The Reduction of β-Iodo Azides. A Stereospecific Synthesis of Aziridines[1a]

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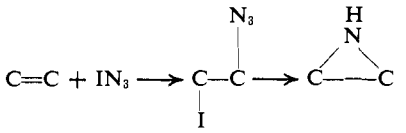
Abstract: A new synthesis of aziridines has been developed and the synthetic potential examined in detail. The substrates for the synthesis, β-iodo azides, were readily obtained from the highly stereoselective and regioselective addition of iodine azide to substituted ethylenes. Aziridine formation requires selective reduction of the azide function followed by base-catalyzed ring closure; competing side reactions are elimination of the elements of iodine azide and hydrogenolysis of the iodo group. The extent of reductive elimination is dependent on the stability of conformers with coplanar iodo and azido groups; aryl groups further enhance elimination in these conformers. Elimination specifically occurred in the LAH reduction of Δ²-cholestene, *trans*-stilbene, and cinnamyl alcohol adducts. Hydrogenolysis of the iodo function becomes competitive with aziridine formation in the sterically less hindered primary iodides. A study of reducing agents by means of product analysis suggests that only reducing agents which may possess Lewis acid properties favor reduction over elimination, *i.e.*, LAH, LAH·$AlCl_3$, or B_2H_6, but not $NaBH_4$, $LiBH_4$, or Zn. The optimum reagent, LAH, was applied to the mild synthesis of mono-, di-, tri-, and tetrasubstituted aziridines.

A convenient and versatile synthesis of aziridines is desirable in order to permit studies of the industrial and chemotherapeutical potentials of this important heterocyclic system.

Pseudohalogen additions to olefins can provide the precursors for an aziridine synthesis, but most of the pseudohalogen reagents possess limitations which restrict their general application. Nitrosyl chloride can only be applied to the synthesis of tetrasubstituted aziridines.[2] Iodine isocyanate was found to be unreactive toward such olefins as stilbenes, α,β-unsaturated esters and ketones, and some trisubstituted olefins.[3] The nonstereospecific addition of N,N-dichlorourethan is further complicated by allylic chlorinations when applied to substituted alkenes.[4] Iodine azide was found to be the most versatile of the pseudohalogens,[5] *i.e.*, high selectivity combined with high reactivity, and could be the reagent of choice for a practical aziridine synthesis.

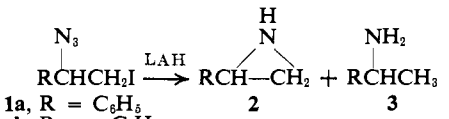


The bifunctionality in β-iodo azides presents several possible reaction sites for reducing agents, such as hydrogenolysis of the iodo function, reduction of the azide group, and reductive elimination[6] of both species. Formation of an aziridine ring requires selective reduction of the azide moiety followed by base-catalyzed ring closure. The properties of lithium aluminum hydride (LAH) such as availability, high hydride to weight ratio, and mild reaction conditions capable of accomplishing both reaction steps make it the reagent of choice. Aziridines, including styreneimine and many others, have been found to be inert to LAH.[7-9] A series of experiments was undertaken to test the predictability of LAH reductions of β-iodo azides and their applicability to the stereospecific synthesis of mono-, di-, tri-, and tetrasubstituted aziridines. A choice of alternate reducing agents is discussed.

Results

Monosubstituted Aziridines. The products from the LAH reduction of IN_3 adducts of terminal olefins are contingent on the regiochemistry[10] of the adducts; those containing a primary iodo group are susceptible to hydrogenolysis.

When α-azido-β-iodoethylbenzene (**1a**) reacted with LAH, the crude product (*ca.* 80%) contained 2-phenylaziridine (**2a**) and α-aminoethylbenzene (**3a**) which were separated in low yield by distillation. Their relative amounts by nmr were 7:3. Similar results were obtained from the reduction of 2-azido-1-iodohexane (**1b**), the aziridine **2b**:amine **3b** ratio being 1:1. Separation of the products was not possible since dimerization occurred, but was accomplished by fractional crystallization of their *p*-nitrobenzoyl derivatives. The aziridine **2c**:amine **3c** ratio derived from 2-azido-1-iodo-3-phenylpropane (**1c**) was 3:2, determined by nmr integration as well as by the weight ratio of the isolated *p*-nitrobenzoyl



1a, R = C_6H_5
b, R = *n*-C_4H_9
c, R = $C_6H_5CH_2$

derivatives. Pure 2-benzylaziridine (**2c**) was readily prepared by a two-step sequence, conversion of **1c** to the

(1) (a) Stereochemistry. XLI. For the previous paper see G. J. Matthews and A. Hassner, *Tetrahedron Lett.*, 1833 (1969). (b) NIH Predoctoral Fellow, 1964–1967. (c) NASA Predoctoral Fellow, 1965–1967.

(2) G. L. Closs and S. J. Brois, *J. Amer. Chem. Soc.*, 82, 6068 (1960).

(3) A. Hassner, M. E. Lorber, and C. Heathcock, *J. Org. Chem.*, 32, 540 (1967), and references therein.

(4) T. A. Foglia and D. Swern, *ibid.*, 31, 3625 (1966); 32, 75 (1967); 33, 766 (1968).

(5) F. W. Fowler, A. Hassner, and L. A. Levy, *J. Amer. Chem. Soc.*, 89, 2077 (1967).

(6) J. F. King and R. G. Pews, *Can. J. Chem.*, 42, 1294 (1964).

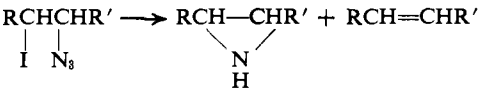
(7) A. Hassner and C. H. Heathcock, *J. Org. Chem.*, 30, 1748 (1965).

(8) K. Kotera, *et al.*, *Tetrahedron*, 24, 1727 (1968); *Tetrahedron Lett.*, 1651 (1968), and references therein.

(9) K. Ichimura and M. Ohta, *Bull. Chem. Soc. Jap.*, 40, 432 (1967).

(10) Regio refers to directional effects in bond making or breaking; see A. Hassner, *J. Org. Chem.*, 33, 2684 (1968).

Table I. Reduction of 1,2-Disubstituted 1-Azido-2-iodoethanes

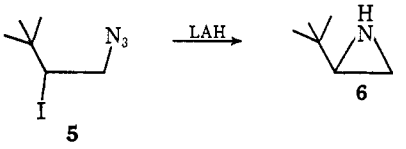


Iodo azide	Reagent	% aziridine	% olefin
7 (*erythro*)			
R = R′ = C_6H_5	LAH		80 (*trans*)
7	LAH, cat.[a]		80 (*trans*)
7	$NaBH_4$[b]		96 (*trans*)
7	$LiAlCl_3H$[c]	**18**, 83 (*trans*)[d,e]	
7	B_2H_6; NaOH	**18**, 87	
8 (*threo*)			
R = R′ = C_6H_5	LAH	**19**, 53 (*cis*) **18**, 11 (*trans*)	36 (*trans*)
9 (*erythro*)			
R = R′ = CH_3	LAH	**20**, 100 (*trans*)[d]	
10 (*threo*)			
R = R′ = CH_3	LAH	**21**, 100 (*cis*)[d]	
11 (*erythro*)			
R = R′ = C_2H_5	LAH	**22**, 100 (*trans*)[d]	
12 (*erythro*)			
R = R′ = *i*-Pr	LAH	**23**, 95 (*trans*)[d]	<5
13 (*erythro*)			
R = C_6H_5; R′ = CH_3	LAH	**24**, 95 (*trans*)[d]	5 (*trans*)
14 (*trans*)			
R,R′ = $(CH_2)_3$	LAH	**25**, 100[d]	
15 (*trans*)			
R,R′ = $(CH_2)_4$	LAH	**26**, 100[d]	
16 (*trans*)			
R,R′ = $(CH_2)_5$	LAH	**27**, 100[d]	
17 (*trans*)			
R,R′ = $(CH_2)_6$	LAH	**28**, 100[d]	
17	$LiBH_4$ or $NaBH_4$		<5
17	Zn–HOAc		100

[a] $CoBr_2$ or $SnCl_2$ was used as catalyst; G. A. Olah, *J. Amer. Chem. Soc.*, **81**, 3165 (1959). [b] In glyme in the presence of cobalt(II) tris(2,2-dipyridyl bromide): K. Ponsold, *J. Prakt. Chem.*, **36**, 148 (1967). Mainly starting material (84–90%) was obtained using $NaBH_4$ in refluxing isopropyl alcohol or $NaBH_4$–$AlCl_3$ in diglyme. [c] Followed by addition of an excess of LAH. [d] As indicated by nmr of crude product. [e] Difficult to purify.

iodoamine salt **4** with diborane and subsequent ring closure with base.

The I-*t*-butyl regiospecific adduct **5** of *t*-butylethylene gave only 2-*t*-butylaziridine (**6**) and no hydrogenolysis product.



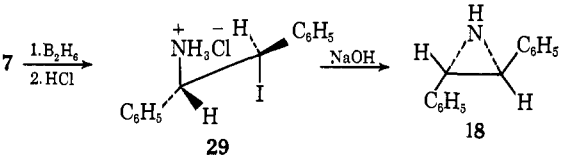
5 **6**

2,3-Disubstituted Aziridines. Another possible competition with reduction of the azido group in β-iodo azides is elimination of IN_3. The formation of olefin side product is most predominant in the reduction of the IN_3 adducts of *sym*-diaryl ethylenes. Accurate determination of the ratio of olefin to aziridine was not possible by gc due to decomposition of the aziridines during distillation and/or irreversible absorption on the column. Analysis was achieved by nmr integration of the easily distinguishable vinylic protons or by measurement of the total volume of gas evolved during the reduction.

Two equivalents of gas (1 equiv of N_2 and 1 equiv of H_2) are expected for complete conversion to an aziridine or amine function (Scheme I), whereas olefin formation by Scheme II produces only 1 equiv of gas.

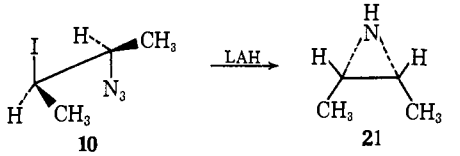
The reduction of *erythro*-1-azido-2-iodo-1,2-diphenylethane gave 80% *trans*-stilbene (83% on the basis of gas evolved). The application of other reducing agents is shown in Table I.

trans-Diphenylaziridine (**18**)[11] is best obtained in a two-step sequence, the intermediate *erythro*-1-amino-2-iodo-1,2-diphenylethane hydrochloride (**29**) being prepared by the diborane reduction of **7**. A considerable yield enhancement for this sluggish reaction is accomplished by heating to 50°, the gross reaction requiring



29 **18**

65 hr for complete loss of the azide absorption at 2100 cm^{-1}. The analogous *threo*-2-azido-3-iodobutane (**10**) gave *cis*-2,3-dimethylaziridine (**21**) exclusively; a quantitative yield was also indicated by the 2 equiv of gas evolved from the reaction.

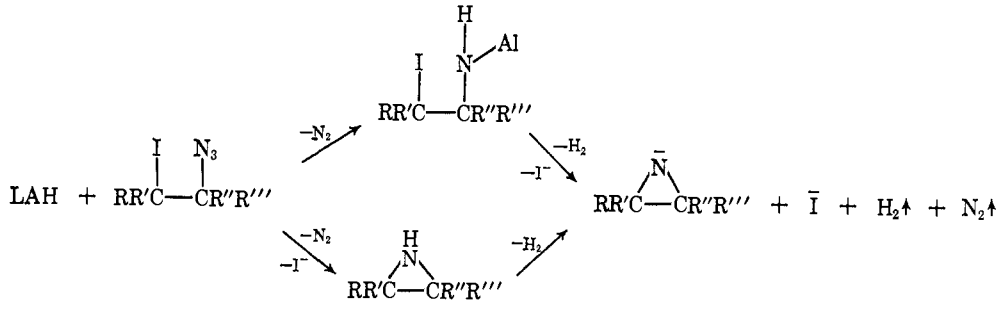


10 **21**

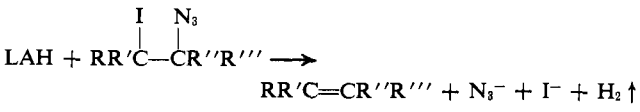
The *trans*-dialkylaziridines **22–24** were obtained from the corresponding *erythro*-iodo azides **11–13** without for-

(11) H. W. Heine, D. C. King, and L. A. Portland, *J. Org. Chem.*, **31**, 2662 (1966).

Scheme I



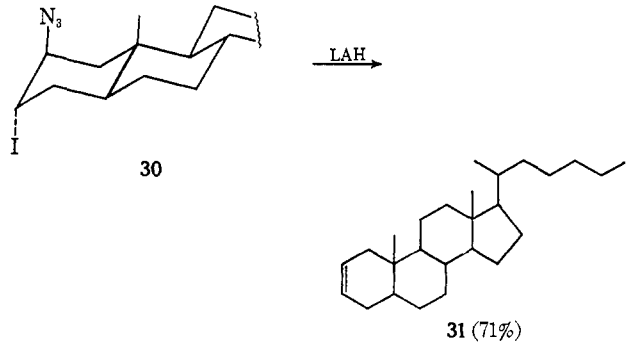
Scheme II



mation of olefins. Only a trace amount, <5%, of diisopropylethylene could be detected in the reduction of **12**.

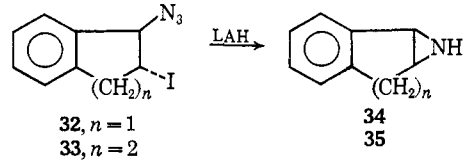
Phenyl substituents appear to favor the elimination reaction as was observed in the reduction of the *erythro*-iodo azide **13**; nmr and the gas evolved indicated 5% *trans*-1-phenylpropene.

The application of this procedure is highly recommended for the synthesis of fused aziridines in good yields. In only one instance, 2β-azido-3α-iodocholestane (**30**), was the olefin obtained in large amounts. This preferred elimination unquestionably arises from the rigid, *trans*-coplanar arrangement of the iodo and azido functions, stereoelectronically favoring E2 eliminations.



30 31 (71%)

Indene and 1,2-dihydronaphthalene were converted to their corresponding aziridines **34** and **35**. The instability of these specific products[12] makes it difficult to obtain reproducible yields.

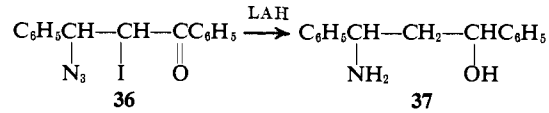


32, $n=1$
33, $n=2$

34
35

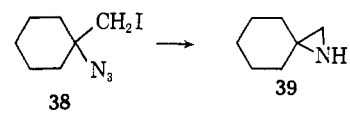
It was hoped that the ability of IN_3 to form adducts with α,β-unsaturated systems would lead to the synthesis of α,β-aziridinyl ketones and carboxylates. LAH was unsuccessful in these attempts since *erythro*-3-azido-2-iodo-3-phenylpropionate gave cinnamyl alcohol as the major product (60% by nmr) and 1,3-diphenyl-3-azido-2-iodo-1-propanone (**36**) gave 1-amino-1,3-diphenyl-3-propanol (**37**) in 67% yield.

(12) A. Hassner and C. Heathcock, *Tetrahedron*, **20**, 1037 (1964).

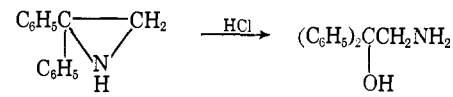


36 **37**

2,2-Disubstituted Aziridines. The LAH reduction of **38** produced 1-azaspiro[2.5]octane (**39**) in quantitative yield (nmr and gas evolution analysis).



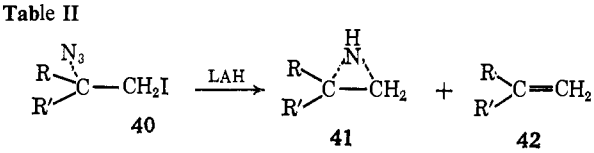
38 **39**



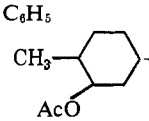
41d **43**

Subtle steric and electronic effects are at play in the syntheses of 2,2-disubstituted aziridines (see Table II).

Table II

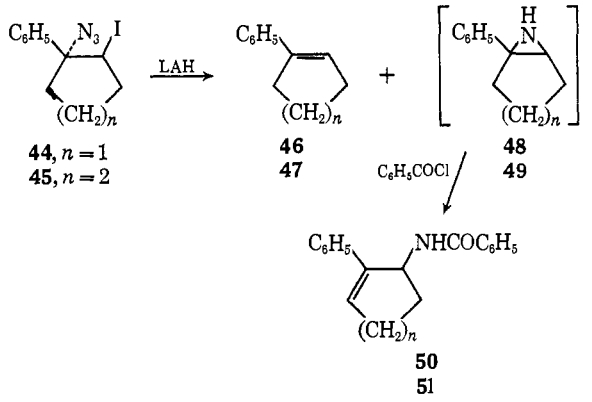


40 **41** **42**

Starting azide	R	R′	Yield of olefin
40a	CH_3	CH_3	0% by gas evolution
40b	C_6H_5	CH_3	10% by nmr
40c		CH_3	30% by nmr
40d	C_6H_5	C_6H_5	22% by nmr

Treatment of 2,2-diphenylaziridine **41** with HCl followed by neutralization gave amino alcohol **43** as well as unchanged **41**.

2,2,3-Trisubstituted Aziridines. Attempts to synthesize aziridines of this structure were thwarted only in the presence of phenyl substituents. (1-Azido-2-iodo-1-phenyl)cyclopentane (**44**) and -cyclohexane (**45**) reacted with LAH to give 22 and 20% (by nmr) of 1-phenylcyclopentene and -cyclohexene, respectively. The formation of the corresponding aziridines (**48** and **49**) could only be inferred by the isolation of (N-benzoyl-3-amino-2-phenyl)cyclopentene and -cyclohexene (**50** and **51**), respectively, from treatment of the crude products with benzoyl chloride. On the other



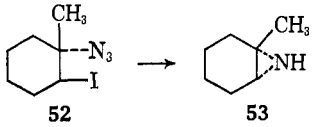
44, $n=1$
45, $n=2$

46
47

48
49

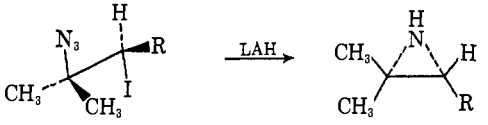
50
51

hand, aziridine **53** was isolated from the reduction of **52** in 81% yield.



52 53

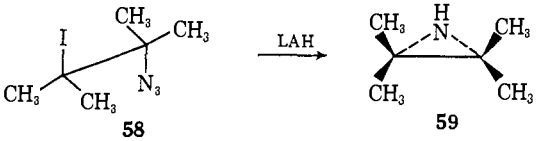
The trialkylethylene adducts **54** and **55** gave fair yields (45 and 60%, respectively) of 3-methyl- and 3-ethyl-2,2-dimethylaziridines (**56** and **57**). The high volatility of these aziridines is responsible for the lower than usual yields.



54, R = CH_3
55, R = C_2H_5

56
57

2,2,3,3-Tetrasubstituted Aziridines. Using the proper precautions for preparing the iodo azide **58**[13] followed by LAH reduction, the volatile 2,2,3,3-tetramethylaziridine (**59**) was obtained in 56% yield; nmr showed the formation of only 2% olefin.



58 59

Discussion

The complete stereospecificity in the reductive ring closure of β-iodo azides to aziridines confirms the *trans* stereochemical assignment[5] made to these IN_3 adducts. In most cases β-iodo azides were converted to aziridines under the mild conditions of LAH in ether at 0°. Any further reactions of the strained aziridine ring (*e.g.*, polymerization) and toxicity hazards[14] are minimized. In addition, an ether solution or an ether concentrate can be used for subsequent reactions after filtration of the aluminum salts and drying over $MgSO_4$. Using this procedure the conversion of crude aziridines to acyl, carbamyl, or other derivatives was accomplished in good yield.

The occurrence of iodide hydrogenolysis as a side reaction in aziridine formation correlates well with the postulated mechanism for halide reduction, an attack of a nucleophilic hydride complex on the halide-bearing carbon atom.[15] This backside attack is very sensitive to steric effects. Accordingly, only unhindered primary iodo functions were displaced by hydride and the amount of displacement decreased in the order of β-*n*-butyl > β-benzyl > β-phenyl. Steric effects in β-trisubstituted iodides (*i.e.*, 1-azido-2-iodo-2,2-dimethylbutane (**5**)) and 2,2-disubstituted 1-iodo-2-azidoethanes completely inhibited iodide hydrogenolysis.

Differentiation of an acyl derivative of the aziridine *vs.* that of a primary amine side product was readily achieved by an examination of the ir and nmr spectra of these products. In this manner an estimate of the ratio of aziridine to primary amine in the crude product was obtained.

2,2-Disubstituted aziridines and their benzoyl derivatives were observed to undergo facile ring opening, indicative of a solvolysis to a tertiary carbonium ion (see formation of **43** from **41d** and of **50** and **51** from **48** and **49**, respectively).

On the basis of the volume of gas evolved during LAH reduction (see Schemes I and II) it is possible to estimate the extent of IN_3 elimination as a side reaction (see Table III). The relative amount of olefin formed depends upon preferred conformations and the nature of substituents in the starting β-iodo azide. Coplanarity, either *syn* or *anti*, is one of the important requirements in E2 eliminations.[16] *erythro* diastereomers have a low-energy conformation (i) with a *anti*-coplanar arrangement of the iodo and azido groups which favors elimination. *threo* diastereomers and adducts from unsymmetrically disubstituted ethylenes have *syn*-coplanar conformers (ii and iii) in which energy lowering may be achieved by London forces between the polarizable iodo and azido groups.[17] Such structural features are con-

Table III. Volume of Gas Evolved from Treatment with LAH in Ether at 0°

Reactant	Moles × 10^3 Reactant	Gas[e]	Gross reaction time	Olefin deduced, %
Aziridine	4.36	4.55	5 min	Standard
1-Iodobutane	3.83	0.00	(3 hr)[c]	Standard
3-Azidocyclohexene	3.98	8.03	<5 min	Standard
1a	1.84	3.70	1 hr	0[a]
1c	2.30	4.52	45 min	3[a]
7	1.15	1.34	4 hr total	83[a]
9	2.29	4.58	1.75 hr	0
10	2.26	4.53	3 hr	0
13	1.96	3.72	2.25 hr	5[a]
14	2.57	4.73	2 hr	17
15	2.88	5.18	1.75 hr	20
16	2.50	4.82	1.5 hr	7
17	2.82	5.56	2.5 hr	3
33	1.45	2.98	1 hr	0
38	2.10	4.23	4.5 hr	0
40	2.44	4.86	1 hr [a,d]	0
41	1.94	3.12	<5 hr	38[b]
52	2.62	4.20	4 hr	39
45	1.72	2.64	4.5 hr	49[b]

[a] Value agrees with the nmr integration of the crude product from the reduction. [b] The nmr integration indicated approximately half as much olefin formation. [c] Observed for 3 hr. [d] Reaction was run at 23°. [e] STP.

(13) A. Hassner and G. J. Matthews, University of Colorado, to be published separately.

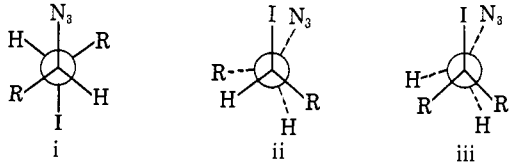
(14) R. M. Acheson, "An Introduction to the Chemistry of Heterocyclic Compounds," 2nd ed, Interscience Publishers, New York, N. Y., 1967, pp 6–17.

(15) N. G. Gaylord, "Reduction With Complex Metal Hydrides," Interscience Publishers, New York, N. Y., 1956.

(16) C. H. Depuy, R. D. Thurn, and G. F. Morris, *J. Amer. Chem. Soc.*, **84**, 1314 (1962).

(17) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y., 1965, Chapter 1.

ducive to a concerted bimolecular elimination of the type proposed to account for a remarkably facile reduction of 8-substituted 1-bromonaphthalenes[18] and *ortho*-substituted anisoles.[19] The percentage of elimination



i ii iii

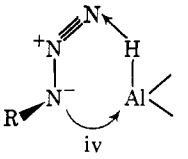
is further enhanced by phenyl substituents which reduce the activation energy for β eliminations involving benzylic substituents.[20]

The contrasting behavior of the reducing agents studied can be correlated on a structure–reactivity basis. The marked difference in the sensitivity of various functional groups to reducing agents has been attributed to the nucleophilicity of the attacking species.[21] A compilation of the reagents which effect a facile reduction of the azide function in β-iodo azides coincides with a list of reducing reagents which possess Lewis acid character, *i.e.*, diborane, LAH, and the "mixed hydrides." A further stipulation is that for maximum effect the Lewis acid should be incorporated in the reducing species and not in the form of "gegen" substances, such as the lithium ion in $LiBH_4$ and mixtures of $CoBr_2$ or $SnCl_2$ with LAH. Both the elimination as well as the reduction of the azide function are enhanced if the reducing species are better hydride donors.

The specific site for electrophilic attack on the azido group has been suggested to be the carbon substituted nitrogen atom.[7,22] This is also substantiated by MO calculations.[7] The results reported here are consistent with this postulate in that compounds bearing a tertiary azide are reduced much slower than secondary azides (see Table III).

In contrast, nucleophilic species, *e.g.*, hydride, should attack the terminal nitrogen. The isolation of unstable disubstituted triazenes from the reaction of azides with cyanide,[7] Grignard reagents,[7,22] and triphenylphosphine[23] strongly support this view. The nucleophilic activity of LAH is apparent in the reductive eliminations of β-iodo azides. A transition state involved in such a process requires the development of a negative charge on the geminal carbon atom. A phenyl substituent, as compared to alkyl substituents, should therefore lower the activation energy of the elimination reaction.

The requirement of both a strong hydride donor and a Lewis acid suggests a five-membered ring cyclic transfer scheme (iv) for the reduction of azido groups. Preliminary coordination of LAH followed by cyclic hydride transfer was advanced to explain products from the reduction of steroid epoxides[24] and propargyl halides.[25] The sluggish reduction by diborane may be explained by the weak hydride donating properties of this Lewis acid.



iv

The contrast in activity of various reducing agents is illustrated in the reduction of *erythro*-1-azido-2-iododiphenylethane (**7**) (see Table I). This suggests that the synthesis of other aziridines unattainable by LAH reduction might be possible by the use of alternate reducing agents.

Experimental Section[26]

General. The general procedure for iodine azide addition was followed as described.[5] Both iodo and azido functions are quite labile in the iodo azide adducts and elemental analysis was precluded with some azides, since extensive decomposition occurred on attempted distillation. However, evidence for complete addition can be obtained from the appearance of very strong asymmetric stretching absorption at *ca.* 2100 cm^{-1} and the disappearance of the vinylic proton absorption in the nmr spectra.

General Procedure for the LAH Reduction of β-Iodo Azides. A mixture of 90 ml of anhydrous ether and 2.50 g of LAH in a 250-ml, three-necked flask fitted with a reflux condenser, mechanical stirrer with a Teflon blade, and an addition funnel, was cooled by an ice bath. To the stirred slurry was added a solution of 0.03–0.045 mol of the β-iodo azide in a minimal amount of ether (usually 15–20 ml).

Caution! The β-iodo azide should be added slowly over a period of 20–30 min to avoid vigorous delayed frothing.

Once the addition was complete, the mixture was allowed to warm to room temperature and to stir for 8–12 hr. Work-up was accomplished by the slow addition of 10 ml of 20% sodium hydroxide followed by 30–45 min of vigorous stirring. The white, granular salts were filtered through a medium porosity sintered-glass funnel and washed well with ether. The dried ($MgSO_4$) filtrate was concentrated *in vacuo*.

Caution! Several of the aziridines decomposed rapidly when concentrated without scrupulous drying.

A separate apparatus was used for the gas evolution experiments (see Table III). The reaction flask was dried in an oven at 120° for several hours. The apparatus consisted of a 200-ml, two-necked flask, one neck sealed with a size 14 rubber septum and one fitted with a reflux condenser which was connected through a Dry Ice trap to a gas buret. The reaction flask was immersed in a 0° constant-temperature bath and 0° water was continually pumped through a condenser. After the reaction vessel was charged with *ca.* 2.0 g of LAH and 50 ml of ether, it was equilibrated for 4–5 hr. The iodo azide sample was dissolved in dry ether in an appropriate volumetric flask. The desired aliquot (5–15 ml) from the volumetric was injected into the reaction vessel with a hypodermic syringe. After injection the volumetric changes were monitored at 15-min intervals. Several measurements were made for each blank volume of ether injected.

LAH Reduction of α-Azido-β-iodoethylbenzene (1a). From 40.0 g of the iodo azide **1a**[5] there was obtained 14.3 g of colorless product which was distilled through a 12-in. spinning-band column. The 2-phenylaziridine (**2a**, 2.14 g, bp 90–94° (11 mm) (lit.[27] 94–95° (10 mm)) was separated from α-aminoethylbenzene (**3a**, 1.44 g, bp

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(20) J. F. Bunnett, *Angew. Chem. Intern. Ed. Engl.*, 1, 225 (1962).
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(24) (a) E. C. Ashby and B. Cooke, *J. Amer. Chem. Soc.*, **90**, 1625 (1968); (b) E. Glotter, S. Greenfield, and D. Lavie, *Tetrahedron Lett.*, 5261 (1967).
(25) J. K. Crandall, D. J. Keyton, and J. Kohne, *J. Org. Chem.*, **33**, 3655 (1968).
(26) All melting points were determined on a Fisher-Johns melting point block and are uncorrected. Infrared spectra were recorded with a Beckman IR-5 spectrometer. Nuclear magnetic resonance spectra were recorded with either a Varian A-60 or A-60A spectrometer. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn. In nmr descriptions, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet; Az connotes protons bonded to the carbon of an aziridine ring. All aziridines showed characteristic NH absorption at or near 3250 cm^{-1}.
(27) S. J. Brois, *J. Org. Chem.*, 27, 3532 (1962).

69–72° (11 mm)). The nmr spectra (CCl_4) of 2-phenylaziridine at τ 2.83 (s, 5), 7.25 (4-band multiplet, 1), 8.08 (d, 1, J = 6 Hz), 8.45 (d, 1, J = 3.5 Hz), and 8.92 (s broad, 1, N*H*), and α-aminoethylbenzene are identical with those previously reported.[27,28] A reexamination of the spectral integrations of the crude product mixture showed the aziridine **2a**:amine **3a** ratio to be 7:3. Extended treatment with LAH produced no change in the product composition.

LAH Reduction of 2-Azido-1-iodohexane (1b). Iodo azide **1b**,[5] 12.04 g, gave 3.99 g of a colorless oil which was judged impure by both an amine N–H shoulder on the aziridine N–H, 3250 cm^{-1} in the ir, and an uninterpretable nmr spectrum. Attempted distillation of this mixture through a spinning-band column was unsuccessful due to an apparent dimerization which led to a crystalline product, identified as 2,6-di-*n*-butylpiperazine: mp 84.5–85° from Skellysolve F; *m/e* 198; nmr (CCl_4) τ 6.9–8.1 (m), 8.38 (s), disappears on addition of D_2O.

Anal. Calcd for $C_{12}H_{26}N_2$: C, 72.66; H, 13.21. Found: C, 72.58; H, 13.02.

To the crude product, 2.63 g, dissolved in 20 ml of dry benzene and 2.72 g (27 mmol) of triethylamine was added 4.97 g (27 mmol) of *p*-nitrobenzoyl chloride dissolved in 30 ml of benzene. After 2 hr the triethylamine salt was filtered and the solvent removed from the filtrate *in vacuo* to give a brown oil. N-(*p*-Nitrobenzoyl)-1-*n*-butylaziridine, 1.58 g, 22%, was obtained from the pentane levigate of the crude oil: mp 33–36° from Skellysolve F–dichloromethane; ir (smear) 1670 (tertiary amide C=O) and 1520 cm^{-1} ($-NO_2$), and no N–H; nmr (CCl_4) showed aziridine ring absorptions at τ 7.49 (m, 2) and 7.82 (m, 1), and no amide N-*H*.

Anal. Calcd for $C_{13}H_{16}O_3N_2$: C, 62.89; H, 6.50. Found: C, 62.83; H, 6.45.

N-(*p*-Nitrobenzoyl)-2-aminohexane was obtained from crystallization of the residue from the above pentane levigate, 1.58 g: mp 89–92°; mp 95–95.5° after several recrystallizations from benzene–cyclohexane; ir (KBr) showed strong N–H, amide I, amide II, and $-NO_2$ bands at 3300, 1640, 1550, and 1520 cm^{-1}, respectively; nmr ($CDCl_3$) showed downfield absorptions at τ 3.28 (d broad, 1, J = 8 Hz, amide N-*H*) and 5.87 (m, 1, $W_{1/2}$ = 20 Hz).

Anal. Calcd for $C_{13}H_{18}O_3N_2$: C, 62.38; H, 7.25. Found: C, 62.26; H, 7.09.

After the nmr absorptions for both *p*-nitrobenzoyl derivatives were characterized, the aziridine:amine ratio resulting from the LAH reduction was interpreted as 1:1 from the respective nmr integrations of the crude N-*p*-nitrobenzoyl derivatives.

LAH Reduction of 2-Azido-1-iodo-3-phenylpropane (1c). The iodo azide **1c** (11.35 g)[5] gave 5.27 g of a colorless oil from which two basic products from the reaction were separated in the form of their N-*p*-nitrobenzoyl derivatives.

To 4.95 g of crude **1c** in 20 ml of benzene and 4.95 g (37 mmol) of triethylamine was added 6.90 g of *p*-nitrobenzoyl chloride in 60 ml of benzene. After 1 hr the triethylamine salt was filtered and the solvent removed *in vacuo* to a volume of about 10 ml. At this point an equal volume of Skellysolve F was added and the solution cooled to 0° to furnish 3.98 g of N-(*p*-nitrobenzoyl)-2-amino-3-phenylpropane: crude mp 140–144°; mp 147–148° after recrystallizations from benzene–cyclohexane (1:1); ir (KBr) showed a strong N–H absorption at 3300 cm^{-1}, and an amide I, amide II, and $-NO_2$ bands at 1640, 1550, and 1520 cm^{-1}, respectively; nmr ($CDCl_3$–DMSO-d_6) τ 1.93 (A_2B_2, 4), 2.75 (s, 5), 5.45 (pentet, 1, J = 7 Hz), 7.07 (m, 2), and 8.75 (d, 3, J = 7 Hz).

Anal. Calcd for $C_{16}H_{16}O_3N_2$: C, 67.59; H, 5.67. Found: C, 67.44; H, 5.75.

The filtrate from the above crystallization was concentrated and levigated with 300 ml of pentane. Concentration to a volume of 70 ml and cooling to −10° gave 0.195 g of N-(*p*-nitrobenzoyl)-2-benzylaziridine: crude mp 87–90°; mp 89–90° from Skellysolve B (lit.[29] mp 85.5–86.5°); ir (KBr) 1670 (*t*-amide C=O) and 1520 cm^{-1} ($-NO_2$); nmr ($CDCl_3$) τ 1.87 (m, 4), 2.82 (s, 5), 7.04 (m, 2), 7.38 (m, 1), and 7.68 (m, 1).

After the nmr absorptions for both pure *p*-nitrobenzoyl derivatives were established, the aziridine:amine ratio in the crude product was interpreted at 60:40 from the respective nmr integrations.

2-Benzylaziridine (2c). To a solution of 5.57 g (0.019 mol) of **1c**[5] in 50 ml of tetrahydrofuran (distilled from LAH) was added 50 ml of a commercial diborane solution (1 *M* BH_3 in tetrahydrofuran). After 12 hr at 50° the excess diborane was decomposed with about 40 ml of ethanol, gaseous hydrogen chloride was bubbled into the reaction mixture for several minutes, and 50 ml of ether was added. Cooling the reaction mixture to 0° and filtration furnished 3.57 g of 1-iodo-2-amino-3-phenylpropane hydrochloride (**4**).

The salt **4**, 1.51 g, was treated with 1.20 g of NaOH in 40 ml of ethanol to give upon work-up 435 mg of 2-benzylaziridine (**2c**) as a colorless oil: nmr (CCl_4) showed absorptions at τ 2.83 (s, 5), 7.43 (m, 2), 2.0 (m, 1), 8.41 (d, 1, J = 5.5 Hz), 8.67 (s, 1, N-*H*, vanishes with D_2O), and 8.75 (d, 1, J = 3 Hz).

The N-*p*-nitrobenzoyl derivative was prepared in 62% yield in benzene,[30] mp 90–91° (from Skellysolve B), identical with an authentic sample described in the preceding preparation.

2-*t*-Butylaziridine (6). LAH reduction of 1-azido-2-iodo-3,3-dimethylbutane,[5] 7.00 g, gave 2.02 g of a volatile colorless liquid: nmr (CCl_4) τ 8.1–8.8 (ABC pattern, 3, Az), 9.14 (s, 9), and 9.42 (s, 1, vanishes in presence of D_2O).

The N-phenylthiocarbamyl derivative (3.6 g from 1.77 g of crude **6**) melted at 84–86°; mp 89–90° after several recrystallizations from Skellysolve B which contained traces of acetone.

Anal. Calcd for $C_{13}H_{18}N_2S$: C, 66.62; H, 7.74. Found: C, 66.73; H, 7.84.

Reduction of *erythro*-1-Azido-2-iodo-1,2-diphenylethane (7) with LAH or $NaBH_4$. See Table I for results.

Reduction of 7 with LAH and Aluminum Chloride. To 75 ml of dry ether cooled in a Dry Ice–acetone bath was added 1.00 g (7.5 mmol) of sublimed aluminum chloride followed by 100 mg (2.5 mmol) of LAH. The mixture was allowed to warm to room temperature and added to a solution of **7** (3.49 g, 10 mmol) in 125 ml of ether dropwise over 0.5 hr. The reaction was stirred an additional hour, then 2.0 g of LAH was added. The stirring was continued for 2 hr followed by the addition of 7.5 ml of 20% NaOH and filtration. Removal of the solvent from the dried filtrate produced 1.86 g of an oil; nmr ($CDCl_3$) showed singlet absorptions at τ 2.74, 6.98, and 8.50 which were characteristic of *trans*-2,3-diphenylaziridine (**18**), and impurities at τ 2.80, 5.88, and 7.08 (an integration of the singlet at 6.98 against the total aromatic protons indicates *ca.* 85% *trans*-2,3-diphenylaziridine). The crude product, 1.55 g, on treatment with hot Skellysolve B and fractional crystallization yielded 690 mg of **18**, mp 43–44° (lit.[31] mp 46–47°).

***trans*-2,3-Diphenylaziridine (18)** was best prepared by diborane reduction of **7**[11] except that the reduction was carried out at 50°. Crude **18** was obtained in 87% yield and was recrystallized from pentane: mp 43–44° (lit.[31] mp 46–47°); ir (pentane smear) 3300, 3050, 1600, 1500, 1450, 1187, 1155, 1105, 1078, 1030, 745, and 695 cm^{-1}; nmr (CCl_4) τ 2.85 (s, 10), 7.15 (s, 2) 8.77 (s, broadened, 1, N–H, disappeared upon addition of D_2O).

***cis*-2,3-Diphenylaziridine (19).** LAH reduction of *threo*-1-azido-2-iodo-1,2-diphenylethane[5] (**8**, 5.00 g) gave 2.59 g of colorless solid. Its nmr spectrum ($CDCl_3$) showed the absence of *cis*-stilbene vinyl protons at τ 3.48. Two upfield singlet absorptions at τ 6.70 and 7.10 in the ratio of 11:2, respectively, were assigned to *cis*- and *trans*-2,3-diphenylaziridines, respectively. To 2.04 g of the crude product was added 30 ml of 10% HCl. The undissolved solid, 0.74 g after drying, was *trans*-stilbene: mp 121–123°, authentic sample mp 124–125°; nmr ($CDCl_3$) showed the characteristic strong singlet at τ 2.96.

Neutralization of the acidic filtrate with 20% NaOH produced colorless crystals of *cis*-2,3-diphenylaziridine (**19**), 1.16 g (41%) after drying: mp 76–80°; mp 81–82° from Skellysolve B (lit.[32] mp 81–82°); nmr (CCl_4) showed singlets at τ 8.95, 6.65, and 8.72 (N–H).

The N-phenylcarbamyl derivative melted at 160–161° (lit.[33] 163–164°).

***cis*-2,3-Dimethylaziridine (21).** The LAH reduction of *threo*-2-azido-3-iodobutane[5] (**10**, 8.45 g) required a modification of the work-up procedure due to the high volatility of the product. The dried ether solution of the aziridine **21** was distilled under reduced pressure (*ca.* 50 mm) from a 40° water bath. The remaining product was analyzed by nmr (CCl_4) which showed, in addition to

(28) "NMR Spectra Catalog," compiled by N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, Varian Associates, 1962.

(29) D. V. Kashelikar and P. E. Fanta, *J. Amer. Chem. Soc.*, **82**, 4927 (1960).

(30) All amine and aziridine derivatives were prepared by mixing equal molar amounts of the amine or aziridine with the reactants in the appropriate solvent unless otherwise stated.

(31) A. Weissberger and H. Bach, *Ber.*, **64**, 1095 (1931); **65**, 631 (1932).

(32) D. A. Darapsky and H. Spannagle, *J. Prakt. Chem.*, 272 (1915).

(33) K. Kotahonoki, K. Kotera, Y. Matsukawa, S. Miyozaki, T. Okada, H. Takahashi, and Y. Takano, *Tetrahedron Lett.*, 1062 (1965).

25% ether, absorptions at τ 8.08 (m, 2), 8.77 (s, 1, vanishes in presence of D_2O), and 8.95 (d, 6, J = 5.5 Hz, CH_3).

The N-phenylthiocarbamyl derivative was prepared in 75% yield: crude mp 87–91°; mp 96–97° from acetone–Skellysolve B.

Anal. Calcd for $C_{11}H_{14}N_2S$: C, 64.04; H, 6.84. Found: C, 64.21; H, 6.95.

The presence of the aziridine **21** in the ether distillate (see above) was determined by treatment with gaseous HCl. The white solid which formed was filtered and dried under vacuum, 0.50 g: mp 141–147°; nmr ($CDCl_3$ and trace of DMSO-d_6) τ 1.53 (s broad, 3, $W_{1/2}$ = 13 Hz), 5.57 (broadened pentet, 1, J = 6 Hz), 6.62 (broadened pentet, 1, J = 6 Hz), and 8.43 (t, 3, J = 7 Hz).

***trans*-2,3-Dimethylaziridine (20).** The product (2.65 g) from LAH reduction of *erythro*-2-azido-3-iodobutane[5] (**9**), 10.0 g, was worked up as described for **21**. The nmr spectrum (CCl_4) showed, in addition to 35% ether, absorptions at τ 8.53 (m, 2, Az), 8.87 (d, *ca.* 6, J = 4.5 Hz, CH_3), and 9.45 (s, 1, vanishes in presences of D_2O). The N-phenylthiocarbamyl derivative was prepared in *ca.* 70% yield: crude mp 85–89°; mp 93.5–95° from acetone–Skellysolve B.

Anal. Calcd for $C_{11}H_{14}N_2S$: C, 64.04; H, 6.84. Found: C, 64.19; H, 6.98.

The presence of **20** in the ether distillate (see above) was determined by treatment with gaseous HCl which gave *erythro*-3-chloro-2-aminobutane hydrochloride: mp 171–172.5° (from acetone–methanol); nmr ($CDCl_3$–DMSO-d_6) τ 1.59 (s broad, 3, $W_{1/2}$ = 20 Hz), 5.32 (q of doublets, J = 6 Hz, J = 3.5 Hz), 6.42 (q of doublets, 1, J = 6.5 Hz, J = 3.5 Hz), 8.43 (d, 3, J = 6.5 Hz), and 8.59 (d, 3, J = 6.5 Hz).

Anal. Calcd for $C_4H_{11}NCl_2$: Cl, 49.22. Found: Cl, 49.13.

***trans*-2,3-Diethylaziridine (22).** LAH reduction of 10.0 g of *erythro*-3-azido-4-iodohexane (**11**) gave 2.18 g of a colorless liquid; nmr ($CDCl_3$) τ 8.2–9.3 (broad).

The crude N-phenylcarbamyl derivative melted at 73–75°; mp 75–77° from Skellysolve B–ethyl acetate.

Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.52; H, 8.31. Found: C, 71.60; H, 8.43.

***erythro*-3-Azido-4-iodo-2,5-dimethylhexane (12)** was prepared from *trans*-2,5-dimethylhexene in 96% yield; nmr (CCl_4) τ 5.94 (d of doublets, 1, J = 11 Hz, J = 2 Hz), 6.48 (d of doublets, J = 11 Hz, J = 2.5 Hz), 7.33 (sextet of doublets, J = 6.5 Hz, J = 2.5 Hz), 8.8 (m, 1, $W_{1/2}$ = *ca.* 20 Hz), 8.95 (t, 3, J = 6.5 Hz), and 9.12 (t, 3, J = 6.5 Hz).

Anal. Calcd for $C_8H_{16}IN_3$: C, 34.18; H, 5.74. Found: C, 34.31; H, 5.84.

***trans*-2,3-Diisopropylaziridine (23).** LAH reduction of *erythro*-3-azido-4-iodo-2,5-dimethylhexane (**12**, 10.5 g) gave after distillation of the ether at *ca.* 15 mm, 3.58 g of a colorless liquid; nmr (CCl_4) τ 8.70 (m, 2), 9.02 (s, 14, $W_{1/2}$ = 4 Hz), and 9.38 (s, 1, N–H, vanishes in presence of D_2O). An nmr spectrum (ether) as well as gc analysis at 25° on Carbowax 20M before the ether distillation was complete indicated a trace amount (<5%) of *trans*-diisopropylethylene.

The N-phenylcarbamyl derivative (91%) melted at 96–97.5°; mp 97–98° after several recrystallizations from Skellysolve B.

Anal. Calcd for $C_{15}H_{22}ON_2$: C, 73.13; H, 9.00. Found: C, 72.92; H, 8.83.

***trans*-2-Phenyl-3-methylaziridine (24).** LAH reduction of *erythro*-2-azido-1-iodo-1-phenylpropane[5] (**13**, 10.3 g) gave 4.93 g of a colorless liquid, the nmr spectrum (CCl_4) of which showed the presence of *ca.* 5% *trans*-1-phenylpropene in addition to the aziridine **24** at τ 2.89 (s, 5), 7.56 (d, 1, J = 2.8 Hz), 8.17 (m, 1), 8.70 (s broad, 1, vanishes in presence of D_2O), and 8.80 (d, 3, J = 5.3 Hz).[34]

The N-phenylcarbamyl derivative was prepared in quantitative yield: mp 125–134°; recrystallized from acetone, mp 144–146°.

Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39. Found: C, 76.12; H, 6.58.

LAH reduction of 2β-azido-3α-iodocholestane (30),[5] 366 mg, led to 228 mg of solid which on trituration with methanol yielded 178 mg of 2-cholestene (**31**), mp 67–69°, identical with an authentic sample.

6-Azabicyclo[3.1.0]hexane (25). LAH reduction of *trans*-1-azido-2-iodocyclopentane (**14**),[6] 10.00 g, gave 2.85 g of a volatile colorless liquid; nmr (CCl_4) τ 7.65 (s broad, 2, $W_{1/2}$ = 3 Hz, Az), 7.9–8.8 (m, 6), and 8.52 (s broad, 1, vanishes with D_2O).

The N-*p*-nitrobenzoyl derivative was prepared in 51% yield: mp 93–99°; after several recrystallizations from Skellysolve F–benzene, mp 108–110°; ir (KBr) 1650 cm^{-1} (tertiary amide); nmr ($CDCl_3$) τ 1.70 (4, A_2B_2 pattern), 6.70 (s broad, 2, $W_{1/2}$ = 3 Hz, Az), and 7.6–8.8 (m, 6).

Anal. Calcd for $C_{12}H_{12}O_3N_2$: C, 62.06; H, 5.21. Found: C, 62.21; H, 5.36.

The N-phenylthiocarbamyl derivative melted at 165–167° (lit.[35] 167–168°).

7-Azabicyclo[4.1.0]heptane (26). LAH reduction of 10.0 g of *trans*-1-azido-2-iodocyclohexane[5] gave 3.97 g of **26**: ir (neat) 3210 cm^{-1}; nmr (CCl_4) τ 7.9–9.1 (complex multiplet), 7.93 (s, broad, 2, $W_{1/2}$ = 6 Hz), 8.49 (s, 1, vanishes with D_2O), and only a trace of vinyl protons at 4.34 attributed to less than 2% of cyclohexene.

The crude aziridine **26**, 3.97 g, was treated with 5.85 g of benzoyl chloride. Work-up gave a colorless oil, which upon treatment with Skellysolve B–benzene (1:3) partially solidified, 0.85 g, mp 148–160°.

The major portion of this solid was insoluble in most solvents. Although vigorous bumping ensued, the product was recrystallized several times from ethanol to give a high-melting product which was assigned the structure **N,N′-dibenzoyl-N-(*trans*-2-chlorocyclohexyl)-*trans*-diaminocyclohexane**: mp 242–244°; ir (KBr) 3300 (N—H), 1645 (amide C=O), 1620 (amide C=O), 1550 (amide II band), and 690 cm^{-1}; the molecular ions at *m/e* 438 and 440 with relative intensities of 3:1 and *m/e* 403 (consistent with one chlorine atom in the molecule).

Anal. Calcd for $C_{26}H_{21}N_2O_2Cl$: C, 71.13; H, 7.12. Found: C, 71.25; H, 7.27.

The Skellysolve B–benzene filtrate (see above) was concentrated *in vacuo* and the residue redissolved in ether. Cooling to −10° effected the crystallization of N-benzoyl-7-azabicyclo[4.1.0]heptane, 3.54 g (38% yield): mp 73–76°; mp 76–77° from ether (lit.[36] mp 77–78°).

The N-phenylcarbamyl derivative of **26** melted at 154–157° (from methanol) (lit.[12] mp 158–159°).

***trans*-1-Azido-2-iodocycloheptane (16)** was prepared by IN_3 addition to freshly distilled cycloheptene in 75% yield; nmr (CCl_4) τ 5.82 (m, 1), 6.05 (m, 1), and 8.0 (m, 10).

8-Azabicyclo[5.1.0]octane (27). LAH reduction of 11.16 g of *trans*-1-azido-2-iodocycloheptane (**16**) gave 4.51 g of **27**; nmr ($CDCl_3$) showed two major envelopes of absorptions at τ 7.92 (s broad, $W_{1/2}$ = 9 Hz) and from 8.0 to 9.1.

The N-*p*-nitrobenzoyl derivative was prepared in 65% yield: mp 91–101°; mp 98–101° after several recrystallizations from Skellysolve F–chloroform.

Anal. Calcd for $C_{14}H_{16}O_3N_2$: C, 64.60; H, 6.20. Found: C, 64.30; H, 6.28.

The N-phenylthiocarbamyl derivative, mp 99–109°, was prepared in 89% yield; mp 119.5–121° (from ethanol) (lit.[37] 120.5°).

9-Azabicyclo[6.1.0]nonane (28). LAH reduction of *trans*-1-azido-2-iodocyclooctane (**17**),[5] 10.00 g, gave 4.44 g of a colorless liquid: nmr (CCl_4) τ 7.75–9.20; picrate, mp 205–209° (lit.[20] 190–195°).

The N-benzoyl derivative was prepared in quantitative yield: mp 68–71°, from Skellysolve B; ir and nmr were identical with those of an authentic sample.[38]

1,2-Indenimine (34). LAH reduction of 10.00 g of *trans*-1-azido-2-iodoindan (**32**) gave 3.95 g of an unstable brown oil. If the product was treated with phenyl isocyanate before it darkened considerably, the N-(phenylcarbamyl)-1,2-indenimine was obtained in variable yield; mp 144–147° (lit.[12] 144–146°).

N-(Benzoyl)-1,2-indenimine was obtained, melting at 128–130°; ir (KBr) 1650 cm^{-1}; nmr ($CDCl_3$) upfield absorptions at τ 3.88 (d, 1), 4.95 (m, 1), and 6.53 (m, 2).

Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57. Found: C, 81.45; H, 5.60.

1,2,3,4-Tetrahydro-1,2-naphthalenimine (35). LAH reduction of **33**,[5] 10.00 g, gave about 4.0 g of a yellow oil after treatment with charcoal. This product was very unstable and began turning black within 1 hr. A portion of this product was crystallized from benzene–pentane: mp 54–56° (lit.[12] 51.5–53°).

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The N-phenylcarbamyl derivative melted at 158–159°, from acetone–Skellysolve B (lit.[12] mp 161–162.5°).

LAH Reduction of 3-Azido-2-iodo-1,3-diphenylpropanone (36). From 7.52 g of **36**[6] 3.77 g of 1-amino-1,3-diphenyl-3-propanol (**37**) was obtained as a colorless oil, which crystallized from benzene–hexane: mp 103–105° (lit.[39] mp 105–108° for the diastereomeric mixture); nmr ($CDCl_3$) τ 2.60 (m, 10), 5.07 (m, 1), 5.88 (m, 1), 6.90 (s broad, *ca.* 3, NH_2 and OH), and 7.79 (m, 2). The α isomer was concentrated by repeated crystallization from benzene: mp 124–125° (lit. mp 124–125°[39] and 122–124°[40]).

LAH Reduction of *erythro*-2-Iodo-3-azido-3-phenylpropionate. From 10.10 g of *erythro*-2-iodo-3-azidophenylpropionate was obtained 4.21 g of a colorless oil. The spectrum showed the presence of cinnamyl alcohol (59% on integration of vinyl protons *vs.* aromatic protons) which was isolated, 2.21 g, by treating an ether solution of the crude product with 10% HCl: mp 29–30° (lit.[41] mp 33°). Basification of the above acid wash gave several products (by nmr) and the isolation of an aziridine appeared futile.

1-Azaspiro[2.5]octane (39). LAH reduction of 9.18 g of 2-azido-1-iodomethylcyclohexane (**38**)[5] gave 3.85 g of a colorless liquid: nmr (CCl_4) τ 8.20–8.80 (envelope of multiplets), 8.62 (sharp singlet extending out of multiplet envelope), and 9.29 (s, 1, vanishes with D_2O).

The N-phenylcarbamyl derivative was prepared in 89% yield: mp 151–151.5° (from acetone) (lit.[3] mp 149.5–150.5°).

2,2-Dimethylaziridine (41a). LAH reduction of 10.3 g of **40a**[5] after work-up as described for **21** gave 2.40 g of **41a** identical by ir with authentic material;[42] nmr τ 9.39 (s, 1, vanishes in presence of D_2O), 8.32 (s, 6, CH_3), and 8.60 (s, 2, Az) in addition to ether absorptions which integrated to *ca.* 50% of the total product.

The N-phenylthiocarbamyl derivative prepared from the crude product melted at 86–89°; mp 92.5–93.5° (from Skellysolve B–trace of acetone).

Anal. Calcd for $C_{11}H_{14}N_2S$: C, 64.04; H, 6.84. Found: C, 63.95; H, 6.90.

1-Iodo-2-azido-2-phenylpropane (40b) was prepared from α-methylstyrene (**42b**) in variable yield (the olefin seemed to polymerize in acetonitrile): nmr (CCl_4) τ 2.68 (s, 5), 6.59 (s, 2), and 8.21 (s, 3).

Anal. Calcd for $C_9H_{10}IN_3$: C, 37.65; H, 3.51. Found: C, 38.68; H, 3.89.

2-Methyl-2-phenylaziridine (41b). LAH reduction of **40b**, 10.30 g, gave 4.78 g of **41b** as an oil: nmr (CCl_4) τ 2.80 (m, 5), 8.28 (d broad, 2, J = 2 Hz, Az), 8.51 (s, 3, CH_3), and 8.98 (s, 1, vanishes in presence of D_2O), as well as 10% of 1-methyl-1-phenylethylene (**42**).

The N-phenylcarbamyl derivative (68%) melted at 92–94° after several recrystallizations from Skellysolve F–dichloromethane.

Anal. Calcd for $C_{16}H_{16}ON_2$: C, 76.16; H, 6.39. Found: C, 76.10; H, 6.52.

8-Azido-9-iodo-menth-2-ol acetate (40c) was prepared from dihydrocarvenyl acetate in 84% yield: nmr (CCl_4) showed characteristic absorptions at τ 5.6 (m, 1, $W_{1/2}$ = 20 Hz) and 6.62 (s, 2, C*H*I). This iodo azide crystallized slowly in pentane at −10°, mp 57–58°.

Anal. Calcd for $C_{12}H_{20}N_3O_2I$: C, 39.46; H, 5.52. Found: C, 39.89; H, 5.17.

LAH Reduction of 8-Azido-9-iodo-menth-2-ol Acetate (40c). From 11.00 g, was obtained 5.19 g of a viscous oil: nmr (CCl_4) τ 5.33 (s broad, $W_{1/2}$ = 5 Hz) and 6.9 (s broad, $W_{1/2}$ = 15 Hz which greatly decreased in intensity upon the addition of D_2O). Integration indicates the presence of 30% of dihydrocarveol. Treatment of an ether solution of the crude product with gaseous HCl produced 4.46 g of a mixture of **ξ-chloro-ξ-aminomenth-2-ol** isomers, mp 122–124°, into a soft glass; the product was not amenable to crystallization. An analytical sample was prepared by washing the salt with ether which had been saturated with HCl.

Anal. Calcd for $C_{10}H_{21}ONCl$: C, 49.59; H, 8.74. Found: C, 51.96; H, 9.01.

2,2-Diphenylaziridine (41d). The LAH reduction of 10.0 g of **40d**[5] gave 3.85 g of a pale yellow liquid, containing 22% of **42d** by nmr. Partitioning between 15% HCl and ether furnished on work-up 0.94 g of 1,1-diphenylethylene (**42d**) and a yellow oil which crystallized giving 2.80 g of **43**: mp 101–104°; mp 108.5–110° from ethyl acetate–Skellysolve B; nmr ($CDCl_3$) τ 7.82 (s broad, 3, $W_{1/2}$ = 35 Hz), 6.68 (s broad, 2, $W_{1/2}$ = 7 Hz), and 2.4–2.9 (m, 10). It was concluded that the aziridine (**41d**) formed in this reduction was hydrolyzed under the aqueous acid treatment to give **2-amino-1,1-diphenylethanol (43).**

Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.79; H, 7.24.

The monobenzoyl derivative of the amino alcohol was obtained by treatment with 1 equiv of triethylamine and benzoyl chloride: mp 180–182°; mp 181.5–182° from chloroform; nmr (DMSO-d_6) τ 5.87 (d, 2, J = 5.5 Hz), 3.80 (s, 1), and 1.8–2.9 (m, 15).

Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03. Found: C, 79.27; H, 5.91.

1-Azido-2-iodo-1-phenylcyclopentane (44) was prepared from 1-phenylcyclopentene (**46**) in 95% crude yield. The iodo azide was recrystallized from methanol (mp 46.5–47°), but decomposed to a black tar upon standing 2 days at room temperature: nmr ($CDCl_3$) τ 2.63 (s, 5), 5.33 (m, 1, C*H*–I), and 6.9–8.2 (m, 6).

Anal. Calcd for $C_{11}H_{12}IN_3$: C, 42.19; H, 3.86. Found: C, 44.60; H, 3.29.

1-Phenyl-6-azabicyclo[3.1.0]hexane (48). The LAH reduction of 2.02 g of **44** gave 1.0 g of the colorless unstable oil containing 22% of **46** by nmr.

Treatment with benzoyl chloride led to N-benzoyl-3-amino-2-phenylcyclopentene (**50**): mp 193.5–194.5° (from methanol); ir (KBr) 3350 (amide N–H), 1620 and 1525 (amide I and II bands) cm^{-1}; nmr ($CDCl_3$) showed a pattern identical with that of **51** (see below).

Anal. Calcd for $C_{18}H_{17}NO$: C, 82.10; H, 6.51. Found: C, 81.44; H, 6.77.

1-Azido-2-iodo-1-phenylcyclohexane (45) was prepared from **47** in 92% yield: mp 75–76° (from methanol); nmr (CCl_4) τ 2.56 (s, 5), 5.3 (s broad, 1, $W_{1/2}$ = 8 Hz, C*H*–I), and 8.1 (m, 8).

Anal. Calcd for $C_{12}H_{14}IN_3$: C, 44.06; H, 4.31. Found: C, 44.24; H, 4.31.

1-Phenyl-7-azabicyclo[4.1.0]heptane (49). LAH reduction of **45**, 10.10 g, gave 4.8 g of a colorless liquid which contained 20% of **47** (by nmr) and decomposed exothermically if left standing (however, the product appeared to be stable in ether solution).

The preparation of the benzoyl derivative (74%) in benzene resulted in rearrangement to N-benzoyl-3-amino-2-phenylcyclohexene (**51**): mp 159–159.5° (from methanol); ir (KBr) 3350 (amide N–H), 1625 and 1520 (amide I and II bands) cm^{-1}; nmr ($CDCl_3$) τ 2.32–2.90 (m, 10), 3.53–4.20 (2, broadened multiplet with a probable triplet at τ 5.67, J = 4 Hz), 4.70 (s broad, 1, $W_{1/2}$ = 15 Hz), and 7.52–8.52 (m, 6).

Anal. Calcd for $C_{19}H_{19}NO$: C, 82.28; H, 6.91. Found: C, 81.80; H, 6.81.

1-Azido-2-iodo-1-methylcyclohexane (52) was prepared from 1-methylcyclohexene in 95% yield: nmr (CCl_4) τ 5.72 (pseudoquartet, 1, C*H*–I), 7.6–8.6 (complex multiplet), and 8.51 (s, 3).

1-Methyl-7-azabicyclo[4.1.0]heptane (53). LAH reduction of 13.3 g of **52** gave 4.56 g of a colorless liquid: nmr (CCl_4) showed an exchangeable N–H at τ 9.19 and a strong singlet extending out of the methylene envelope at τ 8.78.

The N-benzoyl derivative was a gummy solid crystallized from Skellysolve F–ether, mp 46–52°, and recrystallized several times for analysis: mp 51.5–52.5°; ir (KBr) 1650 cm^{-1}.

Anal. Calcd for $C_{14}H_{17}ON$: C, 78.10; H, 7.96. Found: C, 77.61; H, 8.05.

The product underwent slight changes during recrystallization; an insoluble portion was repeatedly filtered off. This more polar product was characterized as **N-benzoyl-2-amino-1-methylcyclohexanol**: ir (KBr) 3450 (OH), 3300 (NH), 1648 and 1550 cm^{-1} (amide I and II); nmr (DMSO-d_6) τ 5.42 (s, 1, *t*-O*H*), 6.10 (s broadened singlet, 1, $W_{1/2}$ = 20 Hz), 8.00–8.80 (m, 8), 8.83 (s, 3), and the aromatic protons. It was observed that these peaks were obviously absent in the ir and nmr of the crude product.

Anal. Calcd for $C_{14}H_{19}O_2N$: C, 72.07; H, 8.21. Found: C, 71.64; H, 8.16.

2-Azido-3-iodo-2-methylbutane (54) was prepared from 2-methyl-2-butene: bp 52° (0.1 mm); nmr (CCl_4) τ 5.86 (q, 1, J = 7 Hz, C*H*–I), 8.10 (d, 3, J = 7 Hz), 8.53 (s, 3), and 8.57 (s, 3).

Anal. Calcd for $C_5H_{10}IN_3$: C, 25.12; H, 4.22. Found: C, 25.44; H, 4.31.

2,2,3-Trimethylaziridine (56). LAH reduction of 10.32 g of **54** gave after distillation of the ether under reduced pressure 2.10 g of a volatile liquid: nmr (CCl_4) τ 8.28 (q broad, 1, J = 6Hz, Az), 8.80 (s, 3), 8.90 (d, 3, J = 6 Hz), 8.92 (s, 3), and 9.03 (s, 1, vanishes in presence of D_2O).

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The N-phenylthiocarbamyl derivative was prepared in 82% yield in Skellysolve B: mp 103–109°; recrystallized from Skellysolve B–acetone, mp 114–115°.

Anal. Calcd for $C_{12}H_{15}N_2S$: C, 65.71; H, 6.89. Found: C, 65.72; H, 7.18.

2-Azido-3-iodo-2-methylpentane (55) was prepared from 2-methyl-2-pentene in 60% yield after purification on an alumina column: nmr (CCl_4) τ 4.11 (m, 1, C*H*–I), 8.20 (m, 2), 8.48 (s, 3), 8.54 (s, 3), and 8.93 (t broad, 3).

Anal. Calcd for $C_6H_{12}IN_3$: C, 28.47; H, 4.78. Found: C, 28.69; H, 4.89.

3-Ethyl-2,2-dimethylaziridine (57). LAH reduction of 10.8 g of **55** gave 2.50 g of a volatile liquid; nmr (CCl_4) τ 9.30 (s broad, 1, $W_{1/2}$ = 6 Hz, exchangeable N–H), 8.40–9.15 (m).

The N-phenylthiocarbamyl derivative was prepared in 88% yield in Skellysolve B: mp 87–90°; recrystallized from Skellysolve B–acetone, mp 90–91°.

Anal. Calcd for $C_{13}H_{18}N_2S$: C, 66.62; H, 7.74. Found: C, 66.67; H, 7.65.

The N-*p*-nitrobenzoyl derivative melted at 55.5–57.5° after recrystallization from pentane.

Anal. Calcd for $C_{13}H_{16}O_2N$: C, 62.89; H, 6.50. Found: C, 62.92; H, 6.52.

A higher melting product was obtained from the mother liquors of the N-*p*-nitrobenzoyl derivative recrystallizations. The side product was characterized as N-*p*-nitrobenzoyl-3-amino-2-methylpentan-2-ol: mp 132–134°; mp 135–137° after recrystallization from Skellysolve F–ethyl acetate; nmr ($CDCl_3$ and a trace of DMSO-d_6) τ 1.80 (A_2B_2 pattern, 4), 2.17 (d broad, 1, J = 10 Hz), 6.08 (t of doublets, 1, J = 10 Hz; J = 3.5 Hz), 2.3 (m, 2), 8.78 (d, 6), and 9.08 (t broad, 3, J = 7 Hz).

Anal. Calcd for $C_{13}H_{18}O_4N_2$: C, 58.63; H, 6.81. Found: C, 58.65; H, 6.77.

2,2,3,3-Tetramethylaziridine. LAH reduction of 10.0 g of 2-azido-3-iodo-2,3-dimethylbutane[13] gave, after distillation of the ether at *ca.* 20 mm, 2.20 g of a volatile liquid, the ir spectrum of which was identical with that reported;[2] nmr (CCl_4) τ 8.80 (s) and 2% of tetramethylethylene by integration of the 8.39 singlet.

The N-*p*-nitrobenzoyl derivative (100%) melted at 135–139°; mp 140–141° after recrystallization from Skellysolve B–trace of benzene; ir (KBr) 1640 cm^{-1}.

Anal. Calcd for $C_{13}H_{16}N_2O$: C, 62.89; H, 6.50. Found: C, 63.04; H, 6.70.

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Acylation Mechanisms in Aprotic Solvents. I. Methanolysis of *p*-Nitrobenzoyl Chloride in Acetonitrile[1]

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Abstract: Contrary to previous proposals, the third-order kinetic term frequently observed for alcoholyses of acyl halides in aprotic solvents does not result from a push–pull mechanism. The methanolysis of *p*-nitrobenzoyl chloride (PNBC) in acetonitrile obeys the kinetic formulation: $d[HCl]/dt = k_2[PNBC][MeOH] + k_3[PNBC][MeOH]^2$. The reaction is not catalyzed by addition of phenol, a more electrophilic but less nucleophilic species than methanol, and an alternative mechanism is proposed in which, for over-all reaction, a first-formed tetrahedral intermediate is deprotonated by either a solvent molecule (second-order kinetics) or a second methanol molecule (third-order kinetics) to give a new tetrahedral intermediate which collapses to products. Consistent with this formulation, addition of chloride ion (a strong base in acetonitrile) leads to a tremendous acceleration and, for a given methanol concentration, this has the formulation: $d[HCl]/dt = k_3'[PNBC][MeOH][Cl^-]$. With increase in [MeOH], there is an appreciable decrease in k_3', consistent with a reduction in chloride ion basicity due to specific solvation. The claim by Briody and Satchell to have excluded the possibility of a tetrahedral intermediate mechanism for acetonitrile reactions of chloroacyl chlorides with phenols, and to have established a synchronous SN2 type mechanism, is questioned and an alternative explanation of their kinetic data in terms of conventional ionization and tetrahedral intermediate mechanisms is presented.

Several studies of the ethanolysis of acyl chlorides in aprotic solvents have led to third-order kinetics, first order in acyl halide and second order in ethanol.[2-4] The apparent involvement of two alcohol molecules has usually been explained[4,5] in terms of a push–pull mechanism of the type postulated by Swain for substitution reactions at a saturated carbon.[6]

Although alcohol molecules can serve as electrophilic as well as nucleophilic reagents,[7] it must be borne in mind that the mechanism for direct nucleophilic attack upon substrate molecules is considered to have different characteristics for attack at a saturated and at a carbonyl carbon. An extension, merely on the basis of kinetic similarities, of theories applied to one class of substitutions to those of the other type must be regarded as, at best, a dubious procedure.

Renewed interest in these reactions arose following studies in our laboratories of the reactions between alkyl chloroformates and silver nitrate in acetonitrile,[8,9] the

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