Debromination of α,α'-Dibromo-ketones with a Zinc–Copper Couple in Methanol. Formation of α-Methoxy-ketones as a Criterion for the Intervention of 2-Oxyallyl Cations

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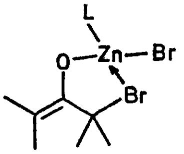
Summary Debromination of α,α'-dibromo-ketones with a zinc–copper couple in methanol yields parent ketone and α-methoxy-ketone in varying amounts; the latter, which is formed in an orientationally specific manner, is suggested to arise *via* a selective 2-oxyallyl cation which is produced in an S_N1 reaction.

Our work with allyl cations[1] has led us to investigate α,α'-dihalogeno-ketones. We have already described two general reactions of these compounds[1b,1c] and recently other workers have reported analogous work.[2] We now described the debromination of α,α'-dihalogeno-ketones in methanol to give α-methoxy-ketone and parent ketone;[1d] this reaction is mechanistically related to those already described.

The α,α'-dihalogeno-ketone (2g) prepared as described previously[1b] dissolved in methanol (10 ml), was added dropwise to a stirred suspension of highly active zinc–copper couple[3] in methanol (15 ml) during *ca.* 45 min at −5° to 0° under deoxygenated nitrogen. The reaction solution was stirred for a further 30 min, filtered, poured into an excess of 0·1N-HCl, and extracted with CCl_4 or CH_2Cl_2. The products which could be analysed by g.l.c., n.m.r., and i.r. spectroscopy, were α-methoxy-ketone and/or parent ketone (see Table).

It is interesting that formation of the α-methoxy-ketone competes so effectively with that of the parent ketone under these conditions. Clearly, methanol has a dual role in that it reacts both as an electrophile by donating a proton, and as a nucleophile by utilising a lone pair on oxygen. The zinc enolate (20) seems a probable intermediate, which is a finely balanced system in that it (a) can ionise to an allyl cation which gives α-methoxy-ketone and (b) contains an electron-rich enolate grouping which can be reduced *via* the monobromo-ketone into the parent ketone. *A priori*, the postulated allyl cation intermediate can be attacked at either carbon terminus and provided that the α- and α′-positions are structurally distinguishable a mixture of α-methoxy-ketones might be expected to be formed. Interestingly, none of our reactions gave such a mixture, a single α-methoxy-ketone being formed to the exclusion of any isomer. Although the α-methoxy-ketones could arise *via* an S_N2 displacement, perhaps on the α,α′-dihalogeno-ketone or the zinc enolate (20), there are several reasons which make this unlikely. The most compelling reason is the formation of tertiary α-methoxy-ketone (12a) from (2) and of (13a) from (3) and (4). Such orientational selectivity is without precedent in the solvolysis of simple methylated allyl halides.[4] It seems relevant that our allyl cations[†] contain an oxygen atom with lone pairs of electrons and that furthermore, the zinc moiety is able to assist electrophilically the departure of the leaving group.



L = solvent

(20)

As to the relative amount of α-methoxy-ketone formed, this route appears to be favoured by increasing methylation and also by a change of leaving group from bromide to iodide [*cf.* (3) and (4)]. Compounds (3) and (4) are unique in that they represent the only α,α′-dihalogeno-ketones which contain a primary carbon and leak into the carbonium ion route. The zinc enolates derived from the most simple α,α′-dihalogeno-ketones (6) and especially (7) appear to be no longer sufficiently prone toward formation of allyl cations under our conditions and 100% parent ketone formation occurs. Since we had shown earlier that (6) and (7) produce neither five-membered rings with dimethylformamide[1b] nor seven-membered systems with conjugated dienes,[1c] the absence of methoxy-ketone was expected.

Table *Dehalogenation of α,α′-dihalogeno-ketones with a zinc-copper couple in methanol at −5° to 0°*

α,α′-Dihalogeno-ketone	Products	
	α-Methoxy-ketone	Parent ketone
$BrCMe_2\cdot CO\cdot CMe_2Br$ (1)	$MeO\cdot CMe_2\cdot CO\cdot CHMe_2$ (11a) (72%)	$Me_2CH\cdot CO\cdot CHMe_2$ (11b) (28%)
$BrCMe_2\cdot CO\cdot CHMeBr$ (2)	$MeO\cdot CMe_2\cdot CO\cdot CH_2Me$ (12a) (76%)	$Me_2CH\cdot CO\cdot CH_2Me$ (12b) (24%)
$BrCMe_2\cdot CO\cdot CH_2Br$ (3)	$MeO\cdot CMe_2\cdot COMe$ (13a) (19% at −35°) (14% at − 5°)	$Me_2CH\cdot COMe$ (13b) (81%) (86%)
$BrCMe_2\cdot CO\cdot CH_2I$ (4)	(33% at −35°) (<5% at −5°)	(67%) (>95%)
$BrCHMe\cdot CO\text{-}$ $\cdot CHMeBr$ (5)	$MeO\cdot CHMe\cdot CO$ $\cdot CH_2Me$ (14a) (62%)	$MeCH_2\cdot CO\cdot CH_2Me$ (14b) (38%)
$BrCHMe\cdot CO\cdot CH_2Br$ (6)		$MeCH_2\cdot COMe$ (15) (100% at 0° and −35°)
$ICH_2\cdot CO\cdot CH_2I$ (7)		$MeCOMe$ (16) (100%)
$BrCMe_2\cdot CO\cdot CHPhBr$ (8)	$MeO\cdot CMe_2\cdot CO\cdot CH_2Ph$ (17a) (84%)	$Me_2CH\cdot CO\cdot CH_2Ph$ (17b) (16%)
$BrCHPh\cdot CO\cdot CHPhBr$ (9)	$MeO\cdot CHPh\cdot CO\cdot CH_2Ph$ (18) (100%)	
$BrCHMe\cdot CO\cdot CHPhBr$ (10)	$MeO\cdot CHMe\cdot CO$ $\cdot CH_2Ph$ (19a) (28%)	$MeCH_2\cdot CO\cdot CH_2Ph$ (19b) (72%)

Thus, the formation of α-methoxy-ketones by the above reaction affords a simple criterion for the feasibility of generating allyl cations and for the orientational selectivity of subsequent nucleophilic attack.

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[†] The specific allusion to 2-oxyallyl cations in the title and discussion has been questioned by three referees who deemed that the intermediacy of these species has not been established clearly. Apart from the arguments presented the following points should be borne in mind. (1) The debromination of the dihalogeno-ketones (1)—(5) with zinc–copper couple in dimethylformamide yields 5-membered heterocycles, the formation of which is subject to the same degree of orientational control[1b] as that of the α-methoxy-ketones described here. (2) The debromination of (1)—(5) with zinc–copper couple in the presence of conjugated dienes and in solvents glyme and acetone affords 7-membered cyclo-adducts.[1c] This reaction in particular must be considered to involve allyl cations.[1a] (3) The α-methoxy-ketones are *not* formed by methanolysis of the α,α′-dihalogeno-ketones, which are inert to methanol in our conditions.

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