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NUCLEOPHILIC SUBSTITUTION AT THE BRIDGEHEAD OF 1,4-DIHALOBICYCLO[2.2.2]OCTANES : AN ABNORMAL LEAVING GROUP MOBILITY ORDER

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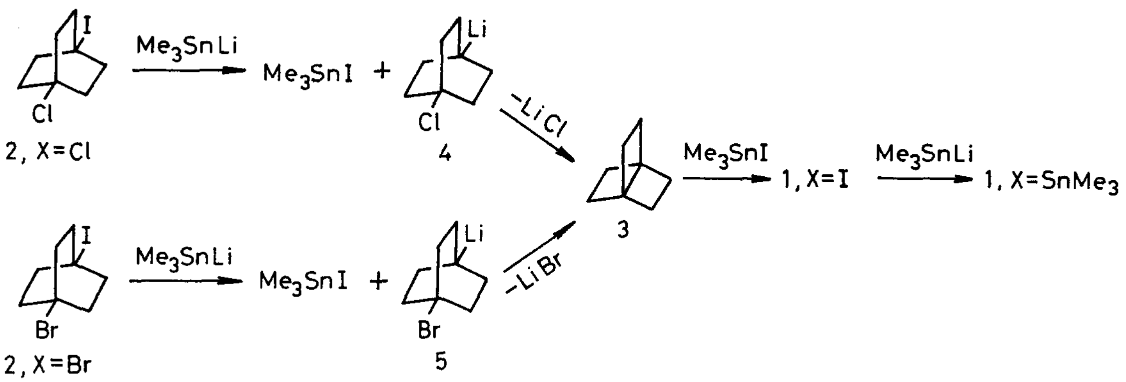
Summary: Stannylation of 1-bromo- and 1-chloro-4-iodobicyclo[2.2.2]octane with (trimethyltin) lithium indicate an abnormal leaving group mobility (Br>I>Cl).

In the course of an investigation of polar substituent effects in the bicyclo[2.2.2]octane (BCO)ring system we had occasion to synthesize a series of 4-substituted bicyclo[2.2.2]octyl-1-trimethylstannanes (1).[1] These compounds were prepared by treating the appropriate 4-substituted bicyclo[2.2.2]oct-1-yl iodides (2) with (trimethyltin)lithium (Me_3SnLi) in tetrahydrofuran at 0°C in the standard way.[2] Although a full description of these syntheses will be presented in a full paper in the near future, completely unexpected aspects of two of the preparations (X=Cl and Br) prompt this report which extends the mechanistic picture for such substitution (stannylation) processes[3-6] by arguing the possibility that the elusive [2.2.2]-propellane (3) (tricyclo[$2.2.2.0^{1,4}$]octane)[7] is functioning as a transient intermediate in these cases.

An analysis (^{13}C and ^{119}Sn nmr and mass spectrometry) of the crude sublimed reaction products from treatment of 2 (X=Cl and Br) with Me_3SnLi (1.3 equivalents; inverse-addition)[2] revealed, in each case, mixtures containing considerable amounts of the unreacted precursor iodide (2, X=Cl (ca. 50%) and Br (ca. 60%)) plus three derivatives of system 1. A small amount of hexamethylditin was also detected in each mixture. For the preparation involving the <u>bromide</u> (2, X=Br), the stannanes present in the appropriate product mixture (1, X=I, Br, and $Sn(CH_3)_3$) were in the ratio 4:2:1, respectively, whilst for the <u>chloride</u> (2, X=Cl) mixture the appropriate stannanes (1, X=Cl, I and $Sn(CH_3)_3$) were in the ratio 7.2:1.4:1, respectively. These results, at their face value, require the conclusion that the relative leaving group mobilities of bridgehead halides towards trimethylstannylation is Br>I>Cl. This order is of particular interest since it appears to conflict with what is known and generally assumed about these anionic replacements at bridgehead positions <u>viz.</u> that I is more mobile than Br and that bridgehead chlorides are unreactive.[3,8-10]

The finding of a distinctly abnormal leaving group order (Br>I>Cl) for the aforementioned anionic replacements raises intriguing mechanistic questions.[3-6] The available evidence suggests that these reactions at the bridgehead of polycyclic alkanes (systems for which typical S_N2 processes are precluded on structural grounds) proceed either by carbanionic[3,11,12] or radical[3] intermediates, or a combination (or mix) of both.[3] We believe the unprecedented results described above can best be explained by the predominance of carbanion formation via



the route outlined. Note, that whereas much of 5 is required to collapse to 3 in order to account for predominance of the iodide (1, X=I) over the bromide (1, X=Br), most of 4 must be trapped by Me$_3$SnI in order to ensure that the chloride (1, X=Cl) dominates in this particular case. This contrasting behaviour is perfectly reasonable given that Br is a much better leaving group than Cl in typical nucleophilic substitution processes.

It is important to emphasize that our results must be considered suggestive rather than definitive evidence for the existence of 3 as a transitory intermediate. Militating against the invocation of 3 is the apparent propensity of 4-halo-BCO-lithium derivatives to readily undergo Grob fragmentation to afford 1,4-dimethylenecyclohexane.[7b,13] However, a plausible explanation in terms of a dominant radical pathway is, at this time, not at all obvious to us since a halogen mobility order (Br>I) is demanded which conflicts starkly with the results of known electron transfer-induced substitution processes.[14] Furthermore, it also requires that bridgehead chlorides possess noticeable reactivity.

Additional studies are now in progress in an attempt to elucidate further the aforementioned situation.

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