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Diastereoselective Peracid Epoxidation: Control of the Face Selectivity via Functional Group Tuning and Proper Choice of Epoxidation Reagent

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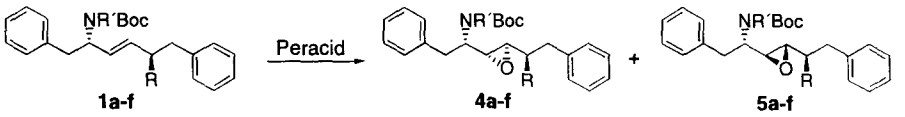
Abstract: Peracid epoxidation of **1a-f** with 3-chloroperbenzoic acid (*m*-CPBA) and trifluoroperacetic acid (CF_3CO_3H) show different stereoselectivities. The olefins are substituted with two directing groups which are expected to direct the peracid to opposite faces of the alkene. Optimal face selectivities could be achieved by the proper choice of directing groups and epoxidation reagent.

We report here on peracid epoxidation reactions of olefins **1a-f**, in which two groups direct the attack of the peracid to opposite faces of the alkene. Two peracids, *m*-CPBA and CF_3CO_3H,[1] were used and remarkable differences in stereoselectivities were observed. The results are summarized in Table I. The stereoselectivity is suggested to emanate from different modes of coordination of the allylic functionalities to the peracid in the transition state.

Table I. *Threo/erythro* Ratios in Epoxidation of Allylic Carbamates 1a-f with *m*-CPBA and CF_3CO_3H



1a-f **4a-f** **5a-f**

		m-CPBA[a]			CF_3CO_3H[b]		
substrate	R and R´	*threo/erythro* ratio[c]	yield (%)	time (h)	*threo/erythro* ratio[c]	yield (%)	time (h)
1a	R= CH_2OH; R´=H	60:40	89	6	48:52	63	0.5
1b	R= CH_2OAc; R´=H	68:32	84	45	36:64	71	0.5
1c	R=COOMe; R´=H	62:38	80	44	37:63	75	0.5
1d	R=CH_2OCOCF_3; R´=H	71:29	64[d]	48	27:73	72[d]	0.5
1e	R=CH_2OTBS; R´=H	81:19	93	48	76:24	93	0.5
1f	R= CH_2OCOCF_3; R´=$COCF_3$	*e*	*e*	*e*	81:19	70[d]	15

[a]*m*-CPBA epoxidations were run in CH_2Cl_2 at room temperature; *see* Refs 2a,b. [b]Epoxidations with CF_3CO_3H were run in buffered CH_2Cl_2 at 0°C; *see* Ref 1. [c]The relative ratio of epoxide isomers has been determined by HPLC and NMR spectroscopy on the crude reaction product. [d]Isolated yields after deprotection to **1a**. [e]After 3 days only a small amount of product had formed together with some byproducts; *see* Refs 2c and 5.

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Treatment of **1a**[2a,b] with trifluoroacetic anhydride and pyridine in THF gave 89% of **1d**. Using excess trifluoroacetic anhydride and triethylamine as a base in CH_2Cl_2 gave **1f** in 93% yield. Silylation of **1a** with TBS-Cl gave **1e** in 95% yield.[3] The configurational assignments of epoxides **4a-c** and **5a-c** have been performed by X-ray crystallography and chemical correlation as described previously.[2a,b] Epoxides **4d-f** and **5d-f** were never isolated but converted to the known alcohol epoxides **4a** and **5a**.[2a,b]

In epoxidations of **1a-f** with *m*-CPBA the *threo* isomer of epoxides dominates, the highest ratio (81:19) obtained for **1e** (R=CH_2OTBS). In contrast, when CF_3CO_3H is used, there is a preference for formation of the *erythro* isomer for **1b** (R=CH_2OAc), **1c** (R=COOMe), and **1d** (R=CH_2OCOCF_3). With **1a** (R=CH_2OH) a 1:1 ratio of isomers is formed and with **1e** (R=CH_2OTBS) and **1f** (R=CH_2OCOCF_3, R´= $COCF_3$) the *threo* isomer is the major product. These results show that CF_3CO_3H has a different preference of coordination to various functional groups compared to *m*-CPBA.[4]

The strong *threo*-selectivity in the *m*-CPBA mediated epoxidations indicates that the peracid coordinates strongest to the allylic carbamate group. The differences in stereoselectivity indicate that *m*-CPBA coordinates stronger to the alcohol, methyl ester and acetate functions than to the trifluoroacetate group, and probably not at all to the TBS-ether. Using the same mode of analyses, CF_3CO_3H appears to coordinate strongest to the trifluoroacetate function, slightly weaker to the acetate and methyl ester groups, and even weaker to the alcohol and carbamate functions. It probably does not coordinate to the TBS-ether. Interestingly, in **1f** it seems as if the directing effect of the carbamate group outweighs that of the trifluoroacetate function. However, the result can instead be due to steric effects outweighing directing effects.

The mode of hydrogen bonding between the peracid and the coordinating group can influence the stereoselectivity in the peracid epoxidations. For allylic carbamates the face selectivity is probably due to hydrogen bonding from NH to O-3 in the peracid. However, the peracid can also donate a hydrogen bond to the carbonyl oxygen of the carbamate group.[2c] Such reverse hydrogen bonding could explain the directing effects of the acetate, methyl ester, and trifluoroacetate functions in the present study. The higher acidity of CF_3CO_3H should make it more prone to coordinate to different functional groups through hydrogen bond donation than *m*-CPBA. The inability of the TBS-ether to direct the incoming peracid is probably due to the low basicity of the oxygen[6] or to steric hindrance preventing optimal hydrogen bond formation.

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