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NOVEL TRANSFORMATIONS WITH BORONTRIFLUORIDE ETHERATE/IODIDE ION : FACILE CONVERSION OF 2-KETOOXIRANES AND 2-BROMO-2-ENONES TO THE α,β-UNSATURATED CARBONYL COMPOUNDS.[1]

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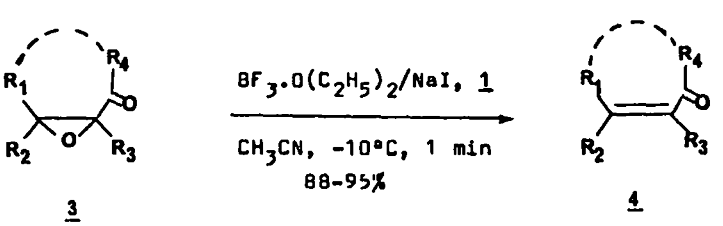
Summary : Borontrifluoride etherate/iodide ion rapidly deoxygenates α-ketooxiranes, 3, to the corresponding α,β-unsaturated carbonyl compounds, 4, in near quantitative yields. In contrast, the reaction of 3 with borontrifluoride etherate/bromide ion, 2, yielded the corresponding 2-bromo-2-enone derivatives, 5, in excellent yields. The reagent 1, also dehalogenates a variety of 2-bromo-2-enones, 5, to the corresponding 2-en-1-one derivatives, 4, in high yields.

We have recently reported that a combination of borontrifluoride etherate/halide ions (X=I, 1; X=Br, 2) performs a number of useful synthetic transformations, e.g., cleavage of alkyl ethers to the halides and alcohols[2], non-aqueous conversion of acetals and ketals to the carbonyl compounds[3], and conversion of activated alcohols to the halides[4]. Vankar et al have also reported independantly the deoxygenation of sulfoxides to sulfide[5] and the selective cleavage of benzyl ethers[6] with the reagent, 1. In continuation of our work, we report herein an efficient deoxygenation of α-ketooxiranes, 3 (eqn.1) and dehalogenation of 2-bromo-2-enone, 5 (eqn.2) to the corresponding α,β-unsaturated carbonyl compounds, 4, with the reagent, 1.

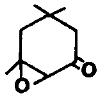
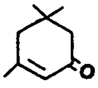
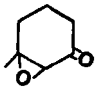
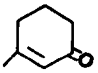
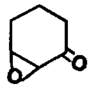
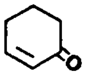
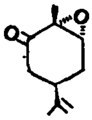
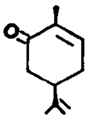
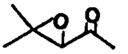
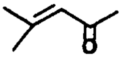
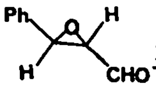
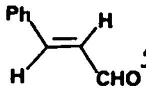
Deoxygenation of α-ketooxiranes 3

Deoxygenation of oxiranes to olefin has been the focus of current interest and a recent review[7] has listed various reagents that can be employed for this purpose. On the other hand, very few systemic studies have been reported on the deoxygenation of α-ketooxiranes, 3, to the α,β-unsaturated carbonyl compounds, 4. We have now found that a variety of α-ketooxiranes 3 can be cleanly converted to the corresponding α,β-unsaturated carbonyl compounds 4 with 1 as the deoxygenation reagent. The results are summarized in Table 1.



(1)

Table - 1 : DEOXYGENATION OF α-KETOOXIRANES, 3 TO α,β-UNSATURATED CARBONYL COMPOUNDS, 4, BY 1[a]

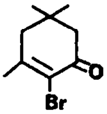
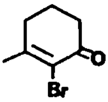
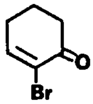
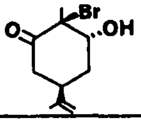
Entry	Substrate[b]		Reaction Condition Temp.°C	Time	Product[c]		Yield[d,e]
1.		3a	-10,	1 min.		4a	85(95)
2.		3a[f]	-do-			4a	82(94)
3.		3a	-25,	1 min.		4a	83(94)
4.		3b	-10,	1 min.		4b	80(92)
5.		3c	-do-			4c	75(90)
6.		3d	-do-			4d	81(94)
7.		3e	-do-			4e	80(93)
8.		3f	-do-			4f	78(92)
9.		3g	-do-			4g	80(92)

[a] The reactions were carried out using 3 (10 mmol), $BF_3.O(C_2H_5)_2$ (23 mmol) and NaI (25 mmol) in acetonitrile (25 ml); [b]The oxiranes were prepared following literature procedures; [c]Purity 95-98% as analysed by GC; [d]Isolated yields by distillation; [e]Figures in parenthesis represent crude isolated yields; [f]Tetraethylammonium iodide as the source of iodide ion CH_2Cl_2 as the reaction medium.

As can be seen from the Table 1, high yields of the products were obtained in all the cases (entries 1-9) and most remarkably the reaction proceeded rapidly even under mild conditions. Thus, while the reported reactions were carried out at -10°C (ice-salt bath), we have found that the reactions were complete within 1 min even when the temperature was as low as -25°C (entry 3) ! Use of equimolar amounts of 3 and 1 in the reaction produced one-half mole of iodine (as estimated by iodometric titration) and a 1 : 1 mixture of 4 and unreacted 3. With two moles of 1, however, one mole of iodine was liberated with concommitant formation of 4 in near quantitative yields.

It is noteworthy that while the reaction of 1 with 3 is facile and yielded 4 in excellent yields, the reaction of 1 with oxiranes, such as cyclohexene oxide[2], and cycloheptene oxide[2] and 1-phenyl-1-cyclohexene oxide[8] yielded the corresponding trans-iodohydrin in almost quantitative yields. In no case, however, were the corresponding olefins detected.

Table - 2 : REACTION OF α-KETOOXIRANES, 3, WITH $BF_3.O(C_2H_5)_2/Br^{\ominus}$, 2, at 25°C[a]

Entry	Substrate	Reaction Time	Product[b]	Yield[c,d]
1.	3a	0.5 h	 5a	85(92)
2.	3a[e]	2 h	5a	80(90)
3.	3b	0.5 h	 5b	82(92)
4.	3c	5 min.	 5c	75(89)
5.	3d	0.5 h	 6	(94)

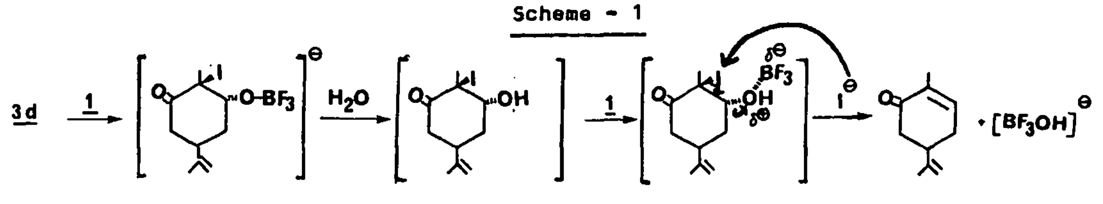
[a] The reactions were carried out using 3 (10 mmol), $BF_3.O(C_2H_5)_2$ (23 mmol) and tetraethylammonium bromide (25 mmol), in CH_2Cl_2 (25 ml) except entry 2.

[b] Purity 93-96%, [c,d] See footnotes d, e of Table-1; [e] NaBr as source of bromide ion in acetonitrile (40 ml).

We have also explored the reaction of 3 with a combination of borontrifluoride etherate and bromide ion, 2 (Table 2). In this case, however, the reaction of 3a-d with 2 yielded high amounts of the corresponding 2-bromo-2-enone derivatives 5a-d (entries 1-5, Table-2), arising possibly from the acid catalysed dehydration of the intermediate bromohydrin derivatives[9]. Indeed, the bromohydrin 6[10] was isolated as the sole product in the case of 3d where dehydration is prevented due to the absence of hydrogen at the 2-position. It is noteworthy that the bromide ion displays an overwhelming preference for the 2-position, even when this place is sterically hindered (entry 5, Table 2).

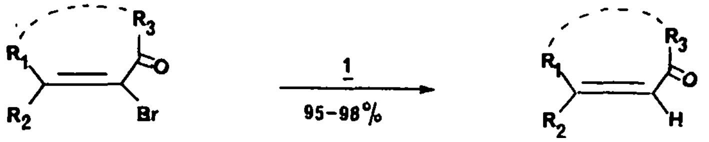
The probable mechanism for the deoxygenation of 3 to 4 is shown in Scheme 1. We speculate that this reaction proceeds through formation of iodo-hydrin 8 via the hydrolysis of the intermediate 7 by the moisture present in the reaction medium (*vide - infra*). The iodo-hydrin, 8 would then react with 1 to yield the thermodynamically stable en-one derivatives 4. This hypothesis is further supported by our observation that the bromohydrin 6[11] reacts instantaneously with a mole of 1 at -10°C to yield the carvone 4d in quantitative yield.

Scheme - 1



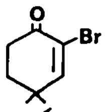
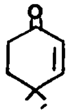
Dehalogenation of 2-bromo-2-enone, 5.

The reaction of 2-bromo-2-enone, 5, with 1 proceeded smoothly to yield the corresponding 2-en-1-one derivatives, 4, in excellent yields (eqn.2). As before the reaction also proceeds with the concommitant formation of a mole of iodine. The results are summarized in Table 3.

 (2)

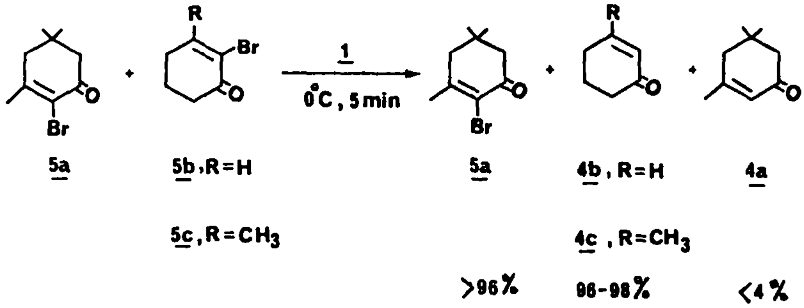
As can be seen from the Table 3, while 5b-d reacts rapidly with 1 to furnish 4b-d in quantitative yields, the corresponding reaction with sterically hindered

Table 3 : DEHALOGENATION OF 2-BROMO-2-ENONE 5 WITH 1

Entry	Substrate	Reaction Condition Temp(°C), Time	Product	Yield^{a,b}
1.	5a	25°,24 h or 82°,2 h	4a	62(73)
2.	5a	85°, 2 h	4a	80(95)
3.	5b	0°, 5 min	4b	85(97)
4.	5c	0°, 5 min	4c	(98)
5.	 5d	25°, 0.5 h	 4d	(96)

[a] Isolated yield, GC purity 95-98%; [b] Figures in the paranthesis indicated GC yields using an internal standard. [c] The reaction was carried out in 1,2-dichloroethane using tetrabutyl ammonium iodide and borontrifluoride etherate.

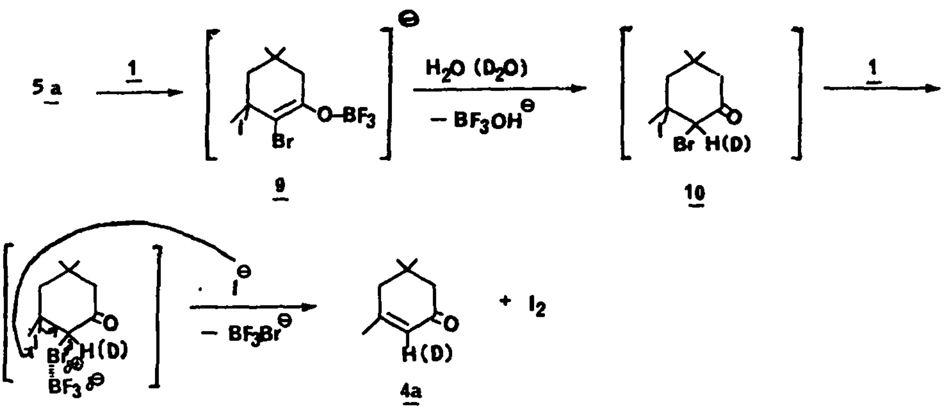
substrate 5a was slow and required forced condition for completion of the reaction (entries 1,2). This difference in the rate of reaction permitted a selective dehalogenation of 5b-c over 5a (eqn.3).



(3)

The probable mechanism of the above dehalogenation reaction (Scheme-2) appears to involve borontrifluoride assisted 1,4-addition of iodide ion to 5 to yield the dihalo-derivative, 9, which is then hydrolysed to the keto-derivative, 10, by the moisture present in the reaction medium. Subsequent reaction of 10 with 1, as shown in Scheme-2, yielded the 2-en-1-one, 4 with concurrent formation of a mole of iodine. This is further supported by (i) deuteration studies which showed the incorporation of deuterum in 4a (50%)[12] and (ii) reaction of 2,3-dibromo-3-methylcyclohexan-1-one with 1 which yielded 4b in good yields.

Scheme-2



In conclusion, we have shown that a combination of borontrifluoride etherate and iodide ion, 1, deoxygenates under exceptionally mild condition a variety of α-keto-oxiranes 3 to the corresponding 2-en-1-one derivatives 4 in quantitative yields. On the other hand the reaction of 3 with a combination of borontrifluoride-etherate and bromide ion, 2 provided, in high yields, the corresponding 2-bromo-2-enone derivatives, 5. Finally, the reaction of 5 with 1 again yielded the dehalogenated products, 4, in excellent yields.

Experimental :

NMR spectra were recorded in $CDCl_3$ on a Bruker CW-80 and Bruker AC-80 spectrometers, with chemical shift reported in ppm downfield of internal standard tetramethylsilane. IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. GLC analyses were carried out on a HP 5890 gas chromatograph using capillary column HP 101 (methyl silicone), 25 m x 0.2 mm x 0.2 μm film thickness.

Preparation of α-ketooxiranes, **3** :

The ketooxirane **3a** was prepared following literature procedure[13]. Similarly α-ketooxiranes **3b**-**3e** were prepared following essentially the above literature procedure. Compounds **3f**[14] and **3g**[15] were prepared following literature procedures. The products were purified by distillation.

3b; b.p 51-53°/0.5 mm of Hg; IR ($CHCl_3$), ν cm^{-1}; 1710; ^1H nmr, δ, 3.05 (s, 1H, $C\underline{H}$-O) 2.50 - 1.50 (*m*, 6H, $3C\underline{H}_2$), 1.45 (s, 3H, $C\underline{H}_3$).

3c; b.p 92-96°/30 mm of Hg; IR ($CHCl_3$), ν cm^{-1}, 1710; ^1H nmr, δ, 3.70-3.50 (*m*, 1H, O-$C\underline{H}$-C=O), 3.10 - 3.30 (m, 1H, O-$C\underline{H}$-C), 2.80 - 1.48 (*m*, 6H, $3C\underline{H}_2$).

3d; b.p 72-75°/ 1 mm of Hg; IR ($CHCl_3$), ν cm^{-1}, 1710; ^1H nmr, δ, 4.87-4.6 (*m*, 2H, =$C\underline{H}_2$), 3.52 - 3.35 (*m*, 1H, $C\underline{H}$-O), 2.95 - 1.80 (*m*, 5H, $2C\underline{H}_2$, 1 $C\underline{H}$), 1.75 (s, 3H, =C-$C\underline{H}_3$), 1.45 (s, 3H, $C\underline{H}_3$-C-O).

3e; b.p 85-86°/30 mm of Hg; IR ($CHCl_3$), ν cm^{-1}, 1745; ^1H nmr, δ, 3.13 (s, 1H, $C\underline{H}$-O), 2.50 - 1.75 (m, 4H, $2C\underline{H}_2$), 1.60 (s, 3H, $C\underline{H}_3$).

General procedure for the deoxygenation of α-ketooxiranes, **3** :

To a stirred solution of **3** (10 mmol), sodium iodide (3.75 g, 25 mmol) in acetonitrile (25 ml) at -10°C was added, freshly distilled borontrifluoride etherate (2.9 ml, 23 mmol) *via* a syringe. After one minute the dark reaction mixture was quenched with 10% aqueous sodium thiosulphate solution. Dichloromethane (50 ml) was added and the organic layer separated, washed with saturated brine solution and dried. Removal of solvent yielded **4** which was further purified by distillation under vacuum.

General procedure for the preparation of 2-bromo-2-enone, **5** :

To a stirred solution of **3** (10 mmol), tetraethyl ammonium bromide (5.78 g, 27.5 mmol) in dry dichloromethane (40 ml) at 25°C was added freshly distilled borontrifluoride etherate (1.6 ml, 12.5 mmol) *via* a syringe. Usual work up as before yielded **5**, which was further purified by distillation under vacuum.

5a ; b.p 90-92°/1 mm of Hg, IR (neat), ν cm^{-1}, 1680, 1610; ^1H nmr, δ, 2.42 (s, 2H, $C\underline{H}_2$-C=O), 2.38 (s, 2H, $C\underline{H}_2$-C=), 2.15 (s, 3H, $C\underline{H}_3$-C=), 1.05 (s, 6H, $2C\underline{H}_3$).

5b ; Kugelrohr distillation (oven temp. 150°C, vacuum 0.8 mm of Hg); IR ($CHCl_3$), ν cm^{-1}, 1680, 1610; ^1H nmr, δ, 2.70 - 2.30 (*m*, 4H, $C\underline{H}_2$-C=O, $C\underline{H}_2$-C=), 2.15 (d, 3H, J=1.0 Hz, $C\underline{H}_3$-), 2.20 - 1.85 (*m*, 2H, $C\underline{H}_2$-).

5c ; m.p 74-76°C; IR ($CHCl_3$), ν cm^{-1}, 1690, 1610; ^1H nmr, δ, 7.42 (t, 1H, J=6.0 Hz, $C\underline{H}$-C=), 2.71 - 2.30 (*m*, 4H, $C\underline{H}_2$-C=O, $C\underline{H}_2$-C=), 2.25 - 1.90 (*m*, 2H, $C\underline{H}_2$-C-).

5d ; Kugelrohr distillation (oven temp. 150°C, vacuum 1 mm of Hg); IR (neat), ν cm^{-1}, 1700, 1605; ^1H nmr, δ, 7.12 (s, 1H, $C\underline{H}$=), 2.66 (dd, 2H, J=8.0 Hz, J=1.0 Hz, -$C\underline{H}_2$-C=O), 1.90 (dd, 2H, J=8.0 Hz, J=1.0 Hz, $C\underline{H}_2$-C-), 1.21 (s, 6H, $2C\underline{H}_3$).

General procedure for the dehalogenation of **5** to **4** :

To a solution of **5** (5 mmol), sodium iodide (2.06 g, 13.75 mmol) in dry acetonitrile (10 ml) at 0°C or 25°C was added freshly distilled borontrifluoride etherate (1.6 ml, 12.5 mmol) as before. Usual workup as before yielded **4** in excellent yields.

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References :

1. Presented in part at the "IMEBORON VI Meeting", 'Bechyne' Czechoslovakia, June, 1987.
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9. Analysis of the initial reaction mixtures revealed the formation of bromohydrins in addition to *5*.
10. *6*; ^{1}H nmr (CDCl$_3$); δ , 4.80-4.65 (*m*, 2H, C*H*$_2$=), 4.4-4.27 (*m*, 1H, C*H*-O), 3.4-2.0 (*m*, 6H, 2C*H*$_2$, 1C*H*, O*H*), 1.83 (s, 3H, C-C*H*$_3$), 1.8-1.6 (*m*, 3H, C*H*$_3$-C=).
11. All our attempts to convert *6* to the corresponding iodohydrin failed.
12. By comparison of the area of vinyl proton (δ,5.89) with the area of the methyl proton (δ,1.94) in the ^{1}H nmr.
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