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TBHP/$R_4N^+X^-$ promoted hydroaroylation of dialkyl azodicarboxylates with methyl arenes, aldehydes, aryl methanols and arylmethyl chlorides

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ABSTRACT

Efficient TBHP/$R_4N^+X^-$ promoted hydroaroylations of dialkyl azo-1,2-dicarboxylates with methyl arenes, aldehydes, aryl methanols and arylmethyl chlorides are described. These oxidation/oxygenation and hydroaroylation processes were carried out by *tert*-butyl hydroperoxide as terminal oxidant/oxygen source, and were catalyzed by tetrabutylammonium bromide and tricaprylmethylammonium chloride as the driving force. During this investigation, all these hydroaroylating sources were found to be highly efficient reagents without the need of any transition-metal.

1. Introduction

C–H functionalization protocol is a rapidly expanding area in organic synthesis as it offers high impetus for developing novel, short and attractive methodologies for synthesizing a variety of complex organic molecules.[1] Moreover, due to their relatively inert nature, the functionalization and activation of C–H bonds plays a vital role in the development of more efficient and sustainable bond forming reactions. From an atom-economical and environmental point of view, the use of un-functionalized starting materials in the construction of C–C and C–heteroatom bonds is one of the major concerns for synthetic chemists.[2]

Methyl arenes,[3] alcohols[4] and arylmethyl halides[4c,5] have been recognized as cheap, simple, stable and easily available starting materials, which made them attractive substrates from both academic and industrial perspective in the synthesis of complex molecules.

Remarkably, construction of various bonds and complex compounds using oxidant/$R_4N^+X^-$ system has emerged as an efficient and unique catalytic methodology which obviates the foregoing impediments of metal-catalyzed reactions.[6]

Dialkyl azodicarboxylates (DAADs) are excellent electrophiles due to the presence of two carboalkoxy groups and electrophilic π bond on the nitrogen atoms of the azo skeleton.[7] Thus, DAADs have been employed as nucleophile acceptors and coupling partners in various reactions such as *N*-arylation,[8] C–H derivatization at the α-position to heteroatoms,[9] electrophilic α-amination of carbonyl compounds,[10] ene-type reactions with olefins[11] and also reactions with zwitterionic intermediates.[12]

On the other hand, acylation of DAADs has also received considerable attention from the synthetic community.[13] In recent

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years, hydrazine imides have been prepared from aliphatic and aromatic aldehydes as hydroacylating agents. While the reaction can be performed under various conditions using metal catalyst such as Rh(II),[14] Cu(II),[15] and Zn(II),[16] aqueous media,[17] ionic liquid,[18] Lewis- and Brønsted-acid catalysis,[19] pyridine-catalysis under microwave irradiation,[20] photocatalytic method,[21a] decatungstate anion photocatalysis,[21b] graphite flakes as the carbocatalyst,[21c] and CoO-Fe_3O_4 as magnetic catalysis.[22]

As part of our continuing effort to develop efficient methods for the preparation of biologically active organic compounds from readily available precursors,[23] recently, we have been particularly interested in oxidant/$R_4N^+X^-$ catalytic systems and have focused our attention on the development of acylation-based novel transformations.[24]

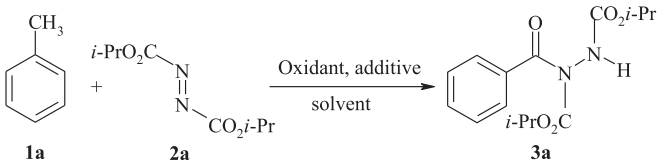
Herein, we present highly efficient and transition metal-free hydroaroylations of DAADs with readily accessible hydroaroylating reagents *via* C(sp^3)–H and C(sp^2)–H oxidation functionalization strategies promoted by oxidant/$R_4N^+X^-$ leading to the corresponding hydrazine imides (Scheme 1).

2. Result and discussion

Initially, we selected toluene **1a** and DAAD **2a** as the model substrates to evaluate the most suitable conditions. In this optimization, various parameters such as the type as well as the quantity of oxidant and additive, solvents, and reaction temperature were examined (Table 1). The reaction between **1a** and **2a** was first started in the presence of *tert*-butyl hydroperoxide (TBHP, 6 equiv.) as oxidant and tetrabutylammonium bromide (TBAB, 30 mol %) as additive at ambient temperature for 1 h, however, no reaction was observed (entry 1). Carrying out the reaction at 50 and 80 °C, gave dialkyl hydrazine-1,2-dicarboxylate (DAHD, **3a**) in 28 and 55% yields, respectively (entries 2 and 3). In order to improve the reaction efficiency, reaction time increased to 2 h, but the yield of **3a** decreased to 35% (entry 4). By increasing the reaction time, the NH group of the formed hydrobenzoylated product may undergo further oxidation and functionalization.[25] By increasing the amount of TBHP and TBAB the efficiency of the reaction improved (entries 5–7) and the best result was observed with 50 mol% of TBAB and 8.0 equiv of TBHP at 80 °C with which **3a** was obtained in 93% yield (entry 6). However, higher TBHP loading did not improve the formation of **3a** (entry 7). An excess amount of TBHP led to the formation of benzoic acid in the reaction mixture. Also, in several reports, increasing the amount of the oxidant has a negative effect on the yield of the product.[5,26] Other additives were also examined (entries 8–13). NBS, TBPB and Aliquat 336 gave **3a** in 10%, 75%, and 48% yields, respectively (entries 8–10) and KI as well as elemental iodine (I_2) were ineffective (entries 11 and 12). Notably, no product was detected by use of BPO, $K_2S_2O_8$, and H_2O_2 as oxidant (entries 13–15). Moreover, the solvent screening studies indicated that no product was formed in solvents such as PhCl, CH_3CN, 1,4-dioxane and DMSO (entries 16–19). Furthermore, the reaction was carried out in the presence of different amounts of toluene (4, 6 and 10 mmol), which led to the formation of **3a** in 40%, 62%, and 79% yields, respectively (entries 20–22). In the absence of TBHP and TBAB, **3a** was not detected (entries 23 and 24), which suggested that both TBHP and TBAB played a crucial role in this reaction. Carrying out the reaction at 100 °C and 120 °C, **3a** was obtained in 93% and 90% yields, respectively, after 30 min (entries 25 and 26). According to the above results, the optimal conditions for synthesis of DAHD **3a** were determined as: DAAD **2a** (0.4 mmol), toluene (8 mmol), TBHP (8 equiv.), 50 mol% of TBAB, at 80 °C for 1 h (entry 6).

With the optimal conditions in hand, various methyl arenes **1** and DAADs **2a**,**b** were used and the corresponding DAHDs **3a**–**q** were obtained in 75–93% yields. The results are summarized in Table 2. The reaction of methyl arenes with neutral and electron-donating substituents such as (one or more) Me and OMe at the *meta*-, *ortho*- and *para*-positions of the aryl ring with DAADs **2a**,**b**

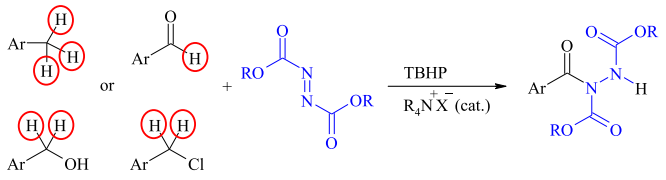
Table 1
Optimization of the reaction conditions for the hydrobenzoylation of **2a** with toluene **1a**.[a]



1a **2a** **3a**

Entry	Oxidant (equiv.)[b]	Additive (mol%)[b]	Solvent	Temp. (°C)	Yield (%)[c]
1	TBHP[d] (6)	TBAB[e] (30)	$PhCH_3$	r.t.	NR[f]
2	TBHP (6)	TBAB (30)	$PhCH_3$	50	28
3	TBHP (6)	TBAB (30)	$PhCH_3$	80	55
4[g]	TBHP (6)	TBAB (30)	$PhCH_3$	80	35
5	TBHP (8)	TBAB (30)	$PhCH_3$	80	52
6	TBHP (8)	TBAB (50)	$PhCH_3$	80	93
7	TBHP (10)	TBAB (50)	$PhCH_3$	80	82
8	TBHP (8)	NBS[h] (50)	$PhCH_3$	80	10
9	TBHP (8)	TBPB[i] (50)	$PhCH_3$	80	75
10	TBHP (8)	Aliquat 336[j] (50)	$PhCH_3$	80	48
11	TBHP (8)	KI (50)	$PhCH_3$	80	NR
12	TBHP (8)	I_2 (50)	$PhCH_3$	80	NR
13	BPO[k] (8)	TBAB (50)	$PhCH_3$	80	NR
14	$K_2S_2O_8$ (8)	TBAB (50)	$PhCH_3$	80	NR
15	H_2O_2[l] (8)	TBAB (50)	$PhCH_3$	80	NR
16[m]	TBHP (8)	TBAB (50)	PhCl	80	NR
17	TBHP (8)	TBAB (50)	CH_3CN	80	NR
18	TBHP (8)	TBAB (50)	Dioxane	80	NR
19	TBHP (8)	TBAB (50)	DMSO	80	NR
20[n]	TBHP (8)	TBAB (50)	$PhCH_3$	80	40
21[o]	TBHP (8)	TBAB (50)	$PhCH_3$	80	62
22[p]	TBHP (8)	TBAB (50)	$PhCH_3$	80	79
23	–	TBAB (50)	$PhCH_3$	80	NR
24	TBHP (8)	–	$PhCH_3$	80	NR
25[q]	TBHP (8)	TBAB (50)	$PhCH_3$	100	93
26[q]	TBHP (8)	TBAB (50)	$PhCH_3$	120	90

[a] Reaction conditions: **1a** (8 mmol), **2a** (0.4 mmol) for 1 h.
[b] In respect to **2a**.
[c] Isolated yields.
[d] 70 wt% *t*-BuOOH in H_2O.
[e] Tetrabutylammonium bromide.
[f] NR = no reaction.
[g] Reaction time of 2 h.
[h] *N*-Bromosuccinimide.
[i] Tetrabutylphosphonium bromide.
[j] Methyltrioctylammonium chloride.
[k] Benzoyl peroxide.
[l] 30 wt% H_2O_2 in H_2O.
[m] Entries 17–20: 0.5 mL solvent.
[n] **1a** (4 mmol).
[o] **1a** (6 mmol).
[p] **1a** (10 mmol).
[q] Reaction time of 30 min.



Scheme 1. Synthesis of hydrazine imides through hydroaroylation of dialkyl azodicarboxylate promoted by the TBHP/$R_4N^+X^-$ system.