

Samarium Diiodide / Hexamethylphosphoramide Promoted Dimerization of Benzaldehydes

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Abstract: Benzaldehyde, its *ortho*- and *meta*-substituted derivatives and acetophenone underwent dimerization reactions on treatment with samarium(II) iodide in the presence of HMPA. Intramolecular phenyl-carbonyl coupling reactions were similarly carried out.

Samarium(II) iodide has been developed as a useful one-electron transfer reducing agent in the past decade.¹ A carbonyl compound is reduced with SmI₂ in THF to give the corresponding alcohols in the presence of a protic cosolvent such as MeOH and *t*-BuOH.² Devoid of the protic solvent, aromatic aldehydes or aromatic ketones couple readily to give pinacols (the hydrodimerization products) on treatment with 1 equiv of SmI₂ in THF.³ In case less than 1 equiv of SmI₂ is used to react with benzaldehyde, several products including benzyl alcohol (1a), hydrobenzoin (2a), benzoin and benzyl benzoate are obtained.⁴ In this *Letter*, we report a novel coupling reaction of benzaldehydes to give dimerization products 3 by mediation of SmI₂ and hexamethylphosphoramide (HMPA).

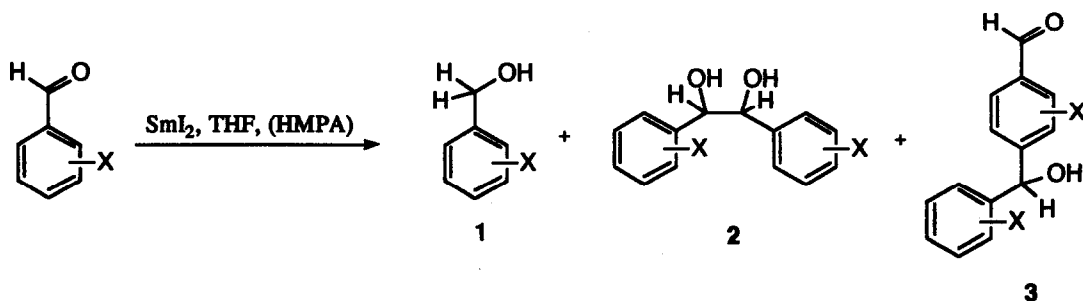
The following procedure is typical. Samarium metal (0.31 g, 2 mmol) and 1,2-diiodoethane (0.38 g, 1.35 mmol) in anhydrous THF (20 mL) was stirred at room temperature under argon atmosphere for 1 h to give a deep blue solution. HMPA (1.4 mL, 8 mmol) was added, after 5 min the resulting deep purple solution was cooled to 0 °C in an ice bath, and benzaldehyde (106 mg, 1 mmol) in THF (2 mL) was added drop-by-drop over a period of 2 min. The mixture was stirred at 0 °C for 1 h and warmed to room temperature over a period of 0.5-2 h. The serum cap was removed, and the reaction mixture was exposed to air to furnish the final oxidative step to resume aromaticity. The mixture was filtered, the filtrate was concentrated under reduced pressure, and the residue was chromatographed on a silica gel column (EtOAc / hexane = 20:80) to give an 80% yield of 3a (81 mg).

The use of HMPA was essential to the dimerization reaction. We repeated the reaction of benzaldehyde with SmI₂ in the absence of HMPA, and obtained a high yield of the pinacol 2a along with a minute amount of the dimer 3a, which was elusive to previous observations.^{3a} A drastic increase of 3a (60%) was achieved by addition of 2.8 equiv of HMPA, and the optimum reaction condition was reached with 8 equiv of HMPA. Other additives⁵ such as *N,N,N',N'*-tetramethylethylenediamine (TMEDA), *N*-methylpyrrolidinone (NMP), *N,N*-dimethylformamide (DMF) and *N,N*-dimethylacetamide (DMA) were inferior to HMPA in promoting the formation of dimers. As shown in the entries 6-8, these additives caused black gelatinous precipitates and lowered reactivity severely.

The *ortho*- or *meta*-substituted benzaldehyde listed in Table 1 also underwent dimerization reaction by means of connecting a *para*-carbon with the carbonyl carbon of the other molecule. No coupling reaction occurred at

either the *ortho*- or *meta*-position. The *para*-orientation preference in these dimerization reactions was different from the *meta*-directed Friedel-Crafts reactions of aromatic compounds containing electron-withdrawing groups. The experiment with acetophenone (entry 19) also showed a similar dimerization process, however, *p*-fluorobenzaldehyde and *p*-methylbenzaldehyde were reduced to give the benzyl alcohols 1h-i and the pinacol 2i. The aldehyde 3a has been prepared by addition of a Grignard reagent PhMgBr to terephthalaldehyde bound on a polymer⁶, while other dimerization products 3b-g and 3j are herein first described. The present method provides a way to the elusive dimers of benzaldehydes and acetophenone.

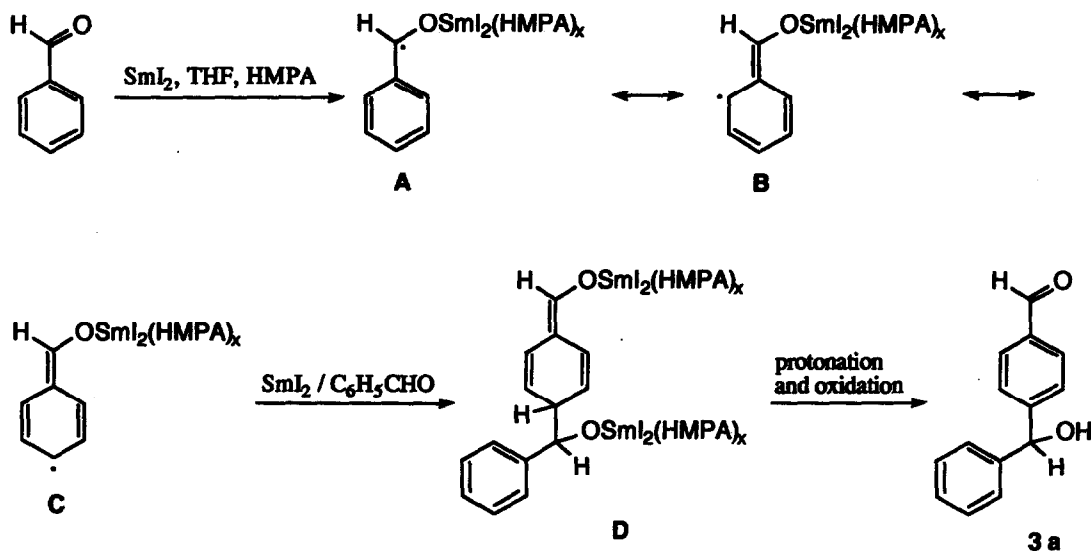
Table 1. Reactions of benzaldehydes and acetophenone with samarium(II) iodide under various conditions.



Entry	Carbonyl compound	Additive (equiv)	Products (isolated yield, %)	Recovery of starting material (%)
1	C ₆ H ₅ CHO		2a (97) + 3a (1)	
2	C ₆ H ₅ CHO	HMPA (2.8)	2a (10) + 3a (60)	not determined
3	C ₆ H ₅ CHO	HMPA (5.6)	3a (72)	not determined
4	C ₆ H ₅ CHO	HMPA (8)	3a (80)	10
5	C ₆ H ₅ CHO	TMEDA (8)	2a (23)	44
6	C ₆ H ₅ CHO	NMP (8)	2a (26) + 3a (4)	58
7	C ₆ H ₅ CHO	DMF (8)	2a (20) + 3a (5)	44
8	C ₆ H ₅ CHO	DMA (8)	2a (11) + 3a (5)	52
9	2-ClC ₆ H ₄ CHO	HMPA (8)	1b (14) + 3b (42)	32
10	2-ClC ₆ H ₄ CHO	HMPA (12)	1b (15) + 3b (44)	21
11	2-ClC ₆ H ₄ CHO	HMPA (16)	1b (20) + 3b (38)	23
12	3-ClC ₆ H ₄ CHO	HMPA (8)	1c (18) + 3c (22)	42
13	3-MeC ₆ H ₄ CHO	HMPA (8)	3d (46)	32
14	2-MeOC ₆ H ₄ CHO	HMPA (8)	3e (30)	46
15	3-MeOC ₆ H ₄ CHO	HMPA (8)	1f (27) + 3f (18)	50
16	2,5-(MeO) ₂ C ₆ H ₃ CHO	HMPA (8)	3g (31)	44
17	4-FC ₆ H ₄ CHO	HMPA (8)	1h (85)	
18	4-MeC ₆ H ₄ CHO	HMPA (8)	1i (10) + 2i (72)	
19	C ₆ H ₅ COMe	HMPA (8)	1j (10) ^a + 3j (32)	42

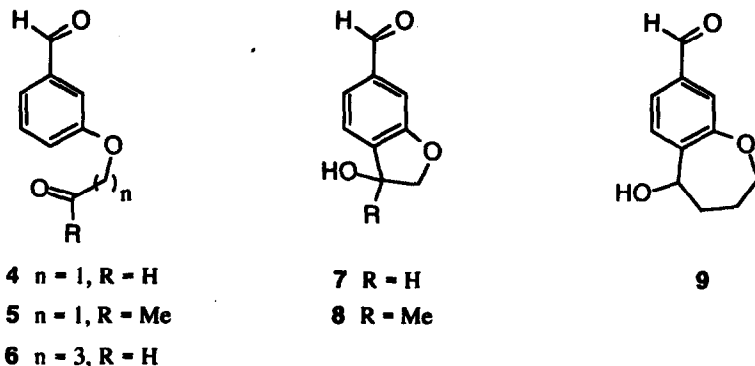
^a Acetophenone is reduced to 1j (80%) in the absence of HMPA, see ref. 2.

Scheme 1.



The use of HMPA has been found to facilitate the reactions involving SmI_2 such as reduction of halides⁷, deoxygenation of sulfones^{7b, 8}, Barbier-type reactions^{5b, 9}, ketone-olefin couplings^{5c, 10}, and in other radical cyclizations of carbon-carbon unsaturated systems¹¹. The precise role of HMPA in these reactions and the present dimerization reactions was not well understood, however, HMPA molecules were presumably to coordinate with samarium ion via their oxygen atoms.^{10b, 12} A possible mechanism is proposed in Scheme 1 without indicating the real nature of samarium ion in the intermediates. In the intermediate A, HMPA molecules would block the ketyl center from taking up a hydrogen atom or proceeding to a subsequent pinacol coupling reaction. Instead,¹³ the second benzaldehyde molecule would have access to the *para*-carbon of the resonance intermediate C to furnish the observed products 3.

The current method was successfully applied to the intramolecular phenyl-carbonyl coupling reactions of the benzaldehydes 4-6 to afford the benzofuran carbaldehydes 7 and 8 and the benzoxepin carbaldehyde 9 in 45%, 88% and 82% yields, respectively.



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