(SO_2); NMR ($CDCl_3$) δ 10.5 (1 H, br, NH and OH), 7.88 (2 H, d, J = 8 Hz, Ar-H), 7.35 (2 H, d, J = 8 Hz, Ar-H), 6.48 (1 H, s, Ar-H), 4.84 (1 H, d, J = 2 Hz, J = 1 Hz, N-CH-O), 4.5–3.3 (6 H, m, CH_2), 2.52 (3 H, s, CH_3), 2.43 (3 H, s, CH_3), 2.21 (3 H, s, CH_3); UV λ_{max} (EtOH) (ϵ) 227 (16 100), 316 (10 100), 400 nm (4490).

Reduction of 1a with Sodium Hydrosulfite. To a solution of **1a** (100 mg) in $CHCl_3$ (20 mL) was added a solution of sodium hydrosulfite (350 mg) in H_2O with stirring. After 30 min, the red–purple mixture became colorless. The chloroform layer was dried over anhydrous Na_2SO_4 and evaporated to dryness. Recrystallization of the residual solid from C_6H_6 gave 62 mg (57%) of 3,6-dihydroxy-4-methyl-2-pyrrolidinoacetophenone tosylhydrazone (**9a**) as colorless crystals: mp 125–126 °C; IR ν_{max} (KBr) 3440 (OH), 3180 (NH), 2960 (CH), 1625 (C=N), 1600, 1160 (SO_2), 675 cm^{-1}; NMR (acetone-d_6) δ 9.0 (1 H, br, NH), 7.66 (2 H, d, J = 8 Hz, Ar-H), 7.24 (2 H, d, J = 8 Hz, Ar-H), 6.37 (1 H, s, Ar-H), 2.92 (6 H, m, 2OH, 2 CH_2), 2.34 (3 H, s, CH_3), 2.17 (3 H, s, CH_3), 2.09 (3 H, s, CH_3), 1.72 (4 H, m, 2 CH_2); UV λ_{max} (ϵ) 309 nm (5200). Anal. Calcd for $C_{20}H_{25}O_4N_3S \cdot C_6H_6$: C, 62.42; H, 6.38; N, 9.50. Found: C, 62.34; H, 6.41; N, 9.46.

From TLC analysis, this compound (**9a**) was not produced by thermolysis and photolysis of **1a**.

Reduction of 1b with Sodium Hydrosulfite. This reaction was carried out in the same procedure as described above. Recrystallization of the crude product gave 49 mg (49%) of 3,6-dihydroxy-4-methyl-2-piperidinoacetophenone tosylhydrazone (**9b**) as colorless crystals: mp 168 °C; IR ν_{max} (KBr) 3480 (OH), 3225 (NH), 2940 (CH), 1625 (C=N), 1600, 1165 (SO_2), 1090, 750, 715 cm^{-1}; NMR (acetone-d_6) δ 9.18 (1 H, br, NH), 7.70 (2 H, d, J = 8 Hz, Ar-H), 7.34 (2 H, br, 2OH), 7.24 (2 H, d, J = 8 Hz, Ar-H), 6.36 (1 H, s, Ar-H), 2.62 (4 H, br, $2CH_2$), 2.36 (3 H, s, CH_3), 2.18 (3 H, s, CH_3), 2.08 (3 H, s, CH_3), 1.46 (6 H, m, $3CH_2$).

Reduction of 1c with Sodium Hydrosulfite. This reaction was carried out in the same procedure as described above. Recrystallization of the crude product from C_6H_6 gave 55 mg (55%) of 3,6-dihydroxy-4-methyl-2-morpholinoacetophenone tosylhydrazone (**9c**) as colorless crystals: mp 205 °C dec; IR ν_{max} (KBr) 3450 (OH), 3250 (NH), 1620 (C=N), 1600, 1415, 1160 (SO_2), 1100, 870, 715 cm^{-1}; NMR (acetone-d_6) δ 9.4 (1 H, br, NH), 7.84 (2 H, d, J = 8 Hz, Ar-H), 7.40 (2 H, d, J = 8 Hz, Ar-H), 6.54 (1 H, s, Ar-H), 3.56 (4 H, t, J = 4 Hz, $2CH_2$), 2.88 (2 H, br, 2 OH), 2.73 (4 H, t, J = 4 Hz, $2CH_2$), 2.41 (3 H, s, CH_3), 2.25 (3 H, s, CH_3), 2.15 (3 H, s, CH_3).

As shown in Tables I and II, **9b** and **9c** were also obtained by thermolysis and photolysis of **1b** and **1c**, respectively.

Acknowledgment. Our sincere thanks are offered to Professor S. Ohki for his continuous interest and encouragement on this work.

Registry No.—**7a**, 64269-21-2; **9a**, 67542-38-5.

References and Notes

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Nuclear Magnetic Resonance Determination of Absolute Configuration and Enantiomeric Compositions of Chiral Oxaziridines Using Chiral Solvating Agents

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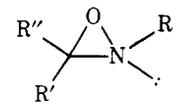
Simultaneous determinations of enantiomeric composition and absolute configuration of chiral oxaziridines (1) are possible by a convenient NMR–chiral solvating agent method. Addition of chiral fluoro alcohols such as 2,2,2-trifluoro-1-(9-anthryl)ethanol (**2a**) to 1 causes the enantiomers of 1 to have nonidentical NMR spectra. This spectral nonequivalence arises as a consequence of the formation of short-lived chelate-like diastereomeric solvates in which the stereochemical disposition of the oxaziridine substituents (with respect to the anthryl group of **2a**) causes the observed anisochronicity of the enantiotopic groups. Evidence is presented that the primary solvation interaction is hydroxyl hydrogen bonding at the ring nitrogen. Weaker carbinyl hydrogen bonding to the ring oxygen or, if present, to aryl ring substituents cis to the nitrogen lone pair of electrons completes the chelation. Coupled with knowledge of the absolute configuration of **2a**, the solvation models allow assignment of absolute configuration to a variety of oxaziridines from the observed "senses of nonequivalence". Enantiomeric compositions are determined by measuring relative intensities of the enantiotopic groups anisochronous resonances.

Oxaziridines (1) have recently received considerable attention as a consequence of the high barrier to inversion and asymmetry at the nitrogen center.[1] Since there are no known



1a, R′ = CH_3; R″ = H; R = *t*-Bu

stereoselective reactions of 1 so as to allow conversion to compounds of established stereochemistry, the first assignments of absolute configuration for oxaziridines were reported only recently on the basis of X-ray structure analysis.[2,3] Subsequently, a claim of configurational correlation with the sign of molecular rotation was made.[4]

We noted earlier that enantiomeric purity of oxaziridines can generally be determined by NMR, using chiral solvating

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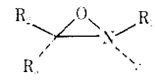
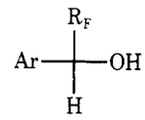
Table I. Coordination Site of Lanthanide Shift Reagents in Oxaziridines



compd	R_1	R_2	R_3	coordination site
1b	*tert*-butyl	H	H	oxygen
1s	*tert*-butyl	H	4-methylphenyl	oxygen
1t	methyl	H	4-methylphenyl	oxygen
1u	methyl	4-methylphenyl	H	nitrogen
1v	methyl	$-CH_2CH_2CH(C(CH_3)_3)CH_2CH_2-$		nitrogen

agents (CSA), and suggested that absolute configurations might potentially be similarly determined.[1] This potential has been realized, and we herein report the experimental data on which the configurational assignment technique is based.

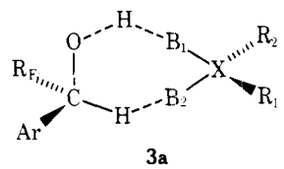
Chiral fluoro alcohols of the general class **2** cause the NMR spectra of oxaziridine enantiomers to differ. For example,



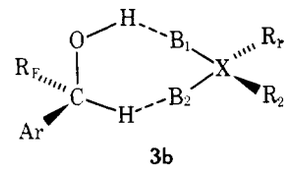
2a, Ar = 9-anthryl; $R_F = CF_3$
b, Ar = 9-(10-methylanthryl); $R_F = CF_3$
c, Ar = 9-(10-bromoanthryl); $R_F = CF_3$
d, Ar = phenyl; $R_F = CF_3$

when (−) enriched 2-*tert*-butyl-3-methyloxaziridine (**1a**) was examined in the presence of (*R*)-(−)-**2b**, separate *tert*-butyl singlets, methyl doublets, and carbinyl quartets were observed for each enantiomer.[1] The *tert*-butyl signal of the major enantiomer is downfield of that from the minor enantiomer (downfield sense of nonequivalence), whereas the remaining doublet and quartet signals show the reverse sense of nonequivalence. Enantiomeric composition could be judged from the relative intensities of the doubled sets of signals.

Type **2** CSA induce enantiomeric spectral nonequivalence in a variety of solutes owing to the formation of short-lived chelate-like diastereomeric solvates **3a** and **3b**. In **3a**, R_1 is

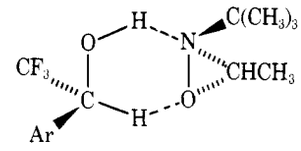


3a

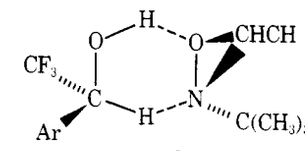


3b

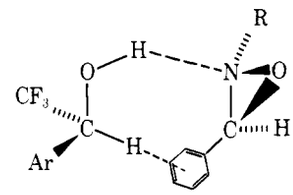
shielded by the aryl substituent to a greater degree than is R_1 in solvate **3b**. The converse is true for the enantiotopic R_2 groups. Alkyloxaziridines have the requisite basic sites (oxygen and nitrogen) to form similar chelate-like solvates. However, assignment of absolute configuration from the observed senses of nonequivalence is dependent upon which ring heteroatom of **1** is chosen as the site of primary hydrogen bonding (e.g., **4a** vs. **4b**). Because we could not state a priori which of the two heteroatoms would be the site of the primary hydrogen bonding interaction,[5] absolute configurations were not assigned to the oxaziridines initially studied. The presence of aryl substituents further complicates interpretation of spectral nonequivalence since chelation as described by **5a** and **5b** might also occur. Attempts were made to determine the prevalent solvation mode of **2a** by an NMR study of the few configurationally known oxaziridines. Originally, these studies were fruitless. However, the absolute configurations of two of these oxaziridines have recently been reassigned,[3] and a pattern of correspondence between observed senses of nonequivalence and absolute configurations is now more evident. This pattern, in conjunction with other data, persuades us that we can describe the NMR-significant solvation behavior of type **2** fluoro alcohols toward numerous oxaziridines.



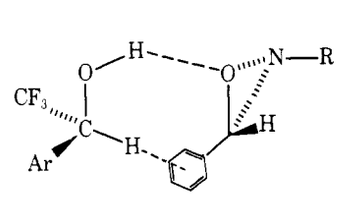
4a



4b



5a



5b

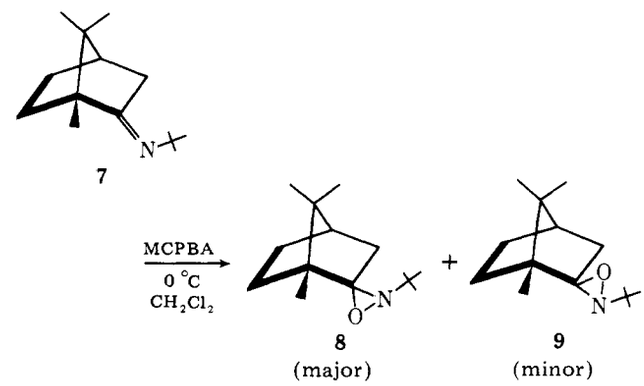
Results and Discussion

Binding of Lanthanide Shift Reagents to Oxaziridines. Typically, lanthanide shift reagents (LSR) and fluoro alcohols such as **2** seem to select the same basic sites in molecules for preferential interaction.[6] By identifying the binding site of LSR in oxaziridines (i.e., oxygen vs. nitrogen), one would presumably determine the principle hydrogen bonding site and thus determine whether **4a** or **4b** represents the predominant solvation mode.

The study of a series of oxaziridines revealed that the LSR binding site is nitrogen for unhindered oxaziridines, but changes to oxygen when bulky substituents are borne either by nitrogen or by the ring carbon, provided that the latter are syn to the nitrogen lone pair of electrons (**1b**, **1s**, and **1t**; Table I). The importance of steric effects in LSR binding is evident from the results of a competition experiment between *cis*-**1u** and *trans*-**1t**. The binding to the cis isomer is clearly much greater in magnitude; while **1u** resonances are shifted, the resonances of **1t** are immobile until the amount of LSR added exceeds the amount of **1u** present.

In so far as the steric requirements of the hydroxyl group on **2** are much less stringent than those of the lanthanide in an LSR, the fluoro alcohol will be much less sensitive to the nature of the nitrogen and carbon substituents. Although it seemed safe to assume that **2** preferentially hydrogen bonds to nitrogen, the more basic of the two heteroatoms, we tested this hypothesis by synthesis and study of an alkyloxaziridine of known absolute configuration.

Reduction of camphor by hydride reagents affords a mixture of exo and endo alcohols in a ratio depending upon the solvent and bulk of the reducing agent. The major product is always the exo alcohol since it is formed by hydride attack at the least hindered face of the camphor system.[7,8] This same argument should be applicable to oxidation of camphorimine



7 → (MCPBA, 0 °C, CH_2Cl_2) → **8** (major) + **9** (minor)

Table II. Properties of Oxaziridines from MPCA Oxidation of Imines

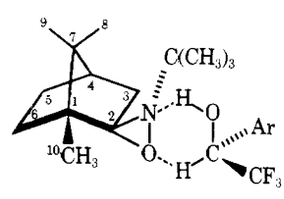
compd	R_1	R_2	R_3	chemical shift in CCl_4, δ R_1	R_2	R_3	CSA	nonequivalence,[a] Hz[b]/sense[c] R_1	R_2	R_3	Enantiomeric excess (%) by NMR	$[\alpha]^{27}_D$, deg	$[\alpha]^{27}_D$ max, deg
1a	*t*-Bu	H	CH_3	1.07	4.00 q	1.37	**2c**	7.5/H	3.0/L	15.0/L	14	−55.19[f]	−37.1
1b	*t*-Bu	H	H	1.03	3.62 AB	3.62	**2b**	9.0/H	35.0/L	30.0/L	6	−2.07	−34.5
1c	*i*-Pr	H	CH_3	1.06	3.61 q	1.32	**2b**			4.6/–	2	0	
				1.16				8.5/–				(neat)	
				1.99									
1d	*i*-Pr		$-(CH_2)_5-$	1.15	1.4–2.4		**2b**	14.1/H			14	−4.37	−31.2
				1.00				3.2/H					
				3.62				1.6/H					
1e	C_2H_5		$-(CH_2)_5-$	1.17	1.4–2.4		**2b**	15.5/H			8	−5.74	−71.7
				2.63									
				2.76									
1f	CH_3		$-(CH_2)_5-$	2.43	1.3–2.0		**2b**	11.0/H			14	−5.39	−38.5
1g	*t*-Bu	H	*i*-Pr	1.02	3.45 d	0.97 d	**2c**	23.0/H	14.0/H	47.0/L	40	−13.05[f]	−32.6
						0.92 d				35.0/L		(neat)	
						1.53 d of sept							
1h	*t*-Bu	H	3-cyclohex-enyl	1.03	3.58 d	1.2–1.3 m	**2c**	9.6/H			58	−20.12[f]	−34.7
						5.61 m							
1i	*t*-Bu	H	benzyl	0.96	3.83 dd	7.18	**2c**	5.5/H	2.0/L	3.0/L	20	−2.44[f]	−12.2
						2.82				14.0/L			
						2.74				12.5/L			
1j	*t*-Bu	H	C_6H_5	1.05	4.63 s	7.1–7.6	**2b**	6.7/L	0		26	−22.3	−85.6
1k	*t*-Bu	H	*p*-BrC_6H_5	1.12	4.35 s	7.40	**2c**	2.2/L	0	3.0/L	60	−44.6[f]	−74.3
1l	*t*-Bu	H	*p*-$NO_2C_6H_5$	1.14	4.62	7.84	**2c**	3.5/L	0	3.0/L	25	−30.9	−124.0
1m	*t*-Bu	H	*p*-MeOC-$_6H_5$	1.10	4.44	3.72	**2c**	4.5/L	0.5/L	0.5/L	20	−17.8	−89.0
						7.00				4.0/L			
1n	*t*-Bu	H	α-naphthyl	1.20	5.16	7.1–8.2	**2c**	6.0/L			51	*f*	
1o	CH_3	H	C_6H_5	2.80	4.25	7.27	**2c**	2.5/L	1.5/L		40	*f*	
1p	CH_3	C_6H_5	H	2.34	7.32	5.02	**2c**	8.5/H		12.0/L	12	*f*	
1q	*i*-Pr	H	C_6H_5	1.13 d	4.26	7.29	**2c**	0	0			*f*	
				1.27 d									
				2.23 sept									
1r	*i*-Pr	C_6H_5	H	0.68 d	7.36 m	4.26	**2c**	8.0/H		12.0/L	35	*f*	
				1.17 d				5.0/H					
				2.20 sept									

[a] Nonequivalence was caused by adding ca. a 3-fold excess of (*S*)-(+)-**2b** or (*S*)-(+)-**2c** to a dilute carbon tetrachloride solution of oxaziridine; all absolute configurations were determined to be *S* at nitrogen. [b] At 100 MHz and 25 °C. [c] H refers to highfield sense and L to lowfield sense. [d] Rotations, unless otherwise specified, were taken in CCl_4 using concentrations of ca. 3%; *cis*-oxaziridines were obtained as mixtures with the corresponding trans isomers, and rotations of these mixtures were not obtained. [e] Obtained as a 1.2:1 mixture of **1o/1p.** After heating for 4 h at 100 °C, a 2.5:1 ratio of **1o/1p** was obtained. [f] See Experimental Section for preparation of oxaziridines.

7. A sample of **7** obtained from 30% enriched (+)-camphor was oxidized with *m*-chloroperoxybenzoic acid (MCPBA) in dichloromethane. Only one oxaziridine isomer could be detected by NMR (>95%), similar to the observation made by Mostowicz and Belžecki for the *n*-propyl analogue of **8.**[4] NMR examination of **8** in the presence of (*S*)-(+)-**2d** shows opposite senses of nonequivalence for the *N-tert*-butyl (highfield) and 10-methyl (lowfield) resonances. This result indicates that primary hydrogen bonding occurs at nitrogen, as depicted in Chart I, in accordance with the conclusions made from the LSR experiments.

Knowledge of the site of primary hydrogen bond formation enables the assignment of absolute configuration by the NMR–CSA method to the kinetically favored enantiomer of a wide variety of partially resolved oxaziridines prepared by oxidation of imines with (+)-monoperoxycamphoric acid (MPCA, **6**). For simplicity of discussion, these oxaziridines will be divided into two categories: oxaziridines bearing only hydrogen or alkyl ring substituents, and oxaziridines bearing aryl ring substituents.

Chart I. Solvation of **8** by (*S*)-(+)-**2c**



Assignment of Absolute Configuration for Alkyloxaziridines. Note from Table II that all 3-(alkyl-substituted)-oxaziridines(**1a–h**) exhibit a highfield sense of nonequivalence for the 2 substituent, and in most instances (where observable)[9] a lowfield sense of nonequivalence for the 3 substituent. Compound **1i,** bearing a benzyl substituent, also falls into this category. Treating nitrogen as the site of primary interaction and using solvation mode **4a,** the *S* configuration at nitrogen is assigned for oxaziridines **1a–i.** The *trans*-oxaziridines among these examples must therefore have the *S* configuration at the ring carbon. A certain degree of additional support for these assignments stems from the observed negative optical rotations since it has been postulated that oxaziridine rings having the *S* configuration at nitrogen provide a negative contribution to the optical rotation of the compound.[4]

Table III. Oxidation of (*R*)- and (*S*)-4-Bromo-*N*-benzylidene-1-phenylethylamine (10)

				ratio of products[b]							
				trans				cis			
entry	absolute configuration of imine	registry no.	oxidation conditions[a]	**11** 4.33[c] *SRR*/*RSS*[d]	registry no.	**12** 4.35[c] *SSS*/*RRR*[d]	registry no.	**13** 5.00[c] *SRS*/*RSR*[d]	registry no.	**14** 5.15[c] *SSR*/*RRS*[d]	registry no.
1	*S*	67463-03-0	MPCA/−78 °C	54/–	60143-68-2	33/–	60183-42-8	9/–	60183-44-0	4/–	60183-43-9
2	*S*		MCPBA/0 °C	61/–		21/–		13/–		5/–	
3	*R*	67463-04-1	MPCA/−78 °C	–/61	63864-70-0	–/7	63813-97-8	–/28	63864-71-1	–/4	63813-98-9
4	*R*		MCPBA/0 °C	–/58		–/20		–/16		–/6	

[a] Solvent was $CHCl_3$–CH_2Cl_2 (4:1). [b] Determined by NMR of crude reaction mixture. [c] ($CDCl_3$) of oxaziridine ring proton. [d] Configurations of the chiral N substituent, nitrogen center, and carbon center, respectively.

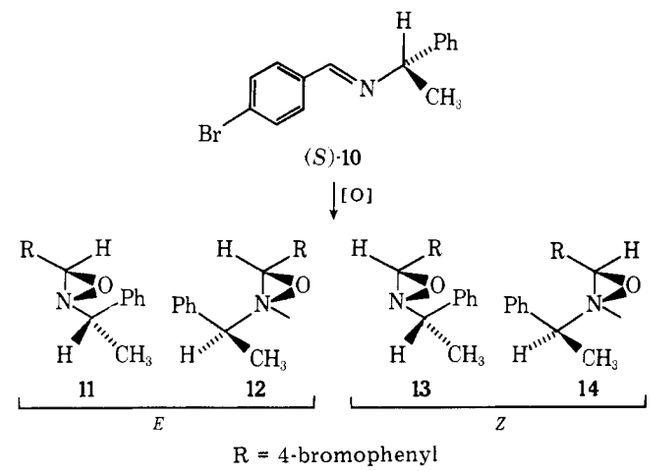
Assignment of Absolute Configuration for Aryloxaziridines. Table II shows that the *trans*-3-aryloxaziridines have *N*-alkyl nonequivalence senses opposite those of the similarly prepared 3-alkyloxaziridines. This raises several questions: (1) are the aryl substituents changing the relative basicities of oxygen and nitrogen, (2) is the chiral oxidizing agent producing oxaziridines having the opposite configuration at nitrogen, or (3) are the aryloxaziridines showing nonequivalence as a result of a different type of solvation (e.g., **5a** or **5b**)? Since unhindered aryl-substituted oxaziridine **1v** coordinates to an LSR at nitrogen (Table I), we can be relatively confident that aryl substituents cause no inversion in relative basicity of the nitrogen and oxygen.

The second of these questions is answered by additional experimental data. First, liquid crystal induced circular dichroism[12] supports the contention that alkyl- and aryloxaziridines formed by asymmetric oxidation with MPCA all have the same predominant absolute configuration at nitrogen.[13] Secondly, the uniformly negative specific rotations are consistent with uniform *S* configurations at nitrogen.[4] The apparent uniformity of asymmetric induction sense by MPCA seems related to the size of the C substituent of an aldimine. As the size of the substituent increases, H < CH_3 < $CH(CH_3)_2$ < benzyl < 3-cyclohexenyl (**1a, 1b, 1i, 1g,** and **1h,** respectively), the extent of asymmetric induction increases (6, 14, 20, 40, and 58% ee, respectively). The C aryl-substituted oxaziridines fit smoothly into this pattern (**1j,** 61% ee and **1k,** 60% ee) since 3-cyclohexenyl and phenyl groups are presumably of similar sizes.

One additional argument can be advanced to support the contention that MPCA has a uniform bias in favor of oxaziridines having the *S* configuration at nitrogen.

The absolute configurations of the diastereomers **11–14,** obtained from oxidation (Scheme I) of (*S*)-*N*-*p*-bromobenzylidene-1-phenylethylamine (**10**) with achiral MCPBA, have been assigned.[3] If chiral MPCA has a consistent intrinsic stereochemical bias, it should be obvious from the resultant change in the ratio of diastereomers **11–14** afforded upon oxidation of imine **10.** Oxidation of (*S*)-**10** with (+)-MPCA affords a lesser amount of oxaziridine having the *R* configuration at nitrogen than does the oxidation with MCPBA (compare entries 1 and 2, Table III). However, oxidation of (*R*)-**10** with (+)-MPCA affords considerably more oxaziridine having the *S* configuration at nitrogen than does MCPBA (entries 3 and 4, Table III). Although the Two MCPBA oxidations are mirror image experiments and should yield identical product ratios, the two MPCA experiments are diastereomeric and may yield rather different results. If the results from the two MCPBA experiments are averaged, it is found that the chiral substituent produces a 73:27 bias in favor of the configuration at nitrogen that is opposite to that of the chiral substituent.[2,10] The much greater preference for the *S* configuration at nitrogen shown by one MPCA oxidation (89:11, entry 4) relative to its diastereomeric counterpart's preference for the *R* configuration (63:37, entry 1) is taken to indicate the stereochemical bias of MPCA for formation of aryloxaziridines having the *S* configuration at nitrogen. This result pertains to both the cis and trans isomers, in accordance with the findings of Boyd et al.[11] that MPCA produces *cis*- and *trans*-aryloxaziridines with the same configuration at nitrogen.

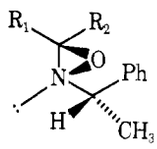
Scheme I



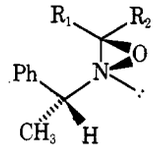
R = 4-bromophenyl

The preceding arguments weigh heavily in favor of the 3-aryloxaziridines in Table II all having the *S* configuration at nitrogen. Accepting this, the solvation mode that accounts for the observed senses of nonequivalence of the trans isomers is that shown in **5a,** where the primary hydrogen bond occurs at nitrogen and the secondary interaction is at phenyl, a type of secondary interaction for which there is ample precedent. This model accounts for the same senses of nonequivalence shown by the *N*-alkyl and methine hydrogens of the *trans*-3-aryloxaziridines. Presumably, aryl groups syn to the nitrogen lone pair block access to the oxygen but offer a readily acceptable substitute site for the secondary interaction. However, for the *cis*-3-aryloxaziridines, the anti relationship of the nitrogen lone pair of electrons and the aryl π system precludes solvation mode **5a.** Hence, the *cis*-3-aryloxaziridines behave as do the alkyl-substituted oxaziridines; solvation mode **4a** accounts for the senses of nonequivalence shown by **1p** and **1r** and affords the *S* configurational assignment at nitrogen for both compounds.

***N*-(1-Phenyl)ethyloxaziridines.** Finally, we return to the study of configurationally known oxaziridines **15–23.** Ob-



15, R_1 = 4-BrC_6H_4; R_2 = H
17, R_1 = H; R_2 = 4-BrC_6H_4
19, R_1 = R_2 = C_6H_5
21, R_1 = R_2 = CH_3
23, R_1 = R_2 = H



16, R_1 = H; R_2 = 4-BrC_6H_4
18, R_1 = 4-BrC_6H_4; R_2 = H
20, R_1 = R_2 = CH_3
22, R_1 = R_2 = H

served nonequivalence senses and magnitudes are given in Table IV for these oxaziridines prepared from 50% *S*-(−)-enriched 1-phenylethylamine. The presence of additional phenyl substituents complicates the interpretation of NMR spectral data owing to the basicity and diamagnetic anisotropy associated with these substituents. In **17** and **18**, the ring aryl substituent is anti to the nitrogen lone pair of electrons and cannot serve as the site of secondary interaction. While contemplating the consequences of solvation mode **4a** for this pair of diastereoisomers, one finds that while all observed senses of nonequivalence for **18** fit this model, only one of two observed senses of nonequivalence for **17** is in accordance with this model. Although we tend to dismiss the significance of this last aberration,[14] it could not have been anticipated. Diastereomers **15**, **16**, and **19** have aryl substituents syn to the nitrogen lone pair of electrons and could utilize the syn C-aryl substituent as a secondary binding site, undergoing solvation as depicted in **5a**. This type of solvation rationalizes the highfield senses of nonequivalence shown by **16** but breaks down for **15** and **19**. Again, we can only point out the complications that arise with these particular diastereomers.[14] Proceeding to the less complicated oxaziridines **20–23**, we find that both pairs of diastereomers show opposite senses of nonequivalence for the nitrogen and ring carbon substituents and that inverting the configuration at nitrogen inverts the senses of nonequivalence. This is exactly in accordance with expectations derived from employment of solvation model **4a**. It is on this basis that the nitrogen absolute configurations implicit in the drawings of **20–23** were assigned.

The assignment of absolute configuration to oxaziridines **20–23** is relevant to a prior suggestion by Italian workers[2] that achiral peracid oxidation of an imine derived from (*R*)-(+)-1-phenylethylamine would preferentially afford the oxaziridine having the *S* configuration at nitrogen. In the case of the diastereomeric pair **20–21**, the kinetic preference shown by MCPBA (0 °C, methylene chloride) is 39:61 (NMR, crude reaction mixture) in favor of the *R* configuration at nitrogen. However, the diastereomeric pair **22** and **23** ($[\alpha]^{25}D$ (*c* 3, $CHCl_3$) −72 and +65°, respectively) is formed in a 60:40 ratio in favor of the *S* configuration at nitrogen. This configurational assignment can also be made from the rotational data.[4]

Conclusions

On the basis of the solvation models herein proposed to account for the enantiomeric spectral nonequivalence shown by oxaziridines in the presence of chiral type **2** alcohols, absolute configurations and enantiomeric purities of oxaziridines can now be determined simultaneously. While this method does not necessarily directly afford the absolute configuration of the ring carbon (should it be chiral), knowledge of the relative configurations at carbon and nitrogen *and the absolute configuration at nitrogen* does provide this information.

This method for assigning absolute configurations to oxaziridines does have limitations in that oxaziridines having additional basic sites may depart from the "normal" model. In such instances, caution must be exercised in using the model to assign absolute configurations, particularly if the "opposite sense of nonequivalence" hallmark is not observed.

Table IV. NMR Data for Enantiomerically Enriched *N*-(1-Phenyl)ethyloxaziridines[a]

	chemical shifts in CCl_4, δ				nonequivalence,[b] Hz[c]/sense[d] in (*R*)-(−)-**2c**			
compd	R_1	R_2	H	CH_3	R_1	R_2	H	CH_3
15		4.50	3.37	1.62		3.5/H		2.7/H
16	4.56		3.25	1.45	0.7/H		2.5/H	7.0/H
17	5.10		3.26	1.55	7.5/H			17.5/H
18		5.21	3.26	1.04		25.0/H		15.0/L
19			3.13	1.58			7.0/H	10.2/H
20	1.55	1.39	3.57	1.30	5.0/H	15.5/H		5.8/L
21	1.27	1.34	3.57	1.49	15.0/L	2.5/L		5.0/H
22	4.07	3.67	3.04	1.46	16.0/H	7.0/H		7.0/L
23	3.60	3.89	2.90	1.62	~0	5.0/L		10.2/H

[a] Obtained from *S*-enriched imines (ca. 50% ee) by oxidation with MCPBA in CH_2Cl_2 at 0 °C. [b] Nonequivalence was caused by addition of a 5–10-fold excess of (*R*)-(−)-**2c** to dilute CCl_4 solutions of the oxaziridines. [c] At 220 MHz and 25 °C. [d] H refers to highfield sense and L to lowfield sense.

Experimental Section

Melting points were determined on a Büchi apparatus. All melting points and boiling points are uncorrected. NMR spectra were recorded on Varian A-60, A56/60, EM-390, HA-100, and HR-220 spectrometers at 27–30 °C. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. Mass spectra were obtained on a Varian MAT CH-5 spectrometer, and IR spectra were obtained on a Beckman IR-12. Elemental analyses were performed by Mr. J. Nemeth and associates, University of Illinois.

NMR determinations of enantiomeric purity were performed using a 2- to 5-fold molar excess of **2** to the oxaziridine dissolved in CCl_4. Relative peak area measurements were performed by relative height measurements and by the cut and weigh method.

Oxaziridines. Oxaziridines were prepared by peracid oxidation of the corresponding imines.[1] All of the oxaziridines mentioned have previously been reported,[15–18] with the exception of **1a, 1h, 1i, 1n,** and **8**. Only the enantiomeric excesses of oxaziridines footnoted in Table II are directly comparable since only these were obtained using one pure isomer of MPCA.[19]

2-*tert*-Butyl-3-methyloxaziridine (1a). This compound is a clear, colorless liquid: bp 55–56 °C (110 mm); NMR (CCl_4) δ 1.07 (s, 9 H, *t*-Bu), 1.37 (d, *J* = 4.5 Hz, 3 H, CH_3), 4.00 (q, *J* = 4.5 Hz, 1 H, CH); IR (neat) 2860–3040, 1420, 1390, 1370, 1280, 1250, 1210, 1125, 1040, 800, 820, 740, 700 cm^{-1}; MS (70 eV) *m/e* (relative intensity) 115 (0.1), 57 (100), 41 (47.9), 29 (38.8).

2-*tert*-Butyl-3-(3-cyclohexenyl)oxaziridine (1h). This compound was obtained as a clear, colorless liquid by molecular distillation (80 °C, 2 mm): NMR (CCl_4) δ 1.03 (s, 9 H, *t*-Bu), 1.2–2.3 (m, 7 H, cyclohexyl), 3.58 (d, *J* = 6.0 Hz, 1 H, OCHN), 5.61 (broad s, 2 H, -HC=CH-); IR (neat) 3040, 2980, 2940, 2860, 1655, 1400–1500, 1390, 1370, 1260, 1210, 1140, 1040, 920,750, 720, 660; MS (70 eV) *m/e* (relative intensity) 181 (0.1), 80 (15.5), 57 (100), 41 (34.1), 29 (18.5).

2-*tert*-Butyl-3-benzyloxaziridine (1i). This compound is a clear, colorless liquid: NMR (CCl_4) δ 0.96 (s, 9 H, *t*-Bu), 2.82 and 2.74 (d of AB pattern, 2 H, CH_2), 3.83 (d of d, 1 H, OCHN), 7.18 (m, 5 H, Ar); IR (neat) 3060, 3020, 2980, 2940, 1600, 1500, 1460, 1390, 1370, 1270, 1220, 1080, 1030, 950, 750, 700 cm^{-1}; MS (70 eV) *m/e* (relative intensity) 191 (1.57), 135 (17.5), 91 (12.5), 77 (6.4), 57 (100), 41 (22.0), 29 (13.4).

2-*tert*-Butyl-3-(1-naphthyl)oxaziridine (1n). This compound is a clear oil: NMR (CCl_4) δ 1.20 (s, 9 H, *t*-Bu), 5.16 (s, 1 H, OCHN), 7.1–8.2 (m, 7 H, Ar); IR (neat) 3070, 2980, 2940, 1600, 1560, 1515, 1480, 1460, 1390, 1370, 1340, 1260, 1240, 1200, 1135, 805, 785; MS (70 eV) *m/e* (relative intensity) 227 (3.0), 171 (33.2), 127 (21.2), 57 (100), 41 (23.7), 29 (16.6).

Chiral Solvating Agents (2). The fluoro alcohols used in this study were synthesized and resolved by a procedure analogous to that reported previously for **2a**.[20] The syntheses, resolutions, and assignments of absolute configuration of **2a–c** have been reported.[21]

(1*R*,4*R*)-*N*-(1,7,7-Trimethylbicyclo[2.2.1]heptylidene)-*tert*-butylamine (7). This compound was prepared by the method of Moretti and Torre.[22] Camphor (15.2 g, 0.10 mol) enriched (33%) in the (+)-1*R*,4*R* isomer, *tert*-butylamine (21.9 g, 31.3 mL, 0.60 mol),

and 500 mL of benzene (distilled over sodium) were placed in an oven-dried 2-L three-neck round-bottom flask equipped with a 500 mL addition funnel, condenser, nitrogen inlet, and overhead stirrer. $TiCl_4$ (9.5 g, 5.5 mL, 0.05 mol) in 100 mL of benzene was added to the reaction mixture with stirring at 0 °C. The mixture was allowed to warm to room temperature over a 5-h period and then was heated at reflux. After several days, a white precipitate began to form. After a reaction period of 3 weeks, IR spectroscopy indicated the absence of carbonyl absorption. The mixture was cooled and filtered, and the solvent was removed. The residue was crystallized from hexane to yield 5.0 g of a tan solid: NMR ($CDCl_3$) δ 0.O7, 1.00, and 1.63 (s, 3 H each, CH_3), 1.71 (s, 9 H, $C(CH_3)_3$), 1.08–2.33 (m, 5 H, $-CH_2CH_2CH$), 2.56 (AB pattern, 1 H, J_{AB} = 19.5 Hz, 1 H, *endo*-HCHC=N), 3.16 (d of AB pattern, J_{AB} = 19.5 Hz, J = 6.0 Hz, 1 H, *exo*-HCHC=N); IR (KBr) 3180, 3040, 2800–3000, 1670, 1445, 1400, 1375, 1250, 1200, 950, 900, 780 cm^{-1}; MS (10 eV) *m/e* (relative intensity) 207 (56.4), 192 (58.5), 150 (44.2), 136 (22.9), 109 (100), 57 (94.8), 36 (30.9).

2-*tert*-Butyl-3-[(1*R*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]hept-yl]oxaziridine (8). *m*-Chloroperoxybenzoic acid (607 mg, 3.0 mmol) in CH_2Cl_2 was added over 30 min to a solution of **7** (500 mg, 2.4 mmol) in CH_2Cl_2 at 0 °C. The mixture was stirred for 4 h at 0 °C, filtered, and extracted twice with 10% Na_2CO_3. The organic layer was dried (K_2CO_3), and the solvent was removed under vacuum to yield a yellow oil: NMR (CCl_4) δ 0.82, 0.07, and 0.91 (s, 3 H each, CH_3), 1.17 (s, 9 H, *t*-Bu), 1.1–2.5 (m, 7 H, $-CH_2CH_2CHCH_2-$); MS (70 eV) *m/e* (relative intensity) 223 (11.6), 208 (16.5), 167 (26.0), 150 (22.6), 57 (100), 41 (69.2), 29 (26.9).

Acknowledgment. This work was partially supported by grants from the National Science Foundation and the National Institutes of Health.

Registry No.—**1a,** 62107-41-9; **1b,** 63017-52-7; **1c,** 67425-86-9; **1d,** 67425-87-0; **1e,** 67425-88-1; **1f,** 63017-53-8; **1g,** 67504-37-4; **1h,** 67425-89-2; **1i,** 67425-90-5; **1j,** 63087-57-0; **1k,** 62058-74-6; **1l,** 59905-68-9; **1m,** 67504-72-7; **1n,** 67425-91-6; **1o,** 67462-99-1; **1p,** 67463-00-7; **1q,** 67463-01-8; **1r,** 67463-02-9; **1s,** 67425-83-6; **1t,** 67425-84-7; **1u,** 67462-98-0; **1v,** 67425-85-8; (*S*)-(+)-**2b,** 63017-54-9; (*S*)-(+)-**2c,** 59153-46-7; (*R*)-(−)-**2c,** 67425-97-2; **7,** 67425-95-0; **8,** 67425-96-1; **19,** 64954-02-5; **20,** 56907-09-6; **21,** 67425-92-7; **22,** 67425-93-8; **23,** 67425-94-9.

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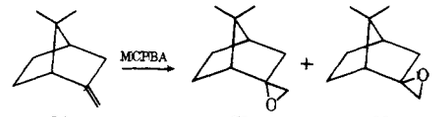

24 25 26

84%, endo 16%, exo

(9) Presumably, **1g** deviates from this behavior because the nonequivalence arises from differential isopropyl rotamer populations for the diastereomeric solvates and actually stems from internal magnetic anisotropy rather than from that of **2.** The magnitude of this type of nonequivalence is usually small relative to that having the usual origin. This phenomenon is most apt to occur for nonsymmetric rotors in molecules having nearby groups possessing substantial magnetic anisotropy.
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Quinazolines and 1,4-Benzodiazepines. 88.[1] Synthesis and Rearrangement of 3a,4,5,6-Tetrahydro-3*H*-imidazo[1,5-*a*][1,4]benzodiazepines

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The chemical and catalytic reduction of the dihydroimidazobenzodiazepine **2** afforded the *trans*-tetrahydroimidazobenzodiazepine **5** and the corresponding cis isomer **6,** respectively. Treatment of these reduced benzodiazepines with tosyl chloride resulted in cyclization to the two epimeric triazatricyclodecanes **7** and **9.** Thermolysis of these compounds led to the vinyl sulfones **13** and **14** involving an unusual 1,3 migration of the sulfonyl group. The structures of **14** and the *N*-nitroso derivative of **13** were determined by single-crystal X-ray analyses.

During the course of synthetic studies related to the preparation of 4*H*-imidazo[1,5-*a*][1,4]benzodiazepines,[2] the 2-aminomethylbenzodiazepine **1** was stereoselectively reduced with zinc and acetic acid to the corresponding tetrahydrobenzodiazepine **4,** which we designate as the trans isomer (Scheme I). Treatment of **4** with triethyl orthoacetate afforded the tetrahydroimidazobenzodiazepine **5** in which the hydrogens at C_2 and C_5 retain their trans stereochemistry. This same compound was also obtained by zinc and acetic acid reduction of the imine function in the dihydroimidazobenzodiazepine **2.**[2] Hydrogenation of **2** using platinum as catalyst gave exclusively the cis isomer, compound **6.** It has been shown[2] that

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