# Phosphoric Amides. 5.[1] Acid-Catalyzed Hydrolysis of Dimethyl *N*-(Alkylphenyl)phosphoramidates

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Studies of the acid-catalyzed hydrolysis of dimethyl *N*-(alkylphenyl)phosphroamidates demonstrate that the LFER between observed rates and basicities of the leaving amines is different for meta/para- and for ortho-substituted derivatives (slopes of log $k_{obsd}$ vs. $pK_a$ are 0.4 and 0.9, respectively). Since the $\Delta S^{\ddagger}$ values and KSIE determined are approximately constant irrespective of the position of an alkyl group, the observed change in the slope of the rate/basicity plot is discussed in terms of the steric effects on solvation rather than as an indication of the change in reaction mechanism.

The acid-catalyzed cleavage of the P–N bond has attracted considerable attention. The remarkably facile fission of this bond under mildly acidic conditions found synthetic application in preparation of chiral organophosphorus compounds[2,3] and in the modification of the Gabriel procedure of preparing aliphatic amines.[4] The main mechanistic studies on phosphoramidate solvolysis were focused on the structure of the substrate's conjugate acid and on the nature and stereochemistry of the substitution step. Detailed investigations carried out by Haake,[5] Koizumi,[6] and Harger[7] and in our laboratory[8] demonstrated that phosphoramidates **1** and phosphinamidates **2** solvolyze via the N-protonated reactive intermediates **3**, which then undergo bimolecular nucleophilic attack by a solvent molecule (Scheme I). The nature of

**Scheme I**

$$X_2P(O)NR_2 + H^+ \underset{}{\overset{K}{\rightleftharpoons}} \underset{\mathbf{3}}{X_2P(O)NHR_2^+} \xrightarrow{SOH,\ k_2} TS$$

1, X = RO, ArO
2, X = R, Ar

the substituents at the nitrogen atom (groups R) are expected to have a weak effect on the overall rate of reaction, since polarity of these groups affects protonation equilibrium ($K$) and substitution step ($k_2$) in opposite directions. However, the exact nature of the relationship between the rate of solvolysis and leaving group structure is a sensitive probe of the mechanism of the cleavage of an amide bond. For the acid-catalyzed hydrolysis of *N*-arylbenzamides $PhCONHC_6H_4$-*p*-X (**4**) the plot of the log $k_{obsd}$ vs. the $pK_a$'s of the corresponding anilinium ions $XC_6H_4NH_3^+$ has a value of −0.19.[9] On the other hand, for the variety of phosphoric systems included in Scheme I, much larger and positive slopes (0.4–1.9) of the log $k_{obsd}/pK_a$ plots were obtained.[5,10-12] This remains in agreement with the different protonation behavior of carboxylic and phosphoric amides. The N-protonation of the latter compounds makes the basicity of a substrate closely related to the basicity of a parent amine $R_2NH$; thus the phosphoramidates derived from more basic amines produce high concentrations of the reactive form **3**. In the case of carboxylic amides which react via the O-protonated species, the substrate's basicity is less sensitive to substitution at nitrogen, but the polar effects of groups R modify the electrophilicity of the resonance-stabilized protonated structure in the rate-determining formation of a tetrahedral intermediate.[13]

Table I. Hydrolysis of 5 in Water/Dioxane (4:1 v/v)[a]

| compd | Ar in 5 | $10^4 \times k_{obsd}$,[b] $s^{-1}$ | $k_{rel}$ | $pK_a$[c] |
|---|---|---|---|---|
| 5a | $C_6H_5$ | 1.19 | 1.00 | 4.60 |
| 5b | 2-$CH_3C_6H_4$ | 0.82 | 0.69 | 4.45 |
| 5c | 3-$CH_3C_6H_4$ | 1.21 | 1.02 | 4.71 |
| 5d | 4-$CH_3C_6H_4$ | 1.89 | 1.59 | 5.08 |
| 5e | 3,4-$(CH_3)_2C_6H_3$ | 1.94 | 1.63 | 5.17 |
| 5f | 2,6-$(CH_3)_2C_6H_3$ | 0.31 | 0.26 | 3.95 |
| 5g | 2-$C_2H_5C_6H_4$ | 0.54 | 0.45 | 4.30 |
| 5h | 4-$C_2H_5C_6H_4$ | 1.67 | 1.40 | 5.00 |
| 5i | 4-*n*-$C_4H_9C_6H_4$ | 1.54 | 1.29 | 4.92 |
| 5j | 2-*t*-$C_4H_9C_6H_4$ | 1.33 | 1.11 | 5.03 |
| 5k | $(CH_3O)_2P(O)$-$N(CH_3)C_6H_5$ | 29.3 | 24.6 | 4.68[d] |

[a] $[H_2SO_4]$ = 3.43 M; temperature 25.0 ± 0.2 °C. [b] Each result is the average of at least two independent measurements and is reproducible to within ±5%. [c] Taken from ref 14. [d] $pK_a$ value of *N*-methylaniline.

In this work we report our results on the acid-catalyzed hydrolysis of a series of dimethyl *N*-arylphosphoramidates, $(MeO)_2P(O)NHAr$ (**5**), substituted in the ring with alkyl groups. We were particularly interested in the correlation between the rates of hydrolysis and basicity of the departing amines $ArNH_2$. Since the structural variations in system **5** involve only alkyl groups, any specific interactions between the substituent and reaction medium should be absent. Analysis of the rates of the P–N bond cleavage in system **5** should therefore provide information about structural effects on the rate-determining transition state, particularly in terms of steric effects on solvation, and the possible change in the reaction mechanism (e.g., from the associative A-2 to the dissociative A-1).

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Table II. Rate Constants and Activation Parameters for Hydrolysis of 5 in Water/Dioxane (4:1 v/v)[a]

| parameter | compd 5a | 5b | 5c | 5d | 5k | 5g | 5h |
|---|---|---|---|---|---|---|---|
| $10^4 k_{obsd}$,[b] $s^{-1}$, at temp (K)[c] | | | | | | | |
| 293 | | | | | 20.2 | | |
| 303 | 1.58 | 1.00 | 1.51 | 2.33 | 34.0 | 0.71 | 2.02 |
| 308 | 2.25 | 1.38 | 2.21 | 3.31 | 45.2 | 0.94 | 2.86 |
| 313 | 3.26 | 1.78 | 2.81 | 4.65 | 58.6 | 1.38 | 3.77 |
| 318 | 4.78 | 2.31 | 4.02 | 6.39 | | 2.20 | 5.54 |
| $E_a$, kcal/mol | 13.6 | 10.7 | 12.0 | 12.6 | 9.4 | 13.5 | 12.0 |
| $\Delta G^{\ddagger}$, kcal/mol | 22.9 | 23.1 | 22.9 | 22.6 | 21.0 | 23.3 | 22.7 |
| $\Delta H^{\ddagger}$, kcal/mol | 13.0 | 10.1 | 11.4 | 13.2 | 8.9 | 12.9 | 11.4 |
| $\Delta S^{\ddagger}$, eu | −33 | −43 | −38 | −32 | −41 | −35 | −38 |

[a] $[H_2SO_4]$ = 3.43 M. [b] Each rate constant is the average of two independent measurements and is reproducible to within ±5%. [c] ±0.2 K.

## Results and Discussion

Phosphoramidates **5** were prepared from dimethyl phosphorochloridate and the corresponding aniline (see Experimental Section). Hydrolysis was studied in a medium consisting of a 3.43 M solution of sulfuric acid in 20% dioxane–water (v/v). Rate constants were obtained by measuring spectrophotometrically the rate of disappearance of a substrate by using the pseudo-first-order rate equation

$$\text{rate} = k_{obsd}[\mathbf{5}]$$

Table I lists the values of $k_{obsd}$ obtained for phosphoramidates **5a–k**, together with the $pK_a$ values of the corresponding anilinium ions $ArNH_3^+$. The plot of the values of log $k_{obsd}$ obtained for substrates **5a–k** vs. the $pK_a$ values of the conjugate acids of the leaving groups is presented in Figure 1. Phosphoramidates **5** yield two linear log $k_{obsd}/pK_a$ correlations, with two different values of the slope. Two substrates, *N*-(*o*-*tert*-butylphenyl) (**5j**) and the tertiary *N*-methyl-*N*-phenyl (**5k**) derivatives, deviate from any of the linear correlations and will be discussed separately. Compounds substituted at the ortho position(s) of the ring (**5b,f,g**) together with the unsubstituted substrate (**5a**) give a linear section with a slope = 0.90 ($r$ = 0.989), while the meta- and para-substituted amidates together with **5a** yield a linear plot with a much lower value of the slope (0.41, $r$ = 0.986). The slope value of 0.41 is practically identical with those reported before for *N*-(para-substituted phenyl) amides of phosphinic acids, $R_2P(O)NHC_6H_4$-*p*-X.[10,11] The observed change in the slope of the log $k_{obsd}/pK_a$ correlation could have been taken as an indication of the mechanistic changeover.[15] For the acid-catalyzed cleavage of the P–N bond, the idea of the transition from an A-2 to an A-1 reaction mechanism as a function of leaving amine nucleophilicity was put forward by Haake et al.[10] for the hydrolysis of phosphinanilides. For substrates **5** any changes from the bimolecular (A-2) to the unimolecular (A-1) rate-determining step would be expected to be followed by variations in the degree of charge development at the nitrogen atom in the transition state (TS) and thus by the change in the response of a rate to the basicity of the parent amine.

The usual criterion applied for a distinction between the A-1 and A-2 mechanisms is the evaluation of the entropy of activation, which is expected to be much more negative for A-2 than for A-1 reactions.[16] We determined the activation parameters for seven substrates, i.e., for the unsubstituted compound (**5a**), two isomeric ethyl derivatives (**5g,h**), and four isomeric methyl substituted amidates (**5b–d,k**). The observed rate constants determined at temperatures higher than 25 °C, together with the estimated activation parameters, are listed in Table II. The most obvious conclusion is that for all substrates included in Table II the activation entropy is approximately constant irrespective of the position of the substituent R, and any variations observed are random in nature.[17] The average value of $\Delta S^{\ddagger}$ for substrates **5** is −37 ± 5 eu, typical for the A-2 process.[18] This value also corresponds well to the average value of $\Delta S^{\ddagger}$ = −32 ± 2 eu obtained for hydrolysis of *N*-alkyl-substituted phosphoramidates,[20] and it is also very similar to the value of $\Delta S^{\ddagger}$ = −35 eu found for the hydrolysis of diphenylphosphinamide.[5] We do not obtain, therefore, any indication of the participation of the A-1 mechanism (for which $\Delta S^{\ddagger}$ values close to zero or slightly positive are expected) in the hydrolysis of all substrates **5**. Since the $\Delta S^{\ddagger}$ for the acid-catalyzed cleavage of the P–N bond in a variety of the phosphoryl derivatives

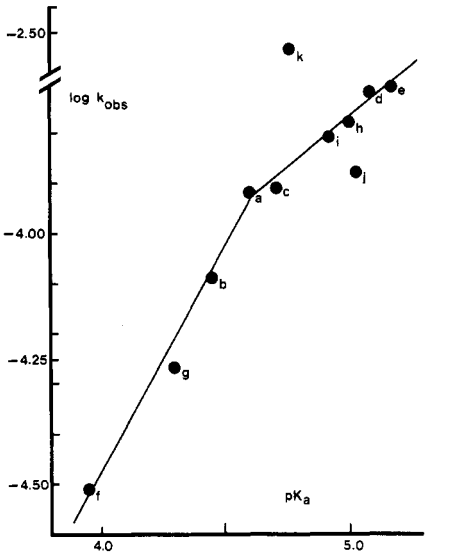


**Figure 1.** Reactivity of phosphoramidates **5** as a function of the basicity of the leaving amine.

(15) See, for example: M. D. Bentley and M. J. S. Dewar, *J. Am. Chem. Soc.*, **92**, 3996 (1970).
(16) A. V. Willi in "Chemical Kinetics", C. H. Bamford and C. F. H. Tipper, Eds., Elsevier, Amsterdam, 1977, Chapter 1, Section 3.2.
(17) Since the $\Delta S^{\ddagger}$ values listed in Table II include the values of $\Delta S^{\circ}$ (protonation) and $\Delta S^{\ddagger}$ (substitution step), any small differences in these two quantities can cause variations in the observed total values of $\Delta S^{\ddagger}$.
(18) The A-1 hydrolyses typically have $\Delta S^{\ddagger}$ values between 0 and 10 kcal $mol^{-1}$ $deg^{-1}$, whereas A-2 hydrolyses have considerably more negative values (−14 to −30 kcal $mol^{-1}$ $deg^{-1}$).[19]
(19) M. Liler, "Reaction Mechanisms in Sulfuric Acid", Academic Press, London, 1971, Chapter 5, Section 2.2.
(20) A. W. Garrison and C. E. Boozer, *J. Am. Chem. Soc.*, **90**, 3486 (1968).

appears to be approximately constant, it is reasonable to postulate that a general and common (A-2) transition-state structure exists for these systems.

Although the ranges of the values of the KSIE for the A-1 and A-2 type reactions overlap,[16] the uniform value of this effect could serve as an additional support for the uniformity of the mechanism of hydrolysis. We determined the $k_H/k_D$ ratio for the unsubstituted substrate (**5a**) and for its two methylated derivatives, the *N*-(2-methylphenyl) derivative **5b** and the tertiary *N*-methyl-*N*-phenyl amidate **5k**. The obtained KSIE values, $k_H/k_D$, are 0.53, 0.48, and 0.55, respectively (average $k_H/k_D = 0.52 \pm 0.04$), again showing no essential differences among substrates which, however, differ significantly in terms of the log $k_{obsd}/pK_a$ behavior.

We believe that the break in the log $k_{obsd}/pK_a$ plot resulting in the two linear sections of slopes 0.4 and 0.9 is a consequence of steric interactions introduced by the ortho substituents in substrates **5b,f,g**. In a series of meta- and para-substituted derivatives of **5**, the polar effects of alkyl groups in the aromatic ring modify the protonation equilibrium and the substitution step (Scheme I), so an LFER is observed with respect to these effects upon the protonation equilibrium of the corresponding anilines ($pK_a$ values). In substrates **5b,f,g** an additional effect is introduced to the system, steric inhibition of solvation of the reaction center by the *o*-alkyl group. Steric hindrance of solvation of the conjugate acid is probably responsible for the decrease in the basicity of the amine group in aniline, caused by alkyl groups in ortho positions.[21] In the acid-catalyzed hydrolysis of phosphoramidates (**5**) ortho substituents interfere with the solvation of the reactive form **3**, as well as with the solvating stabilization of the polar transition state. As a consequence, these new effects produce another LFER, characterized by the different (greater) value of the slope of the log $k_{obsd}/pK_a$ dependence.

Two compounds deviate from the reactivity–basicity relationship presented in the Figure 1, i.e., substrates **5j** and **5k**. There seems to be some uncertainty in the determination of the basicity of 2-*tert*-butylaniline since two apparently contradictory values of $pK_a$ (5.03 and 2.78) have been reported for this compound.[14] The reactivity of **5j** makes us accept the former value of $pK_a$ since in such a case the point obtained for this substrate deviates only slightly from the log $k_{obsd}/pK_a$ plot. It follows that 2-*tert*-butylaniline is therefore a stronger base than aniline, most likely because such a bulky group as $CMe_3$ tends to force the *o*-$NH_2$ group out of the plane of the ring, hence reducing the conjugation with the phenyl group.[22] Since in **5j** the nitrogen atom is substituted not only by the *o*-*tert*-butylphenyl but also by the dimethylphosphoryl group, steric inhibition to solvation of **3** derived from **5j**, as well as to the solvation of the TS, should be greater than in the protonation of the parent amine, hence the deviation of this compound toward lower reactivity in the hydrolysis reaction.

The tertiary amidate **5k** was found to be much more reactive than might have been expected on the basis of the $pK_a$ value for *N*-methylaniline. Part of the reactivity enhancement results certainly from the different protonation behavior of a tertiary substrate relative to the remaining secondary amidates in a nonideal medium. In 3.4 M aqueous $H_2SO_4$ the $H_0$[111] acidity function (describing the acid-base behavior of tertiary amines) is ca. 0.7 H units more negative than the "classical" $H_0$ function. Although this difference does not have to be the same in the 4:1 water–dioxane mixture, roughly half the increase in reactivity of **5k** can be ascribed to the greater acidity of the medium with respect to a tertiary substrate. Another reason for the high value of $k_{obsd}$ obtained for **5k** can be the higher intrinsic basicity of the nitrogen atom in this substrate. Steric crowding at the tertiary nitrogen should disfavor the planarity of the Ph–N–P(O) system and make it more $sp^3$ in character, thus increasing the availability of the lone pair for the interactions with an acid.

In conclusion, we believe that the acid-catalyzed solvolysis of the phosphacyl–nitrogen[23] linkage follows the general, A-2 mechanistic pattern and that a change in the slope of the LFER is not necessarily an indication of a change in basic mechanism. The positive value of the slope of the log $k_{obsd}/pK_a$ (leaving group) relationship remains in agreement with the N-protonated reactive form **3**, but the magnitude of this slope reflects steric interactions operating at the reaction center. It is worthwhile to point out that for the reaction series $Ph_2P(O)NH_2$, $Ph_2P(O)NHMe$, $Ph_2P(O)NMe_2$, where the variations in steric effects occur in a close vicinity to the amide function, a much higher value (1.9) of the slope of the log $k_{obsd}/pK_a$ (leaving group) was obtained.[5] Rates of hydrolysis of the secondary phosphoramidates (MeO)(ArO)P(O)NHR (R = Me, Et, *i*-Pr, *t*-Bu) do not correlate at all with $pK_a$ values of $RNH_3^+$, but a reasonable correlation with steric parameters of the R goups ($E_s$) was reported.[20]

## Experimental Section

Melting points are uncorrected. The solvents used were BDH AnalaR reagents and were purified in the usual manner. The anilines were supplied by BDH or Merck and were all distilled or recrystallized prior to use.

Solutions for hydrolysis were prepared by adding concentrated sulfuric acid (AnalaR, *d* 1.82) to the 20% solution of freshly distilled dioxane in water. The acid concentration was determined by standard titration. The solution of $D_2SO_4$ in 20% dioxane–$D_2O$ was prepared in the same way from concentrated $D_2SO_4$ (MSD, Canada, 96% in $D_2O$, minimum isotopic purity = 99 atom % D). $^1H$ NMR spectra were recorded in $CDCl_3$ at 100 MHz on a Varian XL-100 spectrometer with $Me_4Si$ as an internal standard.

**Substrates.** Dimethyl *N*-arylphosphoramidates were prepared from dimethyl phosphorochloridate[25] and the corresponding aniline according to the following general procedure. Freshly distilled dimethyl phosphorochloridate (0.035 mol) in 20 mL of dry benzene was added dropwise to a stirred solution of the freshly distilled (or recrystallized) aniline (0.035 mol) and triethylamine (0.040 mol) in 80 mL of dry benzene at ca. 15 °C. The mixture was stirred for a further 3–5 h at room temperature and allowed to stand overnight. The precipitate was filtered off and washed with benzene, and the combined benzene solution was washed with water (3 × 10 mL). After removal of the solvent under reduced pressure, the product crystallized on being allowed to stand and was purified by crystallization. All substrates **5** gave $^1H$ NMR spectra in full agreement with the expected structure, as well as satisfactory C, H, and N results.

**5a**: 73%; mp 83–85 °C (from petroleum ether) (lit.[26] mp 84–85.5 °C). **5b**: 59%; mp 110–111 °C (from petroleum ether–benzene, 3:1). **5c**: 70%; mp 81–82 °C (from petroleum ether–benzene, 3:1). **5d**: 65%; mp 110–112 °C (from petroleum ether–benzene, 3:1). **5e**: 62%; mp 121–122 °C (from petroleum ether–benzene, 4:1). **5f**: 36%; mp 122.5–123.5 °C (from petroleum ether). **5g**: 15%; mp 79.5–80.5 °C (from petroleum ether). **5h**: 82%; mp 95–96.5

(21) J. Hine, "Structural Effects on Equilibria in Organic Chemistry", Wiley-Interscience, New York, 1975, Chapter 6, Section 4.
(22) D. H. McDaniel and H. C. Brown, *J. Am. Chem. Soc.*, **77**, 3756 (1955).
(23) This term was proposed by Haake[24] to include phosphoryl, phosphonyl, and phosphinyl groupings.
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(25) B. Fiszer and J. Michalski, *Rocz. Chem.*, **26**, 688 (1952).
(26) T. S. Tung and S. Tsang, *Hua Hsueh Hsueh Pao* **24**, 30 (1959); *Chem. Abstr.*, **53**, 3113*g* (1959).

°C (from petroleum ether). **5i**: 75%; mp 69–71 °C (from petroleum ether). Compound **5j** was obtained in low yield as oily product. The NMR and TLC showed the presence of small quantities of 2-*tert*-butylaniline. This contamination did not, however, interfere with kinetic measurements. **5k**: 56%; bp 96 °C (0.01 mm) [lit.[27] bp 92 °C (0.25 mm)]. Distillation of this product did not allow the removal of small quantities of unreacted *N*-methylaniline. After distillation the product was additionally purified by column chromatography (silica gel, chloroform–acetone, 9:1).

**Kinetics.** All kinetic measurements were done spectrophotometrically by recording the decrease in absorbance at 270–280 nm due to the disappearance of the starting material by using a Beckman UV 5260 spectrophotometer. Pseudo-first-order rate constants were obtained from the plots of ln $(A_t - A_\infty)$ vs. time in the usual manner. Excellent linearity ($r > 0.999$) was obtained in all cases. The identity of the reaction taking place and the identities of the products were determined by recording the UV spectra of the corresponding anilines in the reaction medium.

(27) V. A. Gilyarov, R. V. Kudryavtsev, and M. I. Kabachnik, *Zh. Obshch. Chim.*, **36**, 708 (1966).

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**Registry No. 5a**, 58046-12-1; **5b**, 25626-98-6; **5c**, 25626-99-7; **5d**, 25627-01-4; **5e**, 79639-85-3; **5f**, 75894-86-9; **5g**, 79639-86-4; **5h**, 79639-87-5; **5i**, 79639-88-6; **5j**, 79639-90-0; **5k**, 7006-95-3; dimethyl phosphorochloridate, 813-77-4; benzenamine, 62-53-3; 2-methylbenzenamine, 95-53-4; 3-methylbenzenamine, 108-44-1; 4-methylbenzenamine, 106-49-0; 3,4-dimethylbenzamine, 95-64-7; 2,6-dimethylbenzenamine, 87-62-7; 2-ethylbenzenamine, 578-54-1; 4-ethylbenzenamine, 589-16-2; 4-butylbenzenamine, 104-13-2; 2-(1,1-dimethylethyl)benzenamine, 6310-21-0; *N*-methylbenzenamine, 100-61-8.

# Synthesis of Polycyclic Homocyclopropylcarbinols by Reductive Cyclization of Bromocyclopropyl Epoxides

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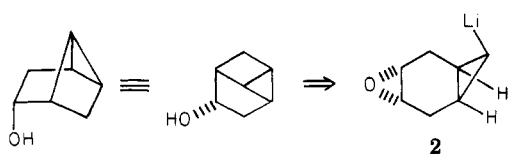
A new synthetic route to polycyclic homocyclopropylcarbinols has been realized by lithiation of bromocyclopropyl epoxides with *n*-butyllithium and subsequent intramolecular attack of the metalated cyclopropane ring onto the epoxide. A series of seven bromocyclopropyl epoxides was prepared from diene precursors in three or four steps by dibromocyclopropanation, epoxidation, and stereoselective reduction of one bromine atom. Thus, *endo*-7-bromobicyclo[4.1.0]hept-3-ene *anti*-oxide (**27**) prepared from 1,4-cyclohexadiene (**3**) underwent cyclization to *endo*-tricyclo[3.2.0.0$^{2,7}$]heptan-4-ol (**1**) in 69% yield. Three dimethyl derivatives of **1** (**34–36**) were synthesized in this manner from 1,2-, 1,4-, and 1,5-dimethyl-1,4-cyclohexadiene. The application of this method to 1,5-cyclooctadiene (**8**) and bicyclo[2.2.2]octa-2,5-diene (**7**) led to efficient syntheses of *endo*-tricyclo[4.3.0.0$^{5,7}$]nonan-2-ol (**38**) and *endo*-tetracyclo[4.3.0.0$^{3,8}$.0$^{7,9}$]nonan-2-ol (**39**). Although most of the lithiation–cyclizations of the bromocyclopropyl epoxides apparently occurred with net retention of configuration at the carbon bearing bromine, the *exo-anti*-bromocyclopropyl epoxide (**24**) from **7** cyclized to **39** with inversion of stereochemistry. Lithiation of a stereoisomeric mixture of the bromocyclopropyl epoxides (**31a–d**) from 1,5-hexadiene afforded the endo and exo isomers of both bicyclo[4.1.0]heptan-3-ol (**40a,b**) and bicyclo[3.1.0]hexane-2-methanol (**41a,b**).

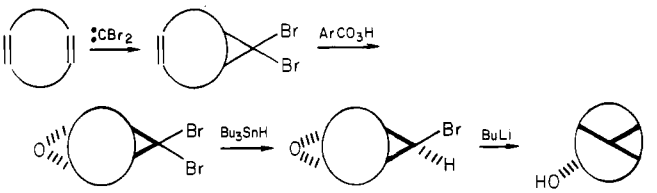
There has been considerable interest in the synthesis and reactions of homocyclopropylcarbinols such as *endo*-tricyclo[3.2.0.0$^{2,7}$]heptan-4-ol (**1**-OH) in connection with investigaitons of long-range cyclopropane participation in solvolytic rearrangements and under stable-ion conditions.[1] For example, ionization of **1**-X proceeds with cyclopropane participation and leads to a bishomo square-pyramidal type of nonclassical carbonium ion.[2] The exo isomer of tricyclic alcohol **1**-OH was prepared as a 73:27 mixture with its 3-isomer by hydroboration of tricyclo[3.2.0.0$^{2,7}$]hept-3-ene.[3] The endo alcohol **1** was obtained by subsequent




**1** **2**

oxidation and reduction.[2] It occurred to us that homocyclopropylcarbinols of this type might be simply prepared by cyclization of lithiated cyclopropyl epoxides (**2**), an approach which would of necessity produce the requisite anti stereochemistry for cyclopropane participation. It is worthy of note that this cyclization involves the formation of a carbon–carbon bond exocyclic to a cyclopropane ring, and therefore the synthetic approach represents a violation of the rules proposed by Corey and co-workers[4] for analysis of bridged polycyclic structures.

Scheme I




Although the synthetic utility of organolithium compounds in intermolecular reactions is widely appreciated, there have been relatively few reports of intramolecular

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