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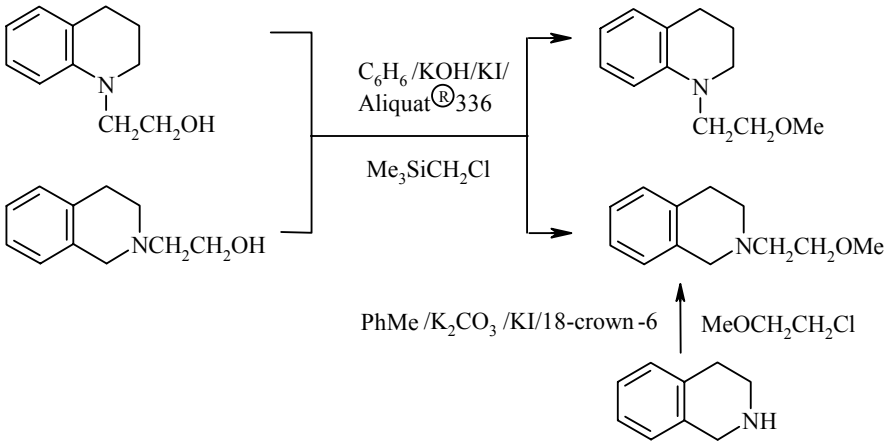
UNEXPECTED O-METHYLATION OF N-(2-HYDROXYETHYL)-1,2,3,4-TETRAHYDRO-QUINOLINE AND -1,2,3,4-TETRAHYDROISOQUINOLINE IN SILYLALKYLATION BY TRIMETHYLCHLORO-METHYLSILANE UNDER PHASE-TRANSFER CATALYSIS CONDITIONS

A. E. Zablotskaya, I. D. Segal, and E. Lukevics

Keywords: tetrahydroisoquinoline, tetrahydroquinoline, alkylation, silylation, phase-transfer catalysis.

In continuing a study of the biological activity of organosilicon derivatives of tetrahydroquinoline and tetrahydroisoquinoline [1-3], we have attempted to obtain trialkylsilylalkyl derivatives of hydroxyethyltetrahydro(iso)quinolines under phase-transfer catalysis conditions.



We have established that as a result of silylalkylation of primary alcohol groups in N-(2-hydroxyethyl)-1,2,3,4-tetrahydroisoquinoline and -tetrahydroquinoline by trimethylchloromethylsilane under phase-transfer catalysis conditions, the major reaction products are N-(2-methoxyethyl)-1,2,3,4-tetrahydroisoquinoline and N-(2-methoxyethyl)-1,2,3,4-tetrahydroquinoline respectively; i.e., instead of the target O-trimethylsilylmethylation, we see that O-methylation of the primary alcohol groups occurs. The reaction was conducted in the system C_6H_6/KOH/KI/Aliquat® 336 for 10 h at a temperature of 80°C and an equivalent reagent ratio of 1:1.05 tetrahydroquinoline:silane. The yield of methylation products is greater than 40%. The structure of the

Latvian Institute of Organic Synthesis, Riga LV-1006; e-mail: aez@osi.lv. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 1110-1111, July, 2004. Original article submitted April 27, 2004.

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N-(2-methoxyethyl)-1,2,3,4-tetrahydroisoquinoline obtained was confirmed by an alternate synthesis: N-alkylation of tetrahydroisoquinoline by 2-chloroethylmethyl ether under phase-transfer catalysis conditions using the system toluene/K_2CO_3/KI/18-crown-6.

General O-Silylalkylation Method. A mixture of the heterocyclic 2-amino alcohol (6.3 g, 35.5 mmol), potassium hydroxide (9.97 g, 178 mmol), potassium iodide (11.79 g, 71 mmol), trimethylchloromethylsilane (4.42 g, 36 mmol), and Aliquat® 336 (0.72 g, 1.78 mmol) in dry benzene (25 ml) was stirred at 80°C for 10 h. Then the precipitate was filtered out, the solvent was distilled off from the filtrate, and the product was isolated by distillation under vacuum.

N-Alkylation. A mixture of tetrahydroisoquinoline (0.49 g, 3.7 mmol), potassium carbonate (1.53 g, 11.1 mmol), potassium iodide (1.24 g, 7.5 mmol), 2-chloroethylmethyl ether (0.42 g, 4.4 mmol), and 18-crown-6 (0.049 mg, 0.2 mmol) in dry toluene (2.3 ml) was stirred at 100°C for 14 h. Then the precipitate was filtered out, the solvent was distilled off from the filtrate, and the product was isolated as a results of chromatographic separation of the reaction products on a column with eluent 52:48 ethyl acetate–hexane. Yield 0.28 g (40%).

N-(2-Methoxyethyl)-1,2,3,4-tetrahydroisoquinoline. Yield 3.25 g (48%); bp 126-128°C (3 mm Hg). Mass spectrum, *m*/*z* (I_{rel}, %): 191 $[M]^+$, 146 $[M^+ - CH_2OCH_3]$. ^{1}H NMR spectrum (90 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 2.77 (2H, t, *J* = 6, NCH_2); 2.83 (4H, m, 3,4-CH_2); 3.37 (3H, s, OCH_3); 3.47 (2H, t, *J* = 6, OCH_2); 3.72 (2H, s, 1-CH_2); 6.92-7.12 (4H, m, arom.). Found, %: C 75.10; H 9.07; N 7.52. $C_{12}H_{17}NO$. Calculated, %: C 75.35; H 8.96; N 7.32.

N-(2-Methoxyethyl)-1,2,3,4-tetrahydroquinoline. Yield 2.78 g (41%); bp 135-137°C (4 mm Hg). Content of the major compound, 98.2%, according to HPLC data (Symmetry C18, 4.6 × 150 mm, system: 70% acetonitrile + 30% [0.1% H_3PO_4 + H_2O], pH 2.5). UV detector (λ = 220 nm). Mass spectrum, *m*/*z* (I_{rel}, %): 191 $[M]^+$, 146 $[M^+ - CH_2OCH_3]$. ^{1}H NMR spectrum (90 MHz, $CDCl_3$), δ, ppm: 1.92 (2H, m, 3-CH_2); 2.75 (2H, t, 4-CH_2); 3.23-3.66 (9H, m, OCH_3 + OCH_2 + 2-CH_2 + NCH_2); 6.47-7.31 (4H, m, arom.). Found, %: C 75.43; H 9.04; N 7.25.$C_{12}H_{17}NO$. Calculated, %: C 75.35; H 8.96; N 7.32.

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