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Solvent-Free Reactions with Hypervalent Iodine Reagents

Mekhman S. Yusubov*,† and Thomas Wirth*,‡

Department of Chemistry, Siberian State Medical University, Moskovski trakt, 2, 634050 Tomsk, Russia, Department of Organic Chemistry, Tomsk Polytechnic University, 30 Lenin st., 634050 Tomsk, Russia, and School of Chemistry, Cardiff University, P.O. Box 912, Cardiff CF10 3TB, UK

yusubov@mail.ru; wirth@cf.ac.uk

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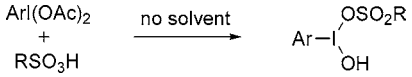
ABSTRACT



We describe solvent-free reactions for the synthesis of hypervalent iodine reagents and their use in solid-state reactions. Improved yields and higher purities of the products are observed.

Hypervalent iodine reagents have found broad application in organic chemistry and are nowadays frequently used in synthesis.[1] It is of great interest to investigate their ability as highly selective oxidants, their electrophilic properties and to develop new reactions using hypervalent iodine compounds. Because these are nonmetallic oxidation reagents, they avoid the issues of toxicity of many transition metals commonly involved in such processes. Therefore, hypervalent iodine compounds bear a high potential for the improvement of known reactions not only from the environmental and pharmaceutical point of view, but also as interesting reagents for the development of completely new synthetic transformations. The continued need for efficient transformations led to the development of solvent-free reactions which we describe here. Solvent-free reactions have many advantages and important aspects are reduced pollution, lower costs and the simplicity of the processes involved.[2] Because many organic solvents are ecologically harmful, strategies for their minimized usage and developments toward benign chemical technologies are highly sought after.[3] Because many hypervalent iodine reagents have low solubilities in most organic solvents, the development of solvent-free reactions is a big step forward and should lead to an increased use of this chemistry. Only iodine(III) compounds should be considered for these reactions, because some iodine(V) compounds are known to be shock and pressure sensitive.[4] The iodine(III) compounds described here have been safely used on a millimolar scale.

For our initial investigations, we used (diacetoxyiodo) benzene **1a** (Ar = Ph) as a hypervalent iodine reagent, which is commercially available and can also easily be prepared.[5] Ligand exchange reactions on this compound are known and have been used frequently to prepare other hypervalent iodine reagents.[6] The reaction of **1a** (Ar = Ph) with *p*-toluenesulfonic acid monohydrate **2a** (R = *p*-Ts) results in the formation of (hydroxytosyloxyiodo)benzene **3a** (Koser's reagent) but has only been carried out in an organic solvent such as dichloromethane or acetonitrile.[7] We find similar or even better yields in the solid-state reaction just by grinding the two reaction partners **1** and **2** for several minutes and evaporating the acetic acid liberated in the ligand exchange reaction.

† Siberian State Medical University and Tomsk Polytechnic University.
‡ Cardiff University.

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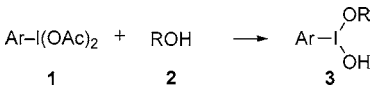
Scheme 1. Solvent-Free Reactions of (Diacetoxyiodo)Arenes **1** and Sulfonic Acids **2**



The reactions investigated usually were complete within several minutes on a millimolar scale.[8] The products are very clean as judged by the NMR spectra of the crude reaction mixtures and only evaporation of acetic acid on high vacuum was necessary. Only for some reactions the removal of excess sulfonic acid by washing with diethyl ether was necessary to obtain pure products. The results are summarized in Table 1. Some of these reactions can be enhanced just by adding a drop of acetic acid to the mixture of the two solid reactants.

Table 1. Solvent-Free Reactions of (Diacetoxyiodo)arenes **1** and Sulfonic Acids **2**

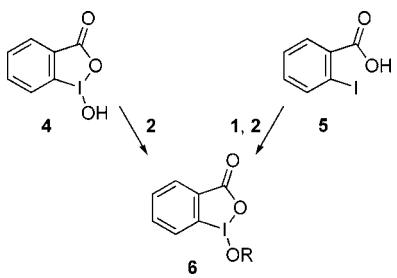
entry	**1**: Ar	**2**: R	product **3** (yield)	lit. yield
1	**1a**: Ph	**2a**: *p*-Ts[a]	**3a** (93%)	93%; ref 9
2	**1a**: Ph	**2b**: Ms[a]	**3b** (98%)	87%; ref 10
3	**1a**: Ph	**2c**: Cs[a]	**3c** (91%)	*b*; ref 11
4	**1b**: 1-naphthyl	**2c**: Cs	**3d** (94%)	this work
5	**1c**: 2-naphthyl	**2a**: *p*-Ts	**3e** (77%)	*b*; ref 6
6	**1c**: 2-naphthyl	**2c**: Cs	**3f** (80%)	this work

[a] *p*-Ts, 4-Me-$C_6H_4SO_2$; Ms, $MeSO_2$; Cs, (1*R*)-10-camphorylsulfonyl. [b] No yield reported.

Also other acids can be used, the solvent-free reaction of **1** (Ar = Ph) with 2.2 equiv of trifluoroacetic acid led in a very clean reaction to the formation of [bis(trifluoroactoxy)-iodo] benzene in 95% yield.[12] This hypervalent iodine reagent, [bis(trifluoroactoxy)iodo] benzene, can be used with similar efficiency in the solid-state ligand exchange reaction with *p*-toluenesulfonic acid monohydrate **2a** (R = *p*-Ts) to give **3a** in 97% yield.

Ligand exchange reactions are also possible using iodosyl benzoic acid (IBA) **4**. Treatment with sulfonic acids led to the formation of the corresponding IBA derivatives **6**[13] in good yields as shown in Scheme 2. These IBA derivatives **6** can be used advantageously for the iodination of aromatic rings[14] or for iodotosylations of alkynes.[15]

Scheme 2. Solvent-Free Reactions to IBA Derivatives **6**



The same products, **6a** and **6b**, can be obtained by a solvent-free reaction of **1** and **2** with 2-iodobenzoic acid **5**. The results are summarized in Table 2.

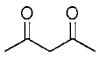
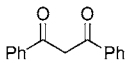
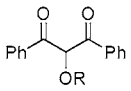
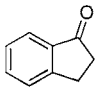
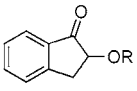
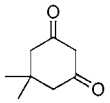
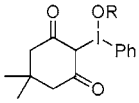
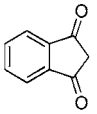
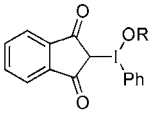
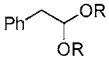
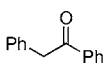
Table 2. Solvent-Free Reactions to IBA Derivatives **6**

entry	starting materials	**2**: R	product **6** (yield)
1	**4**	**2a**: *p*-Ts	**6a** (91%)
2	**4**	**2b**: Ms	**6b** (86%)
3	**1a** (Ar = Ph), **5** (1:1)	**2a**: *p*-Ts	**6a** (86%)
4	**1a** (Ar = Ph), **5** (1:1)	**2b**: Ms	**6b** (80%)

In the reaction with **5**, an intermediate formation of a reagent of type **3** is likely to take place. As reagents such as **3** can react with a variety of different substrates, we investigated the solid-state reaction of a mixture of **1a** (Ar = Ph) and **2** together with a range of substrates **7**. Several of these reactions have already been performed in solution, but the yields are generally higher when performed under solvent-free conditions as shown in Table 3.

The sulfonylations of 1,3-diketones take place in a few minutes to give the products **8** in reasonable yields (Table 3, entries 1−4). The sulfonylation of ketones in α-position with reagents of type **3** is known as well and the yields obtained are still comparable to reactions carried out in

Table 3. Solvent-Free Reactions of **1a** (Ar = Ph), **2**, and Different Substrates **7**

entry	starting material **7**	product **8**	yield	
1			R=Ms:[10]	60%
2			R= *p*-Ts:[17]	90%
3			R=Ms:[10]	67%
4			R= *p*-Ts:[17]	84%
5			R= *p*-Ts:[18]	32%
6			R= *p*-Ts:[17]	50%
7			R=Ms:	90%
8			R= *p*-Ts:[17]	86%
9			R = Ac:[a]	93%
10			R=Ac:[a]	85%
11			R=Ms:	63%
12			R= *p*-Ts:[19]	75%
13			R= *p*-Ts:[19a,20]	92%

[a] Reaction performed without addition of **2**.

solutions (Table 3, entries 5 and 6). The formation of products resulting from a ligand-exchange with dimedone are known, in the solid-state these reactions proceed with very high efficiency as shown in Table 3 (Table 3, entries 7 and 8). If (diacetoxyiodo) benzene is used as reagent without addition of a sulfonic acid **2**, the corresponding hypervalent iodine derivatives with one acetate moiety exchanged to the diketone are obtained (Table 3, entries 9 and 10). The reaction with aryl-substituted alkenes is known to proceed via rearrangements at high concentrations as the aryl moiety stabilizes a positive charge by formation of phenonium ion intermediates.[16] As the concentration in solvent-free reactions is at its maximum, the products are the expected ones and are formed in higher yields than in solution (Table 3, entries 11−13).

In conclusion, by using solvent-free reaction conditions for the synthesis of hypervalent iodine reagents of type **3** and an in situ generation of these reagents for reactions with different substrates we were able to improve the yields and purities of the reaction products considerably. These reaction conditions are contributing to the development of sustainable techniques in organic synthesis and to the simplicity of reactions with hypervalent iodine compounds.

Acknowledgment. We thank Maria A. Arrica for the synthesis of **1** (R = 1-naphthyl, 2-naphthyl) and **4**. M.S.Y. thanks the Ministry of Education (grant 546-05) and RFFI (grant 05-03-32459-a) for support.

Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) **Typical Procedure.** A mixture of (diacetoxyiodo)benzene **1** (Ar = Ph, 184 mg, 0.571 mmol) and *p*-TsOH·H_2O (111 mg, 0.584 mmol) was gently blended in an agate mortar. The resulting homogeneous mixture was then ground for 10 min. The formation of acetic acid and wetting of the reaction mixture was observed. The solid residue was washed with diethyl ether (5 mL) and dried under high vacuum to afford **3a** (218 mg, 97%), mp 134−136 °C.

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