

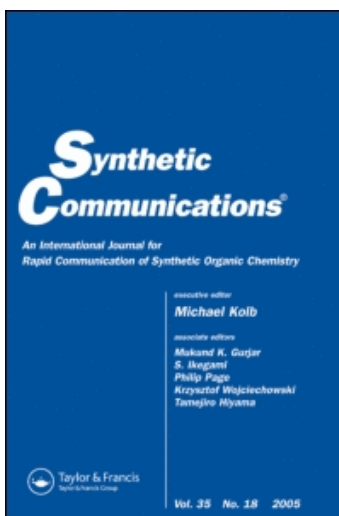
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### NOVEL TITANIUM(IV) CHLORIDE CATALYZED OLEFINATION OF ALDEHYDES: A SIMPLE AND CONVENIENT SYNTHESIS OF *TRANS*-CINNAMIC ACIDS

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**NOVEL TITANIUM(IV) CHLORIDE  
CATALYZED OLEFINATION OF  
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**ABSTRACT**

A variety of aromatic aldehydes were stereoselectively transformed into (*E*)-cinnamic acids *via* the reaction with ethyl bromoacetate and triphenylphosphine in the presence of catalytic amount of titanium tetrachloride, followed by hydrolysis and crystallization.

Stereoselective construction of carbon–carbon double bonds has been and continues to be an important synthetic endeavor in organic chemistry because of the presence of double bond in several natural products and biologically active molecules.<sup>1–6</sup> Various interesting stereoselective methodologies have been developed and the most important ones are Wittig reaction, Peterson's olefination, Tebbe reaction, Julia-Lythgoe olefination

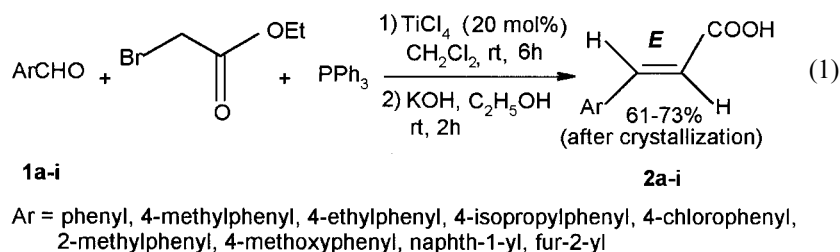
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and their modified versions.<sup>6-13</sup> In continuation of our ongoing research program in the development of synthetic methodologies for stereoselective construction of carbon-carbon double bonds<sup>14-16</sup> herein we report, a simple and convenient synthesis of *trans*-cinnamic acids *via* the reaction of aldehydes with ethyl bromoacetate and triphenylphosphine in the presence of catalytic amount of titanium tetrachloride, followed by hydrolysis and crystallization.

Stereoselective carbon-carbon double bond formation between aldehydes and  $\alpha$ -bromo carboxylic esters in the presence of trialkylphosphine has been achieved using Pd, Zn, or Cd catalysts.<sup>9</sup> Applications of titanium(IV)/PPh<sub>3</sub> reagents in aldol reaction have been reported.<sup>17,18</sup> To the best of our knowledge, titanium tetrachloride/triphenylphosphine system has not been used for the stereoselective olefination of aromatic aldehydes *via* the reaction with  $\alpha$ -bromoacetate to provide the corresponding cinnamic esters. As part of our ongoing research program on applicability of titanium tetrachloride in organic synthesis,<sup>19</sup> we have examined the utility of titanium tetrachloride/triphenylphosphine system for the olefination of aldehydes *via* the reaction with ethyl bromoacetate. During our efforts in this direction, we have first carried out the reaction of benzaldehyde (**1a**) with ethyl bromoacetate in the presence of triphenylphosphine under the influence of titanium tetrachloride at various conditions. The best results were obtained when the aldehyde **1a** (5 mM) was treated with ethyl bromoacetate (7.5 mM) in the presence of triphenylphosphine (7.5 mM) and titanium tetrachloride (1 mM) in dichloromethane at room temperature for six hours, thus providing the desired *trans*-cinnamic acid (**2a**) in 72% yield, after hydrolysis of the resulting ethyl cinnamate followed by crystallization.<sup>20</sup> We have then successfully converted a representative class of aromatic aldehydes (**1b-i**) into (*E*)-cinnamic acids (**2b-i**) (Eq. 1, Table 1) in good yields.

This present olefination reaction did not proceed in the absence of either of the reagents, triphenylphosphine or titanium tetrachloride. Also our attempts to use other reagents such as tri-*n*-butylphosphine, dimethyl

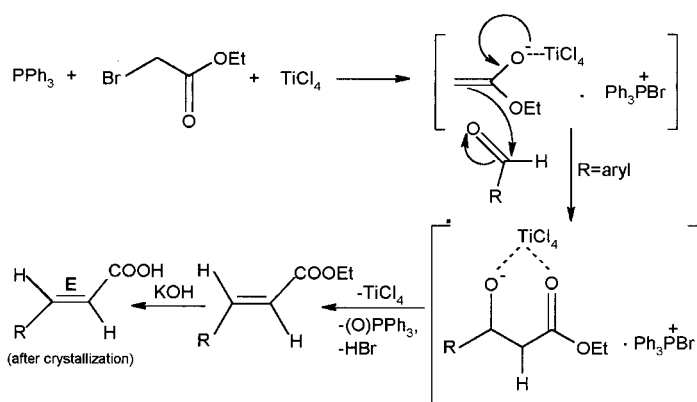


**Table 1.** A Simple and Convenient Synthesis of *trans*-Cinnamic Acids<sup>a,b</sup>

| Aldehyde  | Ar                | Product               | Yield (%) <sup>c</sup> |
|-----------|-------------------|-----------------------|------------------------|
| <b>1a</b> | phenyl            | <b>2a<sup>d</sup></b> | 72                     |
| <b>1b</b> | 4-methylphenyl    | <b>2b</b>             | 70                     |
| <b>1c</b> | 4-ethylphenyl     | <b>2c<sup>e</sup></b> | 67                     |
| <b>1d</b> | 4-isopropylphenyl | <b>2d</b>             | 71                     |
| <b>1e</b> | 4-chlorophenyl    | <b>2e</b>             | 73                     |
| <b>1f</b> | 2-methylphenyl    | <b>2f</b>             | 70                     |
| <b>1g</b> | 4-methoxyphenyl   | <b>2g<sup>e</sup></b> | 68                     |
| <b>1h</b> | naphth-1-yl       | <b>2h</b>             | 69                     |
| <b>1i</b> | fur-2-yl          | <b>2i</b>             | 61                     |

<sup>a</sup>All reactions were carried out on 5 mM scale of aldehyde with triphenylphosphine (7.5 mM) and ethyl bromoacetate (7.5 mM) in the presence of titanium(IV) chloride (20 mol%) in dichloromethane at room temperature for 6 h.<sup>20</sup>; <sup>b</sup>All the compounds are known in the literature and gave satisfactory IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectral analyses; <sup>c</sup>Yields are of isolated pure compounds after crystallization; <sup>d</sup>The reaction was also carried out on 20 mmol scale (of the aldehyde) which provided the cinnamic acid in 75% isolated yield; <sup>e</sup>These compounds are known to possess liquid crystalline properties.<sup>22,23</sup>

sulfide or triethyl phosphite in the place of triphenylphosphine met with failure. Though the exact mechanism is not known, we feel that this transformation might be presumably proceeding through a titanium ester enolate (Scheme 1). It is worth mentioning here a recent report on the application of titanium tetraisopropoxide/triphenylphosphine system for the reductive



**Scheme 1.**



olefination of aldehydes leading to the synthesis of fluorinated *trans*-allylic alcohols.<sup>21</sup>

In conclusion we have described a simple and convenient stereoselective transformation of variety of aldehydes into (*E*)-cinnamic acids *via* the reaction with ethyl bromoacetate and triphenylphosphine under the influence of a catalytic amount of titanium tetrachloride, followed by hydrolysis and crystallization. This methodology represents an alternative to Wittig olefination and also to Perkin reaction.

### EXPERIMENTAL

All melting points were recorded on a Superfit (India) capillary melting point apparatus and are uncorrected. IR spectra were recorded on Jasco-FT-IR model 5300 or Perkin Elmer model 1310 spectrometer using samples as KBr plates. <sup>1</sup>H NMR (200 MHz) and <sup>13</sup>C NMR (50 MHz) spectra were recorded in deuteriochloroform (CDCl<sub>3</sub>) or dimethyl sulfoxide-d<sub>6</sub> (DMSO-d<sub>6</sub>) on Bruker-AC-200 spectrometer using tetramethylsilane (TMS, δ = 0) as internal standard.

**Synthesis of (*E*)-Cinnamic Acids: General Procedure.** To a stirred solution of triphenylphosphine (7.5 mM, 1.967 g) in dichloromethane (10 mL), ethyl bromoacetate (7.5 mM, 1.253 g), aromatic aldehyde (5 mM) and titanium tetrachloride (20 mol%, 0.2 mL, 5 M in dichloromethane) were successively added at 0°C. After stirring at room temperature for 6 h, the reaction mixture was diluted with water (20 mL). Layers were separated, aqueous layer was extracted with dichloromethane (2 × 20 mL). Combined organic layer was successively washed with saturated aqueous sodium bicarbonate solution, water and dried over anhydrous sodium sulfate. Solvent was evaporated and the crude reaction mixture was passed through a small pad of silica gel to remove triphenylphosphine oxide (2% ethyl acetate in hexanes). Solvent was evaporated and the crude product was treated with 85% KOH (1.0 g) in ethanol (10 mL) at room temperature for 2 h. Ethanol was removed under reduced pressure, the residue was diluted with water (20 mL), extracted with dichloromethane (2 × 20 mL) to remove organic impurities. Then the aqueous layer was acidified with dilute HCl, extracted with ether (2 × 50 mL) and the organic layer was dried over anhydrous sodium sulfate. Solvent was evaporated and the crude acid obtained was crystallized from ethyl acetate and hexanes (1:4) to provide the pure (*E*)-cinnamic acids.

**(2*E*)-3-Phenylprop-2-enoic Acid (2a):** Colorless crystals. Yield: 72%; m.p.: 133°C (lit.<sup>24a</sup> 133°C); IR (KBr): 3300–2375, 1684, 1630 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 6.46 (d, 1H, J = 16.1 Hz), 7.35–7.49 (m, 3H), 7.50–7.65 (m, 2H),



7.79 (d, 1H,  $J = 16.1$  Hz), 11.31 (b, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  117.51, 128.44, 129.03, 130.78, 134.20, 147.15, 172.68.

**(2E)-3-(4-Methylphenyl)prop-2-enoic Acid (2b):** Colorless crystals. Yield: 70%; m.p.: 197–198°C (lit.<sup>24b</sup> 198–199°C); IR (KBr): 3250–2350, 1684, 1624  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  2.38 (s, 3H), 6.40 (d, 1H,  $J = 16.1$  Hz), 7.20 (d, 2H,  $J = 7.9$  Hz), 7.45 (d, 2H,  $J = 7.9$  Hz), 7.76 (d, 1H,  $J = 16.1$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  21.57, 116.32, 128.47, 129.79, 131.53, 141.34, 147.15, 172.44.

**(2E)-3-(4-Ethylphenyl)prop-2-enoic Acid (2c):** Colorless crystals. Yield: 67%; m.p.: 154–158°C (lit.<sup>22</sup> (C-N) 152.4°C, (N-I) 157.6°C); IR (KBr): 3350–2360, 1684, 1628  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.24 (t, 3H,  $J = 7.5$  Hz), 2.68 (q, 2H,  $J = 7.5$  Hz), 6.40 (d, 1H,  $J = 15.8$  Hz), 7.23 (d, 2H,  $J = 8.4$  Hz), 7.47 (d, 2H,  $J = 8.4$  Hz), 7.76 (d, 1H,  $J = 15.8$  Hz), 10.09 (b, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  15.27, 28.88, 116.39, 128.54, 131.69, 147.15, 147.58, 172.91.

**(2E)-3-(4-Isopropylphenyl)prop-2-enoic Acid (2d):** Colorless crystals. Yield: 71%; m.p.: 160–162°C (lit.<sup>25</sup> 159–160°C); IR (KBr): 3350–2350, 1684, 1624  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.23 (d, 6H,  $J = 6.8$  Hz), 2.91 (sept. 1H,  $J = 6.8$  Hz), 6.38 (d, 1H,  $J = 16.1$  Hz), 7.23 (d, 2H,  $J = 8.1$  Hz), 7.46 (d, 2H,  $J = 8.1$  Hz), 7.74 (d, 1H,  $J = 16.1$  Hz) 10.25 (b, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  23.76, 34.17, 116.46, 127.13, 128.57, 131.84, 147.13, 152.17, 172.93.

**(2E)-3-(4-Chlorophenyl)prop-2-enoic Acid (2e):** Colorless crystals. Yield: 73%; m.p.: 247–249°C (lit.<sup>25</sup> 248–249°C); IR (KBr): 3250–2325, 1684, 1626  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{DMSO-d}_6$ ):  $\delta$  6.51 (d, 1H,  $J = 16.0$  Hz), 7.45 (d, 2H,  $J = 8.5$  Hz), 7.56 (d, 1H,  $J = 16.0$  Hz), 7.69 (d, 2H,  $J = 8.5$  Hz), 12.48 (b, 1H);  $^{13}\text{C}$  NMR ( $\text{DMSO-d}_6$ ):  $\delta$  120.35, 129.24, 130.11, 133.48, 135.12, 142.83, 167.78.

**(2E)-3-(2-Methylphenyl)prop-2-enoic Acid (2f):** Colorless crystals. Yield: 70%; m.p.: 177–178°C (lit.<sup>26a</sup> 174–176°C); IR (KBr): 3250–2350, 1684, 1622  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  2.46 (s, 3H), 6.38 (d, 1H,  $J = 15.6$  Hz), 7.15–7.38 (m, 3H), 7.52–7.65 (m, 1H), 8.09 (d, 1H,  $J = 15.6$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  19.79, 118.36, 126.51, 126.78, 130.52, 130.97, 133.17, 138.01, 144.80, 172.03.

**(2E)-3-(4-Methoxyphenyl)prop-2-enoic Acid (2g):** Colorless crystals. Yield: 68%; m.p.: 168–170°C (lit.<sup>26b</sup> 170–173°C) and {(C-N) 170°C, (N-I) 182°C}<sup>23</sup>; IR (KBr): 3225–2350, 1685, 1624  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  3.84 (s, 3H), 6.30 (d, 1H,  $J = 15.8$  Hz), 6.91 (d, 2H,  $J = 8.7$  Hz), 7.49 (d, 2H,  $J = 8.7$  Hz), 7.73 (d, 1H,  $J = 15.8$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  55.45, 114.50, 114.72, 126.96, 130.13, 146.72, 161.85, 172.08.

**(2E)-3-(Naphth-1-yl)prop-2-enoic Acid (2h):** Colorless crystals. Yield: 69%; m.p.: 212–213°C (lit.<sup>24c</sup> 211–212°C); IR (KBr): 3250–2340, 1682, 1616  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{DMSO-d}_6$ ):  $\delta$  6.58 (d, 1H,  $J = 15.8$  Hz), 7.45–7.71 (m, 3H), 7.85–8.07 (m, 3H), 8.18 (d, 1H,  $J = 8.0$  Hz), 8.38 (d, 1H,



$J = 15.8$  Hz), 12.64 (b, 1H);  $^{13}\text{C}$  NMR (DMSO- $d_6$ ):  $\delta$  122.22, 123.26, 125.50, 126.02, 126.57, 127.39, 129.03, 130.67, 131.15, 131.40, 133.66, 140.70, 167.95.

**(2E)-3-(Fur-2-yl)prop-2-enoic Acid (2i):** Colorless crystals. Yield: 61%; m.p.: 142–144°C (lit.<sup>24d</sup> 141°C); IR (KBr): 3250–2375, 1691, 1626  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  6.32 (d, 1H,  $J = 15.7$  Hz), 6.46–6.52 (m, 1H), 6.65–6.72 (m, 1H), 7.45–7.60 (m, 2H), 11.19 (b, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  112.50, 115.09, 115.71, 133.10, 145.34, 150.84, 172.66.

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