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A FACILE REDUCTION OF AROMATIC NITRO COMPOUNDS TO AROMATIC AMINES WITH BIS(CYCLOPENTADIENYL)TITANIUM(IV) DICHLORIDE-INDIUM SYSTEM

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ABSTRACT

 Cp_2TiCl_2/In system was found to be a new reagent for reducing various aromatic nitro compounds to the corresponding aromatic amines in good yields under mild and neutral conditions.

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The chemical reactivity of Cp2TiCl2/M system (M=Na, Zn, Al, Mg, Sm) has been the subject of considerable interest and the reducing ability of these systems has been extensively studied.^[1] It has recently been reported that Cp₂TiCl₂/samarium system is used as a reagent for reducing nitroarenes to the corresponding amines.^[2] The synthesis of aromatic amines has been an active area of research for many years and a large number of methods have been developed for the reduction of aromatic nitro compounds.^[3] We considered that Cp₂TiCl₂/In system can be an efficient reducing agent for the conversion of nitroarenes to the corresponding amines. The application of indium reagents in organic synthesis has attracted considerable interest in the last decade.^[4] We have investigated the reaction of Cp2TiCl2/In with various nitroarenes and found that they can be effectively reduced to the corresponding aromatic amines in good yields (Eq. 1). The scope of the reaction is illustrated in Table 1. The new reducing system was generated by the addition of indium powder to a stirred solution of bis(cyclopentadienyl)titanium(IV) dichloride in THF under nitrogen. In continuation of our interest on the applications of indium reagents for various transformations^[5] we would like to report here the reduction of aromatic nitro compounds to aromatic amines by treatment with Cp₂TiCl₂/In under mild conditions. Some control experiments revealed that nitroarenes could not be reduced by Cp₂TiCl₂ or indium alone and were recovered unchanged.

$$\begin{array}{ccc} \operatorname{ArNO}_2 & \xrightarrow{\operatorname{Cp}_2 \operatorname{IrCl}_2/\operatorname{In}} & \operatorname{ArNH}_2 \\ & & & \\ 1 & & & 2 \end{array} \tag{1}$$

The reaction molar ratio of indium and Cp_2TiCl_2 is 1:2. If the molar ratio is changed to $In:Cp_2TiCl_2=1:1$, the reaction is not successful. In comparison with the Cp₂TiCl₂/Sm system, the method of Cp₂TiCl₂/In system resulted in high yields of amino compounds (76-91%). The functional group tolerance of this method is evident from Table 1 which shows that bromo, chloro, methoxy, hydroxy, ketone, carboxyl and ester are not affected under the reaction conditions. All the compounds obtained showed IR, NMR and mass spectral data compatible with the structure. In order to assess the generality of the process, the reaction was studied with a variety of nitroarenes. Thus, we have been able to demonstrate the utility of easily accessible Cp2TiCl2/In system as a convenient reagent for effecting chemoselective reduction of nitroarenes. Although the role of *bis*(cyclopentadienyl)titanium(IV) dichloride is still not clarified, it is assumed that reduction of titanium(IV) with indium provides low valent titanium,^[6] which might be reducing nitroarenes **1** to give the corresponding amines 2. The notable advantages of this methodology are mild reaction

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Entry	Substrate	Product ^a	Reaction Time (h)	Yield (%) ^b
1	C ₆ H ₅ NO ₂	C ₆ H ₅ NH ₂	0.5	91
2	$p-CH_3C_6H_4NO_2$	p-CH ₃ C ₆ H ₄ NH ₂	0.5	91
3	<i>p</i> -HOC ₆ H ₄ NO ₂	<i>p</i> -HOC ₆ H ₄ NH ₂	3	86
4	p-BrC ₆ H ₄ NO ₂	p-BrC ₆ H ₄ NH ₂	0.5	90
5	o-CH ₃ COC ₆ H ₄ NO ₂	o-CH ₃ COC ₆ H ₄ NH ₂	0.5	89
6	<i>p</i> -CH ₃ OOCC ₆ H ₄ NO ₂	<i>p</i> -CH ₃ OOCC ₆ H ₄ NH ₂	2	93
7	o-CH ₃ OC ₆ H ₄ NO ₂	o-CH ₃ OC ₆ H ₄ NH ₂	0.5	79
8	p-HOOCC ₆ H ₄ NO ₂	<i>p</i> -HOOCC ₆ H ₄ NH ₂	1	76
9			0.5	80
10			4	81

Table 1. Reduction of Nitroarenes to Amines with Cp₂TiCl₂/In

^aAll products obtained were fully characterized by spectral analysis. ^bIsolated yield.

condition, simple operation, high yield, tolerance of various functional groups on the aromatic ring.

In conclusion, we believe this procedure using Cp_2TiCl_2/In system will present a useful and convenient alternative to the existing methods for reduction of nitroarenes to the corresponding amines. Further applications of Cp_2TiCl_2/In system as reducing agent in organic synthesis are currently under investigation.

EXPERIMENTAL

Tetrahydrofuran was freshly distilled from sodium/benzophenone ketyl before use. ¹H NMR spectra were recorded on a FT-Bruker AF-300 (300 MHz for ¹H NMR; 75 MHz for ¹³C NMR) using TMS as an internal standard. The solvent was CDCl₃ unless otherwise noted. IR spectra were obtained on a Perkin Elmer 16F PC FT-IR Shimadzu. GC-MS was recorded on a Hewlett-Packard 5890 GC. High resolution mass spectra (HRMS) were obtained on a Varian MATCH-50F instrument.

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General Procedure for the Reaction

Bis(cyclopentadienyl)titanium(IV) dichloride (438 mg, 1.75 mmol, Aldrich, 97%), indium powder (100 mesh, 86 mg, 0.75 mmol, Aldrich, 99.99%) and THF (5 mL) were mixed under nitrogen atmosphere and the resulting mixture was stirred at reflux for 30 min. A dark-red solution of the low-valent titanium–indium complex was obtained and cooled to room temperature. To this solution, nitrobenzene (23.0 mg, 0.25 mmol) was added. The reaction mixture was stirred for 10 min at room temperature under nitrogen. The solvent was evaporated under reduced pressure and the residue was diluted with ether and filtered. The crude product was purified by silica gel column chromatography (hexane:ethyl acetate=6:1) to afford aniline (20.0 mg, 91%).

Entry 1: Oil. ¹H NMR (CDCl₃, 300 MHz): δ 7.23 (t, 2H, J = 8.8 Hz), 6.81 (m, 3H), 3.63 (bs, 2H): IR(film) 3455, 3356, 1606, 1498 cm⁻¹; GC-MS (m/z) 93 (M⁺).

Entry $2^{[7]}$: M.p. 45–46°C (lit: 44–46°C). ¹H NMR (CDCl₃, 300 MHz): δ 6.97 (d, 2H, J = 8.4 Hz), 6.65 (d, 2H, J = 8.4 Hz), 3.38 (bs, 2H), 2.24 (s, 3H); IR(film) 3416, 3334, 1624, 1514 cm⁻¹; GC-MS(m/z) 107 (M⁺).

Entry $3^{[7]}$: M.p. 185–187°C (lit: 188–190°C). ¹H NMR (CDCl₃, 300 MHz): δ 7.23 (d, 2H, J = 8.8 Hz), 6.81 (d, 2H, J = 8.8 Hz), 2.63 (bs, 2H); IR(film) 3340, 3280, 1616, 1508 cm⁻¹; GC-MS(m/z) 93 (M⁺).

Entry $4^{[7]}$: M.p. 62–64°C (lit: 62–64°C). ¹H NMR (CDCl₃, 300 MHz): δ 7.23 (d, 2H, J = 8.6 Hz), 6.56 (d, 2H, J = 8.6 Hz), 3.67 (bs, 2H); IR(film) 3466, 3376, 1610, 1486 cm⁻¹; GC-MS(m/z) 170 (M⁺).

Entry 5: Oil. ¹H NMR (CDCl₃, 300 MHz): δ 7.71 (d, 1H, J = 8.4 Hz), 7.26 (t, 1H, J = 8.6 Hz), 6.65 (m, 2H), 6.27 (bs, 2H), 2.57 (s, 3H): IR(film) 3462, 3342, 1644, 1616, 1550 cm⁻¹; GC-MS(m/z) 135 (M⁺).

Entry $6^{[7]}$: M.p. 109–110°C (lit: 110–111°C). ¹H NMR (CDCl₃, 300 MHz): δ 7.86 (d, 2H, J=8.7 Hz), 6.64 (d, 2H, J=8.7 Hz), 4.06 (bs, 2H), 3.87 (s, 3H); IR(film) 3422, 3340, 1684, 1634, 1596 cm⁻¹; GC-MS(m/z) 151 (M⁺).

Entry 7: Oil. ¹H NMR (CDCl₃, 300 MHz): δ 6.76 (m, 4H), 3.85 (s, 3H), 3.67 (bs, 2H); IR(film) 3454, 3370, 1616, 1506, 1224 cm⁻¹; GC-MS(*m*/*z*) 123 (M⁺).

Entry 8^[7]: M.p. 188–189°C (lit: 187–189°C). ¹H NMR (CDCl₃, 300 MHz): δ 7.23 (d, 2H, J=8.8 Hz), 6.81 (d, 2H, J=8.8 Hz), 3.63 (bs, 2H); IR(film) 3462, 3366, 1690, 1604, 1522 cm⁻¹; GC-MS(m/z) 93 (M⁺).

Entry 9: Oil. ¹H NMR (CDCl₃, 300 MHz): δ 6.98 (d, 1H, J = 7.7 Hz), 6.71 (s, 1H), 6.49 (d, 1H, J = 9.0 Hz), 3.47 (bs, 2H), 2.25 (s, 3H): IR(film) 3445, 3362, 1624, 1500 cm⁻¹; GC-MS(m/z) 141 (M⁺).

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Entry 10^[7]: M.p. 253–255°C (lit: 253–255°C). ¹H NMR (CDCl₃, 300 MHz): δ 8.28 (m, 2H), 7.80(m, 3H), 7.48 (t, 1H, J=9.0 Hz), 6.98 (d, 1H, J=6.0 Hz), 6.88 (bs, 2H); IR(film) 3455, 3336, 1650, 1610, 1495 cm⁻¹; GC-MS (m/z) 223 (M⁺).

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