Synthesis *via* Pummerer Intermediates. II. (1). Disproportionation Reactions of 3-(Methylsulfinyl)chromones and 3-(Methylsulfinyl)quinolinones with Hydrochloric Acid

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Sulfoxides (**1** and **10**) gave oxidation-reduction products when treated with 5*N* hydrochloric acid. 8-Methoxy-3-(methylsulfinyl)-4*H*-1-benzopyran-4-one (**1**) gave 8-methoxy-3-(methylthio)-4*H*-1-benzopyran-4-one (**4**) and 8-methoxy-3-(methylsulfonyl)-4*H*-1-benzopyran-4-one (**5**), whereas 1-methyl-3-(methylsulfinyl)-4(1*H*)quinolinone (**10**) gave 1-methyl-3-(methylthio)-4(1*H*)-quinolinone (**12**) and 1-methyl-4(1*H*)-quinolinone (**13**).

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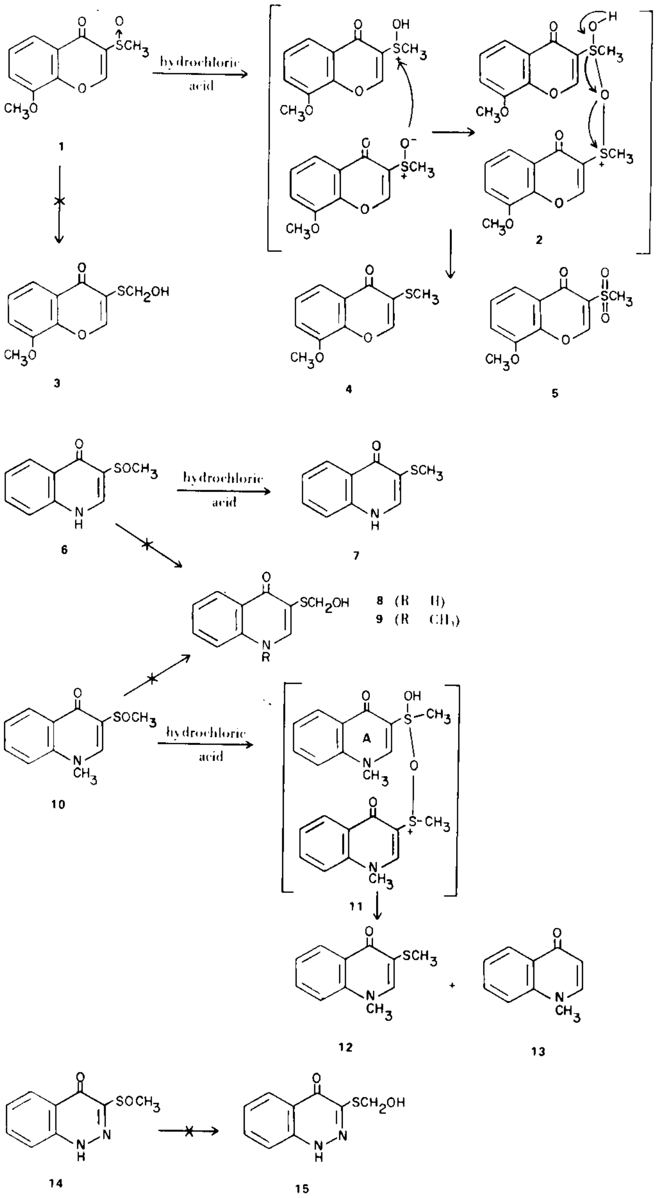
In connection with another project we required 3-thiol derivatives of chromones, quinolinones and cinnolinones. It was expected that treatment of sulfoxides (**1**, **6**, **10** and **14**) with aqueous acid would give the corresponding 3-[(hydroxymethyl)thiol] derivatives [**3**, **8**, **9** and **15**, respectively]. These could then be hydrolyzed to the desired thiols. Instead treatment of sulfoxides (**1**, **6** and **10**) gave disporportionation reactions. Sulfoxide (**1**) gave a mixture of sulfide (**4**), sulfone (**5**) and minor products. Dimer (**2**) may be an intermediate in the production of **5** and an equivalent amount of **4**. Other mechanisms must predominate in this reaction for the nmr of the crude product mixture indicates **4** to be the major product and **5** to be present in a small amount. Sulfone (**5**) was also prepared by the oxidation of **4** with *m*-chloroperbenzoic acid. Sulfoxide (**6**) gave the corresponding sulfide (**7**) and several other products which were not isolated in pure form. Sulfoxide (**10**) also underwent a type of disproportionation giving sulfide (**12**) and 1-methyl-4(1*H*)-quinolinone (**13**). Nmr and tlc indicate **12** and **13** are the only products formed and they are present in equal amounts in the crude product mixture. Thus these products arise from a dimer such as **11**, by protonation at C_3 in ring A followed by fragmentation. To our knowledge these reactions represent the first reported examples of this type of intermolecular oxidation-reduction of sulfoxides under Pummerer conditions. 3-(Methylsulfinyl)-4(1*H*)cinnolinone (**14**) gave recovered starting material on treatment with hydrochloric acid.



EXPERIMENTAL

Melting points were measured with a Thomas-Hoover capillary melting point apparatus without correction. Nmr spectra were recorded on a Perkin-Elmer R-12B spectrometer at 60 MHz with TMS as internal standard. Infrared spectra were recorded on a Beckmann DK-1 spectrometer. Mass spectra were obtained with an AEI MS-902 instrument.

Reaction of 8-Methoxy-3-(methylsulfinyl)-4*H*-1-benzopyran-4-one (1) with Hydrochloric Acid.

A solution of 8-methoxy-3-(methylsulfinyl)-4*H*-1-benzopyran-4-one (3) (2.0 g., 0.0084 mole) in 5*N* hydrochloric acid (40 ml.) was heated at 100° under nitrogen for 5 hours. The reaction mixture was cooled and extracted with chloroform. The extracts were dried over magnesium sulfate and evaporated to give

8-methoxy-3-(methylthio)-4*H*-1-benzopyran-4-one (**4**) (1.1 g., 59%), m.p. 114-115°; (lit. (3) 114-115°). The mother liquor from the recrystallization was evaporated to give an oil. Tlc and nmr indicated it to be a mixture of **4** and 8-methoxy-3-(methylsulfonyl)-4*H*-1-benzopyran-4-one (**5**).

3-(Methylsulfinyl)-4(1*H*)quinolinone (**6**).

Piperidine (8.5 g., 0.1 mole) was added to a solution of 1-(2-aminophenyl)-2-(methylsulfinyl)ethanone (4) (19.7 g., 0.1 mole) in refluxing triethyl orthoformate (200 ml.). The reaction mixture was refluxed under nitrogen for 10 hours. The solvent was removed under reduced pressure to give a viscous purple oil which crystallized from methanol. The product was washed with ethyl acetate and recrystallized from ethanol to give off-white crystals (7.5 g., 36%), m.p. 253-254°; uv: max 244 (20,000), 251 (20,000), 294 (7,000), 317 (9,000) and 329 nm (9,000); ir (nujol): broad 3300-3100 (NH) and 1620 cm^{-1} (CO); nmr (DMSO): δ 11.00 (broad, 1, NH, exchanges with deuterium oxide), 8.40 to 7.10 (m, 5, ArH) and 2.83 (s, 3, SCH_3).

Anal. Calcd. for $C_{10}H_9NO_2S$: C, 57.95; H, 4.38; N, 6.76; S, 15.47. Found: C, 58.10; H, 4.58; N, 6.62; S, 15.32.

3-(Methylthio)-4(1*H*)quinolinone (**7**).

A solution of 3-(methylsulfinyl)-4(1*H*)quinolinone (1.0 g., 0.0048 mole) in 5*N* hydrochloric acid (20 ml.) was refluxed under nitrogen for 6 hours. The solution was cooled, adjusted to *p*H 6 with sodium bicarbonate, and extracted with chloroform. The extracts were dried over magnesium sulfate and evaporated to give the crude product. Recrystallization from methanol-ethyl acetate gave off-white crystals (350 mg., 38%), m.p. 173-175°; nmr (DMSO): δ 12.5 (broad, 1, NH, exchanges with deuterium oxide), 8.30 to 7.20 (m, 5, ArH) and 2.34 (s, 3, SCH_3).

Anal. Calcd. for $C_{10}H_9NOS$: C, 62.80; H, 4.74; N, 7.32; S, 16.77. Found: C, 62.86; H, 4.84; N, 7.37: S, 15.84.

1-Methyl-3-(methylthio)-4(1*H*)quinolinone (**12**) and 1-Methyl-4-(1*H*)quinolinone (**13**).

A solution of 1-methyl-3-(methylsulfinyl)-4(1*H*)quinolinone (3) (1.0 g., 0.0045 mole) in 5*N* hydrochloric acid (20 ml.) was refluxed under nitrogen for 6 hours. The reaction mixture was cooled and extracted with chloroform. No material was extracted. The aqueous solution was neutralized with 10% sodium hydroxide solution and extracted with chloroform. The extracts were dried over magnesium sulfate and evaporated to give a crystalline solid. Recrystallization from ethyl acetate gave 1-methyl-3-(methylthio)-4(1*H*)quinolinone (first crop) as off-white crystals (100 mg., 11%), m.p. 123-124°; nmr (deuteriochloroform): δ 8.45 (d, 1, ArH), 7.75 (s, 1, C_2H), 7.75-7.15 (m, 3, ArH), 3.80 (s, 3, NCH_3) and 2.41 (s, 3, SCH_3).

Anal. Calcd. for $C_{11}H_{11}NOS$: C, 64.38; H, 5.40; N, 6.83; S, 15,58. Found: C, 64.06; H, 5.44; N, 6.73; S, 15.64.

1-Methyl-4(1*H*)quinolinone.

This compound was the second crop (30 mg., 4%), m.p. 145-147° (lit. (4) 145-148°); nmr (deuteriochloroform): δ 8.45 (d, 1, ArH), 7.90-7.20 (m, 3, ArH), 7.50 (d, 1, J = 8 Hz, C_2H), 6.23 (d, 1, J = 8 Hz, C_3H) and 3.80 (s, 3, NCH_3); ms. found: M^+ 159.0633: $C_{10}H_9NO$ requires 159.0684.

8-Methoxy-3-(methylsulfonyl)-4*H*-1-benzopyran-4-one (**5**).

A solution of 8-methoxy-3-(methylsulfinyl)-4*H*-1-benzopyran-4-one (3) (1.8 g., 0.0075 mole) and *m*-chloroperbenzoic acid (2.0 g., 0.0116 mole) in dichloromethane (100 ml.) was stirred at room temperature for 4 hours. The solvent was removed under reduced pressure to give a white solid. The solid was washed with ethanol and recrystallized from ethanol to give white crystals (1.75 g., 91%); m.p. 197-198°; uv: max 252 (12,100) and 308 nm (4,000); ir (nujol): 1655 cm^{-1} (CO): nmr (deuteriochloroform): δ 8.75 (s, 1, C_2H), 7.80 (d, 1, ArH), 7.70 to 7.10 (m, 2, ArH), 3.98 (s, 3, OCH_3), and 3.36 (s, 3, SCH_3).

Anal. Calcd. for $C_{11}H_{10}O_5S$: C, 51.96; H, 3.96; S, 12.61. Found: C, 51.85; H, 3.90; S, 12.77.

REFERENCES AND NOTES

(1) For Part I in this series see D. T. Connor and M. von Strandtmann, *J. Org. Chem.*, **39**, 1594 (1974).

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(3) D. T. Connor, P. A. Young, and M. von Strandtmann, *J. Heterocyclic Chem.*, **15**, 115 (1978).

(4) M. von Strandtmann, S. Klutchko, M. P. Cohen and J. Shavel, Jr., *J. Heterocyclic Chem.*, **9**, 173 (1972).