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Use of [hydroxy(tosyloxy)iodo]benzene in a novel and facile synthesis of 1,4-diaryl-2-(arylamino)but-2-ene-1,4-diones

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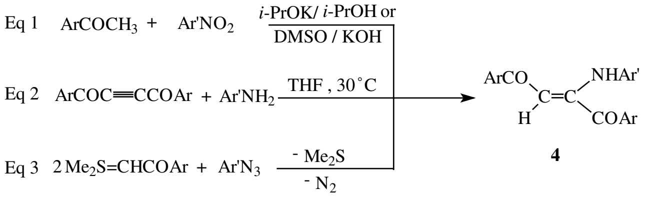
Abstract—The reaction of acetophenones **1** with [hydroxy(tosyloxy)iodo]benzene followed by treatment of the resulting α-tosyloxyacetophenones **2** thus formed with anilines **3** in the presence of sodium carbonate in ethanol provides a novel one-pot synthesis of 1,4-diaryl-2-(arylamino)but-2-ene-1,4-diones **4**.

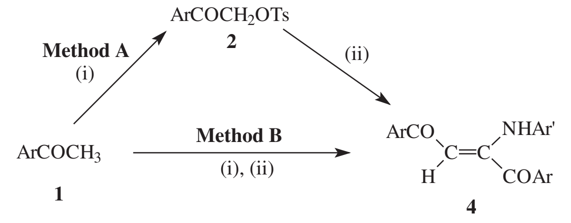
1,4-Diaryl-2-(arylamino)but-2-ene-1,4-diones **4** are important precursors for the synthesis of heterocyclic compounds.[1,2] There are three methods reported in the literature for their synthesis as outlined in Eqs. 1–3.[2–5] The yields in the first two methods (Eqs. 1 and 2) are not good, whereas the third method (Eq. 3) involves aryl azides, which are highly toxic and explosive in nature.



As part of our project[6] directed towards the use of organo-hypervalent iodine reagents[7] such as iodobenzene diacetate (IBD)[8,9] and [hydroxy(tosyloxy)iodo]benzene (HTIB, Koser's reagent)[10,11] in organic synthesis, we earlier reported a convenient synthesis of α-anilinoacetophenones ($ArCOCH_2NHAr'$).[12] In an attempt to synthesize α-anilinoacetophenones from α-tosyloxyacetophenones **2** and anilines **3** in the presence of sodium carbonate in ethanol, we found that instead the reaction resulted in the formation of a mixture containing new products **4** and expected α-anilinoacetophenones products. This observation encouraged us to seek optimum conditions for the synthesis of 1,4-diaryl-2-(arylamino)but-2-ene-1,4-diones **4** and we report here a novel and convenient synthesis of **4**. In addition, a one-pot procedure for the synthesis of **4** starting from acetophenones **1** has been developed and is reported herein.

First, we carried out the reaction between α-tosyloxyacetophenone **2a** and aniline **3a**. We found that an equimolar mixture of **2a** and aniline **3a** in the presence of sodium carbonate in ethanol under reflux for 12 h afforded **4aa** in 70% yield. The generality of this approach was illustrated by reacting different α-tosyloxyacetophenones (**2a**–**e**) and anilines (**3a**–**e**) under similar conditions. The reactions afforded the desired products **4ac**–**ec** in yields ranging from 65% to 77% (Table 1, Scheme 1, Method A).

Based on our earlier success in the development of a one-pot synthesis of α-anilinoacetophenones from acetophenones,[12] we attempted the synthesis of **4** by oxidation of



(i) HTIB, CH_3CN, reflux (ii) $Ar'NH_2$ **3**, Na_2CO_3, C_2H_5OH, reflux

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Keywords: α-Tosyloxyacetophenones; Anilines; α-Anilinoacetophenones; 1,4-Diaryl-2-(arylamino)but-2-ene-1,4-diones.

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1	Ar
a	C_6H_5
b	p-FC_6H_4
c	p-MeC_6H_4
d	p-$MeOC_6H_4$
e	p-BrC_6H_4

3	Ar'
a	C_6H_5
b	p-FC_6H_4
c	p-MeC_6H_4
d	p-$MeOC_6H_4$
e	p-$O_2NC_6H_4$

4	Ar	Ar'
aa	C_6H_5	C_6H_5
ac	C_6H_5	p-MeC_6H_4
ad	C_6H_5	p-$MeOC_6H_4$
ba	p-FC_6H_4	C_6H_5
ca	p-MeC_6H_4	C_6H_5
da	p-$MeOC_6H_4$	C_6H_5
ea	p-BrC_6H_4	C_6H_5
ce	p-MeC_6H_4	p-$O_2NC_6H_4$
ec	p-BrC_6H_4	p-MeC_6H_4

Scheme 1.

Table 1. Physical data of 1,4-diaryl-2-(arylamino)but-2-ene-1,4-diones **4** prepared according to Scheme 1

Compound	Mp (°C)	Lit. mp (°C)	Yield[b,c] (%)
4aa	126–127	128[2]	70 (65)
4ac	144–145	153[4]	71 (67)
4ad	122–123	121–122[15]	70 (63)
4ba	168–169	[a]	76 (68)
4ca	141–142	143[4]	65 (61)
4da	136–137	135–136[2]	67 (61)
4ea	160–161	169–170[4]	72 (67)
4ce	202–203	204[4]	65 (60)
4ec	223–224	[a]	77 (72)

[a] New products and their structures were confirmed by their spectral (IR, ^{1}H NMR, mass) and satisfactory elemental analyses (C, H, N).

[b] Yields of isolated compounds after recrystallization from ethanol with respect to the quantity of pure α-tosyloxyacetophenone **2** starting material (Method A). Compound **2** used in this method were prepared according to the literature procedure and were purified by recrystallization from ethanol.[10a]

[c] Yields in parentheses are of pure products with respect to the quantity of acetophenone starting material (by Method B) presuming that 2 equiv of acetophenone produce 1 equiv of **4**.

acetophenones (**1a**–**e**) with HTIB (**2a**–**e** are generated in situ) followed by reaction with anilines (**3a**–**e**) (Method B).[13] This method worked well for the synthesis of **4aa**–**ec** and the physical data are given in Table 1.

Although the mechanism for the reaction is not certain, preliminary observations from the present study indicate that the conversion **2**→**4** proceeds through the intermediate α-anilinoacetophenones ($ArCOCH_2NHAr'$),[14] which probably undergoes oxidative dimerization in aerobic conditions. Further studies concerning the full scope of the reaction and its mechanism are in progress, and will be published in the future. Finally, the present study provides a novel application of Koser's reagent for a direct one-pot synthesis of 1,4-diaryl-2-(arylamino)-but-2-ene-1,4-diones **4** from acetophenones. The present synthesis is superior to existing methods because of its good yields and the simple experimental procedure involved. The reaction conditions exclusively gave **4** and the intermediate α-anilinoacetophenone can be prepared selectively by omitting the use of base such as Na_2CO_3/K_2CO_3.[12]

Acknowledgements

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13. [Hydroxy(tosyloxy)iodo]benzene (10 mmol) was added to a solution of an acetophenone (**1**, 10 mmol) in acetonitrile (25 mL) and the mixture was refluxed for 1–2 h. The solvent was evaporated in vacuo. Aniline/*p*-substituted aniline (**3**, 10 mmol), sodium carbonate (10 mmol) and ethanol (20 mL) were added and the mixture refluxed for a further 6–12 h, then kept overnight. The solid, thus separated, was filtered, washed with water, dried and recrystallized from ethanol.
14. We were able to isolate the intermediate $PhCOCH_2NHPh$ **5aa** under controlled conditions. In a separate experiment, the intermediate **5aa** was successfully converted into **4aa**.
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