

### 557. 1-Thio-4-pyrone

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The accumulated evidence indicates that 1-thio-4-pyrone, while resembling 4-pyrone (III) in some ways, is more stable, the structure (Ia; R = H) being of considerable importance. No evidence for "aromatic" type chemical properties could be found.

THE title compound (I; R = H) was first prepared in 1930<sup>1</sup> and has subsequently been obtained by several different processes.<sup>2,3</sup> Substituted derivatives are also fairly well known<sup>4-10</sup> but the chemical reactions of 1-thio-4-pyrones have not been much studied although a theoretical paper has appeared.<sup>11</sup> We became interested in the subject since 1-thio-4-pyrone (I; R = H) may be considered as a  $6\pi$ -electron system isosteric with tropone (II) by virtue of participation by electrons from the  $d$ -orbitals of the sulphur atom. This consideration had prompted Czech workers<sup>12</sup> to synthesise 3-hydroxy-1-thio-4-pyrone (I; R = OH) related similarly to tropolone. The infrared<sup>13</sup> and ultraviolet spectra,<sup>14,15</sup> dipole moment,<sup>8</sup> and ionisation constant<sup>16</sup> of 1-thio-4-pyrone have been recorded.

<sup>1</sup> F. Arndt and N. Bekir, *Ber.*, 1930, **63B**, 2393.

<sup>2</sup> R. Mayer, *Chem. Ber.*, 1957, **90**, 2362.

<sup>3</sup> R. Mayer, *Chem. Tech. (Berlin)*, 1958, **10**, 418 (*Chem. Abs.*, 1959, **53**, 2222).

<sup>4</sup> G. Traverso, *Chem. Ber.*, 1958, **91**, 1224.

<sup>5</sup> F. Arndt, *Ber.*, 1925, **58B**, 1633.

<sup>6</sup> V. Horak and M. Cerny, *Chem. listy*, 1952, **46**, 421.

<sup>7</sup> V. Horak, J. Zavada, and A. Piskala, *Chem. and Ind.*, 1958, 1113.

<sup>8</sup> M. Rolla, M. Sanesi, and G. Traverso, *Ann. Chim. (Italy)*, 1952, **42**, 507, 673.

<sup>9</sup> C. Barkenbus, V. C. Midkiff, and R. M. Newman, *J. Org. Chem.*, 1951, **16**, 232, 1047.

<sup>10</sup> G. M. Bennett and L. V. D. Scoria, *J.*, 1927, 194.

<sup>11</sup> R. Zahradnik and J. Koutecky, *Tetrahedron Letters*, 1961, 632.

<sup>12</sup> V. Horak and N. Kucherczyk, *Chem. and Ind.*, 1960, 694.

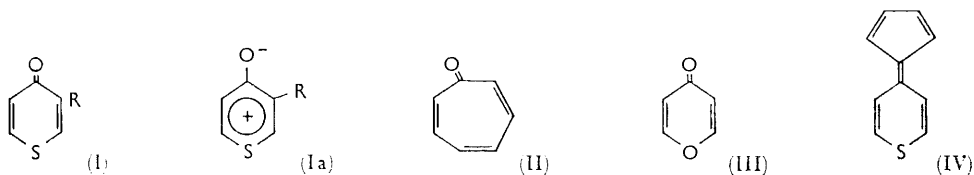
<sup>13</sup> D. S. Tarbell and P. Hoffmann, *J. Amer. Chem. Soc.*, 1954, **76**, 2451.

<sup>14</sup> M. Rolla and P. Franzosini, *Ann. Chim. (Italy)*, 1956, **46**, 582.

<sup>15</sup> G. Traverso, *Ann. Chim. (Italy)*, 1955, **45**, 128.

<sup>16</sup> M. Saresi, *Ann. Chim. (Italy)*, 1960, **50**, 997.

Initial experiments were concentrated on the reactivity of the carbonyl group towards various hydrazines and hydroxylamine. It was found that, in general, these reactions were similar to those of 4-pyrone (III) in which the tendency to ring-opening is of paramount importance. For example, from 1-thio-4-pyrone and hydroxylamine,<sup>17</sup> 4-hydroxyaminopyridine *N*-oxide (cf. Parisi *et al.*<sup>17</sup>) was isolated, and from the 1-thio-4-pyrone and hydrazine,<sup>18a</sup> pyrazole-3-carboxylic acid was obtained after oxidation (cf. Ainsworth



and Jones<sup>18a</sup>). With phenyl- and *p*-nitrophenyl-hydrazine little, if any, reaction was observed but 2,4-dinitrophenylhydrazine gave a 2,4-dinitrophenylhydrazone, in contrast to pyrone from which no carbonyl derivative has been prepared.

Although 4-pyrone is reported to brominate in the 3- and 5-positions, to give both the mono- and di-bromo-products,<sup>19</sup> no evidence of nuclear bromination of 1-thio-4-pyrone was obtained. In various solvents, an orange-red unstable complex was isolated and shown by titration<sup>20</sup> to have the approximate composition  $C_5H_4OS, HBr, 3Br_2$ . This complex, when heated in water, and more rapidly in the presence of acetone, was converted into 4-hydroxythiopyrylium bromide (isolated as the monohydrate) from which 1-thio-4-pyrone could be recovered almost quantitatively by basification. An identical salt was obtained from 1-thio-4-pyrone and hydrogen bromide; the n.m.r. spectrum confirmed that the four nuclear hydrogen atoms were not substituted. Parkanyi and Zahradnik<sup>21</sup> erroneously claimed that 1-thio-4-pyrone is substituted by bromine in acetic acid; repetition of their work led to the same complex as that already described.

The action of Grignard reagents on 1-thio-4-pyrone might be expected by analogy with 4-pyrone<sup>22</sup> to yield 4-substituted thiopyrylium salts, but in fact, with either methylmagnesium iodide or cyclopentadienylsodium, 4-hydroxythiopyrylium salts were obtained identical with those obtained directly from 1-thio-4-pyrone and mineral acids. It is thus deduced that the polar form (Ia; R = H) is important in such situations. The infrared carbonyl band at  $1609\text{ cm}^{-1}$  (4-pyrone  $1658$ ) is further indication of this. Failure to react with cyclopentadienylsodium made a synthesis of the 4-cyclopentadienylidene thiopyran molecule (IV) (cf. ref. 23) impossible by routes involving this step.

Although tropone<sup>24</sup> and thiophen<sup>25</sup> form metal carbonyl derivatives, in the present study 1-thio-4-pyrone was recovered after treatment with iron, cobalt, chromium, and molybdenum carbonyls even under forcing conditions and with irradiation.

The n.m.r. spectrum (in deuteriochloroform) of 1-thio-4-pyrone showed two groups of ten lines centred at  $2.11$  and  $2.91\ \tau$  with further splitting discernible, presumably owing to *meta*-transannular interactions. These chemical shifts are of the order usually encountered in aromatic systems.<sup>26</sup>

<sup>17</sup> F. Parisi, P. Bovina, and A. Quilico, *Gazzetta*, 1960, **90**, 903.

<sup>18</sup> (a) C. Ainsworth and R. G. Jones, *J. Amer. Chem. Soc.*, 1954, **76**, 3172; (b) R. G. Jones and M. J. Mann, *ibid.*, 1953, **75**, 4048.

<sup>19</sup> F. Feist and E. Baum, *Ber.*, 1905, **38**, 3562.

<sup>20</sup> T. Nozoe, T. Mukai, and K. Takase, *Sci. Reports Tôhoku Univ.*, 1956, **39**, 164.

<sup>21</sup> C. Parkanyi and R. Zahradnik, *Coll. Czech., Chem. Comm.*, 1962, **27**, 1355.

<sup>22</sup> G. Kobrich, *Annalen*, 1961, **648**, 114.

<sup>23</sup> D. Lloyd and F. I. Wasson, *Chem. and Ind.*, 1963, **38**, 1559.

<sup>24</sup> W. Hübel and E. Weiss, *Chem. and Ind.*, 1959, 703.

<sup>25</sup> E. O. Fischer and K. Öfele, *Chem. Ber.*, 1958, **91**, 2395.

<sup>26</sup> L. M. Jackman in "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, London, 1962.

## EXPERIMENTAL

N.m.r. spectra were measured at 40 Mc./sec.

**4-Pyrone.**—The original method of Willstätter and Pummerer<sup>27</sup> refined later by Cornubert *et al.*<sup>28</sup> was modified to a simple laboratory preparation as follows. A small retort (100 ml. bulb with delivery tube of length 12 in.) was charged with chelidonic acid (20 g.) (pre-dried at 140°) and dry precipitated copper powder (40 g. commercial quality). This was fitted by ground glass joints to a receiver flask with the open end protected by a calcium chloride tube. The bulb of the retort was immersed in a Wood's metal bath which was heated to 220° in 20 min., and then to 280° in a further 25 min., and finally to 340—350° in a total of 1 hr., this temperature being maintained for 10 min. The crude pyrone (6.5—7.0 g.) that had distilled was dried by refluxing with benzene in a Dean and Stark apparatus and finally distilled at 97°/5 mm.

1-Thio-4-pyrone was prepared from 4-pyrone by the method of Mayer.<sup>2,3</sup>

**Reaction of 1-Thio-4-pyrone with Hydroxylamine.**—1-Thio-4-pyrone (300 mg.), hydroxylamine hydrochloride (600 mg.), dry ethanol (3 ml.), and dry pyridine were refluxed together for 3 hr. After removal of most of the solvent *in vacuo* and addition of water, there was obtained 4-hydroxyaminopyridine *N*-oxide<sup>17</sup> (216 mg., 64%) (Found: C, 47.4; H, 4.9. Calc. for C<sub>5</sub>H<sub>6</sub>N<sub>2</sub>O<sub>2</sub>: C, 47.6; H, 4.9%). This product gave the expected<sup>17</sup> 4,4'-azopyridine 1,1'-dioxide on basification.

**Reaction of 1-Thio-4-pyrone with Hydrazine.**—1-Thio-4-pyrone (200 mg.) was treated with 60% hydrazine hydrate (1 ml.) and ethanol (1 ml.). After the initial exothermic reaction had subsided, the mixture was kept at 100° for 3 hr., treated with potassium permanganate (1.25 g.) in water (20 ml.) at 100° for 30 min., cooled, and filtered. The filtrate was acidified with dilute hydrochloric acid and evaporated to dryness. The residue was extracted with acetone, to yield pyrazole-3-carboxylic acid (127 mg., 63%), m. p. 212° (lit.,<sup>18b</sup> 216—217°), λ<sub>max</sub> 214 mμ (log ε 3.96).

**1-Thio-4-pyrone 2,4-Dinitrophenylhydrazine.**—1-Thio-4-pyrone (500 mg.), 2,4-dinitrophenylhydrazine (1 g.), ethanol (50 ml.), and concentrated hydrochloric acid (1.5 ml.) were warmed on a steam-bath for 15 min. Cooling gave yellow crystals of the *hydrochloride*, m. p. 223° (1 g.) (Found: C, 39.9; H, 3.1; Cl, 11.0; N, 17.0; S, 9.6. C<sub>11</sub>H<sub>9</sub>ClN<sub>4</sub>O<sub>4</sub>S requires C, 40.2; H, 2.8; Cl, 10.8; N, 17.0; S, 9.8%). The free *dinitrophenylhydrazone* was obtained on addition of water; it crystallised from methanol in red needles, m. p. 224° (Found: C, 44.8; H, 3.3; N, 18.9. C<sub>11</sub>H<sub>8</sub>N<sub>4</sub>O<sub>4</sub>S requires C, 45.2; H, 2.8; N, 19.2%), λ<sub>max</sub> 420 mμ (log ε 4.45).

**Reaction of 1-Thio-4-pyrone with Methylmagnesium Iodide.**—To methylmagnesium iodide at 0° [from magnesium (0.22 g.) and methyl iodide (0.56 ml.)] under nitrogen in dry ether (20 ml.) was added 1-thio-4-pyrone (1 g.) in dry ether (100 ml.). The resulting mixture was poured into dilute hydrochloric acid and treated with potassium tri-iodide solution (excess), to give 4-hydroxythiopyrylium tri-iodide (3.5 g., 80%), crystallising from water in green needles, m. p. 95° (Found: C, 12.5; H, 1.05. C<sub>5</sub>H<sub>5</sub>I<sub>3</sub>OS requires C, 12.2; H, 1.0%). Slow evaporation of an aqueous solution of the tri-iodide brought about conversion into the *mono-iodide*. This process was accelerated by addition of acetone. Crystallisation from acetone gave white dichroic plates, m. p. 173° (Found: C, 25.3; H, 2.3. C<sub>5</sub>H<sub>5</sub>IOS requires C, 25.0; H, 2.1%). Treatment of an acidified solution of 1-thio-4-pyrone with potassium tri-iodide solution gave the same tri-iodide, m. p. and mixed m. p. 95°, which could be converted as above into the same mono-iodide, m. p. and mixed m. p. 173°.

**Reaction of 1-Thio-4-pyrone and Cyclopentadienylsodium.**—A solution of sodium (0.4 g.), cyclopentadiene monomer (excess), and dry tetrahydrofuran (5 ml.) was added under nitrogen at -70° to 1-thio-4-pyrone (2 g.) in dry tetrahydrofuran (100 ml.). After 1 hr., the mixture was concentrated *in vacuo* and poured into dilute hydrochloric acid (excess). Addition of potassium tri-iodide gave 4-hydroxythiopyrylium tri-iodide as previously.

**Attempted Reactions of 1-Thio-4-pyrone with Metal Carbonyls.**—1-Thio-4-pyrone was recovered after treatment with the following metal carbonyls under the conditions specified. (a) Iron pentacarbonyl in refluxing benzene, 12 hr. (b) Iron pentacarbonyl at 160° for 6 hr. in a bomb. (c) Iron pentacarbonyl in refluxing ether for 4 hr. with irradiation. (d) Iron dodecacarbonyl in refluxing toluene (8 hr.) and in refluxing diglyme. (e) Iron dodecacarbonyl at 160°

<sup>27</sup> R. Willstätter and R. Pummerer, *Ber.*, 1904, **37**, 3740; 1905, **38**, 1461.

<sup>28</sup> R. Cornubert and P. Robinet, *Bull. Soc. chim. France*, 1933, 565; R. Cornubert, R. Delmas, S. Monteil, and J. Viriot, *ibid.*, 1950, 36.

for 6 hr. in a bomb. (f) Cobalt octacarbonyl in refluxing tetrahydrofuran. (g) Nickel carbonyl in refluxing methylene chloride. (h) Nickel carbonyl at 70° (4 hr.) in a bomb. (i) Chromium carbonyl for 20 hr. in refluxing light petroleum (b. p. 100—120°). (j) Molybdenum carbonyl for 3 hr. in refluxing diglyme.

*Reaction of 1-Thio-4-pyrone with Bromine.*—(a) To 1-thio-4-pyrone (300 mg., 2.7 mmoles) in water (5 ml.) at 0° was added a solution of bromine (1.4 g., 8.8 mmoles) in water (3 ml.) containing potassium bromide (1 g.). An orange-red crystalline product (600 mg.) was obtained, m. p. 110—120°.

(b) To 1-thio-4-pyrone (200 mg., 1.8 mmoles) in carbon tetrachloride (10 ml.) was added bromine (900 mg., 5.6 mmoles) in carbon tetrachloride (5 ml.). The orange-red product (250 mg.) which was slowly precipitated showed no depression of melting point with that obtained in (a).

(c) 1-Thio-4-pyrone (50 mg., 0.45 mmole) in glacial acetic acid (1 ml.), treated with bromine (250 mg., 1.6 mmoles), slowly (2 days) yielded the same compound as in (a) and (b).

(d) The same complex, m. p. 110—120°, was obtained from numerous other reactions, including refluxing in presence of catalysts such as ferric halides, and ultraviolet irradiation.

When the orange-red complex was heated in water and evaporated to dryness or warmed in acetone, a white crystalline solid, m. p. 190°, was obtained and shown to be *4-hydroxythio-pyrylium bromide hydrate* by comparison with the product obtained from 1-thio-4-pyrone and hydrogen bromide-acetic acid in acetone (Found: C, 29.0; H, 3.3.  $C_5H_7BrO_2S$  requires C, 28.5; H, 3.3%). Treatment of this product with sodium hydrogen carbonate solution (excess) and extraction with chloroform gave 1-thio-4-pyrone (quantitative), m. p. and mixed m. p. 112°.

The composition of the freshly prepared orange-red complex was determined (cf. ref. 12) by dissolving a weighed amount (25—30 mg.) in water (10 ml.) containing potassium iodide (0.5 g.), and titrating the liberated iodine with sodium thiosulphate solution (0.01N) to obtain the free bromine value. Further titration with sodium hydroxide (0.01N) allowed calculation of the percentage of hydrogen bromide present. Found:  $Br_2$  (fresh sample), 70.0; after 4 hr., 64.1; after 24 hr., 59.8.  $C_5H_4OS, HBr, 3Br_2$  requires 71.25%. Found: HBr (fresh sample), 14.9; after 4 hr., 16.3; after 24 hr., 17.7.  $C_5H_4OS, HBr, 3Br_2$  requires 12.03%.

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