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Ultrasound promoted regioselective synthesis of β-iodoethers from olefin-I_2-alcohol

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Abstract

Regioselective synthesis of β-iodoethers in high yields by sonicating alkene and alcohol in the presence of iodine in a bath at 35 kHz is reported.

Keywords: β-iodoethers; Ultrasound; Regioselective; Alkenes; Alcohols; Iodine

1. Introduction

β-Iodoethers are versatile compounds because of their inherent features-a reactive carbon-halogen bond, an ether group and acidic hydrogen(s). Owing to these, they can act as intermediates in various organic reactions. Interconversion of olefinic geometrical isomers has been achieved in good to moderate diastereoselectivity *via* these compounds in presence of *n*-butyl lithium [1], they are intermediates in stereoselective radical reactions [2]. Also, reactions specific of each functionality—Wurtz coupling reaction to get diethers with alkali metals, substitution reactions to give different substituted ethers, metallo-de-halogenation reaction (like Grignard reaction) can be carried out on them easily. The ether functional group can be hydrolysed and oxidized to obtain esters or carboxylic acids (from terminal alcohols). Transetherification gives different iodoethers.

For the past two decades, methods like, irradiation by ultrasound (sonochemical reactions), electromagnetic radiation (microwaves assisted reactions) have gained importance as physical substitutes for catalysts used to accelerate chemical reactions. In continuation of our work on sonochemically accelerated reactions [3–7], we became interested in the ultrasound promoted preparation of the β-iodoethers for two reasons (i) contradicting reports regarding the usage of metal salts as catalysts: Tl (I), Cu (II), Ce (IV) salts [8–12], whose presence is required to catalyse the reaction, while in another report by Mattos and coworker [13] excess of iodine is sufficient to obtain β-iodoethers in moderate to good yields (ii) to find the effect of ultrasound (35 kHz, in a sonic bath) for catalytic activity on the reaction and the use of metal salts as catalysts in presence of ultrasound.

In this paper we report our findings of the effect of ultrasound on the regioselective preparation of β-iodoethers and a comparative study of the same at 25 °C. The reaction was studied with a set of nine different alkenes and five different alcohols in presence of varied amounts of iodine. We have found that, under the influence of ultrasound, neither the metal salt nor excess of

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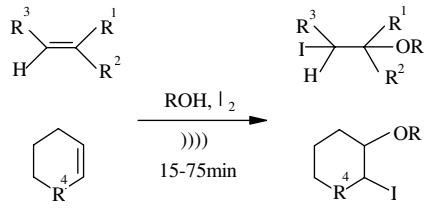


$R^1 = C_6H_5$, $R^2 = R^3 = H$ $R^1 = C_6H_5$, $R^2 = H$, $R^3 = C_6H_5$

$R^1 = C_6H_5$, $R^2 = CH_3$, $R^3 = H$ $R^1 = COOH$, $R^2 = COOH$, $R^3 = H$

$R^1 = C_6H_5$, $R^2 = H$, $R^3 = CHO$ $R^4 = CH_2$, $(CH_2)_3$, $(CH_2)_7$

R = CH_3, C_2H_5, n-C_4H_9, CH $(CH_3)_2$, C $(CH_3)_3$

Scheme 1.

iodine is required but the reaction is accelerated to obtain β-iodoethers in high yields (Scheme 1).

2. Results and discussion

The reaction conditions were optimised by the reaction of styrene and different substituted alcohols (Table 1). Typically, a mixture of styrene, resublimed iodine and dry methanol were (a) stirred at 25 °C and (b) irradiated in a sonic bath, working at 35 kHz, by maintaining the temperature at 25 °C (Table 1). In parallel experiments, the same reactions were carried out in the presence of the metal salts such as copper (II) acetate and ceric ammonium nitrate. In all the cases, the addition of the methoxy group and iodine is regioselective giving the Markovnikov addition product 1-iodo-2-methoxystyrene. Though the β-iodoether was obtained at room temperature in the absence of metal acetates, the yield was very low as the reaction was not proceeding to completion even after stirring for 24 h. Whereas under the influence of ultrasound the reaction went to completion in about 15 min yielding 85% of the 1-iodo-2-methoxystyrene. Hence, it was concluded that, (a) metal salts do not participate in the reaction either to (i) accelerate the reaction by acting as catalysts or (ii) to increase the yield of the product, (b) ultrasound does accelerate the reaction to give the product in high yield. The reaction was also carried out in presence of various amounts of iodine under the influence of ultrasound and it was observed that the reaction can proceed to completion with one equivalent of iodine and increasing the quantity of iodine does not bring about change in either the quantity of the product or decrease the time required for completion of the reaction. However the yield of the product was low when the quantity of iodine used was less than one equivalent.

Apart from styrene, eight other alkenes of varying structure, and methanol were chosen for studying the reaction in detail. Details of the alkenes, yield of the products and the time taken for completion of each reaction is presented in Table 2.

From Table 2 it is clear that, among alkenes, with electron withdrawing groups such as maleic acid and cinnamaldehyde do not react even after sonication for 8 h.

Table 1
Reaction of styrene and alcohols in presence of iodine at 25 °C

Entry	Alkene	Alcohol	Time		Yield (%)	
			25 °C (h)	)))) (min)	25 °C	))))
1.	Styrene	Methanol	24	15	25	85
2.	Styrene	Ethanol	24	20	25	85
3.	Styrene	2-Propanol	24	30	15	75
4.	Styrene	1-Butanol	24	20	20	85
5.	Styrene	*t*-Butanol	24	15	Mixture	

Table 2
Reaction of alkenes and methanol in presence of iodine at 25 °C

Entry	Alkene	Time		Yield (%)	
		25 °C (h)	)))) (min)	25 °C	))))
1.	α-Methylstyrene	24	30	25	85[a]
2.	*trans*-Stilbene	24	480	No reaction	
3.	1-Hexene	24	20	20	92
4.	Cyclohexene	24	25	15	88
5.	Cyclooctene	24	40	05	85
6.	Cyclododecene	24	75	05	70
7.	Maleic acid	24	480	No reaction	
8.	Cinnamaldehyde	24	480	No reaction	

[a] 1:1 mixture of *syn* and *anti* isomers.

3. Experimental

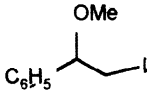
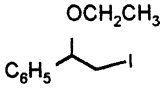
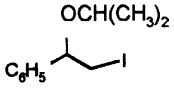
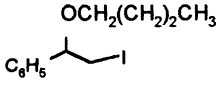
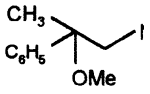
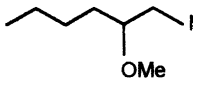
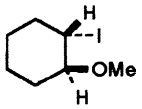
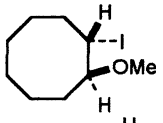
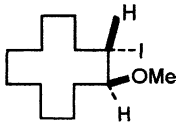
The alkenes (except cyclohexene and *trans*-stilbene), alcohols and iodine were used as obtained commercially. Cyclohexene and *trans*-stilbene were prepared in the laboratory from cyclohexanol and benzoin, respectively by standard procedures.

The reactions at room temperature were carried out by stirring magnetically in properly closed glass apparatus. Sonication was done in a 35 kHz sonic bath (Julabo, German make). During ultrasound irradiation the temperature of the bath was maintained at 25 °C by constant circulation of water. The products were identified by ^{1}H NMR spectra recorded at 500 MHz. *J* values are presented in Hz.

3.1. Preparation of β-iodoethers—General procedure

Alkene (10 mmol), iodine (1.26 g, 10 mmol), alcohol (15 ml) were sonicated in a 50 ml RB flask till the reaction was completed. After the completion of reaction, monitored by TLC (2% EtOAc + 98% pet. ether), 20 ml water was added and then the reaction mixture was extracted into ether (15 ml × 2). The ether layer was washed with sat. $NaHSO_4$ solution (5 ml × 2) and water (10 ml × 2). The ether layer was dried over anhydrous Na_2SO_4 and distilled to get β-iodoether. The product was purified by silica gel column chromatography using first pet. ether and then 1% EtOAc in pet. ether as eluants.

Table 3
^{1}H NMR Spectral data of the products prepared

Entry	Product	^{1}H NMR (δ, ppm)
1		3.31 (s, OMe), 3.32–3.35 (dd, *J* = 4.5, *J* = 9, C<u>H</u>$_2$I), 4.27–4.30 (dd, *J* = 4, *J* = 8, -C<u>H</u>-O), 7.37 (m, 5H) [9].
2		1.23 (t, *J* = 7, C<u>H</u>$_3$), 3.32–3.35 (q, *J* = 4, -C<u>H</u>$_2$-O), 3.43–3.47 (dd, *J* = 6, *J* = 12, C<u>H</u>$_2$I), 4.39–4.42 (dd, *J* = 3, *J* = 6, -C<u>H</u>-O-), 7.32 (m, 5H) [9,13].
3		1.10 (d, *J* = 6, C<u>H</u>$_3$), 1.23 (d, *J* = 6, C<u>H</u>$_3$), 3.30 (d, *J* = 6.5, -C<u>H</u>-), 3.53–3.60 (dd, *J* = 6, *J* = 12, C<u>H</u>$_2$I), 4.50–4.53 (dd, *J* = 6.5 = 6.5, -C<u>H</u>-O-), 7.35 (m, 5H) [13].
4		0.90 (t, *J* = 7, C<u>H</u>$_3$), 1.38–1.45 (sext, *J* = 7, C<u>H</u>$_2$-), 1.55–1.60 (quin, *J* = 7, C<u>H</u>$_2$-), 3.30–3.42 (m, 4H, C<u>H</u>$_2$O- & C<u>H</u>$_2$I, merged), 4.37–4.39 (dd, *J* = 4 = 4, -C<u>H</u>-O-), 7.46 (m, 5H).
5		*syn*-1.54 (s, C<u>H</u>$_3$), 3.15 (s, OMe), 3.43–3.45 (dd, *J* = 10.5, 2H); *anti*-1.71 (s, C<u>H</u>$_3$), 3.08 (s, OMe), 3.51–3.53 (dd, *J* = 10.5, 2H); (*syn* & *anti*) 7.24–7.42 (m, 10H).
6		0.81–0.84 (1, *J* = 7.5, C<u>H</u>$_3$), 0.89–0.93 (m, C<u>H</u>$_2$-), 1.27–1.38 (m, C<u>H</u>$_2$-), 1.56–1.60 (q, *J* = 7, C<u>H</u>$_2$-), 3.24–3.31 (dd, *J* = 5, *J* = 10, C<u>H</u>$_2$I), 3.37 (s, OMe), 3.56–3.68 (dd, *J* = 3, *J* = 7, -C<u>H</u>-O-).
7		1.26–2.40 (m, 8H), 3.21–3.26 (ddd, $J_{1,2} = J_{2,3a} = 8$, $J_{2,3e} = 4$, -C<u>H</u>I-), 3.45 (s, OMe), 4.04–4.09 (ddd, $J_{1,2} = J_{1,6a} = 9$, $J_{1,6e} = 4$, -C<u>H</u>-O-) [8].
8		1.26–2.17 (m, 12H), 3.35 (s, OMe), 3.53–3.57 (dd, *J* = 8, *J* = 9, C<u>H</u>I), 4.31 (m, -C<u>H</u>-O-).
9		1.32–2.05 (m, 20H), 3.23–3.43 (m, C<u>H</u>I), 3.41 (s, OMe), 4.42–4.45 (m, -C<u>H</u>-O-).

3.2. Preparation of 1-iodo-2-methoxy-2-phenylethane

Styrene (1.01 g, 10 mmol), iodine (1.26 g, 10 mmol), methanol (15 ml) were sonicated in a 50 ml RB flask for 15 min. After the completion of the reaction (monitored by TLC, using 2% EtOAc in hexane as eluant) it was worked up by adding 20 ml water and then extracting the reaction mixture into ether (15 ml × 2). The ether layer was washed with sat. $NaHSO_4$ solution (5 ml × 2), water (10 ml × 2) and dried over anhydrous Na_2SO_4. The product was purified by silica gel column chromatography using first pet. ether and then 1% EtOAc in pet. ether as eluants to get 1-iodo-2-methoxy-2-phenylethane in 85% yield. ^1H NMR spectral data of the products is given in Table 3.

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