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Note

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A Palladium-Catalyzed Cyclocarbonylation Approach to Thiadiazafluorenones.

A Correction

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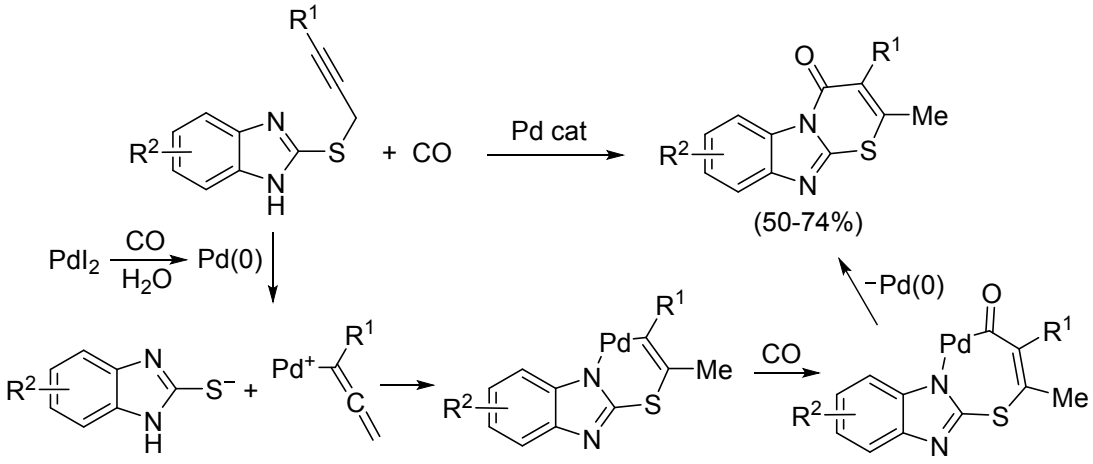


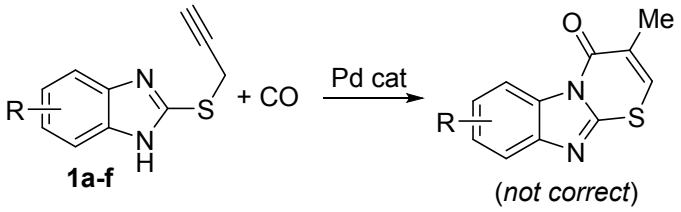
Abstract

The palladium-catalyzed carbonylation of 2-(propynylthio)benzimidazoles bearing a terminal triple bond leads to 2-methyl-1-thia-4a,9-diazafluoren-4-ones, instead of the previously reported 3-methyl isomers, as unequivocally established by XRD analysis of a representative product. A correction is therefore provided here in order to rectify the previous erroneous assignment of the position of the methyl group. Moreover, the process has been generalized to substrates bearing an internal triple bond, which led to 3-alkyl-2-methyl-1-thia-4a,9-diazafluoren-4-ones, whose structure was confirmed by XRD analysis of two representative derivatives.

1-Thiadiazafluoren-4-one derivatives are polyheterocyclic compounds of particular interest, as they are known to possess significant pharmacological activities,[1,2] including cardiotonic activity.[2] Their importance justifies the continuous interest in developing novel synthetic approaches starting from relatively simple and available substrates.[3]

In the course of our studies on carbonylation reactions leading to polyheterocyclic compounds, we investigated the reactivity of 2-(propynylthio)benzimidazoles bearing a terminal triple bond (**1a-f**) with carbon monoxide in the presence of the PdI_2/KI catalytic system under non-oxidative conditions. We published the results obtained, and assigned the structure of the products as 3-methyl-1-thia-4*a*,9-diazafluoren-4-ones (Scheme 1).[4] We here reassign the structure of those products as the corresponding 2-methyl isomers, based on the results obtained with 2-(propynylthio)benzimidazoles bearing an internal triple bond and X-ray structural determination of representative products.

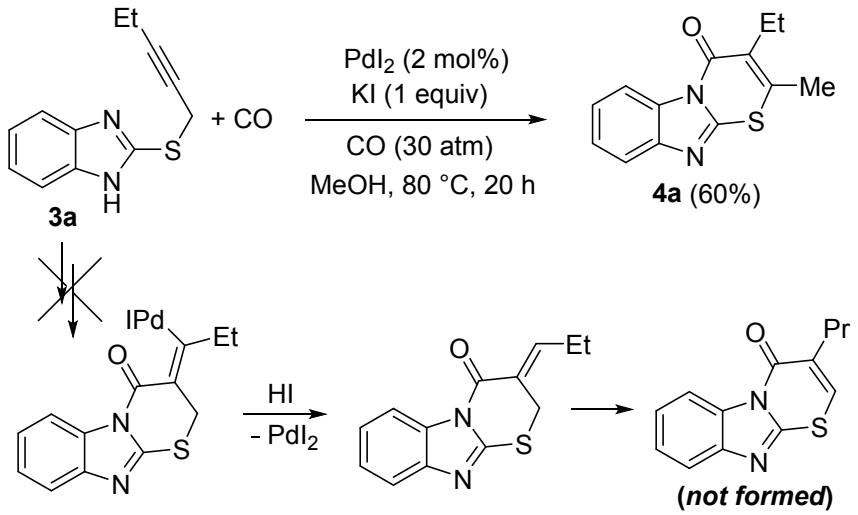
Scheme 1. Previously Reported Palladium-Catalyzed Cyclocarbonylation of 2-(Propynylthio)benzimidazoles Bearing a Terminal Triple Bond 1a-f[4]



We originally optimized the reactivity of **1a-f** and carried out the carbonylation reactions in EtOH at 100 °C for 3 h, under a 5/2 mixture of CO–CO_2 at 70 atm, in the presence of PdI_2 (2 mol%) and KI (1 equiv).[4] Methyl-substituted 1-thia-4*a*,9-diazafluoren-4-ones were obtained, as confirmed by spectrometric and spectroscopic data, by an additive carbonylation process. A relatively simple mechanism, involving *N*-palladation followed by CO insertion, triple bond insertion, protonolysis, and isomerization, seemed in agreement with the formation of 3-methyl-substituted thiadiazafluorenones, as shown in Scheme S1 (Supporting Information).[4]

To further expand the synthetic scope of the process, we have investigated the reactivity of substrates bearing an internal triple bond. Surprisingly, however, the carbonylation reaction of 2-(pent-2-yn-1-ylthio)-1*H*-benzo[*d*]imidazole **3a** did not lead to the expected 3-propyl-substituted derivative, but to thiadiazofluorenone **4a** bearing a methyl group at C-2 and an ethyl group at C-3 (Scheme 2),[5] as confirmed by XRD analysis (Figure 1).[6]

Scheme 2. Formation of 3-Ethyl-2-methyl-1-thia-4*a*,9-diazafluoren-4-one 4a from 2-(Pent-2-yn-1-ylthio)-1*H*-benzo[*d*]imidazole 3a



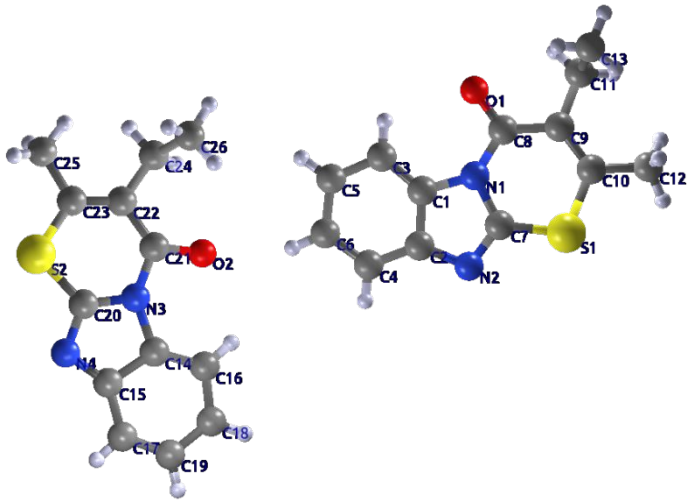


Figure 1. X-Ray Structure of 3-Ethyl-2-methyl-1-thia-4*a*,9-diazafluoren-4-one **4a**, Showing the Atom Labelling Scheme[6]

This unexpected result prompted us to reinvestigate the structure of the methyl-substituted products obtained starting from substrates bearing a terminal triple bond, which, by analogy to **4a**, could actually have corresponded to the 2-methyl-substituted isomers rather than the originally proposed[4] 3-methyl-substituted compounds. A single crystal X-ray analysis of the product obtained from the carbonylation of 2-(prop-2-ynylthio)-1*H*-benzo[*d*]imidazole **1a**[4] indeed confirmed that the methyl group occupies the C-2 rather than the C-3 position, and thus corresponds to 2-methyl-1-thia-4*a*,9-diazafluoren-4-one **2a**, as shown in Figure 2. This means that the structures of all products obtained in our original publication (with the methyl group at C-3)[4] should be corrected to the corresponding 2-methyl-substituted isomers **2a–f**, as shown in Table S1 (Supporting Information).

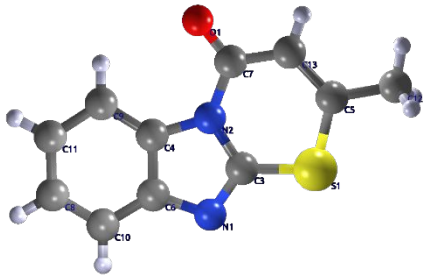


Figure 2. X-Ray Structure of 2-Methyl-1-thia-4*a*,9-diazafluoren-4-one **2a**, Showing the Atom Labelling Scheme[6]

The process has then been generalized to other differently substituted substrates **3b–i**, bearing various alkyl groups on the triple bond and electron-withdrawing as well as π-donating groups on the aromatic ring. As can be seen from the results shown in Table 1, the reaction was quite general, and the corresponding 3-alkyl-2-methyl-1-thia-4*a*,9-diazafluoren-4-ones **4** were isolated in fair yields (50-60 %). The C-2 position of the methyl group was further confirmed by the XRD analysis of product **4f**, bearing two methoxy substituents of the aromatic ring (Figure 3).

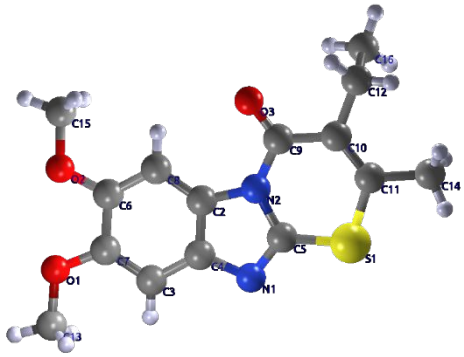
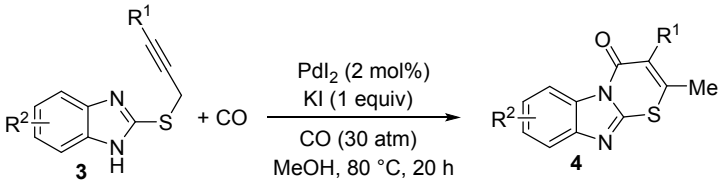
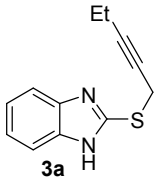
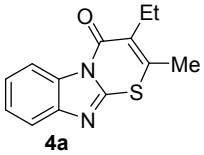
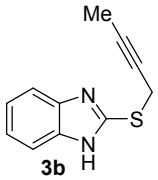
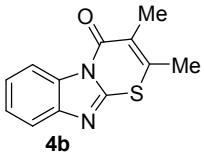
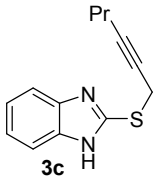
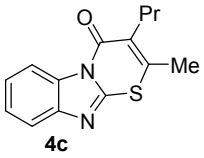
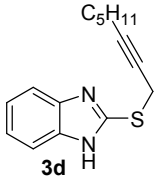
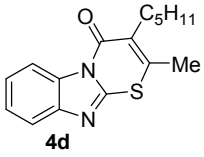
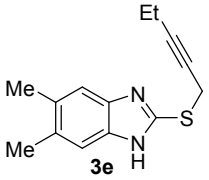
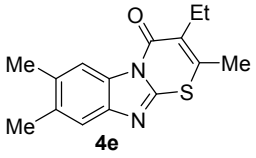
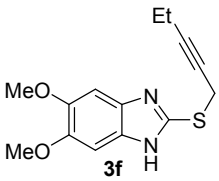
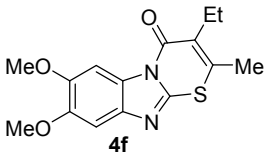
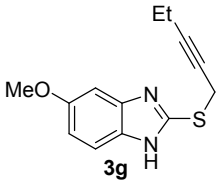
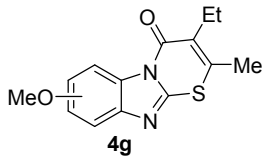
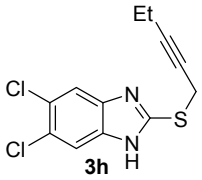
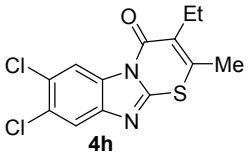
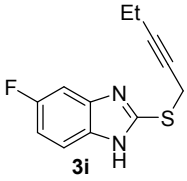
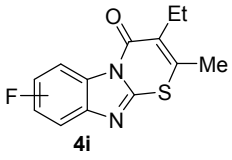


Figure 3. X-Ray Structure of 3-Ethyl-6,7-Dimethoxy-2-methyl-1-thia-4*a*,9-diazafluoren-4-one **4f**, Showing the Atom Labelling Scheme[6]

Table 1. Synthesis 3-Alkyl-2-methyl-1-thia-4*a*,9-diazafluoren-4-ones 4a-i by Palladium-Catalyzed Carbonylation of 2-(Alkynylthio)benzimidazoles 3a-i Bearing an Internal Triple Bond[a]



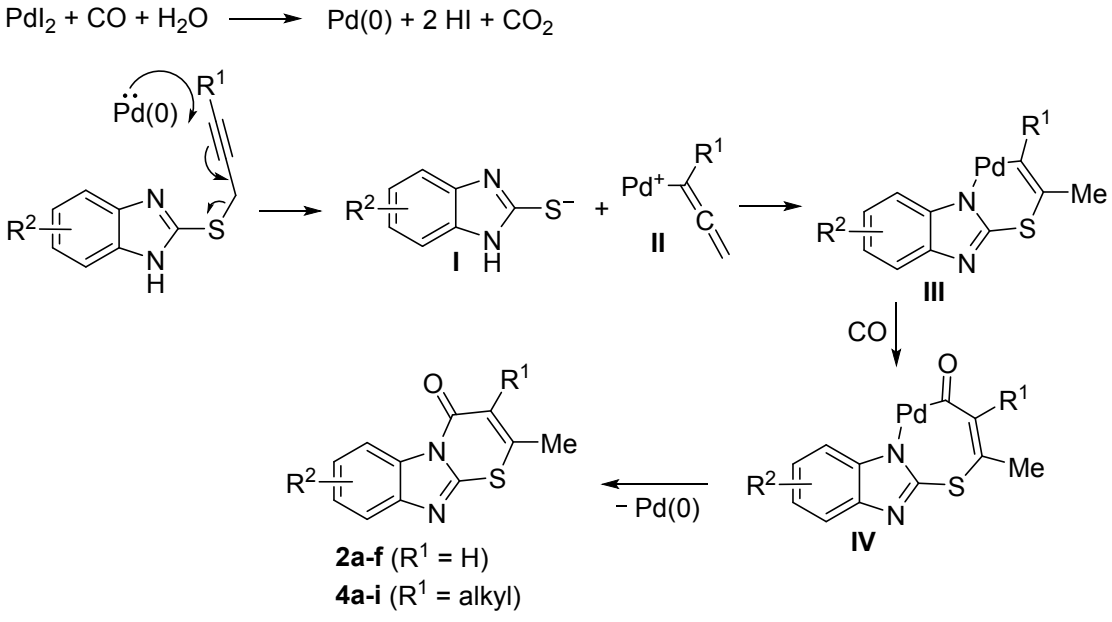
Entry	**3**	**4**	Yield of **4**[b] (%)
1			60
2			55

3	 **3c**	 **4c**	57
4	 **3d**	 **4d**	55
5	 **3e**	 **4e**	56
6	 **3f**	 **4f**	50
7	 **3g**	 **4g**	57[c]
8	 **3h**	 **4h**	59
9	 **3i**	 **4i**	57[d]

[a] All reactions were carried out at 80 °C under 30 atm (at 25 °C) of CO, in MeOH as the solvent (substrate concentration: 0.2 mmol of **1** per mL of solvent), and in the presence of 2 mol% of PdI_2 and 1 equiv of KI. [b] Isolated yield, based on starting material **1**. [c] Mixture of regioisomers (~3/1 by ^{1}H NMR). [d] Mixture of regioisomers (~1.1/1 by ^{1}H NMR).

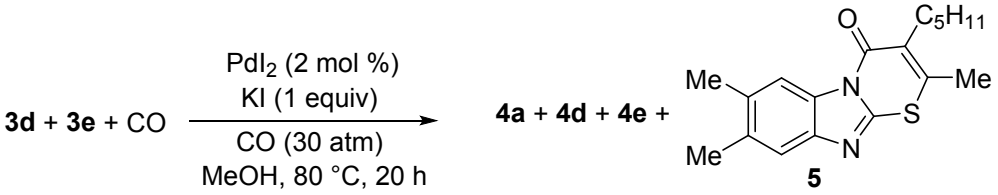
Mechanistically, formation of 2-methyl-substituted products **2a–f** (Table S1, Supporting Information) and **4a-i** (Table 1) must imply some kind of structural rearrangement. Most likely, this takes place by Pd(0)-promoted propargyl-allene rearrangement,[7] occurring through formal Pd(0) attack to the terminal carbon of the triple bond, with elimination of a thiolate **I** and formation of the allenylpalladium intermediate **II** (Scheme 3). Formation of an iodide-stabilized palladium(0) species under our conditions may take place by the water-gas shift reaction between PdI_2, CO and traces of water present in the reaction mixture, as already observed by us under similar conditions.[8] Addition of the thiolate **I** to the allenic moiety of **II** then leads to palladacycle intermediate **III**. The latter undergoes carbon monoxide insertion to give **IV**, from which the final product is formed by reductive elimination (Scheme 3).

Scheme 3. Proposed Mechanistic Pathway for the Palladium-Catalyzed Cyclocarbonylation of 2-(Prop-2-ynylthio)-1*H*-benzo[*d*]imidazoles 1a-f and 3a-i Leading to 2-Methyl-1-thia-4*a*,9-diazafluoren-4-ones 2a-f and 4a-i, respectively



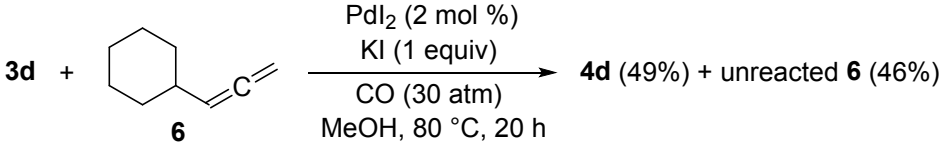
To corroborate this mechanistic hypothesis, we carried out a cross-over experiment, by allowing to react an equimolar mixture of substrates **3d** and **3e** under the optimized conditions (Scheme 4). The GLC-MS analysis of the reaction mixture evidenced the formation of four products (**4a**, **4d**, **4e**, and **5**) (Scheme 4), deriving from the addition of the two different thiolates to the two different allenylpalladium complexes deriving from **3d** and **3e**, which is clearly in agreement with the proposed mechanism (Scheme 3).[9]

Scheme 4. Cross-over Experiment: Formation of a Mixture of Thiadiazafluorenones 4a, 4d, 4e, and 5 from Carbonylation of a Mixture of Substrates 3d and 3e



We also verified if free allenes (possibly deriving from protonolysis of complex **II**) were involved as intermediates in the formation of final bicyclic products. However, as shown in Scheme 5, the carbonylation of **3d** together with commercially available cyclohexylallene **6** only gave the diazafluorenone **4d** (49% yield) without any formation of the mixed product resulting from allene incorporation.[10] This result strongly suggests that protonolysis of complex **II** to give a free allene does not occur in our process, and that, according to Scheme 3, this intermediate preferentially undergoes direct attack by thiolate **I**.

Scheme 5. Carbonylation of 3d in the presence of cyclohexylallene 6



In conclusion, in this Note we have corrected the structure of the products obtained from PdI_2/KI-catalyzed carbonylation of 2-(propynylthio)benzimidazoles bearing a terminal triple bond **1**. In fact, as confirmed by XRD analysis, 2-methyl-1-thia-4*a*,9-diazafluoren-4-ones **2** are formed, instead of the previously reported[4] 3-methyl isomers. We have also extended the process to the use of substrates bearing an internal triple bond **3**, which, in a similar way, led to the corresponding 3-alkyl-2-methyl-1-thia-4*a*,9-diazafluoren-4-ones **4**, as confirmed by XRD analysis. Product formation must ensue from some unexpected kind of structural rearrangement, most likely occurring through palladium-promoted propargyl-allene rearrangement to give a thiolate and an allenylpalladium intermediate, followed by thiolate addition to the central allenic carbon and cyclocarbonylation.

EXPERIMENTAL SECTION

General Experimental Methods. Solvents and chemicals were reagent grade and used without further purification. All reactions were analyzed by TLC on silica gel 60 F254 and by GLC using capillary columns with polymethylsilicone +5% phenylsilicone as the stationary phase. Column chromatography was performed on silica gel 60 (70–230 mesh) or alumina gel 90 (70–230 mesh). Evaporation refers to the removal of solvent under reduced pressure. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C on a 300 or 500 MHz spectrometers in $CDCl_3$, DMSO-d_6, or CD_3OD solutions with Me_4Si as the internal standard. ^{19}F NMR spectra were recorded at 25 °C on a 500 MHz spectrometer in $CDCl_3$ solutions at 471 MHz with CF_2Br_2 or $CFCl_3$ as the internal standard. Chemical shifts (δ) and coupling constants (J) are given in ppm and Hz, respectively. IR spectra were taken with an FT-IR spectrometer. Mass spectra were obtained using a GC-MS apparatus at 70 eV ionization voltage. The HRMS spectra were taken on Q-TOF-MS mass spectrometer, equipped with an electrospray ion source (ESI) operated in dual ion mode. 10 μL of the sample solutions (CH_3OH) were introduced by continuous infusion at a flow rate of 200 L min^{-1} with the aid of a syringe pump. Experimental conditions were performed as following: capillary voltage, 4000 V; nebulizer

pressure, 20 psi; flow rate of drying gas, 10 L/min; temperature of sheath gas, 325 C; flow rate of sheath gas, 10 L/min; skimmer voltage, 60 V; OCT1 RF Vpp, 750 V; fragmentor voltage, 170 V. The spectra data were recorded in the *m/z* range of 100–1000 Da in a centroid pattern of full-scan MS analysis mode. The MS/MS data of the selected compounds were obtained by regulating diverse collision energy (18–45 eV).

Preparation of Substrates 3a-i. 2-(Prop-2-ynylthio)-1*H*-benzo[*d*]imidazoles **3a-i**, bearing an internal triple bond, were prepared with the following procedure. To a solution of the 1*H*-imidazole-2-thione derivative (16.7 mmol) [1,3-dihydrobenzoimidazole-2-thione (commercially available): 2.50 g; 5,6-dimethyl-1,3-dihydrobenzoimidazole-2-thione (commercially available): 2.97 g; 5,6-dichloro-1,3-dihydrobenzoimidazole-2-thione (commercially available): 3.65 g; 5.6-dimethoxy-1,3-dihydrobenzoimidazole-2-thione:[4] 3.51 g; 5-methoxy-1,3-dihydrobenzoimidazole-2-thione (commercially available): 3.00 g; 5-fluoro-1,3-dihydrobenzoimidazole-2-thione:[4] 2.81 g] in anhydrous acetone (100 mL), was added, under nitrogen, K_2CO_3 (2.3 g , 16.7 mmol,) and the 1-bromoalk-2-yne derivative (25.1 mmol) [1-bromopent-2-yne (commercially available): 3.69 g; 1-bromobut-2-yne (commercially available): 3.34 g; 1-bromohex-2-yne:[11] 4.04 g; 1-bromooct-2-yne:[12] 4.75 g]. The mixture was stirred at room temperature for 20 h. After evaporation of the solvent, dichloromethane (30 mL) and water (30 mL) were sequentially added, and phases were separated. The aqueous phase was extracted again with dichloromethane (20 mL) and finally the collected organic phases were dried over Na_2SO_4. After filtration and evaporation of the solvent, products **3a-i** were purified by column chromatography on silica gel using as eluent: 9:1 hexane-AcOEt for **3b**, **3d**, **3h**; 8:2 hexane-AcOEt for **3c**; 7:3 hexane-AcOEt for **3a**, **3e**, **3f**, **3g**, **3i**.

*2-(Pent-2-yn-1-ylthio)-1H-benzo[d]imidazole (**3a**).* Yield: 2.75 g, starting from 2.50 g of 1,3-dihydrobenzoimidazole-2-thione (76%). Colorless solid, mp = 139 – 141 °C. IR (KBr); ν = 2972 (s), 2181 (vw), 1445 (s), 1402 (s), 1270 (m), 1228 (m), 980 (m), 737 (s) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.74 (s, br, 1 H), 7.63 – 7.40 (m, 2 H), 7.24 – 7.13 (m, 2 H), 4.16 (t, *J* = 2.3 , 2 H), 2.16 (qt, *J* = 7.5, 2.3, 2 H), 1.00 (t, *J* = 7.5, 3 H); $^{13}C\{^1H\}$NMR (75 MHz, DMSO-d_6): δ = 149.0, 143.4 (br), 135.7 (br), 122.0, 117.6 (br), 111.0 (br), 85.5, 75.2, 20.8, 13.9, 12.0. GC/MS: *m/z* = 216 (M^+, 77), 201 (100), 187 (27), 150 (27), 122 (42). HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{12}H_{12}N_2SNa^+$ 239.0613; Found 239.0609.

*2-(But-2-yn-1-ylthio)-1H-benzo[d]imidazole (**3b**)*. Yield: 2.70 g, starting from 2.50 g of 1,3-dihydrobenzoimidazole-2-thione (80%). Colorless solid, mp = 169 – 171 °C; IR (KBr): ν = 2972 (m, br), 2239 (vw), 1445 (m), 1402 (s), 1269 (m), 1229 (m), 980 (m) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.59 (s, br, 1 H), 7.51 – 7.41 (m, 2 H), 7.18 – 7.09 (m, 2 H), 4.12 (q, *J* = 2.5, 2 H), 1.77 (t, *J* = 2.5, 3 H); $^{13}C\{^1H\}$NMR (75 MHz, DMSO-d_6): δ = 148.8, 121.5, 79.4, 74.8, 20.3, 3.2 (*Note:* the signals of quaternary carbons were too broad to be detected). GC-MS: *m/z* = 202 (M^+, 100), 201 (72), 187 (31), 169 (81), 149 (42), 122 (77). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{10}N_2SNa^+$ 225.0457; Found: 225.0451.

*2-(Hex-2-yn-1-ylthio)-1H-benzo[d]imidazole (**3c**).* Yield: 2.00 g, starting from 2.50 g of 1,3-dihydrobenzoimidazole-2-thione (52%). Colorless solid, mp = 140 – 142 °C. IR (KBr): ν = 2959 (m, br), 2234 (vw), 1441 (m), 1400 (m), 1269 (m), 1242 (m), 737 (s) cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ = 7.54 – 7.44 (m, 2 H), 7.24 – 7.15 (m, 2 H), 4.98 (s, br, 1 H), 4.03-3.98 (m, 2 H), 2.13 -2.02 (m, 2 H), 1.46 -1.29 (m, 2 H), 0.81 (t, *J* = 7.3, 3 H); $^{13}C\{^1H\}$NMR (75 MHz, CD_3OD): δ = 150.3, 140.4 (br), 123.5, 115.0 (b), 85.4, 75.7, 23.0, 22.5, 21.4, 13.6. GC–MS: *m/z* = 230 (M^+, 60), 201 (100), 187 (24), 169 (28), 150 (28), 122 (29). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{14}N_2SNa^+$ 253.0770; Found: 253.0769.

*2-(Oct-2-yn-1-ylthio)-1H-benzo[d]imidazole (**3d**).* Yield: 3.45 g, starting from 2.50 g of 1,3-dihydrobenzoimidazole-2-thione (80%). Colorless solid, mp = 108 – 111 °C. IR (KBr): ν = 2957 (m br), 2234 (w), 1445 (m), 1402 (s), 1267 (m), 1227 (m), 980 (m), 739 (s) cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ = 12.61 (s, br, 1 H), 7.50 – 7.41 (m, br, 2 H), 7.15 – 7.10 (m, 2 H), 4.12 (t, *J* = 2.3, 2 H), 2.12 (tt, *J* = 7.0, 2.3, 2 H), 1.36-1.31 (m, 2 H), 1.25 – 1.13 (m, 4 H), 0.77 (t, *J* = 7.0, 3 H); $^{13}C\{^1H\}$NMR (125 MHz, DMSO-d_6): δ = 148.6, 121.5, 83.7, 75.7, 30.2, 27.7, 21.5, 20.5, 17.9, 13.7 (*Note:* the signals of two quaternary carbons were too broad to be detected); GC-MS: *m/z* = 258 (M^+, 100), 202 (97), 201 (100), 187 (14), 169 (14), 143 (41). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{18}N_2SNa^+$ 281.1083; Found: 281.1085.

*5,6-Dimethyl-2-(pent-2-yn-1-ylthio)-1H-benzo[d]imidazole (**3e**).* Yield: 2.45 g, starting from 2.97 g of 5,6-dimethyl-1,3-dihydrobenzoimidazole-2-thione (60%). Colorless solid, mp = 164 – 166 °C. IR (KBr): ν = 2974 (m), 2232 (vw), 1449 (m), 1391 (s), 1227 (m), 982 (m); ^1H NMR (300 MHz, DMSO-d_6): δ = 7.26 (s, 2 H), 4.12 (t, *J* = 2.2, 2 H), 2.28 (s, 6 H), 2.14 (qt, *J* = 7.5, 2.2, 2 H), 0.99 (t, *J* = 7.5, 3 H) (*Note:* the NH signal was too broad

to be detected). $^{13}C\{^{1}H\}$NMR (75 MHz, DMSO-d_6): δ = 147.1, 137.4, 130.2, 114.1, 85.2, 75.0, 20.8, 19.9, 13.6, 11.7 (*Note:* the signals of two quaternary carbons were too broad to be detected); GC-MS: *m/z* = 244 (M^+, 100), 243 (23), 229 (53), 171 (6). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{16}N_2SNa^+$ 267.0926; Found: 267.0925.

*5,6-Dimethoxy-2-(pent-2-yn-1-ylthio)-1H-benzo[d]imidazole (**3f**).* Yield: 3.46 g, starting from 3.51 g of 5.6-dimethoxy-1,3-dihydrobenzoimidazole-2-thione (75%). Colorless solid, mp = 102 – 105 °C; IR (KBr): ν = 2950 (m), 2234 (vw), 1393 (s), 1331 (s), 1200 (s), 1138 (s), 1007 (m), 849 (m) cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD): δ = 7.05 (s, 2 H), 4.95 (s, br); 3.90 (t, *J* = 2.4, 2 H), 3.85 (s, 6 H), 2.10 (qt, *J* = 7.5, 2.4, 2 H), 0.98 (t, *J* = 7.5, 3 H); $^{13}C\{^{1}H\}$NMR (75 MHz, CD_3OD): δ = 148.6, 146.9, 97.8 (br), 86.9, 75.0, 56.8, 23.4, 14.1, 13.0 (*Note:* the signal of a quaternary carbon was too broad to be detected); GC-MS: *m/z* = 276 (M^+, 100), 261 (43), 243 (26), 209 (14), 174 (5). HRMS (ESI-TOF) m/z : $[M + Na]^+$ Calcd for $C_{14}H_{16}N_2O_2SNa^+$ 299.0825; Found: 299.0825.

*6-Methoxy-2-(pent-2-yn-1-ylthio)-1H-benzo[d]imidazole (**3g**).* Yield: 3.29 g, starting from 3.00 g of 5-methoxy-1,3-dihydrobenzoimidazole-2-thione (80%). Colorless solid, mp = 112 – 116 °C; IR (KBr): ν = 2875 (m), 2230 (vw), 1628 (m), 1393 (s), 1204 (s), 1161 (s), 1034 (m), 980 (m), 806 (s) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 8.8, 1 H), 7.08 (d, *J* = 2.3, 1 H), 6.87 (dd, *J* = 8.8, 2,3, 1 H), 4.01 (t, *J* = 2.4, 2 H), 3.82 (s, 3 H), 2.12 (qt, *J* = 7.5, 2.4, 2 H), 1.04 (t, *J* = 7.5, 3 H) (*Note:* the NH signal was too broad to be detected); $^{13}C\{^{1}H\}$NMR (75 MHz, $CDCl_3$); δ = 156.4, 148.1, 139.5 (br), 134.3 (br), 115.3, 111.9, 97.2, 86.5, 74.1, 55.8, 22.5, 13.6, 12.5; GC-MS: *m/z* = 246 (M^+, 100), 231 (51), 217 (25), 174 (15), 120 (18). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{14}N_2OSNa^+$ 269.0719; Found: 269.0717.

*5,6-Dichloro-2-(pent-2-yn-1-ylthio)-1H-benzo[d]imidazole (**3h**).* Yield: 3.33 g, starting from 3.65 g of 5,6-dichloro-1,3-dihydrobenzoimidazole-2-thione (70%). Yellow solid. mp = 188 – 193 °C. IR (KBr): ν = 2920 (m), 2234 (vw), 1377 (s), 1319 (m), 1096 (m), 961 (m), 868 (m) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.74 (s, 2 H), 4.15 (t, *J* = 2.4, 2 H), 2.16 (qt, *J* = 7.5, 2.4, 2 H), 1.00 (t, *J* = 7.5, 3 H) (*Note:* the NH signal was too broad to be detected); $^{13}C\{^{1}H\}$NMR (75 MHz, DMSO-d_6): δ = 152.5, 124.0, 114.8 (br), 85.3, 74.8, 20.4, 13.6, 11.8 (*Note:* the signal of a quaternary carbon was too broad to be detected); GC-MS: *m/z* = 288 [$(M+4)^+$, 13], 286 [$(M+2)^+$,

69], 285 [(M+1)$^+$, 21)], 284 (M$^+$, 100), 271 (27), 269 (39), 257 (55), 255 (76), 220 (39), 167 (32). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{12}H_{11}Cl_2N_2S^+$ 285.0015; Found: 285.0015.

*6-Fluoro-2-(pent-2-yn-1-ylthio)-1H-benzo[d]imidazole (**3i**)*. Yield: 1.56 g, starting from 2.81 g of 5-fluoro-1,3-dihydrobenzoimidazole-2-thione: 2.81 (40%). Colorless solid, mp = 175 – 177 °C; IR (KBr): ν = 2914 (m, br), 2237 (vw), 1397 (s), 1142 (s), 988 (m), 845 (s), 799 (s) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.79 (s, br, 1 H), 7.62-7.20 (m, 2 H), 7.01 (t, *J* = 9.7, 1 H), 4.18-4.12 (m, 2 H), 2.22 – 2.11 (m, 2 H), 1.01 (t, *J* = 7.5, 3 H). ^{13}C{^{1}H}NMR (75 MHz, DMSO-d_6): δ = 158.2 (d, *J* = 233.9, C-6 bonded to F), 150.7 (tautomer A), 149.5 (tautomer B), 144.0 (tautomer A or B), 140.2 (tautomer B or A), 135.5 (tautomer A or B), 132.1 (tautomer B or A), 118.1 (tautomer A or B), 110.9 (tautomer B or A), 109.7 (d, *J* = 25.3, C-5 or C-7, tautomer A or B), 109.3 (d, *J* = 25.3, C-5 or C-7, tautomer B or A), 103.3 (d, *J* = 24.3, C-7 or C-5, tautomer A or B), 97.2 (d, *J* = 25.5, C-7 or C-6, tautomer B or A), 85.1, 74.9, 20.4, 13.6, 11.7 (*Note:* some carbon signals were doubled owing to slow tautomerization of the imidazole ring). ^{19}F NMR (471 MHz, DMSO-d_6): δ= –120.0 (s, tautomer A or B), –121.4 (s, tautomer B or A). GC-MS: *m/z* = 234 (M$^+$, 76), 219 (100), 205 (32), 168 (27), 140 (47), 108 (37). HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{12}H_{11}FN_2SNa^+$ 257.0519; Found: 257.0513.

General Procedure for the Synthesis of Thiadiazafluorenones 4a–i (Table 1). A 35 mL stainless steel autoclave was charged in the presence of air with PdI_2 (5.8 mg, 1.61 $\times$ 10^{-2} mmol), KI (133 mg, 0.81 mmol), MeOH (4 mL), and the 2-prop-2-ynylthiobenzimidazole (0.81 mmol; **3a**: 175 mg; **3b**: 164 mg; **3c**: 187 mg; **3d**: 209 mg; **3e**: 198 mg; **3f**: 224 mg; **3g**: 200 mg; **3h**: 231 mg; **3i**: 190 mg). The autoclave was purged at room temperature several times with CO under stirring (5 atm) and eventually pressurized with CO_2 (30 atm). After being stirred at 80 °C for 3 h, the autoclave was cooled, degassed and opened. After evaporation of the solvent, products **4** were purified by column chromatography on neutral alumina using 98:2 hexane-AcOEt as eluent.

*3-Ethyl-2-methyl-1-thia-4a,9-diazafluoren-4-one (**4a**).* Yield: 119 mg, starting from 175 mg of **3a** (60%) (Table 1, entry 1). Colorless solid, mp = 132 – 134°C. IR (KBr): ν = 1675 (s), 1475 (s), 1432 (s), 1358 (m), 1313 (m), 1148 (m), 760 (m) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.57 (d, *J* = 8.1), 7.74 (d, *J* = 8.1), 7.50-7.44 (m, 1 H), 7.44-7.38 (m, 1 H), 2.76 (q, *J* = 7.5, 2 H), 2.43 (s, 3 H), 1.18 (t, *J* = 7.5, 3 H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$):

δ = 160.4, 146.2, 142.4, 140.7, 131.6, 127.8, 125.7, 123.8, 118.4, 116.1, 21.3, 20.6, 13.0. GC-MS: *m/z* = 244 (M^+, 100), 229 (51), 211 (16), 201 (16). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{12}N_2OSNa^+$ 267.0563; Found: 267.0557.

*2,3-Dimethyl-1-thia-4a,9-diazafluoren-4-one (**4b**).* Yield: 103 mg, starting from 164 mg of **3b** (55%) (Table 1, entry 2). Colorless solid, mp = 178 – 183°C. IR (KBr). ν = 1674 (s), 1474 (m), 1435 (m), 1354 (w), 1312 (m), 1150 (m), 768 (s) cm^{-1}. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 8.59 (d, *J* = 8.0), 7.73 (d, *J* = 7.7), 7.50-7.30 (m, 2 H), 2.36 (s, 3 H), 2.21 (s, 3 H). $^{13}C\{^1H\}$NMR (75 MHz, $CDCl_3$): δ = 160.7, 146.1, 142.3, 140.6, 131.4, 125.7, 123.8, 121.8, 118.3, 116.0, 21.3, 13.4. GC-MS: *m/z* = 230 (M^+, 100), 201 (27), 169 (15), 150 (15). HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $[C_{12}H_9N_2OS]^-$ 229.0441; Found: 229.0452.

*2-Methyl-3-propyl-1-thia-4a,9-diazafluoren-4-one (**4c**).* Yield: 119 mg, starting from 187 mg of **3c** (57%) (Table 1, entry 3). Colorless solid, mp = 111 – 112°C. IR (KBr): ν = 1684 (s), 1466 (s), 1431 (s), 1350 (s), 1311 (s), 1152 (m), 746 (s) cm^{-1}. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 8.57 (d, *J* = 8.0), 7.74 (d, *J* = 7.8, 1 H), 7.52-7.35 (m, 2 H), 2.70 (t, *J* = 7.6, 2 H), 2.43 (s, 3 H), 1.59 (sext, *J* = 7.6, 2 H), 1.03 (t, *J* = 7.6, 3 H). $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$): δ = 160.5, 146.2, 142.3, 141.0, 131.5, 126.4, 125.7, 123.8, 118.4, 116.1, 29.8, 22.0, 20.9, 14.1. GC-MS: *m/z* = 258 (M^+, 96), 243 (14), 229 (100), 201 (16), 143 (12). HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{14}H_{13}N_2OS^-$ 257.0754; Found: 257.0764.

*2-Methyl-3-pentyl-1-thia-4a,9-diazafluoren-4-one (**4d**).* Yield: 128 mg, starting from 209 mg of **3d** (55%) (Table 1, entry 4). Colorless solid, mp = 56 – 58°C. IR (KBr): ν = 1684 (s), 1474 (s), 1443 (s), 1383 (s), 1315 (m), 1225 (m), 1155 (m), 760 (s) cm^{-1}. ^{1}HNMR (300 MHz, $CDCl_3$): δ = 8.51 (d, *J* = 7.6, 1 H), 7.68 (d, *J* = 7.9), 7.44-7.28 (m, 2 H), 2.62 (t, *J* = 7.8, 2 H), 2.34 (s, 3 H), 1.57-1.22 (m, 6 H), 0.87 (t, *J* = 6.5, 3 H). $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$): δ = 160.4, 146.1, 142.3, 140.8, 131.4, 126.5, 125.6, 123.7, 118.3, 116.0, 31.8, 28.4, 27.9, 22.5, 20.8, 14.0. GC-MS*: m/z* = 286 (M^+, 47), 229 (37), 202 (31), 137 (100). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{18}N_2OSNa^+$: 309.1032; Found: 309.1036.

*2,6,7-Trimethyl-3-ethyl-1-thia-4a,9-diazafluoren-4-one (**4e**).* Yield: 124 mg, starting from 198 mg of **3e** (56%) (Table 1, entry 5). Colorless solid, mp = 154 – 158°C. IR (KBr): ν = 1667 (s), 1477 (m), 1442 (s), 1350 (s),

1169 (m), 883 (m), 768 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.27 (s, 1 H), 7.43 (s, 1 H), 2.70 (q, *J* = 7.4, 2 H), 2.38 (s, 3 H), 2.36 (s, 6 H), 1.15 (t, *J* = 7.4, 3 H). $^{13}C\{^1H\}$NMR (75 MHz, $CDCl_3$): δ = 160.2, 144.9, 140.8, 140.4, 134.7, 132.9, 129.7, 127.4, 118.3, 116.1, 21.2, 20.52, 20.46, 13.0. GC/MS: *m/z* = 272 (M^+, 100), 257 (44), 239 (13), 229 (19). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{16}N_2OSNa^+$ 295.0876; Found: 295.0871.

*3-Ethyl-6,7-dimethoxy-2-methyl-1-thia-4a,9-diazafluoren-4-one (**4f**).* Yield: 123 mg, starting from 224 mg of **3f** (50%) (Table 1, entry 6). Colorless solid, mp = 167 – 169°C. IR (KBr): ν = 1667 (s), 1462 (s), 1427 (s), 1373 (m), 1318 (s), 1007 (m), 841 (m), 756 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.13 (s, 1 H), 7.20 (s, 1 H), 4.01 (s, 3 H), 3.97 (s, 3 H) 2.76 (q, *J* = 7.5, 2 H), 2.44 (s, 3 H), 1.18 (t, *J* = 7.5, 3 H). $^{13}C\{^1H\}$NMR (75 MHz, $CDCl_3$): δ = 160.5, 148.6, 147.1, 143.6, 140.8, 136.3, 127.2, 125.1, 100.1, 98.7, 56.4, 56.2, 21.3, 20.6, 13.1. GC/MS: *m/z* = 304 (M^+, 100), 289 (60), 261 (9), 167 (32). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{16}N_2O_3SNa^+$ 327.0774; Found: 327.0767.

*Mixture of Regioisomers 3-Ethyl-7-methoxy-2-methyl-1-thia-4a,9-diazafluoren-4-one (A) and 3-Ethyl-6-methoxy-2-methyl-1-thia-4a,9-diazafluoren-4-one (B) (**4g**; A/B ratio about 3.0, by ^{1}HNMR).* Yield: 127 mg, starting from 200 mg of **3g** (57%) (Table 1, entry 7). Colorless solid, mp = 114 – 119°C. IR (KBr): ν = 1670 (s), 1477 (s), 1431 (s), 1358 (m), 1018 (m), 845 (m), 764 (m) cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$): δ = 8.40 (d, *J* = 8.9, 1 H, B), 8.09 (d, *J* = 2.4, 1 H, A), 7.59 (d, *J* = 8.8, 1 H, A), 7.17 (d, *J* = 2.3, 1 H, B), 7.05 (dd, *J* = 8.8, 2.4, 1 H, A), 6.97 (dd, *J* = 8.9, 2.3, 1 H, B), 3.90 (s, 3 H, A), 3.87 (s, 3 H, B), 2.72 (q, *J* = 7.4, 2 H, A+B), 2.40 (s, 3 H, A+B), 1.16 (t, *J* = 7.4, 3 H, A+B); $^{13}C\{^1H\}$NMR (75 MHz, $CDCl_3$): δ = 160.6 (A), 160.0 (B), 158.3 (B), 157.0 (A), 146.4 (B), 144.2 (A), 143.6 (B), 141.0 (A), 140.3 (B), 136.6 (A), 132.1 (A), 127.6 (B), 127.3 (A), 125.8 (B), 118.7 (A), 116.4 (B), 115.3 (A), 112.7 (B), 101.1 (B), 99.4 (A), 55.92 (A), 55.89 (B), 21.3 (A+B), 20.6 (A+B), 13.1 (A+B); GC/MS [A]: *m/z* = 274 (M^+, 100), 259 (55), 231 (18), 180 (10), 165 (11). GC/MS [B]: *m/z* = 274 (M^+, 100), 259 (56), 231 (17), 180 (10), 165 (11). HRMS (ESI - TOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{14}N_2O_2SNa^+$ 297.0668; Found: 297.0663.

*6,7-Dichloro-3-ethyl-2-methyl-1-thia-4a,9-diazafluoren-4-one (**4h**).* Yield: 150 mg, starting from 231 mg of **3h** (59%) (Table 1, entry 8). Colorless solid, mp = 200 – 202°C. IR (KBr): ν = 1670 (s), 1466 (m), 1427 (s), 1350 (m), 914 (m), 872 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.63 (s, 1 H), 7.75 (s, 1 H), 2.75 (q, *J* = 7.5, 2 H), 2.46 (s, 3 H), 1.17 (t, *J* = 7.5, 3 H). $^{13}C\{^1H\}$NMR (75 MHz, $CDCl_3$): δ = 159.7, 148.1, 141.5, 141.4, 130.3, 129.9, 127.84,

127.82, 119.4, 117.3, 21.3, 20.7, 12.9. GC/MS: *m/z* = 316 [$(M+4)^+$, 13], 314 [$(M+2)^+$, 65], 312 (M^+, 100), 299 (22), 297 (30), 279 (17), 277 (18), 271 (11), 269 (16). HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{11}Cl_2N_2OS^+$ 312.9964; Found: 312.9949.

*Mixture of Regioisomers 3-Ethyl-6-fluoro-2-methyl-1-thia-4a,9-diazafluoren-4-one (A) and 3-Ethyl-7-fluoro-2-methyl-1-thia-4a,9-diazafluoren-4-one (B) (**4i**; A/B ratio about 1.1, by ^{1}HNMR).*Yield: 121 mg, starting from 190 mg of **3i** (57%) (Table 1, entry 9). Colorless solid, mp = 107 – 109°C. IR (KBr): ν = 1670 (s), 1468 (s), 1437 (s), 1358 (m), 1130 (m), 845 (m), 814 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.46 (dd, *J* = 8.9, 5.0, 1 H, A), 8.24 (dd, *J* = 8.9, 2.4, 1 H, B), 7.63 (dd, *J* = 8.9, 4.8, 1 H, B), 7.36 (dd, *J* = 8.9, 2.3, 1 H, A), 7.18 (td, *J* = 8.9, 2.4, 1 H, B), 7.09 (dd, *J* = 8.9, 2.3, 1 H, A), 2.79-2.67 (m, 2 H, A+B), 2.43 (s, 3 H, A), 2.43 (s, 3 H, B), 1.22-1.12 (m, 3 H, A+B); ^{13}C{^{1}H}NMR (75 MHz, $CDCl_3$): δ = 160.9 (d, *J* = 242.6, A), 160.09 (B), 159.95 (A), 159.6 (d, *J* = 241.6, B), 147.8 (A+B), 146.2 (B), 143.2 (d, *J* = 12.8, A), 141.0 (d, *J* = 28.9, B), 138.67 (A or B), 138.65 (B or A), 131.4 (d, *J* = 14.2, B), 128.8 (A), 127.6 (d, *J* = 22.0, A), 118.9 (d, *J* = 9.9, B), 116.7 (d, *J* = 9.9, A), 113.8 (d, *J* = 25.1, B), 111.7 (d, *J* = 25.2, A), 104.5 (d, *J* = 24.8, A), 103.3 (d, *J* = 29.6, B), 21.28 (A+B), 20.64 (A), 20.60 (B), 12.99 (A+B). ^{19}F NMR (471 MHz, CD_3Cl): δ = –115.8 (s, A), –117.4 (s, B); GC/MS (A + B): *m/z* = 262 (M^+, 100), 247 (52), 229 (16), 219 (21), 168 (9). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{11}FN_2OSNa^+$ 285.0468; found: 285.0468.

Cross-over Experiment (Scheme 4). A 35 mL stainless steel autoclave was charged in the presence of air with PdI_2 (11.6 mg, 3.22×10^{-2} mmol), KI (267 mg, 1.61 mmol), MeOH (8 mL), **3d** (208.7 mg, 0.81 mmol) and **3e** (197.6 mg, 0.81 mmol). The autoclave was purged at room temperature several times with CO under stirring (5 atm) and eventually pressurized with CO_2 (30 atm). After being stirred at 80 °C for 20 h, the autoclave was cooled, degassed and opened. The resulting crude inseparable mixture was analyzed by GLC and LC-MS, which evidenced the formation of **4a**, **4d**, **4e** and **5** in a ratio **4a**: **4d**: **4e**: **5** = 1: 1.2: 3: 1.9 (determined by GLC).[9] GC/MS (**5**): *m/z* = 314 (M^+, 100), 271 (14), 257 (46), 230 (48), 178 (16), 137 (73).

Carbonylation of 3d in the Presence of Cyclohexylallene (Scheme 5). A 35 mL stainless steel autoclave was charged in the presence of air with PdI_2 (8.3 mg, 2.30×10^{-2} mmol), KI (191.24 mg, 1.15 mmol), MeOH (5.8 mL), **3d** (148.8 mg, 0.58 mmol) and cyclohexylallene **6** (commercially available; 70.4 mg, 0.58 mmol). The

autoclave was purged at room temperature several times with CO under stirring (5 atm) and eventually pressurized with CO_2 (30 atm). After being stirred at 80 °C for 20 h, the autoclave was cooled, degassed and opened. The crude mixture was analyzed in GLC to determinate the cyclohexylallene conversion (54%). After evaporation of the solvent, the crude mixture was purified by column chromatography on neutral alumina (98:2 hexane-AcOEt as eluent) affording **4d** in 49% yield (81.8 mg).[10]

Supporting Information. Scheme S1, Table S1, X-Ray data for compounds **2a**, **4a**, and **4f**. Copy of HRMS, ^{1}H NMR, $^{13}C\{^{1}H\}$NMR, and ^{19}F NMR spectra for Substrates **3a-i** and Products **4a-i**.

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(6) Detailed X-ray structural determination data as well as the CIFs can be found in the Supporting Information.

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(9) The relative amounts of products **4d**, **4e**, **4a**, and **5** were 1: 1.2: 3: 1.9 (determined by GLC). All attempts to isolate at the pure state mixed product **5** failed, owing to the complexity of the reaction mixture; however, its GLC-MS spectrum was compatible with the assigned structure. We thank the Associate Editor, Prof. Scott D. Rychnovsky, for suggesting us to carry out this experiment.

(10) The cyclohexylallene conversion was 54% (determined by GLC analysis of the reaction mixture); partial decomposition occurred with formation of chromatographically immobile materials, which were not investigated further). We thank the Associate Editor and a referee for suggesting us to carry out such an experiment.

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