Table I. ^{1}H and ^{31}P Nmr Data for Phosphoranes **1–4**

Phosphorane	^{31}P chemical shift[a]	^{1}H nmr[b] (benzene)
1	+48.4[1]	δ 1.00 singlet[1]
2	+54.3	δ 1.10 (12 H) singlet δ 3.68 (9 H) doublet $J_{PH} \sim 13$ Hz
3	*c*	δ 1.15 (12 H) singlet δ 1.24 (9 H) triplet $J_{HH} \sim 7$ Hz each peak of which is a doublet $J_{PH} \sim 2$ Hz[d] δ 4.10 (6 H) apparent quintet $J_{HH} \sim J_{PH} \sim 7$ Hz[d]
4	+37.4	δ 1.03 (12 H) singlet δ 3.40 (3 H) doublet $J_{PH} \sim 12$ Hz

[a] All ^{31}P nmr spectra are recorded on a Varian XL-100 nmr spectrometer at 40.5 MHz (^{1}H decoupled, ^{2}H lock, Fourier transform). Spectra were recorded of 0.1 *M* solutions of each phosphorane in benzene–deuteriobenzene (1:1) in 12-mm nmr tubes (solution volume 2.5–3 cm^3). Triphenylphosphine oxide (δ −24.8) was used as external standard. The reported chemical shifts are relative to 85% phosphoric acid. [b] All ^{1}H nmr spectra were recorded on a Varian T-60 nmr spectrometer. [c] Denney and Jones (ref 4) reported δ + 60. [d] (i) Denney and Jones (ref 4) report similar coupling constants for the ethoxy groups for the phosphorane produced from the condensation of triethyl phosphite with β-naphthoquinone. (ii) B. C. Chang, W. E. Conrad, D. B. Denney, D. Z. Denney, R. Edelman, R. L. Powell, and D. W. White, *J. Amer. Chem. Soc.*, **93**, 4004 (1971), report similar coupling constants for the ethoxy groups of a similar triethoxyphosphorane. (iii) D. B. Denney and H. M. Relles, *ibid.*, **86**, 3898 (1964), report similar coupling constants for (EtO)$_5$P.

furic acid in benzene. Phosphoranes **2–4** were found to be very sensitive to moisture.[7] Exposure to moist air resulted in slow hydrolysis of benzene solutions of the phosphoranes.

The kinetics of phosphorane formation was investigated in benzene and in mixed acetonitrile[8]–benzene at 23°. The rate of decay of the intensity of chemiluminescence of TMD in the presence of 9,10-dibromoanthracene was monitored before and after the addition of an excess of a phosphorus compound.[9] The reaction of phosphorus compounds with TMD was found to be of the first order with respect to each reagent. The results have been summarized in Table II.

Table II. Rate Constants for Reaction of Trivalent Phosphorus Compounds with TMD

Reagent	10^{-3} [TMD],[a] *M*	10^{-3} [X$_3$P], *M*	k_2,[c] M^{-1} sec^{-1} Benzene	k_2,[c] M^{-1} sec^{-1} Acetonitrile–benzene[b]
Ph$_2$POMe	2.6	18	12 ± 2	
	3.3	35		10 ± 1
Ph$_3$P	6.6	70	1.0 ± 0.1	
	6.1	65		1.0 ± 0.1
(MeO)$_3$P	6.6	70	0.28 ± 0.03	
	6.6	70–140		0.16 ± 0.05
(EtO)$_3$P	2.6–6.6	35–280	0.30 ± 0.03	
	6.6	70–140		0.18 ± 0.05

[a] All runs contained 7.8×10^{-4} *M* 9,10-dibromoanthracene, $T = 23 \pm 1°$. [b] 550 μl of acetonitrile to 100 μl of benzene. [c] Disappearance of TMD was pseudo-first-order through at least three half lives.

The negligible solvent effect in the reaction of trivalent phosphorus compounds with TMD, as well as with diethyl peroxide,[12] indicates that there is no polar character in the transition state and hence that the reaction must be either concerted or homolytic in character.[13] Since by neither mechanism can **1** be formed with both oxy-substituents apical, an attractive reason is at hand for the tenfold jump in rate of formation from **1** to **4**, namely the unfavorability of forcing a phenyl group into an apical position of the phosphorane. The fact that **2** and **3** form more slowly than **1** is consistent with an opposing depression of the general reactivity of the phosphorus atom as phenyl groups are replaced by alkoxy groups.[14]

Acknowledgments. This work was supported by grants from the National Science Foundation and the National Institutes of Health. C. L. Lerman thanks the National Institutes of Health for a training grant. We thank Dr. T. Wilson for the use of her chemiluminescence-monitoring system.

(7) D. B. Denney and S. T. D. Gough, *J. Amer. Chem. Soc.*, **87**, 138 (1965), report that similar phosphoranes were acid and moisture sensitive.

(8) Each phosphorus compound was added to TMD in dry acetonitrile-d_3. The products and relative yields were similar to those obtained in benzene.

(9) This is one of an increasing number of applications of Wilson and Schaap's kinetic method[10] of converting the excitation energy of a carbonyl triplet into fluorescence by the use of 9,10-dibromoanthracene as an efficient heavy-atom energy acceptor.[11] The luminescence intensity serves as an accurate measure of the instantaneous concentration of the TMD; the spontaneous decomposition responsible for the luminescence is negligibly slow compared to the reaction with the phosphorus compounds being measured. For another recent application of the Vasil'ev–Wilson energy transfer, see N. J. Turro, P. Lechtken, G. Schuster, J. Orell, H.-C. Steinmetzer, and W. Adam, *J. Amer. Chem. Soc.*, **96**, 1627 (1974).

(10) T. Wilson and A. P. Schaap, *J. Amer. Chem. Soc.*, **93**, 4126 (1971).

(11) V. A. Belyakov and R. F. Vasil'ev, *Photochem. Photobiol.*, **11**, 179 (1970).

(12) D. B. Denney, D. Z. Denney, C. D. Hall, and K. L. Marsi, *J. Amer. Chem. Soc.*, **94**, 245 (1972).

(13) Water brings about a change in mechanism, judged by observations on an optically active phosphine and its oxide: D. B. Denney and N. G. Adin, *Tetrahedron Lett.*, 2569 (1966).

(14) A. J. Kirby and S. G. Warren, "The Organic Chemistry of Phosphorus," Elsevier, New York, N. Y., 1967.

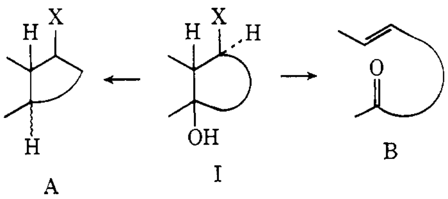
Paul D. Bartlett,* Alfons L. Baumstark
Michael E. Landis, Charles L. Lerman
Converse Memorial Laboratory, Harvard University
Cambridge, Massachusetts 02138

Received April 29, 1974

Epoxynitrile Cyclization. A General Method of Ring Formation

Sir:

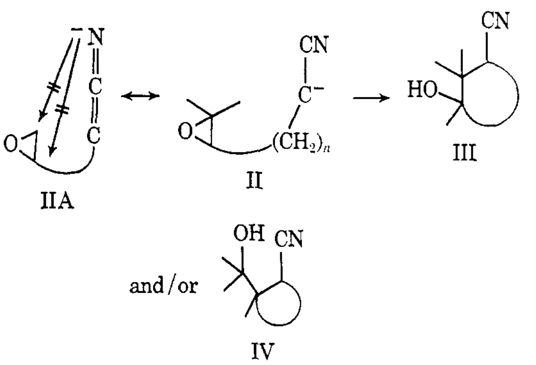
In an effort to find a method for the synthesis of cyclic structures of type I which are of interest, *inter alia*, as precursors of the related desoxy systems (*cf.* A *via* dehydration–reduction) or for use in the Wharton fragmentation[1] (I → B), we have established that the base-catalyzed isomerization of suitably constituted epoxynitriles (II → III and/or IV) constitutes a new and quite general method of ring formation.



There are two important properties of the cyano group which make it the most generally useful of the several possibilities we have investigated. The high nucleophilicity consequent on the low acidity of the α-methy-

---

(1) P. S. Wharton and G. A. Hiegel, *J. Org. Chem.*, **30**, 3254 (1965).

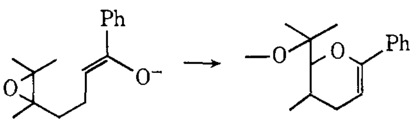


IIA II III

and/or IV

lene group ($\text{p}K$ of $CH_3CN = 29$[2]) made it feasible to explore the possibility of cyclization even at a completely substituted carbon, and, most important, displacement by the anion delocalized on the heteroatom as in IIA is impossible, for normal ring sizes, for geometric reasons.[3]

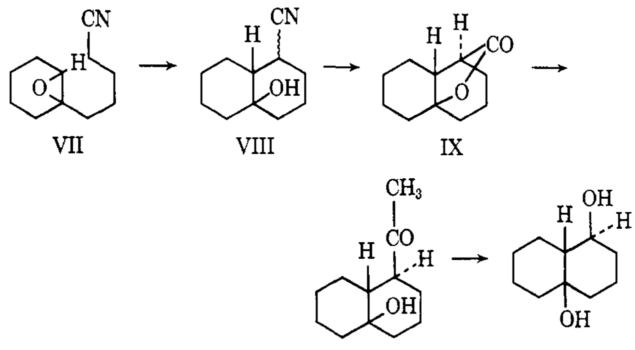
The importance of these considerations is illustrated by the fact that attempted cyclization of epoxy ketones such as V led either to no reaction or to displacement by oxygen (V → VI).[4] Treatment of epoxynitrile VII with



V VI

1 equiv of potassium amide in liquid ammonia–glyme for 7 min followed by addition of *tert*-butyl alcohol, evaporation, and work-up led to a crystalline mixture of nitrile epimers VIII[5] in *ca.* 70% yield. The stereochemistry of the ring junction can safely be assumed to be cis from the mode of formation. It is further possible, in the present and similar cases, to specify the stereochemistry of the center adjacent to the cyano group *via* lactone formation, thus leading to steric control at the three asymmetric centers established in the cyclization. Hydration of the cyclic hydroxynitrile with hydrogen peroxide and aqueous alcoholic sodium hydroxide (0.5 hr, 60°) followed by treatment of the resulting amide with nitric oxide in chloroform at room temperature yielded a mixture of lactone and acid which was converted (potassium acetate–acetic anhydride 120°, 5 hr) to the desired lactone IX, mp 73–74.5°,[5] after evaporative distillation and crystallization from pentane.

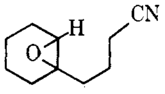
The identity of lactone IX was proved by conversion[6] into the methyl ketone X, mp 104–105°[5] from hexane (ir $\nu_{\max}^{CHCl_3}$ 3600, 3500, 2240, 1695 cm^{-1}; nmr δ 1–2 (15 H, m), 2.1 (3 H, s), 2.25 (1 H, m); mass spectrum *m/e* 196 (M$^+$)) which then (peracetic acid, followed by hydrolysis) gave 1,4a-*cis*-decalindiol (XI), identified as its known[1] crystalline *p*-toluenesulfonate.



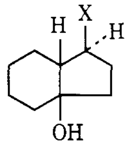
VII VIII IX

X XI

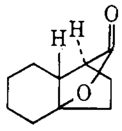
The significant observation was made in the case of the cyclization of the epoxynitrile XII that, under the same conditions used with VII, the cyclization was considerably slower (2 hr *vs.* 7 min). The product XIII, obtained in 75% yield (bp (bath) 140° (1 mm)), was dehydrated (thionyl chloride–pyridine), hydrolyzed (concentrated hydrochloric acid, reflux), and hydrogenated to 1-hydrindanecarboxylic acid (XVI), mp 94.5–96° (reported[7] 95–96°).



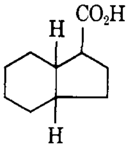
XII



XIII, X = CN
XIV, X = CO$_2$H



XV



XVI

The hydrindanol nitrile (mixture) could be transformed (basic hydrogen peroxide followed by 24 hr of heating with 15% potassium hydroxide) into the crystalline hydroxyacid XIV (47% from XIII) mp 117–118°[5] (chloroform–hexane) (ir $\nu_{\max}^{CHCl_3}$ 3480–2200, 1735, 1695 cm^{-1}; nmr δ 1–3.3 (13 H, m), 2.6 (1 H, m), 7.6 (2 H, s)). The crystalline acid was converted (acetic anhydride, 5 hr) to the corresponding lactone XV, mp 64–65°[5] (ir $\nu_{\max}^{CCl_4}$ 1790, 1010, 950, 900 cm^{-1}).

The remarkable fact that the six-membered ring is formed more readily from VII than the five-membered ring is formed from XII is in contrast with many other cyclizations involving S$_N$2 type transition states.[8] This surprising result is observed *only when cyclization involves the end of the epoxide farther from the carbanion.* Normal behavior favoring the cyclopentane is, however, observed when it involves displacing at the near end of the epoxide. The epoxynitrile XVII was cyclized (20% excess potassium amide in liquid ammonia–glyme; addition of ammonium chloride after 5.5 hr) and gave a 77% yield of the cyanocyclopentane XVIII (91% pure by glc; nmr δ($CDCl_3$) 1.26 (3 H d, J = 6.3 Hz) 2.83 (1 H bq C*H*CN) 3.68 (1 H bm J = 6.3 Hz, C*H*OH), and the structure was confirmed by Jones oxidation to

---

(2) F. G. Bordwell and W. S. Matthews, *J. Amer. Chem. Soc.* **96**, 1216 (1974).

(3) For some simple intermolecular examples, *cf.* M. Mousseron and M. Canet, *Bull. Soc. Chim. Fr.*, 190 (1952).

(4) When displacement by the enolate oxygen is impossible for geometric reasons, the cyclization of epoxy ketones is often a useful reaction; *cf.*, *inter alia*, D. H. R. Barton and A. S. Lindsay, *J. Chem. Soc.*, 2988 (1951); R. B. Woodward, T. Fukunaga, and R. Kelly, *J. Amer. Chem. Soc.*, **86**, 3162 (1964); G. L. Hodgson, D. F. MacSweeney, and T. Money, *Tetrahedron Lett.*, 3683 (1972); J. McMurry and S. J. Isser, *J. Amer. Chem. Soc.*, **94**, 7132 (1972).

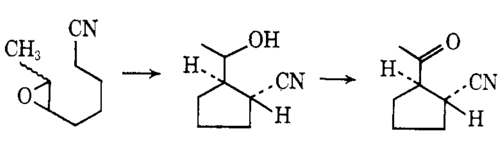
(5) This substance gave reasonable spectral data and acceptable carbon and hydrogen analysis. Nmr spectra are in carbon tetrachloride unless otherwise noted.

(6) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).

(7) D. W. Mathieson, *J. Chem. Soc.*, 3248 (1953).

(8) *Cf.* A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc.*, 67 (1968).

the known[9] methyl ketone XIX (90% yield, 94% pure;



XVII XVIII XIX

nmr $\delta(CDCl_3)$ 2.24 (3 H, s). The stereochemistry follows from the stability of the ketone to potassium *tert*-butoxide in *tert*-butyl alcohol.

It is clear that the oxirane ring imposes on the system a rigidity which makes it difficult to achieve the proper collinear arrangement for displacement at the oxirane carbon further from the nitrile. This point is considered more fully in the accompanying communication[10] which demonstrates that this geometric constraint can be used as the basis of a general method for the synthesis of four-membered rings.[11]

---

[9] R. Trave, L. Marlini, and L. Garanti, *Chim. Ind.* (*Milan*), **40**, 887 (1958); I. N. Nazarov and N. V. Kuznetov, *Izv. Akad. Nauk SSSR*, 354 (1959). This experiment was performed by J. F. Cohen.

[10] G. Stork and J. F. Cohen, *J. Amer. Chem. Soc.*, **96**, 5270 (1974).

[11] We thank the National Science Foundation and the donors of the Petroleum Research Fund administered by the American Chemical Society for the support of this work.

Gilbert Stork,* Lovji D. Cama, D. R. Coulson
Department of Chemistry, Columbia University
New York, New York 10027

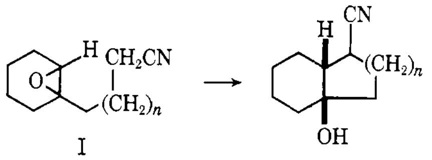
Received March 25, 1974

Ring Size in Epoxynitrile Cyclization. A General Synthesis of Functionally Substituted Cyclobutanes. Application to (±)-Grandisol

Sir:

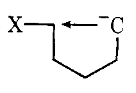
The cyclization of epoxynitriles of type I, which is described in the preceding communication, takes place more rapidly when $n = 2$ than when $n = 1$.[1] The easier formation of a cyclohexane compared to a cyclopentane ring was ascribed to geometric constraints imposed by the oxirane ring.

Examination of models suggests a simple explanation for this result. When the process leading to a five-membered ring involves displacement as illustrated by

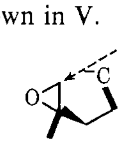


I II

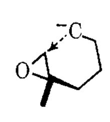
III, there is no particular constraint in locating the carbanion (or indeed any other nucleophile such as oxygen, sulfur, nitrogen, etc.) in the proper position for backside collinear displacement. Reactions of this type generally lead to faster formation of the five- than of the six-membered ring. The situation is very different when the departing group is an epoxide of the type shown in IV. In such a case, the positioning of the carbanion along the dotted line representing collinear approach requires considerable bond distortion.[2] No such distortion is needed for the formation of a six-membered ring, as shown in V.



III

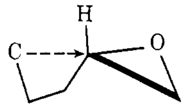


IV



V

While this analysis implies some difficulty in forming a five-membered ring, the fact that such a ring is formed in the particular case of I → II, $n = 1$, implies that the attendant strain in the transition state is not so great as to lead to alternatives such as intermolecular reaction or four-membered ring formation. On the other hand, the transition state for the formation of a four-membered ring seems to allow easy attainment of collinearity (*cf.* VI). It thus became an intriguing possibility that the

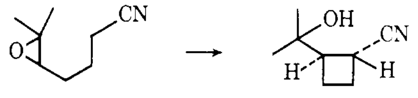


VI

formation of a cyclopentane rather than a cyclobutane ring in the previously studied case of I, $n = 1$, might actually be exceptional and merely reflect the special structural features of I which favor cyclization to a cyclopentane by not requiring displacement at a quaternary center.

We have now found that the epoxynitrile cyclization is unique, in that, *with equal substitution at both ends of the oxirane ring, cyclobutanes always form in preference to cyclopentanes, thus leading to a general, nonphotochemical synthesis of functionally substituted cyclobutanes.*[3] Obviously, this will also be the result when the oxirane carbon further from the nitrile is the more substituted.

Treatment of the cyanoepoxide VII[4] with 1.8 equiv of potassium hexamethyldisalazane in refluxing benzene for 1.25 hr gave (70% yield) the cyanocyclobutyl carbinol VIII, bp (bath) 95–115° (14 mm) (nmr δ-($CDCl_3$) 1.10 (3 H, s), 1.18 (3 H, s), 2.7 (O*H*)).[5] In further confirmation of the tertiary alcohol structure, VIII was completely recovered from attempted Jones



VII VIII

oxidation.

The stereochemistry shown in VIII follows from the much more informative case of the steric course of the cyclization of X, in which epimerization subsequent to cyclization is not possible. The nitrile IX, obtained from the corresponding secondary alcohol[6] (*via* displacement of the tosylate with sodium cyanide in dimethylformamide at 65°), was epoxidized to X which

---

[1] G. Stork, L. D. Cama, and D. R. Coulson, *J. Amer. Chem. Soc.*, **96**, 5268 (1974).

[2] *Cf.* L. Tenud, S. Farooq, J. Seibl, and A. Eschenmoser, *Helv. Chim. Acta*, **53**, 2059 (1970).

[3] For other nonphotochemical routes to cyclobutanes, see B. M. Trost and M. J. Bogdanowicz, *J. Amer. Chem. Soc.*, **95**, 5321 (1973), and references cited therein.

[4] The corresponding olefin was made by Wittig reaction. *Cf.* also C. Agami, M. Andrac-Taussig, and C. Prévost, *Bull. Soc. Chim. Fr.*, 173 (1966).

[5] This substance gave ir, nmr, and high resolution mass spectra in accord with the postulated structure. Reference is made in the text only to some of the more interesting spectral features.

[6] E. Cortes and F. Walls, *Boll. Inst. Quim. Univ. Nacl. Auton. Mex.*, **17**, 34 (1965).