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CONVERSION OF 2-ISOXAZOLINES INTO AZIRIDINES BY LITHIUM ALUMINUM HYDRIDE REDUCTION*

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Abstract—It is shown that the reduction of some of 2-isoxazolines with LAH gives the corresponding aziridines, in a wide range of yields depending upon the substituent effects of the 2-isoxazolines. For example, 2-isoxazolines bearing a Ph group at C_4-position afford the aziridines in almost quantitative yields, but those having a Me group instead of the Ph group at the same position furnish the aziridines in poor yields. In addition, kinetics and mechanism of aziridine formation from 2-isoxazolines are examined in comparison with those of aziridine formation from an oxime and its O-methyl ether. This reaction is a simple and convenient method for the synthesis of aziridines.

RECENTLY, we reported a new method for the synthesis of aziridines by reduction of oximes with LAH.[2] It was also demonstrated that the reduction of not only the oxime itself but also its O-acetate and O-methyl ether yielded the same aziridine in almost equal yields:[3] LAH reduction of dibenzylketoxime (Ia) in THF gave *cis*-2-phenyl-3-benzylaziridine (II) in 92·5% yield, the same treatment of the O-acetate (Ib) and the O-methylether (Ic) afforded the identical aziridine in 87·5 and 90·3% yields, respectively. These findings led us to the expectation that the LAH reduction of 2-isoxazolines might also lead to aziridine derivatives, since 2-isoxazolines can be regarded as internal O-alkyloximes. Actually, the reduction of suitable 2-isoxazolines with LAH was found to give aziridines, in spite of the fact that there have been a few papers concerning the LAH reduction of 2-isoxazolines, which reported the formation of only the corresponding 3-aminopropanols.[4]

This paper deals with aziridine formation from 2-isoxazolines together with its kinetics and mechanistic studies.

(a) *Aziridine formation by* LAH *reduction of 2-isoxazolines.* Perold and von Reiche[4a] reported that the LAH reduction of 3,5-diphenyl-2-isoxazoline[5] (III) in boiling ether gave 1,3-diphenyl-3-aminopropanol (IV) in 62% yield. Our reinvestigation of the LAH reduction of III in boiling ether revealed that the aziridine II, which could be detected by GLC, was formed in 4·6% yield together with the crude aminoalcohol, isolated in 89·8% yield. However, when boiling THF was used instead of ether as a solvent for the LAH reduction of III, the expected *cis*-2-phenyl-3-benzylaziridine (II)[2,3,6] was isolated in 30·5% yield accompanied by 25·6% of the reported amino-alcohol IV. The aziridine was identical with the one obtained from Ia–c as well as from chalcone oxime (V).[7] Similarly, the LAH reduction of 3-phenyl-2-isoxazoline (VI), prepared according to a known method[8] yielded *cis*-2-phenyl-3-methylaziridine (VII) in 36·0% yield, which was identical with the aziridine obtained from 1-phenyl-propanone oxime (IX)[2,9] or phenylvinylketoxime (X),[10] and the amino-alcohol

* The outline of this paper was reported in our preliminary communication.[1]

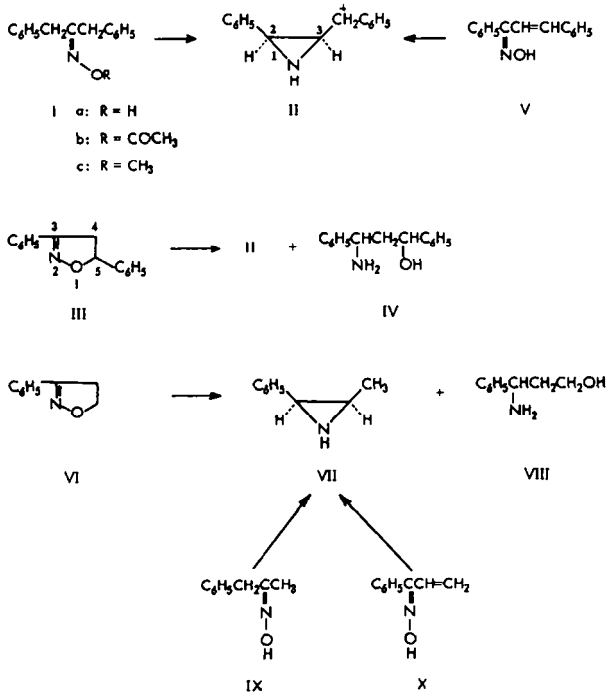


CHART 1

VIII in 46·9% yield. By the two examples mentioned above, it was proved that some 2-isoxazolines were, as expected, transformed to the corresponding aziridines with LAH.

Therefore, the generalization of this reaction was further examined with respect to the effects of substituents of 2-isoxazolines on aziridine formation and a mechanistic study was also carried out. For this purpose, several 2-isoxazolines were synthesized and submitted to LAH reduction.

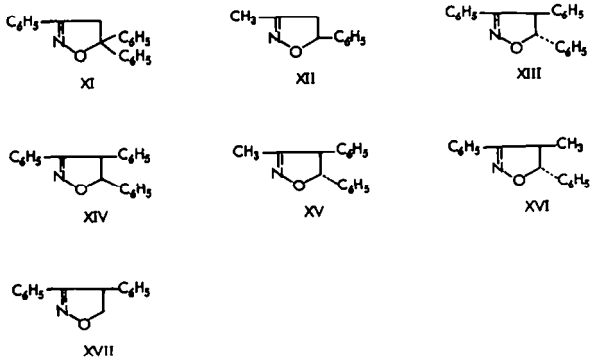


CHART 2

All of 2-isoxazolines (XI–XVII) used here, including newly synthesized XV,[11] b.p. 137°/0·1 mmHg, and XVI, m.p. 81–82°, were prepared by 1,3-dipolar addition using suitable nitrile oxides and olefins except for unknown XVII.

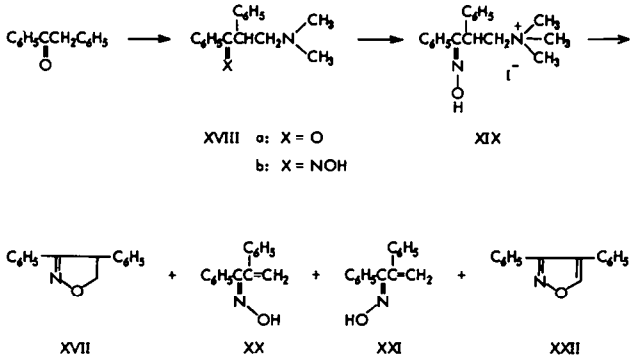


CHART 3

3,4-Diphenyl-2-isoxazoline (XVII) was synthesized as illustrated in Chart 3. In this case alkaline treatment[12] of the methiodide XIX, m.p. 187–187·5° (dec), afforded the 3,4-diphenyl-2-isoxazoline (XVII), m.p. 121–121·5°, in 35% yield, accompanied with two epimers of an oxime, (XX, m.p. 130–132°, and XXI, m.p. 91°) and 3,4-diphenylisoxazole (XXII)[13] in 28, 10 and 5% yields, respectively. For the oximes XX and XXI, *syn* and *anti* configurations were assigned respectively from NMR spectral studies.* The formation of two isomers of the oxime might be attributable to the intermediates, XVIIIb and XIX, which may be a mixture of *syn* and *anti* isomers. The LAH reduction of the 2-isoxazolines (XI–XVII) was carried out in THF and the reduction products were separated into the aziridines, the amino-alcohols and other products by elution-chromatography as shown in Chart 4.

The stereochemistry of the aziridines obtained, XXIII, XXVI, XXVIIIa, XXXa, XXXII, XXXIII, and XXXVI, was readily deduced from their NMR spectra. As shown in Table 1, *cis*-configuration of the aziridine XXIII was established from the value of the coupling constant ($J_{2,3}$ = 6·5 Hz). The determination of the configurations of 2,3,3-trisubstituted aziridines was also based on the NMR data in comparison with those of the aziridines II, VII, and XXXVII-XXXIX having established configurations.[14] For example, the stereochemistry of two aziridines, m.p. 45·5° and 77°, obtained from 3,5-diphenyl-4-methyl-2-isoxazoline (XVI) was established as shown in XXXII and XXXIII, respectively, from the differences between the chemical shifts of the Me and/or the methylene groups attached to the C_3-position in the two aziridines. These assignments were made based on the high-field shifts of the C_3-Me or methylene group, which is *cis*-related to the C_2-phenyl group, due to the shielding effect of the phenyl.[15]

(b) *The effects of the substituents on 2-isoxazolines for aziridine formation.* The effects of the substituents of 2-isoxazolines on aziridine formation were examined. As shown in Table 2, a Ph group at C_5 position in 2-isoxazoline decreased somewhat the yields of the formed aziridines, as in VI, III and XI. In contrast to this, aziridine formation

* See Experimental.

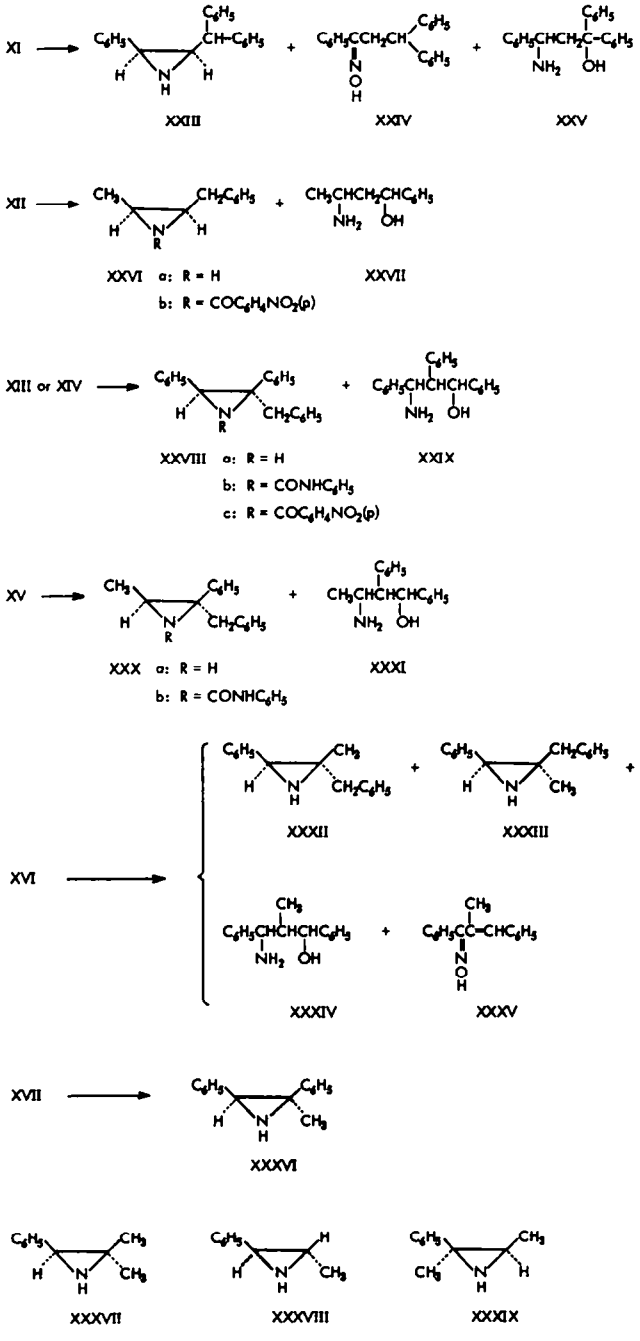


CHART 4

TABLE 1. NMR SPECTRAL DATA OF AZIRIDINES OBTAINED FROM 2-ISOXAZOLINES (60 MC, $CDCl_3$)

Aziridine	Chemical shift (τ)[b]			
	C_2—H	C_3—H	C_4—H	C_2—CH_3
XXXVII	(7·37)[a]	—	CH_3 (9·34)[a] (8·98)[a]	—
XXXVIII	(7·38)[a]	(8·38)[a]	CH_3 (9·17 J = 5·4)[a]	—
VII	(7·38)[a] 6·82 J = 6·5	(8·38)[a] 7·65 J = 6·5, 5·5	CH^3 (9·47 J = 5·4)[a] 9·12 J = 5·5	—
II	6·68d J = 6·0	~7·52	~7·52	—
XXIII	6·58d J = 6·5	7·10d-d J = 6·5, 9·0	6·63d J = 9·0	—
XXVIIIa	6·83	—	6·70	—
XXXa	7·90q J = 5·5	—	6·78, 6·90 q(AB-type)	9·13d J = 5·5
XXXII	~7·00?	—	CH_3 9·08s —CH_2— 6·95, 7·15 q(AB-type)	—
XXXIII	~6·90	—	CH_3 8·68s —CH_2— 7·53	—
XXXVI	~6·68	—	8·27	—
XXXIX	—	7·80q J = 5·0	CH_3 9·14d J = 5·0	8·43s

[a] TMS was used as external reference.
[b] Coupling constants (J-values) are shown by Hz.

from 2-isoxazoline III bearing a Ph group at the C_3-position is superior to that from from XII bearing Me group at the same position. A similar tendency was observed between XIII and XV. Special attention should be paid to the effects of the substituents at the C_4 position of 2-isoxazolines on aziridine formation. While all of the 2-isoxazolines bearing a Ph group at the C_4-position as in the example, XIII, XIV, XV and XVII, gave the aziridines in excellent yields, even if the reaction was carried out at lower temperature and/or shorter reaction time, the 2-isoxazoline XVI bearing Me group at the C_4-position was transformed in only 4·1% yield to the aziridines (XXXII and XXXIII) whereas 3,5-diphenyl-2-isoxazoline (III) having no substituent at the same position was reduced to the aziridine in 30·5% yield. These effects of substituents at 2-isoxazolines should be emphasized in view of not only the mechanism of this reaction but also its preparative application.

(c) *Kinetic studies on the reaction.* As mentioned above, 2-isoxazolines bearing a Ph group at C_4-position were transformed with LAH in THF to the corresponding aziridines in excellent yields as aziridine was formed from dibenzylketoxime (Ia) and further, 2-isoxazoline can be regarded as an internal oxime O-alkyl ether. Therefore, detailed mechanistic study on the LAH reduction of dibenzylketoxime O-methyl ether (Ic) was expected to provide a clue to the reaction mechanism of the aziridine formation from 2-isoxazoline.

When O-methyl ether Ic was stirred with LAH at 40° for 6 hr, GLC analyses

TABLE 2. REDUCTION OF 2-ISOXAZOLINES WITH LAH UNDER DIFFERENT CONDITIONS

Isoxazoline	$[LAH]_c$ (M)	Condition temp	hr	Reaction Aziridine		Product % Aminoalcohol		Another product	
	0·55	reflux	3		36·0	XX	46·9		
VI	0·40	40°	4	VII	(52·4)				
	0·40	20°	2–4		(48·0)				
	0·37	reflux	3		30·5	IV	25·6		
III	0·40	40°	4	II	(38·5)				
	0·40	25°	6		none			III	quantitative
	0·49	reflux	1		20·9	XXV	17·3		
XI	0·49	40°	5	XXIII	10·5			XXIV	21·3, XI 50·1
	0·42	25°	1		none			XI	quantitative
XII	0·51	30°	4	XXVIa	7·3	XXVII	39·4		
	0·17	reflux	3		none	XXIX	33·5		
XIII	0·097	25°	1	XXVIIIa	(93·9)				
	0·22	20°	4		82·6	XXIX	12·9		
XIV	0·097	25°	1	XXVIIIa	(92·3)				
XV	0·35	35–40°	3·5	XXXa	70·1	XXXI	15·2		
XVI	0·33	30–35°	3	XXXII	2·6	XXXIV	67·8	XXXV	6·1
				XXXIII	1·5			XVI	2·4
XVII	0·08	−15°	4	XXXVI	82·7				

[a] Yield of isolated product, figures in parentheses were measured by GLC.

showed the formation of the aziridine II in 95·8% yield accompanied with the liberated MeOH in 89·5% yield. The curves of the reaction product II and starting material Ic *vs* time using different concentrations of LAH are shown in Fig. 1.

Examination of these curves proves that the reaction rate is dependent on the initial

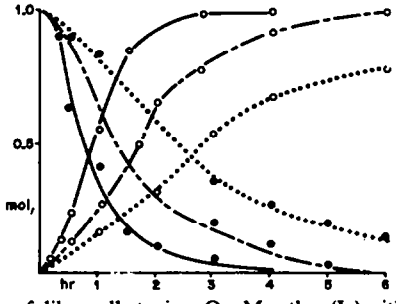


FIG. 1 Reaction of dibenzylketoxime O—Me ether (Ic) with LAH in THF.
Reaction temp: 40·0°.
$[Ic]_0$: 0·04 M
● ● Dibenzylketoxime O-Me ether (Ic)
○ ○ The produced *cis*-2-phenyl-3-benzylaziridine (II)
——— $[LAH]_0$ 0·4M
– – – – $[LAH]_0$ 0·2M
· · · · · $[LAH]_0$ 0·08M

concentration of LAH ([LAH]o). The stoichiometry of the LAH reduction of Ic was also determined at 40° according to Brown *et al.*[16] The hydrogen evolved in the reaction of Ic (0·08M) with LAH (0·2M) in THF was measured after hydrolysis of the solution after 6 hr. A blank reaction without addition of Ic was performed under identical conditions and from the difference of hydrogen volumes the amount of hydride used for the reduction of Ic itself was calculated. The data for dibenzylketoxime O-methyl ether (Ic) are shown in Table 3. Two moles of hydride were consumed per mole of Ic; one for hydrogen abstraction from Ic and one for the reduction of the C=N bond.

TABLE 3. STOICHIOMETRY OF THE REACTION OF LAH (0·2M) WITH DIBENZYLKETOXIME O-METHYLETHER (Ic)[a]

$[Ic]_0$ (M)	Hydrogen evolved mol. eq	Hydride used mol. eq	Hydride used for reduction mol. eq
	1·12	2·10	0·98
0·08	1·05	2·30	1·25
	0·99	2·25	1·26
0·04	1·00	—	—

[a] Reactions were carried out in the following conditions; in THF, at 40·0°, and for 6 hr.

It was recognized that the curve of hydrogen evolved *vs* time fits with that of aziridine formation (as shown by the broken line in Fig. 1) and that this reaction is not affected by the concentration of Ic as shown in Table 3. These results show that the oxime O-methyl ether Ic probably is transformed to the aziridine II by a mechanism similar to that for dibenzylketoxime (Ia) though the reactions differ in two points; the hydrogen does not evolve violently in the initial stage of the reaction, and the reaction rate depends strongly on the initial concentration of LAH. Similar studies were performed on some 2-isoxazolines which, as pointed out above, may be regarded as internal O-alkyl oximes.

As shown in Table 4, the stoichiometry of the LAH reduction of *trans*-3,4,5-triphenyl-2-isoxazoline (XIII)[18] indicated that three moles of hydride were consumed

TABLE 4. STOICHIOMETRY OF THE REACTION OF *trans*-3,4,5-TRIPHENYL-2-ISOXAZOLINE (XIII) WITH LAH IN THF AT 25·0°

$[XIII]_0$ (M)	$[LAH]_0$ (M)	Hydrogen evolved (mol. eq)	Hydride used (mol. eq)	Hydride used for reduction (mol. eq)	Half time of H_2 evolved (min)
0·040	0·097	0·96	3·02	2·06	15
0·061	0·097	1·11	3·10	1·99	15
0·041	0·064	1·08	2·85	1·78	22
0·040	0·048	1·05	2·88	1·83	26
0·021	0·049	1·02	3·09	2·07	25

per mole of XIII under all the different conditions in which the initial concentrations of both LAH and XIII were changed. Since the slow liberation of one mole of hydrogen was observed, two hydrides were used for reduction.

In order to elucidate the mode of hydride consumption, XIII was reduced with LAD instead of LAH to give the dideuterated aziridine, XL, m.p. 85–85·5°. The location of two deuteriums in XL was determined by the comparison of the NMR spectra of XXVIIIa and XL. In the NMR spectrum of XL, in the range of 6–8 τ only one proton signal appeared at 6·73 τ clearly indicating the introduction of two deuteriums at the C_2- and C_4-positions of the aziridine. Similar treatment of 3,5-diphenyl-2-isoxazoline (III)* with LAD gave the dideuterated aziridine, XLIa, m.p. 40–40·5°, which was identical with *cis*-2-phenyl-3-benzyl-2,4-dideuteroaziridine obtained by the reduction of chalcone oxime (V) with LAD. Furthermore, 3,5,5-triphenyl-2-isoxazoline (XI) was transformed on LAD reduction to the corresponding aziridine (XLII), which was proved to be dideuterated at the C_2- and C_4-positions on the basis of the NMR spectra.†

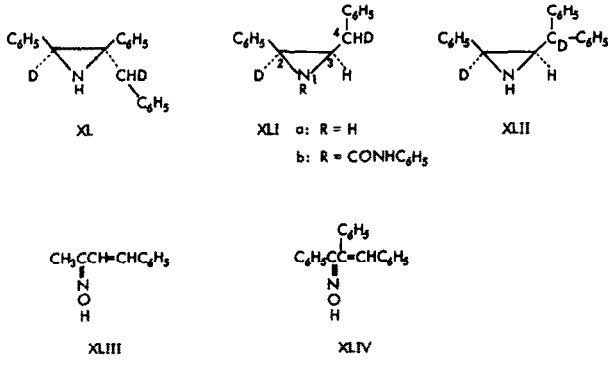


CHART 5

These results clearly show the hydride attack at the C_3- and C_5-positions of the 2-isoxazolines, a fact that should be kept in mind for the later described conclusions about the mechanism.

The time dependence of the hydrogen evolved in the reaction of XIII with LAH was also determined volumetrically. As shown in Fig. 2, the result indicates that the reaction rate is also affected by $[LAH]_0$. On the other hand, it was found that the aziridine formation is neither effected by the initial concentration of XIII nor by the concentration ratio of XIII to LAH if not less than 1·2 moles LAH per mole of XIII is used.

The LAH reduction of 3-phenyl-2-isoxazoline (VI) was also checked by GLC and gasometry. As can be seen in Fig. 3, one mole hydrogen was evolved gradually. This indicates that conversion of VI to the aziridine VII and also to the aminoalcohol VIII proceeded with evolution of one mole of hydrogen, since VI was converted to VII and VIII in a ratio of about 1:1. It is also noted that the rate of reduction of VI is affected by $[LAH]_0$.

* In this case, 1,3-diphenyl-3-amino-3-deuteropropanol-1 was obtained in 26·8% yield instead of IV.

† See Experimental.

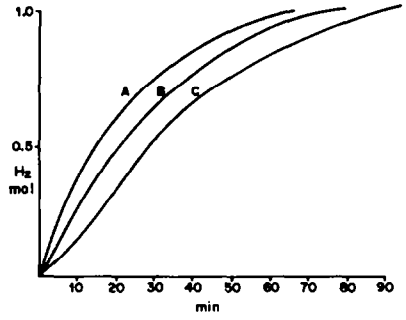


FIG. 2 The evolved H_2 gas in the reaction of *trans*-3,4,5-triphenyl-2-isoxazoline (XIII) with LAH in THF.

Reaction temp: 25·0° $[XIII]_0$: 0·04M $[LAH]_0$ A: 0·097M B: 0·064M C: 0·048M

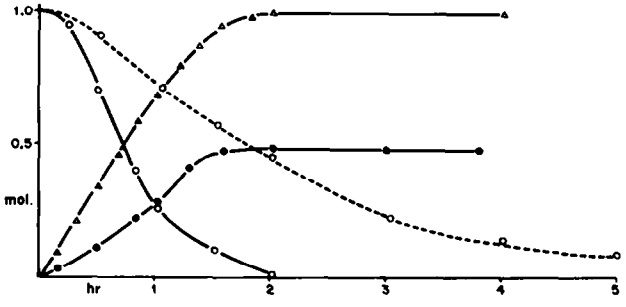


FIG. 3 Reaction of 3-phenyl-2-isoxazoline (VI) with LAH in THF.

Reaction temp: 25·0° $[VI]_0$: 0·04M $[LAH]_0$: 0·4M ○——○ 2-Isoxazoline (VI)
●——● The produced *cis*-2-phenyl-3-methylaziridine (VII)
Δ——Δ H_2 gas evolved
$[LAH]_0$: 0·08M ○·····○ 2-Isoxazoline (VI)

On considering the reaction mechanism, it should be recognized that $[LAH]_0$ affects the reaction rate both in the reduction of 2-isoxazoline and of the oxime O-methyl ether Ic. We first predicted an azirine intermediate in the formation of aziridines from oximes.[2, 19] Kotera *et al.*[17] recently studied the mechanism of the aziridine formation using dibenzylketoxime, based mainly upon its kinetic studies. They showed that an azirine intermediate is most reasonable for the intermediate and the reaction proceeds as illustrated in Chart 6. The azirine intermediate is also supported by the fact that treatment of 2,3-disubstituted azirines with LAH has been reported by Hassner and Fowler[20] to give the corresponding *cis*-aziridines as in our case in good yields.

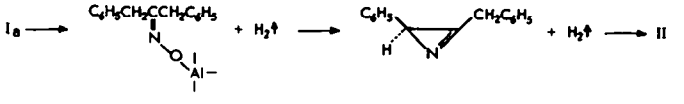


CHART 6

The similarity of the reduction course of 2-isoxazoline and dibenzylketoxime (Ia) or its O-Me ether Ic led us to assume that the reduction of 2-isoxazoline also proceeds *via* an azirine intermediate. On the other hand, *trans*-4-methyl-3,5-diphenyl-2-isoxazoline (XVI) yielded, on LAH reduction, an unsaturated oxime (XXXV) as a by-product in 6·1% yield. Therefore, it seems not inadequate to assume that such unsaturated compounds may represent an intermediate in the course of azirine formation from 2-isoxazoline with LAH.

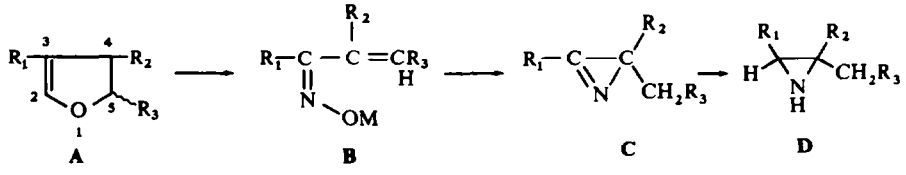
With this in mind, studies on the LAH reduction of benzalacetone oxime (XLIII), benzaldesoxybenzoin oxime (XLIV) and 1,2-diphenyl-2-propen-1-one oxime (XX and XXI) were carried out for comparison with those of phenylvinylketoxime (X)[10] and chalcone oxime (V)[7] previously reported. All of the oximes tested gave the corresponding aziridines, although in varying yields. As portrayed in Table 5, a detailed comparison of the yields of aziridine formation from the unsaturated ketoximes with those from 2-isoxazolines related to them shows that the former are transformed more easily to the corresponding aziridines than are the latter. This result indicates the possibility of the existence of an unsaturated intermediate in the reduction course.

TABLE 5. FORMATION OF AZIRIDINES FROM α,β-UNSATURATED KETOXIMES AND THE RELATED 2-ISOXAZOLINES BY LAH REDUCTION IN THF

Starting material α,β-unsaturated ketoxime	Aziridine % [a]	Starting material 2-isoxazoline	Aziridine % [a]
X	50 (VII)	VI	36[b] (VII)
V	31 (II)	III	31[c] (II)
XLIII	33 (XXVIa)	XII	7 (XXVIa)
XLIV	86 (XXVIIIa)	XIII	83 (XXVIIIa)
XX	98 (XXXVI)	XVII	83 (XXXVI)
XXI	85		

[a] Yield of isolated product.
[b] Ether was used as a solvent.
[c] Isolated as phenylcarboamoyl derivative.

(d) *Conclusion.* From the facts and considerations described above, it may be concluded that 2-isoxazoline (A) is transformed to the aziridine (D) *via* the following sequence; abstraction of a proton from the C_4-position in A with LAH resulting in the evolution of one mole of hydrogen gas and subsequent C—O bond fission leads from



the isoxazoline (A) to an intermediate B, which is further converted to an azirine intermediate C by hydride attack from the C_5-position followed by a cyclization which is accompanied by N—O bond fission. The intermediate C is then reduced to the aziridine (D) by further hydride attack from the opposite side of the bulkier group.

This reaction mechanism, which seems most probable at present, was also supported by the following experimental results. No hydroxyaziridine was obtained in all cases investigated. When 3,5-diphenylisoxazole (XXII), in which a double bond was introduced to C_4 and C_5-positions of 2-isoxazoline, was subjected to the LAH reduction in boiling THF, no aziridine was formed but the starting material was recovered almost quantitatively. In addition, *trans*-4-methyl-3,5-diphenyl-2-isoxazoline (XVI) was reduced to give two stereoisomers of the aziridine, although in poor yields, because of the bulkiness of the two substituents (CH_3 and $CH_2C_6H_5$) at C_3-position of the postulated azirine intermediate (C).

The reduction of 2-isoxazolines, which are easily derived by 1,3-dipolar addition with nitrile oxides and olefins, thus presents a new method for the synthesis of aziridines. These findings also suggest the possibility of aziridine formation from other suitable heterocyclic compounds. We continue to explore these developments.

EXPERIMENTAL

M.ps were taken by capillary and are uncorrected. B.ps are also uncorrected. The NMR spectra were determined at 60 MC with a Varian A-60 spectrometer using TMS as internal standard in $CDCl_3$. Peak multiplicities are represented by s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). The IR spectra were measured using a Jasco Model DS-201B IR double-monochromatic spectrometer. LAH used in the experimental was purified according to the method of Davis *et al.*[21] THF was also purified under Ar atmosphere by refluxing commercially available THF over metallic Na for 2 days and by two redistillation from LAH. Adsorbents, Al_2O_3 and SiO_2 were obtained from M. Woelm.

Preparation of XI *by* 1,3-*dipolar addition*

A soln of anhyd Et_3N (7·3 g) in abs ether (50 ml) was added to an ice-cooled and well stirred soln of benzhydroxamyl chloride (11 g) in abs ether (100 ml) and, after a few min, the ppt of $Et_3N \cdot HCl$ was filtered off rapidly and washed with a small quantity of abs ether. To the combined filtrate, a soln of 1,1-diphenylethylene (11 g) in abs ether was added in one portion under cooling in ice and the mixture was refluxed for 1 hr. After cooling, the ppt of crude XI was filtered off. Recrystallization of the ppt (6·7 g) from EtOH gave pure XI (5·0 g), m.p. 140–141·5°, as needles; ν_{max}^{Nujol} 1604, 908, 750, 693 cm^{-1}; NMR: 6·07 τ (2H, s, C_4—H), ~2·63 τ (15H, m, aromatic H). (Found: C, 84·24; H, 5·52; O, 5·34; N, 4·79. Calc. for $C_{21}H_{17}ON$: C, 84·25; H, 5·72; O, 5·34; N, 4·68%).

Preparation of XVI

To an ice cooled soln of benzonitrile oxide in abs ether (200 ml), prepared from benzhydroxamyl chloride (10·20 g; 0·0653 mole) and Et_3N (6·60 g; 0·0653 mole) in a manner similar to the case of XI, ω-methylstyrene (5·90 g; 0·05 mole) was added and the mixture was stirred at 25° for 2·5 hr. Evaporation of the solvent left a colourless oil (10·5 g), which was chromatographed over neutral Al_2O_3 (320 g, act. I). Elution with ether: n-hexane (1 : 5) gave phenylfluoxane (6·49 g) and fraction eluted with ether: n-hexane (1 : 4) gave the desired 2-isoxazoline (2·172 g; 18·3%) which afforded, on recrystallization from EtOH, needles of pure XVI, m.p. 81·5–82°; ν_{max}^{Nujol} 1073, 923, 876 cm^{-1}; NMR: 4·72 τ (1H, d, J = 5·8 Hz, C_5—H), ~6·33 τ (1H, m, C_4—H), 8·65 τ (3H, d, J = 7·0 Hz, CH_3). (Found: C, 81·13; H, 6·36; N, 6·03. $C_{16}H_{15}ON$ requires: C, 80·88; H, 6·37; N, 5·90%).

Preparation of XV

A soln of nitroethane (2·08 g) and Et_3N (5 drops) in abs benzene (7 ml) was dropwise added at 15° to a soln of phenylisocyanate (6·60 g) and *trans*-stilbene (4·95 g) in abs benzene (42 ml) over a period of 8 min. The reaction mixture was stirred at 30° for 3·5 hr, and then refluxed for further 10 hr, cooled in ice and filtered

to remove the ppts. Evaporation of the yellow benzene soln left an orange residue, which gave, on distillation under reduced press, crude XV (3·10 g), b.p. 143° (0·17 mmHg). Further purification was carried out by column-chromatography over neutral Al_2O_3 (90 g, act. I). Elution with ether: light petroleum (1:9–1:1) gave the pure sample of XV (2·327 g; 35·7%), b.p. 137° (0·11 mmHg); ν_{max}^{film} 1603, 1075, 1025, 947, 871 cm^{-1}; NMR: 4·77 τ (1H, d, J = 7·5 Hz, C_5—H), 5·88 τ (1H, d-q, J = 7·5, 1·0 Hz, C_4—H), 8·20 τ (3H, d, J = 1·0 Hz, CH_3). (Found: C, 80·80; H, 6·45; N, 5·87. $C_{16}H_{15}ON$ requires: C, 80·98; H, 6·37; N, 5·90%).

Preparation of 2-*isoxazoline* XVII *and oximes*, XX *and* XXI, *from desoxybenzoin*

A soln of desoxybenzoin (20·47 g), paraformaldehyde (6·26 g) and $Me_2NH \cdot HCl$ (17·00 g) in EtOH (70 ml) and conc HCl (1 ml) was refluxed for 8 hr, and poured into H_2O (150 ml) containing conc HCl (7·5 ml). After washing with ether, the mixture was basified with 20% KOH, and extracted with ether. The extract was washed with H_2O, dried over anhyd K_2CO_3 and evaporated to dryness leaving a colourless residue (9·44 g; 35·7%), m.p. 77–78·5°, which was recrystallized from n-hexane–ether to yield pure XVIIIa, m.p. 78–79° as prisms; ν_{max}^{Nujol} 1671, 1663 cm^{-1}. (Found: C, 80·44; H, 7·62; N, 5·36. $C_{17}H_{19}ON$ requires: C, 80·57; H, 7·56; N, 5·53%).

A soln of XVIIIa (628 mg) and $NH_2OH \cdot HCl$ (186 mg) in EtOH (3·0 ml) and pyridine (6·0 ml) was left at room temp overnight. Evaporation of the solvent under reduced press left a residue, which was extracted with ether. The ethereal extract was washed with H_2O, dried over K_2CO_3 and evaporated to give a crystalline residue (688 mg), m.p. 128–143°, which yielded, on two recrystallizztions from benzene-AcOEt, needles of pure XVIIIb, (480 mg; 72·7%), m.p. 156–159°. (Found: C, 75·91; H, 7·49; N, 10·34. $C_{17}H_{20}ON_2$ requires: C, 76·08; H, 7·51; N, 10·44%).

A soln of XVIIIb (8·52 g) and MeI (9·0 g) in MeOH (400 ml) was kept at room temp overnight. After evaporation, the residue (13·332 g) was twice recrystallized from EtOH to give pure XIX (10·232 g), m.p. 187–187·5° (dec), as prisms. (Found: C, 52·75; H, 5·98; N, 6·80; I, 31·18. $C_{18}H_{23}ION_2$ requires: C, 52·71; H, 5·65; N, 6·83; I, 30·92%).

A warm soln of XIX (10·23 g) in EtOH (250 ml) was added to the soln of EtONa in EtOH, prepared from metallic Na (5·74 g) and EtOH (180 ml), and the mixture was refluxed for 6 hr. After addition of H_2O (400 ml), the mixture was extracted with ether. The extract was washed with H_2O, dried over anhyd Na_2SO_4 and evaporated to give a crystalline residue (4·913 g), which was twice recrystallized from EtOH to yield the pure sample of XVII (1·517 g), m.p. 121–121·5°; ν_{max}^{Nujol} 1603, 1591, 1073, 1032, 942, 892 cm^{-1}. (Found: C, 80·92; H, 5·90; N, 6·15. $C_{15}H_{13}ON$ requires: C, 80·69; H, 5·87; N, 6·27%). The mother liquor of the recrystallizations was evaporated to dryness leaving a yellow oil residue (3·39 g) which was chromatographed over neutral SiO_2 (170 g, act. II). Elution with benzene:light petroleum (3:7) left crude XXII (262 mg; 4·7%), which was recrystallized from n-hexane-ether to afford the pure sample, m.p. 90–90·5° as rods, undepressed on admixture with an authentic sample of 3,4-diphenylisoxazole. Further elution with benzene: light petroleum (1:1) gave another crop of XVII (438 mg). Total yield of 3,4-diphenyl-2-isoxazoline was 1·955 g (35·1%). Fractions eluted with the same solvent gave *syn*-oxime XX (1·549 g; 27·8%), which, on recrystallization from n-hexane-ether, afforded the pure sample, m.p. 111·5–112·5° as prisms; ν_{max}^{Nujol} 3230, 1614, 1574, 1227, 1020, 939 cm^{-1}; NMR: 3·92 τ and 4·68 τ (2H, s, vinyl-H). (Found: C, 80·45; H, 5·91; N, 6·25. $C_{15}H_{13}ON$ requires: C, 80·69; H, 5·89; N, 6·27%). Further elution with benzene and Chf: benzene (1:19) gave *anti*-isomer XXI, which was recrystallized from n-hexane-ether to afford the pure sample, m.p. 130–132° as rods; ν_{max}^{Nujol} 3248, 1598, 1570, 1075, 982, 908 cm^{-1}; NMR: 4·42 τ and 4·68 τ (2H, d, J = 1·0 Hz, vinyl-H). (Found: C, 80·70; H, 5·91; N, 6·16. $C_{15}H_{13}ON$ requires: C, 80·69; H, 5·89; N, 6·27%).

LAH *reduction of* III

A soln of III (1·018 g) in THF (10 ml) was dropwise added with stirring at 10° to a suspension of LAH (0·692 g) in THF (40 ml) over a period of 5 min and the mixture was refluxed for 3 hr. Under cooling in ice, the excess LAH was decomposed with H_2O and the mixture was extracted with ether. Evaporation of the organic layer, which was dried over anhyd K_2CO_3, left a yellow oily residue (0·997 g), which was chromatographed over neutral Al_2O_3 (40 g, act. I). Elution with n-hexane:ether (19:1) afforded a crystalline aziridine II (0·291 g; 30·5%), which was twice recrystallized from n-hexane-ether to give needles of II, m.p. 46·5–47°, undepressed on admixture with an authentic sample of *cis*-2-phenyl-3-benzylaziridine. Fractions eluted with MeOH:ether (1:9–3:7) afforded, after evaporation a crystalline residue (0·265 g; 25·6%), which was recrystallized 3 times from benzene-AcOEt to give needles of IV, m.p. 115–116·5° (Lit.[4a] m.p. 121–122°): ν_{max}^{Nujol} 3348, 3265, 1607, 1036, 886, 750 cm^{-1}. NMR: 5·01 τ (1-H, t, C_1—H), 5·87 τ (1-H, t, C_3—H), ~8·05 τ (2-H, m, C_2—H). (Found: C, 79·32; H, 7·66; N, 6·15. Calc. for $C_{15}H_{15}ON$: C, 79·26; H, 7·54; N, 6·16%).

LAH *reduction of* VI

A soln of VI (1·019 g) in THF (10 ml) was dropwise added below 10° with stirring to a suspension of LAH (1·050 g) in THF (40 ml) and the mixture was refluxed for 3 hr. Working up left a yellow oily basic residue, which was chromatographed over neutral Al_2O_3 (40 g, act. II). Elution with ether:n-hexane (1:9–1:4) afforded the crude aziridine (337 mg; 36·5%), which was recrystallized from n-hexane to give needles of VII, m.p. 43–44·5°, identical with *cis*-2-phenyl-3-methylaziridine in all respects. Fractions eluted with MeOH:ether (1:19–1:1) gave a crude amino-alcohol (491 mg; 46·9%), which was twice recrystallized from benzene-AcOEt affording needles of pure VIII, m.p. 75·5–76° (Lit.[22] m.p. 73°); ν_{max}^{Nujol} 3308, 3250, 3110 cm^{-1}. (Found: C, 71·47; H, 8·40; N, 9·42. Calc. for $C_9H_{13}ON$: C, 71·48; H, 8·67; N, 9·27%).

LAH *reduction of* XI

A. *Heating under reflux.* A soln of XI (1·217 g) in THF (35 ml) was dropwise added below 10° with stirring to a suspension of LAH (1·40 g) in THF (40 ml) and the mixture was refluxed under Ar and slight press for 1 hr. Working up left a residue (1·226 g), which was chromatographed over neutral Al_2O_3 (94 g, act. II). Elution with ether:light petroleum (1:7–1:1) left a crystalline residue (250 mg; 20·9%), which gave pure aziridine XXIII, m.p. 118·5–120°, on recrystallization from ether-n-hexane; ν_{max}^{Nujol} 3206 cm^{-1} (NH). (Found: C, 88·50; H, 6·80; N, 4·99. $C_{21}H_{19}N$ requires: C, 88·38; H, 6·71; N, 4·91%). Elution with ether and MeOH:ether (1:19) gave 212 mg (17·3%) of crude XXV, which was recrystallized from n-hexane-ether to give needles of pure XXV, m.p. 144–145°. ν_{max}^{Nujol} 3338, 3285 cm^{-1} (NH, OH). (Found: C, 83·18; H, 6·96; N, 4·65. $C_{21}H_{21}ON$ requires: C, 83·13; H, 6·98; N, 4·62%).

B. *At* 40°. To a stirred slurry of LAH (1·4 g) in THF (75 ml), XI (1·20 g) was added under a stream of Ar and the mixture was stirred at 40° under Ar and slight press for 5 hr. Working up left a residue (1·294 g), which was chromatographed over neutral Al_2O_3 (80 g, act. II). Elution with ether:light petroleum (1:19–1:11) left recovered XI (600 mg; 50·1%) and elution with ether:light petroleum (1:5–1:3) left XXIII (119 mg; 10·5%). Fractions eluted with ether:light petroleum (1:1) and ether afforded a crystalline residue (255 mg; 21·3%) which gave pure oxime XXIV, m.p. 143·5–145°, on recrystallization from light petroleum-ether, as needles; ν_{max}^{Nujol} 3240 cm^{-1}, NMR: 6·45 τ (2H, d, J = 8·0 Hz, $-CH_2-$), 5·58 τ (1H, t, J = 8·0 Hz, $CH\diagup\diagdown$). (Found: C, 83·41; H, 6·10; O, 5·20; N, 4·65. $C_{21}H_{19}ON$ requires: C, 83·69; H, 6·35; O, 5·34; N, 4·68%).

C. *At* 25°. To a suspension of LAH (79·2 mg) in THF (15 ml), XI (77·6 mg) was added and the mixture was stirred at 25° for 1 hr. Working up gave quantitative recovery of XI.

LAH *reduction of* XXIV

LAH (140 mg) was added to a soln of XXIV (104 mg) in THF (6 ml) under a stream of Ar and the mixture was stirred at 40° for 4 hr. Working up left a residue (86 mg) which was chromatographed over neutral Al_2O_3 (5·6 g, act. II). Elution with ether:light petroleum (1:9–1:4) gave crude XXIII (21·2 mg; 21·5%) and fractions eluted with ether gave the recovered XXIV (17 mg; 16·4%).

LAH *reduction of* XII

A soln of XII (2·038 g) in THF (20 ml) was dropwise added with stirring at 15° to a suspension of LAH (1·930 g) in THF (80 ml) and the mixture was stirred at 30–31° for 4 hr. Working up left an oily residue (1·677 g) which was chromatographed over neutral Al_2O_3 (80 g, act. II). Elution with ether: light petroleum (1:10) and ether left a mixture (736 mg) including XXVIa, and fractions eluted with MeOH:ether (1:10–1:1) and those with 10% HClaq, which were extracted with ether after basification with KOH, gave oily XXVII (733 mg). The above mixture was further chromatographed over SiO_2 (52 g, act. II). Elution with n-hexane:ether (1:1) left oily aziridine (138 mg; 7·3%), attempted crystallization of which failed, and fractions with 10% HClaq left oily XXVII when extracted with ether after basification of the acidic layer. Total yield of XXVII was 832 mg (39·4%); NMR: 5·17 τ (1H, m, C_1—H), 6·50 τ (3-H, NH_2, and OH), ~6·86 τ (1H, m, C_3-H), 8·35 τ (2H, m, C_2—H), 8·88 τ (3H, d, J = 6·5 Hz, CH_3).

The aziridine XXVIa was characterized as *p*-nitrobenzoate. To a cold soln of XXVIa (126 mg) and Et_3N (63 mg) in abs benzene (4 ml), a soln of *p*-nitrobenzoyl chloride (126 mg) in abs benzene (5 ml) was dropwise added with stirring. The mixture was left at room temp for 1 hr and the ppt was filtered off. Evaporation of the filtrate *in vacuo*, left a crystalline residue (240 mg) (m.p. 100–106°), which was recrystallized from ether to yield the pure sample of *p*- nitrobenzoate XXVIb (91 mg; 60%), m.p. 114·5–115°, as prisms. This was identical with the one obtained from XLIII in all respects as described later; ν_{max}^{Nujol} 1663

cm^{-1}. NMR (100 MC): 8·49 τ (3H, d, J = 6·0 Hz, CH_3), 7·29 τ (1H, broad quintet, J = 5·5 Hz, C_3—H). (Found: C, 68·53; H, 5·59; N, 9·45. $C_{17}H_{16}O_3N_2$ requires: C, 68·90; H, 5·44; N, 9·45%).

LAH *reduction of* XIII

(a) *At* 20°. A soln of XIII (1·455 g) in THF (30 ml) was dropwise added at 4–7° with stirring to a suspension of LAH (0·737 g) in THF (60 ml) and the mixture was stirred at 20° for 4 hr. Working up left an oily residue (1·509 g), which was chromatographed over neutral Al_2O_3 (76 g, act. I). Elution with ether:n-hexane (1:9–1:1) afforded crude XXVIIIa (1·146 g; 82·6%), m.p. 83–84·5°, which gave needles of the pure sample,* m.p. 85·5–86°, after two recrystallization from n-hexane–ether; ν_{max}^{Nujol} 1126, 1073, 1030, 957, 887 cm^{-1}. (Found: C, 88·15; H, 6·65; N, 4·91; MW, 287. $C_{21}H_{19}N$ requires: C, 88·38; H, 6·71; N, 4·91%; MW, 285·37). Elution with ether:n-hexane (3:1) and ether left crude amino-alcohol (189 mg; 12·9%), which was recrystallized 3-times from benzene-AcOEt giving the pure sample of XXIX, m.p. 150–151·5°; ν_{max}^{Nujol} 1097, 1048, 888, 700 cm^{-1}; NMR: 5·20 τ (1H, d, J = 6·0 Hz, C_1—H), ~6·10 τ (1H, d, J = 6·0 Hz, C_3—H), ~6·38 τ (2H, m, C_2—H). (Found: C, 83·06; H, 6·95; N, 4·45; MW, 311. $C_{21}H_{21}ON$ requires: C, 83·13; H, 6·98; N, 4·62%; MW, 303·39).

A soln of phenylisocyanate (25 mg) in abs ether (1·5 ml) was added to a soln of XXVIIIa (50 mg) in abs ether (1·5 ml) and the mixture was left at room temp for 2 days. Filtration of the resultant colourless crystals, m.p. 167–174°, (50 mg; 74%) and three recrystallization from MeOH gave XXVIIIb, m.p. 184–186° as colourless needles; ν_{max}^{Nujol} 3266, 1666 cm^{-1}. (Found: C, 83·29; H, 5·97; N, 6·89. $C_{28}H_{24}ON_2$ requires: C, 83·14; H, 5·98; N, 6·93%).

To a cooled soln of XXVIIIa (43 mg) and Et_3N (25 mg) in abs benzene (2 ml), a soln of *p*-nitrobenzoyl chloride (36 mg) in abs benzene (2 ml) was dropwise added with stirring. The mixture was left at room temp for 1 hr and the ppt was filtered off. Evaporation of the filtrate *in vacuo* left a crystalline residue (65 mg), which was twice recrystallized from ether affording needles of XXVIIIc, m.p. 139·5–140·5°; ν_{max}^{Nujol} 1650, 1604 cm^{-1}. (Found: C, 76·94; H, 4·94; N, 6·53. $C_{28}H_{22}O_3N$ requires: C, 77·40; H, 5·10; N, 6·45%).

(b) *At 20–25° under a stream of Ar.* Ar was passed into a stirred suspension of LAH (1·2 g) in THF (80 ml) at 20–25° for 30 min at a rate of 30 ml/min. To the above mixture, XIII (1·497 g) was added at once with stirring under a stream of Ar and the reaction mixture was stirred at the same temp for 3·5 hr. Working up left crude XVIIIa (1·479 g), which on column-chromatography over neutral Al_2O_3 (115 g, act. II), afforded the pure sample of XXVIIIa (1·255 g; 88·0%) from the fractions eluted with ether:light petroleum (1:14–1:4). No XXIX was obtained from further elution with ether.

(c) *Heating under reflux.* A soln of XIII (1·002 g) in THF (40 ml) was dropwise added at 8–10° to a stirred suspension of LAH (511 mg) in THF (40 ml) and the mixture was refluxed for 3·5 hr. Working up left a crystalline residue (1·128 g), which was chromatographed over neutral Al_2O_3 (40 g, act. II). Elution with n-hexane afforded *trans*-stilbene (101 mg; 16·3%) and elution with ether:n-hexane (3:97–1:9) gave desoxybenzoin (170 mg; 30·0%), m.p. 52–56°, and elution with ether:n-hexane (1:2) gave XXIX (340 mg; 33·5%).

LAH *reduction of* XIV

A soln of XIV (309 mg) in THF (7·0 ml) was dropwise added under cooling in ice to a stirred suspension of LAH (160 mg) in THF (10 ml) and the mixture was stirred at 20° for 5 hr. Working up left a yellow oil (300 mg), which was chromatographed over neutral Al_2O_3 (15 g, act. II). Elution with ether:n-hexane (1:19–1:9) left a crystalline residue which was crystallized from n-hexane–ether giving the pure sample of XXVIIIa, m.p. 85·5–86°, (151 mg, 51·3%), undepressed on admixture with the one obtained from XIII.

LAH *reduction of* XV

A soln of XV (1·049 g) in THF (10 ml) was dropwise added at 10° with stirring to a suspension of LAH (0·670 g) in THF (40 ml) over a period of 3 min and the mixture was stirred at 35–38° for additional 3·5 hr. In this case, XV was found by examination by TLC to disappear after stirring for 30 min. Working up left a residue (912 mg) which was chromatographed over neutral Al_2O_3 (45 g, act. II). Elution with ether:light petroleum (1:20) gave oily aziridine (692 mg; 70·1%), which afforded pure XXXa, on distillation under reduced press, b.p. 131° (1·7 mmHg); ν_{max}^{film} 3281 cm^{-1}. (Found: C, 85·50; H, 7·74; N, 6·12. $C_{16}H_{17}N$ requires: C, 86·05; H, 7·67; N, 6·27%). The derivative XXXb (74 mg; 73·5%), prepared by treatment of XXXa (74 mg) with phenylisocyanate in abs ether had a m.p. of 101–104°, needles from n-hexane–ether; ν_{max}^{Nujol} 3271, 1656. (Found: C, 80·74; H, 6·38; N, 8·27. $C_{23}H_{22}ON_2$ requires: C, 80·67; H, 6·48; N, 8·18%).

* The aziridine XXVIIIa, on refluxing with LAH in THF, decomposed easily to unidentified compounds.

Elution with ether and MeOH:ether (1:5) left the oily XXXI (162 mg; 15·2%). The structure of XXXI was deduced only from the results of IR spectrum and TLC.

LAH *reduction of* XVI

A soln of XVI (1·455 g) in THF (15 ml) was dropwise added at 15° with stirring to a suspension of LAH (0·933 g) in THF (60 ml) and stirring was continued at 30–35° for 3·5 hr. Working up left an oily residue, which was chromatographed over neutral Al_2O_3 (42 g, act. II). After recovery of XVI (62 mg) from the fractions eluted with ether:light petroleum (1:49), elution with the same solvent gave XXIII (20·9 mg; 1·5%), which was recrystallized from n-hexane–ether yielding the pure sample, m.p. 76–77°, as needles. (Found: C, 86·19; H, 7·77; N, 6·23. $C_{16}H_{17}N$ requires: C, 86·05; H, 7·67; N, 6·27%). Further elution with the same solvent afforded XXXII (35·1 mg; 2·6%), which gave needles of the pure sample, m.p. 44·5–45·5°, on recrystallization from n-hexane–ether; ν_{max}^{Nujol} 3226 cm^{-1}. (Found: C, 85·94; H, 7·71; N, 6·08. $C_{16}H_{17}N$ requires: C, 86·05; H, 7·67; N, 6·27%). Elution with ether:light petroleum (1:19–1:5) left a crystalline residue (88·6 mg; 6·1%), which was recrystallized from n-hexane–ether giving the pure sample of XXXV, m.p. 120–121°, as prisms; ν_{max}^{Nujol} 3201 cm^{-1}; NMR: 3·33 τ (1H, d, J = 2·0 Hz, vinyl-H) 7·88 τ (3H, d, J = 2·0 Hz, CH_3). (Found: C, 81·14; H, 6·40; N, 5·77; MW, 221. $C_{16}H_{15}ON$ requires: C, 80·98; H, 6·37; H, 6·37; H, 5·90%; MW, 237·29). Elution with ether and MeOH:ether (1:10), and ether extraction of the eluate with 10% HCl aq after basification gave XXIV, which afforded needles of the pure sample, m.p. 98·5–99°, on recrystallization from n-hexane–ether; ν_{max}^{Nujol} 3311, 3271, 1040 cm^{-1}; NMR: 5·41 τ (1H, d, J = 9·0 Hz, C_1-H), ~7·95 τ (1H, m, C_2-H), 9·70 τ (3H, d, J = 6·0 Hz, CH_3). (Found: C, 79·25; H, 7·85; N, 5·39. $C_{16}H_{19}ON$ requires: C, 79·63; H, 7·94; N, 5·80%).

LAH *reduction of* XVII

(a) *In ether.* A soln of XVII (310 mg) in abs ether (30 ml) was dropwise added at 13° to a stirred suspension of LAH (210 mg) in abs ether (10 ml) over a period of 5 min and the mixture was stirred at 28° for 5 hr. Working up left an oily residue (297 mg), which was chromatographed over neutral Al_2O_3 (15 g, act. II). Elution with ether:n-hexane (1:3) gave crude XXXVI (34 mg; 11·8%), which was recrystallized from n-hexane–ether yielding prisms of the pure sample, m.p. 58·5–59°; ν_{max}^{Nujol} 3285, 1603, 1252, 1071, 1039, 981, 860 cm^{-1}. (Found: C, 85·84; H, 7·35; N, 6·58. $C_{15}H_{15}N$ requires: C, 86·08; H, 7·22; N, 6·69%). Elution with MeOH–ether (1:19) gave 2,3-diphenyl-3-amino-propanol-1 (189 mg; 59·8%), which was characterized as its hydrochloride, m.p. 226–227° needles after two recrystallizations from EtOH; ν_{max}^{Nujol} 3481, 1603, 1568, 1086 cm^{-1}. (Found: C, 68·06; H, 7·04; N, 5·12; Cl, 13·72. $C_{15}H_{17}ON \cdot HCl$: C, 68·30; H, 6·88; N, 5·31; Cl, 13·44%).

(b) *In THF under a stream of Ar.* Ar was passed at −20° for 20 min into a slurry of LAH (60·5 mg) in THF (20 ml). XVII (177·9 mg) was added and the mixture was kept at −15° for 4 hr under a stream of Ar. Working up left crude XXXVI (166 mg), which, on column-chromatography over neutral Al_2O_3 (6·8 g, act. II), afforded pure XXXVI (138 mg; 82·7%) from the fractions eluted with ether:n-hexane (1:4).

When the reduction was carried out without a stream of Ar, neither XXXVI nor XVII was obtained, even though the reaction temp was varied in a range of 0° to reflux (i.e., 0°, 20°, reflux).

LAD *reduction of* XIII

A soln of XIII (224 mg) in THF (5 ml) was dropwise added under cooling in ice to stirred suspension of LAD (125 mg) in THF (8 ml) and stirring was continued for 5 hr at 20°. Working up left a residue (220 mg), which was chromatographed over neutral Al_2O_3 (11 g, act. II). Elution with ether:n-hexane (1:9) gave a residue, which was recrystallized from n-hexane–ether yielding the pure sample of dideuterated XL (85 mg), m.p. 85–85·5° as rods; ν_{max}^{Nujol} 1069, 981, 872 cm^{-1}. (Found: C, 87·97; H, 6·01; D, 1·40; N, 5·27. $C_{21}H_{17}D_2N$ requires: C, 87·77; H, 5·96; D, 1·39; N, 4·87%).

LAD *reduction of* III

A soln of III (500 mg) in THF (5 ml) was dropwise added under cooling in ice to a suspension of LAD (188 mg) in THF (20 ml) and the mixture was refluxed for 3 hr. Working up left an oil (511 mg), which was chromatographed over neutral Al_2O_3 (20 g, act. II). Elution with ether: n-hexane (1:19–1:9) gave crude XLIa (91 mg; 19·1%), which was recrystallized from n-hexane–ether to afford needles of the pure sample, m.p. 40–40·5°. Treatment of XLIa with phenylisocyanate in abs ether afforded XLIb, m.p. 123–124°, as needles from n-hexane–ether, which was identified by mixed m.p. and comparison of the IR spectra with an authentic sample of XLIb prepared by LAD reduction of V. Further elution with MeOH:ether (1:9)

afforded 1,3-diphenyl-3-amino-3-deuteropropanol-1 (137 mg; 26·8%), which, on recrystallization from benzene–AcOEt, yielded the pure sample, m.p. 115° as needles; NMR: 5·03 τ (1H, t, J = 6·5 Hz, C_1-H), 6·87 τ (3H, broad-s, NH_2, and OH) 8·05 τ (2H, d, J = 6·5 Hz, C_2-H). (Found: C, 78·93; H, 7·05; D, 0·88; N, 6·06. $C_{15}H_{16}DON$ requires: C, 78·92; H, 7·06; D, 0·88; N, 6·14%).

LAD *reduction of* XI

Under a stream of Ar, XI (621 mg) was added at 10° to a suspension of LAD (600 mg) in THF (30 ml) and the mixture was refluxed for 75 min. Working up left a residue (610 mg), which, on column-chromatography over neutral Al_2O_3 (45 g, act. II), afforded crystalline XLII (106 mg) from fractions eluted with ether: light petroleum (1:4–1:1). Two recrystallizations from n-hexane gave pure XLII, m.p. 118·5–120°; NMR: 7·08 τ (1H, C_3-H), 8·70 τ (1H, NH). (Found: C, 87·43; H, 5·90; D, 1·38; N, 4·81. $C_{21}H_{17}D_2N$ requires: C, 87·77; H, 5·96; D, 1·39; N, 4·87%).

LAH *reduction of* XLIII

A soln of XLIII (2·022 g) in THF (20 ml) was dropwise added with stirring at 10° to a slurry of LAH (0·96 g) in THF (50 ml) and the mixture was refluxed for 3 hr. Working up left a yellow oil (1·813 g), which was chromatographed over Al_2O_3 (54·3 g, act. I). Fractions eluted with light petroleum: benzene (7:3–1:1), and benzene: Chf (9:1–3:1) gave crude XXVIa (609 mg), almost pure according to TLC. Treatment of the crude XXVIa with *p*-nitrobenzoyl chloride and Et_3N afforded the N-*p*-nitrobenzoyl derivative of XXVIa, which on recrystallization from acetone–ether gave the pure *p*-nitrobenzoyl derivative, m.p. 115–115·5°. This was identical with XXVIb obtained from the aziridine from XII.

LAH *reduction of* XLIV

A soln of XLIV (715 mg) in THF (15 ml) was dropwise added under cooling in ice to a stirred suspension of LAH (363 mg) in THF (25 ml) and the mixture was stirred at 40° for 4 hr. Working up left a yellow oil (666 mg), which was chromatographed over neutral Al_2O_3 (20 g, act. II). Elution with ether: n-hexane (1:9) gave the aziridine (586 mg; 86·1%), which afforded, after three recrystallizations from n-hexane–ether, pure XXVIII, m.p. 85–86° as rods, identical with that obtained by LAH reduction of XIII.

LAH *reduction of* syn-*oxime* XX

A soln of XX (304 mg) in THF (5 ml) was dropwise added at 10° with stirring to a suspension of LAH (207 mg) in THF (10 ml) over a period of 10 min and the mixture was stirred at the same temp for 45 min. Working up left crude aziridine (279 mg; 97·8%), m.p. 49–53°, which was recrystallized from n-hexane–ether to give pure XXXVI, m.p. 58–59° as prisms, identical with that obtained from XVII.

LAH *reduction of* anti-*oxime* XXI

A soln of XXI (58 mg) in THF (1·5 ml) was dropwise added at 5° to a stirred suspension of LAH (39 mg) in THF (2 ml) over a period of 5 min and the mixture was stirred at 10° for 1·5 hr. Working up left crude aziridine (46 mg; 84·6%), which, on column-chromatography over neutral Al_2O_3 (1·5 g, act. II), afforded pure XXXVI, m.p. 58–58·5, identical with that prepared by LAH reduction of XX.

Stoichiometry of the LAH *reduction*

All reactions and solns were kept under a dry Ar atm. In a dry flask, fitted with a rubber syringe cap, magnetic stirring bar, Ar inlet, and connection to a gas buret *via* a spiral reflux condenser and a dry-ice vapour trap, a soln of the compound and LAH in THF stirred at the desired temp in a constant temp bath. The H_2 evolved was collected and measured periodically. After the reaction was stopped, the soln was hydrolyzed by injecting a small quantity of H_2O or 1N-H_2SO_4 and the amount of H_2 evolved was determined. A blank reaction was performed under identical conditions, but without addition of the compound. From the differences in yields of H_2 in two cases, the hydride utilized by the compound and the H_2 evolved were calculated, as shown in Tables 3 and 4.

In the case of XIII, the freeze-thaw method was used because of the sensibility of the reaction to O_2.

GLC *analysis of the* LAH *reduction*

All the reactions were carried out in a dry Ar atm. A mixture of the compound and LAH in THF was stirred in a constant temp bath until the reaction went to completion in a manner similar to the studies on stoichiometry. A suitable internal reference was used in each case. In the cases of XIII and XIV, the reaction

TABLE 6. GLC DATA USED FOR ANALYSES OF THE LAH REDUCTION

The compound to be reduced	Internal ref	Packed column	Conditions Column temp	Carrier gas (N_2) kg		Retention time (min)		
Ic	Dibenzylether	5% polyphenylether (6 ring) on Gaschrom Q (80–100 mesh)	190°	1·0	ref (5·3)	II (16·9)	Ic (8·8)	
VI	Diphenylether	10% KF-54 on Gaschrom Q (80–100 mesh)	110°	1·0	ref (7·3)	VII (25·7)	VII (35·0) VI (43·3)	
III	p-Methylbenzylbenzyl ether	4% KF-54 on Chromosorb W (80–100 mesh)	180°	1·0	ref (5·6)	II (10·1)	III (22·2)	
XIII	9,10-Dimethylanthracene	4% KF-54 on Chromosorb W (80–100 mesh)	220°	1·5	ref (4·4)	XVIIIa (10·4)	XIII (17·5)	
XIV	9,10-Dimethylanthracene	4% KF-54 on Chromosorb W (80–100 mesh)	220°	1·5	ref (4·4)	XVIIIa (10·4)	XVI (16·5)	
MeOH[a]		Porapak Q (100–120 mesh)	160°	1·0	MeOH (1·5)	THF (8·9)		

[a] Formed by LAH reduction of Ic .

mixture was also prepared by the freeze–thaw method. In the cases of Ic and VI, several aliquots, usually 1 ml, were periodically taken out, the residual hydride was decomposed with a small amount of H_2O, and then the filtrate was injected into the gas chromatograph.

GLC was performed using a Hitachi gas chromatograph Model K-53 equipped with flame ionization detector and using N_2 as carrier gas. Standard columns, 1 m × 3 mm, of N_2 as carrier gas. Standard columns, 1 m × 3 mm, of stainless steel tubing were employed in all cases. Table 6 lists all the GLC data in this work.

Characterization of MeOH *produced by treatment of* Ic *with* LAH *as its α-naphthylcarbamoyl derivative*

A mixture of Ic (488·6 mg) and LAH (190 mg) in THF (25 ml) was stirred at 40° for 6 hr. After the decomposition of excess hydride with H_2O, the reaction mixture was subjected to distillation and redistilled after drying over K_2CO_3. To the distillate, α-naphthylisocyanate (355 mg) was added and the mixture was refluxed for 1 hr. After cooling, the ppt was filtered off. After the removal of the solvent, ligroin was added and the mixture was filtered. Evaporation of the filtrate left crude α-naphthylurethane, which was recrystallized from ligroin to afford prisms of the pure sample, m.p. 119–120·5°, undepressed on admixture with an authentic sample prepared from MeOH.

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