Chemistry of Thienopyridines. XIX. Further Studies on Chlorination and *S*-Oxidation in the Thieno[2,3-*b*]pyridine System (1)

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Treatment of thieno[2,3-*b*]pyridine (Ia) with chlorine gas in chloroform (plus water) gave a mixture of two 2,3-dichloro-2,3-dihydrothieno[2,3-*b*]pyridine 1-oxides [*trans-syn* (IIa), and *cis-anti* (IIb)] and 2,3,3-trichloro-2,3-dihydrothieno[2,3-*b*]pyridine *syn*-1-oxide (IVa), as well as a non-isolated fourth product (probably the *anti* isomer of IVa) and sometimes a small amount of thieno[2,3-*b*]pyridine 1,1-dioxide (III). Treatment of Ia in a solvent (water, chloroform-water, or THF-water) with sulfuric acid and sodium hypochlorite gave a mixture of IIb and III. Effects of variations of reaction conditions on the composition of the product mixture were ascertained through chemical isolation and/or pmr analysis. Products formed were rationalized in terms of the chlorine-water-hypochlorous acid equilibrium, plus attack of chlorine variously at positions 1 (*S*-atom), 2, and 3 of Ia, but of hypochlorous acid only at position 1. Thermal and chromatographic limitations on isolation procedures for some of the products were established. Stereochemistries of IIa, IIb, and IVa were assigned by means of pmr spectrometry with the aid of the shift reagent Eu(fod)$_3$. Spin-spin couplings between the proton at position 2 and those at positions 4 and 6 were observed at high resolution.

In exploratory runs, 5-ethyl-Ia was converted into isolable 2,3-dichloro-5-ethyl-2,3-dihydrothieno[2,3-*b*]pyridine 1-oxide, and 5-acetyl-Ia yielded 3-chloro-5-acetylthieno[2,3-*b*]pyridine. Mass spectral fragmentation patterns for the various products are presented.

It has been found that reactions of thienopyridines with elemental chlorine or chlorine-bearing reagents lead to a variety of chlorination and *S*-oxidation products. In particular, thieno[2,3-*b*]pyridine (Ia) was converted into the 3-chloro derivative Ib upon treatment with elemental chlorine in a mixture of silver sulfate-concentrated sulfuric acid at 80-105° (4). Addition of chlorine gas to a refluxing mixture of Ia, chloroform, and water gave a number of products, from which Ib and the 2,3-dichloro derivative of Ia (Ic) were isolated by chromatography on silica gel, Ib hydrochloride was isolated by solvent trituration, and a 2,3-dichloro-2,3-dihydrothieno[2,3-*b*]pyridine 1-oxide (IIa, m.p. 163-164°) (5) was isolated in very low yield (< 3%) by evaporative distillation plus, recrystallization (4,5). Compound IIa was produced in similar yield by treatment of Ia with iodobenzene dichloride in aqueous acetonitrile (6). In contrast, treatment of Ia with dilute hydrochloric acid plus sodium hypochlorite produced the sulfone of Ia (III) (7). The present investigation was conducted in an effort (a) to establish (if possible) conditions for the synthesis of IIa in improved, reproducible yield and (b) to devise a mechanistic rationale for the formation and interrelations of the various products found.

Three sets of experiments (see Table I) were conducted. The first set (runs 1, 2 and 4) comprised variations on the aforementioned method of bubbling chlorine gas into the reaction mixture and isolating products by solvent fractionation. Runs 1 and 2 were conducted in a cold, stirred mixture of chloroform and water (8) under closely similar conditions; while run 4 was made over a longer period of time in refluxing anhydrous chloroform containing the buffer salt dipotassium monohydrogen orthophosphate (9), and water was added only in further processing of the reaction mixture. Two compounds (either dichloro compound Ic or dichlorodihydrosulfoxide IIa, plus a new substance $C_7H_4Cl_3NOS$, m.p. 161.5-162.5°, assigned the structure of the trichlorodihydrosulfoxide IVa) were isolated in each case (see proposed mechanistic Scheme I). From balanced equations for these reactions (equations 1-3) it is apparent that yields of the various products formed should depend on the molar ratios of chlorine/Ia used and on the availability of water in the overall process. While the synthesis of

$$Ia + 2\ Cl_2 \rightarrow Ic + 2\ ClH \qquad 1$$

$$Ia + 2\ Cl_2 + H_2O \rightarrow IIa + 2\ HCl \qquad 2$$

$$Ia + 3\ Cl_2 + H_2O \rightarrow IVa + 3\ HCl \qquad 3$$

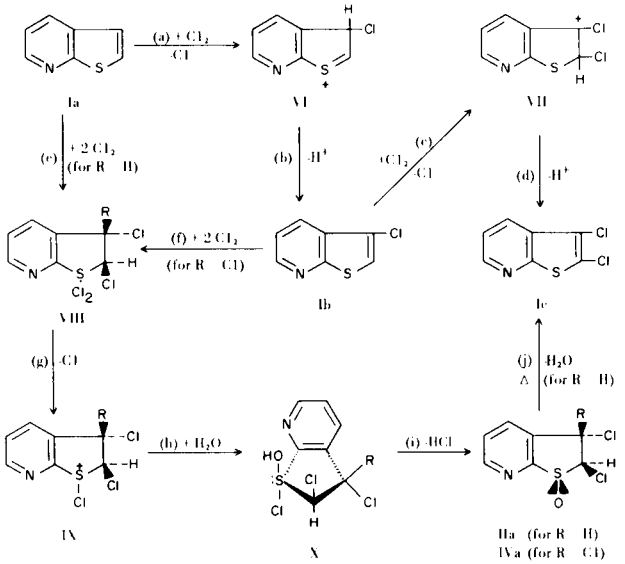
IVa (albeit in variable yield) can be conducted with reason-

TABLE I

Reactions of Thieno[2,3-*b*]pyridine (Ia) with Chlorine Plus Water or with Aqueous Sodium Hypochlorite-Sulfuric Acid under Various Conditions

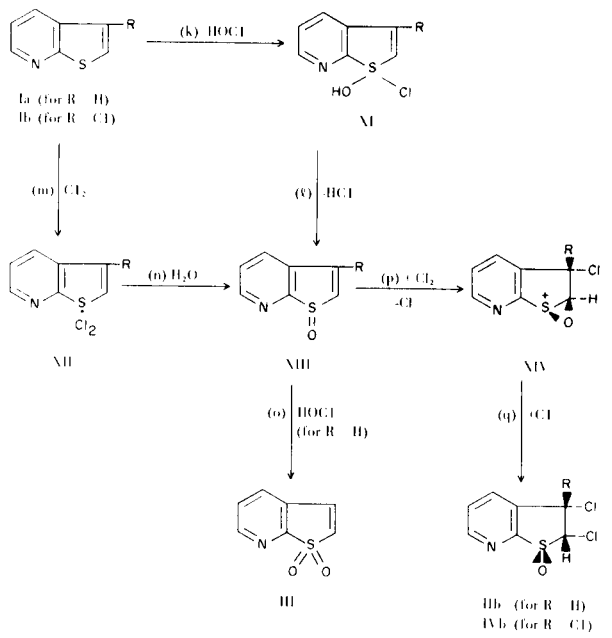
Run No.	Reagents Used: Cl-Bearing Component (A)	Molar Ratio A:Ia	Other Reactant (a)	Solvent System	Reaction Temp. (°C.)	Reaction Time (hr.)	Ic (c)	Product Distribution in % (b): IIa	IIb	III	IVa	IVb
1	Cl_2	(d)	None	$CHCl_3$-H_2O	0-10	3	----	18	----	----	10 (e)	----
2	Cl_2	(d)	None	$CHCl_3$-H_2O	0-10	3	52	----	----	----	22 (f)	----
3	Cl_2	2.3	None	$CHCl_3$-H_2O	0-20 (g)	3	(h)	(43)	(17)	(tr)	(20)	(20)
4	Cl_2	(d)	K_2HPO_4, 1.8	$CHCl_3$ (i)	Reflux	6	24	----	----	----	32 (j)	----
5	Cl_2	4.6	K_2HPO_4, 1	$CHCl_3$ (i)	0-20 (g)	3	(h)	(9)	(15)	(3)	(57) 14	(16)
6	Cl_2	5.0	H_2SO_4, 1	$CHCl_3$-H_2O	0-20 (g)	3	(h)	(8)	(21)	(10)	(39)	(22)
7	Cl_2	6.3	None	THF-H_2O	0-20 (g)	3	(h)	(0)	(54)	(0)	(31)	(15)
8	NaOCl (k)	2	H_2SO_4, 1	H_2O	25	4	(h)	(0)	(19)	(81) 44	(tr)	(0)
9	NaOCl (ℓ)	2	H_2SO_4, 1	$CHCl_3$-H_2O	25	5	(h)	(0)	(31)	(59) 14	(0)	(0)
10	NaOCl (m)	4	H_2SO_4, 2	THF-H_2O	25	5.5	(h)	(0)	(50)	(50)	(0)	(0)
11	NaOCl (ℓ)	6	H_2SO_4, 6	THF-H_2O	25	27	(h)	(tr)	(100) 12	(tr)	(tr)	(0)

(a) Numbers in this column are moles of reactant used per mole of Ia used. Water is also a reactant in every case. (b) Unparenthesized numbers are isolated yields based on quantity of Ia used. Parenthesized numbers are mole percentages of products II-IV in the total crude product mixture, as based on pmr analysis (See Experimental). The symbol tr denotes a trace. (c) Isolation methods would not have yielded Ib or recovered Ia. (d) Chlorine gas was bubbled into the reaction mixture throughout the reaction period, but no quantitative measure of the gas absorbed was made. (e) Products were separated by stirring with cold carbon tetrachloride to leave undissolved IVa. (f) Products were separated by stirring with cold chloroform to leave undissolved IVa. (g) The reaction mixture was cooled in a bath maintained at 0°, but heat evolved during reaction raised the temperature during the first 0.5 hour. (h) The pmr analytical method used would not have detected Ib, Ic, or recovered Ia. (i) Water was added during processing of the reaction mixture. (j) Products were separated by stirring with pentane to leave undissolved IVa. (k) The sodium hypochlorite used was 0.44 *M*. Nearly identical results were obtained with 0.88 *M* solution. (ℓ) Using 0.88 *M* sodium hypochlorite solution. (m) Using 1.1 *M* sodium hypochlorite solution.



able confidence of success, isolation of IIa remains uncertain and capricious (10).

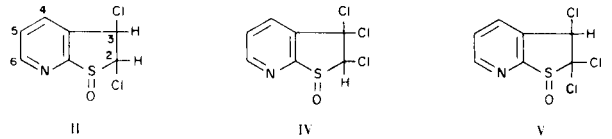
In the second set of experiments (runs 3 and 5-7, Table I) variations were made in solvent used, acidity of the reaction mixture, and the molar ratio of chlorine absorbed (measured by difference in weight) to Ia used. In addition, the crude mixture of products was analysed by means of pmr in the spectral region upfield from $\delta = 7.3$ ppm for the presence of IIa, IVa, and sulfone III (but not for that of Ib, Ic, or recovered Ia). Resonance signals corresponding to the presence of two additional compounds, IIb (m.p. 148-150.5°, isomeric with IIa) and IVb (tentative structural assignment) were also noted. In fact (see run 11), IIb was eventually isolated in pure form, though IVb has not yet been obtained free of other components (see Scheme 2). In run 3, only a 15% excess of chlorine (for the stiochiometric production of II) was added under conditions approximating those of run 1. Nonetheless, just 50% of the chlorine accounted for by identified products resided in II, while the other 50% was found in IV. The predominance of isomer IIa over IIb (molar ratio 2.5:1) is notable. For the one-phase system of aqueous tetrahydrofuran (plus introduction of a much larger excess of chlorine, run 7), however, no IIa was found, while IIb was the dominant identified product. Run 5, a low-temperature variation on run 4, served to confirm the usefulness of dipotassium monohydrogen orthophosphate in the formation of IVa. Somewhat surprisingly, use of sulfuric acid (run 6), instead of the buffer salt, still gave IVa as the main component,



though the reaction conditions were less selective in regard to products formed.

In the runs with chlorine as a reactant yields of sulfone III were small or negligible. As noted in a previous paper (7) treatment of a dilute, aqueous solution of Ia in two equivalents of mineral acid (hydrochloric or sulfuric) with a two molar quantity of sodium hypochlorite produced sulfone III in 37-48% isolated yield. Run 8 corroborated this result and showed that some IIb is also present in the reaction mixture. On changing to aqueous THF as solvent plus increasing the molar ratios of hypochlorite and sulfuric acid (runs 10 and 11) the ratio of IIb/III increased markedly. The low isolated yield of IIb in run 11, however, implies that most of the Ia used was destroyed by excessive oxidation.

Compound IIb was assigned the skeletal structure of II on the bases of elemental analysis, mass spectrum, a sulfoxide absorption band at 1065 cm^{-1}, and a pmr spectrum which showed the usual pattern of signals for pyridine protons H-4 to H-6, plus two upfield doublets of doublets for H-2 and H-3. The skeletal structure of IVa was based on an analogous array of data; except that the upfield portion of the pmr spectrum consisted of only one singlet, for either H-2 or H-3 (corresponding to either structure IV or V). Treatment of IVa with a mixture of hydrochloric acid and potassium iodide in acetic acid, solvent conditions



expected to effect both sulfoxide deoxygenation (6, 11) and vicinal dechlorination (12) of either IV or V, produced 3-chlorothieno[2,3-*b*]pyridine (Ib), identified as its crystalline picrate. Barring the possibility of chlorine migration from C-2 to C-3 during these chemical transformations one can then assign IV as the appropriate skeletal structure of IVa. Stereochemical assignments to IIa, IIb, and IVa were then made with the aid of a europium shift reagent, as detailed in subsequent paragraphs. The rationale for assignment of structure IVb to a non-isolated product is also presented later.

Meanwhile, we considered the possibility that inconsistencies in the production of IIa might be ascribable to facets of the isolation procedure. Two pertinent aspects were found. First, IIa is unstable when heated as a dry solid at atmospheric pressure, whereby it is transformed into 2,3-dichlorothieno[2,3-*b*]pyridine (Ic) (55%) by loss of the elements of water (13). It seems likely that the earlier use of evaporative distillation as a step in the isolation of IIa (5) may have largely thermolyzed the desired product to give Ic. This method of isolation of IIa should be avoided.

Second, thin layer chromatographic studies using silica gel as adsorbent showed that IIa and IVa (like other sulfoxides) (14) are strongly retained on the plate, while Ib and Ic move relatively rapidly on it. In fact, column chromatography on silica gel is an excellent method for freeing Ib and Ic from small amounts of sulfoxides present in crude reaction mixtures, but such chromatography should not be employed when isolation of II or IV is the goal.

For use in investigations of stereostructures Fourier transform proton-decoupled spectra of IIa and IIb (in hexadeuterioacetone) and of IVa (in trideuterioacetonitrile) were determined at a frequency of 100 MHz. At a sweep width of 1000 Hz the spectra appeared to be nearly ideal (*i.e.* approximately first order), but on further expansion of the scale higher multiplicities became apparent (Figures 1-3). For IVa the singlet for H-2 was converted into a pseudotriplet, while the doublets of doublets for H-6 (at lowest field) and H-4 (next to lowest field) became doublets of multiplets. On the other hand, expansion of the H-5 doublet of doublets did not reveal additional complexity. Results with IIa and IIb were similar for H-4, H-5, and H-6 signals. Instead of a singlet at higher field in the 1000-Hz spectrum, however, one has an AB pattern for H-2 and H-3 in these compounds. The downfield pair of this set is assigned to H-2 because of the strong de-shielding effect of the adjacent sulfoxide group (15). The H-2 doublet is seen as a doublet of pseudotriplets in the expanded spectrum, while the H-3 doublet remains unaltered in general appearance. The increased complexity of the expanded spectrum is ascribable to spin-spin coupling between H-2 (on the one

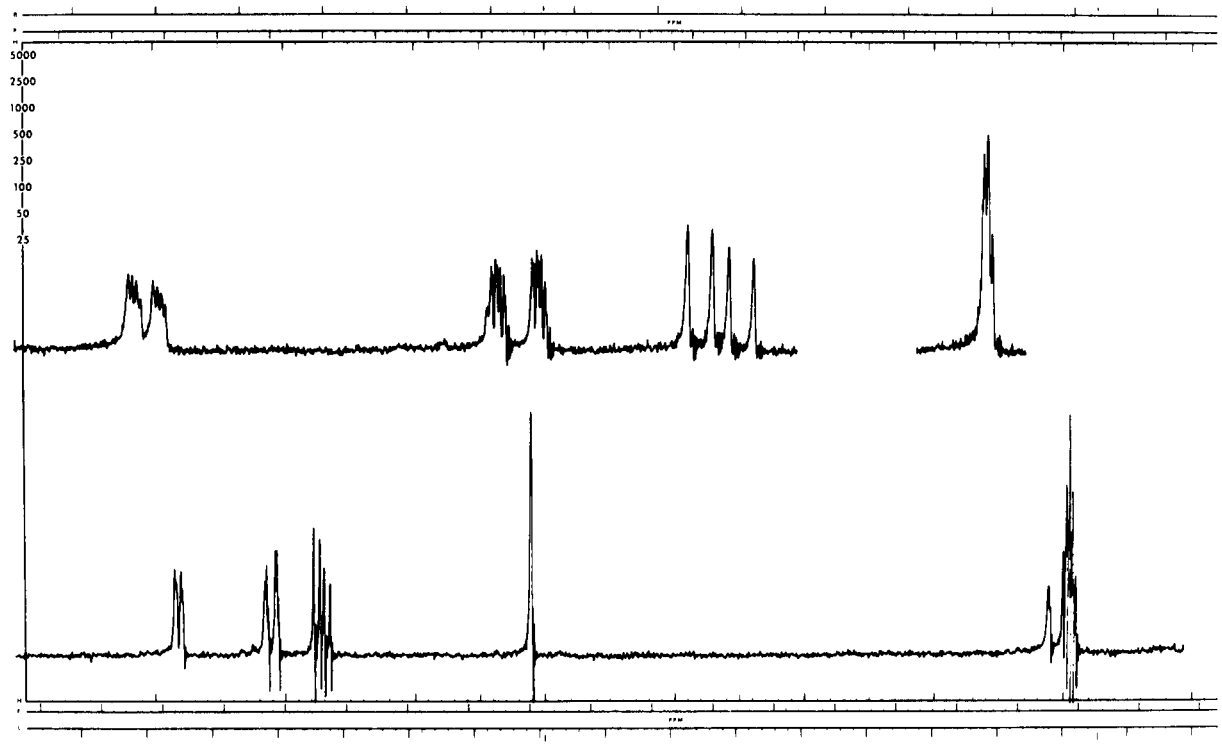


Figure 1. Fourier transform 100 MHz pmr spectrum of IVa in trideuterioacetonitrile. The lower curve was obtained at a sweep width of 1000 Hz and includes an upfield signal for the solvent. The upper curve is an expansion of the substrate signals.

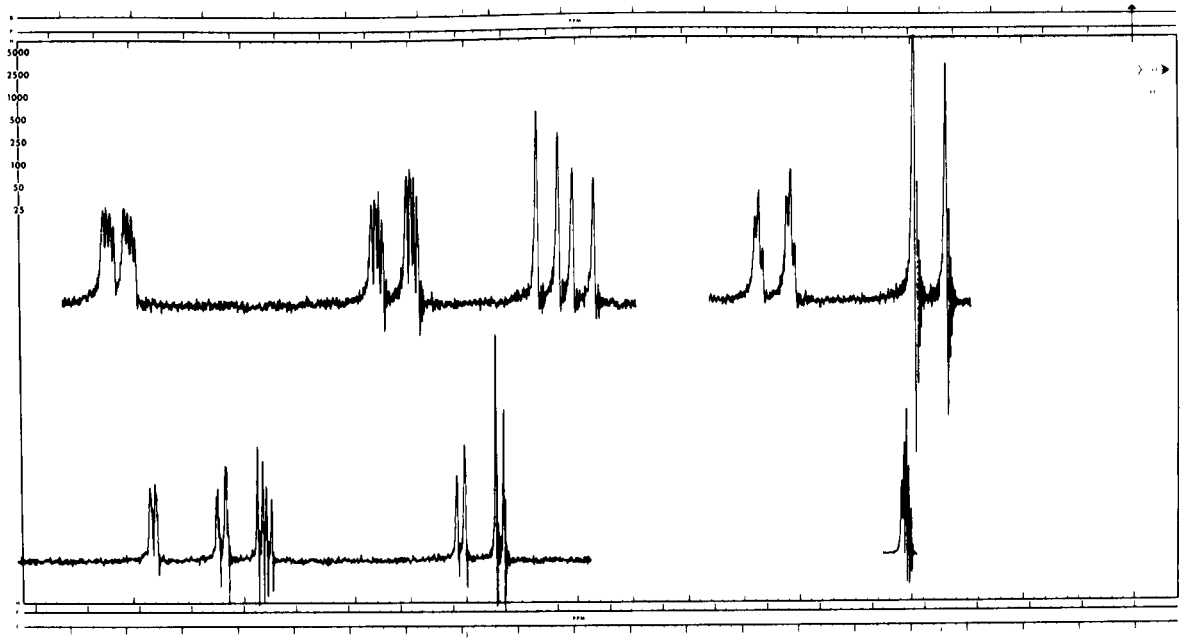


Figure 2. Fourier transform 100 MHz pmr spectrum of IIb in hexadeuterioacetone. See legend for Figure 1 in regard to upper and lower curves.

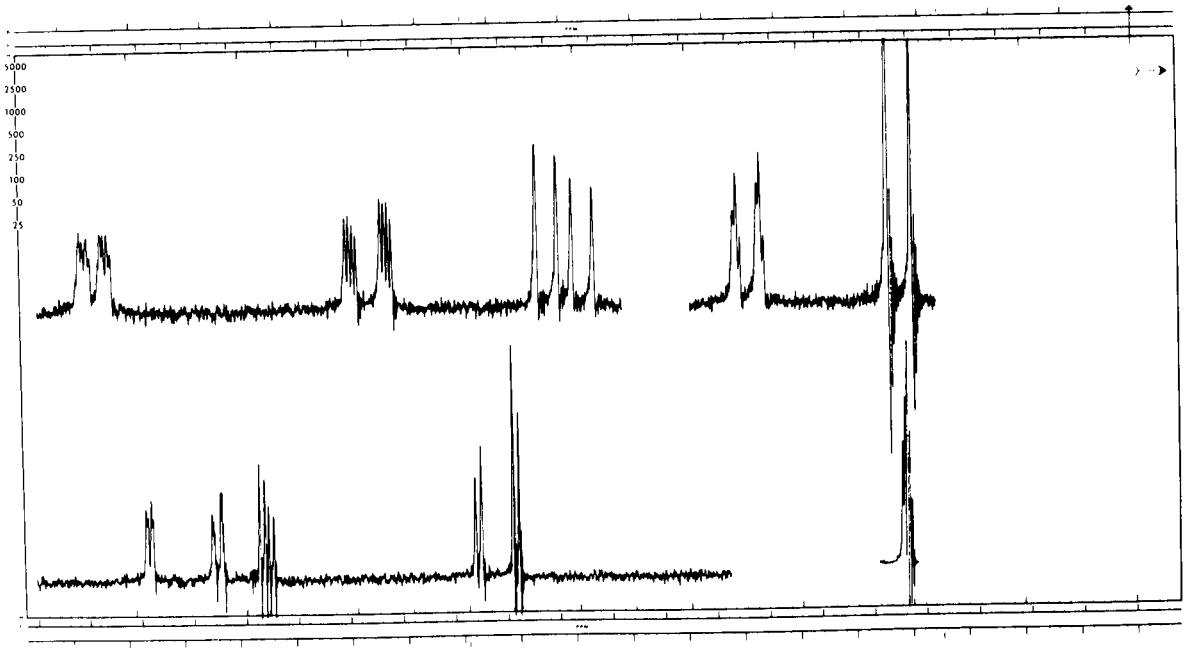


Figure 3. Fourier transform 100 MHz pmr spectrum of IIa in hexadeuterioacetone. See legend for Figure 1 in regard to upper and lower curves.

hand) and H-4 and H-6 (on the other hand), with $J_{2,4} \simeq J_{2,6} \sim 0.8$ Hz. This coupling was corroborated in each case by double irradiation at the frequency of the H-2 signal. Under these conditions the signal for H-6 collapsed to a doublet of doublets and that for H-4 was simplified. Further elucidation of this coupling must await detailed investigation of the system; in particular studies to ascertain whether the coupling is intramolecular (*i.e.* long-range) or is, in fact, intermolecular between (or amongst) units of a molecular aggregate. For present purposes one might note that the occurrence of a non-isolated compound IVb in crude reaction mixtures from chlorination of Ia is based on the presence of an additional singlet (unaccounted for by IIa, IIb, III or IVa) at $\delta < 7.3$ ppm in the 1000-Hz spectrum of the product. Since this singlet becomes a pseudotriplet in the expanded spectrum, we have tentatively assigned structure IVb to this substance, as the most likely possibility.

Stereostructures for substrates IIa, IIb, and IVa were assigned with the aid of the shift reagent Eu(fod)$_3$. The

TABLE II

Induced Proton Magnetic Resonance Shifts from Treatment of Di- and Trichloro-2,3-dihydrothieno[2,3-*b*]pyridine 1-Oxide Substrates with Eu(fod)$_3$ Reagent (a)

Substrate No.	Increment of Eu(fod)$_3$ added	Cumulated Induced Shift in Resonance Signal, $\Delta\delta$ ppm (b)									
		For H-2		For H-3		For H-4		For H-5		For H-6	
		Abs.	Rel.	Abs.	Rel.	Abs.	Rel.	Abs.	Rel.	Abs.	Rel.
IIa	1	0.12	1.2	0.24	2.4	0.08	0.8	0.08	0.8	0.10	1.0
	2	0.21	1.1	0.44	2.3	0.15	0.8	0.14	0.7	0.19	1.0
IIb	1	0.24	3.0	0.21	2.6	0.09	1.1	0.09	1.1	0.08	1.0
	2	0.36	3.0	0.29	2.4	0.14	1.2	0.10	0.8	0.12	1.0
IVa	1	0.07	1.0	----	----	0.06	0.9	0.04	0.6	0.07	1.0
	2	0.07	1.0	----	----	0.05	0.7	0.04	0.6	0.07	1.0

(a) Solvent trideuterioacetonitrile, with tetramethylsilane as internal standard. Eu(fod)$_3$ is tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,5-octanedionato)europium (III). (b) Abs. is the measured induced shift; Rel. is the induced shift compared to that found for the H-6 resonance.

skeletal structures of II and IV are presumed to be nearly planar, with the largest amount of distortion occurring at C-2. The oxygen atom of the sulfoxide group will protrude to one side of this plane. While the coordination site of the substrate molecule for the europium (III) atom is open to question (16), it is assumed that this site is the sulfoxide oxygen atom and that the europium will lie on the same side of the plane as the oxygen does. In Table II are presented data on the induced shifts effected in the resonance signals for the various protons in the three substrates (dissolved in trideuterioacetonitrile) upon addition of successive increments of reagent. Relative shifts are compared to data for H-6 as a standard. Compound IIb is a particularly clear case since shifts for H-2 and H-3 are relatively large – consistent with the location of both hydrogen atoms and the oxygen atom on the same side of the molecular plane. Compound IIa retains a relatively large shift for H-3, but shows much smaller increments for H-2 – as expected for the *trans-syn* geometry shown. Corroborating this difference in stereochemistry at C-2 is the observation that the signal for H-2 in IIb (H *syn* to O) falls downfield from that for H-2 in IIa (H *anti* to O) in hexadeuterioacetone (Figs. 2 and 3) and trideuterioacetonitrile solutions *sans* shift reagent. The stereochemistry assigned to IVa is consistent with that of IIa in that the induced shift in the H-2 signal is relatively small (51).

Despite the complexities of the system we have made an effort (see Schemes 1 and 2) to depict rational mechanistic pathways to the isolated compounds shown in Table I. Important equilibria involved in aqueous solutions (or aqueous phases) during these reactions are shown in equations 4 and 5. Chlorine, chloride ion, water, and hypochlorous acid are potentially available (17) in all runs *per se*, or

$$Cl_2 + 2\,H_2O \rightleftharpoons H_3O^+ + Cl^- + HOCl \quad 4$$

$$HOCl + H_2O \rightleftharpoons H_3O^+ + OCl^- \quad 5$$

during work-up. In addition compound Ia has three pertinent nucleophilic centers, *viz.* the azine nitrogen atom (*N*), the thiole sulfur atom (*S*), and the carbon-carbon double bond between C-2 and C-3 (C=C). From the principle of Hard and Soft Acids and Bases (HSAB) (18) one can list these nucleophilic (basic) centers in order of hardness $N > S > C{=}C$ (19). Likewise, the chlorine-bearing agents (electrophiles or Lewis acids) fall in the order of hardness Cl-OH > Cl-Cl (20) in respect to the displacement reaction 6, where Nu: is the electrically neutral nucleophilic center which attacks the chlorine atom of the reagent ClY with liberation of anion $:Y^-$. In the present reactions

$$Nu: + Cl\overset{\delta+}{-}Y\overset{\delta-}{\rightarrow}(Nu-Cl)^+ + :Y^- \quad 6$$

the hardest and strongest basic center *N* plays only an auxiliary role and will not generally be considered further (21). We believe that hypochlorous acid reacts only at the *S*-center, while chlorine may react either at *S* or at the C=C, in accordance with the generalization that reaction 6 is kinetically favored when Nu: and ClY have closely similar degrees of hardness (22).

In Scheme 1 are shown possible routes to 3-chlorothieno-[2,3-*b*]pyridine (Ib), 2,3-dichlorothieno[2,3-*b*]pyridine (Ic), *trans*-2,3-dichloro-2,3-dihydrothieno[2,3-*b*]pyridine *syn*-1-oxide (IIa), and 2,3,3-trichloro-2,3-dihydrothieno-[2,3-*b*]pyridine *syn*-1-oxide (IVa). Compound Ib results from treatment of a solution of Ia in concentrated sulfuric acid with chlorine in the presence of silver ion catalyst (a soft Lewis acid) which enhances polarization of chlorine by formation of the complex $(Cl\text{-}ClAg)^+$ (4). The transition complex VI (shown without the expected proton on *N*) is analogous to that for deuteriodeprotonation of Ia in concentrated deuteriosulfuric acid (24). Electron availability at C-3 is fostered by conjugation of the sulfur atom with the C=C in Ia. Loss of a proton from VI (step *b*) gives Ib. It appears that in a chloroform phase, steps *a-d* may occur with the formation of Ic. The buffer salt present in run 4 should facilitate proton removal.

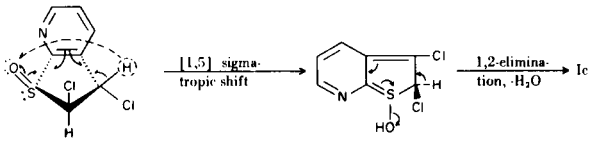
Addition of two molecules of chlorine to Ia or to Ib (steps *e* and *f*) would give structure VIII. It seems likely that addition to the C=C will usually occur first; to give a softer *S*-center, which will then take up chlorine more avidly. In either water or chloroform solution, *trans*-addition to the C=C of Ia should be preferred (as shown) (23, 25) and would lead to IIa (in preference to IIb) as in run 3 (26). On contact with water, VIII should undergo facile hydrolysis to the sulfoxide IIa or IVa (6). We propose that this transformation occurs *via* IX and X; effectively by a reverse pathway from that suggested by Mislow *et al.* and modified by Ciuffarin and Fava (27) for racemization of an optically active sulfoxide by means of concentrated hydrochloric acid. Structure VIII probably involves a trigonal-bipyramidal sulfur atom, as shown for X (28). Loss of a chloride ion from VIII (step *g*) and nucleophilic attack on sulfur by water would produce X (29). Equilibration at the *S*-center of X is expected through breaking and reforming of the S-Cl bond. The thermodynamically more stable structure X (rather than its epimer at position 1) should prevail and lead to IIa and IVa on loss of hydrogen chloride. The yields of IVa are highest in runs 4 and 5 where the molar ratios of chlorine used are large and where buffer salt can foster the formation of Ib. In runs 2 and 4 the relative yields of IVa and Ic should be determined by the relative extents to which steps *f* and *c* proceed.

Scheme 2 depicts the conversion of Ia into *cis*-2,3-dichloro-2,3-dihydrothieno[2,3-*b*]pyridine *anti*-1-oxide (IIb) and thieno[2,3-*b*]pyridine 1,1-dioxide (III), as well as the formation of the postulated 2,3,3-trichloro-2,3-

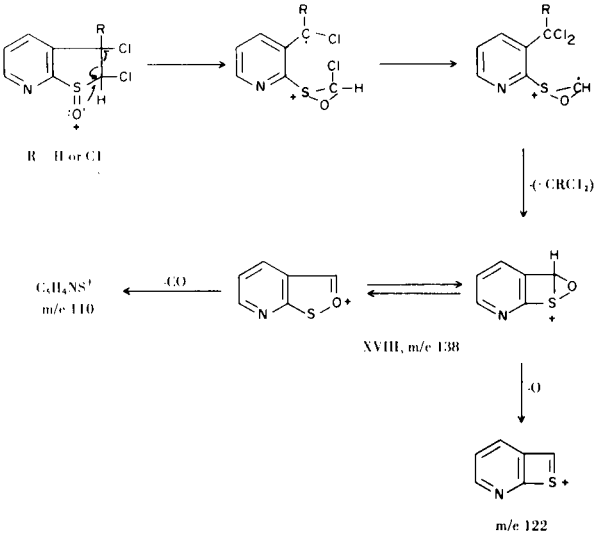
dihydrothieno[2,3-*b*]pyridine *anti*-1-oxide (IVb) from Ib. It is proposed that either chlorine or hypochlorous acid can add directly to the *S*-center of Ia (step *k* or *m*) on the way to the intermediate sulfoxide XIII. Only hypochlorous acid, however, is sufficiently hard as an electrophile to attack the hardened *S*-center of XIII (oxygen withdraws electronic charge from the sulfur) and effect further oxidation to the sulfone III (step *o*). In runs 8 and 9 the high yields of sulfone probably result from reaction of two molecules of hypochlorous acid with one of Ia. Contrariwise, the low yields of III in runs 3 and 5-7 reflect the low availability of hypochlorous acid in these reaction mixtures.

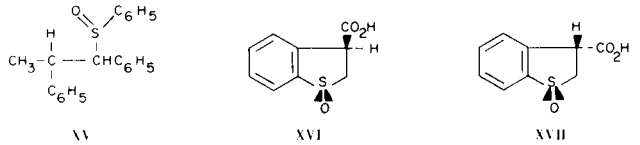
An alternative reaction pathway is open to XIII, namely addition of chlorine to the C=C, a process which is well-documented for α,β-unsaturated sulfoxides in non-polar solvents (30). It is suggested that this addition (at least for XIII as substrate) occurs by electrophilic attack at C-3 with sulfoxide participation (as shown in step *p* and XIV) (31). Backside attack at C-2 by chloride ion would then yield the *cis-anti* geometry observed in IIb. In the two-phase chloroform-water system chlorine should be concentrated in the organic phase and hypochlorous acid should be located largely in the aqueous phase (32). In run 3 (where chlorine is added) no sulfone is found. The IIb produced should be formed *via* XII and XIV, but the yield of IIa is higher than that of IIb due to a more facile initial addition of chlorine to the C=C of Ia than to *S*. In run 9, where the sulfuric acid will help to retain Ia in the aqueous phase, in contact with the hypochlorous acid that forms directly, the yield of III is higher than that of IIb, and neither IIa nor IVa is found. One can visualize that IIb forms *via* XI in this case. In the one-phase system aqueous tetrahydrofuran one expects that the position of equilibrium in equation 4 will lie further toward the left (*i.e.* will correspond to a higher chlorine/hypochlorous acid ratio) than in water alone. In run 10 one can consider that all products form *via* XI and that divergence of pathways occurs at XIII. In run 11 the excess sulfuric acid, excess hypochlorite, and long reaction time probably cause overoxidation and miscellaneous other side-reactions. The results in run 7 might imply that initial addition of chlorine to *S* is much faster than addition to the C=C (in Ia) in aqueous tetrahydrofuran. It is noteworthy that no chlorinated sulfones are formed (33, 34).

The thermolysis of IIa to give Ic appears to be formally related to thermolyses of phenyl 1,2-diphenylpropyl sulfoxide (XV) studied by Kingsbury and Cram (35) and of *cis*- and *trans*-2,3-dihydrobenzo[*b*]thiophene-3-carboxylic acid 1-oxide (XVI and XVII, respectively) investigated by Jonsson (36). The former workers observed that at 80° XV gives predominantly *cis*-elimination of the elements of C_6H_5SOH and proposed that a cyclic 5-membered transition state is involved. Jonsson found that both XVI and XVII undergo loss of water, but that XVII dehydrates considerably more readily than XVI does. In Scheme 3 we represent the thermolysis of IIa as a concerted *supra-supra*-[1,5]-sigmatropic hydrogen shift from C-3 to oxygen of the sulfoxide group, followed by 1,2-elimination of water from C-2 and *S* (37). The same mechanism would be applicable to dehydration of XVII. Compound XVI, on the other hand, would need to undergo epimerization at either C-3 or *S* before dehydration could occur.



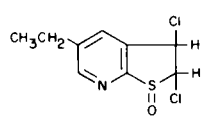
The mass spectra of IIa, IIb, and IVa show many common characteristics, particularly the following: (a) multiple molecular ion peaks for various chlorine isotopic combinations in the parent molecule, (b) successive losses of all chlorine atoms *per se* or as hydrogen chloride molecules (corroborated by the presence of metastable peaks for IVa), and (c) the most abundant peak at m/e 138 for ion XVIII, $C_6H_4NOS^+$ corresponding to the loss of dichloromethyl radical from II and a trichloromethyl radical from IVa. Ion XVIII undergoes the loss of either an oxygen atom or a molecule of carbon monoxide. The formation and decomposition of XVIII are depicted in Scheme 4. The structures proposed for XVIII are similar to those suggested previously for the 138 fragment observed in the mass spectrum of thieno[2,3-*b*]pyridine 1,1-dioxide (7). Compound IVa also loses carbon monoxide



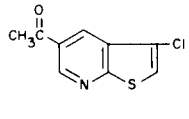


from the mono- and didechlorinated fragment ions. It is noteworthy that neither loss of a molecule of water nor of hydrogen cyanide is apparent in these spectra. However, each spectrum has a series of peaks which correspond to the loss of the elements of hypochlorous acid from the molecular ions. For IIa these peaks are small in intensity, for IVa they are medium, and for IIb one of these peaks (m/e 169) is the second most abundant one in the spectrum. The second most abundant peak in the spectrum of IVa occurs at m/e 136, corresponding to loss of dichloromethyl plus hydrogen chloride from the molecular ion.

In the course of these studies 5-ethylthieno[2,3-*b*]-pyridine and 5-acetylthieno[2,3-*b*]pyridine were treated with acidified hypochlorite in aqueous tetrahydrofuran (according to the procedure of run 10, Table I). In each case there was obtained a complex mixture, from which one product crystallized upon dissolution in acetone. The ethyl derivative gave 2,3-dichloro-5-ethyl-2,3-dihydrothieno-[2,3-*b*]pyridine 1-oxide (XIX) (18%), while the acetyl derivative yielded only 1% of 3-chloro-5-acetylthieno[2,3-*b*]pyridine (XX). The mass spectrum of XIX shows a pattern strikingly similar to that of IIa, but displaced in the region above m/e 100 to +28 mass units for the presence of the ethyl group on the fragment ions. Peaks which result from loss of a methyl group are not apparent (38). The most significant features of the mass spectrum of XX

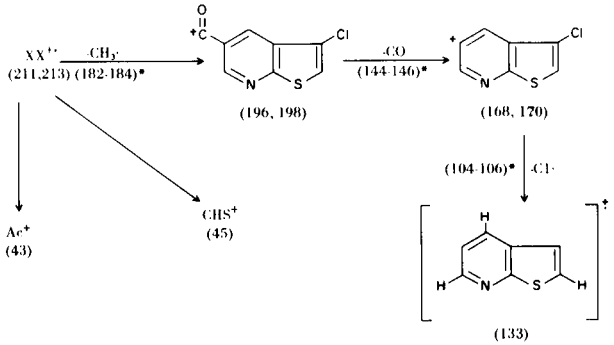


XIX



XX

are presented in Scheme 5. As based on metastable ions observed, the fragmentation process of the molecular ion involves successive losses of a methyl group, carbon monoxide, and a chlorine atom. The first two steps have been



observed in the mass spectra of 2- and 3-acetylthieno[2,3-*b*]pyridines (39). In all three cases the demethylated molecular ion is the most abundant one in the spectrum. Loss of a chlorine atom is also a significant fragmentation process observed in the mass spectrum of 3-chlorothieno-[2,3-*b*]pyridine (4).

EXPERIMENTAL (40)

A. Product Isolation Runs.

Chlorination of Ia in Cold Chloroform-Water.

Run 1. A mixture of 5 g. of thieno[2,3-*b*]pyridine (Ia) (24), 40 ml. of chloroform, and 3 ml. of water was stirred at 0-10° for 3 hours while chlorine gas was bubbled in. The layers were separated, the water layer was discarded, and the organic layer was washed with water, dried (sodium sulfate), and evaporated. The residue was stirred with carbon tetrachloride to leave 0.96 g. (10%) of 2,3,3-trichloro-2,3-dihydrothieno[2,3-*b*]pyridine *syn*-1-oxide (IVa), m.p. 156-160° (see run 2).

Cooling the preceding carbon tetrachloride extract to 0° gave a light yellow solid which was recrystallized from acetonitrile to give prisms (1.5 g., 18%, m.p. 160-164°) of *trans*-2,3-dichloro-2,3-dihydrothieno[2,3-*b*]pyridine *syn*-1-oxide (IIa). Further recrystallizations raised the melting point to 165-166°, undepressed on admixture with a sample obtained previously (5); pmr (trideuterioacetonitrile): (41) δ 5.44 (d, $J_{2,3}$ = 5.5 Hz, H-3), 5.68 (d, H-2), 7.72 (d of d, $J_{4,5}$ = 8 Hz, $J_{5,6}$ = 4.5 Hz, H-5), 8.14 (d of d, $J_{4,6}$ = 1.5 Hz, H-4), 8.84 ppm (d of d, H-6); pmr (hexadeuterioacetone): (42) δ 5.57 (d, $J_{2,3}$ = 5.5 Hz, H-3), 5.91 (d of pseudotriplets, $J_{2,4} \simeq J_{2,6} < 1$ Hz, H-2), 7.82 (d of d, $J_{4,5}$ = 8 Hz, $J_{5,6}$ = 4.5 Hz, H-5), 8.26 (d of d of d, $J_{2,4}$ = 0.8 Hz, $J_{4,6}$ = 1.5 Hz, H-4), 8.87 ppm (d of m, H-6) (see Fig. 3); mass spectrum at 120°, m/e (relative abundance): (43a) 225 (1), 223 (6), 221 (10, M^+), 186 (8, $[M\text{-}Cl]^+$), 170 (6), 169 (6, $[M\text{-}HClO]^+$), 151 (7, $[M\text{-}2Cl]^+$), 140 (9), 139 (8), 138 (100), 135 (12), 123 (7), 122 (15), 110 (11), 103 (5), 102 (34, $C_7H_4N^+$), 78 (6), 77 (11), 75 (15), 74 (5), 63, (8), 51 (11), 50 (11), 45 (5), 39 (6), 38 (5), 36 (5).

Run 2. Run 1 was repeated but on a slightly larger scale (6.6 g. of Ia, 50 ml. of chloroform, and 4 ml. of water). The aqueous layer was separated, brought to *p*H 8 with sodium bicarbonate, and extracted with chloroform. The dried organic layer (combined with the chloroform extract) was evaporated to leave an oily solid. Stirring this residue with cold chloroform left 2.8 g. (22%) of IVa, m.p. 156-159° obtained as prisms (m.p. 161.5-162.5°) on recrystallization from chloroform; positive sulfoxide test (44); ir (chloroform): 1075 (S=O), 1105 cm^{-1}; pmr (deuteriochloroform-hexadeuterio-DMSO): (45a) δ 6.39 (s, 1, H-2), 7.70 (d of d, $J_{4,5}$ = 8.0 Hz, $J_{5,6}$ = 4.5 Hz, 1, H-5), 8.10 (split d, $J_{4,6}$ = 1 Hz, 1, H-4), 8.80 ppm (split d, 1, H-6); pmr (trideuterioacetonitrile: (41) δ 6.10 (pseudotriplet, $J_{2,4} \simeq J_{2,6} < 1$ Hz, H-2), 7.71 (d of d, $J_{4,5}$ = 8.0 Hz, $J_{5,6}$ = 4.7 Hz, H-5), 8.12 (d of m, $J_{4,6} < 2$ Hz, H-4), 8.83 ppm (d of m, H-6) (see Fig. 1); mass spectrum at 110°, m/e (relative abundance): (43b) 261 (1), 259 (5), 257 (14), 255 (14, M^+), 221 (20), 219 (28, $[M\text{-}Cl]^+$), 205 (13), 203 (16, $[M\text{-}HClO]^+$), 194 (25), 192 (36, $[M\text{-}(CO+Cl)]^+$), 187 (11), 186 (11), 185 (27, $[M\text{-}2Cl]^+$), 184 (25, $[M\text{-}(Cl+HCl)]^+$), 174 (10), 172 (19), 169 (17), 159 (10), 158 (15), 157 (15), 156 (36, $[M\text{-}(Cl+HCl+CO)]^+$), 138 (100), 136 (58), 122 (17), 110 (12), 100 (17), 76 (11), 75 (16), 74 (15), 50 (13), 36 (12).

Anal. Calcd. for $C_7H_4Cl_3NOS$: C, 32.8; H, 1.6; Cl, 41.5; N, 5.5; S, 12.5. Found: C, 32.6; H, 1.4; Cl, 41.4; N, 5.3; S, 12.4.

Chlorination of Ia in Chloroform-Buffer Salt. (Run 4).

A mixture of 1.26 g. (9.3 mmoles) of Ia, 2.96 g. (17 mmoles) of anhydrous dipotassium monohydrogen orthophosphate, and 25 ml. of chloroform was stirred and refluxed for 6 hours while chlorine gas was bubbled into it. The yellow-green mixture was diluted with chloroform and water. The dried (sodium sulfate) organic layer was evaporated to leave an oily solid. Suction filtration gave 0.77 g. (32%) of crude IVa, m.p. 154-157°, raised to

161.5-162.5° after washing with pentane and recrystallizations from chloroform.

The residue from evaporation of the mother liquors was crystallized from pentane to give 0.46 g. (24%) of crude Ic, m.p. 59-62°, raised to 65-66° after recrystallizations from pentane and sublimation at 0.4 mm.

Chlorination of Ia with Sulfuric Acid-Hypochlorite. (Run 11).

To a stirred mixture of 1.35 g. of Ia, 6 g. of concentrated sulfuric acid, 10 ml. of water, and 70 ml. of tetrahydrofuran was added dropwise (over a period of 30 minutes) 68 ml. of 0.88 *M* sodium hypochlorite solution. After 26 more hours the mixture was neutralized with sodium bicarbonate and extracted with chloroform. The dried (magnesium sulfate) organic layer was evaporated to leave a liquid which slowly crystallized, yield 0.26 g. (12%) of *cis*-2,3-dichloro-2,3-dihydrothieno[2,3-*b*]pyridine *anti*-1-oxide (IIb), m.p. 140-144°, obtained as platelets (m.p. 148.5-150.5°) on recrystallization from acetone; ir (chloroform) 1065 cm^{-1} (S=O); pmr (trideuterioacetonitrile): (41) δ 5.47 (d, $J_{2,3}$ = 6.5 Hz, H-3), 5.93 (split d, H-2), 7.72 (d of d, $J_{4,5}$ = 8 Hz, $J_{5,6}$ = 4.5 Hz, H-5), 8.11 (broadened d of d, $J_{4,6}$ = 1.5 Hz, H-4), 8.79 ppm (d of d, H-6); pmr (hexadeuterioacetone): (42) δ 5.70 (d, $J_{2,3}$ = 7.0 Hz, H-3), 6.05 (d of pseudotriplets, $J_{2,4} \simeq J_{2,6} \simeq 0.8$ Hz, H-2), 7.81 (d of d, $J_{4,5}$ = 8.0 Hz, $J_{5,6}$ = 4.8 Hz, H-5), 8.20 (d of m, H-4), 8.81 ppm (d of m, H-6) (see Fig. 2); mass spectrum at 150°, m/e (relative abundance): (43b, 46) 225 (2), 223 (10), 221 (14, M^+), 186 (13, $[M-Cl]^+$), 185 (11), 171 (23, 170 (14), 169 (88, $[M-HClO]^+$), 151 (10, $[M-2Cl]^+$), 149 (23), $[M-(HCl+Cl)]^+$), 140 (10), 139 (10), 138 (100), 135 (22), 134 (19), 133 (23), 125 (13), 123 (10), 122 (60), 110 (10), 107 (10), 103 (28).

Anal. Calcd. for $C_7H_5Cl_2NOS$: C, 37.9; H, 2.3; N, 6.3; S, 14.4. Found: C, 37.8; H, 2.2; N, 6.4; S, 14.3.

2,3-Dichloro-5-ethyl-2,3-dihydrothieno[2,3-*b*]pyridine 1-Oxide (XIX) (47).

To a stirred mixture of 1.63 g. (10 mmoles) of 5-ethylthieno-[2,3-*b*]pyridine (24, 48), 2 g. (20 mmoles) of concentrated sulfuric acid, 25 ml. of THF, and 40 ml. of water was added (dropwise) 36.3 ml. (40 mmoles) of 1.1 *M* sodium hypochlorite over a period of 25 minutes. The mixture was stirred for 23.5 hours longer and extracted with chloroform. Recrystallization from acetone of the residue obtained on evaporation of the dried solution gave 0.46 g. (18%) of XIX as prisms, m.p. 167-169°, raised to 170-171° on recrystallization; ir (acetonitrile): 1060 cm^{-1} (S=O); pmr (trideuterioacetonitrile): (41) δ 1.32 (t, J_{Et} = 8 Hz, methyl group), 2.84 (q, methylene group), 5.42 (d, $J_{2,3}$ = 7 Hz, H-3), 5.89 (split d of d, H-2), 7.94 (broadened d, $J_{4,6} \simeq 2$ Hz, H-4), 8.66 ppm (broadened d, H-6); mass spectrum at 180°, m/e (relative abundance): (43a, 46) 253 (3), 251 (12), 249 (16, M^+), 214 (12, $[M-Cl]^+$), 186 (8), 183 (5), 179 (7, $[M-2Cl]^+$), 178 (5), 168 (8), 167 (9), 166 (100, $[M-CHCl_2]^+$), 151 (6), 150 (13, $[M-CHCl_2O]^+$), 148 (5), 138 (5), 130 (11), 104 (6), 103 (7), 102 (5).

Anal. Calcd. for $C_9H_9Cl_2NOS$: C, 43.2; H, 3.6; N, 5.6; S, 12.8. Found: C, 43.1; H, 3.6; N, 5.3; S, 13.0.

3-Chloro-5-acetylthieno[2,3-*b*]pyridine (XX) (49).

In the same manner as used in the preparation of XIX 1.77 g. (10 mmoles) of 5-acetylthieno[2,3-*b*]pyridine (24) was converted into a mixture of products. Recrystallization from acetone plus sublimation at 100° (0.6 mm.) gave 25 mg. (1%) of XX as fine needles, m.p. 134-135°; ir (chloroform): 1680 cm^{-1} (carbonyl); pmr (deuteriochloroform): (45b) δ 2.75 (s, Ac), 7.51 (s, H-2), 8.61 (d, $J_{4,6}$ = 2 Hz, H-4), 9.18 ppm (d, H-6); mass spectrum at 130°, m/e (relative abundance): (43a) 213 (22), 212 (7), 211 (61), 198 (38), 197 (10), 196 (100), 170 (23), 169 (7), 168 (40), 162 (7), 134 (8), 133 (17), 45 (7), 43, (28).

Anal. Calcd. for $C_9H_9Cl_2NOS$: C, 43.2; H, 3.6; N, 5.6; S, 12.8. Found: C, 43.1; H, 3.6; N, 5.3; S, 13.0.

Reaction of IVa with Hydriodic Acid.

A mixture of 130 mg. of IVa, 30 ml. of glacial acetic acid, 6 ml. of concentrated hydrochloric acid, and 0.9 g. of potassium iodide was stirred at room temperature for 24 hours and then poured into water. The neutralized (potassium carbonate) solution was extracted with chloroform. The organic layer was washed with aqueous sodium thiosulfate solution, dried, and evaporated to give a yellow liquid. This liquid was chromatographed on silica gel (20 g.). Elution with carbon tetrachloride gave 20 mg. (19%) of crude 2,3-dichlorothieno[2,3-*b*]pyridine (Ic), m.p. 56-61° (identified by pmr spectrum). Further elution with chloroform gave 70 mg. (81%) of light yellow liquid, identified as 3-chlorothieno[2,3-*b*]pyridine by conversion to the crystalline picrate, m.p. 185-186°, undepressed on admixture with an authentic sample (4).

Thermolysis of IIa.

A sample of 1.1 g. of sulfoxide IIa was heated in an open flask on a hot plate until it became a black tar. Evaporative distillation of the residue at 45-90° (0.4 mm.) gave 0.56 g. (55%) of Ic, m.p. 62-64°, raised to 65-66° on recrystallization.

B. Pmr Studies of Products Formed.

Reaction of Ia with Chlorine.

Run 3. A weighed mixture of 5.4 g. (40 mmoles) of Ia in 50 ml. of chloroform and 4 ml. of water was cooled and stirred while chlorine gas was bubbled in at a rate of 20-30 ml. per minute. Then the mixture was reweighed to determine chlorine uptake and treated with excess aqueous sodium bicarbonate. The organic layer (plus extracts of the aqueous phase) was dried (magnesium sulfate) and evaporated. The residue was dissolved in hexadeuterioacetone and analyzed by pmr (with integration of signals for H-2) and/or H-3) for percentages of IIa, IIb, III (doublet at δ 7.19 ppm) (7), IVa (pseudotriplet for H-2 at δ 6.49), and IVb (pseudotriplet for H-2 at δ 6.54). It should be noted that the H-2 signal for IVb is downfield from that for IVa, consistent with assigned structural relationships between the two compounds.

Fun 6 was similar to run 3, except that concentrated sulfuric acid was added. In run 5 the buffer salt was added, *sans* water. The solvent (50 ml.) for run 7 was 50% THF.

Reaction of Ia with Sulfuric Acid-Sodium Hypochlorite.

A mixture of 1.35 g. (10 mmoles) of Ia, sulfuric acid, and 50-80 ml. of solvent was stirred at room temperature while the sodium hypochlorite solution was added dropwise over a period of 15-40 minutes. Stirring was continued until a negative starch-iodide test was obtained. If the solution was acidic it was neutralized with sodium bicarbonate. The residue from evaporation of a chloroform extract of the reaction mixture was analyzed as in the foregoing case. In run 9 the solvent was 2.5:1 of chloroform/water (by volume). In run 10 the solvent was 33% THF.

Stereochemical Studies of IIa, IIb, and IVa.

Data on the chemical shifts induced in the resonance signals for the protons on IIa, IIb, and IVa upon addition of two successive increments of Eu(fod)$_3$ (Norell Chemical Co., Landing, N. J.) to solutions of these substrates in trideuterioacetonitrile are presented in Table II. Figure 1 shows the spectrum for IVa without added shift reagent.

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(8) *Cf.* a report by B. B. Lampert [Ph. D. thesis, Northwestern University, 1951, p. 167] that treatment of a cold solution of benzo[b]thiophene in carbon tetrachloride with a one-molar quantity of chlorine (plus subsequent shaking with ice-water) gave a 14% yield of 2,3-dichloro-2,3-dihydrobenzo[*b*]thiophene 1-oxide, identified only by carbon-hydrogen elemental analysis, qualitative tests for chlorine and sulfur, and melting point.

(9) The use of this buffer salt to react with evolved hydrogen bromide in the conversion of Ia plus bromine into 3-bromo-Ia was described in an earlier paper (4).

(10) It is apparent that one should follow the composition of the reaction mixture by pmr (as in run 3) in order to ascertain conditions for maximal crude yield of IIa.

(11) R. A. Strecker and K. K. Andersen, *J. Org. Chem.*, 33, 2234 (1968).

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(13) It is hoped that a more systematic study of thermolyses of IIa, IIb, and IVa can be made later.

(14) Unpublished results from this laboratory [see also H. Ertel and L. Horner, *J. Chromatog.*, 7, 268 (1962); L. Fishbein and J. Fawkes, *ibid.*, 22, 323 (1966)]. We ascribe the great adsorbability of a sulfoxide to the formation of a strong hydrogen bond between the silica gel and the sulfoxide group.

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(16) J. Reuben [*J. Am. Chem. Soc.*, 95, 3534 (1973)] found a molar ratio of substrate: reagent >1 for DMSO with $Eu(fod)_3$.

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(19) B. Saville, *Angew. Chem., Intern. Edit. Engl.*, 6, 928 (1967); J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.*, **84**, 16 (1961).

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(21) In these reactions *N* can abstract a proton to affect the solubilities of Ia and of various intermediates in two-phase reaction media and to alter hardness of the other nucleophilic centers. For reaction with hydrogen peroxide in glacial acetic acid, however, the harder acid HO-OH gives exclusive reaction at nitrogen, to form the *N*-oxide (5,6).

(22) The order Cl-Cl $>$ Cl-OH in reactivity toward the carbon-carbon double bond has been indicated (23).

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(26) The preferred stereochemistry of the addition to the C=C of Ib cannot be deduced from the products formed.

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(31) A search of the chemical literature failed to reveal information on the stereochemistry of addition of chlorine to an α,β-unsaturated sulfoxide. 2,3-Dihydrothiophene 1-oxide [R. C. Krug and D. E. Boswell, *J. Heterocyclic Chem.*, 4, 309 (1967)] should be a suitable substrate for use in investigation of this stereochemistry.

(32) Hypochlorous acid is reported to be insoluble in carbon tetrachloride [F. Ephraim, "Inorganic Chemistry," P. C. L. Thorne and A. M. Ward, Eds., 3rd ed., Nordeman Publishing Co., New York, N. Y., 1939, p. 359.

(33) It is reported that chlorine does not add to divinylsulfone under conditions where addition to divinylsulfide and to divinylsulfoxide occur (30).

(34) Reactions with chlorine in the benzo[*b*]thiophene system would appear to be analogous to those in the Ia system (*cf.* 8). A. H. Schlesinger and D. T. Mowry [*J. Am. Chem. Soc.*, 73, 2614 (1951)] found that at room temperature a mixture of chlorine and benzo[*b*]thiophene produces 3-chloro and 2,3-dichloro substitution derivatives. To obtain 2,3-dichloro-2,3-dihydrobenzo[*b*]thiophene 1,1-dioxide a mixture of chlorine and benzo[*b*]thiophene 1,1-dioxide was irradiated with ultraviolet light. While the authors do not comment on the reasons for changing reaction conditions in the two cases, it seems probable that no reaction occurs between chlorine and the sulfone unless irradiation is used.

(35) C. A. Kingsbury and D. J. Cram, *J. Am. Chem. Soc.*, 82, 1810 (1960).

(36) E. Jonsson, *Arkiv Kemi*, 26, 357 (1967).

(37) R. E. Lehr and A. P. Marchand, "Orbital Symmetry," Academic Press, Inc., New York, N. Y., 1972, p. 13.

(38) In contrast, loss of a methyl group is a very significant fragmentation pathway from electron bombardment of 5-ethyl-3-nitrothieno[2,3-*b*]pyridine, 5-ethyl-3-acetylaminothieno[2,3-*b*]-pyridine (48), and various ethylthieno[2,3-*b*]pyridines [unpublished data from this laboratory].

(39) L. H. Klemm and R. E. Merrill, *J. Heterocyclic Chem.*, 11, 355 (1974).

(40) Elemental analyses were performed by M-H-W Laboratories, Garden City, Michigan and by Dr. Susan Rottschaefer of this laboratory. Mass spectra were also determined by Dr. Rottschaefer by means of a CEC model 21-110 instrument at 70 eV. Infrared spectra were obtained by means of a Beckman IR-5A spectrophotometer.

(41) Determined by means of a Varian Associates XL-100 instrument in FT mode (150 transients) with deuterium lock and with the central peak of the pentet for the proton in dideuterioacetonitrile taken at δ 1.96 ppm versus TMS for internal standardization of the scale.

(42) Determined as in (41) but with standardization versus the central peak for pentadeuterioacetone at δ 2.05 ppm.

(43) Except for isotopic molecular ions, only mass spectral peaks of relative abundance (a) $\geq 5\%$, (b) $\geq 10\%$ of the most abundant peak are reported.

(44) E. N. Karaulova and G. D. Gal'pern, *Zh, Obsch. Khim.*, 29, 3033 (1959); *Chem. Abstr.*, 54, 12096 (1960).

(45) Determined by means of a Varian Associates (a) A-60, (b) XL-100 instrument with tetramethylsilane as internal standard.

(46) Because of the presence of multitudinous peaks at m/e $<$ 100 no data are reported for this region of the spectrum.

(47) Based on close similarities in the numerical values of $J_{2,3}$ and $\Delta\delta_{2,3}$ (0.47 for XIX, 0.46 for IIb; *cf.* 0.24 for IIa) for IIb and XIX, the latter is tentatively assigned the same stereochemistry as for IIb.

(48) L. H. Klemm and H. Lund, *J. Heterocyclic Chem.*, 10, 871 (1973).

(49) The assignment of the chlorine atom to C-3 (rather than to C-2) is based on the closely similar chemical shifts of the singlet for the lone proton in XX and Ib (δ = 7.52 ppm) (4).

(50) For simplicity, we designate this compound by the stereostructure which was established in the present study.

(51) We thank Dr. Ishai Sataty of the Israel Institute of Technology, Haifa, for calling our attention to his recent publication [*Org. Mag. Resonance*, 6, 8 (1974)] on configurational assignments of α-hydrogen atoms in cyclic sulfoxides. While it has been found [W. Amman and G. Kresze, *Tetrahedron Letters*, 4909 (1968)] that a *syn* α-hydrogen atom resonates at a lower field than an *anti* α-one in the 2,3-dihydrobenzo[*b*]thiophene 1-oxide system, the reverse order of resonances was established in the 1,3-dihydrobenzo[*c*]thiophene 2-oxide system by Sataty [*loc. cit.*]. The arbitrary stereochemical assignments which we made for α-hydrogen resonances in a 1,3-dihydrothieno[3,4-*b*]pyridine 2-oxide [L. H. Klemm, W. O. Johnson, and D. V. White, *J. Heterocyclic Chem.*, 9, 843 (1972)] must, therefore, be considered doubtful.