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Regeneration of the carbonyl group in the hypervalent iodine oxidation of carbonyl derivatives of dehydroacetic acid and its analogues

Rashmi Pundeer, Vishwas Chaudhri, Mayank Kinger & Om Prakash*

Department of Chemistry, Kurukshetra University, Kurukshetra 136 119, India

E-mail: dromprakash50@rediffmail.com

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Hypervalent iodine oxidation of carbonyl derivatives of dehydroacetic acid and its analogues leads to a mild and efficient regeneration of parent carbonyl compounds leaving pyrone moiety intact.

Keywords: Non-acidic reagents, dehydroacetic acid, oxidative cleavage, iodobenzene diacetate, [hydroxy(tosyloxy)iodo]benzene

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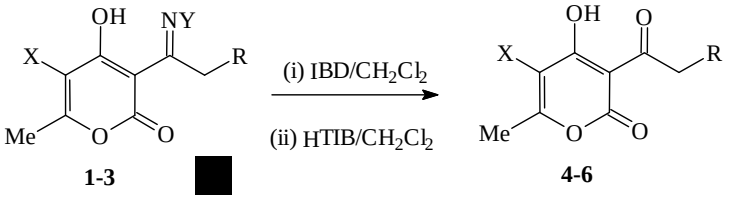
There has been considerable interest in the development of mild and non-acidic reagents for the oxidative regeneration of parent carbonyl compounds from their derivatives. The recovery of the parent aldehydes and ketones has classically involved acid hydrolysis[1,2]. Since this technique limits the scope of the reaction to exclude acid sensitive aldehydes and ketones, a number of new methods for the oxidative and reductive regeneration of carbonyl compounds from their derivatives continue to be developed. Among the many oxidants developed much attention has been paid to hypervalent organoiodine compounds due to the mildness and versatility of the oxidation conditions[3-6].

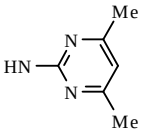
Among the several hypervalent iodine reagents, I(III) compounds such as iodobenzene diacetate (IBD)[7-9] or [hydroxy(tosyloxy)iodo]benzene (HTIB)[10-12] have shown promising results in the regeneration of carbonyl moiety from their derivatives[13-15]. For example, hypervalent iodine oxidation of various hydrazone derivatives of keto esters using IBD and HTIB provides a mild and non-acidic way for the regeneration of parent carbonyl compounds[13]. These reports coupled with the ongoing interest in the reactions of dehydroacetic acid (DHA) derivatives[16-18] led to the examination of the scope of I(III) mediated cleavage of such derivatives. Part of the reason to undertake this study is that carbonyl derivatives of DHA are known to undergo various rearrangements under acidic conditions[19,20]. Herein is reported a simple and efficient I(III) mediated procedure for oxidation of carbonyl derivatives of DHA and its analogues.

The reaction of phenylhydrazone **1a** with 1 equivalent of IBD was first carried out in dichloromethane at RT. The reaction was allowed to stir for 2 hr. The colour of the reaction mixture changed successively from yellow to reddish brown to black. The product isolated in 20% yield was found to be the parent DHA (from the comparison of m.p. and NMR data with the commercially available sample). Besides this, most of the starting material was recovered. Similar results were obtained when other derivatives were treated with IBD.

To optimize the results of the oxidative cleavage, the reaction was carried out with HTIB under different conditions. As a consequence of these efforts, it was found that the oxidative cleavage of hydrazone **1a** smoothly occurred with two equivalents of HTIB in CH_2Cl_2 at RT to give DHA (70%). Similarly, heteroaryl hydrazone (**1b**, *i.e.* 4,6-dimethyl-2-pyrimidylhydrazone of DHA) underwent the oxidative cleavage to regenerate the carbonyl compound (DHA). Encouraged by these observations, reaction was successfully applied to hydrazones of DHA-analogues (**1c, 2a, 2b, 3a**) to give the respective parent carbonyl compounds (**4b, 5a, 5b, 6a**) in good yields. Further, the oxidation reaction also worked for



1-3 **4-6**

Compd	X	Y	R	Compd	X	Y	R
1a	H	NHPh	H	**1f**	H	$NHCSNH_2$	H
1b	H		H	**2a**	H	NHPh	CH_3
1c	Br	NHPh	H	**2b**	Br	NHPh	CH_3
1d	H	OH	H	**3a**	H	NHPh	CH_2CH_3
1e	H	$NHCONH_2$	H				

Scheme I

Table I — Oxidation of carbonyl derivatives of DHA and its analogues

Reactant	Condition	Product	m.p. (Lit. m.p.)	Yield (%)
1a	(i)	**4a**	110-11(111-13) (Ref. 21)	20
1a	(ii)	**4a**	110	70
1b	(ii)	**4a**	111-12	65
1c	(ii)	**4b**	136 (137) (Ref. 22)	71
1d	(ii)	**4a**	111-13	60
1e	(ii)	**4a**	111	62
1f	(ii)	**4a**	110	67
2a	(i)	**5a**	93-4 (94) (Ref. 23)	23
2a	(ii)	**5a**	93-4	68
2b	(ii)	**5b**	90	65
3a	(i)	**6a**	50-51 (52) (Ref. 23)	21
3a	(ii)	**6a**	52	67

other carbonyl derivatives of DHA, namely, oxime **1d**, semicarbazone **1e** and thiosemicarbazone **1f (Scheme I**, **Table I)**.

To study the effect of solvent on the reaction, **1a** was treated with 2 equivalent HTIB in different solvents (methanol and acetonitrile). The reaction proceeded with equal efficacy in acetonitrile (yield 65%) but with poor yield in methanol (40%). So, acetonitrile and dichloromethane are the solvents of choice for the oxidation of carbonyl derivatives of DHA.

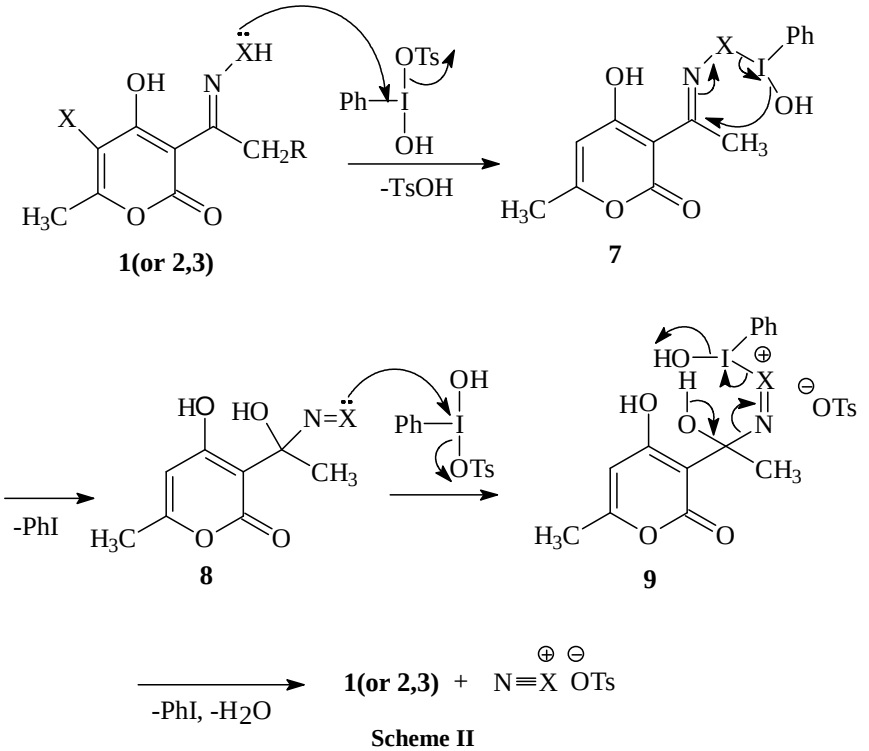
The probable mechanism of the present oxidative cleavage is outlined in **Scheme II** (ref. 13). The electrophilic attack of iodine(III) on the atom X gives the unstable species **7**, which readily undergoes rearrangement to form the intermediate **8**. The intermediate undergoes oxidative hydrolysis with the second equivalent of HTIB to give the respective carbonyl moiety *via* **9 (Scheme II)**.

Finally, it can be concluded that (a) mild regeneration allows the use of hydrazones, oxime, semicarbazone and thiosemicarbazone as protective group for carbonyl functionality in dehydroacetic acid and its analogues; (b) HTIB is a reagent of choice for the oxidative cleavage both in terms of yield and experimentation.

Experimental Section

Melting points were taken in open capillaries in an electrical apparatus and are uncorrected. ^{1}H NMR were recorded on a Brucker 300 MHz instrument using TMS as internal standard. IR spectra were recorded on a Perkin-Elmer 1800 FT-IR spectrophotometer. The known compounds (**1a, 1d, 1e, 1f**)[24-26] were identified by comparing their melting points and spectral data with those reported in literature. The structures of new compounds (**1b, 1c, 2a, 2b, 3a, 5b**) were confirmed by spectral and analytical data. The new hydrazones (**1b, 1c, 2a, 2b, 3a**) were prepared by refluxing equimolar quantities of the respective carbonyl compound with phenyl hydrazine in ethanol for 10 min.

5-Bromo-4-hydroxy-6-methyl-3-propionyl-2*H*-pyran-2-one (**5b**) was prepared by the treatment of 4-



Scheme II

hydroxy-6-methyl-3-propionyl-2*H*-pyran-2-one **(5a)** in $CHCl_3$ with 2.5 equiv of Br_2 containing 1 mol % I_2 according to the procedure reported for 5-bromodehydroacetic acid[22].

General procedure for the cleavage of carbonyl derivatives of DHA and its analogues using HTIB: HTIB (10 mmoles) was added to a stirred solution of carbonyl derivative (5 mmoles) in dichloromethane (20 mL) in portions at RT. The colour of the reaction mixture changed immediately from yellow to violet blue to black. Stirring was continued for 2-3 hr. The solvent was distilled off and the resulting reaction mixture was triturated with pet ether to remove iodobenzene. The solid so obtained was recrystallized from ethanol to get the pure carbonyl compound.

Adopting the same procedure, all other carbonyl derivatives were treated with HTIB.

General procedure for the cleavage of carbonyl derivatives of DHA and its analogues using IBD: A solution of appropriate carbonyl derivative (**1a, 2a, 3a**) in CH_2Cl_2 was treated with one equivalent of IBD in the similar way as with HTIB to obtain the corresponding carbonyl compounds (**4a, 5a, 6a**).

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