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SILVER-ASSISTED DIMETHYLSULFOXIDE OXIDATIONS; AN IMPROVED SYNTHESIS OF ALDEHYDES AND KETONES

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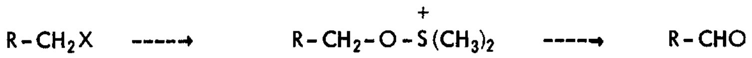
An accompanying paper [1] details our interest in developing a mild method for the oxidation of a primary alkyl bromide to the corresponding aldehyde in the presence of sensitive functionality. Kornblum [2] and subsequent investigators have shown that the direct displacement of primary iodides and tosylates [3] with dimethylsulfoxide (DMSO) occurs at 150°. The resulting oxysulfonium salts 1 have been well characterized [4] and are known to undergo fragmentation thermally[5] or with base to generate aldehydes in moderate yields.



$$R\text{-}CH_2X \dashrightarrow R\text{-}CH_2\text{-}O\text{-}\overset{+}{S}(CH_3)_2 \dashrightarrow R\text{-}CHO$$

1

Unfortunately, simple alkyl bromides are inert to DMSO even at high temperature. Oxysulfonium salts from these compounds have only been prepared by prior conversion to the corresponding tosylates [2]. Hoping to improve the situation, we speculated that a soluble, non-nucleophilic silver salt

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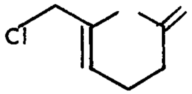
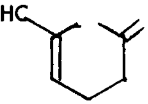
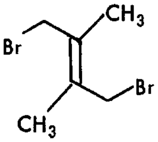
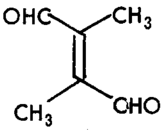
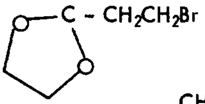
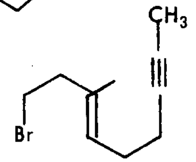
TABLE I

HALIDE	RXN TIME (hrs)	PRODUCT[a]	YIELD (%)
$CH_3(CH_2)_7$ - Br	18	$CH_3(CH_2)_6CHO$	83
$CH_3(CH_2)_5CH(Br)CH_3$	18	$CH_3(CH_2)_5COCH_3$	80
$C_6H_5(CH_2)_3$-Br	12	$C_6H_5(CH_2)_2CHO$	80
$CH_3CO_2(CH_2)_5$-Br	17	$CH_3CO_2(CH_2)_4CHO$	55
$CH_3(CH_2)_7$-Cl	12	no reaction	
 2	1	3 	90
CH_3C C-$(CH_2)_3$-OTs	18	no reaction	
 5	0.75	6[b,c] 	60
 7	18	no reaction	
 8	9	no aldehyde	

(a) Unless otherwise stated, these products were identical with authentic samples, as determined by ir and nmr spectroscopy as well as glc analysis.

(b) nmr (δ) 2.19 (s, 6H), 10.5 (s, 2H); ir (λ max) 5.96μ; uv (EtOH) λ max 250 nm (2630)

(c) Satisfactory elemental analysis was obtained for the bis - 2,4-DNP of this substance, mp 315-320° (d) such as silver tetrafluoroborate might facilitate the oxidation by promoting the displacement of bromide ion at a reasonable temperature. Two disparate preliminary reports [6,7] prompted us to investigate carefully this silver-assisted process. The present note discloses our success in devising such a procedure and applying it to the preparation of a wide variety of carbonyl compounds.

When 1-bromooctane was added at room temperature to a solution of $AgBF_4$ (1.1-1.3 equiv.) in dry DMSO (5ml/g of silver salt), a fine white precipitate slowly developed. Addition of triethylamine (0.5ml/5ml solvent) after 18 hours and ether extraction 15 minutes later afforded an 83% yield of octanal, contaminated with ca 5% of the starting bromooctane [8]. Table I summarizes the results when this method was applied to nine other substances.

Both primary and secondary alkyl bromides are oxidized in excellent yields. In the case of 5-bromopentyl acetate the lower yield is due to appreciable water solubility of the product. Although 1-chlorooctane is unaffected by silver tetrafluoroborate in DMSO, the allylic chloride **2** [9] is quickly transformed to the α, β- unsaturated aldehyde **3**. This aldehyde could not be prepared by direct DMSO oxidation of **2** using Kornblum's procedure [2]. Like octyl chloride, the toluenesulfonate ester **4** was also inert to the reaction conditions. This remarkable selectivity for alkyl bromides in the presence of two other synthetically near-equivalent functional groups may prove useful in a complex synthesis. Particularly noteworthy is the conversion of 1,4-dibromo-trans-2,3-dimethyl-2-butene **5** [10] to 2,3-dimethylfumaraldehyde in 60% isolated yield. In contrast, heating this dibromide in pure DMSO failed to produce any of **6**, illustrating both the versatility and the mildness of silver-assisted oxidation.

Oxidation of both the bromoacetal **7** and the homoallylic bromide **8** [11] failed to produce the desired aldehydes. The former, deactivated halide remains untouched, while the latter gives rise instead to numerous products, apparently derived from homoallyl-cyclopropylcarbinyl rearrangement.

These results demonstrate that a wide variety of bromides, as well as allylic chlorides, now constitutes a convenient source of the corresponding carbonyl compounds using this mild oxidation technique. Although alkyl halides are not generally considered as "masked" precursors for aldehydes and ketones, this may become a significant approach in ribonucleoside synthesis where methods for the selective halogenation of triols have already been developed [12,13].

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References and Footnotes

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