Oxidation of Secondary Alcohols to Tetrahydrofurans by the Silver Oxide–Bromine Reagent: Solvent Effect

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Summary The conversion of secondary unbranched aliphatic alcohols with unactivated δ carbon atoms into tetrahydrofuran derivatives by means of silver oxide and bromine is autocatalysed and the yield is very much improved by adding tetrahydrofuran to the reaction mixture.

RECENTLY Mihailovic and his co-workers[1] reported that the intramolecular cyclisation (by means of bromine and silver salts) of secondary alcohols with geometrically-fixed reaction centres to cyclic 1,4-ethers could be extended to open-chain unbranched aliphatic alcohols, in very good yields. The mechanism of this cyclisation has been much disputed:[2,3] it may result from ionic or free-radical decomposition of the hypohalide formed *in situ*.

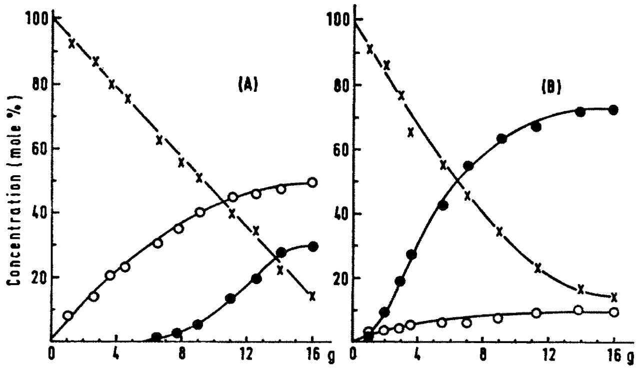


FIGURE. *Reaction products against bromine added*: (A) *without added 2,5-dimethyltetrahydrofuran*: (B) *in the presence of 2,5-dimethyltetrahydrofuran*: + *heptan-3-ol*, ○ *heptan-3-one*, ● *2-ethyl-5-methyl-tetrahydrofuran.*

Our results not only allow us to improve the yield of this reaction but also shed some light on its mechanism.

2-Ethyl-5-methyltetrahydrofuran was prepared by treating heptan-3-ol in pentane solution with bromine in the presence of freshly-prepared silver oxide.[1] The yield was low (even lower in the dark, see Table, run no 5 and 6). We have followed the course of the reaction as a function of bromine added.

By plotting the concentration of the alcohol and the products against the quantity of bromine added (Figure 1) we observe a definite induction period during which the only product observed is the corresponding ketone, formed by the heterolytic oxidation of the alcohol.[4] When about one third of the stoicheiometric quantity of bromine has been added the expected tetrahydrofuran derivative appears, first slowly, then at a higher rate. The S-shape curve indicates the possibility of an autocatalysed type of reaction. We therefore effected the same reaction in the presence of a closely related tetrahydrofuran derivative: 2,5-dimethyltetrahydrofuran. In this case the cyclisation reaction shows no induction period (Figure). The competing ketone formation is suppressed and the yield of the cyclic ether is very much improved (see Table, lines 6 and 8 or 5 and 7).

	Conditions[a]				Reaction products and yields		
No.	Alcohol	T	Light	Solvents	Tetrahydrofuran	Carbonyl compounds	Recovered alcohol
1	Heptan-1-ol	25°	Daylight	Pentane	72	12	12
2	,, ,,	,,	,,	Pentane + DMTHF	68	trace	24
3	Heptan-2-ol	25°	Daylight	Pentane	23 (+10)	59	6
4	,, ,,	,,	,,	Pentane + DMTHF	58	12	26
5	Heptan-3-ol	25°	Daylight	Pentane	32	49	14
6	,, ,,	,,	Dark	,,	20	61	12
7	,, ,,	25°	Daylight	Pentane + DMTHF	70 (+7)[b]	11	8
8	,, ,,	,,	Dark	,, ,,	72	8	14
9	,, ,,	,,	Daylight	Pentane + THF	72 (+8)[b]	9	8
10	,, ,,	,,	,,	Pentane + glyme	74 (+9)[b]	10	4

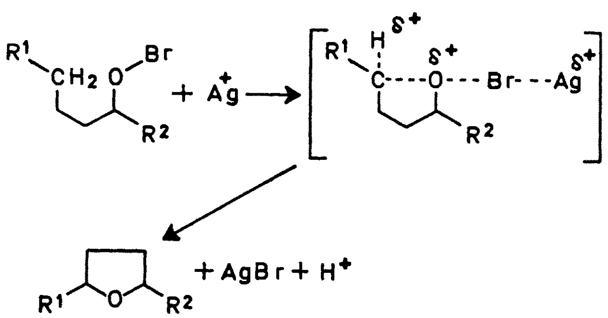
[a] Alcohol (0·05 mole), silver oxide (0·105 mole, prepared as described[1]); bromine (0·1 mole) pentane (150 ml) DMTHF or THF or glyme (0·1 mole).

Bromine was added to the stirred suspension of silver oxide in solvent + alcohol. During the addition we withdrew 0·1 mixture for g.c. analysis (Carbowax, temp 75—140°) in order to follow the course of the reaction. Identification of the reaction products as described in ref. 1.

[b] Corresponding tetrahydropyran.

With heptan-1-ol we obtained only traces of the corresponding carbonyl compound (line 2) and more alcohol is recovered.

This strong solvent effect was also observed when instead of dimethyl tetrahydrofuran we used other solvating agents as tetrahydrofuran or glyme (line 9 and 10). We believe that these results support strongly a mechanism of the type suggested earlier[2] with an ion-pair transition state containing some positive charge on the oxygen. This positive charge is probably solvated by tetrahydrofuran and this makes ketone formation electronically and/or sterically unfavourable.



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