Communication

# Increased Conversion to 2,4,6-Triarylpyrylium Salt: Aldol Cyclotrimerization of Acetophenone in BMImPF<sub>6</sub> Ionic Liquid

Po-Neng Chuang<sup>a,b</sup> ( 莊博能 ), Tsao-Dong Wu<sup>a,c</sup> ( 吳朝棟 ) and Ling-Kang Liu<sup>a,c</sup>\* ( 劉陵崗 ) <sup>a</sup>Institute of Chemistry, Academia Sinica, Nankang, Taipei 115, Taiwan, R.O.C. <sup>b</sup>Department of Chemistry, National Central University, Jhongli, Taoyuan 32001, Taiwan, R.O.C. <sup>c</sup>Department of Chemistry, National Taiwan University, Taipei 106, Taiwan, R.O.C.

Substituted acetophenone 1 in BMImPF<sub>6</sub> ionic liquid, heated at 120 °C for 24 h, produces  $\beta$ -methylchalcone 2, triarylbenzene 3, and triarylpyrylium salt 4. BMImPF<sub>6</sub> catalyzes the self-aldol condensation of 1, whose cyclotrimerization gives an increased conversion to 4 at the expense of 3 normally obtained from the cyclotrimerization of 1 in common organic solvent.

Keywords: Ionic liquid; Acetophenone; Self-aldol condensation.

Room temperature ionic liquids (RTILs), a class of organic salts that melt below 100 °C, are often used as solvent in homogeneous catalysis in order to take advantages of negligible vapor pressure, high thermal stability, tunable polarity, etc.<sup>1</sup> The highly polar nature of RTILs likely increases the life time of a charge-separated transition state during reaction. Seddon et al. found that, employing EMImAl<sub>2</sub>Cl<sub>7</sub> melts in the Friedel-Crafts acetylation reaction of naphthalene, the thermodynamically unfavored 1isomer became the major product whereas the thermodynamically favored 2-isomer exhibited only a 2% yield (Scheme I).<sup>2</sup> Xiao et al. also reported that the Pd-catalyzed Heck arylation reaction of electron rich olefins and aryl halides in BMImBF<sub>4</sub> produced essentially the less common branched products, not the linear ones (Scheme II).<sup>3</sup> These results suggested that as media of reactions, RTILs could shift the reaction to follow the more ionic pathways.

Conventionally aldol condensation reactions were performed in organic solvents.<sup>4</sup> In 2002, Mehnert *et al.* started investigation of the aldol condensation reactions employing imidazolium ionic liquid phases treated with aqueous solution of NaOH as the catalyst.<sup>5</sup> Later, piperidine<sup>6</sup> and L-proline<sup>7</sup> in RTIL, respectively, were studied extensively. Also appeared were the pyrrolidine-functionalized ionic liquids for the aldol condensation reactions.<sup>8</sup> Up to the present time, the base catalyzed aldol condensation reactions in ionic liquids have been documented.





Scheme II Pd-catalyzed Heck arylation reaction of olefin and aryl halide



In this report we wish to present the observation of aldol cyclotrimerization of acetophenone mediated by BMImPF<sub>6</sub>, without the addition of base. The cyclotrimerization was found to produce in substantial amounts the 2,4,6-triarylpyrylium salts<sup>9</sup> in addition to the more familiar 1,3,5-triarylbenzene. That is in sharp contrast to the results of conventional preparation of 1,3,5-triarylbenzene in organic phase with Lewis acid catalyzed aldol cyclocondensation.<sup>4,10-12</sup>

Herein substituted acetophenone 1 and hydrophobic  $BMImPF_6$  ionic liquid were mixed well in a round bottomed flask equipped with a condenser and the solution

<sup>\*</sup> Corresponding author. Fax: +886-2-27831237; E-mail: liuu@chem.sinica.edu.tw

stirred and maintained constantly at 120 °C. During the reaction the mixture became increasingly viscous, even solidified. After 24 h, the reaction was stopped and the reaction mixture extracted with Et<sub>2</sub>O for 3 times. The combined Et<sub>2</sub>O fractions were rotary evaporated and the crude purified with SiO<sub>2</sub> column chromatography. In addition to unused acetophenone,  $\beta$ -methylchalcone **2** and triarylbenzene **3** were obtained (Scheme III, with conversions). Without BMImPF<sub>6</sub> ionic liquid, only acetophenone was recovered after being heated at 120 °C for 24 h. With hydrophilic BMImBr ionic liquid, there was no reaction either.

## Scheme III Aldol condensation reaction of acetophenone in BMImPF<sub>6</sub>



The reaction mixture after Et<sub>2</sub>O extraction was then added with just enough amounts of EtOH in order to keep the ionic liquid in solution. After standing for 24 h, triarylpyrylium PF<sub>6</sub> salt 4 precipitated and the salt was characterized by NMR (<sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F, and <sup>31</sup>P) and other analytical methods. In the <sup>1</sup>H NMR spectra of **4b**, for example, the singlet resonance at  $\delta$  9.06 was assigned to the pyrylium ring protons, downfield shifted by 1.3  $\delta$  units when compared to the singlet resonance at  $\delta$  7.73 assigned to the inner benzene ring protons of **3b**, attributable to the highly electron-withdrawing nature of cationic pyrylium.

Because in the above experiments, 2 is a dimeric intermediate of 1 and both 3 and 4 are trimers of 1, it is interesting to look into more details the ratios of conversion on 4a/3a, 4b/3b, and 4c/3c, at *ca* 0.1, 0.1, and 0.6, respectively. A more electron releasing substituent at 1 favors the production of 4.

Jing *et al.* detailed the treatment of **1** with *p*-tolylsulfonyl acid and a catalytic amount of SnCl<sub>4</sub> in C<sub>5</sub>H<sub>11</sub>OH to produce **3** in good yields without noticing **4**.<sup>11</sup> Alternatively the strategy of Lewis acid promoted cyclotrimerization of acetyl aromatics lead to 1,3,5-triarylbenze formation (100% yield) with conditions of TiCl<sub>4</sub> (1.5 eq), *o*-  $C_6H_4Cl_2$ , 180 °C for 24 h; no 2,4,6-triarylpyrylium formation being indicated.<sup>12</sup> Obviously the aldol cyclotrimerization reaction of **1** in organic solvents produces mainly **3**; similar reaction in hydrophobic BMImPF<sub>6</sub> produces substantially the ionic **4**, in addition to the neutral **3**.

Though formulated as the PF<sub>6</sub> salt, the anions of **4a-c** were not 100% PF<sub>6</sub>, nonetheless. In the <sup>31</sup>P NMR spectra, **4a-c** exhibited a septuplet at *ca*  $\delta$  -145 with <sup>1</sup>J<sub>PF</sub> = 711 Hz (assigned to PF<sub>6</sub>) plus a singlet at *ca*  $\delta$  -1.8 (assigned to H<sub>3</sub>PO<sub>4</sub>) with intensities varying from sample to sample. In the <sup>19</sup>F NMR spectra, **4a-c** exhibited a doublet at *ca*  $\delta$  -70 with <sup>1</sup>J<sub>PF</sub> = 711 Hz (assigned to PF<sub>6</sub>) and a singlet at *ca*  $\delta$  -147 (assigned to HF) with varying intensity, too. These NMR data suggested existence of the H<sub>2</sub>O-HF-P<sub>2</sub>O<sub>5</sub> phase system in that PF<sub>6</sub> and H<sub>3</sub>PO<sub>4</sub> are likely equilibrated by hydrolysis, <sup>13</sup> leading to the existence of fluorides in the system.

Hydrophobic BMImPF<sub>6</sub> ionic liquid was regarded as thermally stable with a thermal decomposition temperature at 349 °C as shown in TGA studies.<sup>14</sup> However, Kosmulski *et al.* reported that wet spots could be observed in crucibles of TGA after conditioning bmimPF<sub>6</sub> at 200 °C for 10 h, i.e. the thermal decomposition temperature based on fast TGA scans does not imply a long term thermal stability.<sup>15</sup> In our experiments, the ionic liquid layer after the reaction was also examined with <sup>1</sup>H NMR, whose spectrum revealed two different sets of BMIm peaks. One set of signals was identical to that of BMImPF<sub>6</sub>; the other set associated with anion(s) other than PF<sub>6</sub><sup>-</sup>. The PF<sub>6</sub><sup>-</sup> anions of the BMImPF<sub>6</sub> ionic liquid at 120 °C in the long term presence of **1** must have degraded to produce at least tracing fluorides and PF<sub>5</sub> to catalyze the aldol condensation of **1**.

The PF<sub>6</sub><sup>-</sup> anion has been known to be weakly coordinating.<sup>16</sup> Gilbert *et al.* reported that in ionic liquids with weakly coordinating anions, tracing water exists as  $H_3O^+$ , not  $H_2O^{17}$ . Under the constraint, the ionic liquids would allow aldol addition followed by slow  $H_2O$  elimination. Loh *et al.* observed that L-proline in BMImPF<sub>6</sub> catalyzes aldol reactions in that  $H_2O$  elimination products could not be observed within 20 h.<sup>7(b)</sup> In line with the slower  $H_2O$  elimination steps, a mechanism is proposed in Scheme IV for the production of **4** in BMImPF<sub>6</sub> ionic liquid. A depronated and activated **1** adds to a second molecule of **1** to form the intermediate structure **A**, which after elimination of  $H_2O$  equivalent, results in **2**. When **2** is depronated and activated, it adds to a third molecule of **1** to form intermediate structure



**B**. Similar elimination gives **C** whose dehydration yields the cyclotrimeric product **3**. Alternatively, if the deprotonated and activated **2** adds to structure **A** (accumulated because of the slower elimination step); the outcome changes to intermediate structures **D** then **E**, in that the formation of a remote double bond is followed by its extrusion *via* the 6-membered cyclic transition state<sup>18</sup> to yield the cyclotrimeric product **4**. The polymeric materials found in these reactions is consistent to the extrusion of ArCMe=CH<sub>2</sub>.

As the imidazolium cations were spectators only, the same chemistry also worked with other dissolving  $PF_6$ salts. The NaPF<sub>6</sub> dissolution in **1** was similarly investigated at 120 °C for 24 h in that the aldol cyclotrimerization reaction also proceeded. The conversion results after the same  $Et_2O$  and EtOH workup were given in Scheme V. Noted were the increasing conversions of both **3** and **4** in the NaPF<sub>6</sub> studies, presumably the reactive dissolution of NaPF<sub>6</sub> in **1** gave high ion concentrations in the mixture and the conversion was seemingly faster than in BMImPF<sub>6</sub>. To avoid solidification of mixtures in flask, a combination of





**1b**/NaPF<sub>6</sub>/BMImPF<sub>6</sub> (10 mmol/10 mmol/2 mL) was also heated at 120 °C for 24 h. In this case the **4**/**3** ratio was found to be 1.6, higher than 0.1 with only BMImPF<sub>6</sub> and 0.7 with only NaPF<sub>6</sub>.

As a conclusion, the BMImPF<sub>6</sub> ionic liquid mediated aldol cyclotrimerization of acetophenones 1 are PF<sub>5</sub> catalyzed processes with a slow H<sub>2</sub>O elimination step; the cyclotrimerization of 1 in BMImPF<sub>6</sub> ionic liquid and the cyclotrimerization of 1 upon reactive dissolution of NaPF<sub>6</sub> in 1 exhibit noted conversion to the trimeric product of 2,4,6-triarylpyrylium salts 4 at the expense of 1,3,5-triarylbenzenes 3.

#### EXPERIMENTAL SECTION General procedures

Into a single-neck round-bottomed flask (50 mL) was introduced a stirring bar, substituted acetophenone (50 mmol) and bmimPF<sub>6</sub> (10 mL, 58 mmol), then fitted with a condenser, before the temperature of the mixture being raised and kept at 120 °C for 24 h with constant stirring. After this, the mixture was cooled down to room temperature and quenched by extraction with  $Et_2O$  (3 × 15 mL). The combined Et<sub>2</sub>O fractions were rotary evaporated. The crude was purified by SiO<sub>2</sub> column chromatography, eluting with 1:10  $Et_2O$ /hexanes, to recover 1, yield oily 2 and solid 3. Compound 2 slowly solidified upon standing at room temperature. Compound 3 was recrystallized from CH<sub>2</sub>Cl<sub>2</sub>/ EtOH. The remaining ionic liquid layer was added with just enough amounts of EtOH and let stand for 24 h to give precipitate 4. Conversions are shown in Scheme III. Similarly, acetophenone reaction with NaPF<sub>6</sub> (10 mmol each) was carried out with conversions shown in Scheme V.

### Characterization data

**2a** yellow solid (CAS 495-45-4), mp 56 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.8-7.5 (m, 10H), 7.2 (s, 1H), 2.6 (s, 3H); MS-

EI: m/z 222.<sup>10(b)</sup> **3a** white solids (CAS 612-71-5), mp 168-169 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.77 (s, 3H), 7.68-7.70 (m, 6H), 7.45-7.49 (m, 6H), 7.36-7.39 (m, 3H); MS-EI: m/z306.<sup>19</sup> **4a** fluorescing yellow powder, <sup>1</sup>H NMR (d<sup>6</sup>-DMSO): δ 9.17 (s, 2H), 8.59-8.61 (m, 6H), 7.86-7.89 (m, 3H), 7.77-7.82 (m, 6H); <sup>13</sup>C NMR (d<sup>6</sup>-DMSO): δ 170.09, 165.13, 135.13, 134.99, 132.49, 130.00, 129.83, 129.80, 129.11, 128.78, 115.20; <sup>19</sup>F NMR (d<sup>6</sup>-DMSO): δ -69.5 (d, J = 711Hz); <sup>31</sup>P NMR (d<sup>6</sup>-DMSO): δ -144.9 (septet, J = 711 Hz); MS-EI: m/z 309 ([M – A]<sup>+</sup>).<sup>20</sup>

**2b** yellow solid (CAS 36201-04-4), mp 57-58 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.92 (d, 2H), 7.49 (d, 2H), 7.26 (d, 2H), 7.22 (d, 2H), 7.17 (s, 1H), 2.61 (s, 3H), 2.41 (s, 3H), 2.39 (s, 3H); MS-EI: *m/z* 250.<sup>10(b)</sup> **3b** white solids (CAS 50446-43-0), mp 167-168 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.73 (s, 3H), 7.59 (d, *J* = 8 Hz, 6H), 7.27 (d, *J* = 8 Hz, 6H), 2.41 (s, 9H); MS-EI: m/z 348.<sup>19(c)</sup> 4b fluorescing yellow powder, <sup>1</sup>H NMR (d<sup>6</sup>-Acetone): δ 9.06 (s, 2H), 8.46-8.54 (m, 6H), 7.60-7.65 (m, 6H), 2.53-2.54 (m, 9H); <sup>13</sup>C NMR (d<sup>6</sup>-DMSO): δ 169.15, 163.79, 146.80, 146.16, 130.43, 129.94, 129.34, 128.48, 126.20, 113.03, 21.40, 21.36; <sup>19</sup>F NMR (d<sup>6</sup>-DMSO):  $\delta$  -72.8 (d, J = 711 Hz), -147.6; <sup>31</sup>P NMR (d<sup>6</sup>-DMSO):  $\delta$  -1.8, -144.9 (septet, J = 711 Hz); MS-EI: m/z $351 ([M - A]^+)$ <sup>21</sup> **2c** yellow solid (CAS 16197-83-4), mp 84-85 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.9-7.8 (m, 8H), 7.1 (s, 1H), 3.8 (s, 6H), 2.5 (s, 3H); MS-EI: m/z 282.<sup>10(b)</sup> 3c white solids (CAS 7509-20-8), mp 139-141 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.65 (s, 3H), 7.62 (d, 6H, J = 9.3 Hz), 7.02 (d, 6H, J = 9.3 Hz), 3.85 (s, 9H); MS-EI: *m/z* 396.<sup>19(c)</sup> 4c fluorescing orange crystals, <sup>1</sup>H NMR (d<sup>6</sup>-DMSO): δ 8.82 (s, 2H). 8.61-8.64 (d, 2H), 8.50-8.53 (d, 4H), 7.29-7.32 (m, 6H), 3.96-3.98 (m, 9H); <sup>13</sup>C NMR (d<sup>6</sup>-DMSO): δ 167.37, 165.21, 164.41, 161.40, 132.25, 130.39, 124.12, 121.00, 115.15, 110.25, 55.97, 55.83; <sup>19</sup>F NMR (d<sup>6</sup>-DMSO):  $\delta$  -70.2 (d, J= 711 Hz), -147.6; <sup>31</sup>P NMR (d<sup>6</sup>-DMSO):  $\delta$  -144.9 (septet, J= 711 Hz); MS-EI: m/z 399 ([M – A]<sup>+</sup>).<sup>10(b)</sup>

Received February 19, 2008.

#### REFERENCES

 (a) Chowdhury, S.; Mohan, R. S.; Scott, J. L. Tetrahedron 2007, 63, 2363-2389. (b) Wasserscheid, P.; Welton, T. Ionic Liquids in Synthesis; Wiley-VCH: Weinheim, Germany, 2003. (c) Rogers, R. D.; Seddon, K. R. Ionic Liquids as Green Solvents: Progress and Prospects; ACS Symp. Ser., 856; ACS: Washington, D. C., 2003. (d) Handy, S. T. Chem. *Eur. J.* 2003, *9*, 2938-2944. (e) Rogers, R. D.; Seddon, K. R. *Ionic Liquids: Industrial Applications for Green Chemistry*; ACS Symp. Ser., 818; ACS: Washington, D. C., 2002. (f) Dupont, J.; De Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* 2002, *102*, 3667-3691. (g) Sheldon, R. *Chem. Commun.* 2001, 2399-2407. (h) Wasserscheid, P.; Keim, W. *Angew. Chem. Int. Ed.* 2000, *39*, 3772-3789. (i) Welton, T. *Chem. Rev.* 1999, *99*, 2071-2083.

- Adams, C. J.; Earle, M. J.; Roberts, G.; Seddon, K. R. Chem. Commun. 1998, 2097-2098.
- Mo, J.; Xu, L.; Xiao, J. J. Amer. Chem. Soc. 2005, 127, 751-760.
- 4. (a) Modern Aldol Reactions; Mahrwald, R. Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vol. 1 and 2. (b) March, J.; Smith, M. Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 5<sup>th</sup> ed.; Wiley: New York, 2001. (c) Evans, D. A. Aldrichimica Acta 1982, 15, 23-32.
- (a) Mehnert, C. P.; Dispenziere, N. C.; Schlosberg, R. H. US Patent 6,552,232,B2, 2003. (b) Mehnert, C. P.; Dispenziere, N. C.; Cook, R. A. Chem. Commun. 2002, 1610-1611.
- Davey, P. N.; Forsyth, S. A.; Gunaratne, H. Q. N.; Hardacre, C.; McKeown, A.; McMath, S. E. J.; Rooney, D. W.; Seddon, K. R. *Green Chem.* 2005, *7*, 224-229.
- (a) Cordova, A. *Tetrahed. Lett.* 2004, *45*, 3949-3952. (b) Loh, T.-P.; Feng, L.-C.; Yang, H.-Y.; Yang, J.-Y. *Tetrahed. Lett.* 2002, *43*, 8741-8743. (c) Kotrusz, P.; Kmentova, I.; Gotov, B.; Toma, S.; Solcaniova, E. *Chem. Commun.* 2002, 2510-2511.
- Luo, S.; Mi, X.; Zhang, L.; Liu, S.; Xu, H.; Cheng, J.-P. *Tetrahedron* 2007, 63, 1923-1930.
- Balaban, T. S.; Balaban, A. T. In Science of Synthesis: Houben-Weyl Methods of Molecular Transformations; Thomas, E. J.; Ed.; Georg Thieme Verlag: Stuttgart, Germany, 2003; Vol. 14.
- (a) Bao, C.; Lu, R.; Jin, M.; Xue, P.; Tan, C.; Xu, T.; Liu, G.; Zhao, Y. *Chem. Eur. J.* **2006**, *12*, 3287-3294. (b) Ruiz-Guerrero, R.; Cardenas, J.; Bautista, L.; Vargas, M.; Vazquez-Labastida, E.; Salmon, M. *J. Mex. Chem. Soc.* **2006**, *50*, 114-118.
- Jing, X.; Xu, F.; Zhu, Q.; Ren, X.; Yan, C.; Wang, L.; Wang, J. Synth. Commun. 2005, 35, 3167-3171.
- Cao, X.-Y.; Liu, X.-H.; Zhou, X.-H.; Zhang, Y.; Jiang, Y.; Cao, Y.; Cui, Y.-X.; Pei, J. J. Org. Chem. 2004, 69, 6050-6058.
- Ames, D. P.; Ohashi, S.; Callis, C. F.; Van Wazer, J. R. J. Am. Chem. Soc. 1959, 81, 6350-6357.
- Huddleston, J. G.; Visser, A. E.; Reichert, W. M.; Willauer, H. D.; Broker, G. A.; Rogers, R. D. *Green Chem.* 2001, *3*, 156-164.
- 15. Kosmulski, M.; Gustafsson, J.; Rosenholm, J. B. Thermo-

chim. Acta 2004, 412, 47-53.

- 16. Krossing, I.; Raabe, I. Angew. Chem. Int. Ed. 2004, 43, 2066-2090.
- 17. Thomazeau, C.; Olivier-Bourbigou, H.; Magna, L.; Luts, S.; Gilbert, B. J. Am. Chem. Soc. **2003**, *125*, 5264-5265.
- 18. To form oligomeric materials. See Barker, S. A.; Riley, T. J. Chem. Soc., Perkin Trans. I **1972**, 809-812.
- (a) Kakeya, M.; Fujihara, T.; Kasaya, T.; Nagasawa, A. Organometallics 2006, 25, 4131-4137. (b) Berthiol, F.; Kondolff, I.; Doucet, H.; Santelli, M. J. Organomet. Chem.

**2004**, *689*, 2786-2798. (c) Tagliatesta, P.; Floris, B.; Galloni, P.; Leoni, A.; D'Arcangelo, G. *Inorg. Chem.* **2003**, *42*, 7701-7703.

- Funston, A.; Kirby, J. P.; Miller, J. R.; Pospisil, L.; Fiedler, J.; Hromadova, M.; Gal, M.; Pecka, J.; Valasek, M.; Zawada, Z.; Rempala, P.; Michl, J. *J. Phys. Chem.* 2005, *A109*, 10862-10869.
- 21. Katritzky, A. R.; Zakaria, Z.; Lunt, E. J. Chem. Soc., Perkin Trans. I 1980, 1879-1987.