

Proceeding Paper

Cp₂TiCl₂—Catalyzed Synthesis of Tertiary Alcohols by the Reaction of AlCl₃ with Ketones and Aryl Olefins [†]

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Abstract: We have previously obtained significant results in the cycloaluminum of olefins with EtAlCl₂ in the presence of magnesium and a Cp₂ZrCl₂ or Cp₂TiCl₂ catalyst. Here we report the development of an efficient one-pot catalytic method for the synthesis of tertiary alcohols from AlCl₃, aryl olefins, and ketones under the action of Cp₂TiCl₂. The developed method for producing tertiary alcohols has a general character and allows the conversion of styrene and substituted styrenes (*ortho*-, *para*-methylstyrenes) into aryl-substituted tertiary alcohols with yields of up to 76% in the reaction with acetone or methyl ethyl ketone. We assume that the reaction proceeds through the formation of a titanacyclopropane intermediate.

Keywords: titanocene; catalysis; arylolefines; ketones; tertiary alcohols



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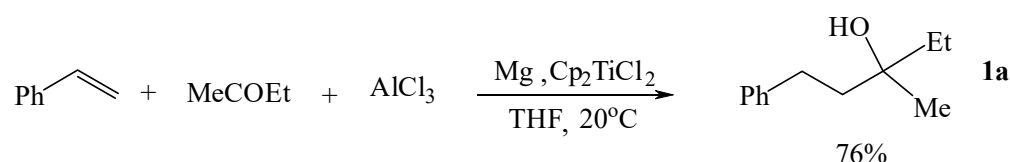
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1. Introduction

Tertiary alcohols are widely used in medicine and industry [1,2]. One of the best methods for the preparation of tertiary alcohols is the reaction of ketones with organo-magnesium compounds [1,3,4]. We have previously obtained significant results in the cycloaluminum of olefins with EtAlCl₂ in the presence of magnesium and a Cp₂ZrCl₂ or Cp₂TiCl₂ catalyst [5–7]. Here we report the development of an efficient one-pot catalytic method for the synthesis of tertiary alcohols from AlCl₃, aryl olefins, and ketones under the action of Cp₂TiCl₂.

2. Results and Discussion

We found that the reaction of styrene with AlCl₃ and methyl ethyl ketone in the presence of metallic Mg as an acceptor of halide anions and Cp₂TiCl₂ as a catalyst (10 mol%) in THF (tetrahydrofuran) solvent at 20 °C for 8 h leads to the formation of 3-methyl-1-phenylpentan-3-ol **1a** in a 76% yield (Scheme 1).

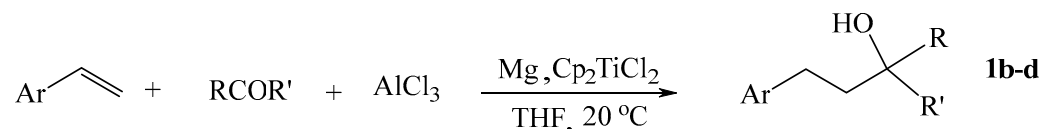


Scheme 1. The reaction of styrene with AlCl₃ and methyl ethyl ketone in the presence of metallic Mg.

In non-ether solvents (hexane, DMSO (dimethyl sulfoxide), DMF (*N,N*-dimethylformamid), and methylene chloride), the yield of reaction product **1a** is less than 11%. Carrying out the reaction at ~0 °C reduces its rate and the conversion of the initial styrene, which does not exceed 20% for 15 h. With an increase in temperature to ~65 °C, the reaction is completed in almost 2 h, but it is less selective. The best results were obtained when the reaction was

carried out in tetrahydrofuran in the presence of Ti-containing catalysts. The reaction does not proceed in the absence of a catalyst.

The developed method for producing tertiary alcohols has a general character and allows the conversion of styrene and substituted styrenes (*ortho*-, *para*-methylstyrenes) into aryl-substituted tertiary alcohols with 66–73% yields in the reaction with acetone or methyl ethyl ketone (Scheme 2).



b: Ar = Ph, R, R' = Me

d: Ar = *p*-methylphenyl, R = Me, R' = Et

c: Ar = *o*-methylphenyl, R = Me, R' = Et

Scheme 2. Cp₂TiCl₂—Catalyzed synthesis of tertiary alcohols by the reaction of AlCl₃ with ketones and aryl olefins.

The structures of compounds 1a–d were identified using one-dimensional (¹H, ¹³C, DEPT135) and two-dimensional (HSQC (heteronuclear single quantum correlation), HMBC (heteronuclear multiple bond correlation) and HHCOSY (HH correlation spectroscopy) NMR (nuclear magnetic resonance spectroscopy, HRMS (high resolution mass-spectrometry).

3. Conclusions

Thus, we have developed a new one-pot method for the production of substituted tertiary alcohols from aryl olefins and ketones in the presence of AlCl₃ and catalytic amounts of Cp₂TiCl₂.

4. Experimental Part

General. ¹H and ¹³C NMR spectra were recorded on a Bruker Avance II 400 Ascend (400 MHz for ¹H and 100 MHz for ¹³C) and Bruker Avance II HD 500 Ascend (500.17 MHz for ¹H and 125.78 MHz for ¹³C) instruments (“Bruker”, Germany) in CDCl₃. Mass spectra were obtained on a Finnigan 4021 instrument (“Thermo Electron Corporation”, Waltham, MA, USA) Chromatographic analysis was performed on a Shimadzu GC-9A instrument (“Shimadzu”, Kyoto, Japan) using a 2000 × 2 mm column, the SE-30 (5%) stationary phase on a Chromaton N-AW-HMDS (0.125–0.160 mm), helium carrier gas (30 mL/min), temperature programming from 50 to 300 °C at an 8 °C/min rate. IR spectra were recorded on a Bruker VE Vertex 70v spectrometer (“Bruker”, Bremen, Germany) as liquid films and are reported in wavenumbers (cm⁻¹). Elemental analysis was performed using a Carlo-Erba CHN 1106 elemental analyzer (“Carlo Erba Instruments”, Cornaredo, Italy). For column chromatography, Acros silica gel (0.060–0.200 mm) (“Acros Organics”, Geel, Belgium) was used. Reactions with organometallic compounds were performed in a dry argon flow. Commercially available styrenes, ketones, Cp₂TiCl₂, Mg, and AlCl₃ (“Sigma-Aldrich”, St. Louis, MO, USA) were used. The solvents were dried and distilled immediately prior to use.

Experimental Procedures. A 50 mL glass reactor equipped with a magnetic stirrer under a dry argon atmosphere at 0 °C was charged under stirring with 5 mL of THF, 2 mmol aryl olefin, 4 mmol AlCl₃, 2 mmol ketone, 4 mmol Mg (powder), and 0.2 mmol Cp₂TiCl₂. The temperature was brought to room temperature (20–21 °C) and the reaction mixture was stirred for 8 h. The reaction mixture was treated with a 7–10% HCl aqueous solution, the reaction products were extracted with diethyl ether, dried over calcined MgSO₄, and the solvent was evaporated on a rotary evaporator. The products were isolated by column chromatography (silica gel L, 180/250 μ, eluent—hexane:ethyl acetate (1:1)).

Compound 1a was isolated by column chromatography and provided 3-methyl-1-phenylpentan-3-ol as a yellow oil (73%). R_f 0.61. IR (film): 3375; 3027; 2930; 2873; 1454;

1379; 1137; 1026; 752 cm^{-1} . ^1H NMR (500.1 MHz, CDCl_3), δ : 0.97 (t 3H, J 7.0 Hz), 1.26 (s 3H), 1.55–1.62 (m 2H), 1.77–1.81 (m 2H), 2.68–2.72 (m 2H), 7.27–7.30 (m 5H). ^{13}C NMR (500.1 MHz, CDCl_3), δ : 8.30, 26.34, 30.35, 34.42, 43.28, 72.85, 125.75, 128.36, 128.43, 142.73. HRMS, m/z : 201.0618 $[\text{M} + \text{Na}]^+$. Found (%): C, 80.82; H, 10.06. Calc. for $\text{C}_{12}\text{H}_{18}\text{O}$ (%): C, 80.85; H, 10.18.

Compound 1b was isolated by column chromatography and provided 2-methyl-4-phenylbutan-2-ol as a yellow oil (69%). R_f 0.61. IR (film): 3376; 3011; 2916; 2902; 1466; 1359; 1131; 828; 744 cm^{-1} . ^1H NMR (500.1 MHz, CDCl_3), δ : 1.32 (s 6H), 1.80–1.84 (m 2H), 2.71–2.75 (m 2H), 7.19–7.33 (m 5H). ^{13}C NMR (500.1 MHz, CDCl_3), δ : 29.35, 30.76, 45.75, 70.92, 125.76, 128.32, 128.42, 142.53. HRMS, m/z : 187.0274 $[\text{M} + \text{Na}]^+$. Found (%): C, 80.40; H, 9.70. Calc. for $\text{C}_{11}\text{H}_{16}\text{O}$ (%): C, 80.44; H, 9.82.

Compound 1c was isolated by column chromatography and provided 3-methyl-1-(2-methylphenyl)pentan-3-ol as a yellow oil (66%). R_f 0.61. IR (film) 3301; 3037; 2902; 1647; 1359; 1016; 746 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 0.98 (t 3H, J 7.0 Hz), 1.28 (s 3H), 1.61–1.64 (m 2H), 1.70–1.74 (m 2H), 2.35 (s 3H), 2.67–2.71 (m 2H), 7.14–7.17, 7.28 (m 4H). ^{13}C NMR (400 MHz, CDCl_3) δ : 8.28, 19.23, 26.28, 27.67, 34.37, 41.98, 72.90, 125.92, 126.09, 128.75, 130.23, 135.81, 140.79. HRMS, m/z : 215.0726 $[\text{M} + \text{Na}]^+$. Found (%): C, 81.17; H, 10.35. Calc. for $\text{C}_{13}\text{H}_{20}\text{O}$ (%): C, 81.20; H, 10.48.

Compound 1d was isolated by column chromatography and provided 3-methyl-1-(4-methylphenyl)pentan-3-ol as a yellow oil (70%). R_f 0.61. IR (film) 3309; 3063; 2935; 1674; 1386; 1081; 751 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 0.97 (t 3H, J 7.0 Hz), 1.21 (s 3H), 1.58–1.61 (m 2H), 1.67–1.71 (m 2H), 2.21 (s 3H), 2.62–2.67 (m 2H), 7.12–7.16 (m 4H). ^{13}C NMR (400 MHz, CDCl_3) δ : 8.26, 21.00, 26.26, 30.01, 34.37, 41.68, 72.90, 126.99, 128.05, 136.11, 139.60. HRMS, m/z : 215.0735 $[\text{M} + \text{Na}]^+$. Found (%): C, 81.18; H, 10.35. Calc. for $\text{C}_{13}\text{H}_{20}\text{O}$ (%): C, 81.20; H, 10.48.

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