A Short Route to (±)-*N*-Hydroxylysine and (±)-Laminine by Palladium-Catalyzed Reactions

Jean Pierre Genet,* Serge Thorimbert, Sergio Mallart, Nathalie Kardos

Laboratoire de Synthèse organique, associé au CNRS; Ecole Nationale Supérieure de Chimie de Paris, 11 Rue Pierre et Marie Curie, F-75231 Paris, France

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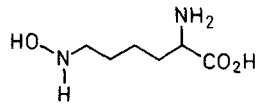
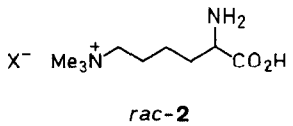
The title compounds were conveniently synthesized by efficient sequential one-pot amination–alkylation starting from (*Z*)-4-acetoxy-2-butenyl ethyl carbonate (**3**) with *tert*-butyl (*tert*-butoxycarbonyloxy)carbamate, dimethylamine and methyl (diphenylmethyleneamino) acetate. Hydrogenation and hydrolysis of the 1,4-adducts afforded N^6-hydroxylysine [2-amino-6-(hydroxyamino)hexanoic acid, **1**) and laminine hydrochloride [2-amino-6-(trimethylammonio)hexanoic acid chloride, **2**] in 65% and 39% yield, respectively.

Mycobactin T is one of the simplest members of the family of mycobactins that were discovered and characterized by Snow.[1] Mycobactins are potent chelators of ferric ion and are important in the study of iron metabolism. The two hydroxamate residues of the mycobactins are both derived from N^6-hydroxylysine **1**. A related *N*-substituted lysine, laminine **2**, is found in the algae extract and in the trypsin moysin-S1.[2]

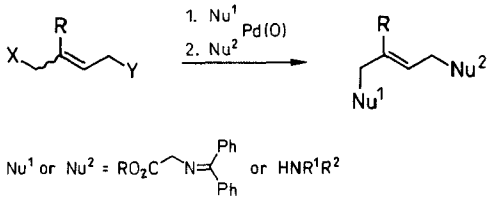


rac-**1**



rac-**2**

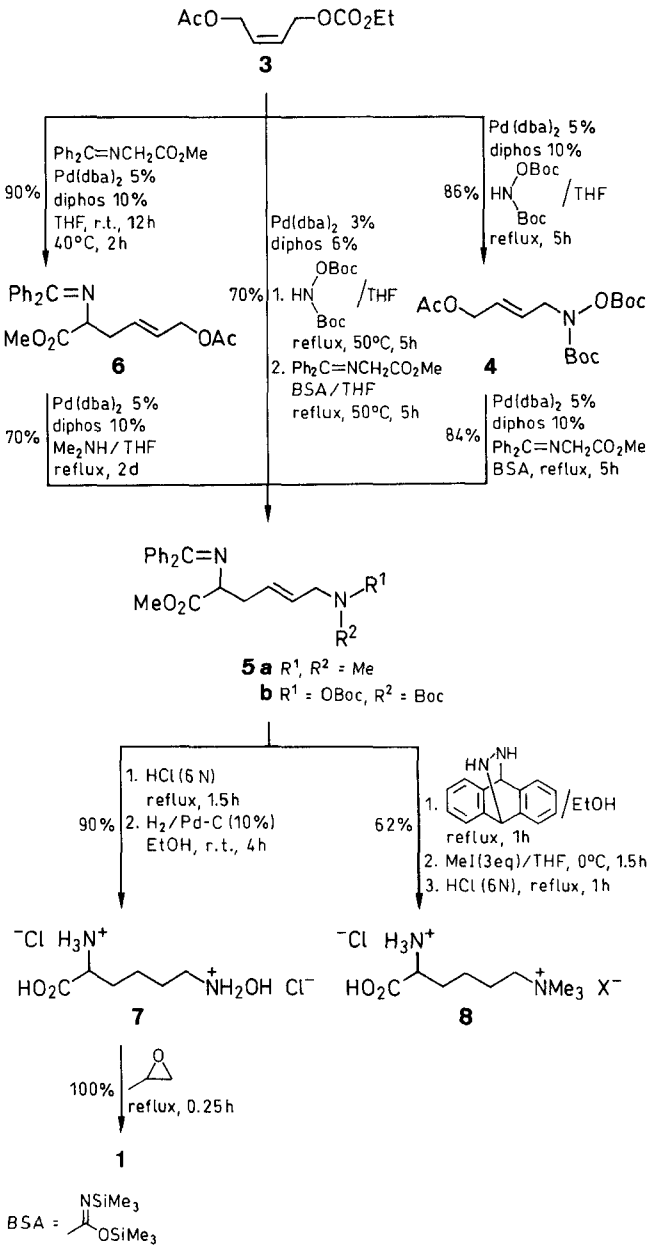
We reported the use of a new type of stabilized carbon nucleophiles in π-allyl chemistry, namely the anions derived from α-imino carboxylates[3] and phosphonic[4] esters. Our methodology for the elaboration of these naturally occurring N^6-substituted lysine derivatives is based on palladium-mediated functionalization of allylic 1,4-diol derivatives discovered by us[5] some years ago. The total regiocontrol for the formation of the new C–C or C–N bonds distal to the hydroxy and acetate groups is of great synthetic value.[6]



We can select the first substitution by using either the nitrogen nucleophile or the imino ester Schiff's base. This

paper presents the successful sequential palladium amination–alkylation and palladium alkylation–amination of (*Z*)-4-acetoxy-2-butenyl ethyl carbonate (**3**) to the fully functionalized hexenoates **5** and their conversion to (±)-N^6-hydroxylysine[1] **1** and (±)-laminine **2**.The preparation of **3** is accomplished in two steps from commercially available (*Z*)-2-butene-1,4-diol. The amination of **3** catalyzed by palladium(0) with *tert*-butyl (*tert*-butoxycarbonyloxy)carbamate[7] in tetrahydrofuran reflux, 5 hours provides (*E*)-4-acetoxy-*N*-*tert*-butoxycarbonyl-*N*-*tert*-butoxycarbonyloxy-2-butenylamine (**4**) in 86% yield.[8] The allylic substitution of **3** with methyl (diphenylmethyleneamino)acetate in the presence of palladium(0) catalyst in tetrahydrofuran leads to the formation of **6** in 90% yield.[8] These newly produced allylic acetates **4** and **6** in the presence of palladium(0) catalyst are selectively substituted with dimethylamine and methyl (diphenylmethyleneamino)acetate to give methyl (*E*)-6-(dimethylamino)-2-(diphenylmethyleneamino)-4-hexenoate (**5a**) and the corresponding 6-[(*tert*-butoxycarbonyl)(*tert*-butoxycarbonyloxy)amino] derivative **5b** in 70% and 84% yield, respectively. In addition, the latter alkylation has been conducted in a one-pot reaction in 70% yield. Simultaneous removal of methyl ester, diphenylmethyleneamino and *N*-*tert*-butoxycarbonyl groups from **5b** is accomplished by refluxing in hydrogen chloride (6N) for 1 hour. Hydrogenation over palladium-carbon in ethanol provides the (±) N^6-hydroxylysine dihydrochloride **7** from which by treatment in ethanol with propylene oxide (±)N^6-hydroxylysine **1** is obtained in 90% yield from **5**.[8] The hydrogenation reaction of imino derivative **5a** with 9,10-dihydro-9,10-biiminoanthracene[9] in dry ethanol at reflux followed by quaternization with three equivalents of methyl iodide at room temperature for 1.5 hours and hydrolysis with 6 M hydrogen chloride at reflux for 1 hour leads to (±)N^6-trimethyllysine hydrochloride **8**.

The above method demonstrates that the reaction is useful for regioselective C–C and C–N bond formation using palladium in both steps. Interestingly the usefulness is augmented by the fact that sequential amination and alkylation of **3** into **5** is also performed in a one-pot reaction.[10]



The following solvents were freshly distilled and stored under Ar prior to use: EtOH from Mg turnings. Et_2O and THF were distilled from sodium/benzophenone under Ar atmosphere. NaH was employed as a 60% dispersion in mineral oil, and weights are recorded for the dispersion. All palladium(0) were prepared in a flame-dried reactor by exchange of $Pd(dba)_2$[11] and phosphine in dry THF and transferred to the reaction mixture after 15–30 min under Ar. BSA [*N*,*O*-bis(trimethylsilyl)acetamide] and 1,2-bis(diphenylphosphino)-ethane (diphos) were purchased from Aldrich and Janssen respectively. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-250 or Bruker AM-200 Fourier transform spectrometers. Spectra were obtained in $CDCl_3$ or D_2O with TMS as an internal reference. IR spectra were recorded on a Perkin-Elmer 297 spectrometer. TLC were performed with commercial aluminum backed silica gel plates. Flash column chromatography was preformed using 230–400 mesh silica gel (E. Merck) or HP20SS (Mitsubishi Kasei Co).

(*Z*)-4-Acetoxy-2-buten-1-ol:
To a suspension of NaH (2.72 g, 68 mmol) in THF (100 mL) was added slowly (*Z*)-2-butene-1,4-diol (18.00 g, 3 eq). After 12 h at r.t. Ac_2O (7.00 g, 1 eq) was added and the solution stirred for 2 h. The solution was then poured into ice (50 mL) and the aqueous layer washed with CH_2Cl_2 (3 × 50 mL). The organic layer was dried ($MgSO_4$), filtered, evaporated and distilled under reduced pressure to yield the desired product and (*Z*)-1,4-diacetoxy-2-butene in 90:10 ratio. The mixture was chromatographed (cyclohexane/EtOAc, 3:7) to yield 4.70 g (50%) of the desired product.

^1H NMR ($CDCl_3$): δ = 5.75 (dtt, 1 H, J = 9.0, 6.6, 1.1 Hz), 5.52 (dtt, 1 H, J = 9.0, 6.7, 1.1 Hz), 4.58 (d, 1 H, J = 6.8 Hz), 4.15 (d, 2 H, J = 6.2 Hz), 3.25 (s, 1 H), 1.98 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 171.1 (OCOMe), 133.4 (=CHCH$_2$OH), 125.1 (=CHCH$_2$OAc), 60.1 (CH$_2$OAc), 58.0 (CH$_2$OH), 20.8 (Me).

IR ($CHCl_3$): ν = 3400, 3030, 2940, 1730, 1650, 1440, 1375 cm^{-1}.

(*Z*)-4-Acetoxy-2-butenyl Ethyl Carbonate (3):
(*Z*)-4-Acetoxy-2-buten-1-ol (4.00 g, 30 mmol) was solubilized in CH_2Cl_2 (30 mL) and the solution cooled to 0°C. Pyridine (2.72 mL, 1.1 eq) and ethyl chloroformate (3.23 mL, 1.1 eq) in CH_2Cl_2 (25 mL) were added to the mixture. The solution was then heated to 20°C (3 h) and hydrolyzed with H_2O (10 mL). The organic layer was washed with HCl 10% (3 × 5 mL) and brine (2 × 5 mL). The solution was dried ($MgSO_4$), filtered and the solvent removed under

reduced pressure. The clear oil was distilled to provide 6.00 g (99%) of the desired product as an colorless liquid. Eb_{14} = 130 °C.

^{1}H NMR ($CDCl_3$): δ = 5.64 (t, 2H, J = 4.2 Hz), 4.64 (d, 2H, J = 4.3 Hz), 5.59 (d, 2H, J = 4.3 Hz), 4.10 (q, 2H, J = 7.1 Hz), 1.97 (s, 3H), 1.21 (t, 3H, J = 7.0 Hz).

^{13}C NMR ($CDCl_3$): δ = 170.5 (OCOMe), 154.7 (OCOOEt), 128.4 (HC=CH), 64.0 (CH_2OAc), 62.9 (CH_2OCO_2Et), 59.6 (CH_3CH_2 OCO), 20.7 ($OCOCH_3$), 14.1 (CH_3CH_2).

IR ($CHCl_3$). ν = 3990, 1755, 1740, 1450, 1375 cm^{-1}.

(*E*)-1-Acetoxy-*N*-*tert*-butoxycarbonyl-*N*-*tert*-butoxycarbonyloxy-2-butenylamine (4):

To a solution of *tert*-butyl (*tert*-butoxycarbonyloxy) carbamate (2.33 g, 10 mmol) and **3** (2.02 g, 10 mmol) in THF (5 mL) was added a solution of $Pd(dba)_2$ (280 mg, 5 mol%) and diphos (400 mg, 10 mol%). The mixture was heated at reflux for 5 h. After evaporation of the solvent, the crude mixture was poured into Et_2O (40 mL), filtered, the solvent removed under reduced pressure and the crude oil chromatographed (cyclohexane/EtOAc, 8.5:2.5) to yield 3.00 g (86%) of **4** as a clear oil.

^{1}H NMR ($CDCl_3$): δ = 5.73 (m, 2H), 4.56 (m, 2H), 4.20 (m, 2H), 2.05 (s, 3H), 1.52 (s, 9H), 1.48 (s, 9H).

^{13}C NMR ($CDCl_3$): δ = 170.3 (OCOMe), 154.4 (NCO_2Bu-*t*), 152.0 (OCO_2Bu-*t*), 128.0, 127.7 (HC=CH), 84.5 [$OCO_2C(CH_3)_3$], 82.3 [$NCO_2C(CH_3)_3$], 63.7 (CH_2OAc), 51.4 (CH_2N), 27.8 [$NCO_2C(CH_3)_3$], 27.3 [$OCO_2C(CH_3)_3$], 20.6 (OCO_2CH_3).

IR ($CHCl_3$): ν = 2980, 1785, 1735, 1370, 1255, 1235 cm^{-1}.

Methyl (*E*)-6-[*tert*-Butoxycarbonyl)(*tert*-butoxycarbonyloxy)-amino]-2-(diphenylmethyleneamino)-4-hexenoate (5b):

To a solution of compound **4** (1.725 g, 5 mmol), BSA (1.015 g, 5 mmol) and methyl (diphenylmethyleneamino)acetate (1.26 g, 5 mmol) in THF (2.5 mL) was added a solution of $Pd(dba)_2$ (143.5 mg, 5 mol%) and diphos (199.2 mg, 10 mol%). The mixture was heated at reflux for 5 h. After evaporation of the solvent, the crude reaction mixture was chromatographed on silica gel cyclohexane/EtOAc, 8.5:2.5) as a clear yellow oil, 2.26 g (84%).

HRMS: m/z, $C_{28}H_{38}N_2O_7$, calc.: 523.2454; found: 523.244.

^{1}H NMR ($CDCl_3$): δ = 7.10–7.60 (m, 10H, H Ar), 5.56 (m, 2H), 4.14 (t, 1H, J = 7.4 Hz), 4.10 (m, 2H), 3.69 (s, 3H), 2.69 (m, 2H), 1.47 (s, 9H), 1.43 (s, 9H).

^{13}C NMR ($CDCl_3$): δ = 171.9 (CO_2Me), 170.6 (N=CPh_2), 154.5 (NCO_2Bu-*t*), 152.2 (OCO_2Bu-*t*), 139.4, 136.3, 130.4, 130.2, 128.7, 128.5, 128.4, 127.9, 127.7, 126.4 (C Ar, HC=CH), 84.3 [$NCO_2C(CH_3)_3$], 82.1 [$OCO_2C(CH_3)_3$], 65.1 ($NCHCO_2$Me), 52.0 (CO_2CH_3),51.8 ($CHCH_2N$), 36.5 (=$CHCH_2$CH), 27.9 [$NCO_2C(CH_3)_3$], 27.5 [$OCO_2C(CH_3)_3$].

IR ($CHCl_3$): ν = 3060–2980, 1785, 1740, 1720, 1625, 1595, 1580, 1450, 1280, 1260, 1235 cm^{-1}.

Compound 5b in a One-Pot Procedure:

To a solution of $Pd(dba)_2$ (17.2 mg, 3 mol%), diphos (23.8 mg, 6 mol%) and **3** (0.202 g, 1 mmol) in THF (0.5 mL) was added in one portion *tert*-butyl (*tert*-butoxycarbonyloxy)carbamate (233 mg, 1 mmol). The mixture was heated at 50 °C for 5 h. Then a solution of catalyst (3 mol%) and methyl(diphenylmethylenamino)acetate (253 mg, 1 mmol) in THF (0.5 mL) were added. The mixture was transferred to BSA (203 mg, 1 mmol) and heated at 50 °C for 5 h. After addition of aq NH_4Cl (2 mL), the solution was extracted with Et_2O (2 × 10 mL). The organic layer was washed with brine (2 × 2 mL) and then dried ($MgSO_4$). Evaporation of the solvent under reduced pressure followed by chromatography (cyclohexane/EtOAc, 1:9) yieled to 379 mg (70%) of the desired product **5b** as a clear oil.

Methyl (*E*)-6-Acetoxy-2-(diphenylmethyleneamino)-4-hexenoate (6):

To a solution of methyl(diphenylmethyleneamino)acetate (1.012 g, 4 mmol) and **3** (0.808 g, 4 mmol) in THF (4 mL) was added a solution of $Pd(dba)_2$ (114.8 mg, 5 mol%) and diphos (159.4 mg, 10 mol%) in THF (2 mL). The mixture was stirred overnight at r.t. and 2 h at 40 °C. After evaporation of the solvent, the crude mixture was poured into Et_2O (40 mL), filtered, the solvent removed under reduced pressure and the crude oil chromatographed (cyclohexane/EtOAc, 8.5:2.5) to yield 1.314 g (90%) of **6** as a clear oil.

^{1}H NMR ($CDCl_3$): δ = 7.80–7.10 (m, 10H, H Ar), 5.65 (m, 2H, H_{4-5}), 4.50 (dm, 2H, J = 5 Hz, H_6), 4.18 (t, 1H, J = 7 Hz, H_2), 3.75 (s, 3H, CO_2CH_3), 2.69 (m, 2H, H_3), 2.00 (s, 3H, $OCOCH_3$).

^{13}C NMR ($CDCl_3$): δ = 172.1 (CO_2Me), 170.9 (C=N), 170.7 (OCOMe), 139.4, 136.3, 131.5, 130.4, 128.9, 128.7, 128.5, 128.0, 127.1 (CAr, HC=CH), 65.0 ($NCHCO_2$Me), 64.7 (=$CHCH_2$OAc), 52.1 (CO_2CH_3), 36.5 (=$CHCH_2$CH), 20.8 ($OCOCH_3$).

IR ($CHCl_3$): ν = 3060–2900, 1740, 1660, 1620, 1600, 1560, 1440 cm^{-1}.

N^6-Hydroxylysine Dihydrochloride (7):

A solution of **5** (1.864 g, 3.46 mmol) in 6N HCl (25 mL) was heated at reflux for 1.5 h. The mixture was washed with Et_2O (3 × 15 mL) and evaporated under reduced pressure. The amorphous solid was poured into a solution of Pd–C (66 mg, 10 mol%) in EtOH (6.5 mL) and hydrogenated under H_2 atmosphere for 4 h at r.t. After filtration, the solvent was removed to yield 730 mg (90%) of **7** as an amorphous solid.

^{1}H NMR (D_2O): δ = 3.84 (t, 1H, J = 6.3 Hz), 3.04 (t, 2H, J = 7.6 Hz), 1.73 (m, 2H), 1.49 (m, 2H), 1.26 (m, 2H).

^{13}C NMR (D_2O): δ = 173.9 (C1), 54.7 (C2), 52.5 (C6), 31.4 (C3), 24.7 (C4), 23.7 (C5).

C.I.M.S. (NH_3): 163 ($MH^+ - 2HCl$, 20), 147 (100).

N^6-Hydroxylysine (1):

To a solution of compound **7** (732 mg, 3.13 mmol) in EtOH (24 mL) was added propylene oxide (12 mL). The solution was heated 15 min at reflux. The precipitate was filtered to yield 507 mg (100%) of **1** as a hygroscopic amorphous solid.

^{1}H NMR (D_2O): δ = 3.35 (t, 1H, J = 5.7 Hz), 2.86 (t, 2H, J = 7.3 Hz), 1.46 (m, 2H), 1.35 (m, 2H), 1.06 (m, 2H).

^{13}C NMR (D_2O): δ = 174.4 (Cl), 54.6 (C2), 50.6 (C6), 30.1 (C3), 22.8 (C4), 21.7 (C5).

IR (neat): ν = 3422, 3185, 3025, 1641, 1326 cm^{-1}.

CIMS (NH_3): m/z (%) = 163 (MH^+, 55), 147 (100), 128 (100).

Methyl (*E*)-6-(Dimethylamino)-2-(diphenylmethyleneamino)-4-hexenoate (5a):

To a solution of **6** (856 mg, 2.34 mmol) in THF (2 mL) was added a solution of $Pd(dba)_2$ (67 mg, 5 mol%) and diphos (92 mg, 10 mol%) in THF (1 mL) and a solution of Me_2NH 2.5 M in THF (9.2 mL, 23 mmol). The solution was warmed at reflux and monitored by TLC. After 2 d the mixture was cooled to r.t., concentrated in vacuo and poured into Et_2O (30 mL). After filtration, the solvent was removed under reduced pressure to give a brown oil which was purified by flash chromatography Et_2O/MeOH, (50:50) to provide 570 mg (70%) of **5a** as a pale yellow oil.

^{1}H NMR ($CDCl_3$): δ = 7.65–7.05 (m, 10H, H Ar), 5.55 (m, 2H, HC=CH), 4.15 (t, 1H, J = 6 Hz, H2), 3.70 (s, 3H, CO_2Me), 2.96 (d, 2H, J = 6 Hz, =$CHCH_2$CH), 2.65 (m, 2H, =$CHCH_2$N), 2.22 (m, 6H, NMe_2).

^{13}C NMR ($CDCl_3$): δ = 172.1 (CO_2Me), 170.5 (C=N), 139.3, 136.1, 130.9, 130.3, 128.7, 128.6, 128.4, 128.3, 128.0, 127.6 (C Ar, HC=CH), 65.2 ($NCHCO_2$Me), 60.7 (=$CHCH_2$N), 52.0 (CO_2CH_3), 43.8 (NMe_2), 36.7 (=$CHCH_2$CH).

IR ($CHCl_3$): ν = 3060–2800, 1740, 1620, 1600, 1580, 1440 cm^{-1}.

Laminine Hydrochloride:

To a solution of **5a** (473 mg, 1.35 mmol) in EtOH (5 mL) was added dropwise 9,10-dihydro-9,10-biiminoanthracene (2.5 g, 12.5 mmol). This heterogeneous solution was then heated 1 h at reflux. The mixture was filtered, the solvent removed under reduced pressure. Et_2O (3 mL) was added to the crude mixture and the solution filtered. After evaporation of the solvent, the brown oil was dissolved in THF (4 mL) and MeI (0.25 mL, 4 mmol) added at 0 °C. After 1.5 h at r.t., the solvent was removed and 6N HCl (5 mL) was added. The

mixture was heated at 100 °C for 1.5 h and the aqueous layer washed with Et_2O (3 × 10 mL). The solvent was removed under reduced pressure and the crude mixture purified by passage through a HP20SS resin column (H_2O) to yield **8** 300 mg (63 %) as a clear amorphous solid.

^1H NMR (D_2O): δ = 3.97 (t, 1 H, J = 12.6 Hz, H_2), 3.18 (t, 2 H, J = 7.3 Hz, H_6), 2.94 (s, 9 H, NMe_3), 1.86 (m, 2 H, H_3), 1.73 (m, 2 H, H_4), 1.33 (m, 2 H, H_5).

^{13}C NMR (D_2O): δ = 173.9 (C1), 68.2 (C6), 55.5 (NMe_3), 55.0 (C2), 31.5 (C3), 24.3 (C5), 23.6 (C4).

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(1) Snow, G.A. *Biochem. J.* **1965**, *97*, 166.
Snow, G.A. *Bacteriol. Rev.* **1970**, *34*, 99.
For synthesis of *N*-acetyl-*N*-hydroxylysine:
Maurer, P.J.; Miller, M.J. *J. Am. Chem. Soc.* **1982**, *104*, 3096.
Isowa, Y.; Ohmori, M. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2672.

(2) Bluden, G.; Gordon, S.; Keysell, G.R. *J. Nat. Prod.* **1982**, *45*, 449.
Mornet, D.; Pantel, R.; Bertrand, R.; Audemard, E.; Kassab, R. *FEBS Lett.* **1981**, *123*, 54.
Watanabe, K.; Matsunaga, S.; Konosu, S. *Tetrahedron Lett.* **1984**, *25*, 2003.

(3) Ferroud, D.; Genet, J.P.; Kiolle, R. *Tetrahedron Lett.* **1986**, *27*, 23.
Cazes, B.; Djahanbini, D.; Gore, J.; Genet, J.P.; Gaudin, J.M. *Synthesis* **1988**, 983.
Genet, J.P.; Ferroud, D.; Juge, S.; Montes, J. *Tetrahedron Lett.* **1986**, *27*, 4573.

(4) Genet, J.P.; Uziel, J.; Juge, S. *Tetrahedron Lett.* **1988**, *29*, 4559.
Genet, J.P.; Uziel, J.; Port, M.; Touzin, A.M.; Roland, S.; Thorimbert, S.; Tanier, S. *Tetrahedron Lett.* **1992**, *33*, 77.

(5) Genet, J.P.; Piau, F.; Ficini, J. *Tetrahedron Lett.* **1980**, *21*, 3183.
For some selected synthetic examples developed in our laboratory using this methodology see:
Genet, J.P.; Piau, F. *J. Org. Chem.* **1981**, *46*, 2414.
Genet, J.P.; Ferroud, D. *Tetrahedron Lett.* **1984**, *25*, 3579.
Genet, J.P.; Ferroud, D.; Gaudin, J.M. *Tetrahedron Lett.* **1986**, *27*, 845.
Genet, J.P.; Gaudin, J.M. Tetrahedron **1987**, *43*, *5315.*
For a recent use of 3-acetoxy-2-alkenyl alkyl carbonate see:
Schink, H.E.; Bäckvall, J.E. *J. Org. Chem.* **1992**, *57*, 1588.

(6) A similar palladium functionalization of 1,4-systems may be obtained by other methods (e.g. dienes monoepoxides, 1-acetoxy-4-chloroalkenes, 1-acetoxy-4-phosphatealkenes) see respectively:
Trost, B.M.; Molander, G.A. *J. Am. Chem. Soc.* **1981**, *103*, 5969;
Tsuji, J.; Kataoka, H.; Kobayashi, Y. *Tetrahedron Lett.* **1981**, *22*, 2575.
Bäckvall, J.E.; Nordberg, R.E.; Nyström, J.E. *Tetrahedron Lett.* **1982**, *23*, 1617.
Tanigawa, Y.; Nishimura, K.; Kawasaki, A.; Murahashi, S.-I. *Tetrahedron Lett.* **1992**, *52*, 5549.
For a recent review see:
Godleski, S.A. In *Comprehensive Organic Synthesis*; Trost, B.M., Ed., Pergamon: **1991**, vol. 4, p. 585.
For a review using allylic carbonates in allyl chemistry see:
Tsuji, J. *Tetrahedron* **1986**, *47*, 4361.

(7) Thorimbert, S. unpublished work: *tert*-butyl (*tert*-butoxycarbonyloxy)carbamate prepared according to:
Carpino, L.A.; Giza, C.A.; Carpino, B.A. *J. Am. Chem. Soc.* **1959**, *81*, 955.

(8) An alternative pathway to the synthesis of the intermediates **4**, **5**, **6** could be the palladium alkylation of the (*E*)-1-acetoxy-4-chloro-2-butene:
Bäckvall, J.E.; Nyström, J.E.; Nordberg, R.E. *J. Am. Chem. Soc.* **1985**, *107*, 3676;
(b) Bäckvall, J.E.; Byström, S.E.; Nyström, J.E. *Tetrahedron* **1985**, *41*, 5761.
However, the use of the (*Z*)-4-acetoxy-2-butenyl ethyl carbonate **(3)** is more convenient: the first allylic substitution is performed under neutral condition without preformation of the corresponding anions.

(9) Diels, O.; Schmidt, S.; Witte, W. *Chem. Ber.* **1938**, *71*, 1186.
Corey, E.J.; Mock, W.L. *J. Am. Chem. Soc.* **1962**, *84*, 685.

(10) For a successful one-pot sequential double allylic C–C substitution using palladium catalysis see:
Nyström, J.E.; Bäckvall, J.E. *J. Org. Chem.* **1983**, *48*, 3947.

(11) Rettig, M.F.; Maitlis, P.M. *Inorg. Synth.* **1977**, *17*, 135.