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Reactivity of 2,1-Benzisoxazole in Palladium-Catalyzed Direct Arylation with Aryl Bromides

Mohand Aidene,[a, b] Fatma Belkessam,[a, b] Jean-François Soulé,*[b] and Henri Doucet*[b]

The Pd-catalyzed direct arylation of 2,1-benzisoxazole with aryl bromides to access 3-arylbenzoisoxazoles proceeds in moderate-to-high yields with 1 mol% $Pd(OAc)_2$ or 2 mol% $PdCl(C_3H_5)(dppb)$ (dppb = 1,4-bis(diphenylphosphino)butane) as the catalysts and KOAc as an inexpensive base. A wide variety of (hetero)aryl bromides have been employed successfully. Moreover, arylations followed by benzisoxazole ring opening allowed the preparation of 2-aminobenzophenones in only two steps.

Introduction

3-Arylbenzisoxazole and 2-aminobenzophenone derivatives exhibit important biological properties.[1] For example, **A** is an inhibitor of the proto-oncogene Pim-1 kinase,[2] and both Bromfenac and Nepafenac are nonsteroidal anti-inflammatory drugs for the treatment of ocular inflammation (Figure 1).

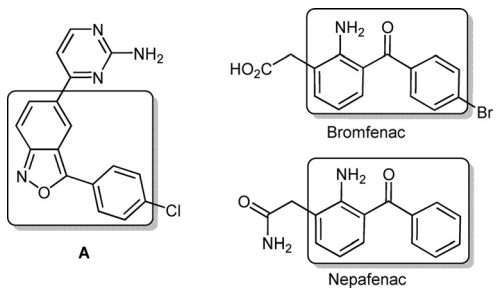
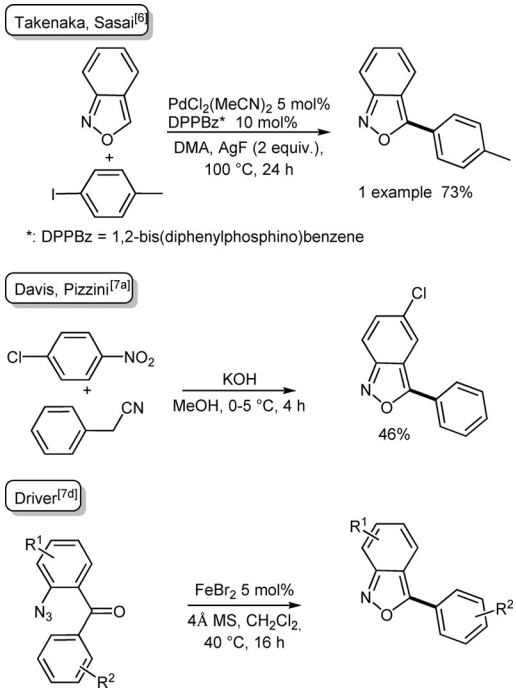


Figure 1. Examples of drugs containing 3-arylbenzisoxazole and 2-aminobenzophenone motifs.

In 1982, Nakamura et al. reported that the 4-arylation of isoxazoles with aryl halides proceeds in moderate yields through a C–H bond activation with Pd catalysts.[3] Since this initial report, the Pd-catalyzed direct arylation[4] of isoxazole derivatives with aryl halides has proved to be a very powerful method for the synthesis of a wide variety of 4-arylated isoxazoles.[3,5] The major byproducts of these reactions are a base associated with HX, instead of the metallic salts that are produced with more classical cross-coupling procedures. Although the 4-arylation of isoxazoles has been studied in detail, only one example of a Pd-catalyzed direct coupling of an aryl halide with a benzisoxazole has been reported.[6] For this reaction, a quite high catalyst loading was employed [5 mol% $PdCl_2(MeCN)_2$ with 10 mol% 1,2-bis(diphenylphosphino)benzene (DPPBz); Scheme 1, top]. Moreover, the expensive base AgF (2 equiv.) was used. In most cases, 3-arylbenzisoxazoles are still prepared through organic reactions such as the intramolecular cyclization of 2-azidobenzophenones or the reactions of nitrobenzene derivatives with phenylacetonitrile derivatives (Scheme 1, middle and bottom).[7] However, for these two methods, the substrate scope is limited because of the dif-

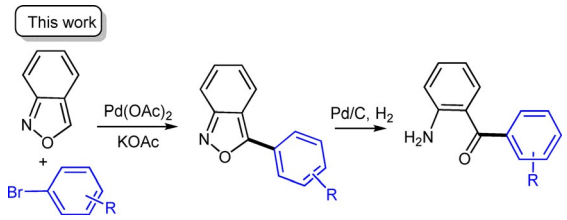


Scheme 1. Reported syntheses of 3-arylbenzoisoxazoles.

[a] Dr. M. Aidene, Dr. F. Belkessam
Département de chimie
Tizi Ouzou University
BP 17 RP 15000 Tizi-Ouzou (Algeria)
[b] Dr. M. Aidene, Dr. F. Belkessam, Dr. J.-F. Soulé, Dr. H. Doucet
Institut des Sciences Chimiques de Rennes
UMR 6226 CNRS-Université de Rennes
"Organométalliques: Matériaux et Catalyse"
Campus de Beaulieu, 35042 Rennes (France)
E-mail: jean-francois.soule@univ-rennes1.fr
henri.doucet@univ-rennes1.fr

ficult access to some substrates and to the poor functional-group tolerance. The convenient synthesis of 2-aminobenzophenones is also an important challenge in organic chemistry, as they are currently prepared through multistep syntheses.[8] Therefore, economically viable reaction conditions that promote the direct arylation of 2,1-benzisoxazole with aryl bromides in the presence of a low loading of a readily available Pd catalyst are needed to provide access to a wide variety of arylated benzisoxazole derivatives.

Here, we report on the reactivity of 2,1-benzisoxazole in Pd-catalyzed direct arylation reactions with a wide variety of aryl bromides and either a phosphine-free Pd catalyst or Pd associated with a simple diphosphine ligand (1,4-bis(diphenylphosphino)butane; dppb) in the presence of an inexpensive base (Scheme 2). The ring opening of benzisoxazole for access to 2-aminobenzophenones is also described.



Scheme 2. Pd-catalyzed direct arylation of 2,1-benzisoxazole followed by ring opening.

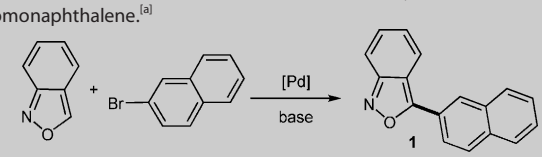
Results and Discussion

Initially, we studied the reactivity of 2,1-benzisoxazole in the presence of 2-bromonaphthalene as the arylation partner (Table 1). The use of 2 mol% of the $PdCl(C_3H_5)$(dppb) catalyst at 150 °C led to **1** in 47% yield with a complete conversion of 2-bromonaphthalene (Table 1, Entry 1). In 2003, de Vries and co-workers demonstrated that if $Pd(OAc)_2$ is employed at elevated temperature as the catalyst precursor without a phosphine ligand, soluble palladium(0) colloids or nanoparticles are formed, which are very efficient catalysts in the Heck and Suzuki reactions.[9] We have recently reported that the use of the "de Vries conditions" promoted the coupling of aryl bromides with several heteroaromatics.[10] The coupling reactions of 2,1-benzisoxazole and 2-bromonaphthalene with 1 or 0.5 mol% $Pd(OAc)_2$ catalyst at 150 °C afforded the target product **1** in very high yields of 78 and 80%, respectively (Table 1, Entries 2 and 3). The use of 1 mol% $PdCl_2$ catalyst was less effective, as **1** was isolated in only 35% yield (Table 1, Entry 4). We also examined the influence of some bases; potassium carbonate, cesium carbonate, and sodium acetate were completely ineffective, and 2-bromonaphthalene was recovered (Table 1, Entries 5–7). The different results obtained with KOAc and NaOAc as bases might come from the poor solubility of NaOAc in dimethylacetamide (DMA). The influence of the nature of the solvent was also examined. The reaction in DMF afforded **1** in a low yield of 33%, whereas the use of *N*-methyl-2-pyrrolidone (NMP) was ineffective (Table 1, Entries 8 and 9). Xylene and cyclopentyl methyl ether (CPME), which are suitable solvents for the Pd-catalyzed direct arylation of several heteroaromatics,[5d] were also ineffective (Table 1, Entries 10 and 11). The reaction performed at 120 °C instead of 150 °C with 1 mol% of $Pd(OAc)_2$ catalyst afforded **1** in only 12% yield because of the very low conversion of 2-bromonaphthalene (Table 1, Entry 12).

Then, we studied the scope of this reaction with various aryl bromides, 1 mol% $Pd(OAc)_2$ as the catalyst, and KOAc as the base in DMA at 150 °C (Scheme 3). First, we examined the reactivity of *para*-substituted aryl bromides. The coupling of 2,1-benzisoxazole with 4-bromobenzaldehyde, 4-bromoacetophenone, 4-bromopropiophenone, 4-bromobenzophenone, and ethyl 4-bromobenzoate proceeded well to afford **2–6** in 82–93% yields. High yields of the desired 3-arylbenzoisoxazoles **7** and **8** were also obtained from 4-(trifluoromethyl)bromobenzene and 4-bromobenzonitrile in the presence of 1 mol% $Pd(OAc)_2$, whereas **9** was only obtained in a moderate yield from the less electron-deficient 4-bromochlorobenzene under these conditions because of the partial conversion of this aryl bromide. This poor conversion is probably caused by the slow oxidative addition of 4-bromochlorobenzene to Pd. Therefore, this phosphine-free Pd catalysis is limited to some electron-deficient aryl bromides. However, **9** could be obtained in a good yield of 86% with 2 mol% $PdCl(C_3H_5)$(dppb) catalyst. For 4-bromofluorobenzene and bromobenzene, 2 mol% $PdCl(C_3H_5)$(dppb) again had to be employed as the catalyst to obtain **10** and **11** in good yields.

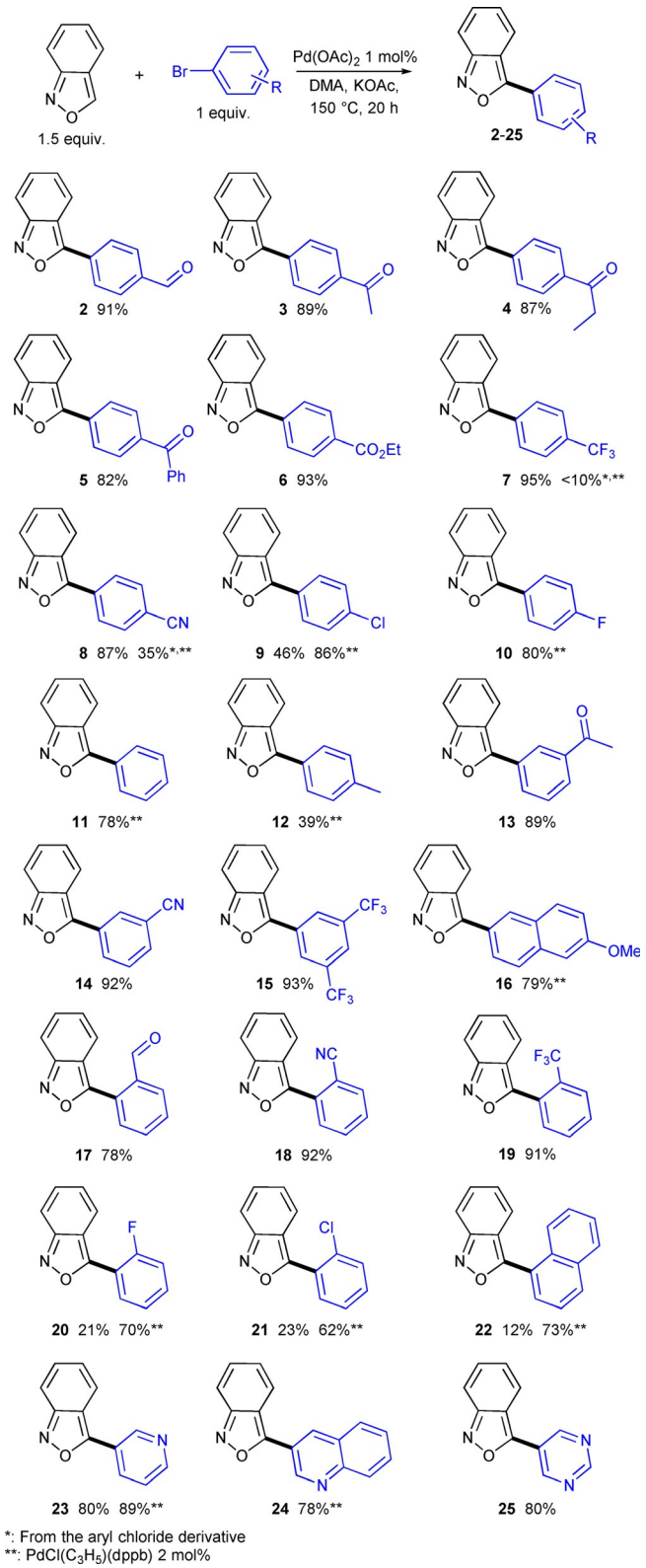
The electron-deficient *meta*-substituted aryl bromides 3-bromoacetophenone, 3-bromobenzonitrile, and 3,5-bis(trifluoromethyl)bromobenzene were also very reactive with 1 mol% $Pd(OAc)_2$ as the catalyst

Table 1. Influence of the reaction conditions on the arylation of 2,1-benzisoxazole with 2-bromonaphthalene.[a]



Entry	Solvent	Base	Catalyst [(mol%)]	*T* [°C]	Conversion[b] [%]	Yield of **1**[c] [%]
1	DMA	KOAc	$PdCl(C_3H_5)$(dppb) (2)	150	100	47
2	DMA	KOAc	$Pd(OAc)_2$ (1)	150	100	78
3	DMA	KOAc	$Pd(OAc)_2$ (0.5)	150	97	80
4	DMA	KOAc	$PdCl_2$ (1)	150	77	35
5	DMA	K_2CO_3	$Pd(OAc)_2$ (1)	150	0	–
6	DMA	Cs_2CO_3	$Pd(OAc)_2$ (1)	150	0	–
7	DMA	NaOAc	$Pd(OAc)_2$ (1)	150	0	–
8	DMF	KOAc	$Pd(OAc)_2$ (1)	150	51	33
9	NMP	KOAc	$Pd(OAc)_2$ (1)	150	30	0
10	Xylene	KOAc	$Pd(OAc)_2$ (1)	140	0	0
11	CPME	KOAc	$Pd(OAc)_2$ (1)	110	0	0
12	DMA	KOAc	$Pd(OAc)_2$ (1)	120	15	12

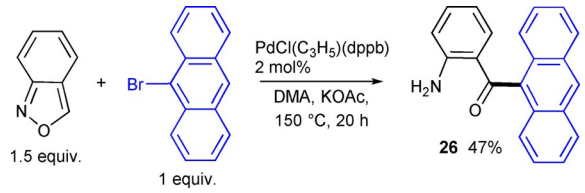
[a] Conditions: 2,1-benzisoxazole (1.5 equiv.), 2-bromonaphthalene (1 equiv.), KOAc (2 equiv.), 20 h. [b] Conversions of 2-bromonaphthalene determined by using GC and NMR spectroscopy. [c] Isolated yields.



Scheme 3. Direct arylation of 2,1-benzisoxazole with a set of aryl bromides.

and afforded **13**–**15** in yields of 89–93%. Next, the reactivity of a set of *ortho*-substituted aryl bromides was investigated. 2-Formyl-, 2-nitrile-, and 2-(trifluoromethyl)bromobenzene in the presence of 1 mol% $Pd(OAc)_2$ gave the desired products **17**–**19** in good-to-high yields. 2-Fluorobromobenzene, 2-chlorobromobenzene, and 1-bromonaphthalene were less reactive, and again 2 mol% $PdCl(C_3H_5)(dppb)$ had to be employed as the catalyst to produce **20**–**22** in good yields. Heteroaryl bromides are also suitable reactants for the C-3-arylation of 2,1-benzisoxazole. The coupling of 3-bromopyridine, 3-bromoquinoline, and 5-bromopyrimidine in the presence of 1 mol% $Pd(OAc)_2$ or 2 mol% $PdCl(C_3H_5)(dppb)$ as the catalyst led to **23**–**25** in yields of 78–89%. The reactivity of two aryl chlorides for such couplings was also examined with 2 mol% $PdCl(C_3H_5)(dppb)$ as the catalyst. From 4-chlorobenzonitrile, the desired product **8** was obtained in 35% yield because of the moderate conversion of this aryl chloride; whereas, a poor yield of **7** (<10%) was obtained from 4-(trifluoromethyl)chlorobenzene.

The Pd-catalyzed coupling of 9-bromoantracene with 2,1-benzisoxazole also proceed well (Scheme 4). However, only the (2-aminophenyl)(anthracen-9-yl)methanone (**26**) was isolated

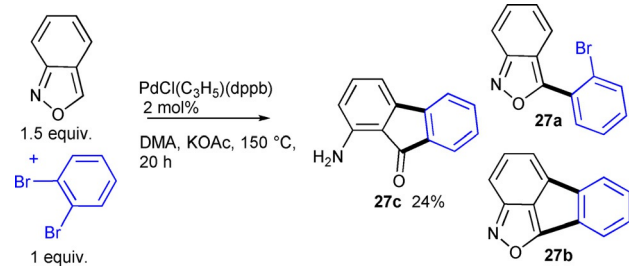


Scheme 4. Direct arylation of 2,1-benzisoxazole with 9-bromoanthracene.

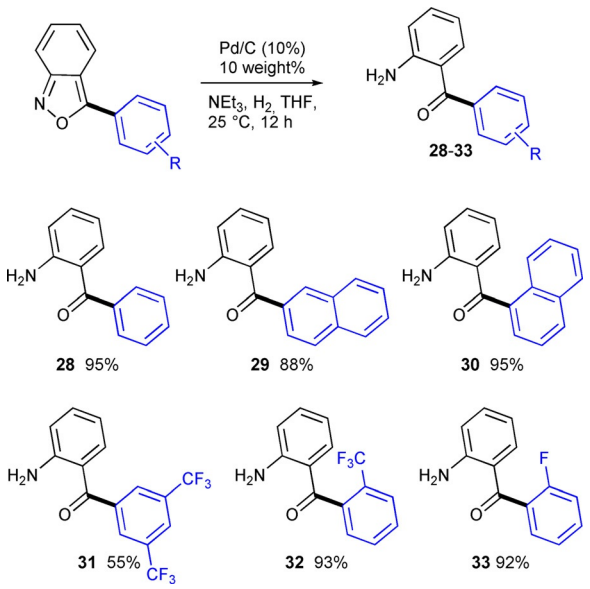
because of the in situ benzisoxazolyl ring opening. GC–MS analysis of the crude mixture only showed the formation of **26**. This ring opening is probably caused by the steric hindrance of the anthracenyl moiety.

From 1,2-dibromobenzene and 2,1-benzisoxazole, the formation of several products, such as the monocoupling product **27a** or the dicoupling product **27b**, was possible (Scheme 5). However, only product **27c** that arose from the coupling at positions C-3 and C-4 of 2,1-benzisoxazole followed by the benzisoxazolyl ring opening was isolated. This method gives a one-step access to 1-amino-9*H*-fluoren-9-ones, which exhibit important physical properties.[11]

The discovery of efficient methods for the synthesis of 2-aminobenzophenones in a limited number of steps is also an important research field in organic synthesis. Therefore, the scope of the benzoisoxazole ring-opening reaction for access to 2-aminobenzophenones under classical conditions was in-



Scheme 5. Direct arylation of 2,1-benzisoxazole with 1,2-dibromobenzene.



Scheme 6. Pd-catalyzed ring opening of 3-arylbenzisoxazoles for access to 2-aminobenzophenones.

vestigated (Scheme 6).[12] In the presence of 10 wt% of Pd/C(10%) and NEt_3 under H_2 in THF, 3-phenylbenzo[*c*]isoxazole (**11**) gave the desired 2-aminobenzophenone (**28**) in an almost quantitative yield. The 3-naphthyl-substituted benzoisoxazoles **1** and **22** also afforded the expected (2-aminophenyl)(naphthyl)methanones **29** and **30** in high yields. From the fluoro- and trifluoromethyl-substituted 3-aryl benzo[*c*]isoxazoles **15**, **19**, and **20**, the target products **31**–**33** were obtained in yields of 55, 93, and 92%, respectively. Notably, one-pot sequential reactions that involve the C-3-arylation of 2,1-benzisoxazole with 1-bromonaphthalene followed by the removal of the solvent and treatment of the crude mixture by Pd/C(10%) and NEt_3 under H_2 in THF failed to afford 2-aminobenzophenone **30**.

Conclusions

We have demonstrated that 2,1-benzisoxazole, which is commercially available at an affordable cost, reacts well in the presence of only 1 mol% of phosphine-free $Pd(OAc)_2$ catalyst and KOAc as an inexpensive base to afford the 3-arylated benzisoxazoles in good to very high yields. This procedure gave the best results using electron-deficient aryl bromides, and several functions such as formyl, acetyl, propionyl, benzoyl, ester, nitrile, and trifluoromethyl were tolerated. This procedure is attractive as the major byproducts of these couplings are AcOH/KBr, it reduces the number of steps to prepare these compounds, and there is no need to eliminate phosphine derivatives at the end of the reaction. For these reasons, the methodology developed here is very promising for the sustainable synthesis of 3-arylbenzisoxazoles. Moreover, sequential C–H bond activation followed by benzisoxazole ring opening using Pd/C as catalyst under hydrogen pressure allowed us to prepare a variety of 2-aminobenzophenones, which are valuable building blocks, in only two steps.

Experimental Section

DMA (99%) and 2,1-benzisoxazole (99%) were purchased from Acros. $Pd(OAc)_2$, $[Pd(C_3H_5)Cl]_2$, 1,4-bis(diphenylphosphino)butane (98%), KOAc (99%), and 1,2-benzisoxazole (97%) were purchased from Alfa Aesar. These compounds were not purified before use.

Preparation of $PdCl(C_3H_5)(dppb)$[13]

An oven-dried 40 mL Schlenk tube equipped with a magnetic stirring bar under Ar was charged with $[Pd(C_3H_5)Cl]_2$ (182 mg, 0.5 mmol) and dppb (426 mg, 1 mmol). Anhydrous dichloromethane (10 mL) was added, and the solution was stirred at RT for 20 min. The solvent was removed in vacuum. The yellow powder was used without purification. ^{31}P NMR (81 MHz, $CDCl_3$): $\delta =$ 19.3 ppm (s).

General procedure for the synthesis of compounds 1–27

Typically, the aryl bromide derivative (1 mmol), 2,1-benzisoxazole (0.179 g, 1.5 mmol), KOAc (0.196 g, 2 mmol), and $PdCl(C_3H_5)(dppb)$ (12.2 mg, 0.02 mmol) or $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) were dissolved in DMA (4 mL) under an Ar atmosphere. The reaction mixture was stirred at 150 °C for 20 h. Then the solvent was evaporated and the product was purified by silica gel column chromatography.

3-(Naphthalen-2-yl)benzo[c]isoxazole (1)[14]

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 2-bromonaphthalene (0.207 g, 1 mmol), **1** was obtained in 80% (0.196 g) yield as a yellow solid. M.p.: 84–86 °C; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.48$ (s, 1H), 8.10 (dd, $J = 8.5$, 2.6 Hz, 1H), 8.00–7.84 (m, 4H), 7.64 (d, $J =$ 8.3 Hz, 1H), 7.60–7.53 (m, 2H), 7.34 (dd, $J = 9.0$, 6.4 Hz, 1H), 7.09 ppm (dd, $J = 8.8$, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 164.7, 157.7, 133.6, 132.9, 130.5, 128.9, 128.5, 127.7, 127.4, 126.8, 126.3, 125.5, 124.5, 123.0, 120.5, 115.3, 114.4 ppm.

4-(Benzo[c]isoxazol-3-yl)benzaldehyde (2)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 4-bromobenzaldehyde (0.185 g, 1 mmol), **2** was obtained in 91% (0.203 g) yield as a yellow solid. M.p.: 174–177 °C; ^1H NMR (400 MHz, $CDCl_3$): $\delta =$ 10.07 (s, 1H), 8.16 (d, $J = 8.3$ Hz, 2H), 8.03 (d, $J = 8.3$ Hz, 2H), 7.83 (d, $J = 8.8$ Hz, 1H), 7.64 (d, $J = 9.0$ Hz, 1H), 7.34 (dd, $J = 9.0$, 6.4 Hz, 1H), 7.13 ppm (dd, $J = 8.8$, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 191.1$, 162.4, 157.9, 136.7, 133.2, 130.8, 130.4, 126.7, 125.8, 120.0, 115.9, 115.5 ppm; elemental analysis calcd (%) for $C_{14}H_9NO_2$ (223.23): C 75.33, H 4.06; found: C 75.21, H 4.22.

1-[4-(Benzo[c]isoxazol-3-yl)phenyl]ethanone (3)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 4-bromoacetophenone (0.199 g, 1 mmol), **3** was obtained in 89% (0.211 g) yield as a yellow solid. M.p.: 152–156 °C; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.10$ (s, 4H), 7.84 (d, $J = 8.8$ Hz, 1H), 7.64 (d, $J = 9.0$ Hz, 1H), 7.35 (dd, $J =$ 9.0, 6.4 Hz, 1H), 7.12 (dd, $J = 8.8$, 6.4 Hz, 1H), 2.66 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 197.1$, 162.8, 157.9, 137.6, 132.1,

130.7, 129.1, 126.4, 125.5, 120.2, 115.8, 115.3, 26.7 ppm; elemental analysis calcd (%) for $C_{15}H_{11}NO_2$ (237.25): C 75.94, H 4.67; found: C 75.74, H 4.54.

1-[4-(Benzo[c]isoxazol-3-yl)phenyl]propan-1-one (4)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 4-bromopropiophenone (0.213 g, 1 mmol), **4** was obtained in 87% (0.218 g) yield as a yellow solid. M.p.: 148–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, J = 8.3 Hz, 2H), 8.08 (d, J = 8.3 Hz, 2H), 7.83 (d, J = 8.8 Hz, 1H), 7.64 (d, J = 9.0 Hz, 1H), 7.35 (dd, J = 9.0, 6.4 Hz, 1H), 7.12 (dd, J = 8.8, 6.4 Hz, 1H), 3.05 (q, J = 7.6 Hz, 2H), 1.26 ppm (q, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.7, 162.9, 157.9, 137.5, 131.8, 130.7, 128.8, 126.4, 125.5, 120.2, 115.8, 115.2, 31.9, 8.1 ppm; elemental analysis calcd (%) for $C_{16}H_{13}NO_2$ (251.28): C 76.48, H 5.21; found: C 76.28, H 5.06.

[4-(Benzo[c]isoxazol-3-yl)phenyl](phenyl)methanone (5)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 4-bromobenzophenone (0.261 g, 1 mmol), **5** was obtained in 82% (0.245 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, J = 8.3 Hz, 2H), 7.99 (d, J = 8.3 Hz, 2H), 7.87 (d, J = 8.8 Hz, 1H), 7.84 (d, J = 8.3 Hz, 2H), 7.68–7.60 (m, 2H), 7.52 (t, J = 8.0 Hz, 2H), 7.36 (dd, J = 9.0, 6.4 Hz, 1H), 7.13 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6, 162.9, 157.9, 138.5, 137.1, 132.8, 131.5, 130.9, 130.8, 130.0, 128.5, 126.2, 125.5, 120.2, 115.8, 115.2 ppm; elemental analysis calcd (%) for $C_{20}H_{13}NO_2$ (299.32): C 80.25, H 4.38; found: C 80.34, H 4.27.

Ethyl 4-(benzo[c]isoxazol-3-yl)benzoate (6)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and ethyl 4-bromobenzoate (0.229 g, 1 mmol), **6** was obtained in 93% (0.248 g) yield as a yellow solid. M.p.: 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, J = 8.3 Hz, 2H), 8.07 (d, J = 8.3 Hz, 2H), 7.82 (d, J = 8.8 Hz, 1H), 7.62 (d, J = 9.0 Hz, 1H), 7.33 (dd, J = 9.0, 6.4 Hz, 1H), 7.10 (dd, J = 8.8, 6.4 Hz, 1H), 4.41 (q, J = 7.6 Hz, 2H), 1.42 ppm (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4, 162.6, 157.6, 131.6, 131.2, 130.5, 130.1, 125.9, 125.2, 120.0, 115.5, 114.9, 61.1, 14.1 ppm; elemental analysis calcd (%) for $C_{16}H_{13}NO_3$ (267.28): C 71.90, H 4.90; found: C 71.69, H 4.67.

3-[4-(Trifluoromethyl)phenyl]benzo[c]isoxazole (7)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 4-(trifluoromethyl)-bromobenzene (0.225 g, 1 mmol), **7** was obtained in 95% (0.250 g) yield as a yellow solid. M.p.: 152–156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, J = 8.3 Hz, 2H), 7.78 (d, J = 8.3 Hz, 3H), 7.62 (d, J = 9.0 Hz, 1H), 7.33 (dd, J = 9.0, 6.4 Hz, 1H), 7.10 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.3, 157.8, 131.5 (q, J = 33.0 Hz), 131.3, 130.7, 126.5, 126.2 (q, J = 3.7 Hz), 125.5, 123.7 (q, J = 272.3 Hz), 119.9, 115.7, 115.1 ppm; elemental analysis: calcd (%) for $C_{14}H_8F_3NO$ (263.21): C 63.88, H 3.06; found: C 63.74, H 3.19.

4-(Benzo[c]isoxazol-3-yl)benzonitrile (8)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 4-bromobenzonitrile (0.182 g, 1 mmol), **8** was obtained in 87% (0.191 g) yield as a yellow solid. M.p.: 208–210 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, J = 8.3 Hz, 2H), 7.82 (d, J = 8.3 Hz, 2H), 7.80 (d, J = 8.3 Hz, 1H), 7.66 (d, J = 9.0 Hz, 1H), 7.37 (dd, J = 9.0, 6.4 Hz, 1H), 7.15 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8, 158.0, 133.1, 132.1, 131.0, 126.8, 126.2, 119.8, 118.2, 116.1, 115.6, 113.4 ppm; elemental analysis calcd (%) for $C_{14}H_8N_2O$ (220.23): C 76.35, H 3.66; found: C 76.42, H 3.80.

3-(4-Chlorophenyl)benzo[c]isoxazole (9)[7d]

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 4-bromochlorobenzene (0.191 g, 1 mmol), **9** was obtained in 86% (0.197 g) yield as a yellow solid. M.p.: 154–157 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, J = 8.3 Hz, 2H), 7.72 (d, J = 8.3 Hz, 1H), 7.58 (d, J = 9.0 Hz, 1H), 7.48 (d, J = 8.3 Hz, 2H), 7.29 (dd, J = 9.0, 6.4 Hz, 1H), 7.03 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 157.5, 136.2, 130.6, 129.4, 127.5, 126.6, 124.8, 120.1, 115.5, 114.3 ppm.

3-(4-Fluorophenyl)benzo[c]isoxazole (10)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 4-bromofluorobenzene (0.175 g, 1 mmol), **10** was obtained in 80% (0.170 g) yield as a yellow solid. M.p.: 102–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (dd, J = 8.3, 6.0 Hz, 2H), 7.77 (d, J = 8.3 Hz, 1H), 7.61 (d, J = 9.0 Hz, 1H), 7.32 (dd, J = 9.0, 6.4 Hz, 1H), 7.25 (t, J = 8.3 Hz, 2H), 7.06 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.4 (d, J = 252.1 Hz), 163.3, 157.7, 130.6, 128.5 (d, J = 8.5 Hz), 124.6, 120.2, 116.4 (d, J = 22.1 Hz), 115.4, 114.0 ppm; elemental analysis calcd (%) for $C_{13}H_8FNO$ (213.21): C 73.23, H 3.78; found: C 73.10, H 3.87.

3-Phenylbenzo[c]isoxazole (11)[15]

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and bromobenzene (0.157 g, 1 mmol), **11** was obtained in 78% (0.152 g) yield as a yellow solid. M.p.: 60–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, J = 8.5 Hz, 2H), 7.81 (d, J = 8.3 Hz, 1H), 7.60 (d, J = 8.2 Hz, 1H), 7.54 (t, J = 8.0 Hz, 2H), 7.47 (t, J = 8.0 Hz, 1H), 7.31 (dd, J = 9.0, 6.4 Hz, 1H), 7.04 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.3, 157.8, 130.5, 130.2, 129.2, 128.3, 126.5, 124.5, 120.5, 115.4, 114.3 ppm.

3-*p*-Tolylbenzo[c]isoxazole (12)[7b]

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 4-bromotoluene (0.171 g, 1 mmol), **12** was obtained in 39% (0.081 g) yield as yellow solid. M.p.: 90–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, J = 8.3 Hz, 2H), 7.81 (d, J = 8.3 Hz, 1H), 7.59 (d, J = 8.2 Hz, 1H), 7.35 (d, J = 8.3 Hz, 2H), 7.31 (dd, J = 9.0, 6.4 Hz, 1H), 7.03 (dd, J = 8.8, 6.4 Hz, 1H), 2.44 ppm (s, 3H).

1-(3-(Benzo[c]isoxazol-3-yl)phenyl)ethanone (13)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 3-bromoacetophenone (0.199 g, 1 mmol), **13** was obtained in 89% (0.211 g) yield as a yellow solid. M.p.: 128–132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (s, 1H), 8.19 (d, J = 8.3 Hz, 1H), 8.04 (d, J = 8.3 Hz, 1H), 7.84 (d, J = 8.3 Hz, 1H), 7.69–7.59 (m, 2H), 7.33 (dd, J = 9.0, 6.4 Hz, 1H), 7.10 (dd, J = 8.8, 6.4 Hz, 1H), 2.69 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.0, 162.9, 157.7, 137.8, 130.7, 130.4, 129.6, 129.5, 128.7, 125.9, 125.1, 120.1, 115.5, 114.6, 26.6 ppm; elemental analysis calcd (%) for $C_{15}H_{11}NO_2$ (237.25): C 75.94, H 4.67; found: C 75.98, H 4.78.

3-(Benzo[c]isoxazol-3-yl)benzonitrile (14)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 3-bromobenzonitrile (0.182 g, 1 mmol), 14 was obtained in 92% (0.202 g) yield as a yellow solid. M.p.: 185–189 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (s, 1H), 8.25 (d, J = 8.3 Hz, 1H), 7.81 (d, J = 8.3 Hz, 1H), 7.77 (d, J = 8.3 Hz, 1H), 7.71 (d, J = 8.3 Hz, 1H), 7.66 (d, J = 8.3 Hz, 1H), 7.37 (dd, J = 9.0, 6.4 Hz, 1H), 7.16 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.4, 157.8, 133.1, 130.9, 130.3, 130.2, 129.6, 129.5, 125.9, 119.6, 117.9, 115.9, 115.0, 113.8 ppm; elemental analysis calcd (%) for $C_{14}H_8N_2O$ (220.23): C 76.35, H 3.66; found: C 76.24, H 3.78.

3-(3,5-Bis(trifluoromethyl)phenyl)benzo[c]isoxazole (15)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 3,5-bis(trifluoromethyl)bromobenzene (0.293 g, 1 mmol), **15** was obtained in 93% (0.308 g) yield as a yellow solid. M.p.: 86–90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.41 (s, 2H), 7.97 (s, 1H), 7.77 (d, J = 8.3 Hz, 1H), 7.65 (d, J = 8.3 Hz, 1H), 7.37 (dd, J = 9.0, 6.4 Hz, 1H), 7.18 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.3, 157.8, 132.8 (q, J = 33.9 Hz), 130.8, 130.0, 126.3, 125.9, 123.1 (m), 122.8 (q, J = 273.0 Hz), 119.2, 115.9, 115.2 ppm; elemental analysis calcd (%) for $C_{15}H_7F_6NO$ (331.21): C 54.39, H 2.13; found: C 54.27, H 2.00.

3-(6-Methoxynaphthalen-2-yl)benzo[c]isoxazole (16)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 2-bromo-6-methoxynaphthalene (0.237 g, 1 mmol), **16** was obtained in 79% (0.217 g) yield as a yellow solid. M.p.: 156–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (s, 1H), 7.99 (d, J = 8.3 Hz, 1H), 7.86 (d, J = 8.3 Hz, 1H), 7.79 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 8.3 Hz, 1H), 7.29 (dd, J = 9.0, 6.4 Hz, 1H), 7.19 (d, J = 8.3 Hz, 1H), 7.10 (s, 1H), 7.03 (dd, J = 8.8, 6.4 Hz, 1H), 3.90 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.6, 158.9, 157.8, 135.2, 130.5, 130.1, 128.5, 127.7, 126.2, 124.2, 123.7, 123.4, 120.7, 119.8, 115.3, 114.1, 105.7, 55.3 ppm; elemental analysis calcd (%) for $C_{18}H_{13}NO_2$ (275.30): C 78.53, H 4.76; found: C 78.60, H 4.89.

2-(Benzo[c]isoxazol-3-yl)benzaldehyde (17)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 2-bromobenzaldehyde (0.185 g, 1 mmol), **17** was obtained in 78% (0.174 g) yield as a yellow solid. M.p.: 142–146 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.20 (s, 1H), 8.17 (d, J = 8.3 Hz, 1H), 7.85–7.75 (m, 2H), 7.75–7.63 (m, 2H), 7.53 (d, J = 8.2 Hz, 1H), 7.37 (dd, J = 9.0, 6.4 Hz, 1H), 7.11 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.6, 162.6, 157.5, 134.2, 134.0, 131.0, 130.7, 130.1, 129.8, 128.8, 125.7, 119.6, 117.2, 115.4 ppm; elemental analysis calcd (%) for $C_{14}H_9NO_2$ (223.23): C 75.33, H 4.06; found: C 75.45, H 4.33.

2-(Benzo[c]isoxazol-3-yl)benzonitrile (18)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 2-bromobenzonitrile (0.182 g, 1 mmol), **18** was obtained in 92% (0.202 g) yield as a yellow solid. M.p.: 140–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–7.85 (m, 2H), 7.78 (t, J = 7.8 Hz, 1H), 7.70 (d, J = 8.2 Hz, 1H), 7.68–7.58 (m, 2H), 7.35 (dd, J = 9.0, 6.4 Hz, 1H), 7.12 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0, 157.5, 134.5, 133.1, 130.9, 130.7, 130.3, 129.7, 125.5, 120.0, 117.4, 116.0, 115.5, 110.8 ppm; elemental analysis calcd (%) for $C_{14}H_8N_2O$ (220.23): C 76.35, H 3.66; found: C 76.17, H 3.87.

3-[2-(Trifluoromethyl)phenyl]benzo[c]isoxazole (19)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 2-(trifluoromethyl)-bromobenzene (0.225 g, 1 mmol), **19** was obtained in 91% (0.239 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, J = 8.3 Hz, 1H), 7.78–7.61 (m, 4H), 7.46 (d, J = 8.3 Hz, 1H), 7.33 (dd, J = 9.0, 6.4 Hz, 1H), 7.04 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 157.0, 131.9, 131.5, 130.8, 130.5, 129.4 (q, J = 31.7 Hz), 127.2 (q, J = 5.1 Hz), 125.8, 124.8, 123.1 (q, J = 273.4 Hz), 119.7, 116.7, 115.1 ppm; elemental analysis calcd (%) for $C_{14}H_8F_3NO$ (263.21): C 63.88, H 3.06; found: C 63.97, H 3.00.

3-(2-Fluorophenyl)benzo[c]isoxazole (20)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 2-bromofluorobenzene (0.175 g, 1 mmol), **20** was obtained in 70% (0.149 g) yield as a yellow solid. M.p.: 52–54 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (td, J = 7.6, 1.5 Hz, 1H), 7.78 (dd, J = 9.0, 3.0 Hz, 1H), 7.62 (d, J = 9.1 Hz, 1H), 7.54–7.45 (m, 1H), 7.39–7.25 (m, 3H), 7.05 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 158.7 (d, J = 253.2 Hz), 157.8, 132.0 (d, J = 8.4 Hz), 130.7, 129.6 (d, J = 2.7 Hz), 124.8 (d, J = 3.4 Hz), 124.4 (d, J = 2.4 Hz), 121.3 (d, J = 12.5 Hz), 116.6 (d, J = 21.7 Hz), 116.3, 115.8, 115.2 ppm; elemental analysis calcd (%) for $C_{13}H_8FNO$ (213.21): C 73.23, H 3.78; found: C 73.10, H 3.87.

3-(2-Chlorophenyl)benzo[c]isoxazole (21)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 2-bromochlorobenzene (0.191 g, 1 mmol), **21** was obtained in 62% (0.142 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.56 (m, 4H), 7.50–7.40 (m, 2H), 7.32 (dd, J = 9.0, 6.4 Hz, 1H), 7.03 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.9, 157.3, 132.7, 131.4, 131.3, 130.7, 130.6, 127.2, 127.0, 124.3, 121.0, 116.2, 115.2 ppm; elemental analysis calcd (%) for $C_{13}H_8ClNO$ (229.66): C 67.99, H 3.51; found: C 68.14, H 3.70.

3-(Naphthalen-1-yl)benzo[c]isoxazole (22)[14]

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 1-bromonaphthalene (0.207 g, 1 mmol), **22** was obtained in 73% (0.179 g) yield as a yellow solid. M.p.: 84–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27–8.20 (m, 1H), 8.03 (d, J = 8.3 Hz, 1H), 7.99–7.93 (m, 1H), 7.85 (d, J = 8.3 Hz, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.65–7.53 (m, 4H), 7.37 (dd, J = 9.0, 6.4 Hz, 1H), 7.03 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6, 157.4, 133.8, 131.0, 130.7, 130.5, 128.5, 128.3, 127.3, 126.5, 125.3, 125.2, 125.0, 124.2, 120.7, 116.4, 115.1 ppm.

3-(Pyridin-3-yl)benzo[c]isoxazole (23)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 3-bromopyridine (0.158 g, 1 mmol), **23** was obtained in 89% (0.174 g) yield as a brown solid. M.p.: 128–130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.28 (bs, 1H), 8.72 (bs, 1H), 8.29 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 8.7 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.53–7.47 (m, 1H), 7.34 (dd, J = 9.0, 6.4 Hz, 1H), 7.11 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.4, 157.7, 150.5, 146.9, 133.4, 130.8, 125.4, 125.0, 124.3, 119.8, 115.6, 114.9 ppm; elemental analysis calcd (%) for $C_{12}H_8N_2O$ (196.20): C 73.46, H 4.11; found: C 73.60, H 4.30.

3-(Quinolin-3-yl)benzo[c]isoxazole (24)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 3-bromoquinoline (0.208 g, 1 mmol), **24** was obtained in 78% (0.192 g) yield as a white solid. M.p.: 182–184 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.51 (s, 1H), 8.68 (s, 1H), 8.13 (d, J = 8.3 Hz, 1H), 7.92 (d, J = 8.3 Hz, 1H), 7.87 (d, J = 8.3 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.66–7.56 (m, 2H), 7.34 (dd, J = 9.0, 6.4 Hz, 1H), 7.12 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.7, 157.8, 148.1, 147.2, 133.3, 130.9, 130.8, 129.5, 128.5, 127.7, 127.4, 125.5, 121.7, 119.9, 115.7, 115.1 ppm; elemental analysis calcd (%) for $C_{16}H_{10}N_2O$ (246.26): C 78.03, H 4.09; found: C 78.20, H 4.33.

3-(Pyrimidin-5-yl)benzo[c]isoxazole (25)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 5-bromopyrimidine (0.159 g, 1 mmol), **25** was obtained in 80% (0.158 g) yield as a brown solid. M.p.: 144–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.37 (s, 2H), 9.31 (s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.39 (dd, J = 9.0, 6.4 Hz, 1H), 7.18 ppm (dd, J = 8.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.9, 158.3, 157.6, 153.7, 131.1, 126.4, 123.3, 119.1, 116.0, 115.8 ppm; elemental analysis calcd (%) for $C_{11}H_7N_3O$ (197.19): C 67.00, H 3.58; found: C 66.88, H 3.41.

(2-Aminophenyl)(anthracen-9-yl)methanone (26)

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 9-bromoanthracene (0.257 g, 1 mmol), **26** was obtained in 47% (0.139 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (s, 1H), 8.05 (d, J = 8.3 Hz, 2H), 7.78 (d, J = 8.3 Hz, 2H), 7.47 (t, J = 8.0 Hz, 2H), 7.41 (t, J = 8.0 Hz, 2H), 7.26 (t, J = 8.0 Hz, 1H), 6.93 (d, J = 8.3 Hz, 1H), 6.69 (d, J = 8.3 Hz, 1H), 6.65 (bs, 2H), 6.32 ppm (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.1, 150.9, 135.3, 135.1, 131.1, 128.5, 128.3, 127.7, 126.3, 125.5, 125.4, 119.6, 116.9, 116.0 ppm; elemental analysis calcd (%) for $C_{21}H_{15}NO$ (297.35): C 84.82, H 5.08; found: C 84.98, H 5.21.

1-Amino-9H-fluoren-9-one (27c)[16]

From 2,1-benzisoxazole (0.179 g, 1.5 mmol) and 1,2-dibromobenzene (0.236 g, 1 mmol), **27c** was obtained in 24% (0.047 g) yield as an orange solid. M.p.: 113–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, J = 8.3 Hz, 1H), 7.48 (d, J = 8.3 Hz, 1H), 7.43 (t, J = 8.0 Hz, 1H), 7.32–7.17 (m, 2H), 6.83 (d, J = 8.3 Hz, 1H), 6.49 (d, J = 8.3 Hz, 1H), 5.52 ppm (bs, 2H).

General procedure for the synthesis of compounds 28–33

Typically, the 3-arylbenzoisoxazole derivative (0.5 mmol), NEt_3 (0.5 mL), Pd/C (10%) (5 mg), and THF (3 mL) were introduced in an autoclave. The autoclave was flushed with hydrogen and pressurized with 10 bars of hydrogen. Then, the reaction mixture was stirred at 25 °C for 12 h. The solvent was evaporated, and the product was purified by silica gel column chromatography.

(2-Aminophenyl)(phenyl)methanone (28)[17]

From 3-phenylbenzo[c]isoxazole **11** (0.098 g, 0.5 mmol) **28** was obtained in 95% (0.093 g) yield as a white solid. M.p.: 109–112 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, J = 8.0 Hz, 2H), 7.50–7.35 (m, 4H), 7.23 (t, J = 7.8 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.53 (t, J = 7.8 Hz, 1H), 6.17 ppm (bs, 2H).

(2-Aminophenyl)(naphthalen-2-yl)methanone (29)[18]

From 3-(naphthalen-2-yl)benzo[c]isoxazole **1** (0.123 g, 0.5 mmol) **29** was obtained in 88% (0.108 g) yield as a yellow solid. M.p.: 102–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (s, 1H), 8.00–7.85 (m, 3H), 7.78 (d, J = 8.2 Hz, 1H), 7.65–7.50 (m, 3H), 7.32 (t, J = 7.8 Hz, 1H), 6.77 (d, J = 8.2 Hz, 1H), 6.63 (t, J = 7.8 Hz, 1H), 6.10 ppm (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.9, 150.7, 137.3, 134.6, 134.5, 134.2, 132.3, 130.0, 129.0, 128.0, 127.8, 127.7, 126.6, 125.7, 118.5, 117.0, 115.6 ppm.

(2-Aminophenyl)(naphthalen-1-yl)methanone (30)[19]

From 3-(naphthalen-1-yl)benzo[c]isoxazole **22** (0.123 g, 0.5 mmol) **30** was obtained in 95% (0.117 g) yield as a yellow solid. M.p.: 142–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.85 (m, 3H), 7.58–7.42 (m, 4H), 7.28 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 6.47 (t, J = 7.8 Hz, 1H), 6.46 ppm (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.6, 151.2, 138.4, 135.1, 134.9, 133.5, 130.5, 129.7, 128.2, 126.7, 126.2, 125.6, 125.5, 124.6, 118.8, 116.9, 115.6 ppm.

(2-Aminophenyl)(3,5-bis(trifluoromethyl)phenyl)methanone (31)

From 3-[3,5-bis(trifluoromethyl)phenyl]benzo[c]isoxazole **15** (0.166 g, 0.5 mmol) **31** was obtained in 55% (0.091 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (s, 2H), 8.03 (s, 1H), 7.37 (t, J = 7.8 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 6.6 (t, J = 7.8 Hz, 1H), 5.91 ppm (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.3, 151.6, 142.0, 135.3, 133.8, 131.7 (q, J = 33.8 Hz), 128.9 (m), 123.0 (q, J = 273.0 Hz), 124.2 (q, J = 3.8 Hz), 117.4, 116.5, 116.0 ppm; elemental analysis calcd (%) for $C_{15}H_9F_6NO$ (333.23): C 54.07, H 2.72; found: C 54.01, H 2.89.

(2-Aminophenyl)(2-(trifluoromethyl)phenyl)methanone (32)[20]

From 3-[2-(trifluoromethyl)phenyl]benzo[c]isoxazole **19** (0.132 g, 0.5 mmol) **32** was obtained in 93% (0.123 g) yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, J = 8.0 Hz, 1H), 7.64–7.52 (m, 2H), 7.36 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.8 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.51 (t, J = 7.8 Hz, 1H), 6.34 ppm (bs, 2H).

(2-Aminophenyl)(2-fluorophenyl)methanone (33)[8a]

From 3-(2-fluorophenyl)benzo[c]isoxazole **20** (0.107 g, 0.5 mmol) **33** was obtained in 92% (0.099 g) yield as a yellow solid. M.p.: 124–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.36 (m, 2H), 7.35–7.20 (m, 3H), 7.15 (t, J = 7.8 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 6.58 (t, J = 7.8 Hz, 1H), 6.30 ppm (bs, 2H).

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