

Catalysis by ionic liquids: solvent-free efficient transthioacetalisation of acetals by molten tetrabutylammonium bromide†

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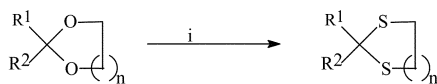
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Tetrabutylammonium bromide in molten state has been demonstrated to be a very efficient and recyclable catalyst for transthioacetalisation of *O,O*-acetals to *S,S*-acetals under solvent-free conditions.

The toxic and volatile nature of many organic solvents, particularly chlorinated hydrocarbons, that are widely used in organic synthesis have posed a serious threat to the environment. Thus, design of solvent-free reactions¹ and use of alternative green solvents like water,² supercritical fluids,³ and ionic liquids⁴ have received a lot of attention in recent times in the area of green synthesis. Although ionic liquids have been successfully employed as solvents with catalytic activities for a variety of important reactions⁴ their use as real catalyst under solvent-free conditions has not been explored to any great extent.⁵ The high cost of most of the conventional ionic liquids prompted us to initiate an investigation to explore the catalytic (minimum) use of less expensive and readily available ionic liquids or molten ionic salts for useful organic transformations.

The transthioacetalisation of *O,O*-acetals to *S,S*-acetals is a synthetically useful transformation and is usually carried out under the catalysis of a variety of Lewis acids such as MgBr_2 ,^{6a} TeCl_4 ,^{6b} WCl_6 ,^{6c} ZrCl_4 ,^{6d} $\text{SiO}_2\text{-SOCl}_2$,^{6e} trichloroisocyanuric acid^{6f} in methylene chloride and other organic solvents. In view of the use of toxic reagents and solvents coupled with other disadvantages like long reaction period in many of these procedures an alternative improved green procedure for this useful transformation would be appreciated.

We wish to report here an efficient transthioacetalisation of acetals to dithioacetals by a simple solvent-free reaction with a thiol or dithiol catalysed by molten tetrabutylammonium bromide, a cheap commercially available ionic salt (Scheme 1).



Scheme 1 Reagents and conditions: i, $\text{HS}(\text{CH}_2)_n\text{SH}$, TBAB, 110 °C.

The experimental procedure is very simple. A mixture of acetal and thiol (or dithiol) was added to molten tetrabutylammonium bromide at 110–115 °C and was stirred at that temperature for several minutes. The product was isolated either by direct distillation under reduced pressure or extraction with a relatively non-hazardous solvent. The tetrabutylammonium bromide remaining in the reaction flask was washed with hexane, dried under vacuum and was recycled for subsequent uses without any loss of efficiency. 30 Mol% of tetrabutylammonium bromide (with respect to acetal) was found to be optimum for an efficient and fast reaction. Although 10–20 mol% is sufficient to catalyse the reaction a longer period for full conversion is necessary. The use of larger quantities of tetrabutylammonium bromide does not make any significant difference.

A wide range of structurally varied acetals derived from aliphatic, aromatic and conjugated aldehydes underwent clean transthioacetalisations with a variety of aliphatic and aromatic thiols and dithiols to provide the corresponding thioacetals in very high yields. The results are summarized in Table 1. The conversion of an acetal to the corresponding acyclic or cyclic dithioacetal has been accomplished efficiently with choice of thiol or dithiol respectively. The presence of electron-withdrawing or electron-donating substituents on the aromatic ring of an acetal does not affect the course of reaction. Although acetals derived from aldehydes undergo transthioacetalisation by this procedure very easily, the acetals from ketones remained inert (entry 18). This makes this process selective for acetals of aldehydes over those of ketones as evident in a couple of cross experiments.⁷ A variety of functionalities such as Cl, NO_2 , OMe, methylenedioxy, allyloxy also survived the present reaction conditions.

The reactions in molten tetrabutylammonium bromide are, in general, very fast and clean. The absence of tetrabutylammonium bromide makes the conversion sluggish and leads to considerable polymeric products particularly in reactions with propane-1,3-dithiol. No conversion has been observed with solid tetrabutylammonium bromide at room temperature or under reflux in dichloromethane and dichloroethane. However, in more polar solvents like dimethyl sulfoxide (DMSO) at 110 °C transthioacetalisation proceeds to a certain extent (40–50%) although the reactions are not always clean being associated with other undesirable side products. For comparison with other salts when the reaction was carried out in the presence of solid sodium bromide without solvent at 110 °C no appreciable reaction (less than 10%) was apparent. However, use of DMSO as solvent leads to some conversion (40%). Presumably, molten tetrabutylammonium bromide acts as a ready source of bromide ion which by co-ordination with thiol makes the thiolate anion a stronger nucleophile and leads to efficient transthioacetalisation, while the partial progress of reaction with solid tetrabutylammonium bromide or sodium bromide in highly polar solvent, DMSO is due to the availability of bromide ion to a certain extent in the reaction media.

In conclusion, the present solvent-free procedure for transthioacetalisation of acetals demonstrates the potential of molten tetrabutylammonium bromide,⁸ a cheap readily available ionic liquid as an efficient catalyst and thus broadens the scope for catalytic uses of molten ionic salts for organic transformations in general. Moreover, this methodology offers significant improvements over many existing procedures with regard to yield of products, mildness of reaction conditions, simplicity in operation, selectivity for acetal of aldehyde over that of ketone, cost-efficiency, and above all, green aspects avoiding toxic catalysts and solvents.

Experimental

Acetals were prepared by standard methods and were purified by distillation or chromatography. Thiols were commercial

† Electronic supplementary information (ESI) available: spectral data of *S,S*-acetals. See <http://www.rsc.org/suppdata/p1/b2/b204363g/>

Table 1 Transthiioacetalisation of *O,O*-acetals catalysed by TBAB









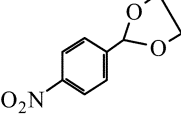
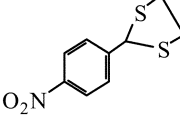
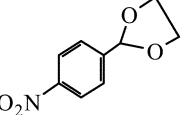
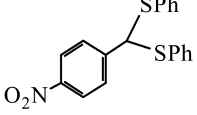
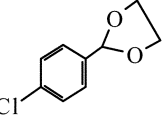
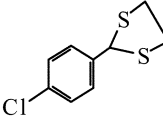
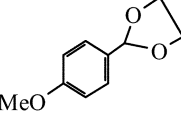
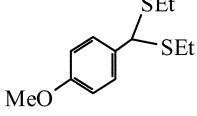
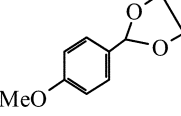
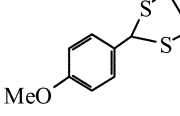
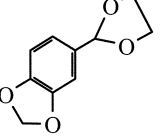
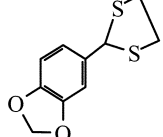
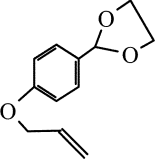
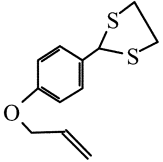
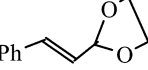
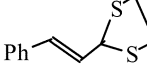
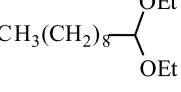
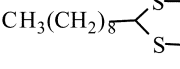
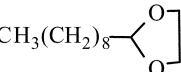
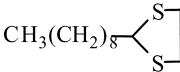
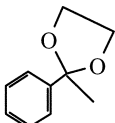
Entry	Acetal	Thiol	<i>t</i> /min	Product	Yield(%) ^a
1	PhCH(OMe) ₂	HS(CH ₂) ₂ SH	40	Ph-CH< 	87
2	PhCH(OMe) ₂	HS(CH ₂) ₃ SH	40	Ph-CH< 	89
3	PhCH(OMe) ₂	EtSH	60	PhCH(SEt) ₂	81
4	PhCH(OMe) ₂	PhSH	40	PhCH(SPh) ₂	89
5	Ph-CH< 	HS(CH ₂) ₂ SH	45	Ph-CH< 	85
6	Ph-CH< 	HS(CH ₂) ₂ SH	45	Ph-CH< 	86
7	Ph-CH< 	HS(CH ₂) ₃ SH	50	Ph-CH< 	89
8		HS(CH ₂) ₂ SH	60		85
9		PhSH	60		87
10		HS(CH ₂) ₂ SH	70		83
11		EtSH	60		86
12		HS(CH ₂) ₂ SH	70		83
13		HS(CH ₂) ₂ SH	50		89
14		HS(CH ₂) ₂ SH	50		81
15		HS(CH ₂) ₂ SH	80		79
16		HS(CH ₂) ₂ SH	60		85
17		HS(CH ₂) ₂ SH	60		83

Table 1 (Contd.)

Entry	Acetal	Thiol	t/min	Product	Yield(%) ^a
18		HS(CH ₂) ₂ SH	120	No reaction	

^a Yields refer to those of pure isolated products characterised by spectral data (IR, ¹H and ¹³C NMR).

materials and were distilled before use. Tetrabutylammonium bromide (Lancaster, UK) was also recrystallised before use.

A representative general procedure

(Entry 1). A mixture of dimethyl acetal of benzaldehyde (456 mg, 3.0 mmol) and ethane-1,2-dithiol (376 mg, 4.0 mmol, a little excess was used to compensate any loss during heating) was added to molten tetrabutylammonium bromide (290 mg, 30 mol%) at 110–115 °C and the whole mixture was stirred at that temperature for 40 minutes (monitored by TLC). The product was isolated by direct distillation under reduced pressure from the reaction mixture as a colourless liquid (475 mg, 87%) whose spectral data (IR, ¹H NMR, ¹³C NMR) are in good agreement with those reported.^{9a}

All other reactions listed in Table 1 were carried out following this procedure. If any reaction was carried out on a 1 mmol (or less) scale and the distillation was not very convenient, the product could be isolated by extraction with diethyl ether followed by washing with 10% NaOH solution and brine and purification by column chromatography. All the products were properly characterised by their IR, ¹H and ¹³C NMR spectral data, many of which have been reported earlier.^{6,9}

Acknowledgements

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