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ASYMMETRIC EPOXIDATION OF NONFUNCTIONALIZED ALKENES WITH HIGH ENANTIOSELECTIVITY USING CHIRAL SULFAMYLOXAZIRIDINES[1]

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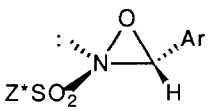
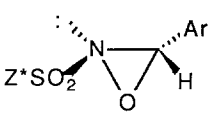
ABSTRACT: High enantioselectivities (19-65% ee) are reported for the asymmetric epoxidation of a series of nonfunctionalized alkenes using chiral sulfamyloxaziridines (1b/2b).

The development of reagents for the asymmetric oxidation of nonfunctionalized alkenes with high enantioselectivities represents a considerable challenge.[2] Low levels of stereoselection (1-8 % ee) are reported for the asymmetric oxidation of alkenes using chiral peracids.[3] Somewhat better results, for selected examples, are obtained with the chiral metal peroxides (up to 35% ee)[4] and the chiral iron porphyrins (up to 51% ee).[5] Enzymatic epoxidations of nonfunctionalized alkenes occurs with high enantioselectivities (70-100 % ee).[6]

We recently described the asymmetric epoxidation of nonfunctionalized alkenes using diastereomeric 2-sulfonyloxaziridines (+)(R,R)-1a and (-)(S,S)-2a (Table, entry 1).[7] The configuration of the oxaziridine three-membered ring controls the product stereochemistry with steric factors being responsible for the chiral recognition.[7] In this communication we report the highest enantioselectivities to date for the asymmetric epoxidation of a series of nonfunctionalized alkenes using 2-[(-)(S)-N-(2-[(-)(S)-N-(α-methylbenzyl)-N-benzyl]sulfamyl-3-(pentafluorophenyl)oxaziridines, (+)(R,R)-1b and (-)(S,S)-2b.



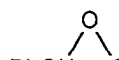
(+) (R,R)-1



(-) (S,S)-2

+ PhCH=CHR

R= H, Me, Ph



+ $Z^*SO_2N{=}CHAr$

a, Z*= (-) 3-bromocamphor, Ar= 2-chloro-5-nitrophenyl
b, Z*= (-) (S) (N-benzyl)-1-phenethylamine, Ar= pentafluorophenyl

2-Sulfamyloxaziridines, 1b/2b, were prepared, as previously reported, by heating equivalent amounts (typically 4.8 mmoles) of (-)(S)-N-(α-methylbenzyl-N-benzylamine)sulfamide[8] and pentafluorobenzaldehyde with 3 mole % Amberlyst 15 ion exchange resin and 5A° powdered molecular sieves, to give an 80% isolated yield of the sulfamylimine ($Z^*SO_2N{=}CHC_6F_5$), mp 99-100 °C (n-pentane); $[\alpha]_D$ -58.8° (c 2.0 $CHCl_3$). Biphasic oxidation of the sulfamylimine, as previously reported,[8] gave a 90 % yield of an approximately 1:1 mixture of the two diastereomeric oxaziridines 1b/2b. Oxaziridines 1b/2b, were separated optically pure by HPLC chromatography.[9,10] The absolute configurations of the oxaziridines three-membered rings in 1b/2b were assigned to the (+)(R,R) and (-)(S,S) configurations, respectively, based on the model of chiral recognition for asymmetric oxidations by 2-sulfonyloxaziridines.[7,8,11,12]

Asymmetric epoxidations were carried out by reacting equivalent amounts (0.5 mmoles) of lb/2b and the alkene in the appropriate solvent. The course of the reaction, monitored by NMR, was complete and nearly quantitative within 48 h at 25 °C. At 60 °C epoxidation was complete within 2 h. Products were isolated by preparative TLC (silica gel) in 60-70% yield. None of the Z-epoxides could be detected, indicating that like 1a/2a, epoxidations using 1b/2b are syn-stereospecific. Optical purities and absolute configurations of the epoxides were determined as previously reported,[7] and are the highest reported for the asymmetric oxidation of nonfunctionalized alkenes. These results are summarized in the Table.

The fact that oxaziridine (+)(R,R)-1b gave epoxides having the R, (R,R) configuration while (-)(S,S)-2b gave epoxides having the S, (S,S) configuration is consistent with a planar transition state geometry, A-B (Figure). These results suggest that, like oxaziridines 1a/2a, the asymmetric induction for the epoxidation of alkenes by 2-sulfamyloxaziridines, 1b/2b, is largely determined by non-bonded steric interactions in the transition state.[8]

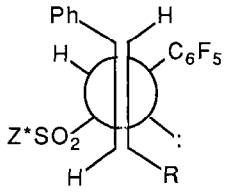
Unlike 1a/1b, however, epoxidations using 2-sulfamylpentafluorophenyloxaziridines, 1b/2b, exhibit modest solvent effects on both the rate of epoxidation and the enantioselectivity. Compared to chloroform, benzene as the solvent slowed the rate of epoxidation to such an extent that styrene and trans stilbene were epoxidized less than 10 % after 80 hr at 25 °C. Acetonitrile increased the rate of epoxidation about two-fold and lowered the enantioselectivity by a factor of two (Table).

While the reasons for these solvent effects are, at present, unclear they seem to be associated with the presence of the pentafluorophenyl group in 1b/2b and the phenyl substituent in the alkenes.[13] This assumption is based on the fact that epoxidation of 1-methylcyclohexene, which lacks a phenyl group, by 1b/2b gave 1-methylcyclohexene oxide in 14.3-l9.4 % optical purity. This is only slightly better than the result observed using 1a/2a (Table).[7] Thus, the high enantioselectivities associated with the phenyl-containing alkenes could result from pi-acid, pi-base interactions via a spiro-C transition state (Figure). However, increasing the size of R in the PhCH=CHR has little effect on the stereoselection. This argues against the spiro-C transition state where the steric interactions between R and Z^*SO_2 become increasingly larger.

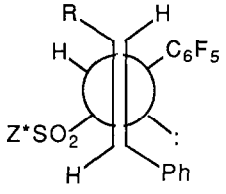
Table: Asymmetric Epoxidation of Alkenes by 2-Sulfamyl-3-(pentafluorophenyl)oxaziridines 1b/2b.

Oxaziridine	Solvent/Temp (°C)	Epoxide % ee (configuration)[a] PhCH=CH$_2$	E-PhCH=CHMe	E-PhCH=CHPh[b]	1-Methyl cyclohexene[c]
(+)(R,R)-1a[a]	$CHCl_3$ (60)	15.9 (R)	27.7 (R,R)	34.9 (R,R)	11.8 (1R,2S)
(-)(S,S)-2a[a]	$CHCl_3$ (60)	15.8 (S)	26.8 (S,S)	30.3 (S,S)	12.7 (1S,2R)
(+)(R,R)-1b	$CHCl_3$ (60)	d	52.5 (R,R)	42.0 (R,R)	
	$CHCl_3$ (25)	44.6 (R)	53.0 (R,R)	49.2 (R,R)	19.4 (1R,2S)
	PhH (25)	e	52.0 (R,R)	e	e
	MeCN (25)	34.2 (R)	32.3 (R,R)	21.0 (R,R)	7.5 (1R,2S)
(-)(S,S)-2b	$CHCl_3$ (25)	61.1 (S)	61.0 (S,S)	56.2 (S,S)	14.1 (1S,2R)
	PhH (25)	e	64.7 (S,S)	e	e
	MeCN (25)	27.3 (S)	27.5 (S,S)	28.5 (S,S)	8.1 (1S,2R)

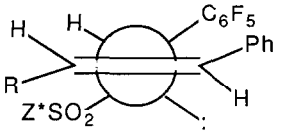
a) Ref. 7. b) % Ee determined using a Daicel Chiral Pak OT (+) HPLC column, 25 cm x 0.46 cm; Solvent, hexane/isopropanol (90/10); Flow rate 0.4 mL/min. First to be eluted was (-)(S,S) enantiomer. c) % Ee determined using Eu(hfc)$_3$. d) Decomposition. e) No reaction at 25 °C.



Planar-A



Planar-B



Spiro-C

Figure: Transition states for the epoxidation of alkenes using oxaziridine (+)(R,R)-1b.

In summary, 2-sulfamyl-3-(pentafluorophenyl)oxaziridines 1b/2b, afford the highest enantioselectivities (50-65 % ee) to date for the asymmetric epoxidation of nonfunctionalized alkenes.

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9. 1b/2b were separated on a Rannin (21.4 mm ID x 25cm L) Dyanmax Silca HPLC column eluting with hexane/methylene chloride (60/40) at a flow rate of 10.75 mL/min, 257 nm; (+)-1b was the first to be eluted. (+)-1b, mp 92-93 °C, $[\alpha]_D$ +22.8° (c 1.6 $CHCl_3$); (-)-2b, mp 105-6 °C, $[\alpha]_D$ -93.2° (c 1.6 $CHCl_3$). Both compounds had NMR and IR spectra consistent with their structures. The NMR spectra of 1b/2b are characterized by the oxaziridine ring protons at δ 5.63 and δ 5.54 ppm, respectively.

10. Additional details of the chemistry of sulfamyloxaziridines will be published elsewhere: Davis, F. A.; McCauley, Jr., J. P.; Chattopadhyay, S., Harakal, M. E.; Watson, W. H.; Tavanaiepour, I, Submitted.

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12. For a review of asymmetric oxidations using chiral 2-sulfonyloxaziridines see: Davis, F. A.; Jenkins, Jr., R. H., in "Asymmetric Synthesis," Morrison, J. D., Ed.; Academic Press: 1984, Vol 4, Chapter 4; pp 313-353.

13. It is known that hexafluorobenzene forms molecular complexes with solvents such as benzene. For a discussion of hexafluorobenzene complexes see: Foster, R. " Organic Charge-Transfer Complexes", Academic Press, New York, 1969; Chapter 10.

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