Iodobenzene-catalysed deprotection of hydrazones using *m*-chloroperbenzoic acid

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Deprotection of phenylhydrazones and tosylhydrazones to their parent aldehydes and ketones has been accomplished using iodobenzene as catalyst in the presence of *m*CPBA as the terminal oxidant at room temperature. The reaction is general, and the target products can be obtained in good to excellent yields.

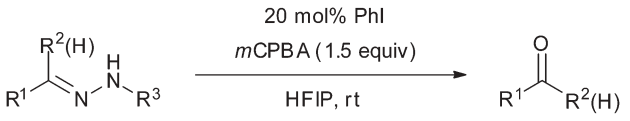
Keywords: deprotection, hydrazones, iodobenzene, *m*-chloroperbenzoic acid, oxidative cleavage

Hydrazones are used in the protection and purification of carbonyl compounds, as they are highly crystalline and stable compounds.[1] The regeneration of carbonyl compounds from their derivatives under mild conditions is an important process in organic synthetic chemistry. Extensive studies on the deprotection of hydrazones have been carried out using various catalysts such as copper (I) chloride,[2] clayfen,[3] potassium bromate,[4] alumina-supported ammonium chlorochromate,[5] quinolinium dichromate (QDC),[6] 1-benzyl-4-aza-1-azoniabicyclO[2.2.2]oc tane dichromate[7] and Amberlyst 15 supported nitrosonium ion.[8] However, these reported procedures require high temperatures, longer reaction times and some of them involve toxic oxidants and metal ions, which are detrimental to the environment. Consequently, there is a need for the development of protocols using readily available and safer reagents.

Hypervalent iodine compounds have recently received attention as mild and selective oxidising agents.[9,10] However, the reported reactions use hypervalent iodine(III) reagents in a stoichiometric amount and generate undesired iodoarenes in an equimolar amount. To overcome these limitations, in 2005, the Ochiai[11] and Kita[12] groups independently reported a catalytic process involving the *in situ* oxidation of iodo(I)arenes using meta-chloroperbenzoic acid (*m*CPBA). Since then, this concept has been extensively used for the synthesis of a variety of organic compounds.[13–17] Here, we report an iodobenzene catalysed deprotection of phenylhydrazones and tosylhydrazones using *m*CPBA as a terminal oxidant at room temperature (Scheme 1).

First, the reaction conditions were optimised using benzaldehyde phenylhydrazone **1a** as model substrate that can be readily prepared from benzaldehyde and phenylhydrazine (Table 1). Treating the substrate **1a** with 20 mol% of iodobenzene and 1.5 equiv. of *m*CPBA as an oxidant in CH_2Cl_2 as solvent for 2 h at room temperature did not afford the target benzaldehyde **2a** (entry 1). Further screening of solvents such as MeOH, DMSO, DMF, and CF_3COOH proved unsuccessful (entries 2–5). However, the target benzaldehyde was obtained in 96% conversion using 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) as solvent (entry 6). Employing other substituted iodoarenes gave inferior results (entries 7 and 8). In addition, oxidants such as *tert*-butyl hydroperoxide (TBHP), H_2O_2 and oxone were not successful (entries 9–11). Lowering the quantity of iodobenzene to 10 mol% led to the formation of the product with a 79% conversion (entry 12). A control experiment showed that, without iodobenzene, no product **2a** was formed (entry 13). Moreover, in the presence of 1.0 equiv. of PhIO in HFIP, **1a** underwent decomposition to give **2a** in 73% yield (Scheme 2).

With the optimised conditions in hand, the scope of the procedure was studied with a series of substituted phenylhydrazones and tosylhydrazones (Table 2). As is evident from the results, our experiments show that phenylhydrazones, *p*-nitro phenylhydrazones and tosyldrazones were smoothly converted to their corresponding aldehydes and ketones in good to excellent yields (78–95%). Other functional groups such as methyl, methoxyl, halogen, and nitro were compatible with this catalytic system. Furthermore, the over-oxidation of aldehydes to their carboxylic acids was not observed. Interestingly, the α,β-unsaturated phenylhydrazones underwent deprotection



R^1, R^2 = aryl, alkyl;
R^3 = Ph, Tosyl

Scheme 1 Iodobenzene-catalysed deprotection of hydrazones using *m*CPBA.

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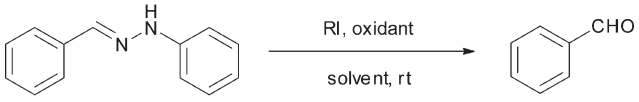
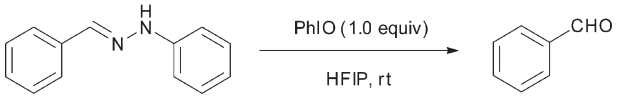
Table 1 Optimisation of the reaction conditions[a]



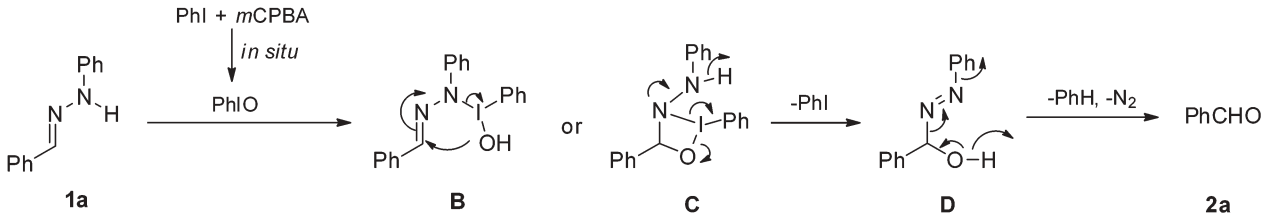
1a **2a**

Entry	R	Oxidant	Solvent	Conversion/%[b]
1	C_6H_5	*m*CPBA	CH_2Cl_2	0
2	C_6H_5	*m*CPBA	MeOH	0
3	C_6H_5	*m*CPBA	DMSO	0
4	C_6H_5	*m*CPBA	DMF	0
5	C_6H_5	*m*CPBA	CF_3COOH	15
6	C_6H_5	*m*CPBA	HFIP	96
7	4-$OMeC_6H_4$	*m*CPBA	HFIP	41
8	4-MeC_6H_4	*m*CPBA	HFIP	68
9	C_6H_5	TBHP	HFIP	12
10	C_6H_5	H_2O_2	HFIP	5
11	C_6H_5	Oxone	HFIP	0
12[c]	C_6H_5	*m*CPBA	HFIP	79
13	-	*m*CPBA	HFIP	0

[a]Reaction conditions: **1a** (1 mmol), aryl iodide (20 mol%), oxidant (1.5 equiv), solvent (2 mL), rt, 2 h.
[b]Determined by GC-MS.
[c]Iodobenzene (10 mol%) used.

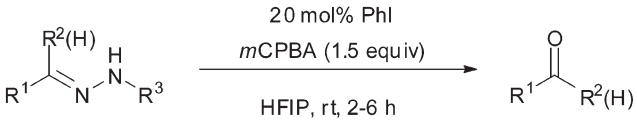


Scheme 2 Control experiment.



Scheme 3 Proposed reaction mechanism.

Table 2 Deprotection of phenylhydrazones and tosylhydrazones[a]



Entry	Substrate	Product	t/h	Yield /%
1	$C_6H_5CHNNHC_6H_5$	C_6H_5CHO	2	91
2	4-$CH_3C_6H_4CHNNHC_6H_5$	4-$CH_3C_6H_4CHO$	2	90
3	4-$OCH_3C_6H_4CHNNHC_6H_5$	4-$OCH_3C_6H_4CHO$	5	87
4	4-$ClC_6H_4CHNNHC_6H_5$	4-ClC_6H_4CHO	2	92
5	2-$ClC_6H_4CHNNHC_6H_5$	2-ClC_6H_4CHO	2	85
6	4-$BrC_6H_4CHNNHC_6H_5$	4-BrC_6H_4CHO	2	90
7	4-$NO_2C_6H_4CHNNHC_6H_5$	4-$NO_2C_6H_4CHO$	2	95
8	Cinnamaldehyde tosylhydrazone	Cinnamaldehyde	2	89
9	$C_6H_5C(CH_3)NNH(p\text{-}NO_2C_6H_4)$	$C_6H_5CO(CH_3)$	4	86
10	$(C_6H_5)_2CNNHTs$	$(C_6H_5)_2CO$	4	85
11	Cyclohexanone tosylhydrazone	Cyclohexanone	6	80
12	$CH_3(CH_2)_5C(CH_3)NNHTs$	$CH_3(CH_2)_5CO(CH_3)$	6	78

[a]Reaction conditions: hydrazones (1 mmol), iodobenzene (20 mol%), *m*CPBA (1.5 equiv.), HFIP (2 mL), rt, isolated yield.

very efficiently without rearrangement of the C=C bond and the reactions were essentially chemoselective.

A possible reaction mechanism is shown in Scheme 3. The oxidation of iodobenzene using *m*CPBA may give the active hypervalent iodine(III) species that could react with **1a** to generate the unstable species **B** which readily undergoes rearrangement to form an α-hydroxy phenylazo compound **D** and iodobenzene. The latter can be reoxidised to hypervalent iodine(III) species by *m*CPBA. Then decomposition of compound **D** gives the target product **2a** accompanied by the formation of benzene and nitrogen, which were confirmed by GC-MS. An alternative mechanism might involve the addition of the iodosobenzene to the imine carbon followed by a fragmentation with the loss of iodobenzene to give intermediate **D**, and a second fragmentation to release benzene and nitrogen to afford the product **2a**.

In summary, we have developed an efficient protocol for the deprotection of hydrazones using iodobenzene as catalyst in the presence of *m*CPBA as terminal oxidant at room temperature. The reaction is simple and general affording the products with good to excellent yields in short reaction times.

Experimental

The hydrazones were prepared according to the described procedure.[18] *m*CPBA (75 wt%) was purchased from Aladdin (Shanghai, China). Iodosobenzene (PhIO) was purchased from TCI (Shanghai, China). Other reagents were obtained from local commercial suppliers and used without further purification. The reaction was monitored by GC-MS (QP2010 Ultra, Japan). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Advance III 500 analyser. All the products are known compounds and were identified by comparing of their physical and spectra data with those reported in the literature.

Deprotection of hydrazones; typical procedure:
*m*CPBA (1.5 equiv.) was added to a stirred solution of hydrazone (1 mmol, 1.0 equiv.) and iodobenzene (20 mol%) in HFIP (2 mL) at room temperature under air. The mixture was stirred and the progress of the reaction was monitored by TLC using ethyl acetate and *n*-hexane as eluent. After the appropriate time, saturated $NaHCO_3$ (5 mL) was added to the reaction mixture. The resulting solution was extracted with ethyl acetate (3 × 10 mL) and washed with brine (2 × 5 mL). Drying over Na_2SO_4 and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as eluent to afford analytically pure carbonyl compounds.

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