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REDUCTIVE DECHLORINATION OF gem-CHLOROFLUOROCYCLOPROPANES WITH LITHIUM ALUMINIUM HYDRIDE. A STEREOSELECTIVE PROCESS.

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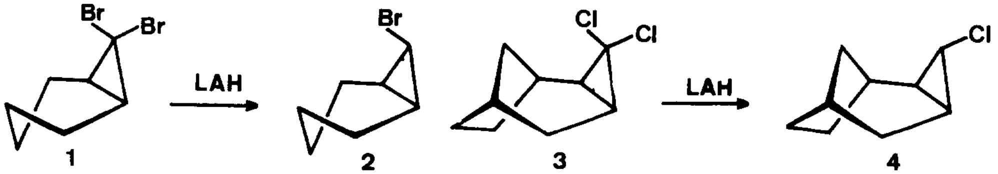
We have recently reported that lithium aluminium hydride (LAH), contrary to expectations of long standing, can bring about reductive dehalogenation of a wide variety of so-called inert organic halides in high yields (>80%)[1]. In particular, *gem*-dihalocyclopropanes undergo stepwise dehalogenation to give monohalocyclopropanes and cyclopropanes[2]. Furthermore, the environment of the *gem*-dihalo grouping appears to control the reduction course. 7,7-Dibromobicyclo-[4.1.0]heptane (1) gives mainly the *endo* product 2, while 3,3-dichlorotricyclo-$[4.2.1.0^{2,4}]$nonane (3) gives chiefly the *exo* product 4. This hint of a stereoselective process, taken together with the uncanny parallelism of the macroscopic behaviour of organotin hydrides and LAH[1,3], leads us to examine afresh the reactivity of *gem*-chlorofluorocyclopropanes on treatment with LAH[4].



Two pairs of syn-anti isomers (5, 8 and 9, 12) were prepared[5], separated and treated individually with a threefold excess of LAH in diglyme at 100° for 1.5 hours. In each case, reductive dechlorination occurred quantitatively to give a pair of fluoro epimers in which the original skeleton remains intact[7] (Table). Not only is the second epimer formed in sizeable amounts under these relatively mild reaction conditions, but the isomer ratio clearly reveals the operation of steric factors in the substrate. For the syn and anti-fluoronorcaranes 5 and 8, the overall course is one of retention of configuration at the fluorine-bearing carbon atom. Nevertheless, less retention is observed for the more strained anti isomer 8. The effect is more pronounced for the tricyclic pair 9 and 12 in which the syn-disposed substituents encounter severe non-bonded interactions with the contiguous methylene bridge. The anti isomer 12 still favours formation of retained product, but to a less marked extent. This trend away from retention takes a dramatic turn with syn isomer 9; the overall stereochemical course being inversion of configuration.

These findings are particularly informative about the mechanism of reduction of cyclopropyl halides. Firstly, the macroscopic process is stereoselective and not stereospecific as previously claimed[4]. Secondly, the product composition cannot be rationalized in terms of the simultaneous operation of two different transition states. Obviously both S_N1 and S_N2 processes as well as the recently proposed four-centre mechanism can all be ruled out[4]. It therefore follows that the results can only be explained by the formation of a cyclopropyl intermediate which tends to retain its configuration, but may invert if compelled to do so by virtue of intramolecular non-bonded interactions. Only two intermediates fit these criteria; a cyclopropyl radical or carbanion. In both cases, direct attack by metal hydride on chlorine can account for their formation. However, the two intermediates should subsequently react differently, and in distinguishable fashion, especially if lithium aluminium deuteride (LAD) is used as reagent.

Taking compound 8 by way of illustration, the derived cyclopropyl radical

(13) and carbanion (15) should display markedly different behaviour. The radical 13 confronted with its immediate, but inert, environment (deuterium chloride and aluminium deuteride radical) will abstract hydrogen preferentially from the protonic solvent. A mixed isotopic product 14 should result. In contrast, the carbanion 15 will capture a deuteron from its most acidic neighbour, deuterium chloride or aluminium deuteride, but not from the weakly acidic solvent. Thus the completely deuterated product 16 is expected.

In the actual experiment, 8 was heated with LAD in anhydrous diglyme at 100° for 1.5 hours under nitrogen. Extraction of the mixture with dry pentane afforded the deuterio analogues of 6 and 7 in which 100% incorporation of deuterium had occurred at the fluorine-bearing cyclopropyl carbon[8].

Apart from this strong indication that LAD and LAH reduction of gem-dihalocyclopropanes occurs via a cyclopropyl carbanion, it is also seen that reduction is already complete prior to the stage of the conventional aqueous work-up. Accordingly, the intermediacy of organometallic compounds derived from carbanions (or even radicals) is most unlikely.

REFERENCES

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(2) R.E. Erickson, R. Annino, M.D. Scanlon and G. Zon, J. Amer. Chem. Soc. 91, 1767 (1969); H. Yamanaka, R. Oshima, K. Teramura and T. Ando, J. Org.Chem. 37, 1734 (1972); D. Seyferth, H. Yamazaki and D.L. Alleston, ibid. 28, 703 (1963); S.J. Cristol, R.M. Segueira and C.H. DePuy, J. Amer. Chem. Soc. 87, 4007 (1965); W.E. Barnett and R.F. Koebel, Chem. Comm. 875 (1969).

(3) T. Ando, F. Namigata, H. Yamanaka and W. Fumasaka, J. Amer. Chem. Soc. 89, 5719 (1967), J. Org. Chem. 35, 33 (1970).

(4) H. Yamanaka, T. Yagi, K. Teramura and T. Ando, Chem. Comm. 380 (1971).

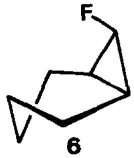
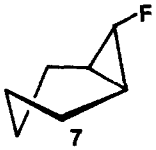
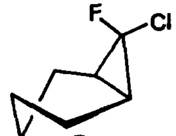
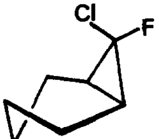
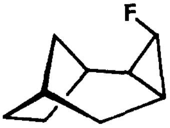
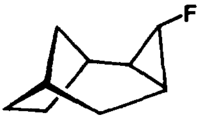
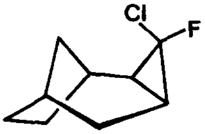
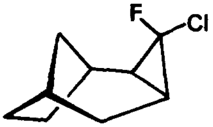
(5) Compounds 5, 8, 9 and 12 were prepared by the addition of chlorofluorocarbene (ref. 6) to cyclohexene and bicyclo[3.2.1]oct-2-ene. Separations were effected by gas chromatography (20% FFAP on Chromosorb W, 5 m, 80° and 100°C. Structure assignments were based on the values of $^3J_{FH}$, viz. 5.0, 18.0, 6.0 and 20.0 Hz respectively.

(6) P. Weyerstahl, D. Klamann, C. Finger, F. Nerdel and J. Bu-drus, Chem. Ber. 100, 1858 (1967).

(7) All products were separated by g.c. and gave correct elemental and mass spectral analyses. Structures of 6, 7, 10 and 11 were attributed on the basis of the $^2J_{FH}$ values, viz. 68.0, 65.0, 68.0, 61.1 Hz and the cyclopropylic $^3J_{HH}$ values, viz. 6.3, 2.0, 6.5 and 1.7 Hz respectively.

(8) The major product, 7,7-deuteriofluorobicyclo[4.1.0]heptane (analogous to 7) showed values of 10.0 and 22.0 Hz for $^2J_{FD}$ and $^3J_{FH}$ respectively.

Table. Reductive Dechlorination of Some Chlorofluorocyclopropanes with Lithium Aluminium Hydride

Reactant	Products **Syn**	 **Anti**	Isomer Ratio	Overall Course
	 **6**	 **7**		
 **5**	94 %	6 %	15	Retention
 **8**	10 %	90 %	9	Retention
	 **10**	 **11**		
 **12**	17 %	83 %	5	Retention
 **9**	29 %	71 %	2 5	Inversion