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Diastereoselective Epoxidation of Olefins by Organo Sulfonic Peracids, II.[1]

R. Kluge, M. Schulz* and S. Liebsch[2]

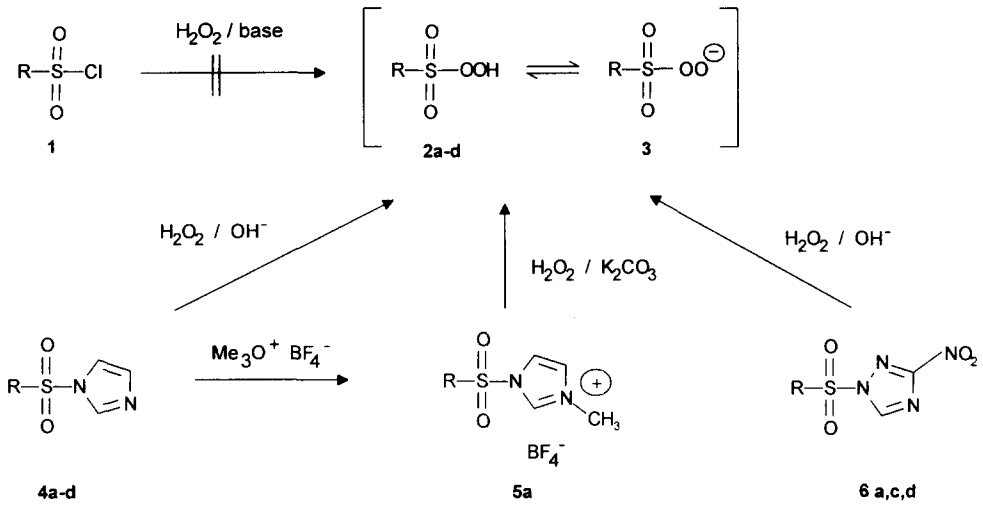
Martin-Luther-Universität Halle-Wittenberg, Institut für Organische Chemie, Geusaer Straße, D-06217 Merseburg, Germany

Abstract: We have investigated the behaviour of sulfonic peracids **2** *in situ* generated towards olefins **7a,7b,9,11,14,16,18**, allylic and homoallylic alcohols **20,22,24,26,28,30,33** and α,β-unsaturated ketones **35,37,39**. Generally, the epoxidation proceeds in a peracid-like manner with greater diastereoselectivity than those by common oxidants. In particular, the epoxidation of Δ^4 3-ketosteroids **39a-i** led to 4α,5α-epoxides **40a-i** with remarkable high de-values. Enhanced α-selectivity was also found in the epoxidation of cholesterol **28b**. Due to the mild reaction conditions, even acid sensitive epoxides **8a,8b,10,12,13,15,17,19** were obtained in good yields.

Until now the application of arene or hetarene sulfonic peracids has been almost a grey area in the field of organic oxidation chemistry. These peracids are not available by the reaction of sulfonyl chlorides **1** with hydrogen peroxide.[3] Furthermore, mixtures of perfluoroalkylsulfonic acids (or sulfonic anhydrides) with anhydrous H_2O_2 which are supposed to form sulfonic peracids[4] could not be widely used for oxidations because of the strong acidic media.

The reaction of sulfonyl chlorides with KO_2, reported by Kim and coworkers[5] led to sulfonyl peroxy radicals, and not to the anions of the corresponding sulfonic peracids, as was first proposed. This was proven both by trapping the intermediate radicals as well as by the nonstereospecific epoxidation of *cis*- and *trans*-olefins. In a previous paper, we described new strong oxidants, probably the sulfonic peracids **2**, formed by the reaction of hydrogen peroxide with corresponding sulfonyl imidazolides **4** under alkaline conditions.[1] We investigated their oxidizing ability by examinating the epoxidation of different types of olefins.

The present publication deals with the application of the sulfonic peracids **2** in particular for the preparation of acid sensitive epoxides and for the epoxidation of allylic and homoallylic alcohols, as well as for the epoxidation of α,β-unsaturated ketones with low reactivity. The oxidants **2** were generated from corresponding sulfonyl imidazolides **4**, sulfonyl N-methylimidazolium salts **5** (easily prepared by methylation of **4** with Me_3O^+ BF_4^-)[6] or from 1-sulfonyl-5-nitro-1,2,4-triazoles **6** with H_2O_2 in the presence of a base (NaOH or K_2CO_3). Special attention was also paid to the stereochemical course of the oxidations by comparing the oxidants with typical epoxidation agents in order to obtain more evidence for the postulated structure **2**.



a : R = 4-$CH_3C_6H_4$
b : R = 1-Imidazolyl
c : R = 2,4,6-$(CH_3)_3C_6H_2$
d : R = 2,4,6-$(i\text{-}Pr)_3C_6H_2$

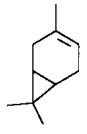
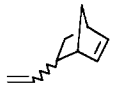
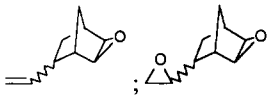
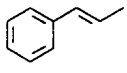
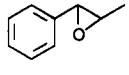
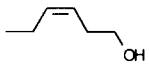
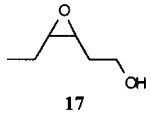
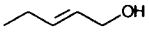
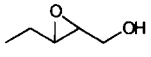
Scheme 1

Epoxidation of Olefins

In general the epoxidation reactions with **4a-d** were performed in MeOH or ^{t}BuOH at 5 - 10 °C by the slow addition of aqueous NaOH to the mixture of the corresponding olefin, sulfonyl imidazolides **4a-d** and excess H_2O_2. The pH range during the reaction was 7 - 8.5 reaching pH 9 as maximum at the end of the reaction when **4** was almost completely consumed. Epoxidations with **5a** were carried out at 0-5°C in CH_3CN/CH_2Cl_2 using H_2O_2 and solid K_2CO_3 as base under PTC-conditions (10 Mol-% $Bu_4N^+HSO_4^-$). **6a,c,d** were allowed to react with H_2O_2/NaOH in an analogous manner to **4a-d** in THF at -5°C with a slightly decreased pH of 5-6 at the beginning of the reaction due to the more acidic character of the liberated nitrotriazole and reached a pH of 8 on complete consumption of **6a,c,d**.

The results obtained in the epoxidation of terpenes and other olefins are summarized in table 1.

Table 1: Epoxidation of Olefins by *p*-Toluenesulfonic Peracid **2a** Generated *in situ*

Entry	Olefin	Product(s) [a]	Method[b]	Conversion [%][c]	Yield [%][d]	de [%] [e]
1	 **7a**	 **8a**	A (**4a**)	95 [f]	79	> 99 [g]
2	 **7b**	 **8b**	A (**4a**)	90 [f]	47	> 99 [g]
3	 **9**	 **10**	A (**4a**)	62	90	> 99 [g]
4	 **11**	 **12** **13**	A (**4a**)	80	36 ; 14	
5	 **14**	 **15**	A (**4a**)	90	66	> 99 [g]
6	**14**	**15**	B (**5a**)	> 95	82	> 99 [g]
7	**14**	**15**	Ts_2O /H_2O_2 / K_2CO_3	76	22	> 99 [g]
8	 **16**	 **17**	A (**4a**)	1 00	93	> 99 [g]
9	 **18**	 **19**	A (**4a**)	100	85	> 99 [g]

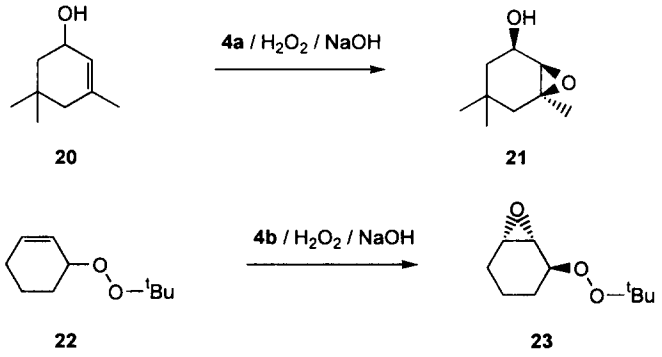
a) Main diastereomer shown. b) For details see experimental part. c) Conversion with reference to recovered starting material. d) With reference to conversion, isolated yield of the main diastereomer. e) Analysis of the crude product. f) Determined by GLC. g) Other diastereomer was not detected.

In common with the results obtained using other peracids,[7] the epoxidation of α-pinene (**7a**), β-pinene (**7b**) and 3-carene (**9**) described here occurred exclusively *anti* to the dimethyl substituted bridge, and the corresponding epoxides were isolated in good yields. Epoxidation of 5-vinyl-norbornene (**11**) (*exo/endo*-mixture) led to a mixture of the monoepoxide **12** (main product) and bisepoxide **13**. In both compounds the *exo*-position of the epoxide group was determined by ^{1}H NMR. Other peracid oxidations of norbornene derivatives gave mainly *exo*-isomers in accord with this result.[8]

In contrast to the non stereoselective oxidations obtained using Kim's oxidant RSO_2Cl / KO_2[5] (a result of the radical character of the epoxidizing sulfur intermediate), the epoxidation of *cis*- or *trans*-olefins with the *in situ* generated oxidants **2** occurred with complete retention of the stereochemistry (entries 5-9). In a similar process to the *in situ* generation of hydroperoxyphosphonic acids from phosphinic anhydrides,[9] tosyl anhydride (Ts_2O) was used for the generation of **2a**, but only a poor yield of epoxide was obtained together with some polar byproducts (entry 7).

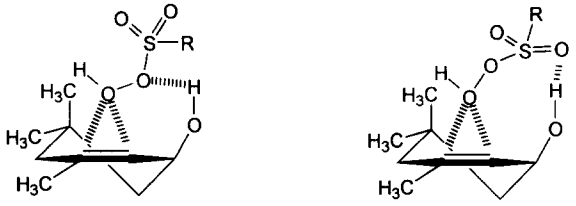
Epoxidation of Allylic and Homoallylic Alcohols

The epoxidation of various allylic and homoallylic alcohols including steroids with different types of oxidants ($VOacac_2$ / ^{t}BuOOH, $TiOR_4$ / ^{t}BuOOH, peracids, imidoperacids) is well documented.[10-12] In the case of peracids as epoxidation agents, a predominant attack *syn* to the OH-group was observed which is due to an association between the peracid and the OH group. Even higher *syn*-selectivity was found for the $VOacac_2$ / ^{t}BuOOH system where a vanadyl ester is the key intermediate in the oxidation step. The limiting factor for the *syn*-selectivity observed for both types of oxidants is sterical hindrance within the substrate molecule. This may result in lower *syn*-selectivity or even in the predominant formation of the *anti*-product in the case of peracids, while the oxidation of sterical hindered allylic alcohols by $VOacac_2$ / ^{t}BuOOH leads to the corresponding α,β-unsaturated ketones as main or byproducts.[12]



Scheme 2

Different cyclic allylic and homoallylic alcohols were oxidized with the mixture of the sulfonyl azolides **4-6** / H_2O_2 / base and the results compared with those obtained with other common oxidants. The epoxidation of isophorol (**20**) with **4a** or **4b** / H_2O_2 gave the corresponding epoxy alcohol **21** in good yield (76%)(scheme 2). The observed diastereoselectivity (de >> 95%) with **2a** and **2b** *in situ* generated is higher than that reported for the epoxidation of **20** using *p*-nitroperbenzoic acid (de 92%)[13] and similar to the de-value obtained in $VOacac_2$ / ^tBuOOH epoxidation (de ≈ 99%) and that of the recently reported epoxidation using hydroperoxyphosphonic acids *in situ* generated.[9] (For dioxirane epoxidation see ref. 14.) This points unambiguously to a strongly preferred *syn*-attack of the sulfonic peracid due to the intermediate association of the oxidant **2** and the substrate in the transition state as shown in scheme 3.



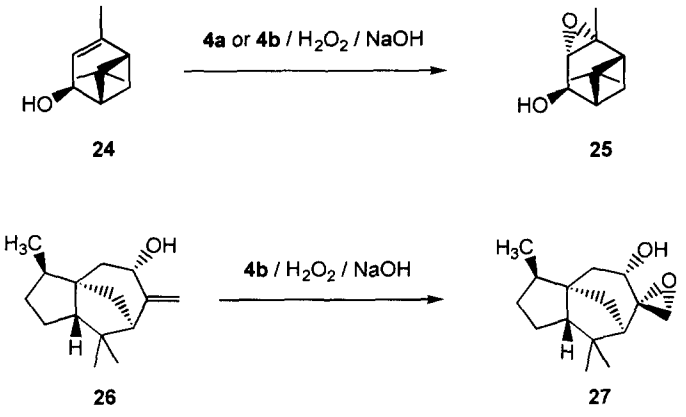
Possible transition states for the *syn* selective epoxidation by the sulfonic peracid **2**

Scheme 3

In contrast to this our recent studies[15] concerning the epoxidation of different cyclic allylic peroxides with various oxidants have shown that the *tert*-butylperoxy group exhibits an *anti* directing effect similar to the known *anti*-directing effect shown by acetate or ether functions.[16] Again, a significantly higher diastereoselectivity was observed with **2b** *in situ* generated(de 91 %) in comparison with mCPBA (de 56 %) or PhCN / H_2O_2 / HO^- (de 13 %). One example, the conversion of **22** into **23** (major diastereomer), is given in scheme 2.

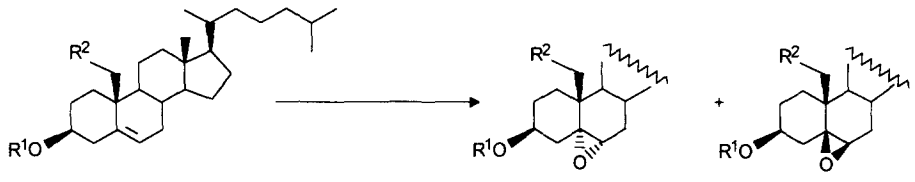
The epoxidation of *cis*-verbenol (**24**) is difficult to achieve with common oxidants because of the high sensitivity of **24** and its epoxide to acidic medium and also because of the steric hindrance within the molecule. Thus, attempts to epoxidize **24** with mCPBA resulted only in "mixtures of polar compounds" whilst the $VOacac_2$ catalyzed oxidation with ^tBuOOH led to the formation of the corresponding α,β-unsaturated ketone verbenone.[12b] By employing **2a** or **2b** *in situ* generated we were able to epoxidize **24**. The epoxide **25** was obtained as the sole product in moderate yield (conv. 60 % ; yield 75 %) and epoxidation occurred exclusively *anti* to the dimethyl substituted bridge as previously observed for α-pinene (**7a**). The epoxidation of the similar acid sensitive (+)-8(15)-cedren-9-ol (**26**) with either **4a** or **4b** / H_2O_2 / HO^- gave the corresponding epoxide **27** in high yield (conv. 93 % ; yield 89 %) . **27** was obtained as a single diastereoisomer and is formed by exclusive *syn*-attack with respect to the OH group of the intermediate oxidants **2a,b**. This was proven by ^1H

NMR spectroscopy (H,H-NOESY experiments) of **27**. To our knowledge this compound has not been described in the literature until now.



Scheme 4

The epoxidation of 19-hydroxycholesterol (**28a**) using **2a** generated *in situ* proceeds with very high diastereoselectivity yielding only the 19-hydroxy-5β,6β-epoxycholesterol (**29a**) comparable to epoxidations of 19-hydroxycholesteryl derivatives by $VOacac_2$ / ^tBuOOH or by peroxy acids (scheme 5). Presumably, the OH group at the C-19 atom controls the direction of the epoxidation by an analogous association as discussed above (scheme 3).



a : R^1 = H, R^2 = OH
b : R^1, R^2 = H
c : R^1 = CH_3CO, R^2 = H

Scheme 5

In contrast to the foregoing, the equatorial OH group in cholesterol (**28b**) should have no directing influence on the diastereomeric course of the epoxidation due to the fixed skeleton. Indeed, using the same oxidation system (as shown for the reaction of **28a**) the α-epoxide **29b** is formed as the major product (table 2, entry 2) and almost the same α:β-selectivity is found for the epoxidation of cholesteryl acetate (**28c**) (entry 7). In agreement

with other authors [11,12] we deduce that the axial 10-CH_3 group of **28b** must hinder the β-attack of the persulfonic acid and an association between **2** and the equatorial 3β-OH group cannot play any significant role.

Compared to other oxidants, the sulfonic peracids show significant differences in the diastereoselectivity. The reaction of **28b** with peroxy acids gives also mainly the α-epoxide but with lower diastereoselectivity (mCPBA: α : β ~ 1,5 : 1[17] ; perlauric acid: α : β ~ 3:1[18]). The β-epoxide is the major product employing the $Feacac_3$ / H_2O_2 - system [19] (α : β = 1: 4) whilst oxidation with dioxiranes appears to be nondiastereoselective (α : β = 2 : 3) in the case of 3β-acetoxy-5,16-pregnadien-20-acetate.[20]

We employed the four different methods to generate the persulfonic acid **2a**, but could observe no significant effect on the α:β-selectivity (starting from **4a**, **5a**, **6a** or toluenesulfonic anhydride Ts_2O). Only conversions and yields were influenced by the method of generation (entries 1-4). By contrast, variation of the number and the bulkiness of the substituents in the aromatic part of **2** led to remarkable changes in the observed diastereoselectivities as illustrated in entries 4-6.

Table 2: Epoxidation of **28b,c** with Sulfonic Peracids **2a,c,d** Generated *in situ*

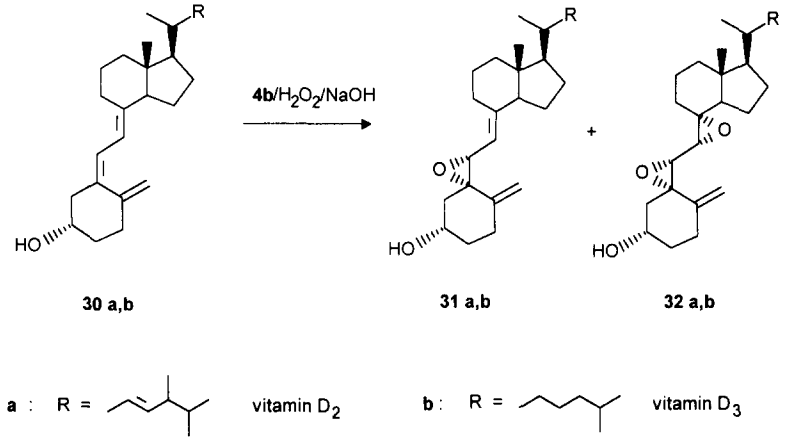
Entry	Starting material	Oxidant	Product	Conv. [%][a)]	Yield [%][b)]	Isomer ratio [c)] α : β
1	**28b**	**4a**/H_2O_2/HO^-	**29b**	46[d)]	70	4 : 1
2	**28b**	**5a**/H_2O_2/K_2CO_3	**29b**	100	93	5.2 : 1
3	**28b**	Ts_2O/H_2O_2/K_2CO_3	**29b**	45	44[e)]	4.8 : 1
4	**28b**	**6a**/H_2O_2/HO^-	**29b**	100	90	4.8 : 1
5	**28b**	**6c**/H_2O_2/HO^-	**29b**	100	95 (80)[f)]	11 : 1
6	**28b**	**6d**/H_2O_2/HO^-	**29b**	100	90	3.5 : 1
7	**28c**	**5a**/H_2O_2/HO^-	**29c**	100	89	5.1 : 1

a) Conversion refers to recovered starting material. b) Isolated yield of the diastereomeric mixture (α/β–epoxides) based on conversion. c) Determined by ^1H NMR analysis of the crude reaction product. d) Low conversion caused by the low solubility of **28b** in MeOH. e) Accompanied by the formation of polar byproducts. f) Isolated yield of pure 5α,6α-**29b**.

The application of the *o,o'*-CH_3-substituted compound **6c** (entry 5) led to a dramatic improvement of the α-selectivity (α:β = 11 : 1). We believe that an enhanced steric interaction between the *o,o'*-CH_3-substituents of **2c** and the axial arranged 10-CH_3 group of **28b** (β-side) causes a preferred attack of **2c** from the less hindered α-side. When more bulky *o,o'*-substituents are introduced into the aromatic ring of **2**, i.e. isopropyl groups (**6d**, entry 6) the α-selectivity drops to an unexpected extent. A possible reason may be an additional steric repulsion

between the axial H-atoms of the A- and B ring (α-side) of the steroidal skeleton of **28b** and the bulky isopropylgroups, thus α-side attack is less dominant than with **2c**.

Remarkable differences were observed between the epoxidations of **30a,b** (vitamins D_2 and D_3) using the sulfonic peracids **2** and their epoxidations using perbenzoic acids. While the extremely acid sensitive vitamin D_2 (**30a**) can only be oxidized by peroxy acids when the OH-group is protected (otherwise mixtures of polar oxidation products are obtained)[21], **30b** gave the corresponding 7,8-epoxide using mCPBA with high regio- and diastereoselectivity.[22] By contrast, oxidation of **30a,b** with **2b** generated *in situ* yielded mixtures of the 5,6-epoxides **31a,b** and the bisepoxides **32a,b**, depending on the reaction conditions (only the *syn*-products, with respect to the OH-group, were obtained; scheme 6).

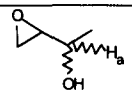
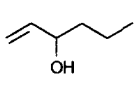
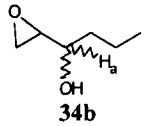
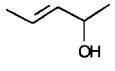
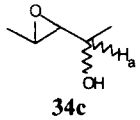


Scheme 6

In the epoxidation of the vitamin D_2 (**30a**) the sulfonic peracid **2b** showed an analogous behaviour to imidoperbenzoic acid [21] leading to the same products **31a** and **32a**, depending on the amount of oxidant used.

Epoxidations of aliphatic allylic alcohols with the oxidants **2** were carried out with 3-buten-2-ol (**33a**), 1-hexen-3-ol (**33b**) and *trans*-3-penten-2-ol (**33c**) respectively, yielding the corresponding epoxy alcohols **34a-c** as diastereomeric mixtures of the *threo*- and *erythro*-isomers. The results listed in table 3 demonstrate the peracid-like formation of the *threo*-isomer as the major product. The observed *threo : erythro* selectivities are similar to those observed with mCPBA, whilst $VOacac_2$ catalyzed epoxidation leads mainly to the *erythro*-products.[23,24] An obvious explanation for this contrary behaviour has been postulated by Sharpless[24] who has discussed the different C=C-C-O dihedral angles in the oxygen transfer step. Not surprisingly, no significant effects on the *erythro : threo* - selectivity were found when different substituted sulfonic peracids **2** were employed.

Table 3: *erythro / threo* - Selectivity in the Epoxidation of Acyclic Allylic Alcohols

Entry	Starting material	Product	Oxidant	Isomer ratio [a] *erythro* : *threo*
1	 **33a**	 **34a**	**4a** / H_2O_2 / NaOH	40 : 60
2	**33a**	**34a**	**4b** / H_2O_2 / NaOH	38 : 62
3	**33a**	**34a**	mCPBA [b]	40 : 60
4	**33a**	**34a**	$VOacac_2$ / ^tBuOOH [b]	80 : 20
5	 **33b**	 **34b**	**4a** / H_2O_2 / NaOH	37 : 63
6	**33b**	**34b**	**4b** / H_2O_2 / NaOH	38 : 62
7	**33b**	**34b**	**4c** / H_2O_2 / NaOH	36 : 64
8	**33b**	**34b**	**6d** / H_2O_2 / NaOH	42 : 58
9	 **33c**	 **34c**	**4a** / H_2O_2 / NaOH	33 : 67
10	**33c**	**34c**	**4b** / H_2O_2 / NaOH	30 : 70
11	**33c**	**34c**	mCPBA [b]	36 : 64
12	**33c**	**34c**	$VOacac_2$ / ^tBuOOH [b]	71 : 29

a) Determined by ^1H NMR analysis of the crude product (integration of the signals of the H_a protons). b) Taken from ref. 24.

Epoxidation of α, β-Unsaturated Ketones

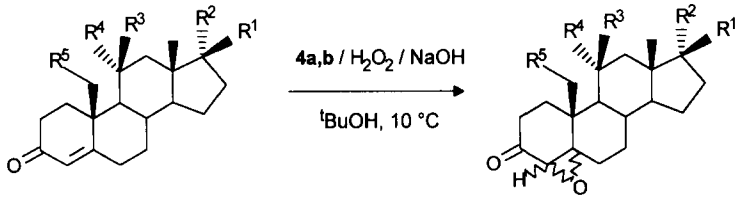
In our previous paper[1] we reported the oxidation of carvone with the new oxidant **2** and obtained epoxides both at the *exo*- and *endo*cyclic double bond. This result indicated that the more reactive sulfonic peracids may be able to oxidize α,β-unsaturated ketones too. This is shown here in the epoxidation of isophorone (**35**) and verbenone (**37**) to their epoxides **36** (yield 34 %) and **38** (yield 68 %), respectively (scheme 7).

35 **36** **37** **38**

Scheme 7

Since in the case of **35** and **37** the peracid-route cannot be clearly distinguished from the possible side reaction with H_2O_2/HO^- ("Weitz-Schaeffer" oxidation), the „Adam-Test" using thianthrene-5-oxide (SSO) to distinguish between nucleophilic and electrophilic oxidants[25] was carried out and led to X_{nu}-values of about 0.5, depending on the reaction conditions. As this result does not permit a clear distinction between nucleophilic and electrophilic oxidation (for comparison see ref. 26), the oxidation was carried out with a series of Δ^4-unsaturated 3-keto steroids **39a-i** (scheme 8). The stereochemistry of the epoxidation of α,β-unsaturated ketones described above had been investigated very carefully by Henbest and coworkers [27,28] and later by other groups.[29] It is well established that the epoxidations of these compounds with H_2O_2/HO^- (HOO^-) afford mainly β-epoxides[27] and cannot be achieved with the anion of *tert*-butyl hydroperoxide in the case of **35** or Δ^4-3-ketosteroids **39** because of steric hindrance,[29] whilst the major products of epoxidation by peroxy acids are the diastereomeric α-epoxides.[28,29] Therefore the oxidation of compounds **39a-i** was considered by us to be a good mechanistic test to see whether the epoxidizing agent resulting from **4a,b**/H_2O_2/HO^- is an anion (Weitz-Schaeffer-type of epoxidation) or an organo sulfonic peracid. The results of the epoxidation of **39a-i** are summarized in table 4.

From the results listed in table 4, it is evident that the new epoxidation reaction generally yields 4α,5α-epoxy compounds with high diastereomeric excesses (up to 96 % de) which therefore excludes Weitz-Schaeffer-type epoxidation. The observed rates of conversion are somewhat lower than are found for H_2O_2/HO^- oxidations, but up to 5 - 6 times higher than in the case of peroxy acids. Additionally, the reaction is faster even at lower temperature (10 °C, 3h). In a comparable experiment it was shown that the epoxidation of **39b** with PhCN / H_2O_2 / K_2CO_3 leads to a nearly equal yield of **40b** (entry 7) but resulted in a complete loss of diastereoselectivity. The epoxidation of steroidal α,β-unsaturated ketones by "isolated dioxiranes" gave higher conversion rates but lower diastereoselectivities (the α-epoxides are also the major products)[20] when compared to the oxidant **2**.



39 a - i **40 a - i**

Scheme 8

Table 4: Epoxidation of Δ^4-Unsaturated 3-Ketosteroids **39a-i** with **4a,b**/H_2O_2/NaOH [a]

Entry	Starting material	Substituents	Oxidant	Product [b]	Conversion [c] [%]	Yield [d] [%]	de [e] [%]
1	**39a**	$R^1 = C_8H_{17}$ $R^2,R^3,R^4,R^5 = H$	**4a**	4α,5α - **40a**	35	80	66
2	**39a**	"	**4b**	4α,5α - **40a**	37	90	82
3	**39a**	"	H_2O_2/NaOH	4β,5β - **40a**	33	45	71
4	**39a**	"	$C_{11}H_{23}CO_3H$	4α,5α - **40a**	15	66	n.d. [f]
5	**39b**	R^1 = -$COCH_3$ $R^2,R^3,R^4,R^5 = H$	**4a**	4α,5α - **40b**	30	83	90
6	**39b**	"	**4b**	4α,5α - **40b**	50	78	90
7	**39b**	"	PhCN/H_2O_2/ K_2CO_3	**40b**	58	52	0
8	**39c**	R^1-R^2 = O $R^3,R^4 = H$; R^5 = OH	**4a**	4β,5β - **40c**	66	61	82
9	**39c**	"	**4b**	4β,5β - **40c**	70	84	82
10	**39d**	R^1-R^2 = O $R^3,R^4,R^5 = H$	**4b**	4α,5α - **40d**	73	73	92
11	**39e**	R^1 = OH R^2,R^3,R^4,R5 = H	**4b**	4α,5α - **40e**	62	69	93
12	**39f**	R_1 = -$COCH_3$ $R^2,R^3,R^5 = H$; R^4 = OH	**4b**	4α,5α - **40f**	64	58	67
13	**39g**	R^1-R^2 = O; R^3-R^4 = O; $R^5 = H$	**4b**	4α,5α - **40g**	35	88	96
14	**39h**	R^1 = -$COCH_3$ R^2 = OH; $R^3,R^4,R^5 = H$	**4b**	4α,5α - **40h**	51	68	92
15	**39i**	R^1 = -CO-CH_2OAc; $R^2,R^3,R^4,R^5 = H$	**4b**	4α,5α - **40i**	71 [g]	88	94

a) All reactions were carried out in ^{t}BuOH (except entry 7) at 10 °C, for details see the experimental part. b) Main diastereomer. c) Conversion refers to introduced ketone and was determined by isolation of unchanged starting material. d) Isolated main diastereomer, based on conversion. e) Determined by ^{1}H NMR analysis of the crude reaction mixture. f) Taken from ref. 28, there only 4α,5α-**40a** was isolated, the de value was not determined from the crude reaction mixture. g) Starting material was recovered as 21-hydroxy-4-pregnene-3,20-dione.

It is noteworthy that no complications were observed with the different subtituents within the steroid skeleton, epimerizations or oxidative side reactions for example Baeyer-Villiger oxidation did not occur to any significant extent. No dramatic effects of the different substituents on the diastereoselectivity were observed with exception of **39c**. Epoxidation of **39c**, whose structure differs from **39d** only by the 19-OH group, resulted in the complete opposite diastereoselectivity yielding the 4β,5β-epoxide **40c**. Again, this result may be explained by an association of the intermediate peracid with the homoallylic OH group thus leading to high *syn*-selectivity in accord with the high *syn*-selectivity found in the epoxidation of isophorol (**20**), cedrenol (**26**), 3β,19-dihydroxy-5-cholestane **28a** and in the epoxidation of steroidal allylic and homoallylic alcohols by m-CPBA.[12]

Summary

From the results presented here, it is evident that the sulfonyl azolide derivatives **4-6** in combination with H_2O_2 / base generate a powerful oxidant which epoxidizes olefins, allylic and homoallylic alcohols and electron- poor α,β-unsaturated ketones under mild conditions. Because of the weakly alkaline medium (especially when **4a-d** were introduced) even acid-sensitive epoxides could be isolated in acceptable to good yields.

The behaviour of the mixture **4-6** / H_2O_2 / base in oxidation reactions is in excellent agreement with the postulated O-transferring intermediate, the sulfonic peracid **2**. The peracid-like character of the oxidant was demonstrated by the observed diastereoselectivities in the epoxidation of olefinic substrates, i.e. high *anti*-selectivity found in the epoxidation of terpenes (**5**, **7a,b**, **9**, **24**), with allylic peroxide (**22**), the *syn*-selective epoxidation of cyclic allylic and homoallylic alcohols (**20**, **26**, **28a**, **39d**) and the preferred *threo*-selectivity in the epoxidation of acyclic allylic alcohols (**33a-c**). In addition to this, the dominant α-attack of **2** using different steroids (**28b,c**, **39a-i**) supports this conclusion.

Surprisingly, in most cases the observed diastereoselectivies were higher than those reported for various peroxy acids or imidoperacids. This may be explained by increased steric repulsion caused by the tetrahedral configuration of the sulfur atom in **2**, in contrast to the planar structure of common peracids.

EXPERIMENTAL PART

Unless otherwise noted ^1H and ^{13}C NMR-investigations were performed in $CDCl_3$ as solvent on a Varian Gemini 300 (300 MHz) using hexamethyldisiloxane (HMDSO) as internal reference. GLC-MS analyses were performed on a Varian Saturn II spectrometer. Melting points were recorded on a Boetius Hotstage apparatus and are uncorrected.

4a,c,d were prepared according to the method of Staab[30], **4b** and **6a,c,d** were commercially available from Aldrich. Compounds (**7a,b,9,11,14,16,18,20,24,26,28a-c,30a,b,33a-c,35,37,39a-i**) were commercially available

(Aldrich, Fluka, Sigma). Their purity was verified prior use by GLC, HPLC or TLC. H_2O_2 was a commercial product and used as 33 % (Merck) or 70 % aqueous solution (Peroxid-Chemie GmbH). The content of peroxide was determined by iodometric titration before use. Solvents for column chromatography were purified and distilled prior use.

1-Methyl-3(4-methylphenyl)sulfonylimidazolium tetrafluoroborate (5a) : 1.111 g (5 mmol) **4a** were added to a solution/suspension of 0.739 g (5 mmol) trimethyloxonium tetrafluoroborate Me_3O^+ BF_4^- in 10 ml of anhydrous CH_2Cl_2 and stirred for 24 h at room temperature. Then the solvent was reduced to about 1/3 and the resulting white precipitate was filtered off. The crude white solid was dissolved in a minimum of acetone and again filtered. Anhydrous Et_2O was added dropwise to the clear solution until small colourless needles precipitated. The product was filtered off, washed with ice-cold ether and dried. Yield: 1.344 g (83 %).
mp.: 120 - 122 °C , elemental analysis: $C_{11}H_{13}BF_4N_2O_2S$ (324.17) calc.: C, 40.75; H, 4.04; N, 8.69; S, 9.89; found: C, 40.35; H, 3.66; N, 8.80; S, 10.01 %.
^{1}H NMR (acetone-d_6) : 2.49 (s, 3H, C**H**$_3$), 4.12 (s, 3H, N-C**H**$_3$), 7.62 (d, 2H, J = 8.3 Hz), 7.91 (s, 1H), 8.13 (d, 2H, J = 8.4 Hz), 8.19 (s, 1H), 9.74 (s, 1H)

General Procedure for the Epoxidation Reactions

Method A : One equivalent of the appropriate olefin, 1.5 to 8 equivalents of **4a-d** and an excess H_2O_2 (33 % or 70 % aqueous solution) were dissolved in ^{t}BuOH or MeOH and a 2N or 10N NaOH (10N NaOH was used if the substrates were poorly soluble in water) were added dropwise with stirring to the mixture over a period of 2-3 h so that the base was consumed immediately and the mixture was only weakly alkaline. The end of the reaction was indicated by the consumption of **4a-d** (TLC) and the pH of the mixture (about 8 - 9).
After addition of ice-cold water the mixture was extracted with CH_2Cl_2 or Et_2O. The combined organic phases were washed with saturated aqu. $NaHCO_3$, water and brine and finally dried over $MgSO_4$. After evaporation of the solvent in vacuo the crude product was purified by Kugelrohr distillation or by column chromatography using silica gel 60 (Fluka, 0.04 - 0.063 mm). The de values were determined directly from the crude mixtures integrating the signals of the epoxy protons of the corresponding diastereomers.

Method B : One equivalent of the olefin, 2 equivalents of the 1-methyl-3(4-methylphenyl)sulfonylimidazolium tetrafluoroborate (**5a**), 2 equivalents K_2CO_3 and 0.1 equivalent n-Bu_4N^+ HSO_4^- were dissolved/suspended in CH_3CN / CH_2Cl_2 (~ 3:1) with stirring and 4 equivalents of aqueous H_2O_2 (70 %) were added over a period of about 2 hours at 0-5°C. After additional stirring for 1 hour the reaction was terminated and the solvent mixture was evaporated. The residue was taken up in Et_2O or CH_2Cl_2 and washed with saturated $NaHCO_3$, water and brine. After drying with $MgSO_4$ and evaporation of the solvent the crude product was analyzed by ^{1}H NMR (determination of the de-value) and chromatographed.

Method C : The corresponding olefin (1 equivalent) was dissolved in anhydrous THF with stirring and cooled down to -5°C while stirring. Two equivalents of **6a**, **6c** or **6d** were then added and the resulting solution was treated with 4 equivalents of aqueous H_2O_2 (70 %). At the same temperature, aqueous 2N NaOH was added in small portions with stirring so that the base was immediately consumed (pH control, pH ~ 5-6). The end of the reaction (~ 0.5 h) was reached when all **6a,c,d** was consumed and the pH was about 8. Excess THF was removed in vacuo and the residue was treated with 10 ml H_2O, followed by extraction with ether (5x). The combined organic phases were washed with saturated $NaHCO_3$, water and brine and dried over $MgSO_4$. After evaporation of the solvent the crude product was purified by column chromatography.

2α,3α-Epoxypinane (8a): According to *method A* 2 mmol (272 mg) α-pinene (**7a**) were oxidized in 5 ml MeOH using 888 mg (4 mmol) **4a**, 8 mmol H_2O_2 and 2N NaOH to yield 229 mg (75 %) **6** after Kugelrohr distillation. ^{1}H NMR data of **8a** were in agreement with the literature.[7] GLC-MS (EI): m/z: 152 [M+].

2α,10α-Epoxypinane (8b): As described above 2 mmol (272 mg) β-pinene (**7b**) were oxidized yielding 125 mg (41 %) **8b** after Kugelrohr distillation. ^{1}H NMR data of **8b** were in accord with the published data.[31] GLC-MS (EI) m/z: 152 [M+].

3α,4α-Epoxycarane (10): 2 mmol (272 mg) 3-carene (**9**) were oxidized as described for **8a** in 5 ml ^{t}BuOH to yield 170 mg (56 %) **10** after column chromatography (EtOAc/n-hexane 1:10). 103 mg of **9** were recovered. ^{1}H NMR data of **10** agree with the published data.[31] GLC-MS (EI) m/z: 152 [M+].

Epoxidation of 11 with 4a/H_2O_2 : As described above 2 mmol (240 mg) 5-vinyl-norbornene (**11**) (*exo/endo*-mixture) were oxidized to give 78 mg (29 %) **12** and 35 mg (11.5 %) **13** after column chromatography (EtOAc/n-hexane 1:1). ^{1}H NMR data of **12** were in agreement with the published data.[32] **12**: ^{1}H NMR: δ[ppm] 0.8 (d, 1H, J = 9.8 Hz); 1.09 (m, 1H); 1,35(dd, 1H, J_1 = 7.9 Hz, J_2 = 2 Hz); 1.77 (m, 1H), 2.48 (m, 2H), 2.61 (m, 1H), 3.13 (m, 2H), 5.00 (m, 2H), 5.75 (m, 1H). GLC-MS (EI) m/z: 136 [M+]. **13**: ^{1}H NMR: δ[ppm] 0.75-1.9 (m, 4H), 2.47 (m, 2H), 2.70 (m, 2H), 2.86 (m, 1H), 3.01 (m, 1H), 3.17 (m, 1H), 3.35 (m, 1H). GLC-MS (EI) m/z: 152 [M+]. The stereochemistry of the 5-vinyl-group in **12** and of the 5-oxiranyl-group in **13** was not determined.

***trans*-2-Methyl-1-phenyl-oxirane (15):**
a) Oxidation with 4a / H_2O_2 / NaOH : *Trans*-ω-methylstyrene (**14**) (2 mmol, 236 mg) was oxidized with 1.776 g (8 mmol) **4a**, 16 mmol H_2O_2 (33 %) and 2N NaOH in 10 ml MeOH to give 160 mg (60 %) **15** after column chromatography (EtOAc/n-hexane 1:10). 24 mg of unchanged **14** (10%) were recovered. **15**: GLC-MS (EI) m/z: 134 [M+]. ^{1}H NMR δ[ppm] 1.42 (d, 3H, J = 5 Hz), 3.01 (q*d, 1H, J_1 = 2 Hz, J_2 = 5 Hz), 3.55 (d, 1H, J = 2 Hz), 7.2-7.35 (m, 5H). ^{1}H NMR data were in agreement with the published data.[33]
b) Oxidation with 5a / H_2O_2 / K_2CO_3 : According to *method B* 29 mg (0.25 mmol) **14** were oxidized using 162 mg (0.5 mmol) **5a**, 41 mg (0.3 mmol) K_2CO_3 , 7 mg (0.02 mmol) n-Bu_4N^+ HSO_4^- and 1mmol H_2O_2 (70 %). After the usual work up and evaporation of the solvent 61 mg of crude product (**15**, N-methylimidazole, PTC) were obtained. The crude product was dissolved in 5 ml of EtOAc/n-hexane (1:1) and filtered through a short column (alkaline Al_2O_3, ~ 3 cm). After flushing the column with another 15 ml of EtOAc/n-hexane (1:1) the filtrate was evaporated *in vacuo* to yield 28 mg (82 %) of pure **15** (all data were consistent with those obtained for *a)*).
c) Oxidation with Ts_2O / H_2O_2 : Tosyl anhydride (Ts_2O, 173 mg, 0.53 mmol, Fluka) and 41 mg **14** (0.35 mmol) were dissolved in 2 ml anhydrous THF. 145 mg (1.03 mmol) K_2CO_3 were added and the mixture was cooled to -5°C with stirring. At this temperature a solution of 0.2 ml H_2O_2 (70 %) in 2 ml THF was added over 0.5 h and then stirred overnight.. After consumption of the Ts_2O (TLC) the reaction mixture was worked up according to *method B* and the crude product chromatographed yielding 8 mg (17 %) **15** and 10 mg (24 %) recovered **14**. The polar side products from the reaction were neither isolated nor characterized.

***cis*-3,4-Epoxyhexan-1-ol (17):** According to *procedure A* 200 mg (2 mmol) *cis*-3-hexen-1-ol (**16**) were oxidized as described for **11** in 10 ml MeOH to yield 215 mg (93 %) **17** as a colourless oil after column chromatography (EtOAc/n-hexane 1:1). ^{1}H NMR: δ[ppm] 1.02 (t, 3H, J = 7.5 Hz), 1.55 (m, 2H), 1.69 (m, 1H), 1.85 (m, 1H), 2.91 (q, 1H, J = 6 Hz), 3.09 (m, 1H), 3.83 ("q", 2H, J = 6Hz).

***trans*-3,4-Epoxyhexan-1-ol (19):** In an analogous manner 200 mg (2 mmol) *trans*-3-hexen-1-ol (**18**) were oxidized in 10 ml MeOH to yield 198 mg (85 %) **19** as a colourless oil after column chromatography (EtOAc/n-hexane 1:1).
^{1}H NMR δ[ppm] 0.96 (t, 3H, J=7.5 Hz) 1.55 (m, 2H), 1.76 (m, 2H), 1.95 (m, 1H), 2.75 (m, 1H), 2.85 (s, broad, 1H), 3.76 (t, 2H, J = 5.5 Hz).

***cis*-4,4,6-Trimethyl-7-oxabicyclo[4.1.0]heptan-2-ol (21):** Following *method A* 71 mg (0.5 mmol) isophorol (**20**) were oxidized with 396 mg (2 mmol) **4b**, 5 mmol H_2O_2 (70 %) 5 ml in ^{t}BuOH to yield 60 mg (76 %) **21**

after column chromatography (EtOAc/n-hexane 1:1). 12 mg (17 %) unreacted **20** were also recovered. ^{1}H NMR data of **21** correspond to the published data.[13]

(1R, 2R, 3S, 4R, 5S)-2,3-Epoxypinan-4-ol (25): According to *method A* 76 mg (0.5 mmol) (1S)-*cis*-verbenol (**24**) (Fluka) were oxidized with 198 mg (1 mmol) **4b**, 2 mmol H_2O_2 (70 %) and 2N NaOH in 10 ml MeOH at 10 °C (3h). After the usual work up the crude material was chromatographed on silica gel (EtOAc/n-hexane 1:3) yielding 31 mg (40 %) of unreacted **24** and 38 mg (45 %) **25** as colourless oil. (All analytical data of **25** were identical with those of a sample prepared by an independent procedure from **38**.[34]) Nearly similar results were obtained when **4a** was used instead of **4b**.

(1R, 2R, 5S, 7R, 8S, 9S)-8,15-Epoxycedran-9-ol (27): The epoxidation of 0.11 g (0.5 mmol) (+)-8(15)-cedren-9-ol **26** (Fluka) according to *method A* was carried out with 198 mg (1 mmol) **4b**, 2 mmol H_2O_2 (70 %) and 2N NaOH in 10 ml MeOH at 10 °C (3h). After column chromatography (EtOAc/n-hexane 1:3) of the crude material 8 mg (7 %) **26** were recovered and 98 mg (83 %) pure **27** isolated. After recrystallization from n-hexane white needles, mp. 106.5 - 107 °C, were obtained. Elemental analysis : $C_{15}H_{24}O_2$ (236.35), calc: C, 76.23; H, 10.23; found : C, 76.12; H, 10.32%. MS (EI) : m/z: 236 [M+]. ^{1}H NMR: δ [ppm] 0.86 (d, 3H, CH_3, J = 7 Hz), 0.95 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.21 (dd, 1H, J_1 = 12 Hz, J_2 = 10.6 Hz), 1.28-1.86 (m, 10 H), 2.13 (ddd, 1H, CH, J_1 = 12 Hz, J_2 = 7.3 Hz, J_3 = 2.6 Hz), 2.62 (d, 1H, epoxy-H, J = 4.7 Hz), 3.05 (d, 1H, epoxy-H, J = 4.7 Hz), 4.06 (t*d, 1H, **CH**OH, J_1 = 10.6 Hz, J_2 = 7.3 Hz). ^{13}C NMR : δ [ppm] 15.30 (CH_3), 25.44 (CH_2), 25.61 (CH_3), 26.66 (CH_3), 36.50 (CH_2), 41.20 (C), 41.50 (CH), 41.58 (CH_2), 42.92 (CH_2), 51.44 (CH), 54.16 (C), 56.22 (CH_2-O), 57.52 (CH), 61.44 (C-O), 65.60 (CH-O). The H,H-NOESY experiments were carried out on a Varian Unity 500 (500 MHz) NMR spectrometer. NOE's were found between the CH_3-group (δ = 1.09 ppm) and the epoxy proton at δ = 2.62 ppm and, additionally, between the CH_3-group (δ = 1.09 ppm) and the C**H**-OH proton at δ = 4.06 ppm.

3β, 19-Dihydroxy-5β,6β-epoxycholestane (29a) : Following *method B* 20 mg (0,05 mmol) 3β,19-dihydroxy-5-cholestene **28a** (Sigma) were oxidized using 32 mg (0.1 mmol) **5a**, 0.2 mmol H_2O_2 (70 %), 14 mg (0.1 mmol) K_2CO_3 and 3 mg (0.01 mmol) n-Bu_4N^+ HSO_4^- in 2 ml CH_2Cl_2 / CH_3CN (1:3) at 0-5 °C. After the usual work up the crude product was crystallized from acetone/water yielding 19 mg (90 %) pure 5β-**29a**, mp. 176 °C (lit.-mp. [35] 177-178 °C). ^{1}H NMR : δ [ppm] 3.01 (d, 1H, J = 1.7 Hz), 3.54 (d, 1H, J = 11.7 Hz) 3.67 (m, 1H), 4.18 (d, 1H, J = 11.7 Hz). The data were in accord with those published.[35] The corresponding 5α,6α-isomer could not be detected by ^{1}H NMR analysis of the crude reaction mixture.

5,6-Epoxycholestan-3β-ol (29b) :
entry 1: According to *method A* 77 mg (0,2 mmol) **28b** (Fluka) were oxidized using 133 mg (0.6 mmol) **4a**, 1.2 mmol H_2O_2 (70 %) and 2N NaOH in 15 ml of a MeOH/THF (2:1)-mixture (the solubility of **28b** in MeOH is poor). After the usual work up and column chromatography (EtOAc/n-hexane 3:1), 44 mg (57%) of recovered **28b** and 27 mg (33%) of **29b** as diastereomeric mixture were isolated. Determination of the ratio 5α-**29b** : 5β-**29b** in the crude product was carried out by ^{1}H NMR spectroscopy and found to be 5α : 5β = 4 : 1 (Integration of the signals at δ = 2.86 ppm (d, J = 4.4 Hz, α-epoxide) and δ = 3.05 ppm (d, J = 1.7 Hz, β-epoxide)).
entry 2: According to *method B* 77 mg (0.2 mmol) **28b** were oxidized with 97 mg (0.3 mmol) **5a**, 0.6 mmol H_2O_2 (70 %), 40 mg (0.3 mmol) K_2CO_3 and 7 mg (0.02 mmol) n-Bu_4N^+ HSO_4^- in 4 ml CH_2Cl_2 / CH_3CN (1:3) at 0-5 °C. The following work up and column chromatography (EtOAc/n-hexane 3:1) gave 75 mg (93 %) pure **29b** as diastereomeric mixture. The isomer ratio 5α : 5β = 5.2 : 1 was determined from the crude reaction mixture by ^{1}H NMR. The ^{1}H NMR data are in full agreement with data reported in the literature.[36]
entry 3: *Oxidation with Ts_2O / H_2O_2* : The reaction was carried out in the same way as described for the oxidation with diphenylphosphinic acid anhydride / H_2O_2.[9] Compound **28b** (97 mg, 0.25 mmol) and 124 mg (0.38 mmol) tosyl anhydride (Ts_2O, Fluka) were dissolved in 2 ml anhydrous THF. 104 mg (0.75 mmol) solid K_2CO_3 was added and the mixture was stirred and cooled to -5 °C. A solution of 0.15 mmol H_2O_2 (70 %) in 2 ml THF was added within 0.5 h at this temperature and stirred overnight. Consumption of Ts_2O was monitored by TLC. After the usual work up (*method C*) the crude product was chromatographed on silica gel (EtOAc/n-hexane

3:1) yielding 20 mg (20 %) **29b** as diastereomeric mixture, 53 mg (55 %) of unreacted **28b** were recovered (polar byproducts were also detected by TLC but not isolated or characterized). The isomer ratio 5α-**29b** : 5β-**29b** = 4.8 : 1 was determined by ^{1}H NMR analysis of the crude reaction mixture.
entry 4: According to *method C* 193 mg (0.5 mmol) **28b** were oxidized using 268 mg (1 mmol) **6a**, 2 mmol H_2O_2 (70 %) and 2N NaOH in 5 ml THF at -5 °C (0.5 h). The work up and following chromatography (EtOAc/n-hexane 3:1) gave 180 mg (90 %) **29b** as a diastereomeric mixture of α- and β-epoxides. The isomer ratio in the crude product was found to be 5α-**29b** : 5β-**29b** = 4.8 : 1.
entry 5: As described above 193 mg (0.5 mmol) **28b** were oxidized with 296 mg (1 mmol) **6c**, 2 mmol H_2O_2 (70 %) and 2N NaOH as described above. ^{1}H NMR analysis of the crude product **29b** (191 mg, 95 %) showed an isomer ratio 5α-**29b** : 5β-**29b** = 11 : 1. After column chromatography (EtOAc/n-hexane 3:1) and crystallization from acetone 160 mg (80 %) pure 5α-**29b** were obtained as white crystals, mp 142-143 °C (lit.-mp. 141-142 °C [36]).
entry 6: As described above 193 mg (0.5 mmol) **28b,** 380 mg (1 mmol) **6d** and 2 mmol H_2O_2 (70 %) were allowed to react yielding, after the work up and purification (see entry 4), 180 mg (90 %) **29b** as a diastereomeric mixture of α- and β-epoxides. The isomer ratio determined from ^{1}H NMR analysis of the crude product was found to be 5α-**29b** : 5β-**29b** = 3.5 : 1.

3β-Acetoxy-5,6-epoxycholestane (29c) : Cholesteryl acetate (**28c**) (64 mg, 0.15 mmol, Aldrich) was epoxidized following *method B* with 97 mg (0.3 mmol) **5a**, 0.6 mmol H_2O_2 (70 %), 41 mg (0.3 mmol) K_2CO_3 and 6 mg (0.02 mmol) n-Bu_4N^+ HSO_4^- in 4 ml CH_2Cl_2/CH_3CN (1:3) at 0-5 °C. After work up, the crude product was chromatographed on silica gel (EtOAc/n-hexane 1:4) yielding 69 mg (89 %) **29c** as a diastereomeric mixture of 5α,6α- and 5β,6β-epoxide. ^{1}H NMR data were in accord with those reported earlier.[19] The α/β-ratio (5α-**29c** : 5β-**29c** = 5.1 : 1) of **29c** was determined from the crude reaction mixture by integration of the signals in the ^{1}H NMR spectrum at δ = 2.86 ppm (d, J = 4.4 Hz, α-epoxide) and δ = 3.05 ppm (d, J = 1.7 Hz, β-epoxide).

Epoxidation of ergocalciferol (vitamin D_2) (30a) : According to *method A* 99 mg (0.25 mmol) ergocalciferol (**30a**), 459 mg (2.5 mmol) **4b** and 5 mmol H_2O_2 (70 %) were allowed to react in MeOH in the dark yielding 54 mg (50 %) (3S, 5S, 6R, 7R)-5,6;7,8-diepoxy-9,10-seco-ergosta-10(19),22*t*-dien-3-ol (**32a**) after the usual work up (column chromatography EtOAc/n-hexane 1:1) and recrystallization from n-hexane, mp 192-194 °C (lit.-mp[21] 175-176 °C).
The same reaction carried out in ^{t}BuOH instead of MeOH as described above yielded 36 mg (35 %) (3S, 5S, 6R, 7*E*)-5,6-epoxy-9,10-seco-ergosta-7,10(19),22*t*-trien-3-ol (**31a**) and 21 mg (20 %) **32a**.
31a ^{1}H NMR : δ [ppm] 0.46 (s, 3H, CH_3), 0.78 (d, 3H, J = 5 Hz, CH_3), 0.81 (d, 3H, J = 5 Hz, CH_3), 0.88 (d, 3H, J = 6.9 Hz, CH_3), 0.98 (d, 3H, J = 6.6 Hz, CH_3), 3.62 (d, 1H, J = 8.6 Hz, epoxy-H), 3.90 (m, 1H, C**H**OH), 4.64 (d, 1H, J = 8.6 Hz, epoxy-H), 4.90 Hz (s, 1H, =CH_2), 4.94 (s, 1H, =CH_2), 5.15 (m, 2H, olef.)
32a ^{1}H NMR : δ [ppm] 0.61 (s, 3H, CH_3), 0.78 (d, 3H, J = 5.2 Hz, CH_3), 0.80 (d, 3H, J = 5.1 Hz, CH_3), 0.87 (d, 3H, J = 6.9 Hz, CH_3), 0.98 (d, 3H, J = 7.9 Hz, CH_3), 2.74 (d, 1H, J = 7.9 Hz, epoxy-H), 2.83 (d, 1H, J = 7.9 Hz, epoxy-H), 3.85 (m, 1H, C**H**OH), 4.96 (s, 1H, =CH_2), 5.11 (s, 1H, =CH_2), 5.14 (m, 2H, olef.). The ^{1}H NMR data of **31a** and **32a** are in complete agreement with the literature.[21]

Epoxidation of cholecalciferol (vitamin D_3) (30b) : According to *method A* 77 mg (0,2 mmol) cholecalciferol (**30b**), 119 mg (0.6 mmol) **4b** and 1.2 mmol H_2O_2 (70 %) were dissolved in MeOH in the dark and 2N NaOH was added dropwise until **4b** had been completely consumed (TLC). After the work up and column chromatography 38 mg (47 %) pure (5S)-5,6-epoxy-9,10-seco-7,10(19)-cholestadien-3β-ol (**31b**), 6 mg (7 %) (5S)-5,6;7,8-diepoxy-9,10-seco-10(19)-cholesten-3β-ol (**32b**) and 12 mg of a mixture of **31b** and **32b** were obtained.
31b mp.: 52-53 °C (lit.[22]: colourless oil); **32b** decomposes from 45 °C.
31b: ^{1}H NMR : δ [ppm] 0.46 (s, 3H, CH_3), 0.83("d", 6H, 2*CH_3), 0.88 (d, 3H, CH_3), 3.62 (d, 1H, J = 8.6 Hz, epoxy-H), 3.89 (m, 1H, C**H**OH), 4.64 (d, 1H, J = 8.6 Hz, epoxy-H), 4.91 (s, 1H, =CH_2), 4.94 (s, 1H, =CH_2). The data are in agreement with the published data.[22] **32b:** ^{1}H NMR : δ [ppm] 0.60 (s, 3H, CH_3), 0.84(„d", 6H,

2*CH_3), 0.89 (d, 3H, CH_3), 2.75 (d, 1H, J = 8 Hz, epoxy-H), 2.83 (d, 1H, J = 8 Hz, epoxy-H), 3.86 (m, 1H, CHOH), 4.96 (s, 1H, =CH_2), 5.12 (s, 1H, =CH_2).

Epoxidation of 33a-c with 4a-c, 6d/H_2O_2 : 2 mmol of one of the allylic alcohols 1-buten-3-ol (**33a**) (144 mg), 1-hexen-3-ol (**33b**) (200 mg) or *trans*-3-penten-2-ol (**33c**) (172 mg) were oxidized with 4 mmol of **4a** (0.888g), **4b** (0.792 g) or **4c** (1.0 g)(*method A*) or with **6c** (1.522 g). After the usual work up, the *threo / erythro*-selectivity was determined by ^{1}H NMR of the crude products by integration of the CH-OH protons (the chemical shifts are given below). Isolation of the pure products was carried out only for the reaction mixtures obtained in the reaction of **33a-c** in the presence of **4b**. For all other experiments the crude product was weighed and the yield determined by ^{1}H NMR and gave very similar results to those obtained with **4b**. Pure 1,2-epoxybutan-3-ol (**34a**) (90 mg, 51 %, *erythro / threo*-mixture) was isolated by Kugelrohr distillation followed by column chromatography (EtOAc/n-hexane 1:1); 1,2-epoxyhexan-3-ol (**34b**) (180 mg, 78 %, *erythro / threo*-mixture) and pure *trans*-2,3-epoxypentan-4-ol (**34c**) (173 mg, 85 %, *erythro / threo*-mixture) were isolated by column chromatography (EtOAc/n-hexane 1:1).

34a ^{1}H NMR : δ [ppm] 1.24 (d, J = 6.4 Hz, CH_3, *erythro*), 1.29 (d, J = 6.4 Hz, CH_3, *threo*), 2.67-2.81 (m, epoxy-CH_2, *erythro / threo*), 3.60 („quint", J ≈ 6.3 Hz, CH-OH, *threo*), 3.99 (q*d, J_1 = 6.4 Hz, J_2 = 3 Hz, CH-OH, *erythro*) .

34b ^{1}H NMR : δ [ppm] 0.93 (t, 3H, CH_3), 1.53 (m, 4H, 2*CH_2), 2.81 (m, 1H, epoxy-CH_2, *erythro / threo*), 3.00 (m, 1H, epoxy-H, *erythro / threo*), 3.43 (m, CH-OH, *threo*), 3.84 (m, CH-OH, *erythro*).

34c ^{1}H NMR : δ [ppm] 1.21-1.30 (m, 6H,2*CH_3, *erythro / threo*), 2.66 (d*d, J_1 = 2.2 Hz, J_2 = 5.1 Hz, epoxy-H, *threo*), 2.70 („t", J ≈ 2.8 Hz, epoxy-CH, *erythro*), 2.95 (q*d, J_1 = 2.2 Hz, J_2 = 5.2 Hz, epoxy-H, *threo*), 3.04 (q*d, J_1 = 2.2 Hz, J_2 = 5.2 Hz, epoxy-H, *erythro*), 3.60 („quint", J ≈ 6.4 Hz, CH-OH, *threo*), 3.90 (q*d, J_1 = 3.1 Hz, J_2 = 6.4 Hz, CH-OH, *erythro*). The ^{1}H NMR data and the chromatographic behaviour of **34a-c** were in agreement with the assignments made in ref. 23 and 24.

2,3-Epoxy-3,5,5-trimethylcyclohexan-1-one (36): According to *method A* 138 mg (1 mmol) isophorone (**35**) were oxidized using 792 mg (4 mmol) **4b**, 10 mmol H_2O_2 (70 %) and 10N NaOH in 10 ml ^{t}BuOH at 10 °C. After column chromatography (EtOAc/n-hexane 1:3) 52 mg **36** (34 %) were obtained as colourless oil. 63 mg (46 %) of starting material **35** were recovered. **36**: ^{1}H NMR: δ[ppm] 0.88 (s, 3H, CH_3), 0.99 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.66 (d, 1H, J = 14.5 Hz), 1.78 (d, 1H, J = 13.4 Hz), 2.05 (d, 1H, J = 14.5 Hz), 2.59 (d, 1H, J = 13.4 Hz), 3.03 (s, 1H). GLC-MS (EI): m/z 154 [M+]. The product was identical with a sample prepared according to literature.[37]

2α,3α-Epoxypinan-4-one (38): As described above 75 mg (0.5 mmol) verbenone (**37**) were transformed using 396 mg (2 mmol) **4b**. After usual work up and purification by column chromatography (EtOAc/n-hexane 1:10) 57 mg (68 %) **38** were isolated as colourless oil. 7 mg (9 %) of unchanged starting material **37** were also recovered. The structure of **38** was determined by ^{1}H NMR spectroscopy by comparison with an authentic sample, prepared according to literature and by reduction to 2α,3α-epoxy-4β-hydroxypinane with $LiAlH_4$.[34]

4,5-Epoxycholestan-3-one (40a): According to *method A* 212 mg (0.55 mmol) 4-cholesten-3-one (**39a**) were oxidized in 10 ml ^{t}BuOH at 10 °C with 245 mg (1.1 mmol) **4a**, 5 mmol H_2O_2 (70 %) and 10N NaOH . After column chromatography (EtOAc/n-hexane 1:10) 40 mg (20 %) 4α,5α-**40a** were isolated as white crystals, followed by 143 mg of unchanged **39a**. Starting from 96 mg (0.25 mmol) **39a**, 396 mg (2 mmol) **4b**, 4 mmol H_2O_2 (70 %) and 10N NaOH 33 mg 4α,5α-**40a** (33 %) and 60 mg **39a** (63 %) were isolated.

The crude 4α,5α-**40a** obtained after chromatography was crystallized from MeOH, mp 122-123 °C (lit-mp[28] 122-124 °C). The de value was measured with the crude material by ^{1}H NMR (δ = 3.0 ppm α-epoxide, δ = 2.95 ppm β-epoxide). The enantiomeric purity of the crystallized product was measured by HPLC using a Diacel Chiracel OD column (n-hexane / ^{i}PrOH 9:1, detector: Knauer chiral detector and Merck L-6000 diode array detector) to be > 99 %.

Epoxidation of 39a with H_2O_2 / NaOH: Oxidation of 192 mg (0.5 mmol) **39a** was carried out by treatment with 2 mmol H_2O_2 (70 %) and 1 mmol 2N NaOH in 10 ml ^{t}BuOH at 10 °C. After 3 h stirring at the same temperature, the mixture was worked up as described in the general procedure. 30 mg 4β,5β-**40a** (15 %) and 128 mg **39a** (67 %) were obtained after chromatography (EtOAc/n-hexane 1:10). Crystallization of crude 4β,5β-**39a** gave the pure product mp 115-116 °C (lit.-mp[27] 116 - 116.5 °C).

4,5-Epoxy-pregnane-3,20-dione (40b): Epoxidation of 157 mg (0.5 mmol) 4-pregnene-3,20-dione (**39b**) (*method A*) with 222 mg (1 mmol) **4a**, 2 mmol H_2O_2 (33 %) and 1 mmol 2N NaOH yielded 41 mg 4α,5α-**40b** (25 %) and 110 mg (70 %) unreacted **39b** after chromatography (EtOAc / n-hexane 1:1). The reaction of 77 mg (0.25 mmol) **39b** with 396 mg (2 mmol) **4b**, 4 mmol H_2O_2 (70 %) and 10N NaOH and after work up as described above gave 32 mg 4α,5α-**40b** (39 %) and 39 mg (50 %) unreacted **39b**. Pure 4α,5α-**40b** was obtained by crystallization from EtOAc mp 176-178 °C (lit.-mp[27] 177-178 °C). The de-values were determined from the crude reaction mixtures by integration of the signals at δ = 3.02 ppm (α-epoxide) and δ = 2.96 ppm (β-epoxide) in the ^{1}H NMR spectrum.

Oxidation of 39b with PhCN / H_2O_2: 39b (157 mg, 0.5 mmol) in 10 ml MeOH was treated at 10 °C with stirring with 0.75 mmol PhCN, 1.25 mmol H_2O_2 (33 %) and 0.15 mmol K_2CO_3. After 1 h stirring the same amounts of PhCN, H_2O_2 and K_2CO_3 were added and after further 1 h the addition of the oxidant was repeated and the stirring continued for 1 h. The crude mixture obtained after usual work up was purified by chromatography as described above yielding 50 mg **40b** (30 %) and 66 mg (42 %) unreacted **39b**. ^{1}H NMR analysis of the crude **40b** showed a 1:1-mixture of α- and β-epoxide.

4,5-Epoxy-19-hydroxyandrostane-3,17-dione (40c): According to *method A* using 198 mg (1 mmol) **4b**, 2 mmol H_2O_2 (70 %) and 1 mmol 2N NaOH, 151 mg (0.5 mmol) 19-hydroxy-4-androstene-3,17-dione (**39c**) were oxidized (^{t}BuOH, 10 °C) yielding 97 mg 4β,5β-**40c** (59 %) and 47 mg (30 %) unreacted **39c** after chromatography (EtOAc/n-hexane 3:1). Pure 4β,5β-**40c** was obtained after crystallization from EtOAc, mp 202 °C (lit-mp[38] 201-203 °C). ^{1}H NMR: δ [ppm] 2.90 (s, 1H, epoxy-H), 3.78 (d, 1H, J = 11 Hz), 4.13 (d, 1H, J = 11 Hz). Measurement of the de-value by ^{1}H NMR at δ = 3.01 (α-epoxide) and δ = 2.90 (β-epoxide).

4,5-Epoxyandrostane-3,17-dione (40d): 4-Androstene-3,17-dione (**39d**) (72 mg, 0.25 mmol) was oxidized with 396 mg (2 mmol) **4b**, 4 mmol H_2O_2 (70 %) and 10N NaOH in 10 ml ^{t}BuOH at 10 °C. After chromatography (EtOAc/n-hexane 1:1) 40 mg 4α,5α-**40d** (53 %) and 19 mg **39d** (27 %) were isolated. Crystallization from EtOAc yielded pure 4α,5α-**40d**, mp 197-199 °C (lit-mp[27] 197-198 °C). Measurement of the de-value by ^{1}H NMR at δ = 3.04 ppm (α-epoxide) and δ = 2.98 (β-epoxide).

4,5-Epoxy-17β-hydroxyandrostan-3-one (40e): Epoxidation of 72 mg (0.25 mmol) 17β-hydroxy-4-androsten-3-one (**39e**) as described above yielded after chromatography (EtOAc / n-hexane 1:1) 32 mg 4α,5α-**40e** (43 %) and 27 mg unreacted **39e** (38 %). 4α,5α-**40e** was crystallized from EtOAc, mp 169-171 °C (lit-mp[27] 169-171 °C). ^{1}H NMR: δ[ppm] 3.02 (s, 1H, epoxy-H), 3.65 (m, 1H, **CH**-OH). Measurement of the de-value at δ = 3.02 (α-epoxide) and δ = 2.96 (β-epoxide).

4,5-Epoxy-11α-hydroxypregnane-3,20-dione (40f): As described above 83 mg (0.25 mmol) 11α-hydroxy-4-pregnene-3,20-dione (**39f**) were epoxidized. Chromatography (EtOAc/n-hexane 3:1) yielded 32 mg 4α,5α-**40f** (37 %) and 30 mg **39f** (36 %). Crude **40f** was crystallized from MeOH / H_2O: mp 161-162 °C (lit-mp[39] 167-168 °C). ^{1}H NMR: δ [ppm] 2.99 (s, 1H, epoxy-H), 3.93 (m, 1H, **CH**OH). Measurement of the de-value: δ = 2.99 ppm (α-epoxide) and δ = 2.95 ppm (β-epoxide).

4,5-Epoxyandrostane-3,11,17-trione (40g): Starting from 75 mg (0.25 mmol)) 4-androstene-3,11,17-trione (**39g**) according to the above procedure 24 mg 4α,5α-**40g** (31 %) and 49 mg **39g** (65 %) were isolated after chromatography (EtOAc / n-hexane 1:1). Crystallization from EtOAc gave pure 4α,5α-**40g**, mp 279-281 °C (lit-

mp[39] 275-278 °C). Measurement of the de-value was done by ^{1}H NMR at δ = 3.05 ppm (α-epoxide) and δ = 2.97 ppm (β-epoxide).

4,5-Epoxy-17α-hydroxypregnane-3,20-dione (40h): 83 mg (0.25 mmol) 17α-hydroxy-4-pregnene-3,20-dione (**39h**) were oxidized in the same way as described above for **39g**. After chromatography (EtOAc/n-hexane 3:1) 30 mg 4α,5α-**40h** (35 %) were isolated and 40 mg (49 %) unreacted **39h** recovered. Crystallization from EtOAc gave pure 4α,5α-**40h**, mp 215-216 °C (lit-mp[40] 216-217 °C). Measurement of the de-value by ^{1}H NMR at δ = 3.02 ppm (α-epoxide) and δ = 2.96 ppm (β-epoxide).

4,5-Epoxy-21-hydroxypregnane-3,20-dione (40i): The oxidation of 93 mg (0.25 mmol) 21-acetoxy-4-pregnene-3,20-dione (**39i**) was carried out according to the procedure above. After chromatography (EtOAc/n-hexane 1:1) 54 mg 4α,5α-**40i** (62 %) and 24 mg 21-hydroxy-4-pregnen-3,20-dione (29 %) were isolated. Pure 4α,5α-**40i** was obtained after crystallization from EtOAc, mp 168 - 172 °C (lit-mp[39] 170 - 172 °C). ^{1}H NMR: δ [ppm] 3.02 (s, 1H, epoxy-H), 3.23 (s, broad, 1H, OH), 4.17 (s, 2H, CH_2OH); the de-value was measured at 3.02 ppm (α-epoxide) and 2.96 ppm (β-epoxide).

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REFERENCES AND NOTES

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1. Part I : Schulz, M.; Kluge, R.; Lipke, M.; *Synlett* **1993**, 915-918.
2. Liebsch, S., Dissertation in progress, Martin-Luther-Universität Halle-Wittenberg
3. (a) Hoffmann, R. V. in *The Chemistry of Functional Groups, Peroxides,* Patai S. Ed. John Wiley & Sons, Inc., **1983** p. 259 ff.
   (b) Hoffmann, R. V. *Organic Preparation and Precedure Int.* **1986**, *18*, 179-201.
4. (a) Eschwey, M.; Sundermeyer, W.; Stephenson, D.S.; *Chem. Ber.* **1983**, *116*, 1623 - 1630.
   (b) Nielsen, A.T.; Atkins, R.L.; Novis, W.P.; Coon, C.L.; Sitzmann, M.E.; *J. Org. Chem.*, **1980**, *45*, 2341 - 2347.
5. Kim, Y. H. in *Modern Methodology in Organic Synthesis*, Shono, T. Ed. VCH Publishers, **1992**, p. 303 ff and lit. therein.
6. Analogous methylation of 1-acylimidazolides was reported by: Olofson, R. A.; Kendall, R. V.; *J. Org. Chem.* **1970**, *35*, 2246 - 2248.
7. (a) Suzuki, A.; Miki, M.; *Tetrahedron* **1967**, 3621 - 3629.
   (b) Bessiere, Y; El Gaied, M. M.; Meklati, B.; *Bull. Soc. Chim. France* **1972**, 1000 - 1008.
   (c) Cocker, W.; Grayson, D. H.; *J. Chem. Soc. Perkin Trans 1* **1975**, 1217 - 1220.
8. Bartok, M.; Lang, K. L. in *Small Ring Heterocycles Part 3,* p. 1 - 196.
9. Kende, A. S.; Delair, P.; Blass, E. B. *Tetrahedron Lett.* **1994**, *35*, 8123-8126.
10. Sharpless, K.B.; Michaelson, R.C.; *J. Am. Chem. Soc.* **1973**, 95, 6136 - 6137.
11. (a) Henbest, H. B.; Wilson, R. A. L.; *J. Chem. Soc.* **1957**, 1958-1965.
    (b) Henbest, H. B.; *Proc. Chem. Soc.* **1963**, 159 - 166.
    (c) Chamberlain, P.; Roberts, M. L.; Whitham, G. H.; *J. Chem. Soc. (B)* **1970**, 1374-1381.
12. (a) Hoveyda, A.H.; Evans, D.A.; Fu, G.C.; *Chem. Rev.*, **1993**, *93*, 1307 - 1370 and ref. cited therein.

(b) Kocovsky, P.; *J. Chem. Soc. Perkin Trans. 1* **1994**, 1759-1763 and ref. cited therein.
13. Chautemps, P.; Pierre, J. L. *Tetrahedron* **1976**, *32*, 549 - 557.
14. The epoxidation of allylic alcohols with „isolated" dioxiranes is characterized by the competetive oxidation of the allylic OH-group: Adam, W.; Prechtl, F.; Richter, M.-J.; Smerz, A.-K.; *Tetrahedron Lett.* **1993**, *34*, 8427 - 8430.
15. Schulz, M., Kluge, R.; Liebsch, S.; Lessig, J.; Halik, M.; manuscript in preparation.
16. Chamberlain, P.; Roberts, M. L.; Whitham, G. H., *J. Chem. Soc. (B)* **1970**, 1374-1381.
17. Mousseron-Canet, M.; Guilleux, J.C.; *Bull. Soc. Chim. Fr.* **1966**, 3853 - 3858.
18. Bingham, K.D.; Blaiklock, T.M.; Coleman, R.C.B.; Meakins; G.D.; *J. Chem. Soc. (C)* **1970**, 2330 - 2332.
19. Tohma, M.; Tomita, T.; Kimura, M.; *Tetrahedron Lett.* **1973**, 4359 - 4362.
20. Bovicelli, P.; Lupattelli, P.; Mincione, E.; *J. Org. Chem.* **1992**, *57*, 2182 - 2184.
21. LeBoulch, N.; Raoul, Y.; Ourisson, G.; *Bull. Soc. Chim. Fr.* **1965**, 646 - 649.
22. Nakayama, K.; Yamada, S.; Takayama, H; *J. Org. Chem. 1984*, **49**, 1537 - 1539.
23. Mihelich, E.D.; *Tetrahedron Lett.* **1979**, 4729 - 4732.
24. Rossiter, B.E.; Verhoeven, T.R.; Sharpless, K.B.; *Tetrahedron Lett.* **1979**, 4733 - 4736.
25. (a) Adam, W.; Haas, W.; Lohray, B.B.; *J. Am. Chem. Soc.* **1991**, *113*, 6202 - 6208.
(b) Adam, W.; Golsch, D.; *Chem. Ber* **1994**, *127*, 1111-1113.
26. Ballistieri, F.P.; Tomaselli, G.A.; Toscano, R.M.; Bonchio, M; Conte, V.; DiFuria, F.; *Tetrahedron Lett.* **1994**, *35*, 8041-8044.
27. Henbest, H. B.; Jackson, W. R.; *J. Chem. Soc. (C)* **1967**, 2459 - 2465.
28. Henbest, H. B.; *J. Chem. Soc. (C)* **1967**, 2469 - 2471.
29. Berti, G.; *Top in Stereochem.*, **1973**, *7*, 93 - 251 and ref. cited therein.
30. Staab, H. A.; *Angew. Chem.* **1962**, *74*, 407 - 423.
31. Arbuzov, B. A.; Samitov, Y. Y.; Bikeev, Sh. S.; *Dokl. Akad. Nauk SSSR* **1974**, *216*, 550 - 553.
32. Ishii, K.; Yamawaki, K.; Ura, T.; Yamamoto, H.; Yoshida, T.; Ogawa, M.; *J. Org. Chem.* **1988**, *53*, 3587 - 3593.
33. Imuta, M.; Ziffer H.; *J. Org. Chem.* **1979**, *44*, 1351-1352.
34. Uzarewicz, A.; Segiet-Kujawa, E.; *Pol. J. Chem.* **1978**, *52*, 63-70.
35. Mastalerz, H.; Morand, P.; *J. Chem. Soc. Perkin Trans 1* **1981**, 154-160.
36. Houminer, Y.; *J. Chem. Soc. Perkin Trans 1* **1975**, 1663-1669.
37. Wasson, R. L.; House, H. O.; *Org. Synth.* **1963**, *Coll. Vol 4*, 552 - 553.
38. Hosoda, H.; Fishman, J.; *J. Am. Chem. Soc.* **1974**, *96*, 7325 - 7329.
39. Camarino, Patelli; *Farmaco Ed. Scient.* **1956**, *11*, 579-585.
40. Tomoeda, M.; Ishida, A.; Koga, T.; *Chem. Pharm. Bull.* **1967**, *15*, 887 - 894.

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