

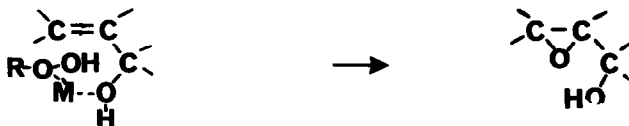
THE TEMPLATE-DIRECTED REMOTE EPOXIDATION OF OLEFINS

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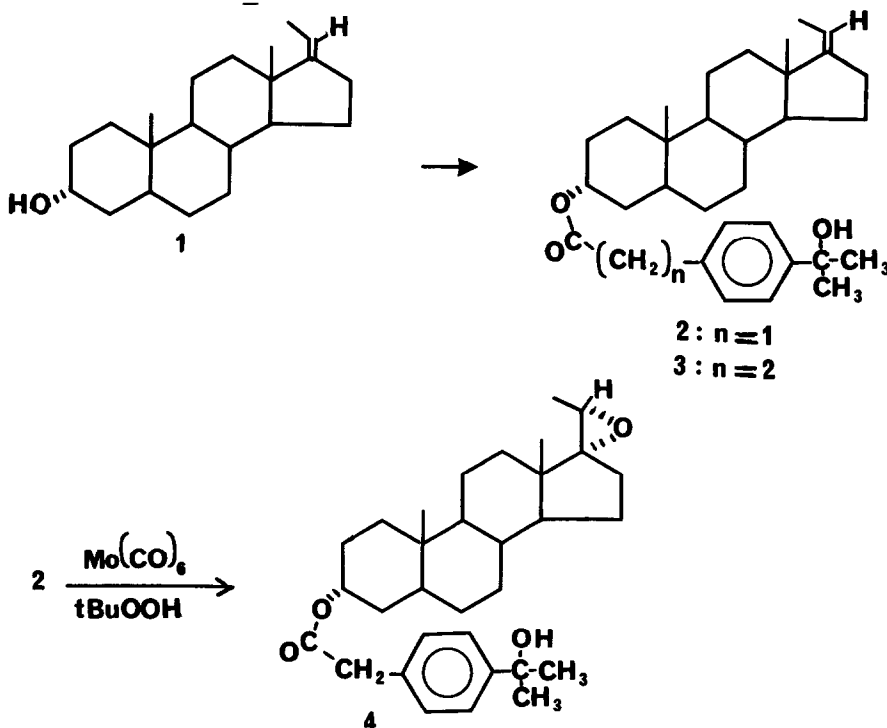
The epoxidation of olefins by alkyl peroxides, catalyzed by metals such as molybdenum, tungsten, chromium, or vanadium, has been the object of much recent interest. Sharpless¹ has greatly extended earlier observations² that olefins bearing allylic hydroxyl groups are particularly reactive. With an allylic hydroxyl group present the epoxidation is both regioselective and stereoselective, as predicted if the metal atom is complexed to the substrate hydroxyl group when it delivers an oxygen atom to the double bond.¹



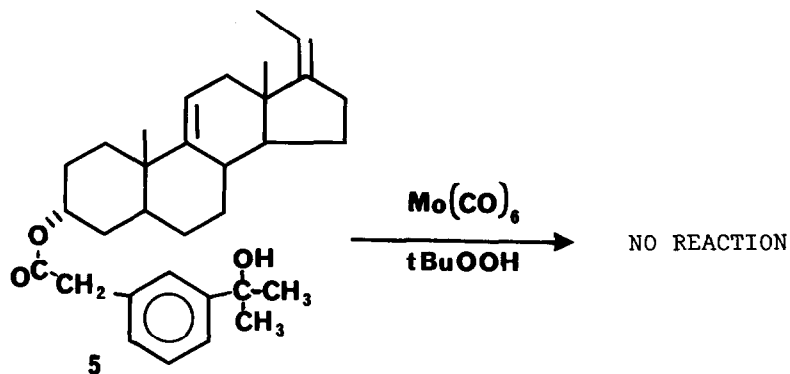
For some years we have been exploring the directive effects possible through the use of template molecules attached or complexed to substrates.³ With such methods an intramolecular or intracomplex reaction is freed from the geometrical constraints imposed by the functional groups of the substrate. Typically the chemistry of a molecule is directed by its functional groups, either by chemical activation (e.g. enolization next to carbonyl) or by geometric activation (e.g. the allylic hydroxyl effect on epoxidation described above). Our template methods use a functional group of the substrate as the point of attachment for a template or spacer. The geometric activation is then determined by the exact geometry of the template. We now wish to report the application of such a template method to olefin epoxidation.

17(20) (5 α)-Pregnen-3 α -ol(1)⁴, mp 184-186^o, was prepared by Wittig re-

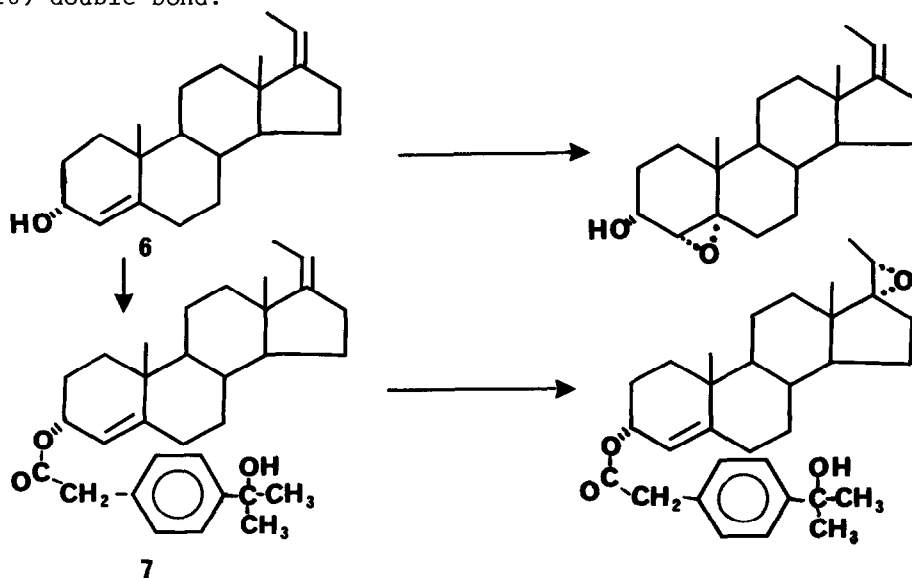
action on androstanolone. With the appropriate acetophenone acid chloride this was converted to ketoesters which, with methyl magnesium iodide in ethers, afforded the ester carbinols^{4,6} 2 and 3. Treatment of 2 with 0.03 equiv. $\text{Mo}(\text{CO})_6$ and 2.0 equiv. *t*-butyl hydroperoxide in refluxing benzene for 8 hr. afforded 25% of the corresponding epoxide^{4,6} 4 along with 75% recovered starting material. With more catalyst and peroxide the conversion of 2 to 4 was raised to 60%, and undoubtedly can be quantitative since the only other product is recovered 2.



By contrast, under these conditions 3 undergoes no epoxidation and is recovered unchanged. This establishes several points. First of all, the reaction is catalyzed by complexing of the molybdenum to the template hydroxyl in 2, while in 3 the corresponding complex must have the wrong geometry. Secondly, attack by uncomplexed reagent, or intermolecular reaction, is not appreciable under these conditions. Further, the small change in geometry between 2 and 3 suggests that the geometric requirements of this reaction are quite strict. This is also indicated by our finding, with a related steroid^{4,6} 5 that the meta isomer of the template in 2 cannot produce detectable epoxidation of a 17(20) double bond.



As expected from these results, we can direct epoxidation in an appropriate steroid diene 6 by adding or omitting the correct template. Thus 6 itself undergoes allylic epoxidation in 61% conversion, 100% yield, with $\text{Mo}(\text{CO})_6$ and *t*-butyl hydroperoxide under our standard conditions.⁵ However the addition of a template to produce 7 now directs epoxidation to the remote double bond, in 25% conversion, 100% yield.⁵ While in principle such a result might involve simple shielding of the 4(5) double bond, our studies described above show clearly that simple intermolecular epoxidations do not proceed at a detectable rate under our conditions⁵, as evidenced by the results with 3 and 5. Thus in 7 the template is catalyzing attack at the 17(20) double bond.



We have also attached such templates to flexible polyenes⁶, in particular to geraniol, farnesol, and geranylgeraniol. In these cases, which will be described elsewhere, the templates produce a product distribution in accord with the conformational preferences of the flexible polyene chain. Such studies are useful in determining these conformational preferences.

Acknowledgements. This work was supported by the National Institutes of Health and the National Science Foundation.

References

1. K.B. Sharpless and R.C. Michaelson, J. Amer. Chem. Soc., 95, 6136 (1973), and subsequent papers.
2. Reviewed by R. Hiatt in R.C. Augustine and D.L. Trecker, "Oxidation" Vol.2, Marcel Dekker, Inc., New York, 1971.
3. e.g. R. Breslow, R.L. Wife, and D. Prezant, Tetrahedron Lett., 1925(1976); R. Breslow, H. Kohn, and B. Siegel, Tetrahedron Lett., 1645 (1976); and references therein.
4. The structure was consistent with spectroscopic data.
5. The standard conditions are those described above, with only 0.03 equiv. of $\text{Mo}(\text{CO})_6$ and 2.0 equiv. of t-butyl hydroperoxide. The synthetic reaction is apparently limited by loss of the metal catalyst, whose quantity should be increased for preparative work.
6. See L. Maresca, Ph.D. thesis, Columbia University, 1976, for details.