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Reductive coupling of aromatic aldehydes and imines by the low valent titanium species generated in the reaction of $TiCl_4$ with Et_3N

Mariappan Periasamy*, Gadthula Srinivas, Galla V. Karunakar and Pandi Bharathi

School of Chemistry, University of Hyderabad, Central University P.O.,
Hyderabad 500 046, India.

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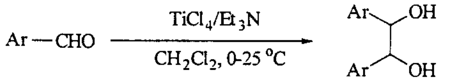
Abstract: Aromatic aldehydes and imines are converted to the corresponding diols and diamines using the low valent titanium species generated by the reaction of $TiCl_4$ with triethylamine. **© 1999 Published by Elsevier Science Ltd. All rights reserved.**

Keywords: Aromatic aldehydes; diols; diamines; coupling reactions.

The reduction of $TiCl_4$ to lower valent titanium species and the synthetic utility of such species are well documented chemistry of wide interest.[1] Generally, reducing agents such as Mg, Zn, Li, Pb-Te and $LiAlH_4$ are used for the reduction of $TiCl_4$.[2] In most cases, reactions of such species with carbonyl compounds give olefins (eg. McMurry reaction). During the course of studies on the synthetic applications of the $TiCl_4/Et_3N$ reagent system,[3] we became interested in the low valent titanium species that would be formed in the reaction of R_3N with $TiCl_4$. Herein, we report the reductive coupling of aromatic aldehydes and imines by the titanium species formed in this way.

The aromatic aldehydes and imines react with species generated using $TiCl_4/Et_3N$ to give the corresponding diols (Table 1) and diamines (Table 2) respectively.[4] Whereas benzaldehyde, *p*-chloro benzaldehyde and *o*-methyl benzaldehyde gave a mixture of *dl/meso* isomers, *p*-methyl benzaldehyde yielded the *dl* isomer only. The reaction with enolizable ketones, such as acetophenone was not clean under these conditions.

Table 1. Conversion of aromatic aldehydes to 1,2-diols using $TiCl_4/Et_3N$



	Ar	Yield (%)	dl/meso
1	C_6H_5	71	74/26
2	*p*-ClC_6H_4	58	83/17
3	*p*-MeC_6H_4	61	100/0
4	*o*-MeC_6H_4	63	75/25

a. The products were identified using the spectral data (IR, ^{1}H-nmr, ^{13}C-nmr and ms) and comparison with reported data.[5]

b. Yields are based on the aldehyde used.

c. The dl/meso ratio in the mixture was determined by comparison with reported ^{1}H-nmr data.[5]

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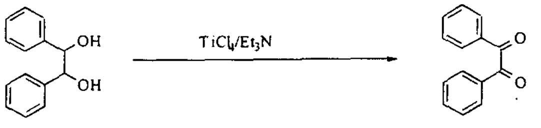
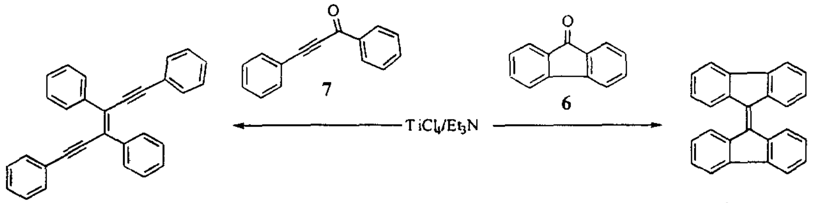
Also, it was observed that when excess $TiCl_4$ was used in the reaction with benzaldehyde, benzil (**5**) was isolated besides 12% of diol.[6] Presumably, the diol is oxidized to the diketone under these reaction conditions. This was further confirmed by carrying out the reaction with diol. When $TiCl_4$ and Et_3N were taken in 1:1 ratio and 1,2-diphenyl-1,2-ethanediol (0.25 equivalents), benzil (**5**) was isolated in 77% yield (eq 1).



------- (1)

5 77%

The fluorenone (**6**) and the alkynyl ketone (**7**) gave the corresponding McMurry products (**6a** and **7a**) under these conditions (eq 2).[7]

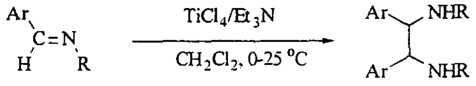


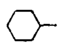
---- (2)

7a 43% **6a** 64%

The reaction of aromatic imines gives the *dl/meso* mixture of 1,2-diamines (60-65%) under these conditions.

Table 2. Conversion of aromatic imines to diamines using $TiCl_4/Et_3N$



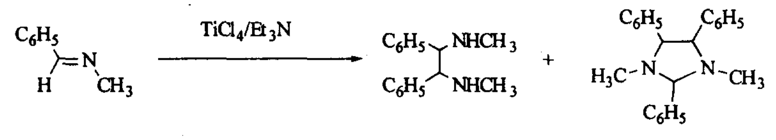
	Ar	R	Yield (%)	dl/meso
7[8a]	C_6H_5	C_6H_5	65	80/20
8	C_6H_5	p-ClC_6H_4	63	85/15
9	p-ClC_6H_4	C_6H_5	62	76/24
10[8b]	C_6H_5		60	16/84
11[8a]	C_6H_5	$(CH_3)_3C$	62	33/67

a. The products were identified using the spectral data (IR, ^{1}H-nmr, and ^{13}C-nmr) and comparison with reported data. (for **7**, **10** and **11**) [8]

b. Yields are based on the imines used.

c. The dl/meso ratio in the mixture was determined by comparison with reported ^{13}C-nmr data.[8]

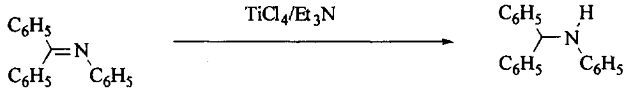
The imine **12** gave imidazolidine **12b** in 48% yield besides the diamine **12a** (21%) (eq 3).



(3)

12 **12a** 21% **12b** 48%

The anil **13** was reduced to corresponding secondary amine **13a** in 31% yield (eq 4).

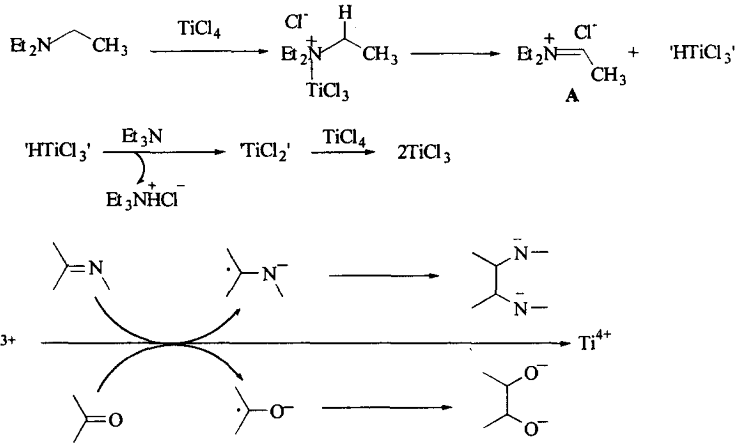


(4)

13 **13a** 31%

The $TiCl_4/Et_3N$ system has been extensively used for the generation of titanium enolates for applications in aldol reactions.[9] Recently, it has been used for the oxidative coupling of phenylacetic acid esters and amides to the corresponding 2,3-diphenylsuccinic acid derivatives.[10] We have observed the formation of 2,5-diarylpyrroles in the reaction of aryl methyl ketimines with $TiCl_4/Et_3N$.[3] In all these reactions, the Ti(IV) species is reduced to Ti(III). In 1955, it was reported that the reaction of $TiCl_4/Me_3N$ gives $TiCl_3/Me_3N$ complexes and α-haloamines.[11] Based on these observations, the transformation described here can be explained by the sequence of reactions outlined in Scheme 1.

Scheme 1.



Whereas the '$HTiCl_3$' species may be expected to cause reductions, the Ti(II) and Ti(III) species would lead to coupling reactions described here. In conclusion, a simple way of making low valent titanium species without using metals or metal hydrides has been achieved. The results described here illustrate the synthetic possibilities of these species.

Acknowledgement

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3. Periasamy, M., Srinivas, G., Bharathi, P. *J. Org. Chem.* **1999,** *64,* 4204.
4. <u>**The reaction of aldehydes:**</u> Dichloromethane (25 ml) and Et_3N (15 mmol) were taken under N_2 atmosphere. $TiCl_4$ (10 mmol) was added under N_2 at 0°C. The reaction mixture was stirred for 1h at 0°C and the aldehyde (5 mmol) was added to this reaction mixture and stirred further for 5h at 0-25°C. It was quenched with saturated NH_4Cl solution (20 ml). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 25 ml). The combined organic extract was washed with brine solution (10 ml) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column. The product diol was isolated using 10% EtOAc/hexane mixture as eluent. <u>**The reaction of imines**</u>: Dichloromethane (25 ml), Et_3N (15 mmol) and imine (10 mmol) were taken under N_2 atmosphere. $TiCl_4$ (10 mmol) in CH_2Cl_2 (10 ml) was added dropwise under N_2 at 0°C for 15 min. The reaction mixture was stirred for 0.5h at 0°C and stirred further for 7-8h at 25°C. It was quenched with saturated K_2CO_3 solution (30 ml) and filtered through Buchner funnel. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 25 ml). The combined organic extract was washed with brine solution (10 ml) and dried over anhydrous K_2CO_3. The solvent was removed and the residue was chromatographed on a silica gel column with 5% EtOAc/hexane mixture as eluent
5. Compounds **1-4** were reported; Raubenheimer, H. G., Seebach, D. *Chimia.* **1986,** *40,* 12..
6. The reaction was carried out by using PhCHO (10 mmol), $TiCl_4$ (15 mmol) and Et_3N (10 mmol).
7. Compound **6a** mp 247°C (Lit[12]. mp 244-247°C), ^{13}C-nmr (δ ppm) 141.35, 141.04, 138.32, 129.16, 126.85, 126.75, 119.89. **7a.** ^{13}C-nmr (δ ppm) $CDCl_3$: 139.14, 131.44. 129.29, 128.71, 128.47, 128.32, 127.88, 123.33, 98.68, 90.99. M^+ (e/m) 380.
8. (a) Mangeney, P. Tejero, T., Alexakis, A., Grosjean, F., Normant, J. *Synthesis*, **1988,** 255. (b) Enholm, E. J., Forbes, D. C., Holub, D. P. *Synth. Commun.* **1990**, 981. **Spectral data for the compounds 1-4, 7-11, 12b and 13a.** ^{1}H-NMR (200 MHz, $CDCl_3$) data for the compounds **1-4.** **1** δ: 2.91 (s, broad, 2H), 4.72 (s, 2H, *dl*), 4.8 (s, 2H, *meso*), 7.11-7.35 (m, 10H). **2** δ: 3.05 (s, broad, 2H), 4.60 (s, 2H, *dl*), 4. 85 (s, 2H, *meso*), 7.12-7.32 (m, 8H). **3** δ: 2.30 (s, 6H), 2.8 (s, 2H), 4.68 (s, 2H, *dl*), 7.10-7.25 (m, 8H). **4** δ: 1.71 (s, 6H), 2.92 (s, broad, 2H), 5.0 (s, 2H, *dl*), 5.15 (s, 2H, *meso*), 6.81-7.71 (m, 8H). ^{13}C-NMR (50 MHz, $CDCl_3$) data for the compounds **7-11.** **7** δ: *dl:* 147.15, 140.01, 129.17, 128.44, 127.55, 118.16, 114.18, 64.06.7. *meso:* 146.66, 138.34, 129.17, 128.44, 127.55, 118.0, 113.86, 62.11. **8** δ: *dl:* 145.54, 139.25, 128.61-127.34, 122.99, 115.35, 63.99. *meso:* 145.05, 137.58, 128.61-127.34, 122.69, 115.03, 62.12. **9** δ: *dl*: 146.60, 138.33, 133.47, 129.26, 128.79, 118.67, 114.25, 63.58; *meso*: 146.08, 136.67, 129.26, 128.79, 118.42, 113.92, 61.54. **10** δ: *dl*: 142.23, 128.33-126.55, 66.38, 53.93, 34.87, 32.62, 26.10, 24.92, 24.51; *meso*: 141.99 128.34-126.56, 65.16, 53.12, 34.63, 32.38, 26.10, 24.92, 24.51. **11** δ: *dl*: 145.52, 128.57-126.19, 64.18, 51.02, 30.12; *meso*: 145.13, 128.57-126.19, 63.88, 50.84, 29.91. **12b** δ: 140.79, 140.13, 129.4, 128.90, 128.65, 128.32, 127.31, 126.52, 92.09, 73.78, 37.76. ^{1}H-NMR (δ ppm): 7.9-7.1 (m, 15H), 4.1 (s, 2H), 3.8 (s, 1H), 2.1 (s, 6H). **13a** ^{13}C-NMR (δ ppm) 143.05, 125.19, 126.82, 127.53, 127.43, 117.76, 113.60, 63.13. ^{1}H-NMR (δ ppm): 7.9-6.6 (m, 15H), 5.7 (s, 1H), 4.4 (s, 1H).
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