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The role of atropisomers on the photo-reactivity and fatigue of diarylethene-based metal–organic frameworks

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ARTICLE TYPE

Metal-free denitrative arylation of β-nitrostyrenes using benzoyl peroxide: an easy access to *trans*-stilbenes†

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†Electronic supplementary information (ESI) available: Experimental details and copies of ^{1}H & ^{13}C spectra for the products, See DIO: 10.1039/c0xx00000x

A simple, novel and stereoselective synthesis of *trans*-stilbenes has been described using denitrative arylation of β-nitrostyrenes in the presence of benzoyl peroxide under metal-free conditions. The reaction is assumed to involve homolytic clevage of the benzoyl peroxide followed by decarboxylation to generate phenyl radical, which brings about *ipso*-substitution of the nitro group of nitrostyrenes to afford the *trans*-stilbenes.

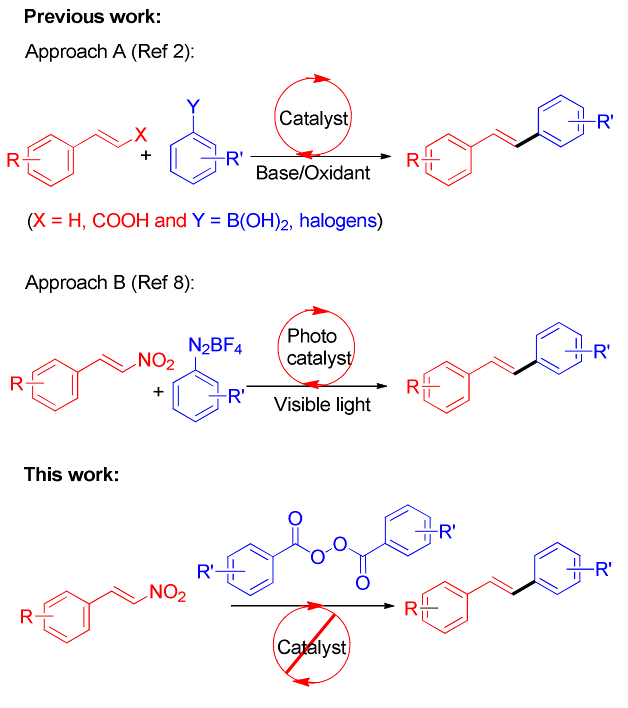
Introduction

Stilbenes have broad applications in the synthesis of small to medium ring cyclic compounds, enantiomerically pure 1,2-diphenylethanes, 1,2-diamines, 1,2-diols and phenanthrene alkaloids.[1] They are also used as optical brighteners and therapeutic agents for liver disorders.[1] Because of their importance in the synthesis of such valuable molecules, a variety of preparative methods for stilbenes have been developed.[2] Among them, Heck reaction is one of the most frequently used methods for the synthesis of aryl-substituted olefins (Scheme 1, Approach A). However, metal (Pd/Ni/Co/Cu/Fe) and ligand based methods in general have some limitations, such as high cost, generation of toxic waste, protection from air and moisture, and substrate limitations (not applicable to halogen substituent).[2,3] Some other useful alternative methodologies to prepare stilbenes include condensation of aldehyde tosylhydrazones with stabilized carbanions,[1d] Wittig type reaction,[4] reductive coupling of carbonyl compounds,[5] and self-coupling of α-lithiated benzylic sulfones.[6]

β-Nitrostyrenes constitute an important class of synthetic intermediate and are easily prepared by the Henry reaction. They have been successfully used for C-C/C-S bond formation by denitrative addition-elimination reaction to prepare a variety of biologically and pharmaceutically important compounds.[7] The process involves the cross-coupling of nitroalkenes, where NO_2 eventually acts as a leaving group. Further exploration on the application of this stable and easily available intermediate is highly demanding and interesting in organic synthesis.

Recently, König and Wang groups have developed new methodologies for the synthesis of stilbenes from β-nitrostyrene using visible light photoredox catalysts (Scheme 1, Approach B).[8] Despite their intrinsic advantages, yet, photoredox catalysts are often expensive, potentially toxic and undergo decomposition on long irradiation. The recovery of the photocatalyst from the reaction mixture is also cumbersome, and requires longer reaction time. Therefore, a facile and efficient alternative to synthesize *trans*-stilbenes is exigent and useful.

Inspired by the recent work on β-nitrostyrenes under transition metal catalysis by Yuan and Yadav groups,[9] it was envisioned that the phenyl radical generated from *tert*-butylperoxybenzoate (TBPB) or benzoyl peroxide (BPO) could be judiciously used for its coupling with β-nitrostyrenes. This is worthwhile to mention that benzoyl peroxide has been recently utilized as phenyl radical source,[10] but the use of benzoyl peroxide as a phenyl radical source under metal-free conditions is rather limited.[11] Further, there is no report on the free radical reactions of β-nitrostyrene without the use of a catalyst. In view of the above and as a part of our ongoing research programme in organic synthesis,[12] we describe herein a novel, metal-free and stereoselective synthesis of *trans*-stilbenes adoping denitrative arylation of β-nitrostyrenes using benzoyl peroxides (**Scheme 1, This work**).



Scheme 1 Synthesis of *trans*-stilbenes.

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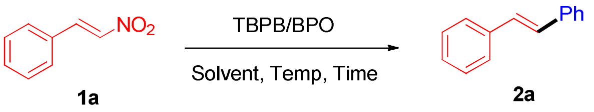
Results and discussion

In order to optimize the reaction conditions, a detailed study employing β-nitrostyrene (**1a**) as model reactant was undertaken by varying different parameters and the findings are given in Table 1. The reaction was initially carried out using equimolar quantities (1.0 mmol) of **1a** and *tert*-butylperoxybenzoate (TBPB) in CH_3CN (3 mL) at 110 °C for 4 h in a sealed tube, which did not give the desired product (Table 1, entry 1). Then was added a catalytic amount (10 mol%) of $Cu(OAc)_2$ to the same blend, which gave rise to the *trans*-stilbene (**2a**) in 38% yield (Table 1, entry 2).

Table 1 Optimization of reaction conditions. [a]



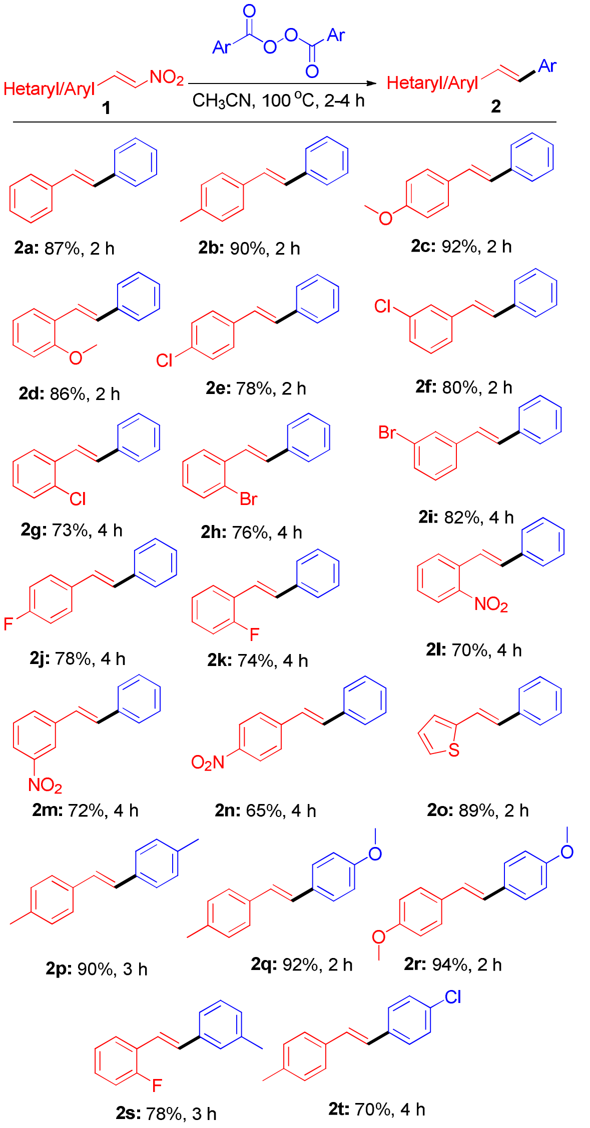
Entry	Catalyst (mol%)	Ph Source (mmol)	Solvent	Temp.	Time (h)	Yield (%)[b]
1	-	TBPB (1)	CH_3CN	110	4	traces
2	$Cu(OAc)_2$ (10)	TBPB (1)	CH_3CN	110	4	38
3	$Cu(OTf)_2$ (10)	TBPB (1)	CH_3CN	110	4	32
4	$CuCl_2$ (10)	TBPB (1)	CH_3CN	110	4	27
5	$Ni(OAc)_2$ (10)	TBPB (1)	CH_3CN	110	4	35
6	$Cu(OAc)_2$ (10)	TBPB (1)	DCE	110	4	30
7	$Cu(OAc)_2$ (10)	TBPB (1)	DMF	110	4	37
8	$Cu(OAc)_2$ (10)	TBPB (1)	DMSO	110	4	34
9	$Cu(OAc)_2$ (10)	BPO (1)	CH_3CN	110	2	90
10	-	BPO (1)	CH_3CN	110	2	88
11	-	BPO (0.5)	CH_3CN	110	2	87
12	**-**	**BPO** (0.5)	**CH_3CN**	**100**	**2**	**87**
13	-	BPO (0.5)	CH_3CN	90	2	70

[a] Reaction conditions: **1** (1.0 mmol), Catalyst (10 mol%), Phenyl source (1-0.5 mmol), Solvent (3 mL), 100-110 °C, 2-4 h, in sealed tube. [b] Isolated product yield.

Thereafter, some other catalysts such as $Cu(OTf)_2$, $CuCl_2$ and $Ni(OAc)_2$ were used under identical conditions to test their efficacy (entries 3 to 5), but none of them could match the productivity of $Cu(OAc)_2$. Then was tested the effect of some other solvents like DCE, DMF and DMSO, yet no improvement in the product yield was observed (entries 6-8). Then, we resorted to the use of benzoyl peroxide (BPO) as phenyl radical source, as BPO is readily available, inexpensive, and easy to handle. To our utmost delight, when the reaction was carried out using BPO in the presence of $Cu(OAc)_2$, a dramatic increase in the product yield and a considerable reduction in the reaction time (2h) was observed (entry 9). Encouraged by this result, the reaction was afterwards conducted with BPO in the absence of $Cu(OAc)_2$, which delightedly led to almost identical product yield (entry 10). In order to avoid the use of metal salt, entry 10 was opted as the best fit. The molar ratio of reactants and the effect of temperature were also optimized, which came out to be 0.5 mmol of BPO at 100 °C (entries 11-13).

Under the established set of reaction conditions (entry 12), the generality and scope of the present protocol was examined in detail by using cross-coupling reaction of diversely substituted β-nitrostyrenes with benzoyl peroxide to afford a variety of *trans*-stilbenes **2a-2o**. The outcome is given in Table 2. The reaction works well in almost all the cases of β-nitrostyrenes containing substituent like Me, MeO, Cl, Br, F and NO_2 at different positions; and also with a heteroaromatic ring. However, aromatic substrates bearing electron-donating substituent afford somewhat higher yield of the products in comparison to those bearing electron-withdrawing group (*cf.* **Table 2**; **2b-2n**). This is perhaps due to the formation of the benzylic intermediate during the course of reaction, which is destablised by an electron-withdrawing substituent. In order to establish the scope and utility of the chemistry, diversely substituted BPOs containing *p*-Me, *m*-Me, *p*-MeO and *p*-Cl were also prepared from the corresponding carboxylic acids, and then allowed to undergo reaction with β-nitrostyrenes having substituent like *p*-Me, *p*-MeO and *o*-F under the established conditions, which successfully led to the formation of the *trans*-stilbenes **2p-2t** (*cf.* Table 2).

Table 2 Substrate scope. [a,b]



[a] Reaction conditions: **1** (1.0 mmol), benzoyl peroxide/substituted benzoyl peroxide (0.5 mmol), CH_3CN (3 mL), 100 °C, 2-4 h, in a sealed tube. [b] Isolated product yield (For general procedure and characterization of the product, see: ESI†).

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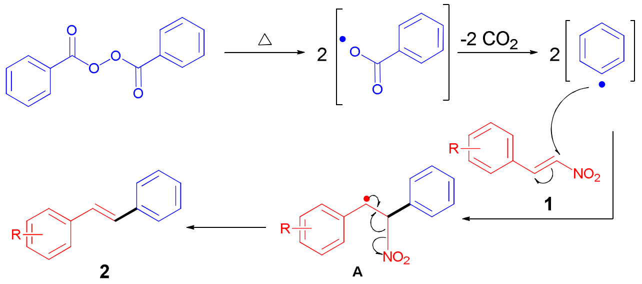
To demonstrate the workability of the reaction, a gram scale reaction using **1a** (0.74 g) and BPO (0.60 g) was carried out, which afforded the product **2a** in 82% yield (0.73 g) without compromising the reaction conditions.

To look into the mechanistic insights of the reaction, a typical reaction of **1a** with BPO was carried out in the presence of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO, 2 equiv.), which completely suppressed the formation of **2a**, thereby revealing the involvement of a radical pathway. Based on this observation, isolation of products and literature precedents,[8,9,11] a plausible mechanism is outlined in Scheme 2. Benzoyl peroxide on thermolysis undergoes successive cleavage of O-O bond and decarboxylation to afford the phenyl radical, which subsequently reacts with β-nitrostyrene to form the benzylic radical species **A**, followed by denitration giving rise to the product **2**.



Scheme 2 Plausible reaction mechanism.

Conclusions

In conclusion, a convenient, metal-free and efficient method for the synthesis of *trans*-stilbenes has been developed by the cross coupling of easily accessible β-nitrostyrenes and benzoyl peroxide. The protocol describes the first-time free radical reaction of β-nitrostyrenes without using a catalyst.

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Metal-free denitrative arylation of β-nitrostyrenes using benzoyl peroxide: an easy access to *trans*-stilbenes

Arvind Kumar Yadav and Krishna Nand Singh*

A novel, efficient and stereoselective synthesis of *trans*-stilbenes has been achieved from β-nitrostyrenes and benzoyl peroxide without using any catalyst.