A New Heterocyclic Structure. The 6H-[1,3]Benzoxathiepino[5,4-*d*]pyrimidine 5,5-Dioxide

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The novel benzoxathiepinopyrimidines **6a-d** were synthesized by ring transformations of 3-chloromethylsulfonylchromone (**2**) with amidines **3a-d**.

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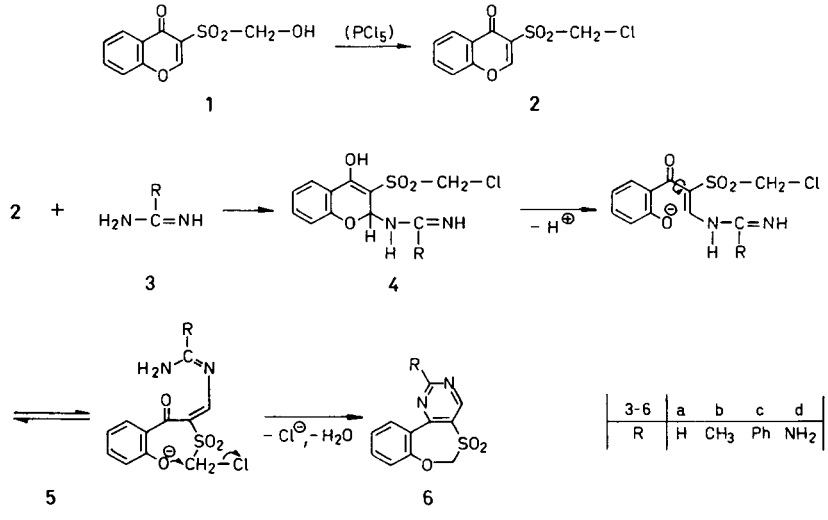
In this paper we report a further development of our research in the synthesis of sulfur containing heterocycles *via* ring transformation reactions of chromone-3-sulfonyl-compounds [2-6]. The starting chloromethyl sulfone **2** was prepared in 78% yield by the reaction of **1** [7] with phosphorus pentachloride. Treatment of **2** with the amidines **3a-d** in the presence of sodium acetate resulted in high yields of the desired compounds **6a-d**. The structures of **6a-d** have been established on the basis of their analytical and spectral data. Thus, the compounds show in their ir spectral bands at 1305-1320 cm^{-1} and 1120-1150 cm^{-1} for the SO_2-absorptions. In the proton nmr spectra signals of the pyrimidine protons for **6a** appear at 9.65 ppm (H-2) and 9.32 ppm (H-4), the signals of H-4 of **6b-d** in range 9.36-8.63 ppm. The methylene protons of **6a-d** were observed to be singlets between 5.55 and 5.84 ppm. The aromatic ring proton absorptions for the compounds designated **6a-d** were consistent with fused structures. The mass spectrum indicated the ion peaks $(M-30)^{+\cdot}$ [8,9] and $(M-64)^{+\cdot}$ corresponding to the eliminations of CH_2O and SO_2 from the molecular ion.

The tentative reaction sequence for the ring transformation is outlined in Scheme I. The conversion of **2** into **6a-d** could involve an initial attack of the amidines **3a-d** at the electrophilic C-2 position of **2**, forming **4**, followed by deprotonation leading to a ring open intermediate **5**. Subsequent recyclisation of **5** accompanied by elimination of chloride and water results in the formation of **6a-d**. The most likely mechanism for this ring closure is a SN_2-reaction of the phenolate anion with the halomethyl-sulfone group [10].

EXPERIMENTAL

General Methods.

Melting points were determined on a Linström apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 297 spectrometer. The ^{1}H-nmr spectra (250 MHz) were recorded on a Bruker WM 250 spectrometer. Mass spectra were obtained on a Finnigan MAT Bremen CH 7A spectrometer. Elemental analyses were performed by the Institut für Pharmazie Analytical Service Laboratory.



3-Chloromethylsulfonyl-4*H*-[1]benzopyran-4-one (**2**).

To a solution of **1** [7] (0.72 g, 3 mmoles) in 12 ml of chloroform, phosphorus pentachloride (0.62 g, 3 mmoles) was added. Then, the mixture was stirred at room temperature for 15 hours. After evaporation *in vacuo* the syrupy residue was treated with ethanol. The crude product was recrystallized from ethanol to give 0.6 g (78%) of colorless crystals.

The compound had mp 209°; ir (potassium bromide): 1660 (CO), 1325, 1165 (SO_2) cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 5.32 (s, 2H), 7.64-8.21 (m, 4H), 9.19 (s, 1H); ms: m/z 258 (M^+, 56%).

Anal. Calcd. for $C_{10}H_7ClO_4S$: C, 46.43; H, 2.73; Cl, 13.70; S, 12.39. Found: C, 46.51; H, 2.69; Cl, 13.89; S, 12.40.

General Procedure for the Synthesis of **6a-d**.

A mixture of **2** (0.5 g 1.9 mmoles), **3a** (1.0 g, 9.6 mmoles) and sodium acetate (1.0 g) was heated at 140° for 20 minutes. In the case of **3b** (0.5 g, 5.3 mmoles), **3c** (0.5 g, 3.2 mmoles) and **3d** (0.5 g, 5.2 mmoles) the mixtures were heated at 160° for 30 minutes. After cooling to room temperature, water (10 ml) was added. The resulting mixtures were stirred for 2 hours. The compounds **6a-d** separated out under these conditions and were recrystallized from ethanol/charcoal.

6*H*-[1,3]Benzoxathiepino[5,4-*d*]pyrimidine 5,5-Dioxide (**6a**).

This compound had mp 188°, pale yellow crystals, yield 0.35 g, (73%); ir (potassium bromide): 1320, 1120 (SO_2) cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 5.84 (s, 2H), 7.46-8.01 (m, 4H), 9.32 (s, 1H), 9.65 (s, 1H); ms: m/z 248 (M^+, 40%), 218 ($M-CH_2O)^{+\cdot}$, 184 ($M-SO_2)^{+\cdot}$.

Anal. Calcd. for $C_{11}H_8N_2O_3S$: C, 53.22; H, 3.25; N, 11.29. Found: C, 52.86; H, 3.04; N, 11.03.

2-Methyl-6*H*-[1,3]benzoxathiepino[5,4-*d*]pyrimidine 5,5-Dioxide (**6b**).

This compound had mp 192°, ocher yellow crystals, yield 0.22 g, (43%); ir (potassium bromide): 1310, 1140 (SO_2) cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 2.84 (s, 3H), 5.79 (s, 2H), 7.44-7.96 (m, 4H), 9.18 (s, 1H); ms: m/z 262 (M^+, 35%), 232 ($M-CH_2O)^{+\cdot}$, 198 ($M-SO_2)^{+\cdot}$.

Anal. Calcd. for $C_{12}H_{10}N_2O_3S$: C, 54.98; H, 3.84; N, 10.69. Found: C, 55.16; H, 3.91; N, 10.82.

2-Phenyl-6*H*-[1,3]benzoxathiepino[5,4-*d*]pyrimidine 5,5-Dioxide (**6c**).

This compound had mp 212°, pale yellow crystals, yield 0.44 g, (70%); ir (potassium bromide): 1305, 1150 (SO_2) cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 5.84 (s, 2H), 7.47-8.58 (m, 9H), 9.36 (s, 1H); ms: m/z 324 (M^+, 35%), 294 ($M-CH_2O)^{+\cdot}$, 260 ($M-SO_2)^{+\cdot}$.

Anal. Calcd. for $C_{17}H_{12}N_2O_3S$: C, 62.95; H, 3.73; N, 8.64. Found: C, 62.63; H, 3.60; N, 8.55.

2-Amino-6*H*-[1,3]benzoxathiepino[5,4-*d*]pyrimidine 5,5-Dioxide (**6d**).

This compound had mp 248°, colorless crystals, yield 0.27 g, (53%); ir (potassium bromide): 3400, 3320 (NH_2), 1320, 1150 (SO_2) cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 5.55 (s, 2H), 7.36-7.74 (m, 4H), 8.00 (s, 2H), 8.65 (s, 1H); ms: m/z 263 (M^+, 35%), 233 ($M-CH_2O)^{+\cdot}$, 199 ($M-SO_2)^{+\cdot}$.

Anal. Calcd. for $C_{11}H_9N_3O_3S$: C, 50.18; H, 3.45; N, 15.96. Found: C, 49.99; H, 3.51; N, 15.97.

REFERENCES AND NOTES

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