

25°, then neutralized dropwise with concd. hydrochloric acid until the red color disappeared and filtered to remove stilbene. Excess sodium perchlorate was added to precipitate the insoluble sulfonium perchlorate, which was removed by filtration and dried. The infrared spectrum had two major C-D stretching bands, at 2210 and 2130  $\text{cm}^{-1}$ , which were not present in the spectrum of the (undeuterated) sulfonium perchlorate isolated by precipitation from  $\text{H}_2\text{O}$  solution with sodium perchlorate. Therefore the

formation of the carbanion is reversible. Similar results have been obtained with *p*-nitrobenzyl chloride in 50% aqueous dioxane at 30°.<sup>6</sup>

Isotope effects were measured as described previously.<sup>2</sup> Two separate runs gave 1.00601 and 1.00713.

(6) S. B. Hanna, S.M. Thesis in Chemistry, Alexandria University, Egypt, 1957; S. B. Hanna, Y. Iskander and Y. Riad, *J. Chem. Soc.*, 217 (1961); S. B. Hanna, Y. Iskander and A. Salama, *ibid.*, 221 (1961).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA, MINNEAPOLIS 14, MINN.]

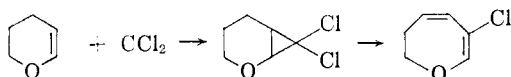
## The Reaction of Dichlorocarbene with 2H-1-Benzothiopyran and 4H-1-Benzothiopyran<sup>1</sup>

BY WILLIAM E. PARHAM<sup>1</sup> AND ROBERT KONCOS<sup>2</sup>

RECEIVED MAY 3, 1961

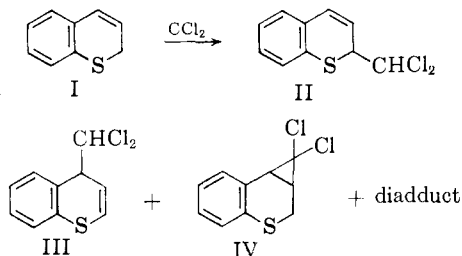
The reaction of 2H-1-benzothiopyran (I) with dichlorocarbene gives the insertion products 2-dichloromethyl-2H-1-benzothiopyran (II) and 4-dichloromethyl-4H-1-benzothiopyran (III). There was no evidence for formation of the expected cyclopropane IV. The reaction of dichlorocarbene with the isomeric 4H-1-benzothiopyran gives only the cyclopropyl adduct XIV. Thermal decomposition of XIV in hot quinolines gives 2-chloronaphthalene.

We previously observed<sup>3</sup> that halocarbenes react with dihydrothiopyran to give cyclopropyl adducts, which afford dihydrooxepines, in high yield, by subsequent ring expansion and elimination of hydrogen chloride. This reaction sequence



appears to offer considerable promise as a synthetic method for oxepin, thiopin and azepine, or derivatives of these unsaturated heterocycles, and experiments directed toward these objectives are in progress. We now wish to report studies of the reaction of dichlorocarbene with 2H-1-benzothiopyran (I) and 4H-1-benzothiopyran (X).

Dichlorocarbene was generated by reaction of ethyl trichloroacetate<sup>4</sup> and sodium methoxide, and was allowed to react with 2H-1-benzothiopyran (I) in petroleum ether at 0 to 25°. The products



isolated from the reaction mixture were: (1) recovered I, when one equivalent of ethyl trichloroacetate was employed, (2) an oil (b.p. 108–115° (0.65 mm.), 31% yield) with the composition calculated for a monoadduct (II, III or IV), and (3) a solid (m.p. 125°, 8.4% yield) diadduct derived apparently from one equivalent of I and two equivalents of dichlorocarbene.

(1) This work was supported by a grant from the National Science Foundation (NSF-G14458), and by a grant (1959-1960) from the Office of Ordnance Research (Contract No. DA-11-022-ORD-2616).

(2) NSF predoctoral fellow, 1960-1961.

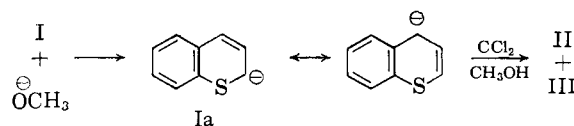
(3) E. E. Schweizer and W. E. Parham, *J. Am. Chem. Soc.*, **82**, 4085 (1960).

(4) W. E. Parham and E. E. Schweizer, *J. Org. Chem.*, **24**, 1733 (1959).

The monoadduct partially crystallized, and the solid fraction (m.p. 57–58°) was subsequently identified as II. Nuclear magnetic resonance studies of this solid established its structure to be II or III,<sup>5</sup> furthermore, nuclear magnetic resonance studies of the oil, obtained subsequent to the removal of II, established that this product was a mixture of II and III (approximately 40 and 60%, respectively). Thus, the ratio of II to III in the crude monoadduct was approximately 2.4/1 (22% yield and 9.1% yield, respectively). There was no evidence for the formation of the expected cyclopropane IV.

The structure of the solid monoadduct, and the composition of the mixed monoadducts, were further confirmed by their reduction with Raney nickel in ethanol. The solid (II) gave *n*-butylbenzene (72.5% yield), while the mixture obtained subsequent to removal of solid II afforded nearly equal amounts of *n*-butylbenzene and *sec*-butylbenzene (37 and 40.5%, respectively). The products in each case were analyzed by vapor phase chromatography.

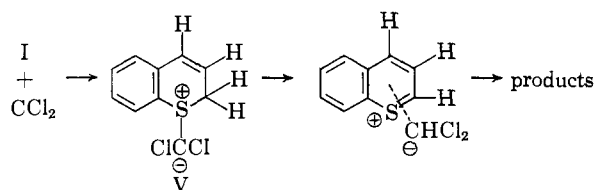
Although insertion reactions are common for methylene,<sup>6</sup> this is the first reported example of preferential insertion involving a halocarbene. The distribution of products in the allylic system suggests, of course, that a resonance ion is involved, and the reaction may occur as shown in the accompanying equation. It is reasonable, however,



to assume that the sulfur atom in I can compete as a nucleophilic site with the conjugated double bond for the electrophilic carbene, and we are inclined to believe that the reaction is more properly

(5) A variety of structures with an expanded ring, derivatives of benzothiopin, also were considered; however, the n.m.r. spectrum was incompatible with such assignment.

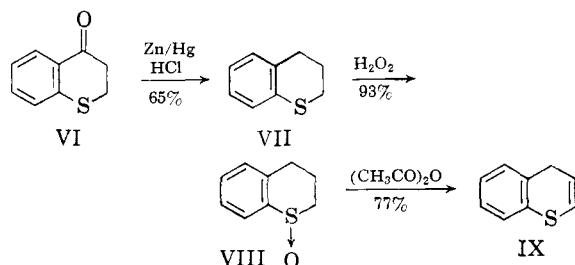
(6) Cf. (a) W. von E. Doering, R. G. Buttery, R. G. Laughlin and N. Chaudhuri, *J. Am. Chem. Soc.*, **78**, 3224 (1956); (b) D. B. Richardson, M. C. Simmons and I. Dvoretzky, *ibid.*, **82**, 5001 (1960).



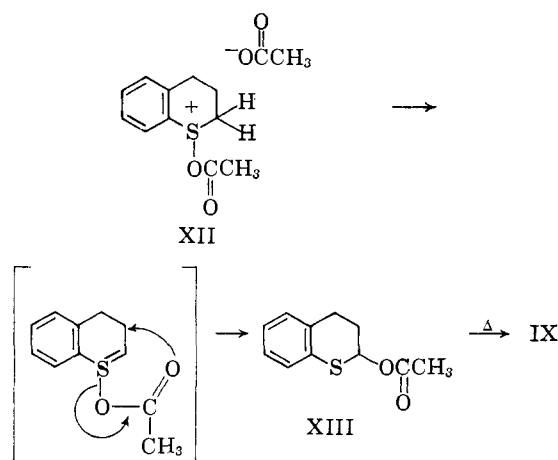
described by assuming a prior reaction of the olefin with dichlorocarbene to give V.

It is interesting to note, in this respect, that II and III were also formed when Compound I was allowed to react with dichlorocarbene generated by the thermal ( $80^\circ$ ) decomposition of sodium trichloroacetate in 1,2-dimethoxyethane. The ratio of II to III in the isolated monoadduct, as determined by nuclear magnetic resonance studies, was somewhat different ( $\sim 1:1$ ), but again there was no evidence for the formation of IV.

4H-1-Benzothiopyran (IX) was unknown; its synthesis was accomplished as summarized in the accompanying equation.

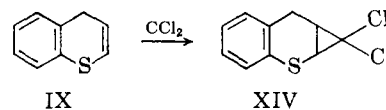


The conversion of VIII to IX can be formulated as shown (XII  $\rightarrow$  XIII  $\rightarrow$  IX), which is analogous to the reaction described by Sorenson.<sup>7</sup> In one experiment the intermediate acetate XIII was isolated.



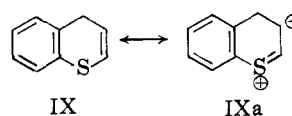
The reaction of 4H-1-benzothiopyran (IX) with dichlorocarbene, generated from ethyl trichloroacetate, was carried out under the same conditions as described for I. In this case, however, a single monoadduct was obtained in 85% yield, which has been assigned structure XIV. The same product was obtained though in much lower yield (24%), when dichlorocarbene was generated by

(7) W. R. Sorenson, *J. Org. Chem.*, **24**, 978 (1959).



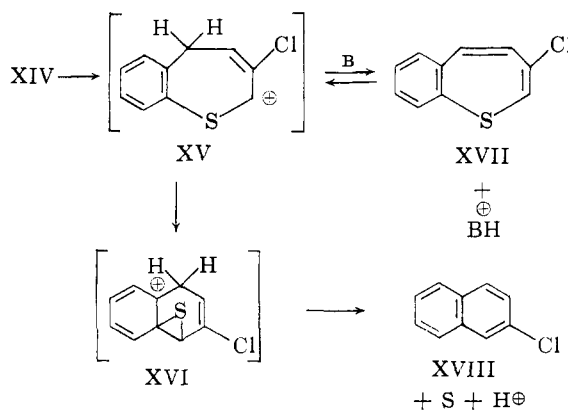
the thermal decomposition ( $80^\circ$ ) of sodium trichloroacetate in 1,2-dimethoxyethane. Infrared and nuclear magnetic resonance studies showed the absence of olefinic unsaturation, and were consistent only with the 1,1-dichlorocyclopropane structure XIV.

The remarkable difference noted for the course of reaction of I and IX with dichlorocarbene establishes the fact that a common intermediate ion, such as Ia and Ib, is not involved. While the difference noted is subject to considerable speculation as to mechanism, we feel that reasonable rationalization is provided by the difference in conjugation by sulfur in the two cases. Sulfur 3-p orbital interaction with the olefinic bond in IX (IXa)



effectively activates the double bond relative to sulfur for reaction with the electrophilic carbene.<sup>7a</sup>

Preliminary experiments have revealed that the cyclopropane XIV is more stable than anticipated. The adduct is recovered unchanged after prolonged reflux of its solution in pyridine. It is probable that the rigid system provided by the benzene ring inhibits participation<sup>3</sup> by the sulfur atom in the ring breaking step. The adduct XIV was decomposed when its solution in quinoline was heated at  $210^\circ$ . Some hydrogen sulfide was evolved, and 2-chloronaphthalene was formed (isolated in 26.9% yield). It is reasonable to expect that the desired thiopin



XVII would be thermodynamically less stable than 2-chloronaphthalene, and obviously there is a suitable path (possibly XVII  $\rightarrow$  XV  $\rightarrow$  XVI  $\rightarrow$  XVIII) for the formation of the latter. These results suggest that alternate, and less vigorous, conditions will have to be employed for the synthesis of benzothiopin derivatives. These studies, together with those related to the syntheses of the oxepine analogs, are under investigation.

(7a) A study of the reaction of other vinyl sulfides and allyl sulfides with carbene and halocarbenes is in progress.

The authors wish to express their appreciation to Professor Maurice M. Kreevoy for helpful suggestions, in particular with reference to interpretation of the nuclear magnetic resonance spectra.

### Experimental

**4-Thiochromanone (VI).**—A mixture of  $\beta$ -phenylmercaptopyropionic acid<sup>8-11</sup> (543.6 g., 2.98 moles, m.p. 57–59°) and 1550 g. of polyphosphoric acid was stirred by hand with intermittent heating on a hot-plate until a deep red homogeneous solution was obtained (about 1.5 hours). The solution was allowed to stand at room temperature an additional 5 hours and then was poured onto 3 liters of water. This mixture of product and water was cooled overnight and extracted with four portions of ether which were combined, washed with water, 5% sodium bicarbonate solution, and then dried ( $\text{Na}_2\text{SO}_4$ ). The product was distilled through a helices packed column and 463.2 g. (94.6%) of 4-thiochromanone was obtained, b.p. 117–123° (1.2 mm.),  $n_D^{25}$  1.6376 (lit. b.p.<sup>12</sup> 112–114° (1.5 mm.),  $n_D^{20}$  1.6397, m.p. 29–29.5°; b.p.<sup>11</sup> 112–113 (1 mm.)).

**4-Thiochromanol (XIX).**—4-Thiochromanol (323.7 g., 93.7% yield, m.p. 67–69°; reported<sup>13</sup> m.p. 68–69°) was prepared from 4-thiochromanone (341 g., 2.08 moles) by reduction with lithium aluminum hydride (23.7 g., 0.625 mole) as described by Lüttringhaus and Engelhard.<sup>13</sup>

**4-Thiochromanyl Acetate (XX).**—A mixture of 4-thiochromanol (XIX) (40 g., 0.241 mole), 150 ml. of acetic anhydride and 10 ml. of pyridine was refluxed for 4 hours. The excess acetic anhydride and pyridine were removed by distillation at aspirator vacuum. The residue was distilled through a semi-micro column and 43.2 g. (86.2%) of the acetate was obtained, b.p. 116–117° (0.4 mm.),  $n_D^{25}$  1.5786. A sample, b.p. 110° (0.4 mm.),  $n_D^{25}$  1.5793, was redistilled for analysis.

*Anal.* Calcd. for  $\text{C}_{11}\text{H}_{12}\text{O}_2\text{S}$ : C, 63.42; H, 5.81. Found: C, 63.26; H, 5.86.

**2H-1-Benzothiopyran (I).** (A). **By Dehydration of 4-Thiochromanol (XIX).**—4-Thiochromanol (200 g., 1.2 moles) and freshly fused potassium acid sulfate (20 g.) were placed in a flask and evacuated to 1 mm. The flask was immersed in an oil-bath and rapidly heated at 90° (bath temperature) or until the alcohol melted. The magnetic stirrer was started and the bath slowly brought to about 120°. Dehydration was very rapid at this temperature and a mixture of the product and water distilled, and was collected in an ice-cooled receiver. When only the solid salt remained in the flask, heating was stopped. The product was taken up in ether and dried ( $\text{Na}_2\text{SO}_4$ ). The crude product was distilled through a helices packed column and gave 162.7 g. (91.2%) of 2H-1-benzothiopyran, b.p. 86–87° (0.85 mm.),  $n_D^{25}$  1.6468 (lit.<sup>13</sup> b.p. 123–124° (12 mm.),  $n_D^{25}$  1.6379).

A redistilled sample had b.p. 95° (1.4 mm.),  $n_D^{25}$  1.6438; infrared spectrum (neat): 3025s, 2930w, 2870m, 2800w, 1943w, 1907w, 1797w, 1702w, 1627w, 1627w, 1611m, 1584m, 1565w, 1470s, 1442s, 1420s, 1390m, 1321w, 1267s, 1259m, 1213m, 1173m, 1160m, 1127m, 1074s, 1036s, shoulder 980w, 969m, 952m, 909w, 865m, 843m, 772s, 748s, 733s, 714w, 695s, 649s.

The nuclear magnetic resonance spectrum of 2H-1-benzothiopyran, run as 10% in carbon tetrachloride with 1% tetramethylsilane as reference, gave: 3.18 $\tau$ , a singlet, weight 4.00, designated as the aromatic hydrogens; 3.64 $\tau$ , a doublet, weight 1.02, designated as the C-4 hydrogen; 4.18 $\tau$ , a multiple, weight 1.21, designated as the C-3 hydrogen; 6.65 $\tau$ , a doublet, weight 2.23, designated as the C-2 hydrogens.

(8) J. C. Petropoulos, M. A. McCall and D. S. Tarbell, *J. Am. Chem. Soc.*, **75**, 1130 (1953).

(9) F. Krollpfeiffer and H. Schultze, *Ber.*, **56**, 1819 (1923).

(10) F. Arndt, *et al.*, *ibid.*, **56**, 1269 (1923).

(11) S. F. Birch, R. A. Dean and E. V. Whitehead, *J. Inst. Petrol.*, **40**, 76 (1954).

(12) W. E. Truce and J. P. Milionis, *J. Am. Chem. Soc.*, **74**, 974 (1952).

(13) A. Lüttringhaus and M. Engelhard, *Chem. Ber.*, **93**, 1525 (1960).

The ultraviolet spectrum showed  $\lambda_{\text{max}}^{95\% \text{ EtOH}}$  243 m $\mu$  ( $\log \epsilon$  4.288), 277 m $\mu$  ( $\log \epsilon$  3.350), 298 m $\mu$  (shoulder) ( $\log \epsilon$  3.122), 327 m $\mu$  ( $\log \epsilon$  3.000).

*Anal.* Calcd. for  $\text{C}_6\text{H}_6\text{S}$ : C, 72.93; H, 5.44. Found: C, 72.74; H, 5.69.

**B. By Pyrolysis of 4-Thiochromanyl Acetate (XX).**—4-Thiochromanyl acetate (14.96 g., 0.72 mole) was added over 30 minutes to a vertical 2  $\times$  32 cm. glass helices packed column which was heated by an automatically controlled electric furnace set at 400°. Nitrogen was used as a carrier gas and set at 3–4 bubbles/sec. The column was flushed with 30 ml. of benzene which was collected along with the product in a Dry Ice-cooled receiver. The benzene solution was washed with water, 5% sodium bicarbonate solution and dried ( $\text{K}_2\text{CO}_3$ ). The product was distilled through a semi-micro column and 6.85 g. (64.5%) of 2H-1-benzothiopyran was obtained, b.p. 96–97° (1.5 mm.),  $n_D^{25}$  1.6447–1.6460.

The infrared spectrum of a redistilled sample, b.p. 95° (1.3 mm.),  $n_D^{25}$  1.6437, was identical with that of the material prepared by dehydration of 4-thiochromanol.

**Conversion of 2H-1-Benzothiopyran (I) to Thiochroman-S-dioxide (XXI).**—Four grams of 30% palladium-on-charcoal was shaken in a Parr apparatus for 1.5 hours with 150 ml. of absolute methanol under 32 p.s.i.g. of hydrogen.<sup>14</sup> Concentrated sulfuric acid (1.4 ml.) and 0.57 g. (0.00385 mole) of 2H-1-benzothiopyran were added. This mixture was shaken for 15 minutes under 32 p.s.i.g. of hydrogen, the catalyst was filtered and washed with 20 ml. of absolute methanol, and the filtrate and washings stored for 2 hours over anhydrous potassium carbonate. The solids were removed and the filtrate concentrated to about 2 ml. in a rotary evaporator. Glacial acetic acid (12 ml.) and 30% hydrogen peroxide (1.2 ml.) were added. This solution was refluxed 45 minutes, poured onto 50 ml. of ice-water, and made basic by the addition of solid potassium carbonate. The basic solution was extracted four times with methylene chloride, which was dried briefly over magnesium sulfate and evaporated to dryness. The sulfone was crystallized from methylene chloride–petroleum ether (b.p. 30–60°) and 0.24 g. (34.2%) was obtained, m.p. 84–86° (uncor.). The reported<sup>15</sup> m.p. is 87–88°. A mixture m.p. with authentic thiochroman-S-dioxide was undepressed.

**Thiochroman (VII).**—Thiochroman (130.8 g., 64.9% yield, b.p. 93–97° (2 mm.),  $n_D^{25}$  1.6136; reported b.p.<sup>12</sup> 121–122° (11 mm.),  $n_D^{20}$  1.6148; b.p.<sup>11</sup> 76–78 (1.2 mm.),  $n_D^{25}$  1.6122) was prepared by reduction of 4-thiochromanone (333.8 g., 2.03 moles) with zinc amalgam as described by Truce and Milionis.<sup>12</sup>

The product had a weak carbonyl band in the infrared and was purified further by chromatography on alumina (300 g.) using petroleum ether (b.p. 30–60°) as eluent. Pure thiochroman (120.1 g., 59.7%) was obtained by distillation, b.p. 81.5–82.5° (1.2 mm.),  $n_D^{25}$  1.6118; infrared spectrum (neat): 3045m, 3000m, 2930s, 2845m, 1943w, 1902w, 1792w, 1583m, 1570m, 1483s, 1445s, 1350w, 1299s, 1272s, 1219m, 1199w, 1177m, 1162w, 1126m, 1079s, shoulder 1075s, 1039m, 936m, 892m, 864w, 840w, 776s, 748s, 709w, 690m, 668m.

The nuclear magnetic resonance spectrum, run as before, had: at 3.10 $\tau$ , a singlet, weight 4.00, assigned to the aromatic hydrogens; 7.18 $\tau$ , a quintet, weight 4.39, assigned to the C-2 and C-4 hydrogens; 8.10 $\tau$ , a complex multiplet, weight 1.93, assigned to the C-3 hydrogens.

The ultraviolet spectrum showed  $\lambda_{\text{max}}^{95\% \text{ EtOH}}$  259 m $\mu$  ( $\log \epsilon$  3.988), 299 m $\mu$  (shoulder) ( $\log \epsilon$  2.938), 310 m $\mu$  (shoulder) ( $\log \epsilon$  2.711).

**Thiochroman-S-oxide (VIII).**—Thiochroman (99.3 g., 0.661 mole) dissolved in glacial acetic acid (270 ml.) and cooled to 5° was treated with 75 ml. (0.75 mole) of 30% hydrogen peroxide (in approximately 8-ml. portions added at 5-minute intervals). The maximum temperature rise was to 20°. The reaction was stirred (magnetic stirrer) an additional hour after the addition was complete, and then allowed to warm up overnight. The purple reaction mixture was made basic by slow addition to an ice-cooled solution of sodium hydroxide (260 g.) in water (900 ml.). During this time, the temperature of the basic solution was not allowed to rise above 30°. The product, after extraction with methylene chloride and drying ( $\text{MgSO}_4$ ), was distilled.

(14) R. Mazingo, *et al.*, *J. Am. Chem. Soc.*, **67**, 2092 (1945).

(15) F. Krollpfeiffer, *et al.*, *Ber.*, **56**, 1654 (1925).

Thiochroman-S-oxide (102.1 g., 93%) was obtained as a colorless liquid, b.p. 117–120° (0.04 mm.),  $n_D^{20}$  1.6087.

A sample of this liquid crystallized from benzene-petroleum ether (b.p. 30–60°) was isolated as a white, hard, deliquescent solid, m.p. 31–33° (reported<sup>11</sup> m.p. 31–34°); infrared spectrum (neat liquid): 3040m, shoulder 3000m, 2925s, shoulder 2885m, 1707w, 1675m, 1657w, 1592w, 1568w, 1479s, 1442s, 1407m, 1348w, 1327w, 1288m, 1261m, 1197w, 1173m, 1162m, 1126m, 1073s, 1040s, 1002s, 952w, 930m, 888m, 869w, 834w, 782s, 757s, 711m, 693w, 674w, 649w.

*Anal.* Calcd. for  $C_9H_{10}OS$ : C, 65.02; H, 6.06. Found: C, 64.72; H, 5.83.

**4H-1-Benzothiopyran (IX).**—A mixture of thiochroman-S-oxide (100 g., 0.602 mole) and acetic anhydride (150 ml.) was heated for 5 hours on a water-bath set at 90°. The reaction was distilled through a helices-packed column and only one fraction (b.p. 66–83° (0.1 mm.)) was collected. The residue from the distillation (about 50 g.) was heated for 3 hours on a steam-bath with acetic anhydride (100 mg.). Again, only one fraction (b.p. 50–78° (0.03 mm.)) was collected in a crude distillation. These two fractions were redistilled and gave 70 g. (77.6%) of pure 4H-benzothiopyran, b.p. 70–71.5° (0.85 mm.),  $n_D^{25}$  1.6245.

A redistilled sample had b.p. 64° (0.7 mm.),  $n_D^{25}$  1.6242; infrared spectrum (neat): 3045m, shoulder 3005m, 2940w, 2843w, 2800m, 1952w, 1912w, 1826w, 1804w, 1677w, 1640w, 1613m, 1588m, 1570m, 1484s, 1473s, 1448s, 1426m, 1324m, 1289w, 1262m, shoulder 1213w, 1202m, 1162m, 1129m, shoulder 1077m, 1072s, 1043s, 1011w, 984s, 973w, 942m, 912w, 869w, 839m, 778s, 768s, 750s, 716w, 699s, 676s.

The nuclear magnetic resonance spectrum, run as before, had: at 2.94  $\tau$ , a singlet, weight 4.00, assigned to the aromatic hydrogens; 3.70  $\tau$ , a doublet, weight 1.02, assigned to the C-2 hydrogen; 4.11  $\tau$ , a quintet, weight 1.01, assigned to the C-3 hydrogen; 6.76  $\tau$ , a doublet, weight 2.11, assigned to the C-4 hydrogens.

The ultraviolet spectrum showed  $\lambda_{max}^{95\% EtOH}$  224 m $\mu$  (log  $\epsilon$  3.82), 236 m $\mu$  (shoulder (log  $\epsilon$  3.72)), 243 m $\mu$  (shoulder (log  $\epsilon$  3.71)), 274 m $\mu$  (log  $\epsilon$  3.615).

*Anal.* Calcd. for  $C_9H_8S$ : C, 72.93; H, 5.44. Found: C, 72.66; H, 5.47.

In one experiment, a small amount of material (b.p. 118–119° (0.95 mm.)),  $n_D^{25}$  1.5828) was obtained. The infrared spectrum of this material suggested that it was the expected 2-thiochromanyl acetate.

*Anal.* Calcd. for  $C_{11}H_{12}O_2S$ : C, 63.42; H, 5.81. Found: C, 63.38; H, 5.75.

**Conversion of 4H-1-Benzothiopyran (IX) to Thiochroman-S-dioxide (XXI).**—4H-1-Benzothiopyran (0.6 g., 0.00405 mole) was reduced and the product subsequently oxidized as described for 2H-1-benzothiopyran. Thiochroman-S-dioxide (0.18 g., 24.4%) was isolated as before, m.p. 85–87°. A mixture m.p. with authentic material was undepressed.

**Reaction of 2H-1-Benzothiopyran with Dichlorocarbene.** (A) **Ethyl Trichloroacetate—Sodium Methoxide Method.**<sup>14</sup>—Ethyl trichloroacetate (38.36 g., 0.2 mole) was added all at once to a cold (0–5°) mixture of 2H-1-benzothiopyran (15.16 g., 0.102 mole), olefin-free petroleum ether (b.p. 30–60°) and commercial sodium methoxide (11 g., 0.204 mole). The mixture was allowed to stir under a nitrogen atmosphere for 8 hours at 0–5° and then allowed to warm up overnight. Water (100 ml.) was added, the organic layer separated, and the aqueous layer extracted with petroleum ether (b.p. 30–60°). The combined and dried ( $MgSO_4$ ) organic layers were concentrated in a rotary evaporator to 50° (20 mm.). The residue gave, when distilled through a semi-micro column, 7.34 g. (31%) of monoadduct, b.p. 108–115° (0.65 mm.),  $n_D^{27.5}$  1.6329–1.6346, and a residue (14.55 g.) from which a diadduct was isolated (see below). A sample of monoadduct, b.p. 107.5–108° (0.25 mm.),  $n_D^{28.5}$  1.6308, was redistilled for analysis.

*Anal.* Calcd. for  $C_{10}H_8Cl_2S$ : C, 51.96; H, 3.49; Cl, 30.68; S, 13.87. Found: C, 52.11; H, 3.19; Cl, 30.61; S, 14.02.

The crude adduct partially crystallized and the solid (3.25 g.) was isolated by filtration, using small amounts of petroleum ether to wash the crystals, m.p. 56–58°. This product, later shown to be 2-dichloro-methyl-2H-1-benzothiopyran (II), was crystallized from petroleum ether

(b.p. 30–60°) and melted at 57–58°; infrared spectrum (Nujol): shoulder 3045w, shoulder 2985s, shoulder 2955s, 2940s, 2870m, 2490w, 1639w, 1595w, 1480s, 1447m, 1387m, 1370w, 1274m, 1262w, 1217m, 1198m, 1179w, 1166w, 1079m, 1035w, 949w, 885w, 847w, 795s, 784m, 774s, 749s, 724s, 695m, 690m, 670w.

The nuclear magnetic resonance spectrum, run as before, had: at 2.90  $\tau$ , a singlet, weight 4.00, assigned to the aromatic hydrogens; 3.33  $\tau$ , a doublet, weight 1.08, assigned to the C-4 hydrogen; 3.98  $\tau$ , a quartet, weight 1.17, assigned to the C-3 hydrogen; 4.59  $\tau$ , a doublet, weight 1.18, assigned to the hydrogen of the dichloromethyl group; 6.21  $\tau$ , a triplet, weight 1.16; assigned to the C-2 hydrogen.

The ultraviolet spectrum showed  $\lambda_{max}^{95\% EtOH}$  240 m $\mu$  (log  $\epsilon$  4.44), 273 m $\mu$  (shoulder (log  $\epsilon$  3.36)), 280 m $\mu$  (log  $\epsilon$  3.39), 291 m $\mu$  (shoulder (log  $\epsilon$  3.26)), 322 m $\mu$  (log  $\epsilon$  3.13).

*Anal.* Calcd. for  $C_{10}H_8Cl_2S$ : C, 51.96; H, 3.49. Found: C, 51.74; H, 3.55.

The filtrate remaining after the separation of II was redistilled to remove solvents. The nuclear magnetic resonance spectrum of this distillate indicated the presence of a mixture of II (2.90, 3.35, 3.98, 4.58, 6.21  $\tau$ ) and an isomeric structure (2.77, 3.35, 3.89, 4.38, 5.88  $\tau$ ), believed to be 4-dichloromethyl-4H-1-benzothiopyran (III). Vapor phase chromatographic analysis of the Raney nickel reduction products of this mixture (see below) served to confirm these structures, and establish the composition of the mixture as approximately 48% II and 52% III. Thus, the yields of II and III determined partially by isolation and partially by calculation were 22% and 9.1%, respectively.

The distillation residue (14.45 g.) remaining after the isolation of the monoadduct was dissolved in benzene (150 ml.) and diluted to 600 ml. with petroleum ether (b.p. 30–60°). The solid which separated was removed and the filtrate concentrated in a rotary evaporator. The dark residue which remained was distilled in a 2-bulb flask (0.1 mm.). The distillate quickly crystallized and was purified by recrystallization from petroleum ether (b.p. 30–60°). The solid diadduct (2.7 g., 8.4% yield) melted at 122–125°. The sample, prepared for analysis, was crystallized from petroleum ether (b.p. 30–60°), m.p. 124–125°; infrared spectrum (Nujol): 3055w, 3010m, 2930s, 2865s, 2325w, 1990w, 1927w, 1593w, 1475s, 1452s, 1428w, 1380m, 1307w, 1290w, 1276m, 1261s, 1239s, 1233s, 1211m, 1186w, 1172w, 1141m, 1111w, 1083m, 1071m, 1042m, 986m, 942w, 927w, 914m, 893w, 883m, 856s, 817s, 780s, 763s, 754s, 727m, 680m.

The nuclear magnetic resonance spectrum had: at 2.79  $\tau$ , a singlet, weight 4.00, assigned to the aromatic hydrogens; 3.65  $\tau$ , a doublet, weight 0.98; 6.60  $\tau$ , a doublet, weight 0.93; 6.90  $\tau$ , a doublet, weight 1.00; 7.38  $\tau$ , a doublet, weight 0.80.

No further attempt has been made to investigate the structure of this diadduct.

*Anal.* Calcd. for  $C_{11}H_8Cl_4S$ : C, 42.06; H, 2.57; S, 10.21. Found: C, 41.92; H, 2.71; S, 10.55.

(B) **Sodium Trichloroacetate Method.**<sup>16</sup>—2H-1-Benzothiopyran (15.05 g., 0.102 mole) was added to a mixture of sodium trichloroacetate (38.65 g., 0.208 mole) suspended in dry 1,2-dimethoxyethane (100 ml.). This mixture was refluxed for 22 hours under nitrogen. The solids were removed and the filtrate concentrated in a rotary evaporator to 50° (20 mm.). The residue which remained was distilled through a semi-micro column and gave 5.78 g. (30.9% based on starting material consumed) of adduct, b.p. 98–108° (0.1 mm.),  $n_D^{27.5}$  1.6308. A redistilled sample had b.p. 94° (0.15 mm.),  $n_D^{28.5}$  1.6317.

The nuclear magnetic resonance spectrum of the product showed the presence of II (2.94, 3.35, 3.97, 4.57, 6.20  $\tau$ ) and III (2.81, 3.35, 3.89, 4.38, 5.90  $\tau$ ). The composition of the mixture was estimated to be 50% of II and 50% of III.

*Anal.* Calcd. for  $C_{10}H_8Cl_2S$ : C, 51.96; H, 3.49. Found: C, 52.08; H, 3.74.

No adduct would be isolated by processing the residues by a procedure similar to that described above.

**Proof of Structure of 2-Dichloromethyl-2H-1-benzothiopyran (II).**—2-Dichloromethyl-2H-1-benzothiopyran (1.00 g., 0.00433 mole) dissolved in 75% ethanol–water (100 ml.), was refluxed for 30 minutes with freshly prepared Raney

(16) W. M. Wagner, *Proc. Chem. Soc.*, 229 (1959).

nickel (about 30 g.).<sup>17</sup> Warm water (100 ml.) was added and the mixture was distilled with steam. About 200 ml. of distillate was collected. This distillate was diluted to 500 ml. with water and potassium chloride (30 g.) was added. The product was extracted with petroleum ether (b.p. 30–60°) and dried (MgSO<sub>4</sub>). The solvent was distilled until a 1- to 2-ml. residue remained in the distillation flask.

A sample of this residue was analyzed in a Perkin-Elmer vapor phase chromatograph using a diisodecyl phthalate column set at 148°, and a carrier gas (helium) flow rate of 8.5. The spectrum showed the presence of 5 components (other than solvent peaks). Four of the components were present in 1% or less concentration (not identified) and the major component was shown to be *n*-butylbenzene by the addition of authentic *n*-butylbenzene to a second sample. The calculated yield of *n*-butylbenzene was 0.42 g. (72.5%).

**Degradation of the Mixture of 2-Dichloromethyl-2H-1-benzothiopyran (II) and 4-Dichloromethyl-4H-1-benzothiopyran (III).**—A mixture of II and III (1.09 g., 0.00472 mole) was treated with Raney nickel by a procedure identical with that described above. Chromatographic analysis of the product showed 8 components, 6 of which were present in 1% or less concentration and not identified. The two major components were identified as *n*-butylbenzene and *sec*-butylbenzene (by the addition of knowns to separate samples). The calculated yields of *n*-butyl and *sec*-butylbenzene were 0.234 g. (37%) and 0.256 g. (40.5%), respectively thus indicating an approximately equal distribution of dichloromethyl derivatives in the starting mixture.

The nuclear magnetic resonance spectrum of the mixture of II and III indicated that the ratio (II/III) was approximately 4/6.

**Reaction of 4H-1-Benzothiopyran (IX) with Dichlorocarbene.** (A) **Ethyl Trichloroacetate-Sodium Methoxide Method.**—The procedure used was identical with that described for 2H-1-benzothiopyran. Ethyl trichloroacetate (38.78 g., 0.202 mole) was added to a mixture of 4H-1-benzothiopyran (15.48 g., 0.105 mole) in petroleum ether (b.p. 30–60°) and sodium methoxide (11 g., 0.204 mole). The product was processed as previously described and 1,1-dichlorocyclopropa[b][1]benzothiopyran (IV) (20.52 g., 84.9%) was obtained by distillation, b.p. 100–105° (0.06–0.08 mm.), *n*<sub>D</sub><sup>20</sup> 1.6211. A sample, redistilled for analysis, was collected at 101° (0.2 mm.), *n*<sub>D</sub><sup>20</sup> 1.6213; infrared spectrum (neat): 3075m, 3025m, 2980m, 2940w, 2860w, 1958w, 1918w, 1822w, 1800w, 1749w, 1627w, 1598m, 1582m, shoulder 1488s, 1479s, 1460s, 1445s, 1359w, 1338w, 1293w, 1278m, 1260s, 1227s, 1206m, 1167w, 1135m, 1096m, 1076s,

1070m, 1045s, shoulder 1008s, 984w, 956m, 938m, 921s, 874m, 857s, broad 810s, broad 755s, 721w, 687m.

The nuclear magnetic resonance spectrum of this product showed the following peaks: 2.94  $\tau$ , a singlet, weight 4.00, assigned to the aromatic hydrogens; 6.79 and 7.09  $\tau$ , doublets, weight 2.39, assigned to the C-7 hydrogens<sup>14</sup>; 7.42  $\tau$ , a doublet, weight 0.77 assigned to the C-9 hydrogen; 7.88  $\tau$ , a complex multiplet, weight 1.62, assigned to the C-8 hydrogen.

The ultraviolet spectrum showed  $\lambda_{\max}^{95\% \text{ EtOH}}$  241 m $\mu$  (shoulder) (log  $\epsilon$  3.691), 255 m $\mu$  (log  $\epsilon$  3.813).

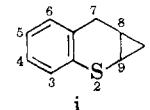
*Anal.* Calcd. for C<sub>10</sub>H<sub>8</sub>Cl<sub>2</sub>S: C, 51.96; H, 3.49. Found: C, 51.76; H, 3.91.

(B) **Sodium Trichloroacetate Method.**—The procedure used was identical with that described for 2H-1-benzothiopyran. A mixture of 4H-1-benzothiopyran (15.33 g., 0.104 mole), sodium trichloroacetate (38.6 g., 0.208 mole) and 1,2-dimethoxyethane (100 ml.) was refluxed for 22 hours. The product was distilled and 1,1-dichlorocyclopropa[b][1]benzothiopyran (5.76 g., 24.1%) was obtained, b.p. 102–118° (0.3 mm.), *n*<sub>D</sub><sup>20</sup> 1.6225. A pure sample, b.p. 94–96° (0.07 mm.), *n*<sub>D</sub><sup>20</sup> 1.6234, was obtained by redistillation of the crude material.

The spectra (infrared, n.m.r., ultraviolet) of this material were identical with those of the material prepared by the ethyl trichloroacetate-sodium methoxide procedure.

**Attempted Ring Expansion of 1,1-Dichlorocyclopropa[b][1]benzothiopyran (IV) with Quinoline.**—A solution of 1,1-dichlorocyclopropa[b][1]benzothiopyran (4.33 g., 0.0187 mole) and quinoline (4.86 g.) was heated to reflux in an atmosphere of nitrogen. Soon after refluxing had started, the odor of hydrogen sulfide was apparent. After 15 minutes of refluxing, the reaction was cooled and ether and water were added. The layers were separated and the ether layer was extracted with water and 10% hydrochloric acid solution. The ether was dried (MgSO<sub>4</sub>) and evaporated. The dark red solid which remained was chromatographed on alumina using petroleum ether (b.p. 30–60°) as eluent. Crude 2-chloronaphthalene (m.p. 56–58°, 1.11 g., 36.4%) was obtained. After recrystallization from ethanol-water, the product (0.82 g., 26.9%) melted at 57–58°. A mixture m.p. with authentic material was undepressed.

(18) The numbering system (Patterson, "Ring Index," 2nd Edition, p. 275) refers to i.



(17) R. Mozingo, *et al.*, *J. Am. Chem. Soc.*, **65**, 1013 (1943).

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## Potential Purine Antagonists. XXVII. Synthesis and Reactions of Some Purinesulfonyl Fluorides<sup>1</sup>

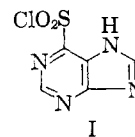
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The introduction of the fluorosulfonyl group has been accomplished for the first time in a nitrogen heterocyclic system. The appropriate heterocyclic thiol upon oxidation with chlorine in the presence of potassium fluoride and hydrofluoric acid affords the desired compound. Thus, the synthesis of purine-6-sulfonyl fluoride (III) has been accomplished from 6-purine-thiol (6-mercaptapurine). This reaction is also successful in the presence of other groups on the heterocyclic ring. The reactivity of the fluorosulfonyl group at various positions in the purine ring has been studied. A number of interesting and previously inaccessible purinesulfonamide derivatives have been prepared from the corresponding purinesulfonyl fluorides.

Very few organic sulfonyl fluorides have been reported,<sup>2</sup> and the fluorosulfonyl group has not previously been introduced into heterocyclic compounds. In the oxidation of a mercaptapurine<sup>3</sup>

with chlorine gas a probable reactive intermediate may be the sulfonyl chloride, such as I. Thus, Roblin and Clapp<sup>4</sup> isolated several chlorosulfonylpyri-



(1) Supported by Research Contract No. SA-43-ph-1928 with the Cancer Chemotherapy National Service Center of the National Cancer Institute, National Institutes of Health, Public Health Service.

(2) See Friedrich Muth in Houben-Weyl, "Methoden der Organischen Chemie," edited by Eugen Müller, Vol. 9, p. 561, Georg Thieme Verlag, Stuttgart, 4th edition, 1955 (Literature covered until 1955).

(3) R. K. Robins, *J. Org. Chem.*, **26**, 447 (1961).

(4) R. O. Roblin, Jr., and J. W. Clapp, *J. Am. Chem. Soc.*, **72**, 4890 (1950).