ISSN 1070-4280, Russian Journal of Organic Chemistry, 2013, Vol. 49, No. 12, pp. 1848–1850. © Pleiades Publishing, Ltd., 2013.
Original Russian Text © A.I. Moskalenko, V.I. Boev, 2013, published in Zhurnal Organicheskoi Khimii, 2013, Vol. 49, No. 12, pp. 1863–1865.

SHORT COMMUNICATIONS

Palladium-Catalyzed Reactions of Allyl Acetates with N-Substituted 4-Trimethylstannyl-1,2,3,6-tetrahydropyridines

A. I. Moskalenko[a] and V. I. Boev[b]

[a] *Lipetsk State Pedagogical University, ul. Lenina 42, Lipetsk, 398020 Russia*
e-mail: kaf_himii@lspu.lipetsk.ru

[b] *Russian State Agrarian University, Moscow, Russia*

Received June 21, 2013

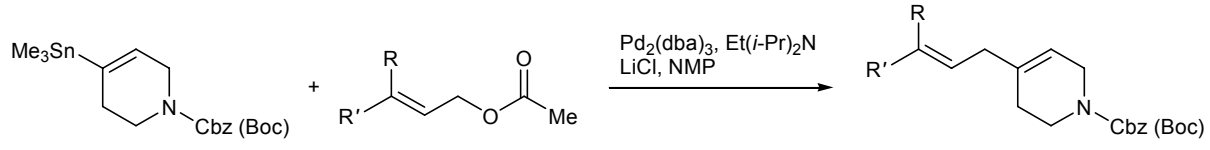
DOI: 10.1134/S1070428013120269

Palladium-catalyzed cross-coupling reactions are widely used in organic synthesis [1]. Diversity of reactants that could be involved in cross-coupling reactions ensures purposeful synthesis of organic molecules with a required structure. In the present communication we report on the reactions of previously obtained N-substituted 4-trimethylstannyl-1,2,3,6-tetrahydropyridines **I** and **II** [2] with a number of allyl acetates **III**–**VII**, including those containing natural alcohol residues (geraniol, nerol, and farnesol). The reactions were carried out according to modified procedures [3, 4] with the use of tris(dibenzylideneacetone)palladium(0) [$Pd_2(dba)_3$] [5], ethyl(diisopropyl)amine, and anhydrous lithium chloride as catalytic system in *N*-methylpyrrolidin-2-one (NMP) at 50–55°C. We thus isolated in high yields the corresponding N-protected (Cbz, Boc) 1,2,3,6-tetrahydropyridine derivatives **VIII**–**XIII** containing unsaturated hydrocarbon substituents in the 4-position, which attract interest as potential biologically active substances [6] and building blocks for organic synthesis (Scheme 1).

Compound **VIII** was oxidized at both endocyclic and exocyclic double bonds with 3-chloroperoxybenzoic acid in methylene chloride to produce a mixture of diastereoisomeric mono- and diepoxides **XIV** and **XV**. The Boc protection was readily removed from compound **XV** by treatment of the latter with trimethylsilyl trifluoromethanesulfonate, the epoxide rings being conserved, and the subsequent addition of acetic anhydride to the reaction mixture afforded the corresponding *N*-acetyl derivative **XVI** (Scheme 2).

1,2,3,6-Tetrahydropyridines VIII–XIII (*general procedure***).** To a mixture of 0.23 g (0.243 mmol) of $Pd_2(dba)_3$ and 0.42 g (9.9 mmol) of anhydrous lithium chloride we added under stirring in an argon atmosphere in succession 2.2 mmol of allyl acetate **III**–**VII** in 6 mL of *N*-methylpyrrolidin-2-one, 2.16 mmol of pyridine derivative **I** and **II** in 6 mL of NMP, and 0.75 mL (5 mmol) of ethyl(diisopropyl)amine. The resulting dark red mixture was stirred for 10 min, heated for 3–8 h at 50–55°C (TLC), cooled, and filtered through a thin layer of celite, the precipitate was washed on a filter with 60 mL of ethyl acetate, the filtrate was poured into 100 mL of a saturated solution of ammonium chloride, the mixture was stirred for 10 min, the organic layer was separated, and the aque-

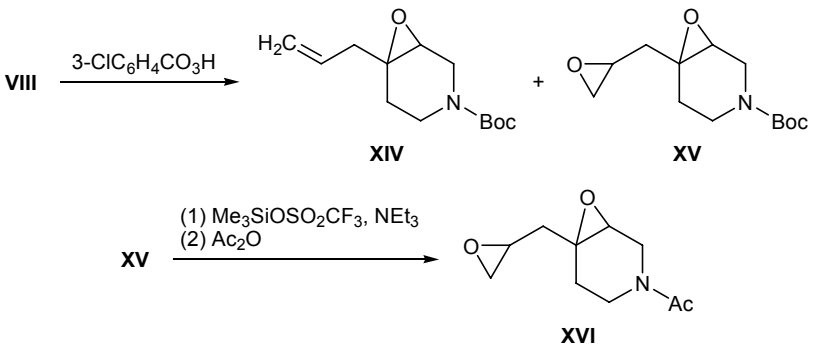
Scheme 1.



I, **II** **III**–**VII** **VIII**–**XIII**

I, **X**, **XII**, **XIII**, Cbz = $PhCH_2OC(O)$; **II**, **VIII**, **IX**, **XI**, Boc = *t*-BuOC(O); **II**, **VIII**, R = R′ = H; **IV**, **IX**, R = R′ = Me; **V**, **X**, **XI**, R = Me, R′ = (*E*)-$Me_2C{=}CHCH_2$; **VI**, **XII**, R = Me, R′ = (*Z*)-$Me_2C{=}CHCH_2$; **VII**, **XIII**, R = Me, R′ = (*E*,*E*)-$Me_2C{=}CHCH_2CH_2C(Me){=}CHCH_2$.

Scheme 2.



ous layer was extracted with ethyl acetate (2×50 mL). The extracts were combined with the organic phase, washed with two portions of water and with brine, and dried over sodium sulfate. The solvent was removed under reduced pressure, and the residue was subjected to column chromatography on silica gel using hexane–ethyl acetate (5:1 to 3:1) as eluent.

***tert*-Butyl 4-allyl-3,6-dihydropyridine-1(2*H*)-carboxylate (VIII).** Yield 79%, light yellow oily substance. IR spectrum, ν, cm^{-1}: 1686 (C=O), 1636, 1625 (C=C). ^{1}N NMR spectrum, δ, ppm: 1.48 s (9H, *t*-Bu), 2.02 s (2H, CH_2), 2.73 d (2H, CH_2C=, *J* = 8.3 Hz), 3.47 t (2H, NCH_2, *J* = 7.4 Hz), 3.83 s (2H, NCH_2), 5.02 d (2H, CH_2=C, *J* = 9.6 Hz), 5.31 s (1H, 5-H), 5.78 m (1H, CH=C). Mass spectrum, *m*/*z* (I_{rel}, %): 224.26 (100) $[M + H]^+$, 168.18 (23.4) $[M – 57 + 2H]^+$. Found, %: C 69.74; H 9.17; N 6.12. $C_{13}H_{21}NO_2$. Calculated, %: C 69.96; H 9.42; N 6.28. *M* 223.31.

***tert*-Butyl 4-(3-methylbut-2-en-1-yl)-3,6-dihydropyridine-1(2*H*)-carboxylate (IX).** Yield 83%, light yellow oily substance. IR spectrum, ν, cm^{-1}: 1685 (C=O), 1632, 1620 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.49 s (9H, *t*-Bu), 1.67 s (3H, CH_3), 1.72 s (3H, CH_3), 2.03 m (2H, CH_2), 2.71 m (2H, CH_2C=), 3.45 t (2H, NCH_2, *J* = 7.8 Hz), 3.82 s (2H, NCH_2), 5.30 s (1H, 5-H), 5.73 m (1H, CH=C). Mass spectrum, *m*/*z* (I_{rel}, %): 252.31 (5.2) $[M + H]^+$, 196.25 (100) $[M – 57 + 2H]^+$, 152.37 (18.4) $[M – 101 + 2H]^+$. Found, %: C 71.67; H 10.08; N 5.43. $C_{15}H_{25}NO_2$. Calculated, %: C 71.73; H 10.23; N 5.64. *M* 251.42.

Benzyl 4-[(2*E*)-3,7-dimethylocta-2,6-dien-1-yl]-3,6-dihydropyridine-1(2*H*)-carboxylate (X). Yield 76%, light yellow oily substance. IR spectrum, ν, cm^{-1}: 1694 (C=O), 1638, 1624 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.61 s (6H, CH_3), 1.72 s (3H, CH_3), 2.03 m (6H, CH_2), 2.70 d (2H, CH_2, *J* = 8.7 Hz), 3.56 t (2H, NCH_2, *J* = 7.5 Hz), 3.97 s (2H, NCH_2), 5.12 d (1H, CH=, *J* = 9.6 Hz), 5.17 m (3H, OCH_2, CH=), 5.36 s (1H, CH=), 7.27–7.37 m (5H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 354.11 (18.2) $[M + H]^+$, 310.21 (100) $[M – 44 + H]^+$, 218.18 (15.6) $[M – 136 + H]^+$. Found, %: C 78.02; H 8.57; N 4.03. $C_{23}H_{31}NO_2$. Calculated, %: C 78.15; H 8.85; N 4.12. *M* 353.24.

***tert*-Butyl 4-[(2*E*)-3,7-dimethylocta-2,6-dien-1-yl]-3,6-dihydropyridine-1(2*H*)-carboxylate (XI).** Yield 92%, light yellow oily substance. IR spectrum, ν, cm^{-1}: 1685 (C=O), 1636, 1628, 1617 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.48 s (9H, *t*-Bu), 1.62 s (6H, CH_3), 1.73 s (3H, CH_3), 1.98–2.05 m (6H, CH_2), 2.71 d (2H, CH_2, *J* = 8.8 Hz), 3.48 t (2H, NCH_2, *J* = 7.4 Hz), 3.85 s (2H, NCH_2), 5.08 t (1H, CH=, *J* = 9.2 Hz), 5.13 t (1H, CH=, *J* = 9.4 Hz), 5.34 s (1H, CH=). Mass spectrum, *m*/*z* (I_{rel}, %): 320.24 (36.7) $[M + H]^+$, 264.18 (100) $[M – 57 + 2H]^+$, 220.30 (58.8) $[M – 101 + 2H]^+$. Found, %: C 75.04; H 10.36; N 4.58. $C_{20}H_{33}NO_2$. Calculated, %: C 75.28; H 10.43; N 4.45. *M* 319.48.

Benzyl 4-[(2*Z*)-3,7-dimethylocta-2,6-dien-1-yl]-3,6-dihydropyridine-1(2*H*)-carboxylate (XII). Yield 76%, light yellow oily substance. IR spectrum, ν, cm^{-1}: 1695 (C=O), 1637, 1625 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.54 s (3H, CH_3), 1.58 s (3H, CH_3), 1.67 s (3H, CH_3), 2.05 m (6H, CH_2), 2.69 t (2H, CH_2, *J* = 7.8 Hz), 3.46 t (2H, NCH_2, *J* = 7.8 Hz), 3.81 s (2H, NCH_2), 5.05–5.17 m (4H, OCH_2, CH=), 5.31 s (1H, CH=), 7.24–7.46 m (5H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 354.28 (100) $[M + H]^+$, 310.32 (21.4) $[M – 44 + H]^+$. Found, %: C 77.96; H 8.63; N 3.84. $C_{23}H_{31}NO_2$. Calculated, %: C 78.02; H 8.85; N 4.12. *M* 353.24.

Benzyl 4-[(2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl]-3,6-dihydropyridine-1(2*H*)-carboxylate (XIII). Yield 89%, yellow oily substance. IR spectrum, ν, cm^{-1}: 1697 (C=O), 1643, 1631, 1624 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.50–1.68 m (12H, CH_3), 1.97–2.05 m (10H, CH_2), 2.62 d (2H, CH_2, *J* = 9.3 Hz), 3.47 t (2H, NCH_2, *J* = 7.6 Hz), 3.81 s (2H, NCH_2), 5.12 d (1H, CH=, *J* = 9.6 Hz), 5.01–5.12 m (5H,

OCH_2, CH=), 5.38 s (1H, CH=), 7.26–7.37 m (5H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 422.30 (100) $[M + H]^+$, 378.34 (12.4) $[M - 44 + H]^+$. Found, %: C 79.63; H 9.18; N 3.42. $C_{28}H_{39}NO_2$. Calculated, %: C 79.84; H 9.36; N 3.38. *M* 421.62.

***tert*-Butyl 6-allyl-7-oxa-3-azabicyclo[4.1.0]heptane-3-carboxylate (XIV) and *tert*-butyl 6-(oxiran-2-yl)methyl-7-oxa-3-azabicyclo[4.1.0]heptane-3-carboxylate (XV).** A mixture of 1.34 g (6 mmol) of compound **VIII** and 15 mL of anhydrous methylene chloride was cooled to 0°C, 2.58 g (15 mmol) of 3-chloroperoxybenzoic acid was added under stirring, and the mixture was stirred for 50 h at room temperature (until initial diene **VIII** disappeared). The mixture was filtered, the filtrate was washed with three portions of 7% aqueous potassium hydroxide and with water and dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel to isolate first monoepoxide **XIV** (eluent ethyl acetate–hexane, 1:5) and then diepoxide **XV** (ethyl acetate).

Compound **XIV**. Yield 23%, colorless oily substance. IR spectrum, ν, cm^{-1}: 1686 (C=O), 1628 (C=C), 873 (oxirane). ^1H NMR spectrum, δ, ppm: 1.48 s (9H, *t*-Bu), 1.78–1.91 m (2H, CH_2), 2.37 d (2H, H_2CC=, *J* = 8.1 Hz), 3.06 t (2H, NCH_2, *J* = 7.5 Hz), 3.48 m (1H, NCH), 3.58 d (1H, NCH, *J* = 7.8 Hz), 3.88 br.s (1H, OCH), 5.08–5.15 d (2H, CH_2=, *J* = 9.8 Hz), 5.73 m (1H, CH=). Mass spectrum, *m*/*z* (I_{rel}, %): 240.19 (88.4) $[M + H]^+$, 184.26 (100) $[M - 57 + 2H]^+$, 140.39 (52.3) $[M - 101 + 2H]^+$. Found, %: C 65.03; H 8.56; N 5.67. $C_{13}H_{21}NO_3$. Calculated, %: C 65.17; H 8.78; N 5.85. *M* 239.31.

Compound **XV**. Yield 37%, colorless thick oily substance. IR spectrum, ν, cm^{-1}: 1685 (C=O), 921, 870 (oxirane). ^1H NMR spectrum, δ, ppm: 1.48–1.52 m (9H, *t*-Bu), 1.71–2.05 m (4H, CH_2), 2.48 m (1H, CH), 2.75 m (1H, CH), 2.98–3.07 m (2H, NCH_2), 3.47–3.71 m (2H, NCH_2), 3.78–4.01 m (2H, OCH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 256.16 (18.4) $[M + H]^+$, 200.17 (25.2) $[M - 57 + 2H]^+$, 156.33 (100) $[M - 101 + 2H]^+$. Found, %: C 60.84; H 8.17; N 5.32. $C_{13}H_{21}NO_4$. Calculated, %: C 61.10; H 8.23; N 5.48. *M* 255.31.

1-[6-(Oxiran-2-ylmethyl)-7-oxa-3-azabicyclo-[4.1.0]hept-3-yl)ethanone (XVI). Trimethylsilyl trifluoromethanesulfonate, 1.33 g (6 mmol), was added dropwise to a mixture of 0.51 g (2 mmol) of compound **XV** and 0.41 g (4 mmol) of triethylamine in 6 mL of anhydrous methylene chloride, maintaining the temperature not higher than 20°C. The mixture was stirred for 25 h (TLC), 0.41 g of triethylamine in 6 mL of methylene chloride and 0.61 g (6 mmol) of acetic anhydride were added in succession, and the mixture was stirred for 3 h. It was then poured into 20 mL of a saturated aqueous solution of sodium hydrogen carbonate, the organic phase was separated, and the aqueous phase was extracted with 30 mL of methylene chloride. The extract was combined with the organic phase and dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was purified by chromatography on silica gel using ethyl acetate as eluent. Yield 0.26 g (66%), colorless thick oily substance which slowly crystallized. IR spectrum, ν, cm^{-1}: 1701 (C=O), 920, 867 (oxirane). ^1H NMR spectrum, δ, ppm: 1.70–2.08 m (7H, CH_2, CH_3), 2.51 m (1H, CH), 2.78 m (1H, CH), 2.96–3.04 m (2H, NCH_2), 3.45–3.69 m (2H, NCH_2), 3.81–4.03 m (2H, OCH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 198.31 (100) $[M + H]^+$. Found, %: C 60.73; H 7.41; N 6.95. $C_{10}H_{15}NO_3$. Calculated, %: C 60.84; H 7.60; N 7.10. *M* 197.24.

The IR spectra were recorded on a Specord 75 IR spectrometer from thin films. The ^1H NMR spectra were measured on a Varian Mercury Plus-400 spectrometer (400 MHz) from solutions in $CDCl_3$ (**VIII**, **IX**, **XI**, **XIV**–**XVI**) or DMCO-d_6 (**X**, **XI**, **XIII**); hexamethyldisiloxane was used as internal standard. The mass spectra (atmospheric pressure chemical ionization) were obtained on a Thermo Finnigan Surveyor MSQ instrument (USA).

REFERENCES

1. Tsuji, J., *Palladium Reagents and Catalysts. Innovations in Organic Synthesis*, Chichester: Wiley, 1995, p. 549.
2. Moskalenko, A.I. and Boev, V.I., *Russ. J. Gen. Chem*., 2013, vol. 83, p. 2347.
3. Valle, L.D., Stille, J.K., and Hegedus, L.S., *J. Org. Chem*., 1990, vol. 55, p. 3019.
4. Snyder, S.A. and Corey, E.J., *J. Am. Chem. Soc*., 2006, vol. 128, p. 740.
5. Ukai, T., Kawazura, H., Ishii, Y., Bonnet, J.J., and Ibers, J.A., *J. Organomet. Chem*., 1974, vol. 65, p. 253.
6. Buchheit, K., Gamses, R., Giger, R., Hoyer, D., Klein, F., Kloppner, E., Pfannkuche, H., and Mattes, H., *J. Med. Chem*., 1995, vol. 38, p. 2326.