resulting polymer was filtered, washed, and dried as described for **1a-g**. The content of bonded cryptand units was evaluated by oxygen and nitrogen elemental analysis (Table IV).

Polymer-Supported Cryptands 2a-b. A sample of carboxylated polystyrene corresponding to 1 mmol of COOH group in 15 mL of thionyl chloride was stirred and refluxed for 3 h. The polymer was filtered in an argon atmosphere and washed with anhydrous toluene and ethyl ether. The conversion of the carboxylic acid into the corresponding chlorocarbonyl function was found quantitative by IR (KBr pellets). This polymer was added to a solution of 1.2 mequiv of **12** and 1.5 mequiv of anhydrous triethylamine in 15 mL of $CHCl_3$. The mixture was stirred and refluxed for 15 h. After filtration the polymer was washed with methanol, water, methanol, methylene chloride, and twice with ethyl ether and dried for 3 h (65 °C, 2 torr). The amount of bonded cryptand was estimated by nitrogen elemental analysis (Table I).

Kinetic Measurements. Kinetics were run in a 50-mL flask equipped with a Teflon-lined screw cap and magnetic stirrer and thermostated at 60 °C with circulating butyl phthalate. The temperature was controlled to within ±0.01 °C by a Exacal 200 Bath Circulator. Stirring speed (1300 ± 50 rpm) was controlled by using a strobe light. The flask was charged with 12.5 mL of a 4 M aqueous solution of potassium salt (KX, X = I, Br, Cl), 3 mL of toluene, tetradecane as internal standard (2 mL of a 0.1 M solution in toluene), and 0.25 mequiv of catalyst. The mixture was left at 60 °C for 12 h at 200 rpm stirring speed in order to condition the catalyst. *n*-Octyl methanesulfonate or *n*-octyl bromide (5 mL of a 1 M solution in toluene) was added at zero time and the mixture stirred at 1300 rpm. The reactions were followed by GLC analysis. The pseudo-first-order rate constants (k_{obsd}) were obtained by plotting ln [substrate] vs. time and determining the slope of the straight lines.

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Registry No. **5**, 4799-67-1; **6**, 104911-02-6; **7**, 80525-59-3; **8**, 104911-03-7; **8** diethyl ester, 104911-07-1; **9**, 104911-04-8; **10**, 104911-05-9; **11**, 104911-08-2; **12**, 104911-09-3; **13**, 74339-03-0; **14**, 104911-06-0; **15**, 23978-09-8; n-$C_8H_{17}Br$, 111-83-1; I^-, 20461-54-5; n-$C_8H_{17}OMe_5$, 16156-52-8; Br^-, 24959-67-9; Cl^-, 16887-00-6; chloroacetic acid, 79-11-8; oxalyl chloride, 79-37-8; 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane, 23978-55-4.

2-(4-Pyridyl)ethyl as a Protective Group for Sulfur Functionality

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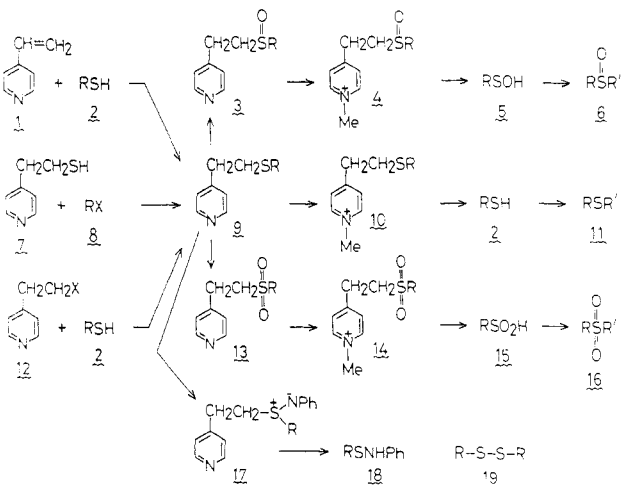
2-(4-Pyridyl)ethyl sulfides have been prepared from a variety of alkyl and aryl thiols and from alkyl and acyl halides. These sulfides and their corresponding sulfoxides and sulfones were each depyridylethylated by quaternization and subsequent treatment with mild base to give respectively the thiols, sulfenic acids, sulfinic acids, and sulfenamides. During one of these protection-deprotection sequences, methyl 1-octyl sulfoxide was readily converted by aerial oxidation into the corresponding sulfone.

Other publications[1,2] from this laboratory have reported the use of 2-(4-pyridyl)ethyl as a protective group, which is easily removed by quaternizing agents such as methyl iodide. In particular, we have shown that carboxylic acids[1] and heterocyclic NH groups[2] can be protected in this way. Other workers have utilized 2-(4-pyridyl)ethyl as a constituent of the group $PyCH_2CH_2OCO-$, used in the protection of amino functionality.[3,4] The technique of pyridylethylation has also been used to activate the cyano group in 4-cyanopyridine by easily reversible quaternization.[5] This paper records some applications of 2-(4-pyridyl)ethylation in the manipulation of sulfur functionality.

Strategy

Our overall strategy is outlined in Scheme I. Pyridylethyl sulfides **9a-g** and thiol esters **9h,i** were prepared (i) by the pyridylethylation of thiols **2a-d**, (ii) by the alkylation or acylation of 2-(4-pyridyl)ethanethiol (**7**), and (iii) by the alkylation of thiol **2d** using the 2-(4-pyridyl)-ethyl alkylating agent **12j**. The 2-(4-pyridyl)ethyl sulfides **9** could be converted by oxidation to sulfoxides **3** and sulfones **13**. Each of these three classes of compounds **3**, **9**, and **13** could then be quaternized to give the corresponding methyl quaternary salts **4**, **10**, and **14**. In practice, these now decomposed either spontaneously or on treatment with mild base to give, respectively, the corresponding sulfenic acid **5**, thiol **2**, or sulfinic acid **15**. These products were usually trapped as the sulfoxide **6**, the

Scheme I



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sulfide **11**, or the sulfone **16**, respectively, by using an excess of the methyl iodide quaternizing agent: however, it should be possible to utilize the intermediate anion to form other products.

Results and Discussion

The 2-(4-pyridyl)ethylations of *p*-toluene- (**2b**),[1] phenylmethane- (**2e**),[6] and benzenethiol (**2d**)[7] to give **9b**, **9e**, and **9d**, respectively have been described previously. We have now carried out Michael additions of 4-vinylpyridine (**1**) to 1-octanethiol (**2a**) and 2-naphthalenethiol (**2c**), to give the products **9a** (99%) and **9c** (99%), respectively. 2-(4-Pyridyl)ethanethiol (**7**) and the corresponding hydrochloride (**7**·HCl) have previously been reported.[6,8,9] We prepared **7**·HCl by the literature method[8] in 96% yield and found that it was readily converted by alkylation or acylation into sulfides and thiol esters **9**. In this way, the following sulfides and thiol esters were prepared in the yields indicated: the 1-butyl sulfide **9f** (71%) and the 5-nitro-2-pyridyl sulfide **9g** (75%); the thiol benzoate **9h** (49%) and the thiol (phenylthio)carbonate **9i** (62%). The reaction of **12j** with thiophenol **2d** afforded the phenyl compound **9d**, but in only 11% yield, whereas Michael addition gave 100% (see below).

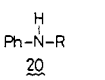
Sulfoxides **3a–c** were prepared from the corresponding sulfides **9a–c** by sodium periodate oxidation[10] at 0 °C in respective yields of 85%, 71%, and 58%. Treatment of sulfoxide **3a** with excess methyl iodide, followed by 1 equiv of potassium carbonate at 20 °C gave methyl 1-octyl sulfoxide (**6n**) quantitatively: the excess methyl iodide alkylates **5** as well as quaternizing **3**. Attempts to purify crude **6n** by recrystallization afforded the pure sulfoxide **6n** in 27% yield. On the other hand, attempts to purify crude **6n** by chromatography on silica gel afforded only the sulfone **16n** in 57% yield. That the latter was formed by aerial oxidation was established by filtration through silica of a sample of sulfoxide **6n** prepared by a well-known procedure;[11] again, only sulfone **16n**, in 52% yield, was obtained. There appear to be no previous reports of such a facile oxidation of a sulfoxide. Moreover, when crude **6o** and **6p** were subjected to chromatography, methyl *p*-tolyl sulfoxide (**6o**) and methyl 2-naphthyl sulfoxide (**6p**) were recovered in respective yields of 64% and 40%; apparently, aerial oxidation of alkyl aryl sulfoxides does not readily occur.

We have previously reported[1] the preparation of *p*-toluenethiol (**2b**) by the route **9** → **10** → **2**, as shown in Scheme I. We have applied this strategy to 2-(4-pyridyl)ethyl thiolbenzoate (**9h**). Treatment of thiol ester **9h** with excess methyl iodide (16 mol) at 20 °C gave the corresponding quaternary salt **10h** in 96% yield. Treatment of salt **10h** with 1 equiv of potassium carbonate in aqueous acetone at 20 °C afforded only benzoic acid (quantitatively), presumably by the attack of hydroxide ion at the carbonyl carbon. Thermolysis of salt **10h** resulted in either the recovery of or the complete decomposition of **10h**. Finally, treatment of salt **10h** with 1 equiv of diisobutylamine at 20 °C afforded the ammonium salt of thiol benzoic acid (**2h**-*i*-Bu_2NH),[12] but in only 5% yield.

Sulfones **13a** and **13c** were prepared from the corresponding sulfides **9a** and **9c** by H_2O_2 oxidation[1] in yields of 76% and 67%, respectively. Treatment of sulfones **13a** and **13c** with excess methyl iodide (16 mol) at 20 °C gave the corresponding quaternary salts **14a** and **14c**, quantitatively. Treatment of **14a** and **14c** with 1 equiv of potassium carbonate in the presence of excess methyl iodide afforded methyl 1-octyl sulfone (**16n**) and methyl 2-naphthyl sulfone (**16p**) (75% and 97%, respectively). Additionally, treatment of **14a** with 1 equiv of potassium carbonate in the presence of excess ethyl iodide or 1-bromooctane afforded ethyl 1-octyl sulfone (**16q**) and di-1-octyl sulfone (**16r**) in respective yields of 74% and 19%.

It was hoped that reaction of a sulfide (**9**) in the presence of an aniline would provide a new route to sulfenanilides **18**, via the sulfimides **17**, as shown in Scheme I. The reaction of sulfides **9b** and **9c** with aniline and *tert*-butyl hypochlorite indeed gave *p*-toluenesulfenanilide (**18b**) and the novel 2-naphthalenesulfenanilide (**18c**) (57% and 60%, respectively). However, sulfide **9a** with aniline and *N*-chlorosuccinimide gave di-1-octyl disulfide (**19a**) as the major product (67%); 1-octanesulfenanilide (**18a**) was formed in only 6% yield. When *tert*-butyl hypochlorite was used in place of *N*-chlorosuccinimide, disulfide **19a** was obtained in 89% yield, together with the recovered sulfide **9a** (11%). In none of these examples were sulfimides **17**, the expected intermediates, detected.

When benzothiazole-2-thione (**21k**) was heated at reflux with 4-vinylpyridine (**1**) in acetic acid, the major product (56%) was the *N*-alkylated thione **21l**; the *S*-alkylated isomer **22l** was obtained, but in only 8% yield. An analogous reaction with 2-vinylpyridine was previously reported.[13]



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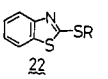

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a, R = 1-octyl; **b**, R = *p*-tolyl; **c**, R = 2-naphthyl; **d**, R = phenyl; **e**, R = benzyl; **f**, R = 1-butyl; **g**, R = 5-nitro-2-pyridyl; **h**, R = benzoyl; **i**, R = (phenylthio)carbonyl; **j**, X = Cl; **k**, R = H; **l**, R = 2-(4-pyridyl)ethyl; **m**, R = $C(=NH)NH_2$·2TsOH; **n**, R = 1-octyl, R′ = Me; **o**, R = *p*-tolyl, R′ = Me; **p**, R = 2-naphthyl, R′ = Me; **q**, R = 1-octyl, R′ = Et; **r**, R = R′ = 1-octyl

It has been shown that the 2-(4-pyridyl)ethyl group can be used to prepare sulfoxides which act as masked sulfenic acids and sulfones which act as masked sulfinic acids. These synthetic equivalents are deprotected under very mild condition (MeI; K_2CO_3, 20 °C). Investigations of the efficiency of the 2-(4-pyridyl)ethyl group in protection–deprotection sequences involving substituted (R) sulfur compounds other than those discussed here are planned.

Experimental Section

Melting points were measured with a Kofler hot-stage melting point apparatus and a Thomas-Hoover capillary melting point apparatus. All melting and boiling points are uncorrected. IR spectra were measured with a Perkin-Elmer 283B infrared spectrophotometer. NMR spectra measurements were carried out with a Varian EM360L NMR spectrometer (60 MHz, ^1H), a JEOL JNM-PMX60 NMR spectrometer (60 MHz, ^1H), and a JEOL JNM-FX100 Fourier transform NMR spectrometer (25 MHz, ^{13}C). All signals are expressed as parts per million downfield from tetramethylsilane (Me_4Si) (or sodium 4,4-dimethyl-4-sila-

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Table I. Analytical Data for the Compounds 9 and 10[a]

compd	(formula)	% yield	mp, °C	IR,[b] cm^{-1}
9a	($C_{15}H_{25}NS$)	99	oil[c]	1600, 1560, 1410 (C—S), 800
9c	($C_{17}H_{15}NS$)	99	80.5–82[c,d]	1620, 1595, 1410 (C—S), 800
9d	($C_{13}H_{13}NS$)	100	oil[c]	1600, 1580, 1410 (C—S), 800
9e	($C_{14}H_{15}NS$)	69	oil[c]	1600, 1555, 1410 (C—S), 800
9f	($C_{11}H_{17}NS$)	71	oil[c]	1600, 1555, 1410 (C—S), 800
9g	($C_{12}H_{11}N_3O_2S$)	75	89–90[e]	1600, 1585, 1505 (NO_2), 1340 (NO_2), 1410 (C—S), 800[f]
9h	($C_{14}H_{13}NOS$)	49	41–45[c]	1655 (C=O), 1595, 1410 (C—S), 1200 (C—S), 800[f]
9i	($C_{14}H_{13}NOS_2$)	62	oil[c]	1640 (C=O), 1595, 1410 (C—S), 800
10h	($C_{15}H_{16}INOS$)	96	130–135[g]	1655 (C=O), 1640 (pyridinium), 1590, 1445 (C—S), 1210 (C—S), 770[f]

[a] Satisfactory analytical values (±0.4% for C, H, N) were obtained for all new compounds except for **9i** (**9d**[7] and **9e**[6] reported previously). High-resolution mass spectrum calculated for **9i**: m/z 275.0439. Found for **9i**: m/z 275.0439. Mass spectral M^+ peaks shown for all compounds except **9h**, where $M^+ - 48$ (SO) was shown. [b] Except where otherwise stated, IR spectra were obtained on neat liquid. [c] Purified by chromatography. [d] Pale orange prisms. [e] Pale brown needles. [f] Obtained in bromoform. [g] Pale yellow plates from acetone–ether.

pentane-1-sulfonate (DSS) in D_2O) used as an internal standard. Mass spectra were taken with an AEI MS30 spectrometer. Combined organic extracts obtained in each experiment were dried over anhydrous $MgSO_4$ before filtration and concentration in vacuo.

The following compounds were prepared by literature methods: 2-(4-pyridyl)ethyl *p*-tolyl sulfide (**9b**), bp 145 °C (3.5 mmHg) (lit.[1] 124 °C (2.4 mmHg)); *S*-(2-(1*H*-4-pyridinio)ethyl)isothiuronium bis(*p*-toluenesulfonate) (**9m**), mp 197 °C with decomposition with darkening at 183 °C (lit.[8] mp 201–202 °C); 2-(4-pyridyl)ethanethiol hydrochloride (**7**-HCl), melted at 189–193 °C, resolidified at 235 °C, and remelted at 256–266 °C with decomposition (lit.[8] melted at 189 °C, resolidified and remelted at 250 °C with decomposition); 2-(4-pyridyl)ethyl chloride hydrochloride (**12j**-HCl), mp 201–203 °C (lit.[14] mp 260 °C with decomposition); methyl 1-octyl sulfoxide (**6n**), mp 37–38 °C (lit.[11] mp 40–40.5 °C); diisobutylammonium thiolbenzoate (**11h**-*i*-Bu_2NH), mp 118–122 °C (with decomposition) (lit.[12] mp 124 °C); methyl 1-octyl sulfide (**11n**), bp 102–104 °C (25 mmHg) (lit.[11] bp 108 °C (40 mmHg); bis(2-(4-pyridyl)-ethyl)disulfide dihydrochloride (**19l**-HCl), mp 199–202 °C (with decomposition) with darkening at 169 °C and 182 °C (lit.[8] mp 199–200 °C (with decomposition) with darkening at 185 °C).

Typical Procedures for the Preparation of Compounds 9a–i. (A) By Michael Addition. Part 1. 1-Octyl 2-(4-Pyridyl)ethyl Sulfide (9a). 4-Vinylpyridine (**1**; 1.95 g, 18.5 mmol) in ethanol (15 mL) at 20 °C was treated with a solution of 1-octanethiol (**2a**; 2.78 g, 19.0 mmol) and sodium ethoxide (0.15 g, 2.2 mmol) in ethanol (10 mL) over 20 min. The mixture was stirred for 5 h at 20 °C, the solvent evaporated, and the resulting oil (5.53 g) chromatographed on silica gel eluted with benzene–ethyl acetate (4:1) to give 4.63 g (99%) of **9a** as a yellow viscous oil. Other data are listed in Tables I–III.

(B) By Michael Addition. Part 2. 2-Naphthyl 2-(4-Pyridyl)ethyl Sulfide (9c). A solution of 4-vinylpyridine (**1**; 0.63 g, 6.21 mmol) and 2-naphthalenethiol (**2c**; 1.01 g, 6.30 mmol) in benzene (15 mL) was heated at reflux for 6 h with stirring. The reaction mixture was stored overnight at 20 °C, the solvent evaporated, the resulting oil (1.94 g) chromatographed on silica gel eluted with benzene–ethyl acetate (3:1) to give 1.63 g (99%) of **9c** as an orange viscous oil, which solidified after storage at 0 °C to prisms, mp 80.5–82 °C. Other data are listed in Tables I–III.

A similar procedure was used for the preparation of phenyl 2-(4-pyridyl)ethyl sulfide (**9d**), which was characterized as **9d**-HCl [mp 148–149 °C (lit.[7] mp 149–151 °C)] which was prepared by treatment of sulfide **9d** with concentrated hydrochloric acid, followed by recrystallization from ethanol–ether in 83% yield. Data are listed in Tables I–III for compound **9d**.

(C) By Alkylation of Thiol 7. Part 1. 5-Nitro-2-pyridyl 2-(4-Pyridyl)ethyl Sulfide (9g). To an ice-cold, stirred suspension of 2-(4-pyridyl)ethanethiol hydrochloride (**7**-HCl; 1.10 g, 6.26 mmol) in anhydrous ethanol (10 mL) was added a solution of sodium ethoxide in anhydrous ethanol (20 mL, prepared from 0.36 g, 15.7 mmol, of sodium) over 10 min with stirring. The mixture was then stirred for 5 min at 0 °C and 2-chloro-5-nitropyridine (**8g**, X = Cl; 1.00 g, 6.31 mmol) added in portions over 10 min at 0 °C with stirring, followed by anhydrous ethanol (5 mL). The whole mixture was stirred for 140 min at 20 °C, filtered, and evaporated, and the residue was dissolved in methylene chloride. Filtration and evaporation then gave crude sulfide **9g** as a brown-red solid (1.63 g). Chromatography on silica gel eluted with benzene–ethyl acetate (4:1) gave 1.23 g (75%) of **9g** as yellow-brown needles, mp 89–90 °C.

Similar procedures were used for the preparation of **9e**, **9f**, **9h**, and **9i**. For the preparation of thiol ester **9i**, potassium *tert*-butoxide in *tert*-butyl alcohol was used as the base. Data for **9e**, **9f**, **9g**, **9h**, and **9i** are listed in Tables I–III. Benzyl 2-(4-pyridyl)ethyl sulfide (**9e**) was characterized as **9e**-HCl [mp 141–144 °C (lit.[7] mp 139–142 °C)] which was prepared by treatment of sulfide **9e** with concentrated hydrochloric acid, followed by recrystallization from ethanol in 80% yield.

(D) By Alkylation of Thiol 7. Part 2. Phenyl 2-(4-Pyridyl)ethyl Sulfide (9d). To a solution of sodium ethoxide in anhydrous ethanol (15 mL, prepared from 0.41 g, 17.8 mmol, of sodium) was added benzenethiol (**2d**; 0.90 g, 8.18 mmol) dropwise over 2 min at 20 °C with stirring, followed by anhydrous ethanol (5 mL). The mixture was stirred for 10 min at 20 °C, and then a solution of 2-(4-pyridyl)ethyl chloride hydrochloride (**12**-HCl; 1.57 g, 8.12 mmol) in anhydrous ethanol (25 mL) was added dropwise over 25 min at 0 °C, followed by anhyrous ethanol (5 mL). The whole mixture was stirred for 1 h at 0 °C and then 1.5 h at 20 °C. After workup as described in procedure C, purification by chromatography on silica gel eluted with benzene–ethyl acetate (4:1) gave 0.20 g (11%) of **9d**, identical by TLC and spectral data with the sample prepared by procedure A.

Typical Procedure for the Preparation of Compounds 3a–c: 1-Octyl 2-(4-Pyridyl)ethyl Sulfoxide (3a). 1-Octyl 2-(4-pyridyl)ethyl sulfide (**9a**; 1.10 g, 4.37 mmol) was added dropwise over 6 min to a stirred solution of sodium periodate (0.94 g, 4.39 mmol) in water (10 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C, followed by 2 h at 20 °C, and then extracted with ether (40 mL) and then chloroform (2 × 40 mL). The combined extracts were washed with water (2 × 20 mL), dried, and evaporated to give an oil which was chromatographed on silica gel and eluted successively with benzene–ethyl acetate (3:1), benzene–ethyl acetate (1:7), and benzene–acetone (1:3). Evaporation afforded respectively (i) 0.09 g (8%) of recovered sulfide **9a**, (ii) 0.08 g (6%) of sulfone **13a**, and (iii) 1.00 g (85%) of sulfoxide **3a** as a yellow oil. Sulfoxide **3a** solidified after storage in a refrigerator (mp <30 °C).

Similar procedures were used for the preparation of sulfoxides **3b** and **3c**. In the preparation of **3c**, 50% methanol was used as the solvent, in place of water. Data for **3a**, **3b**, and **3c** are listed in Tables IV–VI.

Typical Procedure for the Preparation of *N*-Methylpyridinium Iodides (10h, 4b, 14a, and 14c): 2-(1-Methyl-4-pyridinio)ethyl Thiolbenzoate Iodide (10h). Methyl iodide (2.28 g, 16.1 mmol) was added dropwise over 5 min to a stirred solution of 2-(4-pyridyl)ethyl thiolbenzoate (**9h**; 0.25 g, 1.03 mmol) in acetone (5 mL) at 20 °C. The mixture was stirred for 24 h at 20 °C. Evaporation of the solvent gave 0.38 g (96%) of a solid, mp 126–131 °C, which was recrystallized from acetone–ether to give an analytical sample of *N*-methylpyridinium iodide **10h**, mp 130–135 °C; other data are given in Tables I–III.

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Table II. ^{1}H NMR Spectra of the Compounds 9 and 10[a-d]

	H	9a	9c	9d	9e	9f	9g	9h	9i	10h
pyridine	2,6 (2 H, d)	8.48	8.44	8.66	8.39	8.52	8.68	8.68[e]	8.65[e]	9.06[f]
	3,5 (2 H, d)	7.43	7.10	7.19	6.96	7.21	7.29	7.28[e]	7.18[e]	8.21[f]
ethylene	α,β (4 H, m)	2.82	2.65–3.45	2.70–3.40	2.70	2.86	2.85–3.80	2.75–3.65	2.60–3.50	3.30–3.80
alkyl	1′ (2 H)	2.52 t[e]			3.67 s	2.54 t[e]				
	8′ (3 H, t)	0.88								
phenyl	2″,6″ (2 H)							8.08 dd[g]		8.01 dd[g]
	3″–5″ (3 H)			7.20–7.60 m	7.22 s			7.35–7.95 m	7.1–7.8 m	7.35–7.95 m

[a] In tables, in order to indicate a certain proton or carbon, the following numbering is adopted: (i) numbers (including α and β) *without prime* are used for the 2-(4-pyridyl)ethyl group; (ii) numbers *with single prime* are used for the alkyl group attached to a sulfur atom (the protons or carbon adjacent to a sulfur atom are numbered 1′); (iii) numbers *with double prime* are used for the other aromatic ring (phenyl, naphthyl, or pyridyl) in the substituent on the sulfur atom. [b] Spectra were run in $CDCl_3$ except for **10h** (Me_2SO-d_6). Chemical shift (δ) in ppm from Me_4Si. Multiplicity: s = singlet, d = doublet, t = triplet, m = multiplet. [c] Except where otherwise stated, J = 5 Hz. [d] Other signals were as follows: **9a**, 1.28 (12 H, m, H-2′ to H-7′); **9c**, 7.10–8.00 (7 H, m, naphthyl); **9f**, 0.70–1.20 (3 H, m, H-4′), 1.15–1.90 (4 H, m, H-2′ and H-3′); **9g**, 7.38 (1 H, d, J = 9 Hz, H-3″), 8.43 (1 H, dd, J = 3 and 9 Hz, H-4″), 9.41 (1 H, d, J = 3 Hz, H-6″); **10h**, 4.40 (3 H, s, N^+CH_3). [e] J = 6 Hz. [f] J = 7 Hz. [g] J_{meta} = 2 Hz; J_{ortho} = 7 Hz.

Table III. ^{13}C NMR Spectra of the Compounds 9 and 10[a]

	C	9a	9c	9d	9e	9f	9g	9h	9i	10h
pyridine	2	149.8	149.8	149.8	149.7	149.7	149.9	149.8	149.9	144.8
	3	123.8	123.8	123.8	123.8	123.8	123.9	123.9	123.8	129.1
	4	149.3	148.8	148.7	149.1	149.4	148.6	148.7	148.1	159.0
ethylene	α	35.5	34.7	34.7	35.0	35.5	34.7	35.2	35.2	34.1
	β	31.8	33.9	34.0	31.4	31.7	30.4	29.0	30.9	27.5
alkyl (′) and/or other aromatic ring (″)	1′	32.4			36.4	32.0[b]				
	1″		127.1[b]	135.6	138.0			136.8	135.2	136.0
	2′/2″	29.6	133.7	129.7	128.8	32.4[b]	166.9	128.6	129.3[b]	127.5[b]
	3′/3″	28.9	127.5[b]	129.0	128.5	21.9	121.7	127.2	135.2[b]	126.7[b]
	4′/4″	29.2	128.6	126.4	127.1	13.6	130.4	133.5	130.1	134.0
	4″a		131.9							
	5′/5″	29.2	127.6	129.0	128.5		141.2	127.2	135.2[b]	126.7[b]
	6′/6″	32.4	126.7[c]	129.7	128.8		145.0	128.6	129.3[b]	127.5[b]
	7′/7″	22.7	125.8[c]							
	8′/8″	14.1	127.6							
	8″a		133.0							
others	N^+Me									47.3
	CO							191.1	188.5	190.5

[a] See footnote *a*, Table II, for explanation of numbering. Spectra were run in $CDCl_3$ except for **10h** (Me_2SO-d_6). Chemical shift (δ) in ppm. [b,c] Assignments bearing the same superscript could be reversed.

Table IV. Analytical Data for the Compounds 3, 13, and 14[a]

compd	(formula)	% yield	mp, °C	IR,[b] cm^{-1}	M$^+$, *m/z*
3a	($C_{15}H_{25}NOS$)	85	<30[c,d]	1595, 1410 (C—S), 1030 (S=O), 800	251[e,f]
3b	($C_{14}H_{15}NOS$)	71	36–40[c,g]	1595, 1410 (C—S), 1065 (S=O), 1035 (S=O), 800[h]	245
3c	($C_{17}H_{15}NOS$)	58	104–107.5[c,g]	1600, 1415 (C—S), 1065 (S=O), 1035 (S=O), 800[h]	281
13a	($C_{15}H_{25}NO_2S$)	76	oil[c]	1600, 1415 (C—S), 1340–1250 (SO_2), 1140 (SO_2), 810	284[e,i]
13c	($C_{17}H_{15}NO_2S$)	67	97.5–98.5[c]	1595, 1415 (C—S), 1300 (SO_2), 1270 (SO_2), 1140 (SO_2), 830[j]	297
14a	($C_{16}H_{28}INO_2S$)	96	<30[d,k]	1645 (pyridinium), 1575, 1300 (SO_2), 1120 (SO_2), 830[j]	

[a] Satisfactory analytical values (±0.4% for C, H, N) were reported for all new compounds except for **3a** and **3c**. Calcd for **3a**: C, 67.37; H, 9.42; N, 5.24. Found for **3a**: C, 67.15; H, 9.84; N, 5.00. Calcd for **3c**: C, 72.57; H, 5.37; N, 4.98. Found for **3c**: C, 72.99; H, 5.56; N, 4.81. [b] Except where otherwise stated, IR spectra were obtained on neat liquid. [c] Purified by chromatography. [d] Gradually melted at 25 °C. [e] M$^+$ was not observed. [f] m/z = M$^+$ − 16 (O). [g] Pale yellow prisms. [h] Obtained in bromoform. [i] m/z = M$^+$ + 1. [j] Obtained in Nujol. [k] Pale yellow wax from acetone–ether.

Table V. ^{1}H NMR Spectra of the Compounds 3, 13, and 14[a-c]

	H		3a	3b	3c	13a	13c	14a
pyridine	2,6	(2 H, d)	8.68	8.44	8.63	8.69	8.59	9.40[d]
	3,5	(2 H, d)	7.28	7.04	7.16	7.29	7.14	8.52[d]
ethylene	α,β	(4 H, m)	2.75–3.45	3.00	2.75–3.50	3.25	2.85–3.75	3.30–4.20
alkyl	1′	(2 H, m)	2.50–2.95			2.80–3.20		3.15–3.65
	2′	(2 H, m)	1.50–2.10			1.50–2.20		1.50–2.20
	3′–7′	(10 H, m)	1.33			1.30		1.37
	8′	(3 H, m)	0.50–1.10			0.60–1.10		0.50–1.10
naphthyl	1″	(1 H, s)			8.33		8.65	
	3″–8″	(6 H, m)			7.35–8.25		7.50–8.30	

[a] Spectra were run in $CDCl_3$ except for **14a** (Me_2CO-d_6). Chemical shifts (δ) in ppm from Me_4Si. Multiplicity: s = singlet, d = doublet, t = triplet, m = multiplet. [b] Except where otherwise stated, J = 5 Hz. [c] Other signals were as follows: **3b**, 2.42 (3 H, s, Ar-CH_3), 7.29 (2 H, d, J = 8 Hz, H-3″ and H-5″), 7.46 (2 H, d, J = 8 Hz, H-2″ and H-6″); **14a**, 4.72 (3 H, s, N^+CH_3). [d] J = 6 Hz.

Similar procedures were used for the preparation of **4b**, **14a**, and **14c**.

Compound 4b: yield 100%, hygroscopic brown oil; ^{1}H NMR (acetone-d_6) δ 2.38 (3 H, s, CH_3-arom), 3.1–3.7 (4 H, m, pyridinium-CH_2CH_2-S), 4.57 (3 H, s, N^+Me), 7.0–7.8 (4 H, m, aryl), 8.08 (2 H, d, J = 6 Hz, β-pyridinium), 9.05 (2 H, d, J = 6 Hz, α-pyridinium). This sample was immediately subjected to the procedure below without further purification.

Table VI. ^{13}C NMR Spectra of the Compounds 3, 13, and 14[a]

	C	3a	3b	3c	13a	13c	14a
pyridine	2	150.1	150.0	150.0	150.1	150.0	146.0
	3	123.9	123.8	123.7	123.7	123.6	129.1
	4	148.0	147.9	147.7	147.0	146.4	159.8
ethylene	α	28.1	27.1	27.0	27.1	28.1	28.7
	β	52.2[b]	56.5	56.1	52.5[b]	56.0	52.1[b]
alkyl (′) or other aromatic ring (″)	1′/1″	52.7[b]	141.6	124.8	53.4[b]	129.8	53.7[b]
	2′/2″	22.6	130.0	140.2	21.9[c]	135.6	22.5[c]
	3′/3″	28.8[c]	130.0	119.6	28.4[d]	122.5	29.0[d]
	4′/4″	28.9[c]	139.9	129.6	28.9[d]	130.0	29.7[d]
	4″a			134.4		135.3	
	5′/5″	29.1[c]	130.0	128.4[b]	29.0[d]	129.4	29.7[d]
	6′/6″	31.7	130.0	127.9[c]	31.6	127.9[b]	32.5
	7′/7″	22.6		127.4[c]	22.5[c]	128.0[b]	23.2[c]
	8′/8″	14.1		128.0[b]	14.0	129.4	14.0
	8″a			132.8		132.1	
others	ArMe		21.3				
	N^+Me						48.9

[a] Spectra were run in $CDCl_3$ except for **14a** (Me_2CO-d_6). Chemical shift (δ) in ppm. [b-d] Assignments bearing the same superscript could be reversed.

Compound 14a: yield 96%, hygroscopic yellow wax; mp <30 °C. Other data are listed in Tables IV–VI.

Compound 14c: yield 100%, hygroscopic brown wax; ^1H NMR (acetone-d_6) δ 3.5 (4 H, m, pyridinium-CH_2CH_2-S), 4.48 (3 H, s, N^+Me), 7.6–8.5 (6 H, m, naphthyl), 8.20 (2 H, d, J = 6 Hz, β-pyridinium), 8.72 (1 H, s, H^1-naphthyl), 9.05 (2 H, d, J = 6 Hz, α-pyridinium). This sample was immediately subjected to the procedure below without further purification.

Typical Procedure for the Preparation of Compounds 6o from 4b and Compounds 16n, 16p, 16q, and 16r from 14: Deprotection–Trapping Method. Methyl *p*-Tolyl Sulfoxide (6o). To a solution of the *N*-methylpyridinium iodide **4b** (0.40 g, 0.86 mmol) and methyl iodide (1.82 g, 12.9 mmol) in acetone (8.0 mL) was added aqueous potassium carbonate (0.12 g, 0.87 mmol; 1.0 mL) in one batch. The mixture was stirred for 24 h at 20 °C, ether (20 mL) was added, and the mixture was stirred an additional 10 min at 0 °C. Collection of the precipitate and washing with ether (2 × 10 mL) afforded a solution which was evaporated. The residue was chromatographed on silica gel, eluting with benzene–ethyl acetate (1:1), to give 85 mg (64%) of sulfoxide **6o**, as pale yellow prisms: mp 37–41 °C (lit.[15] mp 42–43 °C); IR ($CHBr_3$) 1610, 1595, 1500, 1490, 1400 (C—S), 1065 (S=O), 1030 (S=O), 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 (3 H, s, CH_3-aryl), 2.68 (3 H, s, CH_3SO), 7.25 (2 H, d, J = 8 Hz, H^3-phenyl), 7.46 (2 H, d, J = 8 Hz, H^2-phenyl); ^{13}C NMR ($CDCl_3$) δ 142.6 (s), 141.4 (s), 130.0 (d), 123.5 (d), 44.0 (q), 21.3 (q); mass spectrum, m/z (relative intensity) 154 (M^+, 55), 139 (100), 123 (14), 108 (8), 91 (49), 77 (20), 65 (18), 51 (6).

Similar procedures were used for the preparation of **16n**, **16p**, **16q**, and **16r**.

Compound 16n: yield 75%, leaflets; mp 60.5–62.5 °C (lit.[11] mp 62 °C); IR (Nujol) 1400 (C—S), 1320–1240, 1120 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.60–1.15 (3 H, m, CH_3CH_2), 1.30 (10 H, m, $(CH_2)_5CH_3$), 1.6–2.2 (2 H, m, $CH_2CH_2SO_2$), 2.85 (3 H, s, CH_3SO_2), 3.00 (2 H, t, J = 7 Hz, CH_2SO_2); ^{13}C NMR ($CDCl_3$) δ 54.9 (t), 40.4 (q), 31.7 (t), 29.0 (t), 28.9 (t), 28.4 (t), 22.6 (t), 22.5 (t), 14.0 (q); mass spectrum, m/z (relative intensity) 193 (M^+ + 1, 2), 177 (3), 175 (2), 107 (12), 94 (10), 83 (17), 81 (100).

Compound 16p: yield 97%, leaflets from ethanol; mp 106–107 °C (lit.[16] mp 142–143 °C); IR (Nujol) 1585, 1390, 1145 (SO_2), 1120, 820, 770 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.13 (3 H, s, CH_3-aryl), 7.3–8.4 (6 H, m, naphthyl), 8.68 (1 H, s, H^1-naphthyl); ^{13}C NMR ($CDCl_3$) δ 137.5 (s), 135.3 (s), 132.2 (s), 129.7 (d), 129.4 (d), 129.3 (d), 129.0 (d), 128.0 (d), 127.8 (d), 122.1 (d), 44.5 (q); mass spectrum, m/z (relative intensity) 206 (M^+, 22), 191 (8), 143 (9), 128 (9), 127 (97), 115 (23), 101 (5). Anal. Calcd for $C_{11}H_{10}O_2S$: C, 64.06; H, 4.89. Found: C, 64.23; H, 4.87.

Compound 16q: ethyl iodide was used in place of methyl iodide; yield 74%, leaflets; mp 65–67 °C (lit.[17] mp 68 °C); IR (Nujol) 1310 (SO_2), 1290, 1270, 1250, 1230, 1120 (SO_2), 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.5–1.1 (3 H, m, $CH_3CH_2CH_2$), 1.35 (10 H, m, $(CH_2)_5CH_3$), 1.40 (3 H, t, J = 6 Hz, $CH_3CH_2SO_2$), 1.6–2.2 (2 H, m, $CH_2CH_2SO_2$), 2.98 (2 H, t, J = 7 Hz, $CH_2CH_2SO_2$), 3.05 (2 H, q, J = 6 Hz, $CH_3CH_2SO_2$); ^{13}C NMR ($CDCl_3$) δ 52.1 (t), 47.0 (t), 31.7 (t), 29.0 (t), 28.9 (t), 28.6 (t), 22.6 (t), 21.9 (t), 14.0 (q), 6.6 (q); mass spectrum, m/z (relative intensity) 206 (M^+, 1), 189 (2), 177 (12), 121 (9), 112 (4), 95 (97), 85 (3), 71 (75), 57 (100), 43 (91).

Compound 16r: 1-bromooctane was used in place of methyl iodide; yield 19%, needles from petroleum ether; mp 75–76 °C (lit.[17] mp 76 °C); IR (Nujol) 1415 (C—S), 1325 (SO_2), 1300, 1275, 1240, 1210, 1200 (SO_2), 1125 (SO_2), 1110 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.6–1.1 (6 H, m, CH_3CH_2), 1.33 (20 H, m, $(CH_2)_5CH_3$), 1.6–2.2 (4 H, m, $CH_2CH_2SO_2$), 2.80–3.25 (4 H, m, CH_2SO_2); ^{13}C NMR ($CDCl_3$) δ 52.8 (t), 31.7 (t), 29.05 (t), 28.95 (t), 28.6 (t), 22.6 (t), 22.0 (t), 14.0 (q); mass spectrum, m/z (relative intensity) 290 (M^+, 0.3), 273 (0.6), 205 (1), 179 (52), 161 (4), 113 (3), 112 (3), 71 (75).

Methyl 1-Octyl Sulfoxide (6n). Methyl iodide (4.56 g, 32.1 mmol) was added dropwise over 5 min to a stirred solution of sulfoxide **3a** (0.56 g, 2.09 mmol) in acetone (12 mL) at 20 °C. After the mixture was stirred for 4 h at 20 °C, acetone (12 mL) and aqueous potassium carbonate (0.30 g, 2.17 mmol; 2.4 mL) were added, and the mixture was stirred for 24 h at 20 °C. Extraction with ether (3 × 50 mL) and evaporation of the combined extracts afforded a green wax (0.51 g), which on recrystallization from petroleum ether gave 0.10 g (27%) of sulfoxide **6n** as pale yellow needles, mp 37–38 °C (lit.[11] mp 40–40.5 °C). This sample was identical with sulfoxide **6n** obtained from the sulfide **11n** as compared by TLC, spectra, and mixed melting point (no depression was observed): IR (film) 1420 (C—S), 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.6–1.2 (3 H, m, CH_3CH_2), 1.35 (10 H, m, $(CH_2)_5CH_3$), 1.4–2.1 (2 H, m, $CH_2CH_2SO_2$), 2.62 (3 H, s, CH_3SO_2), 2.5–3.0 (2 H, m, CH_2SO_2); ^{13}C NMR ($CDCl_3$) δ 54.8 (t), 38.6 (q), 31.7 (t), 29.1 (t), 29.0 (t), 28.8 (t), 22.6 (t), 14.0 (q).

A similar procedure was used for the preparation of **6p**.

Methyl 1-Octyl Sulfone (16n). Sulfoxide **6n** (0.190 g, obtained from 0.224 g of sulfoxide **3a**) was chromatographed on silica gel and eluted with benzene–ethyl acetate (3:1); the sole product isolated by evaporation of the solvent was 92 mg (57%) of **16n** as prisms, mp 61.5–62 °C (lit.[11] mp 62 °C). This sample was identical with sulfone **16n** obtained from the sulfone **13a** as compared by TLC, spectra, and mixed melting point (no depression was observed).

Analytically pure sulfoxide **6n** (150 mg, 0.851 mmol) was chromatographed on silica gel and eluted with benzene–ethyl acetate (3:1); the sole product isolated by evaporation of the solvent was 85 mg (52%) of **16n** as prisms, mp 59–60 °C, identical with **16n** obtained above.

Methyl 2-Naphthyl Sulfoxide (6p). After workup, crude **6p**

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(17) Fenton, G. W.; Ingold, C. K. *J. Chem. Soc.* **1928**, 3127.

was chromatographed on silica gel eluted with benzene–acetone (2:1). In this case, there was no evidence that oxidation of sulfoxide **6p** to sulfone **16p** occurred: yield 40%, prisms; mp 109–110 °C (lit.[18] mp 104–105 °C); IR ($CHBr_3$) 1585, 1490, 1420 (C—S), 1060 (S=O), 1035 (S=O), 815, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.80 (3 H, s, CH_3SO), 7.35–7.80 (3 H, m, β-naphthyl), 7.80–8.25 (3 H, m, α-naphthyl), 8.35 (1 H, s, H^1-naphthyl); ^{13}C NMR δ 142.9 (s), 134.4 (s), 132.9 (s), 129.5 (d), 128.5 (d), 128.0 (d), 127.7 (d), 127.3 (d), 124.0 (d), 119.3 (d), and 43.8 (q); mass spectrum, *m/z* (relative intensity) 190 (M^+, 49), 175 (100), 159 (18), 147 (28), 144 (8), 143 (7), 128 (15), 127 (37), 126 (16), 115 (56), 101 (8), 93 (1), 77 (13), 65 (2), 51 (8).

Procedure for the Preparation of Compounds 13a and 13c: 1-Octyl 2-(4-Pyridyl)ethyl Sulfone (13a). Aqueous hydrogen peroxide (30%; 4.0 mL) was added dropwise over 5 min to a stirred solution of sulfide **9a** (1.00 g, 3.98 mmol) in acetic acid (4.0 mL). After the solution was stirred for 38 h at 20 °C, the mixture was evaporated and treated with saturated aqueous sodium bicarbonate (30 mL) and the suspension extracted with ethyl acetate (3 × 40 mL). The combined extracts were washed with saturated aqueous sodium chloride (20 mL), dried, and evaporated to give an oil which was chromatographed on silica gel and eluted with benzene–ethyl acetate (3:1). Evaporation afforded 0.86 g (76%) of **13a** as a colorless viscous oil.

A similar procedure was used for the preparation of sulfone **13c**. Data for **13a** and **13c** are listed in Tables IV–VI.

Reaction of 1-Octyl 2-(4-Pyridyl)ethyl Sulfide (9a) with Aniline and a Chlorinating Agent. Method A. Using *N*-Chlorosuccinimide. *N*-Chlorosuccinimide (0.59 g, 4.42 mmol) was added during 8 min to a stirred solution of sulfide **9a** (1.01 g, 4.02 mmol) and aniline (0.39 g, 4.19 mmol) in methylene chloride (20 mL) at 0 °C. The mixture was stirred for 2 h at 0 °C and then 55 h at 20 °C. Addition of methylene chloride (30 mL), shaking, and washing with aqueous sodium hydroxide (5%; 2 × 30 mL) gave an organic layer which was washed with water (2 × 30 mL), dried, and evaporated to give a tarry residue (1.19 g). Chromatography on silica gel and elution with benzene gave 0.39 g (67%) of di-1-octyl disulfide (**19a**)[19] as an oil: IR (film) 1440 (C—S) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.5–1.2 (6 H, m, CH_3), 1.30 (20 H, m, $(CH_2)_5CH_3$), 1.5–2.2 (4 H, m, CH_2CH_2S), 2.70 (4 H, t, *J* = 7 Hz, CH_2CH_2S); ^{13}C NMR ($CDCl_3$) δ 39.3 (t), 31.9 (t), 29.3 (t), 28.6 (t), 22.7 (t), 14.1 (q); mass spectrum, *m/z* (relative intensity) 290 (M^+, 10), 182 (9), 178 (7), 105 (8), 93 (28), 84 (100), 77 (37). Subsequent chromatography by elution with benzene–ethyl acetate (3:1) gave 60 mg (6%) of 1-octanesulfenanilide (**18a**) as an oil [IR (film) 3300 (NH), 1595, 1495, 1455, 1325, 1230, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.60–1.20 (3 H, m, CH_3), 1.25–1.50 (12 H, m, $(CH_2)_6$), 3.10 (2 H, t, *J* = 7 Hz, CH_2S), 3.40 (1 H, b s, NH), 6.35–7.50 (5 H, m, phenyl); mass spectrum, *m/z* (relative intensity) 290 (6), 184 (3), 145 (28), 93 (15), 43 (100)], 0.10 g (13%) of *N*-(2-(4-pyridyl)ethyl)aniline (**20l**) as brown prisms [mp 57–62 °C (lit.[20] mp 61.5 °C); IR ($CHBr_3$) 3400 (NH), 3300 (NH), 1600, 1565, 1500, 1320 (C—N), 1260 (C—N), 810, 800, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.80 (2 H, t, *J* = 7 Hz, CH_2-pyridyl), 3.35 (2 H, t, *J* = 7 Hz, CH_2CH_2-pyridyl), 3.67 (1 H, b s, NH), 6.20–7.50 (5 H, m, phenyl), 7.01 (2 H, d, *J* = 5 Hz, β-pyridyl), 8.38 (2 H, d, *J* = 5 Hz, α-pyridyl)] and a recovery of 0.20 g (20%) of sulfide **9a**.

Method B. Using *tert*-Butyl Hypochlorite. To a stirred solution of aniline (0.48 g, 5.15 mmol) in methylene chloride (10 mL) at −78 °C was added a solution of *tert*-butyl hypochlorite (0.56 g, 5.16 mmol) in methylene chloride (10 mL) over 20 min. The mixture was stirred for an additional hour at −78 °C, and this was followed by addition of sulfide **9a** (1.27 g, 5.05 mmol) in methylene chloride (25 mL) over 20 min. The mixture was stirred a further 2 h at −78 °C and then allowed to reach the ambient temperature during another 2-h period. The mixture was washed with aqueous sodium hydroxide (0.24 g; 20 mL) and then with water (20 mL). The organic layer was dried and evaporated to give a tarry residue which was chromatographed on silica gel, eluting successively with benzene and benzene–ethyl acetate (3:1). Di-1-octyl disulfide (**19a**) was eluted first (0.65 g, 89%), followed by recovered 1-octyl 2-(4-pyridyl)ethyl sulfide (**9a**; 0.14 g, 11%).

***p*-Toluenesulfenanilide (18b).** To a stirred solution of aniline (0.47 g, 5.05 mmol) in methylene chloride (10 mL) at −78 °C was added a solution of *tert*-butyl hypochlorite (0.55 g, 5.07 mmol) in methylene chloride (10 mL) over 15 min. A solution of sulfide **9b** (1.15 g, 5.01 mmol) in methylene chloride (25 mL) was then added at −78 °C, over 20 min. The mixture was stirred for a further 2 h at −78 °C and then allowed to reach the ambient temperature during another 2-h period. The mixture was washed with aqueous sodium hydroxide (0.27 g; 20 mL) and then with water (20 mL). The organic layer was dried and evaporated to give a tarry residue which was chromatographed on silica gel, eluting successively with benzene and benzene–ethyl acetate (3:1). *p*-Toluenesulfenanilide (**18b**; 0.62 g, 57%) crystallized as needles from petroleum ether: mp 73–75 °C (lit.[21] mp 80–81 °C); IR ($CHBr_3$) 3370 (NH), 1595, 1490, 1470, 1390, 1285, 1230, 800, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.30 (3 H, s, CH_3), 5.20 (1 H, b s, NH), 6.50–7.70 (9 H, m, aryl); ^{13}C NMR ($CDCl_3$) δ 146.8 (s), 137.9 (s), 135.5 (s), 129.7 (d), 129.3 (d), 123.2 (d), 120.4 (d), 114.7 (d), 20.9 (q); mass spectrum, *m/z* (relative intensity) 215 (M^+, 100), 182 (14), 123 (63), 92 (47), together with recovered sulfide **9b** (0.31 g, 27%).

2-Naphthalenesulfenanilide (18c): prepared by method B, yield 60%, pale orange prisms; mp 96–99 °C; IR ($CHBr_3$) 3365 (NH), 1620, 1590, 1490, 1470, 1390, 1285, 1230, 800, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.13 (1 H, b s, NH), 6.70–8.15 (12 H, m, aryl); ^{13}C NMR ($CDCl_3$) δ 146.6 (s), 139.0 (s), 133.7 (s), 131.7 (s), 129.3 (d), 128.6 (d), 127.9 (d), 127.1 (d), 126.6 (d), 125.3 (d), 121.1 (d), 120.6 (d), 120.1 (d), 114.7 (d); mass spectrum, *m/z* (relative intensity) 251 (M^+, 100), 218 (24), 159 (67), 128 (21), 115 (92), 93 (39). Anal. Calcd for $C_{16}H_{13}NS$: C, 76.46; H, 5.21; N, 5.57. Found: C, 76.16; H, 5.28; N, 5.64, together with recovered sulfide (**9c**, 37%).

Reaction of 4-Vinylpyridine (1) with Benzothiazole-2-thione (21k). 4-Vinylpyridine (**1**; 0.975 g, 9.27 mmol) and benzothiazole-2-thione (**21k**; 1.56 g, 9.33 mmol) in acetic acid (10 mL) was heated at reflux for 7.5 h. Evaporation afforded a residue which was treated with saturated aqueous sodium bicarbonate (20 mL). The mixture was extracted with ethyl acetate (3 × 40 mL), and the combined extracts were washed with saturated aqueous sodium chloride (30 mL), dried, and evaporated to give an oil. Chromatography on silica gel and elution with benzene–ethyl acetate (7:1) gave 0.20 g (8%) of thiene **22l** as an orange oil: IR (film) 1595, 1560, 1420 (C=N), 1410 (C—S), 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.90–3.40 (2 H, m, CH_2-pyridyl), 3.30–3.80 (2 H, m, CH_2CH_2-pyridyl), 6.80–8.20 (4 H, m, benzothiazole), 7.11 (2 H, d, *J* = 5 Hz, β-pyridyl), 8.46 (2 H, d, *J* = 5 Hz, α-pyridyl); ^{13}C NMR ($CDCl_3$) δ 165.8 (s), 153.1 (s), 149.7 (d), 148.5 (s), 135.2 (s), 126.0 (d), 124.3 (d), 123.9 (d), 121.5 (d), 121.0 (d), 34.8 (t), 33.1 (t); mass spectrum, *m/z* (relative intensity) 272 (M^+, 14), 180 (11), 167 (85), 135 (21), 106 (100), 93 (13), 78 (44), 65 (17), 51 (47). Anal. Calcd for $C_{14}H_{12}N_2S_2$: C, 61.73; H, 4.44; N, 10.28. Found: C, 61.83; H, 4.48; N, 10.26. Subsequent elution with benzene–ethyl acetate (7:1) gave 1.42 g (56%) of thione **21l** as pale yellow prisms from ethanol: mp 123–126 °C; IR ($CHBr_3$) 1595, 1565, 1410 (C—S), 1370, 1310, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.85–3.35 (2 H, m, CH_2-pyridyl), 4.40–4.80 (2 H, m, CH_2CH_2-pyridyl), 6.80–7.60 (4 H, m, benzothiazole), 7.16 (2 H, d, *J* = 5 Hz, β-pyridyl), 8.46 (2 H, d, *J* = 5 Hz, α-pyridyl); ^{13}C NMR ($CDCl_3$) δ 188.7 (s), 149.9 (d), 146.2 (s), 140.9 (s), 127.4 (s), 127.0 (d), 124.8 (d), 124.1 (d), 121.5 (d), 111.9 (d), 46.3 (t), 31.9 (t); mass spectrum, *m/z* (relative intensity) 272 (M^+, 37), 209 (19), 167 (100), 135 (22), 106 (50), 93 (15). Anal. Calcd for $C_{14}H_{12}N_2S_2$: C, 61.73; H, 4.44; N, 10.28. Found: C, 61.88; H, 4.44; N, 10.14.

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Registry No. 1, 100-43-6; **2a**, 111-88-6; **2c**, 91-60-1; **2d**, 100-53-8; **3a**, 105163-65-3; **3b**, 105163-66-4; **3c**, 105163-67-5; **4b**, 105163-68-6; **6n**, 3079-27-4; **6o**, 934-72-5; **6p**, 35330-76-8; **7**·HCl, 6298-11-9; **8g** (X = Cl), 4548-45-2; **9a**, 105163-69-7; **9b**, 62237-49-4; **9c**, 105163-70-0; **9d**, 21070-67-7; **9d**·HCl, 21070-68-8; **9e**, 21181-90-8; **9e**·HCl, 21181-91-9; **9f**, 105163-71-1; **9g**, 105163-72-2; **9h**, 105163-73-3; **9i**, 105163-74-4; **10h**, 105163-75-5; **11n**, 3698-95-1; **12**·HCl (X = Cl), 85673-15-0; **13a**, 105163-76-6; **13b**, 105163-77-7; **14a**, 105163-78-8; **14b**, 90158-96-6; **16n**, 7560-60-3; **16p**, 35330-75-7; **16q**, 34008-69-0; **16r**, 7726-20-7; **18a**, 105163-79-9; **18b**, 14933-92-7; **18c**, 105163-80-2; **19a**, 822-27-5; **20l**, 28683-44-5; **21k**, 149-30-4; **21l**, 27410-87-3.

New Total Synthesis of (±)-Indolmycin

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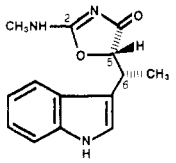
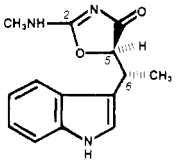
A convergent total synthesis of the antibiotic (±)-indolmycin (1) is presented. *N*-Carbobenzoxy-3-(1-chloroethyl)indole (12) is prepared in three steps from indole-3-carboxaldehyde (9). Alkylation of the lithium anion of 2-(dimethylamino)-4(5*H*)-oxazolone (4) with chloride 12 provides a mixture of the (±)-2-dimethylamino derivative of indolmycin (13) and its diastereomer (14) in a ratio of 2.2:1. Amine exchange is effected by treatment of 13 with methylamine, affording (±)-1 in five steps from commercially available 9. Efforts to extend this technology toward an asymmetric synthesis of (−)-1 are described.

Indolmycin (1), isolated from an African strain of *Streptomyces albus*,[1] exhibits an antibacterial spectrum that includes the pathogenic species *Pasteurella*, *Haemophilus*, and *Mycoplasma*,[2] which are responsible for many of the respiratory diseases in farm animals. It was shown by Schach von Wittenau and Els[3] that indolmycin (1) is 5-[1-(1*H*-indol-3-yl)ethyl]-2-(methylamino)-4(5*H*)-



(5*S*, 6*R*)-**1**
(−)-Indolmycin

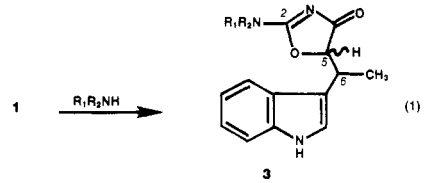


(5*R*, 6*R*)-**2**
(+)-Isoindolmycin

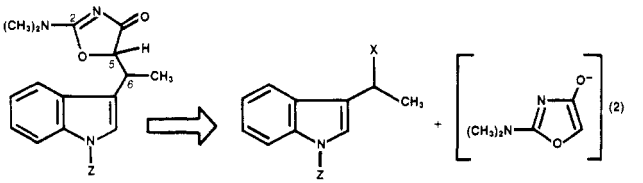
oxazolone, and the absolute configuration was later determined as 5*S*,6*R* by Chan and Hill.[4] In an alkaline medium indolmycin readily epimerizes at C-5 to afford isoindolmycin (2). In contrast to indolmycin, this unnatural diastereomer (5*R*,6*R*) possesses no antibacterial activity.[3] We wished to prepare a variety of analogues, related to indolmycin, and in particular some benzo-substituted compounds. Synthetic attempts were made using two published routes[3,5] for indolmycin itself, but these were found to be unacceptable when starting with the requisite substituted indoles (e.g., 5-methoxyindole, 5-fluoroindole, etc.).[6] Takeda and Mukaiyama[7] have reported a 14-step asymmetric synthesis of indolmycin that could be used for the preparation of certain analogues; however, we were interested in the development of a shorter sequence. In the present paper we report the successful use of the enolate anion derived from 2-(dimethylamino)-4(5*H*)-oxazolone (4) as a key intermediate in the synthesis of (±)-indolmycin. This new synthesis can also be readily adapted for the preparation of some compounds related to this antibiotic.

Results and Discussion

Shortly after we initiated work in the area of indolmycin chemistry, we found that a simple amine exchange reaction[8] affords 2-amino analogues of indolmycin in the manner illustrated below (eq 1). In principle, this reaction



could be used as the last step in a total synthesis of 1 (using methylamine), allowing facile manipulation of intermediates that do not possess an acidic hydrogen on the exocyclic nitrogen atom. The idea was conceived that the 2-(dimethylamino)-4(5*H*)-oxazolone ring could be constructed at an early stage in the synthetic sequence and then connected at C-5–C-6 by a displacement reaction with a suitably substituted 3-ethylindole nucleus, as shown retrosynthetically in eq 2. This new method, if successful,



would circumvent some problems encountered in previous

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