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Reduction of benzoyl tributylphosphonium chlorides by samarium diiodide as a novel access to 4-benzoylbenzaldehydes

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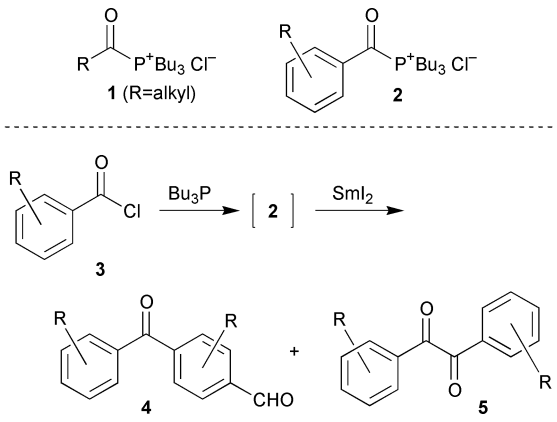
Addition of samarium diiodide to a well-stirred THF solution of benzoyl tributylphosphonium chlorides generated *in situ* from benzoyl chlorides and tributylphosphine at −40 °C gave 4-benzoylbenzaldehydes as predominant products from benzoyl chlorides without *para*-substituents, while benzoyl chloride bearing *p*-methyl or chloro groups was exclusively converted into the corresponding α-diketone.

Recently it was found that the reduction potentials of alkanoyl- and benzoyltributylphosphonium ions (**1** and **2**, respectively) (Scheme 1), anodically generated from carboxylic acids and tributylphosphine (Bu_3P) or formed from acid chlorides and Bu_3P, are much more positive than those of the corresponding acid chlorides;[1,2] hence **1** and **2** are converted into aldehydes without over-reduction to alcohols by reduction using a cathode,[1] Zn or Zn–Cu couple[3] more feasibly than the corresponding carboxylic acids or acid chlorides. In addition, electrochemical reduction of **1** was shown to provide a novel tool for the generation of acyl radical or acyl anion equivalents, which are utilized in intramolecular C–C bond formation.[4] However, the synthetically intriguing species generated from **1** or **2** have not been applied to intermolecular reactions. This is probably because **1** and **2** are highly reactive acylating reagents.[4–6] During electrochemical generation of an acyl radical or acyl anion equivalent from **1** or **2**, excess of the acylating reagent remains. Such circumstances may have induced formation of a complex mixture in the cathodic reaction of **1** or **2** with an electrophile or radical acceptor through acylation of all anionic species generated during the electrolysis. Thus, it is speculated that an immediate and total transformation of **1** or **2** into the corresponding acyl radical or acyl anion equivalent prevents such an undesired process. It was reported that benzoyl chlorides **3** were reduced by samarium diiodide (SmI_2)[7] as a one-electron reducing reagent, leading to formation of the corresponding α-diketones (**5**).[8,9] Based on the reduction potentials, it was postulated that **2** will be more feasibly reduced by SmI_2 than the corresponding **3**, namely, that SmI_2-reduction will satisfy the above requirement for the reduced species of **2** to enter intermolecular reaction. Thus, we examined the reduction of **2** itself by SmI_2 as a preliminary study to develop the intermolecular reaction of an acyl radical or acyl anion equivalent generated from **1** or **2**, and obtained interesting results different from those for the case of **3** itself. We report herein that SmI_2–reduction affords benzoylbenzaldehydes **4** as predominant products from **2** without *para*-substituents and **5** exclusively from **2** bearing *para*-substituents (Scheme 1).



Scheme 1

It was reported that **4** can be prepared by the following methods: (1) SmI_2-induced coupling of benzaldehydes followed by PDC oxidation;[10] (2) benzylic bromination of 4-methylbenzophenone followed by periodate oxidation;[11] (3) oxidative transformation of 4-methylbenzophenone into the corresponding benzaldiacetate followed by acid hydrolysis,[12,13] (4) photolysis of benzaldehyde–cyclodextrin complexes in the solid state.[12] However, the following factors seem to attenuate their synthetic utilities: in the first method, the yields of coupling products from substituted benzaldehydes were rather low; it is unlikely that starting materials with a variety of substituents for the second and the third methods are easily available; the fourth method was applied only to unsubstituted benzaldehyde and its generality is unknown. Thus, it is worthwhile developing a simple and general method for preparing **4**, taking into consideration not only the drawbacks of these methods but also the facts that **4** was used as an important intermediate for synthesis of an HIV-1 integrase inhibitor[11] and antifungal agents.[14]

The typical procedure is as follows: to a THF solution of **3** (1.0 mmol) cooled to −40 °C, Bu_3P (1.1 mmol) was added under an argon atmosphere and the resulting mixture was stirred for 20 min. To the vigorously† stirred mixture, a THF solution (0.1 M, 20 ml) of SmI_2 was added using a syringe. After stirring for 5 min at the same temperature, the reaction was quenched by addition of 1 M HCl (5 ml). The entire mixture was poured into H_2O (20 ml) and extracted with ether (50 ml × 3). The combined organic layer was washed with 5% K_2CO_3 and brine (40 ml each), and dried over $MgSO_4$. After removal of the solvent, the residue was subjected to column chromatography (SiO_2, hexane–AcOEt). Thus obtained products were characterized by ^{1}H-NMR, ^{13}C-NMR, IR, and mass spectra or by comparison with spectroscopic data in the literature.[10,11,15] The regiochemistry in **4b**, **4c**, **6**, and **4f** (*cf.* Table 1) was tentatively assigned to be *para* with respect to the aldehyde groups, based on the results for **2** with *para*-substituents as described below.

The results obtained for benzoyltributylphosphonium chlorides **2** derived from several benzoyl chlorides **3** are shown in Table 1. Reduction of phosphonium chloride **2a** with SmI_2 afforded keto aldehyde **4a** as a sole product in an excellent yield (run 1). Without *in situ* transformation into **2a**, benzoyl chloride was converted only to the corresponding α-diketone in 38% yield under essentially the same conditions, suggesting that reduction of **2** by SmI_2 proceeds in a different manner from that of **3** itself. Similarly, **2b** and **2c** bearing *o*- or *m*-methyl groups were transformed into **4b** and **4c**, respectively, in excellent yields, although formation of the corresponding α-diketone in small amounts was noted (runs 2 and 3). In contrast to the case of **2b** and **2c**, reduction of **2d** with a *p*-methyl group resulted in exclusive formation of α-diketone **5d** (run 4), suggesting that

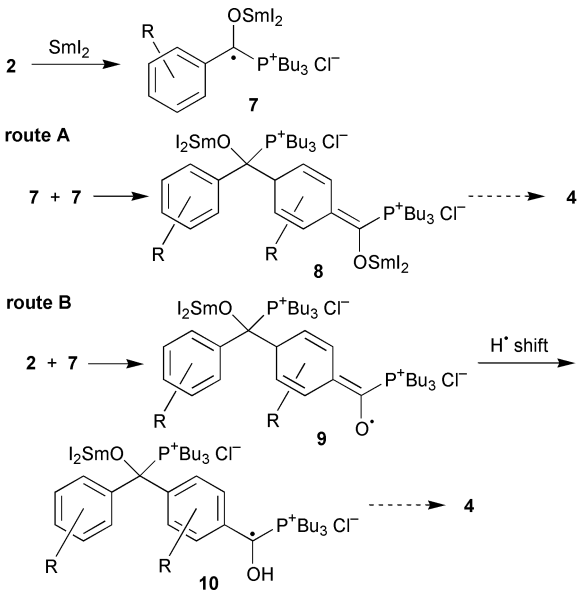
Table 1 Reduction of benzoyl tributylphosphonium ions (**2**) *in situ* generated from benzoyl chlorides and Bu_3P by SmI_2

Run	2	Product
1	**2a** (R=H)	**4a** (80%)[a,b]
2	**2b** (R=2-CH_3)	**4b** (80%), **5b** (10%)[c]
3	**2c** (R=3-CH_3)	**4c** (71%), **5c** (13%)
4	**2d** (R=4-CH_3)	**5d** (59%)[c]
5	**2e** (R=2-Cl)	**6** (50%)
6	**2f** (R=3-Cl)	**4f** (45%), **5f** (42%)
7	**2g** (R=4-Cl)	**5g** (56%)[c]

[a–c] Physical data are available in ref. 10, 12 and 11 respectively.

SmI_2-reduction of **2** favors formation of **4** *via* coupling at the *para*-position. In reaction with SmI_2, **2f** and **2g** with *m*- or *p*-chloro groups exhibited a tendency similar to **2c** and **2d**; in the former case, **4f** was obtained as a major product and the latter case predominantly afforded α-diketone **5g** (runs 6 and 7). Interestingly, reduction of **2e** bearing an *o*-chloro group led to the formation of a triply coupled product **6** in 50% yield (run 5). These results demonstrated that SmI_2-reduction of **2** provided a novel access to **4** from **3** without *para*-substituents, and the transformation seems to prefer electron-donating substituents to electron-withdrawing substituents on the aromatic ring of **3**. It should be mentioned here that the decanoyl tributylphosphonium ion (**1** with R = n-$C_{10}H_{21}$ in Scheme 1) generated from decanoyl chloride and Bu_3P was reduced under essentially the same conditions, affording only decanal in 39% yield.

For formation of **4** by SmI_2-reduction of **2**, two plausible routes can be considered as depicted in Scheme 2, although the detailed mechanism is not clear at present. By one-electron reduction, characteristic of SmI_2,[7] a neutral radical **7** would be formed from **2**. One of the routes to **4** includes a head-to-tail coupling of the radical (route A). The other comprises radical addition of **7** to **2** (route B). When the procedure with a reverse addition was utilized, namely, when **2** was added to a THF solution of SmI_2 cooled at −40 °C, the yields of **4** were markedly decreased: **4a** (57%) and benzil (9%) from **2a**; **4b** (33%) and **5b** (61%) from **2b**; **4c** (32%) and **5c** (61%) from **2c**. These results suggest that effective formation of **4** needs generation of **7** in the presence of excess **2**, namely, that route B is more likely than route A. In addition, route B seems to provide a reasonable explanation that formation of the triply



Scheme 2

coupled product **6** is initiated by addition of a radical such as **10** to **2**.

Since benzoyl chlorides **3** with a wide variety of substituents are commercially available and the present transformation is carried out in one-pot, the SmI_2 reduction of benzoylphosphonium ions **2** is thought to be more straightforward and applicable for the preparation of various types of **4**. Further work is under way to examine the generality of the present methodology as a method of preparing **4** and to shed light on the mechanism of its formation.

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Notes and references

† Vigorous stirring was essential for the formation of **4** in high yields, when SmI_2 was added to a THF solution of **2**.

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