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A green procedure for the protection of carbonyl compounds catalyzed by iodine in ionic liquid

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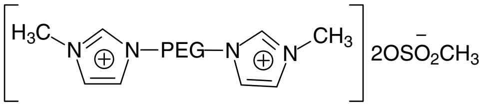
ABSTRACT

Aldehydes and ketones are protected with ethylene glycol in the presence of a catalytic amount of iodine in PEG ionic liquid (IL 400) under mild conditions to afford the corresponding ketals in good yields. The recovery of iodine is facilitated by the ionic liquid. The recovered catalyst was reused six times with consistent activity.

The protection of carbonyl groups plays an important role in organic synthesis as well as in the chemistry of drug design.[1] In general, this aim could be achieved via the formation of ketals in the presence of protonic acids, Lewis acids, and a number of transitional metal complexes including Rh, Pd, and Pt as catalysts.[2] However, most of the traditional processes suffer from a variety of disadvantages, such as pollution, use of noble metals and expensive reagents, high temperature, stoichiometric amounts of reagent, and tedious work-up procedures. Therefore, the development of a catalytic system that may be stable, easily separable, and reusable has been long awaited.

In recent years, the usage of molecular iodine has drawn considerable attention as an inexpensive, nontoxic, and readily available catalyst for various organic transformations to afford the corresponding products in excellent yields with high selectivity. The mild Lewis acidity associated with iodine enhances its usage in organic synthesis to realize several organic transformations using stoichiometric levels to catalytic amounts.[3] However, the reuse of iodine is difficult because it has a good solubility in most organic solvents and easy sublimation at high temperature. Previously, the iodine supported on polyvinylpyrrolidone (I_2/PVP),[4a] aminopropyl silica gel (I_2/APSG),[4b] neutral alumina surface (I_2/Al_2O_3),[4c,d] or natural phosphate (I_2/NP)[4e] had been reported for some reactions. The above supports were the preferred choice as supports to keep the reaction medium under mild and neutral conditions. However, the reuse of iodine was also difficult. So simple, efficient supports for reusable iodine are still desirable.

Room-temperature ionic liquids have been emerging as promising green solvents for the past decade.[5] Their nonvolatile nature gives them significant advantage in minimizing solvent consumption. Their polarity renders them good solvents for various organic, inorganic, and polymeric compounds, and therefore good media for homogeneous reactions.[5b] Because of their unique solubility properties, that is, miscibility gap between water and organic solvents, they have become interesting candidates for separation processes by simple liquid–liquid extraction with either aqueous or conventional organic solvents.[6] Furthermore, ionic liquids are found to be an efficient reaction media for the immobilization of transition metal-based catalysts, Lewis acids, and enzymes.[7] Now, we synthesize novel PEG ionic liquids (Scheme 1),[8,10] the ionic liquids and toluene have the advantages of both homogeneous and heterogeneous phase at different temperatures (biphasic conditions at lower temperatures and monophasic at higher temperatures) with the ease of product as well as catalyst separation. Herein, we present the preparation of 1,3-dioxolanes using a catalytic amount of iodine in the PEG ionic liquid (IL 400) under mild conditions with good yields (Scheme 2).



Scheme 1. PEG ionic liquids.

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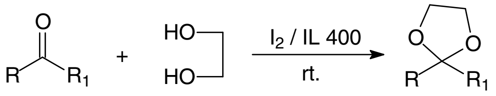

Scheme 2.

First, the addition of molecular iodine (25 mg) to a mixture of IL 400 (1 mL) and toluene (1 mL). The mixture was stirred at 80 °C for several minutes. After the mixture was cooled to room temperature, we found that most of iodine was dissolved in IL 400 (Fig. 1). The light yellow of toluene was changed to light lavender after the toluene was washed with water (1 mL). Then the titration was processed by adding to toluene standard $Na_2S_2O_3$ solution. It only has about 0.1 mg iodine in the toluene. The result shows that the iodine can be excellently distributed in the IL 400.

Next, the condensation of benzaldehyde and ethylene glycol using molecular iodine as catalyst was examined with several PEG ionic liquids at room temperature, and the results are summarized in Table 1. According to Banik's previously reported reaction conditions using molecular iodine,[9] the appreciable amount of I_2 was 5 mol % to benzaldehyde, and the reaction time was 16 h in the present reaction. As shown in Table 1, IL 400 was more satisfied to obtain excellent yield (entry 3) than other PEG ionic liquids. The PEG with larger molecular weight, such as PEG 2000 and PEG 4000, was not a good choice, because the IL 2000 and IL 4000 remain in the solid state at room temperature which had to have a high reaction temperature for the stir. However, a low yield was obtained without iodine or ionic liquid (entries 1 and 3). So, the IL 400 was chosen as reaction medium for the reaction.

Several carbonyl compounds had been used as substrates to react with ethylene glycol in the system of iodine immobilized in the IL 400, and the results are shown in Table 2. It was shown that both aldehydes and ketones were converted to the corresponding 1,3-dioxolanes in good yields. However, the reaction of aliphatic carbonyl compounds under the same conditions gave the corresponding products in higher yields than aromatic carbonyl compounds, because the conjugation effect in aromatic carbonyl compounds induced by the direct connection to the aromatic rings made the carbonyl group less positive and therefore, reduced its activity in nucleophilic addition reaction.

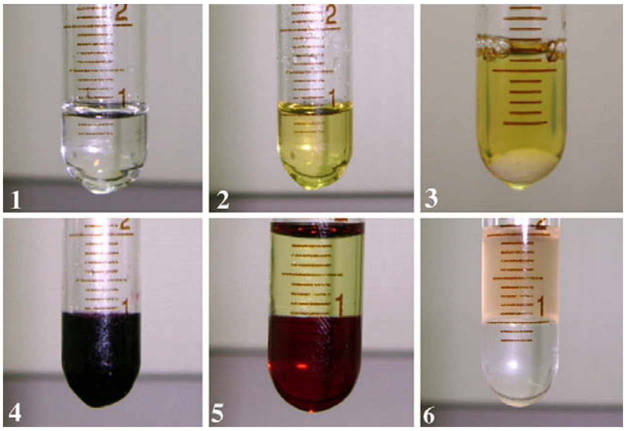

Figure 1. Photographic plates. (1) toluene: 1 mL; (2) IL 400: 1 mL; (3) 1 mL toluene and 1 mL IL 400 at 80 °C; (4) 25 mg iodine in 1 mL toluene; (5) 25 mg iodine in a mixture of IL 400 (1 mL) and toluene (1 mL), the upper layer was toluene; (6) the toluene of photo 5 was washed with 1 mL water, the upper layer was toluene.

Table 1
Effect of ionic liquids on the reaction of benzaldehyde and ethylene glycol

Entry	IL	Yield[a] (%)
1	—	70[9]
2	IL 200	80
3	IL 400	83 25[b]
4	IL 1000	79

[a] Isolated yields.
[b] Without iodine.

Table 2
Protection of carbonyl compounds as ketals using iodine as catalyst in IL 400[11]

Entry	Carbonyl compounds	Yield[a] (%)
1	Benzaldehyde	83
2	4-Nitro-benzaldehyde	72
3	4-Chloro-benzaldehyde	75
4	4-Methoxy-benzaldehyde	80
5	Butanal	95
6	Propanal	96
7	Acetophenone	60
8	2-Hydroxy-acetophenone	56
9	4-Methoxy-acetophenone	58
10	Cyclohexanone	96
11	4-Methyl-cyclohexanone	94
12	Cyclopentane	93

[a] Isolated yields.

Table 3
Reusing of iodine immobilized in IL 400

Run	Yield[a] (%)
1	83
2	83
3	82
4	83
5	82
6	81
7	65

[a] Isolated yields.

The recycling performance of iodine immobilized in the IL 400 was investigated in the reaction of benzaldehyde and ethylene glycol. The data listed in Table 3 show that I_2/IL 400 could be reused six times with consistent activity.

In conclusion, we have developed a simple, inexpensive, and effective method for the protection of carbonyl compounds catalyzed by iodine in ionic liquid. The advantages of the present reaction are the elimination of the metals, and toxic reagents, operational simplicity and good yields of products. Moreover, the simple experimental procedure being combined with ease of recovery and reuse of iodine is expected to contribute to the development of a green strategy for the other iodine-catalyzed reaction. Further studies on the reuse of iodine are now in progress.

Acknowledgments

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10. *Typical procedure for the synthesis of IL 400*: To a solution of PEG 400 (60 mmol) and triethylamine (120 mmol) in toluene (200 mL) was added methylsulfonyl chloride (10 mL) within 30 min under nitrogen atmosphere. The mixture was stirred at room temperature. After 3 h, the mixture was filtrated. The filtrate was added to 1-methylimidazol (120 mmol), and the mixture was stirred at 86 °C for 17 h. After the reaction, the ionic liquid layer was separated and washed with petroleum ether (3 × 10 mL). Evaporation of solvent under reduced pressure gave the desired pure product IL 400 in 86% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 2.85 (s, 6H, $2OSO_2CH_3$), 3.75 (t, 36H, $J = 4.3$ Hz $(OCH_2CH_2)_n$), 3.88 (s, 6H, $2NCH_3$), 7.48 (s, 2H, 2CH), 7.60 (s, 2H, 2CH), 8.92 (s, 2H, 2CH); ^{13}C NMR (500 MHz, $CDCl_3$): δ 37.1, 39.5, 49.5, 69.1, 70.3, 70.4, 122.8, 123.6, 137.1; ESI-MS: 294.12, $M^{2+}/2$, $n = 9$, 316.42, $M^{2+}/2$, $n = 10$, 338.13, $M^{2+}/2$, $n = 11$, 360.33, $M^{2+}/2$, $n = 12$, 382.13, $M^{2+}/2$, $n = 13$, 108.9 (95); IR (KBr, cm^{-1}): 3445, 3182, 2985, 1456, 1321, 1194, 1101, 1059, 895, 594.
    The spectra data for IL 200: ^1H NMR (500 MHz, $CDCl_3$) δ 2.84 (s, 6H, $2OSO_2CH_3$), 3.70 (t, 17H, $J = 8.0$ Hz $(OCH_2CH_2)_n$), 3.94 (s, 6H, $2NCH_3$), 7.52 (s, 2H, 2CH), 7.58 (s, 2H, 2CH), 8.78 (s, 2H, 2CH); ESI-MS: 184.22, $M^{2+}/2$, $n = 4$, 206.12, $M^{2+}/2$, $n = 5$, 228.31, $M^{2+}/2$, $n = 6$, 250.11, $M^{2+}/2$, $n = 7$, 272.23, $M^{2+}/2$, $n = 8$, 83.14 (100); IR (KBr, cm^{-1}): 3454, 3153, 2985, 1435, 1350, 1207, 1051, 858, 623.
    The spectra data for IL 1000: ^1H NMR (500 MHz, $CDCl_3$) δ 2.85 (s, 6H, $2OSO_2CH_3$), 3.70–3.76 (m, 97H, $J = 15.0$ Hz $(OCH_2CH_2)_n$), 3.82 (s, 6H, $2NCH_3$), 7.52 (s, 2H, 2CH), 7.59 (s, 2H, 2CH), 8.81 (s, 2H, 2CH); ESI-MS: 448.17, $M^{2+}/2$, $n = 16$), 470.20, $M^{2+}/2$, $n = 17$, 492.20, $M^{2+}/2$, $n = 18$, 514.27, $M^{2+}/2$, $n = 19$, 558.27, $M^{2+}/2$, $n = 21$, 580.30, $M^{2+}/2$, $n = 22$, 602.33, $M^{2+}/2$, $n = 23$, 624.36, $M^{2+}/2$, $n = 24$, 646.36, $M^{2+}/2$, $n = 25$, 668.37, $M^{2+}/2$, $n = 26$, 690.43, $M^{2+}/2$, $n = 27$, 712.43, $M^{2+}/2$, $n = 28$, 153.07 (100); IR (KBr, cm^{-1}): 3447, 3153, 2985, 1447, 1352, 1205, 1117, 1060, 858, 587.
11. *Typical procedure for the protection of carbonyl groups catalyzed by iodine immobilized in the IL 400*: To a solution of carbonyl compounds (1 mmol) and ethylene glycol (1 mL) in IL 400 (1 mL) was added I_2 (0.05 mmol). The mixture was stirred at room temperature. After the reaction, toluene (2 × 1 mL) was added to the mixture. The mixture was stirred at 80 °C for several minutes. After the mixture was cooled to room temperature, the upper toluene containing the expected product was separated by decantation. The toluene was evaporated, and the pure products were obtained by purification through basic alumina using ethyl acetate–hexane (10:90) as the eluent. The bottom phase was the ionic liquid containing the iodine and the produced water. The system of I_2/IL 400 was reused after removal of the water under reduced pressure.