

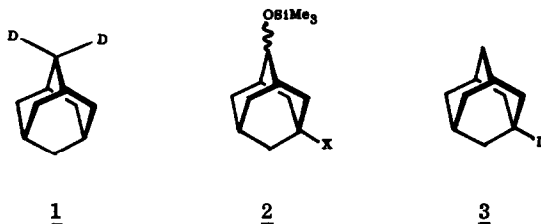
SET MECHANISM IN THE LITHIUM ALUMINUM DEUTERIDE REDUCTION
OF CHLOROADAMANTANES, AND ITS INDUCTION BY REMOTE SUBSTITUENTS

Sushil Srivastava and W. J. le Noble*

Department of Chemistry, State University of New York
Stony Brook, New York 11794, U.S.A.

Summary: The title reduction may lead to very incomplete isotopic substitution as a result of SET intrusion and the related intermediacy of radicals and hydrogen abstraction from the solvent, even though the halogen to be replaced is chlorine. Two examples are reported. In one of them, this mechanism is shown to be induced through five single bonds by an ether substituent separated from the chlorine by a rigid W-chain of saturated carbons.

We had a recent need to prepare 2,2-dideuterioadamantane (1), and the E- and Z-5-deuterio-2-adamantyl trimethylsilyl ethers 2-D. A survey of the information available on how best to deuterate either one of the two positions in adamantane turned up a report by Dubois et al¹ mentioning that they had obtained adamantane-1-d₁ (3) with 99% enrichment simply by treating 1-chloroadamantane with lithium aluminum deuteride (LAD) in refluxing n-butyl ether. This claim appeared to be supported by an extensive literature² on the reduction of



organic halides with lithium aluminum hydride (LAH), which has gradually evolved from the original view that it is simply an S_N2 displacement,^{3,4} to the assumption that hydride transfer must occur via a four-membered cyclic transition state,^{5,6} to the insight that free radicals must be involved,^{7,8} and recently, to the understanding that single electron transfer^{9,10} (SET) is the mode of reaction. Stereochemistry, substituent effects, deuterium incorporation and EPR were the criteria used in most of these studies; Chung⁹ has employed the ingenious

device of internal trapping of the intermediate radicals by means of an allyl group with especially telling effect.

All of this literature suggests that deuteriodehalogenation may be inefficient with respect to the isotope, but only if the halogen to be replaced is bromine or iodine. Indeed, Brown⁵ has been able to reduce mixed halocarbons such that the bromo- or iodo substituents are replaced by hydrogen but chlorine is not. Likewise, Ashby¹¹ reports that the hydride reduction of 1-hex-5-enyl bromides gives substantial amounts of cyclization products, but that of the corresponding chlorides does not. We could in fact find no mention in the literature of radical products arising from the LAH reduction of aliphatic or alicyclic monochlorides.

We attempted to prepare 1 from adamantanone by LAD reduction to the 2-adamantanol- α -d₁, conversion to the chloride with SOCl₂, and LAD reduction of this halide under Dubois' conditions (10:1 mole ratio of LAD to chloride in refluxing n-butyl ether). The first deuteration step was successful (99% D-incorporation, by mass spectrometry), but the last phase was not (45% incorporation of D₂; this second stage was somewhat variable, but the maximum isotopic yield of 1 observed was only 54%). The problem was then solved by an application of Djerassi's method¹² (reduction of the tosylhydrazone by means of NaBD₄ in methanol-d₁).

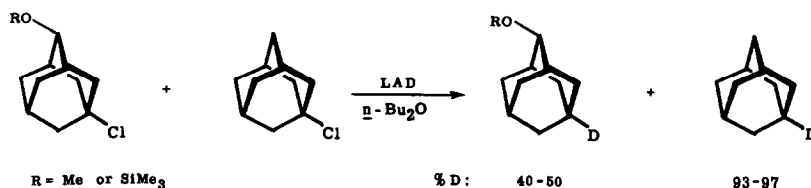
We fared no better with the LAD reduction of E-2-Cl under Dubois' conditions; only an average of 53% of D-incorporation was achieved in several experiments. A brief study was undertaken with both E-2-Cl and -Br in several solvents (Table I). The results show that the chloride consistently gives rise to somewhat higher isotopic substitution, but it is far from complete; the solvent effects are roughly parallel. However, any doubt that Dubois' report might be in error (the use to which 3 was put would not have revealed more modest enrichment) was subsequently removed by him by means of a mass spectrometric analysis of a sample still available: about 95% D-incorporation was found.¹³ A duplicate experiment with 1-chloroadamantane in our own laboratory confirmed this result exactly. Ultimately, we resorted to the use of THF-d₈ (99%) in order to achieve our goal. Even then, the E-2-D produced had only about 94% enrichment; this result supports the conclusion by Engel *et al* that hydrogen abstraction by the 1-adamantyl radical is strongly affected by tunnelling ($k_H/k_D = 26$).¹⁴

Table I
Percent^a Deuterium Incorporation^b into E-2-X

X	THF	Solvent ^c		
		Ether	Glyme	n-Bu ₂ O
Cl	35 ± 10 (18)	50 ± 2 (96)	53 ± 3 (4)	53 ± 3 (4)
Br	20 ± 5 (30) ^d	40 ± 5 (48)	45 ± 3 (4)	45 ± 3 (3)

(a) By mass spectrometry. (b) With LAD in the refluxing solvent. (c) Time is given in hrs in parentheses. (d) At room temperature.

While these samples were adequate for our purposes, we were intrigued by the contrasting behavior of E-2-Cl and 1-chloroadamantane. To make sure that we were not victimized by accidental minor differences in conditions—a factor so characteristic of free radical chemistry—, we reduced equimolar amounts of these two compounds together in the same mixture, and checked each mass-spectrometrically after GC separation. This experiment accurately confirmed the findings that had been made with each separately: 40% and 94%, respectively. Further experiments then showed that the effect is due to the oxygen atom rather than to the silicon: the E-methoxy analog also gives only limited deuteration (50%, and 97% in 1-chloroadamantane).



Clearly, the distant ether functionality is sufficient to depolarize the carbon-chlorine bond to such an extent that it begins to mimic the carbon-bromine bond in its behavior vis-à-vis hydride reducing agents, and it becomes subject to at least a major SET component in the reduction. Finally, we call attention to the fact that not only can this substituent exert surprisingly large effects across the rigid six membered ring, but the effect has a strong directional component as well. Thus, E- and Z-2-Cl, each together with 1-chloroadamantane, were deuterated to different extents: there is barely more than half as much D-incorporation in the E- isomer as in the Z-. We have reported on the symmetry-perturbing effects of 5-substituents in adamantanes elsewhere,¹⁵ and hope to comment further on these and related findings in a future publication.¹⁶

Acknowledgment. — We thank the National Science Foundation and the Donors of the Petroleum Research Fund for support, and Drs. J. E. Dubois and E. W. Della for correspondence.

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16. The possibility that the symptoms of a SET mechanism are mimicked by nucleophilic displacement of the tertiary adamantyl carbanions from chlorine by LAD (suggested by a Referee) can be excluded, in our opinion. The solvents were carefully freed from any proton donors before use by distillation from LAH, and the red color so typical of carbanions in THF is not observed even transiently. Furthermore, deuteration results are unchanged if D₂O work-up is used.

(Received in USA 2 July 1984)