Improved Synthesis of 2-(4-Propylphenyl)ethanol

A. Stephen K. Hashmi[a], Tobias Burkert[a], Jan W. Bats[b], and Aleksandra Martyniak[c]

[a] Institut für Organische Chemie, Universität Stuttgart, Pfaffenwaldring 55, D-70569 Stuttgart, Germany
[b] Institut für Organische Chemie und Chemische Biologie, Universität Frankfurt, Marie-Curie-Str. 11, D-60439 Frankfurt, Germany
[c] Institut für Physikalische Chemie, Universität Stuttgart, Pfaffenwaldring 55, D-70569 Stuttgart, Germany

Reprint requests to Dr. A. S. K. Hashmi. E-mail: hashmi@hashmi.de

Z. Naturforsch. **61b,** 179 – 181 (2006); received November 8, 2005

A new procedure for the synthesis of 2-(4-propylphenyl)ethanol is provided. This new procedure significantly reduces side-products as 1-(4-propylphenyl)ethanol and 2-bromoethanol, which are obtained when using the previously known procedure. Only with the new procedure an efficient purification on the large scale needed for avoided-level-crossing muon-spin resonance experiments was possible.

Structural details of the title compound could be derived from an X-ray structure analysis of a crystalline derivative, the nitrobenzoyl ester.

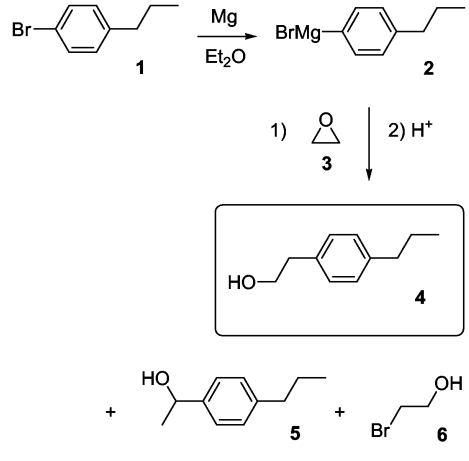
Key words: Alcohols, Epoxides, Esters, Grignard Reagents, Nitro Compounds

Introduction

The title compound **4** is a known compound [1]. In the context of a project investigating the solvation thermodynamics of phenyl-substituted alcohols in lamellar phase surfactant dispersions by avoided-level-crossing muon-spin resonance [2], we needed to prepare a pure sample of **1** on an multigram scale and in addition to obtain detailed spectroscopic characterization and structural information.

Results and Discussion

Using the original procedure of McKusick [1], the *in situ* generation of the Grignard compound **2** from commercially available 1-bromo-4-propylbenzene (**1**) and its reaction with oxirane **3**, only material with significant amounts of side-products as impurities was obtained. On a multigram scale it was impossible to separate these impurities from the product, even by column chromatography. As the major side-products we could identify the known compounds 1-(4-propylphenyl)ethanol (**5**) [3] and 2-bromoethanol (**6**) [4]. The formation of **6** consumes oxirane at the expense of the yield of the desired product **4**, but the formation of magnesium bromide could not be avoided. Thus a higher excess of **3** than in the original procedure was used. Alcohol **5** is probably formed from the magnesium salt of **4** upon heating to 95 °C or during the acidic work-up (pouring the hot reaction mixture directly into the saturated ammonium chloride solution) by ionization and rearrangement to the more stable benzylic cation. In order to avoid this, the reaction and the work-up was conducted at room temperature. Only then the small amounts of impurities formed could conveniently be removed by column chromatography after removal of **6** in high vacuum.



A crystal structure analysis would have provided detailed structural information, but **4** was a liquid. Thus

Table 1. Selected bond lengths (Å) and bond angles (°) of **8**.

O(3)-C(8)	1.4565(17)	O(3)-C(8)-C(9)	111.93(12)
C(8)-C(9)	1.513(2)	C(8)-C(9)-C(10)	109.03(12)
C(9)-C(10)	1.5169(19)	C(9)-C(10)-C(11)	118.70(14)
C(13)-C(16)	1.5144(16)	C(15)-C(10)-C(9)	123.23(15)
C(16)-C(17)	1.5203(19)	C(14)-C(13)-C(16)	121.33(12)
C(17)-C(18)	1.5154(17)	C(13)-C(16)-C(17)	112.02(10)
C(7)-O(3)-C(8)	116.04(13)	C(16)-C(17)-C(18)	112.97(11)

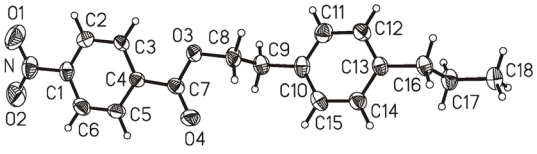


Fig. 1. Solid state structure of **8**.

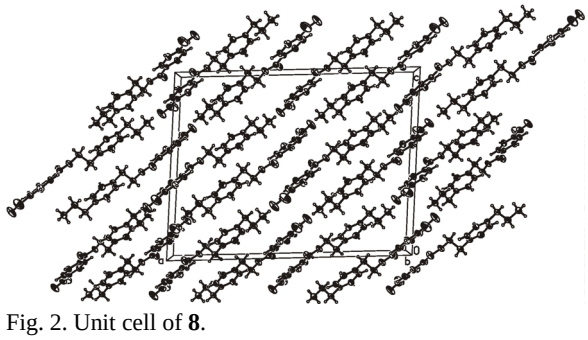
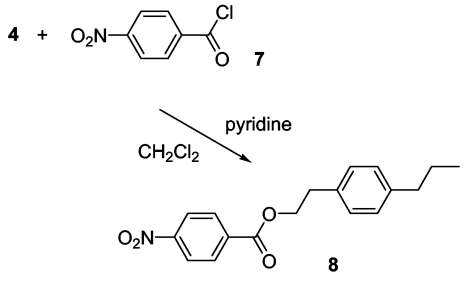


Fig. 2. Unit cell of **8**.

we decided to prepare a crystalline derivative, which would at least deliver that information for the 2-(4-propylphenyl)ethoxy group. We chose an esterification with 4-nitrobenzoyl chloride (**7**), which gave a 99% yield of the desired ester **8** as a slightly yellow solid.



Single crystals of **8** could be grown from petrol ether/dichloromethane. The solid state structure is depicted in Fig. 1 [5]. Both six-membered rings are planar, the mean deviations from the planes are 0.002 and 0.001 Å, respectively. The angle between the planes C1/N/O1/O2 and C1/C2/C3/C4/C5/C6 is 8.7°. The angle between the planes C4/C7/O3/O4 and C1/C2/C3/C4/C5/C6 is 0.3°. The shortest intramolecular contacts are: H2…O1 2.42 Å, H6…O2 2.44 Å, H3…O3 2.46 Å, H5…O4 2.51 Å and H8A…O4 2.43 Å. The crystal packing shows three intermolecular C-H…O contacts with H…O distances between 2.46 and 2.59 Å, two intermolecular C-H…π(benzene) interactions with H…Cg distances of 2.83 and 2.84 Å (Cg is the centroid of a benzene ring) and a $\pi\cdots\pi$ contact of 3.52 Å between two parallel benzene rings. The unit cell is shown in Fig. 2. Selected bond lengths and bond angles of the 2-(4-propylphenyl)ethoxy substructure are provided in Table 1.

Table 2. Crystallographic data for **8**.

Empirical formula	$C_{18}H_{19}NO_4$
Formula weight	313.34
Temperature [K]	156(2)
Wavelength [Å]	0.71073
Crystal system, space group	monoclinic, *C*2/c
Unit cell dimensions	$a = 24.732(6)$ Å, $\alpha = 90°$ $b = 6.9064(9)$ Å, $\beta = 93.818(12)°$ $c = 18.974(2)$ Å, $\gamma = 90°$
Volume [Å^3]	3233.7(9)
Z, Calculated density [Mg/m^3]	8, 1.287
Absorption coefficient [mm^{-1}]	0.091
F(000)	1328
Crystal size [mm]	$0.74 \times 0.70 \times 0.30$
θ Range for data collection [°]	1.65 to 30.96
Limiting indices	$-35 \le h \le 2$, $-9 \le k \le 9$, $-26 \le l \le 26$
Reflections collected / unique	25573 / 4701 [R(int) = 0.0293]
Completeness to $\theta = 30.96$	91.7 %
Absorption correction	Empirical, SADABS (Sheldrick, 2000)
Max. and min. transmission	1.000 and 0.872
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4701 / 0 / 241
Goodness-of-fit on F^2	1.552
Final R indices [I¿2σ(I)]	$R1 = 0.0576$, w$R2 = 0.1954$
R Indices (all data)	$R1 = 0.0763$, w$R2 = 0.2112$
Largest diff. peak and hole [e·Å^{-3}]	0.593 and −0.323

Experimental Section

Synthesis of **4**

From 46.3 g (232 mmol) of 1-bromo-4-propylbenzene (**1**) and 5.65 g (232 mmol) of magnesium turnings in diethyl ether (125 ml), Grignard compound **2** was formed. The reaction started spontaneously at room temperature and proceeded under slight reflux. When the formation of **2** was finished, diethyl ether was added to reach a total volume of 500 ml and an acetone/dry ice condenser was placed on the flask. Then 12.0 g (272 mmol) of oxirane were added during one hour while stirring. A colourless precipitate formed.

Stirring was continued overnight, then a hydrolysis with saturated ammonium chloride solution at room temperature followed. The aqueous phase was extracted with 3×50 ml of diethyl ether, the combined organic layers were dried over magnesium sulfate, and the solvent was removed under reduced pressure. Most of **6** was then removed from the crude product by applying 0.01 mbar at 30 – 40 °C for 24 h. Column chromatography of the crude product (silica gel, petrol ether/ethyl acetate = 15:1) delivered 21.1 g (55%) of pure **4** as a colourless liquid. – R_f (PE:EE, 3:1) = 0.23. – IR (film): ν = 3306 (O-H), 2956, 2930 (=C-H), 2870 (-C-H), 1514, 1116, 655 cm^{-1}. – ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.3 Hz, 3 H, Me), 1.42 (bs, 1 H, OH), 1.63 (m, 2 H, CH_2-C*H*$_2$-Me), 2.57 (t, ^3J = 7.6 Hz, 2 H, C*H*$_2$-CH_2-Me), 2.84 (t, ^3J = 6.5 Hz, 2 H, C*H*$_2$-CH_2-OH), 3.85 (t, ^3J = 6.5 Hz, 2 H, CH_2-C*H*$_2$-OH), 7.14 (s, 4 H, aryl-*H*). – ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.0 (q, 1 C), 24.7 (t, 1 C), 37.8 (t, 1 C), 48.9 (t, 1 C), 63.9 (t, 1 C), 128.8 (d, 2 C), 129.0 (d, 2 C), 135.7 (s, 1 C), 141.0 (s, 1 C). – MS (EI, 70 eV): *m/z* (%) = 164 (51) [M^+], 133 (100), 105 (36), 91 (36). – $C_{11}H_{16}O$ (164.2): calcd. C 80.44, H 9.82; found C 79.91, H 9.88.

*Synthesis of 2-(4-propylphenyl)ethyl 4-nitrobenzoate (**8**)*

231 mg (1.41 mmol) of **4** were dissolved in dichloromethane (5 ml) and 196 mg (2.47 mmol) of pyridine were added. At 0 °C a solution of 262 mg (1.41 mmol) of **7** in dichloromethane (5 ml) was added within 10 min drop by drop. Stirring at 0 °C was continued for 15 min, then at room temperature for 45 min. After hydrolysis, from the organic phase the solvent was removed under reduced pressure. Column chromatography (silica gel, petrol ether/ethyl acetate = 20:1) provided 437 mg (99%) of **8** as a slightly yellow solid. Single crystals for the structure analyis were obtained by slow evaporation of a solution in petrol ether/dichloromethane at room temperature. Details concerning the crystal structure analysis are provided in Table 2. – M. p. 49 °C. – R_f (PE:EE, 3:1) = 0.42. – IR (film): ν = 1715 (C=O), 1524, 1269, 1098, 829, 714 cm^{-1}. – ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 0.94 (t, ^3J = 7.4 Hz, 3 H, Me), 1.64 (m, 2 H, CH_2-C*H*$_2$-Me), 2.57 (t, J = 7.6 Hz, 2 H, C*H*$_2$-CH_2-Me), 3.07 (t, ^3J = 7.1 Hz, 2 H, C*H*$_2$-CH_2-O), 4.57 (t, ^3J = 7.1 Hz, 2 H, CH_2-C*H*$_2$-O), 7.11 – 7.23 (m, 4 H, dialkylaryl-H), 8.13 – 8.32 (m, 4H, nitroaryl-H). – ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 13.8 (q, 1 C), 24.51 (t, 1 C), 34.7 (t, 1 C), 37.6 (t, 1 C), 66.4 (t, 1 C), 123.5 (d, 2 C), 128.71 (d, 2 C), 128.73 (d, 2 C), 130.7 (d, 2 C), 134.5 (s, 1 C), 135.7 (s, 1 C), 141.2 (s, 1 C), 150.5 (s, 1 C), 164.6 (s, 1 C). – MS (EI, 70 eV): *m/z* (%) = 313 (5) [M^+], 150 (6), 146 (100), 117 (64). – $C_{18}H_{19}NO_4$ (313.3): calcd. C 68.99, H 6.11, N 4.46; found C 68.93, H 6.11, N 4.46.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] B. C. McKusick, J. Am. Chem. Soc. **72**, 1982 (1948).
[2] A. Martyniak, R. Scheuermann, H. Dilger, I. M. Tucker, T. Burkert, A. S. K. Hashmi, D. Vujoševic, E. Roduner, Physica B, in press (2005).
[3] O. Cervinka, A. Fabryova, I. Brozova, M. Holik, Collect. Czech. Chem. Commun. **51**, 684 (1986). Y. Kobayashi, K. Kodama, K. Saigo, Org. Lett. **6**, 2941 (2004).
[4] S.-K. Kang, W.-S. Kim, B.-H. Moon, Synthesis 1161 (1985).
[5] Crystallographic data for the structure have been deposited with the Cambridge Crystallographic Data Centre, CCDC-288953. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: int.code+(1223)336-033; e-mail for inquiry: fileserv AT ccdc.cam.ac.uk).