SHORT PAPER

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Formation of α-ethylcinnamaldehydes by the reaction of aromatic aldehydes with *n*-$Bu_3N/TiCl_4$†

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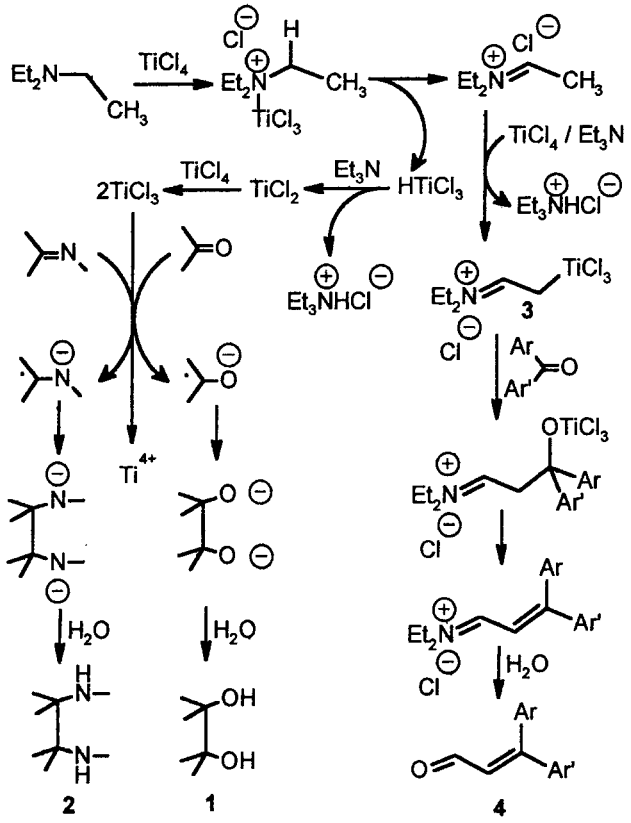
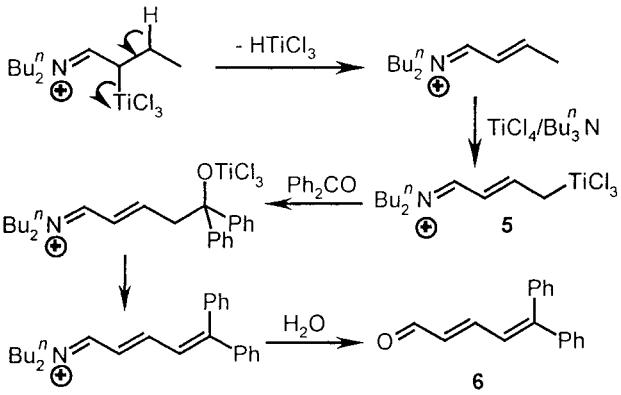
The reaction of various aromatic aldehydes with *n*-Bu_3N in the presence of $TiCl_4$ gave the corresponding α-ethylcinnamaldehydes in 18–31% yield; when *p*-chlorobenzaldehyde was used, *p*-chlorobenzyl alcohol was also isolated besides α-ethyl-*p*-chlorocinnamaldehyde.

Titanum (IV) is usually more stable than titanium in lower oxidation states. Therefore, low valent titanium has the tendency to transform to titanium (IV), thus effecting reduction of a variety of organic compounds en route[1]. Consequently, the reverse of this reaction, that is oxidation by titanium (IV) is usually an unfavourable reaction and has been only rarely observed. In this regard, the $TiCl_4$-promoted oxidative couplings of lithium ester enolates[2] and their silylated analogues,[3] phenylacetic acid esters[4] and arylacetic acid amides[4] are noteworthy. These reactions have recently been used for asymmetric synthesis of α, α′-disubstituted succinic acid derivatives.[4a,5] Aryl methyl ketimines have also been reported to undergo oxidative coupling with $TiCl_4/Et_3N$ to 2,5-diaryl pyrroles.[6]

Although reduction of $TiCl_4$ by simple tertiary amines such as Me_3N [7] and Et_3N [8] was reported about 45 years ago, a mixture of $TiCl_4$ and Et_3N which had been stirred for 1 hour, has only recently been used as a source of low valent titanium for reductive coupling of aldehydes and ketones including diaryl ketones to *vic*-diols **1** and imines to *vic*-diamines **2** (Scheme 1).[9] The iminium ion intermediate, which was proposed to be formed by the oxidation of Et_3N with $TiCl_4$ in the reaction, was more recently shown to condense with diaryl ketones under slightly different conditions (adding Et_3N to a stirred solution of $TiCl_4$ and diaryl ketones) to give 3,3-diarylpropenals **4** as the condensation products in high yields.[10] Under these conditions, the reductive coupling of the ketone was not observed. The products were proposed to arise by the reaction of α-titanated iminium ion **3** with the diaryl ketones followed by hydrolysis of the iminium group during aqueous workup. The reaction of some higher tertiary amines such as *n*-Pr_3N, *n*-Bu_3N, *N*-ethyl-, *N*-*n*-pentyl-, and *N*-*n*-hexyl- piperidines with $TiCl_4$ in the presence of benzophenone also gave the condensation products albeit in low yields (18–25%). A curious feature of these latter reactions is that the acyclic alkyl group of the amine ends up in the product and 5,5-diphenyl-2,2-pentadienals such as **6** (Scheme 2) and not the propenals **4** are formed as the products if the alkyl group of the amine has four or more carbons. *e.g.* in the cases of *n*-Bu_3N, *N*-*n*-pentyl-, and *N*-*n*-hexyl- piperidines. The formation of these products was proposed to involve β-elimination of '$HTiCl_3$' from the α-titanated iminium ion to give the conjugated iminium ion intermediate **5**, which underwent retitanation at the γ-position followed by condensation with benzophenone. The reaction of higher tertiary amines with aldehydes was, however, not investigated. The only reaction in which an aldehyde was used was the reaction of benzaldehyde with $Et_3N/TiCl_4$ whereby cinnamaldehyde was isolated in low yield along with some polar unidentified products and the unreacted benzaldehyde. In this context, we wish to report our observation on the reaction of *n*-Bu_3N with aromatic aldehydes in the presence of $TiCl_4$, which in contrast to the reported reactions with diary ketones, yielded α-ethyl-cinnamaldehydes and not the conjugated dienals.



Scheme 1



Scheme 2

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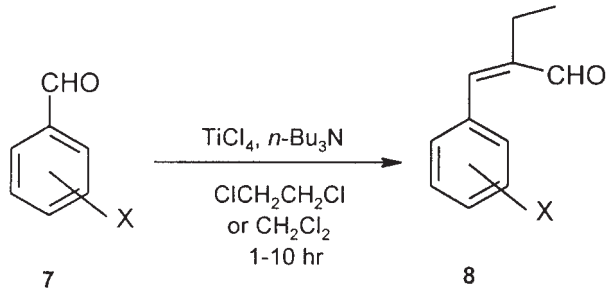
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Thus, when to an equimolar mixture of aromatic aldehydes and $TiCl_4$ in 1,2-dichloroethane or dichloromethane was added to two equivalents of *n*-Bu_3N slowly with stirring at room temperature and the solution was stirred for 1–10 hours a complex mixture of products was obtained after work up, which on column chromatography gave α-ethylcinnamaldehydes in 18–31% yields (Scheme 3). The results are shown in Table 1. In the case of *p*-chlorobenzaldehyde, 19% of *p*-chlorobenzyl alcohol was also isolated, which arose probably by reduction of the aldehyde with the low valent titanium formed in the reaction.

All the compounds were characterised by IR and ^1H NMR spectroscopy and in the case of α-ethylcinnamaldehyde, by comparison with the authentic sample prepared by aldol condensation of benzaldehyde with *n*-butyraldehyde.[11] The geometry of these compounds was found to be Z using ^1H NMR spectroscopy. Interestingly, electron-withdrawing groups in the aldehyde impede the reaction, though such groups are expected to increase the reactivity of the aldehyde in nucleophilic additions. Thus, *p*-nitro- and *p*-chlorobenzaldehyde required 10 hours for the completion of the reaction.



X = H, *p*-Me, *m*-Me, *o*-Me, *p*-NO_2, *p*-Cl

Scheme 3

In order to optimise the yields, the reaction was performed with different proportions and different modes of mixing of the reactants and under N_2 and O_2 atmospheres taking benzaldehyde as a test case. The reaction proceeded smoothly and took 1 hour for completion if the ratio of benzaldehyde: $TiCl_4$: *n*-Bu_3N was 1:1:2. The reaction was found to be incomplete in comparable amounts of time with lower proportions of $TiCl_4$ and *n*-Bu_3N (benzaldehyde:$TiCl_4$:*n*-Bu_3N=2:1:2). When the reaction was carried out with equimolar mixture of benzaldehyde, $TiCl_4$ and *n*-Bu_3N, some unreacted benzaldehyde was detected by TLC, which disappeared on addition of one more equivalent of *n*-Bu_3N without causing any improvement in the yield of the product. When to an equimolar mixture of benzaldehyde and $TiCl_4$ in 1,2-dichloroethane, 4 equivalents of *n*-Bu_3N was added, the reaction was over immediately but the yield of the product (26%) did not improve.

Addition of one equivalent of $TiCl_4$ to a stirred solution containing one equivalent of benzaldehyde and 2 equivalents of *n*-Bu_3N also gave α-ethylcinnamaldehyde in 30% yield. Stirring a solution of $TiCl_4$ and *n*-Bu_3N in 1,2-dichloroethane for 5 minutes followed by the addition of benzaldehyde produced 2% of the 1,2-diphenyl-1,2-ethanediol besides 26% of α-ethylcinnamaldehyde. When the addition was carried out as reported for reductive coupling[9] (stirring *n*-Bu_3N with $TiCl_4$ in 1,2-dichloromethane for 1 hour followed by addition of benzaldehyde and further stirring at room temperature for 6 hours), reductive coupling to 1,2-diphenyl-1,2-ethanediol was indeed observed without the formation of α-ethylcinnamaldehyde.

The extent of the diol formation depended on how long the mixture of $TiCl_4$ and *n*-Bu_3N was stirred in the absence of aromatic aldehyde. Probably, under our conditions also the mechanism of the reaction is similar to that shown in the Scheme 1. The reason why different products were formed under these two conditions is not clear. The main difference between the two reaction conditions is that for the reductive coupling, $TiCl_4$ and *n*-Bu_3N were allowed to react with each other for longer time (one hour) in the absence of the carbonyl compound. Probably under these conditions, the higher concentration of the low valent titanium produced by the redox reaction, made the reductive coupling of the carbonyl compound compete so effectively with the condensation reaction that the latter was considerably suppressed. This could probably also explain why under our conditions some reduction of the aldehyde to alcohol and not reductive coupling to *vic*-diol was observed.

The reaction under nitrogen atmosphere did not help in improving the yield, whereas, the reaction under oxygen atmosphere took 12 hours for completion, yielding 18% yield of α-ethylcinnamaldehyde indicating that O_2 can not be used to make the reaction catalytic with respect to $TiCl_4$. The reaction with *n*-Pr_3N also followed the same course to give α-methylcinnamaldehyde whereas the reaction did not occur within comparable times with Et_3N and *n*-octyl$_3$N under our conditions and unreacted benzaldehyde was isolated to the extent of 46% and 44% respectively.

Experimental

Melting points were recorded in a glass capillary with electrical heating and are uncorrected. The IR spectra were recorded on a Nicolet 5DX FTIR Spectrometer on samples taken neat or as KBr discs. The ^1H NMR spectra were recorded on Bruker Spectrospin DX-300MHz NMR spectrometer in $CDCl_3$ with tetramethylsilane as the internal standard. All the aldehydes and titanium tetrachloride are commercially available and were used as received. All the amines are also commercially available and were distilled over calcium hydride before use.

General procedure: To a solution of 10 mmol of aldehyde in 10 ml of 1,2-dichloroethane (or dichloromethane) was added 1.1 ml (10 mmol) of $TiCl_4$ and the resulting heterogeneous mixture was stirred for 10 minutes at room temperature (25°C). To this solution was added 4.8 ml (20 mmol) of *n*-Bu_3N slowly drop wise with stirring through a separatory funnel at the same temperature. The addition required 10 minutes. The solution became homogeneous after the addition of *n*-Bu_3N. The stirring was continued and the progress of the reaction was monitored by TLC. After the reaction was complete (see Table 1 for time), the solution was diluted with 50 ml of ether, washed with 5% H_2SO_4 (2 × 20 ml) solution to remove the excess of the amine, and 10 ml of brine and dried over anhydrous Na_2SO_4. The organic layer after evaporation gave a crude liquid, which was purified by column chromatography (silica gel, 5% EtOAc in *n*-hexane) to get the α-ethylcinnamaldehyde **8**.

Table 1 Reaction of aromatic aldehydes with *n*-BuN_3/$TiCl_4$

S. no.	Aromatic aldehyde **7**	Time/h	Yield of α-ethyl cinnamaldehyde **8** (%)
1	Benzaldehyde	1	31
2	*p*-Tolualdehyde	2	26
3	*m*-Tolualdehyde	2	26[a]
4	*o*-Tolualdehyde	2	20[a]
5	*p*-Nitrobenzaldehyde	10	18
6	*p*-Chlorobenzaldehyde	10	26[b]

[a]Isolated as its 2,4-DNP derivative; [b]19 % of *p*-chlorobenzyl alcohol was also isolated.

In the reaction of *p*-chlorobenzaldehyde with tributylamine, 19% of *p*-chlorobenzyl alcohol was also isolated by column chromatography as a colourless solid besides α-ethyl-*p*-chlorocinnamaldehyde.

Spectral data of α-ethylcinnamaldehydes (8) compounds (3), (4), (5) and (6) and the 2,4-DNP (2,4-dimitrophenylhydrazine) derivatives of (1) and (2) have not been reported previously.

(1) *(2Z)-2-ethyl-3-phenylprop-2-enal*[11]*:* m.p. (2,4-DNP derivative) 210°C. IR: ν_{max} 1685(s, C=O), 1626(s, C=C), 1597(m), 1584(w), 1574(m), 1182(s), 1057(s) cm^{-1}. ^1H NMR: δ 1.15 (t, *J*=7.51Hz, 3H), 2.57 (q, *J*=7.52Hz, 2H), 7.21 (s, 1H), 7.37–7.56 (m, 5H), 9.55(s, 1H) ppm; Analysis: calculated for $C_{17}H_{16}O_4N_4$ (2,4-DNP derivative): C 60.0, H 4.74, N 16.47. Found: C 59.64, H 4.51, N 16.37.

(2) *(2Z)-2-ethyl-3-(4-methylphenyl)prop-2-enal*[12]*:* m.p. (2,4-DNP derivative) 180°C. IR: ν_{max} 1685 (s, C=O), 1626 (s, C=C), 1592(s), 1328(s), 1138(s), 1085(s) cm^{-1}. ^1H NMR: δ 1.13 (t, *J*=7.45Hz, 3H), 2.39 (s, 3H), 2.56 (q, *J* = 7.49Hz, 2H), 7.14 (s, 1H), 7.18–7.5 (m, 4H), 9.5 (s, 1H) ppm; Analysis: calculated for $C_{18}H_{17}O_4N_4$ (2,4-DNP derivative): C 61.0, H 4.84, N 15.82. Found: C 60.82, H 4.63, N 15.71.

(3) *(2Z)-2-ethyl-3-(3-methylphenyl)prop-2-enal (2,4-dinitrophenyl)hydrazone:* m.p. 170°C. IR: ν_{max} 3289(w, sh, N-H), 1614 (s, C=N), 1592(s), 1514(s), 1330(s), 1309(m) cm^{-1}. ^1H NMR: δ 1.32 (t, *J* = 7.45, 3H), 2.4 (s, 3H), 2.76 (q, *J* = 7.42Hz, 2H), 6.78 (s, 1H), 7.15-7.34 (m, 4H), 7.83 (s, 1H), 7.99 (d, *J* = 9.60Hz, 1H), 8.34 (dd, *J* = 9.56, 2.45Hz, 1H), 9.15 (d, *J* = 2.55Hz, 1H), 11.6 (s, 1H, D_2O exchangeable) ppm; Analysis: calculated for $C_{18}H_{17}O_4N_4$: C 61.0, H 4.84, N 15.82. Found: C 60.79, H 4.65, N 15.73.

(4) *(2Z)-2-ethyl-3-(2-methylphenyl)prop-2-enal (2,4-dinitrophenyl)hydrazone:* m.p. 172°C. IR: ν_{max} 3279(w, sh, N-H), 1613(s, C=N), 1595(s), 1515(s), 1328(s), 1311(m), 1263(m), 1134(m), 1084(w) cm^{-1}. ^1H NMR: δ 1.24 (t, *J* = 7.44Hz, 3H), 2.3 (s, 3H), 2.59 (q, *J* = 7.43Hz, 2H), 6.9 (s, 1H), 7.24-7.28 (m, 4H), 7.9 (s, 1H), 7.98 (d, *J* = 9.57Hz, 1H), 8.34 (dd, *J* = 9.47, 2.48Hz, 1H), 9.15 (d, *J* = 2.55Hz, 1H), 11.22 (s, 1H, D_2O exchangeable) ppm; Analysis: calculated for $C_{18}H_{17}O_4N_4$: C 61.0, H 4.84, N 15.82. Found: C 60.80, H 4.67, N 15.71.

(5) *(2Z)-2-ethyl-3-(4-nitrophenyl)prop-2-enal:* m.p. 88–90°C. IR: ν_{max} 1683(s, C=O), 1624(w, C=C), 1508(s), 1344(s), 1181(m), 1054(m) cm^{-1}. ^1H NMR: δ 1.15 (t, *J*=7.53, 3H), 2.54 (q, *J*=7.52Hz, 2H), 7.27 (s, 1H), 7.64 (d, *J* = 8.70Hz, 2H), 8.31 (d, *J* = 8.78Hz, 2H), 9.6 (s, 1H) ppm; Analysis: calculated for $C_{11}H_{11}O_3N$: C 64.38, H 5.40, N 6.83. Found: C 64.19, H 5.27, N 6.79.

(6) *(2Z)-3-(4-chlorophenyl)-2-ethylprop-2-enal:* m.p. (2,4-DNP derivative) 188°C. IR: ν_{max} 1678(s, C=O), 1624(s, C=C), 1589(s), 1491(s), 1180(s), 1091(s), 1055(s) cm^{-1}. ^1H NMR: δ 1.13 (t, *J*=7.52Hz, 3H), 2.54 (q, *J*=7.51Hz, 2H), 7.15 (s, 1H), 7.43(≈s, 4H), 9.54(s, 1H) ppm; Analysis: calculated for $C_{11}H_{11}OCl$: C 67.87, H 5.70. Found: C 67.69, H 5.59.

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References

1 (a) G.M. Robertson *Comprehensive Organic Synthesis*, B.M. Trost, I. Fleming and G. Pattenden (eds.); Pergamon: Oxford, 1991, **3**, 563; (b) J.E. McMurry *Chem. Rev.*, 1989, **89**, 1513; (c) A. Fürstner and B. Bogdanovic *Angew. Chem Int. Ed. Engl.*, 1996, **35**, 2442; (d) D. Lenoir *Synthesis*, 1989, 883; (e) J. E. McMurry *Acc. Chem. Res.*, 1974, **7**, 281; (f) M. Ephritikhine *Chem. Commun.*, 1998, 2549; (g) T.–L. Ho and C.M. Wong *Syn. Commun*., 1973, **3**, 237; (h) T.–L. Ho and C.M. Wong *Syn. Commun*., 1973, **3**, 37; (i) S.V. Kuz'min, M.D. Mizhiritskii and L. M. Kogan *J. Org. Chem. USSR*, 1989, **25**, 596.
2 I. Ojima, S.M. Brandstadter and R.J. Donavan *Chem. Lett*., 1992, 1591.
3 (a) K. Hirai and I. Ojima *Tetrahedron Lett*., 1983, **24**, 785; (b) S. –I. Inaba and I. Ojima *Tetrahedron Lett*., 1977, **23**, 2009.
4 (a) V.D. Rao and M. Periasamy, *Tetrahedron: Asymmetry*, 2000, **11**, 1151; (b) Y. Matsumura, M. Nishimura, H. Hiu, M. Watanabe and N. Kise, *J. Org. Chem*., 1996, **61**, 2809.
5 (a) N. Kise, K. Kumada, Y. Terao and N. Ueda. *Tetrahedron*, 1998, **54**, 2697; (b) N. Kise, K. Tokioka, Y. Aoyama and Y. Matsumura *J. Org. Chem*., 1995, **60**, 1100.
6 M. Periasamy, G. Srinivas and P. Bharathi *J. Org. Chem*., 1999, **64**, 4204.
7 M. Antler and A.W. Laubengayer *J. Am. Chem. Soc*., 1955, **77**, 5250.
8 W.R. Trost *Can. J. Chem*., 1952, **30**, 835.
9 M. Periasamy, G. Srinivas, G.V. Karunakar and P. Bharathi *Tetrahedron Lett.*, 1999, **40**, 7577.
10 P. Bharathi and M. Periasamy *Org. Lett.*, 1999, **1**, 857.
11 Kraft, W.M. *J. Am. Chem. Soc.*, 1948, **70**, 3570.
12 M.T. Bogert and G. Powell *Am. Perfumer*, 1930, **25**, 617, 620; *Chem. Abstr.*, 1931, **25**, 1230.