

New domino radical synthesis of aminoalcohols
promoted by TiCl_4 -Zn/*t*-BuOOH system:
selective hydroxyalkylation of amines in alcohol
or in cyclic ether cosolvents.

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Supplementary Information

Contents:

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^1H -NMR and ^{13}C -NMR spectral data	S4-S18

Experimental

General

All materials were purchased from commercial suppliers without further purification. All reactions were performed at room temperature (20°C) under atmosphere of nitrogen. The following solutions were used: 1 M solution of TiCl_4 in CH_2Cl_2 , 35 wt % aqueous solution of H_2O_2 , 15 wt% acidic aqueous solution of TiCl_3 and 80 wt% aqueous solution of *t*-BuOOH.

NMR spectra were recorded at 400 MHz for ^1H and 100 MHz for ^{13}C in CDCl_3 or DMSO and chemical shifts were presented in parts per million (δ) using TMS as reference.

ESI-MS were performed with an Esquire 3000 plus ion-trap mass spectrometer equipped with an ESI source. Tandem mass spectra were obtained by CID with helium collision gas after isolation of the precursor ion. Mass spectra were alternatively performed with a GC-MS instrument, using a gas chromatograph equipped with an SBP-1 fused silica column (30 m×0.2 mm i.d., 0.2 μm film thickness) and helium as carrier gas.

Flash column chromatography was performed by using 40-63 μm silica gel packing: the eluent was chosen in order to move the desired components to $R_f = 0.35$ on analytical TLC.

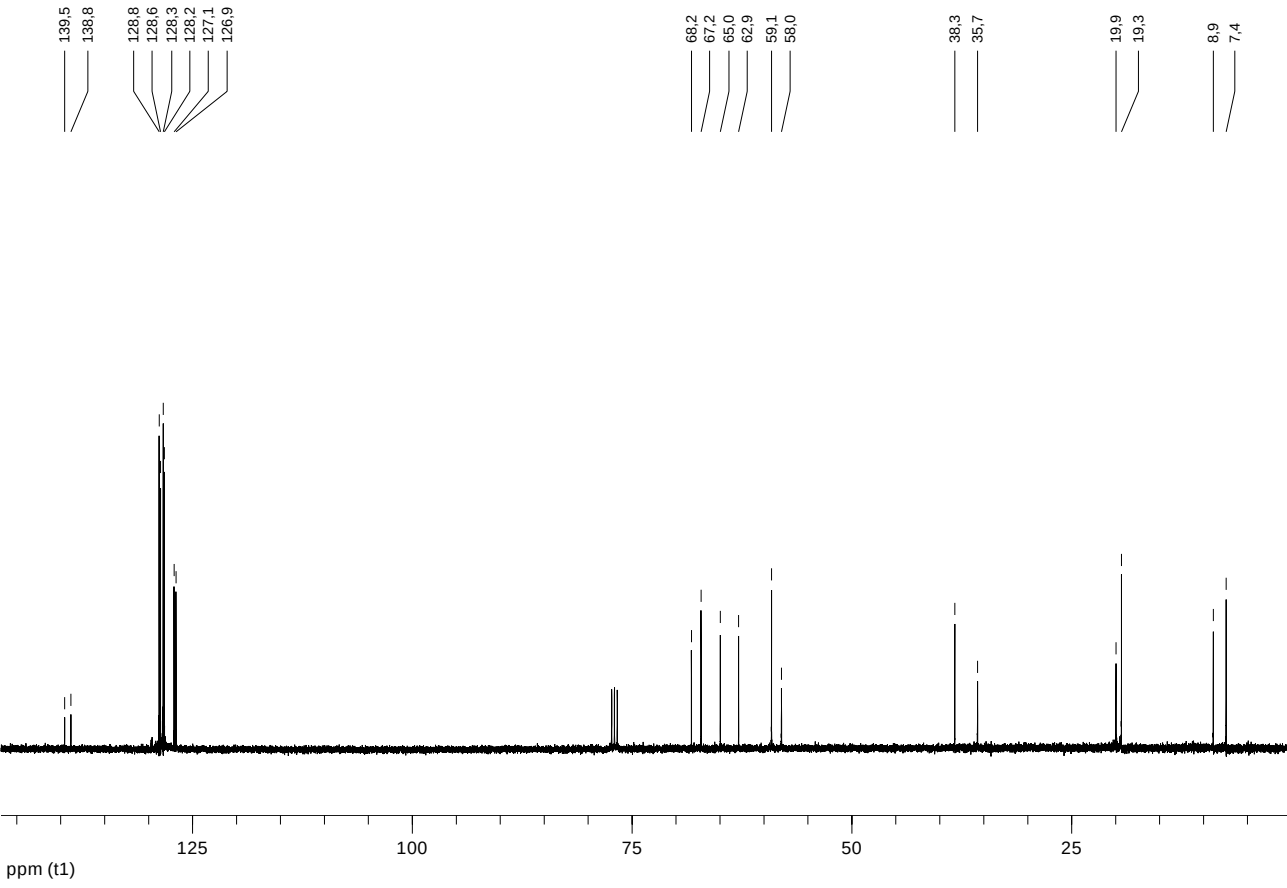
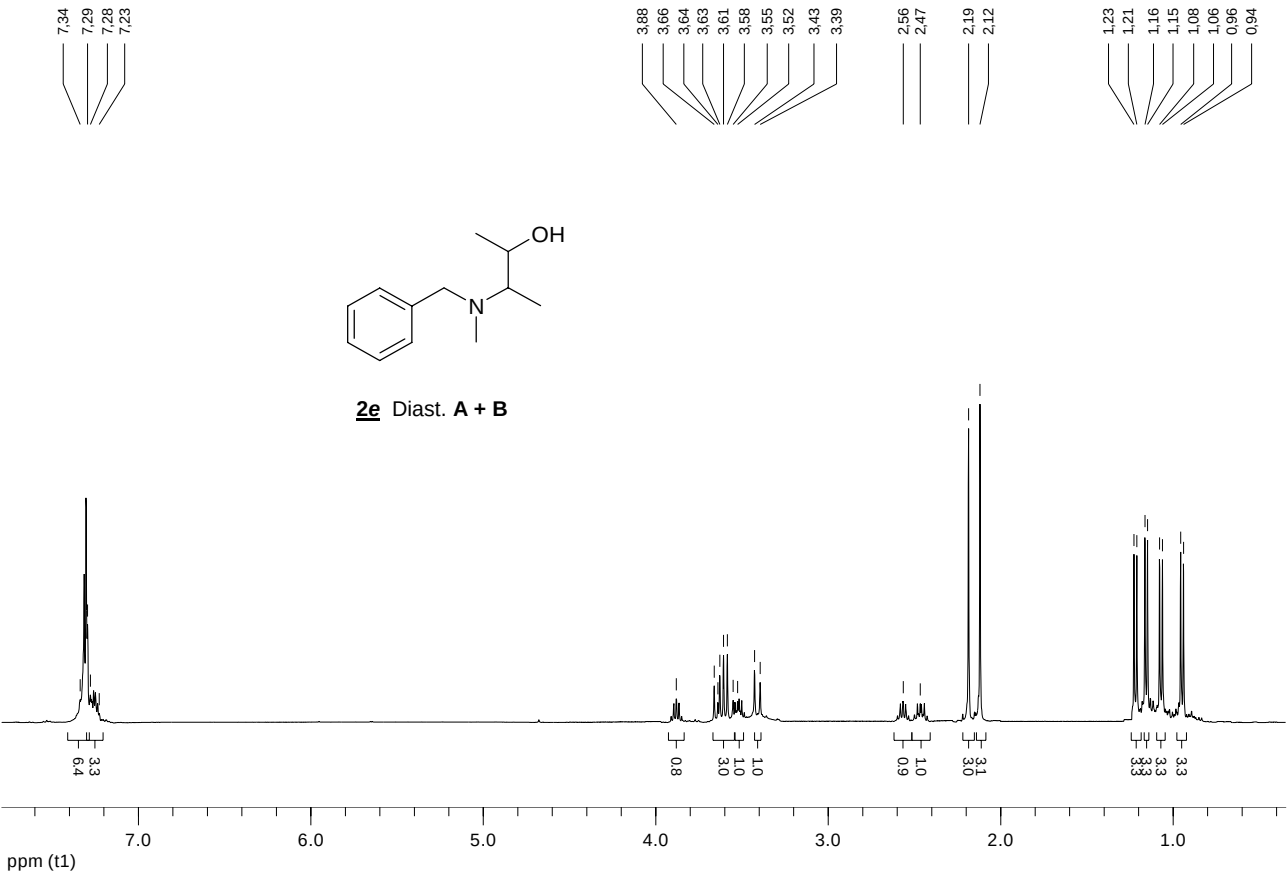
General procedure for the synthesis of aminoalcohols starting from amines **1a-f** in alcoholic or cyclic ether solvent triggered by TiCl_4 -Zn/*t*-BuOOH.

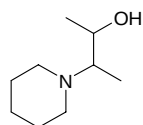
A aqueous 80 wt% *t*-BuOOH solution (5 mmol, ca. 0.5 mL), diluted in 4.5 mL of alcohol (EtOH or PrOH) or cyclic ether (THF, THP or dioxane), was added dropwise to a well stirred homogeneous solution of the same solvent (10 mL) containing the amine (2 mmol), TiCl_4 (2.5 mmol) and AcOH (1 mL), with Zn powder in suspension (300 mg, ca. 5 mmol). The reaction looks like a titration which proceeds with periodic changes of color from orange to violet, and *t*-BuOOH was added until a pale orange was barely maintained upon further addition of Zn. At this point, the reaction was quenched with 5 mL of H_2O and added with a 30% aqueous NH_3 solution until basic

pH (a white precipitate of Ti(IV) hydroxide was observed) and extracted with EtOAc (3x50 mL). The solution was then washed twice with 5 mL of H₂O in order to remove the formamide leftover, which is insoluble in CHCl₃ but very soluble in H₂O. The organic layers were then dried over Na₂SO₄ and concentrated in *vacuum*. Purification by flash chromatography of the crude residue afforded the desired products **2**, **3**, **4**, **5**, **6** and **7**. Yields of isolated products are based on the starting amine.

General procedure for the synthesis of aminoalcohols starting from amines *1a-f* in alcoholic or cyclic ether solvent triggered by TiCl₃/*t*-BuOOH.

To 10 mL of a well stirred homogeneous solution of alcohol (EtOH or PrOH) or cyclic ether (THF, THP or dioxane) containing primary arylamines **1a-c** (2 mmol) and the hydroperoxide (5 mmol of 80 % *t*-BuOOH, ca. 0.5 mL), a 15 wt% TiCl₃ solution was added dropwise such that a pale blue color was just maintained to ensure the complete decomposition of the peroxide. The solvent was removed in *vacuum* and a 30% aqueous NH₃ solution was added to the leftover solution until basic pH was achieved (a white precipitate of Ti(IV) hydroxide was observed) and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with water (2 x 5 mL), dried over Na₂SO₄ and then concentrated.





2f Diast. A + B

