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HALOKETONE DEHALOGENATION BY IODIDE ION

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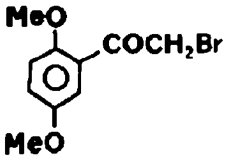
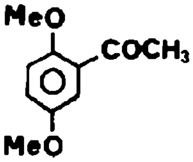
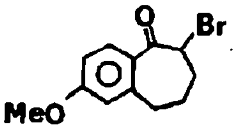
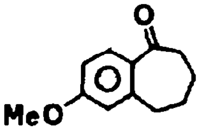
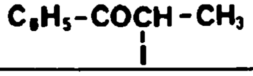
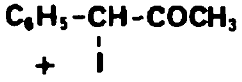
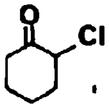
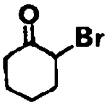
Summary : NaI in aqueous acid-THF is an efficient reagent for dehalogenation of α-haloketones.

Due to our current interest in the applications of lanthanoid derivatives in organic syntheses[1], the recently reported use of cerium triiodide for the dehalogenation of α-haloketones attracted our attention[2]. Various reagents, some quite sophisticated, have been suggested for effecting this transformation: zinc in acetic acid[3], metal carbonyls[4], transition metals in low valency state[5], $LiI-BF_3$ [6], $NaI-SO_2$-amine[7], pyridine followed by sodium dithionite[8], triphenylphosphine[9]. Many of these procedures suffer from one or more drawbacks: lack of selectivity, unsatisfactory yields, cost or toxicity of the reagent, necessity of anhydrous conditions. These limitations prompted us to further investigate the simple method employing CeI_3 which offers the advantage to be run in an aqueous medium. We found that the iodide ions act as the reducing species as postulated, but that cerium is unnecessary. We discovered that a more efficient reducing system is NaI in THF-water (1:1) in the presence of 5% aqueous H_2SO_4. By using this combination, α-bromoacetophenone is converted to acetophenone in 74% yield at room temperature in less than 1/2 hour.

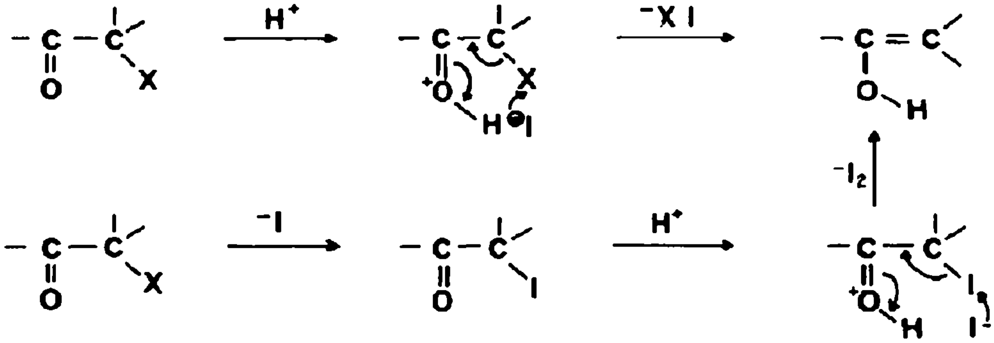
As our procedure is experimentally quite simple[10], it is of synthetic interest. Results of our study are given in the table[11]. Bromo and iodo arylalkyl ketones are easily reduced to the parent compound. Aliphatic ketones are more resistant to reduction and consequently require more drastic conditions, i.e. refluxing in dioxane water. Hindered ketones such as α-bromocamphor and 16-bromo 3β-hydroxyandrostane 17-one, however, could not be reduced.

Table

Entry	Starting Material	Method[a]	Product	Reaction (hrs)	Yield %
1	$C_6H_5COCH_2Br$	A	$C_6H_5COCH_3$	0.4	74[b]
2	$C_6H_5COCH_2Cl$	A	$C_6H_5COCH_3$	3	53[b]
3		A		0.75	81[b]
4		A		24	95[c]
5	$C_6H_5CH_2COCH_2Br$	A	$C_6H_5CH_2COCH_3$	0.5	88[c]
6	 $C_6H_5\text{-}CO\underset{I}{C}H\text{-}CH_3$	A	$C_6H_5COCH_2CH_3$	2	70[c]
7	 $C_6H_5\text{-}\underset{I}{C}H\text{-}COCH_3$ + $C_6H_5CH_2COCH_2I$	A	$C_6H_5CH_2COCH_3$	2	70[d]
8		B		6	55[d]
9		B		2[e]	78[de]

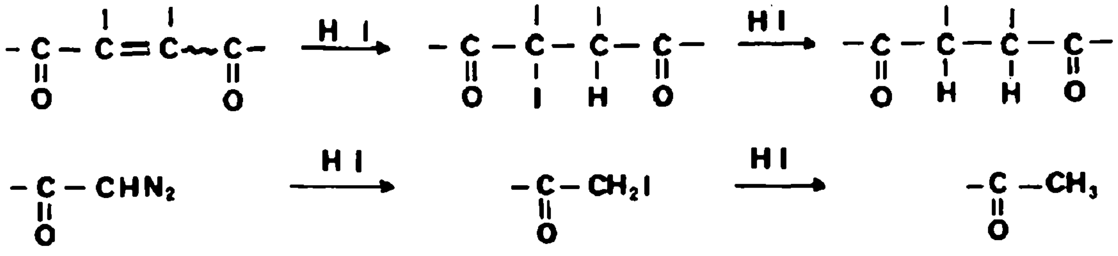
a) A : in THF:water (1:1) at room temperature. B : in refluxing 1:1 water dioxane. b) After distillation. c) Determined by NMR. d) After purification by column chromatography. e) 22% of the iodo ketone was isolated.

In the reaction, iodine and/or interhalogen species are observed almost immediately. In some instances, the corresponding iodoketone could be isolated from the mixture. From a mechanistic point of view, this result suggests that the reaction might proceed by two pathways: a direct reduction of the C-X bond by I^-, or an halogen exchange leading to the iodoketone which is then reduced in a second step. Both processes yield the dehalogenated ketone via the enol form :



Conversion to the iodoketone[12], as expected, is the only process observed in the absence of acid.

Our results cast some light on two reactions: the reduction of enediones to saturated diketones[13], and the formation of methylketones from diazoketones[14]. In both reactions one might postulate that I^- or HI reacts in a first step to give an iodo compound which is further reduced in a process analogous to the one described here.



Though it is not general, the present dehalogenation reaction offers a simple and easily performed alternative to other known methods.

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(10) These conditions resemble those employed by Zimmerman who dehalogenated a small number of bromoketones by using concentrated HI in acetone. See : Zimmerman H.E. and Chang W.H., *J. Am. Chem. Soc.* **1959**, *81*, 3634.

(11) The standard procedure is as follows : 4 mmol (600 mg) of NaI, 1 mmol of haloketone and 0.5 mL of 5% aqueous H_2SO_4 are stirred at room temperature in 5 mL THF and 5 mL H_2O. After disappearance of the starting material (TLC or GLC), the deep brown color is discharged through the addition of 10% aqueous sodium thiosulfate and the mixture is extracted with ether. The organic layer is washed with brine, dried ($MgSO_4$) and the solvent is evaporated. The residue is purified by distillation, column chromatography, or crystallization. The reduction products were identified by spectral comparison and by comparison with authentic samples[10].

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