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Base-Promoted Domino Reaction of 5-Substituted 2-Nitrosophenols with Bromomethyl Aryl Ketones: A Transition-Metal-Free Approach to 2-Aroylbenzoxazoles

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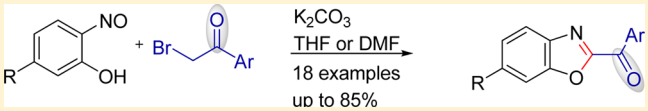
Supporting Information

ABSTRACT: The reaction of 5-substituted 2-nitrosophenols with bromomethyl aryl ketones and related compounds employing K_2CO_3 as a base in refluxing THF and DMF at 80 °C, respectively, delivers 2-aroylbenzoxazoles in a single step with yields up to 85%. The new method involves an intermolecular nucleophilic substitution followed by intramolecular 1,2-addition and elimination. It allows an efficient and practical access to 2-aroylbenzoxazoles under transition-metal-free conditions.



INTRODUCTION

Natural as well as unnatural benzoxazoles are heterocyclic compounds with a wide range of interesting biological and pharmacological properties.[1,2] In addition, they are important building blocks and intermediates in organic synthesis. Of particular interest are α-ketobenzoxazoles, which are well-known in drug discovery due to their significant biological activities such as the inhibition of fatty acid amide hydrolase inhibitors,[3] cysteine protease inhibitors,[4] and channel-activating protease inhibitors.[5]

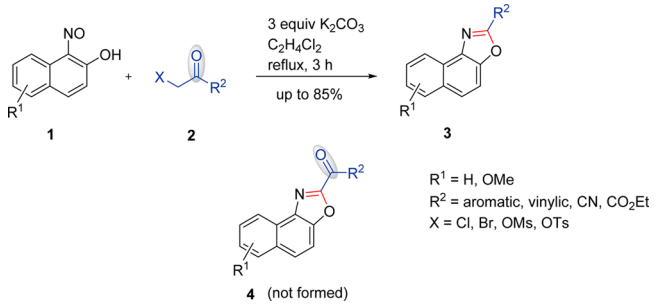
This is the reason why a number of methods have been developed for the preparation of α-ketobenzoxazoles. Some of them are based on the modification of the benzoxazoles skeleton, such as the functionalization at C-2. Among them are the deprotonation/metalation of benzoxazoles followed by transition-metal-catalyzed acylation,[3c,d,6] the Pd-catalyzed carbonylative coupling of benzoxazoles with aryl halides,[7] and the Pd-[8] and Ni-catalyzed[9] decarboxylative coupling of benzoxazoles with α-oxocarboxylic acids. Another method is the NHC-catalyzed C−H arylation of benzoxazole-2-carboxaldehydes.[10] In addition, some methods have been reported that are based on the formation of the benzoxazole moiety as the key step. They include the Ru-catalyzed reaction between 2-aminophenols and 1,2-dibromoethenes,[11] the Fe-catalyzed reaction of 2-aminophenols with alkynyl bromides,[12] and the hypoiodite-catalyzed oxidative cycloetherification of *N*-(2-hydroxyphenyl)-4-methyl-*N*-(phenacyl)benzenesulfonamides.[13] Our intention was to develop a method for the selective preparation of 2-aroylbenzoxazoles in a single step that uses cheap and easily available starting materials and reagents and can be performed under transition-metal-free conditions. Here, we disclose the formation of 2-aroylbenzoxazoles from the reaction of 5-substituted 2-nitrosophenols with α-bromo acetophenones and related compounds.

RESULTS AND DISCUSSION

Recently, we have reported on the reaction between 1-nitroso-2-naphthols **1** and α-functionalized ketones, such as α-bromo, α-chloro, α-mesyloxy, α-tosyloxy, and α-hydroxy ketones **2**, under basic conditions to deliver 2-substituted naphtho[1,2-*d*]-[1,3]oxazoles **3** in a single synthetic operation with yields up to 85% (Scheme 1).[14] The formation of the naphtho[1,2-*d*][1,3]oxazoles **3** was accompanied by the unexpected loss of the C═O group from the α-functionalized ketones. The expected α-ketonaphtho[1,2-*d*][1,3]oxazoles **4** could not be detected even in trace amounts. In this context, it should be mentioned that 2-aryl-annulated oxazoles can be obtained by reaction of 2-nitrosophenols and 1-nitroso-2-naphthols with benzyl halides.[15]

We wondered whether the reaction between 2-nitrosophenols **5** and bromomethyl aryl ketones **6** delivers the required 2-aroylbenzoxazoles **7** or whether this transformation

Scheme 1. Unexpected Formation of 2-Substituted Naphtho[1,2-*d*][1,3]oxazoles 3



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is also accompanied by formal loss of a CO group and produces 2-arylbenzoxazoles **8** (Figure 1). For this purpose, the

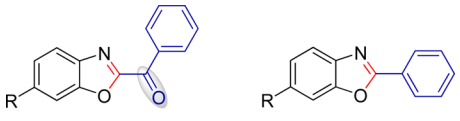
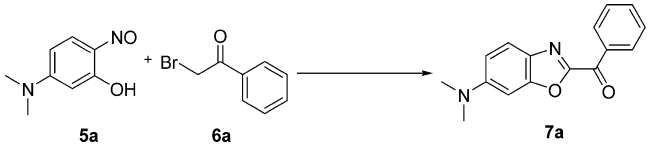


Figure 1. Potential products from the reactions between 2-nitrosophenols **5** and bromomethyl aryl ketones **6**.

transformation of 5-substituted 2-nitrosophenols, such as 5-(dimethylamino)-2-nitrosophenol (**5a**), 5-(diethylamino)-2-nitrosophenol (**5b**), and 5-methoxy-2-nitrosophenol (**5c**), with bromomethyl aryl ketones **6** was studied. The required 5-substituted nitrosophenols **5a−c** were obtained by nitrosation of the corresponding phenols in one step.[16−18]

The reaction between 5-(dimethylamino)-2-nitrosophenol (**5a**) and 2-bromoacetophenone (**6a**) was selected as model reaction. Equimolar amounts of **5a** and **6a** were reacted under the conditions that had proven successful for the preparation of the 2-arylnaphtho[1,2-*d*][1,3]oxazoles **3**,[14] i.e., with 3 equiv of K_2CO_3 in $C_2H_4Cl_2$ under reflux (Table 1, entry 1). Surprisingly,

Table 1. Influence of Solvents and Bases on the Outcome of the Model Reaction 5a + 6a → 7a[a]



entry	solvent	base (equiv)	time (h)	*T* (°C)	yield of **7a** (%)
1	$C_2H_4Cl_2$	K_2CO_3 (3)	16	reflux	16
2	toluene	K_2CO_3 (3)	7	85	20
3	acetone	K_2CO_3 (3)	5	reflux	60
4	DMSO	K_2CO_3 (3)	5.5	85	74
5	DMF	K_2CO_3 (3)	5.5	85	70
6	DMA	K_2CO_3 (3)	5.5	85	56
7	CH_3CN	K_2CO_3 (3)	5	reflux	66
8	NMP	K_2CO_3 (3)	5.5	85	40
9	1-nitropropane	K_2CO_3 (3)	4	85	42
10	*i*-PrOH	K_2CO_3 (3)	6	85	68
11	THF	K_2CO_3 (3)	5	reflux	85
12	THF	Cs_2CO_3 (3)	5	reflux	78
13	THF	K_3PO_4 (3)	5	reflux	69
14	THF	DABCO (3)	5	reflux	10
15	THF	K_2CO_3 (2)	5	reflux	66
16	THF	K_2CO_3 (1)	5	reflux	50

[a]All reactions were performed using 1 mmol of **5a** and 1 mmol of **6a**.

under these conditions, 2-benzoyl-6-(dimethylamino)-benzoxazole (**7a**) was formed exclusively. The product resulting from C═O loss, i.e., 6-(dimethylamino)-2-phenylbenzoxazole (**8a**), could not be detected. However, the yield of **7a** amounted to only 16% after 16 h of reflux. In order to optimize the reaction conditions, the model reaction of equimolar amounts of **5a** and **6a** with 3 equiv of K_2CO_3 as base was performed in a number of nonpolar, dipolar aprotic and protic solvents at 85 °C and under reflux, respectively (Table 1, entries 2−11). It was observed that **7a** was obtained in yields up to 74% when the reaction was run in dipolar aprotic solvents (Table 1, entries 3−9). Polar protic solvents are also suitable as reaction media. With *i*-PrOH, **7a** was isolated in 68% yield (Table 1, entry 10). However, the best results were observed when the transformation was run in dry THF. After 5 h under reflux, 2-benzoylbenzoxazole (**7a**) could be isolated as a single product in 85% yield (Table 1, entry 11).

Next, the influence of the base on the result of the model reaction was studied (Table 1). For this purpose, equimolar amounts of **5a** and **6a** were refluxed in THF with a 3-fold excess of Cs_2CO_3, K_3PO_4, and DABCO, respectively. The yields obtained with Cs_2CO_3 and K_3PO_4 amounted to 78% and 69% (Table 1, entries 12 and 13). With DABCO as the base, the yield dropped to 10% (Table 1, entry 14). Obviously, the yield achieved with 3 equiv of K_2CO_3 could not be improved (Table 1, entry 11). Next, the influence of decreasing amounts of K_2CO_3 on the outcome of the model reaction was examined. This measure didn't pay off, since the yield of **7a** decreased to 66% and 50%, respectively, when the excess of K_2CO_3 was reduced to 2 equiv and 1 equiv, respectively (Table 1, entries 15 and 16). It should be mentioned that irrespective of the solvent and the base employed 2-benzoyl-6-(dimethylamino)-benzoxazole (**7a**) was formed exclusively.

After optimization of the conditions for the model reaction, the scope and limitation of the new method for the preparation of 2-aroylbenzoxazoles with regard to the 2-bromoacetophenone moiety **6** was studied. For this purpose, 5-(dimethylamino)-2-nitrosophenol (**5a**) was reacted with the substituted 2-bromoacetophenones **6b−i** (Table 2) as well as with related substrates, such as bromomethyl 2-naphthyl ketone (**6j**) and bromomethyl 1-pyrenyl ketone (**6k**) (Table 2) under the conditions of the model reaction.

The 2-aroyl-substituted benzoxazoles **7b−i** were formed exclusively with yields in the range between 59 and 74%. In particular, the transformation can be performed successfully with a number of 4′-substituted 2-bromoacetophenones, such as 2-bromo-4′-methylacetophenone (**6b**), 2-bromo-4′-methoxyacetophenone (**6c**), 2-bromo-4′-fluoroacetophenone (**6d**), 2-bromo-4′-chloroacetophenone (**6e**), 4′-(2-bromoacetyl)-benzonitrile (**6f**), and 4′-methyl(2-bromoacetyl)benzoate (**6g**) (Table 2, entries 1−6). The reactions with 2-bromo-3′-bromoacetophenone (**6h**) and 2-bromo-3′,4′-dichloroacetophenone (**6i**) clearly demonstrate that the transformations can also be run with 3′-aryl-substituted 2-bromoacetophenones and 2-bromoacetophenones carrying more than one substituent at the aryl moiety (Table 2, entries 7 and 8).

In addition to the 2-bromoacetophenones **6a−i**, the naphthyl ketone **6j** and the pyrenyl ketone **6k** were also suitable substrates (Table 2, entries 9 and 10). The yields of the corresponding 2-aroylbenzoxazoles **7j** and **7k** amounted to 71 and 75%. It is worth mentioning that irrespective of the structure of the bromomethyl aryl ketone the 2-aroylbenzoxazoles were formed exclusively. The 2-aryl-substituted benzoxazoles could not be detected at all.

5-(Dimethylamino)-2-nitrosophenol (**5a**) is not the only nitrosophenol that was tolerated as a substrate for the transformation presented. It could be replaced with 5-(diethylamino)-2-nitrosophenol (**5b**) and with 5-methoxy-2-nitrosophenol (**5c**) (Table 3). Remarkably, the reactions with 5-(diethylamino)-2-nitrosophenol (**5b**) need to be run in DMF at slightly higher temperatures to achieve reasonable yields of **7**. In particular, **5b** was reacted with 2-bromoacetophenone (**6a**), 2-bromo-4′-methoxyacetophenone (**6c**), 2-bromo-4′-chloroacetophenone

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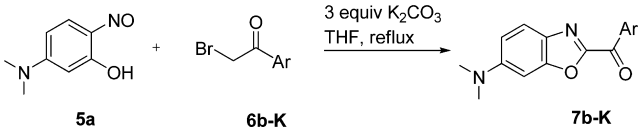
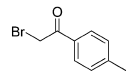
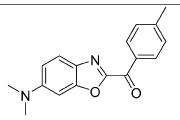
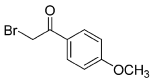
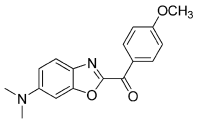
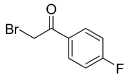
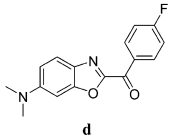
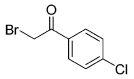
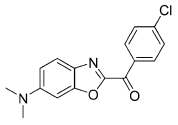
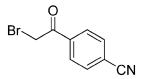
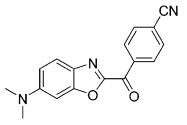
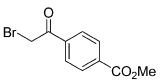
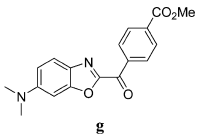
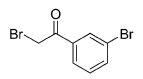
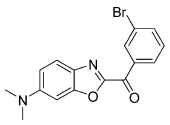
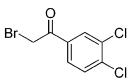
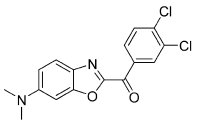
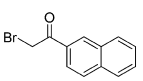
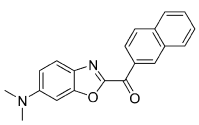
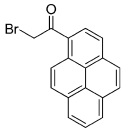
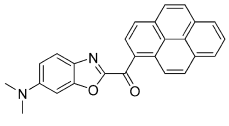
Table 2. Synthesis of 2-Aroylbenzoxazoles 7b−k[a]

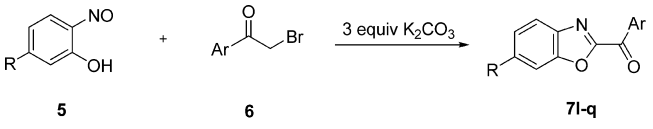


5a 6b-K 7b-K

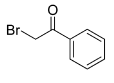
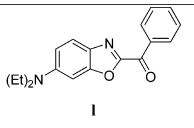
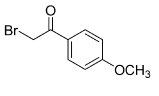
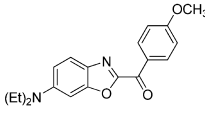
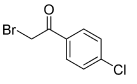
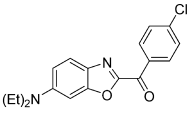
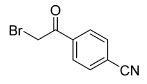
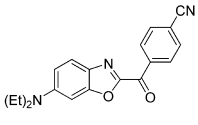
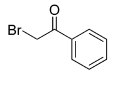
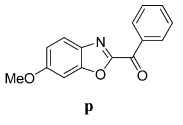
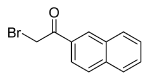
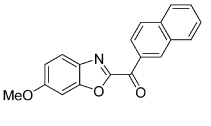
entry	6	t (h)	7	yield of 7 (%)
1	 b	6.5	 b	73
2	 c	8	 c	74
3	 d	5.5	 d	74
4	 e	10	 e	63
5	 f	8	 f	74
6	 g	7.5	 g	59
7	 h	8	 h	67
8	 i	6	 i	64
9	 j	7	 j	71
10	 k	15	 k	75

[a]All reactions were performed using 1 mmol of **5** and 1 mmol of **6**.

Table 3. Synthesis of 2-Aroylbenzoxazoles 7l−q[a]



5 6 7l-q

entry	5	R	6	t (h)	7	yield of 7 (%)
1	b	$N(Et)_2$	 a	3	 l	70[b]
2	b	$N(Et)_2$	 c	4	 m	70[b]
3	b	$N(Et)_2$	 e	3	 n	66[b]
4	b	$N(Et)_2$	 f	3	 o	68[b]
5	c	OMe	 a	3	 p	63[c]
6	c	OMe	 j	3	 q	51[c]

[a]All reactions were performed using 1 mmol of **5** and 1 mmol of **6**. [b]The reaction was performed in DMF at 80 °C. [c]The reaction was performed in refluxing THF.

(**6e**), and 4′-(2-bromoacetyl)benzonitrile (**6f**) in DMF at 80 °C to give 2-benzoyl-6-(diethylamino)benzoxazole (**7l**), 2-(5′-methoxybenzoyl)-6-(diethylamino)benzoxazole (**7m**), 2-(5′-chlorobenzoyl)-6-(diethylamino)benzoxazole (**7n**), and 2-(5′-cyanobenzoyl)-6-(diethylamino)benzoxazole (**7o**) with yields of 70, 70, 66, and 68%, respectively (Table 3, entries 1−4). Finally, it was demonstrated that 5-methoxy-2-nitrosophenol (**5c**) could be reacted with 2-bromoacetophenone (**6a**) and bromomethyl 2-naphthyl ketone (**6j**) under the conditions of the model reaction (Table 3, entries 5 and 6) to produce the benzoyl and the naphthoyl derivatives **7p** and **7q** in 63 and 51% yield, respectively. The reaction also tolerated bromoacetonitrile (**6l**) as a substrate. The corresponding 2-cyano-6-(dimethylamino)benzoxazole (**7r**) was formed in 55% yield (Scheme 2).

With respect to the reaction mechanism, it is assumed that the reaction sequence between the nitrosophenols **5** and the bromomethyl aryl ketones **6** starts with a base-mediated intermolecular nucleophilic substitution with the OH group of the nitrosophenol as the nucleophile to form the ether **9** as an intermediate (Scheme 3). Deprotonation at the α-position to the keto group produces carbanion **10**, which in turn undergoes

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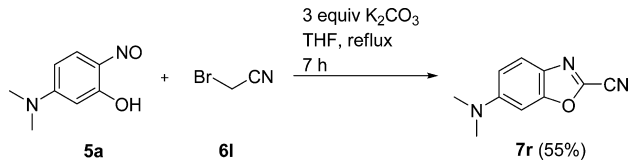
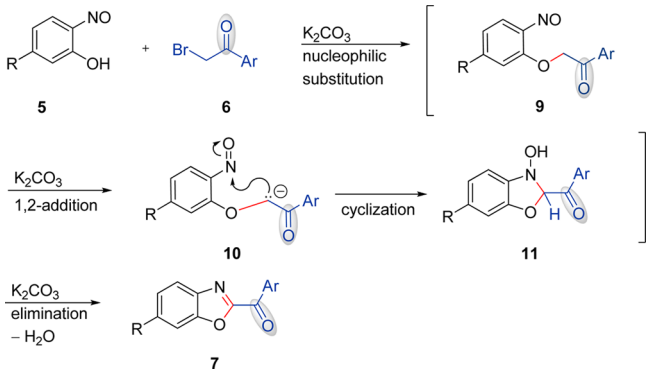
Scheme 2. Formation of 2-Cyano-6-(dimethylamino)benzoxazole (6r)[a]



[a]The reaction was performed using 1 mmol of **5a** and 1 mmol of **6l**.

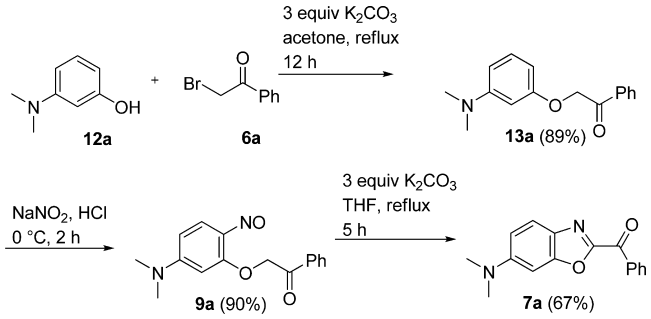
Scheme 3. Proposed Reaction Mechanism for the Formation of 2-Aroylbenzoxazoles 7



intramolecular cyclization followed by base-mediated dehydration to give the 2-aroylbenzoxazole **7**.

In order to provide support for the proposed reaction mechanism, the cyclization precursor **9a** was prepared and reacted under the conditions of the benzoxazole formation (Scheme 4). The synthesis of 2-(5-(dimethylamino)-2-nitrosophenoxy)-1-phenylethanone (**9a**) was achieved by nitrosation of 2-(3-(dimethylamino)phenoxy)-1-phenylethanone (**13a**) with sodium nitrite in hydrochloric acid at 0 °C for 2 h. For the preparation of 2-(3-(dimethylamino)phenoxy)-1-phenylethanone (**13a**), 3-(dimethylamino)phenol (**12a**) was reacted with 2-bromoacetophenone (**6a**). When **9a** was treated with 3 equiv of K_2CO_3 in boiling THF for 5 h, 2-benzoyl-6-(dimethylamino)benzoxazole (**7a**) was isolated in 67% yield (Scheme 4). The outcome of the cyclization of **9a** provides strong evidence for the reaction mechanism proposed in Scheme 3. However, it remains unclear what the reason is for the different behavior of 1-nitroso-2-naphthols **1** and 1-nitroso-2-phenols **5** upon reaction with α-functionalized ketones. While the reaction of the 1-nitroso-2-naphthols **1** is accompanied by a formal loss of CO to produce the 2-arylnaphtho[1,2-*d*][1,3]-oxazoles,[14] the reaction of the 2-nitrosophenols with α-functionalized aromatic ketones produces the 2-aroylbenzoxazoles **7** exclusively. It seems that the differences with respect to the products formed are due to differences regarding the reactivity of the underlying aromatic ring systems since neither the structure of the α-functionalized ketones nor additional substituents of the 1-nitroso-2-naphthols **1**[14] and 1-nitroso-2-phenols **5** have an influence on the type of product formed.

Scheme 4. Synthesis and Cyclization of 2-(5-(Dimethylamino)-2-nitrosophenoxy)-1-phenylethanone (9a)



The structures of all 2-aroylbenzoxazoles were unambiguously elucidated by NMR spectroscopy and mass spectrometry. Full assignment of the ^1H and ^{13}C chemical shifts was achieved by evaluating their gCOSY, gHSQC, and gHMBC spectra. Future work is intended to investigate the solvent-dependent UV/vis absorption and fluorescence properties of the 2-aroylbenzoxazoles **7**.

CONCLUSIONS

In summary, a straightforward and selective new method for the efficient preparation of 2-aroylbenzoxazoles by reaction between substituted 2-nitrosophenols and bromomethyl aryl ketones has been developed. The transformations were performed under basic conditions in refluxing THF or in DMF at 80 °C and delivered the 2-aroylbenzoxazoles exclusively with yields up to 85%. There is evidence that the reaction proceeds as a domino intermolecular nucleophilic substitution/intramolecular 1,2-addition/elimination. The method not only allows for the preparation in a single step but also is an example of a transition-metal-free access to 2-aroylbenzoxazoles.

EXPERIMENTAL SECTION

General Remarks. Starting materials and reagents were purchased from commercial suppliers and were used without further purification. Solvents used in reactions, extraction, and purification were distilled (over proper drying agents) prior to use. Glassware was dried for 4 h at 140 °C in an oven. Reaction temperatures are reported as bath temperatures. Thin-layer chromatography (TLC) was performed on silica gel 60 F254. Compounds were visualized with UV light (λ = 254 nm) and by immersion in an ethanolic vanillin solution or by immersion in $KMnO_4$ solution followed by heating. Products were purified by flash chromatography on silica gel, 0.04−0.063 mm. Melting points were determined on a melting point apparatus with open capillary tubes and are uncorrected. IR spectra were measured on an FT-IR spectrometer. UV/vis spectra were recorded with a spectrophotometer. ^1H NMR and $^{13}C\{^1H\}$ NMR spectra were recorded at 300 (75) and 500 (125) MHz using $CDCl_3$ and DMSO as the solvents. The ^1H and ^{13}C chemical shifts were referenced to residual solvent signals at δ H/C 7.26/77.0 ($CDCl_3$), 2.50/39.5 (DMSO) relative to TMS as internal standard. HSQC, HMBC, and COSY spectra were recorded on a NMR spectrometer at 300 or 500 MHz. Coupling constants J (Hz) were directly taken from the spectra and are not averaged. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad), and app (apparent). 1D and 2D homonuclear NMR spectra were measured with standard pluse sequences. Low-resolution electron-impact mass spectra (MS) and exact mass electron-impact mass spectra (HRMS) were obtained at 70 eV using a double-focusing sector field mass spectrometer. Intensities are reported as percentages relative to the base peak (I = 100%).

Synthesis of Starting Materials. 5-(Dimethylamino)-2-nitrosophenol (**5a**), 5-(diethylamino)-2-nitrosophenol (**5b**),[17] 5-methoxy-2-nitrosophenol (**5c**),[18] methyl 4-(2-bromoacetyl)benzoate (**6g**),[19] and bromomethyl 1-pyrenyl ketone (**6k**)[20] were prepared according to the reported procedures.

General Procedure for the Preparation of 2-Aroylbenzoxazoles 7 and Related Compounds. A mixture of the 2-nitrosophenol **5** (1 mmol), the bromomethyl aryl ketone **6** (1 mmol), and

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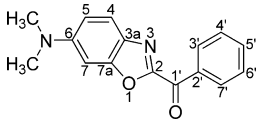
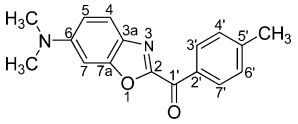
K_2CO_3 (417 mg, 3 mmol) was heated under argon in dry THF (5 mL) under reflux or in dry DMF (5 mL) at 80 °C until the starting materials were consumed (TLC). After being cooled to room temperature, the reaction mixture was poured into water and extracted with diethyl ether (3 × 30 mL). The combined organic extracts were washed with brine (30 mL). After drying over anhydrous $MgSO_4$ and concentration in vacuo, the resulting residue was purified by flash chromatography over silica gel to afford the desired product.

Synthesis of 2-Aroylbenzoxazoles 7. *2-Benzoyl-6-(dimethylamino)benzoxazole (**7a**).*



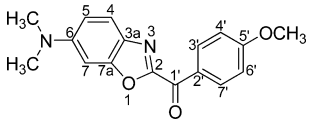
According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), 2-bromoacetophenone (**6a**) (199 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 5 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 4:1) to give **7a** as an orange solid in 85% yield (226 mg, 0.85 mmol): mp 165−166 °C; R_f = 0.50 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1642, 1613, 1509, 1308, 1281, 1175, 1065, 901, 798, 724 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 420 (4.34), 257 (4.26) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 6H; $N(CH_3)_2$), 6.83 (d, ^4J (5-H, 7-H) = 2.3 Hz, 1H, 7-H), 6.89 (dd, ^4J (5-H, 7-H) = 2.4 Hz, ^3J (4-H, 5-H) = 8.9 Hz, 1H, 5-H), 7.54 (app t, J = 7.3 Hz, J = 7.7 Hz, 2H, 4′-H and 6′-H), 7.64 (app d, J = 7.3 Hz 1H, 5′-H). 7.73 (d, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 4-H), 8.52 (app d, J = 7.4 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.9 ($N(CH_3)_2$), 92.6 (C-7), 112.6 (C-5), 122.3 (C-4), 128.4 (C-4′), 130.8 (C-3′), 131.6 (C-3a), 133.6 (C-5′), 135.7 (C-2′), 151.7 (C-6), 152.9 (C-7a), 155.6 (C-2), 180.0 (C-1′); MS (EI, 70 eV) m/z 266 (84) [M^+], 238 (4), 161 (3), 133 (4), 105 (100); HRMS (EI, M^+) calcd for $C_{16}H_{14}N_2O_2$ (266.1055), found 266.1050.

*2-(5′-Methylbenzoyl)-6-(dimethylamino)benzoxazole (**7b**).*



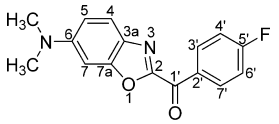
According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), 2-bromo-4′-methylacetophenone (**6b**) (213 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 6.5 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7b** as an orange solid in 73% yield (204 mg, 0.73 mmol): mp 161−162 °C; R_f = 0.49 (cyclohexane/EtOAc = 2:1); IR (ATR) $\tilde{\nu}$ 1642, 1614, 1512, 1306, 1283, 1179, 915, 797, 755 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 418 (3.82), 290 (3.41) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, CH_3), 3.08 (s, 6H, $N(CH_3)_2$), 6.83 (brd, ^4J (5-H, 7-H) = 2.2 Hz, 1H, 7-H), 6.91 (dd, ^4J (5-H, 7-H) = 2.3 Hz, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 5-H), 7.34 (app d, J = 8.1 Hz, 2H, 4′-H and 6′-H), 7.72 (d,^3J (4-H, 5-H) = 8.9 Hz, 1H, 4-H), 8.43 (app d, J = 8.2 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 21.8 (CH_3), 40.8 ($N(CH_3)_2$), 92.6 (C-7), 112.4 (C-5), 122.2 (C-4), 129.2 (C-4′), 130.9 (C-3′), 131.6 (C-3a), 133.2 (C-2′), 144.6 (C-5′), 151.6 (C-6), 152.9 (C-7a), 155.6 (C-2), 179.6 (C-1′); MS (EI, 70 eV) m/z 280 (100) [M^+], 252 (32), 237 (10), 209 (4), 140 (4), 125 (8), 119 (68), 91 (24); HRMS (EI, M^+) calcd for $C_{17}H_{16}N_2O_2$ (280.1212), found 280.1213.

*2-(5′-Methoxybenzoyl)-6-(dimethylamino)benzoxazole (**7c**).*



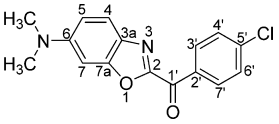
According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), 2-bromo-4′-methoxyacetophenone (**6c**) (230 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 8 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7c** as an orange solid in 74% yield (218 mg, 0.74 mmol): mp 148−149 °C; R_f = 0.38 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1634, 1600, 1505, 1308, 1285, 1171, 1062, 1033, 845, 796 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 415 (3.86), 307 (3.60) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.01 (s, 6H, $N(CH_3)_2$), 3.91 (s, OCH_3), 6.83 (d, ^4J (5-H, 7-H) = 2.2 Hz, 1H, 7-H), 6.89 (dd, ^4J (5-H, 7-H) = 2.3 Hz, ^3J (4-H, 5-H) = 9.0 Hz, 1H, 5-H), 7.02 (app d, J = 9.2 Hz, 2H, 4′-H and 6′-H), 7.71 (d, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 4-H), 8.59 (app d, J = 9.2 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.9 ($N(CH_3)_2$), 55.5 (OCH_3), 92.7 (C-7), 112.4 (C-5), 113.8 (C-4′), 122.1 (C-4), 128.6 (C-2′), 131.6 (C-3a), 133.3 (C-3′), 151.5 (C-6), 152.9 (C-7a), 155.6 (C-2), 164.1 (C-5′), 178.3 (C-1′); MS (EI, 70 eV) m/z 296 (64) [M^+], 268 (4), 253 (4), 135 (100), 107 (6); HRMS (EI, M^+) calcd for $C_{17}H_{16}N_2O_3$ (296.1161), found 296.1163.

*2-(5′-Fluorobenzoyl)-6-(dimethylamino)benzoxazole (**7d**).*



According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), 2-bromo-4′-fluoroacetophenone (**6d**) (217 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 5.5 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7d** as an orange solid in 74% yield (210 mg, 0.74 mmol): mp 178−179 °C; R_f = 0.24 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1640, 1609, 1512, 1371, 1283, 1206, 829, 792, 777 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 422 (3.82), 257 (3.75) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.10 (s, 6H, $N(CH_3)_2$), 6.82 (d, ^4J (5-H, 7-H) = 2.2 Hz, 1H, 7-H), 6.90 (dd, ^4J (5-H, 7-H) = 2.3 Hz, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 5-H), 7.21 (app t, J = 8.6 Hz, J = 8.6 Hz, 2H, 4′-H and 6′-H), 7.71 (d,^3J (4-H, 5-H) = 9.2 Hz, 1H, 4-H), 8.62 (app dd, J = 8.9 Hz, J = 5.5 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.8 ($N(CH_3)_2$), 92.5 (C-7), 112 (C-5), 115.6 (d, ^2J (^{19}F, ^{13}C) = 21.9 Hz, C-4′), 122.3 (C-4), 131.5 (C-3a), 131.98 (d, ^4J (^{19}F, ^{13}C) = 8.1 Hz, C-2′), 133.6 (d, ^3J (^{19}F, ^{13}C) = 9.3 Hz, C-3′), 151.7 (C-6), 152.9 (C-7a), 155.4 (C-2), 166.1 (d, ^1J (^{19}F, ^{13}C) = 255.7 Hz, C-5′), 178.2 (C-1′); MS (EI, 70 eV) m/z 284 (100) [M^+], 256 (3), 123 (100), 95 (40); HRMS (EI, M^+) calcd for $C_{16}H_{13}FN_2O_2$ (284.0961), found 284.0958.

*2-(5′-Chlorobenzoyl)-6-(dimethylamino)benzoxazole (**7e**).*



According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), 2-bromo-4′-chloroacetophenone (**6e**) (233 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 10 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7e** as an orange solid in 63% yield (188 mg, 0.63 mmol): mp 186−187 °C; R_f = 0.42 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1643, 1612, 1511, 1373, 1282, 1206, 1088, 1066, 847, 796, 758 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 429 (3.78), 263 (3.69) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 6H, $N(CH_3)_2$), 6.80 (d, ^4J (5-H, 7-H) = 2.4 Hz, 1H, 7-H), 6.90 (dd, ^4J (5-H, 7-H) = 2.5 Hz, ^3J (4-H, 5-H) = 9.0 Hz, 1H, 5-H), 7.51 (app d, J = 8.7 Hz, 2H, 4′-H and 6′-H), 7.71 (d, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 4-H), 8.52 (app d, J = 8.7 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.8 ($N(CH_3)_2$), 92.3 (C-7), 112.6 (C-5), 122.3 (C-4), 128.7 (C-4′), 131.5 (C-3a), 132.2 (C-3′), 133.9 (C-2′), 140.2 (C-5′), 151.7 (C-6), 153.0 (C-7a), 155.3 (C-2), 178.4 (C-1′); MS (EI, 70 eV) m/z 300 (100) [M^+], 272 (4), 139 (88), 111 (20); HRMS (EI, M^+) calcd for $C_{16}H_{13}ClN_2O_2$ (300.0666), found 300.0653.

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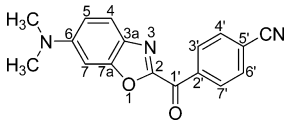
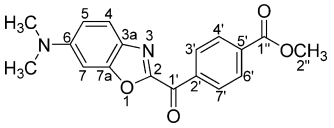
*2-(5′-Cyanobenzoyl)-6-(dimethylamino)benzoxazole (**7f**).*



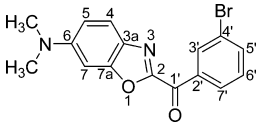
According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), 4′-(2-bromoacetyl)-benzonitrile (**6f**) (224 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 8 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7f** as a red solid in 74% yield (218 mg, 0.74 mmol): mp 200−202 °C; R_f = 0.40 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 2222, 1650, 1620, 1514, 1310, 1284, 1206, 862, 795, 763 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 443 (3.76), 240 (3.77) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.10 (s, 6H, $N(CH_3)_2$), 6.80 (d, ^4J (5-H, 7-H) = 2.4 Hz, 1H, 7-H), 6.92 (dd, ^4J (5-H, 7-H) = 2.4 Hz, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 5-H), 7.71 (d, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 4-H), 7.83 (app d, J = 8.2 Hz, 2H, 4′-H and 6′-H), 8.64 (app d, J = 8.3 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.8 ($N(CH_3)_2$), 92.2 (C-7), 113.0 (C-5), 116.5 (C-5′), 118.2 (CN), 122.5 (C-4), 131.2 (C-3′), 131.5 (C-3a), 132.1 (C-4′), 138.9 (C-2′), 152.1 (C-6), 153.2 (C-7a), 155.0 (C-2), 177.97 (C-1′); MS (EI, 70 eV) m/z 291 (92) [M^+], 262 (4), 130 (100), 102 (66); HRMS (EI, M^+) calcd for $C_{17}H_{13}N_3O_2$ (291.1008), found 291.0989.

*Methyl 4-(5-(Dimethylamino)benzo[d]oxazole-2-carbonyl)-benzoate (**7g**).*



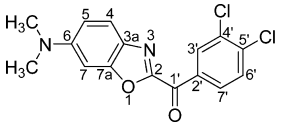
According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), methyl 4′-(2-bromoacetyl)-benzoate (**6g**) (258 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 7.5 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7g** as a red solid in 59% yield (191 mg, 0.59 mmol): mp 177−178 °C; R_f = 0.23 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1725, 1646, 1628, 1515, 1275, 904, 789, 732 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 436 (3.93), 267 (3.91) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.01 (s, 6H, $N(CH_3)_2$), 3.97 (s, 3H, 2″-H), 6.82 (brd, ^4J (5-H, 7-H) = 2.3 Hz, 1H, 7-H), 6.92 (dd, ^4J (5-H, 7-H) = 2.3 Hz, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 5-H), 7.73 (d, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 4-H), 8.19 (app d, J = 8.5 Hz, 2H, 4′-H and 6′-H), 8.58 (app d, J = 8.5 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.8 ($N(CH_3)_2$), 52.4 (C-2″), 92.3 (C-7), 112.8 (C-5), 122.4 (C-4), 129.5 (C-4′), 130.6 (C-3′), 131.6 (C-3a), 134.0 (C-5′), 151.8 (C-6), 153.1 (C-7a), 155.4 (C-2), 166.3 (C-1″), 179.1 (C-1′); MS (EI, 70 eV) m/z 324 (60) [M^+], 293 (4), 265 (4), 193 (30), 163 (56); HRMS (EI, M^+) calcd for $C_{18}H_{16}N_2O_4$ (324.1110), found 324.1104.

*2-(4′-Bromobenzoyl)-6-(dimethylamino)benzoxazole (**7h**).*



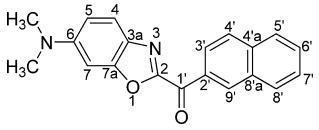
According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), 2-bromo-3′-bromoacetophenone (**6h**) (278 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 8 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7h** as an orange solid in 67% yield (231 mg, 0.67 mmol): mp 168−169 °C; R_f = 0.46 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1642, 1613, 1509, 1310, 1282, 1166, 1070, 917, 795, 737 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 433 (3.56), 260 (3.54) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.01 (s, 6H, $N(CH_3)_2$), 6.80 (brd, ^4J (5-H, 7-H) = 2.2 Hz, 1H, 7-H), 6.91 (dd, ^4J (5-H, 7-H) = 2.3 Hz, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 5-H), 7.42 (dd, ^3J (5′-H, 6′-H) = 7.90 Hz, ^3J (6′-H, 7′-H) = 7.92 Hz, 1H, 6′-H), 7.45−7.71 (m, 2H, 4-H and 5′-H), 8.51 (d, ^3J (6′-H, 7′-H) = 7.8 Hz, 1H, 7′-H), 8.67 (brs, 1H, 3′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.8 ($N(CH_3)_2$), 92.3 (C-7), 112.7 (C-5), 122.5 (C-4), 122.6 (C-4′), 129.4 (C-6′), 129.9 (C-7′), 131.5 (C-3a), 133.5 (C-3′), 136.3 (C-5′), 137.4 (C-2′), 151.8 (C-6), 153.0 (C-7a), 155.2 (C-2), 178.2 (C-1′); MS (EI, 70 eV) m/z 344 (100) [M^+], 316 (4), 185 (70), 183 (74), 155 (20); HRMS (EI, M^+) calcd for $C_{16}H_{13}BrN_2O_2$ (344.0160), found 344.0155.

*2-(4′,5′-Dichlorobenzoyl)-6-(dimethylamino)benzoxazole (**7i**).*



According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), 2-bromo-3′,4′-dichloroacetophenone (**6i**), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 6 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7i** as an orange solid in 64% yield (215 mg, 0.64 mmol): mp 204−205 °C; R_f = 0.57 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1648, 1618, 1510, 1371, 1283, 1206, 836, 800, 758 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 438 (3.82), 267 (4.08) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.10 (s, 6H, $N(CH_3)_2$), 6.79 (d, ^4J (5-H, 7-H) = 2.4 Hz, 1H, 7-H), 6.91 (dd, ^4J (5-H, 7-H) = 2.4 Hz, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 5-H), 7.61 (d, ^3J (6′-H, 7′-H) = 8.4 Hz, 1H, 6′-H), 7.72 (d, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 4-H), 8.44 (dd, ^4J (3′-H, 7′-H) = 2.0 Hz, ^3J (6′-H, 7′-H) = 8.4 Hz, 1H, 7′-H), 8.70 (d, ^4J (3′-H, 7′-H) = 2.0 Hz, 1H, 3′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.8 ($N(CH_3)_2$), 92.3 (C-7), 112.8 (C-5), 122.5 (C-4), 129.9 (C-7′), 130.5 (C-6′), 131.5 (C-3a), 132.7 (C-3′), 133.1 (C-2′), 135.1 (C-4′), 138.2 (C-5′), 151.9 (C-6), 152.1 (C-7a), 155.0 (C-2), 177.1 (C-1′); MS (EI, 70 eV) m/z 335 (24) [M^+], 307 (4), 175 (60), 173 (90), 145 (20), 109 (4); HRMS (EI, M^+) calcd for $C_{16}H_{12}Cl_2N_2O_2$ (334.0276), found 334.0263.

*5-(Dimethylamino)benzo[d]oxazole-2-yl)(naphthalene-1-yl)-methanone (**7j**).*



According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), 2-(bromoacetyl)naphthalene (**6j**) (249 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 7 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7j** as an orange solid in 71% yield (225 mg, 0.71 mmol): mp 223−224 °C; R_f = 0.38 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1642, 1611, 1514, 1308, 1285, 1069, 1033, 901, 793, 778 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 429 (3.81), 267 (4.09) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 3.09 (s, 6H, $N(CH_3)_2$), 6.85 (brd, ^4J (5-H, 7-H) = 1.9 Hz, 1H, 7-H), 6.91 (dd, ^4J (5-H, 7-H) = 2.1 Hz, ^3J (4-H, 5-H) = 8.9 Hz, 1H, 5-H), 7.55−7.65 (m, 2H, 6′-H and 7′-H), 7.77 (d, ^3J (4-H, 5-H) = 8.9 Hz, 1H, 4-H), 7.90 (d, ^3J (5′-H, 6′-H) = 7.9 Hz, 1H, 5′-H), 7.96 (d, ^3J (3′-H, 4′-H) = 8.6 Hz, 1H, 4′-H), 8.08 (brd, ^3J (7′-H, 8′-H) = 7.9 Hz, 1H, 8′-H),), 8.40 (d, ^3J (3′-H, 4′-H) = 8.6 Hz, 1H, 3′-H), 9.28 (brs, 1H, 9′-H); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO) δ 40.5 ($N(CH_3)_2$), 92.3 (C-7), 112.8 (C-5), 122.1 (C-4), 125.4 (C-7′), 127.1 (C-9′), 127.8 (C-6′), 128.1 (C-5′), 129.1 (C-4′), 129.9 (C-8′), 130.7 (C-8a′), 131.9 (C-3a), 132.7 (C-4′a), 132.8 (C-3′), 135.2 (C-2′), 151.7 (C-6), 152.5 (C-7a), 155.2 (C-2), 182.8 (C-1′); MS (EI, 70 eV) m/z 316 (96) [M^+], 288 (5), 156 (12), 155 (100), 127 (80); HRMS (EI, M^+) calcd for $C_{20}H_{16}N_2O_2$ (316.1212), found 316.1217.

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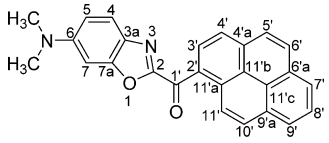
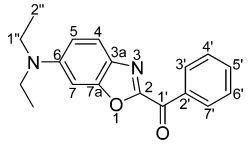
*5-(Dimethylamino)benzo[d]oxazol-2-yl)(pyren-1-yl)methanone (**7k**).*



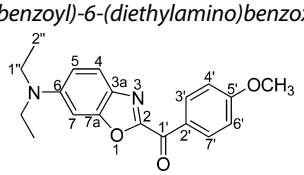
According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (84 mg, 0.5 mmol), 1-(bromoacetyl)pyrene (**6k**) (162 mg, 0.5 mmol), and K_2CO_3 (209 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 15 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7k** as a red solid in 75% yield (146 mg, 0.37 mmol): mp 210−212 °C; R_f = 0.59 (cyclohexane/EtOAc = 2:1); IR (ATR) $\tilde{\nu}$ 1648, 1627, 1541, 1366, 1279, 1192, 1056, 1052, 841, 833, 794, 714 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 434 (3.75), 241 (4.09) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 3.07 (s, 6H, $N(CH_3)_2$), 6.85 (d, ^4J (5-H, 7-H) = 2.04 Hz, 1H, 7-H), 6.87 (dd, ^4J (5-H, 7-H) = 2.04 Hz, ^3J (4-H, 5-H) = 9.0 Hz, 1H, 5-H), 7.69 (d, ^3J (4-H, 5-H) = 8.9 Hz, 1H, 4-H), 8.05 (overlapped, 1H, 8′-H), 8.10 (d, ^3J (5′-H, 6′-H) = 8.6 Hz, 1H, 5′-H), 8.18 (d, ^3J (5′-H, 6′-H) = 9.2 Hz, 1H, 6′-H), 8.21 (d, ^3J (10′-H, 11′-H) = 9.5 Hz, 1H, 10′-H),), 8.25 (overlapped, 2H, 7′-H and 9′-H),), 8.25 (d, ^3J (3′-H, 4′-H) = 7.9 Hz, 1H, 4′-H), 8.75 (d, ^3J (3′-H, 4′-H) = 8.1 Hz, 1H, 3′-H), 8.79 (d, ^3J (10′-H, 11′-H) = 9.4 Hz, 1H, 11′-H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 40.8 ($N(CH_3)_2$), 92.5 (C-7), 112.6 (C-5), 122.4 (C-4), 123.7 (C-4′), 124.2 (C-11′c), 124.4 (C-11′), 124.8 (C-11′b), 126.2 (C-9′), 126.3 (C-8′), 126.4 (C-7′), 127.2 (C-5′), 129.1 (C-3′), 129.6 (C-10′), 129.86 (C-6′), 129.98 (C-2′), 130.6 (C-9′a), 130.7 (C-11′a), 131.0 (C-6′a), 131.9 (C-3a), 134.3 (C-4′a), 151.7 (C-6), 153.3 (C-7a), 157.0 (C-2), 182.8 (C-1′); MS (EI, 70 eV) *m*/*z* 390 (100) [M^+], 362 (6), 288 (3), 229 (98), 201 (72), 181 (8); HRMS (EI, M^+) calcd for $C_{26}H_{18}N_2O_2$ (390.1368), found 390.1393.

*2-Benzoyl-6-(diethylamino)benzoxazole (**7l**).*



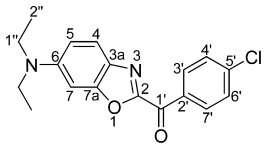
According to the general procedure, a mixture of 5-(diethylamino)-2-nitrosophenol (**5b**) (194 mg, 1 mmol), 2-bromoacetophenone (**6a**) (199 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry DMF (5 mL) was heated at 80 °C under argon for 3 h. After workup, the crude product was purified by flash chromatography over silica gel (PE/EtOAc = 8:1) to give **7l** as an orange solid in 70% yield (206 mg, 0.70 mmol): mp 88−89 °C; R_f = 0.53 (PE/EtOAc = 4:1); IR (ATR) $\tilde{\nu}$ 1645, 1614, 1509, 1319, 1253, 1179, 1068, 911, 797, 728 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 432 (4.28), 261 (4.21) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (t, ^3J (1″-H, 2″-H) = 7.4 Hz, 6H, 2″-H), 3.45 (q, ^3J (1″-H, 2″-H) = 7.4 Hz, 4H, 1″-H), 6.80 (d, ^4J (5-H, 7-H) = 2.6 Hz, 1H, 7-H), 6.86 (dd, ^4J (5-H, 7-H) = 2.8 Hz, ^3J (4-H, 5-H) = 8.9 Hz, 1H, 5-H), 7.54−7.58 (m, 2H, 4′-H and 6′-H), 7.62−7.65 (m, 1H, 5′-H), 7.69 (d, ^3J (4-H, 5-H) = 8.9 Hz, 1H, 4-H), 8.51 (app d, *J* = 8.5 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 12.4 (C-2″), 45.2 (C-1″), 91.8 (C-7), 112.2 (C-5), 122.6 (C-4), 128.4 (C-4′), 130.7 (C-3′), 131.1 (C-3a), 133.5 (C-5′), 135.8 (C-2′), 149.2 (C-6), 153.3 (C-7a), 155.5 (C-2), 179.9 (C-1′); MS (EI, 70 eV) *m*/*z* 294 (14) [M^+], 265 (100), 250 (84); HRMS (EI, M^+) calcd for $C_{18}H_{18}N_2O_2$ (294.1368), found 294.1359.

*2-(5′-(Methoxybenzoyl)-6-(diethylamino)benzoxazole (**7m**).*



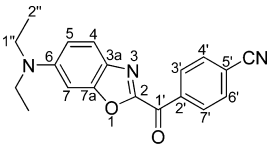
According to the general procedure, a mixture of 5-(diethylamino)-2-nitrosophenol (**5b**) (194 mg, 1 mmol), 2-bromo-4′-methoxyacetophenone (**6c**) (230 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry DMF (5 mL) was heated at 80 °C under argon for 4 h. After workup, the crude product was purified by flash chromatography over silica gel (PE/EtOAc = 8:1) to give **7m** as an orange solid in 70% yield (226 mg, 0.70 mmol): mp 125−126 °C; R_f = 0.58 (PE/EtOAc = 4:1); IR (ATR) $\tilde{\nu}$ 1653, 1619, 1599, 1504, 1252, 1168, 1118, 1076, 1014, 911, 768, 714 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 427 (4.34), 307 (4.06), 255 (4.10) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 1.23 (t, ^3J (1″-H, 2″-H) = 7.4 Hz, 6H, 2″-H), 3.44 (q, ^3J (1″-H, 2″-H) = 7.4 Hz, 4H, 1″-H), 3.90 (s, 3H, OCH_3), 6.80 (d, ^4J (5-H, 7-H) = 2.6 Hz, 1H, 7-H), 6.84 (dd, ^4J (5-H, 7-H) = 2.6 Hz, ^3J (4-H, 5-H) = 9.0 Hz, 1H, 5-H), 7.02 (app d, *J* = 9.6 Hz, 2H, 4′-H and 6′-H), 7.69 (d, ^3J (4-H, 5-H) = 9.0 Hz, 1H, 4-H), 8.58 (app d, *J* = 8.9 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 12.4 (C-2″), 45.2 (C-1″), 55.5 (OCH_3), 92.0 (C-7), 112.0 (C-5), 113.7 (4′-C), 122.3 (C-4), 128.6 (C-2′), 131.0 (C-3a), 135.3 (C-3′), 149.2 (C-6), 153.2 (C-7a), 155.7 (C-2), 164.1 (C-5′), 178.3 (C-1′); MS (EI, 70 eV) *m*/*z* 324 (12), 295 (20), 280 (4); HRMS (EI, M^+) calcd for $C_{19}H_{20}N_2O_3$ (324.1474), found 324.1462.

*2-(5′-Chlorobenzoyl)-6-(diethylamino)benzoxazole (**7n**).*



According to the general procedure, a mixture of 5-(diethylamino)-2-nitrosophenol (**5b**) (194 mg, 1 mmol), 2-bromo-4′-chloroacetophenone (**6e**) (233 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry DMF (5 mL) was heated at 80 °C under argon for 3 h. After workup, the crude product was purified by flash chromatography over silica gel (PE/EtOAc = 8:1) to give **7n** as a brown solid in 66% yield (218 mg, 0.66 mmol): mp 104−105 °C; R_f = 0.48 (PE/EtOAc = 4:1); IR (ATR) $\tilde{\nu}$ 1650, 1616, 1510, 1318, 1253, 1176, 1073, 912, 800, 730 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 441 (4.28), 266 (4.16) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 1.24 (t, ^3J (1″-H, 2″-H) = 7.1 Hz, 6H, 2″-H), 3.46 (q, ^3J (1″-H, 2″-H) = 7.1 Hz, 4H, 1″-H), 6.79 (d, ^4J (5-H, 7-H) = 2.6 Hz, 1H, 7-H), 6.86 (dd, ^4J (5-H, 7-H) = 2.4 Hz, ^3J (4-H, 5-H) = 9.0 Hz, 1H, 5-H), 7.49−7.53 (m, 2H, 4′-H and 6′-H), 7.69 (d, ^3J (4-H, 5-H) = 9.2 Hz, 1H, 4-H), 8.50 (app d, *J* = 8.5 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 12.4 (C-2″), 45.2 (C-1″), 91.2 (C-7), 112.3 (C-5), 122.6 (C-4), 128.7 (C-4′), 131.0 (C-3a), 132.2 (C-3′), 133.9 (C-5′), 140.2 (C-2′), 149.4 (C-6), 153.4 (C-7a), 155.2 (C-2), 178.3 (C-1′); MS (EI, 70 eV) *m*/*z* 328 (33) [M^+], 299 (100), 284 (44); HRMS (EI, M^+) calcd for $C_{18}H_{17}ClN_2O_2$ (328.0979), found 328.0983.

*2-(5′-Cyanobenzoyl)-6-(diethylamino)benzoxazole (**7o**).*



According to the general procedure, a mixture of 5-(diethylamino)-2-nitrosophenol (**5b**) (194 mg, 1 mmol), 4′-(2-bromoacetyl)-benzonitrile (**6f**) (224 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry DMF (5 mL) was heated at 80 °C under argon for 3 h. After workup, the crude product was purified by flash chromatography over silica gel (PE/EtOAc = 8:1) to give **7o** as an orange solid in 68% yield (215 mg, 0.68 mmol): mp 160−161 °C; R_f = 0.39 (PE/EtOAc = 4:1); IR (ATR) $\tilde{\nu}$ 1646, 1614, 1585, 1510, 1398, 1370, 1320, 1253, 1191, 1179, 1138, 1072, 997, 913, 803, 716 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 458 (4.36), 262 (4.34) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 1.24 (t, ^3J (1″-H, 2″-H) = 7.1 Hz, 6H, 2″-H), 3.46 (q, ^3J (1″-H, 2″-H) = 7.1 Hz, 4H, 1″-H), 6.78 (d, ^4J (5-H, 7-H) = 2.6 Hz, 1H, 7-H), 6.88 (dd, ^4J (5-H, 7-H) = 2.6 Hz, ^3J (4-H, 5-H) = 9.2 Hz, 1H, 5-H), 7.69 (d, ^3J (4-H, 5-H) = 9.3 Hz, 1H, 4-H), 7.81−7.84 (m, 2H, 4′-H and 6′-H), 8.61−8.65 (m, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 12.4 (C-2″), 45.2 (C-1″), 91.5 (C-7), 112.7 (C-5), 116.4 (C-5′), 118.1 (CN), 122.8 (C-4), 131.1 (C-3′), 132.1 (C-4′), 131.0

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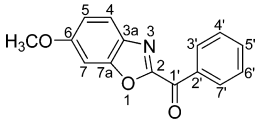
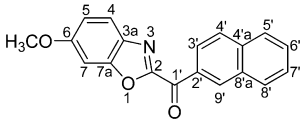
(C-3a), 139.0 (C-2′), 149.7 (C-6), 153.6 (C-7a), 154.9 (C-2), 177.8 (C-1′); MS (EI, 70 eV) *m*/*z* 319 (26), 290 (100), 275 (83); HRMS (EI, M^+) calcd for $C_{19}H_{17}N_3O_2$ (319.1321), found 319.1315.

*2-Benzoyl-6-methoxybenzoxazole (**7p**).*



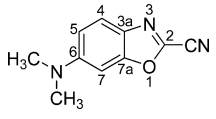
According to the general procedure, a mixture of 5-methoxy-2-nitrosophenol (**5c**) (153 mg, 1 mmol), 2-bromoacetophenone (**6a**) (199 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 3 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/EtOAc = 10:1) to give **7p** as a yellow solid in 63% yield (160 mg, 0.63 mmol): mp 219−221 °C; R_f = 0.38 (cyclohexane/EtOAc = 2:1); IR (ATR) $\tilde{\nu}$ 1646, 1523, 1248, 1112, 962, 913, 820, 728, 684 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 340 (4.22), 258 (3.92) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.91 (s, OCH_3), 7.09 (dd, ^4J (5-H, 7-H) = 2.5 Hz, ^3J (4-H, 5-H) = 9.0 Hz, 1H, 5-H), 7.16 (brd, ^4J (5-H, 7-H) = 2.3 Hz, 1H, 7−H), 7.56 (app t, *J* = 7.7 Hz, *J* = 7.4 Hz, 2H, 4′-H and 6′-H), 7.67 (app d, *J* = 7.4 Hz, 1H, 5′-H), 7.81 (d, ^3J (4-H, 5-H) = 9.0 Hz, 1H, 4-H), 8.53 (app d, *J* = 7.6 Hz, 2H, 3′-H and 7′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 56.0 (OCH_3), 95.1 (C-7), 115.6 (C-5), 122.6 (C-4), 128.5 (C-4′), 130.9 (C-3′), 134.0 (C-5′), 134.6 (C-3a), 135.2 (C-2′), 151.8 (C-7a), 156.7 (C-2), 160.9 (C-6), 180.1 (C-1′); MS (EI, 70 eV) *m*/*z* 253 (100) [M^+], 225 (8); HRMS (EI, M^+) calcd for $C_{15}H_{11}NO_3$ (253.0739), found 253.0733.

*6-Methoxybenzo[d]oxazole-2-yl)(naphthalen-1-yl)methanone (**7q**).*



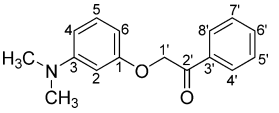
According to the general procedure, a mixture of 5-methoxy-2-nitrosophenol (**5c**) (153 mg, 1 mmol), 2-(bromoacetyl)naphthalene (**6j**) (249 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 3 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 1:4) to give **7q** as an orange solid in 51% yield (154 mg, 0.51 mmol): mp 202−203 °C; R_f = 0.44 (cyclohexane/EtOAc = 2:1); IR (ATR) $\tilde{\nu}$ 1643, 1611, 1464, 1258, 1225, 1104, 1021, 969, 907, 831, 779, 773, 704 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 342 (3.87), 260 (4.15) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 3.92 (s, OCH_3), 7.11 (dd, ^4J (5-H, 7-H) = 2.4 Hz, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 5-H), 7.19 (brd, ^4J (5-H, 7-H) = 2.3 Hz, 1H, 7-H), 7.56−7.68 (m, 2H, 6′-H and 7′-H), 7.86 (d, ^3J (4-H, 5-H) = 9.1 Hz, 1H, 4-H), 7.92 (d, ^3J (5′-H, 6′-H) = 7.8 Hz, 1H, 5′-H), 7.98 (d, ^3J (3′-H, 4′-H) = 8.6 Hz, 1H, 4′-H), 8.09 (brd, ^3J (7′-H, 8′-H) = 7.8 Hz, 1H, 8′-H), 8.45 (d, ^3J (3′-H, 4′-H) = 8.7 Hz, 1H, 3′-H), 9.31 (brs, 1H, 9′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 56.0 (OCH_3), 95.1 (C-7), 115.6 (C-5), 119.7 (C-8′a), 122.6 (C-4), 125.4 (C-7′), 126.8 (C-9′), 127.8 (C-6′), 128.4 (C-5′), 129.1 (C-4′), 130.3 (C-8′), 132.4 (C-4′a), 132.5 (C-3′), 134.0 (C-3a), 136.0 (C-2′), 151.8 (C-7a), 156.9 (C-2), 160.9 (C-6), 179.9 (C-1′); MS (EI, 70 eV) *m*/*z* 303 (14) [M^+], 275 (4), 155 (26); HRMS (EI, M^+) calcd for $C_{19}H_{13}NO_3$ (303.0895), found 303.0881.

*2-Cyano-6-(dimethylamino)benzoxazole (**7r**).*



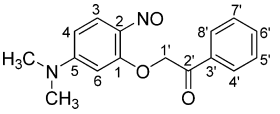
According to the general procedure, a mixture of 5-(dimethylamino)-2-nitrosophenol (**5a**) (167 mg, 1 mmol), bromoacetonitrile (**6l**) (119 mg, 1 mmol), and K_2CO_3 (417 mg, 3 mmol) in dry THF (5 mL) was refluxed under argon for 7 h. After workup, the crude product was purified by flash chromatography over silica gel (cyclohexane/EtOAc = 8:1) to give **7r** as a yellow solid in 55% yield (102 mg, 0.55 mmol): mp 113−114 °C; R_f = 0.58 (cyclohexane/EtOAc = 2:1); IR (ATR) $\tilde{\nu}$ 2234, 1616, 1520, 1370, 1296, 1247, 1221, 1119, 1071, 966, 806, 737 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 367 (4.04) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 6H, $N(CH_3)_2$), 6.70 (d, ^4J (5-H, 7-H) = 2.4 Hz, 1H, 7-H), 6.89 (dd, ^4J (5-H, 7-H) = 2.4 Hz, ^3J (4-H, 5-H) = 9.2 Hz, 1H, 5-H), 7.62 (d, ^3J (4-H, 5-H) = 8.1 Hz, 1H, 4-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.8 ($N(CH_3)_2$), 92.2 (C-7), 110.0 (CN), 112.8 (C-5), 121.5 (C-4), 129.9 (C-3a), 134.3 (C-2), 151.8 (C-6), 152.9 (C-7a); MS (EI, 70 eV) *m*/*z* 187 (83) [M^+], 170 (7), 115 (4), 93 (4); HRMS (EI, M^+) calcd for $C_{10}H_9N_3O$ (187.0746), found 187.0736.

Preparation of 13a and 9a and Cyclization to 7a. *2-(3-(Dimethylamino)phenoxy)-1-phenylethanone (**13a**).*



A mixture of 3-(dimethylamino)phenol (**12a**) (802 mg, 5.85 mmol), 2-bromoacetophenone (**6a**) (2.33 g, 11.7 mmol), and K_2CO_3 (2.50 g, 18 mmol) in dry acetone (20 mL) was refluxed for 12 h. After being cooled to room temperature, the reaction mixture was poured into water (70 mL) and extracted with ether (3 × 40 mL). The combined organic extracts were washed with brine. After drying over anhydrous $MgSO_4$ and concentration in vacuo, the resulting residue was purified by flash chromatography over silica gel (cyclohexane/EtOAc = 10:1) to give **13a** as a white solid in 89% yield (1.32 g, 5.18 mmol): mp 100−102 °C; R_f = 0.46 (cyclohexane/EtOAc = 1:2); IR (ATR) $\tilde{\nu}$ 1698, 1610, 1503, 1326, 1274, 1153, 1063, 818, 738, 683 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 293 (3.14), 248 (3.92) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 2.93 (s, 6H, $N(CH_3)_2$), 5.24 (s, 2H, 1′-H), 6.27 (dd, ^4J (2-H, 4-H) = 2.0 Hz, ^3J (4-H, 5-H) = 8.1 Hz, 1H, 4-H), 6.38−6.41 (m, 2H, 2-H and 6-H), 7.13 (dd, ^3J (4-H, 5-H) = 8.2 Hz, ^3J (5-H, 6-H) = 8.8 Hz, 1H, 5-H), 7.50 (dd, *J* = 7.3 Hz, *J* = 7.6 Hz, 2H, 5′-H and 7′-H), 7.52−7.61 (m, 1H, 6′-H), 8.0 (d, *J* = 7.3 Hz, 2H, 4′-H and 8′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.5 ($N(CH_3)_2$), 70.9 (C-1′), 100.2 (C-6), 101.6 (C-4), 106.6 (C-2), 128.2 (C-4′), 128.7 (C-5′), 129.7 (C-5), 133.7 (C-6′), 134.7 (C-3′), 152.0 (C-3), 159.1 (C-1), 194.9 (C-2′); MS (EI, 70 eV) *m*/*z* 255 (76) [M^+], 221 (12), 208 (8), 194 (8), 165 (16), 105 (50); HRMS (EI, M^+) calcd for $C_{16}H_{17}NO_2$ (255.1259), found 255.1270.

*2-(5-(Dimethylamino)-2-nitrosophenoxy)-1-phenylethanone (**9a**).*



A solution of sodium nitrite (668 mg, 9.69 mmol) in water (8 mL) was gradually added to a stirred solution of 2-(3-(dimethylamino)phenoxy)-1-phenylethanone (**13a**) (2.03 g, 7.95 mmol) in concd HCl (12 mL) and water (8 mL) at 0 °C. After being stirred for 2 h slightly below 0 °C, the product was filtered using a Buchner funnel, and the residue was washed with HCl (50 mL, 1 M). The solid was placed in a beaker and treated with aqueous $NaHCO_3$ (50 mL, 1 M). After filtration using a Buchner funnel, the crude product was purified by flash chromatography on silica gel (cyclohexane/EtOAc = 2:1) to give **9a** as a green solid in 90% yield (2.03 g, 7.14 mmol): mp 87−88 °C; R_f = 0.10 (cyclohexane/EtOAc = 1:2); IR (ATR) $\tilde{\nu}$ 1695, 1595, 1536, 1325, 1277, 1166, 1066, 812, 769, 690 cm^{-1}; UV/vis (MeCN) λ_{max} (log ε) 417 (3.99), 329 (3.05), 273 (3.48), 241 (3.75) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.12 (s, 6H, $N(CH_3)_2$), 5.81 (s, 2H, 1′-H), 6.16 (dd, ^4J (4-H, 6-H) = 2.3 Hz, ^3J (3-H, 4-H) = 9.4 Hz, 1H, 4-H), 6.21 (d, ^4J (4-H, 6-H) = 2.3 Hz, 1H, 6-H), 6.65 (d, ^3J (3-H, 4-H) = 9.4 Hz, 1H, 3-H), 7.44−7.49 (m, 2H, 5′-H and 7′-H), 7.56−7.61 (m, 1H, 6′-H), 8.05 (dd, *J* = 1.2 Hz, *J* = 7.3 Hz, 2H, 4′-H and 8′-H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 40.5 ($N(CH_3)_2$), 74.2 (C-1′), 96.3 (C-6), 105.3 (C-4), 113.1 (C-3), 128.3 (C-4′), 128.8 (C-5′), 133.9 (C-6′), 134.4 (C-3′), 156.4 (C-2), 157.3 (C-5), 163.5 (C-1), 194.8 (C-2′); MS (EI, 70 eV) *m*/*z* 284 (20) [M^+], 266 (70), 252 (16), 237 (12), 161 (16), 105 (100); HRMS (EI, M^+) calcd for $C_{16}H_{16}N_2O_3$ (284.1161), found 284.1153.

*Cyclization of 2-(5-(Dimethylamino)-2-nitrosophenoxy)-1-phenylethanone (**9a**) to 2-Benzoyl-6-(dimethylamino)benzoxazole*

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(7a). A mixture of 2-(5-(dimethylamino)-2-nitrosophenoxy)-1-phenylethanone (**9a**) (200 mg, 0.71 mmol) and K_2CO_3 (296 mg, 2.13 mmol) in dry THF (5 mL) was refluxed under argon for 5 h. After being cooled to room temperature, the reaction mixture was poured into water and extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine. After drying over anhydrous $MgSO_4$ and concentration in vacuo, the resulting residue was purified by flash chromatography over silica gel (cyclohexane/CH_2Cl_2 = 4:1) to give **7a** as an orange solid in 67% yield (126 mg, 0.47 mmol).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02000.

^1H and ^{13}C NMR spectra for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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