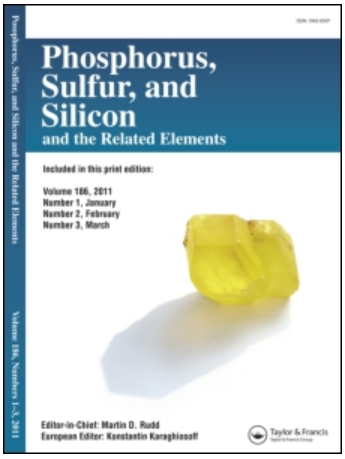


## Phosphorus, Sulfur, and Silicon and the Related Elements

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# Preparation of New *tert*-Butyl Substituted Coumarins, Thiocoumarins and Dithiocoumarins

Jürgen Voss[a]; Ronald Edler[a]; Gunadi Adiwidjaja[b]
[a] Department of Chemistry, Organic Chemistry, University of Hamburg, Hamburg, Germany [b] Department of Geosciences, University of Hamburg, Hamburg, Germany

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# Preparation of New *tert*-Butyl Substituted Coumarins, Thiocoumarins and Dithiocoumarins

**Jürgen Voss**
**Ronald Edler**
University of Hamburg, Department of Chemistry, Organic Chemistry, Hamburg, Germany

**Gunadi Adiwidjaja**
University of Hamburg, Department of Geosciences, Hamburg, Germany



*6*-tert-*Butyl-4-methyl- and 6,8-di*-tert-*butyl-4-methylcoumarin were prepared from tert-butylphenols and diketene via the corresponding aryl acetoacetates. 6*-tert-*Butyl-4-methyl-thiocoumarin (**6**) was obtained from 6*-tert-*butylthiophenol. Thionation with* LAWESSON*'s or* DAVY*'s reagent led to the related thion- and dithiocoumarins. The structures were proved by NMR spectroscopy and an X-ray structure analysis of 6.*

**Keywords** Coumarins; dithiocoumarins; keto-enol tautomerism; thiocoumarins; X-ray structure

## INTRODUCTION

Within the context of our studies on the EPR spectra of ester,[1] thioester,[2] and, in particular, of dithiopyrone[3] radical anions, we became interested in the preparation and investigation of the corresponding benzoanellated compounds, i.e., the coumarins (2*H*-1-benzopyran-2-ones) and thiocoumarins (2*H*-1-benzothiopyran-2-ones). In order to simplify the expected complexity of the EPR spectra and in consideration of an unequivocal experimental assignment of the proton hyperfine structure coupling constants,[3] we needed *tert*-butyl derivatives. A preliminary

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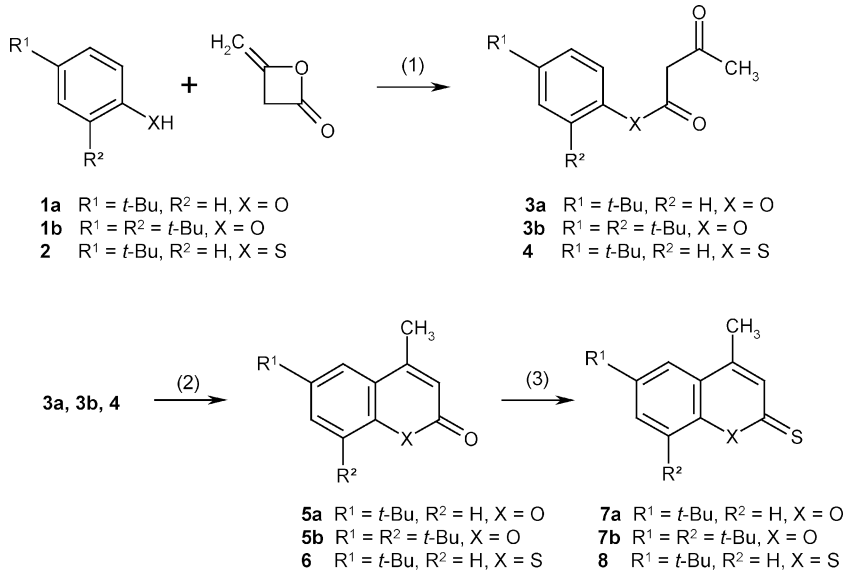
Address correspondence to Jürgen Voss, University of Hamburg, Department of Chemistry, Organic Chemistry, Martin-Luther-King-Platz 6, Hamburg D-20146, Germany. E-mail: juergen.voss@chemie.uni-hamburg.de

study[4] had shown that coumarin radical anions are only persistent enough as to give resolved EPR spectra if they are substituted with a methyl group in the 4-position. We describe here the synthesis of 4-methyl-coumarins with *tert*-butyl substituents in the benzene ring and of the corresponding thio derivatives. Our EPR results have been published elsewhere.[5]

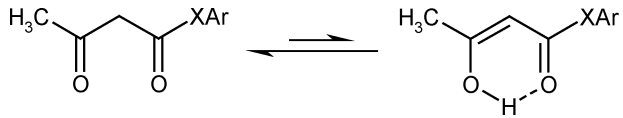
## RESULTS AND DISCUSSION

We obtained 6-*tert*-butyl-4-methylcoumarin (**5a**) from commercially available 4-*tert*-butylphenol (**1a**) and 4-methylene-2-oxetanone (diketene) *via* the $\beta$-keto-ester **3a** with an overall yield of 44% using the general method of LACEY[6] (Scheme 1). According to its $^1$H NMR spectrum, **3a** consisted of a 2:1 mixture of the keto and enol tautomers (Scheme 2).






**SCHEME 1** (1): $NEt_3$, $CHCl_3$; (2): $H_2SO_4$, 75% or $AlCl_3$, $CS_2$; (3): **LR** or **DR**, toluene.




**SCHEME 2** Keto-Enol-Tautomerism of **3a**, **3b**, **4**, **11a**, and **11b** (X = O, S).

The $^{13}C$ NMR signals were assigned by comparison of the experimentally observed shifts with the theoretical ones (Table I). The latter were calculated from data for 4-methylcoumarin, thiolcoumarin, thioncoumarin and dithiocoumarin,[7] and the increments of a *tert*-butyl substituent.[8]

Thionation of **5a** with 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 1,3-disulfide (LAWESSON's reagent, **LR**)[9,10] gave a 84% yield of the thioncoumarin **7a** (Scheme 1).

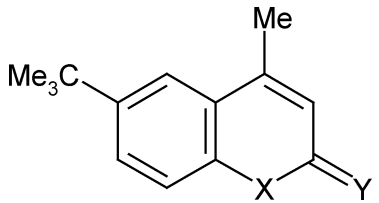
The base-catalyzed reaction of 2,4-di-*tert*-butylphenol (**1b**) with diketene led to the $\beta$-ketoester **3b**, again as a 2:1 mixture of the keto-enol tautomers (Scheme 2). Obviously due to steric hindrance, the yield was only 37%. Cyclodehydration with sulfuric acid gave a very small amount (5% yield) of the desired 6,8-di-*tert*-butyl-4-methylcoumarin (**5b**). In this case, dealkylation was observed. Under the strongly acidic conditions, **3a** (2.3%) was formed as byproduct. Furthermore, ester cleavage with formation of **1b** took place.

The thionation of **5b** to **7b** was achieved with 45% yield by using 2,4-bis(methylthio)-1,3,2,4-dithiadiphosphetane 2,4-disulfide, the so-called DAVY's reagent (**DR**),[11] which is more reactive than **LR**. It produces even dithioesters on reaction with carboxylic acids. No dithiocoumarin was formed from **5b**, however.

An analogous synthesis[12,13] of the thiocoumarine **6** required 4-*tert*-butylthiophenol (**2**) as starting material. The preparation of arenethiols by reduction of arenesulfonyl chlorides with lithium alanate is described in the literature.[14] In our hands, however, the use of the much cheaper zinc dust in sulfuric acid as the reductive reagent[15,16] turned out to give a higher yield of **2**. The reaction of **2** with diketene led to the $\beta$-keto-thioester **4**. As one would expect according to the literature,[12,13] **4**, as well as the acetothioacetates **11a** and **11b**, also exist as mixtures (ca. 2:1) of the keto and the enol tautomers (Scheme 2). Cyclization under dehydration of **4** with aluminum trichloride eventually led to the thiocoumarin **6** (Scheme 1). The very low yield of only 4.5% is obviously due to a rapid decomposition of **6** under the rather harsh reaction conditions.

According to the NMR spectra of **6**, no dealkylation or migration of the *tert*-butyl substituent had occurred, which could have happened in the presence of the strong LEWIS-acid aluminum trichloride.[17] The correct structure of **6** and, in particular, the 6-position of the *tert*-butyl substituent, was corroborated by an X-ray structure analysis (Figure 1). The bicyclic thiocoumarin skeleton of the molecule does not deviate significantly from planarity. The relevant bond lengths and angles (see the legend of Figure 1) exhibit the expected values and are

**TABLE I $^{13}C$ Chemical Shifts $\delta$ [ppm][a] in the Coumarin 5a, the Thiocoumarins 6 and 7a, and the Dithiocoumarin 8**




| | X | Y | C-2 | C-3 | C-4 | C-4a | C-5 | C-6 | C-7 | C-8 | C-8a | Me | C-6′ | $Me_3$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **5a** | O | O | 160.8 | 114.9 | 152.6 | 119.3 | 120.6 | 147.2 | 129.3 | 116.5 | 151.5 | 18.6 | 34.6 | *31.4* |
| | | | 160.5 | 115.1 | 152.3 | 119.6 | 121.2 | 146.3 | 128.3 | 116.5 | 150.4 | | | |
| **6** | S | O | 184.5 | [b] | 151.2 | 126.9 | 123.7 | 149.7 | 127.6 | 125.9 | 133.9 | 22.1 | 34.8 | *31.2* |
| | | | 185.5 | 125.2 | 152.4 | 127.0 | 123.1 | 146.1 | 128.1 | 126.1 | 134.2 | | | |
| **7a** | O | S | 197.1 | 129.8 | 144.5 | 120.8 | 120.4 | 148.5 | 128.8 | 116.4 | 154.3 | 18.0 | 34.8 | *31.3* |
| | | | 198.1 | 128.4 | 143.4 | 121.3 | 120.9 | 147.4 | 128.7 | 116.9 | 153.2 | | | |
| **8** | S | S | 206.9 | 137.1 | 142.6 | 127.8 | 123.4 | 151.1 | 128.5 | 123.5 | 137.5 | 21.7 | 35.0 | *31.2* |
| | | | 209.1 | 134.7 | 140.1 | 128.8 | 123.4 | 145.3 | 130.9 | 127.8 | 136.8 | | | |

[a]Calculated shifts (see text) in italics; [b]not detected, possibly due to overlap with some other signal.

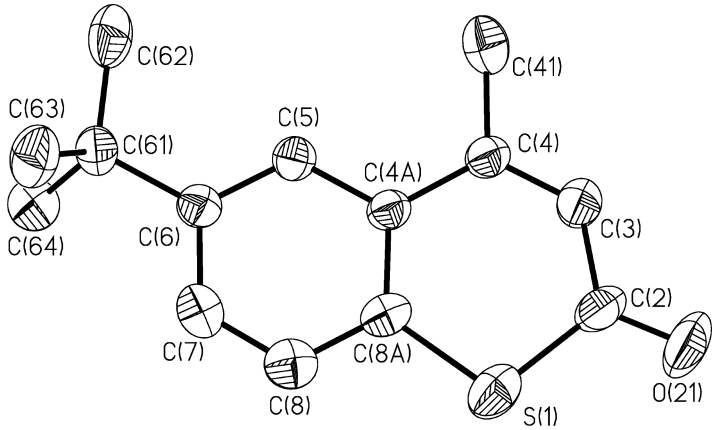



**FIGURE 1** ORTEP view of the thiocoumarin **6**. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms are not shown. Relevant functional bond lengths (pm): S–C-2: 175.9, S–C-8a: 173.9, C-2–O: 122.4, C-2–C-3: 144.6, C-3–C-4: 133.6, C-4–C-4a: 146.5, C-4a–C-8a: 140.4; and bond angles (°): C-2–S–C-8a: 105.0, S–C-2–O: 117.5, S–C-2–C-3: 118.1, O–C-2–C-3: 124.4, C-2–C-3–C-4: 128.5.

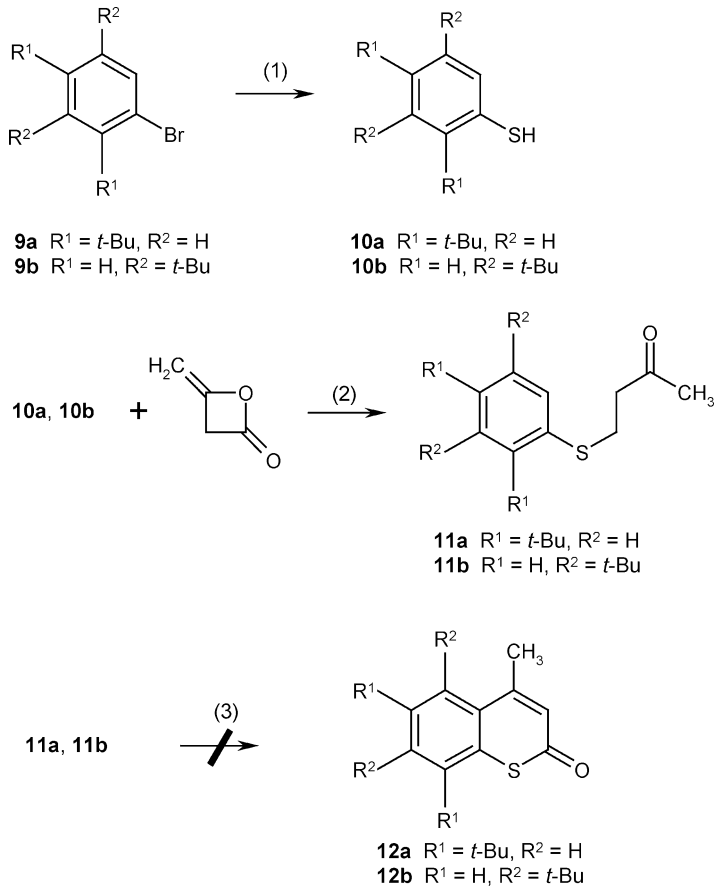


in reasonable agreement with values found for the related 6-methyl-4-morpholinomethyl-thiocoumarin.[18]

The thiocoumarin **6** was readily transformed into the corresponding dithiocoumarin **8** with 62% yield by use of **LR**.

The di-*tert*-butylthiophenols **10a**[19] and **10b**[19] can be obtained from 1-bromo-2,4-di-*tert*-butylbenzene (**9a**)[20] and 1-bromo-3,5-di-*tert*-butylbenzene (**9b**),[21] respectively, by GRIGNARD reaction with elemental sulfur and reduction of the intermediate disulfide with lithium alanate. Both thiophenols reacted with diketene to form the corresponding *S*-aryl acetothioacetates **11a** and **11b** (Scheme 3). An intramolecular cyclization of **11a** and **11b** with aluminum trichloride under formation of the thiocoumarins **12a** or **12b** could, however, not be achieved (Scheme 3). Instead, a *tert*-butyl substituent was split off from **11a** to form **4**, and ester cleavage led to **2**. The thioester **11b** was completely unreactive because the cyclization is sterically hindered due to the *tert*-butyl substituents in the two ortho-positions of **11b**. The thioester **11b** was recovered unchanged from the reaction mixture.

When we tried to prepare 3,6-di-*tert*-butylcoumarin (**14a**) from 4-*tert*-butylphenol (**1a**) and the known ethyl 2-*tert*-butylacetoacetate (**13**)[22,23] only **5a** and **5b** instead of **14a** were formed as products *via* cleavage (**5a**) or rearrangement (**5b**) of a *tert*-butyl group (Scheme 4). An attempt

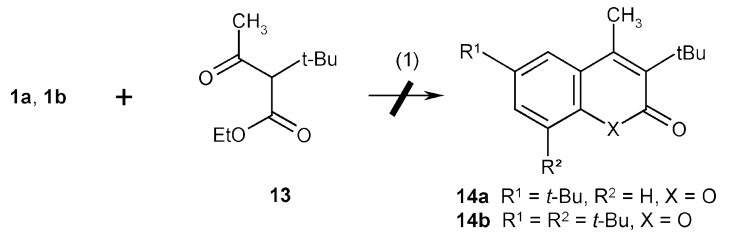



**SCHEME 3** (1): 1. Mg, THF, 2. $S_8$, 3. $LiAlH_4$; (2): $NEt_3$,$CH_2Cl_2$; (3): $AlCl_3$, $CS_2$.

to prepare 3,6,8-tri-*tert*-butylcoumarin (**14b**) from **1b** and **13** was also unsuccessful. Again, only a low yield of **5b** was formed in this case.

## EXPERIMENTAL

Melting points (m.p., uncorrected) were determined with a Leitz-Heiztischmikroskop. Boiling points (b.p.) were determined during distillation. Thin layer chromatography (TLC) was performed on Al foils coated with $SiO_2$ $F_{254}$ (Merck, Darmstadt). The spots were detected by the extinction of the fluorescence or by spraying with the iodine/sodium azide reagent.[24] Column chromatography (CC) was performed on Kieselgel 60, (Merck, Darmstadt), 0.063–0.200 mm




**SCHEME 4** (1): $H_2SO_4$ or $AlCl_3$, $CS_2$.

(70–230 mesh). Eluents [$CH_2Cl_2$, petroleum ether (PE)] were distilled prior to use. Solvents were purified and dried by standard laboratory procedures.[25] Removal of solvents was performed in a vacuum rotatory evaporator.

IR spectra were measured as KBr pellets or films on Perkin-Elmer spectrometers 297 and 399.

NMR spectra were measured in $CDCl_3$ on Varian T60 (60 MHz for $^1H$) or Bruker WM 400 (400 MHz for $^1H$, 100.62 MHz for $^{13}C$) spectrometers. The $^{13}C$ NMR data are compiled in Table I. Chemical shifts $\delta$ are related to $SiMe_4$ ($\delta = 0.00$ ppm) as internal standard. Coupling constants $J$ are given in Hz.

Mass spectra were measured on a Varian MAT CH 7 spectrometer at 70 eV.



## X-Ray Structure Analysis

The crystal data of **6** and a summary of the experimental details are given in Table II. Data collection was performed with a CAD 4 SDP (Enraf Nonius) diffractometer with graphite-monochromated Cu-$K_\alpha$, (Ni-filter, 1.54184 Å) in the $\theta/2\theta$ scan mode at 298 K. The structure was solved by the direct method MULTAN.[26] All non-hydrogen atoms were localized. After refinement of these parameters the hydrogen atoms were localized by differential FOURIER-synthesis.[27] The final refinement was performed by least squares methods. An experimental correction for absorption[28] was performed in addition to the usual LORENTZ-correction for polarization. Crystallographic data of **6** have been deposited with the Cambridge Crystallographic Data Centre as a supplementary publication No. CCDC-612426. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 IEZ, UK [Fax: (international) +44-1223/336-033; E-mail: deposit@ccdc.cam.uk].

**TABLE II Crystal Data and Structure Refinement for 6**

| Compound | |
|---|---|
| Empirical formula | $C_{14}H_{16}OS$ |
| Formula weight | 232.35 |
| Crystal system | Tetragonal |
| Space group | $P4_12_12$ |
| $a = b$ [pm] | 916.6 (1) |
| $c$ [pm] | 2937.4 (2) |
| $V$ [pm$^3$] | 2468 $10^6$ |
| $Z$ | 8 |
| $\rho_{calcd.}$ [g cm$^{-3}$] | 1.32 |
| $\mu$ [cm$^{-1}$] | 21.05 |
| $F(000)$ | 992 |
| $\theta$-limits [°] | 2/60 |
| $h/k/l$-Limits | 0, 7/ 0, 8/0, 32 |
| Reflections collected ($I > 3\sigma_I$) | 1777 |
| Number of parameters | 210 |
| $R$-Index | 0.038 |
| $R_w$-Index ($w = \sigma_I^{-2}$) | 0.039 |



### 4-tert-Butylphenyl 3-Oxobutanoate (3a)

4-*tert*-Butylphenol (**1a**, 100 g, 0.67 mol) was dissolved in $CHCl_3$ (150 mL). $NEt_3$ (5 drops) was added and the solution was heated to 55°C. Freshly distilled diketene was dropped in within 1 h and the reaction mixture was heated to 55°C for another 1.5 h. The solvent was removed and the residue was recrystallized from PE to yield **3a** (143 g, 91%) as colorless crystals, m.p. 40.5–41.5°C. IR: $\nu$ 3060, 2970 (s), 2870, 1760 (s, C=O), 1715 (s, C=O), 1660 (C=C), 1620 (C=C), 1600, 1500, 1400, 1360, 1305, 1260, 1100, 1015, 920, 840, 550 cm$^{-1}$. $^1$H NMR (60 MHz); ketone: $\delta$ 1.22 [s, 9H, $C(CH_3)_3$], 1.90 (s, 3H, $CH_3$), 3.48 (s, 2H, $CH_2$), 7.03 (m, 4H, $H_{ar}$); enol: $\delta$ 1.22 [s, 9H, $C(CH_3)_3$], 2.17 (s, 3H, $CH_3$), 5.10 (s, 1H, 2-H), 7.03 (bs, 4H, $H_{ar}$), 9.60 (bs, 1H, OH). Anal. calcd. for $C_{14}H_{18}O_3$ (234.30): C, 71.77; H, 7.74; Found: C, 71.70; H, 7.59.

### 6-tert-Butyl-4-methylcoumarin (5a)

The ester **3a** (100 g, 0.43 mol) was dissolved in 75% $H_2SO_4$ (300 mL) and stirred at 20°C for 24 h. The reaction mixture was poured into $H_2O$ (1 L) and repeatedly extracted with diethyl ether. The extract was washed with dilute aqueous KOH and $H_2O$ and dried over $Na_2SO_4$. The solvent was removed and the residue was washed with icy-cold PE and then recrystallized from PE to give **5a** (45 g, 48%) as long, colorless needles, m. p. 120.5–121°C. IR: $\nu$ 3050, 2960, 2870, 1720 (s, C=O), 1620 (C=C), 1600 (C=C), 1570, 1490, 1380, 1270, 1220, 1180, 1065, 1000, 920

(s), 895, 880 (s), 640 $cm^{-1}$. $^1H$ NMR (400 MHz): $\delta$ 1.34 [s, 9H, $C(CH_3)_3$], 2.44 (d, $^4J_{H,CH3} = 0.7$ Hz, 3H, $CH_3$), 6.22 (q, $^4J_{H,CH3} = 0.7$ Hz, 1H, 3-H), 7.22 (d, $^3J_{H7,H8} = 6.7$ Hz, 1H, 8-H), 7.57 (m, 2H, 7-H, 8-H). MS (70 eV) $m/z$ (%) = 216 (18) [$M^+$], 202 (14), 201 (100) [$M^+ - CH_3$], 173 (22), 161 (12), 145 (11), 28 (59). Anal. calcd. for $C_{14}H_{16}O_2$ (216.28): C, 77.75; H, 7.46; Found: C, 77.82; H, 7.40.

### *6-tert-Butyl-4-methylthionocoumarin (7a)*

The coumarin **5a** (10.0 g, 46.0 mmol) and **LR** (18.6 g, 46.0 mmol) were refluxed in toluene (200 mL) for 2.5 h. The toluene was removed and the residue was extracted with hot EtOH/$H_2O$ (1:1). After drying and removal of the solvent, a residue (9.5 g, m. p. 125–126°C) containing 2% of $S_8$ according to its elemental analysis was obtained. Column chromatography (PE) and subsequent recrystallization (EtOH/$H_2O$, 1:1) gave pure **7a** (9.0 g, 84%) as bright yellow crystals, m. p. 127–128°C. IR: $\nu$ 3060, 3040, 2960 (s), 2900, 2860, 1605 (s, C=C), 1560 (s), 1280, 1255 (s), 1150 (s), 1120, 1100 (s), 1065, 980, 820 (s) $cm^{-1}$. $^1H$ NMR (400 MHz): $\delta$ 1.34 [s, 9H, $C(CH_3)_3$], 2.37 (d, $^4J_{H,CH3} = 0.7$ Hz, 3H, $CH_3$), 7.11 (q, $^4J_{H,CH3} = 0.7$ Hz, 1H, 3-H), 7.35 (d, $^3J_{H7,H8} = 6.7$ Hz, 1H, 8-H), 7.59 (d, $^4J_{H5,H7} = 1.3$ Hz, 1H, 5-H), 7.63 (dd, $^3J_{H7,H8} = 6.7$ Hz, $^4J_{H5,H7} = 1.3$ Hz, 1H, 7-H). Anal. calcd. for $C_{14}H_{16}OS$ (232.35): C, 72.37; H, 6.94, S, 13.80; Found: C, 72.56; H, 6.98; S, 13.65.

### *4-tert-Butylthiophenol (2)[15,16]*

Ice (720 g) and conc. $H_2SO_4$ (1.30 L) were mixed in a three-necked round-bottomed flask equipped with a high-performance reflux-cooler and a mechanical stirrer. Under cooling with an ice/NaCl mixture and vigorous stirring, powdered 4-*tert*-butylbenzenesulfonyl chloride[29] (79.1 g, 0.34 mol) and subsequently, as quickly as possible, Zn dust (120 g, 1.83 mol) were added. After stirring at 0°C for 1 h, subsequent refluxing for 3.5 h, and cooling, the reaction mixture was repeatedly extracted with diethyl ether. The extracts were dried over $K_2CO_3$, and the solvent was removed. Distillation of the residue gave **2** (48.1 g, 85%) as a colorless liquid, b.p. 55°C/0.3 Torr. IR: $\nu$ 3080, 3020, 2960 (s), 2860, 2560 (SH), 1500 (s), 1480, 1460, 1360, 1265, 1200, 1120 (s), 1010, 920, 820 (s), 740, 720 $cm^{-1}$. $^1H$ NMR (60 MHz): $\delta$ 1.20 [s, 9H, $C(CH_3)_3$], 3.17 (s, 1H, SH), 7.02 (m, 4H, $H_{ar}$).

### *S-4-tert-Butylphenyl 3-Oxobutanethioate (4)*

Thiophenol **2** (9.0 g, 54 mmol) was dissolved in dry $CH_2Cl_2$ (200 mL). Freshly distilled diketene (4.56 g, 54 mmol) and $NEt_3$ (3 drops) were added, and the solution was stirred at 20°C for 12 h. A quantitative

yield of **4** was obtained on removal of the solvent. Purification by CC ($CH_2Cl_2$) gave **4** (12.0 g, 89%) as a colorless liquid. IR: $\nu$ 2960 (s), 2900, 2870, 1720 (s, C=O), 1695 (s, C=O), 1620 (s, C=C), 1490, 1400, 1360, 1265, 1190, 1155, 1080, 1010, 970, 855 $cm^{-1}$. $^1H$ NMR (60 MHz); ketone: $\delta$ 1.28 [s, 9H, $C(CH_3)_3$], 2.13 (s, 3H, $CH_3$), 3.63 (s, 2H, $CH_2$), 7.30 (m, 4H, $H_{ar}$); enol: $\delta$ 1.28 [s, 9H, $C(CH_3)_3$], 1.83 (s, 3H, $CH_3$), 5.42 (s, 1H, 2-H), 7.30 (m, 4H, $H_{ar}$), 11.4 (bs, 1H, OH).

### *6-tert-Butyl-4-methyl-thiocoumarin (6)*

The thioester **4** (5.0 g, 20 mmol) was added to a suspension of $AlCl_3$ (20 g) in dry $CS_2$ (20 mL). The mixture was refluxed for 7 h. After cooling, it was poured into icy-cold $H_2O$ and repeatedly extracted with diethyl ether. The ether was removed, and the residue was chromatographed ($CH_2Cl_2$). Recrystallization (2×) from $CH_2Cl_2$ gave pure **6** (0.21 g, 4.5%) as colorless crystals, m.p. 94–95°C. IR: $\nu$ 3050, 2960, 2900, 2860, 1620 (s, C=O), 1580, 1530, 1470, 1370, 1260, 1220, 900, 820 $cm^{-1}$. $^1H$ NMR (400 MHz): $\delta$ 1.37 [s, 9H, $C(CH_3)_3$], 2.52 (d, $^4J_{CH3,H} = 0.7$ Hz, 3H, $CH_3$), 6.43 (q, $^4J_{CH3,H} = 0.7$ Hz, 1H, 3-H), 7.29 (d, $^3J_{H7,H8} = 6.7$ Hz, 1H, 8-H), 7.46 (dd, $^3J_{H7,H8} = 6.7$ Hz, $^4J_{H5,H7} = 1.7$ Hz, 1H, 7-H), 7.75 (d, $^4J_{H5,H7} = 1.7$ Hz, 1H, 5-H). MS (70 eV) $m/z$ (%) = 234 (4), 232 (59) [$M^+$], 217 (53) [$M^+ - CH_3$], 204 (30) [$M^+ - CO$], 189 (100) [$M^+ - CO - CH_3$], 161 (25), 149 (25), 147 (13), 115 (11), 81 (12), 80 (11). Anal. calcd. for $C_{14}H_{16}OS$ (232.35): C, 72.37; H, 6.94; S, 13.80; Found: C, 72.33; H, 7.03; S, 13.97.

### *6-tert-Butyl-4-methyl-dithiocoumarin (8)*

The thiocoumarin **6** (0.60 mg, 2.60 mmol) and **LR** (1.12 g, 2.70 mmol) were refluxed in toluene under stirring for 2 h. The toluene was removed, and the residue was extracted with hot EtOH/$H_2O$ (1:1). Pure **8** (0.40 g, 62%) was obtained from the extract as orange crystals, m.p. 118–119°C. IR: $\nu$ 2965 (s), 2875, 1580 (s), 1530 (s), 1450, 1380, 1240, 1220 (s), 1020 (s), 995 (s), 890, 825 $cm^{-1}$. $^1H$ NMR (400 MHz): $\delta$ 1.34 [s, 9H, $C(CH_3)_3$], 2.45 (s, 3H, $CH_3$), 7.30 (d, $^3J_{H7,H8} = 6.7$ Hz, 1H, 8-H), 7.34 (s, 1H, 3-H), 7.53 (dd, $^3J_{H7,H8} = 6.7$ Hz, $^4J_{H5,H7} = 0.7$ Hz, 1H, 7-H), 7.81 (d, $^4J_{H5,H7} = 0.7$ Hz, 1H, 5-H). MS $m/z$ (%) = 250 (9), 248 (93) [$M^+$], 235 (11), 233 (100) [$M^+ - CH_3$], 204 (20), 189 (51), 161 (16), 147 (11), 115 (11). Anal. calcd. for $C_{14}H_{16}S_2$ (248.41): C, 67.69; H, 6.49; S, 25.82; Found: C, 67.59; H, 6.57; S, 25.81.

### *2,4-Di-tert-butylphenyl 3-Oxobutanoate (3b)*

Diketene (40.7 g, 0.48 mol) was dropped into a boiling solution of 2,4-di-*tert*-butylphenol (**1b**, 100 g, 0.48 mol) and $NEt_3$ (5 drops) in $CHCl_3$ (150 mL) within 1 h. The reaction mixture was refluxed for 7 h. Most of the solvent was removed and the residue was triturated with PE. The

mixture crystallized on cooling and the solid was filtered. Recrystallization from PE gave **3b** (51 g, 37%), m.p. 55–56°C. IR: $\nu$ 3060, 2960, 2870, 1760 (C=O), 1660 (C=C), 1620, 1600, 1500, 1460, 1400, 1360, 1300, 1260, 1100, 1015, 920, 840, 745 $cm^{-1}$. $^1H$ NMR (60 MHz); ketone: $\delta$ 1.32 [s, 9H, $C(CH_3)_3$], 1.35 [s, 9H, $C(CH_3)_3$], 2.30 (s, 3H, $CH_3$), 3.63 (s, 2H, $CH_2$), 6.83–7.33 (m, 3H, $H_{ar}$); enol: $\delta$ 1.32 [s, 9H, $C(CH_3)_3$], 1.35 [s, 9H, $C(CH_3)_3$], 1.98 (s, 3H, $CH_3$), 5.18 (s, 1H, 2-H), 7.10 (m, 3H, $H_{ar}$), 11.63 (bs, 1H, OH). Anal. calcd. for $C_{18}H_{26}O_3$ (290.40): C, 74.45; H, 9.02; Found: C, 75.79; H, 9.17.

### *6,8-Di-tert-butyl-4-methylcoumarin (5b)*

Ester **3b** (29 g, 0.1 mol) was slowly added to 75% $H_2SO_4$ (120 mL). The reaction mixture was stirred at 20°C for 24 h, then poured into $H_2O$ (360 mL) and repeatedly extracted with diethyl ether. The extract was washed with aqueous KOH and $H_2O$ and dried over $Na_2SO_4$. The solvent was removed and the residue was chromatographed ($CH_2Cl_2$). The fractions containing **5b** were collected, concentrated and triturated with a small amount of PE. On cooling to –30°C, **5a** (0.50 g, 2.3%) crystallized from the solution and was removed by filtration. The solvent was removed from the filtrate and the residue was crystallized from a small amount of PE to yield pure **5b** (1.36 g, 5%), m.p. 90–92.5°C. IR: $\nu$ 3080, 2960 (s), 1710 (s, C=O), 1620 (C=C), 1575 (s), 1480, 1460, 1425, 1380, 1360, 1280, 1235, 1065, 1100 (s), 940 (s), 905, 880 (s), 770, 645 $cm^{-1}$. $^1H$ NMR (60 MHz): $\delta$ 1.37 [s, 9H, $C(CH_3)_3$], 1.50 [s, 9H, $C(CH_3)_3$], 2.38 (d, $^4J_{H,CH3} = 0.7$ Hz, 3H, $CH_3$), 6.08 (q, $^4J_{H,CH3} = 0.7$ Hz, 1H, 3-H), 7.37–7.53 (AB-system, 2H, 5-H, 7-H). Anal. calcd. for $C_{18}H_{24}O_2$ (272.39): C, 79.37; H 8.88; Found: C, 79.90; H, 8.94.

### *6,8-Di-tert-butyl-4-methyl-thionocoumarin (7b)*

Coumarin **5b** (0.38 g, 1.30 mmol) and **DR**[11] (0.74 g, 2.60 mmol) were refluxed in toluene (5 mL) under stirring for 50 min. The solvent was removed and the residue was purified by preparative scale TLC (2 mm $SiO_2$ layer, $CH_2Cl_2$) to yield **7b** (0.18 g, 45%) as bright yellow crystals, m.p. 127–128°C. IR: $\nu$ 2980 (s), 1620 (s, C=C), 1580 (s), 1470, 1410, 1395, 1380, 1320, 1280, 1160, 1100, 890, 780 $cm^{-1}$. $^1H$ NMR (60 MHz): $\delta$ 1.35 [s, 9H, $C(CH_3)_3$], 1.51 [s, 9H, $C(CH_3)_3$], 2.38 (s, 3H, $CH_3$), 7.01 (s, 1H, 3-H), 7.40–7.65 (m, 2H, 5-H, 7-H).

### *S-2,4-Di-tert-butylphenyl 3-Oxobutanethioate (11a)*

2,4-Di-*tert*-butylthiophenol (**10a**,[19,20] 4.0 g, 18 mmol) was dissolved in $CH_2Cl_2$ (60 mL). Diketene (1.51 g, 18 mmol) and $NEt_3$ (4 drops) were added and the reaction mixture was stirred at 20°C for 12 h. The solvent was removed. The residue was chromatographed ($CH_2Cl_2$) to yield **11a** (4.4 g, 80%). IR: $\nu$ 3070, 2960, 1725 (C=O), 1695 (C=C), 1480, 1400,

1360, 1280, 1240, 1195, 1080, 965, 870, 705 $cm^{-1}$. $^1H$ NMR (60 MHz); ketone: $\delta$ 1.32 [s, 9H, $C(CH_3)_3$], 1.43 [s, 9H, $C(CH_3)_3$], 1.98 (s, 3H, $CH_3$), 3.45 (s, 2H, $CH_2$), 6.97–7.37 (m, 3H, $H_{ar}$); enol: $\delta$ 1.32 [s, 9H, $C(CH_3)_3$], 1.43 [s, 9H, $C(CH_3)_3$], 1.70 (s, 3H, $CH_3$), 5.25 (s, 1H, 3-H), 7.2 (m, 3H, $H_{ar}$), 11.13 (bs, 1H, OH). Anal. calcd. for $C_{18}H_{26}O_2S$ (306.47): C, 70.55; H, 8.55; S, 10.46; Found: C, 71.11; H, 8.66; S, 10.45.

### *S-3,5-Di-tert-butylphenyl 3-Oxobutanethioate (11b)*

Thioester **11b** (85%) , colorless crystals, m.p. 44–45 °C, was prepared from 3,5-di-*tert*-butylthiophenol (**10b**)[19,21] as described for **11a**. IR: $\nu$ 3070, 2970, 1725 (C=O), 1695 (C=C), 1620, 1480, 1400, 1380, 1240, 1190, 1080, 965, 870, 705 $cm^{-1}$. $^1H$ NMR (60 MHz); ketone: $\delta$ 1.30 [s, 18H, $C(CH_3)_3$], 2.08 (s, 3H, $CH_3$), 3.55 (s, 2H, $CH_2$), 7.12–7.40 (m, 3H, $H_{ar}$); enol: $\delta$ 1.30 [s, 18H, $C(CH_3)_3$], 1.83 (s, 3H, $CH_3$), 5.37 (s, 1H, 3-H), 7.12–7.40 (m, 3H, $H_{ar}$), 12.07 (bs, 1H, OH). Anal. calcd. for $C_{18}H_{26}O_2S$ (306.47): C, 70.55; H, 8.55; S, 10.46; Found: C, 71.15; H, 8.65; S, 10.23.



### *Ethyl 2-tert-Butyl-3-oxobutanoate (13)*[22,23]

Ethyl acetoacetate (63.3 mL, 65 g, 0.50 mol) and *tert*-butyl alcohol (113 mL, 88.8 g, 1.20 mol) were mixed in a 500-mL three-necked flask under exclusion of moisture. Under cooling with ice, dry, purified (absorption flask with $B_2O_3/H_2SO_4$) gaseous $BF_3$ was introduced for 5 h (until saturation) through a glass tube, which reached about 1 cm above the level of the liquid. The ice-bath was removed and the reaction mixture was left at 20°C for 14 h. A solution of $NaOAc{\cdot}3H_2O$ (100 g) in $H_2O$ (300 mL) was added. The product was extracted with diethyl ether (3 $\times$ 150 mL), the extract was dried over $Na_2SO_4$, and the solvent was removed. Vacuum distillation by use of a spinning band column gave 19 g (20%) of **13**, b.p. 98–100°C/20 Torr. IR: $\nu$ 2960, 2910, 2870, 1740 (C=O), 1720 (C=O), 1470, 1390, 1220, 1200, 1140, 1040, 600 $cm^{-1}$. $^1H$ NMR (60 MHz): $\delta$ 1.05 [s, 9H, $C(CH_3)_3$], 1.20 (t, $^3J = 7.0$ Hz, 3H, $CH_2CH_3$), 2.15 (s, 3H, $COCH_3$), 3.22 (s, 1H, CH), 4.10 (q, $^3J = 7.0$ Hz, 2H, $CH_2$).

### *Reaction of 1a and 1b with 13 (Attempted Preparation of 14a or 14b)*

An intimate mixture of **1a** (32 g, 0.21 mol) and **13** (20 g, 0.107 mol) was slowly added with stirring to 75% $H_2SO_4$ (180 mL). The mixture was heated to 85°C for 1 h and then poured into $H_2O$ (1 L). The solution was repeatedly extracted with diethyl ether, the extract was washed with aqueous KOH and $H_2O$ and dried over $Na_2SO_4$. The solvent was removed and the residue was chromatographed ($CH_2Cl_2$). No **14a** was found. Instead, **5a** (0.8 g, 3.5%) and **5b** (0.1 g, 0.4%) were isolated, which were identical with the authentic compounds.

An analogous reaction of **1b** with **13** gave only **5b** as product.

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