had been continued at 35–40° for 4 hr, the reaction mixture was worked up as usual to give 1.5 g (15.2%) of VII as a colorless oil [bp 94–96° (3 mm); ir $\nu_{\max}^{\text{liquid}}$ 2230 cm^{-1} (C≡N); nmr (CDCl$_3$) τ 7.83 (s, CH$_3$ of 2-methyl derivative), 7.80 (s, CH$_3$ of 3-methyl derivative), 6.60 (s, CH$_2$CN of the former), 6.57 (s, CH$_2$CN of the latter), 2.77–3.23 (m, aromatic protons)] and 6.2 g (47.1%) of XIV as a colorless oil, bp 114–116° (3 mm), both of which were separated to the following two components by the preparative gas chromatography. The first fraction afforded 2-methyl-1-morpholinobenzene [nmr (CDCl$_3$) τ 7.72 (3 H, s, CH$_3$), 7.18 (4, H, t, CH$_2$NCH$_2$), 6.20 (4 H, t, CH$_2$OCH$_2$), 3.71–2.65 (4 H, m, aromatic protons)], whose hydrochloride was recrystallized from ethanol–ether to give colorless needles, mp 185–186°.

Anal. Calcd for C$_{11}$H$_{15}$ON·HCl: C, 62.08; H, 7.58; N, 6.59. Found: C, 62.12; H, 7.65; N, 6.60.

The second fraction gave 3-methyl-1-morpholinobenzene: mp 40.5–42° (from petroleum ether); nmr (CDCl$_3$) τ 7.70 (3 H, s, CH$_3$), 6.91 (4 H, t, CH$_2$NCH$_2$), 6.18, (4 H, t, CH$_2$OCH$_2$), 3.45–2.65 (4 H, m, aromatic protons).

Anal. Calcd for C$_{11}$H$_{15}$ON: C, 74.50; H, 8.52; N, 7.90. Found: C, 74.65; H, 8.61; N, 7.92.

A Mixture of 1-(2-Methylphenyl)-1-phenylacetonitrile and 1-(3-Methylphenyl)-1-phenylacetonitrile (VIII).—To a mixture of 60 ml of tetrahydrofuran, 9.6 g of sodium amide, and 16.4 g of phenylacetonitrile was added 8.9 g of 2-chlorotoluene. The reaction mixture was refluxed for 4 hr and worked up as usual to give 7 g (48.9%) of VIII as a pale yellowish oil: bp 141–143° (1 mm); ir $\nu_{\max}^{\text{liquid}}$ 2230 cm^{-1} (C≡N); nmr (CDCl$_3$) τ 7.80 (s, CH$_3$ of 2-methyl derivative), 7.76 (s, CH$_3$ of 3-methyl derivative), 5.03 (s, >CHCN of 3-methyl derivative), 4.79 (s, >CHCN of 2-methyl derivative), 2.61–3.12 (m, aromatic protons).

Registry No.—IV, 26926-49-8; V, 1529-41-5; VI, 26926-51-2; VII, 2947-60-6; VIII, 26926-53-4; XI, 14318-66-2; XI hydrochloride, 26926-55-6; XIII, 26926-56-7; XIII hydrochloride, 26926-57-8; XIV, 7025-91-4; 2-methyl-1-morpholinobenzene hydrochloride, 26926-59-0; acetonitrile, 75-05-8; phenylacetonitrile, 140-29-4; *o*-chloroanisole, 766-51-8; 2-benzyloxy-1-chlorobenzene, 949-38-2; 1,2-dichlorobenzene, 95-50-1; 2-chlorotoluene, 95-49-8.

Acknowledgment.—We thank President A. Yanagisawa and Director O. Takagi of the Grelan Pharmaceutical Co., Ltd., for their encouragement. We also thank Miss A. Kawakami and Miss C. Yoshida for microanalyses, and Mr. O. Koyama for technical assistance. We are also grateful to Dr. K. Fukumoto, Pharmaceutical Institute, Tohoku University, for his helpful suggestions.

Alkali Metal Reductions of Epoxides, Ketals, and Related Heterocycles. Intermediacy of Carbanions[1]

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Solutions of alkali metals in liquid ammonia reduce aromatic epoxides from the "most hindered" position to afford isomerically pure alcohols. Such reductions proceed *via* the most stable of two possible carbanions as demonstrated by alkylation and deuteration experiments. Aliphatic epoxides are likewise reduced to alcohols. Similar cleavages of aromatic, but not aliphatic, ketals and thioketals afford the corresponding hydrocarbons in good to excellent yield, though a deficiency of metal in such systems gives hydroxy ethers or their sulfur analogs. Monocarbanions, not *gem*-dicarbanions, have been shown to be intermediates in the reductions of ketals. Aromatic aziridines are reduced to give amines, but a reverse aldol-type condensation has been observed with one highly unsymmetrically arylated aziridine.

Although small heterocyclic ring systems such as epoxides and cyclic ketals have been reductively cleaved by a variety of reagents,[3] similar reactions effected by means of alkali metals in liquid ammonia and other inert solvents have been accomplished only in a few cases. For example, ethylene oxide,[4] indene oxide,[5] and propylene oxide[6] have been reduced by sodium in ammonia, but products were either not isolated or yields of alcohols were only fair. Certain steroidal epoxides have been cleaved by the more potent lithium–ethylamine system, but reduction of olefinic double bonds was also realized.[7,8] In similar, but unrelated studies, benzophenone diethylketal has been reported to afford a variety of products upon treatment with sodium or potassium in liquid ammonia.[9] Certain other ketals have been likewise cleaved in ammonia,[10,11] but alcohol coreagents were often present which led to concomitant reduction of aromatic rings; in addition, the yields in these reactions were only fair or not reported. Two related classes of compounds, aziridines and thioketals, appear not to have been reduced by alkali metals in ammonia. However, two bisthioketals were cleaved by lithium–ethylamine, but reduction of olefins occurred in one case,[12] and no yield was reported in the other.[13]

It has been suggested that dissolving metal reductions of epoxides and ketals proceed *via* carbanionic intermediates, but this has not been experimentally demonstrated. Indeed, one report[9] surprisingly postulates that *gem*-dialkali derivatives of diphenylmethane are intermediates in the reduction of benzophenone diethylketal in liquid ammonia.

Thus, it was the intent of the present research to not only determine the best conditions, and the scope and limitations of such reductions, but also to prove the intermediacy of carbanions. The latter was to be accom-

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[1] Supported by the Undergraduate Education Division of the National Science Foundation on Grants GY-3072 and GY-6144 and by the Petroleum Research Fund, administered by the American Chemical Society, on Grant 959-G.

[2] (a) Author to whom correspondence should be directed; (b) Undergraduate Research Participant.

[3] "Reduction," R. L. Augustine, Ed., Marcel Dekker, New York, N. Y., 1968.

[4] C. B. Wooster, H. D. Segool, and T. T. Allan, Jr., *J. Amer. Chem. Soc.*, **60**, 1666 (1938).

[5] C. M. Suter and H. B. Milne, *ibid.*, **65**, 582 (1943).

[6] A. J. Birch, *J. Proc. Roy. Soc. N. S. W.*, **83**, 245 (1950).

[7] W. Reusch and R. LeMahieu, *J. Amer. Chem. Soc.*, **86**, 3068 (1964).

[8] W. Reusch, R. LeMahieu, and R. Guynn, *Steroids*, **5**, 109 (1965).

[9] C. B. Wooster and J. G. Dean, *J. Amer. Chem. Soc.*, **57**, 112 (1935).

[10] A. J. Birch, *J. Chem. Soc.*, 102 (1947).

[11] A. R. Pinder and H. Smith, *ibid.*, 113 (1954).

[12] N. S. Crossley and H. B. Henbest, *ibid.*, 4413 (1960).

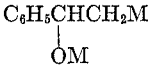
[13] R. D. Stolow and M. M. Bonaventura, *Tetrahedron Lett.*, 95 (1964).

plished by performing appropriate trapping experiments. Of particular interest was the possibility that the small number of known *gem*-diorganometallics[14] might be expanded by reduction of ketals, especially in nonprotic solvents like THF or monoglyme. Finally, it was of interest to determine if aziridines might similarly be reduced to amines.

Results with Epoxides.—First, optimum conditions for the reduction of styrene oxide were established. Thus, treatment of this epoxide with 2 equiv of sodium in liquid ammonia cleanly afforded 2-phenylethanol (**1**) in 83% yield after only a 45-min reaction period. Similar amounts of alcohol **1** were obtained by employing lithium, sodium, or potassium in ammonia either at −33° or at −80°. Lower yields of **1** were obtained, though, using sodium–alcohol–ammonia or lithium–methylamine, perhaps because of ring opening by the more nucleophilic solvents. Interestingly, 1-phenylethanol (**3**), the alcohol obtained upon reduction of styrene oxide with lithium aluminum hydride,[3] was not observed in any of the above reductions. This fact suggests that the reductions of styrene oxide proceed *via* 1,3-dianion **2**, a relatively stable benzylic-type carbanion, rather than *via* the less stable **4**, a primary carbanion.

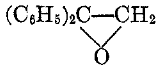

$C_6H_5\overset{M}{\overset{|}{C}}HCH_2OM$

1, M = H
2, M = Na, K, Li


$C_6H_5\underset{OM}{\underset{|}{C}}HCH_2M$

3, M = H
4, M = Na, Li, K

Similarly, *trans*-stilbene oxide and 1,1-diphenylethylene oxide (**5**) were reduced by sodium in ammonia to afford 1,2-diphenylethanol and 2,2-diphenylethanol (**6**) in yields of 77 and 89%, respectively. In the latter reaction, 1,1-diphenylethanol (**8**) was not observed indicating that this reaction apparently proceeds *via* dianion **7** rather than the less stable **9**.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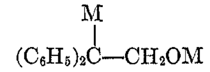
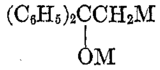
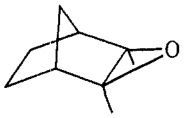

$(C_6H_5)_2\overset{M}{\overset{|}{C}}{-}CH_2OM$

6, M = H
7, M = Na


$(C_6H_5)_2\underset{OM}{\underset{|}{C}}CH_2M$

8, M = H
9, M = Na

Next, strictly aliphatic epoxides were found to also undergo reduction by sodium in ammonia. Thus, cyclohexene oxide and *exo*-norbornene oxide (**10**) afforded cyclohexanol and *exo*-norbornanol (**11**) in yields of 60 and 82%, respectively. Likewise, 1,2-epoxybutane afforded 2-butanol in 55% yield.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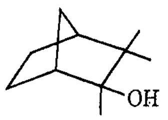
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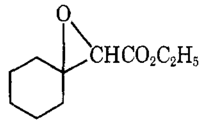
Finally, ethyl β,β-pentamethyleneglycidate (**12**), an epoxy ester, was reduced by 2 equiv of lithium in ammonia to afford hydroxy ester **13** in 46% yield; as above, the reaction apparently proceeded *via* the more stable resonance stabilized dianion **14** since no isomeric alcohol was observed. The use of sodium rather than lithium in the reduction of **12** was not satisfactory since a mixture of products was obtained which presumably arose from Claisen-type condensations.[15]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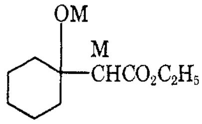
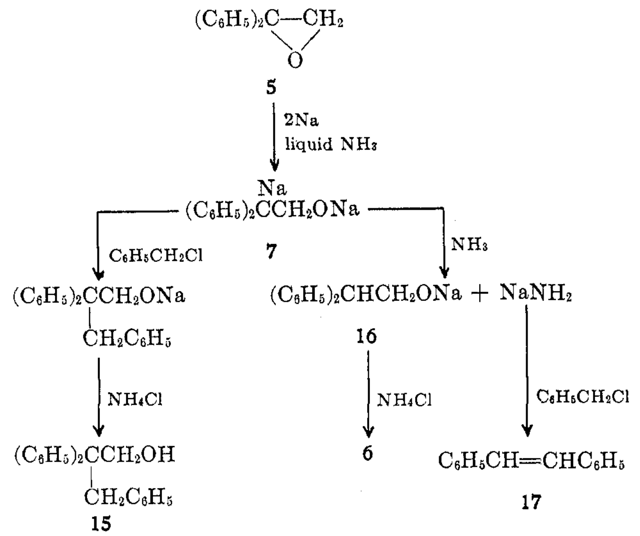

13, M = H
14, M = Li

Attention was then directed toward trapping intermediate 1,3-dianions in the reductions of epoxides by dissolving metals. 1,1-Diphenylethylene oxide (**5**) was selected as the model substrate since dianion **7**, its apparent reduction intermediate, was expected to be somewhat stable to ammonolysis. This was a reasonable assumption because related alkali alkyldiphenylmethides have a finite lifetime in this solvent.[16] Thus, when a mixture of epoxide **5** and benzyl chloride in ether was added to 2 equiv of sodium in ammonia, alkyl derivative **15** was indeed obtained in low yield; the remainder of the product consisted of alcohol **6** and stilbene (**17**). Such products can be rationalized by considering dianion **7** to undergo not only C-alkylation to afford **15**, but also rapid ammonolysis to give alkoxide **16** and sodium amide (Scheme I). It is well known that sodium amide reacts with benzyl chloride[17] to afford stilbene.

SCHEME I



Surprisingly, alkyl derivative **15** could not be obtained unless the epoxide and alkyl halide were simultaneously added to the reducing media; otherwise, only alcohol **6** and stilbene were realized. This would suggest that despite the fact that dianion **7** consists of a benzhydrylic carbanion, it is too basic to survive in liquid ammonia. This was verified by attempting the reverse reaction, *viz.*, treating alcohol **6** with 2 equiv of

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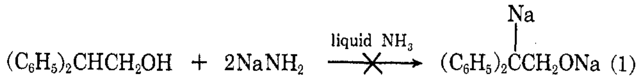
(14) For example, see E. M. Kaiser, F. E. Henoch, and C. R. Hauser, *J. Amer. Chem. Soc.*, **90**, 7287 (1968); E. M. Kaiser and C. R. Hauser, *ibid.*, **88**, 2348 (1966).

(15) W. R. Dunnavant and C. R. Hauser, *J. Org. Chem.*, **25**, 1693 (1960).

(16) W. S. Murphy and C. R. Hauser, *ibid.*, **31**, 1781 (1966).

(17) C. R. Hauser, W. R. Brasen, P. S. Skell, S. W. Kantor, and A. E. Broadhag, *J. Amer. Chem. Soc.* **78**, 1653 (1956).

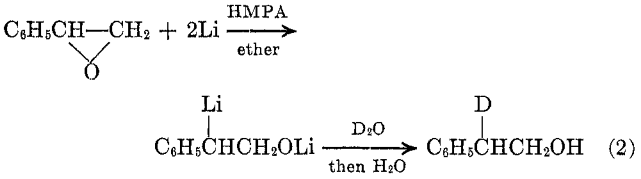
sodium amide in ammonia; however, no color developed and work-up gave only recovered **6** (eq 1).



$$(C_6H_5)_2CHCH_2OH + 2NaNH_2 \xrightarrow[\quad]{\text{liquid } NH_3} (C_6H_5)_2\overset{Na}{C}CH_2ONa \quad (1)$$

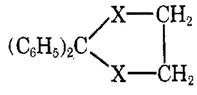
6 **7**

In order to avoid the ammonolysis described above, styrene oxide was reduced by 2 equiv of lithium in hexamethylphosphoramide–ether to afford an intense red solution. That a benzylic type carbanion was indeed present was demonstrated by treatment of the solution with deuterium oxide to afford α-deuterated 2-phenylethanol (eq 2); the nmr spectra of the compound indicated that it contained 0.8 benzylic deuterium atom per molecule.



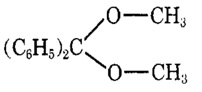
$$C_6H_5\overset{Li}{C}HCH_2OLi \xrightarrow[\text{then } H_2O]{D_2O} C_6H_5\overset{D}{C}HCH_2OH \quad (2)$$

Results with Ketals and Related Compounds.—The results obtained in liquid ammonia will be discussed first. Benzophenone ethyleneketal (**18**) was cleaved by 4 equiv of sodium or potassium to afford diphenylmethane (**20**) in 60% yield; the yield of **20** was increased to 94% by the use of 5 equiv of metal during a 3-hr period. The latter conditions were also used to convert benzophenone ethylenethioketal (**19**) and dimethoxydiphenylmethane (**21**) to diphenylmethane in yields of 98 and 88%, respectively. Similar reduction of 1-naphthaldehyde ethyleneketal (**22**) gave 1-methylnaphthalene (**23**) in 58% yield; however, 2-nonanone ethyleneketal (**24**) failed to undergo reduction and only starting material was recovered.



18, X = O
19, X = S

$(C_6H_5)_2CH_2$
20



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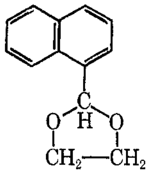

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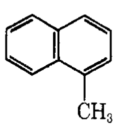

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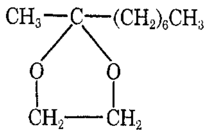

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Incidentally, in contrast to previous reports,[10] reduction of ketal **18** under "Birch" conditions using 4 equiv each of sodium and ethanol gave diphenylmethane in about the same yield as obtained in the absence of the alcohol. Although an advantage the current method enjoys is that a large excess of reducing agent need not be employed as is often the case with Raney nickel,[3] at least stoichiometric amounts of metal must be used to avoid underreduction of the ketal functional group. Thus, treatment of **18** or of **19** with only 2 equiv of sodium in the absence of alcohol cleanly afforded hydroxy ether **25** and mercapto thioether **26** in good to excellent yields, respectively.

$(C_6H_5)_2CHOCH_2CH_2OH$
25

$(C_6H_5)_2CHSCH_2CH_2SH$
26

Next, attention was directed toward trapping intermediate carbanions from these reductions in ammonia. Thus, ketal **18** was reduced by 5 equiv of sodium for 3 hr and the reaction mixture alkylated with *n*-butyl bromide to afford only 1,1-diphenylpentane (**27**); none of the dialkylated product **28** was present. This result implies that *gem*-dianion **29** was not present in the reaction mixture[14] and that the earlier workers[9] were probably in error by postulating the existence of such species in ammonia.

$(C_6H_5)_2CHC_4H_9$
27

$(C_6H_5)_2C(C_4H_9)_2$
28

$(C_6H_5)_2CNa_2$
29

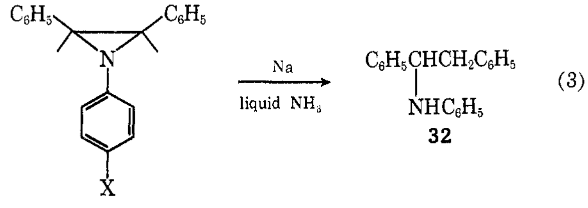
Similar trapping experiments were performed in ammonia on ketal **21** and on thioketal **19** using sodium and *n*-butyl bromide to also afford hydrocarbon **27**.

Two solvents related to ammonia were employed in the reduction of ketal **18** but neither one afforded the clean results realized in ammonia. Surprisingly, reduction of **18** by the more potent system, lithium in methylamine,[18] afforded only 17 and 31% of diphenylmethane (**20**) after 15 min and 3 hr, respectively; in the latter experiment, hydroxy ether **25** was obtained in 43% yield despite the use of 4 equiv of lithium. Reduction of **18** by the still more potent lithium–ethylamine system not only caused cleavage of the dioxalane ring, but also resulted in extensive reduction of the aromatic rings to give mixtures of olefinic compounds which were not further studied.

Next, certain reductions of ketals were performed in ethereal-type solvents in anticipation that *gem*-dicarbanions might be realized. However, reduction of ketal **18** by 4 equiv of lithium in THF for 4 hr afforded only hydroxy ether **25** in 73% yield. The yield of **25** was increased to 79% by allowing the reaction to proceed for 20 hr. Similarly, reduction of thioketal **19** by 4 equiv of lithium in monoglyme gave mercapto thioether **26** in 86% yield.

Finally, treatment of thioketal **19** with 4 equiv of lithium in hexamethylphosphoramide for 24 hr followed by excess deuterium oxide afforded deuterated diphenylmethane (**20**) in 70% yield. However, that deuterium was present only to the extent of 0.82 atom per molecule appears to indicate that the reduction proceeded *via* monolithiodiphenylmethane rather than dialkali salt **29** (M = Li).

Results with Aziridines.—Three arylated aziridines were likewise reduced by sodium in liquid ammonia. Thus, cleavage of 1,2,3-triphenylaziridine (**30**) and of *cis*-1-*p*-chlorophenyl-2,3-diphenylaziridine (**31**) by 2 and 4 equiv of sodium, respectively, gave 1-anilino-1,2-diphenylethane (**32**) in 66–73% yield (eq 3). The



$$\xrightarrow[\text{liquid } NH_3]{Na} C_6H_5\underset{NHC_6H_5}{C}HCH_2C_6H_5 \quad (3)$$

32

30, R = H
31, R = Cl

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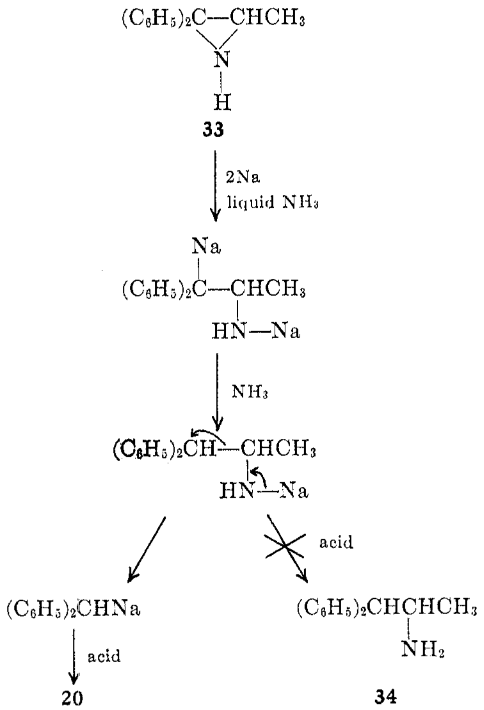
[18] For example, see R. A. Benkeser, R. K. Agnihotri, M. L. Burrous, E. M. Kaiser, J. M. Mallan, and P. W. Ryan, *J. Org. Chem.*, **29**, 1313 (1964).

excess sodium metal was successfully employed in the latter reduction to ensure complete removal of the aryl chlorine.

Similar cleavage of 2,2-diphenyl-3-methylaziridine (**33**), however, surprisingly gave diphenylmethane (**20**) rather than the expected amine **34**. Hydrocarbon **20** apparently arose *via* a reverse "aldol-type" condensation (Scheme II) despite the use of the inverse neutralization technique, a procedure which has previously been shown to minimize such reversions in liquid ammonia.[19]

SCHEME II



In summary, it is now clear that aliphatic and aromatic epoxides, aromatic ketals and thioketals, and aromatic aziridines can be rapidly and conveniently reduced by alkali metals in liquid ammonia. Qualitatively, alkali metal reductions of epoxides and aziridines occur more easily than those of ketals as evidenced by more extensive cleavages of the former ring systems than of the latter during similar reaction periods. Also, and more importantly, strictly aliphatic epoxides, but not aliphatic ketals, readily undergo such reductions. These differences in reactivity can be ascribed to greater release of steric strain upon opening of the three-membered epoxides compared to the five-membered ketals. Such reductions appear to be quite general and presumably could be extended to a wide variety of other similar heterocyclic ring systems. Although the above reactions have been unequivocally shown to proceed *via* carbanion intermediates, no evidence for the existence of *gem*-dicarbanions was obtained either in ammonia or in ethereal-type solvents.

Experimental Section[20]

Reduction of Epoxides by Alkali Metals in Liquid Ammonia.—To a solution of 0.0125–0.5 mol of the epoxide in 300 ml of commercial, anhydrous, liquid ammonia, was added 2 equiv of sodium spheres as rapidly as caution permitted. After stirring until the blue color disappeared (35–90 min), the mixture was treated with excess solid ammonium chloride (directy neutralized) or poured into ammonia containing ammonium chloride, (inversely neutralized) and the ammonia was allowed to evaporate. The resulting residue was hydrolyzed (100 ml of 3 *N* HCl) and the aqueous layer extracted (ether). After drying ($CaSO_4$ or $MgSO_4$), the product was isolated by vacuum distillation or by recrystallization. Specific examples are listed in Table I.

Reductive Benzylation of 1,1-Diphenylethylene Oxide in Ammonia.—To a solution of 0.96 g (0.042 g-atom) of sodium in 300 ml of ammonia was added during 1 min, a solution of 4.0 g (0.021 mol) of 1,1-diphenylethylene oxide and 2.53 g (0.021 mol) of benzyl chloride in 100 ml of ether. After 30 min, the mixture was poured into 200 ml of ammonia containing 10 g of ammonium chloride, and the ammonia was allowed to evaporate. The residue was worked up as above to afford an oily material which was chromatographed on neutral alumina using ethanol–benzene solvent to give 0.85 g (22.5%) of stilbene, mp and mmp 123–124°, and 2.1 g (50%) of 2,2-diphenylethanol (**6**), mp and mmp 61–63°, mp and mmp of phenylurethan derivative 135–137°. The infrared spectra of the above compounds were identical with those of authentic samples. Also 0.9 g (15%) of 2,2,3-triphenyl-1-propanol (**15**) was obtained, mp 85–87° (lit.[21] mp 80°); the phenylurethan derivative was prepared: mp 170–173°, lit.[21] mp 169–170°; ir (mull) 3220 (OH), 775, 699 cm^{-1} (ArH); nmr ($CDCl_3$) δ 6.91 (m, 15, ArH), 3.90 (d, 2, CH_2O), 3.43 (s, 2, $ArCH_2$), 1.23 (s, 1, OH).

When the benzylation was repeated by adding the epoxide to the sodium–ammonia solution followed after 7 min, or after 30 sec, by the benzyl chloride, only stilbene and 2,2-diphenylethanol were obtained in yields of 83 and 85%, respectively.

Reductive Deuteration of Styrene Oxide in Hexamethylphosphoramide–Ether.—To a solution of 6.0 g (0.05 mol) of styrene oxide in 45 ml of hexamethylphosphoramide and 75 ml of ether was added 0.7 g (0.1 g-atom) of lithium wire cut into 1-cm pieces. Heat was applied and the mixture was gently refluxed for 2 hr. Upon cooling to 0°, the intensely red mixture was treated with 6 ml of deuterium oxide added all at once. After stirring briefly, the mixture was treated with 200 ml of ether and the resulting solution was washed with three 100-ml portions of water. Drying ($CaSO_4$), concentrating, and distilling the residue gave 1.5 g (24%) of 2-phenylethanol, bp 90–92° (3.5 mm). The nmr of the product indicated the presence of 0.8 benzylic deuterium atom per molecule.

Reduction of Ketals by Alkali Metals in Liquid Ammonia.—To a solution of 2–5 equiv of an alkali metal in 300 ml of liquid ammonia was added 0.025 mol of a given ketal dissolved in ethyl ether. After an appropriate time, the mixture was treated with excess solid ammonium chloride and the ammonia was allowed to evaporate. The residue was taken up into 100 ml each of water and ether, the aqueous layer was extracted with four 50-ml portions of ether, and the combined extracts were dried ($CaSO_4$) and concentrated. Products were purified by vacuum distillation or by recrystallization. Specific examples are listed in Table II.

Preparation of β-Hydroxyethyl Benzhydryl Ether (25).—To 1.1 g (0.048 g-atom) of sodium in 300 ml of ammonia was added 5.65 g (0.025 mol) of benzophenone ethyleneketal (**18**). After stirring the resulting mixture for 3 hr, it was worked up as above to afford 3.3 g (58%) of β-hydroxyethyl benzhydryl ether (**25**): bp 148–150° (1 mm); ir (neat) 3280 (OH), 1105, 1055, and 1022 (COC), 735 and 695 cm^{-1} (ArH); nmr (CCl_4) δ 7.23 (m, 10, ArH), 4.08 (s, 1, OH), 3.4 (t, 2, CH_2), 2.26 (t, 2, CH_2).

Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.90; H, 7.02. Found: C, 78.71; H, 6.93.

Hydroxy ether **25** was also prepared by stirring a mixture of 5.65 g (0.025 mol) of ketal **18** with 0.69 g (0.1 g-atom) of lithium in 75 ml of THF for 4 hr. At the end of this time, the mixture was hydrolyzed by 100 ml of water, worked up as above, and

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(19) For example, see E. M. Kaiser and C. R. Hauser, *J. Org. Chem.*, **31**, 3316 (1966).

(20) All starting epoxides, ketals, thioketals, and aziridines were purchased from Aldrich Chemical Co., or prepared by standard methods. Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 137 either neat or as Nujol mulls. Nmr spectra were obtained with a Varian Associates A-60 using tetramethylsilane as internal standard. Analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

(21) M. Ramart and M. Amagat, *C. R. Acad. Sci., Ser. C*, **182**, 1342 (1926).

TABLE I

REDUCTION OF EPOXIDES BY ALKALI METALS[a]

Epoxide (mol)	Conditions (hr)	Product (%)	Nmr spectral data (δ)[b]
Styrene oxide (0.05)	2Na–NH_3 (0.75)	2-Phenylethanol (83)[c]	(neat) 7.08 (s, 5, ArH), 4.46 (s, 1, OH), 3.63 (t, 2, CH_2O), 2.70 (t, 2, CH_2)
trans-Stilbene oxide (0.0125)	2Na–NH_3 (1.0)	1,2-Diphenylethanol (77)[d]	($CDCl_3$) 7.0 (d, 10 ArH), 4.53 (t, 1, HCOH), 2.72 (d, 2, CH_2), 1.97 (s, 1, OH)
1,1-Diphenylethylene oxide (0.05)	2Na–NH_3 (1.0)[e]	2,2-Diphenylethanol (89)[f]	(CCl_4) 7.1 (s, 10, ArH), 3.91 (m, 2, CH_2O), 2.03 (t, 1, Ar_2CH)
Cyclohexene oxide (0.1)	2Na–NH_3 (0.75)	Cyclohexanol (60)[g]	
exo-2,3-Epoxynorbornane (0.05)	2Na–NH_3 (1.5)	*exo*-2-Norborneol (82)[h]	(CCl_4) 3.5 (s, 1, OH), 2.1 (m, 1, HCOH), 1.25 (m, 10, CH)
1,2-Epoxybutane (0.5)	2Na–NH_3 (1.0)	2-Butanol (55)[i]	
Ethyl β,β-pentamethyleneglycidate[j] (0.04)	2.2Li–NH_3 (0.8)	Ethyl 1-cyclohexanolacetate[k] (46)	(neat) 4.1 (q, 2, OCH_2), 3.65 (s, 1, OH), 2.43 (s, 2, CH_2CO), 1.5 (m, 10, $(CH_2)_5$), 1.23 (t, 3, CH_3)

[a] All reactions were directly neutralized unless otherwise indicated. [b] The ir spectra either were identical with authentic samples or were in agreement with the assigned structures. [c] Bp 69–70° (1.6 mm) [lit. bp 98–100° (12 mm)]: "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1965, p 2687. [d] Mp 62–63° (lit. mp 62°): see footnote *c*, p 1280. [e] Inversely neutralized. [f] Mp 61–63° (lit. mp 64–65°), phenylurethan, mp 134–136° (lit. mp 135–137°: see footnote *c*, p 1280. [g] Bp 160–161° (lit. bp 161°): see footnote *c*, p 785. [h] Mp 127–128° (lit. mp 126–127°), phenylurethan, mp 145–147° (lit. mp 146°): G. Komppa and S. Beckmann, *Justus Liebigs Ann. Chem.*, **512,** 172 (1934). [i] Bp 97.5–99.5° (lit. bp 100°): see footnote *c*, p 505. [j] Prepared by the method of R. H. Hunt, L. J. Chinn, and W. S. Johnson, *Org. Syn.*, **IV,** 459 (1963). [k] Bp 119–122° (17 mm) [lit. bp 143–146° (37 mm)]: E. H. Charlesworth, J. A. McRae, and H. M. MacFarlane, *Can. J. Res.*, **21B,** 37 (1943).

TABLE II

REDUCTION OF KETALS AND RELATED COMPOUNDS BY ALKALI METALS

Compd (mol)	Conditions (hr)	Product (%)[a]
Benzophenone ethyleneketal (0.025)	5Na–NH_3 (3.0)	Diphenylmethane (94)[b]
	4Na–NH_3 (0.25)	Diphenylmethane (60)[b]
	4K–NH_3 (0.25)	Diphenylmethane (60)[b]
	4Na–$4C_2H_5OH$ NH_3 (0.25)	Diphenylmethane (63)[b]
Benzophenone ethylenethioketal (0.025)	5Na–NH_3 (3.0)	Diphenylmethane (98)[b]
Dimethoxydiphenylmethane (0.025)	5Na–NH_3 (3.0)	Diphenylmethane (88)[b]
Naphthaldehyde ethyleneketal (0.025)	5Na–NH_3 (3.0)	1-Methylnaphthalene (58)[c]
2-Nonanone ethyleneketal (0.025)	5Na–NH_3 (3.0)	2-Nonanone ethyleneketal (88%)[d]

[a] See footnote *b*, Table I. [b] Bp 84–85° (1 mm) [lit. bp 120° (10 mm)]: footnote *c*, Table I, p 1285. [c] Bp 77–78° (1 mm) [lit. bp 110° (12 mm)]: footnote *c*, Table I, p 2242. [d] Nmr (neat) δ 3.76 (s, 4, OCH_2CH_2O), 1.0 (m, 18, CH).

distilled to give 4.15 g (73%) of **25**, bp 148–150°. Similarly, the use of a 20-hr reaction period instead of a 3-hr one gave 4.5 g (79%) of this product, bp 148–150° (1 mm).

Preparation of β-Mercaptoethyl Benzhydryl Thioether (26).—To 1.15 g (0.05 g-atom) of sodium in 300 ml of ammonia was added 6.45 g (0.025 mol) of thioketal **19** to afford a red-brown mixture, the color of which changed to a bright red within 15 min. After 3 hr, the mixture was neutralized by the addition of 15 g of ammonium chloride and worked up in the usual fashion to give 5.7 g (88%) of β-mercaptoethyl benzhydryl thioether (**26**): bp 135–137° (2 mm); ir (neat) 733 and 695 cm^{-1} (ArH); nmr (CCl_4) δ 7.3 (m, 10, ArH), 5.0 (s, 1, Ar_2CH), 2.54 (m, 4, $-SCH_2CH_2S-$), 1.4 (m, 1, SH). The latter absorption was decreased upon mixing the sample with deuterium oxide.

Anal. Calcd for $C_{15}H_{16}S_2$: C, 69.23; H, 6.15; S, 24.62. Found: C, 69.27; H, 5.93; S, 24.67.

Compound **26** was also prepared by refluxing 0.69 g (0.1 g-atom) of lithium and 6.45 g (0.025 mol) of thioketal **19** in 75 ml of THF for 24 hr to give 3.1 g (48%) of the compound.

When the reaction was repeated by employing 4 equiv of lithium in refluxing monoglyme for 22 hr, the yield of **26** was increased to 5.6 g (86%).

Reductive Alkylation of Benzophenone Ketals in Ammonia.—To a solution of 2.88 g (0.125 g-atom) of sodium in 300 ml of ammonia was added 5.65 g (0.025 mol) of ketal **18**. After 3 hr, the mixture was treated with a solution of 3.8 g (0.0275 mol) of *n*-butyl bromide in 50 ml of ether. The resulting solution was then stirred for 1 hr before it was treated with excess ammonium chloride and worked up as above. Distillation of the crude product afforded 1.12 g (27%) of diphenylmethane (**20**), bp 84–85° (1 mm), and 3.3 g (60%) of 1,1-diphenylpentane (**27**), bp 125–127° (1 mm) [lit.[22] bp 80–81° (0.005 mm)]. The nmr of product **27** was identical with that of an authentic sample prepared by the method of Murphy and Hauser.[16]

When the reaction was repeated employing 6.45 g (0.025 mol) of thioketal **19** and 6.85 g (0.05 mol) of *n*-butyl bromide, 3.03 g (54%) of 1,1-diphenylpentane (**27**) was obtained, bp 125–127° (1 mm). Similarly, reduction of 5.76 g (0.025 mol) of ketal **19** followed by 3.8 g (0.0275 mol) of *n*-butyl bromide gave 3.95 g (71%) of 1,1-diphenylpentane (**27**), bp 125–127° (1 mm).

Reductive Deuteration of Benzophenone Ethylenethioketal (19) in Hexamethylphosphoramide.—A mixture of 6.45 g (0.025 mol) of thioketal **19** and 0.69 g (0.1 g-atom) of lithium in 50 ml of HMPA was stirred at room temperature for 24 hr. At the end of this time, the reddish mixture was treated with excess deuterium oxide, then washed with four 50-ml portions of water and worked up as usual to afford 2.95 g (70%) of diphenylmethane, bp 85–86° (1 mm). The nmr of the product indicated the presence of 0.82 benzhydrylic deuterium atom per molecule.

Reduction of Aziridines by Alkali Metals in Liquid Ammonia. A. 1,2,3-Triphenylaziridine (30).—To a solution of 0.115 g (0.005 g-atom) of sodium in 250 ml of ammonia was added 0.62 g (0.0025 mol) of solid aziridine **30** to afford, within 15 min, a yellow solution. After 1 hr, the solution was treated with 10 g

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[22] H. Gilman and B. J. Gaj, *J. Amer. Chem. Soc.*, **82,** 6326 (1960).

of solid ammonium chloride, the ammonia was allowed to evaporate, and the crude product was worked up in the usual fashion to give 0.45 g (66%) of 1-anilino-1,2-diphenylethane (**32**), bp 168–170° (1 mm) [lit.[23] bp 168–170° (1 mm)]: hydrochloride, mp 198–199° (lit.[23] mp 192°); ir (neat) of **32**, 3115 (NH), 745, 728 and 689 cm^{-1} (ArH); nmr (CCl$_4$) of **32** δ 6.77 (m, 16, ArH, NCH), 4.08 (d, 2, ArCH$_2$), 3.67 (broad s, 1, NH).

B. ***cis*-1-*p*-Chlorophenyl-2,3-diphenylaziridine** (**31**).[24]—This reaction was effected essentially as described in part A by employing 0.92 g (0.04 g-atom) of sodium and 3.2 g (0.01 mol) of aziridine **31** to afford 2.2 g (73%) of 1-anilino-1,2-diphenylethane (**32**), bp 168–170°,[23] hydrochloride mp and mmp 198–199°. The ir and nmr of this product were identical with those in part A.

C. **2,2-Diphenyl-3-methylaziridine** (**33**).—This reaction was effected as described in part A by reducing 5.23 g (0.025 mol) of aziridine **33** by 1.15 g (0.05 g-atom) of sodium to give a reddish brown mixture which was, after 1 hr, poured into 200 ml of ammonia containing 15 g of ammonium chloride. The usual work-up gave 2.9 g (69%) of diphenylmethane, bp 84–85° (1 mm). The ir and nmr of this compound were identical with those of authentic samples.

Registry No.—Styrene oxide, 97-09-3; *trans*-stilbene oxide, 1439-07-2; **5**, 882-59-7; cyclohexene oxide, 286-20-4; **10**, 3146-39-2; 1,2-epoxybutane, 106-88-7; **12**, 6975-17-3; **18**, 4359-34-6; **19**, 6317-10-8; **21**, 2235-01-0; **22**, 26963-79-1; **24**, 14447-29-1; **25**, 26926-47-6; **26**, 26926-48-7.

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[23] M. Busch and A. Rinck, *Ber.*, **38**, 1761 (1905).

[24] Kindly provided by R. N. Loeppky and D. H. Smith.

A Stereochemical Reaction Cycle with Chiral Phosphorus[1]

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Cholesteryl and menthyl methylphenylphosphinates diastereomerically pure gave *N*-phenyl methylphenylphosphinic amide of the same rotation. The lithium salt of α-phenylethylamine with the same phosphinate esters gave the corresponding diastereomerically pure phosphinic amide of the same rotation. Treatment of these same esters with benzyl Grignard reagent gave benzylmethylphenylphosphine oxide of the same rotation. These results, coupled with reactions and configurational assignments of others, completed a three-reaction stereochemical cycle with three chiromers. The two reactions reported here proceed with inversion of configuration and high stereospecificity. Cholesteryl methylphenylphosphinate, absorbed on a solid support, failed to separate a series of racemates in a glc column.

From analogies drawn between the reactions of sulfinate[3, 1b] and phosphinate esters, we anticipated the possibility that phosphinate esters might react with Grignard reagents and with substituted lithium amides to produce phosphine oxides and phosphinic amides, respectively. The stereochemical course of these reactions was of interest, particularly since they lead to compounds with phosphorus as the only chiral center. Indeed, since Horner and Winkler[4] had already demonstrated that benzylmethylphenylphosphine oxide was converted stereospecifically and with retention to *N*-phenyl methylphenylphosphinic amide, we envisioned closing a three-reaction stereochemical cycle by converting the same methylphenylphosphinate ester to these two substances. Finally, we planned to use these optically active compounds as liquid phases in attempts to resolve racemates by gas–liquid chromatography.

While our work was in progress, that of Korpium and Mislow[5a] appeared which established that in general, alkylarylphosphinate esters of menthol react with Grignard reagents to give phosphine oxides with high stereospecificity and inversion of configuration. In particular, they converted menthyl methylphenylphosphinate to benzylmethylphenylphosphine oxide. The absolute configuration of menthyl methylphenylphosphinate was known,[6] and that of the oxide was established.[5] Thus, by the time our work matured, the configurations of all three chiromers[7] II, III, and IV were in hand.

Initially, we failed to separate the diastereomers of menthyl methylphenylphosphinate, but successfully obtained pure one diastereomer of cholesteryl methylphenylphosphinate (I). Korpium and Mislow's[5a] recipe led us to the pure menthyl diastereomers (II). Treatment of either ester with benzylmagnesium Grignard reagent gave benzylmethylphenylphosphine oxide (IV) of essentially the same maximum rotation, a fact that establishes that both starting phosphinate esters possess the same configuration at phosphorus (*S*) (Scheme I). Both esters with lithium anilide gave *N*-phenyl methylphenylphosphinic amide (III) of the same sign and magnitude of rotation as that reported[4] by conversion of (+)-(*R*)-IV to (−)-(*S*)-III. These facts establish that the conversion of the phosphinic esters with lithium anilide proceeds with essentially complete inversion of configuration. The two, *three*-reaction stereochemical cycles are formulated. They are triligostatic (three ligands common to the three chiromers),[7] podal (number of chiromers equals the number of reactions),[7] contain no ligand metathesis,[7] and two of the reactions proceed with inversion and one with retention of configuration.

To determine the generality of the conclusion that lithium amides and phosphinate esters give phosphinic amides with high stereospecificity, (−)-(*S*)-I and (−)-(*S*)-II were treated with the lithium salt of optically

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[1] (a) This investigation was supported by the U. S. Public Health Service Research Grant No. GM 12640-04 from the Department of Health, Education and Welfare. (b) This work was reported in preliminary form: A. Nudelman and D. J. Cram, *J. Amer. Chem. Soc.*, **90**, 3869 (1968).

[2] This author thanks the Dow Chemical Co. and U. S. Rubber Co. for nonresident tuition grants.

[3] K. K. Andersen, *Tetrahedron Lett.*, 93 (1962).

[4] L. Horner and H. Winkler, *ibid.*, 3265 (1964).

[5] (a) O. Korpium and K. Mislow, *J. Amer. Chem. Soc.*, **89**, 4784 (1967); (b) O. Korpium, R. A. Lewis, J. Chickos, and K. Mislow, *ibid.*, **90**, 4842 (1968).

[6] E. B. Fleischer and R. Dewar, unpublished results, referred to in ref 5b, coupled with the results of ref 5b.

[7] D. C. Garwood and D. J. Cram, *J. Amer. Chem. Soc.*, **92**, 4575 (1970).