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LETTERS TO THE EDITOR

Synthesis of *N*-Substituted 4-Trimethylstannyl-3,6-dihydro-2*H*-pyridines as Promising Synthons in the Preparative Chemistry of Piperidine

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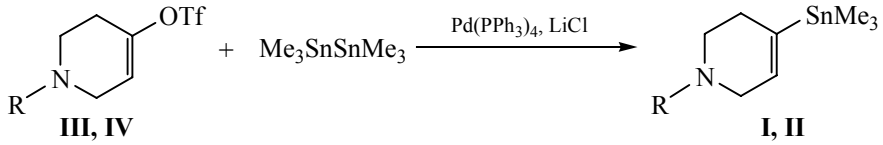
Piperidine derivatives are of interest due to a broad spectrum of their biological activity [1, 2].

In this work, we synthesized previously unknown piperidine derivatives, *N*-substituted 4-trimethylstannyl-3,6-dihydro-2*H*-pyridines **I** and **II** starting from preparatively available *tert*-butyl or benzyl 1,2,3,6-tetrahydro-4-[(trifluoromethyl)sulfonyl]pyridine-1-carboxylates **III**, **IV** [3]. The latter react with hexamethyldistannane in the presence of catalyst systems $Pd(PPh_3)_4$–anhydrous LiCl [4] under reflux in dioxane for 1.5 h to afford **I** and **II** as pale yellow oily substances in a yield of 80–90%.



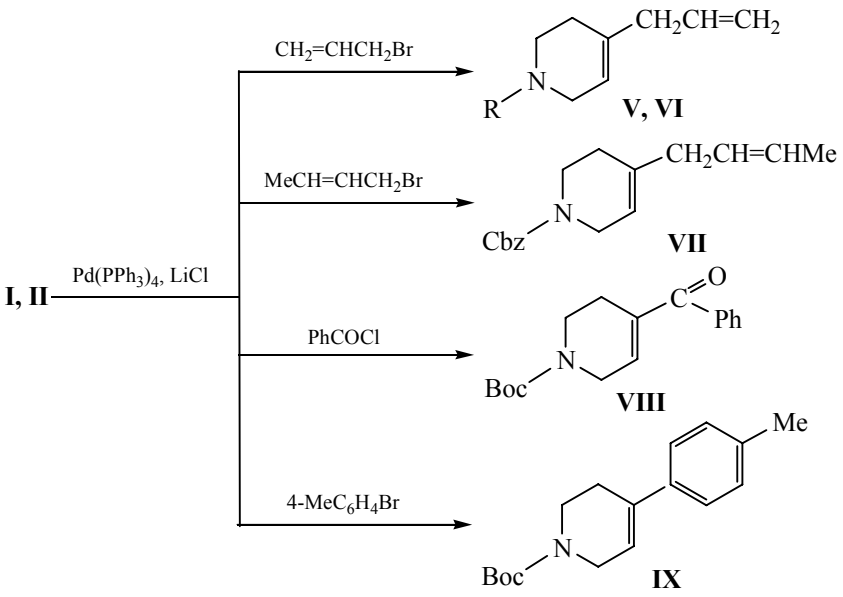
III, IV **I, II**

R = —C(=O)—O—CMe_3 (Boc, **I, III**); —C(=O)—O—CH_2Ph (Cbz, **II, IV**).

Organotin compounds are well known [5–7] to be widely used as convenient synthons for catalytic synthesis of various functionally substituted organic compounds. Indeed, we found that compounds **I**, **II** react with a range of electrophilic reagents in the Stille reaction conditions [8–10] to form the corresponding piperidine derivatives **V**–**IX** in 64–87% yields.

The synthesized compounds **V**–**IX** are highly reactive due to the presence of double bond and labile protecting groups, therefore they can be used in preparative molecular design of piperidine derivatives.

***tert*-Butyl 4-trimethylstannyl-3,6-dihydro-2*H*-pyridine-1-carboxylate (I).** A mixture of 6.34 g of **III** [3], 6.56 g of hexamethyldistannane, 2.52 g of anhydrous lithium chloride, and 1.20 g of tetrakis(triphenylphosphine)palladium in 75 mL of anhydrous dioxane was heated with stirring for 1.5 h under argon. After cooling, 200 mL of ethyl acetate and 200 mL of saturated aqueous sodium chloride solution were added to the mixture. Then the mixture was stirred for 0.5 h, after which the organic layer was separated. The aqueous layer was extracted with 150 mL of ethyl acetate. The combined organic solutions were washed with water, with saturated sodium chloride, and dried over anhydrous Na_2SO_4. After distilling off the solvent in a vacuum, the residue was purified by chromatography on silica gel eluting with ethyl acetate–hexane, 1 : 10. Yield 6.45 g (93%). IR spectrum, ν, cm^{-1}: 1686 (C=O), 1632 (C=C). ^1H NMR spectrum, δ, ppm: 0.10 s (9H, $SnMe_3$, J_{HSn} 27.64 Hz), 1.48 s (9H, CMe_3), 2.28 t (2H, CH_2, *J* 9.2 Hz), 3.41 t (2H, NCH_2, *J* 9.2 Hz), 3.89 d (2H, NCH_2, *J* 10.4 Hz), 5.78 t (1H, CH=C, *J* 10.4 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 347.13 (100) $[M + H]^+$.



R = Boc (**V**), Cbz (**VI**).

Found, %: C 45.23; H 7.18; N 3.96. $C_{13}H_{25}NO_2Sn$. Calculated, %: C 45.09; H 7.23; N 4.05. *M* 346.05.

Benzyl 4-trimethylstannyl-3,6-dihydro-2*H*-pyridine-1-carboxylate (II) was prepared similarly. Yield 81%. IR spectrum, ν, cm^{-1}: 1693 (C=O), 1635 (C=C). ^1H NMR spectrum, δ, ppm: 0.07 s (9H, $SnMe_3$, J_{HSn} 31.26 Hz), 2.21 s (2H, CH_2), 3.48 t (2H, NCH_2, *J* 8.6 Hz), 3.91 s (2H, NCH_2), 5.04 s (2H, OCH_2), 5.77 t (1H, CH=C, *J* 9.6 Hz), 7.26–7.38 m (5H, C_6H_5). Found, %: C 50.34; H 6.17; N 3.75. $C_{16}H_{23}NO_2Sn$. Calculated, %: C 50.53; H 6.05; N 3.68.

***tert*-Butyl 4-allyl-3,6-dihydro-2*H*-pyridine-1-carboxylate (V)** was prepared by procedure [10] using anhydrous dioxane as solvent. Yield 83%, pale yellow oil. IR spectrum, ν, cm^{-1}: 1685 (C=O), 1636, 1624 (C=C). ^1H NMR spectrum, δ, ppm: 1.48 s (9H, CMe_3), 2.01 s (2H, CH_2), 2.70 d (2H, CH_2C=C, *J* 6.7 Hz), 3.48 t (2H, NCH_2, *J* 8.4 Hz), 3.86 s (2H, NCH_2), 5.01 d (2H, CH_2=C, *J* 12.8 Hz), 5.31 s (1H, CH=CN), 5.76 m (1H, CH=C). Mass spectrum, *m*/*z* (I_{rel}, %): 224.26 (22) $[M + H]^+$, 168.33 (100) $[M - 57 + 2H]^+$. Found, %: C 69.87; H 9.31; N 6.15. $C_{13}H_{21}NO_2$. Calculated, %: C 69.96; H 9.42; N 6.28. *M* 223.31.

Benzyl 4-allyl-3,6-dihydro-2*H*-pyridine-1-carboxylate (VI) was prepared similarly to **V**. Yield 80%, colorless solid. IR spectrum, ν, cm^{-1}: 1695 (C=O), 1637, 1626 (C=C). ^1H NMR spectrum, δ, ppm: 2.01 s (2H, CH_2), 2.70 d (2H, CH_2C=C, *J* 6.2 Hz), 3.48 t (2H, NCH_2, *J* 7.9 Hz), 3.86 s (2H, NCH_2), 5.01 d (2H, CH_2=C, *J* 11.9 Hz), 5.05 s (2H, OCH_2), 5.38 s (1H, CH=CN), 5.75–5.79 m (1H, CH=C), 7.25–7.34 m (5H, C_6H_5). Mass spectrum, *m*/*z* (I_{rel}, %): 258.20 (100) $[M + H]^+$. Found, %: C 74.63; H 7.28; N 5.51. $C_{16}H_{19}NO_2$. Calculated, %: C 74.71; H 7.39; N 5.45. *M* 257.33.

Benzyl 4-[(*E*)-but-2-enyl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (VII) was prepared similarly to **V**. Yield 62%, pale yellow solid. IR spectrum, ν, cm^{-1}: 1695 (C=O), 1632, 1620 (C=C). ^1H NMR spectrum, δ, ppm: 1.61 d (3H, CH_3, *J* 11.0 Hz), 2.01 s (2H, CH_2), 2.68 d (2H, CH_2C=C, *J* 7.4 Hz), 3.48 t (2H, NCH_2, *J* 8.1 Hz), 3.81 d (2H, NCH_2, *J* 10.6 Hz), 5.01 s (2H, OCH_2), 5.04 t (1H, CH=CN, *J* 10.6 Hz), 5.32 t ($1H^a$, CH^a=CH^b, *J* 16.4 Hz), 5.72–5.77 m ($1H^b$, CH^a=CH^b, *J* 16.4 Hz), 7.25–7.38 m (5H, C_6H_5). Mass spectrum, *m*/*z* (I_{rel}, %): 272.23 (100) $[M + H]^+$. Found, %: C 75.09; H 7.63; N 5.24. $C_{17}H_{21}NO_2$. Calculated, %: C 75.28; H 7.75; N 5.17. *M* 271.35.

***tert*-Butyl 4-benzoyl-3,6-dihydro-2*H*-pyridine-1-carboxylate (VIII)** was prepared by procedure [8]. Yield 78%, pale yellow substance. IR spectrum, ν, cm^{-1}: 1702, 1686 (C=O), 1658 (C=C). ^1H NMR spectrum, δ, ppm: 1.49 s (9H, CMe_3), 2.02 s (2H, CH_2), 3.54 t (2H, NCH_2, *J* 6.7 Hz), 3.92 d (2H, NCH_2, *J* 8.5 Hz), 6.51 s (1H, CH=C), 7.46–7.74 m (5H, C_6H_5). Mass spectrum, *m*/*z* (I_{rel}, %): 288.32 (100) $[M + H]^+$. Found, %: C 70.56; H 7.18; N 4.73. $C_{17}H_{21}NO_3$. Calculated, %: C 70.83; H 7.32; N 4.88. *M* 287.41.

***tert*-Butyl-4-(*p*-tolyl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (IX)** was prepared by procedure [3]. Yield 81%, pale yellow substance. IR spectrum, ν, cm^{-1}: 1687 (C=O), 1618 (C=C). ^1H NMR spectrum, δ, ppm: 1.49 s (9H, CMe_3), 2.34 s (3H, CH_3), 2.50–2.54 m (2H, CH_2), 3.49–3.54 m (2H, NCH_2), 4.06 d (2H, NCH_2, *J* 7.6 Hz), 6.00–6.04 m (1H, CH=C), 7.18 d (2H, C_6H_2, *J* 8.2 Hz), 7.30 d (2H, C_6H_2, *J* 8.2 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 274.48 (100) $[M + H]^+$. Found, %: C 74.61; H 8.34; N 5.06. $C_{17}H_{23}NO_2$. Calculated, %: C 74.73; H 8.42; N 5.13. *M* 273.74.

IR spectra were recorded on a Specord 75 IR instrument from KBr pellets. ^1H NMR spectra were taken on a Varian Mercury Plus-400 spectrometer (400 MHz). GC-MS spectra were registered on a Surveyor MSQ Thermo Finnigan instrument (USA) by chemical ionization at atmospheric pressure.

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