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LETTERS TO THE EDITOR

Fe-Catalyzed Cross-Coupling of 3-Chloroprop-2-en-1-ylamines with *sec*-Butylmagnesium Bromide

R. N. Shakhmaev, A. Sh. Sunagatullina, and V. V. Zorin

Ufa State Petroleum Technological University, ul. Kosmonavtov 1, Ufa, 450062 Russia
e-mail: biochem@rusoil.net

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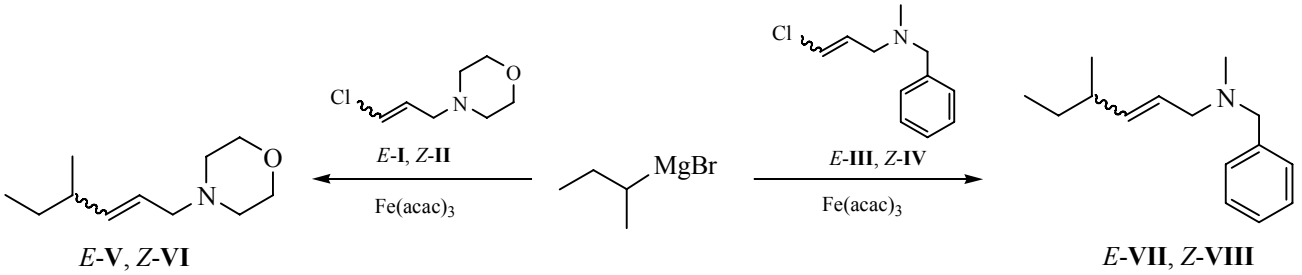
Pd- and Ni-catalyzed cross-coupling reaction of aryl(vinyl)halides with the Grignard reagents (Kumada–Tamao–Corriu reaction [1]) has limited synthetic use due to the low tolerance of many functional groups towards the highly reactive organomagnesium compounds. Recently, Fe-catalyzed cross-coupling reactions between alkylmagnesium halides and aryl(vinyl)halides, tosylates and triflates have been reported [2–8]. The doubtless advantages of Fe-catalyzed cross-coupling include high reaction rate, low toxicity, and the catalyst availability [9].

Allylamines are widespread in nature [10–12]; they attract attention of researchers because of their high synthetic potential [13–15] and the successful use in the drug design [16, 17].

In this work we investigated the possibility of stereoselective synthesis of allylamines via Fe-catalyzed cross-coupling of *sec*-butylmagnesium bromide and (*E*)/(*Z*)-3-chloroprop-2-en-1-ylamines. The latter were prepared by nucleophilic substitution of allylic chlorine atom with amines [18–20].

Reactions of *sec*-butylmagnesium bromide with stereochemically pure (*E*)- and (*Z*)-4-(3-chloroprop-2-en-1-yl)morpholines **I** and **II**, or (*E*)- and (*Z*)-*N*-benzyl-*N*-methyl-3-chloroprop-2-ene-1-ylamines **III** and **IV** proceeded in a tetrahydrofuran–*N*-methylpyrrolidone mixture in the presence of catalytic amounts of $Fe(acac)_3$ to form the corresponding isomers of 4-(4-methylhex-2-en-1-yl)morpholine **V** and **VI**, or *N*-benzyl-*N*,4-dimethylhex-2-en-1-ylamine **VII** and **VIII**. (*E*)-Allilamines **V** and **VII** were formed stereosspecifically (without changing the configuration of the substituents at the double bond) in high yields (86 and 88%, respectively). In the case of (*Z*)-allylamines **VI** and **VIII** some decrease in the yields (74 and 71%, respectively) and stereoselectivity (*Z* : *E* = 97 : 3 and 86 : 14, respectively) was observed. In the absence of $Fe(acac)_3$, the reaction did not occur. When $Pd(OAc)_2$

Scheme 1.



or $Pd(PPh_3)_4$ was used, the desired products were formed in yields of 4–15%, which was probably due to the low activity of vinylchlorides **I**–**IV** at the rate-limiting step of oxidative addition to Pd(0) [21]. Content of *N*-methylpyrrolidone (4–8 equiv) had a decisive influence on the efficiency of Fe-catalyzed cross-coupling reaction. In particular, increase or decrease in amount of *N*-methylpyrrolidone led to reduced yields of the allylamines (Scheme 1).

Structure, stereochemical purity, and configuration of the substituents at the double bond of the obtained compounds were confirmed by GC analysis, IR, NMR spectroscopy and GC–mass spectrometry. Reliable proof of the stereoconfiguration of the synthesized allylamines was downfield shifting the signals of allylic C-atoms of *trans*-allylamines by 4–6 ppm in comparison with the signals of the same carbon atoms of the corresponding *cis*-isomers [22].

4-[(2*E*)-4-Methylhex-2-en-1-yl]morpholine (V). 3.7 mL of 0.7 M solution of *sec*-BuMgBr in THF was added dropwise to a solution of 0.210 g (1.3 mmol) of 4-[(2*E*)-3-chloroprop-2-en-1-yl]morpholine **I** and 9.2 mg (2 mol%) $Fe(acac)_3$ in a mixture of 2 mL of THF and 0.8 mL of *N*-methylpyrrolidone at 0°C under argon. The mixture was stirred at room temperature during 1.5 h, and then poured into a mixture of 2 mL of water and 5 mL of diethyl ether. The organic layer was separated, and the aqueous layer was treated with diethyl ether (2 × 5 mL). The combined organic layers were washed with saturated NaCl, dried with Na_2SO_4, and concentrated. The reaction product was isolated by column chromatography (SiO_2, hexane–EtOAc, 9 : 1 → 3 : 1). Yield 0.205 g (86%), oil. IR spectrum, ν, cm^{-1}: 2959, 2926, 2853, 2805, 1454, 1119, 1005, 976, 868. ^1H NMR spectrum, δ, ppm: 0.85 t (3H, C^6H_3, *J* 7.4 Hz), 0.98 d (3H, $C\underline{H}_3C^4H$, *J* 6.6 Hz), 1.31 quintet (2H, C^5H_2, *J* 7.4 Hz), 1.98–2.11 m (1H, C^4H), 2.43 br.s (4H, NCH_2), 2.94 d (2H, C^1H_2, *J* 6.4 Hz), 3.72 t (4H, OCH_2, *J* 4.7 Hz), 5.37–5.52 m (2H, C^2H,C^3H). ^{13}C NMR spectrum, δ_C, ppm: 11.70 (C^6), 22.02 ($\underline{C}H_3C^4H$), 29.52 (C^5), 38.15 (C^4), 53.45 ($2NCH_2$), 61.39 (C^1), 66.93 ($2OCH_2$), 124.00 (C^2), 140.78 (C^3). Mass spectrum, *m*/*z* (I_{rel}, %): 183 (8) $[M]^+$, 126 (44), 124 (51), 100 (41), 96 (76), 88 (43), 87 (67), 86 (66), 56 (40), 55 (100), 41 (45).

4-[(2*Z*)-4-Methylhex-2-en-1-yl]morpholine (VI) was obtained similarly. Yield 0.176 g (74%), oil. IR spectrum, ν, cm^{-1}: 2959, 2927, 2855, 2802, 1455, 1292, 1119, 1005, 867. ^1H NMR spectrum, δ, ppm: 0.85 t (3H, C^6H_3, *J* 7.4 Hz), 0.94 d (3H, $C\underline{H}_3C^4H$, *J* 6.6 Hz), 1.15–1.43 m (2H, C^5H_2), 2.31–2.49 m (5H, C^4H, NCH_2), 3.03 d (2H, C^1H_2, *J* 6.4 Hz), 3.73 t (4H, OCH_2, *J* 4.6 Hz), 5.29–5.46 m (2H, C^2H,C^3H). ^{13}C NMR spectrum, δ_C, ppm: 11.87 (C^6), 20.71 ($\underline{C}H_3C^4H$), 30.05 (C^5), 33.59 (C^4), 53.54 ($2NCH_2$), 55.70 (C^1), 66.93 ($2OCH_2$), 124.19 (C^2), 139.71 (C^3). Mass spectrum, *m*/*z* (I_{rel}, %): 183 (5) $[M]^+$, 96 (67), 88 (60), 87 (100), 86 (86), 81 (93), 57 (64), 56 (30), 55 (67), 42 (22), 41 (40).

(2*E*)-*N*-Benzyl-*N*,4-dimethylhex-2-en-1-amine (VII) was obtained similarly. Yield 0.249 g (88%), oil. IR spectrum, ν, cm^{-1}: 2961, 2926, 2783, 1454, 1366, 1023, 973, 737, 698. ^1H NMR spectrum, δ, ppm: 0.86 t (3H, C^6H_3, *J* 7.3 Hz), 0.98 d (3H, $C\underline{H}_3C^4H$, *J* 6.8 Hz), 1.31 quintet (2H, C^5H_2, *J* 7.3 Hz), 1.99–2.10 m (1H, C^4H), 2.17 s (3H, NCH_3), 2.97 d (2H, C^1H_2, *J* 6.4 Hz), 3.48 s (2H, $PhC\underline{H}_2$), 5.41–5.54 m (2H, C^2H, C^3H), 7.20–7.33 m (5H, CH_{Ar}). ^{13}C NMR spectrum, δ_C, ppm: 11.79 (C^6), 20.20 ($\underline{C}H_3C^4H$), 29.61 (C^5), 38.24 (C^4), 41.92 (NCH_3), 59.72 (C^1), 61.51 ($Ph\underline{C}H_2$), 125.35 (C^2), 126.85 (CH_{Ar}), 128.14 ($2CH_{Ar}$), 129.12 ($2CH_{Ar}$), 139.04 (C_{Ar}), 140.06 (C^3). Mass spectrum, *m*/*z* (I_{rel}, %): 217 (4) $[M]^+$, 160 (12), 134 (20), 122 (18), 121 (22), 120 (31), 92 (11), 91 (100), 55 (19), 44 (12), 42 (15).

(2*Z*)-*N*-Benzyl-*N*,4-dimethylhex-2-en-1-amine (VIII) was obtained similarly. Yield 0.200 g (71%), oil. IR spectrum, ν, cm^{-1}: 2959, 2928, 2779, 1455, 1362, 1021, 739, 700. ^1H NMR spectrum, δ, ppm: 0.83 t (3H, C^6H_3, *J* 7.3 Hz), 0.93 d (3H, $C\underline{H}_3C^4H$, *J* 6.6 Hz), 1.17–1.39 m (2H, C^5H_2), 2.23 s (3H, NCH_3), 2.29–2.41 m (1H, C^4H), 3.11 d (2H, C^1H_2, *J* 6.6 Hz), 3.54 s (2H, $PhC\underline{H}_2$), 5.35 t (1H, C^3H, J_{cis} 11.0 Hz), 5.51 d. t (1H, C^2H, J_{cis} 11.0, 6.6 Hz), 7.20–7.36 m (5H, CH_{Ar}). ^{13}C NMR spectrum, δ_C, ppm: 11.94 (C^6), 20.77 ($\underline{C}H_3C^4H$), 30.12 (C^5), 33.71 (C^4), 41.86 (NCH_3), 54.08 (C^1), 61.48 ($Ph\underline{C}H_2$), 124.63 (C^2), 127.21 (CH_{Ar}), 128.29 ($2CH_{Ar}$), 129.27 ($2CH_{Ar}$), 138.20 (C_{Ar}), 139.73 (C^3). Mass spectrum, *m*/*z* (I_{rel}, %): 217 (3) $[M]^+$, 122 (27), 121 (36), 120 (83), 92 (14), 91 (100), 81 (19), 65 (12), 55 (18), 44 (22), 42 (15).

IR spectra were recorded with the IR Prestige-21 Shimadzu FTIR spectrophotometer (thin layer). ^1H and ^{13}C NMR spectra of the solutions in $CDCl_3$ were obtained using the Bruker AM-300 spectrometer [300.13 (^1H) and 75.47 MHz (^{13}C)] relative to internal TMS reference. Gas chromatography–mass spectrometry analysis was performed with the GCMS-QP2010S Shimadzu instrument (EI, 70 eV, *m*/*z* 33–350 Da).

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