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OXIDATION OF β HYDROXY ESTER DIANIONS:
A NEW STRATEGY FOR EPOXIDE FORMATION

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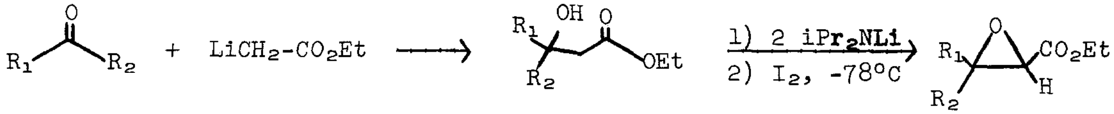
Common methods for the construction of α,β epoxy esters are the Darzens condensation[1] and the reaction of hydroperoxides[2] or peracids[3] with α,β unsaturated esters. The effectiveness of the peracid route is dependent upon the absence of other unsaturated units in the molecule. While significant improvements have been developed[4] to render the Darzens condensation preparatively useful, a major disadvantage is the production of diastereomeric mixtures. We wish to communicate a new strategy for epoxide formation which is outlined below.



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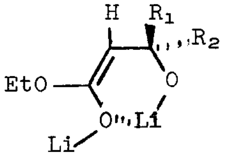
An outstanding feature of this method is the stereochemical purity of the resulting epoxyester - the exclusive formation of the least hindered compound. This has been established by VPC comparison with mixtures of epoxides prepared independently. While it is conceivable that at -78°C there are great differences in the rates of reaction for the two diastereomeric transition states, another possible explanation involves complexation between the ester enolate and the alkoxide. Reaction of the iodine molecule on the least hindered side of 3 will produce the observed product upon the elimination of lithium iodide. Complex 3 is illustrated below:



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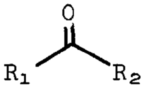
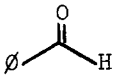
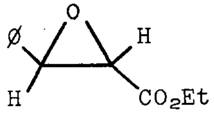
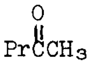
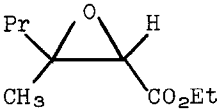
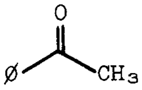
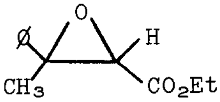
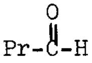
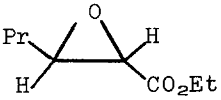
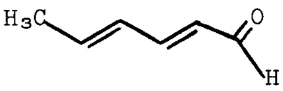
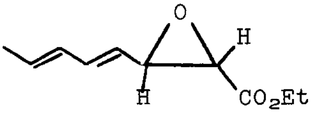
This method works well for the preparation of di- and trisubstituted epoxides. Tetrasubstituted epoxides are obtained in low yield due to incomplete formation of the dianion.[5] An additional advantage of our method is that it is sufficiently selective to allow the preparation of sensitive unsaturated epoxy esters, as seen in the Table below. In a typical experiment, 10 mmoles of hydroxy ester[6] dissolved in 3 ml THF was added dropwise over 5 min to a solution of 23 mmoles of lithium diisopropylamide in 20 ml THF at -78°C. The solution was stirred at -78°C for 40 minutes, then added via syringe to 10 mmoles of iodine dissolved in 20 ml THF at -78°C. The reaction was worked up by addition of 23 mmoles of acetic acid, followed by dilution with ether and extraction with sodium bisulfite solution. The organic layer was dried over sodium sulfate and concentrated.[10] Filtration through a silica gel column using ether:pentane provided pure product.[11] This epoxidation method, by virtue of its convergence and selectivity, should find wide use in synthetic chemistry. We are currently examining the utility of this method to construct optically active compounds from carbohydrate precursors.

ACKNOWLEDGEMENTS - We would like to thank DuPont for a Young Faculty Grant which provided partial support of this research.

	Product	% Overall Yield	Ref.
		48%	7
 $\mathrm{Pr}\overset{O}{\overset{\parallel}{C}}\mathrm{CH_3}$		31%	8
		43%	9
 $\mathrm{Pr}-\overset{O}{\overset{\parallel}{C}}-\mathrm{H}$		31%	8
		45%	

REFERENCES AND NOTES

1. M. Ballester, Chem. Rev., 55, 283 (1955).
2. H. O. House, Modern Synthetic Reactions (second edition), 306.
3. Ibid., p. 307.
4. R. Borch, Tet. Lett., 3761 (1972).
5. Quenching experiments with benzaldehyde showed that dianion formation was not complete. The use of higher temperatures or the addition of two equivalents of HMPA did not improve the yield of epoxy ester. Quenching experiments involving β-hydroxyesters having no α-substituent showed that dianion formation was complete.
6. N. W. Rathke, J. Amer. Chem. Soc., 92, 3222 (1970). See also, Organic Synthesis, 53, 66 (1973).
7. V. R. Valente and J. L. Wolfhagen, J. Org. Chem., 31, 3509 (1966).
8. W. S. Johnson, J. Belew, L. Chinn and R. Hunt, J. Amer. Chem. Soc., 75, 4995 (1953). This method was used to prepare the epoxide mixture.
9. F. W. Bachelor and R. K. Basal, J. Org. Chem., 34, 3600 (1969).
10. The use of a bromine solution instead of iodine led to inferior yields. The other identifiable product which could readily be separated by chromatography was the original β hydroxy ester.
11. Purity was based upon VPC analysis of column chromatographed material.