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Ultrasound Promoted Hypervalent Iodine Reactions: α-Tosyloxylation of Ketones with [Hydroxy(Tosyloxy)Iodo]Benzene

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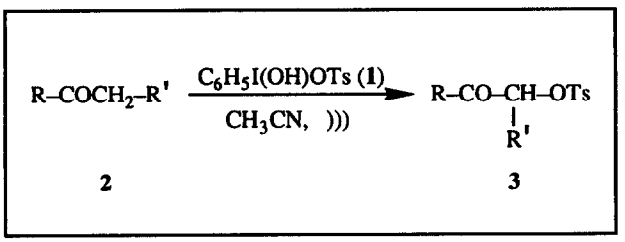
Abstract: Ultrasound enhances substantially the rates of α-tosyloxylation of ketones with [hydroxy(tosyloxy)iodo] benzene and thus provides a direct, quick, and mild method of tosyloxylation of ketones without the generation of time-consuming intermediates such as trimethylsilyl enol ether derivatives and α-hydroxy ketones. The present method also provides convenient access to the tosylates of alicyclic ketones such as cyclopentanone and cycloheptanone which are otherwise very difficult to obtain.

The chemistry of α-sulfonyloxy ketones has received little attention[1-3] even though the related α-haloalkyl ketones have been widely investigated.[4] The most common method for the synthesis of α-sulfonyloxy ketones involves condensation of α-hydroxyalkyl ketones with a sulfonyl chloride but this often involves multiple steps.[5] α-Tosyloxy ketones in particular, have been obtained by the base-catalyzed rearrangement of deoxybenzoin oxime tosylate,[6] by treatment of α-diazoacetophenone with p-toluenesulphonic acid[7] and by the action of silver tosylate on α-bromodeoxybenzoin[8] and thallium (III) p-tolylsulphonate[9] on enolizable ketones. These methods involve multiple steps with limited scope. Recently, [hydroxy(tosyloxy)iodo]benzene has been found to be an effective reagent by Koser[10] for one-step conversion of enolizable ketones to the corresponding α-tosyloxy ketones. Reactions have to be conducted mostly in acetonitrile at the reflux temperature. Such conditions are, however, too severe for alicyclic ketones. A complementary method reported recently[11] utilizes the silyl enol ether derivatives which are time-consuming and sometimes difficult to obtain. We report here that ultrasound dramatically enhances the rates of α-tosyloxylation of ketones with [hydroxy(tosyloxy)iodo]benzene **1**.

1

Ultrasound has been utilized recently to accelerate a number of synthetically useful reactions.[12,13] Many of the observed effects are due to cavitation:[12] the formation, growth and collapse of bubbles in an irradiated liquid with consequent high local temperatures and pressures. We therefore investigated the enhancement of this hypervalent iodine reaction by ultrasound (Scheme I). The results are summarized in Table I.



Scheme I

Table 1. Reaction Conditions and Yields[a,b]

Ketone	Product (mp)	Time	% Yield
CH_3COCH_3	CH_3COCH_2OTs (35°)	15 min	74
$CH_3COCH_2CH_3$	$CH_3COCH(OTs)CH_3$ and $CH_2(OTs)COCH_2CH_3$ (oil)	10 min	91
$CH_3CH_2COCH_2CH_3$	$CH_3CH(OTs)COCH_2CH_3$ (43°-44°)	10 min	92
c-$C_3H_5COCH_3$	c-$C_3H_5COCH_2OTs$ (73°-74°)	15 min	86
$PhCOCH_3$	$PhCOCH_2OTs$ (89°-91°)	30 min	55
$CH_3COCH_2COCH_3$	$CH_3COCH(OTs)COCH_3$ (81°-82°)	10 min	74[c]
Cyclopentanone	2-(tosyloxy)cyclopentanone (oil)	10 min	42[d]
Cyclohexanone	2-(tosyloxy)cyclohexanone (74°-76°)	15 min	55
Cycloheptanone	2-(tosyloxy)cyloheptanone (oil)	15 min	58

[a] Yields are based upon isolated pure products. In the absence of ultrasound no products were detectable (< 5% yield).

[b] Satisfactory spectral data (MS, IR, ^1H and ^{13}C NMR) were obtained on all the products.

[c] Crude

[d] Heat and light sensitive

[Hydroxy(tosyloxy)iodo]benzene is largely insoluble in acetonitrile under ambient conditions. Upon application of ultrasound, however, it does disperse and react with dissolved ketones to give yellow solutions, affording the α-tosyloxy derivatives in short reaction times with very good yields. In a typical experiment,[14] 0.65 g (1.67 mmol) of **1** was added to a solution of 2 ml of the ketone in 15 ml acetonitrile in a reaction vessel immersed in water bath. The vessel was purged with Ar for 10 minutes and subjected to sonication under Ar using a Vibracell Ultrasonic Processor (Sonics and Materials, 20 kHz, 0.5 in. Ti horn at ≈50 W/cm^2) for 10-30 minutes with a reaction temperature of 55°. The reaction solution was concentrated in vacuo, the residue was dissolved in 15 mL of dichloromethane, washed with saturated aq. $NaHCO_3$ and then water, and finally dried over $MgSO_4$. The solvent was distilled off under reduced pressure to yield the crude product which afforded, the corresponding α-tosyloxy derivative upon trituration with hexane.

The regiochemistry of the α-tosyloxylation reaction with ultrasound was also investigated with 2-butanone as the substrate. The oil obtained after work-up was subjected to ^{1}H NMR analysis and was found to consist of 1-(tosyloxy)-2-butane and 3-(tosyloxy)-2-butanone in a 1 : 1.5 ratio.

The reaction also works well with alicyclic ketones, tosyloxylation of which was previously inaccessible. For example, cycloheptanone (2 mL), **1** (0.65g), and acetonitrile (15 mL) were subjected to ultrasound for 15 minutes as described above. After the work-up, 2-tosyloxycycloheptanone was obtained in 58% yield. Under similar conditions, cyclopentanone and cyclohexanone were also converted to the corresponding tosyloxy derivatives (Table 1).

Ultrasound promises to be a new and powerful technique in hypervalent iodine chemistry. The methodology reported here provides rapid and convenient one-step access to α-tosyloxy ketones, which are important synthetic intermediates. We presume the increase in reactivity originates from the rapid dispersion of the insoluble [hydroxy(tosyloxy)iodo]benzene into acetonitrile during ultrasonic irradiation. We are currently investigating the scope of this technique in other hypervalent iodine reactions.

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