propylene oxide (1.5 Eq.)	Acetone	47%
8	Pd_2dba_3-$CHCl_3$ dppf	Propylene oxide (10 Eq.)	Acetone	42%

a) for a typical procedure, see the experimental section.



Scheme 4.



Scheme 5.

MHz, respectively, or at 250 and 63 MHz, in $CDCl_3$ as solvent: chemical shifts are given in ppm. Column chromatography was performed on silica gel 230–400 mesh. THF was distilled from sodium/benzophenone. Dichloromethane and acetone were distilled over CaH_2 prior to use. NMP was degassed using argon bubbling. Elemental analyses were carried out by 'laboratoire de micro-analyse ICSN—Gif/Yvette'. IR spectra were recorded with an FTIR spectrometer. Mass spectra were recorded by Navigator LC/MS (source AQA) for electrospray ionisation. Optical rotations were determined operating at the sodium D line.

3.1. Typical reaction procedure for the preparation of aryl and vinyl sulfides

To a solution of aryl or vinyl halide (0.21 mmol), Pd_2dba_3-$CHCl_3$ (5.5 mg, 5.5 μmol) and dppf (12 mg, 21 μmol) in 1.6 ml of proper solvent (acetone or NMP, see Tables 1 and 2) was added triethylamine (60 μl, 0.42 mmol). The solution was stirred for 20 min at room temperature (r.t.) and then heated to 60 °C (or 70 °C). Boc-L-Cysteine ethyl ester (73 mg, 0.29 mmol) in 1 ml of solvent was added over 30 min. The mixture was stirred for an additional 2.5 h, cooled to r.t. and the solvent was evaporated under reduced pressure. Chromatography on silica gel (3/1 heptane/EtOAc) gave the desired product.

3.2. (2S)-2-tert-Butoxycarbonylamino-3-phenylsulfanyl)-propionic acid ethyl ester (**2**)

Compound **2** was obtained in 80% yield by using the typical procedure. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.20 (t, $J = 7.2$ Hz, 3H), 1.44 (s, 9H), 3.41 (bd, $J = 4.0$ Hz, 2H), 4.07 (q, $J = 7.2$ Hz, 2H), 4.57 (m, 1H), 5.39 (bd, 7.1 Hz, 1H), 7.23–7.44 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.0, 28.3 (3C), 37.2, 53.4, 61.6, 80.0, 126.9, 129.0 (2C), 130.9 (2C), 135.0, 154.7, 170.5; IR (KCl, cm^{-1}) ν 691, 742, 1025, 1165, 1368, 1500, 1716, 2979; MS (ESI) m/z 348 [M+Na$^+$], 292, 248; HRMS ES+ Calc. for $C_{16}H_{23}NO_4SNa$: 348.1245, Found: 348.1214. $[\alpha]_D = 40°$ ($c = 1.0$, $CHCl_3$).

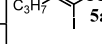
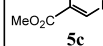
3.3. (2S)-2-tert-Butoxycarbonylamino-3-[4-((2S)-2-tert-butoxycarbonylamino-2-methoxycarbonyl-ethyl)-phenylsulfanyl]-propionic acid ethyl ester (**4**)

Compound **4** was obtained in 66% yield by using the typical procedure. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.18 (t, $J = 7.1$ Hz, 3H), 1.40 (s, 9H), 1.41 (s, 9H), 2.98 (dd, $J = 13.8$ Hz, $J = 6.0$ Hz, 1H), 3.07 (dd, $J = 13.8$ Hz, $J = 5.7$ Hz, 1H), 3.34 (bd, $J = 4.7$ Hz, 2H), 3.69 (s, 3H), 4.04 (q, $J = 7.1$ Hz, 2H), 4.51 (m, 2H), 4.95 (bd, $J = 7.8$ Hz, 1H), 5.33 (bd, $J = 7.6$ Hz, 1H), 7.02 (d, $J = 8.1$ Hz, 2H), 7.30 (d, $J = 8.1$ Hz, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.0, 28.3 (6C), 37.2, 37.7, 52.3, 53.2, 54.3, 61.6, 80.0 (2C), 129.9 (2C), 130.9 (2C), 133.6, 134.9, 155.0 (2C), 170.5, 172.1; IR (KCl, cm^{-1}) ν 756, 1020, 1055, 1166, 1367, 1497, 1714, 1745, 2929, 2978; MS (ESI) m/z 549 [M+Na$^+$]; HRMS ES+ Calc. for $C_{25}H_{38}N_2O_8SNa$: 550.2313, Found: 550.2325. $[\alpha]_D = 53°$ ($c = 1.0$, $CHCl_3$).

3.4. 2-Iodo-hex-2-enoic acid ethyl ester (**5a**)

According to the procedure described in Ref. [8], to a solution of triethylphosphonoacetate (200 μl, 1 mmol) in anhydrous THF (4 ml) were successively added NaH (60% dispersion in mineral oil) (88 mg, 2.2 mmol) and *N*-iodosuccinimide (300 mg, 1.3 mmol). The solution

Table 2
Palladium catalyzed reactions of Boc-Cys-OEt with various vinyl and alkynyl halides **5a**–**e**

Entry	vinylhalide	Conditions	Product	Yield
1	 **5a**	NMP 70° C, 3h NEt_3	**6a**	70%
2		Acetone reflux, 6h NEt_3		20%
3		NMP 70° C, 6h Propylene oxide		30%
4	 **5b**	NMP 70° C, 3h NEt_3	**6b**[b]	60%
5	 **5c**		**6c**	74%
6	**5d**		**6d**	25%
7	**5e**		**6e**	NR

a) for a typical procedure, see the experimental section.
b) This reaction was carried out with Z-Cys-OtBu

was stirred for an hour at r.t. and butyraldehyde (88 μl, 1 mmol) was added dropwise. Stirring was maintained for an additional 15 min and the solution was quenched with a saturated solution of ammonium chloride (1 ml). The mixture was filtered through silica gel (diethyl ether), the organic layer was washed with a saturated $Na_2S_2O_3$ solution, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. Chromatography on silica gel (30/1 heptane/ethyl acetate) gave **5a** (196 mg, 73% yield) as an inseparable *Z*/*E* mixture (80/20).

^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.94 (t, $J = 7.4$ Hz, 0.6H), 1.00 (t, $J = 7.3$ Hz, 2.4H), 1.34 (t, $J = 7.1$ Hz, 3H), 1.48 (m, 0.4H), 1.56 (m, 1.6H), 2.30 (q, $J = 7.2$ Hz, 1.6H), 2.44 (q, $J = 7.7$ Hz, 0.4H), 4.26 (q, $J = 7.1$ Hz, 0.4H), 4.27 (q, $J = 7.2$ Hz, 1.6H), 6.90 (t, $J = 7.7$ Hz, 0.2H), 7.21 (t, $J = 7.2$ Hz, 0.8H); ^{13}C-NMR ($CDCl_3$, 75 MHz) (*Z* isomer) δ 14.3, 14.6, 21.3, 39.4, 63.0, 95.7, 153.4, 163.3; (*E* isomer) δ 14.0, 14.5, 35.7, 62.5, 95.7, 156.3, 164.3; IR (KCl, cm^{-1}) *v* 668, 757, 1034, 1216, 1253, 1613, 1711, 2930; MS (EI) *m*/*z* 268 [$M^{+\bullet}$], 198, 67, 55, 53, 43, 41; Anal. Calc. for $C_8H_{13}IO_2$: C, 35.84; H, 4.89; Found: C, 36.01; H 4.94%.

3.5. 2-((2S)-2-tert-Butoxycarbonylamino-2-ethoxycarbonyl-ethylsulfanyl)-hex-2-enoic acid ethyl ester (**6a**)

Compound **6a** was obtained in 68% yield by using the typical procedure. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.92 (t, $J = 7.4$ Hz, 0.6H), 0.95 (t, $J = 7.3$ Hz, 2.4H), 1.22–1.38 (m, 8H), 1.44 (bs, 9H), 2.41 (m, 0.4H), 2.45 (m, 1.6H), 3.11 (bd, $J = 4.2$ Hz, 0.4H), 3.21 (bd, $J = 4.7$ Hz, 1.6H), 4.07–4.30 (m, 4H), 4.45 (m, 1H), 5.41 (bd, $J = 7.6$ Hz, 1H, NH), 6.51 (t, $J = 7.6$ Hz, 0.2H), 7.21 (t, $J = 7.4$ Hz, 0.8H); ^{13}C-NMR ($CDCl_3$, 75 MHz) (*Z* isomer) δ 13.9, 14.0, 14.2, 21.6, 28.2 (3C), 32.9, 35.8, 53.6, 61.3, 61.6, 79.9, 126.5, 152.3, 155.0, 164.9, 170.6; (*E* isomer) δ 13.8, 14.1, 14.1, 22.2, 28.1, 33.1, 35.8, 53.3, 61.3, 61.6, 79.9, 126.5, 150.2, 155.0, 164.9, 170.7; IR (KCl, cm^{-1}) *v* 756, 1165, 1369, 1499, 1712, 2360, 2981, 3400; ESI-MS *m*/*z* 412.2 [$M+Na^+$], 290.2; Anal. Calc. for $C_{18}H_{31}NO_6S$: C, 55.50; H, 8.02; N, 3.60; Found: C, 55.72; H, 8.24; N, 3.89%.

3.6. (5R)-2-Iodo-5-methoxymethoxy-hex-2-enoic acid ethyl ester (**5b**)

To a solution of (*R*)-3-hydroxy-butyric acid ethyl ester (500 μl, 3.78 mmol) in $CH_2(OCH_3)_2$ (10 ml) were added dropwise allyltrimethylsilane (720 μl, 4.54 mmol) and iodine (50 mg, 0.189 mmol). The mixture was stirred overnight at r.t. and poured into a saturated solution of $Na_2S_2O_3$. After extraction with diethyl ether, the organic layers were washed with brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude residue was taken up in CH_2Cl_2 (30 ml) and the solution was cooled to -78 °C. Dibal-H (1 mol l^{-1} in hexane) (4.6 ml) was added dropwise over 30 min. The mixture was stirred for 30 min, methanol (2 ml) was added dropwise and the solution was poured into 1 N HCl. After stirring for an additional 1 h at r.t., the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure to give crude aldehyde, which was used without further purification in the next step.

To a solution of triethylphosphonoacetate (750 μl, 3.78 mmol) in anhydrous THF (16 ml) were added NaH (60% dispersion in mineral oil) (335 mg, 7.56 mmol) and *N*-iodosuccinimide (1.1 g, 4.91 mmol). The solution was stirred for an hour at r.t. and crude aldehyde in CH_2Cl_2 (2 ml) was added dropwise. The stirring was maintained for 15 additional min and the solution was quenched with saturated solution of ammonium chloride (1 ml). The mixture was filtered over silica gel (diethyl ether), the organic layer was washed with a saturated solution of $Na_2S_2O_3$, dried with $MgSO_4$ and the solvent was evaporated under reduced pressure. Chromatography on silica gel (4/1 heptane/ethyl acetate) gave **5b** (750 mg, 60% yield over three steps) as an inseparable *Z*/*E* mixture (80/20). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.20 (d, $J = 6.2$ Hz, 0.6H), 1.25 (d, $J = 6.2$ Hz, 2.4H), 1.33 (t, $J = 7.1$ Hz, 3H), 2.53 ($\sim$t, $J = 6.5$ Hz, 1.6H), 2.69 ($\sim$t, $J = 6.8$ Hz, 0.4H), 3.39 (s, 3H), 3.83 ($\sim$sex, $J = 6.0$ Hz, 0.2H), 3.95 ($\sim$sex, $J = 6.1$ Hz, 0.8H), 4.26 (q, $J = 7.1$ Hz, 0.4H), 4.28 (q, $J = 7.1$ Hz, 1.6H), 4.62 (d, $J = 6.6$ Hz, 0.2H), 4.64 (d, $J = 7.0$ Hz, 0.8H), 4.69 (d, $J = 4.9$ Hz, 0.2H), 4.71 (d, $J = 7.0$ Hz, 0.8H), 7.03 (t, $J = 7.4$ Hz, 0.2H), 7.30 (t, $J = 6.8$ Hz, 0.8H); ^{13}C-NMR ($CDCl_3$, 75 MHz) (*Z* isomer) δ 14.6, 20.8, 44.6, 55.8, 63.0, 71.6, 86.8, 95.2, 149.9, 163.0; (*E* isomer) δ 14.5, 20.6, 40.6, 55.8, 62.6, 72.2, 88.0, 97.3, 152.8, 164.0; IR (KCl, cm^{-1}) *v* 741, 918, 1035, 1247, 1718, 2976; ESI-MS *m*/*z* 367 [$M+K^+$], 351 [$M+Na^+$], 329 [$M+H^+$], 253; Anal. Calc. for $C_{10}H_{17}IO_4$: C, 36.68; H, 5.28; Found: C, 36.60; H, 5.22%.

3.7. (5R)-2-((2S)2-Benzyloxycarbonylamino-2-tert-butoxycarbonyl-ethylsulfanyl)-5-hydroxy-hex-2-enoic acid ethyl ester (**6b**)

Compound **6b** was obtained in 63% yield by using the typical procedure. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.13 (bd, 6.3 Hz, 0.6H), 1.20 (bd, 2.4H), 1.23 (t, 7.1 Hz, 0.4H), 1.29 (t, 7.1 Hz, 1.6H), 1.46 (s, 9H), 2.47–2.64 (m, 1H), 2.73–2.84 (m, 1H), 3.02 (dd, 4.6 Hz, 13.2 Hz, 0.2H), 3.12 (dd, 4.8 Hz, 14.4 Hz, 0.8H), 3.27 (m, 0.2H), 3.32 (m, 0.8H), 3.31 (s, 2.4H), 3.36 (s, 0.6H), 3.79 (m, 0.2H), 3.85 (m, 0.8H), 4.22 (q, 7.1 Hz, 2H), 4.46 (m, 1H), 4.55 (bd, 6.7 Hz, 1H), 4.64 (bd, 6.7 Hz, 1H), 5.06 (bs, 2H), 5.64 (bd, 8 Hz, 0.2H), 5.8 (bd, 7.4 Hz, 0.8H), 6.54

(dt, 1.4 Hz, 7.4 Hz, 0.2H), 7.21 (bt, 7.2 Hz, 0.8H), 7.33 (bs, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) (*Z* isomer) 14.2, 20.3, 27.9 (3C), 35.6, 38.2, 55.1, 55.3, 61.6, 66.9, 71.7, 82.6, 94.6, 128.1 (3C), 128.3, 128.5 (2C), 136.3, 148.1, 155.6, 164.7, 169.2. (*E* isomer) 14.2, 20.4, 27.9 (3C), 35.7, 37.9, 55.1, 55.3, 61.4, 66.9, 72.6, 82.7, 95.0, 128.1 (3C), 128.3, 128.5 (2C), 136.3, 144.7, 155.6, 164.7, 169.2; IR (KCl, cm^{-1}) *v* 1037, 1154, 1247, 1506, 1718, 2339, 2360, 2933, 2977; ESI-MS *m/z* 550.3 [$M+K^+$], 534.3 [$M+Na^+$], 478.4; HRMS ES+ Calc. for $C_{25}H_{37}NO_8SNa$: 534, 2137 [M+Na]; Found: 534, 2163.

3.8. (2E)-3-((2S)-2-tert-Butoxycarbonyl-2-ethoxycarbonyl-ethylsulfanyl)-2-methyl-acrylic acid methyl ester (**6c**)

Compound **6c** was obtained in 74% yield by using the typical procedure. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.27 (t, $J=7.1$ Hz, 3H), 1.42 (s, 9H), 1.81 (s, 3H), 3.30 (m, 2H), 3.67 (s, 3H), 4.19 (q, $J=7.1$ Hz, 2H), 4.58 (m, 1H), 5.38 (bd, $J=6.9$ Hz, 1H), 7.33 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.8, 14.0, 28.2 (3C), 36.9, 51.6, 53.8, 62.0, 80.2, 123.6, 141.6, 154.6, 165.9, 169.9; IR (KCl, cm^{-1}) *v* 737, 1024, 1165, 1241, 1368, 1709, 1743, 2979; MS (ESI) *m/z* 370.1 [$M+Na^+$], 314, 270; m.p. 65–66 °C; Anal. Calc. for $C_{15}H_{25}NO_6S$: C, 51.86; H, 7.25; N, 4.03; Found: C, 52.37; H, 7.35; N, 3.49%; $[\alpha]_D=56^\circ$ ($c=0.44$, $CHCl_3$).

3.9. (2S)-2-tert-Butoxycarbonyl-3-oct-1-enylsulfanyl-propionic acid ethyl ester (**6d**)

Compound **6d** was obtained in yield by using the typical procedure. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.85 (m, 3H), 1.21–1.31 (m, 11H), 1.43 (s, 9H), 2.02 (m, 2H), 3.05 (bd, $J=4.5$ Hz, 2H), 4.18 (q, $J=7.1$ Hz, 2H), 4.52 (m, 1H), 5.32 (bd, $J=6.6$ Hz, 1H), 5.73 (td, $J=15.1$ Hz, $J=6.3$ Hz, 1H), 5.84 (d, $J=15.1$ Hz, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.0, 14.1, 22.6, 28.3, 28.8 (3C), 29.0, 31.6, 33.1, 35.7, 53.6, 61.6, 80.0, 121.7, 134.0, 155.0, 170.7; IR (KCl, cm^{-1}) *v* 1023, 1163, 1364, 1499, 1716, 1740, 2848, 2923, 2954; MS (ESI) *m/z* 382 [$M+Na^+$]; Anal. Calc. for $C_{18}H_{33}NO_4S$: C, 60.13; H, 9.25; N, 3.90; Found: C, 59.97; H, 9.24; N, 3.76%; $[\alpha]_D=21^\circ$ ($c=1.0$, $CHCl_3$).

Acknowledgements

We thank the CNRS for financial support and MENRT for a grant (X.M.).

References

[1] (a) P. Johannesson, G. Lindenberg, A. Johansson, G.V. Nikiforovich, A. Gogoll, B. Synnergren, M. Le Grèves, F. Nyberg, A. Karlén, A. Hallberg, J. Med. Chem. 45 (2002) 1767;
(b) J. Hynes, Jr., T. Nasser, L. Overmann, D.A. Watson, Org. Lett. 4 (2002) 929;
(c) H. Kuniyasu, H. Kurosawa, Chem. Eur. J. 8 (2002) 2661;
(d) N. Kuznik, S. Krompiec, T. Bieg, S. Baj, K. Skutil, A. Chrobok, J. Organomet. Chem. 665 (2003) 167;
(e) D.J. Procter, J. Chem. Soc. Perkin Trans. 1 (1999) 641;
(f) A. Ogawa, T. Ikeda, K. Kimura, T. Hirao, J. Am. Chem. Soc. 121 (1999) 5108.

[2] Reviews: (a) J.F. Hartwig, Acc. Chem. Res. 31 (1998) 852. (b) T. Kondo, T.-A. Mitsudo, Chem. Rev. 100 (2000) 3205. (c) D. Prim, J.M. Campagne, D. Joseph, B. Andrioletti, Tetrahedron 58 (2002) 2041.

[3] (a) M. Kosugi, T. Shimizu, T. Migita, Chem. Lett. (1978) 13;
(b) P.G. Ciattini, E. Morera, G. Ortar, Tetrahedron Lett. 36 (1995) 4133;
(c) I.W. Still, F.D. Toste, J. Org. Chem. 61 (1996) 7677;
(d) S. Rajagopalan, G. Radke, M. Evans, J.M. Tomich, Synth. Commun. 26 (1996) 1431;
(e) S. Wendeborn, S. Berteina, W.K.D. Brill, A. De Mesmaeker, Synlett (1998) 671;
(f) G.Y. Li, J. Org. Chem. 67 (2002) 3643.

[4] Copper catalyzed reactions: (a) P.S. Herradura, K.A. Pendola, R.K. Guy, Org. Lett. 2 (2000) 2019. (b) C.G. Bates, R.K. Gujadhur, D. Venkataraman, Org. Lett. 4 (2002) 2803. (c) F.Y. Kwong, S.L. Buchwald, Org. Lett. 4 (2002) 3517.

[5] Nickel catalyzed reactions: (a) H.J. Cristau, B. Chabaud, A. Chene, H. Christol, Synlett (1981) 892. (b) H.J. Cristau, B. Chabaud, R. Labaudinière, H. Christol, J. Org. Chem. 51 (1986) 875.

[6] For preliminary accounts, see: (a) C.J. Brennan, J.M. Campagne, Tetrahedron Lett. 42 (2001) 5195. (b) X. Moreau, J.M.J. Campagne, Org. Chem., in press.

[7] For a mechanistic study on the reductive elimination, see Ref. [2a].

[8] N.A. Braun, I. Klein, D. Spitzner, B. Vogler, S. Braun, H. Borrmann, A. Simon, Liebigs Ann. Org. Bioorg. Chem. (1995) 2165.