Oxidations with Metal Oxide–Halogen Reagents. Cyclization of Primary and Secondary Aliphatic Alcohols to Tetrahydrofurans

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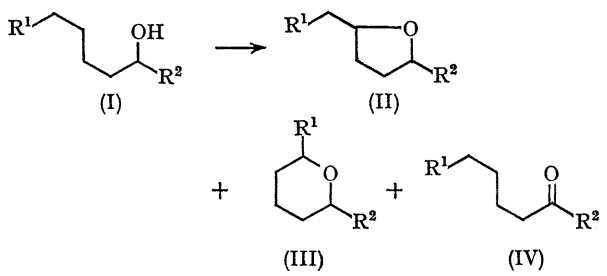
Summary Primary and secondary unbranched aliphatic alcohols with unactivated δ-carbon atoms are readily converted into tetrahydrofuran derivatives by means of silver oxide and bromine or mercuric oxide and iodine.

As shown recently,[1–4] primary and secondary aliphatic alcohols containing unactivated δ-carbon atoms can be converted in 40—55% yield into the corresponding tetrahydrofurans by oxidation with lead tetra-acetate in benzene, either under thermal or u.v.-photolytic conditions. On the other hand, it has been reported that secondary and tertiary alcohols in which one or both reacting centres are geometrically fixed (*e.g.* steroid alcohols) undergo intramolecular ring closure to cyclic 1,4-ethers when treated either with iodine and mercuric oxide (in carbon tetrachloride, chloroform or methylene chloride at room temperature in the presence of u.v. light or at reflux temperature in the dark),[5] or with bromine and silver salts (oxide or acetate) in pentane (at room temperature in the dark).[6,7] With mercuric oxide and iodine, 4-phenylbutanol, *i.e.* an open-chain alcohol with an activated (benzylic) δ-carbon atom, is cyclized to 2-phenyltetrahydrofuran,[8] and with silver oxide and bromine two tertiary acyclic alcohols have also been in part oxidized to 5-membered cyclic ethers.[6,9]

In order to improve the preparative scale synthesis of tetrahydrofurans from open-chain alcohols, we have now studied the action of silver oxide–bromine and mercuric oxide–iodine on some primary and secondary unbranched aliphatic alcohols with unactivated δ-carbon atoms, and have found that both reagents effect readily intramolecular ting closure of 1- and 2-alkanols (I) to the corresponding tetrahydrofurans (II) in very good yields of 60—73% (Tables 1 and 2). In addition to recovered alcohol (I), the only other major reaction product is the carbonyl compound (IV) of the starting alcohol, whereas tetrahydropyrans of type (III) are formed in only small amounts (corresponding to the yields obtained in the lead tetra-acetate oxidations[1–4]). Intramolecular cyclization of cyclo-octanol (as a representative of secondary cycloalkanols) to the bicyclic 1,4-ether occurs in a yield (45—50%) which is superior to that observed in the lead tetra-acetate reaction (36%).[10]

It should be particularly noted that oxidations with silver oxide–bromine do not require the absence of light (as stated previously,[6,7,9]), and that reactions performed in (indirect) daylight at room temperature afford somewhat



R^1 = H, Me, Et, Pr^n; R^2 = H, Me

TABLE 1

Oxidation of primary and secondary alcohols with silver oxide and bromine

				Reaction products and yields (%)		
Alcohol (I)	Solvent	Conditions[a] Temp.	Light	Tetrahydrofuran (II)	Carbonyl compound (IV)	Recovered alcohol (I)
Hexan-1-ol	Pentane	25°	Dark	61	14	11
	,,	0	Daylight	51	5	31
	,,	25	,,	71	15	6
	$CHCl_3$	25	,,	56	8	25
Heptan-1-ol	Pentane	25	,,	70	14	8
Octan-1-ol	,,	25	,,	73 (+3·7)[b]	15	4
Hexan-2-ol	,,	25	,,	69	16	8
Octan-2-ol	,,	25	Dark	57	13	20
	,,	0	Daylight	50	7	33
	,,	25	,,	62 (+3)[b]	20	8
	,,	36	,,	61 (+3)[b]	20	10
	$CHCl_3$	0	,,	47	10	32
	,,	61	,,	33	5	56
Cyclo-octanol	Pentane	25	,,	45[c]	23[c]	15

[a] Alcohol (0·05 mole), finely divided, freshly prepared ("neutral") silver oxide (0·105 mole), bromine (0·1 mole), solvent (150 ml.). Silver oxide was prepared by treating aqueous $AgNO_3$ with dilute aqueous NaOH; the precipitate was filtered, washed thoroughly with water and EtOH, dried at 40—45°, and kept in the dark. Bromine was added to the stirred suspension over a period of 3 hr., and stirring was continued for another 1·5 hr. The resulting mixture was filtered, and the filtrate was washed successively with aqueous $Na_2S_2O_3$, $NaHCO_3$ and water. After drying, the reaction products were separated by fractional distillation through a spinning-band column and/or by gas chromatography (Carbowax, temp. 100—130°). The products were identified on the basis of their i.r., n.m.r. and mass spectra.[1] [b] Corresponding tetrahydropyran (III).[1] [c] See ref. 7.

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higher yields of cyclic ethers than those which were carried out in the dark (Table 1). When mercuric oxide and iodine were used as oxidation agent, the irradiation of the reaction mixture at room temperature was performed with an ordinary 500 w tungsten lamp (and not with a high pressure mercury u.v. lamp[3,8]).

In the case of the secondary alcohols hexan-2-ol (I; $R^1 = H$, $R^2 = Me$) and octan-2-ol (I; $R^1 = Et$, $R^2 = Me$), the corresponding 2,5,-dialkyl tetrahydrofurans (II) which are obtained upon oxidation (with either of both reagents) consist of a mixture of diastereomers, the ratio *cis* : *trans* being about 40 : 60. These results parallel the nonstereoselective formation of 2,5-disubstituted five-membered cyclic ethers in the lead tetra-acetate reaction of alcohols.[1–4]

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TABLE 2

Oxidation of primary and secondary alcohols with mercuric oxide and iodine in carbon tetrachloride at 25°

	Reaction products and yields (%)		
Alcohol (I)[a]	Tetrahydrofuran (II)	Carbonyl compound (IV)	Recovered alcohol (I)
Octan-1-ol	60	20	8
Octan-2-ol	61	18	7
Cyclo-octanol	50[b]	23[b]	10

[a] Alcohol (0·015 mole), finely divided yellow mercuric oxide (prepared from mercuric nitrate as described in footnote a, Table 1 for silver oxide) (0·09 mole), iodine (0·12 mole), carbon tetrachloride (400 ml.). The mixture was vigorously stirred and irradiated with a 500 w tungsten lamp (water cooling),[4] over a period of 5·5 hr. The reaction mixture was worked up and the products isolated and identified as described in footnote a, Table 1. [b] See ref. 7.

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