calcd for $C_{11}H_{10}O_2S$), 128 (100), 115 (43) 77 (20).

(1*R,5*S**,5a*S**,8a*R**,8b*S**)-5,5a,6,8,8a,8b-Hexahydro-6,8-dioxo-5,7-diphenyl-2*H*,7*H*-3-oxa-1-thia-7-aza-*as*-indacene *S*-Oxide (7b). Representative Procedure for Preparing Cycloadducts 7.**[19] A solution of NPM (23.0 mg, 0.131 mmol), **4b** (27.0 mg, 0.131 mmol), and toluene (0.13 mL) was maintained at 70 °C for 7 days. The reaction mixture was allowed to cool to room temperature, concentrated, and the resulting crude material was chromatographed (silica gel 240-400 mesh, 30:1 CH_2Cl_2/EtOH) to give 43.0 mg (87%) of **7b** as a pale yellow solid. An analytical sample was prepared by recrystallization from *i*-PrOH, giving **7b** as a fine yellow powder (mp 222.5-223.0 °C): ^{1}H NMR (500 MHz, $CDCl_3$) 7.5-7.1 (m, PhH), 5.64 (dd, J = 2.9, 5.8 Hz, =CH), 5.20 (dd, J = 1.0, 9.5 Hz, OC*H*HSO), 4.90 (d, J = 9.5 Hz, OCH*H*SO), 4.24 (dd, J = 5.1, 8.9 Hz, OCCHCSO), 3.95 (ddd, J = 8.2, 2.64, 2.63 Hz, C*H*Ph), 3.77 (m, CHSO), 3,54 (t, J = 8.4 Hz, OCC*H*CHPh); ^{13}C NMR (125 MHz, $CDCl_3$) 42.4, 43.4, 45.6, 67.5, 91.6, 99.7, 125.8, 127.8, 128.5, 128.7, 128.9, 129.2, 131.0, 137.9, 154.9, 173.3, 176.3 ppm; IR (KBr) 1704, 1498, 1389, 1207, 1166, 1151, 1047, 1003 cm^{-1}; MS (CI), m/e 380 (MH^+); MS (EI), m/e (relative intensity) 379.0879 (1, 379.0878 calcd for $C_{21}H_{17}NO_4S$), 160 (54), 148 (100), 115 (47). Anal. Calcd for $C_{21}H_{17}NO_4S$: C, 66.48; H, 4.52; N, 3.69. Found: C, 66.21; H, 4.60; N, 3.69.

Acknowledgment. Financial support from the National Science Foundation (CHE 8618451) is gratefully acknowledged.

(19) All cycloadducts were prepared following this general procedure.
(20) Winkle, M. R.; Lahsinger, J. M.; Ronald, R. C. *J. Chem. Soc., Chem. Commun.* **1980**, 87.

The Regiospecific Pummerer-Like Introduction of Chlorine Atoms into Pyrrol-3-yl and Indol-3-yl Sulfoxides†

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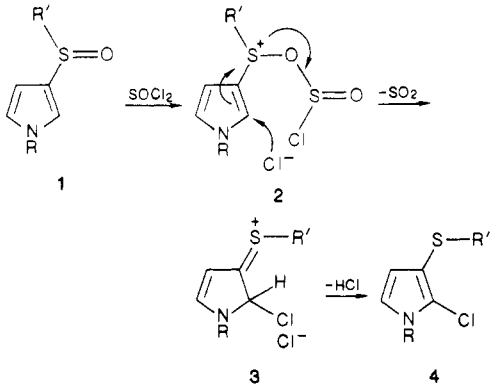
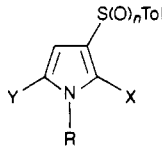
Recent work from this laboratory made available for the first time a general synthesis of pyrrol-3-yl sulfoxides from the corresponding 2-isomers by acid-catalyzed isomerization.[1] In subsequent studies of the chemistry of this novel class of compounds, we sought to exploit the known reactions of sulfoxides to introduce a substituent regiospecifically into the 2-position (e.g., chloro) and thus prepare 2,3-disubstituted pyrroles from pyrrole itself.

From the outset, we expected that in a Pummerer-like reaction[2] with thionyl chloride and the sulfoxide **1**, a sulfoxonium chloride **2** would be formed. With such an intermediate, *the only reasonable point of attack by Cl⁻ on the ring to enable the elimination of SO_2 would be the 2-position.* The sulfonium salt **3** upon loss of a proton would give the chloro sulfide **4**. In fact 3-(*p*-tolylsulfinyl)pyrrole (**5a**)[1] reacted virtually instantaneously at 0 °C with thionyl chloride to give a less polar compound, which, although reasonably stable in solution protected from oxygen, decomposed to tar upon attempted isolation. When the reaction was carried out in the presence of suspended sodium bicarbonate followed by excess *m*-chloroperoxybenzoic acid, the products were obtained as



the stable sulfones. Thus formed were 2-chloro-3-(*p*-tolylsulfonyl)pyrrole (**6a**) in 38% yield and 2,5-dichloro-3-(*p*-tolylsulfonyl)pyrrole (**7a**) in 10% yield. Likewise *N*-methyl-3-(*p*-tolylsulfinyl)pyrrole (**5b**) afforded similar yields of **6b** and **7b**. When the acid chloride was changed to oxalyl chloride and the reaction carried out at −78 °C, only traces of dichloropyrroles were observed and the monochlorosulfones were obtained in substantially higher yields (see Table I). Moreover, by limiting the quantity of oxidizing agent to 1.1 equiv, the corresponding 2-chloro-3-(*p*-tolylsulfinyl)pyrroles (**8**) were obtained as stable crystalline solids in good yields.



5a, R=H, X=Y=H, n=1
b, R=CH_3, X=Y=H, n=1
c, R=CH_2Ph, X=Y=H, n=1
6a, R=H, X=Cl, Y=H, n=2
b, R=CH_3, X=Cl, Y=H, n=2
c, R=CH_2Ph, X=Cl, Y=H, n=2
7a, R=H, X=Y=Cl, n=2
b, R=CH_3, X=Y=Cl, n=2
8a, R=H, X=Cl, Y=H, n=1
b, R=CH_3, X=Cl, Y=H, n=1
c, R=CH_2Ph, X=Cl, Y=H, n=1
9a, R=H, X=Cl, Y=H, n=0
b, R=CH_3, X=Cl, Y=H, n=0
c, R=CH_2Ph, X=Cl, Y=H, n=0

Though mechanistically reasonable, the structures of the chlorinated pyrroles **6** and **8** were easily confirmed by their NMR spectra (Table II), which all show the expected value for $J_{4,5}$ of 3.2 to 3.4 Hz. Entry of the chlorine atom at either of the other available positions would give instead a coupling constant of 1.35-1.80 Hz for $J_{2,4}$ or 1.95-2.30 Hz for $J_{2,4}$, which are well established values in the pyrrole series.[3] The origin of dichloropyrroles **7a** and **7b** is mechanistically less clear, but having suppressed their formation, we did not investigate them further.

The reaction was extended to indol-3-yl sulfoxides with analogous results in higher yields. Furthermore, due to their greater inherent stability, the indolyl sulfides **11** could be isolated and characterized as such, thus supporting the presumed identity of the initially formed products **9** in the pyrrole series. Some of the indole products were then

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† Contribution 689 from the Syntex Institute of Organic Chemistry.

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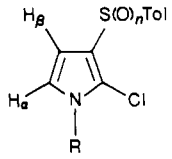
Table I. Yields and Physical Data of Products

cmpd	mp, °C	% yield	method[a]	analysis[b]
6a	209–210	38 (61)	a (b)	CHNClS
6b	167–168	32 (41)	a (b)	CHNClS
6c	145–146	83	b	CHNS
7a	180–181	10	a	CHN
7b	171–172	9	a	CHNClS
8a	125–127	56	c	CHNS
8b	85.5–86	66	c	CHNS
8c	78–79	83	c	CHNS
11a	98–99	58	d	CHNClS
11b	85–86	82	d	CHNClS
11c	107–108	94	d	CHNClS
11d	107–108	98	d	CHNClS
11e	114–114.5	96	d	CHNClS
11f	49–50	81	d	CHN
12c	151–152	84	e	CHN
12d	154–155	98	e	CHN
13a	197–198	98	f	CHN
13c	190–191	86	f	CHNClS
13d	135.5–136.5	59	f	CHNClS
13e	158–159	95	f	CHNClS
13f	157–158	86	f	CHN

[a] Methods (see Experimental Section): (a) $SOCl_2$, $NaHCO_3$, CH_2Cl_2, 0 °C; 3 equiv of *m*-CPBA, CH_2Cl_2; (b) ClCOCOCl, $NaHCO_3$, CH_2Cl_2, −78 °C; 3 equiv of *m*-CPBA, CH_2Cl_2; (c) ClCOCOCl, $NaHCO_3$, CH_2Cl_2, −78 °C; 1.1 equiv *m*-CPBA, CH_2Cl_2; (d) $SOCl_2$, $NaHCO_3$, CH_2Cl_2, 0 °C; (e) 1.1 equiv *m*-CPBA, CH_2Cl_2 (f) 3 equiv *m*-CPBA, CH_2Cl_2. [b] All analyses listed are within ±0.4% of calculated values.

Table II. Partial NMR Spectral Data of Chlorinated Pyrroles 6 and 8

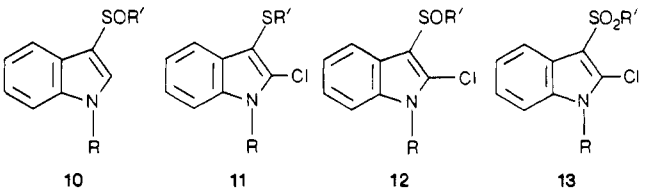


cmpd	R	*n*	δ(Hα)	δ(Hβ)	$J_{\alpha\beta}$, Hz
6a	H	2	6.89	6.51	3.2
6b	CH_3	2	6.61	6.59	3.4
6c	CH_2Ph	2	6.56	6.47	3.4
8a	H	1	6.61	6.08	3.3
8b	CH_3	1	6.57	6.08	3.3
8c	CH_2Ph	1	6.59	6.10	3.3

oxidized to the sulfoxides or sulfones. The reaction conditions, yields, and physical properties of the products are summarized in Table I.

Several points are worth mentioning in reference to the indole reaction. First, all the reactions proceeded satisfactorily at 0 °C using the relatively inexpensive thionyl chloride instead of the milder but more expensive oxalyl chloride. Second, while the thionyl chloride induced chlorination of 3-(phenylsulfinyl)indole (**10a**) gave **11a** in 58% yield, the same product was isolated in only 20% yield when sulfuryl chloride was used to chlorinate 3-(phenylthio)indole. In the latter reaction several other unidentified products were observed. Finally, the chlorination goes in nearly quantitative yield when the indole nitrogen is protected with a benzoyl or phenylsulfonyl group (**10d,e**). Since these groups are easily removed by mild base treatment, they are useful protecting groups which raise the yield of the chlorination reaction in cases where the indole nitrogen does not bear an alkyl substituent.

The reaction herein described has precedent in the so-called additive Pummerer reaction[4] of vinyl sulfoxides.



a, R=H, R′=Ph
b, R=CH_3, R′=Ph
c, R=CH_2Ph, R′=Ph
d, R=COPh, R′=Ph
e, R=SO_2Ph, R′=Ph
f, R=CH_2Ph, R′=CH_3

These compounds afford moderate to excellent yields of β-substituted sulfides when treated with typical Pummerer initiators such as thionyl chloride,[5,6] trifluoroacetic anhydride,[5] and others.[7-11] A mechanism which involves a cyclic transition state and simultaneous transfer of the Cl anion and loss of SO_2 has been proposed[6] in the reaction of β-(methylsulfinyl)styrene with thionyl chloride, the closest analogy in the literature to the present work. Although several examples of vinyl sulfoxides undergo a similar reaction, to our knowledge no example of a diaryl sulfoxide, such as those described in the present study, is among them. In fact Parham et al. have reported[12] that phenyl *p*-tolyl sulfoxide is inert to forced Pummerer conditions (benzoic anhydride, 187 °C). Furthermore we found that treatment of diphenyl sulfoxide with oxalyl chloride merely effected reduction of the sulfoxide without substitution, affording diphenyl sulfide in good yield.[13] Thus the present work is novel in that aromatic substitution with a nucleophile is facilitated by an intramolecular redox reaction between sulfur and the substituted carbon. The replaced H thus leaves as a proton rather than as a hydride as would be required by normal nucleophilic aromatic substitution. A reaction similar in form to this occurs when *N*-methylgramine methiodide reacts with cyanide ion to give 1,3-dimethyl-2-cyanoindole.[14]

Further chemistry of the novel intermediates described here will be reported shortly.

Experimental Section

The melting points were determined on a Mel-Temp melting point apparatus and are corrected. The NMR spectra were measured with a Varian EM-390 or a Bruker WM-300 spectrometer and are expressed in parts per million (δ) from internal tetramethylsilane. The infrared spectra were recorded with a Perkin-Elmer Model 237 grating infrared spectrometer. The ultraviolet spectra were obtained with a Perkin-Elmer Model 402

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(12) Parham, W. E.; Edwards, L. D. *J. Org. Chem.* **1968**, *33*, 4150.

(13) It has been reported that diphenyl sulfoxide reacts with $SiCl_4$ or BCl_3 to afford phenyl *p*-chlorophenyl sulfide in quantitative yield (Lappert, M. F.; Smith, J. K. *J. Chem. Soc.* **1961**, 3224; **1965**, 7102). Since the product is alleged to be the para isomer, identified apparently only by IR, it is not clear what, if any, mechanistic similarity the result has to the present work or other examples of the additive Pummerer reaction. Complete absence of the ortho isomer would indeed be surprising were it similar in mechanism.

(14) Snyder, H. R.; Eliel, E. L. *J. Am. Chem. Soc.* **1948**, *70*, 1857.

(15) (a) Gossauer, A. *Die Chemie der Pyrrole*; Springer-Verlag: West Berlin, 1974; p 120ff. (b) Jones, R. A.; Bean, G. P. *The Chemistry of Pyrroles*; Academic: New York, 1977; p 192ff.

ultraviolet–visible spectrometer.

Method A: Preparation of 2-Chloro-3-(*p*-tolylsulfonyl)-pyrroles by $SOCl_2$ Chlorination and *m*-CPBA Oxidation. The 3-(*p*-tolylsulfinyl)pyrrole[1] was dissolved in anhydrous methylene chloride (10 mL/mmol) and stirred at 0 °C. Sodium bicarbonate (5–8 equiv) was added, and thionyl chloride (1.4 equiv) dissolved in methylene chloride (ca. 2.5 mL/mmol) was added dropwise with efficient stirring. Upon termination of the addition, the suspension was stirred another 5 min. *m*-Chloroperoxybenzoic acid (3.0 equiv) was then added in one portion, and the temperature was allowed to reach 25 °C. The mixture was then washed with saturated aqueous bicarbonate, and the organic phase was dried over sodium sulfate, filtered, and evaporated to dryness. The product mixture was separated on preparative silica gel chromatography using hexane/ethyl acetate mixtures. The dichloro sulfones were somewhat less polar than the monochloro sulfones.

Method B: Preparation of 2-Chloro-3-(*p*-tolylsulfonyl)-pyrroles by Oxalyl Chloride Chlorination and *m*-CPBA Oxidation. The 3-(*p*-tolylsulfinyl)pyrrole was dissolved in anhydrous methylene chloride (10 mL/mmole) and sodium bicarbonate (3 times the weight of starting material) was added. With stirring under an inert atmosphere, the temperature was lowered to −78 °C. To this suspension was added 1.1 equiv of oxalyl chloride dissolved in methylene chloride, dropwise. The reaction was instantaneous, and upon completion of the addition, the reaction mixture was poured into a saturated solution of sodium bicarbonate. The phases were thoroughly mixed and then separated. To the organic phase was added *m*-chloroperoxybenzoic acid (2.1 equiv), and the reaction mixture was stirred for 30–60 min at room temperature. Upon completion of the oxidation, the solution was washed with sodium carbonate solution, dried, and evaporated. The crude products were purified either by silica gel chromatography (**6a,b**) or simply crystallized (**6c**).

Method C: Preparation of 2-Chloro-3-(*p*-tolylsulfinyl)-pyrroles by Oxalyl Chloride Chlorination and *m*-CPBA Oxidation. The reactions were carried out in an identical manner with method B, except that the oxidations were done by adding 1.1 equiv of *m*-chloroperoxybenzoic acid and stirring 10–90 min as necessary. In each case the product was purified by column chromatography silica gel).

Method D: Preparation of 2-Chloro-3-(aryl(or alkyl)-thio)indoles by $SOCl_2$ Chlorination. The reactions of 3-(phenyl(or methyl)sulfinyl)indoles with thionyl chloride were carried out in a manner identical with method A, except that the oxidation step was omitted. The products were purified by silica gel preparative TLC (**11a**), column chromatography (**11d,f**), or simply by crystallization (**11b,c,e**).

Method E: Preparation of 2-Chloro-3-(phenylsulfinyl)-indoles from 2-Chloro-3-(phenylthio)indoles by *m*-CPBA Oxidation. The sulfide dissolved in anhydrous methylene chloride was treated dropwise at 0 °C with 1.1 equiv of *m*-chloroperoxybenzoic acid dissolved in methylene chloride. The reaction mixture was allowed to reach room temperature and stirred for 10–20 min. When the reaction was complete, the solution was washed with saturated sodium carbonate solution, dried, and evaporated. The crude sulfoxide was recrystallized from an appropriate solvent system.

Method F: Preparation of 2-Chloro-3-(phenyl(or methyl)sulfonyl)indoles from 2-Chloro-3-(phenyl(or methyl)-thio)indoles by *m*-CPBA Oxidation. The reactions were carried out in a manner identical with method E, except that 2–3 equiv of oxidant was used. The products were either directly crystallized (**13a,c,f**) or purified by preparative silica gel TLC (**13d,e**).

Preparation of the Starting Materials. Heterocyclic Sulfoxides. 3-(*p*-**Tolylsulfinyl)pyrrole** (**5a**) and *N*-methyl-3-(*p*-tolylsulfinyl)pyrrole (**5b**) were prepared as described.[1]

3-(Phenylsulfinyl)indole (10a). To a solution of 3-(phenylthio)indole[16] (2.0 g) in dry methylene chloride, stirred at 0 °C, was added *m*-chloroperoxybenzoic acid (1.93 g) in small portions. After the addition was complete, the solution was stirred for 5 min more and then washed with saturated sodium bicarbonate solution, dried, and evaporated to give the pure product (1.96 g, 91%), which was recrystallized from ether–hexane: mp 126–127 °C; IR ($CHCl_3$) 3490, 1000, 975 cm^{-1}; NMR 10.01 (br s, 1 H), 7.68 (m, 2 H), 7.50–7.43 (m, 3 H), 7.33 (d, 1 H), 7.28–7.24 (m, 2 H), 7.13 (t, 1 H), 7.00 (t, 1 H); MS, *m/e* 241 (M^+). Anal. Calcd for $C_{14}H_{11}NOS$ (241.298): C, 69.68; H, 4.60. Found: C, 69.43; H, 4.52.

3-(Methylsulfinyl)indole. A solution of 3-(methylthio)-indole[17] (29.26 g) in absolute methanol (300 mL) was previously cooled to −70 °C. Oxone (55.02 g, 49.5% $KHSO_5$) dissolved in water (250 mL) was added dropwise as the reaction temperature was allowed to rise to 0 °C (ice–water bath). Upon completion of the addition of the oxidizing solution, the mixture was stirred at 0 °C for 30 min. The mixture was partitioned between water and chloroform. The aqueous layer was saturated with salt, and the phases were separated. Upon drying and evaporating, the organic layer yielded 22.20 g (69%) 3-(methylsulfinyl)indole after crystallization from chloroform–ethyl acetate: mp 134–135 °C; IR ($CHCl_3$) 3495, 1050 cm^{-1}; NMR 11.09 (br s, 1 H), 7.92 (m, 1 H), 7.5–7.1 (m, 4 H), 3.01 (s, 3 H); MS, *m/e* 179 (M^+). Anal. Calcd for C_9H_9NOS (179.233): C, 60.32; H, 5.16; N, 7.76. Found: C, 60.30; H, 5.26; N, 7.81.

N-Substituted Pyrrol-3-yl and Indol-3-yl Derivatives. N-Substitution of the heterocycles was accomplished by treatment of the sodium salt of the compound with the requisite alkylating or acylating agent in dimethylformamide. A general procedure is exemplified by the benzylation of 3-(*p*-tolylsulfinyl)pyrrole.

***N*-Benzyl-3-(*p*-tolylsulfinyl)pyrrole (5c).** To a solution of 3-(*p*-tolylsulfinyl)pyrrole[1] (1.0 g) in anhydrous dimethylformamide (10 mL) was added sodium hydride (60% in oil, 0.24 g) at 0 °C under an inert atmosphere. The suspension thus formed was stirred for 30 min. To the resulting pyrrolyl anion was added benzyl bromide (0.916 g) in one portion. After being stirred for 5 min, the reaction was diluted with water and extracted with ether (2 × 50 mL). After washing the ether layer with water, the solution was dried and evaporated. The crude product (1.36 g) was recrystallized from methylene chloride–ether to afford 1.17 g of the pure product (**5c**) as a colorless solid (81%): mp 104 °C; IR ($CHCl_3$) 1066 cm^{-1}; NMR 7.58 (d, 2 H, J = 8 Hz), 7.26 (m, 7 H), 7.08 (t, H_2, $J_{apparent}$ = 3.0 Hz), 6.66 (t, H_5, $J_{apparent}$ = 2.3 Hz), 6.29 (dd, H_4, $J_{4,5}$ = 1.8 Hz), 5.03 (s, 2 H), 2.41 (s, 3 H); MS, *m/e* (relative intensity) 295 (M^+), 247, 91 (100). Anal. Calcd for $C_{18}H_{17}NOS$ (295.42): C, 73.18; H, 5.80; N, 4.74; S, 10.86. Found: C, 72.90; H, 5.77; N, 4.72; S, 10.89.

N-Methyl-3-(phenylsulfinyl)indole (**10b**), prepared from 3-(phenylsulfinyl)indole and methyl iodide, had mp 120 °C (ethyl acetate–ether): IR ($CHCl_3$) 1010 cm^{-1}; NMR 7.71 (m, 2 H), 7.52 (s, 1 H), 7.36 (m, 6 H), 7.07 (m, 1 H) 3.82 (s, 3 H); MS, *m/e* 255 (M^+), 239, 207, 178, 77. Anal. Calcd for $C_{15}H_{13}NOS$ (255.337): C, 70.55; H, 5.13; N, 5.48; S, 12.55. Found: C, 70.55; H, 5.11; N, 5.43; S, 12.69.

N-Benzyl-3-(phenylsulfinyl)indole (**10c**), prepared from 3-(phenylsulfinyl)indole and benzyl bromide, had mp 148–149 °C (methylene chloride–hexane): IR ($CHCl_3$) 1050 cm^{-1}; NMR 7.72 (m, 2 H), 7.59 (s, 1 H), 7.45 (m, 4 H), 7.31 (m, 4 H), 7.18 (m, 3 H), 7.05 (m, 1 H), 5.32 (s, 2 H); MS, *m/e* 332 (M^+), 283, 192, 91 (100). Anal. Calcd for $C_{21}H_{17}NOS$ (331.435): C, 76.10; H, 5.17; N, 4.22. Found: C, 75.91; H, 5.18; N, 4.24.

N-Benzoyl-3-(phenylsulfinyl)indole (**10d**), prepared from 3-(phenylsulfinyl)indole and benzoyl chloride, was an oil purified by TLC: IR ($CHCl_3$) 1700, 1020 cm^{-1}; NMR 8.35 (m, 1 H), 7.52 (m, 14 H); MS, *m/e* (relative intensity) 345 (M^+), 297, 224, 105 (100). Anal. Calcd for $C_{21}H_{15}NO_2S$ (345.404): C, 73.01; H, 4.37; N, 4.05. Found: C, 73.00; H, 4.63; N, 3.98.

N-(Phenylsulfonyl)-3-(phenylsulfinyl)indole (**10e**), prepared from 3-(phenylsulfinyl)indole and benzenesulfonyl chloride, had mp 184–185 °C (methylene chloride–hexane): IR ($CHCl_3$) 1440, 1370, 1170, 1160, 1010 cm^{-1}; NMR 7.98 (m, 4 H), 7.41 (m, 1 H); MS, *m/e* 381 (M^+), 333, 192. Anal. Calcd for $C_{20}H_{15}NO_3S_2$ (399.905): C, 62.96; H, 3.96; N, 3.67; S, 16.81. Found: C, 63.02; H, 4.03; N, 3.58; S, 16.95. Alternatively, to a mixture of benzene (25 mL) and sodium hydroxide solution (50%, 25 mL) was added benzyltriethylammonium chloride (0.188 g), 3-(phenylsulfinyl)-indole (0.200 g), and benzenesulfonyl chloride (0.116 mL). With efficient stirring, the mixture was refluxed for 30 min. Upon

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cooling, the phases were separated, and the organic phase was diluted with methylene chloride, washed with water, dried, and evaporated to dryness. Purification of the crude product by preparative silica gel TLC (hexane/ethyl acetate, 3:2) yielded 0.264 g (88%) with mp 184–185 °C after recrystallization from methylene chloride–hexane. In addition 0.010 g of 3-(phenylsulfinyl)indole was recovered.

N-Benzyl-3-(methylsulfinyl)indole (**10f**), prepared from 3-(methylsulfinyl)indole and benzyl bromide, had mp 110–111 °C (methylene chloride–hexane): IR ($CHCl_3$) 1050 cm^{-1}; NMR 7.95 (m, 1 H), 7.53 (s, 1 H), 7.45–7.05 (m, 8 H), 5.30 (s, 2 H), 3.00 (s, 3 H); MS, *m/e* 269 (M^+). Anal. Calcd for $C_{16}H_{15}NOS$ (269.351): C, 71.34; H, 5.61; N, 5.20. Found: C, 71.35; H, 5.66; N, 5.17.

The Chlorination of 3-(Phenylthio)indole with Sulfuryl Chloride. To a solution of 3-(phenylthio)indole[16] (0.20 g) in anhydrous methylene chloride, maintained at 0 °C, was added dropwise sulfuryl chloride (0.071 mL), via microsyringe. The reaction was stirred at 0 °C for (1 h) and then washed with saturated sodium bicarbonate solution. The organic phase was dried and evaporated to dryness. The crude mixture, composed of several compounds, was separated on preparative silica gel TLC, by eluting with hexane–ethyl acetate (7:3), and the band corresponding to the previously characterized 2-chloro-3-(phenylthio)indole (**11a**) was isolated. The product weighed 0.046 g (20%) and had mp 98–99 °C after recrystallization from methylene chloride–pentane.

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Registry No. **5a**, 75421-89-5; **5b**, 75421-91-9; **5c**, 113976-52-6; **6a**, 98207-68-2; **6b**, 113976-53-7; **6c**, 113976-54-8; **7a**, 113976-55-9; **7b**, 113976-56-0; **8a**, 113976-57-1; **8b**, 113976-58-2; **8c**, 113976-59-3; **10a**, 98508-67-9; **10b**, 108698-57-3; **10c**, 98508-70-4; **10d**, 113976-64-0; **10e**, 113976-65-1; **10f**, 108698-58-4; **11a**, 98508-68-0; **11b**, 108698-59-5; **11c**, 98508-72-6; **11d**, 113976-60-6; **11e**, 113997-01-6; **11f**, 108726-69-8; **12c**, 108698-77-7; **12d**, 113976-61-7; **13a**, 98508-69-1; **13c**, 98508-74-8; **13d**, 113976-62-8; **13e**, 113976-63-9; **13f**, 108698-64-2; 3-(phenylthio)indole, 54491-43-9; 3-(methylthio)indole, 40015-10-9; 3-(methylsulfinyl)indole, 86925-06-6.

Enzymes in Organic Synthesis. 43.[1] Investigation of the Preferred Orientations of Ester Groups in Pig Liver Esterase Catalyzed Hydrolyses Using Conformationally Rigid Substrates[2]

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Of the many enzymes that are useful in asymmetric synthesis,[3] pig liver esterase (PLE, EC 3.1.1.1) is one that has already proven of great value[3] and for which there remains considerable potential, as reflected by the degree of current interest in its synthetic applications.[4] One of the active-site models[5] for PLE has been proposed by the group of Tamm.[5a] In this, the preferred orientation for hydrolysis of an ester group at the active site was postulated to be equatorial when attached to a cyclohexane ring. This assumption, a key one for all PLE active-site model formulations, has now been verified in a study of the PLE-catalyzed hydrolyses of the conformationally rigid *tert*-butylcyclohexanecarboxylic acid esters **1a–4a**.

Table I. Relative Rates of PLE-Catalyzed Hydrolyses of 1a–4a[a]

substrate	rel rate
ethyl butyrate	100
1	29
2	127
(±)-**3**	57
(±)-**4**	8

[a] Determined at 23 °C. [S] = 0.5 nM in 0.1 M KCl (pH 7) containing 5% MeOH.

Table II. Preparative-Scale PLE-Catalyzed Hydrolyses of (±)-3a and (±)-4a[a]

substrate	product acid (% yield, % ee)	recovd ester (% yield, % ee)
(±)-**3a**	(−)-(1*R*,3*S*)-**3b** (quant, 5)	(+)-(1*S*,3*R*)-**3a** (85, 6)
(±)-**4a**	(+)-(1*S*,3*S*)-**4b** (93, 4)	(−)-(1*R*,3*R*)-**4a** (80, 5)

[a] At pH 7, 20 °C. Reactions terminated after 50% of hydrolysis.

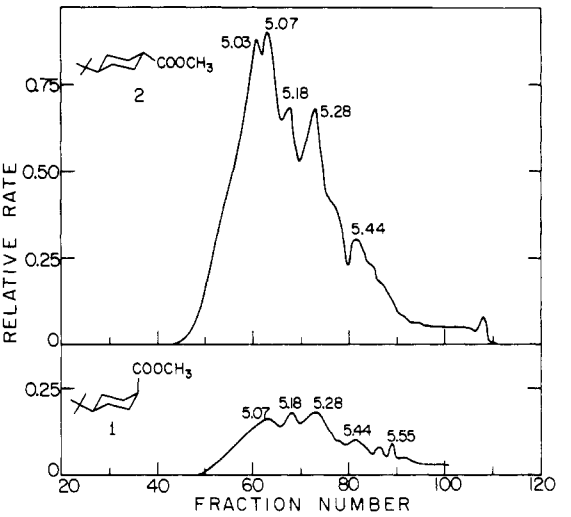

Figure 1. PLE-isozyme activity toward the equatorially and axially oriented ester groups of **2a** and **1a**, respectively, determined at pH 7 in 5% aqueous MeOH at 25 °C. The rates are relative to ethyl butyrate = 100. The fraction numbers are those from the isoelectric focusing separation. The numbers at the peaks are the p*I* values of the major isozyme fractions.

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