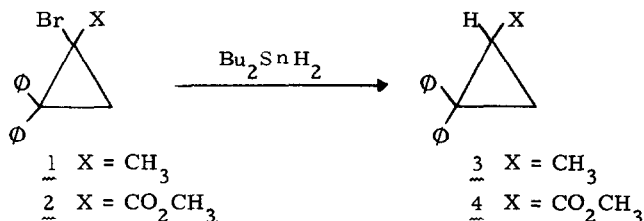# NET RETENTION IN THE REDUCTION OF OPTICALLY ACTIVE CYCLOPROPYL

BROMIDES BY DI-n-BUTYLTIN DIHYDRIDE. CAGE

REDUCTION OF A RAPIDLY INVERTING CYCLOPROPYL RADICAL.

L. J. Altman and Timothy R. Erdman

Department of Chemistry, Stanford University, Stanford, California 94305

In a preceding communication[1] we described the reduction of optically active cyclopropyl

bromides in neat triphenyltin hydride to yield products with net inversion of stereochemistry.

This result was ascribed to the backside cage reduction of a rapidly inverting cyclopropyl

radical,[2] the front side of which was shielded by the departing triphenyltin bromide. If this

explanation is correct, one would predict the possibility of the front side cage reduction of a

rapidly inverting cyclopropyl radical by an appropriate choice of reducing agent.[3] We wish

to report our observation of such a reduction.

$$\underline{1} \quad X = CH_3 \qquad \underline{3} \quad X = CH_3$$
$$\underline{2} \quad X = CO_2CH_3 \qquad \underline{4} \quad X = CO_2CH_3$$

The results of the reduction of optically active cyclopropyl bromides by di-n-butyltin

dihydride are reported in Table I. Evidence for the free-radical nature of these reductions is

obtained from the observation that addition of 1% of the radical scavenger galvinoxyl to the

reaction mixture of $\underline{1}$ in hexadecane strongly inhibits the reduction (an inhibition period of

somewhat greater than 24 hours was observed).

It is interesting to note that the enantiomeric excess[4] of the product increases as the

concentration of reducing agent decreases! This trend is inconsistent with the rapid non-cage

reduction of a cyclopropyl radical whose inversion rate is on the same order as the rate of

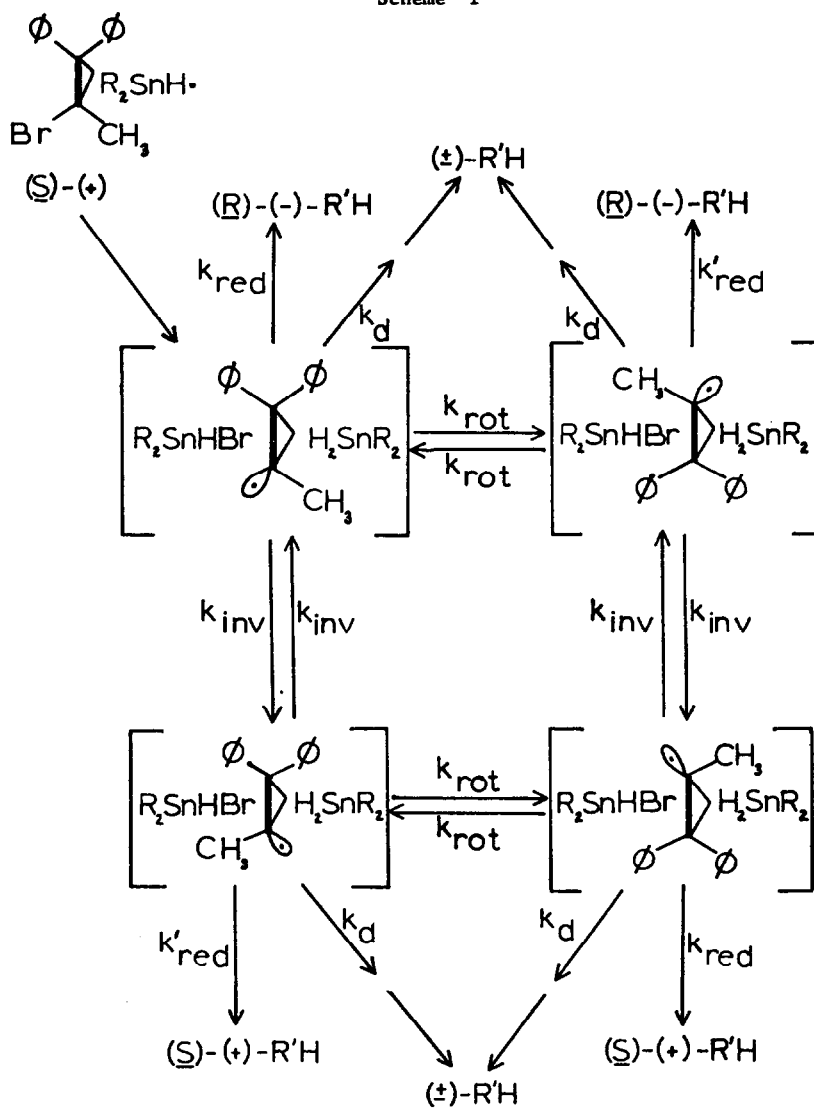Table I.   Results of Di-n-butyltin Dihydride Reductions [a]

Starting Material	(Bu_2SnH_2) M	Solvent	η (c.p.)	$[\alpha]_D$ [b] Product	% Enantiomeric Excess[4]
(+)-1	.60	hexane	0.48	$-0.18 \pm .02$	0.14
(+)-1	.59	hexadecane	2.25	$-1.35 \pm .17$	1.06
(-)-1	.61	paraffin oil	29	$+3.17 \pm .17$	2.50
(-)-1	.40	paraffin oil	43	$+4.41 \pm .19$	3.47
(-)-1	4.98	Bu_2SnH_2	1.05	$+0.55 \pm .04$	0.43
(-)-2	.71	paraffin oil	22.3	$+5.81 \pm .15$	2.77
(-)-2	.31	paraffin oil	51	$+8.45 \pm .10$	4.03
(-)-2	.173	paraffin oil	66	$+12.26 \pm .29$	5.84
(-)-2	.088	hexane	0.45	$+0.87 \pm .06$	0.41
(-)-2	.088	hexadecane	2.47	$+3.71 \pm .13$	1.77
(+)-2	.088	paraffin oil	75.8	$-12.32 \pm .15$	5.87

(a)   All reductions were carried out at 30° by the addition of a tenfold molar excess of the tin hydride to a solution of the starting material except for the reaction in neat tin hydride.

(b)   All products had net retention of configuration and were chromatographically pure; analyses of all samples gave satisfactory C, H values and showed less than 0.01% Br.

reduction. We prefer to interpret our results in terms of the mechanism presented in Scheme I, where k_{red} and k'_{red} are not the usual second order rate constants, but are first order rate constants for the conversion of the cage material to reduced product, k_{rot} is the rate constant for a 180° change in orientation of the cyclopropyl radical with respect to the asymmetric environment, and the inversion rate is assumed to be fast in comparison with the out of cage reduction rate. An extrapolation of our results obtained at low concentrations of reducing agent to infinite viscosity should yield the enantiomeric excess[4] in the pure cage reduction. The results of such an extrapolation yield an enantiomeric excess for the reduction of 2 of approximately 6%.[5] The only way to get inverted product in the cage reduction at low concentrations of reducing agent is by both an inversion and rotation of the initially produced radical. Thus, both inversion and rotation at high viscosities are faster than reduction.

Scheme I

ϕ ϕ

$R_2SnH\cdot$

Br CH₃

(S)-(+)

(R)-(-)-R'H   (±)-R'H   (R)-(-)-R'H

k_{red} k_d k_d k'_{red}

ϕ ϕ CH₃

R_2SnHBr H_2SnR_2 $\xrightarrow{k_{rot}}$ R_2SnHBr H_2SnR_2

CH₃ $\xleftarrow{k_{rot}}$ ϕ ϕ

k_{inv} k_{inv} k_{inv} k_{inv}

ϕ ϕ CH₃

R_2SnHBr H_2SnR_2 $\xrightarrow{k_{rot}}$ R_2SnHBr H_2SnR_2

CH₃ $\xleftarrow{k_{rot}}$ ϕ ϕ

k'_{red} k_d k_d k_{red}

(S)-(+)-R'H   (±)-R'H   (S)-(+)-R'H

REFERENCES

1.   L. J. Altman and B. W. Nelson, J. Amer. Chem. Soc., 91, 5163 (1969).

2.   (a) L. J. Altman and J. C. Vederas, Chem. Commun., 895 (1969); R. W. Fessenden and R. H. Schuler, J. Chem. Phys., 39, 2147 (1963); H. M. Walborsky, C. Chen, and J. L. Webb, Tetrahedron Lett., 3551 (1964); D. E. Applequist and A. H. Peterson, J. Amer. Chem. Soc., 82, 2372 (1960).

(b) T. Ando et al, J. Org. Chem., 35, 33 (1970) report a case of reduction of a slowly inverting cyclopropyl radical.

3.   (a) The only authenticated example of a cage reduction in the cyclopropyl series is that of H. M. Walborsky and J. Chen, J. Amer. Chem. Soc., 89, 5499 (1967).

(b) Other radical reductions in the cyclopropyl series which possibly have cage components are J. Jacobus and D. Pensak, Chem. Commun., 400 (1969); M. J. S. Dewar and J. M. Harris, J. Amer. Chem. Soc., 91, 3652 (1969); and H. M. Walborsky, F. P. Johnson and J. B. Pierce, ibid., 90, 5222 (1968).

4.   The percent enantiomeric excess is defined as $100 \times (A-B)/(A+B)$ where A is the major enantiomer.

5.   Obtained by plotting $1/\eta$ vs. 1/e. e. (see R. M. Noyes in "Progress in Reaction Kinetics", G. Porter, Ed., Pergamon Press Ltd., London, 1961), and assuming that k_d is the only rate constant that is viscosity dependent. The viscosity dependence of k_{rot} is open to question (see C. P. Smyth, Special Publication No. 20, The Chemical Society, London, 1965, pp. 1-14 and references cited therein). Clearly, even at the relatively high viscosities employed k_{rot} is still fast in comparison to k_{red}.

This can be compared to a value of approximately 35% obtained by Walborsky and Chen[3] in the cage disproportionation of the 1-methyl-2, 2-diphenylcyclopropyl radical. Thus, Bu_2SnHBr must be a poorer hydrogen atom donor than another radical.