Synthesis of thiiranes through direct sulfur transfer to cycloalkenes in the thermolysis of a thiophene endoperoxide

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Thiophene endoperoxide 2, which was prepared by photo-oxygenation of thiophene 1, transfers a sulfur atom to form thiiranes when thermolysed in the presence of cycloalkenes, an unexpectedly efficient process which can be catalysed by the cobalt–tetraphenylporphine complex.

Alkyl-substituted thiophenes react with singlet oxygen[1–4] by [4 + 2] cycloaddition to form endoperoxides. In the case of 2,5-dimethylthiophene, the thiaozonide structure was assigned by reduction of the C=C bond with diimine to the persistent dihydro derivative[5] and NMR spectroscopy at low temperature.[6] The thermolysis of this endoperoxide leads to thiocarbonyl-(*S*)-oxide (sulfine) and *cis*-enedione with extrusion of elemental sulfur.[5–7] Matturro *et al.*[7a] performed this thermolysis in the presence of excess norbornene or 2,5-dimethylhex-3-ene and observed low yields of the corresponding thiiranes, along with other products. Here we report on a thiophene endoperoxide, which affords efficiently thiiranes in the presence of cycloalkenes, either thermally or Co^{II}-induced.

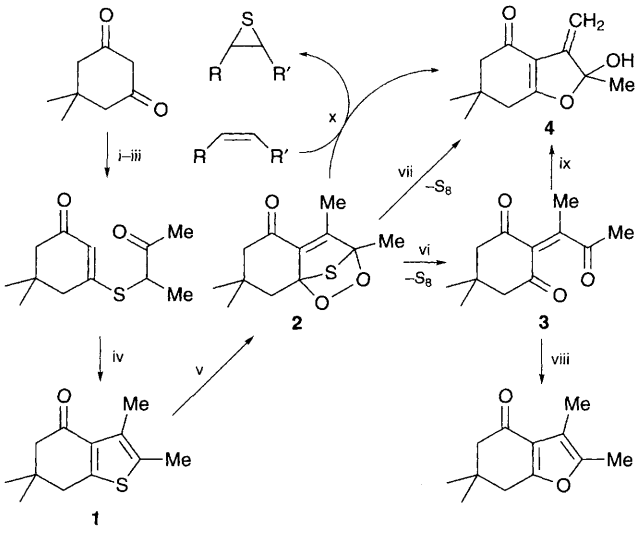
The synthesis of the thiophene **1**† is presented in Scheme 1, analogous to the method described by Lawesson[8] (steps i–iii), followed by cyclisation with polyphosphoric acid (step iv). Photo-oxygenation of thiophene **1** at −30 °C led entirely to endoperoxide **2**† (step v), which is persistent in solution at −20 °C for some days. The endoperoxide structure is consistent with all ^1H and ^{13}C NMR data (δ 105.7 and 106.5 for the characteristic heteroatom-substituted carbon atoms).[6]

At room temperature, endoperoxide **2** is transformed to hemiacetal **4** (step vii), which was synthesized independently from the furan by way of the enetrione **3**[9] (steps viii and ix). Therefore, entrione **3** is the primary product in the thermolysis of endoperoxide **2**, which was also verified by ^1H NMR monitoring of the thermolysis (step vi), but the expected thiocarbonyl-(*S*)-oxide was not observed as in the case of the 2,5-dimethylthiophene endoperoxide.[5–7]

When the thermolysis of endoperoxide **2** was performed in the presence of norbornene,[7a] 50% of the corresponding episulfide was obtained (Scheme 1, step x and Table 1, entry 1). With an excess of norbornene (4.2 equiv.), the yield of sulfur transfer was >95% (entry 2).

To assess the scope of this sulfur transfer process, a series of alkenes was investigated (entries 3–8). In all cases thiiranes were formed, which were identified by comparison with literature-known ^1H NMR data[10,11] and the ^{13}C NMR chemical shifts [δ_c (CS) = 37.5–41.6 (d)].[12] The yields for the cycloalkenes are lower than for norbornene, which is known to possess a high reactivity in such addition reactions,[13] and increase in the order cyclopentene (entry 7, 25%), cycloheptene (entry 4, 30%) and cyclooctene (entry 3, 38%), while cyclohexene (entry 6, 5%) is a poor sulfur atom acceptor.

Since the cleavage of the peroxide bond in endoperoxides is known to be catalysed by redox-active metals at low temperature,[14] this methodology was utilized for the sulfur transfer from endoperoxide **2**. Indeed, in the presence of norbornene and 10 mol% of CoTPP [tetraphenylporphine cobalt(II) complex], the thiirane was obtained efficiently (68%) at −40 °C (entry 9), an unprecedented metal-assisted sulfur atom transfer. Although the



Scheme 1 (i) Oxalyl chloride, CH_2Cl_2, reflux, 4 h, 92% (ref. 8: 92%); (ii) Na_2S, H_2O, 80 °C, 16 h; (iii) 3-chlorobutan-2-one, H_2O, room temp., 16 h, 73%; (iv) polyphosphoric acid, 95 °C, 6 h, 66%; (v) O_2, tetraphenyl porphine (TPP), *hν*, $CDCl_3$, −30 °C, 2.5 h; (vi) $CDCl_3$, 0 °C, 1 h, conversion 13%, yield 13%; (vii) $CDCl_3$, room temp., 16 h, 59%; (viii) dimethyldioxirane, acetone, −20 °C, 2.5 h, >95%; (ix) room temp., $CDCl_3$, 3 h, 74%; (x) *cf.* Table 1

Table 1 Sulfur transfer from thiophene endoperoxide **2** to alkenes

Entry	Alkene (equiv.)	Conditions	Products (%)[a] 3	4	Thiirane[b]
1	norbornene (1.0)	$CDCl_3$, room temp., 2 h	38	54	50
2	norbornene (4.2)	$CDCl_3$, room temp., 2 h	35	65	>95 (52)
3	cyclooctene (1.0)	$CDCl_3$, room temp., 2 h	28	45	38 (31)
4	cycloheptene (1.0)	$CDCl_3$, room temp., 2 h	30	60	30
5	cycloheptene (7.0)	$CDCl_3$, room temp., 2 h	—[c]	—[c]	(22)
6	cyclohexene (1.0)	$CDCl_3$, room temp., 4 h	26	37	5
7	cyclopentene (1.0)	$CDCl_3$, room temp., 2 h	33	51	25
8	cyclopentene (7.0)	$CDCl_3$, room temp., 2 h	22	48	38 (25)
9	norbornene (7.0)	CoTPP[d], $CDCl_3$, −40 °C, 20 min	>95	—	68

[a] Yields were determined from the ^1H NMR spectra of the crude products (1,4-dibromobenzene as internal standard); the values in brackets are yields of isolated material after Kugelrohr destillation. [b] Based on thiophene endoperoxide **2**. [c] Not determined. [d] Tetraphenylporphine cobalt(II) complex.

mechanistic details of the sulfur atom transfer are still obscure, *i.e.* whether carbonyl-*O*-sulfide or oxathiirane serve as intermediates,[6,7] the effective CoTPP catalysis suggests that peroxide bond homolysis is involved as the initiating event.

The present work establishes an interesting reaction mode for thiophene endoperoxides, namely the direct sulfur atom transfer to cycloalkenes. In the case of norbornene, the most efficient sulfur atom acceptor, it should be stressed that its episulfide cannot be readily made by the usual methods,[15] especially from its epoxide.[16] The limitation of the present method is the competition between the menacing extrusion of elemental sulfur[6,7] and the desired sulfur atom transfer[17] to the alkene. Further studies will be necessary to learn how to suppress elemental sulfur extrusion and optimize thiirane formation by searching for appropriate thiophene endoperoxide derivatives.

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Footnote

† All new substances except the labile endoperoxide **2** gave correct elemental analysis. *Selected data* for **1**: mp 51–52 °C, colourless plates; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.07 (6 H, s), 2.26 (3 H, s), 2.30 (3 H, s), 2.35 (2 H, s) and 2.78 (2 H, s); ^{13}C NMR (63 MHz, $CDCl_3$) δ 12.4 (q), 13.7 (q), 28.1 (2 × q), 35.6 (s), 39.0 (t), 52.7 (t), 129.6 (s), 132.1 (s), 133.5 (s), 152.0 (s) and 194.4 (s). For **2**: ^{1}H NMR (200 MHz, $CDCl_3$, −20 °C) δ 1.08 (6 H, s), 2.00 (3 H, s), 2.28 (3 H, s), 2.35 (2 H, s), 2.32 (1 H, d, *J* 15.4 Hz), 2.50 (1 H, d, *J* 15.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$, −20 °C) δ 11.8 (q), 13.0 (q), 28.3 (q), 28.9 (q), 32.6 (s), 37.0 (t), 53.5 (t), 105.7 (s), 106.5 (s), 136.4 (s), 157.6 (s) and 194.5 (s). For **4**: mp 143–144 °C, colourless powder; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.11 (6 H, s), 1.62 (3 H, s), 2.27 (2 H, s), 2.41 (2 H, s), 3.68 (1 H, s, OH), 5.09 (1 H, s) and 5.80 (1 H, s); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 26.3 (q), 28.5 (q), 28.7 (q), 34.0 (s), 38.1 (t), 51.1 (t), 105.2 (t), 110.9 (s), 112.5 (s), 144.5 (s), 179.3 (s) and 194.9 (s).

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