Reaction of Enol Ethers with Carbenes. II. 3-Chloro-2-methylthiochromone from 4-Ethoxy-3,4-thiochromene[1]

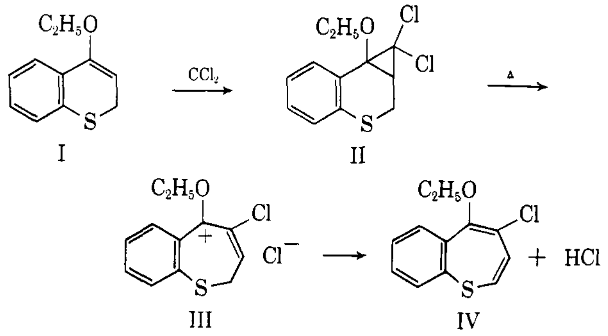
WILLIAM E. PARHAM AND M. D. BHAVSAR

Department of Chemistry, Institute of Technology, University of Minnesota, Minneapolis, Minnesota

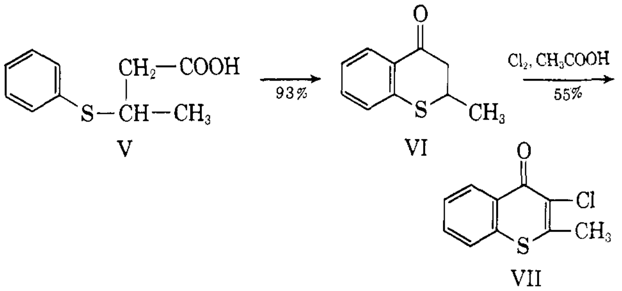
Received October 21, 1963

Decomposition of the dichlorocarbene adduct of 4-ethoxy-2H-1-benzothiapyran in hot quinoline leads to the formation of 3-chloro-2-methylthiochromone (VII); ethyl chloride also was shown to be a product of the thermal decomposition of the adduct. Evidence cited suggests that it is unlikely that the 2,3-benzothiepin ring system can be prepared by reactions which involve protonated intermediates with carbonium ion centers in the 2- and 3-positions.

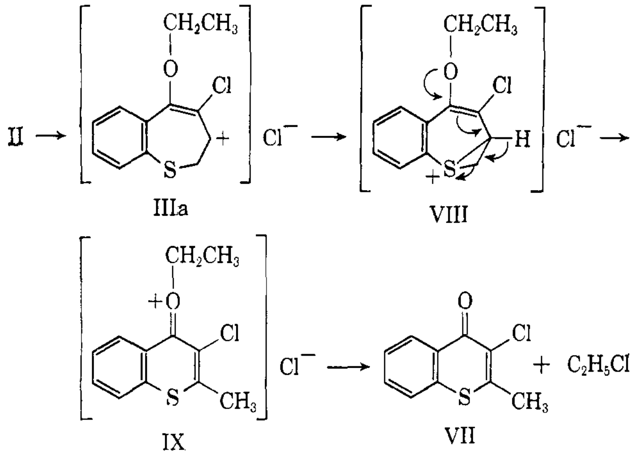
The facile conversion[2] of 1-ethoxyclohexene into 1-ethoxy-1,3,5-cycloheptatriene, by ring expansion of the derived dichlorocarbene adduct, prompted us to explore the decomposition of 3,4-(dichloromethano)-4-ethoxythiochroman (II) as a route to the synthesis of 4-chloro-5-ethoxybenzthiepin (IV).



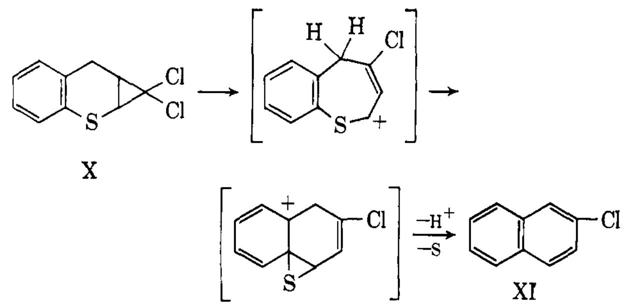
The benzothiapyran I was prepared in 88% yield from the corresponding thiochromanone and was converted into II in 33% yield by reaction with ethyl trichloroacetate and sodium methoxide.[3] The cyclopropane II was stable to hot acidic alcohol–water mixtures and stable in boiling pyridine; however, it decomposed to a solid (~48% yield), m.p. 153–154°, in hot (210°) quinoline. The composition of the solid, together with its infrared, ultraviolet, and nuclear magnetic resonance (n.m.r.) spectra (see Experimental) established that it was not the desired thiepin IV, but most probably the unknown 3-chloro-2-methylthiochromone (VII). The identity of the product as 3-chloro-2-methylthiochromone was confirmed by its independent synthesis as shown in V–VII.



The formation of VII is thought to occur in this sequence: III → IIIa → VIII → VII.[4] Ethyl chloride was shown to be one of the thermal decomposition products of II. The ring contraction IIIa → VIII → VII seems reasonable in view of the known rearrangements of sulfides substituted in the β-position in a manner which permits formation of three-membered cyclic sulfonium intermediates.[5]



In a previous paper[6] we reported that the decomposition of X in hot quinoline leads to 2-chloronaphthalene and suggested the reaction sequence as shown in X → XI. In view of these reactions it would appear unlikely that the 2,3-benzothiepin ring system can be prepared by reactions which involve protonated intermediates with carbonium ion centers in the 2- or 3-positions.



Experimental

4-Ethoxy-2H-1-benzothiapyran (I).—A mixture of thiochromanone[7] (20.0 g., 0.121 mole), absolute alcohol (20 ml.), triethyl

---

[1] This work was supported by the Office of Ordnance Research, U. S. Army, Contract No. DA-ORD-31-124-61-G13.

[2] W. E. Parham, R. W. Soeder, and R. M. Dodson, *J. Am. Chem. Soc.*, **84**, 1755 (1962).

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

[4] For discussion and references related to the ring expansion of 1,1-dihalocyclopropanes, see W. E. Parham and E. E. Schweizer, *Org. Reactions*, **13**, 71 (1963).

[5] (a) *Cf.* W. E. Parham, J. Heberling, and H. Wynberg, *J. Am. Chem. Soc.*, **77**, 1169 (1955); (b) C. C. Price and S. Oae, "Sulfur Bonding," The Ronald Press Co., New York, N. Y., 1962, pp. 9-15.

[6] W. E. Parham and R. Koncos, *J. Am. Chem. Soc.*, **83**, 4034 (1961).

[7] J. C. Petropoulous, M. A. McCall, and D. S. Tarbell, *ibid.*, **75**, 1130 (1953).

orthoformate (40.0 g., 0.27 mole), and *p*-toluenesulfonic acid (~0.1 g., dried by azeotroping water with benzene) was added to a flask equipped with a magnetic stirrer, reflux condenser, and drying tube (calcium chloride). A slow stream of nitrogen gas was passed into the flask throughout the reaction. The mixture was stirred at room temperature for 24 hr. and then at the reflux temperature for 3 hr. The mixture was then concentrated at 70° (15-16 mm.) using a rotary evaporator. Additional dry *p*-toluenesulfonic acid (~0.1 g.) was added to the residue which was then heated under vacuum at 15-16 mm. in a flask equipped with a long (~18 in.) Claisen head. After some additional ethyl orthoformate had distilled, the temperature was raised slowly to 175°. At this point vigorous reflux, but no distillation, occurred. The mixture was cooled and distilled through a spiral wire column. 4-Ethoxy-2H-1-benzothiapyran was collected as a pale yellow oil, b.p. 105-107° (0.22 mm), $n^{25.8}\text{D}$ 1.6113, 20.7 g., 88.4% yield. The product darkens in air and was stored under nitrogen at 0°.

Anal. Calcd. for $C_{11}H_{12}OS$: C, 68.75; H, 6.25. Found: C, 68.46; H, 6.24.

Infrared spectrum (neat liquid) showed strong absorption at 1630 cm.$^{-1}$ assigned to the olefinic band. Ultraviolet spectrum (in chloroform) was $\lambda_{\max}$ 256 mμ (ϵ 10,540) and 323 (1456). N.m.r. spectrum[8] (in carbon tetrachloride) was the following: aromatic CH (multiplets at 423.6 and 399.4 c.p.s.); =C—H (triplet at 279.7, 275.2, and 268.6 c.p.s., J = 5.7); OCH_2 (quartet at 224.7, 217.6, 210.4, and 203.8 c.p.s., J = 6.8); SCH_2 (doublet at 193.9 and 188.4 c.p.s., J = 7.5); CH_3 (triplet at 54.1, 77.5, and 69.8 c.p.s., J = 6.8).

3,4-(Dichloromethane)-4-ethoxythiochroman (II).—A mixture of 4-ethoxy-3,4-thiochromene (18.3 g., 0.095 mole), sodium methoxide (18.0 g., 0.33 mole), and olefin-free petroleum ether (b.p. 30-60°, 180 ml.) was cooled to 0-5° and ethyl trichloroacetate (46.0 g., 0.24 mole) was added all at once. The mixture was stirred (magnetic stirrer) under nitrogen at 0-5° for 8 hr. and then allowed to warm up slowly to room temperature overnight; a water condenser was employed to prevent evaporation of solvent. The dark brown mixture was filtered, the residue was washed with petroleum ether, and the combined organic layers were stirred vigorously with 200 ml. of 10% sodium hydroxide for 80 min. The ether layer was separated and the water layer was extracted with additional petroleum ether. The combined ether layers were dried (magnesium sulfate) and concentrated, and the dark-brown viscous liquid (29 g.) was chromatographed on aluminum (610 g., Alcoa, grade F-20) using petroleum ether (b.p. 30-60°) as eluent. Most of the fractions contained oils which partially or completely solidified when free of solvent. The principal product was II, isolated as white plates (8.7 g., 33% yield) melting at 68° from pentane.

Anal. Calcd. for $C_{12}H_{12}Cl_2OS$: C, 52.36; H, 4.36; Cl, 25.82; S, 11.63; mol. wt., 275. Found: C, 52.40; H, 4.57; Cl, 25.75; S, 11.69; mol. wt., 235 (cryoscopic in benzene).

Ultraviolet spectrum was $\lambda_{\max}$ (in 95% alcohol) 223 mμ (ϵ 13,650), 262 (6720), 295 (1222). N.m.r. spectrum[8] (in carbon tetrachloride) was the following: aromatic CH (multiplets at 422.6 and 403.2 c.p.s.); OCH_2 and SCH_2 (complex region with peaks at 206.1, 199.3, 191.4, 185.7, and 183.3 c.p.s.); -CH (triplet at 135.5, 127.6, and 119.6 c.p.s., J = 8.5); $-CH_3$ (triplet at 69.4, 62.6 and 55.8, J = 6.9).

A minor unidentified component of the mixture was isolated (~0.5 g.) from the earlier fractions of the chromatogram as colorless plates, m.p. 107-107.5° from pentane), which turned yellow on standing.

Anal. Found: C, 54.10; H, 4.86; S, 10.23.

Conversion of II to 3-Chloro-2-methylthiochromone.—A mixture of II (3.00 g., 0.0109 mole) in dry and refined quinoline (5.0 ml., 0.042 mole) was heated under nitrogen in a flask provided with an air condenser. The temperature was raised rapidly; the mixture darkened at 160° and boiled vigorously at 210-215°. The mixture was maintained for 2 min. at 210-215°, and was then cooled and diluted with ether (150 ml.). The ether solution was extracted with three 200-ml. portions of 2% hydrochloric acid and three 200-ml. portions of water, and was then dried and concentrated. The brown semisolid residue (~1.99 g.) was triturated with petroleum ether and the solid thus obtained (1.4 g.) was processed by sublimation at 50-155° (1.0 mm.). The pale yellow solid (1.1 g., 48% yield) gave white crystals of VII, m.p. 153-155°, by recrystallization from carbon tetrachloride. The product was identical (infrared, n.m.r., ultraviolet, and mixture melting point) with the authentic 3-chloro-2-methylthiochromone described below.

Thermal Decomposition of II.—A small sample of II (1.0 g.) was decomposed thermally in a round-bottom flask containing a short air condenser and distilling head in such a way that any highly volatile material such as ethyl chloride would be collected in a cold (ice-salt) solution of carbon tetrachloride (1 ml.) containing 0.5% tetramethylsilane. The sample turned brown at 170° and boiled vigorously with decomposition during a 2-min. heating period at 200°. The dark tarry residue was not processed. An n.m.r. spectrum of the carbon tetrachloride solution showed that it contained a high concentration of ethyl chloride.

2-Methylthiochromanone (VI).—A mixture of β-(phenylmercapto)-*n*-butyric acid[7,9] (39.7 g., 0.20 mole) and polyphosphoric acid (120 g.) was heated to 75-85° for 2 hr. with occasional stirring. The mixture was allowed to stand at room temperature for 5 hr., and was then diluted with water (240 ml.). The cooled mixture was extracted with ether (920-ml. total), and the ether extract was washed with two 200-ml. portions of water and two 125-ml. portions of 5% aqueous sodium bicarbonate. The ether extract was dried and distilled to give 33.4 g. (93% yield) of 2-methylthiochromanone, b.p. 93-95° (0.15 mm), $n^{26.5}\text{D}$ 1.6083 [lit.[7,9] b.p. 146-147° (9 mm.), 152° (13 mm.); $n^{20}\text{D}$ 1.6125]. The ketone showed strong absorption in the infrared at 1683 and 1673 cm.$^{-1}$, and gave a semicarbazone melting at 171-172° (lit.[7,9] m.p. 167-168° and 168-169°).

Conversion of VI to 3-Chloro-2-methylthiochromone (VII).—A solution of 2-methylthiochromanone (6.8 g., 0.038 mole) in glacial acetic acid (80.0 ml.) was placed in a 1-l. three-necked flask provided with a magnetic stirrer and a calcium chloride tube. The stirred mixture was cooled in a water bath (20-25°) and chlorine gas was admitted until approximately 2 molar equiv. of chlorine (5.4-5.5 g., 0.076 mole) had been adsorbed (~3 hr.). The solution was then stirred for 31 hr. at 30-34° and finally heated on a steam bath for 15 min. during which time hydrogen chloride was evolved. The resulting mixture was diluted with water and the pale yellow solid which precipitated (8.3 g.) was collected. Recrystallization of this solid from alcohol gave 3-chloro-2-methylthiochromone (VII) as pale yellow crystals (3.56 g., 43.4% yield, m.p. 152-154°). The thiochromone VII, m.p. 153-154° from carbon tetrachloride, gave a colorless solution in concentrated sulfuric acid with blue fluorescence in ultraviolet light.

Anal. Calcd. for $C_{10}H_7ClOS$: C, 57.00; H, 3.32; Cl, 16.86; S, 15.20; mol. wt., 210.5. Found: C, 57.06; H, 3.56; Cl, 16.85; S, 15.21; mol. wt., 182 (Rast in camphor).

Infrared spectrum was the following (perfluorocarbon mull): 3070 (w), 3025 (w), 1625 (s), 1586 (s), shoulder at 1570 (m), 1535 (m), 1450 (w), 1440 (s), shoulder at 1425 (m), 1380 (m), 1320 (s), and 1300 cm.$^{-1}$ (m); Nujol mull, 1625 (s), 1585 (s), shoulder at 1566 (m), 1535 (m), 1310 (s), 1300 (s), 1240 (w), 1160 (m), 1088 (s), 1068 (m), 1023 (m), 835 (s), 808 (s), 790 (m), 745 (s), shoulder at 730 (m), 680 (m), and 640 cm.$^{-1}$ (m). Ultraviolet spectrum (95% alcohol) was $\lambda_{\max}$ 215.5 mμ (ϵ 10,090), 226.5 (11,130), 250.5 (21,800), shoulder at 255 (21,590), 280 (3456), 291.5 (3046), 344 (10,810). N.m.r. spectrum[8] (deuteriochloroform) was the following: aromatic =CH (multiplets 478.3 and 423.9 c.p.s., τ 1.5 and 2.5) and CH_3 (singlet at 143.9 c.p.s., τ 7.44).

The alcoholic mother liquior was concentrated and ~0.5 g. of VII precipitated. Water was added to the residue and the solid that precipitated was recrystallized from petroleum ether. The solid thus obtained was recrystallized from petroleum ether (b.p. 60-68) and the pink solid (1.1 g.) was chromatographed on alumina (Alcoa, grade F-20). Three products were eluted: (A) with benzene, a product, m.p. 148-149°, with the composition in reasonable agreement for trichloro-2-methylthiochromanone [*Anal.* Calcd. for $C_{10}H_7Cl_3OS$: C, 42.93; H, 1.78. Found: C, 43.05; H, 1.98.]; (B) additional 3-chloro-2-methylthiochromone (4.46 g., 55.6% yield); and (C) an unidentified purple solid, sparingly soluble in alcohol.

---

[8] The n.m.r. spectra were determined on a Varian V 4302 at 56.44 Mc.

[9] F. Knollpfeiffer, H. Schultze, E. Schlumbohm, and E. Sommermeyer, *Ber.*, **58**, 1654 (1925).