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Arene synthesis by extrusion reaction

X *. Synthesis of arenes by deoxygenation of endoxides with cyclopentadienyltitanium trichloride / lithium aluminum hydride and dicyclopentadienyltitanium dichloride / lithium aluminum hydride

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Abstract

The two homogeneous systems, cyclopentadienyltitanium trichloride/lithium aluminum hydride and dicyclopentadienyltitanium dichloride/lithium aluminum hydride have been utilized to deoxygenate 1,4-endoxides in tetrahydrofuran. The results show that they can provide corresponding arenes in fair yields.

Introduction

Deoxygenation of 1,4-endoxide compounds (**1**) is perhaps one of the most useful routes to polysubstituted benzene nuclei (**2**) [2]. Low valent titanium generated by reduction of titanium tetrachloride [3,4], has been utilized by us in the synthesis of arenes **2** from 1,4-endoxides **1**. Ample examples have proved that $TiCl_4$–$LiAlH_4$–Et_3N in THF is extremely effective in converting **1** into **2** [5,6]. However, it should be mentioned that reactions involving $TiCl_4$–$LiAlH_4$–Et_3N in THF generally result in only moderate yields. The reason for this shortcoming might be attributed in part to the heterogeneous nature of the reaction systems. Perhaps more importantly, it has been observed that the insoluble titanium oxides produced during the deoxygenation process could interfere with the subsequent extraction procedure. Thus, a tedious filtration step must precede extraction in order to remove the fine powdery titanium oxides. We thought that these difficulties would be best obviated by

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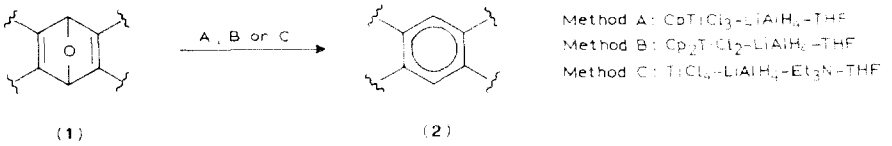
carrying out the deoxygenation reactions under homogeneous conditions. After some experimentation, we found out that cyclopentadienyltitanium trichloride ($CpTiCl_3$)/lithium aluminum hydride as well as dicyclopentadienyltitanium dichloride (Cp_2TiCl_2)/lithium aluminum hydride were both effective for deoxygenation. To this end, the two organotitanium reagents were used to remove oxygen atoms from several 1,4-endoxides **1**, resulting to yield their corresponding arenes **2**.



(1) (2)

Results and discussion

The $CpTiCl_3$–$LiAlH_4$–THF system (method A) was first used on three model oxygen-bridged compounds, namely dimethyl 7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (**3**) [5,8], dimethyl 1-methyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (**4**) [5] and dimethyl 1,4-dimethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (**5**) [5,9]. Hence, when compounds **3**, **4** and **5** were allowed to react with a mixture of $CpTiCl_3$ and $LiAlH_4$ in THF for 24 h at 55–70 °C under nitrogen, followed by the usual work-up, the corresponding phthalates **6** [5], **7** [5] and **8** [5,9,10] were obtained in moderate yields (see Table 1). Similarly, dimethyl 3-acetoxymethylphthalate (**12**), 13,14-dihydrotrinaphtho[*a*,*c*,*e*]cyclooctene (**13**) [11] and 6,7 : 14,15-dibenzotetraphenylene (**14**) [11] were also obtained from dimethyl 1-acetoxymethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (**9**). 1,6-endoxo-1,6 : 13,14-tetrahydrotrinaphtho[*a*,*c*,*e*]cyclooctene (**10**) [11] and 1,4 : 9,12-diendoxo-1,4 : 9,12-tetrahydro-6,7 : 14,15-dibenzotetraphenylene (**11**) [11] respectively. It is noteworthy that isolation of **13** and **14** involved only direct recrystallization whereas isolation of **6**, **7**, **8** and **12** required purification by thick layer chromatography.

The Cp_2TiCl_2–$LiAlH_4$–THF system (method B) has been used previously to convert the endoxides, **3** and **10** into the arenes **6** and **13** respectively (see Table 1).

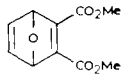
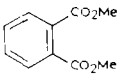
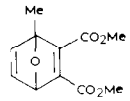
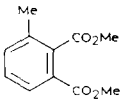
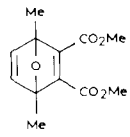
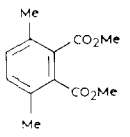
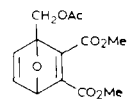
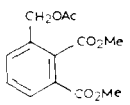
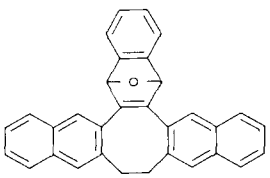
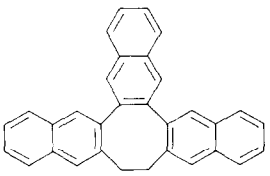
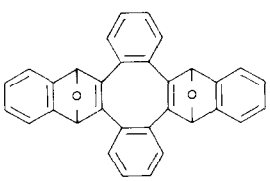
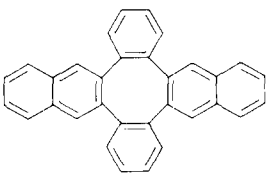
The structures of the reactants, and the structures and yields of the products, of method A and method B, are listed in Table 1, together with the yields of products obtained by use of method C ($TiCl_4$–$LiAlH_4$–Et_3N–THF) [5,11]. As can be seen from the Table, methods A,B and C generally provide comparable yields. Nevertheless, we believe that although methods A and B do not seem to afford significant improvements in the yields of products, it does not hamper their applicability because the extraction procedure for methods A and B is much easier to perform than that of method C. Furthermore, handling of $CpTiCl_3$ and Cp_2TiCl_2 is safer and more convenient than that of $TiCl_4$.

Experimental

Proton nuclear magnetic resonance spectra were recorded in $CDCl_3$ solution on a Bruker cryospec WM 250 (250 MHz) spectrometer or on a JEOL PMX 60 SI (60 MHz) spectrometer. The absorptions are reported in parts per million downfield (δ

Table 1

Reactants, yields and products of compounds by use of methods A–C

Reactant	Yield (%) Method A	Yield (%) Method B	Yield (%) Method C	Product
 (3)	56	57	64 [5]	 (6)
 (4)	73		78 [5]	 (7)
 (5)	48		54 [5]	 (8)
 (9)	42		33	 (12)
 (10)	54	80	93 [11]	 (13)
 (11)	75		89 [11]	 (14)

scale) from Me_4Si as internal reference. Mass spectra were recorded on a VG Micromass 7070F spectrometer. Analytical thin-layer chromatography (TLC) was carried out on precoated thin layers of silica gel F_{254} (Merck) on aluminum foil. Preparative layer chromatography was carried out on 0.5–1.0 mm thick layers of Merck Kieselgel 60 PF_{254} on 20×20 cm^2 glass plates. Solvents used were redistilled or purified and dried by standard procedures [12]. All evaporations of solvents were carried out by a rotatory evaporator in conjunction with a water aspirator. Compounds in organic solvents were dried over anhydrous Na_2SO_4.

*(a) Dimethyl phthalate (**6**) (method A)*

To a solution of $CpTiCl_3$ (0.53 g, 2.4 mmol) in THF (10 ml) under N_2 was cautiously added $LiAlH_4$ (80 mg, 2.11 mmol) in THF (5 ml). The reaction mixture was stirred at 55°C for 1 h and was then cooled to room temperature. Endoxide **3** (95 mg, 0.45 mmol) in THF (9 ml) was then introduced. The mixture was stirred for 24 h at 55°C. It was allowed to cool to room temperature and was poured into sat. aq. K_2CO_3 solution (150 ml) and filtered. The residue was washed with $CHCl_3$ several times. The filtrate was extracted with $CHCl_3$ (3 × 50 ml). The combined $CHCl_3$ solution was dried and evaporated. A yellow oil was obtained and was chromatographed on preparative layer of silica gel (EtOAc/hexanes 1/3) to give the phthalate **6**: 49 mg (56%); ^{1}H NMR 3.80(s,6H), 7.20–7.68 (AA′BB′,4H); MS *m/e* 194(M^+).

*(b) Dimethyl phthalate (**6**) (method B)*

To a solution of Cp_2TiCl_2 (1.2 g, 4.8 mmol) in THF (5 ml) under N_2 was added $LiAlH_4$ (0.2 g, 5.3 mmol) in THF (10 ml). The reaction mixture was stirred for 30 min at 80°C, then endoxide **3** (0.2 g, 1 mmol) was added and the mixture was stirred at 80°C for 24 h, after which sat. aq. K_2CO_3 (50 ml) was added to the mixture. The organic compound was extracted with $CHCl_3$ (3 × 70 ml). The $CHCl_3$ solution was dried and evaporated to give phthalate **6** which was purified by thick layer chromatography on silica gel (EtOAc/hexanes 1/4): 105 mg (57%); the spectral data are identical with an authentic sample [5].

*(c) Dimethyl 3-methylphthalate (**7**) (method A)*

To a solution of $CpTiCl_3$ (0.46 g, 2.12 mmol) in THF (10 ml) under N_2 was added $LiAlH_4$ (88 mg, 2.31 mmol) in THF (3 ml). The reaction mixture was stirred at 55°C for 1 h and was then cooled to room temperature. Endoxide **4** (95 mg, 0.42 mmol) in THF (8 ml) was then added. The mixture was stirred for 24 h at 55°C, and was allowed to cool to room temperature. It was then poured into sat. aq. K_2CO_3 (150 ml) and filtered. The residue was washed with $CHCl_3$ several times. The filtrate was extracted with $CHCl_3$ (3 × 50 ml). The combined $CHCl_3$ solution was dried and evaporated. A yellow oil was obtained and was chromatographed on silica gel (EtOAc/hexanes 1/3) to give phthalate **7**: 64 mg (73%); ^{1}H NMR 2.28(s,3H), 3.82(s,3H), 3.90(s,3H), 7.22–7.35(m,2H), 7.75(d,1H); MS *m/e* 208 (M^+).

*(d) Dimethyl 3,6-dimethylphthalate (**8**) (method A)*

To a solution of $CpTiCl_3$ (0.56 g, 2.56 mmol) in THF (14 ml) under N_2 was added $LiAlH_4$ (91 mg, 2.39 mmol) in THF (7 ml). The reaction mixture was stirred at 55°C for 1 h and was then cooled to room temperature. Endoxide **5** (0.11 g 0.46 mmol) in THF (7 ml) was then added, and the mixture was stirred for 24 h at 55°C, and allowed to cool to room temperature. It was poured into sat. aq. K_2CO_3 (150 ml) and filtered. The residue was washed with $CHCl_3$ several times, and the filtrate was extracted with $CHCl_3$ (3 × 50 ml). The combined $CHCl_3$ solution was dried and evaporated to leave a yellow oil which was purified by chromatography on silica gel (EtOAc/hexanes 1/3) to give phthalate **8**: 49 mg (48%); m.p. 73–75°C (ref. 9: 72–73°C); ^{1}H NMR 2.40(s,6H), 3.90(s,6H), 7.20(s,2H); MS *m/e* 222 (M^+).

*(e) Dimethyl 3-acetoxymethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (**9**)*

Dimethyl acetylenedicarboxylate (3.56 g, 25 mmol) and furfuryl acetate (2.97 g, 21 mmol) were placed in a sealed tube and heated at 110°C for 24 h. The reaction

mixture was chromatographed on a silica gel column (EtOAc/hexanes 1/1) to give the endoxide **9**: 3.17 g (49%); ^{1}H NMR 2.10(s,3H), 3.85(s,3H), 3.90(s,3H), 4.92(s,2H), 5.90(s,1H), 7.20–7.65(m,2H).

*(f) Dimethyl 3-acetoxymethylphthalate (**12**) (method A)*

To a solution of $CpTiCl_3$ (0.72 g, 3.28 mmol) in THF (9 ml) under N_2 was added $LiAlH_4$ (0.10 g, 2.73 mmol) in THF (2 ml). The reaction mixture was stirred at 70 °C for 1.5 h and was then allowed to cool to room temperature. Endoxide **9** (0.16 g, 0.58 mmol) in THF (6 ml) was introduced. The mixture was stirred for 24 h at 70 °C, and was allowed to cool and poured into sat. aq. K_2CO_3 (150 ml). The resulting mixture was filtered and the residue was washed with $CHCl_3$ several times. The filtrate was extracted with $CHCl_3$ (3 × 50 ml). The combined $CHCl_3$ solution was dried and evaporated. The yellow oil obtained was chromatographed on a preparative layer of silica gel (EtOAc/hexanes 1/3) to give the phthalate **12**: 65 mg (42%); ^{1}H NMR 2.10(s,3H), 3.90(s,3H), 3.96(s,3H), 5.18(s,2H), 7.52(t,1H), 7.62(d,1H), 7.98(d,1H); MS calc. for $C_{12}H_{10}O_5$ 234.0526, measured 234.0525.

*(g) Dimethyl 3-acetoxymethylphthalate (**12**) (method C)*

To a solution of $TiCl_4$ (2 ml, 17 mmol) in THF (8 ml) under N_2 was cautiously added $LiAlH_4$ (0.31 g, 8 mmol) in THF (8 ml) and was followed by Et_3N (0.28 g, 30 mmol) in THF (2 ml). The reaction mixture was stirred at 65 °C for 1 h and then cooled to room temperature. Endoxide **9** (0.72 g, 3 mmol) in THF (3 ml) was then added. The mixture was stirred at room temperature for 24 h. It was then poured into sat. aq. K_2CO_3 (150 ml) and filtered. The aqueous layer was washed with $CHCl_3$ (3 × 50 ml). The combined $CHCl_3$ solution was dried and evaporated. A yellow oil was obtained and was chromatographed on a preparative layer of silica gel (EtOAc/hexanes 1/3) to give the phthalate **12**: 0.22 g (33%); the spectral data were identical with those reported for (f).

*(h) 13,14-Dihydrotrinaphtho[a,c,e]cyclooctene (**13**) (method A)*

To a solution of $CpTiCl_3$ (0.13 g, 0.61 mmol) in THF (6 ml) under N_2 was added $LiAlH_4$ (19 mg 0.51 mmol) in THF (3 ml). The reaction mixture was stirred at 70 °C for 1 h and was then cooled to room temperature. Endoxide **10** (21 mg, 0.05 mmol) in THF (4 ml) was then introduced. The mixture was stirred for 24 h at 70 °C, and was allowed to cool to room temperature. It was then poured into sat. aq. K_2CO_3 (150 ml) and filtered, and the residue washed with $CHCl_3$ several times. The filtrate was extracted with $CHCl_3$ (3 × 50 ml). The combined $CHCl_3$ solution was dried and evaporated. The residue was recrystallized from absolute EtOH to give **13**: 11 mg (54%); m.p. 290–292 °C (ref. 11: 290–292 °C); ^{1}H NMR 3.22(d,4H), 7.24–7.40(m,4H), 7.45–7.60(m,6H), 7.62–7.70(m,4H), 7.90(s,2H), 7.92–8.00(m,2H); MS calc. for $C_{32}H_{22}$ 406.1721, measured 406.1726.

*(i) 13,14-Dihydrotrinaphtho[a,c,e]cyclooctene (**13**) (method B)*

To a solution of Cp_2TiCl_2 (158 mg, 0.635 mmol) in THF (10 ml) under N_2 was added $LiAlH_4$ (49 mg, 1.3 mmol) in THF (5 ml). The mixture was stirred and refluxed at 90 °C for 2 h. The endoxide **10** (11.6 mg, 0.02 mmol) was added and the mixture was stirred at 85 °C for 3 h. It was then allowed to cool to room temperature and sat. aq. K_2CO_3 (50 ml) was added. The mixture was extracted with

$CHCl_3$ (3 × 70 ml) and the $CHCl_3$ solution was dried and evaporated. The residue was purified by chromatography on silica gel (EtOAc/hexanes 1/4). The compound was further purified by recrystallization from absolute EtOH to give **13**: 9 mg (80%); the spectral data were identical with those reported for (h).

*(j) 6,7:14,15-Dibenzotetraphenylene (**14**) (method A)*

To a solution of $CpTiCl_3$ (94 mg, 0.43 mmol) in THF (9 ml) under N_2 was added $LiAlH_4$ (12 mg, 0.31 mmol) in THF (3 ml). The reaction mixture was stirred at 70°C for 2 h and was then cooled to room temperature. Endoxide **11** (23 mg, 0.05 mmol) in THF (6 ml) was then introduced, and the mixture was stirred for 24 h at 70°C, and allowed to cool to room temperature. It was then poured into sat. aq. K_2CO_3 (150 ml) and filtered. The residue was washed with $CHCl_3$ several times. The filtrate was extracted with $CHCl_3$ (3 × 50 ml). The combined $CHCl_3$ solution was dried and evaporated. The residue was recrystallized from absolute EtOH to give **14**: 16 mg (75%); m.p. 288–291°C (ref. 11: 288–291°C); ^1H NMR 7.24–7.34(AA'BB',8H), 7.36–7.76(AA'BB',8H), 7.63(s,4H); MS calc. for $C_{32}H_{20}$ 404.1565, measured 404.1564.

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