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Oxidation of Allylic Alcohols by Dimethyldioxirane: Competition Reaction between Epoxidation and C-H Insertion

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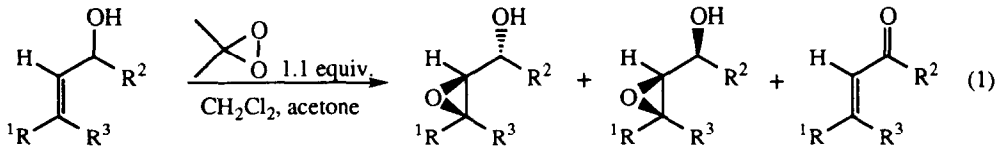
Abstract: Epoxidation of allylic alcohols with dimethyldioxirane is accompanied by oxidation of the hydroxy functionality; thus enone formation increases with decreasing substitution at the C-C double bond; nonetheless, selective epoxidation can be obtained by acylation of the alcohol functionality.

Dioxiranes have proven highly versatile oxidizing reagents in the past few years.[1] Especially isolated dimethyldioxirane[2] (as acetone solution) has found numerous applications in organic synthesis as it performs valuable olefin epoxidation, C-H insertion[3], and heteroatom oxidations. While the individual transformations have been studied extensively, little is still known on the chemoselectivity of dioxiranes. In view of the fact that with *in situ* generated[4] and with isolated[5] dimethyldioxirane the oxyfunctionalization of allylic alcohols affords usually epoxy alcohols. it was generally accepted that olefin epoxidation is preferred over C-H insertion in the oxidation of alcohols. Herein we report that alcohol oxidation can effectively compete with olefin epoxidation.

A number of secondary allylic alcohols **1** were allowed to react with isolated dimethyldioxirane and the product distribution was analyzed directly after removal of the solvent (Eq. 1). The results are



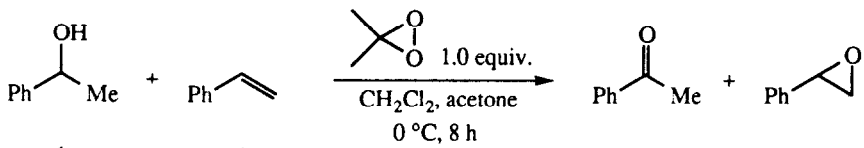
1 **2α** **2β** **3**

compiled in Table 1. In all cases, except **1a** and **1c**, considerable amounts of α,β-unsaturated ketones **3** were formed, besides the expected diastereomeric epoxy alcohols **2**. Authentic samples of the latter, prepared by *m*-chloroperbenzoic acid epoxidation, were on hand for comparison. The results for allylic alcohol **1a** nicely match those reported[4] for *in situ* generated dimethyldioxirane in both chemo- and diastereoselectivity; however, as the results in Table 1 manifest, substrate **1a** is apparently an exception; presumably conformational effects of the cyclooctene ring play a decisive role. Also an intermolecular competition experiment showed that ketone formation can compete with epoxidation (Eq. 2).

Table 1: Oxidation of Allylic Alcohols by Dimethyldioxirane[a)]

	R^1	R^2	R^3	temp. [°C]	conv.[b)] [%]	product distribution[b)] **2 : 3**	d.r.[b)] **2α : 2β**
1a	H	$-(CH_2)_5-$		0	>95	>95 : 5	>95 : 5
1b	H	$-(CH_2)_3-$		-20	>95	46 : 54	72 : 28
1b	H	$-(CH_2)_3-$		0	80	70 : 30	53 : 47
1c	Me	Me	Me	-78	>95	>95 : 5	76 : 24
1c	Me	Me	Me	0	87	>95 : 5	77 : 23
1d	Me	Me	H	0	78	81 : 19	53 : 47
1e	Me	*i*-Pr	H	-20	>95	47 : 53	63 : 37
1e	Me	*i*-Pr	H	0	>95	90 : 10	65 : 35
1f	Me	*n*-Bu	H	-20	96	47 : 53	52 : 48
1f	Me	*n*-Bu	H	0	>95	71 : 29	52 : 48
1g	H	*n*-Pent	H	0	>95	51 : 49	66 : 34

a) Dimethyldioxirane was used as a 0.070 - 0.100 M solution in acetone. b) Determined by ^1H NMR analysis directly on the crude reaction mixture (error ± 5 %).



(2)

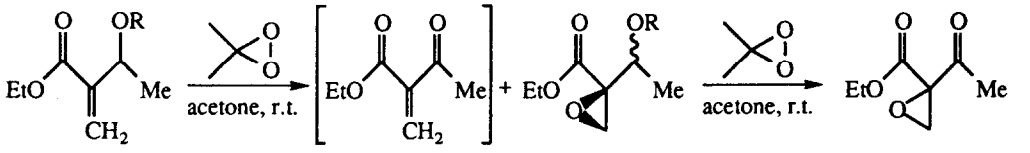
At a constant temperature, the amount of enone **3** decreased with increasing substitution at the C-C double bond (Table 1); in fact, for the trisubstituted olefin **1c** no enone **3c** was observed. In view of the electrophilic character of dimethyldioxirane, olefin epoxidation is expected to be more facile with the more substituted electron-rich double bond, while the rate of C-H insertion should not be affected significantly, as in agreement with our results (Table 1).

The ratio of products **2** and **3** showed a pronounced temperature dependence. At lower temperature, more enone is formed in all cases, except for the trimethyl derivative **1c**; its double bond is so readily epoxidized, that enone formation cannot compete even at -78 °C. This temperature effect can be rationalized in terms of entropy control in the epoxidation *versus* C-H insertion pathways. A large negative entropy of activation has been determined for the olefin epoxidation by dimethyldioxirane,[6] but the activation enthalpy is expected to be relatively small. Thus, the $T\Delta S^{\neq}$ term comprises the major contribution to the total free energy of activation in the epoxidation process. On the other hand, for C-H insertion into alcohols $\Delta S^{\neq}$ appears to have a less negative value than for epoxidation,[7] so that this reaction pathway is mainly enthalpy driven and, thus, the $T\Delta S^{\neq}$ term of less importance; however, in view of the relatively low $\Delta H^{\neq}$ value anyway, a low temperature coefficient

applies and, therefore, a small temperature effect is expected. Indeed, as our product data in Table 1 reveal, lower temperatures slow down the rate of epoxidation and those of enone formation are favored.

The diastereoselectivity of the epoxidation reaction showed no temperature dependence and was generally low; the *threo* or *cis* epoxy alcohols[8] were obtained as the major products in all cases. These results imply insignificant interaction of the dioxirane with the chirality center of the substrate, especially with the hydroxyl group through hydrogen bonding, which is in contrast to peracids[11a]. This is further substantiated by the fact that the major epoxy alcohol formed from substrate **1b** has *trans* stereochemistry.

Further insight into the chemoselectivity of dimethyldioxirane was acquired in the oxidation of the rather sluggish α,β-unsaturated hydroxyester **1h** (Eq. 3). Reaction with one equivalent of dimethyldioxirane yielded a



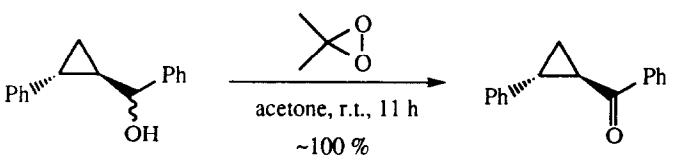
3 **2** **4**

(3)

		t [h]	conv. [%]	mb [%]				
1h	R = H	18	>95	37	0	:	0	: 100
1i	R = Ac	48	>95	~100	0	:	100 (65 : 35)	: 0

mixture of epoxy alcohol **2h** and epoxy ketone ester **4**.[9] Additional signals indicated the formation of undefined higher-molecular-weight products, which presumably derived from the labile enone ester **3h**, obtained through oxidation of the alcohol functionality in **1h**. The formation of the epoxy ketone **4** at partial conversion of **1h** indicates that for electron-deficient double bonds enone formation is favored, but oxidation of the epoxy alcohol **2h** competes. Treatment of **1h** with excess oxidant allowed complete conversion, the epoxy ketone ester **4** was isolated in 37 % yield; however, the major product was undefined material, presumably derived from the enone ester **3h**. Again the pronounced preference of alcohol oxidation in the first step becomes apparent.

Protection of the hydroxyl group in form of its acetate **1i** completely prevents ketone formation (Eq. 3); thus, the epoxy acetate **2i** was isolated in high yield. Furthermore, the primary allylic alcohol functionality in *geraniol* resisted C-H oxidation, since the 6,7-epoxide was the major product, besides smaller amounts of the 2,3-epoxide and the *bis*-epoxide.[10] Finally, oxidation of alcohol **1j** proceeded cleanly and quantitatively to ketone **3j** (Eq. 4) and no products derived from cyclopropane ring-opening were observed. This mechanistically significant result excludes radicals as intermediates in the C-H insertion during oxidation of the alcohols to



1j **3j** (4)

ketones by dimethyldioxirane, in agreement with theoretical investigations.[7]

In conclusion, it has been shown that the oxidation of secondary allylic alcohols to ketones by dimethyldioxirane can efficiently compete with olefin epoxidation. Nevertheless, the chemoselectivity of this oxidant can be promoted towards epoxide formation by alcohol protection or by employing higher reaction temperatures.

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References and Notes

1. (a) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205-211. (b) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187-1201. (c) Curci, R. in *Advances in Oxygenated Processes;* Baumstark, A. L., Ed.; JAI: Greenwich, CT, 1990; Vol 2, Chapter I. (d) Adam, W.; Hadjiarapoglou, L. P.; Curci, R.; Mello, R. in *Organic Peroxides;* Ando, W., Ed.; Wiley, New York, 1992; Chapter 4, pp 195-219. (e) Adam, W.; Hadjiarapoglou, L. *Top. Curr. Chem.* **1993**, *164*, 45-62.
2. (a) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847-2853. (b) Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377.
3. (a) Mello, R.; Cassidei, L.; Fiorentino, M.; Fusco, C.; Hümmer, W.; Jäger, V.; Curci, R. *J. Am. Chem. Soc.* **1991**, *113*, 2205-2208. (b) Curci, R.; D' Accolti, L.; Detomaso, A.; Fusco, C.; Takeuchi, K.; Ohga, Y.; Eaton, P. E.; Yip, Y. C. *Tetrahedron Lett.* **1993**, *28*, 4559-4562. (c) D' Accolti, L.; Detomaso, A.; Fusco, C.; Rosa, A.; Curci, R. *J. Org. Chem.* **1993**, *58*, 3600-3601.
4. Cicala, G.; Curci, R.;Fiorentino, M.; Laricchiuta, O. *J. Org. Chem.* **1982**, *47*, 2670-2673.
5. Abou El-Zahab, M.; Adam, W.;Saha-Möller, C. R. *Liebigs Ann. Chem.* **1991**, 445-450.
6. Murray, R. W.; Shiang, D. L. *J. Chem. Soc., Perkin Trans. 2*, **1990**, 349-352.
7. Bach, R. D.; Andrés, J. L.; Su, M.-D.; McDouall, J. J. W. *J. Am. Chem. Soc.* **1993**, *115*, 5768-5775.
8. The diastereomers of **2** were assigned on the basis of NMR shift data[11] and by comparison with authentic samples.
9. The previously unknown compounds **4** and **2i** gave satisfactory analytical data; all other substances reported herein are literature known. *threo*-**2i**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.19 - 1.32 (m, 6 H), 2.01 (s, 3 H), 2.91 (d, J = 5.95 Hz, 1 H), 3.03 (d, J = 5.95 Hz, 1 H), 4.19 (q, J = 7.19 Hz, 2 H), 5.52 (q, J = 6.53 Hz, 1 H).- ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.9 (q), 15.8 (q), 20.8 (q), 49.9 (t), 57.3 (s), 61.9 (t), 66.9 (d), 168.2 (s), 169.7 (s).- *erythro*-**2i**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20 - 1.32 (m, 6 H), 2.00 (s, 3 H), 2.85 (d, J = 5.7 Hz, 1 H), 3.98 (d, J = 5.7 Hz, 1 H), 4.20 (q, J = 7.2 Hz, 2 H), 5.52 (q, J = 6.5 Hz, 1 H).- ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.9 (q), 14.8 (q), 20.7 (q), 49.0 (t), 58.1 (s), 61.7 (t), 67.1 (d), 168.2 (s), 169.7 (s).- **4**: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (t, J = 7.1 Hz, 3 H), 2.28 (s, 3 H), 3.11 (d, J = 5.9 Hz, 1 H), 3.32 (d, J = 5.9 Hz, 1 H), 4.30 (q, J = 7.1 Hz, 2 H).- ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.9 (q), 26.0 (q), 50.9 (t), 59.8 (s), 62.5 (t), 164.9 (s), 203.0 (s).-
10. The oxidation of geraniol by 1.0 equiv. of dimethyldioxirane at 0 °C resulted in 72 % of 6,7-epoxide, 23 % of the 2,3-epoxide, and 5 % of the bis-epoxide.
11. (a) Mihelich, E. D. *Tetrahedron Lett.* **1979**, 4729-4732. (b) Adam, W.; Braun, M.; Griesbeck, A.; Lucchini, V.; Staab, E.; Will, B. *J. Am. Chem. Soc.* **1989**, *111*, 203-212.

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