Chlorination of Heterocyclic and Acyclic Sulfonhydrazones[1]

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Received September 14, 1970

Chlorination of 2*H*-1,2,3-benzothiadiazine 1,1-dioxide (**1**) in wet methylene chloride gives *o*-formylbenzenesulfonyl chloride (**4**), but in dry methylene chloride at 0° yields the chlorosultine 3-chloro-3*H*-2,1-benzoxathiole 1-oxide (**2**); the latter is readily hydrolyzed to the "pseudo-acid" 3*H*-2,1-benzoxathiol-3-ol 1-oxide (**3**) which on further chlorination forms **4**. In 1,2-dichloroethane at −20° chlorination of **1** gave the "coupled product" **14**, whereas in dimethylformamide at room temperature the cyclic acyl chloride hydrazone 4-chloro-2*H*-1,2,3-benzothiadiazine was isolated in poor yield. The acyl chloride hydrazones (**16**) were the products obtained following chlorination of some representative aromatic acyclic tosylhydrazones (**15**). 3*H*-2,3,4-Benzothiadiazepine 2,2-dioxide (**19**), a previously unknown heterocyclic system, was synthesized in two steps from 1,3-dihydrobenzo[*c*]thiophene (**17**). Chlorinolysis of **19** gave *o*-chloromethylbenzal chloride (**21**). These reactions are believed to involve formation of the α-chloroazo compound (*e.g.* **22**) as the first step. The formation of **2** from **1** is discussed in terms of three possible routes, two which involve the sulfene **23**.

La chloration de la 2*H*-benzothiadiazine-1,2,3 dioxyde-1,1 (**1**) dans du chlorure de méthylène humide conduit au chlorure de l'*o*-formylbenzènesulfonyle (**4**), mais donne dans le chlorure de méthylène sec à 0 °C une chlorosultine à savoir la chloro-3 3*H*-benzoxathiole-1,2 oxyde-1 (**2**); celle-ci est rapidement hydrolysée en "pseudo acide" 3*H*-benzoxathiol-1,2 ol-3 oxyde-1 (**3**) qui est transformé en **4** par chloration ultérieure. La chloration de **1** à −20° dans le dichloro-1,2 éthane donne un "produit couplé" **14** alors que dans la diméthylformamide à la température de la pièce, l'hydrazone cyclique du chlorure d'acyle, la chloro-4 2*H*-benzothiadiazine-1,2,3 est obtenue avec un faible rendement. Les hydrazones (**16**) des chlorures d'acyle sont les produits obtenus par chloration de tosylhydrazones (**15**) aromatiques et acycliques caractéristiques. Un système hétérocyclique inconnu jusqu'à présent, la 3*H*-benzothiadiazépine-2,3,4 dioxyde-2,2 (**19**) a été synthétisé en deux étapes à partir du dihydro-1,3 benzo[*c*]thiophène (**17**).

L'ouverture de **19** par le chlore conduit au chlorure de l'*o*-chlorométhylbenzal (**21**). Il est supposé que ces réactions procèdent dans la première étape, par la formation de composés α-chloroazo (*e.g.* **22**). La formation de **2** à partir de **1** est discutée en considérant trois voies possibles, dont deux impliquant le sulfène **23**.

Canadian Journal of Chemistry, 49, 943 (1971)

As described in the preceding paper (1), our interest in the generation of sulfenes led us to synthesize 2*H*-1,2,3-benzothiadiazine 1,1-dioxide (**1**). Some observations made in the course of attempting to improve our early synthetic procedure led us to examine the effect of chlorine on **1**. Once we had determined the general features of this reaction, it appeared that one of the more likely mechanisms involved a sulfene. This prompted us to carry out a comparatively detailed investigation of the course of this transformation and also a study of the chlorination of other sulfonhydrazones, to find out whether the reaction of **1** was typical or exceptional. Some of the earlier results in this study have been described in a preliminary communication (2).

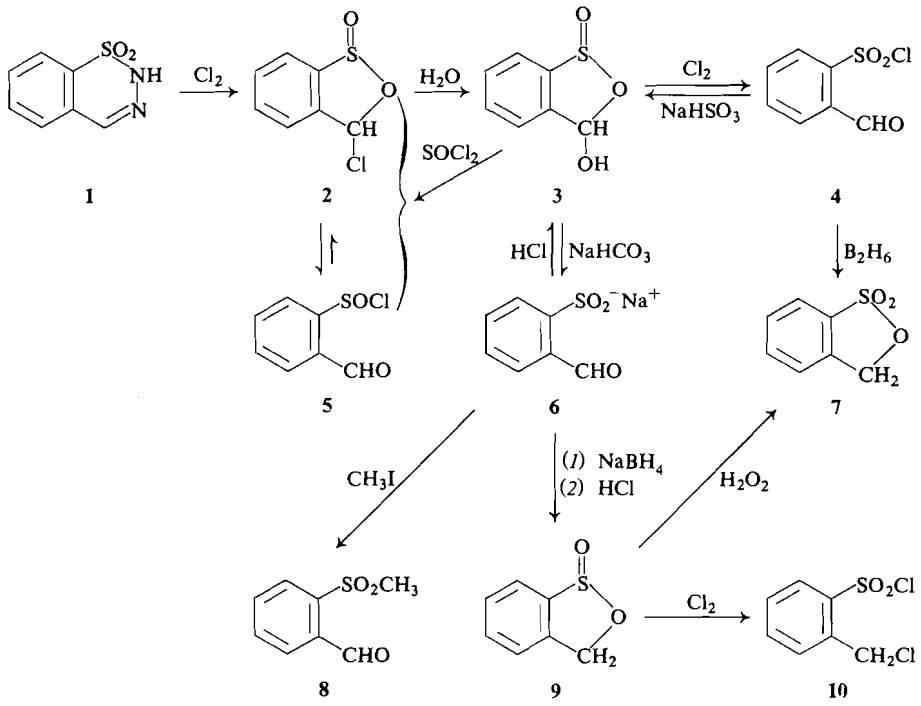
Results and Discussion

The Products of the Chlorinolysis and Subsequent Interconversions (Scheme 1)

When chlorine was bubbled into a solution of **1** in chloroform (reagent grade, containing 0.75% ethanol) or wet methylene chloride at room temperature, we observed effervescence (presumably due to nitrogen) and isolated a white crystalline solid melting at 33–35°. Structure **4** for the product readily follows from elemental analysis and spectra, the latter showing a singlet (1*H*) at 10.9 p.p.m. in addition to aromatic proton signals (4*H*) around 7.9 p.p.m. in the n.m.r., and bands at 1700 and 2900 due to the aldehyde group and at 1385, 1192, and 366 cm^{-1} characteristic (3, 4) of the $—SO_2Cl$ function. The peak at 2900 cm^{-1}, though at the high end of the range for such absorption was confirmed as due to the formyl group by observation of the combination band (5, 6) at 4600 cm^{-1} in the near i.r.

On adding a solution of **1** to a solution of chlorine in methylene chloride with careful exclusion of water, we again observed effervescence but the product obtained on evaporating the solvent showed only a small carbonyl maximum in the i.r., no significant bands attributable to a sulfonyl group, but absorption at 1140 and 960 cm^{-1} suggestive of a sulfinic ester (3). After shaking this material with a mixture of water and methylene chloride and evaporating the

[1]Organic Sulfur Mechanisms. Part 9. For part 8 see the accompanying paper (1).



SCHEME 1

organic phase, we obtained a good yield of a crystalline solid, m.p. 98–102°, shown as described below to be 3*H*-2,1-benzoxathiol-3-ol 1-oxide (**3**). This structure is the cyclic tautomer of *o*-formylbenzenesulfinic acid, and because of the complexity of the systematic name **3** is referred to here as the "pseudo-acid".

The pseudo-acid character of this material is shown by titration with base, which gave an equivalent weight of 171 (theoretical for **3** is 170); this taken with the elemental analysis establishes the empirical formula $C_7H_6O_3S$. The i.r. spectrum of the sodium salt (**6**) shows bands at 2750, 1706, and 1686, and a very strong complex absorption centered around 1020 cm^{-1}, as expected for the aldehyde and sulfinate (3) functions. Structure **6** is confirmed by conversion of the sodium salt to *o*-methylsulfonylbenzaldehyde (**8**) by reaction with methyl iodide; **8** had previously been made (7) by oxidation of the sulfide. The pseudo-acid (**3**) itself is not very soluble in the usual solvents for i.r. spectroscopy. A Nujol mull spectrum showed strong bands at 3180, 1137 (sh), 1125, and 1085 and no absorption around 1700 cm^{-1}, whereas the spectrum of a dilute (but saturated) solution in methylene chloride showed absorption at 3540 and 3300, a strong band centered around 1140, and a rather weak peak at 1705 cm^{-1}. This last peak is presumably due to a small amount of aldehyde in the methylene chloride solution, though whether this means the presence of *o*-formylbenzenesulfinic acid itself or the conjugate base is not certain. The very strong absorption around 1140 cm^{-1} is in agreement with the cyclic sulfinate formulation (**3**) (3); the differences between the solid and liquid phase spectra could merely be a reflection of the differences in phase, but ring–chain tautomerism (acid $\rightleftharpoons$ pseudo-acid), ionization, and *cis–trans* isomerism in **3** may well contribute also.

The n.m.r. spectrum of the pseudo-acid (**3**) in D_2O showed complex aromatic absorption from 7.7–8.0 (4H) and an apparent singlet at 8.11 p.p.m. (1H). Addition of 1 equiv of sodium bicarbonate resulted in a broadening of the four-hydrogen aromatic absorption, complete removal of the singlet at 8.11, and its replacement by a sharp singlet at 10.60 p.p.m. (1H); with 0.5 equiv of $NaHCO_3$ the one-hydrogen peak is a broadened singlet at 9.33 p.p.m. Addition of perchloric acid caused a small upfield shift of the 8.11 p.p.m. peak so that it became superimposed

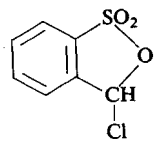
on the aromatic absorption. In acetone-d_6 **3** showed absorption in the aromatic region (5H) as well as a signal at 5.7 p.p.m. (1H) which disappeared on adding D_2O. The above results indicate that the pseudo-acid (**3**) and the conjugate base (and perhaps the "true" acid) are in rapid equilibrium with **3** predominating in the absence of added base. Phthalaldehydic acid shows comparable behavior (8).

Reduction of a solution of **3** in sodium hydroxide (*i.e.* **6**) with sodium borohydride, followed by acidification with hydrochloric acid led to **9**, a cyclic sulfinic ester or "sultine" (*cf.* refs. 9 and 10). Sultine **9** is also produced on thermolysis of **1**, as described in the accompanying paper (1), and its formation and n.m.r. spectrum were of interest in connection with the formation of sultines by thermal rearrangement of thiete 1,1-dioxide and derivatives (10). The anisotropy of the sulfinyl group is such that in a group of these sultines (10) the chemical shifts of the two methylene protons were found to differ by as much as 0.67 p.p.m. Confirmation of the sultine formulation (**9**) was obtained by oxidation to the sultone (**7**), identical to a specimen prepared from the cyclic chloride **11** by the procedure of Helberger *et al.* (11), and also from **4** by reduction with diborane.

It seemed from the results already described that **3** was probably the precursor of **4** in the chlorination of **1** in wet methylene chloride and that chlorination of **3** should yield **4**; this was found to be so. In addition, reduction of **4** with sodium bisulfite gave back **3**. Chlorination of the sultine **9** led to **10**, a previously unknown material which would appear to have potential as a synthetic intermediate. Chlorinolysis of a sulfinic ester has been observed before in the formation of methyl chloride from methyl methanesulfinate (12), and would also appear to have analogy in the cleavage of sulfite esters (13). *o*-Chloromethylbenzenesulfonyl chloride (**10**) is more conveniently prepared from sodium *o*-formylbenzenesulfonate by reduction with sodium borohydride followed by treatment with $POCl_3$–PCl_5.

Remaining to be discussed are the transformations involving **2** and **5**. The material obtained on chlorination of **1** in dry methylene chloride at room temperature proved intractable but when the reaction was carried out at 0–2°, again with exclusion of moisture, careful removal of solvent left a crystalline product melting at 64–66°. Structure **2** for this material follows from elemental analysis and spectra, the latter showing strong bands at 1150 and 970 cm^{-1} in the i.r., characteristic of sulfinic esters (3), while in addition to the aromatic absorption (4H) in the n.m.r. there was a sharp singlet (1H) at 7.08 p.p.m. appropriate to the methine hydrogen. When the n.m.r. sample was allowed to stand for a time, the singlet at 7.08 diminished and one at 9.88 p.p.m. grew. The latter peak is due (as is shown below) to presence of some of the ring–chain isomer **5**. On further standing (and addition of HCl) the 7.08 peak diminished further and the 9.88 grew until an equilibrium mixture consisting of about 17% of **2** and 83% of **5** was obtained. The equilibration was evidently catalyzed by hydrogen chloride and since the absence of HCl was difficult to ensure (or its concentration difficult to control) owing to the ease with which **2** and **5** may be hydrolyzed, no attempt was made to determine the rate of spontaneous equilibration.

The same equilibrium mixture of **2** and **5** is obtained by treatment of the pseudo-acid (**3**) with thionyl chloride. From the mixture so obtained we isolated a sample of **5** (m.p. 103–105°); the structure again follows from elemental analysis and spectra (see Experimental). A solution of **5**, showing initially no sign of **2** in the n.m.r., was found gradually to develop a small peak due to **2** at 7.08 p.p.m., eventually giving the spectrum of the equilibrium mixture. It should perhaps be mentioned that the purest specimen of **2** obtained showed no sign of the 9.88 peak in the n.m.r. but did show a very small carbonyl absorption at 1700 cm^{-1}; the i.r. sample at least would appear to have been contaminated with a small amount of **5**.

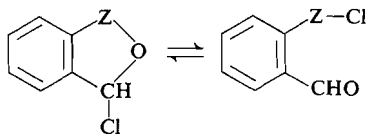


11

The ring–chain isomerism (**2** ⇌ **5**) observed here offers an interesting contrast with related systems. The analogous sulfonyl compounds **4** and **11** are reasonably stable species which show no sign of equilibrating under any circumstances in which we have observed them. With the carbonyl system on the other hand the only form that has been observed (see for example ref. 14)

has the cyclic (phthalide) structure; the failure to observe the open form ("normal" acid chloride) is assumed to be due to rapid conversion to the ring tautomer.

It is of interest to consider the variation in relative stabilities of "ring" *vs.* "chain" isomers in the light of Pearson's "hard–soft–acid–base" (HSAB) theory (15). If we symbolize the general situation by the equilibrium **12** ⇌ **13** and focus

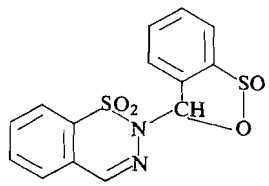


12 **13**

attention initially only on bond energies, it is evident that any change in equilibrium constant accompanying changing from one Z to another, reflects as a first approximation a change in the bond energy difference, $E_{Z-Cl} - E_{Z-O}$. Kice and Guaraldi have shown (16) that the sulfinyl group is a distinctly "softer" Lewis acid than the sulfonyl and carbonyl groups, which are "hard" (15, 17). Since Cl^- is "softer" than RO^- (15), we would expect the difference $(E_{Z-Cl} - E_{Z-O})$ to be larger for the sulfinyl compounds than for the sulfonyl or carbonyl analogues. With the sulfinyl *vs.* the carbonyl compounds this is evidently so, the equilibrium proportion of the open form **13** being much higher for the former than the latter. This would in turn suggest that the equilibrium mixture of **4** and **11** would be almost entirely **11**, but the point has not been tested. Another factor which could influence the position of the equilibrium **12** ⇌ **13** is variation in ring strain associated with change from one Z group to another, but the ring strain in these compounds is probably not large and its variation would not seem to us to be the most important influence.

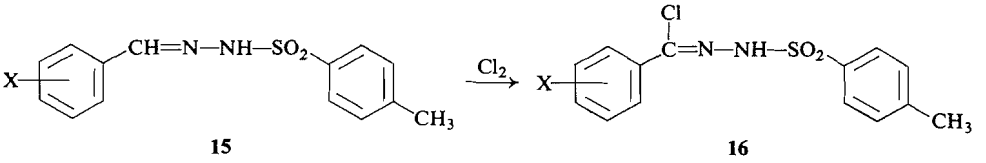
A similar comparison of the isomerization **2** ⇌ **5** with the ring–chain tautomerization "pseudo-acid" (**3**) ⇌ *o*-formylbenzenesulfinic acid is also explicable in HSAB terms. The change in equilibrium constant in this case is a direct function of the change in the quantity $E_{S-X} - E_{C-X}$, where X may be Cl or OH. By the same reasoning as before the equilibrium proportion of the open-chain isomer is predicted to be greater with the acid chlorides than the acids; the same conclusion is drawn from experiment. Steric effects would be expected to be of even less significance in this case, since the cyclic compounds are derived from the same ring system.

Finally, mention should be made of two further variations in the course of the chlorination of the benzothiadiazine (**1**) accompanying change in reaction conditions. In 1,2-dichloroethane at −20°, a product melting at 198–200° was obtained; the yield of this high-melting material was improved (to 82%) by adding the chlorine to **1**, rather than the other way around. This material analyzed for $C_{14}H_{10}S_2O_4N_2$ and showed i.r. bands characteristic of both sulfinyl and sulfonyl groups, but no sign of N–H absorption. These points suggested that the material arose from reaction of **2** (or **5**) with unreacted **1**. In confirmation of this the mixture of **2** and **5** obtained by reaction of **3** with thionyl chloride, gave, when treated with an equimolar quantity of **1**, a 90% yield of the compound melting at 198–200°. Also, alkaline hydrolysis of the high-melting material gave back **3** and **1** in good yield. The simplest formulation for this "coupled product" that fits the above data is **14**, though the zwitterionic structure with the "sultinyl" residue attached to the other nitrogen is not excluded.



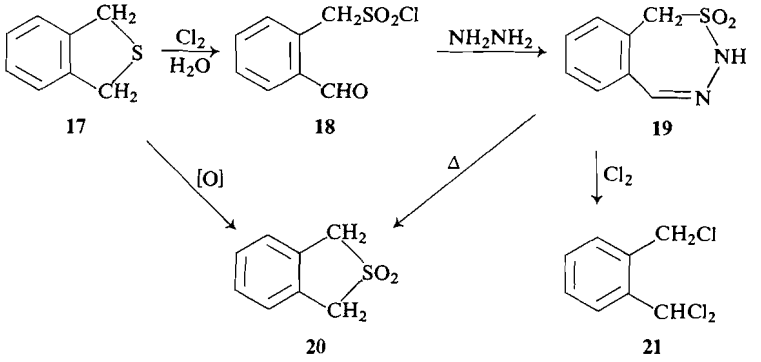
14

Use of cold dimethylformamide as the solvent in the chlorination of **1** led to another result. Part of the material suffered loss of nitrogen and, presumably via solvolysis, led to *o*-formylbenzenesulfonic acid, which was characterized by conversion to **11**. Some of the material, however, retained the nitrogen to give a material which, on the basis of analytical, i.r., n.m.r., and mass spectrometric data is evidently 4-chloro-2*H*-1,2,3-benzothiadiazine 1,1-dioxide, *i.e.* the cyclic acyl chloride hydrazone. As is described immediately below, the formation of acyl chloride hydrazones is the reaction found with acyclic sulfonhydrazones in both methylene chloride or dimethylformamide, though the yield is higher with the latter solvent. The properties of the 4-chloro-derivative of **1** are such that if it had been formed



a X = H
b X = *p*-OCH_3
c X = *o*-SO_2CH_3

SCHEME 2



SCHEME 3

in significant amount in the chlorinations in the other solvents then it would probably have been readily detected.

Chlorination of Acyclic Sulfonhydrazones (Scheme 2)

It appeared that the reaction of aromatic sulfonhydrazones with chlorine had not been studied before, and that information on this reaction might be of use in helping to understand the nature of the chlorinolysis of the thiadiazine (**1**). Accordingly the sulfonhydrazones **15***a–c* were treated with chlorine at room temperature. The principal product in each case was the acyl chloride hydrazone (hydrazonoyl chloride) (**16***a–c*); this is the expected result on the basis of previous workers' findings on the halogenation of other hydrazones (18). In addition, small amounts of the aldehyde and *p*-toluenesulfonyl chloride were also formed.

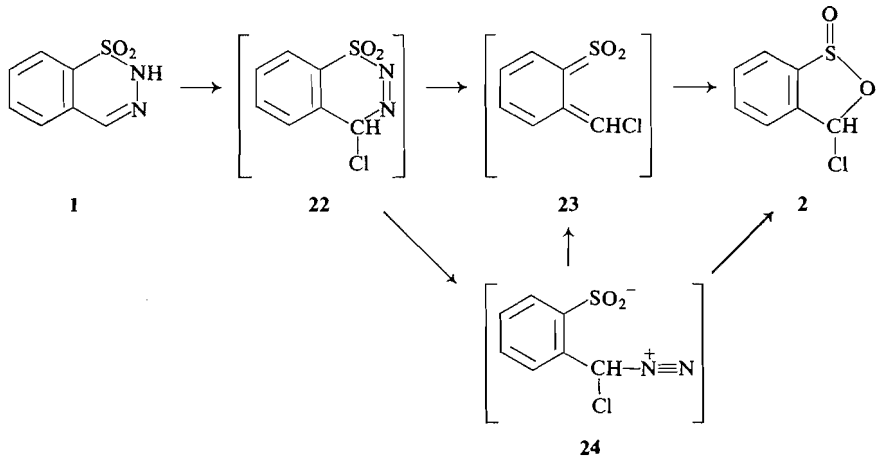
Synthesis and Chlorinolysis of 3H-2,3,4-Benzothiadiazepine 2,2-Dioxide (19) (Scheme 3)

For reasons described more fully in the discussion of the mechanism (below) we decided to synthesize the previously unknown heterocycle 3*H*-2,3,4-benzothiadiazepine 2,2-dioxide (**19**) and to treat it with chlorine. The thiadiazepine **19** was readily obtained from the dihydrothiophene **17** via the sulfonyl chloride (**18**) produced by treatment of an aqueous suspension of **17** with chlorine. The thiadiazepine (**19**) was obtained as a white solid melting (with evolution of gas) at 169–170°, the mode of synthesis and its analytical and spectroscopic properties of which (see Experimental) support the thiadiazepine formulation (**19**). On heating just above its melting point for a few minutes the evolution of gas ceases and the sulfone (**20**) is obtained in good yield. The latter compound (**20**) on further heating (at 280°) has been previously shown (19) to undergo loss of sulfur dioxide to give products derivable from *o*-quinodimethane.

3*H*-2,3,4-Benzothiadiazepine 2,2-dioxide (**19**) reacts readily with chlorine at 0° with loss of both nitrogen and sulfur dioxide to give *o*-chloromethylbenzal chloride (**21**).

The Mechanism of the Chlorinolysis of 2H-1,2,3-Benzothiadiazine 1,1-Dioxide (1)

Three possible routes from **1** to the chlorosultine (**2**) are summarized in Scheme 4. The first step is common to the three mechanisms and



SCHEME 4

involves attack of chlorine at the α-carbon with formation of the α-chloroazosulfone (**22**), a reaction for which there is precedent from different quarters. As has been mentioned above halogenation of aldehyde hydrazones, including sulfonhydrazones, gives the acyl chloride hydrazone, most probably via the α-chloroazo compound. In agreement with such a formulation is the actual isolation of the azo compound on chlorination of ketazines (20, 21).

The cyclic α-chloroazo compound **22**, once formed, is well set up to undergo cycloreversion to the sulfene (**23**), which, following the route proposed for the formation of the sultines (1, 10), would be expected to give the chlorosultine **2**. Reverse Diels–Alder reactions with extrusion of nitrogen can be estimated to be strongly exothermic (by about 45 kcal/mol), and, though apparently not very frequently observed, would appear to be facile reactions taking place readily below room temperature (for examples see reference 22). A particularly close analogy to the present case is the formation of *o*-quinodimethane dimer by mercuric oxide oxidation of 1,2,3,4-tetrahydrophthalazine observed by Carpino (23). This reaction is believed to involve oxidation to the cyclic azo compound followed by extrusion of nitrogen to give *o*-quinodimethane.

Though the formulation **22** → **23** → **2** is attractive to us, it is not the only imaginable route from **22** to **2**. To judge from the work of Overberger and co-workers (24, 25) and more recently by Kice and Gabrielsen (26), azosulfones react by free radical processes under certain circumstances, but heating is normally required to induce the homolysis even in apparent free radical chain processes; such reaction would seem unlikely under the conditions of the chlorinolysis of **1**. Ionic cleavage of azosulfones to form the diazonium sulfinate is well-known; from **22** this would lead to **24** which could go to the chlorosultine (**2**), either directly or via the sulfene (**23**). Lewis and co-workers (27) have estimated that the half-life for the formation of benzenediazonium benzenesulfinate ($PhN^{+}{\equiv}N\ {}^{-}SO_2{-}Ph$) from the azosulfone ($PhN{=}NSO_2Ph$) in methanol is about 5 min at 29°. The formation of an aliphatic diazonium ion would not be expected to be much faster and at first glance such a process (*i.e.* via **24**) would seem a little slow to account for the rapid formation of **2** from **22** in non-polar solvents even at 0° and lower. These observations are also consistent with the formation of the hydrazonoyl chlorides (**16**), the prototropic shift in the presumed intermediate α-chloroazo compound taking place faster than the heterolysis to the *p*-toluenesulfinate and benzylic diazonium ions. In these chlorinations, however, small amounts of both *p*-toluenesulfonyl chloride and the aromatic aldehyde are, in fact, observed, suggesting that the decomposition to the diazonium sulfinate does compete to some extent. However, substituents on the azo group in **22** are held in a *cis* configuration whereas it is likely that in the azo compound from **15** they are *trans*, and it is by no means impossible that a *cis*-azosulfone (*e.g.* **22**) because of the favorable *anti* arrangement of the sulfonyl group and the free electron

pair, could undergo heterolysis a good deal more quickly than the *trans* analogues. Unfortunately, unlike a number of other azo compounds (including the closely related diazosulfonates), there is comparatively little information on geometrical isomerism in azosulfones, and in no instance has a pair of *cis–trans* isomers been isolated, or even been unambiguously shown to exist (27, 28); a study of the dipole moments of a number of azosulfones led to the conclusion that each of these compounds had the *trans* configuration (28).

It was hoped that the chlorination of 2*H*-2,3,4-benzothiadiazepine 2,2-dioxide (**19**) might be instructive, since the α-chloroazosulfone presumably formed initially would have a *cis* azo double bond but at the same time be less favorably arranged for cycloreversion than **22**. The result shows that the six-membered ring arrangement as in **22** is not *required* for easy loss of nitrogen, though, at the same time, it does not exclude the reverse Diels–Alder mechanism when the molecule is well set up for it. It would appear that it is not possible to determine at this stage which reaction path the reaction is actually proceeding by, and further discussion should await further information.

Experimental

Experimental procedures, materials, and apparatus are the same as in the accompanying paper. The i.r. spectra below 600 cm^{-1} were determined on a Beckman IR-5A spectrometer equipped with CsBr optics and using KBr cells; the near i.r. determination was made on a Cary 14 spectrophotometer.

Chlorinolysis of 2H-1,2,3-Benzothiadiazine 1,1-Dioxide (1)

(i) In Hydroxylic Media

2*H*-1,2,3-Benzothiadiazine 1,1-dioxide (**1**) (1) (1.005 g) was dissolved in chloroform (55 ml; Fisher Spectranalyzed, containing 0.75% ethanol), and dry chlorine gas was bubbled through. When the solution began to effervesce the passage of chlorine was stopped and when no more gas was given off (about 5 min) the solvent was evaporated under reduced pressure. The product, 1.265 g of a colorless oil, was recrystallized four times from carbon tetrachloride – petroleum ether (35–60°) cooled in an acetone – Dry Ice mixture, giving **4** as fine white crystals melting at 33–35°. The i.r. spectrum showed peaks at: 2900 (w), 2770 (vw), 1700 (s), 1585 (m), 1570 (m), 1445 (w), 1400 (sh), 1380 (vs), 1300 (w), 1265 (m), 1180 (vs), 1120 (m), 1060 (m), 1035 (w), 995 (w), 965 (vw), 820 (m), 700 (m), 640 (w), 570 (s), 505 (w), 470 (m), 435 (vw), and 370 (m) cm^{-1}. The n.m.r. spectrum (CCl_4) showed multiplets in the aromatic region at 7.9 p.p.m. (4H) and a singlet (1H) at 10.9 p.p.m.

Anal. Calcd. for $C_7H_5SO_3Cl$: C, 41.08; H, 2.46; S, 15.67; Cl, 17.23. Found: C, 41.05; H, 2.76; S, 15.47; Cl, 17.16.

In another experiment chlorine (~ 0.5 g) was dissolved in methylene chloride (50 ml) and water (0.1 ml) was added. To this mixture a solution of 2*H*-1,2,3-benzothiadiazine 1,1-dioxide (**1**) (387 mg) in methylene chloride (20 ml) was added dropwise over a period of about 10 min. When the strong effervescence, which accompanied addition of **1**, had subsided, a portion of the reaction mixture was examined by i.r. spectroscopy which showed the presence of unreacted **1**. The mixture was then left overnight, dried, and the solvent evaporated giving a colorless oil (251 mg, 52%) shown by its i.r. spectrum to be *o*-formylbenzenesulfonyl chloride (**4**). Recrystallization from cold petroleum ether–carbon tetrachloride gave crystals melting at 31–35°.

(ii) In Dry Methylene Chloride Followed by Aqueous Work-up

A solution of 2*H*-1,2,3-benzothiadiazine 1,1-dioxide (**1**) (1.02 g) in methylene chloride previously dried by distillation from lithium aluminum hydride, was added dropwise over a period of 20 min to a solution of chlorine (about 2.0 g) in dry methylene chloride (50 ml). Within a few minutes the mixture began to bubble and when the effervescence had stopped (1 h) the solvent was evaporated leaving a colorless oil showing bands at 1710, 1140, and 960 cm^{-1} in the i.r. Water (10 ml) was added to the product and the mixture warmed on the water bath (10 min) before being extracted with methylene chloride. The methylene chloride extract was dried and the solvent evaporated giving crude **3** as white crystals (75%), which after recrystallization from methylene chloride melted at 98–102°. The i.r. spectrum of a Nujol mull of **3** showed bands at 3180 (s), 1598 (w), 1585 (w), 1337 (m), 1325 (w), 1295 (s), 1253 (s), 1213 (s), 1137 and 1125 (vs), 1085 (vs), 1055 (s), 1020 (w), 957 (w), 888 (m), 840 (vs), 770 (s), 725 and 713 (vs), and 678 (m) with no absorption around 1700 ± 25 cm^{-1}, whereas a dilute (saturated) solution in methylene chloride showed bands at 3540 and 3300 (w), 3080 (w), 1705 (w), 1452 (w), 1425 and 1420 (w), 1305 (w), 1280 (w), 1220 (m), 1140 and 1125 (s and broad), 1055 (w), 883 (m), 850 (w), and 790 (m) cm^{-1}.

Anal. Calcd. for $C_7H_6SO_3$: C, 49.34; H, 3.55; S, 18.89. Found: C, 49.46; H, 3.78; S, 18.83.

The n.m.r. spectrum of **3** in acetone-d_6 showed complex absorption from 7.2 to 7.9 and a broad singlet at 5.7; the latter band disappeared in addition of D_2O. In D_2O solution, using external tetramethylsilane as the standard, **3** showed aromatic absorption as a relatively narrow band from 7.8 to 8.0 (4H) and a slightly broadened singlet (1H) due to the methine hydrogen at 8.11 p.p.m. Upon addition of 1 equiv of $NaHCO_3$ the aromatic absorption broadened 7.6–8.2 (4H) and a new sharp singlet appeared at 10.60 p.p.m. With only 0.5 equiv of $NaHCO_3$ there was aromatic absorption at 7.7–8.2 (4H) and a broadened singlet at 9.33 p.p.m. (1H). After addition of a few drops of 30% perchloric acid to the solution of **3** in D_2O, the n.m.r. spectrum showed only a relatively narrow band between 7.7 and 8.0 p.p.m. The integrated intensity of the 7.8–8.3 region (5H) in the spectrum of **3**, relative to that of a small amount of acetone added to the D_2O to serve as an integration standard, was found to be about the same as the relative

integrated intensity of the 7.7–8.0 band found after addition of perchloric acid; this was interpreted as showing that the band at 8.11 in **3** had moved upfield upon addition of perchloric acid and was obscured by the aromatic hydrogens.

Titration of **3** (18.9 mg) with 0.01 *N* sodium hydroxide led to consumption of 11.05 ml, corresponding to an equivalent weight of 171; theoretical equivalent weight, 170. On evaporation of the water sodium *o*-formylbenzenesulfinate (**6**) was left as a crystalline solid. The i.r. spectrum of this material (Nujol mull) showed peaks at 3060 (w), 2750 (w), 1710 and 1686 (vs), 1586 (s), 1567 (m), 1304 (m), 1255 (m), 1200 (s), 1162 (w), 1133 (w), 1118 (w), a very strong complex absorption with the following peaks, 1063, 1045, 1018, 1000, 987 and 972, 888 (w), 837 (m), 825 (m), 763 (s), 725 (m), 695 (m), and 682 (m) cm^{-1}.

When sodium *o*-formylbenzenesulfinate (**6**) (31 mg) was suspended in methylene chloride and hydrogen chloride bubbled through the mixture, the yellow salt disappeared and a white precipitate formed. After 15 min when there were no traces of **6** remaining, the solution was filtered and the solvent removed from the filtrate under reduced pressure without heating leaving a colorless oil (24 mg) the i.r. spectrum of which showed it to be the pseudo-acid (**3**). After crystallization from methylene chloride, the product melted at 92–96°.

(iii) In Dry Methylene Chloride at 1 ± 1°

A solution of 2*H*-1,2,3-benzothiadiazine 1,1-dioxide (**1**) (589 mg) in a mixture of dry methylene chloride (25 ml) and dry chloroform (5 ml) was added slowly to a stirred solution of chlorine (636 mg) in methylene chloride (15 ml), maintained at 0–2° by means of an ice-bath, over a period of 1 h. After addition was complete, the mixture was stirred for a further 1/2 h and then the solution was evaporated to about 5 ml under reduced pressure at room temperature. The concentrated solution was transferred to a Craig tube and solvent removed in a stream of dry nitrogen until crystallization took place. The white crystals of **2** (269 mg) were collected. The n.m.r. spectrum showed a singlet (1H) at 7.25 p.p.m. and a multiplet (4H) at 7.7 p.p.m. The i.r. spectrum (CH_2Cl_2) showed the following peaks: 3040 (w), 1700 (w), 1585 (w), 1465 (w), 1450 (m), 1300 (w), 1235 (w), 1200 (m), 1145 (vs), 1060 (m), 1020 (w), 970 (vs), 880 (w), 865 (s), 640 (s); the peak at 1700 cm^{-1} (and perhaps also that at 1200 cm^{-1}) is probably due to the aldehyde – sulfinyl chloride (**5**) present as impurity.

The analytical sample, prepared by recrystallization (twice) from methylene chloride, melted at 64–66°.

Anal. Calcd. for $C_7H_5SO_2Cl$: C, 44.57; H, 2.67; S, 16.99. Found: C, 44.49; H, 2.87; S, 17.11.

In some preparations the crude crystalline product showed a small peak at 9.88 p.p.m. in the n.m.r. due to the presence of **5**. One such sample, in which integration of the 7.08 and 9.88 peaks indicated a ratio of **2** to **5** of 94:6 was let stand at room temperature for 80 min. The n.m.r. showed a change in the intensities of the 7.08 and 9.88 peaks corresponding to a change in composition to 74% **2** and 26% **5**; the aromatic region also became broader. Dry hydrogen chloride was then bubbled into the sample and the mixture let stand for 10 min; the ratio of **2** to **5** was judged from the n.m.r. spectrum to be 49:51, and after a further 15 min to be 35:65. After standing overnight the above ratio was estimated as 17:83.

(iv) In 1,2-Dichloroethane at −20°

A solution of 2*H*-1,2,3-benzothiadiazine 1,1-dioxide (**1**) 364 mg, 2 mmol in dichloroethane (55 ml) was added dropwise with stirring to a solution of chlorine (168 mg) in dichloroethane (14 ml) cooled to −20°. The mixture was stirred for 1 h at −20°, and the solvent removed under reduced pressure at room temperature to give a sticky, colorless solid (317 mg). Recrystallization from methylene chloride gave crystals (177 mg) melting at 194–196° (dec.); further recrystallization from methylene chloride – acetone gave an analytical sample of the coupled product (**14**) melting at 198–200° (dec.). The i.r. spectrum of a dilute (saturated) solution in $CHCl_3$ showed prominent bands at 1350, 1185, and 1130 with weaker bands at 3000, 1440, 905, 890, and 655 cm^{-1}.

Anal. Calcd. for $C_{14}H_{10}N_2O_4S_2$: C, 50.28; H, 3.01; N, 8.38; S, 19.17. Found: C, 50.15; H, 2.89; N, 8.34; S, 19.35.

In another experiment in which chlorine (1 mmol) in dichloroethane (14 ml) was added to **1** (366 mg, 2 mmol) in dichloroethane at −20° as above, a higher yield (82%) of recrystallized **14** was obtained.

(v) In Dimethylformamide

2*H*-1,2,3-Benzothiadiazine 1,1-dioxide (**1**) (1.31 g) was dissolved in a mixture of dimethylformamide (18 ml) and water (3 ml) and the solution was cooled to 0°. Chlorine was passed into the solution until the yellow color persisted and after a further 2 min the reaction mixture was evacuated on a water aspirator to remove much of the excess chlorine. It was then poured into water (300 ml) and the product extracted with methylene chloride (4 × 100 ml, 2 × 50 ml). The combined extracts were dried and evaporated to give an oil which on standing overnight *in vacuo* partly solidified. Crystallization from methylene chloride gave 4-chloro-2*H*-1,2,3-benzothiadiazine 1,1-dioxide (327 mg, 21%), melting at 143–144°. The i.r. spectrum (CH_2Cl_2) showed absorption at 3310 (m), 1585 (w), 1560 (w), 1370 (m), 1345 (s), 1245 (w), 1185 (s), 1145 (m), 1040 (m), 990 (m), 865 (m), and 630 (m) cm^{-1}. The n.m.r. spectrum (CD_2Cl_2) exhibited a multiplet (4H) at 7.8–8.2 and a broad signal (1H) at 8.3–9.2 p.p.m. removed by addition of D_2O. In the mass spectrum the molecular ion was principally a doublet at 216 (Cl^{35}) and 218 mu (Cl^{37}), relative abundance 29:12.

Anal. Calcd. for $C_7H_5ClN_2O_2S$: C, 38.81; H, 2.33; Cl, 16.36; N, 12.93; S, 14.80. Found: C, 38.72; H, 2.23; Cl, 16.53; N, 12.93; S, 14.74.

In another experiment 2*H*-1,2,3-benzothiadiazine 1,1-dioxide (**1**) (239 mg) was dissolved in dimethylformamide (4.6 g) and solid calcium carbonate (480 mg) was added to the solution. The mixture was then cooled to 0° and added to a cooled, freshly prepared solution of chlorine (460 mg) in dimethylformamide (4.4 g). After 5 min the reaction mixture was filtered and the filtrate evaporated to give an oil which was partitioned between chloroform and water in three stages. The organic phase on evaporation gave an oil (104 mg) which was crystallized from chloroform–pentane to give needles of 4-chloro-2*H*-

1,2,3-benzothiadiazine 1,1-dioxide (52 mg, 18%), identified by direct comparison (i.r., mixed m.p., t.l.c.) with a specimen prepared as described above. Evaporation of the aqueous phase also gave an oil (456 mg) which was dissolved in water (5 ml) and passed through Dowex 50W-X8 ion exchange resin. Evaporation of the eluate gave an acidic oil (195 mg) whose i.r. absorption at 1020 (s) and 1240 (s) cm^{-1} suggested the presence of some sulfonic acid. It was treated with thionyl chloride (5 ml) on the steam bath for 15 min and evaporated to dryness under reduced pressure; crystallization of the resultant oil from chloroform gave **11** (55 mg, 22%), m.p. 111–114°, identified by direct comparison (mixed m.p., i.r.) with an authentic specimen (29).

Preparation of o-Formylbenzenesulfinyl Chloride (5) from the Pseudo-acid (3)

The pseudo-acid (**3**) (522 mg) was dissolved in thionyl chloride (5 ml) and left at room temperature for 0.5 h. The excess thionyl chloride was removed under reduced pressure leaving a pale yellow crystalline product (530 mg), which on recrystallization five times from methylene chloride containing a few drops of thionyl chloride and evaporating the excess solvent under a stream of dry nitrogen, gave *o*-formylbenzenesulfinyl chloride (**5**), m.p. 103–105° (vacuum capillary). The i.r. spectrum (CH_2Cl_2) showed bands at 3060 (w), 2850 (m), 2750 (w), 1700 (vs), and 1680 (sh), 1585 (m), 1575 (m), 1390 (w), 1305 (m), 1205 (s), 1145 (vs), 1050 (w), 1030 (w), 845 (s), and 650 cm^{-1} (s). The n.m.r. spectrum (CD_2Cl_2) showed complex aromatic absorption in the range 7.5–8.3 (4H) and a sharp singlet at 9.88 p.p.m. (1H).

Anal. Calcd. for $C_7H_5ClO_2S$: C, 44.57; H, 2.67; S, 16.99. Found: C, 44.54; H, 2.93; S, 17.04.

In other experiments the n.m.r. spectrum of the material obtained by dissolving **3** in thionyl chloride showed in addition to the peaks characteristic of **5**, a singlet at 7.08 p.p.m. and a prominent peak around 7.5 p.p.m. ascribable to the presence of about 20% of **2**.

Chlorination of 3H-2,1-Benzoxathiol-3-ol 1-Oxide (3) (the "Pseudo-acid")

The "pseudo-acid" **3** (84 mg) was dissolved in methylene chloride (25 ml) and a solution of chlorine (about 0.2 g) in methylene chloride (8 ml) was added. The mixture was shaken for 5 min and then allowed to stand for 1 h. When the solvent was evaporated 85 mg (83%) of a colorless oil was obtained. An i.r. spectrum (CCl_4) of the product was identical to that of *o*-formylbenzenesulfonyl chloride (**4**) prepared as above. The product was crystallized from carbon tetrachloride – petroleum ether cooled in an acetone – Dry Ice mixture; m.p. 31–35°.

Reduction of o-Formylbenzenesulfonyl Chloride (4) to the "Pseudo-acid" 3

o-Formylbenzenesulfonyl chloride (1.94 g, 9.5 mmol), sodium sulfite (2.5 g), and water (20 ml) were stirred at room temperature for 4.5 h. The solution was acidified with concentrated sulfuric acid and heated to 90–100° on the steam bath for 1 h. The solution was cooled and extracted with methylene chloride. The extracts were dried and the solvent evaporated under reduced pressure giving a colorless solid (1.01 g, 63%), melting at 97–98°. After recrystallization, it melted at 97–100°; mixed m.p. with a specimen of **3** prepared from **1**, 97–100°. The i.r. was also identical with that of authentic **3**.

Formation of o-Methylsulfonylbenzaldehyde (8) from the "Pseudo-acid" 3

A solution of sodium bicarbonate (504 mg, 6 mmol) in water (8 ml) was added to a solution of the "pseudo-acid" **3** (1.02 g, 6 mmol) in ethanol (10 ml) and the mixture let stand for 5 min. The mixture was then evaporated to dryness, benzene was added and the mixture evaporated again to dryness (3 ×); the last traces of volatile material were removed by means of an oil pump. The pale yellow solid (**6**) was then dissolved in absolute ethanol and methyl iodide (1 ml) added. The mixture was refluxed for 4.5 h, whereupon the dark red mixture was allowed to cool and was poured into water and extracted with methylene chloride. The extracts were washed with 0.1 *N* sodium thiosulfate (10 ml) and then with saturated potassium chloride solution. Evaporation of the solvent gave a colorless oil (1.39 g), the spectrum of which indicated the major portion of the material to be the diethyl acetal of **8**. The oil was suspended in 5% hydrochloric acid (10 ml) and warmed on the steam bath for 0.5 h. The mixture was then cooled in an ice-bath and the crystals of **8** (832 mg; 75%) removed by filtration. The crystals melted at 97–99°; reported for **8**, 97–98° (7). The i.r. spectrum ($CHCl_3$) showed peaks at 3000 (m), 1695 (s), 1585 (m), 1570 (w), 1395 (m), 1315 (vs), 1260 (w), 1185 (m), 1150 (vs), 1115 (w), 1060 (w), and 955 (m); the n.m.r. spectrum showed a singlet at 3.25 (3H), a complex multiplet around 7.6–8.2 (4H), and a singlet at 10.52 p.p.m. (1H).

Reduction of the "Pseudo-acid" 3 with Sodium Borohydride

3*H*-2,1-Benzoxathiol-3-ol 1-oxide (**3**) (1.76 g, 0.010 mol) was dissolved in 1.0 *N* sodium hydroxide (10.3 ml) and water (70 ml). Sodium borohydride (4 g, 0.106 mol) was added and the reaction mixture was left stirring overnight at room temperature. Concentrated hydrochloric acid (120 ml) was added slowly. The reaction mixture was extracted with methylene chloride which in turn was dried and evaporated under reduced pressure to yield 3*H*-2,1-benzoxathiole 1-oxide (**9**) (1.4 g, 88%). The crude product was distilled, b.p. 165°/0.005 mm. The distillate when cooled to −30° crystallized; recrystallization from ether and pentane yielded crystals of **9** melting at 40–41°.

Anal. Calcd. for $C_7H_6O_2S$: C, 54.52; H, 3.92; S, 20.80. Found: C, 54.60; H, 3.96; S, 20.78.

The i.r. spectrum (CCl_4) showed absorption bands at 3070 (w), 2930 (w), 2870 (w), 1580 (w), 1468 (m), 1450 (m), 1340 (w), 1298 (w), 1255 (w), 1210 (m), 1185 (w), 1130 (s), 1060 (m), 1020 (w), 1005 (w), 950 (s), 710 (s), 705 (s), 690 (s), 645 (s), and 560 cm^{-1} (m). The n.m.r. spectrum (CCl_4) showed an AB quartet, $\delta_A = 5.42$ and $\delta_B = 5.78$ p.p.m., $J_{AB} = 13.5$ Hz., and aromatic hydrogen absorption between 7.3–7.75 p.p.m., relative areas 1:2.

Oxidation of 3H-2,1-Benzoxathiole 1-Oxide (9) with Hydrogen Peroxide in Acetic Acid

A 2.1 ml aliquot of a solution made by mixing glacial

acetic acid (3 ml) with hydrogen peroxide (30%) (0.8 ml), was added to **9** (0.10 g, 0.65 mmol). The reaction mixture was heated under reflux for 1½ h, and was then poured into water (4 ml) and extracted three times with methylene chloride. The methylene chloride solution was washed with sodium carbonate solution, dried, and the solvent evaporated to yield 3*H*-2,1-benzoxathiole 1,1-dioxide (**7**) (0.06 g, 55%). Recrystallization from benzene gave white crystals, m.p. 113–114°, identified by mixed m.p. and comparison of i.r. and n.m.r. spectra with an authentic specimen prepared as described by Helberger *et al.* (11); reported m.p. 112.5° (11).

Reduction of o-Formylbenzenesulfonyl Chloride (4) with Diborane

o-Formylbenzenesulfonyl chloride (**4**) (0.14 g, 0.72 mol) was dissolved in diglyme (15 ml) which had been dried by distilling from calcium hydride. Diborane (13 mmol), generated by mixing sodium borohydride and boron trifluoride etherate in diglyme, was bubbled slowly into the diglyme solution under anhydrous conditions. The reaction mixture was poured into water (150 ml) to destroy unreacted diborane, and the water was evaporated from the diglyme under reduced pressure. Methylene chloride (30 ml) was added and then the solution was washed five times with water (25 ml portions). The methylene chloride was dried and evaporated to yield crude 3*H*-2,1-benzoxathiole 1,1-dioxide (**7**) (0.042 g, 35%). Recrystallization from methylene chloride and petroleum ether yielded crystals melting at 110–113°, and with an i.r. spectrum identical to that of an authentic specimen prepared by the method of Helberger *et al.* (11); reported m.p. 112.5° (11).

Chlorination of 3H-2,1-Benzoxathiole 1-Oxide (9)

3*H*-2,1-Benzoxathiole 1-oxide (**9**) (2.2 g, 14 mmol) was dissolved in methylene chloride which had been dried by distillation from lithium aluminum hydride. Chlorine was dissolved in methylene chloride (0°) until the solution was 0.6 *N*, as determined by titration with sodium thiosulfate. An aliquot of 48 ml (14.4 mmol of chlorine) was added dropwise under anhydrous conditions to the magnetically stirred solution of **9**. The reaction mixture was stirred for 3 h at room temperature. The methylene chloride was evaporated under reduced pressure without heating, to yield *o*-chloromethylbenzenesulfonyl chloride (**10**) (3.15 g, 98%). Recrystallization from methylene chloride and petroleum ether yielded short thin crystals (2.56 g, 80%), m.p. 46–47°.

Anal. Calcd. for $C_7H_6Cl_2O_2S$: C, 37.36; H, 2.69; Cl, 31.50; S, 14.24. Found: C, 37.25; H, 2.83; Cl, 31.16; S, 14.41.

The i.r. absorption bands (CH_2Cl_2) were found at 3060 (w), 1590 (w), 1570 (w), 1470 (m), 1442 (m), 1372 (s), 1305 (m), 1180 (s), 1115 (w), 1060 (m), 1040 (w), 962 (w), 820 (m), 675 (m), 585 (s), 570 (s), 547 (s), 490 (m), 445 (w), 373 cm^{-1} (w); n.m.r. spectrum (CCl_4) showed absorption bands at 5.10 (s, 2H) and 7.35–8.2 p.p.m. (4 aromatic hydrogens).

Preparation of o-Chloromethylbenzenesulfonyl Chloride (10) from Sodium o-Formylbenzenesulfonate

Sodium *o*-formylbenzenesulfonate (practical grade) (1 g, 0.048 mol) was dissolved in water (60 ml). Sodium borohydride (0.18 g, 4.74 mmol) was added. The reaction was stirred for 20 h at room temperature. Hydrochloric acid was added until the solution was slightly acidic. The water was evaporated under reduced pressure with heating. The white residue was leached with hot ethanol (70 ml) and the ethanol evaporated to yield crude sodium *o*-hydroxymethylbenzenesulfonate (0.75 g, 75%); i.r. bands (Nujol) at 3560 (w), 3490 (w), 3280 (m), 3060 (w), 1300 (w), 1240–1140 (s), (partially resolved), 1095 (m), 1058 (w), 1035 (s), 1010 (s), 955 (w), 890 (w), 835 (w), 760 (s), 710 (s), and 625 cm^{-1} (s).

The crude sodium *o*-hydroxymethylbenzenesulfonate as prepared above (12.2 g, 58 mmol) was cooled in ice. Phosphorus oxychloride (60 ml, 0.66 mol) was added slowly with stirring. Phosphorus pentachloride (12.2 g, 59 mmol) was added. The reaction was stirred at 50° for 3 days and then poured slowly with stirring onto ice. After the evolution of heat had subsided (3 h), the aqueous mixture was extracted with methylene chloride (400 ml). The methylene chloride solution was washed with water, dried, and the solvent evaporated under reduced pressure without heating. The crude yield of yellow viscous liquid was 12.7 g. Crystallization from methylene chloride and petroleum ether at −60° yielded *o*-chloromethylbenzenesulfonyl chloride (**10**) (6.1 g, 46%). Recrystallization from the same solvents gave 2.81 g, m.p. 46–47°. The i.r. spectrum and m.p. were identical to the sample of *o*-chloromethylbenzenesulfonyl chloride (**10**) prepared from **9**.

Formation of the "Coupled Product" 14 by Reaction of 1 with the Chlorosultine – Sulfinyl Chloride (2 ⇌ 5) Mixture

The pseudo-acid **3** (73 mg, 0.43 mmol) was added to thionyl chloride (5 ml) and left at room temperature for 15 min. The pale yellow solution was evaporated to dryness. The residual pale yellow solid (a mixture of **2** and **5**) was dissolved in dry methylene chloride and a solution of 2*H*-1,2,3-benzothiadiazine 1,1-dioxide (**1**) (78 mg, 0.43 mmol) in dry methylene chloride (5 ml) added. The mixture was left at room temperature for 1 h. Evaporation of the solvent gave colorless crystals which on recrystallization from methylene chloride – pentane melted at 197–198°; yield 122 mg (90%). The i.r. spectrum was identical to that of the "coupled product" **14** prepared by chlorination of **1** in dichloroethane at −20°.

Hydrolysis of the "Coupled Product" 14

The coupled product **14** (100 mg) was suspended in 5% sodium hydroxide solution (5 ml) and swirled for 10 min, whereupon most of the solid had dissolved to give a pale yellow solution. The mixture was left at room temperature for 1 h, and then acidified with 20% hydrochloric acid to give a white precipitate (41 mg, m.p. 135–140°). Recrystallization from chloroform gave **1**, m.p. 139–140°, mixed m.p. with a specimen of **1** prepared as described above 138–141°.

The filtrate was extracted with methylene chloride; removal of the solvent from the extracts gave a colorless oil (45 mg), which on recrystallization from methylene chloride gave crystals identified as the pseudo-acid **3** by

m.p. (97–100°) and mixed m.p. with an authentic specimen (98–101°).

Preparation of the Tosylhydrazones ***15***

Approximately equimolar amounts of the aldehyde and *p*-toluenesulfonylhydrazine were refluxed in absolute ethanol. The crude product was obtained either by cooling the reaction mixture and filtering off the crystalline product or by evaporating the solvent. Recrystallization from the indicated solvent gave the following samples with the indicated melting points: benzaldehyde tosylhydrazone (**15***a*) (ethanol), m.p. 128–129°, reported m.p. 127–128° (30); anisaldehyde tosylhydrazone (**15***b*) (methylene chloride – pentane), m.p. 109–111°, reported m.p. 112–114° (30); *o*-methylsulfonylbenzaldehyde tosylhydrazone (**15***c*) (ethanol), m.p. 209.5–211°, with the following elemental analysis.

Anal. Calcd. for $C_{15}H_{16}N_2O_4S_2$: C, 51.11; H, 4.57; N, 7.95; S, 18.19. Found: C, 50.96; H, 4.53; N, 7.85; S, 18.05.

Chlorination of the Tosylhydrazones ***15****: Formation of the Acyl Chloride Hydrazones*

*(a) Benzoyl Chloride Tosylhydrazone (**16a**)*

(*i*) A solution of benzaldehyde tosylhydrazone (**15***a*) (549 mg, 2.0 mmol) in dry methylene chloride (25 ml) was cooled to −20° and added dropwise to a stirred solution of chlorine (154 mg, 2.2 mmol) in dry methylene chloride (19 ml) maintained at −20°. The mixture was stirred for 1 h and the solvent then removed at reduced pressure and room temperature. The dark yellow oily residue was dissolved in methylene chloride and filtered from a trace of insoluble residue. Removal of the solvent gave a dark brown oil (342 mg) which was dissolved in benzene and filtered through a column of silica gel (B.D.H. Reagent). Removal of the solvent gave a colorless solid which was recrystallized from methylene chloride – pentane to give colorless crystals of **16***a* (163 mg, 26%), m.p. 112–114°, mixture m.p. with authentic **16***a* (prepared as described below) 112–114°; the i.r. spectra were indistinguishable.

(*ii*) To a solution of benzaldehyde tosylhydrazone (**15***a*) (367 mg, 1.34 mmol) in dimethylformamide (DMF) (3.0 ml, dried over Linde 4A molecular sieves) at 0° was added a solution of chlorine in DMF (0.23 *M*) to a permanent end point. After 5 min, the reaction mixture was evaporated to dryness to give a colorless oil (469 mg). Crystallization from methylene chloride gave **16***a* (295 mg, 71%), m.p. 112–114°, identical to an authentic sample (i.r., mixed m.p.).

*(b) Anisoyl Chloride Tosylhydrazone (**16b**)*

A solution of anisaldehyde tosylhydrazone (**15***b*) (238 mg, 0.78 mmol) in the minimum quantity of DMF was titrated to a permanent end point with a solution of chlorine (0.63 *M*) in the same solvent. When t.l.c. showed that all the starting material had been consumed, the reaction mixture was evaporated to dryness to give a yellow oil, which crystallized from methylene chloride to give **16***b* (143 mg, 54%), m.p. 146–149°. The i.r. ($CHCl_3$) showed peaks at 3245 (w), 1610 (s), 1510 (m), 1410 (m), 1310 (m), 1255 (s), 1175 (s), 1075 (m), 1040 (m), 975 (m), 910 (m), 865 (m), 840 (m), 815 (m), 705 (w), 675 (m), and 660 (m) cm^{-1}. The n.m.r. ($CDCl_3$) comprised a singlet (3H) at 2.4, a singlet (3H) at 3.8, an apparent AB quartet (4H), $\delta_A = 6.9$, $\delta_B = 7.75$, $J_{AB} = 10$ Hz, another apparent AB quartet (4H), $\delta_A = 7.3$, $\delta_B = 7.9$, $J_{AB} = 8$ Hz, and a broad singlet (1H), removed by addition of D_2O, at 8.2 p.p.m.

Anal. Calcd. for $C_{15}H_{15}ClN_2O_3$: C, 53.17; H, 4.46; Cl, 10.47; N, 8.27; S, 9.46. Found: C, 53.22; H, 4.40; Cl, 10.66; N, 8.24; S, 9.63.

*(c) o-Methylsulfonylbenzoyl Chloride Tosylhydrazone (**16c**)*

A solution of *o*-methylsulfonylbenzaldehyde tosylhydrazone (**15***c*) (352 mg, 1.0 mmol) in dichloroethane (65 ml) was added dropwise to a stirred solution of chlorine (75 mg, 1.05 mmol) in dichloroethane (7.5 ml), cooled to −20°. The solution was stirred for 1 h and the solvent then removed at room temperature and reduced pressure to give a pale yellow oil (369 mg). Trituration with methylene chloride gave some colorless solid (81.8 mg, m.p. 209–211°) which was removed by filtration. Addition of pentane to the filtrate afforded pale yellow crystals, recrystallized from acetone to give colorless crystals of **16***c* (108 mg, 28%), melting at 166.5–168° (dec.). Absorption in the i.r. (Nujol) occurred at 3200 (w), 1590 (w), 1295 (s), 1240 (m), 1170 (s), 1150 (s), 1125 (m), 1070 (m), 955 (m), 850 (m), 820 (w), 765 (m), 705 (w), 665 (m), 630 (w) cm^{-1}.

Anal. Calcd. for $C_{15}H_{15}ClN_2O_4S_2$: C, 46.56; H, 3.91; Cl, 9.16; N, 7.24; S, 16.57. Found: C, 46.68; H, 3.84; Cl, 9.23; N, 7.18; S, 16.64.

*Benzoyl Chloride Tosylhydrazone (**16a**)*

1-Benzoyl-2-(*p*-tolylsulfonyl)-hydrazine (31) (100 mg) was dissolved in thionyl chloride (5 ml) and the solution was refluxed for 2 h. The excess thionyl chloride was evaporated at reduced pressure and the residue was pumped *in vacuo*. The solid product was recrystallized from methylene chloride – pentane to give colorless needles of **16***a* (68 mg, 64%), m.p. 113–115°. The i.r. spectrum ($CHCl_3$) showed bands at 3280 (m), 1605 (m), 1500 (w), 1455 (w), 1400 (s), 1360 (s), 1265 (m), 1180 (s), 1090 (s), 1075 (s), 980 (m), 870 (s), 630 (m), 620 (m), 545 (m) cm^{-1}. The n.m.r. spectrum ($CDCl_3$) showed a singlet (3H) at 2.4, a multiplet (5H) at 7.35, a multiplet (4H) at 7.8, and a broad singlet (1H) at 8.3 p.p.m.

Anal. Calcd. for $C_{14}H_{13}ClN_2O_2S$: C, 54.45; H, 4.24; Cl, 11.48; N, 9.07; S, 10.38. Found: C, 54.26; H, 4.31; Cl, 11.62; N, 9.08; S, 10.22.

*Preparation of 1,3-Dihydrobenzo[c]thiophene (**17**)*

Sodium sulfide nonahydrate (51 g, 0.21 mol) was partially dissolved in a mixture of alcohol (500 ml) and water (100 ml) in a 1 l round-bottomed flask. The flask was fitted with a Soxhlet extraction apparatus (sintered disc type) charged with α,α′-dichloro-*o*-xylene (Aldrich 25 g, 0.14 mmol). The solution was heated to reflux and the α,α′-dichloro-*o*-xylene extracted into the solution. The mixture was refluxed for a further 0.75 h and then steam distilled until the distillate was clear. The distillate was extracted with ether and the extracts washed with water and dried. Evaporation of the solvent gave a colorless oil (16.49 g, 87%) showing i.r. and n.m.r. absorption

appropriate to 1,3-dihydrobenzo[*c*]thiophene (**17**). The oil solidified on cooling in the refrigerator, the solid melting at 23–24.5°; reported m.p. 22.5–23.5° (32).

*o-Formylphenylmethanesulfonyl Chloride (**18**)*

Ice water (2 l) was saturated with chlorine gas. The solution was rapidly stirred and a suspension of 1,3-dihydrobenzo[*c*]thiophene (**17**) (5.50 g) in water (50 ml) was injected below the surface over a period of 15 min. The reaction was stirred for a further 45 min with slow passage of chlorine and addition of more ice as necessary. The white crystalline solid (mixed with a little black tar) was collected, washed with water, and dissolved in methylene chloride. The solution was dried (Na_2SO_4), treated with animal charcoal, and the solvent evaporated to leave a dark solid (7.22 g). Crystallization from benzene–pentane gave a material (5.7 g, 70%) melting at 72–76°. To obtain the analytical specimen a methylene chloride solution was filtered through silica gel and the material recrystallized twice from carbon tetrachloride to give **18** m.p. 76.5–78°. The i.r. spectrum ($CHCl_3$) showed peaks at 2840 (w), 2750 (w), 1705 (s), 1600 (w), 1585 (m), 1380 (s), 1170 (s), 865 (m), and 625 (m) cm^{-1}. The n.m.r. spectrum ($CDCl_3$) showed a singlet (2H) at 5.6, a multiplet (4H) at 7.5–8.0, and a singlet (1H) at 10.1 p.p.m.

Anal. Calcd. for $C_8H_7ClO_3S$: C, 43.94; H, 3.22; Cl, 16.21; S, 14.66. Found: C, 43.84; H, 3.32; Cl, 15.99; S, 14.52.

*3H-2,3,4-Benzothiadiazepine 2,2-Dioxide (**19**)*

o-Formylphenylmethanesulfonyl chloride (**18**) (2.0 g, 9.2 mmol) was dissolved in methylene chloride (20 ml) and added dropwise at room temperature to a stirred solution of hydrazine hydrate (5.0 g, 100 mmol) in methylene chloride (50 ml) over a period of 20 min. After a further 10 min, the reaction mixture was poured into aqueous sodium hydroxide (2.0 g NaOH, 150 ml H_2O), shaken, and the brown organic phase discarded. The aqueous phase was added to methylene chloride (300 ml) and the rapidly stirred mixture treated dropwise with 8% hydrochloric acid until it was distinctly acidic. The layers were then separated, the aqueous phase re-extracted with methylene chloride (100 ml), and the combined extracts washed once with water (100 ml), dried, and concentrated to *ca.* 5 ml. The crystalline **19** (1.36 g, 76%) was collected by filtration; m.p. 163–167° (dec.). Repeated crystallization from ethanol gave material melting at 169–170° (dec.). The i.r. spectrum (Nujol) showed peaks at 3250 (m), 1325 (s), 1310 (s), 1170 (s), 1135 (s), 1005 (m), 885 (m), and 770 cm^{-1}.

Anal. Calcd. for $C_8H_8N_2O_2S$: C, 48.91; H, 4.11; N, 14.32; S, 16.33. Found: C, 48.76; H, 4.09; N, 14.09; S, 16.18.

*Thermolysis of 3H-2,3,4-Benzothiadiazepine 2,2-Dioxide (**19**)*

The benzothiadiazepine **19** (250 mg) was heated at 175–180° under slightly reduced pressure to remove evolving gases. After 5 min, gas evolution had ceased and the reaction product was cooled to room temperature, dissolved in methylene chloride (40 ml), and filtered through silica to remove colored impurities. Evaporation of the eluate gave a colorless solid (181 mg) whose i.r. and n.m.r. spectra were identical to those of an authentic sample of 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide (**20**) obtained by oxidation of **17** (19); yield 85%. On recrystallization from methylene chloride – hexane it melted at 151–151.5°; mixed m.p. with authentic **20**, 148–150.5°.

*Chlorinolysis of 3H-2,3,4-Benzothiadiazepine 2,2-Dioxide (**19**)*

The benzothiadiazepine **19** (250 mg) was stirred in dry methylene chloride (25 ml) and the suspension was cooled in an ice-bath. Chlorine gas was passed through the mixture until all the material had dissolved, and the solution was then diluted with methylene chloride (50 ml) and washed with sodium thiosulfate solution (50 ml, 10%) and water (2 × 50 ml). The organic phase was dried and evaporated to give a liquid (280 mg) whose n.m.r. spectrum indicated that it was essentially pure α,α,α′-trichloro-*o*-xylene (**21**) (100% yield). A redistilled sample (73°/0.05 mm) had n_D^{29} 1.5695 (reported (33) n_D^{18} 1.5740). In the i.r. ($CHCl_3$) it showed bands at 1490 (w), 1460 (m), 1270 (s), 1210 (w), 1185 (m), 860 (s), 695 (vs), and 680 (vs) cm^{-1}. The n.m.r. spectrum ($CDCl_3$) showed a singlet (2H) at 4.7, a singlet (1H) at 7.1, a multiplet (3H) at 7.3–7.5, and a further multiplet (1H) at 7.8–8.0 p.p.m.

Anal. Calcd. for $C_8H_7Cl_3$: C, 45.85; H, 3.37; Cl, 50.77. Found: C, 45.83; H, 3.48; Cl, 50.89.

Reaction of **19** with only 1 equiv of Cl_2 under similar conditions to the above, afforded a mixture of starting material and α,α,α′-trichloro-*o*-xylene (**21**).

We gratefully acknowledge the support of the National Research Council of Canada, the Petroleum Research Fund (administered by the American Chemical Society), and the Alfred P. Sloan Foundation.

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