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Soluble Polymer Supported (Diacetoxy)iodobenzene in Synthesis

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Abstract: Polyethylene glycol (PEG) supported (diacetoxy)iodobenzene as soluble polymer reagent can smoothly oxidize acid hydrazides into corresponding dimmers in good yields under very mild conditions.

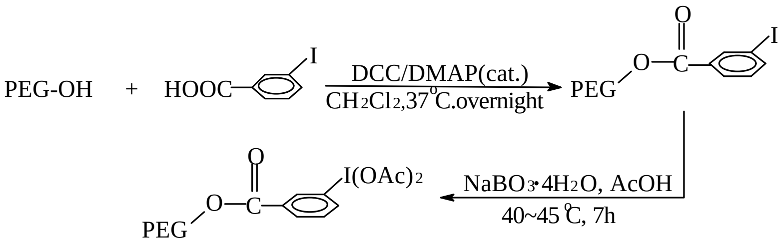
Keywords: PEG supported (diacetoxy)iodobenzene, oxidation, hydrazides, dimmers.

N, N-diacylhydrazines are the essential precursors to 1,3,4-oxadiazoles derivatives which are important substances in medicines and agrochemistry due to their special biochemical properties[1]. It was reported that N, N-diacylhydrazines could be prepared by oxidation of corresponding hydrazides with lead tetraacetate[2], selenium oxidants[3] or halogens[4]. However, these reagents are either very toxic or hard to operate, accompanying with environmental pollution. Recently, hypervalent iodine compounds are widely used in organic synthesis[5]. Among them, (diacetoxy)iodobenzene is the most useful and versatile oxidant for many compounds, especially for compounds containing N atoms[6], due to its advantages for mild conditions, easy handling, high selectivity and low toxicity. According to its oxidative mechanism, iodobenzene is the general byproduct which is hard to be reused in solution phase. Nevertheless, polymer supported (diacetoxy)iodobenzene enables to solve the trouble. It has been reported[7] that cross-linked polystyrene resin supported (diacetoxy)iodobenzene could be used to solve the problem of recycling iodobenzene. However, owning to the drawback of heterogeneity, the cross-linked polystyrene supported (diacetoxy)iodobenzene reagent is prepared under harsh conditions, such as iodine pentoxide in nitrobenzene at 90°C for 50 hours and peracetic acid at 40°C for 24 hours.

Recently, liquid-phase synthesis using soluble polymer supported substrates or reagents has increasingly becoming an attractive field thanks to its combination of the advantages of liquid-phase and solid-phase methodology[8]. Among all kinds of soluble polymers, polyethylene glycol is most useful and promising. In connection with our research on the PEG as soluble support in liquid-phase synthesis[9], we herein report our first example of oxidative reaction with PEG 4000 supported (diacetoxy)iodobenzene.

The PEG 4000 supported (diacetoxy)iodobenzene was prepared as following (**Scheme 1**): the 3-iodobenzioc acid was bound to PEG 4000 with DCC/DMAP in anhydrous CH_2Cl_2 at 37°C overnight to form the PEG 4000 linked 3-iodobenzoic acid, which was then treated with sodium perborate tetrahydrate in acetic acid at 40~45°C for 7 hours. The product was obtained by precipitation and washing with Et_2O and could be stored under dry condition in a refrigerator for several months.

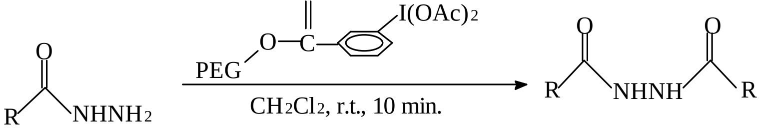
Scheme 1



Due to the homogeneity, PEG 4000 supported (diacetoxy)iodobenzene could be synthesized under very mild conditions with the loading capacity of 0.46 mmol/g (based on the ^{1}H-NMR analysis[10]). Because of the electron-withdrawing group of carboxyl, only 3-iodobenzoic acid was able to carry out the oxidative step while 2 or 4-iodobenzoic acid was stunt to provide the supported (diacetoxy)iodobenzene. PEG supported 2 or 4-iodobenzoic acid was recycled almost quantitatively by precipitation with ether after reaction.

We applied the soluble polymer supported (diacetoxy)iodobenzene into the dimerization of acid hydrazides (**Scheme 2**). The reaction was completed at room temperature within 10 minutes in good yields with the strong evolution of nitrogen gas. The results were shown in **Table 1**. It appeared that electron-donating and electron-withdrawing groups had little effect on the reaction in term of yields. As for entry f, due to the presence of oxidizable phenolic group, the yield of corresponding N, N-diacylhydrazine was lower.

Scheme 2



After reaction the byproduct of PEG supported 3-iodobenzoate was recycled by precipitation and washing with Et_2O and oxidized with sodium perborate tetrahydrate in acetic acid once again, offering the refreshed PEG supported (diacetoxy)iodobenzene which could be used for oxidation without the decrease of oxidizing property (entry h).

In conclusion, N, N-diacylhydrazines were synthesized smoothly in good fields under mild conditions with the soluble polymer supported (diacetoxy) iodobenzene as oxidant, which could be prepared readily with the advantages of environmental friend and low cost.

Table 1 Oxidation of hydrazides with PEG supported (diacetoxy)iodobenzene[i]

Entry	R	Yield (%)[ii]	mp (°C)	mp (℃) (Lit)
a	Ph	71	238~239	238~240[11]
b	p-ClC_6H_4	74	288~290	292[12]
c	p-CH_3 C_6H_4	76	254~256	254~255[13]
d	p-CH_3 OC_6H_4	66	225~227	228[12]
e	p-NO_2 C_6H_4	62	286~288	289[14]
f	o-HO C_6H_4	44	298~300	301[15]
g	C_6 H_5CH_2	78	234~235	236~237[16]
h	Ph	69		

i. all the products are characterized by ^{1}H-NMR and FT-IR; ii. Isolated yields.

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10. The H-NMR signal peaks of double CH_2 on PEG terminus were at 4.38 ppm, which were well-separated from the large backbone peak (centered at 3.51 ppm) due to influence of carboxyl groups linked to them, while the ^{1}H-NMR signal peaks of CH_3 in PEG supported (diacetoxy)iodobenzene was at 2.05 ppm. The loading capacity of PEG supported (diacetoxy)iodobenzene could be calculated on the integral of CH_2 and CH_3 since the formation of PEG supported 3-iodobenzoic acid under DCC/DMAP was quantitative.

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