Functionalization of Photochromic Dithienylmaleimides

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Supporting Information

Non-hydrolytic methyl ester deprotection of 12

Synthesis of compounds 11S, 12S, 13S and 21S

¹H- and ³C-NMR spectra of all prepared compounds
Non-hydrolytic methyl ester deprotection of 12

**Table S1.** Non-hydrolytic methyl ester deprotection of 12.

<table>
<thead>
<tr>
<th>Entry</th>
<th>LiI [eq]</th>
<th>Solvent</th>
<th>T [°C]</th>
<th>Isolated yield[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.0</td>
<td>EtOAc</td>
<td>r.t.</td>
<td>--</td>
</tr>
<tr>
<td>2</td>
<td>3.0</td>
<td>EtOAc</td>
<td>reflux</td>
<td>--</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>EtOAc</td>
<td>reflux</td>
<td>26%</td>
</tr>
<tr>
<td>4</td>
<td>3.0</td>
<td>acetone</td>
<td>reflux</td>
<td>--</td>
</tr>
<tr>
<td>5</td>
<td>30</td>
<td>acetone</td>
<td>reflux</td>
<td>35%</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>MeCN</td>
<td>reflux</td>
<td>--</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>DMSO</td>
<td>100 °C</td>
<td>--</td>
</tr>
</tbody>
</table>

[a] If conversion was too low the product 13b was not isolated.

**Synthesis of compounds 11S, 12S, 13S and 21S**

**Scheme S1.** Perkin condensation of 10 and 11S yielding dithienylmaleimide 12 and 12S.

**Scheme S2.** Hydrolytic ester cleavage yielding maleic anhydride 13S.

**Scheme S3.** Synthesis of ethyl ester 11S.
Ethyl 4-(2-methoxy-2-oxoethyl)-5-methylthiophene-2-carboxylate (11S): Thallium trinitrate (2.20 g, 4.94 mmol) and 70% HClO₄ (2 mL) were added to a suspension of 21S (875 mg, 4.12 mmol) in MeOH (10 mL) at room temperature. After stirring for 24 h the mixture was concentrated under reduced pressure and diluted with water (10 mL). The aqueous phase was extracted with chloroform (3 x 15 mL) and the combined organic layers were dried over MgSO₄. The solvent was evaporated and purification of the crude product by automated flash column chromatography (PE/EtOAc, 3% - 15% EtOAc) yielded compound 11S (816 mg, 82%) as yellowish oil. R_f: 0.23 (PE/EtOAc: 9/1); IR (neat) v_max: 3081, 2987, 2922, 1730, 1705, 1460, 1254, 1201, 1172, 1061; ¹H-NMR (400 MHz, CDCl₃): δ = 1.35 (t, J = 7.1 Hz, 3H, O−CH₂−C₃H₇), 2.42 (s, 3H, thiophene-C₃H₃), 3.54 (s, 2H, C−C₃H₂−CO), 3.70 (s, 3H, CO−O−C₃H₃), 4.31 (q, J = 7.1 Hz, 2H, O−C₃H₂−CH₃), 7.60 (s, 1H, thiophene-Η); ¹³C-NMR (75 MHz, CDCl₃): δ = 13.8 (+), 14.4 (+), 33.8 (−), 52.2 (+), 61.0 (−), 129.6 (q), 130.6 (q), 135.4 (+), 143.8 (q), 162.2 (q), 171.0 (q); HR-MS (ESI): calcd. for C₁₁H₁₄NaO₄S (M+Na)⁺ 265.0505; found 265.0502.

Methyl/Ethyl 4-(4-(5-(((allyloxy)carbonyl)amino)methyl)-2-methyl-thiophen-3-yl)-2,5-dioxo-2,5-dihydro-1Η-pyrrol-3-yl)-5-methylthiophene-2-carboxylate (12/12S): KOtBu (1 M in THF, 1.34 mL, 1.34 mmol) was added to a solution of 10 (316 mg, 1.12 mmol) in anhydrous THF (6 mL) at 0 °C under nitrogen atmosphere. After stirring for 90 min at 0 °C, diester 11S (326 mg, 1.34 mmol) was added and stirred for 15 h at room temperature. Then the reaction was heated to 60 °C for 1 h, quenched with 1 M HCl solution (4 mL) and diluted with EtOAc (10 mL). The organic phase was washed with water (3 x 5 mL), brine (5 mL) and dried over MgSO₄. The solvent was removed under reduced pressure and purification of the crude product by automated reversed phase flash column chromatography (H₂O/EtOH, 20% - 45% EtOH) yielded 12S (40 mg, 8%) as orange foam, 12 (74 mg, 14%) as yellow foam and a mixed fraction of both (65 mg). Analytical data of 12S: R_f: 0.25 (PE/EtOAc: 2/1); IR (neat) v_max: 3288, 3071, 2980, 1710, 1541, 1458, 1252, 995, 916, 760; UV/Vis (50 µM in MeOH): open isomer: Λ_max = 250 nm; closed isomer: Λ_max = 232 nm, 378 nm, 554 nm; ¹H-NMR (400 MHz, CDCl₃): δ = 1.36 (t, J = 7.1 Hz, 3H, O−CH₂−CH₃), 1.91 (s, 3H, thiophene-CH₃), 1.97 (s, 3H, thiophene-CH₃), 4.33 (q, J = 7.1 Hz, 2H, O−CH₂−CH₃), 4.45 (d, J = 5.9 Hz, 2H, C−CH₂−NH), 4.60 (d, J = 4.8 Hz, 2H, O−CH₂−CH), 5.14 – 5.26 (m, 2H, CH₂=CH−CH₂ and CH₂−NH−CO), 5.31 (dd, J = 17.2, 1.1 Hz, 1H, CH₂=CH−CH₂), 5.92 (ddt, J = 16.3, 10.8, 5.6 Hz, 1H, CH₂=CH−CH₂), 6.90 (s, 1H, thiophene-Η), 7.75 (s, 1H, thiophene-Η), 7.97 (bs, 1H, CO−NH−CO); ¹³C-NMR (101 MHz, CDCl₃): δ = 14.3 (+), 15.0 (+), 15.3 (+), 39.9 (−).
61.4 (−), 65.9 (−), 117.9 (−), 125.8 (q), 127.4 (q), 131.4 (q), 132.7 (+), 132.8 (q), 134.7 (+), 139.4 (q), 142.1 (q), 148.4 (q), 156.0 (q), 161.7 (q), 170.0 (q), 170.1 (q); HR-MS (ESI): calcd. for C_{22}H_{23}N_{2}O_{6}S_{2} (M+H)^{+} 475.0993; found 475.0992.

4-(4-(5-((((Allyloxy)carbonyl)amino)methyl)-2-methylthiophen-3-yl)-2,5-dioxo-2,5-dihydrofuran-3-yl)-5-methylthiophene-2-carboxylic acid (13S): A mixture of 12 and 12S (62 mg) in 10 mL of H_{2}O/MeOH/THF (2:5:3, v/v/v) was stirred for 20 h with NaOH (78 mg, 1.95 mmol) at room temperature. After addition of water (10 mL) the reaction mixture was washed with EtOAc (2 x 10 mL) and then acidified with conc. HCl to pH 1. The aqueous phase was extracted with EtOAc (3 x 10 mL) and the combined organic phases were dried over MgSO_{4}. Evaporation of the solvent and purification of the crude product by automated reversed phase flash column chromatography (H_{2}O/MeCN, 20% - 55% MeCN) yielded 13S (29 mg)^{A} as green solid. R_{f}: 0.02 (PE/EtOAc: 1/1); m.p.: 84 °C; IR (neat) \nu_{\max}: 3327, 3164, 3020, 2925, 1764, 1702, 1541, 1458, 1254, 931, 750; UV/Vis (50 µM in MeOH): open isomer: \lambda_{\max} = 246 nm; closed isomer: \lambda_{\max} = 384 nm, 568 nm; ^{1}H-NMR (400 MHz, DMSO-d_{6}): \delta = 1.90 (s, 3H, thiophene-CH_{3}), 1.96 (s, 3H, thiophene-CH_{3}), 4.28 (d, J = 6.1 Hz, 2H, thiophene-CH_{2}NH), 4.49 (d, J = 5.3 Hz, 2H, CH_{2}CH\text{=CHCH}_{2}O), 5.17 (dd, J = 10.5, 1.4 Hz, 1H, CH\text{=CHCH}_{2}), 5.27 (dd, J = 17.2, 1.5 Hz, 1H, CH\text{=CHCH}_{2}), 5.90 (ddt, J = 17.2, 10.6, 5.3 Hz, 1H, CH\text{=CHCH}_{2}), 6.86 (s, 1H, thiophene-H), 7.65 (s, 1H, thiophene-H), 7.92 (t, J = 6.0 Hz, 1H, CH\text{=NHCO}), 13.30 (bs, 1H, COOH); ^{13}C-NMR (75 MHz, DMSO-d_{6}): \delta = 14.1 (+), 14.5 (+), 38.8 (−), 64.4 (−), 116.9 (−), 124.9 (q), 125.5 (+), 126.8 (q), 131.6 (q), 133.5 (+), 133.9 (q), 134.1 (+), 135.6 (q), 140.8 (q), 141.4 (q), 148.6 (q), 155.9 (q), 162.2 (q), 164.9 (q), 164.9 (q); HR-MS (ESI): calcd. for C_{20}H_{18}NO_{7}S_{2} (M+H)^{+} 448.0519; found 448.0516.

Ethyl 4-acetyl-5-methylthiophene-2-carboxylate (21S): A solution of acetyl chloride (128 µL, 1.80 mmol) in anhydrous chloroform (2 mL) was added to AlCl_{3} (480 mg, 3.60 mmol) at room temperature under nitrogen atmosphere. After stirring for 10 min a solution of 20S (204 mg, 1.20 mmol) in anhydrous chloroform (2 mL) was dropped to the suspension. The mixture was heated to 60 °C for 9 h, then the reaction was quenched with ice/water and the aqueous phase was extracted with chloroform (2 x 30 mL). The combined organic phases were washed with saturated aqueous solution of NaHCO_{3} (50 mL) and brine.

^A Yield could not be determined because the ratio of 12 to 12S in the mixture was not calculated.
(50 mL). The organic phase was dried over MgSO₄ and the solvent was evaporated. The crude product was purified by automated flash column chromatography (PE/EtOAc, 8% - 30% EtOAc) and 21S (180 mg, 71%) was obtained as colorless solid. R_f: 0.15 (PE/EtOAc: 9/1); m.p.: 103 °C; IR (neat) νmax: 3008, 2985, 2944, 1713, 1670, 1540, 1452, 1250, 1236, 1082, 1021, 747; ¹H-NMR (400 MHz, CDCl₃): δ = 1.37 (t, J = 7.1 Hz, 3H, O−CH₂−CH₃), 2.52 (s, 3H, thiophene-CH₃), 2.75 (s, 3H, acetyl-CH₃), 4.34 (q, J = 7.1 Hz, 2H, O−CH₂−CH₃), 8.02 (s, 1H, thiophene-H); ¹³C-NMR (101 MHz, CDCl₃): δ = 14.3 (+), 16.8 (+), 29.6 (+), 61.4 (−), 129.0 (q), 134.7 (+), 136.3 (q), 155.6 (q), 161.6 (q), 193.7 (q); HR-MS (ESI): calcd. for C₁₀H₁₃O₃S (M+H)⁺ 213.0580; found 213.0581.
$^1$H- and $^{13}$C-NMR spectra of all prepared compounds

$^1$H-NMR (300 MHz, DMSO-$d_6$) for compound 4:

$^{13}$C-NMR (75 MHz, DMSO-$d_6$) for compound 4:
$^1$H-NMR (300 MHz, DMSO-$d_6$) for compound 6:

$^{13}$C-NMR (75 MHz, DMSO-$d_6$) for compound 6:
$^{1}$H-NMR (400 MHz, DMSO-$d_6$) for compound 7:

$^{13}$C-NMR (101 MHz, DMSO-$d_6$) for compound 7:
$^1$H-NMR (400 MHz, DMSO-$d_6$) for compound 8:

$^{13}$C-NMR (101 MHz, DMSO-$d_6$) for compound 8:
1H-NMR (300 MHz, CDCl₃) for compound 9:

13C-NMR (75 MHz, CDCl₃) for compound 9:
$^{1}$H-NMR (400 MHz, CDCl$_3$) for compound 10:

$^{13}$C-NMR (101 MHz, CDCl$_3$) for compound 10:
$^{1}H$-NMR (400 MHz, CDCl$_3$) for compound 11:

$^{13}C$-NMR (101 MHz, CDCl$_3$) for compound 11:
$^1$H-NMR (400 MHz, CDCl$_3$) for compound 11S:

$^{13}$C-NMR (101 MHz, CDCl$_3$) for compound 11S:
$^1$H-NMR (400 MHz, CDCl$_3$) for compound 12:

$^{13}$C-NMR (101 MHz, CDCl$_3$) for compound 12:
$^{1}$H-NMR (400 MHz, CDCl$_3$) for compound 12S:

$^{13}$C-NMR (101 MHz, CDCl$_3$) for compound 12S:
$^1$H-NMR (600 MHz, MeOD) for compound 13a:

$^{13}$C-NMR (151 MHz, MeOD) for compound 13a:
$^1$H-NMR (300 MHz, CD$_3$CN) for compound 13b:

$^{13}$C-NMR (75 MHz, CD$_3$CN) for compound 13b:
$^{1}$$H$-NMR (300 MHz, DMSO-$d_6$) for compound 13S:

$^{13}$$C$-NMR (75 MHz, DMSO-$d_6$) for compound 13S:
$^1$H-NMR (400 MHz, CDCl$_3$) for compound 17:

$^{13}$C-NMR (101 MHz, CDCl$_3$) for compound 17:
$^1$H-NMR (400 MHz, CDCl$_3$) for compound 18:

$^{13}$C-NMR (101 MHz, CDCl$_3$) for compound 18:
$^1$H-NMR (300 MHz, CDCl$_3$) for compound 21:

$^{13}$C-NMR (75 MHz, CDCl$_3$) for compound 21:
$\text{H-NMR (400 MHz, CDCl}_3\text{)}$ for compound $21S$:

$\text{C-NMR (101 MHz, CDCl}_3\text{)}$ for compound $21S$:

$\text{13C-NMR (101 MHz, CDCl}_3\text{)}$ for compound $21S$:
$^1$H-NMR (300 MHz, DMSO-$d_6$) for compound 23:

$^{13}$C-NMR (75 MHz, DMSO-$d_6$) for compound 23:
$^1$H-NMR (400 MHz, DMSO-$d_6$) for compound 24:

$^{13}$C-NMR (101 MHz, DMSO-$d_6$) for compound 24:
$^1$H-NMR (300 MHz, CDCl$_3$) for compound 26:

$^{13}$C-NMR (75 MHz, CDCl$_3$) for compound 26:
$^1$H-NMR (300 MHz, CDCl$_3$) for compound 27:

$^{13}$C-NMR (75 MHz, CDCl$_3$) for compound 27:
$^{1}$$H$-NMR (300 MHz, CDCl$_3$) for compound 30:

$^{13}$$C$-NMR (75 MHz, CDCl$_3$) for compound 30:
$^1$H-NMR (300 MHz, CDCl$_3$) for compound 31:

$^{13}$C-NMR (75 MHz, CDCl$_3$) for compound 31:
$^1$H-NMR (300 MHz, DMSO-$d_6$) for compound 33:

$^{13}$C-NMR (75 MHz, DMSO-$d_6$) for compound 33:
$^1$H-NMR (300 MHz, DMSO-$d_6$) for compound 34:

$^{13}$C-NMR (75 MHz, DMSO-$d_6$) for compound 34:
$^1$H-NMR (300 MHz, DMSO-$d_6$) for compound 35:

$^{13}$C-NMR (75 MHz, DMSO-$d_6$) for compound 35:
$^1$H-NMR (300 MHz, DMSO-$d_6$) for compound 36:

$^{13}$C-NMR (75 MHz, DMSO-$d_6$) for compound 36:
$^1$H-NMR (300 MHz, DMSO-$d_6$) for compound 37:

$^{13}$C-NMR (75 MHz, DMSO-$d_6$) for compound 37: