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Intramolecular Iodine-Mediated Oxygen Transfer from Nitro Groups to C≡C Bonds

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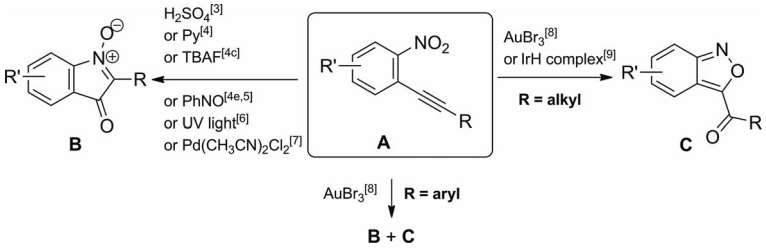
Highly regioselective oxygen transfer from nitro groups to C≡C bonds has been achieved by employment of iodine monochloride or molecular iodine. The precursors are heterocyclic, aromatic or acyclic compounds, each bearing a nitro group *ortho* to an internal alkyne. The developed methodology is general for the preparation of a wide range of fused isoxazoles, each bearing a carbonyl function in the fifth position in the isoxazole ring. It is very important to note that the outcomes of the cycloisomerizations are not dictated by the natures of the heterocycle or alkyne substituents. Moreover, this is a unique example of iodine-mediated ring closure of internal alkynes without introduction of halogen into the newly formed rings.

Introduction

Cyclization of alkynes containing adjacent nucleophilic centers is currently of considerable interest and developing into one of the most effective strategies for heterocyclic ring construction. This chemistry provides a straightforward approach to the synthesis of functionalized carbo- and heterocycles through regio- and stereoselective addition of a nucleophile to an unsaturated carbon unit across the carbon-carbon triple bond.[1] A variety of transition-metal- or electrophile-induced 5-*exo*-*dig* or 6-*endo*-*dig* cyclization reactions have been reported.[2] *ortho*-Alkynyl nitrobenzenes **A** (Scheme 1) are well known as precursors for the preparation of isatogens **B**. Since Baeyer's pioneering work,[3] a variety of intramolecular cyclizations of *o*-alkynylnitrobenzenes have been reported. The classical cycloisomerizations of starting compounds **A** to afford isatogens **B** can be initiated by concentrated sulfuric acid,[3] pyridine,[4] tetrabutylammonium fluoride (TBAF),[4c] nitrosobenzene,[4e,5] or UV light.[6]

Usually these classic reactions take long times and require high temperatures. On the other hand, nitro-alkyne cycloisomerization can be effectively catalyzed by metal catalysts under relatively mild reaction conditions. In metal-mediated nitro-alkyne cycloisomerizations, however, formation of two products – isatogens **B** and/or anthranils **C** (Scheme 1) – is possible. *o*-Alkynylnitrobenzenes thus selectively formed isatogens **B** in the presence of a catalytic amount of $Pd(CH_3CN)_2Cl_2$,[7] whereas *o*-arylalkynylnitrobenzenes formed mixtures of isatogens **B** and anthranils **C** in the presence of gold(III) bromide.[8] On the other hand, *o*-alkylalkynylnitrobenzenes were converted selectively into anthranils **C** in the presence of gold(III) bromide[8] or iridium hydride complex.[9]



Scheme 1. Literature results.

Several years ago we developed a concise and high-yielding route to pyrrolo[3,2-*d*]pyrimidin-7-one 5-oxides **E** (Scheme 2) through smooth cycloisomerization of 2,4-disubstituted 6-arylethynyl-5-nitropyrimidines **D** in the presence of pyridine. We showed that the triple bonds in the starting compounds are electron-poor, so cycloisomeriza-

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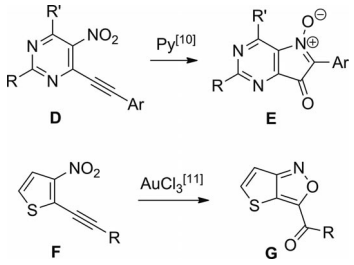
tion takes only few minutes and does not require transition-metal catalysts, UV initiation, or harsh conditions.[10] It was also shown by us that electron-rich 2-alkynyl-3-nitrothiophenes **F** (Scheme 2) underwent smooth regioselective intramolecular cycloisomerization to afford thieno[2,3-*c*][1,2]-oxazoles **G** in the presence of gold(III) chloride or silver(I) trifluoroacetate. It is notable that the outcomes of the cyclizations of 2-alkynyl-3-nitrothiophenes **F** were not dictated by the natures of the alkyne substituents.[11]



Scheme 2. Our previous results.

Molecular iodine has recently been reported to function as a Lewis acid and to impart high regio- and chemoselectivity in various transformations.[12] Use of iodine as a Lewis acid has been increasing exponentially for the last decade, due to its high tolerance to air and moisture, low cost, and high catalytic activity both under dilute and under highly concentrated conditions, as well as under solvent-free reaction conditions. It is also known that I^+ is a soft electrophilic reagent that can promote the intramolecular attack of carbon, oxygen, and nitrogen nucleophiles on alkynes.[13] In continuation of our research into cycloisomerizations of various substrates containing various functional groups and alkynyl moieties in close proximity to one another, it was envisioned that electrophilic iodine could well activate C≡C bonds in nitro-alkyne cycloisomerizations. Indeed, highly regioselective iodine-mediated nitro-alkyne cycloisomerizations of various substrates were observed. Here we report the results of our investigations.

Results and Discussion

The starting compounds, each bearing a nitro group and an ethynyl moiety in close proximity (Figure 1), were synthesized by classical Sonogashira coupling[14] between halogen derivatives and terminal acetylenes. 2-Alkynyl-3-nitrothiophenes **1a**–**g**, 3-alkynyl-2-nitrothiophenes **2a**, **2b**, 2-alkynylnitrobenzenes **3a**, **3b**, 2-alkynyl-3-nitropyridines **4a**–**f**, and 4-alkynyl-5-nitropyrimidines **5a**, **5b** were prepared.

The prepared heteroaryl and aryl substrates, each bearing a nitro group and an alkynyl substituent in close proximity to one another, can undergo cycloisomerization reactions into products containing either pyrrol-3-one 1-oxide or isoxazole rings (Scheme 3), so the scope of nitro-alkyne cycloisomerization of various substrates bearing both phenyl and alkyl substituents on their alkyl moieties was explored first. The results of cycloisomerizations of thio-

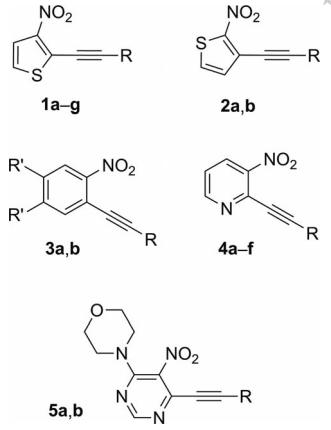
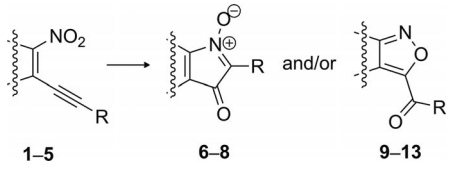


Figure 1. Nitro-alkyne precursors. **1**: R = Ph (**a**), Bu (**b**), 4-$CH_3C_6H_4$ (**c**), 4-$C_2H_5C_6H_4$ (**d**), 2-Py (**e**), *t*Bu (**f**), H (**g**). **2**: R = Ph (**a**), *c*-Pr (**b**). **3**: R = Ph, R′ = OCH_3 (**a**), R = *c*-Pr, R′ = H (**b**). **4**: R = Ph (**a**), Bu (**b**), 4-$CH_3C_6H_4$ (**c**), 4-$C_2H_5C_6H_4$ (**d**), *c*-Pr (**e**), H (**f**). **5**: R = Ph (**a**), Bu (**b**).

phenes **1a**, **1b**, and **2a**, benzenes **3a** and **3b**, pyridines **4a** and **4b**, and pyrimidines **5a** and **5b** under the different conditions are presented in Table 1.



Scheme 3. Cycloisomerization of nitro-alkyne precursors.

The feasibility of the nitro-alkyne cycloisomerization was examined with the catalysts most commonly described in the literature: gold(III) bromide (Table 1, Method A), $PdCl_2(CH_3CN)_2$ (Table 1, Method B) and pyridine (Table 1, Method C). Moreover, the potential for the use of iodine monochloride to initiate nitro-alkyne cycloisomerization was also studied (Table 1, Method D).

Use of gold(III) bromide in dichloromethane at room temperature (Table 1, Method A, Entries 1–3) led to the selective formation of (thieno[2,3-*c*][1,2]oxazol-3-yl)-methanones **9a** and **9b** (Figure 2, below) and phenyl(thieno[2,3-*c*][1,2]oxazol-3-yl)methanone (**10a**). Treatment of benzene derivative **3a** with $AuBr_3$ (5 mol-%) in dichloromethane at room temperature gave the mixture of isatogen **6a** and the 2,1-benzoxazol **11a** (Table 1, Method A, Entry 4). On the other hand, 1-cyclopropylethynyl-2-nitrobenzene (**3b**) was selectively converted into 2,1-benzoxazol **11b** in the presence of $AuBr_3$ (Table 1, Method A, Entry 5). However, pyridine and pyrimidine systems **4a**/**4b** and **5a**/**5b** with nitro-alkyne substrates were completely unreactive toward cycloisomerization conditions on exposure to $AuBr_3$. In all these cases (Table 1, Method A, Entries 6–9) the starting materials were recovered after workup of the reaction mixtures.

Next, the scope of the cycloisomerization described by Ramana et al. (Table 1, Method B)[7] was studied. $Pd(CH_3CN)_2Cl_2$ worked well with benzene substrates **3a** and **3b**. Both compounds were converted selectively into

Table 1. Study of cycloisomerization of selected nitro-alkyne precursors.

Entry	Starting compound	R	Products of cycloisomerization reactions (yield, %) Method A[a]	Method B[b]	Method C[c]	Method D[d]
1	**1a**	Ph	**9a** (97%)	**9a** (33%) [e]	no reaction	**9a** (98%)
2	**1b**	Bu	**9b** (91%)	**9b** (37%) [e]	no reaction	**9b** (99%)
3	**2a**	Ph	**10a** (45%)[e]	**10a** (15%)[e]	no reaction	**10a** (88%)
4	**3a**	Ph (R′ = OCH_3)	**6a** (60%) and **11a** (29%)	**6a** (55%)	no reaction	**6a** (3%) and **11a** (87%)
5	**3b**	*c*-Pr (R′ = H)	**11b** (76%)	**6b** (49%)[e]	no reaction	**11b** (99%)
6	**4a**	Ph	no reaction	no reaction	**7** (82%)	**12a** (92%)
7	**4b**	Bu	no reaction	no reaction	no reaction	**12b** (93%)
8	**5a**	Ph	no reaction	no reaction	**8** (96%)	**13** (69%)
9	**5b**	Bu	no reaction	no reaction	no reaction	complicated[f]

[a] Reaction conditions: $AuBr_3$ (5 mol-%), DCM, r.t., 2 h. [b] Reaction conditions: $PdCl_2(CH_3CN)_2$ (5 mol-%), CH_3CN, r.t., 6 h. [c] Reaction conditions: heating of the starting material at reflux in dry pyridine (20 min for **5a** and 2 h for **4a**). [d] Reaction conditions: ICl (3 mol-%), DCE, reflux (30 min for **1**–**3**, 1 h for **4**, 4 h for **5**). [e] Incomplete conversion of the starting material after 24 h. [f] A lot of byproducts were formed.

3*H*-indol-3-one 1-oxides **6a** and **6b** (Table 1, Method B, Entries 4 and 5). However, the palladium complex gave different selectivity with thiophene substrates **1a**, **1b**, and **2a**, which were converted into methanones **9a**, **9b**, and **10a** in low yields (Table 1, Method B, Entries 1–3). It should be also noted that the conversions of the starting thiophenes were incomplete after prolonged heating of the reaction mixtures. Pyridine and pyrimidine derivatives **4a/4b** and **5a/5b** remained unchanged on treatment with $Pd(CH_3CN)_2Cl_2$ (Table 1, Method B, Entries 6–9).

The pyridine-initiated cycloisomerization was successful only in cases of electron-poor heterocycles bearing phenylethynyl moieties in close proximity to their nitro groups. The pyridine derivative **4a** and the pyrimidine **5a** were converted into the corresponding heterocyclic isatogen analogues **7** and **8** on heating at reflux in dry pyridine (Table 1, Method C, Entries 6 and 8).

It was therefore possible to conclude at this stage of the investigation that metal catalysts $AuBr_3$ and $Pd(CH_3CN)_2Cl_2$ gave satisfactory results only in the cases of benzene derivatives and electron-rich thiophene heterocycles. Whereas gold(III) bromide usually leads to the formation of isoxazoles, the palladium complex catalyzes the cycloisomerization of *o*-alkynylnitrobenzenes to 3*H*-indol-3-one 1-oxides **6a** and **6b**, but also leads to the formation of thieno-isoxazoles **9a**, **9b**, and **10a** in low yields. The nucleophilic initiation of nitro-alkyne cycloisomerization by pyridine is possible only in cases of electron-poor heterocycles bearing aryl substituents on their alkyne moieties.

Next the possibility of using iodine monochloride as a mild Lewis acid for the promotion of nitro-alkyne cycloisomerization was studied. The starting nitro-alkyne substrates were heated at reflux in dichloroethane in the presence of ICl (3 mol-%). A pleasant surprise was to see that the regioselective cycloisomerization reactions of compounds **1**–**5** into products **9**–**13**, containing isoxazole rings, took place in almost all cases (Table 1, Method D, Entries 1–8). The exception was the cycloisomerization of 6-(hex-1-ynyl)-4-morpholinyl-5-nitropyrimidine **5b**. The reaction behavior of compound **5b** was complicated, leading to a mixture of various products (Table 1, Method D, Entry 9).

After these intriguing results, the best conditions for triggering iodine-mediated regioselective oxygen transfer from nitro groups to alkyne moieties were optimized. First of all, some other sources of iodine were also studied. It should be noted that iodine monochloride gave the best results in terms of yields, amount of the catalyst, and reaction time. Another good catalyst for nitro-alkyne cycloisomerization is molecular iodine. To determine its effectiveness, reactions were run with different concentrations of it (1 mol-%, 5 mol-%, 10 mol-%, 20 mol-%, and 50 mol-%). The reaction took place at all concentrations, but 20 mol-% of iodine was found to be the best. Bis(pyridine)iodonium tetrafluoroborate, however, did not promote the cycloisomerization effectively.

1,2-Dichloroethane was found to be the most suitable solvent in comparison with acetonitrile, methanol, tetrahydrofuran, dimethylformamide, and 1,4-dioxane. The iodine-mediated cycloisomerization reactions of the starting nitro-alkyne precursors proceeded readily and in the most cases showed excellent regioselectivity independently of alkyne substituent and the nature of the heterocycle (Figure 2). However, it should be noted that 2-ethynyl-3-nitrothiophene (**1g**) and 2-ethynyl-3-nitropyridine (**4f**) did not undergo cycloisomerization on heating at reflux in dichloroethane in the presence of molecular iodine. In these two cases the slow formation of diiodo compounds **14** and **15** took place. Probably, the absence of a substituent on the alkyne moiety favors electrophilic 1,2-addition of iodine to the triple bond. On the other hand, the presence of an alkyl or aryl substituent on the alkyne moiety and of the nitro group in the *ortho*-position sterically disfavor 1,2-addition, and intramolecular oxygen transfer from the nitro group takes place.

A possible mechanism of the cycloisomerization reaction is presented in Scheme 4. It seems that the iodine catalyst behaves in a way very similar to that in related gold-catalyzed oxygen functionality transfer reactions.[15] After the direct iodonium activation (intermediate **I**) of the triple bond, the intramolecular 6-*endo-dig* nucleophilic attack of the oxygen of the nitro group takes place, leading to the formation of the intermediate **II**. Cleavage of the N–O bond gives the intermediate **III**, which undergoes recyclization to

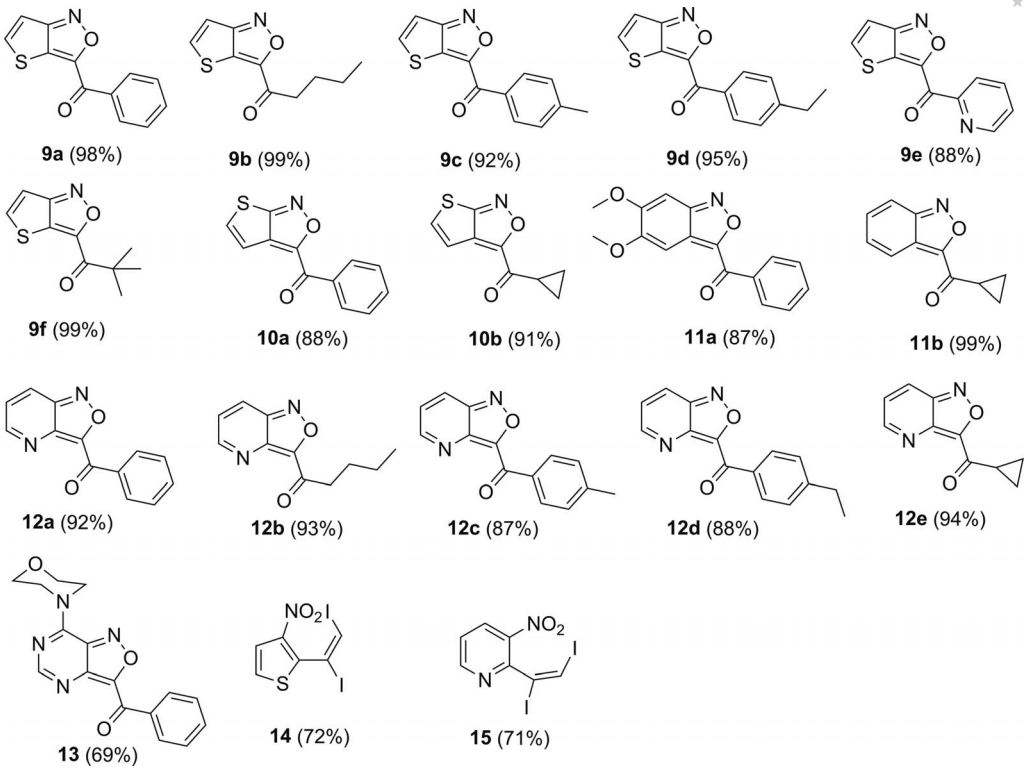
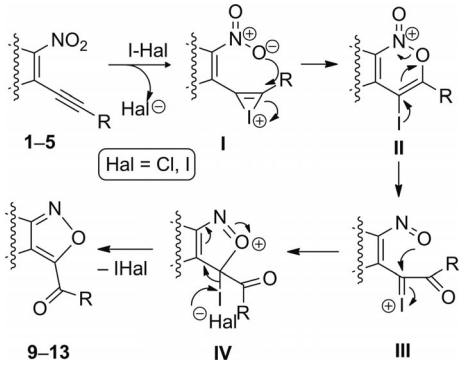


Figure 2. Compounds prepared through iodine-mediated cycloisomerization of various nitro-alkyne precursors.

IV. Finally, abstraction of iodine by an anion leads to the aromatization of the isoxazole moiety and regeneration of the catalyst.



Scheme 4. Possible mechanism for the iodine-mediated nitro-alkyne cycloisomerization.

It is well known from the literature that various intramolecular transformations of functionally substituted alkynes can be carried out either with gold catalysts or with iodine electrophiles to access the same core unit in an analogous manner.

In almost all cases electrophilic cyclization results in incorporation of iodine in the final product,[13] whereas gold catalysis typically results in hydrogen at the same position, due to the protodeauration step required for catalyst regeneration.[15,16] The method presented here is a unique example of iodine-mediated ring closure of internal alkynes without the introduction of halogen or oxygen from the solvent into the newly formed ring. Moreover, the developed method can be used broadly for the preparation of fused isoxazoles through nitro-alkyne cycloisomerization of either electron-rich or electron-poor substrates. The reaction conditions employed are catalytic in nature and mild, accommodating both aryl and alkyl substituents on the alkyne moieties.

Conclusions

The first examples of iodine-mediated regioselective nitro-alkyne cycloisomerization have been demonstrated. The method has several advantages over metal-mediated reactions, such as low cost, tolerance to air and moisture, and high regioselectivity. The outcomes of the cycloisomerizations are not dictated by the natures of the heterocycles or the alkyne substituents. Moreover, they represent unique examples of iodine-mediated ring closure of internal alkynes without introduction of halogen into the newly formed rings, and constitute the first report of highly regioselective nitro-alkyne cycloisomerization through a 6-*endo*-*dig* process. A new, simple, and high-yielding synthetic route to a range of compounds containing the isoxazole framework is therefore presented.

Experimental Section

IR spectra were measured with a Perkin–Elmer FT Spectrum BX II spectrophotometer (KBr discs). ^{1}H and ^{13}C NMR spectra were re-

corded with a Varian Unity INOVA spectrometer (300 MHz) with use of residual solvent peaks as internal standards. HRMS spectra were obtained with a Dual-ESI Q-TOF 6520 mass spectrometer (Agilent Technologies). All reactions and the purities of the synthesized compounds were monitored by TLC with silica gel 60 F254 aluminum plates (Merck). Visualization was accomplished by use of UV light.

General Procedure for the Preparation of Compounds 1–5: A mixture of the appropriate nitroaryl halide (5 mmol), $PdCl_2(PPh_3)_2$ (5 mol-%), and Et_3N (1.01 g; 10 mmol) was suspended in anhydrous THF (8 mL). The appropriate acetylene (1.1 equiv.) was then injected under argon, followed by addition of CuI (2.5 mol-%). The reaction mixture was stirred under argon at 40 °C temperature until full completion (normally 1–3 h, completion observed by TLC). Solvent was evaporated under the reduced pressure; the crude residue was purified by column chromatography (elution by mixtures of hexane and ethyl acetate).

3-Nitro-2-(phenylethynyl)thiophene (1a): Yellowish solid; yield 69%; m.p. 62–64 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.25 [d, J = 6.0 Hz, 1 H, C(4)-H], 7.42–7.45 (m, 3 H, ArH), 7.63–7.66 (m, 2 H, ArH), 7.64 [d, J = 6.0 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 79.6, 102.8, 121.7, 123.7, 125.2, 125.4, 128.5, 129.7, 131.9, 147.9 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2207 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{12}H_8NO_2S$ [M + H]$^+$ 230.0270; found 230.0269.

2-(Hex-1-ynyl)-3-nitrothiophene (1b): Yellow oil; yield 90%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.93 (t, J = 7.5 Hz, 3 H, $CH_2CH_2CH_2CH_3$), 1.44–1.52 (m, 2 H, $CH_2CH_2CH_2CH_3$), 1.58–1.67 (m, 2 H, $CH_2CH_2CH_2CH_3$), 2.53 (t, J = 7.5 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 7.10 [d, J = 5.7 Hz, 1 H, C(4)-H], 7.50 [d, J = 5.7 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 13.5, 19.8, 21.9, 30.0, 71.1, 105.9, 123.2, 124.1, 126.4, 147.5 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2225 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{10}H_{12}NO_2S$ [M + H]$^+$ 210.0583; found 210.0566.

2-[(4-Methylphenyl)ethynyl]-3-nitrothiophene (1c): Yellow solid; yield 74%; m.p. 70–71 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.39 (s, 3 H, CH_3), 7.18–7.21 [m, 3 H, ArH and C(4)-H], 7.49 (d, J = 8.1 Hz, 2 H, ArH), 7.60 [d, J = 5.7 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 21.9, 79.6, 103.7, 118.9, 123.9, 125.3, 126.1, 129.6, 132.2, 140.6, 148.1 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2196 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{13}H_{10}NO_2S$ [M + H]$^+$ 244.0427; found 244.0439.

2-[(4-Ethylphenyl)ethynyl]-3-nitrothiophene (1d): Yellow solid; yield 88%; m.p. 72–74 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.25 (t, J = 7.5 Hz, 3 H, CH_3), 2.68 (q, J = 7.5 Hz, 2 H, CH_2), 7.18–7.24 [m, 3 H, ArH and C(4)-H], 7.53 (d, J = 8.1 Hz, 2 H, ArH), 7.59 [d, J = 5.7 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 14.8, 28.5, 78.8, 99.5, 102.9, 118.4, 123.1, 124.5, 127.7, 131.5, 132.0, 146.0 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2203 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{14}H_{12}NO_2S$ [M + H]$^+$ 258.0583; found 258.0577.

2-[(3-Nitrothien-2-yl)ethynyl]pyridine (1e): Yellow solid; yield 71%; m.p. 112–114 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.30 [d, J = 5.7 Hz, 1 H, C(4)-H], 7.30–7.34 (m, 1 H, ArH), 7.61 [d, J = 5.7 Hz, 1 H, C(5)-H], 7.64 (dt, J = 7.8, 1.2 Hz, 1 H, ArH), 7.71–7.78 (m, 1 H, ArH), 8.64–8.66 (m, 1 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 79.0, 100.3, 123.7, 123.9, 125.1, 126.7, 128.0, 136.6, 141.9, 148.8, 150.1 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2211 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{11}H_7N_2O_2S$ [M + H]$^+$ 231.0223; found 231.0218.

2-(3,3-Dimethylbut-1-ynyl)-3-nitrothiophene (1f): Yellowish oil; yield 69%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.35 (s, 9 H, *t*Bu), 7.31 [d, J = 6.0 Hz, 1 H, C(4)-H], 7.55 [d, J = 6.0 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 28.2, 30.5, 70.2, 100.3, 120.3, 124.3, 126.2, 143.6 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2224 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{10}H_{12}NO_2S$ [M + H]$^+$ 210.0583; found 210.0570.

2-Ethynyl-3-nitrothiophene (1g): Compound **1g** was prepared from the intermediate 3-nitro-2-trimethylsilylthiophene (obtained by Sonagashira coupling) by treatment with potassium fluoride in methanol solution at room temperature for 20 min. Purification was accomplished by column chromatography. Yellowish solid; yield 85%; m.p. 89–90 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.90 (s, 1 H, ≡C–H), 7.25 [d, J = 5.7 Hz, 1 H, C(4)-H], 7.58 [d, J = 5.7 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 73.1, 90.7, 123.5, 123.7, 126.1, 139.3 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 3268 (≡C–H), 2104 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_6H_4NO_2S$ [M + H]$^+$ 153.9957; found 153.9966.

2-Nitro-3-(phenylethynyl)thiophene (2a): Yellowish oil; yield 80%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.15 [d, J = 5.4 Hz, 1 H, C(4)-H], 7.38–7.41 (m, 3 H, ArH), 7.45 [d, J = 5.4 Hz, 1 H, C(5)-H], 7.61–7.64 (m, 2 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 82.3, 99.4, 121.9, 128.5, 129.2, 129.6, 130.1, 131.3, 132.1, 132.4 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2205 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{12}H_8NO_2S$ [M + H]$^+$ 230.0270; found 230.0275.

3-(Cyclopropylethynyl)-2-nitrothiophene (2b): Yellowish oil; yield 84%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.94–1.01 (m, 4 H, *c*-Pr), 1.51–1.59 (m, 1 H, *c*-Pr), 7.00 [d, J = 5.7 Hz, 1 H, C(4)-H], 7.38 [d, J = 5.7 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 0.9, 9.6, 69.3, 105.9, 124.3, 129.9, 131.6, 147.8 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2220 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_9H_8NO_2S$ [M + H]$^+$ 194.0270; found 194.0272.

1,2-Dimethoxy-4-nitro-5-(phenylethynyl)benzene (3a): Yellow solid; yield 67%; m.p. 117–118 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.02 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 7.12 (s, 1 H, ArH), 7.40–7.43 (m, 3 H, ArH), 7.63–7.65 (m, 2 H, ArH), 7.73 (s, 1 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 56.3, 56.5, 85.7, 95.8, 107.6, 115.0, 127.5, 128.3, 128.4, 128.9, 131.8, 142.5, 148.7, 152.7 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2211 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{14}NO_4$ [M + H]$^+$ 284.0917; found 284.0930.

1-(Cyclopropylethynyl)-2-nitrobenzene (3b): Yellowish oil; yield 91%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.90–0.98 (m, 4 H, *c*-Pr), 1.48–1.57 (m, 1 H, *c*-Pr), 7.38 (td, J = 7.1, 2.1 Hz, 1 H, ArH), 7.49–7.58 (m, 2 H, ArH), 7.96–7.99 (m, 1 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 0.6, 9.1, 71.1, 102.6, 119.3, 124.3, 127.5, 132.5, 134.5, 149.8 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2232 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{11}H_{10}NO_2$ [M + H]$^+$ 188.0706; found 188.0711.

3-Nitro-2-(phenylethynyl)pyridine (4a): Beige solid; yield 82%; m.p. 107–109 °C (propan-2-ol). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.42–7.51 (m, 4 H, ArH), 7.70–7.73 (m, 2 H, ArH), 8.42 [dd, J = 8.1, 1.2 Hz, 1 H, C(4)-H], 8.84 [d, J = 3.6, 1 H, C(6)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 85.0, 97.8, 121.3, 122.6, 128.5, 130.1, 132.5, 132.6, 137.5, 146.2, 153.5 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2223 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{13}H_9N_2O_2$ [M + H]$^+$ 225.0659; found 225.0666.

2-(Hex-1-ynyl)-3-nitropyridine (4b): Brownish oil; yield 89%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.90 (t, J = 7.2 Hz, 3 H, $CH_2CH_2CH_2CH_3$), 1.40–1.50 (m, 2 H, $CH_2CH_2CH_2CH_3$), 1.57–1.66 (m, 2 H, $CH_2CH_2CH_2CH_3$), 2.50 (t, J = 6.9 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 7.34–7.38 [m, 1 H, C(5)-H], 8.24 [dd, J = 8.25; 1.5 Hz, 1 H, C(4)-H], 8.73 [br s, 1 H, C(6)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 13.4, 19.4, 21.9, 29.8, 76.5, 100.8, 122.2,

128.2, 132.1, 137.5, 153.0 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2228 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{11}H_{13}N_2O_2$ $[M + H]^+$ 205.0972; found 205.0992.

2-[(4-Methylphenyl)ethynyl]-3-nitropyridine (4c): Beige solid; yield 83%; m.p. 88–90 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.38 (s, 3 H, CH_3), 7.20 (d, J = 7.8 Hz, 2 H, ArH), 7.41 [dd, J = 8.4, 4.8 Hz, 1 H, C(5)-H], 7.56 (d, J = 7.8 Hz, 2 H, ArH), 8.39 [dd, J = 8.4, 1.5 Hz, 1 H, C(4)-H], 8.82 [dd, J = 4.8, 1.5 Hz, 1 H, C(6)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 21.9, 84.9, 98.7, 118.5, 122.7, 129.6, 132.7, 132.8, 137.9, 140.9, 146.0, 153.7 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2217 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{14}H_{11}N_2O_2$ $[M + H]^+$ 239.0815; found 239.0823.

2-[(4-Ethylphenyl)ethynyl]-3-nitropyridine (4d): Beige solid; yield 81%; m.p. 90–92 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.19 (t, J = 7.8 Hz, 3 H, CH_3), 2.52 (q, J = 7.8 Hz, 2 H, CH_2), 7.19 (d, J = 7.8 Hz, 2 H, ArH), 7.40 [dd, J = 8.4, 4.8 Hz, 1 H, C(5)-H], 7.52 (d, J = 7.8 Hz, 2 H, ArH), 8.40 [dd, J = 8.4, 1.5 Hz, 1 H, C(4)-H], 8.81 [dd, J = 4.8, 1.5 Hz, 1 H, C(6)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 14.3, 28.9, 85.9, 97.7, 117.5, 121.7, 129.5, 132.2, 132.9, 136.9, 140.5, 146.4, 153.9 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2216 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{15}H_{13}N_2O_2$ $[M + H]^+$ 253.0972; found 253.0980.

2-Cyclopropyl-3-nitropyridine (4e): Brown oil; yield 79%. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.98–1.01 (m, 4 H, *c*-Pr), 1.52–1.60 (m, 1 H, *c*-Pr), 7.37 [dd, J = 8.25, 4.5 Hz, 1 H, C(5)-H], 8.28 [dd, J = 8.25, 1.5 Hz, 1 H, C(4)-H], 8.74 [br s, 1 H, C(6)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 0.9, 9.8, 72.4, 104.7, 122.2, 128.8, 132.5, 137.9, 153.5 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2226 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{10}H_9N_2O_2$ $[M + H]^+$. 189.0658; found 189.0670.

2-Ethynyl-3-nitropyridine (4f): Compound **4f** was prepared from the intermediate 3-nitro-2-(trimethylsilyl)pyridine (obtained by Sonagashira coupling) by treatment with potassium fluoride in methanol solution at room temperature for 20 min. Purification was accomplished by column chromatography. Brownish solid; yield 53%; m.p. 65–67 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.69 (s, 1 H, ≡C–H), 7.53 [dd, J = 8.25, 4.5 Hz, 1 H, C(5)-H], 8.39 [dd, J = 8.25, 1.5 Hz, 1 H, C(4)-H], 8.87 [dd, J = 4.5, 1.5 Hz, 1 H, C(6)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 78.2, 85.4, 123.4, 132.1, 133.9, 136.0, 153.2 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 3264 (≡C–H), 2214 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_7H_5N_2O_2$ $[M + H]^+$ 149.0346; found 149.0364.

4-Morpholinyl-5-nitro-6-(phenylethynyl)pyrimidine (5a): Yellow solid; yield 62%; m.p. 142–144 °C (propan-2-ol). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.63–3.66 [m, 4 H, $N(CH_2)_2$], 3.79–3.83 [m, 4 H, $O(CH_2)_2$], 7.39–7.48 (m, 3 H, ArH), 7.63–7.67 (m, 2 H, ArH), 8.60 [s, C(2)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 46.4, 66.3, 82.7, 99.6, 120.5, 128.5, 130.5, 132.8, 144.2, 144.4, 153.6, 157.3 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2219 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{15}N_4O_3$ $[M + H]^+$ 311.1139; found 311.1145.

6-(Hex-1-ynyl)-4-morpholinyl-5-nitropyrimidine (5b): Brownish oil; yield 74%. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.90 (t, J = 7.2 Hz, 3 H, $CH_2CH_2CH_2CH_3$), 1.37–1.48 (m, 2 H, $CH_2CH_2CH_2CH_3$), 1.52–1.62 (m, 2 H, $CH_2CH_2CH_2CH_3$), 2.44 (t, J = 6.9 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 3.52–3.56 [m, 4 H, $N(CH_2)_2$], 3.70–3.73 [m, 4 H, $O(CH_2)_2$], 8.47 [s, 1 H, C(2)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 13.4, 19.3, 21.8, 29.6, 46.2, 66.2, 74.4, 102.9, 133.6, 144.5, 153.3, 157.1 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 2223 (C≡C) cm^{-1}. HRMS (ES): calcd. for $C_{14}H_{19}N_4O_3$ $[M + H]^+$ 291.1452; found 291.1459.

Palladium(II)-Mediated Cycloisomerization: The palladium(II)-mediated cycloisomerization was performed by the method reported by Ramana et al.[7]

5,6-Dimethoxy-2-phenyl-3*H*-indol-3-one 1-Oxide (6a): Violet solid; yield 55%; m.p. 200–202 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.01 (s, 3 H, OCH_3), 4.08 (s, 3 H, OCH_3), 7.17 (s, 1 H, ArH), 7.30 (s, 1 H, ArH), 7.48–7.53 (m, 3 H, ArH), 8.63–8.66 (m, 2 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 56.7, 56.9, 98.6, 104.3, 114.4, 126.1, 127.5, 128.5, 130.1, 130.4, 143.1, 151.0, 154.3, 186.6 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1701 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{14}NO_4$ $[M + H]^+$ 284.0917; found 284.0922.

2-Cyclopropyl-3*H*-indol-3-one 1-Oxide (6b): Orange solid; yield 49%; m.p. 137–139 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.08–1.15 (m, 2 H, *c*-Pr), 1.53–1.58 (m, 2 H, *c*-Pr), 2.15–2.25 (m, 1 H, *c*-Pr), 7.41–7.48 (m, 2 H, ArH), 7.52–7.57 (m, 1 H, ArH), 7.60–7.63 (m, 1 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 6.5, 6.9, 113.1, 120.7, 122.6, 130.3, 134.3, 138.8, 146.8, 185.9 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1708 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{11}H_{10}NO_2$ $[M + H]^+$ 188.0706; found 188.0700.

General Procedure for the Pyridine-Mediated Cycloisomerization: A solution of the alkyne **4a** or **5a** (1 mmol) in pyridine (5 mL) was heated at reflux for 30 min. After the system had cooled to room temperature, the precipitate was filtered off and recrystallized to give the product as a dark red (**7**) or violet (**8**) solid.

2-Phenyl-3*H*-pyrrolo[3,2-*b*]pyridin-3-one 1-Oxide (7): Dark red solid; yield 92%; m.p. 190–192 °C (propan-2-ol). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.50–7.53 (m, 3 H, ArH), 7.57 [dd, J = 7.8, 5.1 Hz, 1 H, C(6)-H], 8.00 [dd, J = 7.8, 1.2 Hz, 1 H, C(7)-H], 8.63–8.67 (m, 2 H, ArH), 8.81 [dd, J = 5.1, 1.4 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 121.6, 125.2, 126.4, 127.4, 128.0, 128.7, 131.4, 142.9, 143.6, 152.2, 185.3 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1726 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{13}H_9N_2O_2$ $[M + H]^+$ 225.0659; found 225.0666.

4-(4-Morpholinyl)-6-phenyl-7*H*-pyrrolo[3,2-*d*]pyrimidin-7-one 5-Oxide (8): Dark violet solid; yield 96%; m.p. 184–186 °C. ^1H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 3.89–3.92 [m, 4 H, $N(CH_2)_2$], 4.02–4.05 [m, 4 H, $O(CH_2)_2$], 7.50–7.54 (m, 3 H, ArH), 8.48–8.52 (m, 2 H, ArH), 8.89 [s, 1 H, C(2)-H] ppm. ^{13}C NMR (75 Hz, [D$_6$]DMSO, 25 °C): δ = 49.7, 66.9, 125.0, 127.7, 128.6, 130.5, 130.9, 132.8, 150.9, 151.3, 159.7, 186.4 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1710 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{15}N_4O_3$ $[M + H]^+$ 311.1139; found 311.1145.

General Procedure for the Iodine-Mediated Cycloisomerization: Iodine monochloride (2.44 mg, 0.015 mmol) or iodine (25 mg, 0.1 mmol) was added to a solution of the appropriate compound **1**–**5** (0.5 mmol) in 1,2-dichloroethane (10 mL), and the resulting solution was heated at reflux until full completion (1–4 h.). The reaction mixture was diluted with dichloromethane and washed with saturated aqueous $Na_2S_2O_3$ solution (2 × 40 mL) and then with water (2 × 30 mL). The organic layer was dried with anhydrous sodium sulfate and concentrated, and the obtained residue was purified by column chromatography (ethyl acetate in hexane) to afford the corresponding compound **9**–**13**.

Phenyl(thieno[2,3-*c*][1,2]oxazol-3-yl)methanone (9a): White solid; yield 98%; m.p. 114–115 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.15 [d, J = 5.4 Hz, 1 H, C(6)-H], 7.57–7.63 (m, 2 H, ArH), 7.68–7.73 (m, 1 H, ArH), 7.70 [d, J = 5.4 Hz, 1 H, C(5)-H], 8.35–8.38 (m, 2 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 112.0, 127.0, 128.8, 130.1, 134.0, 135.0, 143.1, 158.2, 170.5, 179.3 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1635 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{12}H_8NO_2S$ $[M + H]^+$ 230.0270; found 230.0279.

1-(Thieno[3,2-*c*][1,2]oxazol-3-yl)pentan-1-one (9b): White solid; yield 99%; m.p. 62–63 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.95 (t, J = 7.5 Hz, 3 H, $CH_2CH_2CH_2CH_3$), 1.44 (sext., J = 7.5 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 1.76 (pent., J = 7.5 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 3.04 (t, J = 7.5 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 7.09 [d, J = 5.4 Hz, 1 H, C(6)-H], 7.63 [d, J = 5.4 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 13.8, 22.3, 25.5, 39.3, 111.9, 123.4, 142.7, 157.4, 170.9, 188.6 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1681 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{10}H_{12}NO_2S$ [M + H]$^+$ 210.0583; found 210.0577.

(4-Methylphenyl)(thieno[2,3-*c*][1,2]oxazol-3-yl)methanone (9c): White solid; yield 92%; m.p. 117–118 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.49 (s, 3 H, CH_3), 7.14 [d, J = 5.7 Hz, 1 H, C(6)-H], 7.39 (d, J = 8.1 Hz, 2 H, ArH), 7.69 [d, J = 5.7 Hz, 1 H, C(5)-H], 8.27 (d, J = 8.1 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 21.8, 111.9, 126.8, 129.6, 130.2, 132.5, 143.0, 145.2, 158.5, 170.4, 178.9 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1636 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{13}H_{10}NO_2S$ [M + H]$^+$ 244.0427; found 244.0439.

(4-Ethylphenyl)(thieno[2,3-*c*][1,2]oxazol-3-yl)methanone (9d): White solid; yield 95%; m.p. 69–70 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.29 (t, J = 7.8 Hz, 3 H, CH_3), 2.75 (q, J = 7.8 Hz, 2 H, CH_2), 7.10 [d, J = 5.7 Hz, 1 H, C(6)-H], 7.38 (d, J = 8.1 Hz, 2 H, ArH), 7.66 [d, J = 5.7 Hz, 1 H, C(5)-H], 8.27 (d, J = 8.1 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 14.9, 28.9, 111.8, 126.7, 128.3, 130.3, 132.5, 143.0, 151.2, 158.4, 170.3, 178.8 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1637 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{14}H_{12}NO_2S$ [M + H]$^+$ 258.0583; found 258.0569.

(2-Pyridinyl)(thieno[2,3-*c*][1,2]oxazol-3-yl)methanone (9e): White solid; yield 88%; m.p. 195–196 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.15 [d, J = 5.7 Hz, 1 H, C(6)-H], 7.59–7.64 (m, 1 H, ArH), 7.61 [d, J = 5.7 Hz, 1 H, C(5)-H], 7.95–8.00 (m, 1 H, ArH), 8.31–8.34 (m, 1 H, ArH), 8.85 (ddd, J = 4.5, 1.8, 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 112.6, 123.7, 127.9, 128.9, 137.6, 143.2, 148.3, 151.9, 154.8, 170.3, 176.4 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1656 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{11}H_7N_2O_2S$ [M + H]$^+$ 231.0223; found 231.0233.

2,2-Dimethyl-1-thieno[2,3-*c*][1,2]oxazol-3-ylpropan-1-one (9f): White solid; yield 99%; m.p. 75 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.44 (s, 9 H, *t*Bu), 7.06 [d, J = 5.4 Hz, 1 H, C(6)-H], 7.63 [d, J = 5.4 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 25.9, 43.6, 111.9, 126.5, 143.2, 157.7, 170.1, 193.6 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1664 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{10}H_{12}NO_2S$ [M + H]$^+$ 210.0583; found 210.0575.

Phenyl(thieno[2,3-*c*][1,2]oxazol-3-yl)methanone (10a): Beige solid; yield 88%; m.p. 53–55 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.14 [d, J = 5.4 Hz, 1 H, C(5)-H], 7.40 [d, J = 5.4 Hz, 1 H, C(4)-H], 7.54–7.60 (m, 2 H, ArH), 7.67–7.70 (m, 1 H, ArH), 8.23–8.26 (m, 2 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 115.0, 128.8, 130.0, 132.8, 133.9, 135.6, 136.8, 148.6, 156.3, 180.3 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1652 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{12}H_8NO_2S$ [M + H]$^+$ 230.0270; found 230.0266.

Cyclopropyl(thieno[2,3-*c*][1,2]oxazol-3-yl)methanone (10b): Beige solid; yield 91%; m.p. 61–63 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.17–1.23 (m, 2 H, *c*-Pr), 1.33–1.39 (m, 2 H, *c*-Pr), 2.84–2.92 (m, 1 H, *c*-Pr), 7.10 [d, J = 5.4 Hz, 1 H, C(5)-H], 7.36 [d, J = 5.4 Hz, 1 H, C(4)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 12.9, 18.7, 114.6, 116.3, 129.5, 136.6, 155.9, 188.9 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1663 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_9H_8NO_2S$ [M + H]$^+$ 194.0270; found 194.0288.

(5,6-Dimethoxy-2,1-benzisoxazol-3-yl)phenylmethanone (11a): Beige solid; yield 87%; m.p. 165–166 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.99 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 6.88 (s, 1 H,ArH), 7.31 (s, 1 H, ArH), 7.53–7.56 (m, 2 H, ArH), 7.61–7.68 (m, 1 H,ArH), 8.28–8.31 (m, 2 H, ArH), ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 56.3, 56.5, 91.7, 96.3, 119.2, 127.5, 128.6, 130.0, 133.5, 136.2, 153.5, 155.2, 155.3, 181.6 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1650 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{14}NO_4$ [M + H]$^+$ 284.0917; found 284.0929.

(2,1-Benzisoxazol-3-yl)cyclopropylmethanone (11b): Yellowish solid; yield 99%; m.p. 79–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.23–1.28 (m, 2 H, *c*-Pr), 1.40–1.43 (m, 2 H, *c*-Pr), 3.04–3.13 (m, 1 H, *c*-Pr), 7.24–7.29 (m, 1 H, ArH), 7.39–7.44 (m, 1 H, ArH), 7.74 (d, J = 9.0 Hz, 1 H, ArH), 8.04 (d, J = 8.7 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 12.8, 18.9, 115.8, 118.6, 121.4, 128.4, 131.3, 157.6, 160.1, 190.1 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1671 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{11}H_{10}NO_2$ [M + H]$^+$ 188.0706; found 188.0752.

(Isoxazolo[4,3-*b*]pyridin-3-yl)phenylmethanone (12a): Beige solid; yield 92%; m.p. 95–96 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.37 [dd, J = 9.15, 3.6 Hz, 1 H, C(6)-H], 7.54–7.59 (m, 2 H, ArH), 7.66–7.71 (m, 1 H, ArH), 7.14 [dd, J = 9.15, 1.5 Hz, 1 H, C(7)-H], 8.20–8.23 (m, 2 H, ArH), 8.84 [dd, J = 3.6, 1.5 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 124.2, 125.8, 128.0, 128.7, 130.4, 134.2, 135.8, 151.4, 155.6, 160.4, 181.1 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1661 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{13}H_9N_2O_2$ [M + H]$^+$ 225.0659; found 225.0677.

1-([1,2]Oxazolo[4,3-*b*]pyridin-3-yl)pentan-1-one (12b): White solid; yield 93%; m.p. 73–74 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.95 (t, J = 7.5 Hz, 3 H, $CH_2CH_2CH_2CH_3$), 1.45 (sext., J = 7.5 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 1.79 (pent., J = 7.5 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 3.32 (t, J = 7.5 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 7.32 [dd, J = 9.15; 3.6 Hz, 1 H, C(6)-H], 8.09 [dd, J = 9.15; 1.5 Hz, 1 H, C(7)-H], 8.81 [dd, J = 3.6; 1.5 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 13.8, 22.3, 25.8, 40.7, 124.4, 125.6, 132.6, 151.6, 155.4, 159.5, 188.7 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1687 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{11}H_{13}N_2O_2$ [M + H]$^+$ 205.0972; found 205.0970.

(4-Methylphenyl)([1,2]oxazolo[4,3-*b*]pyridin-3-yl)methanone (12c): Beige solid; yield 87%; m.p. 117–119 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.49 (s, 3 H, CH_3), 7.35–7.41 (m, 3 H, ArH), 8.14–8.18 (m, 3 H, ArH), 8.85–8.86 [m, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 21.8, 124.2, 125.7, 129.4, 130.5, 133.2, 133.4, 145.4, 151.3, 155.4, 160.7, 180.7 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1648 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{14}H_{11}N_2O_2$ [M + H]$^+$ 239.0815; found 239.0874.

(4-Ethylphenyl)([1,2]oxazolo[4,3-*b*]pyridin-3-yl)methanone (12d): Beige solid; yield 88%; m.p. 91–92 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.28 (t, J = 7.8 Hz, 3 H, CH_3), 2.74 (q, J = 7.8 Hz, 2 H, CH_2), 7.32–7.39 (m, 3 H, ArH), 8.11–8.16 (m, 3 H, ArH), 8.81–8.83 [m, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 14.9, 29.0, 124.2, 125.7, 127.3, 128.2, 130.6, 133.4, 151.3, 151.5, 155.4, 160.7, 180.7 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1646 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{15}H_{13}N_2O_2$ [M + H]$^+$ 253.0972; found 253.0971.

Cyclopropyl([1,2]oxazolo[4,3-*b*]pyridin-3-yl)methanone (12e): Beige solid; yield 94%; m.p. 129–130 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.20–1.27 (m, 2 H, *c*-Pr), 1.43–1.46 (m, 2 H, *c*-Pr), 3.44–3.53 (m, 1 H, *c*-Pr), 7.33 [dd, J = 9.15, 3.9 Hz, 1 H, C(6)-H], 8.10 [dd, J = 9.15, 1.5 Hz, 1 H,C(7)-H], 8.81 [dd, J = 3.9, 1.5 Hz, 1 H, C(5)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$): δ = 13.3, 19.6, 124.4, 125.5, 132.7, 151.5, 155.3, 159.6, 188.4 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1672 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{10}H_9N_2O_2$ [M + H]$^+$ 189.0658; found 189.0666.

[7-(4-Morpholinyl)-[1,2]oxazolo[4,3-*d*]pyrimidin-3-yl]phenylmethanone (13): Yellow solid; yield 69%; m.p. 139–140 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.92–3.94 [m, 4 H, $N(CH_2)_2$], 4.21 (br s, 2 H,OCH_2), 4.24 (br s, 2 H, OCH_2), 7.57–7.62 (m, 2 H, ArH), 7.69–7.74 (m, 1 H, ArH), 8.22 (d, J = 7.5 Hz, 1 H, ArH), 8.47 [s, 1 H, C(2)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$, 25 °C): δ = 44.8, 48.9; 66.7, 66.9, 128.7, 130.3, 134.2, 135.7, 135.9, 145.8, 152.5, 157.7, 158.3, 180.8 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 1645 (C=O) cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{15}N_4O_3$ $[M + H]^+$ 311.1139; found 311.1178.

General Procedure for the 1,2-Addition of Iodine: Iodine (0.132 g, 0.52 mmol) was added to a solution of compound **1g** or **4f** (0.5 mmol) in 1,2-dichloroethane (10 mL) and the resulting solution was heated at reflux for 2 h. The reaction mixture was diluted with dichloromethane and washed with saturated aqueous $Na_2S_2O_3$ solution (2 × 40 mL) and then with water (2 × 30 mL). The organic layer was dried with anhydrous sodium sulfate and concentrated, and the obtained residue was purified by column chromatography (ethyl acetate in hexane) to afford compound **14** or **15**.

2-[(*E*)-1,2-Diiodoethenyl]-3-nitrothiophene (14): Yellowish solid; yield 72%; m.p. 80–81 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.40 [, J = 5.7 Hz, 1 H, d C(5)-H], 7.56 [s, 1 H, C(sp^2)-H], 7.58 [d, J = 5.7 Hz, 1 H, C(4)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$): δ = 80.6; 89.9, 124.0, 125.7, 143.0, 145.9 ppm. HRMS (ES): calcd. for $C_6H_4I_2NO_2S$ $[M + H]^+$ 407.8047; found 407.8039.

2-[(*E*)-1,2-Diiodoethenyl]-3-nitropyridine (15): Yellowish wax; yield 71%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.37 [s, 1 H, C(sp^2)-H], 7.59 [dd, J = 8.4, 4.8 Hz, 1 H, C(5)-H], 8.46 [dd, J = 8.4, 1.5 Hz, 1 H, C(4)-H], 8.97 [dd, J = 4.8, 1.5 Hz, 1 H, C(6)-H] ppm. ^{13}C NMR (75 Hz, $CDCl_3$): δ = 83.8, 89.6, 124.4, 133.2, 152.4, 153.8, 154.1 ppm. HRMS (ES): calcd. for $C_7H_5I_2N_2O_2$ $[M + H]^+$ 402.8435; found 402.8444.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra of final products **6**–**15**.

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