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A Palladium Iodide-Catalyzed Cyclocarbonylation Approach to Thiadiazafluorenones

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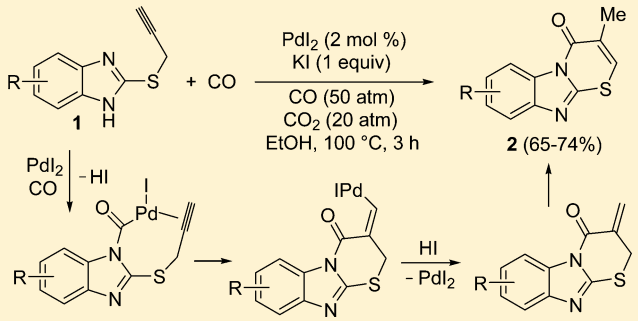
Supporting Information

ABSTRACT: The first example of an additive cyclocarbonylation process leading to 1-thia-4*a*,9-diazafluoren-4-ones is reported. This process is based on the reaction of readily available 2-(propynylthio)benzimidazoles with carbon monoxide carried out in EtOH at 100 °C under a 5/2 mixture of CO−CO_2 at 70 atm in the presence of the PdI_2/KI catalytic system. Experimental evidence suggests a mechanistic pathway involving *N*-palladation of the substrate followed by CO insertion, triple bond insertion, protonolysis, and isomerization.



1-Thiadiazafluoren-4-ones are an important class of polyheterocyclic compounds known to possess important pharmacological activities.[1,2] In particular, some 1-thiazafluorenone derivatives have shown a positive inotropic effect and strong cardiotonic activity,[2] while other derivatives are known to be antihyper secretion agents.[2] They are usually prepared by intramolecular amidation of 3-(1*H*-benzo[*d*]imidazol-2-ylthio)-propanoic acid and its derivatives.[3] Clearly, the possibility to synthesize them by a direct carbonylation procedure involving the use of the simplest and most available C-1 unit (carbon monoxide) would represent a very attractive alternative synthetic approach. Currently, cyclocarbonylation constitutes a method of primary importance for the construction of a ring with direct incorporation of the carbonyl group into the cycle starting from CO.[4] In particular, palladium-catalyzed cyclocarbonylation reactions of unsaturated substrates bearing a nucleophilic group in a suitable position for cyclization have been proven to be particularly significant for the synthesis of carbonylated heterocycles, with many important examples being reported in the recent literature.[4−6]

Herein, we report a novel cyclocarbonylation route to 1-thia-4*a*,9-diazafluoren-4-one **2** starting from readily available 2-(prop-2-ynylthio)-1*H*-benzo[*d*]imidazoles **1**.[7] The process, catalyzed by a simple catalytic system consisting of PdI_2 in conjunction with KI and promoted by an excess of carbon dioxide, corresponds to a 6-*exo*-*dig* carbonylative cyclization in which the nitrogen of the imidazole ring of **1** acts as nucleophile, followed by in situ isomerization of the ensuing double bond from the exocyclic to the endocyclic position (Scheme 1).

2-(Prop-2-ynylthio)-1*H*-benzo[*d*]imidazole **1a** was used as model substrate for optimizing the reaction conditions that would lead to the polyheterocyclic derivatives **2**. This substrate was initially allowed to react with carbon monoxide (30 atm) at 100 °C in MeOH as the solvent (**1a** concentration = 0.1 mmol per milliliter of solvent) in the presence of PdI_2 (2 mol %) and KI (1 equiv). After 3 h, substrate conversion was quantitative, and analysis of the reaction mixture evidenced the formation of the desired product, 3-methyl-1-thia-4*a*,9-diazafluoren-4-one **2a**, in 37% yield, together with heavy unidentified compounds (chromatographically immobile materials) (Table 1, entry 1).[8] Although the yield of **2a** was modest, this initial result confirmed the possibility to realize the direct synthesis of a thiadiazafluorenone by a PdI_2-catalyzed cyclocarbonylation route. With the aim of improving the selectivity of **2a**, we then changed the reaction parameters, such as the nature of the catalyst, substrate concentration, reaction temperature, and solvent (Table 1). The use of $PdCl_2$/KCl instead of PdI_2/KI led to less-satisfactory results (Table 1, entry 2), while practically the same yield of **2a** was obtained by replacing KI with

Scheme 1. PdI_2-Catalyzed Cyclocarbonylation of 2-(Prop-2-ynylthio)-1*H*-benzo[*d*]imidazoles 1 Followed by Double Bond Isomerization Leading to 1-Thia-4*a*,9-diazafluoren-4-one 2

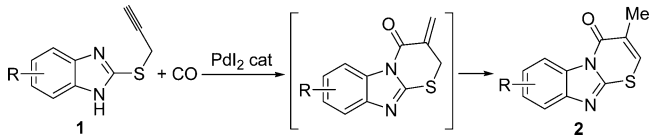


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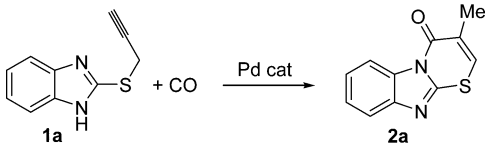
Table 1. Carbonylation Reaction of 2-(Prop-2-ynylthio)-1*H*-benzo[*d*]imidazole 1a under Different Conditions[a]



	catalyst	cocatalyst	*T* (°C)	solvent	P(CO) (atm)	yield of **2a**[b] (%)
1	PdI_2	KI (1 equiv)	100	MeOH	30	37
2	$PdCl_2$	KCl (1 equiv)	100	MeOH	30	14[c]
3	PdI_2	$Et_2NH_2^+I^-$ (1 equiv)	100	MeOH	30	36
4	$PdCl_2(PPh_3)_2$		100	MeOH	30	17
5	$Pd(dba)_2$		100	MeOH	30	<5
6	PdI_2	KI (0.2 equiv)	100	MeOH	30	30
7	PdI_2	KI (1 equiv)	80	MeOH	30	25[d]
8	PdI_2	KI (1 equiv)	100	MeOH	30	18[e]
9	PdI_2	KI (1 equiv)	100	MeOH	30	40[f]
10	PdI_2	KI (1 equiv)	100	MeOH	50	45
11	PdI_2	KI (1 equiv)	100	MeOH	30	53[g]
12	PdI_2	KI (1 equiv)	100	EtOH	30	44
13	PdI_2	KI (1 equiv)	100	dioxane	30	0
14	PdI_2	KI (1 equiv)	100	DME	30	0
15	PdI_2	KI (1 equiv)	100	MeCN	30	12
16	PdI_2	KI (1 equiv)	100	DMA	30	10

[a]Unless otherwise noted, all reactions were carried out under CO at 30 atm (25 °C) for 3 h with a substrate concentration of 0.1 mmol of **1a** per milliliter of solvent in the presence of 2 mol % of the palladium catalyst. Unless otherwise noted, substrate conversion was quantitative. [b]Isolated yield based on starting amount of **1a**. [c]Substrate conversion was 76% by isolation of unreacted substrate. [d]Substrate conversion was 68% by isolation of unreacted substrate. [e]The reaction was carried out using 2-(prop-2-ynylthio)-1*H*-benzo[*d*]imidazolium bromide **1a′** as the substrate instead of **1a**. [f]The reaction was carried out with a substrate concentration of 0.2 mmol per milliliter of solvent. [g]The reaction was carried out under a 3/2 mixture of CO−CO_2 at 50 atm (25 °C).

diethylammonium iodide (Table 1, entry 3). On the other hand, lower yields of **2a** were observed using $PdCl_2(PPh_3)_2$ (Table 1, entry 4) or a Pd(0) complex such as $Pd(dba)_2$ (Table 1, entry 5). A lower yield was also observed with 10 mol % KI rather than 1 equiv (Table 1, entry 6), working at 80 °C rather than 100 °C (Table 1, entry 7), and using 2-(prop-2-ynylthio)-1*H*-benzo[*d*]imidazolium bromide **1a′** as the substrate instead of **1a** (Table 1, entry 8). Selectivity toward **2a** was instead improved when working under more concentrated conditions (0.2 rather than 0.1 mmol of **1a** per milliliter of MeOH Table 1, entry 9) or under higher CO pressure (50 atm, Table 1, entry 10). Interestingly, the use of a CO−CO_2 mixture (30/20 atm) also tended to augment the product yield (Table 1, entry 11). The nature of the solvent was also very important for product selectivity. In particular, the process worked well not only in MeOH but also in another protic solvent such as EtOH (Table 1, entry 12), while less-satisfactory results were obtained in aprotic solvents such as dioxane, DME, MeCN, or DMA (Table 1, entries 13−16).

Under the final optimized conditions (2 mol % PdI_2 and 1 equiv of KI at 100 °C for 3 h in EtOH (**1a** concentration = 0.2 mmol per milliliter of solvent) under a CO/CO_2 mixture (50/20 atm) at 70 atm), the desired thiadiazafluorenone was isolated in 65% yield (Table 2, entry 1). The process was then extended to differently substituted substrates **1b−f**.

As can be seen from the results shown in Table 2, entries 2−6, the process was quite general, as it worked nicely with substrates bearing electron-withdrawing groups as well as electron-donating groups on the aromatic ring. 5-Fluoro-2-(prop-2-ynylthio)-1*H*-benzo[*d*]imidazole **1f** was less reactive than the other substrates tested; thus, its carbonylation was carried out for 15 h with a 5 mol % PdI_2 (Table 2, entry 6). Quite predictably, on the basis of the similar reactivity of the two nitrogens of the benzimidazole ring due to conjugation, a mixture of regioisomers was formed, starting from mono-substituted substrates **1e** and **1f** (Table 2, entries 5 and 6, respectively).

Based on our experiences with PdI_2/KI-catalyzed carbonylation reactions[5a,c,9] and the experimental results obtained in this work, we propose the mechanism shown in Scheme 2 for rationalizing the formation of thiadiazafluorenones **2** from (propynylthio)benzimidazoles **1** under our conditions (anionic iodide ligands are omitted for clarity). The fact that practically no reaction occurs with a classical Pd(0) catalyst such as $Pd(dba)_2$ (Table 1, entry 4) seems to rule out a Pd(0)-mediated mechanism initiated by oxidative addition of the N−H group of the substrate to a Pd(0) species formed in situ under the reaction conditions. Accordingly, a Pd(II)-catalyzed process initiated by *N*-palladation of **1** with PdI_2 to give complex **I** and HI appears much more likely (Scheme 2). Carbon monoxide insertion into the N−Pd bond of **I** would lead to carbamoylpalladium intermediate **II**, from which the final product would be obtained by triple bond insertion to give **III**, protonolysis by HI (leading to intermediate **IV**), and isomerization. This mechanistic hypothesis is also in agreement with the higher activity displayed by the PdI_2/KI system with respect to $PdCl_2$/KCl because, on one hand, iodide is a better leaving group in the *N*-palladation step and, on the other hand, HI is a stronger acid in the protonolysis step.[10] The importance of an effective protonolysis step with regeneration of the Pd(II) catalyst is further demonstrated by the experimental observation that the process works much better in protic solvents, where HI dissociation is more favored, rather than in aprotic ones. Finally, although the favorable effect exerted by CO_2 is difficult to interpret, the excess CO_2 may also favor the protonolysis step by slightly augmenting the acidity of the reaction medium. It may also act as a ligand to Pd(II),[11] suitably stabilizing the key organometallic intermediates leading to **2**.

In conclusion, we developed a novel cyclocarbonylative method for the direct synthesis of thiadiazafluorenones **2** starting from readily available (propynylthio)benzimidazoles **1**. The process, catalyzed by the simple catalytic system PdI_2/KI, occurs in EtOH under relatively mild conditions (100 °C, under a 5/2 mixture of CO−CO_2 at 70 atm) and takes place through an ordered sequence of steps involving *N*-palladation, CO insertion, triple bond insertion, protonolysis, and isomerization. To the best of our knowledge, this is the first example of synthesis of polyheterocycles **2** by a direct additive carbonylation approach.

EXPERIMENTAL SECTION

General Experimental Methods. Solvents and chemicals were reagent grade and used without further purification. All reactions were

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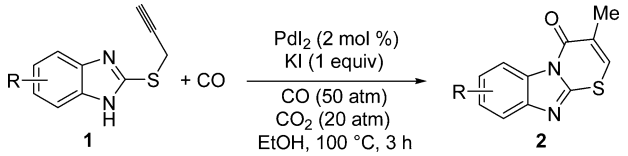
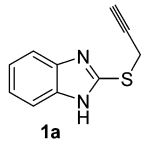
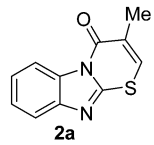
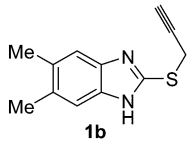
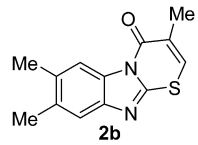
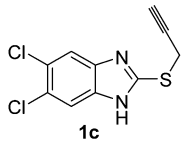
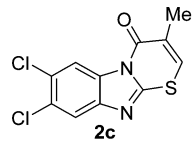
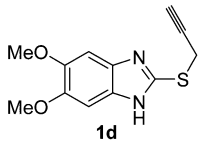
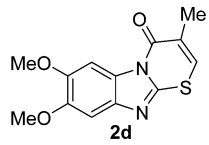
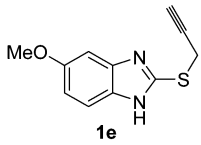
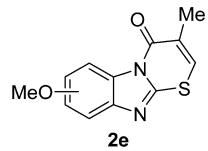
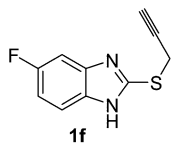
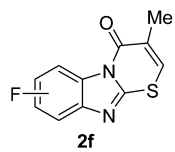
Table 2. Synthesis of 1-Thia-4*a*,9-diazafluoren-4-one 2 by PdI_2-Catalyzed Cyclocarbonylation of 2-(Prop-2-ynylthio)-1*H*-benzo[*d*]imidazoles 1[a]



Entry	1	2	Yield of 2[b] (%)
1	 1a	 2a	65
2	 1b	 2b	72
3	 1c	 2c	71
4	 1d	 2d	67
5	 1e	 2e	74[c]
6	 1f	 2f	68[d,e]

[a]Unless otherwise noted, all reactions were carried out at 100 °C for 3 h in EtOH as the solvent (0.2 mmol of **1** per milliliter of EtOH) under a 5/2 mixture of CO−CO_2 at 70 atm (25 °C) in the presence of PdI_2 (2 mol %) in conjunction with KI (1 equiv). Substrate conversion was quantitative in all cases. The formation of heavy products (chromatographically immobile materials) accounted for the difference between product yield and substrate conversion. [b]Isolated yield based on starting amount of **1**. [c]Mixture of regioisomers (~1.2/1, by GLC). [d]Mixture of regioisomers (~1.4/1, by ^{1}H NMR). [e]The reaction was carried out with 5 mol % PdI_2 for 15 h.

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 and by electrospray ionization using an ESI-MS spectrometer. The LC-MS was operated in the positive ion mode. The experimental conditions were as follows: ion spray voltage 4000 V; curtain gas 35 psi; temperature 25 °C; ion source gas 15 psi; declustering and focusing potentials 50 and 400 V, respectively. Microanalyses were carried out in our analytical laboratory.

Preparation of Substrate Precursors. Starting materials 1,3-dihydrobenzimidazole-2-thiones were commercially available except for 5,6-dimethoxy-1,3-dihydrobenzimidazole-2-thione and 5-fluoro-1,3-dihydrobenzimidazole-2-thione, which were prepared according to the following procedure:[12] to a three-necked flask were introduced, under nitrogen, 4-fluorobenzene-1,2-diamine (2.0 g, 16.0 mmol) or 1,2-diamino-4,5-dimethoxybenzene[13] (2.7 g, 16.0 mmol), carbon disulfide (2.4 g, 32.0 mmol), and a solution of KOH (1.8 g, 32 mmol) in anhydrous EtOH (26 mL). The mixture was refluxed under

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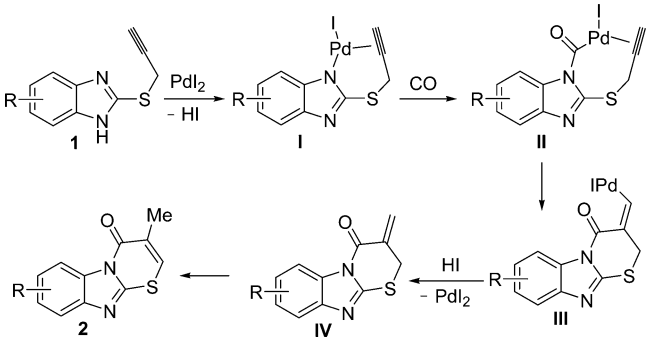
Scheme 2. Proposed Mechanistic Pathway for the PdI_2-Catalyzed Cyclocarbonylation of 2-(Prop-2-ynylthio)-1*H*-benzo[*d*]imidazoles 1 Leading to 1-Thia-4*a*,9-diazafluoren-4-one 2



stirring for 4 h. After being cooled, glacial acetic acid (30 mL) was added to the mixture. The solvent was evaporated, and to the solid residue was added aq NaOH (2.5 wt %, 200 mL) containing a few drops of $NaHSO_3$. The mixture was refluxed until dissolution of the solid was observed, and after being cooled to 0 °C, the pH of the solution was adjusted to neutral by addition of concd HCl. To the resulting mixture was added AcOEt (100 mL); the phases were separated, and the aqueous phase was extracted with AcOEt (3 × 50 mL). The collected organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvent, the product was purified by column chromatography on silica gel using 6/4 hexane AcOEt for 5-fluoro-1,3-dihydrobenzimidazole-2-thione and 7/3 hexane-acetone for 5,6-dimethoxy-1,3-dihydrobenzoimidazole-2-thione.

5-Fluoro-1,3-dihydrobenzimidazole-2-thione. Yield: 2.2 g starting from 2 g of 4-fluorobenzene-1,2-diamine (80%). Yellow solid, mp: 227−229 °C; IR (KBr): ν 1630 (m), 1503 (s), 1471 (m), 1344 (s), 1252 (m), 1194 (m), 1145 (s), 985 (m), 837 (s), 703 (s), 658 (s) cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 7.20−7.11 (m, 1 H), 7.00−6.86 (m, 2 H); ^{13}C NMR (75 MHz, CD_3OD): δ 170.9, 161.1 (d, J = 239), 134.4 (d, J = 13), 130.3, 111.6 (d, J = 10), 111.1 (d, J = 25), 98.3 (d, J = 29); ^{19}F NMR (471 MHz, CD_3OD): δ −119.9 (s, 1 F); MS (ESI^+, direct infusion): m/z 169 [$(M + H)^+$]; Anal. calcd for $C_7H_5FN_2S$ (168.19): C, 49.99; H, 3.00; F, 11.30; N, 16.66; S, 19.06; found C, 49.97; H, 3.02; F, 11.28; N, 16.61; S, 19.12.

5,6-Dimethoxy-1,3-dihydrobenzimidazole-2-thione. Yield: 2.0 g starting from 2.69 g of 1,2-diamino-4,5-dimethoxybenzene (60%). Yellow solid, mp: 289−290 °C, lit.[12b] 289−290 °C; IR (KBr): ν 2360 (m), 1638 (m), 1510 (s), 1472 (m), 1460 (m), 1350 (s), 1249 (m), 1212 (m), 1186 (m), 1150 (m), 1014 (m), 901 (m), 829 (m), 729 (m) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 12.31 (s, br, 2 H), 6.75 (s, 2 H), 3.76 (s, 6 H); ^{13}C NMR (75 MHz, DMSO- d_6): δ 166.1, 145.9, 125.4, 94.5, 56.0; MS (ESI^+, direct infusion): m/z 211 [$(M + H)^+$]; Anal. calcd for $C_9H_{10}N_2O_2S$ (210.25): C, 51.41; H, 4.79; N, 13.32; S, 15.25; found C, 51.60; H, 4.81; N, 13.29; S, 15.22.

Preparation of 2-(Prop-2-ynylthio)-1*H*-benzo[*d*]imidazoles 1.[14] To a solution of the 1,3-dihydrobenzimidazole-2-thione derivative (16.7 mmol) [1,3-dihydrobenzimidazole-2-thione: 2.50 g; 5,6-dimethyl-1,3-dihydrobenzimidazole-2-thione: 2.97 g; 5,6-dichloro-1,3-dihydrobenzimidazole-2-thione: 3.65 g; 5,6-dimethoxy-1,3-dihydrobenzimidazole-2-thione: 3.51 g; 5-methoxy-1,3-dihydrobenzimidazole-2-thione: 3.00 g; 5-fluoro-1,3-dihydrobenzimidazole-2-thione: 2.81 g] in anhydrous acetone (100 mL) was added, under nitrogen, K_2CO_3 (2.3 g, 16.7 mmol) followed by propargyl bromide (2.96 g, corresponding to 2.8 mL of a 80 wt % solution in toluene, 25.1 mmol). 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 the 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 **1a−f** were purified by column chromatography on silica gel using as eluent 9/1 hexane-AcOEt for **1a−c** and **1e** and 7/3 hexane-AcOEt for **1d** and **1f**. 2-(Prop-2-ynylthio)-1*H*-benzo[*d*]imidazolium bromide **1a′** was prepared as we already reported.[12b]

*2-(Prop-2-ynylthio)-1H-benzo[d]imidazole (**1a**).* Yield: 2.51 g starting from 2.50 g of 1,3-dihydrobenzimidazole-2-thione (80%). Colorless solid, mp: 165−167 °C, lit.[15]: 164−165 °C and 165−167;[12b] IR (KBr) ν 3048 (m), 2958 (m), 2888 (m), 2106 (vw), 1506 (w), 1444 (m), 1405 (s), 1351 (m), 1267 (m), 1227 (m), 1012 (m), 977 (m), 745 (s), 657 (m)cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 12.7 (s, br, 1 H), 7.56−7.42 (m, 2 H), 7.21−7.10 (m, 2 H), 4.16 (d, J = 2.6, 2 H), 3.22 (t, J = 2.6, 1 H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 148.3, 121.5, 114.3 (br), 80.0, 73.9, 19.7; MS (ESI^+, direct infusion): m/z 189 [$(M + H)^+$]; Anal. calcd for $C_{10}H_8N_2S$ (188.25): C, 63.80; H, 4.28; N, 14.88; S, 17.03; found C, 63.89; H, 4.30; N, 14.85; S, 16.96.

*5,6-Dimethyl-2-(prop-2-ynylthio)-1H-benzo[d]imidazole (**1b**).* Yield: 3.25 g starting from 2.97 g of 5,6-dimethyl-1,3-dihydrobenzimidazole-2-thione (90%). Colorless solid, mp: 163−164 °C; IR (KBr) ν 3051 (m), 2920 (m), 2122 (vw), 1451 (s), 1415 (m), 1389 (s), 1299 (w), 1234 (w), 974 (m), 854 (m) cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 7.24 (s, 2 H), 4.92 (s, br, 1 H), 3.99−3.93 (m, 2 H), 2.65−2.57 (m, 1 H), 2.32 (s, 6 H); ^{13}C NMR (75 MHz, CD_3OD): δ 148.5, 139.2, 132.8, 115.4, 79.8, 73.2, 22.3, 20.2; MS (ESI^+, direct infusion): m/z 217 [$(M + H)^+$]; Anal. calcd for $C_{12}H_{12}N_2S$ (216.30): C, 66.63; H, 5.59; N, 12.95; S, 14.82; found C, 66.29; H, 5.61; N, 12.90; S, 15.20.

*5,6-Dichloro-2-(prop-2-ynylthio)-1H-benzo[d]imidazole (**1c**).* Yield: 3.21 g starting from 3.65 g of 5,6-dichloro-1,3-dihydrobenzimidazole-2-thione (75%). Colorless solid, mp: 185−188 °C; IR (KBr) ν 3270 (m), 2923 (m), 2122 (w), 1492 (w), 1402 (m), 1332 (m), 1260 (m), 1095 (m), 967 (m), 866 (m), 660 (s) cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 7.60 (s, 2 H), 4.92 (s, br, 1 H), 4.07 (d, J = 2.6, 2 H), 2.68 (t, J = 2.6, 1 H); ^{13}C NMR (75 MHz, CD_3OD): δ 153.5, 140.3, 127.4, 116.5, 79.2, 73.5, 21.6; MS (ESi^+, direct infusion): m/z 257 [$(M + H)^+$]; Anal. calcd for $C_{10}H_6Cl_2N_2S$ (257.139): C, 46.71; H, 2.35; Cl, 27.57; N, 10.89; S, 12.47; found C, 46.79; H, 2.33; Cl, 27.61; N, 10.86; S, 12.41.

*5,6-Dimethoxy-2-(prop-2-ynylthio)-1H-benzo[d]imidazole (**1d**).* Yield: 3.43 g starting from 3.51 g of 5,6-dimethoxy-1,3-dihydrobenzimidazole-2-thione (83%). Yellow solid, mp: 95−97 °C; IR (KBr) ν 3287 (m), 2116 (w), 1665 (m), 1632 (m), 1597 (m), 1511 (m), 1497 (m), 1453 (m), 1368 (m), 1339 (m), 1243 (m), 1216 (m), 1147 (m), 1012 (m), 989 (m), 857 (m), 734 (s) cm-1; ^1H NMR (300 MHz, DMSO-d_6): δ 12.45 (s, br, 1 H), 7.03 (s, 2 H), 4.06 (d, J = 1.9, 2 H), 3.77 (s, 6 H), 3.22−3.16 (m, 1 H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 146.2, 144.9, 133.5, (br), 97.2 (br), 80.2, 73.9, 55.9, 20.5; MS (ESI^+, direct infusion): m/z 249 [$(M + H)^+$]; Anal. calcd for $C_{12}H_{12}N_2O_2S$ (248.30): C, 58.05; H, 4.87; N, 11.28; S, 12.91; found C, 57.91; H, 4.89; N, 11.26; S, 12.88.

*5-Methoxy-2-(prop-2-ynylthio)-1H-benzo[d]imidazole (**1e**).* Yield: 2.20 g starting from 3.00 g of 5-methoxy-1,3-dihydrobenzimidazole-2-thione (60%). Colorless solid, mp: 140−142 °C; IR (KBr) ν 3262 (m), 2122 (vw), 1622 (m), 1456 (m), 1396 (s), 1342 (m), 1301 (m), 1272 (w), 1227 (m), 1158 (m), 1113 (w), 981 (m), 815 (m) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 12.6 (s, br, 1 H), 7.50−7.34 (m, 1 H), 7.17−6.93 (m, 1 H), 6.81 (dd, J = 8.6, 2.3, 1 H), 4.15 (d, J = 2.5, 2 H), 3.79 (s, 3 H), 3.22 (t, J = 2.5, 1 H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 155.4, 147.0, 137.1, 117.9, 110.7, 100.2, 94.5, 80.1, 73.9, 55.4, 20.0; MS (ESI^+, direct infusion): m/z 219 [$(M + H)^+$]; Anal. calcd for $C_{11}H_{10}N_2OS$ (218.27): C, 60.53; H, 4.62; N, 12.83; S, 14.69; found C, 60.32; H, 4.60; N, 12.88; S, 14.72.

*5-Fluoro-2-(prop-2-ynylthio)-1H-benzo[d]imidazole (**1f**).* Yield: 2.10 g starting from 2.81 g of 5-fluoro-1,3-dihydrobenzimidazole-2-thione (61%). Yellow solid, mp: 132−134 °C; IR (KBr) ν 3303 (m), 1633 (m), 1498 (s), 1461 (m), 1427 (m), 1362 (m), 1274 (m), 1242 (m), 1159 (m), 997 (m), 860 (m), 677 (m) cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 7.44 (dd, J = 8.8, 4.7, 1 H), 7.20 (dd, J = 9.1, 2.3, 1 H), 7.06−6.92 (m, 1 H), 4.06−4.01 (m, 2 H), 2.69−2.63 (m, 1 H); ^{13}C NMR (75 MHz, CD_3OD): δ 161.1 (d, J = 238), 151.5, 141.1 (br), 137.4 (br), 116.0 (br), 111.5 (d, J = 26), 101.4 (d, J = 26), 79.8, 73.5, 73.4, 22.0; ^{19}F NMR (471 MHz, CD_3OD): δ −113.5 (s); MS (ESI^+,

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direct infusion): m/z 207 [$(M + H)^+$]; Anal. calcd for $C_{10}H_7FN_2S$ (206.24): C, 58.24; H, 3.42; F, 9.21; N, 13.58; S, 15.55; found C, 58.29; H, 3.40; F, 9.18; N, 13.61; S, 15.52.

General Procedure for the Synthesis of Thiadiazafluorenones 2a–f (Table 2). A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (5.8 mg, 1.61×10^{-2} mmol for **1a–e** and 14.6 mg, 4.05×10^{-2} mmol for **1f**), KI (134.0 mg, 0.81 mmol), anhydrous EtOH (4.0 mL), and 2-(prop-2-ynylthio)-1*H*-benzo[*d*]imidazole (0.81 mmol) (**1a**: 153 mg; **1b**: 175 mg; **1c**: 208 mg; **1d**: 201 mg; **1e**: 177 mg; **1f**: 167 mg). The autoclave was purged at room temperature several times with CO_2 under stirring (5 atm) and eventually pressurized with CO_2 (20 atm) and CO (up to 70 atm). After being stirred at 100 °C for 3 h (for **1a–e**) or 15 h (for **1f**), the autoclave was cooled, degassed, and opened. After evaporation of the solvent, products **2** were purified by column chromatography on alumina using 9/1 hexane-AcOEt (**2b** and **2c**) or 8/2 hexane-AcOEt (**2a**, **2e**, **2d**, and **2f**) as the eluent.

*3-Methyl-1-thia-4a,9-diazafluoren-4-one (**2a**).* Yield: 114 mg, starting from 153 mg of **1a** (65%) (Table 2, entry 1). Colorless solid, mp: 170–172 °C; IR (KBr): ν 1680 (s), 1639 (m), 1618 (m), 1472 (m), 1401 (m), 1360 (m), 1310 (m), 1200 (w), 771 (m) cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$): δ 8.54 (d, J = 7.8, 1 H), 7.76 (d, J = 7.7, 1 H), 7.54–7.36 (m, 2 H), 6.56–6.51 (m, 1 H), 2.48 (d, J = 0.9, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.6, 148.8, 146.7, 142.5, 131.2, 125.8, 124.2, 118.6, 116.1, 115.6, 22.8; GC-MS: m/z 216 (M^+, 100), 188 (29), 175 (4), 150 (33), 143 (6), 129 (4), 122 (5), 108 (4), 90 (9); Anal. calcd for $C_{11}H_8N_2OS$ (216.26): C, 61.09; H, 3.73; N 12.95; S, 14.83; found C, 61.35; H, 3.71; N 12.91; S, 14.89.

*3,6,7-Trimethyl-1-thia-4a,9-diazafluoren-4-one (**2b**).* Yield: 142 mg, starting from 175 mg of **1b** (72%) (Table 2, entry 2). Colorless solid, mp: 115–121 °C; IR (KBr): ν 1677 (s), 1377 (m), 1347 (m), 1315 (m), 1286 (m), 1184 (m), 1094 (w), 846 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.24 (s, 1 H), 7.45 (s, 1 H), 6.48–6.43, (m, 1 H), 2.44 (d, J = 1.1, 3 H), 2.39 (s, 3 H), 2.38 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.6, 148.2, 145.6, 141.6, 134.9, 133.5, 130.0, 119.0, 116.1, 115.8, 22.5, 20.2; GC-MS: m/z 244 (M^+, 100), 229 (20), 216 (16), 201 (7), 178 (23), 163 (10), 157 (3), 122 (7), 91 (7), 67 (10); Anal. calcd for $C_{13}H_{12}N_2OS$ (244.31): C, 63.91; H, 4.95; N 11.47; S, 13.12; found C, 63.80; H, 4.96; N 11.49; S, 13.09.

*6,7-Dichloro-3-methyl-1-thia-4a,9-diazafluoren-4-one (**2c**).* Yield: 164 mg, starting from 208 mg of **1c** (71%) (Table 2, entry 3). Yellow solid, mp: 153–155 °C; IR (KBr): ν 1692 (s), 1467 (w), 1375 (m), 1340 (m), 1297 (m), 1190 (m), 1095 (m), 842 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.64 (s, 1 H), 7.82 (s, 1 H), 6.56 (q, J = 1.2, 1 H), 2.52 (d, J = 1.2, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.5, 140.3, 127.4, 116.5, 79.2, 73.5, 21.6; GC-MS: m/z 286 [$(M + 2)^+$, 69], 284 (M^+, 100), 258 (23), 256 (33), 220 (18), 218 (25), 199 (3), 181 (8), 158 (4), 142 (4), 100 (4), 88 (6), 67 (61); Anal. calcd for $C_{11}H_6Cl_2N_2OS$ (285.15): C, 46.33; H, 2.12; Cl, 24.87; N 9.82; S, 11.24; found C, 46.21; H, 2.14; N 9.86; S, 11.27.

*6,7-Dimethoxy-3-methyl-1-thia-4a,9-diazafluoren-4-one (**2d**).* Yield: 150 mg, starting from 201 mg of **1d** (67%) (Table 2, entry 4). Yellow solid, mp: 187–188 °C; IR (KBr): ν 1678 (s), 1465 (s), 1436 (s), 1340 (m), 1307 (m), 1193 (m), 1153 (m), 1016 (m), 862 (m), 830 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.02 (s, 1 H), 7.18 (s, 1 H), 6.48 (s, 1 H), 3.99 (s, 3 H), 3.96 (s, 3 H), 2.47 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.7, 149.6, 148.4, 144.2, 137.1, 132.2, 125.4, 115.5, 101.7, 100.0, 56.9, 56.6, 22.5; GC-MS: m/z 276 (M^+, 100), 261 (28), 233 (6), 207 (11), 193 (5), 167 (5), 135 (5), 73 (6); Anal. calcd for $C_{13}H_{12}N_2O_3S$ (276.31): C, 56.51; H, 4.38; N 10.14; S, 11.60; found C, 56.66; H, 4.36; N 10.17; S, 11.64.

*Mixture of 6-Methoxy-3-methyl-1-thia-4a,9-diazafluoren-4-one and 7-Methoxy-3-methyl-1-thia-4a,9-diazafluoren-4-one (1.2/1 Mixture of Isomers A/B, by GLC) (**2e**).* Yield: 148 mg, starting from 177 mg of **1e** (74%) (Table 2, entry 5). Yellow solid, mp: 125–130 °C; IR (KBr): ν 1689 (s), 1594 (w), 1478 (s), 1432 (m), 1366 (m), 1303 (m), 1277 (m), 1200 (m), 1155 (m), 1023 (m), 839 (m) cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$): δ 8.37 (d, J = 9.0, A), 8.05 (d, J = 2.5, B), 7.61 (d, J = 8.8, B), 7.19 (d, J = 2.4, 1 H, A), 7.07 (dd, J = 8.8, 2.5, 1 H, B), 7.01 (dd, J = 9.0, 2.4, A), 6.51 (q, J = 1.1, 1 H, B), 6.48 (q, J = 1.1, 1 H, A), 3.91 (s, 3 H, B), 3.88 (s, 3 H, A), 2.48 (d, J = 1.2, 3 H, A), 2.47 (d, J = 1.1, 3 H, B) (Note: The A/B isomer assignments are based on ^1H NMR peak integration data: A refers to the major isomer and B refers to the minor isomer); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.5, 158.79, 158.75, 157.5, 149.1, 148.5, 147.1, 144.9, 135.3, 131.7, 130.9, 128.8, 125.0, 118.5, 116.7, 115.7, 115.4, 114.1, 100.3, 99.5, 56.0, 55.8, 29.7, 22.8; GC-MS [A (major isomer)]: m/z 246 (M^+, 100), 231 (42), 218 (7), 203 (14), 180 (21), 165 (29), 152 (4), 137 (4), 67 (36); GC-MS [B (minor isomer)]: m/z 246 (M^+, 100), 231 (41), 218 (9), 203 (10), 180 (15), 165 (27), 152 (4), 137 (6), 123 (3), 89 (4), 67 (34); Anal. calcd for $C_{12}H_{10}N_2O_2S$ (246.28): C, 58.52; H, 4.09; N 11.37; S, 13.02; found C, 58.37; H, 4.07; N 11.39; S, 13.05.

*Mixture of 6-Fluoro-3-methyl-1-thia-4a,9-diazafluoren-4-one and 7-Fluoro-3-methyl-1-thia-4a,9-diazafluoren-4-one (1.4:1 mixture of isomers A:B, by ^1H NMR) (**2f**).* Yield: 129 mg, starting from 167 mg of **1f** (68%) (Table 2, entry 6). Colorless solid, mp: 125–128 °C; IR (KBr): ν 1679 (s), 1466 (s), 1429 (s), 1355 (m), 1305 (m), 1135 (m), 958 (m), 862 (m), 813 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.47 (dd, J = 9.0, 5.0, 1 H, A), 8.24 (dd, J = 8.8, 2.4, 1 H, B), 7.67 (dd, J = 8.9, 4.8, 1 H, B), 7.40 (dd, J = 8.6, 2.3, 1 H, A), 7.28–7.09 (m, 1 H, A + 1 H, B), 6.55 (s, br, 1 H, A), 6.52 (s, br, 1 H, B), 2.50 (s, 3 H, A + 3 H, B) (Note: The A/B isomer assignments are based on ^1H NMR peak integration data: A refers to the major isomer and B refers to the minor isomer); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.9 (d, J = 243), 159.8 (d, J = 243), 159.4, 159.3, 149.3, 148.9, 143.3 (d, J = 12.5), 138.3 (d, J = 1.4), 131.1 (d, J = 13.9), 127.6 (d, J = 1.4), 119.2 (d, J = 9.7), 116.8 (d, J = 9.7), 115.5, 115.3, 114.1 (d, J = 25.0), 112.2 (d, J = 25.0), 104.8 (d, J = 25.0), 103.3 (d, J = 29.8), 22.9, 22.8; ^{19}F NMR (471 MHz, $CDCl_3$): δ −108.5 (s), −109.7 (s); GC-MS [A + B]: m/z 234 (M^+, 100), 206 (32), 191 (3), 168 (32), 162 (8), 147 (5), 136 (4), 108 (16), 95 (5); Anal. calcd for $C_{11}H_7FN_2OS$ (234.25): C, 56.40; H, 3.01; F 8.11; N, 11.96; S, 13.69; found C, 56.29; H, 3.02; N 11.99; S, 13.65.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01028.

Copies of ^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra for all products (PDF)

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Notes

The authors declare no competing financial interest.

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(7) Substrates **1** were easily prepared by propargylation of 1,3-dihydrobenzimidazole-2-thiones, as described in the Experimental Section.

(8) A blank experiment, carried out on **1a** under the same conditions as those of entry 1 (Table 1) but in the absence of carbon monoxide, resulted in partial substrate decomposition. On the other hand, when product **2a** was heated under the same conditions as those of entry 1 (Table 1), it could be recovered practically unreacted. These results show that **2a** was stable under the reaction conditions and that the formation of chromatographically immobile materials observed in the carbonylation reaction of **1a** reported in entry 1 (Table 1) must be due to partial substrate decomposition rather than product instability.

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