

An efficient synthesis of 1,8-dioxo-octahydro-xanthene derivatives promoted by a room temperature ionic liquid at ambient conditions under ultrasound irradiation

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Abstract

The condensation reaction involving an aldehyde and diketone was efficiently promoted by the Ionic liquid, [Hbim]BF₄ (IL) as a reaction medium with methanol as co-solvent at ambient temperature under ultrasonic irradiation to afford the corresponding 1,8-dioxo-octahydroxanthene (xanthene) derivatives in excellent yields. The advantages of this method include among others the use of a recyclable, non-volatile ionic liquid, which promotes this protocol under ambient temperature without the requirement of any added catalyst. The reaction times and yields are compared with *p*-TSA catalyzed synthesis of xanthenes under thermal conditions, which is also reported for the first time under our reaction conditions.

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Keywords: Aldehydes; Dimedone; Xanthenes; Ionic liquid; Brønsted acidity; Ultrasound; Ambient conditions

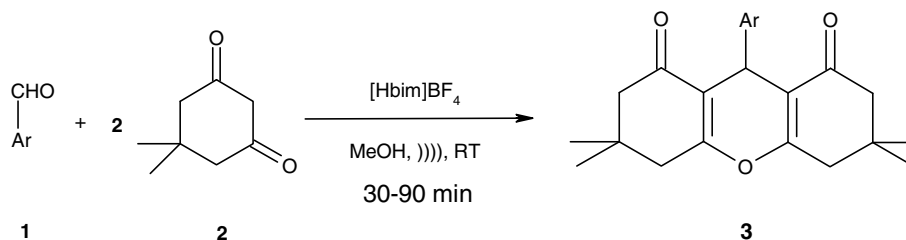
1. Introduction

The use of ultrasound in organic transformation is now well known to enhance reaction rates and yields/selectivity of reactions, and in several cases facilitates organic transformation at ambient conditions which otherwise require drastic conditions of temperature and pressure [1,2]. The driving energy is provided by cavitation, the formation and collapse of bubbles, which liberates considerable energy in short times. It follows then that the molecules that can be activated for sonochemical transformation are those that can penetrate the atmosphere of the bubble, which in turn constitutes a limitation for the method. This limitation may be addressed to by the use of non-volatile solvents to force even less volatile substrates to undergo the cavitation activation. In recent times, the use of non-aqueous room temperature ionic liquids (ILs) as

green' solvents in organic synthetic processes has gained considerable importance due to their negligible vapour pressure, solvating ability and easy recyclability [3]. These ionic liquids have no vapour pressure, which should change considerably the characteristics of cavitation in the bulk. We had recently shown that sonochemistry in ILs is a versatile tool to promote important organic transformations at ambient conditions in enhanced reaction rates. Indeed, by practising sonochemistry in ILs, we have succeeded in promoting Sonogashira, Heck and Suzuki reactions at ambient conditions, without the need for a phosphine ligand, nitration of phenols in significantly enhanced reaction rates as well as high *para*-selectivity, acylation of alcohols and MCR synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones [4a,4b,4c,4d,4e,4f]. The significance of this work is brought out by two reviews of the entire work done in recent literature [5a,5b].

Even though there are many methods reported in the literature for the synthesis of xanthenes [6–14], we thought that there is scope for further innovation towards milder reaction conditions, short reaction time and better yields

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in the synthesis of xanthenes, which was achieved by using ‘green’ imidazolium ionic liquid, [Hbim]BF₄(IL) as reaction media as well as promoter in the absence of any added catalyst under ultrasound irradiation at ambient conditions. We have compared the reaction times and yields for the *p*-TSA catalyzed synthesis of xanthenes under thermal conditions.

It is noteworthy that the products, xanthenes, were isolated in excellent yields in short reaction times employing simple workup procedures and the non-volatile IL could be efficiently recovered and reused, and the process does not need any additional acidic/basic catalyst (Scheme 1).

2. Results and discussion

The Ionic liquid, [Hbim]BF₄, was synthesized by the method reported by us [4f]. A model reaction involving 5,5-dimethyl-1,3-cyclohexanedione (dimedone) and benzaldehyde to afford the xanthenone **3k** under various reaction conditions was performed for an appropriate time. The results are recorded in Table 1.

The sonochemical synthesis of xanthenes using IL containing 25 vol.% of MeOH was observed to be the most optimum condition for the synthesis of xanthenes in maximum yields at ambient temperature in the absence of any added catalyst. Hence, all further reactions with other aldehydes were carried out under these conditions. The IL

acts as a Brønsted acid catalyst as well as a solvent at ambient temperature (30 °C) under ultrasonic irradiation (Scheme 1). The MeOH was added as co-solvent to solubilize dimedone under this condition. A variety of aldehydes including aryl-, cinnamyl- and furyl- were subjected to the sonochemical conditions in the IL to afford the products (xanthenes) in very good yields in short reaction times. All the reactions were monitored by TLC and taken to completion. The time taken for complete conversion and the isolated yields are recorded in Table 2. We also compared our results with the reaction rates for the *p*-TSA catalyzed synthesis of xanthenes under thermal conditions (Table 2), which were comparable. All the known and new products were well characterized by melting point, IR, ¹H NMR and LC–MS analyses. For the known compounds, the values were in agreement with those reported in the literature.

No significant formation of product (**3k**) was observed, when the reaction was conducted under silent conditions, even after 6 h of stirring (stirring at 30 °C under silent conditions). The replacement of IL by molecular solvents such as DMSO, MeOH, hexadecane and PEG-400 did not result in the formation of the product (**3k**) even after 6 h of sonication and the unreacted starting materials were recovered. The process tolerates aromatic aldehydes containing both electron donating and electron withdrawing substituents. It can be observed that all the aldehydes have reacted

Table 1
The synthesis of xanthenone **3k** under various reaction conditions

S. No.	Catalyst/solvent	Reaction conditions	Product	Yield ^a (%)
1	2 mL of MeOH + no catalyst	RT, 6 h,))))	3k	0
2	2 mL of [Hbim]BF ₄ + no co-solvent	RT, 6 h,))))	3k	5 ^b
3	2 mL of [Hbim]BF ₄ + 0.5 mL of MeOH	RT, 6 h,))))	3k	85
4	2 mL of DMSO + no catalyst	RT, 6 h,))))	3k	0
5	2 mL of hexadecane + no catalyst	RT, 6 h,))))	3k	0
6	2 mL of NMP + no catalyst	RT, 6 h,))))	3k	0
7	2 mL of PEG-400 + no catalyst	RT, 6 h,))))	3k	0
8	2 mL of [Hbim]BF ₄ + 0.5 mL of MeOH	RT stirring, 6 h	3k	<5 ^c
9	<i>p</i> -TSA (5 mol%) + 4 mL of MeOH + 2 mL of water	50 °C, 20 min	3k	80
10	<i>p</i> -TSA (5 mol%) + 4 mL of MeOH + 2 mL of water	RT stirring, 24 h	3k	0
11	4 mL of MeOH + 2 mL of water + no catalyst	75–80 °C, 1 h	3k	0
12	<i>p</i> -TSA (5 mol%) + 2 mL of water	75–80 °C, 1 h	3k	0

^a Isolated yields.

^b The substrate, dimedone, is sparingly soluble under this condition.

^c Dimedone (92%) and benzaldehyde (86%) were recovered back from the reaction mixture.

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