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LETTERS TO THE EDITOR

UNUSUAL REACTION OF N-(2-METHOXYETHYL)-1,2,3,4-TETRAHYDROISOQUINOLINE WITH ETHYL ACETATE IN THE PRESENCE OF SILICA GEL

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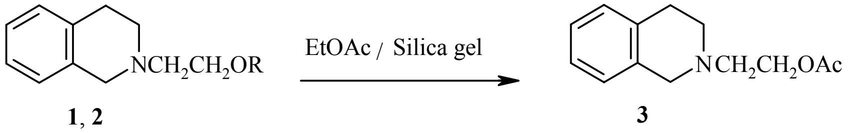
Silica gel can initiate various reactions [1, 2] which, on the one hand, can cause difficulty in the separation of compounds by column chromatography and, on the other, can be used as alternative (in several cases the only) methods for the synthesis of different compounds.

The separation of the products of the alkylation reaction of N-(2-hydroxyethyl)-1,2,3,4-tetrahydroisoquinoline (**1**) on silica gel using ethyl acetate gave the N-(2-acetoxyethyl)-1,2,3,4-tetrahydroisoquinoline (**3**) [3].

We have found that an increase in the amount of silica gel and the reaction time cause the yield of acetate **3** in the reaction of the alkanol **1** with ethyl acetate to increase to 25%.



1 R = H; **2** R = Me

The N-(2-hydroxyethyl)-1,2,3,4-tetrahydroquinoline (**4**) [3] is similarly acetylated to give the acetate **5**.

Unexpectedly, we found that the methyl ether of the N-(2-hydroxyethyl)-1,2,3,4-tetrahydroisoquinoline **2** [4] was also converted to the acetate **3** in 25% yield. However, the methyl ether of N-(2-hydroxyethyl)-1,2,3,4-tetrahydroquinoline **6** [4] did not react with ethyl acetate.

The silicon-containing ethers of N-[2-(3'-dimethylheptylsilylpropoxy)ethyl]-1,2,3,4-tetrahydroisoquinoline (**7**) [3] and N-[2-(3'-dimethylheptylsilylpropoxy)ethyl]-1,2,3,4-tetrahydroquinoline (**8**) [3] also do not react with ethyl acetate.

Mass spectra were recorded on an HP 6890 GC-MS instrument. ^{1}H NMR and ^{13}C NMR spectra were taken on a Varian Mercury 200 (200 and 50 MHz respectively) spectrometer using CDCl$_3$ with HMDS (δ 0.055 ppm) as internal standard. IR spectra were recorded on a Shimadzu IR Prestige 21 instrument. Elemental analysis was performed on a Carlo Erba 1108 analyzer. Preparative column chromatography was carried out using Acros silica gel grade (0.060-0.220 mm). The reagents and materials used came from the Acros and Aldrich companies.

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Acetylation of Hydroxy and Alkoxyethyl Derivatives of 1,2,3,4-Tetrahydroisoquinolines using Ethyl Acetate (General Method). Alcohol **1** or **4** or ether **2,6,7** and **7** (1 mmol) was dissolved in ethyl acetate (10 ml) and silica gel was added in different ratios to the substrate (2.5-, 10-, or 25-fold excess). The mixture was held at room temperature for 3, 8, 40, 48, or 72 h with periodic shaking. The silica gel was filtered off and the filtrate was analyzed using chromato-mass spectrometer and evaporated to determine the mass of the residue. The silica gel was treated with ethanol with gentle heating over 2 h, filtered, and the filtrate was analyzed using chromato-mass spectrometry and evaporated to determine the mass of the residue. The yield of the acetyl derivative was calculated using chromato-mass spectrometry data and the mass of the residues produced.

According to the work done the reaction needs a significant excess of silica gel, hence with a 2.5-fold excess and reaction time in excess of 40 h the acetylation of alcohol **1** and its methyl ether **2** were not seen. When increasing the excess of silica gel to 25-fold and with the same reaction time the formation of the acetyl derivative occurs in both cases with a 25% yield. Exchange of the silica gel from Acros grade to Chemapol under the same reaction conditions has almost no effect on the product yield. An increased yield of the acetate **5** with increases in the amount of silica gel is also observed in the case of the tetrahydroquinoline alcohol **4**. With use of a 25-fold excess the yield of **5** reaches 13%.

The amount of the acetylation product **3** formed both from alcohol **1** and from the methyl ether **2** increases with a longer reaction time. Hence an increases from 3 to 48 h raises the yield of product **4** from alcohol **1** from 6 to 25%.

N-(2-Acetoxyethyl)-1,2,3,4-tetrahydroisoquinoline (3) was prepared from compound **1** or **2**. A solution of compound **2** (1.9 g, 10 mmol) in ethyl acetate (100 ml) was treated with silica gel (48 g). The mixture was held at room temperature for 48 h. The silica gel was filtered off and the filtrate was evaporated to minimum volume and chromatographed on silica gel with ethyl acetate eluent. Yield of compound **4** 0.55 g (25%). IR spectrum (thin film), ν, cm^{-1}: 1739. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.07 (3H, s, CH_3); 2.77-2.89 (6H, m, 3,4-CH_2 + NCH_2); 3.70 (2H, s, 1-CH_2); 4.28 (2H, t, *J* = 6.0, OCH_2); 7.09-7.14 (4H, m, arom.). ^{13}C NMR spectrum, δ, ppm: 21.02 (CH_3); 28.81 (C-4); 51.06 (C-1); 59.01 (NCH_2); 62.01 (OCH_2); 125.62, 126.16, 126.34 (C-6, C-7, C-8); 128.65 (C-5); 134.04, 134.38 (C-9, C-10); 171.05 (C=O). Mass spectrum (EI, 70 eV), *m/z* (I_{rel}): 218 [M^+-H] (1), 176 [M^+-$COCH_3$] (1), 159 [M^+-$OCOCH_3$-H] (10), 146 [M^+-CH_2OCOCH_3] (100), 132 [M^+-$CH_2CH_2OCOCH_3$] (13). Found, %: C 71.55; H 7.78; N 6.38. $C_{13}H_{17}NO_2$. Calculated, %: 71.23; H 7.76; N 6.39.

The product obtained from compound **1** by an analogous method was identical to **4**.

N-(2-Acetoxyethyl)-1,2,3,4-tetrahydroquinoline (5) was prepared from alcohol **4** by the method given for compound **4**. IR spectrum (thin layer), ν, cm^{-1}: 1739. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.95 (2H, m, 3-CH_2); 2.07 (3H, s, CH_3); 2.77 (2H, t, *J* = 6.3, 4-CH_2); 3.13 (2H, t, *J* = 6.1, 2-CH_2); 3.28 (2H, t, *J* = 5.8, NCH_2); 4.28 (2H, t, *J* = 5.8, OCH_2); 7.03-7.13 (4H, m, arom.). Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 218 [M^+-H] (1), 176 [M^+-$COCH_3$] (1), 159 [M^+-$OCOCH_3$-H] (6), 146 [M^+-CH_2OCOCH_3] (100), 132 [M^+-$CH_2CH_2OCOCH_3$] (16).

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