

SYNTHESIS OF 1-OXASPIRO[2.2]PENTANES.

REARRANGEMENT TO CYCLOBUTANONES^{1,2}

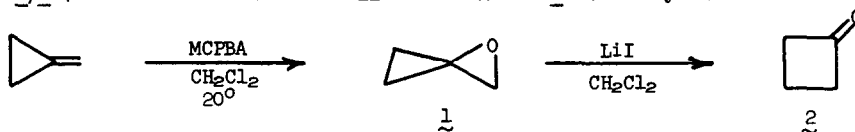
Donald H. Aue*, Michael J. Meshishnek and Dale F. Shellhamer

Department of Chemistry, University of California,
Santa Barbara, California 93106

(Received in USA 11 September 1973; received in UK for publication 16 October 1973)

Oxaspiro[2.2]pentanes have recently been reported;^{3,4} the synthesis and reactivity of this new heterocyclic system promises to be of considerable synthetic and mechanistic interest. We have found peracid oxidation of methylenecyclopropanes provides a convenient synthesis of several 1-oxaspiro[2.2]pentanes. We report here on the formation of some oxaspiropentanes, their thermal reactivity, and their conversion to cyclobutanones with Lewis acids.

The parent spiroepoxide 1 is obtained in 48% yield by m-chloroperbenzoic acid (MCPBA) oxidation of methylenecyclopropane.⁵ Low temperature distillation from o-dichlorobenzene solvent affords pure 1, bp 36° (200 mm); ir (CCl₄) 2960, 1395, 905 cm⁻¹; nmr (CCl₄) δ 3.10 (s, 2H), 0.95 (m, 4H); m/e 70.0416.^{4,6} When a distilled solution of 1 in methylene chloride is treated with







anhydrous lithium iodide, cyclobutanone, 2, is obtained in quantitative yield. By an analogous procedure, 3,3-dimethyl-1-oxaspiro[2.2]pentane 3 is obtained from 2,2-dimethyl-methylenecyclopropane⁷ in 54% isolated yield, bp 61° (350 mm); ir (CCl₄) 2960, 1450, 1370, and 855 cm⁻¹; nmr (CCl₄) δ 3.02 (s, 2H), 1.15 (s, 3H), 1.10 (s, 3H) and 0.80 (m, 2H); m/e 98.0735.

The rates of epoxidation of these methylenecyclopropanes are remarkably slower than for methylenecyclopentane by a factor of 75 (Table I).⁸ This is in direct contrast to the 40-fold increase in the rate of addition of phenyl azide to methylenecyclopropane because of strain relief relative to methylenecyclopentane.⁹ The epoxidation rates of methylenecyclopropane and a large number of other alkenes and cycloalkenes correlate quantitatively, however, with π -electron energies of the olefins as indicated by ionization potentials.¹⁰ The lack of any correlation

of epoxidation rates with the strong strain relief effects found in phenyl azide additions⁹ supports arguments^{11b} favoring a "spiro" transition state with partial 3-membered ring formation over a suggested 5-member ring 1,3-dipolar transition state.^{11,12} In forming the 3-membered ring no significant changes in strain energies are expected (Table I).

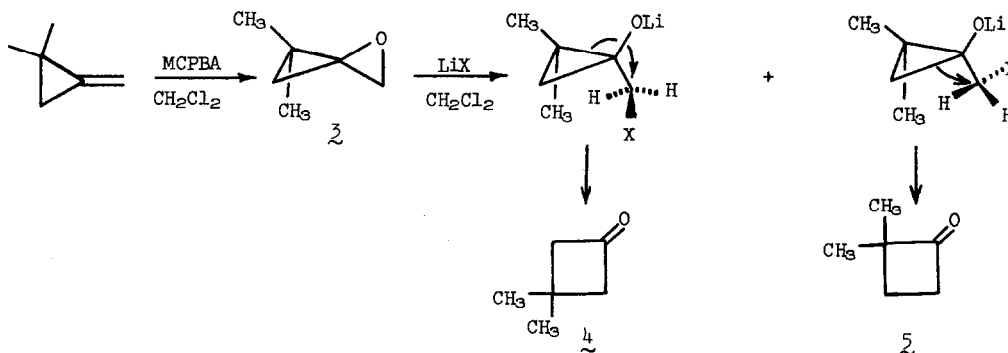
TABLE I - Relative Rates of Epoxidation with MCPBA, 15°, CH₂Cl₂

	k_{rel}	Vertical IP (eV)	Increase in Strain Energy on Epoxidation ^a (kcal/mole)
	0.8	-	23
	1.0	9.50 ^c	23
	24	9.19 ^c	ca. 26
	74	9.16 ^c	ca. 29
propene	ca. 1.1 ^b	9.74	28

(a) P. v. R. Schleyer, J. C. Williams and K. R. Blanchard, *J. Amer. Chem. Soc.*, **92**, 2377 (1970).
 (b) Relative to methylenecyclopentane with peracetic acid; D. Swern, *ibid.*, **69**, 1692 (1947), A. Endo, M. Saito, T. Ogura, and Y. Fushizaki, *Nippon Kagaku Zasshi*, **85**, 786 (1964). (c) D. W. Turner, *Molecular Photoelectron Spectroscopy*, Wiley-Interscience, New York (1970).

On heating above 100° in decalin both 1 and 2 rearrange to cyclobutanones in a catalyzed reaction.¹³ In gas phase pyrolysis of 1 small amounts of methyl vinyl ketone and methacrolein are formed along with cyclobutanone (90%). The new products and higher preexponential factor in the gas phase experiments suggest that less catalytic reaction is taking place than in solution.^{13,14}

Epoxide 2 rearranges with Lewis acids to form ketones 4 and 5. The ratio of 4:5 (Table II) is strongly dependent on the nature of the catalyst and in an unexpected way. The dependence of



the product ratio on the nature of the catalyst provides strong evidence for a mechanism involving nucleophilic ring opening to lithio-halohydrin-type intermediates.¹⁵ The amount by which tertiary migration to give 4 is favored over primary migration to give 5 may depend on the degree of positive charge development at the migrating center in the rearrangement. These results

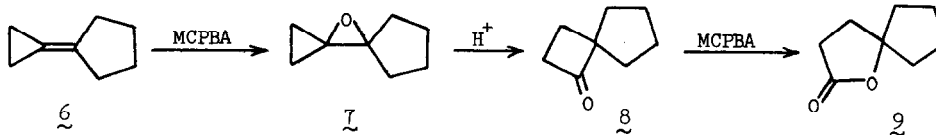
suggest that tosylate and perchlorate add to the epoxide in an S_N2 -like fashion.¹⁶ Lithium perchlorate normally, however, opens epoxides to products suggestive of carbonium ion intermediates in contrast to S_N2 -like lithium halide catalyzed opening.^{15a,b} The specific formation of 4 with lithium iodide or lithium bromide in nitromethane allows the preparation of nearly pure 4. In contrast, the diazomethane-dimethylketene reaction¹⁷ leads to a 1.9:1 mixture of 4:5.

TABLE II - Product Ratios in Rearrangement of 3,3-Dimethyl-1-oxaspiro[2.2]pentane, 3

Reaction Medium	Reaction Time	Yield of <u>4</u> + <u>5</u>	Ratio of <u>4</u> to <u>5</u>
LiI, CH ₂ Cl ₂ , 30°	< 1 min	100%	7.5
LiClO ₄ , CH ₂ Cl ₂ , 30°	24 hr	83%	10
LiBr, CH ₂ Cl ₂ , 30°	72 hr	100%	3.5
LiBr, CH ₃ NO ₂ , 30°	3 hr	-	14
LiOSO ₂ C ₆ H ₄ CH ₃ , CH ₃ NO ₂ , 70°	10 hr	-	15
HOSO ₂ C ₆ H ₄ CH ₃ ·H ₂ O, CH ₂ Cl ₂ , 30°	3 hr	76%	11
Decalin, in base-washed glass, 150°	30 min	65%	11

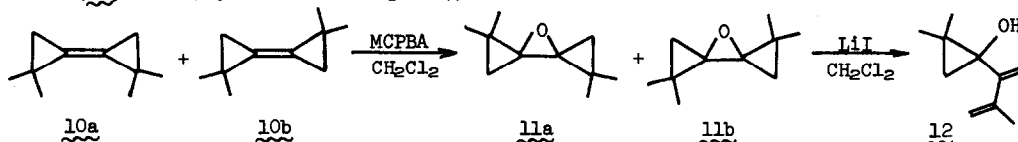
Typically, acid catalyzed opening of epoxides leads to mixtures of products in which opening at the site of the more stable carbonium ion is favored.^{18,19} Spiroepoxide 3 however, opens preferentially at the primary center, even with catalysts expected to give S_N1 -type opening.¹⁴ The parent oxaspiropentane 1 also opens only toward the primary center with lithium iodide, hydrogen chloride, perchloric acid-methanol, and sulfuric acid.^{20,21} I-strain destabilization of the tertiary carbonium ion may in part account for the direction of the ring opening; but hydrogen bromide,²¹ formic acid²² and trifluoroacetic acid²² additions to methylenecyclopropane give only products derived from the tertiary cyclopropyl cation.

The tertiary cyclopentyl center in 9-oxadispiro[2.0.4.1]nonane 7 makes it very unstable to acid, but it can be isolated from the peracid oxidation of cyclopropylidenecyclopentane, 6,²³ by low temperature distillation.^{3c} Spiro[3.4]octanone, 8,²⁴ is obtained in 68% isolated yield from 6, and ketone 8 gives the butyrolactone 9^{3c} in 88% yield. This sequence provides a synthetically useful three carbon extension of ketones to butyrolactones in a two step procedure (ketone - 6 -> 9).



Epoxidation of a 70:30 mixture of cis- and trans-2,2,2',2'-tetramethyl-1,1'-biscyclopropylidene (10a + 10b) gives the oxa-dispiroheptanes 11a and 11b in 54% yield. These epoxides are relatively stable. They do not give cyclobutanones but instead rearrange to the ring-opened

dien-ol, 12, in 76% yield on heating to 75° with lithium iodide.



References

- The authors acknowledge support from the Petroleum Research Fund administered by the American Chemical Society. We thank Prof. B. Rickborn for helpful discussions and Mr. W. J. Nakata.
- Presented in part at 7th Western Regional Meeting of the American Chemical Society, Anaheim, California, October 1971.
- a) J. K. Crandall and D. R. Paulson, *J. Org. Chem.*, **33**, 991 (1968); *ibid.*, **33**, 3291 (1968); b) J. R. Wiseman and H. F. Chan, *J. Amer. Chem. Soc.*, **92**, 4749 (1970); c) M. J. Bogdanowicz and B. M. Trost, *Tetrahedron Lett.*, 887 (1972); B. M. Trost and M. J. Bogdanowicz, *J. Amer. Chem. Soc.*, **95**, 289 (1973); *ibid.*, **95**, 5311 (1973); *ibid.*, **95**, 5321 (1973); d) C. R. Johnson G. F. Katekar, R. F. Huxon and E. R. Janiga, *ibid.*, **93**, 3771 (1971).
- While this work was in progress a similar study of 1 appeared; J. R. Salaün and J. M. Conia, *Chem. Commun.*, 1579 (1971).
- R. Köster, S. Arora and P. Binger, *Synthesis*, 322 (1971).
- This structure has been confirmed by microwave spectroscopy, W. D. Slafer, D. O. Harris, D. H. Aue, D. F. Shellhamer, to be published.
- W. Rahman and H. G. Kuivila, *J. Org. Chem.*, **31**, 772 (1966).
- The yield of 1 is low because epoxidation is competitive with m-chlorobenzoic acid addition to 1.
- D. H. Aue and G. S. Helwig, preceding paper.
- Log k and ionization potential correlate linearly (correlation coefficient = 0.96), with methyl-encyclopentane falling somewhat low, by a factor of 4 in k.
- a) H. Kwart and D. M. Hoffman, *J. Org. Chem.*, **31**, 821 (1952), H. Kwart, P. S. Starchen and S. W. Tinsley, *Chem. Commun.*, 335 (1967). b) For another criticism based on strain energies see K. D. Bingham, G. D. Meakins, and G. H. Whitam, *ibid.*, 445 (1966).
- A concerted mechanism involving no carbonium ion intermediate is supported by the lack of any of the ring opening products expected from a cyclopropyl cation (ref. 14).
- Even in purified decalin and base-washed glassware, the reactions appear to be catalyzed from the low preexponential factors: for 1 log A \approx 5, $E_a \approx$ 10 kcal/mole; for 3 log A \approx 8, $E_a \approx$ 13 kcal/mole. The rate of reaction of 1 is much slower in the gas phase with $t_{1/2} \approx$ 70 min. at 230°. Apparent Arrhenius parameters are log A \approx 11, $E_a \approx$ 33 kcal/mole.
- For analogous azaspiropentanes see D. H. Aue, R. B. Lorens and G. S. Helwig, preceding paper.
- a) B. Rickborn and R. M. Gerkin, *J. Amer. Chem. Soc.*, **93**, 1693 (1971); b) B. C. Hartman and B. Rickborn, *J. Org. Chem.*, **37**, 943 (1972); c) D. L. Garin, *J. Org. Chem.*, **36**, 1697 (1971).
- Perchlorate can act as a nucleophile in organic solvents, K. Baum, *J. Amer. Chem. Soc.*, **92**, 2927 (1970).
- H. Audier, J. M. Conia, M. Fetizon and J. Gore, *Bull. Soc. Chim. France*, 787 (1967); N. J. Turro and R. B. Gagosian, *J. Amer. Chem. Soc.*, **92**, 2036 (1970), and references therein.
- N. B. Chapman and V. Wray, *J. Chem. Soc. (B)*, 71, (1971).
- I. G. Guest and B. A. Marples, *J. Chem. Soc. (C)*, 1626 (1970); B. N. Blackett, J. M. Coxon, M. P. Hartshorn and K. E. Richards, *Tetrahedron*, **25**, 4999 (1969).
- Cf. K. L. Erickson and K. Kim, *J. Org. Chem.*, **36**, 2915 (1971).
- B. C. Anderson, *ibid.*, **27**, 2720 (1962).
- D. H. Aue, W. J. Nakata and D. F. Shellhamer, unpublished results.
- E. E. Schweizer, C. J. Berninger and J. G. Thompson, *J. Org. Chem.*, **33**, 336 (1968).
- J. R. Salaün, and J. M. Conia, *Tetrahedron Lett.*, 2849 (1972).