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Direct Formation of Benzoins from Diarylmethanones via a Rearrangement Reaction Promoted by Samarium Metal in DMF

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Abstract: Diarylmethanones react readily with DMF when promoted by samarium metal in DMF with TMSCl or iodine as an activator, to afford benzoins in good to excellent yields via rearrangement of aryl groups. As for asymmetric diarylmethanones, products resulting from the migration of either aryl group were obtained, where the migration of aryl groups shows certain priority.

Key words: samarium, DMF, diarylmethanone, rearrangement reaction, benzoin, benzil

Although samarium diiodide (SmI₂) is a very useful reducing reagent,¹ however, its application in organic synthesis is limited to some extent. Its storage is difficult because of its sensitivity to air oxidation. Besides, Sm²⁺ can only donate one electron in the reaction and the lack of atom economy seriously restricts its application on a large scale. Therefore, direct use of metallic samarium as a reducing agent in organic transformations has attracted the attention of many organic chemists.² Usually, reactions promoted directly by samarium metal are carried out in THF³ and metallic samarium has to be activated by other reagents such as iodine, hydrochloric acid, alkyl halides, TMSCl, etc.^{1,3,4} so as to ensure the reactions proceed smoothly. We have recently found that metallic samarium exhibits some interesting properties in organic synthesis when DMF is used as a solvent instead of THF.5

The diarylmethanone dianion is a known species⁶ whose reactions with carbonyl compounds or benzonitrile have been observed long time before.⁷ Reduced by SmI_2 , diarylmethanone forms ketyl readily, which has considerable stability and constitutes the important intermediate in cross-coupling reactions with ketones, aldehydes, imines, aroyl chlorides, conjugated carbon-carbon double bonds, and so on.¹

However, when diphenylmethanone was treated with samarium metal activated with TMSCl in DMF, surprisingly, benzoin was obtained in excellent yield (Scheme 1).





The unexpected formation of benzoin indicates that the additional carbonyl group comes from the dimethylformamide and dimethylamino group acts as a leaving group in this reaction. Despite the fact that the carbonyl groups of amides are unreactive toward many carbon nucleophiles and are employed consequently as solvents in carbon-carbon bond-formation reactions,⁸ DMF as a good formylation reagent is well known (Vilsmeier–Hack reaction).⁹ Besides, such necleophiles as Grignard reagents,^{10a} organolithium^{10a,b} and the radical anions^{10c} resulting from the reduction by sodium in THF can attack the carbonyl group in DMF to afford the corresponding aldehydes. In the reactions mentioned above, the formoyl group in DMF was introduced into the products with dimethylamino anion acting as a leaving group.

To have some idea about the mechanism of the present reaction, we undertook an extensive literature survey and were fortunate to find some clues to this reaction in the electron spin resonance study of the radicals obtained from acetophenone and benzaldehyde.¹¹ At high reduction potentials and by an irreversible electrode process, the conversion of acetophenone to 1-phenyl-propane-1,2semidione in DMF was proposed to undergo a carbene rearrangement.^{11b}

To have an in-depth understanding of the reaction, a series of diarylketones were subjected to the same conditions and the desired benzoins were formed smoothly. In some cases, benzils were also obtained as the unexpected byproducts (Scheme 2). The results of the reactions are described in Table 1. The reaction of diarylketones with electron-donating group attached to the aromatic rings proceeds efficiently. In contrast, diarylketones with electron-withdrawing group require relatively harsh reaction conditions and give lower total yields. As can be seen, bis(p-methylphenyl)-methanone (**1b**) and bis(p-methoxyphenyl)-methanone (**1c**) can give 4,4'-dimethylbenzoin

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Scheme 2

En- try	R^1 , R^2 in substrate 1	Temp (°C)	Time (h)	Total yield of 2 , 3 (%) ^a	Ratio of $2/3^{b}$	Yield of 4 (%)
1	H, H (1a)	90	10	91 (2a)		0 (4a)
2	$CH_3, CH_3 (\mathbf{1b})$	80	6	74 (2b)		18 (4b)
3	CH ₃ O, CH ₃ O (1c)	80	4	53 (2c)		35 (4c)
4	4-(CH ₃) ₂ N, 4-(CH ₃) ₂ N (1d)	120	36	_		-
5	4-Cl, 4-Cl (1e)	120	12	-		_
6	4-CH ₃ , H (1f)	90	8	77 (2f , 3f)	68/32	14 (4f)
7	4-Ph, H (1g)	80	5	47° (2g , 3g)	19/81	16 (4g)
8	4-Cl, H (1h)	120	24	52 ^d (2a , 3h)	0/100	0
9	4-Br, H (1i)	120	24	53 ^e (2a)		0

^a Products **2** and **3** were inseparable and the overall yields were given. ^b The ratio was determined by HPLC and ¹H NMR.

^c A considerable amount of reductive product biphenyl-4-yl-phenyl-methanol was detected.

^d Dechlorination reaction affording 26% of **2a** occurred simultaneously in the formation of the corresponding benzoin.

^e Exclusive debromination product 2a was formed.

and anisoin respectively (entries 2 and 3) in good yields, while bis(*p*-chlorophenyl)-methanone (**1e**) failed to afford the corresponding types of products **2** and **3**. It is surprising to find bis(*p*-dimethylaminophenyl)-methanone (**1d**) did not undergo the reaction under the same conditions. The amino group may form a salt with TMSCl and thus bear an electron-withdrawing character, which makes the reaction difficult to occur just like the case of bis(*p*-chlorophenyl)-methanone (**1e**). As for asymmetric diarylmethanones, two kinds of benzoins can be obtained, with the carbonyl groups adjacent to the electron-richer aryl groups predominant. This may indicate the reaction follows a certain rule in the rearrangement.

It is worth noting that besides the 4'-chlorobenzoin (3h), benzoin (2a) was also obtained. The formation of 2aobviously results from a dechlorination process under the reaction conditions accompanying the rearrangement. As for phenyl *p*-bromophenyl methanone, the debromination

Table 2Reaction of Diarylmethanones with DMF Promoted by Sm/I_2 in DMF

En- try	$\mathbf{R}^{1}, \mathbf{R}^{2}$ in substrate 1	Temp (°C)	Time (h)	Total yield of 2 , 3 (%)	Ratio of 2/3	Yield of 4 (%)
1	H, H (1a)	80	2	90 (2a) ^{12b}		0
2	$CH_3, CH_3 (\mathbf{1b})$	70	1	79 (2b) ^{12b}		15 (4b) ^{12f}
3	CH ₃ O, CH ₃ O (1c)	50	1	78 (2c) ^{12b}		16 (4c) ^{12f}
4	4-(CH ₃) ₂ N, 4- (CH ₃) ₂ N (1d)	80	1	63 (2d) ^{12d}		21 (4d) ^{12f}
5	4-Cl, 4-Cl (1e)	120	5	_		-
6	4-CH ₃ , H (1f)	70	1	82 (2f , 3f) ^{12c}	68/32	11 (4f) ^{12g}
7	4-Ph, H (1g)	50	1	87 $(2g, 3g)^{12e}$	81/19	9 (4g) ^{12h}
8	4-Cl, H (1h)	100	5	41 (2h , 3h) ^{12c}	0/100	13 (4h) ^{12f}
9	4-Br, H (1i)	100	5	58 (2a)		0

reaction proceeds to such an extent that benzoin (2a) was isolated as the only product. An attempt was also made but with a negative result in investigating if acetophenone and benzaldehyde could undergo such a reaction.

Considering TMSCl is an acidic activator, we explored neutral activator iodine in a further investigation. To our delight, better results were obtained in the presence of I_2 , as shown in Table 2.

With iodine as an activator, the reaction proceeded more easily with milder reaction conditions and higher total yields than that activated with TMSCl, except that substrate bis-(*p*-chlorophenyl)-methanone (**1e**) still failed to give encouraging result (entry 5). Bis-(*p*-dimethylaminophenyl)-methanone, to our expectation, can undergo the same kind of reaction under this conditions and afford the corresponding benzoin and benzil in high total yield (entry 4). The benzoins with the carbonyl groups adjacent to the electron-richer aryl groups still predominate in the products when asymmetric diarylmethanones are used as substrates under the Sm/DMF/I₂ conditions. An exception is biphenyl-4-yl-phenyl-methanone (**1g**) gives the benzoin with the carbonyl group adjacent to the biphenyl group as a major product (entry 7).



Electron donating ability R¹ > R²

Scheme 3

The formation of benzils may be explained as a result of the auto-oxidation of benzoins. The reports that some metal salts such as copper(I)^{13a} and Ce(IV)^{13b} can easily catalyze the autoxidation of benzoins to the corresponding benzils make us deduce that the presence of samarium salts here may accelerate the formation of benzils from benzoins during the treatment process. Further investigation showed that the benzil could also be obtained when benzoin was treated under the same reaction conditions. This validates our suggestion.

We attempted the reaction without activator (TMSCl or I_2) and found that the reaction did not occur at all, and further attempts to expand the reaction to other metals such as zinc failed. We also tried other solvents such as THF, DMSO, and toluene instead of DMF but did not find any benzoin formed. This result may indicate the additional carbonyl group comes from DMF. On the other hand, the result that no obvious reaction between Sm/activator and DMF was observed without diarylmethanone in the reaction system shows the reaction must be initiated by ketyl resulting from diarylmethanone. Based on our experimental results and the ESR study on the relevant radicals,^{11b} a possible mechanism was suggested (Scheme 3).

Due to the strongly electrophilic character of carbene,¹⁴ **A** undergoes a rearrangement (intramolecular insertion reaction) with the electron-richer aryl group of the two preferably migrates to form enol intermediates (**B**>**C**), which tautomerizes immediately followed by protonation to give the corresponding benzoins respectively.

In conclusion, with TMSCl or iodine as the activator, the reaction between diarylketones and DMF via a rearrangement process promoted by samarium metal can afford benzoins and benzils in good overall yields. The complexing of DMF with samarium ion¹⁵ may play an important role in promoting the reaction to occur, and studies on the exact mechanism are currently in progress.

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