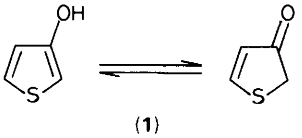
Simple 3-Hydroxythiophenes [Thiophen-3(2*H*)-ones]

Gordon A. Hunter and Hamish McNab*

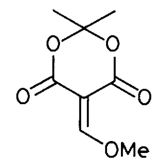
Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, U.K.

We report a simple and flexible synthetic route to simple 3-hydroxythiophenes [thiophen-3(2*H*)-ones], including the parent compound (**1a**).

'Hydroxythiophenes are often very unstable, air-sensitive and acid-sensitive compounds which decompose easily.'[1] Simple members of the series therefore have been prepared only with difficulty, by low yielding and/or multi-step sequences, and little is known of their chemistry.[1] Here we report a convenient and general solution to problems of 3-hydroxythiophene [thiophen-3(2*H*)-one] (**1**) synthesis, by using a flexible and efficient two-step route which relies on gas-phase methodology to overcome the sensitive nature of the products. The route follows from the well-established formation of the 1*H*-pyrrol-3(2*H*)-one nucleus by thermolysis of aminomethylene Meldrum's acid derivatives.[2] Very recently, Pom-



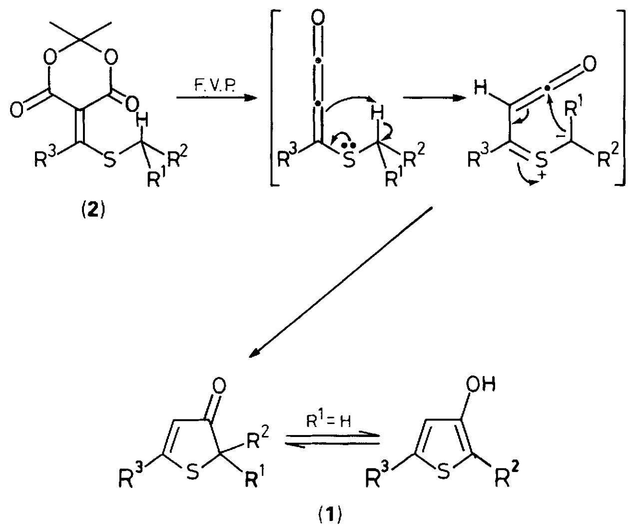
(**1**)



(**3**)

Table 1

Compounds (**1**) and (**2**)	R^1	R^2	R^3	Yield of (**1**)/%
a	H	H	H	80
b	H	Me	H	50
c	H	Ph	H	92
d	H	CO_2Et	H	76
e	Me	Me	H	45
f	$-(C_5H_{10})-$		H	60
g	H	H	Me	75
h	H	H	Ph	80
i	H	H	$4\text{-}Bu^t\text{-}C_6H_4$	86
j	H	H	MeS	80

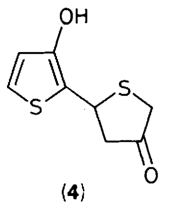


Scheme 1

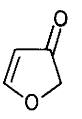
melet, Chuche, and co-workers[3] have adopted a similar strategy for compounds (**1g**) and (**1j**), and have characterised methyleneketene intermediates *en route* to the thiophenones.

We have found that pyrolysis of the Meldrum's acid derivatives (**2**) at 625 °C (10^{-3} Torr) proceeds cleanly and efficiently to give the thiophenones (**1**) in high yield (Scheme 1).† The method is applicable to 2-alkyl, 2-aryl, or 2-functionalised derivatives [(**1b**), (**1c**), and (**1d**), respectively] and 2,2-disubstituted compounds [(**1e**) and (**1f**)]. The precursors (**2b—f**) are readily available in *ca.* 85% yield by treatment of methoxymethylene Meldrum's acid[4] (**3**) with the appropriate thiol in acetonitrile solution.[5] Similarly, 5-alkyl, 5-aryl, and 5-functionalised thiophenones (**1g—j**) can be obtained from the known derivatives (**2g—j**).[6,7]

Of particular importance, the parent thiophen-3(2*H*)-one (**1a**), which hitherto has been only poorly characterised[8] is now available in high yield (80%) and in sufficient quantity that its properties can be studied. The precursor (**2a**) is obtained directly from Meldrum's acid and the commercially available tris(methylthio)methane in the presence of aluminium trichloride (80%). The thiophenone (**1a**) is indeed[8] an unstable compound, and dimerises relatively cleanly to the bithiophene (**4**) over a period of days, even at low temperature. In contrast with the corresponding furanone (**5**)[9] and pyrrolone (**6**)[10] which show, at most, only traces of enol tautomer in chloroform solution, (**1a**) exists as a 2.9 : 1 mixture of thiophenone and hydroxythiophene forms.[11] This result shows the enhanced resonance stability of the thiophene nucleus over the furan and pyrrole ring systems. Reaction of (**1a**) with electrophiles under basic conditions is illustrated by regiospecific *O*-acylation (acetyl chloride/triethylamine) and *O*-alkylation (methyl toluene-*p*-sulphonate/sodium hydride) to give (**7**) and (**8**), respectively. Under acidic conditions ([^{2}H]trifluoroacetic acid), deuterium exchange reactions at the 2-, 4-, and 5-positions take place *via* the hydroxythiophene tautomer.

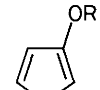


(**4**)



(**5**)

(**6**)



(**7**) R = COMe
(**8**) R = Me

Further chemical and spectroscopic studies of the thiophenones (**1**) are in progress.

We thank the University of Edinburgh for the award of the Colin and Ethel Gordon Scholarship (to G. A. H.) and Lonza Ltd. for a generous gift of Meldrum's acid.

Received, 23rd November 1989; Com. 9/05027B

References

1 S. Gronowitz and A.-B. Hornfeldt, in 'Thiophene and its Derivatives. Part 3,' ed. S. Gronowitz, Wiley-Interscience, New York, 1986, ch. 1.
2 H. McNab and L. C. Monahan, *J. Chem. Soc., Perkin Trans. 1*, 1988, 863, and references cited therein.
3 A. Ben Cheikh, H. Dhimane, J. C. Pommelet, and J. Chuche, *Tetrahedron Lett.*, 1988, **29**, 5919.
4 G. A. Bihlmayer, G. Derflinger, J. Derkosch, and O. E. Polansky, *Monatsh. Chem.*, 1967, **98**, 564.
5 *Cf.* F. Bellini and J. Bagli, U.S. Pat. 4, 547, 516 (1985); *Chem. Abstr.*, 1986, **104**, P129914w.
6 X. Huang and B.-C. Chen, *Synthesis*, 1986, 967.
7 X. Huang and B.-C. Chen, *Synthesis*, 1987, 480.
8 M. C. Ford and D. Mackay, *J. Chem. Soc.*, 1956, 4985.
9 A. Hofmann, W. v. Philipsborn, and C. H. Eugster, *Helv. Chim. Acta*, 1965, **48**, 1322.
10 A. J. Blake, H. McNab, and L. C. Monahan, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1455.
11 See also B. Capon and F.-C. Kwok, *J. Am. Chem. Soc.*, 1989, **111**, 5346.

---

† All new compounds were characterised by their spectra and by elemental analysis.