Note

LAH induced stereoselective dehalogenation of vicinal-dihalides *via* single electron transfer

Jitender M Khurana*[†] & Amita Puri (née Gogia)

Department of Chemistry, University of Delhi,
Delhi 110 007, India

Received 29 April 1997; accepted 8 July 1997

Vicinal-dihalides have been observed to undergo dehalogenation to alkenes with LAH under nitrogen atmosphere. The elimination is stereoselective and no reduced products are formed. The possibility of LAH acting as a hydride transfer reagent or as a base has been eliminated and a SET mechanism has been proposed for these reactions.
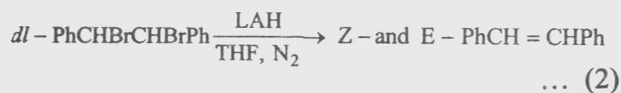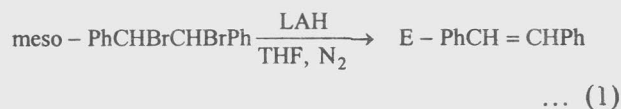
Complex metal hydrides are extremely versatile reagents for the reduction of a wide variety of organic functional groups[1,2]. Among these, lithium aluminium hydride (LAH) is the reagent of choice for rapid reduction of alkyl, aryl and aralkyl halides[3]. Different mechanisms have been proposed for the reduction of halides. A four-centered transition state[3a] an S_N2 displacement pathway[4] or prior ionization of halides followed by hydride attack[5] have been proposed. But aryl, vinyl, bridgehead and cyclopropyl halides are generally inert towards an S_N2 displacement and a significant contribution of radicals has been reported in their reactions with LAH[6]. Ashby *et al.*[7] have also proposed significant evidence in favour of the radical pathway.

The *gem*-dihalocyclopropanes are also reported to undergo reduction *via* four-centered transition state[8], carbanion[9] or radicals[10]. However, the lack of investigations on the reduction of vicinal-dihalides is conspicuous. Trevoy and Brown[11] reported either the formation of alkenes or a reduced product from three different vicinal-dihalides and proposed alkene formation by nucleophilic displacement on halogen and the reduced product by the hydride attack on the dihalide. However, both

[†]Address for correspondence: Chemistry & Chemical Engineering Laboratories, SRI International, 333 Ravenswood Avenue, Menlo Park, CA 94025, USA.

these pathways appear to be improbable. King and Pews[12] proposed ionic pathways in the dehalogenation of certain vicinal-dihalides but overlooked the radical pathways. We, therefore, decided to investigate the reactions of some 1, 2-dihalides with LAH. We chose meso- and *dl*-stilbene dibromides as model substrates which could also serve as mechanistic probes to understand the stereochemistry of the products.

Results and Discussion

In this paper, we report the dehalogenation of vicinal-dihalides with LAH to alkenes in THF under inert atmosphere. Though LAH is known to reduce halides, no reduction products (bibenzyls) were obtained in any of the reactions. We observed complete debromination of meso-stilbene dibromide to *E*-stilbene by refluxing with LAH in THF or with a clear solution of LAH in THF under nitrogen atmosphere. Though *E*-stilbene was obtained exclusively from meso-stilbene dibromide, *dl*-stilbene dibromide resulted in a mixture of *E*- and *Z*-stilbenes with *Z*-stilbene as the predominant products (Eqs 1 and 2). This observation suggests that the dehalogenations are proceeding

$$\text{meso} - \text{PhCHBrCHBrPh} \xrightarrow[\text{THF, N}_2]{\text{LAH}} E - \text{PhCH} = \text{CHPh}$$

$$\qquad \dots (1)$$

$$dl - \text{PhCHBrCHBrPh} \xrightarrow[\text{THF, N}_2]{\text{LAH}} Z - \text{and } E - \text{PhCH} = \text{CHPh}$$

$$\qquad \dots (2)$$

stereoselectively (runs 1-10; Table I). The exclusive formation of substituted stilbenes has also been observed in the reactions of meso-*p*, *p'*-dichlorostilbene dibromide (run 11), meso-*p*, *p'*-dimethylstilbene dibromide (run 12), meso-*m*, *m*-dimethylstilbene dibromide (run 13) and meso-stilbene dichloride (run 14). The reactions of 9, 9'-dibromobifluorenyl and tolan dibromide with LAH also produced the alkenes, namely bifluorenylidene (run 15) and tolan (run 16), respectively. No debromination was observed in the reactions of *trans*-1, 2-dibromocyclohexane (run 17) and 1, 2-

Table I—Reactions of vicinal-dihalides with lithium aluminium hydride in THF

Run	Substrate ArCHBrCHBrAr	Mode[a]	Molar ratio Substrate:LAH[b]	Time (hr)	% Yield[c] E-ArCH=CHAr
1	meso-Stilbene dibromide	~	1:4	36	59
2	meso-Stilbene dibromide	~	1:6	36	70
3	meso-Stilbene dibromide	Δ	1:4	7	76
4	meso-Stilbene dibromide	Δ	1:6	7	96
5	meso-Stilbene dibromide	Δ	1:4	7	72
6	meso-Stilbene dibromide	Δ	1:6	7	76
7	meso-Stilbene dibromide	Δ	1:8	7	89
8	dl-Stilbene dibromide	~	1:6	36	31.37[d]
9	dl-Stilbene dibromide	Δ	1:6	48	21.20[e]
10	dl-Stilbene dibromide	~	1:6	24	−f
11	meso-p, p′-Dichloro stilbene dibromide	Δ	1:6	7	87
12	meso-p, p′-Dichloro stilbene dibromide	Δ	1:6	7	73
13	meso-p, p′-Dichloro stilbene dibromide	Δ	1:1	15	81
14	meso-Stilbene dichloride	Δ	1:6	15	41.77[g]
15	9, 9′-Dibromobifluorenyl	Δ	1:6	7	45
16	Tolan dibromide	Δ	1:6	9	85
17	trans-1, 2-Dibromocyclohexane	~	1:6	48	h
18	1, 2-Dibromooctane	~	1:6	48	h

[a]Mode ~=Stirring at ambient temperature; Δ=Reflux.
[b]Solid LAH was used in all the reactions except in runs 5, 6, 7 and 10 in which a clear solution of LAH was used.
[c]Isolated yields unless otherwise specified.
[d]HPLC yield: 50.76% of Z-stilbene was also formed.
[e]HPLC yield: 40.62% of Z-stilbene was also formed.
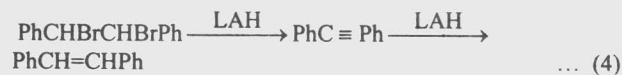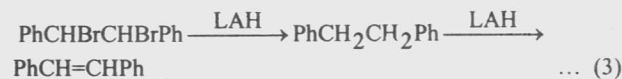[f]31.56% of Z-stilbene (HPLC yield) was also formed.
[g]HPLC yield.
[h]No reaction.

dibromooctane (run 18) even after 48 hr. The results are listed in Table I.

The absence of any completely reduced or partially reduced product eliminates the possibility of a direct hydride transfer (nucleophilic substitution, S_N2) in our reactions. The absence of any bibenzyl derivative or 9, 9′-bifluorenyl also eliminates the possibility of a four-centred transition state in our reactions.. The formation of stilbenes from 1, 2-dihalides wherein LAH acts as a hydride transfer reagent can also be conceived to be proceeding by (i) dehydrogenation of the initially formed bibenzyl derivative, (ii) by two successive HBr eliminations to give alkynes followed by reduction, (iii) by E_2 elimination of vicinal-dihalides or (iv) by single electron transfer from LAH via radical-anions. The first possibility has been eliminated as no bibenzyl was detected in the reactions of meso- and dl-stilbene dibromides when monitored at regular intervals. The recovery of unchanged bibenzyl from its reaction with LAH under reflux for 24 hr (Eq. 3) further eliminates the first possi-

bility. In a similar manner, absence of tolan in the reactions of meso- and dl-stilbene dibromides when monitored continuously as well as the quantitative recovery of tolan from its reaction with LAH under reflux for 24 hr in an independent reaction rules out the second possibility (Eq. 4). The formation of bifluorenylidene in the reaction of 9, 9′-dibromobifluorenyl—which has no α-hydrogen—further substantiates this proposal.

$$PhCHBrCHBrPh \xrightarrow{LAH} PhCH_2CH_2Ph \xrightarrow{LAH}$$
$$PhCH=CHPh \qquad \qquad \cdots (3)$$

$$PhCHBrCHBrPh \xrightarrow{LAH} PhC \equiv Ph \xrightarrow{LAH}$$
$$PhCH=CHPh \qquad \qquad \cdots (4)$$

Since the eliminations in question are stereoselective and not stereospecific, E_2 elimination is highly unlikely in our reactions (third possibility). However, the stereoselective elimination could be conceived to be resulting from isomerization of Z-stilbenes—formed initially by E_2 elimination—to E-stilbene with LAH under experimental condi-
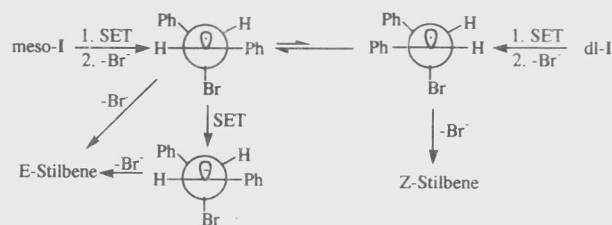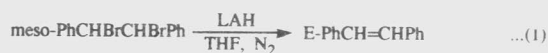
tions. But the absence of any *E*-stilbene in the reaction of *Z*-stilbene with LAH under reflux for 24 hr eliminates the possibility of any isomerization during the course of our reactions. The eliminations are, therefore, undoubtedly stereoselective and not stereospecific as would be expected from E_2 eliminations.

Therefore, we propose that LAH acts as a single electron transfer (SET) reagent to give radical-anions of the vicinal-dihalides which undergo heterolytic cleavage to the halobenzylic radicals and halide ion. The halobenzylic radicals could lose a halogen atom rapidly to give the corresponding olefin or accept another electron[6,7] to give the halo-carbanion. Alkenes are obtained from the carbanions by loss of a halide ion (E_2 elimination). The *anti* alignment of halo radical/carbanion from meso-stilbene dibromide does not favour any bond-rotation unlike the halo radical/carbanion from *dl*-stilbene dibromide which can equilibrate rapidly to a more stable conformation[13], before the halide radical/ion is lost, resulting in a mixture of *E*- and *Z*-stilbenes as shown in Scheme I.

The observed order of reactivity in our reactions is Br>Cl since only ~42% of dechlorination was observed in the reaction of meso-stilbene dichloride with LAH after 10 hr under reflux (run 14) unlike meso-stilbene dibromide which yielded *E*-stilbene quantitatively (run 4) in 7 hr. This order is in agreement with the known order of reactivity I>Br>Cl>F in electron transfer reactions[14]. The formation of a small amount of 1-bromo-1, 2-diphenylethane in the raction of meso-stilbene dibromide in the presence of ten molar excess of cumene further supports our proposal. The absence of any debromination in the reactions of *trans*-1, 2-dibromocyclohexane and 1, 2-dibromooctane may be due to large difference in HOMO-LUMO. Recently we have observed the formation of *E*-stilbene in the reactions of benzal bromide and benzal chloride with LAH under reflux (50.1% and 26.6%) after 10 and 24 hr, respectively. This also suggests the intervention of free radicals in the reactions of benzylic dihalides.

Experimental Section

General. Melting points were recorded on Labequip apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Perkin-Elmer model R-

$$meso\text{-PhCHBrCHBrPh} \xrightarrow[\text{THF, N}_2]{\text{LAH}} E\text{-PhCH=CHPh} \quad \ldots(1)$$

$$dl\text{-PhCHBrCHBrPh} \xrightarrow[\text{THF, N}_2]{\text{LAH}} Z\text{- and } E\text{-PhCH=CHPh} \quad \ldots(2)$$

$$\text{PhCHBrCHBrPh} \xrightarrow[\text{X}]{\text{LAH}} \text{PhCH}_2\text{CH}_2\text{Ph} \xrightarrow[\text{X}]{\text{LAH}} \text{PhCH=CHPh} \quad \ldots(3)$$

$$\text{PhCHBrCHBrPh} \xrightarrow[\text{X}]{\text{LAH}} \text{PhC}\equiv\text{CPh} \xrightarrow[\text{X}]{\text{LAH}} \text{PhCH=CHPh} \quad \ldots(4)$$

Scheme I

32 (90 MHz) and Hitachi FT-NMR (60 MHz). HPLC analyses were carried out using ODS-18 Zorbax (150 mm×4.6 mm) column using methanol as eluent on Shimadzu instrument model LC-4A. All the dibromides were prepared by known procedures. LAH (Aldrich) was used after estimation by the amount of hydrogen gas evolved on reaction with aqueous glycerol[2]. The clear solution of LAH in THF was estimated by determining the amount of iodine which reacts with LAH[15].

General procedure. In a typical procedure (run 6), 1 mmole of meso-stilbene dibromide (0.340 g) was dissolved in 50 mL of THF in a 100 mL 2-necked round-bottomed flask fitted with a reflux condenser and a mercury trap. The reaction mixture was flushed with nitrogen for 15 min and LAH (6 mmoles, 0.2277 g) added to the solution. The system was sealed and a vigorous reaction ensued. The reaction mixture was refluxed (see Table I). The progress of the reaction was monitored by TLC. After disappearance of the starting material (7 hr), the unreacted LAH was destroyed by careful dropwise addition of water followed by 30 mL of 10% HCl. The product(s) were extracted with dichloromethane (3×20 mL). The combined dichloromethane extract was washed with 5% NaHCO$_3$ solution (1×10 mL), water (1×10 mL) and dried over anhyd. MgSO$_4$. The solvent was removed on a Buchi rotary evaporator and the product dried under vacuum. The dried product was

identified to be *E*-stilbene (0.173 g, 96%) by m.p., mixed m.p. and NMR spectra.

The products in runs 1-5 were separated by ether from the starting material. The product in run 12 was separated by methanol. The reactions with clear solution of LAH were performed by addition of LAH solution to the substrate under nitrogen atmosphere followed by stirring or reflux (see Table I).

Acknowledgement

References and Notes

1   *Modern synthetic reactions,* 2nd edition, edited by H O House (W.A. Benjamin Inc., Menlo Park, CA) 1972.

2   *Advanced organic chemistry; Reaction mechanisms and structure,* 3rd edition, edited by J March, Wiley Eastern Ltd, 1991.

3   (a) Brown H C & Krishnamurthy S, *J Org Chem,* 34, **1969,** 3918.
    (b) Krishnamurthy S & Brown H C, *J Org Chem,* 45, **1980,** 849.
    (c) Krishnamurthy S, *J Org Chem,* 45, **1980,** 2550.
    (d) Krishnamurthy S & Brown H C, *J Org Chem,* 47, **1982,** 276.

4   (a) Eliel E L, *J Am Chem Soc,* 71, **1940,** 3970.
    (b) Eisenbaumer R L & Mosher H S, *J Org Chem,* 44, **1979,** 600.
    (c) Maiter D J, Wotiz H J & Hollingsworth C A, *J Am Chem Soc,* 78, **1956,** 1311.
    (d) Cram D J & Rickborn B, *J Am Chem Soc,* 83, **1961,** 2178.
    (e) Parry R J & Kunitani H G, *J Am Chem Soc,* 98, **1976,** 4024
    (f) Levine S G & Gopalkrishnan B, *Tetrahedron Lett,* **1979,** 699.

5   (a) Paquette L A & Storm P C, *J Org Chem,* 35, **1970,** 3390.

    (b) Story R P & Saunders M, *J Am Chem Soc,* 84, **1962,** 4876.
    (c) Corriu R J P, Fernandez J M & Guerin C, *Tetrahedron Lett,* **1978,** 3391

6   (a) Chung S K & Chung F, *Tetrahedron Lett,* **1979,** 2473.
    (b) Chung S K, *J Org Chem,* 45, **1980,** 3513.
    (c) Chung S K & Filmore K L, *J Chem Soc Chem Commun,* **1983,** 358.
    (d) Beckwith A L J & Goh S H, *J Chem Soc, Chem Commun,* **1983,** 905.
    (e) Singh P R, Nigam A & Khurana J M, *Tetrahedron Lett,* **1980,** 4753.
    (f) Singh P R, Khurana J M & Nigam A, , *Tetrahedron Lett,* **1981,** 2901.

7   (a) Ashby E C, Goel A B & Depriest R N, *Tetrahedron Lett,* **1981,** 3729.
    (b) Ashby E C, Depriest R N & Goel A B, , *Tetrahedron Lett,* **,1981,** 1763.
    (c) Ashby E C, Depriest R N & Pham T N, *Tetrahedron Lett,* **1983,** 2825.
    (d) Ashby E C, Depriest R N, Goel A B, Wenderoth B & Pham T N, *J Org Chem,* 49, **1984,** 3545.
    (e) Ashby E C & Pham T N, *J Org Chem,* 51, **1986,** 3598.
    (f) Ashby E C, *Acc Chem Res,* 21, **1988,** 414.
    (g) Ashby E C, Weldor C O & Doctorovich F, *Tetrahedron Lett,* **1993,** 7235 and references cited therein.

8   Yamanaka H, Yagi T, Terarnura K & Ando T, *J Chem Soc Chem Commun,* **1971,** 380.

9   Jefford C W, Kirkpatrick D & Delay F, *J Am Chem Soc,* 94, **1972,** 8905.

10 Jefford C W, Burger U, Laffer M H & Kabengele T, *Tetrahdron Lett,* **1973,** 2483.

11 Trevoy L W & Brown W C, *J Am Chem Soc,* 71, **1949,** 1675.

12 King J F & Pews R G, *Can J Chem,* 42, **1964,** 1294.

13 The anti alignment in meso- and *dl*-stilbene dichlorides though favoured by orbital symmetry rules is opposed in the latter case conformationally by a free energy difference of 4.4 cal/mol; Fischer G, Muszkat K A & Fischer E, *J Chem Soc B,* **1968,** 1156.

14 Bunnet J F, *Acc Chem Res,* 11, **1978,** 413.

15 Vogel A I, *Textbook of practical organic chemistry,* 4th edition (ELBS/Longman) 1987.