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A Hydrogen-bonded Model for the *Syn* Epoxidation of Cyclic Allylic Ethers under Payne Conditions

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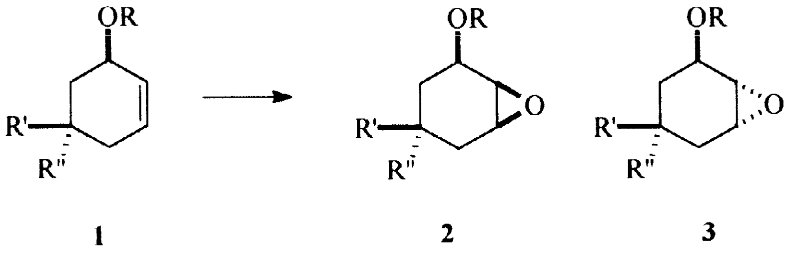
Abstract: The *syn* selectivity observed for the Payne (PhCN/H_2O_2) epoxidation of cyclohexenyl ethers is consistent with an hydrogen-bonded model implying the allylic ether oxygen and the imino hydrogen of the *in situ* generated perbenzimidic acid. The geometry of the two most stable conformers, deduced from AM1 calculations, allows both hydrogen bonding and oxygen transfer.

Many reagents (and conditions) have been introduced to carry out regio- and diastereoselective epoxidations. Among them, peracids (*m*CPBA, monoperphthalic acid,...) are the most widely used.[1] The structurally related perbenzimidic acid [Ph-C(=NH)OOH], generated *in situ* from PhCN and H_2O_2 has been much less studied in spite of non-acidic conditions ($KHCO_3$ or K_2CO_3, MeOH) and chemoselectivity (Payne reaction).[2] An interesting aspect is the variation of diastereoselectivity usually observed between these reagents for unsaturated carbohydrates or other oxygen substituted derivatives.[3] To our knowledge no model has been put forward to explain the observed selectivity in the Payne epoxidation.[4] Therefore a study of the epoxidation of cyclohexenol derivatives **1a-d**, **4a-b** (pseudo-equatorial OR) and **7a-c** (pseudo-axial OR) with perbenzimidic acid has been carried out in order to compare these data with those already published by Ganem[5] using *m*CPBA and trifluoroperacetic acid (TFPA).



R'= R''= H	**1**	**2**	**3**
R'= *t*Bu, R''= H	**4**	**5**	**6**
R'= H, R''= *t*Bu	**7**	**8**	**9**

a: R= H; **b**: R= TBDMS; **c**: R= Bn; **d**: R=Ac; **e**: R= O*t*Bu

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Reactions with *m*CPBA were repeated to correlate our results with the reported diastereoselectivities[5,6] and also to use the same analytical method for each mixture of epoxides (^{1}H NMR for entries 1 and 5-9 or capillary GLC for entries 2-4). Results reported in Table 1 are for reactions carried out under standard procedures.[7]

Table 1. Epoxidation of **1a-d**, **4a,b** and **7a-c** with *m*CPBA and PhCN/H_2O_2 (this work) and TFPA (ref 5).

Entry	Substrate	Products	Isolated Yield (%)		*Syn/anti* ratio		
			*m*CPBA	Payne	*m*CPBA[c]	Payne	TFPA (ref 5)
1	**1a**	**2a/3a**	71	65	21/1	24/1[g]	50/1
2	**1b**	**2b/3b**	74	56	1/5.2[d]	3.7/1	4.5/1
3	**1c**	**2c/3c**	95	83	1/2.2	8/1	1.4/1
4	**1d**	**2d/3d**	78	22[a]	1/1.3[e]	7/1	1/1.1
5	**4a**	**5a/6a**	69	56	17/1	12/1	100/1
6	**4b**	**5b/6b**	80	59	1/3.6	5/1	1/5.5
7	**7a**	**8a/9a**	49	57	5.3/1	12/1	100/1
8	**7b**	**8b/9b**	68	47[b]	1/4.3	1/1	12.4/1
9	**7c**	**8c/9c**	87	57[b]	1/3	4/1	5/1
10[f]	**1e**	**2e/3e**	90	94	1/3.5	1/1.3	/

[a] Acetate hydrolysis is also observed. [b] yield based on starting material consumption (conversion *c.a.* 70 %). [c] *Syn/anti* ratios similar in ref 5. [d] Ratio 1/4.5 in ref 8. [e] *id.* in ref 9. [f] Ref 10. [g] Ratio 4.5/1 in ref 7.

Except for acetate **1d** and the less reactive ethers **7b,c** the Payne reaction affords a moderate to good yield of epoxides with a *syn* selectivity (except for **7b**). It is interesting to note that the *syn/anti* ratio is higher for benzyl ethers than for TBDMS ethers (entries 3 *vs* 2, 9 *vs* 8) and for pseudoequatorial ethers than for pseudoaxial ones (entries 6 *vs* 8). However, the observed selectivities are different from those of the TFPA reactions which mainly occur *syn* with pseudoaxial ethers (selectivity: TBDMS > Bn) and *anti* with pseudoequatorial ones.

These results may be explained by a hydrogen-bonded transition structure. This hypothesis is consistent with the unselective Payne epoxidation[10] of the allylic peroxide **1e** (entry 10) whose oxygen atoms are less negatively charged. In order to rationalize these results, we may first consider the well-known *syn* epoxidation of cyclic allylic alcohols which occurs through hydrogen bonding of an oxygen of the peracid with the hydroxyl group.[11] In the case of allylic ethers and esters no such interaction is available with common peracids and *anti* epoxidation is mainly observed. However, in the TFPA case, the peroxide hydrogen is more acidic than for *m*CPBA and hydrogen-bonded model **A** has been proposed by Ganem.[5] This "butterfly" arrangement is more favorable for pseudoaxial ethers (see Table 1).

In order to search for possible interactions of perbenzimidic acid, a conformational analysis was carried out at the AM1 level (AMPAC).[12] The most stable conformers are **C_1** (ΔH_f= 25.03 kcal/mol, E_{rel}= 0) and **C_2** (ΔH_f= 25.22 kcal/mol, E_{rel}= + 0.19) which correspond to a *quasi* planar O-O-C=N-H substructure (*syn* imine) with the remaining hydrogen located out of this plane with a H-O-O-C torsion angle of *c.a.* 103° (Figure 1). These conformers only differ by the up or down twisting (**C_1**: 25°; **C_2**: -29°) of the phenyl ring. The next conformer **C_3** (ΔH_f= 27.49 kcal/mol, E_{rel}= +2.45) corresponds to an *anti* imine structure with an internal hydrogen bond between the nitrogen and the hydroxyl group (as in peracids).

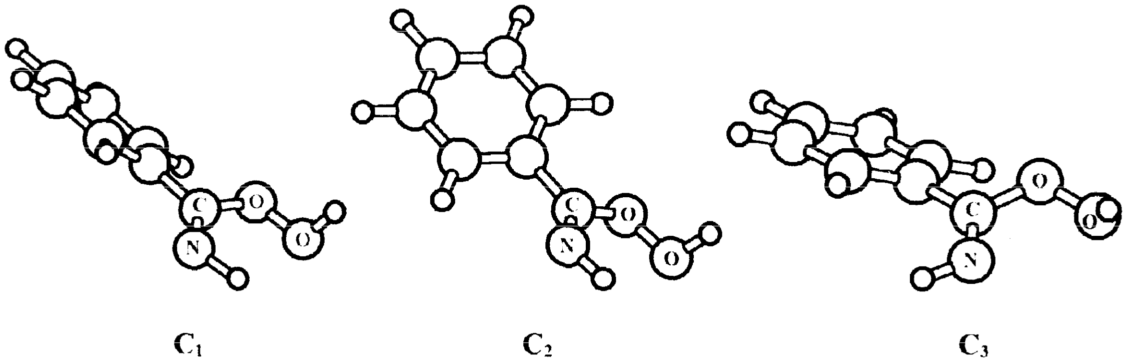

Figure 1. Representation of the three most stable conformers of perbenzimidic acid.

To explain our results, we assume that the epoxidation results from a peracid-like approach, i.e. with a perpendicular location of the H-O-O and the C=C bond planes (spiro arrangement) in agreement with Houk recent high level density functional calculations for peracid epoxidation.[13] Thus, taking into account conformers **C_1/C_2**, we propose the transition state model **B** for epoxidation of allylic ethers. This allows the formation of an hydrogen bond between the imino hydrogen and the ether oxygen (Figure 2). Undoubtedly, such a model is more sensitive to steric hindrance than the peracid transition state and this may explain the higher *syn* selectivity for pseudo-equatorial ethers (the *syn* epoxidation of pseudoaxial ethers is more sterically hindered) and for benzyl ethers compared to bulky TBDMS ones (although the latter oxygen is more negatively charged).

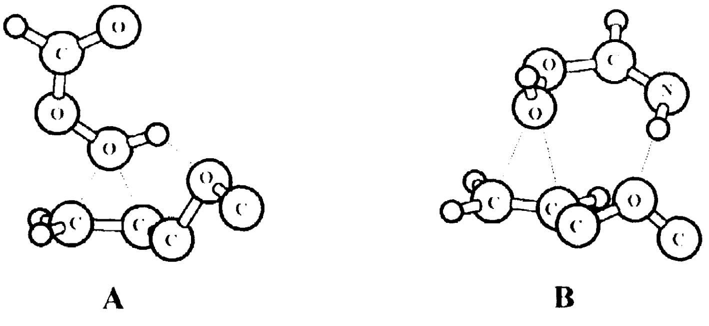

Figure 2. Proposed transition structures for epoxidation of allylic ethers by TFPA (**A**, Ganem[5]) and under Payne conditions (**B**). For clarity, HCOOOH and HC(=NH)OOH are shown here and hydrogens have been omitted for the C-O-C moiety.

In conclusion, the proposed model appears to be consistent with the selectivity observed in the Payne epoxidation. Since this reaction is conducted in MeOH, further hydrogen bonding of the perbenzimidic acid nitrogen and hydroxyl by MeOH may also be considered in such a transition structure. Other experiments and higher level calculations are underway in order to probe this model.

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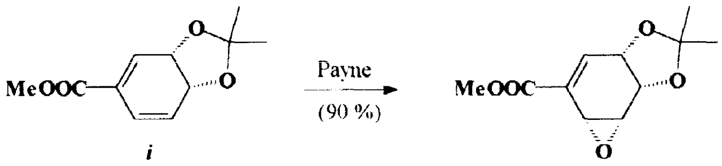
4. A doubly hydrogen-bonded model between perbenzimidic acid and both the ester (with NH) and allylic ether (with OH) has been proposed by Sainsbury[3c] to explain the preferred *syn* epoxidation of ***i***. Such a model, close to the **C_3** conformer, does not allow an appropriate location of the transferred oxygen.



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