5–48 h in 40 mL of dry toluene in a Dean–Stark apparatus. Water (about 1.5 mL) was removed. Toluene was removed at 60 °C/30 mmHg and the residue was treated with 200 mL of diethyl ether. The crude product was recrystallized from the appropriate solvent or purified by column chromatography.

Registry No. **1a**, 82894-56-2; **1b**, 116368-50-4; **1c**, 66730-27-6; **1d**, 5267-50-5; **1f**, 6583-59-1; **1i**, 117067-56-8; **1j**, 117067-57-9; **2a**, 117067-58-0; **2b**, 117067-59-1; **2e**, 117067-60-4; **2g**, 117067-61-5; **2h**, 97469-74-4; **3a**, 117067-46-6; **3b**, 117067-47-7; **3c**, 117067-48-8; **3d**, 117067-49-9; **3f**, 117067-50-2; **4a**, 117067-51-3; **4b**, 117067-52-4; **4e**, 117067-53-5; **4g**, 117067-54-6; **4h**, 117067-55-7.

Supplementary Material Available: Table of ^{13}C NMR spectral data for compounds 1 and 2 (1 page). Ordering information is given on any current masthead page.

Oxidation of Amines with 2-Sulfonyloxaziridines (Davis' Reagents)

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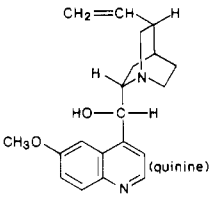
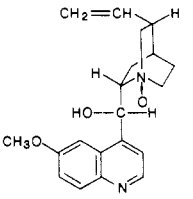
2-(Phenylsulfonyl)-3-aryloxaziridines (Davis' Reagents) react rapidly with amines that are more basic than pyridine to give products that are dependent upon the structure of the amine. Tertiary aliphatic amines are oxidized to the corresponding *N*-oxides in high yields, while secondary aliphatic amines give the N,N-disubstituted hydroxylamines and corresponding nitrones in variable, stoichiometrically dependent ratios. Primary aliphatic amines give 10–35% yields of nitroso compounds and 50–65% yields of *N*-arylideneamines formed by the transimination reaction of the amine with the *N*-arylidenebenzenesulfonamide generated following oxygen transfer from the 2-(phenylsulfonyl)-3-aryloxaziridine.

Numerous reagents have been used to oxidize primary amines to nitro compounds,[1] among them the small ring heterocycle dimethyldioxirane.[2] Our need to effect the amine to nitro transformation under convienent, mild, and anhydrous reaction conditions prompted us to explore the use of another class of heterocyclic oxidants, the 2-(phenylsulfonyl)-3-aryloxaziridines (Davis' Reagents). These easy to prepare and handle solids are useful aprotic and neutral oxidizing reagents, which have been employed for the oxidation of a wide variety of functionalities.[3] Although it had been demonstrated that pyridine was not oxidized to pyridine *N*-oxide by 2-(phenylsulfonyl)-3-(4-nitrophenyl)oxaziridine,[4] we hypothesized that amines more basic than pyridine would prove sufficiently nucleophilic to be oxidized by these reagents. We now report our study on the oxidation of a wide variety of amines with 2-(phenylsulfonyl)-3-aryloxaziridines.

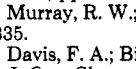
Although our primary interest was the conversion of primary amines into nitro compounds, we first examined the oxidation of tertiary amines more basic than pyridine to test the aforementioned basicity hypothesis. The oxidations were carried out by adding the sulfonyloxaziridine in a single portion to a deuteriochloroform solution of the amine. Any precipitate that formed was removed by filtration, and a ^{13}C NMR analysis of the filtrate was performed. In some instances the reactions were carried out on a preparative scale, the products were isolated and characterized, and the yields were determined. The results

Table I. Percent Yield of Tertiary Amine *N*-Oxide from Oxidation of Tertiary Amine

R_3N	R_3NO, %	ref
triethylamine	>95[a]	5
pyridine	0[a]	
N-methylpiperidine	>95[a]	6
1-azabicyclo[2.2.2]octane[b]	>95[a]	7
(1*R*,2*S*)-$C_6H_5CH(OH)CH(CH_3)N(CH_3)_2$[c]	>95,[a] 67[d]	8
 (quinine)	 >95,[a] 94[d]	7

[a] Estimated from the ^{13}C NMR spectra. The *N*-oxides were observed to be the only amine derived products present in the crude reaction mixtures where oxidation had occurred. [b] Quinuclidine. [c] (−)-*N*-Methylephedrine. [d] Isolated by preparative-layer chromatography.

Table II. ^{13}C NMR Chemical Shifts of *tert*-Butylamine Oxidation Products

	δ in ppm		
compd (R = *tert*-butyl)	*C*N	*C*H$_3$	*C*H
RN=O	95.9	25.2	
RNO_2	84.9	27.7	
$(RNO)_2$	76.3	23.0	
$RN(O)=CHC_6H_5$	70.6	28.1	*a*
	58.3	25.1	73.5
$RN=CHC_6H_5$	56.9	29.5	154.8
RNH_2	47.2	32.4	

[a] In aromatic region, 126–132.

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0022-3263/88/1953-5856$01.50/0

of the tertiary amine oxidations are summarized in Table I. The ^{13}C NMR spectra of the crude reaction mixtures for the tertiary amines examined, with the exception of pyridine, displayed resonances only for the corresponding *N*-oxides and the oxaziridine reduction product *N*-benzylidenebenzenesulfonamide (**3**). As expected, quinine (entry 6, Table I), which possesses both a quinoline and a quinuclidine nitrogen atom, undergoes oxidation only at the more basic quinuclidine site. Furthermore, the chemoselectivity of Davis' reagent is apparent as neither the olefinic double bond or the secondary alcohol group in quinine are affected.

Encouraged by our ability to oxidize tertiary amines to the corresponding *N*-oxides under mild conditions and in very high yields, we extended our investigation to our targeted primary amines. *tert*-Butylamine was studied initially because the intermediate oxidation products have been well characterized[9] and their simple ^{13}C NMR spectra are readily interpreted (Table II). Furthermore, the nitroso derivative, 2-methyl-2-nitrosopropane, exists substantially as a monomer in solution, a situation we have found that facilitates the subsequent oxidation to the desired nitro compound.

When 1 equiv of 2-(phenylsulfonyl)-3-phenyloxaziridine (**1**) was added in a single portion to a deuteriochloroform solution of *tert*-butylamine, a deep blue color, characteristic of aliphatic nitroso monomers, developed rapidly. A copious white precipitate of benzenesulfonamide formed within 1 h. The ^{13}C NMR spectrum of the solution clearly showed that while all of the amine had been consumed, a large quantity of oxidant (δ 76.2 ppm) remained. Also conspicuously absent from the reaction mixture was the signal at δ 170.5 ppm corresponding to the methine carbon of the sulfonimine byproduct **3**. The major product (65%) in the reaction mixture was determined to be the imine, *N*-benzylidene-*tert*-butylamine[10] (**4**) (δ 56.9 and 29.5 ppm), presumably formed by the reaction of unreacted *tert*-butylamine and sulfonimine **3**, which was generated during the oxidation (vide infra). The imine was accompanied by 30% of 2-methyl-2-nitrosopropane (**5**) (monomer, δ 95.9 and 23.0 ppm; dimer, δ 76.3 and 25.2 ppm). Two other components in the reaction mixture were present in trace amounts and were determined to be the desired 2-methyl-2-nitropropane (**6**) (δ 84.9 and 27.7 ppm) and *N*-*tert*-butyl-α-phenylnitrone[1] (**7**) (δ 70.6 and 28.1 ppm). The nitrone is presumably formed by the reaction of *N*-*tert*-butyl-hydroxylamine[9] (**2**) (δ 55.0 and 26.1 ppm), the putative intermediate on the pathway to the nitroso compound, and the in situ generated sulfonimine **3** (vide supra). After 7 days a ^{13}C NMR spectrum of the reaction mixture showed that the remaining oxidant had been consumed and sulfonimine **3** was present. The levels of the nitro compound and nitrone had substantially increased relative to the levels initially observed in the reaction mixture but had not formed in synthetically significant amounts.

Table III. Percent Yields of Oxidation Products of Primary Amines[a]

RNH_2	RNO/$(RNO)_2$,[11] %	RN=CHC_6H_5, %	other[b]
R = benzyl	35	50[c]	15
R = *endo*-2-norbornylmethyl	10	50[c]	40
R = cyclohexyl	20	60[13]	20
R = *endo*-2-norbornyl	trace	15[c]	80[d]
R = *exo*-2-norbornyl	20	60[c]	20
R = 2-adamantyl	10	60[14]	30
R = *tert*-butyl	30	65[10]	5
R = 1-adamantyl	30	65[14]	15
R = 3-noradamantyl	15	60[c]	25

[a] The percentages were estimated by using ^{13}C NMR peak height ratios (see the Experimental Section). [b] The remainder of the product was a mixture of nitrone, azoxy compound and/or oxime in varying ratios. [c] See the Experimental Section. [d] The oxidation proceeds very slowly and mostly unreacted amine was present after the 1-h reaction period.

A number of other primary amines were examined and gave essentially the same results as *tert*-butylamine on oxidation, i.e., the *N*-benzylideneamine was the major product with the remainder primarily nitroso compound (see Table III).

Several experiments were conducted to test our presumption that the imine and nitrone were formed via a transimination process between the sulfonimine **3** and the amine and hydroxylamine **2**, respectively. The reaction of equimolar amounts of *tert*-butylamine and the sulfonimine **3** in deuteriochloroform resulted in the rapid precipitation of benzenesulfonamide. A ^{13}C NMR spectrum of the crude reaction mixture displayed resonances corresponding to *N*-benzylidene-*tert*-butylamine (**4**) and a small amount of benzenesulfonamide only, suggesting that the transimination process had proceeded in very high yield. The nitrone **7** was obtained in a similar fashion from the reaction of the hydroxylamine **2** with the sulfonimine **3**. These transimination reactions emerged as a synthetically useful method for the synthesis of imines and nitrones under neutral and mild conditions.

Several other experiments were conducted to elucidate the pathways by which the various products arose in the reaction mixtures as well as to gain a qualitative feel for the relative rates of these chemical processes, which might permit us to circumvent the undesired side reactions. The addition of 1 equiv of oxidant to a solution of *N*-*tert*-butylhydroxylamine (**2**) resulted in the instantaneous development of a deep blue color. A ^{13}C NMR spectrum showed that the nitroso compound **5** and the nitrone **7** were the sole products in 60% and 40% yields, respectively. Pure 2-methyl-2-nitrosopropane (**5**) was reacted with 1 equiv of the oxidant. After 7 days, a ^{13}C NMR spectrum revealed that 2-methyl-2-nitropropane was present in the crude reaction mixture but was accompanied by substantial amounts of unidentified side products as well as the starting nitroso compound. The nitrone **7** was formed only very slowly by the action of the oxidant on the imine **4** and may arise via the intermediacy of its isomeric oxaziridine whose presence was also detected in the crude reaction mixture. The sequence of observed reactions and their relative rates appear in Scheme I. The large relative rate for the transimination reactions relative to nitroso oxidation (k_3 and $k_4 \gg k_5$) suggested that these side reactions could not be easily overcome. Indeed, the observed product distributions showed little variation when the order and period of addition of the reactants was al-

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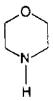
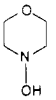
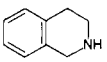
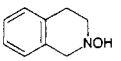
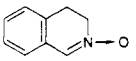
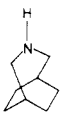
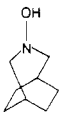
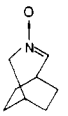
Table IV. % Yields of Oxidation Products of Secondary Amines[a]

amine	equiv of oxaziridine 1	hydroxylamine	nitrone	other,[b] %	ref
Ph_2NH		Ph_2NHOH			
	1	(0)		100	
$(PhCH_2)_2NH$		$(PhCH_2)_2NOH$	$PhCH_2N(O)=CHPh$		15
	1	(70)	(10)	20	
	2	(0)	(85)	15	
					16
	1	(70)	(15)	15	
	2	(0)	(80)	20	
					17
	1	(65)	(20)	15	
	2	(0)	(85)	15	
					17a
	2	(0)	(42)[c]		
					17
	2	(0)	(80)	20	
					
	1	(60)	(20)	20	
	2	(0)	(66)[d]		

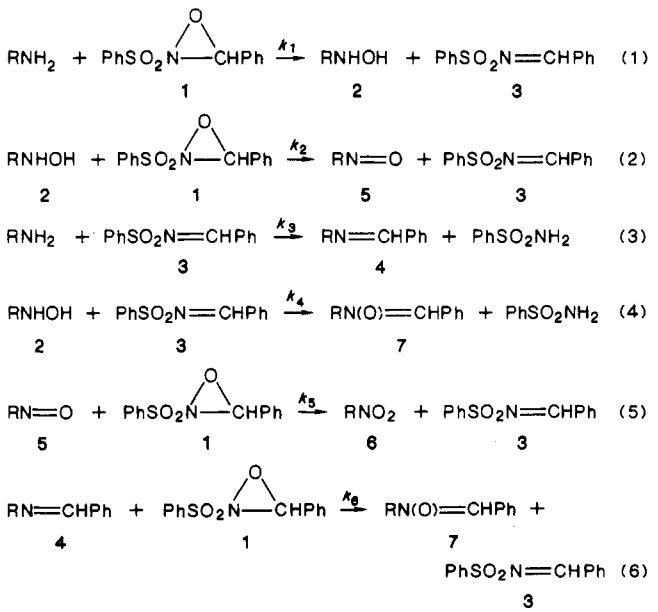
[a] The percentages were estimated using ^1H NMR integrations or ^{13}C NMR peak height ratios (see the Experimental Section). [b] The other products detected in the crude reaction mixtures were the unreacted amines and an uncharacterized product demonstrated to arise from the addition of the amine to the sulfonimine 3 when 1 equiv of the oxaziridine was used. The addition product proved stable to the reaction conditions and was observed to be the only other amine derived product when 2 equiv of the oxaziridine were employed. [c] Isolated as the adduct of diethyl fumarate. [d] Oxidized with ozone at −78 °C to *cis*-4-(nitromethyl)cyclohexanecarboxylic acid.

tered and the oxaziridine to amine stoichiometry was raised to 5:1.

When a secondary amine was reacted with 1 equiv of a 2-sulfonyloxaziridine, the ^{13}C NMR spectrum of the reaction mixture indicated that two major products were present along with some unreacted amine. The products were identified as the hydroxylamine and the nitrone. The formation of nitrone results from the elimination of water from the hydroxylamine *N*-oxide formed when the hydroxylamine reacts with a second molecule of oxidant. When 2 equiv of a 2-sulfonyloxaziridine were used to oxidize the secondary amines, the nitrone was the major product, which was accompanied by a small amount of an unidentified product (see Table IV). In most cases the analysis of the reaction mixtures of the secondary amines was carried out by ^{13}C NMR because of the ease of identifying compounds in the mixtures, and the yields in most cases are estimated from the NMR data. In some instances the utility of this reaction was demonstrated by using the nitrone produced in a subsequent chemical reaction without purification (entries 5 and 7, Table IV). It should be noted that diphenylamine, which is less basic than pyridine, was not oxidized (entry 1, Table IV). Although most of the oxidations of the amines were carried out with 2-(phenylsulfonyl)-3-phenyloxaziridine (1), we found that the same results were obtained with 2-(phenylsulfonyl)-3-(4-nitrophenyl)oxaziridine.

Finally a set of experiments was carried out to determine the relative nucleophilicities of nitrogen and sulfur toward the oxygen atom in a sulfonyloxaziridine. Equivalent amounts of dibenzylamine and dibenzyl sulfide were allowed to react with varying deficient amounts of 2-(phenylsulfonyl)-3-phenyloxaziridine in deuteriochloroform, and the resulting ^1H NMR spectra were recorded. The benzylic protons of the starting materials, dibenzylamine (δ 3.77 ppm) and dibenzyl sulfide (δ 3.56 ppm), and the products, *N*,*N*-dibenzylhydroxylamine (δ 3.72 ppm) and dibenzyl sulfoxide (δ 3.91 ppm) are sufficiently separated

Scheme I[a]



[a] R = $(CH_3)_3C$. Relative rates: $k_2 \gg k_3 = k_4 > k_1 \gg k_5 = k_6$.

from each other so that accurate integration is possible. From the ratios of the signals it was determined that sulfur is about 20 times more reactive that nitrogen toward oxidation by the sulfonyloxaziridine. This finding is consistent with the proposed mechanism[3] which suggests that the sulfur nucleophile should be more reactive.

$$(PhCH_2)_2NH + (PhCH_2)_2S \xrightarrow{1} (PhCH_2)_2NOH + (PhCH_2)_2SO \quad 1{:}20$$

In summary, we have found that from a preparative standpoint 2-(phenylsulfonyl)-3-aryloxaziridines (Davis' Reagents) are useful oxidants for the conversion of tertiary amines more basic than pyridine to the corresponding *N*-oxides. Nitrones are also available on a preparative scale by the oxidation of selected secondary amines with 2 equiv of a sulfonyloxaziridine. Furthermore, it was also discovered that *N*-benzylidenebenzenesulfonamide (**3**) ($PhSO_2N{=}CHPh$) is a useful transiminating reagent that converts primary amines and N-substituted hydroxylamines into imines and nitrones, respectively, in very high yields and under neutral and anhydrous conditions (see Scheme I, eq 3 and 4).

Experimental Section

Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were obtained on an Analect FX-6160 FT-IR instrument. ^1H and ^{13}C NMR spectra were obtained on a Varian XL-200 spectrometer in $CDCl_3$ as the solvent and TMS as the internal standard. Chemical shifts are in ppm, and coupling constants are in hertz. Preparative-layer chromatography (PLC) was carried out on 0.1 × 20 × 20 cm silica gel 60 F254, Merck. Microanalyses were performed by Gailbraith Laboratories, Knoxville, TN. 2-(Phenylsulfonyl)-3-phenyloxaziridine and 2-(phenylsulfonyl)-3-(*p*-nitrophenyl)oxaziridine were prepared as previously described.[18] (Note: The oxaziridine precursor and transiminating reagent *N*-benzylidenebenzenesulfonamide is now available from the Aldrich Chemical Co.)

The ^{13}C NMR spectra used for semiquantitative evaluation of crude reaction mixtures were acquired with use of a 45° pulse width and a 0.4-s acquisition time. The final signal to noise ratios were generally greater than 250:1 to facilitate the detection of minor components. The semiquantitative evaluation was conducted by taking an average of the ratios of peak heights for several corresponding carbons in each compound. Care was taken to exclude the resonances for carbons whose relaxation times may have been altered by a change in proximal functionality. Even so, the anticipated accuracy of the estimation is no greater than 10%.

Oxidation of Amines with Davis' Reagents. General Procedure. To a solution of the amine (1 mmol) in 3 mL of $CDCl_3$ was added in a single portion 2-(phenylsulfonyl)-3-phenyloxaziridine (**1**) (1 mmol). The reaction mixture was stirred for 1 h. Any solid that precipitated was removed by filtration, and a ^{13}C NMR spectrum of the filtrate was obtained. After the spectrum had been recorded the $CDCl_3$ solution was evaporated, and the residue was either recrystallized or chromatogrpahed.

***N*-Benzylideneamines: Reaction of an Amine with *N*-Benzylidenebenzenesulfonamide.** *N*-Benzylidenebenzenesulfonamide (**3**) (0.671 g, 2.73 mmol) was added to a solution of *tert*-butylamine (0.20 g, 2.73 mmol) in 5 mL of $CHCl_3$. A slight exotherm was detected on mixing. The heterogeneous mixture that resulted was stirred at room temperature for 15 min. Pentane (5 mL) was added, and stirring was continued for an additional 5 min. The solid was removed by filtration and washed with 2–3 mL of pentane. The solvent of the filtrate was removed by rotary evaporation, providing 0.419 g (95%) of a colorless viscous liquid. A ^{13}C NMR of the residue was obtained and was identical with that reported for *N*-benzylidene-*tert*-butylamine[10] (**4**): ^{13}C NMR δ 154.9, 136.7, 129.9, 128.2, 127.6, 56.9, 29.5. Similarly, the following imines were prepared in excellent yields (89% to 102% mass balance) and displayed high purity by ^{13}C NMR with only trace quantities of benzenesulfonamide observed to be accompanying the imine.

***N*-Benzylidenebenzylamine:**[13b] ^{13}C NMR δ 161.9, 139.3, 135.9, 130.6, 128.4, 128.3, 128.1, 126.8, 64.8.

***N*-Benzylidene-*endo*-2-(aminomethyl)norbornane:** ^{13}C NMR δ 160.3, 136.1, 130.2, 128.3, 127.8, 64.2, 41.0, 39.6, 38.8, 36.8, 34.8, 30.0, 22.4 (major isomer); 160.3, 135.7, 130.8, 129.3, 127.7, 64.2, 41.8, 38.3, 38.0, 36.5, 34.3, 29.5, 22.1 (minor isomer).

***N*-Benzylidenecyclohexylamine:**[13] ^{13}C NMR δ 159.2, 136.4, 130.2, 128.3, 127.8, 69.8, 34.1, 25.4, 24.6.

***N*-Benzylidene-*endo*-2-norbornylamine:** ^{13}C NMR δ 158.9, 136.7, 130.0, 128.3, 127.8, 70.9, 43.8, 38.6, 37.8, 37.4, 30.1, 22.0.

***N*-Benzylidene-*exo*-2-norbornylamine:** ^{13}C NMR δ 157.4, 136.5, 130.0, 128.3, 127.8, 73.6, 44.2, 39.7, 36.1, 35.5, 29.0, 26.7.

***N*-Benzylidene-2-adamantylamine:**[14] ^{13}C NMR δ 157.5, 137.0, 130.0, 128.3, 74.2, 37.9, 37.2, 35.4, 31.9, 28.1, 27.3.

***N*-Benzylidene-1-adamantylamine:**[14] ^{13}C NMR δ 154.8, 137.1, 130.0, 128.3, 127.7, 57.3, 43.0, 36.5, 29.5.

***N*-Benzylidene-3-noradamantylamine:** ^{13}C NMR δ 157.0, 137.0, 130.1, 128.4, 127.7, 74.8, 49.6, 44.9, 43.8, 37.5, 34.8.

Oxidation of *N*-*tert*-Butylhydroxylamine (2) with Davis' Reagent. 2-(Phenylsulfonyl)-3-phenyloxaziridine (0.523 g, 2.00 mmol) was added to a $CHCl_3$ solution of *N*-*tert*-butylhydroxylamine (0.178 g, 2.00 mmol). The reaction mixture was stirred for 15 min, and then the solvent was removed by rotary evaporation. The residue was suspended in $CDCl_3$ (3 mL), and the solid that did not dissolve was removed by filtration. A ^1H NMR spectrum of the filtrate revealed the presence of two products: 74% 2-methyl-2-nitrosopropane[10] (monomer and dimer) and 26% *N*-*tert*-butylphenylnitrone.[11]

***N*-*tert*-Butyl-α-phenylnitrone**[11] **(7).** *N*-*tert*-Butylhydroxylamine hydrochloride (0.251 g, 2.00 mmol) was added to 25 mL of 0.1 M aqueous NaOH solution in a separatory funnel. The aqueous solution was extracted with CH_2Cl_2 (2 × 25 mL). To the dried (Na_2SO_4) organic solvent was added *N*-benzylidinebenzenesulfonamide (0.491 g, 2.00 mmol). The solution was stirred for 15 min, pentane (10 mL) was added, and the mixture was stirred for an additional 5 min. The precipitate that formed was removed by filtration, and the filtrate was concentrated by rotary evaporation to give a white solid residue (0.360 g, 102%). ^1H and ^{13}C NMR analysis of the residue indicated that it was largely (>95%) *N*-*tert*-butyl-α-phenylnitrone: ^{13}C NMR δ 130.8, 130.1, 128.3, 70.2, 28.2. Also present was a small amount of benzenesulfonamide, which did not precipitate when the pentane was added to the reaction mixture.

Oxidation of 3-Azabicyclo[3.2.2]nonane with 2 equiv of Davis' Reagent. To a solution of 2-(phenylsulfonyl)-3-phenyloxaziridine (0.523 g, 2.0 mmol) in $CHCl_3$ (10 mL) was added 3-azabicyclo[3.2.2]nonane (0.125 g, 1 mmol). The reaction mixture was stirred for 15 min. The solvent was removed by rotary evaporation and replaced by CH_2Cl_2. This solution was ozonized at −78 °C. The CH_2Cl_2 solution was then extracted with a saturated $NaHCO_3$ solution. The aqueous layer was neutralized with HCl and then extracted with CH_2Cl_2. The CH_2Cl_2 solution was rotary evaporated, and the residue was subjected to PLC. The major fraction that was isolated was recrystallized from ethanol to provide a 66% yield (0.123 g) of *cis*-4-(nitromethyl)cyclohexanecarboxylic acid: mp 83–85 °C; R_f 0.2 ($CHCl_3$); ^1H NMR δ 10.1 (s, 1 H), 4.28 (d, 2 H, J = 7 Hz), 2.72 (m, 1 H), 2.31 (m, 1 H), 2.12 (m, 2 H), 1.66 (m, 4 H), 1.44 (m, 2 H); ^{13}C NMR δ 181.3, 80.4, 39.1, 35.2, 26.2, 24.4. Anal. Calcd for $C_8H_{13}NO_4$: C, 51.33; H, 7.00; N, 7.48. Found: C, 51.79; H, 7.01; N, 6.75.

1,3-Cycloaddition of Morpholine Nitrone and Diethyl Fumarate. Morpholine (0.087 g, 1 mmol) was added to a solution of 2-(phenylsulfonyl)-3-phenyloxaziridine (0.523 g, 2 mmol) in $CHCl_3$ (15 mL). The reaction mixture was stirred at room temperature for 1 h, and then diethyl fumarate (0.172 g, 1 mmol) was added. The reaction mixture was purged with nitrogen and then heated at vigorous reflux for 1 h. The solvent was reduced to half the volume, and the precipitate that formed was removed by filtration. The solvent in the filtrate was removed by rotary evaporation, and the residue was subjected to PLC. The cyclo-

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adduct was isolated in 42% yield as a yellow viscous oil whose proton NMR spectrum was identical with that reported previously.[17a]

Competitive Oxidation of Dibenzylamine and Dibenzyl Sulfide with Davis' Reagents. Dibenzylamine (0.197 g, 1.00 mmol) and dibenzyl sulfide (0.214 g, 1.00 mmol) were dissolved in $CDCl_3$ (3 mL). 2-(Phenylsulfonyl)-3-phenyloxaziridine (0.150 g, 0.57 mmol) was added in one portion, and the reaction mixture was stirred for 30 min. The ^1H NMR spectrum of the reaction mixture was obtained. The integral ratio of the methylene protons of dibenzyl sulfoxide (δ 3.91) and dibenzyl sulfide (δ 3.56) was 30.5 to 25.5, indicating that 54% of the 1 mmol of dibenzyl sulfide had been oxidized to dibenzyl sulfoxide. Thus 0.54 mmol (54% of 1 mmol) of the available 0.57 mmol of oxidant (95%) had reacted at sulfur. A similar experiment using a 1:1:1 ratio of reactants was carried out, and the reaction mixture was analyzed by ^{13}C NMR. Similar results were obtained as in the previous experiment.

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Transvesicular Reactions of Thiols with Ellman's Reagent

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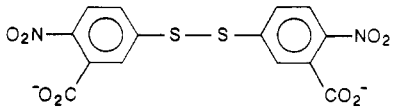
The cleavage of Ellman's reagent [5,5'-dithiobis(2-nitrobenzoic acid)], **1**, to chromophoric anion **2** by various thiols has been studied in pH 8 buffer, micellar cetyltrimethylammonium bromide (**4**), and vesicular dihexadecyldimethylammonium bromide (**5**) or dioctadecyldimethylammonium chloride (**6**) solutions. The thiols included thiocholesterol, thiophenol, 2-thionaphthol, DL-cysteine, glutathione, 1-butanethiol, and 1-octanethiol. Vesicles of **6** at 25 °C sequester **1** in distinct exovesicular and endovesicular binding sites, where reactions with added thiols are kinetically differentiated. Differences in thiol acidity and structure influence their rates of permeation and reaction with vesicle-bound **1**. Small quantities of covesicallized 1-hexanol (0.2 wt %) lower the gel to liquid crystalline transition temperature of vesicular **1** (from ~39 °C to 24 °C), enhance vesicular fluidity, accelerate the thiol/**1** reactions, and destroy the kinetic distinction between the exovesicular and endovesicular reactions.

Ellman's reagent [5,5'-dithiobis(2-nitrobenzoic acid)], **1**, is readily cleaved at its disulfide bond by a variety of nucleophiles to afford chromophoric anion **2**.[1] In the case of (excess) thiolate nucleophile, **1** is cleaved to 2 equiv of **2** via an intermediate "mixed disulfide",[2] whereas nucleophiles such as sulfite,[1b] or dithionite[3,4] give 1 equiv of **2**, together with a "Bunte" salt (e.g., $ArSSO_3^-$ from **1** + sulfite[1b]). In either case, conditions can be selected to make



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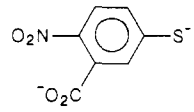

2

the reductive cleavage of **1** rapid and quantitative, so that the reaction assumes analytical importance due to the intense (log ϵ 4.14) and conveniently located (λ_{max} 407 nm) absorption of Ellman's anion, **2**.[5]

Accordingly, Ellman's reagent has been used as a probe of reactions occurring on or within micelles, vesicles, and liposomes. Micelles are thermodynamically stable aggregates that form spontaneously from single chain surfactants, typically carrying 12–16 carbons in their alkyl chains. Vesicles or liposomes are usually composed of twin-tailed ionic surfactants or phospholipids. These form multilamellar or unilamellar vesicles depending upon the method of preparation. The unilamellar vesicles contain a central water core surrounded by a surfactant bilayer that has both inner and outer charged interfaces covering the hydrocarbon chain region. Micelles, on the other hand, contain a hydrophobic core composed of the alkyl chain hydrocarbons, surrounded by a single charged interface or Stern layer in contact with the aqueous solution.

Fendler and Hinze examined the hydroxide mediated cleavage of **1** in cetyltrimethylammonium (CTA) bromide micelles and in dioctadecyldimethylammonium chloride (18_2, DODAC) vesicles. In the latter case, reaction was slow, relative to OH^- permeation across the bilayer membrane, leading to a monophasic chemical process.[6] In contrast, the very rapid reactions of **1** with added sulfite or dithionite ions in dihexadecyldimethylammonium bromide vesicles (16_2) were kinetically biphasic, with dynamic behavior indicative of a rapid but kinetically resolvable equilibration (k_{equil} ~ 2–4 s^{-1}) of **1** between "subvesicular" (possibly intercalation) and exovesicular binding sites.[7] When **1** was *encapsulated* inside DODAC (18_2) vesicles, the more permeation-resistant 18_2 bilayers prevented the leakage of **1** and "shut off" exovesicular reactions with dithionite.[8]

Bizzigotti, analyzed reactions of **1** with thiol-functionalized 16_2, finding evidence that the reaction of 16_2S-SEll (the "mixed" disulfide) and 16_2S^- was unexpectedly slow.[9] This may have reflected a general phenomenon when the reactants were both integral parts of the bilayer. In the

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