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Convenient *in situ* Generation of an Active Titanium(III)-Reagent for Stereoselective Pinacolization of Aromatic Aldehydes

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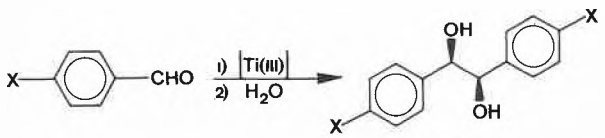
Abstract: Addition of butyllithium to titanium tetrachloride in diethylether produces a mixture capable of reducing the aromatic aldehydes RCHO (R = C_6H_5, *p*-MeC_6H_4, *p*-ClC_6H_4, or *o*-MeC_6H_4) stereoselectively to 1,2-diols $(RCHOH)_2$ with relative topicity *lk*.

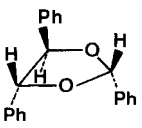
The reductive coupling of carbonyl compounds to afford mixtures of *meso*- and (±)-pinacols[1] or the corresponding alkenes by consecutive deoxygenation[2] has attracted much interest. Different reagents amongst which a variety of titanium-containing mixtures of known[3] and unknown[4] constitution have been employed to effect these transformations. Highly selective reductions have only been found with stannylene (stannandiyl) precursors, but not always in satisfactory yields[5]. We report here on a unique one-pot pinacolization which affords predominantly *like*-products under mild conditions.

Reaction of *n*-butyllithium with an equimolar quantity of the yellow $TiCl_4$-diethylether adduct suspended in ether at −50 °C, gave a grey, extremely air-sensitive solid suspended in a dark-brown solution. The mixture turned purple or yellow on addition of each of the aromatic aldehydes *p*-XC_6H_4CHO (X = H, Me, or Cl). Upon treatment with a saturated aqueous K_2CO_3 solution, the corresponding pinacols (**1**, **2**, and **3**, respectively, of *like*-configuration) were formed in more than 90% yields.



1: X = H
2: X = Me
3: X = Cl

Due to in situ condensation of the diol **1** with the starting aldehyde, the dioxolane **4** was formed as a side product (< 5% yield). These yields were directly determined by ^{1}H-NMR spectroscopy by comparison of the intensities of the aldehyde proton signal and the sharp resonances of the benzylic protons in the products. Isolated yields were somewhat lower (compare Experimental Section). No trace of any corresponding *unlike*- or *meso*-diol was detected. When employing *ortho*-tolualdehyde, however, steric factors came into play and both *l*- and *u*-isomers (**5** and **6**, respectively) of the diol were formed still selectively (ratio 8:1), but in lower yield.



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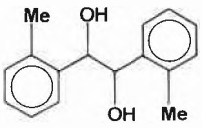


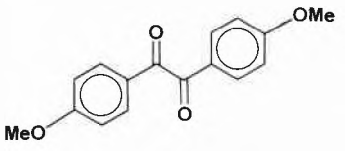
5: *l*-configuration
6: *u*-configuration

It has been proposed[6] that $BuTiCl_3$ disproportionates according to:

$$2\ BuTiCl_3 \rightarrow 2\ TiCl_3 + BuH + CH_3CH_2CH{=}CH_2$$

Titanium trichloride, however, effected no coupling of the aldehydes under the present reaction conditions[7] indicating that the active Ti^{III} was present in a «more complicated form». We established that the active species was present both in the dark ether solution and in the grey precipitate formed at −50 °C. After some hours at room temperature the solid turned dark-brown with concomitant loss in reactivity of the mixture which might be due to the eventual formation of $TiCl_3$. Although Ti^0 and Ti^{II} were previously used in such coupling reactions, the essential features of the applicable reaction mechanism[8, 9] still apply and need not be repeated here (compare also the discussion of V^{IV}-mediated aminative coupling of aromatic aldehydes[10]). Since the Ti^{III}-compound Cp_2TiCl_2 furnishes well-defined 1:1 dimeric oxygen-donor complexes with benzaldehyde[11], we also favour similar compounds to be formed in the present study, rather than five-membered bidentate chelates considered before[9].

Although a reductive coupling apparently occurred with *p*-methoxybenzaldehyde, subsequent hydride abstraction and pinacol rearrangement[12] produced the benzil **7** and the aldehyde **8**, respectively. No significant conversion was observed with *p*-nitrobenzaldehyde, pivalaldehyde, or acetophenone, and 3-phenylpropanal was converted to the aldol condensation product[13] (58%).



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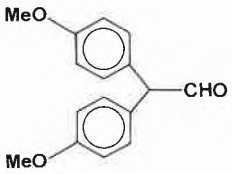

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Experimental

The synthesis of *l*-1,2-bis(4-chlorophenyl)-1,2-ethanediol (**3**) is described as a typical example: BuLi (10 mmol, 1.6 M in hexane) was slowly added to a suspension formed from $TiCl_4$ (10 mmol, 1.7 M in hexane) and diethylether (60 cm^3) at −50 °C. After 20 min the reaction mixture was warmed up slowly (30 min) to 0 °C. Upon addition of 1.0 g (7.1 mmol) *p*-chlorobenzaldehyde to the grey suspension, the mixture immediately turned yellow-green and later dark-yellow. After stirring for 2 h at room temperature under argon, 6 cm^3 of saturated aqueous K_2CO_3 solution was added and stirring continued for further 20 min. Diethylether (40 cm^3) was added, the mixture filtered through Celite, extracted twice with saturated aqueous NaCl solution, and dried over $MgSO_4$. Removal of the solvent under vacuum left the crude product as a white solid. ^{1}H-NMR indicated that no other product was formed in significant yield and that no unreacted aldehyde remained. Crystallization from ether/pentane afforded thin needles of the analytically pure diol **3** (0.92 g, 92%).

Compounds **1**, **2**, and **5**/**6** were prepared similarly (using ca. 10 mmol of each aldehyde) but remaining

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aldehyde in the crude product mixture was removed by washing with cold (−10 °C) hexane before crystallization. The dioxolane **4** was separated from **1** by flash column chromatography (SiO_2; diethylether/hexane, 1:6). A ^{1}H-NMR spectrum of the crude products obtained from *o*-tolualdehyde revealed a *l*/*u* product ratio of 8:1. When treated in the same manner with the Ti^{III}-reagent anisaldehyde gave a mixture of compounds which was treated with a saturated aqueous $Na_2S_2O_5$ solution (12 h) to remove unreacted aldehyde, and then subjected to a flash column chromatographic separation (SiO_2; diethylether/hexane, 1:5) to afford compounds **7** and **8**.

Yields and selected physical data for the products obtained are given in Table 1. Satisfactory elemental analyses for **3** and **5** were obtained. Analytical data for all the other products have been reported before.

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Table 1. Yields and selected characterization data for the compounds **1**–**8**.

l-1,2-Bis(phenyl)-1,2-ethanediol (**1**): ca. 90% (crude, by ^{1}H-NMR), 80% (isolated); *m.p.* 119 °C (Lit.[14] 119–120 °C); ^{1}H-NMR ($CDCl_3$): δ = 3.03 (s, broad, 2 H, 2 × OH), 4.66 (s, 2 H, 2 × PhCH), 7.0–7.3 (m, 10 H, 2 × C_6H_5).

l-1,2-Bis(4-methylphenyl)-1,2-ethanediol (**2**): ca. 90% (crude, by ^{1}H-NMR), 82% (isolated); *m.p.* 160 °C (Lit.[15] 163 °C); ^{1}H-NMR ($CDCl_3$): δ = 2.30 (s, 6 H, 2 × CH_3), 4.64 (s, 2 H, 2 × ArCH), 7.0–7.2 (m, 8 H, 2 × C_6H_4).

l-1,2-Bis(4-chlorophenyl)-1,2-ethanediol (**3**): > 98% (crude, by ^{1}H-NMR), 92% (isolated); *m.p.* 157 °C (*m.p. meso*-form 109–110 °C[14]); ^{1}H-NMR ($CDCl_3$): δ = 2.93 (s, broad, 2 H, 2 × OH), 4.60 (s, 2 H, 2 × ArCH), 6.8–7.3 (m, 8 H, 2 × C_6H_4); MS (70 eV): *m*/*z* 282 (*M*), 265(*M* − OH), 248 (100%, *M* − Cl), 141 (*M*/2).

l-2,4,5-Triphenyl-1,3-dioxolane (**4**): < 5% (crude, by ^{1}H-NMR), 3% (isolated); *m.p.* 84 °C (Lit.[16] 84–85 °C); ^{1}H-NMR ($CDCl_3$) δ = 4.93 (s, 2 H, $H^{4,5}$), 6.38 (s, 1 H, H^2), 7.2–7.7 (m, 15 H, 3 × C_6H_5).

l-1,2-Bis(2-methylphenyl)-1,2-ethanediol (**5**): ca. 62% (crude, by ^{1}H-NMR), 50% (isolated); *m.p.* 115 °C (*m.p. meso*-form 104–105 °C[17]); ^{1}H-NMR ($CDCl_3$): δ = 1.63 (s, 6 H, 2 × CH_3), 3.19 (s, broad, 2 H, 2 × OH), 4.91 (s, 2 H, 2 × ArCH), 6.7–7.5 (m, 8 H, 2 × C_6H_4); MS (70 eV). *m*/*z* 242 (*M*), 225 (*M* − OH), 208 (*M* − 2 × OH), 121 (100%, *M*/2).

u-1,2-Bis(2-methylphenyl)-1,2-ethanediol (**6**): ca. 7% (crude, by ^{1}H-NMR); ^{1}H-NMR ($CDCl_3$)[17]: δ = 2.13 (s, 6 H, 2 × CH_3), ca. 3.2 (s, broad, 2 H, 2 × OH), 5.14 (s, 2 H, 2 × ArCH), 6.7–7.5 (m, 8 H, 2 × C_6H_4).

4,4′-Dimethoxybenzoin (**7**): 34% (isolated); *m.p.* 132 °C (Lit.[18] 133 °C); ^{1}H-NMR ($CDCl_3$): δ = 3.87 (s, 6 H, 2 × CH_3); 7.34 (m, AA′XX′-system, J_{AX} = 9.5 Hz); IR ($CHCl_3$): ν(CO) = 1640 cm^{-1}.

Bis(4-methoxyphenyl)acetaldehyde (**8**): 14% (isolated); *m.p.* 100 °C (Lit.[19] 100–102 °C); ^{1}H-NMR ($CDCl_3$): δ = 3.80 (s, 6 H, 2 × CH_3), 4.77 (s, 1 H, ArCH), 6.8–7.3 (m, 8 H, 2 × C_6H_4), 9.83 (s, 1 H, CHO); IR ($CHCl_3$): ν(CO) = 1720 cm^{-1}.

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