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# CYCLOPROPYL HALIDES. ELECTRON TRANSFER IN THE LITHIUM ALUMINUM HYDRIDE REDUCTION OF GEM-DIBROMO AND MONOBROMOCYCLOPROPANES.

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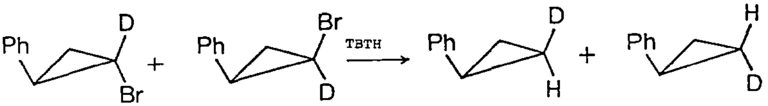
SUMMARY: The stereochemistry of reduction of mixtures of r-1-bromo-1-deuterio-c- and t-2-phenylcyclopropane and the cyclized products from 1,1-dibromo-2-(3-butenyl) cyclopropane upon reduction with lithium aluminum hydride give evidence of a configurationally equilibrated cyclopropyl radical as a reaction intermediate.

The reductive dehalogenation of *gem*-dihalocyclopropanes can be brought about with a variety of reagents.[1,2] Two of the more interesting reagents mechanistically are lithium aluminum hydride (LAH) and sodium bis(2-methoxyethoxy) aluminum hydride (SMEAH). Based on stereochemical results and the amount of deuterium incorporation in LAD reductions, four-centre,[3] radical,[4] and anion[5] mechanisms have been proposed for LAH reduction of *gem*-dihalocyclopropanes. Reductions with SMEAH have been proposed to proceed by an anion mechanism.[6] Recent studies have shown that reductions of aryl,[7] vinyl[8] and primary alkyl bromides[9] with LAH involve radical intermediates. The results presented herein give definitive evidence for configurationally equilibrated cyclopropyl radicals as intermediates in the LAH reductions of monobromo and *gem*-dibromocyclopropanes.

We have reduced mixtures of r-1-bromo-1-deuterio-c-2-phenylcyclopropane (*cis*-1-Br)[10] and its isomer, *trans*-1-Br, with tributyltin hydride (TBTH), LAH and SMEAH. The results are listed in Table I. Reduction of 70:30 and 3:97 mixtures, respectively, of *cis*-1-Br and *trans*-1-Br with TBTH (entries 1 and 5 in Table I) led to the similar 6:96 mixture of the cyclopropanes, trans- and



*trans*-1-Br *cis*-1-Br *cis*-2 *trans*-2 *cis*-2. This demonstrates that configurational equilibration of the radical[13] intermediate is complete before it is trapped by the TBTH. This is in keeping with the known properties of cyclopropyl radicals in general[16] and the 2-phenyl cyclopropyl radical in particular.[14] The reduction of mixtures of *cis*- and *trans*-1-Br with LAH in tetrahydrofuran or ether gives similar results (entries 3, 7 and 4,8 in Table I). Thus the LAH reductions, like those with TBTH, appear to proceed through a radical intermediate.

Table I. Stereochemistry of the TBTH, SMEAH and LAH Reductions of *cis*-1-Br and *trans*-1-Br.

| Entry | Reaction Conditions[a] | *cis*-1-Br : *trans*-1-Br[b] | *trans*-2 : *cis*-2[c] |
|---|---|---|---|
| 1 | A | 70:30 | 7:93 |
| 2 | B | 70:30 | 80:20 |
| 3 | C | 66:34 | 8:92 |
| 4 | D | 70:30 | 4:96 |
| 5 | A | 3:97 | 5:95 |
| 6 | B | 3:97 | 4:96 |
| 7 | C | 11:89 | 3:97 |
| 8 | D | 12:88 | 5:95 |

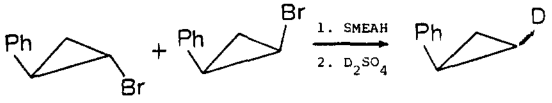
[a] A: TBTH, 100°, 90 min; B: SMEAH, PhH, 100°, 5.5 h followed by quench with 20% $H_2SO_4$; C: LAH (1 M in THF), 70°, 12 h, followed by quench with saturated aqueous $Na_2SO_4$; D: LAH (1 M in $Et_2O$), 26°, 48h followed by quench with saturated aqueous $Na_2SO_4$.

[b] Ratios determined by GPC; estimated error ± 2%.

[c] Ratios determined by $^1H$ NMR integration with comparison to authentic samples of *trans*-[8] and *cis*-2[9].

To rule out an anion as an intermediate in the LAH reductions we reduced a mixture of *cis*-1-Br and *trans*-1-Br (70:30) with SMEAH, a reagent known[6] to produce cyclopropyl anions. The result was predominant (entry 2 in Table I) retention of configuration. Cyclopropyl anions are known to undergo slow configuration inversion, the rate of inversion depending on the reaction conditions (solvent, gegen ion, etc.) and the α-substituent.[15]

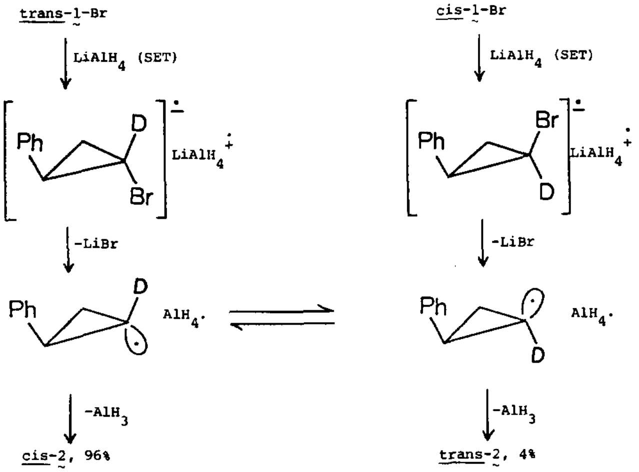
Insight into the nature of the product forming step in the LAH and SMEAH reductions was gained by testing for deuterium incorporation through the work-up media. Thus, reduction of a 66:34 mixture of *cis*- and *trans*-3-Br with SMEAH followed by a quench of the reaction mixture with 20% $D_2SO_4$ produced phenylcyclopropane (2) with 94% deuterium incorporation. In marked contrast, reduction of a similar mixture of *cis*- and *trans*-3-Br with LAH followed by a $D_2O$ quench



*trans*-3-Br *cis*-3-Br 2

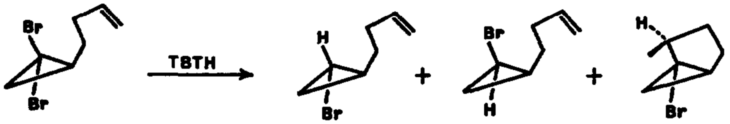
gave phenylcyclopropane with no deuterium incorporation. However, reduction with LAD in THF followed by an $H_2O$ quench gave phenylcyclopropane with 75% deuterium incorporation. These results are consistent with the intermediates proposed above. The anion produced in the SMEAH reduction survived the reduction conditions to be protonated (deuterated) upon work up with sulfuric acid. However, the radical produced in the LAH (LAD) reductions did not survive the reaction conditions but abstracted a hydrogen or deuterium from the reaction media before work-up.

A mechanism for the LAH reductions consistent with our results and recent findings concerning the LAH reduction of aryl[7], vinyl[8], and primary alkyl bromides[9] is outlined below.



A single electron transfer (SET) from LAH to *cis*- or *trans*-**1**-Br gives a radical-anion-radical-cation pair. Loss of lithium bromide produces a radical pair which gives reduction products by hydrogen atom transfer. Inversion of the secondary cyclopropyl radical occurs faster than hydrogen atom transfer.[13] However, hydrogen atom transfer to the equilibrated radical must be faster than a second electron transfer to give a cyclopropyl anion which would have incorporated deuterium upon work-up with $D_2O$.

Finally, a critical test of a mechanistic scheme invoking radicals as intermediates is the generation of such an intermediate in a system where cyclization or rearrangement can occur. A classical example of such a system is the 5-hexenyl radical which cyclizes irreversibly ($k_c$ ~$1 \times 10^{-5}$ $s^{-1}$) to the cyclopentylmethyl radical.[17] The 2-(3-butenyl) cyclopropyl radical has also been shown to cyclize when generated in the TBTH reduction[18] of 1,1-dibromo-2-(3-butenyl) cyclopropane (**4**). A comparison of the results obtained in the reduction of **4** with TBTH, LAH and SMEAH are shown below[19].



4 5 6 7

| | | | | | |
|---|---|---|---|---|---|
| TBTH, neat | 33 | : 52 | : | 13 |
| 1 M, LAH | 30 | : 33 | : | 37 |
| SMEAH, 70% in PhH | 74 | : 26 | : | - |

The formation of cyclized product (7) in the LAH reduction and its absence under SMEAH reaction conditions gives further support to the mechanistic conclusions discussed above.

## REFERENCES AND NOTES

1. For reviews see R. Barlet and Y. Vo-Quang, Bull. Soc. Chim. Fr., 10, 3729 (1969) and A. R. Pinder, Synthesis, 425 (1980).
2. J. T. Groves and K. M. Ma, J. Am. Chem. Soc., 96, 6527 (1974), and references therein.
3. H. Yamanaka, T. Yagi, K. Teramura and T. Ando, Chem. Commun., 380 (1970).
4. J. Hatern and B. Waegell, Tetrahedron Lett., 2023 (1973).
5. C. W. Jefford, U. Burger, M. H. Laffer and T. Kabengele, Tettrahedron Lett., 2483 (1973).
6. L. K. Syndes and L. Skattebol, Acta Chem. Scand. B 32, 632 (1978).
7. S. Chung and F. Chung, Tetrahedron Lett., 2473 (1979).
8. S. Chung and F. Chung, J. Org. Chem., 45, 3513 (1980).
9. E. C. Ashby, R. N. DePriest, and A. B. Goel, Tetrahedron Lett., 1763 (1981).
10. Mixtures of cis-1-Br and trans-1-Br were prepared from 1,1-dibromo-2-phenylcyclopropane by reduction with Zn(Cu)-$Et_2O$-$D_2O$[11] and n-butyllithium at -95 C followed by a quench with EtOD[12]. The former reduction conditions giving a cis-1-Br rich mixture and the latter a trans-1-Br mixture.
11. R. M. Blankenship, K. A. Burdett and J. S. Swenton, J. Org. Chem., 39, 2300 (1974).
12. K. Kitatani, T. Kujamo and H. Nozaki, Bull. Chem. Soc. Jpn., 50, 3288 (1970).
13. The same radical (undeuterated) was found to equilibrate rapidly when generated from mixtures of cis- and trans-1-Br with napthalene radical anion[14].
14. G. Boche and D. R. Schneider, Tetrahedron Lett., 2327 (1978); see also G. Boche, D. R. Schneider and H. Wintermayr, J. Am. Chem. Soc., 102, 5697 (1980).
15. M. P. Periasamy and H. M. Walborsky, J. Am. Chem. Soc., 99, 2631 (1977) and references therein.
16. H. M. Walborsky, Tetrahedron, 37, 1625 (1981).
17. C. Walling, J. H. Cooley, A. A. Ponaras and E. J. Racah, J. Am. Chem. Soc., 88, 5361 (1966); D. Lal, D. Griller, S. Husband and K. U. Ingold, J. Am. Chem. Soc., 96, 6355 (1974).
18. C. Descains, M. Julia and H. V. Sang. Bull. Soc. Chim., Fr., 4087 (1971).
19. The details of these experiments will be reported in a full paper, J. Org. Chem. to be submitted.

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