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## Indole-3-Acetic Acids and Hetero Analogues by One Pot Synthesis including Heck Cyclisation

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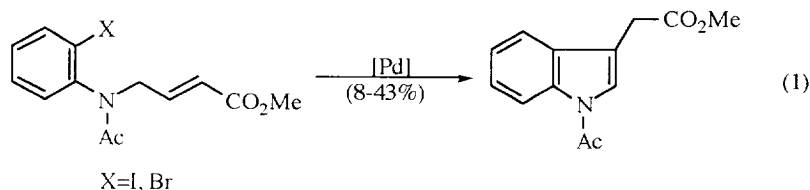
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**Abstract:** Bz-substituted indole-3-acetic acid ethyl esters (**14e-g**) and heteroanalogues, i.e. thienopyrroles (**14a, c**) and selenolopyrrole (**14d**), were prepared starting from N-BOC protected *o*-iodo aryl amines. Allylation with ethyl 4-bromocrotonate, followed by palladium-catalysed ring closure in a one pot reaction, yielded N-BOC protected indoles (**13e-g**), thienopyrroles (**13a-c**), and selenolopyrrole (**13d**). The BOC group was readily removed thermally after adsorption on silica. Oxothienopyrroles (**11a-c**) were similarly prepared.

### INTRODUCTION

Indole-3-acetic acid and derivatives thereof are of great biological and medicinal interest. Compounds of this type have been shown to possess for example plant growth, antiinflammatory, analgesic, antipyretic, antirheumatic, muscle relaxant, and serotonin-like activities.<sup>1</sup> General synthetic methods of substituted and modified indole-3-acetic acids are therefore of importance. The Heck cyclisation<sup>2</sup> of N-allyl substituted *o*-halo anilines<sup>3</sup>, has previously been utilized for the synthesis of indole-3-acetic acid derivatives<sup>4</sup> (eq. 1).

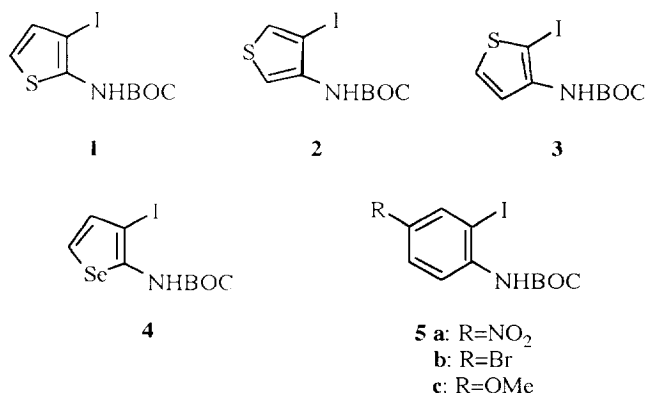


In connection with our previous work<sup>5</sup> on finding synthetic methods toward 3-substituted indoles<sup>6</sup> and hetero condensed pyrroles we decided to investigate this pathway. The synthetic strategy was thus to introduce a suitably substituted allyl or acryloyl group on the nitrogen atom of a ringsubstituted *o*-halo aniline or *o*-halo hetarylamine, and thereafter achieve palladium-catalysed ring closure to form the pyrrole moiety.

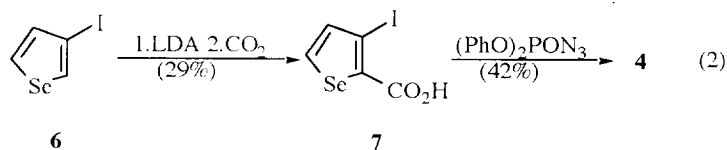
Other methods, concerning the synthesis of Bz-substituted indole-3-acetic acid derivatives have been developed in recent years.<sup>7,8</sup> The Heck cyclisation approach has however not, until now, attracted any attention. This paper deals with improvement of this procedure towards synthesis of Bz-substituted indole-3-acetic acid derivatives, and is applied to the preparation of isosteric heterocondensed pyrroles, by employment of N-BOC-*o*-iodo-arylamines as precursors. Existing procedures for construction of thienopyrroles usually seem quite circumstantial.<sup>9-11</sup>

## RESULTS AND DISCUSSION

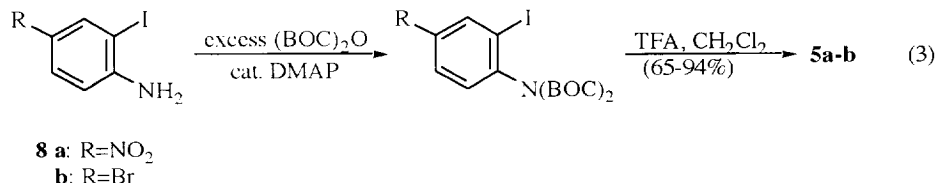
*N*-BOC-*o*-iodo-arylamines. The *o*-halo-hetarylamine precursor has to bear an electron-withdrawing substituent due to the instability of electron rich hetarylamines<sup>12</sup>. The *tert*-butoxycarbonyl (BOC) group was selected as N-protective group in the starting hetarylamines, and as N-substituent in the anilines, for the following reasons: (a) These compounds are readily accessible by the modified Curtius rearrangement<sup>13</sup>, starting from the corresponding carboxylic acid, or directly from the anilines by substitution. (b) The NHBOC-substituent might serve as directing group, for introduction of the *o*-iodine, via *o*-lithiation.<sup>14</sup> (c) Selective removal of the BOC-group in the final product could be achieved under mild thermolytic conditions<sup>15</sup>, thus giving access to sensitive electron rich systems such as the thienopyrrole nucleus.<sup>9</sup>



Aminothiophenes **1** and **2** were prepared from the corresponding carboxylic acids by treatment with diphenylphosphoryl azide in *tert*-butanol.<sup>16</sup> The N-BOC protected 3-amino-2-iodothiophene **3** was prepared in 71 % yield, in a fashion similar to corresponding bromination<sup>17</sup>, by iodination of 3-(*N*-*tert*-butoxycarbonylamino)thiophene with N-iodosuccinimide in carbon tetrachloride. Lithiation of 3-iodoselenophene **6** with LDA in diethyl ether, followed by quenching with carbon dioxide, gave 29 % yield of the carboxylic acid **7**. Treatment of this with diphenylphosphoryl azide and triethyl amine (TEA) in *tert*-butanol at reflux gave N-BOC protected 2-amino-3-iodoselenophene **4** in 42 % yield (eq. 2).



The N-BOC substituted anilines **5a-b** were prepared by the introduction of two N-BOC substituents on the free anilines **8a-b**, with excess BOC-anhydride in THF under 4-(N,N-dimethylamino)pyridine (DMAP) catalysis, followed by selective removal of one N-BOC group with trifluoro acetic acid (TFA) in methylene chloride<sup>18</sup>, in 94 and 65 % yield respectively (eq. 3).



It was found that treatment of these anilines with equimolar quantities of BOC-anhydride in THF at room temperature, with or without DMAP catalysis, resulted in formation of both N-mono- and N,N-diBOC substituted products. Aniline **5e** was prepared by *o*-lithiation / iodination starting from N-BOC substituted 4-methoxy aniline.<sup>8</sup>

*Allylation and acryloylation of N-BOC protected aminothiophenes 1 and 3 (eq. 4).* Initial attempts to allylate N-BOC protected aminothiophenes **1** and **3**, using excess ethyl 4-bromocrotonate as allylating agent, under influence of strong bases, such as sodium hydride or potassium *tert*-butoxide, resulted in rapid decomposition of the ethyl 4-bromocrotonate. Only trace amounts of the desired N-allylated products **12a** and **12e** could be isolated or detected, along with most of the unreacted starting material.

Table 1. Allylation of N-BOC Protected Aminothiophenes with Ethyl 4-Bromo-Crotonate Under Different Conditions.

entry	substrate product	base (equiv.)	solvent	ethyl 4-bromo-crotonate (equiv.) <sup>a</sup>	time (h) / temp.	isolated yield (%)
1	<b>3 / 12e</b>	KF · Al <sub>2</sub> O <sub>3</sub> (11) <sup>19</sup>	DME	1.5+1.0	39+10 / r.t.+55°C	64 <sup>b</sup>
2	"	K <sub>2</sub> CO <sub>3</sub>	DMF	1.5+0.5	48 / r.t.	72 <sup>b</sup>
3	"	Cs <sub>2</sub> CO <sub>3</sub> <sup>20</sup>	"	1.5	40min / r.t.	80 <sup>b, c</sup>
4	<b>1 / 12a</b>	KF · Al <sub>2</sub> O <sub>3</sub> (10) <sup>19</sup>	DME	"	72 / r.t.	37 <sup>b</sup>
5	"	<i>n</i> -Bu <sub>4</sub> NF (3)	"	"	"	57 <sup>b</sup>
6	"	<i>n</i> -Bu <sub>4</sub> NF (3) · K <sub>2</sub> CO <sub>3</sub> (1.5)	"	"	2 / r.t.	87
7	"	<i>n</i> -Bu <sub>4</sub> NF (0.1) · K <sub>2</sub> CO <sub>3</sub> (1.5)	"	"	46 / r.t.	88
8	"	-	DiPrA <sup>d</sup>	"	96 / r.t.	trace <sup>b</sup>
9	"	K <sub>2</sub> CO <sub>3</sub> (3)	DMF	"	2.5 / r.t.	91 <sup>c, e</sup>

a Additional ethyl 4-bromocrotonate was added when consumed as indicated by TLC. b Unconsumed substrate could be isolated or detected (TLC) when the reaction was stopped. c Also see experimental section. d Diisopropyl amine was used as both solvent and base. e A byproduct 97 of compound **12a**<sup>21</sup> was also isolated.

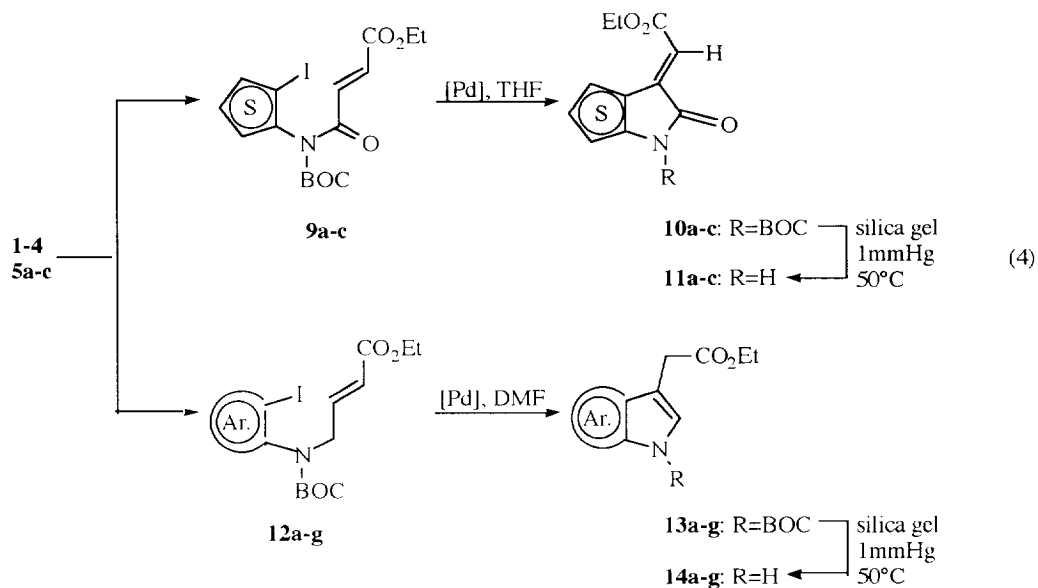
When the relatively insensitive allyl bromide was used under the same conditions, N-allylation proceeded rapidly and in quantitative yields, showing that allylation with ethyl 4-bromocrotonate might be possible if proper conditions were chosen. In order to evaluate better methods, the two N-BOC protected aminothiophenes **1** and **3** were allylated with ethyl 4-bromocrotonate, using different bases in DMF or DME as solvent (Table 1). It was found that allylation could be achieved more effectively by use of weaker bases such as potassium or cesium carbonate, or fluoride, to give N-allylated products **12a** and **12c** in yields ranging from 37 to 91 %. Corresponding acryloylation with ethoxyfumaroyl chloride under different conditions were also investigated, and found to give the expected N-acryloylated products **9a** and **9c** in yields from 51 to 83 % (Table 2). The overall lower yield of **9c** and **12c**, compared to **9a** and **12a** respectively, indicates lower nucleophilicity of the nitrogen atom in the 3-, compared to 2-position of the thiophene ring.

Table 2. Acryloylation of N-BOC Protected Aminothiophenes with Ethoxyfumaroyl chloride Under Different Conditions.

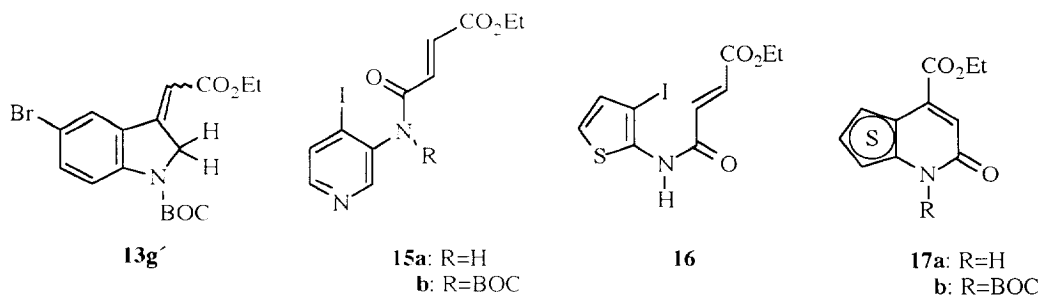
entry	substrate product	base (equiv.)	solvent	ethoxyfumaroyl chloride(equiv.) <sup>a</sup>	time (h) / temp.	isolated yield (%)
1	<b>1</b> <b>9a</b>	TEA (5)	THF / cat. DMAP <sup>d</sup>	1.5	2 / r.t.	83 <sup>c</sup>
2	"	K <sub>2</sub> CO <sub>3</sub> (5)	DMF / cat. DMAP <sup>d</sup>	"	5 / r.t.	68 <sup>b</sup>
3	<b>3</b> <b>9c</b>	TEA (5)	THF / cat. DMAP <sup>d</sup>	1.5+0.5+0.5	72 / r.t.	51 <sup>b</sup>
4	"	"	"	"	72 / 50 °C	60 <sup>b, c</sup>

a. Additional ethoxyfumaroyl chloride was added when consumed as indicated by TLC. b/ Unconsumed substrate could be isolated or detected (TLC) when the reaction was stopped. c. Also see experimental section. d. 10 mol % relative to substrate.

*Palladium-catalysed cyclisation (eq. 4).* Cyclisation of the N-allylaminothiophene **12a** in DMF as solvent, gave thienopyrrole **13a** in 85 % yield when treated with a mixture of sodium carbonate (3 equiv.), palladium acetate (0.05 equiv.), and triphenylphosphine (0.1 equiv) for 4 h at 60–65 °C. Longer reaction time was found necessary for complete reaction, and lower yield of thienopyrrole was obtained when triphenylphosphine was omitted (47 h, 69 %). Incomplete reaction, and pronounced formation of by-products, resulted surprisingly if tetrabutylammonium chloride (1 equiv.) was present under otherwise similar conditions. This result is contrary to the normally positive effects of this reagent in Heck reactions.<sup>22</sup> The use of TEA as base, instead of sodium carbonate, gave essentially the same yield and reaction time. Cyclisation of the N-acryloyl aminothiophenes **9a** and **9c**, in THF as solvent, gave the oxothienopyrroles **10a** and **10c** in 60 and 18 % yield when treated with TEA (10 equiv.), palladium acetate (0.05 equiv.), and triphenylphosphine (0.1 equiv) for 5 h at reflux and 96 h at room temperature respectively. Attempted cyclisation of **9c** in THF at reflux, DMF or MeCN at room temperature, with or without added triphenylphosphine, resulted in all cases in rapid formation of a deep blue color, with only trace amounts (TLC) of **9c** and **10c** present in the reaction mixture. Cyclisation to the desired condensed pyrroles from pyridines<sup>23</sup> **15a-b**, or N-acryloyl aminothiophene **16**, also failed. Only complex mixtures or unreacted materials were obtained. The presence of **16** was found to inhibit the cyclisation of its N-BOC substituted analog **9a**. Without any **16** present, **9a** cyclised at room temperature to give 43 % yield of **10a** after 10 h. reaction. Under the same conditions (DMF, 3 equiv. potassium carbonate, 0.05 equiv. palladium acetate, 0.1 equiv. triphenylphosphine) and reaction times, yields decreased to 14 and 0 %, in presence of 15 and 100 mol% of **16** respectively.



- a: 2-N, 3-I thiophene / thieno[2,3-b]pyrrole  
 b: 3-N, 4-I thiophene / thieno[3,4-b]pyrrole  
 c: 3-N, 2-I thiophene / thieno[3,2-b]pyrrole  
 d: 2-N, 3-I selenophene / selenolo[2,3-b]pyrrole  
 e: 4-NO<sub>2</sub>, 2-I aniline / 5-NO<sub>2</sub> indole  
 f: 4-OMe, 2-I aniline / 5-OMe indole  
 g: 4-Br, 2-I aniline / 5-Br indole



Since the same base and solvent could be used in both steps, cyclisation of N-allyl and N-acryloyl arylamines (**12a-g**, **9a-b**) could advantageously be achieved directly without isolation. After having introduced the allyl or acryloyl unit, heterocondensed pyrroles and indoles were formed by addition of catalytic amounts of palladium acetate and triphenylphosphine (table 3). To our knowledge, this is a novel approach toward selenolo- and thienopyrroles. Although the cyclisation step demanded longer reaction times in this “one pot procedure”, no significant decrease in yield was found, compared to the two step process with isolation of intermediate product. In one case only the two step process was found preferable. Thus 18 % yield of oxothienopyrrole **10c** was obtained by cyclisation of N-acryloyl aminothiophene **9c**, while the “one pot procedure”, starting from aminothiophene **3**, only resulted in trace amounts of the desired product (table 3, entry 11).

Table 3. One Pot Synthesis of Indole-, Thienopyrrole-, and Selenopyrrole Acetic Acid Ethylester Derivatives from N-BOC Protected *o*-Iodo-Arylamines<sup>d</sup>.

entry	substrate product	solvent	reagent <sup>b</sup> equiv.	time 1 (h) <sup>c</sup> time 2 (h)	temp. 1 (°C) <sup>d</sup> temp. 2 (°C)	isolated yield (%)
1	<b>1</b> <b>13a</b>	DMF	1.5	2.5 24	r.t. / 60-65	72
2	<b>2</b> <b>13b</b>	"	1.5+0.5	48 5	"	66
3	<b>3</b> <b>13c</b>	"	"	"	"	66
4	<b>4</b> <b>13d</b>	"	1.5	3 24	"	59
5	<b>5a</b> <b>13e</b>	"	1.5	3 19	"	68
6	<b>5c</b> <b>13f</b>	"	1.5+0.5+0.5	94 5	"	67 <sup>e</sup>
7	<b>5b</b> <b>13g</b>	"	1.5	30 4	r.t. / r.t.	48 <sup>f</sup>
8	"	"	"	30 24	"	67
9	<b>1</b> <b>10a</b>	THF	"	1 5	r.t. / reflux	54
10	<b>2</b> <b>10b</b>	"	1.5+0.5	50 72	reflux 40	27 <sup>e</sup>
11	<b>3</b> <b>10c</b>	"	1.5	35 144	reflux r.t.	trace

a For general procedures see experimental section. b Entry 1 to 8: Ethyl 4-bromocrotonate was used as allylating agent. Entry 9-11: Ethoxyfumaroyl chloride, together with 10 mol % DMAP relative to substrate, was used as acryloylating agent. c/ Time 1 indicates the time for allylation or acryloylation. Time 2 indicates the time for ring closure, after having added catalytic amounts of palladium acetate and triphenylphosphine. d Temp 1 indicates the temperature while performing allylation or acryloylation. Temp 2 indicates the temperature during palladium catalysed ring closure. e Unconsumed substrate was isolated together with product. f/ As byproduct 8 % of the tautomeric compound **13g'** was also isolated.

It was observed, in agreement with others<sup>3,24</sup>, that 5-exo- was favoured over 6-endo-cyclisation. Products resulting from 6-endo-cyclisation could in no case be detected. Substrates such as anilines with electron-donating groups (Table 3, entry 6), or 3-aminothiophenes (Table 3, entry 2, 3, 10), needed extra addition of ethyl 4-bromocrotonate or ethoxyfumaroyl chloride for allylation / acryloylation to proceed satisfactorily. Unreacted aryl iodides could, in some of those cases, be isolated after cyclisation (Table 3, entry 6, 10). In one case, when the cyclisation was stopped after 4 h, could the tautomer **13g'** be isolated together with the desired indole (Table 3, entry 7). Tautomerisation of this compound to indole could easily be monitored by proton NMR in deuteriochloroform, under influence of a catalytic amount of TEA. No trace of this tautomer could be detected when the same cyclisation was continued for 24 h (Table 3, entry 8).

X-ray crystallographic analysis<sup>25</sup> of N-unprotected oxothienopyrrole **11a** was performed to ensure the structure of this compound, and its N-BOC protected precursor **10a**. Assignment of the (E)-stereochemistry at the exocyclic double bond in **10a** and **11a** could, by this analysis, be made with certainty. The regio- and stereochemistry of the two differently fused isomers **10b** and **10c**, as well as the unprotected analogues **11b** and **11c**, was thereby also confirmed since all three isomers, with and without N-BOC protection, showed very similar spectroscopical properties. Without reference material these N-BOC protected (**10a-c**), or N-unprotected (**11a-c**), oxothienopyrroles proved otherwise impossible to distinguish (<sup>1</sup>H shifts and J<sub>C-H</sub>) from the thienopyridinones **17a** and **17b**, which would result from imaginable 6-endo-cyclisation. The three N-unprotected isomers **11a-c** showed similarities in their <sup>1</sup>H shifts ( $\delta$  (H-vinyl, deuteriochloroform)=6.52, 6.70, 6.71 respectively), and <sup>1</sup>H-<sup>13</sup>C coupling constants (<sup>3</sup>J (H-vinyl-CON, deuteriochloroform)=7.1, 6.5, 5.8 Hz respectively). The corresponding N-BOC protected compounds **10a-c** also showed similarities in their <sup>1</sup>H shifts ( $\delta$  (H-vinyl, deuteriochloroform)=6.57, 6.76, 6.53 respectively), and <sup>1</sup>H-<sup>13</sup>C coupling constants (<sup>3</sup>J (H-vinyl-CON, deuteriochloroform)=7.2, 6.8, 6.0 Hz respectively). It might be concluded that only one stereoisomer is formed during cyclisation of N-acryloyl aminothiophenes **9a-c**, since no other isomer could be detected by TLC-analysis of the crude products, or by <sup>1</sup>H NMR of the purified compounds.

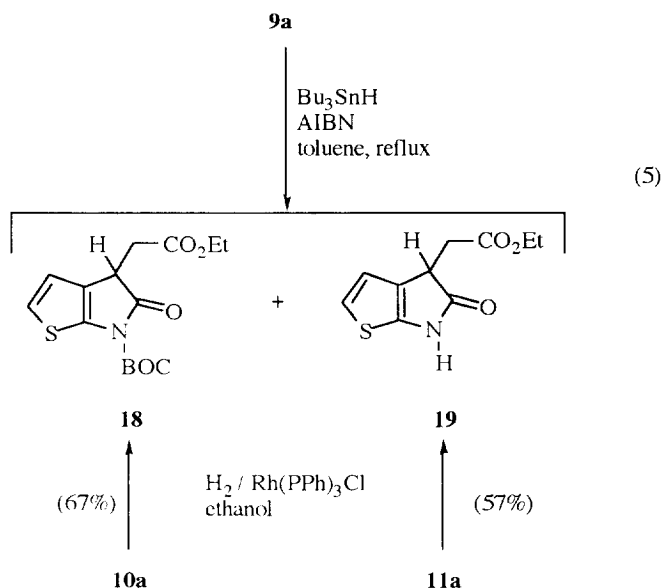
*Thermal removal of N-BOC substituents.* In order to remove the N-BOC substituent from the indoles and heterocondensed pyrroles obtained, we used a modified thermal procedure of Rawal and Cava.<sup>15</sup> Although the original procedure - to heat the substrate to about 180 °C - has been used for deprotection of indoles<sup>26</sup> and other nitrogen protected compounds<sup>27</sup>, we experienced it less suitable. Along with the desired products, the N-BOC protected thienopyrroles **13a** and **13c** also gave large amounts of dark resinous material at this temperature. The substrate was instead adsorbed onto silica gel and kept at only 50 °C under reduced pressure to remove the BOC group (table 4, eq. 4). When the reaction was performed at atmospheric pressure, under otherwise identical conditions, it was slow and only trace amounts of product could be detected after 24 h. Only in the case of the highly instable 3,4-b fused thienopyrrole **13b**, the product **14b** could not be obtained (Table 4, entry 2). The silica gel became black and neither starting material nor product could be detected.

Table 4. Thermal Removal of the N-BOC Substituent from Various Substrates.<sup>a</sup>

entry	substrate	product	isolated yield (%)
1	<b>13a</b>	<b>14a</b>	92
2	<b>13b</b>	<b>14b</b>	—
3	<b>13c</b>	<b>14c</b>	86
4	<b>13d</b>	<b>14d</b>	58
5	<b>13e</b>	<b>14e</b>	89
6	<b>13f</b>	<b>14f</b>	89
7	<b>13g</b>	<b>14g</b>	79
8	<b>10a</b>	<b>11a</b>	87
9	<b>10b</b>	<b>11b</b>	77
10	<b>10c</b>	<b>11c</b>	76
11	<b>9a</b>	<b>16</b>	81

a/ See experimental section for a general procedure.

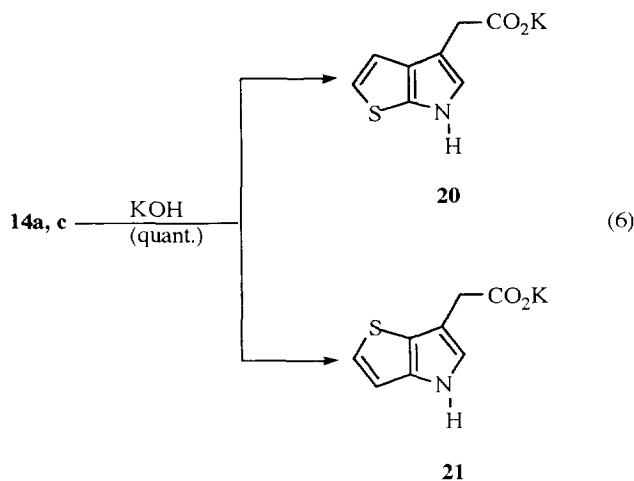
Comparison with radical cyclisation (eq. 5). Comparison of the palladium catalysed, and the radical induced pathways for ringclosure of N-acryloyl substituted aminothiophene **10a** was made.



Saturated oxothienopyrroles **18** and **19** could be obtained by hydrogenation of unsaturated oxothienopyrroles **10a** and **11a** by employment of Wilkinson's catalyst in 67 and 57 % (67 % based on consumed **11a**) yield respectively. The N-BOC protected oxothienopyrrole **10a** proved to be more smoothly hydrogenated than the N-unprotected analogue **11a**, which demanded longer reaction time and still was not totally consumed. The best total yield starting from **9a**, using palladium-catalysis as the key step, was thus 36 % of **18**. When radical cyclisation<sup>28</sup> was performed, by reaction of **9a** with 1.2 equiv. tributyltin hydride in refluxing toluene for 5 h with 12.2 mM AIBN as initiator, a mixture of **18** (9 %) and **19** (4 %) was obtained. The crude product after this reaction was more complex compared to that from the Heck cyclisation. Despite two successive purifications by chromatography on silica gel, the products were not pure according to <sup>1</sup>H-NMR. Attempted radical cyclisation of the isomeric N-acryloylated aminothiophene **9c** under the same conditions failed.

*Saponification of thienopyrrole esters 14a and 14c.* Saponification of esters **14a** and **14c** with potassium hydroxide gave, in quantitative yields, potassium salts **20** and **21** respectively (eq. 6). These salts were stable neat or in water solution for several weeks at room temperature if protected from light. All efforts to obtain the corresponding acids, by mild acidic treatment of the salts and extractive workup, resulted in resinous products. Similar results have been found by Snyder and coworkers<sup>11</sup> in attempts to obtain the corresponding acid of **21**. Degradation of this *in situ* generated acid, in 0.8 M DOAc / deuteriumoxide, could be monitored by <sup>1</sup>H-NMR overnight.





#### ACKNOWLEDGEMENT

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#### EXPERIMENTAL

All reactions were performed under nitrogen. Starting materials, **1**<sup>16</sup>, **2**<sup>16</sup>, **5c**<sup>8</sup>, 3-(*N-tert*-butoxycarbonyl-amino)thiophene<sup>16</sup>, **8a**<sup>29</sup>, **8b**<sup>29</sup>, **6**<sup>30</sup>, and ethoxyfumaroyl chloride<sup>31</sup> were prepared according to literature procedures. Ethyl 4-bromo-crotonate was purchased from Janssen Chimica, diphenylphosphoryl azide from Merck, *N*-iodo succinimide from Fluka, and palladium acetate from Riedel-de Haën. DMF, DME, and solvents used as eluents for chromatography, was distilled and stored over 4 Å molecular sieves. Dry diethyl ether was distilled over sodium prior to use. THF were distilled over sodium under nitrogen atmosphere. Flash column chromatography was performed on TLC-silica gel (60H, Merck), and is referred to as "chromatography". TLC analyses were performed on silica coated aluminium plates. The spots were visualized in UV light, and by anisaldehyde/sulfuric acid/ethanol-spray followed by heating. <sup>1</sup>H NMR spectra were recorded on a Varian XL 300-, or XL 200 NMR-spectrometer, operating at 300 and 200 MHz (proton) respectively. <sup>13</sup>C NMR spectra were recorded on the same Varian XL 300 NMR-spectrometer. Chemical shifts ( $\delta$ ) are reported in parts per million downfield from TMS. Mass spectra were obtained on a Jeol SX 102 spectrometer using electron impact ionization at 70 eV. Elemental analyses were performed by H. Kolbe Mikroanalytisches Laboratorium (Mülheim, Germany). Uncorrected melting points were performed on a Wetzlar microscope.

**2-Iodo-3-(N-tert-butoxycarbonylamino)thiophene (3):**

A solution of 7.10 g (35.6 mmol) 3-(N-tert-butoxycarbonylamino)thiophene and 8.02 g (35.6 mmol) of N-iodosuccinimide in carbon tetrachloride (50 ml) was refluxed for 2 h. After allowing the mixture to reach room temperature, the precipitated succinimide was removed by filtration, followed by washing with carbon tetrachloride (20 ml). The crude product obtained after concentration was purified by chromatography (EtOAc/n-heptane 5:95) to yield an oil, that slowly crystallised when stored at 0 °C, to give 8.22 g (71.0 %) of **3** as white crystals. mp 71-72 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ 8.55 (bs, 1H), 7.66 (d, J=5.5 Hz, 1H), 6.97 (d, J=5.5 Hz, 1H), 1.46 (s, 9H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>) δ 153.06, 140.92, 130.17, 125.38, 79.11, 28.03; MS *m/z* (%): 325 (M<sup>+</sup>, 26), 269 (98), 225 (100), 210 (49), 57 (60); HRMS observed: 324.9627. Calcd: 324.9632; Anal. Calcd for C<sub>9</sub>H<sub>12</sub>INO<sub>2</sub>S: C 33.24, H 3.72, N 4.31. found: C 33.49, H 3.46, N 4.52.

**(3-Iodo-2-selenophene)carboxylic acid (7):**

A solution of LDA was prepared by adding 28 ml (1.91 M, 53.7 mmol) BuLi /cyclohexane while stirring to 5.43 g (53.7 mmol) diisopropyl amine in dry diethyl ether (100 ml) at room temperature. After cooling (-70 °C) this solution, 11.5 g (44.8 mmol) of **6** in dry diethyl ether (50 ml) was added at such a rate that the temperature did not exceed -70 °C. The mixture was stirred for another 20 min. at this temperature before addition of excess solid carbon dioxide. After allowing the mixture to reach room temperature it was extracted with three portions (50 ml) of 1 M NaOH (aq.). Acidification of the combined extracts with conc. HCl and cooling (0°C over night) resulted in precipitation of the product. Filtration, washing with cold water, and drying gave 3.93 g (29 %) of **7** as a slightly colored solid which was used in next step without further purification. mp ~160-170 °C (dec.); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ 11.05 (bs, 1H), 8.42 (d, J=5.7 Hz, 1H), 7.63 (d, J=5.7 Hz, 1H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>) δ 166.06, 164.04, 139.40, 137.37, 131.91; MS *m/z* (%): 302 (M<sup>+</sup>+1, 100), 256 (2), 175 (13); HRMS observed: 301.8343 (M<sup>+</sup>). Calcd: 301.8342.

**3-Iodo-2-(N-tert-butoxycarbonylamino)selenophene (4):**

A solution of 2.65 g (8.81 mmol) **7**, 0.98 g (9.69 mmol) of TEA, and 2.67 g (9.69 mmol) of diphenyl phosphoryl azide in *tert*-butanol (50 ml) was refluxed for 6 h. The reaction mixture was thereafter evaporated with 5 g silica gel (100-200 mesh), and purified by chromatography (EtOAc/n-heptane 5:95), to give 1.38 g (42 %) of **4** as yellowish crystals. mp 57-60 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ 9.37 (bs, 1H), 7.65 (d, J=6.5 Hz, 1H), 7.08 (d, J=6.5 Hz, 1H), 1.49 (s, 9H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>) δ 153.17, 141.30, 133.96, 125.16, 80.80, 27.89; MS *m/z* (%): 373 (M<sup>+</sup>+1, 16), 317 (56), 273 (34), 57 (100); HRMS observed: 372.9079 (M<sup>+</sup>). Calcd: 372.9077; Anal. Calcd for C<sub>9</sub>H<sub>12</sub>INO<sub>2</sub>Se: C 29.05, H 3.25, N 3.77. found: C 29.41, H 3.43, N 3.64.

**4-Bromo-2-iodo-N-(tert-butoxycarbonyl)aniline (5b):**

A solution of 3.10 g (10.4 mmol) **8b**, 5.45 g (25.0 mmol) of BOC-anhydride, and 127 mg (1.04 mmol) of DMAP in THF (50 ml) was stirred at room temperature for 31 h. The solvent was removed in vacuo, and the residue redissolved in methylene chloride (100 ml), followed by filtration through 50 g silicagel. The silicagel was washed with another portion methylene chloride (200 ml). After concentration of the combined solutions 5.15 g (99 %) of the corresponding N,N-diBOC substituted aniline was obtained as a pale red solid. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.98 (d, J=2.2 Hz, 1H), 7.47 (dd, J=8.4, 2.2 Hz, 1H), 7.06 (d, J=8.4 Hz, 1H), 1.41 (s, 18H). This solid, and 1.78 g (15.6 mmol, 1.20 ml) of TFA, was dissolved in methylene chloride (100 ml) and stirred at room temperature for 18 h before quenching with 5 ml TEA.

The crude product obtained after concentration was purified by chromatography (EtOAc/n-heptane 1:9) to give 3.89 g (94 % total yield) of **5b** as a pale red waxy solid.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.96 (d,  $J=9.0$  Hz, 1H), 7.86 (d,  $J=2.3$  Hz, 1H), 7.42 (dd,  $J=9.0, 2.3$  Hz, 1H), 6.79 (bs, 1H), 1.52 (s, 9H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  152.33, 140.45, 138.16, 132.08, 120.86, 115.80, 88.72, 81.46, 28.28; MS  $m/z$  (%): 397 / 399 ( $\text{M}^+$ , 12), 341 / 343 (38), 297 / 299 (51), 57 (100); HRMS observed: 396.9180 ( $\text{M}^+$ ). Calcd: 396.9173; Anal. Calcd for  $\text{C}_{11}\text{H}_{13}\text{BrINO}_2$ : C 33.19, H 3.29, N 3.52. found: C 33.28, H 3.34, N 3.56.

#### **2-Iodo-4-nitro-N-(tert-butoxycarbonyl)aniline (5a):**

The title compound was prepared according to the procedure above with the following exceptions: 2.8 g (10.6 mmol) of **8a** was used as starting material. Intermediate N,N-diBOC substituted aniline, 4.88 g (99 %), was obtained as a pale brown solid.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  8.70 (d,  $J=2.5$  Hz, 1H), 8.23 (dd,  $J=8.7, 2.5$  Hz, 1H), 7.38 (d, 8.7 Hz, 1H), 1.41 (s, 18H). The crude product (4.1 g) was purified by recrystallization from n-heptane (60 ml), by aid of activated carbon, to give 2.5 g (65 % total yield) of **5a** as yellow crystals. mp 110.5-111.5 °C;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  8.64 (d,  $J=2.6$  Hz, 1H), 8.34 (d,  $J=9.3$  Hz, 1H), 8.21 (dd,  $J=9.3, 2.6$  Hz, 1H), 7.19 (bs, 1H), 1.56 (s, 9H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  151.65, 144.68, 142.58, 134.43, 124.91, 117.65, 85.85, 82.60, 28.18; MS  $m/z$  (%): 364 ( $\text{M}^+$ , 10), 308 (13), 264 (75), 234 (26), 57 (100); HRMS observed: 363.9920 ( $\text{M}^+$ ). Calcd: 363.9919; Anal. Calcd for  $\text{C}_{11}\text{H}_{13}\text{IN}_2\text{O}_4$ : C 36.28, H 3.60, N 7.70. found: C 36.35, H 3.66, N 7.76.

#### **N-(Ethyl-4-crotonyl)-3-iodo-2-(N-tert-butoxycarbonylamino)thiophene (12a):**

To a stirred mixture of 163 mg (0.50 mmol) **1** and 207 mg (1.50 mmol) of potassium carbonate in DMF (5 ml), was added 193 mg (0.75 mmol) of ethyl 4-bromocrotonate in one portion. The mixture was stirred for another 2.5 h at room temperature, and then added to 100 ml of diethyl ether, followed by washing with water (2x25 ml), drying ( $\text{MgSO}_4$ ), and concentration in vacuo. Purification was done by chromatography (EtOAc/n-heptane 15:85) to give 198 mg (91 %) of **12a** as a colorless oil.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.09 (d,  $J=5.8$  Hz, 1H), 6.91 (dt,  $J=15.7, 5.9$  Hz, 1H), 6.88 (d,  $J=5.8$  Hz, 1H), 5.87 (dt,  $J=15.7, 1.6$  Hz, 1H), 4.24 (dd,  $J=5.9, 1.6$  Hz, 2H), 4.12 (q,  $J=7.1$  Hz, 2H), 1.37 (s, 9H), 1.21 (t,  $J=7.1$  Hz, 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  165.73, 153.37, 143.32, 142.31, 132.88, 125.69, 123.36, 81.65, 81.40, 60.40, 51.32, 28.10, 14.24; MS  $m/z$  (%): 437 ( $\text{M}^+$ , 4), 381 (1), 337 (99), 308 (7), 264 (8), 136 (20), 57 (100); HRMS observed: 437.0155 ( $\text{M}^+$ ). Calcd: 437.0157; Anal. Calcd for  $\text{C}_{15}\text{H}_{20}\text{INO}_4$ : C 41.20, H 4.61, N 3.20. found: C 41.14, H 4.68, N 3.17. Also 24 mg (9%) of the reesterified compound **12a**<sup>21</sup> (cf. table 1, entry 9) was isolated as a byproduct. The proposed structure of this compound is based on its spectroscopic data:  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.15 (d,  $J=5.8$  Hz, 1H), 7.04 (dt,  $J=15.7, 5.9$  Hz, 1H), 6.94 (d,  $J=5.8$  Hz, 1H), 6.94 (dt,  $J=15.7, 4.5$  Hz, 1H), 6.02 (dt,  $J=15.7, 2.0$  Hz, 1H), 5.97 (dt,  $J=15.7, 1.6$  Hz, 1H), 4.80 (dd,  $J=4.5, 2.0$  Hz, 2H), 4.32 (dd,  $J=5.9, 1.6$  Hz, 2H), 4.20 (q,  $J=7.2$  Hz, 2H), 1.42 (s, 9H), 1.28 (t,  $J=7.1$  Hz, 3H); MS  $m/z$  (%): 521 ( $\text{M}^+$ , 2), 421 (92), 308 (13), 224 (7), 113 (28), 57 (100).

#### **N-(Ethyl-4-crotonyl)-2-iodo-3-(N-tert-butoxycarbonylamino)thiophene (12c):**

To a stirred mixture of 163 mg (0.50 mmol) **3** and 489 mg (1.50 mmol) of cesium carbonate in DMF (4 ml), was added a solution of 193 mg (0.75 mmol) ethyl 4-bromocrotonate in DMF (1 ml) during 5 min. The mixture was stirred for another 40 min. at room temperature, and then added to 100 ml of diethyl ether, followed by washing with water (2x25 ml), drying ( $\text{MgSO}_4$ ), and concentration in vacuo. Purification was done by chromatography (EtOAc/n-heptane 2:8) to give 175 mg (80 %, 97 % based on consumed **3**) of **12c** as a

colorless oil, together with 29 mg of **3**.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.40 (d,  $J=5.7$  Hz, 1H), 6.95 (dt,  $J=15.7, 6.0$  Hz, 1H), 6.72 (bs, 1H), 5.91 (d,  $J=15.7$  Hz, 1H), 4.26 (d,  $J=6.0$  Hz, 2H), 4.19 (q,  $J=7.1$  Hz, 2H), 1.39 (s, 9H), 1.28 (t,  $J=7.1$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  165.91, 153.73, 144.74, 143.11, 130.26, 126.63, 123.02, 80.97, 75.90, 60.42, 50.11, 28.21, 14.23; MS  $m/z$  (%): 437 ( $\text{M}^+$ , 4), 381 (9), 337 (43), 308 (27), 264 (11), 136 (77), 57 (100); HRMS observed: 437.0157 ( $\text{M}^+$ ). Calcd: 437.0157; Anal. Calcd for  $\text{C}_{15}\text{H}_{20}\text{INO}_4\text{S}$ : C 41.20, H 4.61, N 3.20. found: C 41.36, H 4.84, N 3.08.

**N-(Ethoxyfumaroyl)-2-iodo-3-(N-tert-butoxycarbonylamino)thiophene (9c):**

To a stirred solution of 975 mg (3.00 mmol) **3**, 37 mg (0.30 mmol) of DMAP, and 1.52 g (15.0 mmol, 2.10 ml) of TEA in THF (10 ml), was added portionwise under 1 h, a solution of 732 mg (4.50 mmol) of ethoxyfumaroyl chloride in THF (3 ml). The mixture was thereafter heated (50 °C) for 72 h, with addition of two 244 mg (1.50 mmol) portions of ethoxyfumaroyl chloride, after 24 and 48 h of reaction respectively. The mixture was then, after cooling to room temperature, poured into diethyl ether (100 ml). The ethereal solution was washed with water (2x25 ml), dried ( $\text{MgSO}_4$ ), and concentrated in vacuo. Purification by chromatography (EtOAc/n-heptane 2:8) gave 805 mg (60 %, 79 % based on consumed **3**) of **9c** as white crystals together with 242 mg of **3**. mp 116-119 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.78 (d,  $J=15.5$  Hz, 1H), 7.48 (d,  $J=5.6$  Hz, 1H), 6.80 (d,  $J=15.5$  Hz, 1H), 6.75 (d,  $J=5.6$  Hz, 1H), 4.26 (q,  $J=7.1$  Hz, 2H), 1.44 (s, 9H), 1.31 (t,  $J=7.1$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  166.02, 165.29, 151.09, 140.63, 136.16, 131.53, 130.62, 126.57, 84.65, 61.24, 27.82, 14.18; MS  $m/z$  (%): 451 ( $\text{M}^+$ , 3), 395 (6), 351 (45), 251 (74), 224 (100), 225 (55), 127 (58), 99 (84), 57 (86); HRMS observed: 450.9951 ( $\text{M}^+$ ). Calcd: 450.9949; Anal. Calcd for  $\text{C}_{15}\text{H}_{18}\text{INO}_5\text{S}$ : C 39.92, H 4.02, N 3.10. found: C 39.84, H 3.95, N 3.13.

**N-(Ethoxyfumaroyl)-3-iodo-2-(N-tert-butoxycarbonylamino)thiophene (9a):**

The title compound was prepared as above from 975 mg (3.00 mmol) of **1**, with following exceptions: No additional ethoxyfumaroyl chloride was added. The reaction was run for 2 h at room temperature. After workup 1.12 g (83 %) of **9a** was obtained as white crystals. mp 100.5-101.5 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.73 (d,  $J=15.4$  Hz, 1H), 7.30 (d,  $J=5.8$  Hz, 1H), 7.00 (d,  $J=5.8$  Hz), 6.79 (d,  $J=15.4$  Hz, 1H), 4.24 (q,  $J=7.1$  Hz, 2H), 1.45 (s, 9H), 1.31 (t,  $J=7.1$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  166.06, 165.18, 150.83, 138.34, 135.71, 133.19, 131.97, 127.29, 85.22, 83.31, 61.29, 27.78, 14.17; MS  $m/z$  (%): 451 ( $\text{M}^+$ , 2), 395 (2), 351 (96), 251 (100), 225 (74), 224 (11), 127 (97), 99 (45), 57 (94); HRMS observed: 450.9963 ( $\text{M}^+$ ). Calcd: 450.9949; Anal. Calcd for  $\text{C}_{15}\text{H}_{18}\text{INO}_5\text{S}$ : C 39.92, H 4.02, N 3.10. found: C 39.99, H 4.04, N 3.17.

**General procedure for synthesis of acetic acid ethyl esters (13a-g) by one pot reaction (table 3):**

In one portion with stirring, 1.5 equiv. of ethyl 4-bromocrotonate was added to a mixture of N-BOC substituted *o*-iodoaniline/aminothiophene (2.5 mmol/ml), and 4 equiv. of dry finely divided potassium carbonate, in DMF at room temperature. Normally the mixture was stirred until the starting aniline/aminothiophene was totally consumed (TLC). If the reaction was slow, and the crotonate was consumed before completion, another 0.5 equiv. portion of this material was added. Thereafter 0.1- and 0.05 equiv. respectively of triphenylphosphine and palladium acetate were added. After stirring for another 30 min. at room temperature the mixture was heated to 60-65 °C, unless otherwise stated, until TLC indicated total consumption of the previously formed N-allylated intermediate. The mixture was then allowed to reach room

temperature before dissolving in diethyl ether. The ethereal solution was washed with water, dried ( $\text{MgSO}_4$ ), and evaporated with silica gel (100-200 mesh), followed by purification by chromatography.

**Ethyl (6-(tert-butoxycarbonyl)-4-thieno[2,3-b]pyrrolyl)acetate (13a):**

The reaction was carried out on 1.62 g (5.00 mmol) of **1**. Allylation and ringclosure was carried out for 2.5 and 24 h respectively. EtOAc/n-heptane 15:85 as eluent gave 1.11 g (72 %) of **13a** as white crystals. mp 69-71 °C;  $^1\text{H}$  NMR (DMSO-*d*<sub>6</sub>)  $\delta$  7.37 (s, 1H), 7.22 (dd, *J*=5.3, 0.8 Hz, 1H), 7.02 (d, *J*=5.3 Hz, 1H), 4.10 (q, *J*=7.1 Hz, 2H), 3.69 (d, *J*=0.8 Hz, 2H), 1.60 (s, 9H), 1.17 (t, *J*=7.1 Hz, 3H);  $^{13}\text{C}$  NMR (DMSO-*d*<sub>6</sub>)  $\delta$  170.49, 147.53, 132.62, 122.64, 122.29, 117.20, 114.10, 84.41, 60.27, 31.39, 27.50, 14.01; MS *m/z* (%): 309 ( $\text{M}^+$ , 25), 253 (94), 209 (31), 136 (100), 57 (70); HRMS observed: 309.1033 ( $\text{M}^+$ ). Calcd: 309.1035; Anal. Calcd for  $\text{C}_{15}\text{H}_{19}\text{NO}_4\text{S}$ : C 58.23, H 6.19, N 4.54. found: C 58.18, H 6.23, N 4.50.

**Ethyl (1-(tert-butoxycarbonyl)-3-thieno[3,4-b]pyrrolyl)acetate (13b):**

The reaction was carried out on 1.62 g (5.00 mmol) of **2**. Allylation and ringclosure was carried out for 48 and 5 h respectively, with another addition of crotonate after 24 h. EtOAc/n-heptane 15:85 as eluent gave 1.02 g (66 %) of **13b** as a colorless oil that rapidly darkened.  $^1\text{H}$  NMR (DMSO-*d*<sub>6</sub>)  $\delta$  7.52 (s, 1H), 7.23 (d, *J*=2.5 Hz, 1H), 7.00-7.26 (bs, unresolved, 1H), 4.10 (q, *J*=7.1 Hz, 2H), 3.63 (d, *J*=0.9 Hz, 2H), 1.58 (s, 9H), 1.20 (t, *J*=7.1 Hz, 3H);  $^{13}\text{C}$  NMR (DMSO-*d*<sub>6</sub>, 40°C)  $\delta$  170.10, 148.36, 137.85, 130.30, 110.87, 108.97, 101.54, 82.90, 60.27, 31.06, 27.67, 13.99; MS *m/z* (%): 309 ( $\text{M}^+$ , 12), 253 (54), 209 (37), 136 (100), 57 (41); HRMS observed: 309.1042 ( $\text{M}^+$ ). Calcd: 309.1035; Anal. Calcd for  $\text{C}_{15}\text{H}_{19}\text{NO}_4\text{S}$ : C 58.23, H 6.19, N 4.54. found: C 58.29, H 6.22, N 4.65.

**Ethyl (4-(tert-butoxycarbonyl)-6-thieno[3,2-b]pyrrolyl)acetate (13c):**

The reaction was carried out on 1.62 g (5.00 mmol) of **3**. Allylation and ringclosure was carried out for 48 and 5 h respectively, with another addition of crotonate after 24 h. EtOAc/n-heptane 15:85 as eluent gave 1.03 g (66 %) of **13c** as white crystals. mp 91-96 °C;  $^1\text{H}$  NMR (DMSO-*d*<sub>6</sub>)  $\delta$  7.47 (dd, *J*=5.2, 1.3 Hz, 1H), 7.41 (m, 1H), 7.26 (d, *J*=5.2 Hz, 1H), 4.11 (q, *J*=7.1 Hz, 2H), 3.68 (d, *J*=1.0 Hz, 2H), 1.61 (s, 9H), 1.21 (t, *J*=7.1 Hz, 3H);  $^{13}\text{C}$  NMR (DMSO-*d*<sub>6</sub>)  $\delta$  170.09, 147.87, 137.43, 126.77, 126.47, 122.28, 114.39, 113.51, 83.80, 60.39, 31.56, 27.52, 14.02; MS *m/z* (%): 309 ( $\text{M}^+$ , 16), 253 (68), 209 (42), 136 (100), 57 (44); HRMS observed: 309.1034 ( $\text{M}^+$ ). Calcd: 309.1035; Anal. Calcd for  $\text{C}_{15}\text{H}_{19}\text{NO}_4\text{S}$ : C 58.23, H 6.19, N 4.54. found: C 58.28, H 6.24, N 4.48.

**Ethyl (6-(tert-butoxycarbonyl)-4-selenolo[2,3-b]pyrrolyl)acetate (13d):**

The reaction was carried out on 558 mg (1.50 mmol) of **4**. Allylation and ringclosure was carried out for 3 and 24 h respectively. EtOAc/n-heptane 1:9 as eluent gave 315 mg (59 %) of **13d** as a yellowish oil.  $^1\text{H}$  NMR (DMSO-*d*<sub>6</sub>)  $\delta$  7.72 (d, *J*=5.8 Hz, 1H), 7.37 (bs, 1H), 7.24 (d, *J*=5.8 Hz, 1H), 4.09 (q, *J*=7.1 Hz, 2H), 3.70 (d, *J*=0.8 Hz, 2H), 1.60 (s, 9H), 1.19 (t, *J*=7.1 Hz, 3H);  $^{13}\text{C}$  NMR (DMSO-*d*<sub>6</sub>)  $\delta$  170.56, 134.01, 131.79, 126.98, 122.40, 119.72, 115.46, 84.35, 60.26, 31.39, 27.49, 14.02; MS *m/z* (%): 357 ( $\text{M}^+$ +1, 28), 301 (100), 257 (26), 184 (81), 57 (93); HRMS observed: 357.0482 ( $\text{M}^+$ ). Calcd: 357.0479; Anal. Calcd for  $\text{C}_{15}\text{H}_{19}\text{NO}_4\text{Se}$ : C 50.57, H 5.38, N 3.93. found: C 50.63, H 5.44, N 4.06.

**Ethyl (5-nitro-1-(*tert*-butoxycarbonyl)-3-indolyl)acetate (13e):**

The reaction was carried out on 560 mg (1.54 mmol) of **5a**. Allylation and ringclosure was carried out for 3 and 19 h respectively. methylene chloride/*n*-heptane 7:3 as eluent gave 363 mg (68 %) of **13e** as brownish crystals. mp 84-86 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.49 (d, J=2.1 Hz, 1H), 8.27 (d, J=9.2 Hz, 1H), 8.22 (dd, J=9.2, 2.1 Hz, 1H), 7.72 (bs unresolved, 1H), 4.20 (q, J=7.1 Hz, 2H), 3.75 (d, J=1.0 Hz, 2H), 1.68 (s, 9H), 1.29 (t, J=7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 170.42, 148.79, 143.67, 138.60, 130.08, 127.37, 119.83, 115.75, 115.49, 114.10, 85.13, 61.38, 30.88, 28.10, 14.17; MS m/z (%): 348 (M<sup>+</sup>, 7), 292 (35), 248 (38), 175 (66), 57 (100); HRMS observed: 348.1324 (M<sup>+</sup>). Calcd: 348.1322; Anal. Calcd for C<sub>17</sub>H<sub>20</sub>N<sub>2</sub>O<sub>6</sub>: C 58.61, H 5.79, N 8.04. found: C 58.96, H 5.95, N 7.80.

**Ethyl (5-methoxy-1-(*tert*-butoxycarbonyl)-3-indolyl)acetate (13f):**

The reaction was carried out on 529 mg (1.50 mmol) of **5c**. Allylation and ringclosure was carried out for 94 and 5 h respectively, with two additions of crotonate after 28 and 49 h. EtOAc/*n*-heptane 15:85 as eluent gave 337 mg (67 %, 72 % based on consumed **5c**) of **13f** as a slight yellow oil, together with 36 mg **5c**. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.02 (bd, J=9.0 Hz, 1H), 7.55 (bs, unresolved, 1H), 7.00 (d, J=2.5 Hz, 1H), 6.94 (dd, J=9.0, 2.5 Hz, 1H), 4.18 (q, J=7.1 Hz, 2H), 3.86 (s, 3H), 3.67 (d, J=1.0 Hz, 2H), 1.65 (s, 9H), 1.27 (t, J=7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 171.02, 155.89, 149.55, 130.93, 130.13, 125.03, 116.00, 113.17, 113.01, 101.84, 83.43, 61.02, 55.70, 31.32, 28.21, 14.24; MS m/z (%): 333 (M<sup>+</sup>, 24), 277 (100), 233 (23), 204 (25), 188 (2), 160 (99), 57 (37); HRMS observed: 333.1576 (M<sup>+</sup>). Calcd: 333.1576; Anal. Calcd for C<sub>18</sub>H<sub>23</sub>NO<sub>5</sub>: C 64.85, H 6.95, N 4.20. found: C 64.93, H 6.98, N 4.26.

**Ethyl (5-bromo-1-(*tert*-butoxycarbonyl)-3-indolyl)acetate (13g):**

The reaction was carried out on 596 mg (1.50 mmol) of **5b**. Allylation and ringclosure was carried out for 30 and 24 h respectively. Ringclosure was in this case performed at room temperature. EtOAc/*n*-heptane 2:8 as eluent gave 381 mg (67 %) of **14g** as a colorless oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.02 (bd, J=8.9 Hz, 1H), 7.67 (d, J=1.9 Hz, 1H), 7.56 (s, 1H), 7.40 (dd, J=8.9, 1.9 Hz, 1H), 4.19 (q, J=7.1 Hz, 2H), 3.65 (d, J=1.0 Hz, 2H), 1.67 (s, 9H), 1.29 (t, J=7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 170.70, 149.22, 134.20, 131.83, 127.35, 125.56, 121.93, 116.72, 116.01, 112.55, 84.09, 61.16, 31.04, 28.16, 14.20; MS m/z (%): 381/383 (M<sup>+</sup>, 15), 325 / 327 (52), 281 / 283 (32), 252 / 254 (14), 208 / 210 (79), 57 (100); HRMS observed: 383.0555 (M<sup>+</sup>). Calcd: 383.0556; Anal. Calcd for C<sub>17</sub>H<sub>20</sub>BrNO<sub>4</sub>: C 53.41, H 5.27, N 3.67. found: C 53.32, H 5.25, N 3.74.

**General procedure for synthesis of carbethoxymethylene-oxothienopyrrole carboxylic acid ethyl esters (10a, b) by one pot reaction (table 3):**

In one portion with stirring, 488 mg (3.00 mmol) of ethoxyfumaroyl chloride was added to a mixture of 650 mg (2.00 mmol) *o*-iodo-*N*-(*tert*-butoxycarbonylamino)thiophene (**1**, **2**), 2.02 g (20 mmol, 2.80 ml) of TEA, and 24 mg (0.20 mmol) of DMAP in THF (10ml). The mixture was stirred at the indicated temperature until starting aminothiophene was totally consumed as monitored by TLC. If the reaction was slow, and the ethoxyfumaroyl chloride was consumed before completion, another 163 mg (1 mmol) portion of this material was added. Thereafter, 24 mg (0.10 mmol) of palladium acetate and 52 mg (0.20 mmol) of triphenylphosphine, was added. The mixture was thereafter stirred for the time, and at the temperature indicated. Purification was achieved by evaporating the reaction mixture with 3 g silica gel (100-200 mesh) followed by chromatography (EtOAc/*n*-heptane 1:9).

**(E)-4-(Carboethoxymethylene)-5-oxo-6-(tert-butoxycarbonyl)-4,5-dihydro-thieno[2,3-b]pyrrole (10a):**

The acryloylation and ringclosure respectively was carried out for 1 h at room temperature, and 5 h at reflux. After purification, 352 mg (54 %) of **10a** was obtained as yellow crystals. mp 123-125 °C;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.71 (d,  $J=5.5$  Hz, 1H), 6.90 (d,  $J=5.5$  Hz, 1H), 6.57 (s, 1H), 4.30 (q,  $J=7.2$  Hz, 2H), 1.65 (s, 9H), 1.38 (t,  $J=7.2$  Hz, 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  166.41, 165.49, 149.93, 147.02, 134.83, 124.28, 120.87, 119.84, 117.21, 85.60, 61.09, 28.04, 14.23; MS  $m/z$  (%): 323 ( $\text{M}^+$ , 7), 223 (100), 150 (49), 57 (39); HRMS observed: 323.0826 ( $\text{M}^+$ ). Calcd: 323.0828; Anal. Calcd for  $\text{C}_{15}\text{H}_{17}\text{NO}_5\text{S}$ : C 55.71, H 5.30, N 4.33. found: C 55.82, H 5.41, N 4.38.

**(E)-3-(Carboethoxymethylene)-2-oxo-1-(tert-butoxycarbonyl)-2,3-dihydro-thieno[3,4-b]pyrrole (10b):**

The acryloylation was carried out for 50 h at reflux, with another addition of ethoxyfumaryl chloride after 28 h. Ringclosure was carried out at 40 °C for 72 h. After purification, 173 mg (27 %, 37 % based on consumed **2**) of **10b** was obtained as yellow crystals, together with 183 mg **2**. mp 118-120 °C;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  8.46 (dd,  $J=2.7, 0.6$  Hz, 1H), 7.00 (d,  $J=2.7$  Hz, 1H), 6.76 (d,  $J=0.6$  Hz, 1H), 4.31 (q,  $J=7.1$  Hz, 2H), 1.64 (s, 9H), 1.36 (t,  $J=7.1$  Hz, 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  167.57, 165.65, 148.21, 138.83, 134.45, 129.44, 124.95, 119.92, 104.44, 84.77, 61.20, 28.05, 14.20; MS  $m/z$  (%): 323 ( $\text{M}^+$ , 9), 223 (100), 150 (24), 57 (48); HRMS observed: 323.0821 ( $\text{M}^+$ ). Calcd: 323.0828; Anal. Calcd for  $\text{C}_{15}\text{H}_{17}\text{NO}_5\text{S}$ : C 55.71, H 5.30, N 4.33. found: C 54.78, H 5.42, N 4.31.

**(E)-6-(Carboethoxymethylene)-5-oxo-4-(tert-butoxycarbonyl)-5,6-dihydro-thieno[3,2-b]pyrrole (10c):**

A solution of 226 mg (0.50 mmol) **9c**, 506 mg (5.0 mmol, 0.69 ml) of TEA, 6 mg (0.025 mmol) of palladium acetate, and 13 mg (0.050 mmol) of triphenylphosphine was stirred at room temperature for 96 h. The mixture was thereafter evaporated with 1.5 g silica gel (100-200 mesh) and purified by chromatography (EtOAc/n-heptane 2:8) to give 29 mg (18 %, 21 % based on consumed **9c**) of **10c** as a yellow oil, together with 36 mg **9c**.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.61 (dd,  $J=5.3, 0.7$  Hz, 1H), 7.31 (d,  $J=5.3$  Hz, 1H), 6.53 (d,  $J=0.7$  Hz, 1H), 4.32 (q,  $J=7.1$  Hz, 2H), 1.63 (s, 9H), 1.38 (t,  $J=7.1$  Hz, 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  167.18, 166.57, 148.23, 147.54, 135.88, 135.39, 117.28, 116.95, 114.39, 84.64, 61.30, 28.08, 14.28; MS  $m/z$  (%): 323 ( $\text{M}^+$ , 7), 223 (100), 151 (34), 57 (46); HRMS observed: 323.0824 ( $\text{M}^+$ ). Calcd: 323.0828.

**General procedure for thermal removal of N-BOC substituent (table 4):**

A solution of the corresponding N-BOC-substituted substrate (**10a-c**, **13a**, **c-g**, **9a**) in methylene chloride, was evaporated with 10 times its weight of silica gel (100-200 mesh). This gel was then evacuated (1 mmHg) at 50 °C using Kugelrohr equipment with protection from light for 24 h. Purification was achieved on a short silica gel column to remove minor polar impurities.

**Ethyl (6-H-4-thieno[2,3-b]pyrrolyl)acetate (14a):**

The reaction was carried out on 317 mg (1.02 mmol) of **13a**.

Methylene chloride was used as eluent to give 198 mg (92 %) of **14a** as a yellowish oil.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 200 mg / ml)  $\delta$  8.53 (bs, 1H), 7.04 (d,  $J=5.3$  Hz, 1H), 6.85 (dd,  $J=5.3, 1.0$  Hz, 1H), 6.74 (m, 1H), 4.23 (q,  $J=7.1$  Hz, 2H), 3.71 (s, 2H), 1.31 (t,  $J=7.1$  Hz, 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  172.24, 133.68, 130.88, 122.60, 118.08, 117.00, 108.65, 60.86, 32.68, 14.26; MS  $m/z$  (%): 209 ( $\text{M}^+$ , 43), 136 (100); HRMS observed: 209.0508 ( $\text{M}^+$ ). Calcd: 209.0511;

Anal. Calcd for C<sub>10</sub>H<sub>11</sub>NO<sub>2</sub>S: C 57.39, H 5.30, N 6.70. found: C 57.27, H 5.22, N 6.75.

**Ethyl (4-H-6-thieno[3,2-b]pyrrolyl)acetate (14c):**

The reaction was carried out on 290 mg (0.937 mmol) of **13c**. Methylene chloride was used as eluent to give 169 mg (86 %) of **14c** as a yellowish oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.10 (dd, J=5.2, 1.3 Hz, 1H), 6.86 (d, J=5.2 Hz, 1H), 6.79 (s, 1H), 4.22 (q, J=7.1 Hz, 2H), 3.67 (s, 2H), 1.32 (t, J=7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 171.96, 138.82, 123.85, 123.56, 121.68, 111.49, 108.63, 61.04, 32.88, 14.30; MS m/z (%): 209 (M<sup>+</sup>, 48), 136 (100); HRMS observed: 209.0511 (M<sup>+</sup>). Calcd: 209.0511; Anal. Calcd for C<sub>10</sub>H<sub>11</sub>NO<sub>2</sub>S: C 57.39, H 5.30, N 6.70. found: C 57.44, H 5.27, N 6.75.

**Ethyl (6-H-4-selenolo[2,3-b]pyrrolyl)acetate (14d):**

The reaction was carried out on 215 mg (0.603 mmol) of **13d**. EtOAc/n-heptane 3:7 was used as eluent to give 89 mg (58 %) of **14d** as a yellowish oil that rapidly darkened. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.38 (dd, J=5.7, 0.9 Hz, 1H), 7.24 (d, J=5.7 Hz, 1H), 6.82 (m, 1H), 4.18 (q, J=7.1 Hz, 2H), 3.68 (d, J=0.9 Hz, 2H), 1.28 (t, J=7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 172.32, 132.42, 131.25, 122.69, 121.47, 120.04, 110.08, 60.90, 32.71, 14.27; MS m/z (%): 257 (M<sup>+</sup>+1, 68), 184 (100); HRMS observed: 256.9953 (M<sup>+</sup>). Calcd: 256.9955; Anal. Calcd for C<sub>10</sub>H<sub>11</sub>NO<sub>2</sub>Se: C 46.88, H 4.33, N 5.47. found: C 46.50, H 4.14, N 5.35.

**(E)-4-(Carboethoxymethylene)-5-oxo-4,5-dihydro-6-H-thienol[2,3-b]pyrrole (11a):**

The reaction was carried out on 116 mg (0.360 mmol) of **10a**. EtOAc/n-heptane 3:7 was used as eluent to give 70 mg (87 %) of **11a** as deep red crystals. mp 160-162 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.36 (bs, 1H), 7.61 (d, J=5.3 Hz, 1H), 6.71 (d, J=5.3 Hz, 1H), 6.52 (s, 1H), 4.31 (q, J=7.1 Hz, 2H), 1.37 (t, J=7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 172.08, 165.89, 152.00, 135.59, 124.91, 121.15, 116.53, 116.04, 61.00, 14.27; MS m/z (%): 223 (M<sup>+</sup>, 100), 195 (18), 178 (30), 151 (22), 150 (86); HRMS observed: 223.0311 (M<sup>+</sup>). Calcd: 223.0303.

**(E)-3-(Carboethoxymethylene)-2-oxo-2,3-dihydro-1-H-thienol[3,4-b]pyrrole (11b):**

The reaction was carried out on 125 mg (0.387 mmol) of **10b**. EtOAc/n-heptane 3:7 was used as eluent to give 67 mg (77 %) of **11b** as bright yellow crystals. mp 158-159 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.81 (bs, 1H), 8.33 (d, J=2.5 Hz, 1H), 6.70 (s, 1H), 6.31 (d, J=2.5 Hz, 1H), 4.32 (q, J=7.2 Hz, 2H), 1.37 (t, J=7.2 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 172.35, 165.90, 140.63, 135.79, 129.87, 126.76, 119.04, 96.98, 61.10, 14.26; MS m/z (%): 223 (M<sup>+</sup>, 100), 195 (8), 178 (45), 151 (32), 150 (73); HRMS observed: 223.0300 (M<sup>+</sup>). Calcd: 223.0303; Anal. Calcd for C<sub>10</sub>H<sub>9</sub>NO<sub>3</sub>S: C 53.80, H 4.06, N 6.28. found: C 53.68, H 3.92, N 6.34.

**(E)-6-(Carboethoxymethylene)-5-oxo-5,6-dihydro-4-H-thienol[3,2-b]pyrrole (11c):**

The reaction was carried out on 18 mg (56 μmol) of **10c**. EtOAc/n-heptane 3:7 was used as eluent to give 9 mg (76 %) of **11c** as orange crystals. mp ~190 °C dec.; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.74 (bs, 1H), 7.57 (dd, J=5.2, 0.7 Hz, 1H), 6.74 (d, J=5.2 Hz, 1H), 6.71 (d, J=0.7 Hz, 1H), 4.34 (q, J=7.1 Hz, 2H), 1.37 (t, J=7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 171.63, 166.88, 149.62, 136.65, 136.42, 115.35, 113.78, 112.31, 61.18, 14.34; MS m/z (%): 223 (M<sup>+</sup>, 100), 195 (15), 178 (48), 151 (71), 150 (39); HRMS observed: 223.0306 (M<sup>+</sup>). Calcd: 223.0303.



**Ethyl (5-nitro-1-H-3-indolyl)acetate (14e):**

The reaction was carried out on 310 mg (0.890 mmol) of **13e**. EtOAc/n-heptane 1:1 was used as eluent to give 197 mg (89 %) of **14e** as yellow crystals. mp 86-88 °C (lit.<sup>32</sup> 109-110 °C); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.69 (bs, 1H), 8.60 (d, J=2.2 Hz, 1H), 8.18 (dd, J=9.0, 2.2 Hz, 1H), 7.34 (d, J=9.0 Hz, 1H), 6.99 (m, 1H), 4.21 (q, J=7.1 Hz, 2H), 3.81 (d, J=0.8 Hz, 2H), 1.31 (t, J=7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 171.54, 142.69, 141.81, 139.12, 126.75, 126.28, 117.86, 116.45, 111.23, 61.24, 31.04, 14.20; MS m/z (%): 248 (M<sup>+</sup>, 37), 175 (100), 129 (38); HRMS observed: 248.0790 (M<sup>+</sup>). Calcd: 248.0797; Anal. Calcd for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>4</sub>: C 58.06, H 4.87, N 11.29. found: C 57.93, H 4.81, N 11.19.

**Ethyl (5-methoxy-1-H-3-indolyl)acetate (14f):**

The reaction was carried out on 139 mg (0.417 mmol) of **13f**. EtOAc/n-heptane 3:7 was used as eluent to give 86 mg (89 %) of **14f** as pale crystals. mp 90-92 °C (lit.<sup>33</sup> 89-91 °C). The <sup>1</sup>H NMR-spectra was in accordance with previously reported<sup>33,34</sup>.

**Ethyl (5-bromo-1-H-3-indolyl)acetate (14g):**

The reaction was carried out on 324 mg (0.848 mmol) of **13g**. EtOAc/n-heptane 3:7 was used as eluent to give 189 mg (79 %) of **14g** as redish crystals. mp 39-40 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.21 (bs, 1H), 7.75 (m, 1H), 7.26 (dd, J=8.7, 1.8 Hz, 1H), 7.17 (d, J=8.7 Hz, 1H), 7.10 (m, 1H), 4.19 (q, J=7.1 Hz, 2H), 3.72 (d, J=0.8 Hz, 2H), 1.29 (t, J=7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 171.89, 134.76, 129.00, 125.03, 124.36, 121.60, 112.94, 112.66, 108.24, 60.99, 31.24, 14.24; MS m/z (%): 281 / 283 (M<sup>+</sup>, 36), 208 / 210 (100), 129 (28); HRMS observed: 283.0036 (M<sup>+</sup>). Calcd: 283.0032; Anal. Calcd for C<sub>12</sub>H<sub>12</sub>BrNO<sub>2</sub>: C 51.08, H 4.29, N 4.97. found: C 51.17, H 4.25, N 5.08.

**2-(N-Ethoxyfumaroylamino)-3-iodothiophene (16):**

The reaction was carried out on 667 mg (1.48 mmol) of **9a**. EtOAc/n-heptane 3:7 was used as eluent to give 422 mg (81 %) of **16** as bright yellow crystals. mp 137-138 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.16 (bs, 1H), 7.13 (d, J=15.2 Hz, 1H), 7.04 (d, J=5.6 Hz, 1H), 7.00 (d, J=15.2 Hz, 1H), 6.04 (d, J=5.6 Hz, 1H), 4.29 (q, J=7.2 Hz, 2H), 1.35 (t, J=7.2 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 165.07, 159.79, 136.25, 134.07, 132.85, 130.41, 120.58, 66.04, 61.57, 14.16; MS m/z (%): 351 (M<sup>+</sup>, 83), 225 (99), 127 (100), 99 (53); HRMS observed: 350.9432 (M<sup>+</sup>). Calcd: 350.9425; Anal. Calcd for C<sub>10</sub>H<sub>10</sub>INO<sub>3</sub>S: C 34.20, H 2.87, N 3.99. found: C 34.08, H 2.87, N 3.89.

**Ethyl (5-oxo-6-(tert-butoxycarbonyl)-4,5-dihydro-4-thieno[2,3-b]pyrrolyl)acetate (18):**

A solution of 309 mg (0.956 mmol) **10a** and 88 mg (96 μmol) of (PPh<sub>3</sub>)<sub>3</sub>RhCl in abs. ethanol (100 ml) was hydrogenated (Parr, 6 kg / cm<sup>2</sup>, room temperature) for 58 h. The reaction mixture was thereafter evaporated with 2 g silica gel (100-200 mesh), and purified twice by chromatography (EtOAc/n-heptane 2:8) to give 209 mg (67 %) of **18** as a yellow oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 6.92 (d, J=5.2 Hz, 1H), 6.82 (d, J=5.2 Hz, 1H), 4.12 (dq, 1.4 Hz, J=7.1 Hz, 2H), 3.91 (dd, J=8.8, 4.3 Hz, 1H), 3.05 (dd, J=16.8, 4.3 Hz, 1H), 2.73 (dd, J=16.8, 8.8 Hz, 1H), 1.62 (s, 9H), 1.21 (t, J=7.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 175.91, 170.51, 147.48, 140.06, 123.89, 121.09, 119.96, 85.10, 61.08, 43.96, 35.46, 28.05, 14.06; MS m/z (%): 325 (M<sup>+</sup>, 4), 269 (4), 225 (36), 151 (100), 57 (33); HRMS observed: 325.0981 (M<sup>+</sup>). Calcd: 325.0984; Anal. Calcd for C<sub>15</sub>H<sub>19</sub>NO<sub>5</sub>S: C 55.37, H 5.89, N 4.31. found: C 55.45, H 5.82, N 4.39.

**Ethyl (5-oxo-4,5-dihydro-6-H-4-thieno[2,3-b]pyrrolyl)acetate (19):**

A solution of 11 mg (50  $\mu\text{mol}$ ) **11a** and 4.6 mg (5.0  $\mu\text{mol}$ ) of  $(\text{PPh}_3)_3\text{RhCl}$  in abs. ethanol (10 ml), was hydrogenated (Parr, 6 kg /  $\text{cm}^2$ , 60 °C) for 120 h. The reaction mixture was thereafter evaporated with 0.5 g silica gel (100-200 mesh), and purified by chromatography (EtOAc/n-heptane 3:7) to give 6.4 mg (57 %, 67 % based on consumed **11a**) of **19**, together with 1.5 mg of **11a**.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.08 (bs, 1H), 6.81 (d,  $J=5.2$  Hz, 1H), 6.74 (d,  $J=5.2$  Hz, 1H), 4.16 (q,  $J=7.1$  Hz, 2H), 3.78 (dd,  $J=9.4, 4.4$  Hz, 1H), 3.04 (dd,  $J=16.7, 4.4$  Hz, 1H), 2.66 (dd,  $J=16.7, 9.4$  Hz, 1H), 1.25 (t,  $J=7.1$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  181.73, 171.04, 141.13, 126.22, 122.00, 116.34, 61.00, 43.00, 35.02, 14.15; MS  $m/z$  (%): 225 ( $\text{M}^+$ , 33), 180 (9), 179 (9), 151 (100); HRMS observed: 225.0460 ( $\text{M}^+$ ). Calcd: 225.0460.

**Potassium (6-H-4-thieno[2,3-b]pyrrolyl)acetate (20):**

To 77 mg (0.368 mmol) of **14a**, 2.20 ml (0.167 M, 1.0 equiv.) potassium hydroxide in ethanol (95 %) was added. The mixture was stirred for 24 h at room temperature, followed by removal of the solvent in vacuo. The residue was thereafter dissolved in water (10 ml), and washed with diethyl ether (5 ml). Lyophilisation of the water phase yielded 81 mg (quant. yield) of **20** as a slightly colored solid.  $^1\text{H}$  NMR ( $\text{D}_2\text{O}$ )  $\delta$  7.01 (d,  $J=5.5$  Hz, 1H), 6.95 (s, 1H), 6.92 (d,  $J=5.5$  Hz, 1H), 3.51 (s, 2H);  $^{13}\text{C}$  NMR ( $\text{D}_2\text{O}$ )  $\delta$  184.25, 136.25, 132.91, 125.67, 121.11, 119.48, 113.61, 37.89.

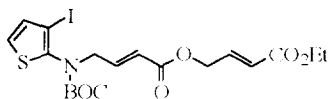
**Potassium (4-H-6-thieno[3,2-b]pyrrolyl)acetate (21):**

The title compound was synthesised as above, with the following exceptions: As starting material was used 116 mg (0.554 mmol) of **14e** to give 121 mg (quant. yield) of **21** as a slightly colored solid.  $^1\text{H}$  NMR ( $\text{D}_2\text{O}$ )  $\delta$  7.12 (dd,  $J=5.2, 1.4$  Hz, 1H), 6.97 (d,  $J=5.2$  Hz, 1H), 6.90 (m, 1H), 3.42 (d,  $J=0.8$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{D}_2\text{O}$ )  $\delta$  183.52, 141.47, 126.56, 125.32, 124.81, 114.86, 113.71, 38.10.

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