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Visible-Light-Induced Decarboxylative C–H Adamantylation of Azoles at Ambient Temperature

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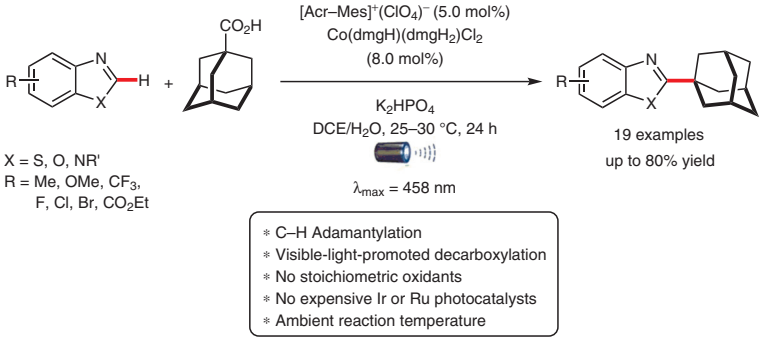

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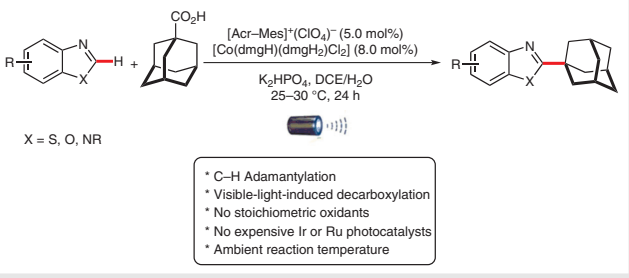
Abstract The visible-light-promoted oxidant-free decarboxylative C–H adamantylation of azoles was accomplished under ambient reaction conditions. The novel acridinium photocatalyst and cobalt synergistic catalysis enabled the C–H adamantylation under oxidant-free reaction conditions. This C–H adamantylation strategy proved viable for a wide range of substituted azoles, including benzothiazole, benzoxazole, and benzimidazoles as well as caffeine derivatives, providing an expedient access to 2-adamantyl-substituted azoles.

Key words photocatalysis, C–H functionalization, decarboxylation, cobalt, acridinium salts, oxidant-free, adamantylation, azoles

Adamantane, a strain-free molecule consisting of three fused cyclohexane rings, has attracted significant attention because of its unique structural features and properties.[1] For instance, the adamantyl moiety represents a key scaffold in several biologically active compounds[2] and clinical therapeutics.[3] The incorporation of the adamantyl group to polymers[4] and functional materials[5] significantly improves their physical properties, such as thermal stability and solubility.[6] Furthermore, the specific features of the adamantyl scaffold, including lipophilicity, steric demand, dispersion attraction, and conformational stability and rigidity expanded their presence and influence in several other important areas of research, such as supramolecular chemistry,[7] and molecular syntheses.[8] Despite the great importance of adamantyl-substituted organic compounds, the incorporation of adamantyl group into organic molecules largely relies on conventional nucleophilic substitution reactions with adamantyl halides.[8e,9] Recently, selected examples of C–H adamantylation were reported as the part of the scope of transition-metal-catalyzed C–H alkylation protocols.[10] However, no specific methods have as of yet been reported for the C–H adamantylation of heteroarenes, in detail delineating its scope and limitations. Within our program on transition-metal-catalyzed C–H alkylation[11] and photoredox catalysis,[12] we have now devised an exceedingly mild method for the C–H adamantylation of azoles by a photoinduced[13] decarboxylative[14] C–H alkylation strategy.[15] Notable features of our approach include (i) expedient C–H adamantylation on diversely decorated azoles, (ii) non-directing group-assisted C–H functionalization, (iii) easily accessible and inexpensive 1-adamantanecarboxylic acid as reagent, (iv) visible-light-promoted C–H functionalization, (v) no stoichiometric oxidants and iridium or ruthenium photocatalysts, (vi) key mechanistic insights, and (vii) ambient reaction temperature (Scheme 1).



Scheme 1 Visible-light-induced decarboxylative C–H adamantylation

We initiated our studies by examining suitable photocatalysts (PCs) (Figure 1), bases, and solvents under oxidant-free conditions, using an easily accessible cobaloxime complex[16] as cocatalyst for the envisioned decarboxylative C–H adamantylation of benzothiazole (**1a**) with adamantanecarboxylic acid (**2**) (Table 1). Thus, among a set of representative photocatalysts, 9-mesityl-10-methylacridinium perchlorate (**PC1**) provided optimal results in a mixture of

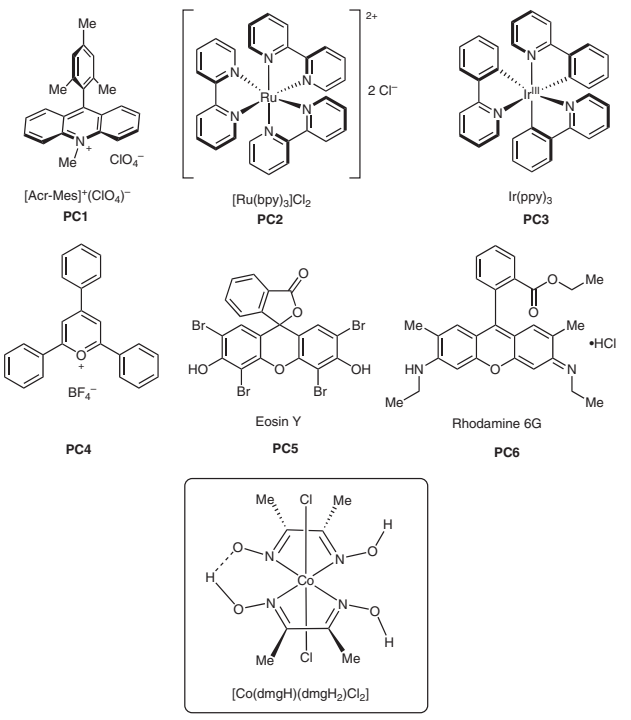
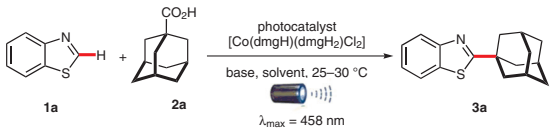


Figure 1 Photocatalysts (PCs) tested in this study

Table 1 Optimization Studies[a]



Entry	PC	Base (equiv)	Solvent	Yield (%)
1	**PC1**	**K_2HPO_4 (3)**	**DCE/H_2O (3:1)**	**83**
2	**PC2**	K_2HPO_4 (3)	DCE/H_2O (3:1)	trace
3	**PC3**	K_2HPO_4 (3)	DCE/H_2O (3:1)	11
4	**PC4**	K_2HPO_4 (3)	DCE/H_2O (3:1)	0
5	**PC5**	K_2HPO_4 (3)	DCE/H_2O (3:1)	0
6	**PC6**	K_2HPO_4 (3)	DCE/H_2O (3:1)	0
7	**PC1**	K_2HPO_4 (3)	CH_2Cl_2/H_2O (3:1)	74
8	**PC1**	K_2HPO_4 (3)	$CHCl_3$/H_2O (3:1)	9
9	**PC1**	K_2HPO_4 (3)	H_2O	7
10	**PC1**	K_2HPO_4 (3)	DCE	trace
11	**PC1**	Na_2HPO_4 (3)	DCE/H_2O (3:1)	77
12	**PC1**	$NaHCO_3$ (3)	DCE/H_2O (3:1)	66
13	**PC1**	K_2HPO_4 (2)	DCE/H_2O (3:1)	71
14	**PC1**	K_2CO_3	DCE/H_2O (3:1)	25
15	**PC1**	KOAc	DCE/H_2O (3:1)	24
16	**PC1**	K_3PO_4	DCE/H_2O (3:1)	21
17	**PC1**	–	DCE/H_2O (3:1)	trace
18	–	K_2HPO_4 (3)	DCE/H_2O (3:1)	0
19	**PC1**	K_2HPO_4 (3)	DCE/H_2O (3:1)	0[b]
20	**PC1**	K_2HPO_4 (3)	DCE/H_2O (3:1)	21[c]
21	**PC1**	K_2HPO_4 (3)	DCE/H_2O (3:1)	15[d]

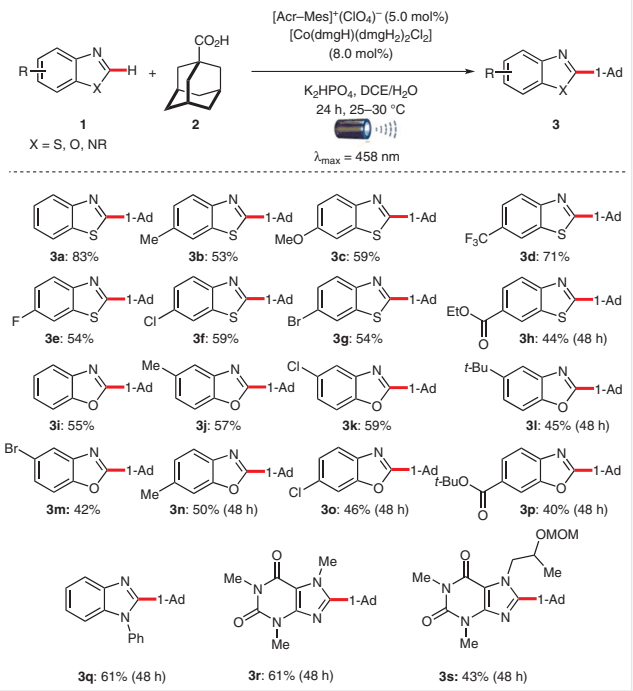
[a] Reaction conditions: benzothiazole (**1a**; 0.4 mmol), 1-adamantanecarboxylic acid (**2a**; 1.2 mmol), photocatalyst PC (5.0 mol%), [Co(dmgH)(dmgH$_2$)Cl$_2$] (8.0 mol%), solvent (2.0 mL), 24 h under blue light irradiation (λ_{max} = 458 nm), yield of isolated product.
[b] Reaction performed in the dark.
[c] 22 W CFL.
[d] 2 W green LED.

DCE/H_2O (3:1) as the reaction medium (Table 1, entry 1). While a variety of bases could be utilized, the photoinduced C–H adamantylation was most effective in the presence of K_2HPO_4. The key importance of the photocatalyst, base, and light irradiation in the decarboxylative C–H adamantylation manifold was verified by probing the transformation in the absence of each component under otherwise identical reaction conditions (entries 17–19). Notably, the use of blue light was found beneficial to realize satisfactory yields (entries 20 and 21).

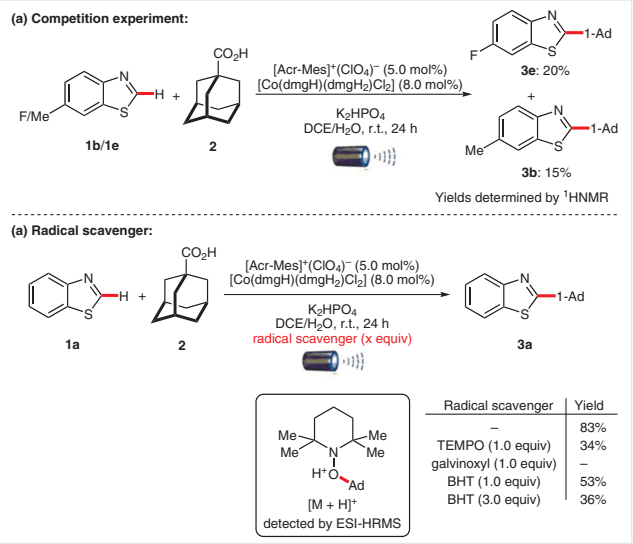
With the optimized reaction conditions in hand, we probed the scope of the reaction with a range of azoles **1** (Scheme 2). To our delight, the visible-light-enabled decarboxylative C–H adamantylation proved broadly applicable towards a range of azoles. Thus, differently substituted benzothiazoles **1a–h** and benzoxazoles **1i–p** were efficiently transformed into the desired adamantyl-substituted products **3a–p** in satisfactory yields. Notably, the challenging benzimidazole **1q** and caffeine derivatives **1r**,**s** were successfully functionalized under identical reaction conditions.

In consideration of the unique reactivity of the photoinduced decarboxylative C–H functionalization, we were attracted to delineate its mode of action. To probe the catalyst's working mode, we performed an intermolecular competition experiment, which revealed electron-deficient benzothiazole **1e** to be preferentially converted (Scheme 3a). Further, we investigated a SET-type regime by the use of typical radical scavengers TEMPO, galvinoxyl, and BHT (Scheme 3b), which significantly suppressed the catalytic efficacy.

To further elucidate the reaction mechanism of the photoinduced C–H adamantylation, we performed a series of additional experiments (Figure 2). First, we monitored the conversion profile of the photocatalytic reaction of **1a** and **2** to give **3a**, which revealed the reaction being completely suppressed in the absence of light (Figure 2a). These findings provided strong evidence for the beneficial influence of visible-light irradiation. Second, fluorescence-quenching experiments (Figure 2b–d) revealed no quenching of the free acid **2**, while both benzothiazole and the carboxylate salt quenched the excited state of acridinium photocatalyst



Scheme 2 Visible-light-induced decarboxylative C–H adamantylation of azoles **1**



Scheme 3 Key mechanistic findings

PC1. Based on these observations, we propose the single-electron transfer to occur from **PC1*** to adamantane carboxylate as the key step.

In light of these mechanistic findings, a plausible catalytic cycle for the photoinduced decarboxylative C–H adamantylation protocol is elaborated in Scheme 4. The acridinium photocatalyst [Arc-Mes+] is initially excited to [Acr-Mes+]* by blue light absorption, which oxidizes the adamantane carboxylate anion to the oxygen-centered carboxyl radical. Then, decarboxylation forms the adamantyl radical. Subsequently, the [Acr-Mes•] radical is re-oxidized to [Arc-Mes+] by the cobalt(III) species to complete the photo-

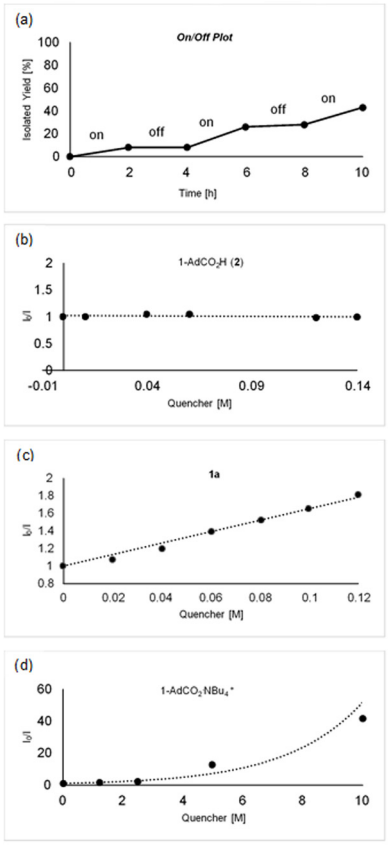
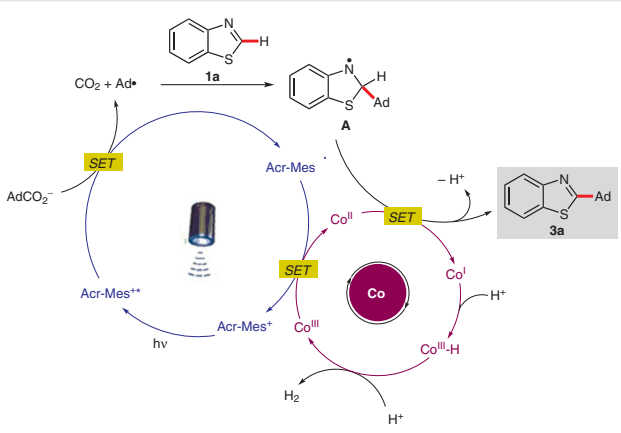


Figure 2 (a) The on/off light experiments. (b) Fluorescence quenching experiments of **PC1*** with **2**. (c) Fluorescence quenching experiments of **PC1*** with **1a**. (d) Fluorescence quenching experiments of **PC1*** with adamantane carboxylate.



Scheme 4 Proposed mechanism for the decarboxylative C–H adamantylation

catalytic cycle. In the meantime, the attack of the adamantyl radical at the electrophilic C2 position of benzothiazole (**1a**) generates radical intermediate **A**. Upon deprotonation, reduction of the cobalt(II) species to cobalt(I) through SET from species **A** then delivers the adamantylated product **3a**. Concurrently, the cobalt(III)-hydride species could be formed from the cobalt(I) species by capturing a proton generated in the reaction. Release of H_2 through a reaction with another proton will regenerate the cobalt(III) species.[16c–f]

In summary, we have reported on the unprecedented visible-light-enabled decarboxylative C–H adamantylation of azoles at ambient reaction temperature. The oxidant-free decarboxylative adamantylation was efficiently achieved by the aid of catalytic amounts of easily available cobalt oxime complex. A range of substituted azoles, including benzothiazole, benzoxazole, and benzimidazoles as well as caffeine derivatives, were well tolerated, providing a new general strategy to access adamantyl-substituted heterocycles motifs.

Catalytic reactions were carried out in pre-dried 10 mL vials under N_2 atmosphere. In cases wherein air- or moisture-sensitive reagents were used, reactions were performed under N_2 atmosphere using standard Schlenk techniques. The following substrates were prepared according to previously described procedures: Benzothiazoles **1b–h**,[17] benzoxales **1l–p**,[18] benzimidazole **1q**,[19] [Co(dmgH)(dmgH$_2$)Cl$_2$],[20] and tetrabutylammonium adamantane carboxylate.[21] Other chemicals were obtained from commercial sources and were used without further purification, unless otherwise noted. Yields refer to isolated compounds, estimated to be >95% pure as determined by ^{1}H NMR spectroscopy. TLC: Merck TLC silica gel 60 F_{254}, TLC plates; detection under UV light at 254 nm. Chromatography: Separations were carried out on Merck Geduran® Silica 60 (0.040–0.063 mm, 70–230 mesh ASTM) using distilled solvents. Melting points: Stuart melting point apparatus SMP3, Barloworld Scientific, the reported values are not corrected. NMR: Spectra were recorded on Varian VX 300, Varian VNMRS 300, Bruker Avance 300, Bruker Avance 400 and 500 or Varian Inova 500 and 600 spectrometers in the solvent indicated; chemical shifts (δ) are given in ppm and referenced to the residual solvent peak. All IR spectra were recorded on a Bruker ATR FT-IR Alpha device. MS: ESI-MS-spectra as well as high-resolution mass spectrometry (HRMS) were recorded with a micrOTOF (ESI-TOF-MS), Bruker Daltonik; EI-spectra were recorded with an AccuTOF (EI-TOF) instrument from Jeol. Fluorescence emission data in solution were recorded on a Jasco® FP-8500 spectrofluorometer. The widths of excitation and emission slits were held constant at 2.5 and 5.0 nm, respectively. The scan speed was adjusted to 500 nm/min.

Visible-Light-Promoted Decarboxylative C–H Adamantylation; General Procedure

To an oven-dried 10 mL vial were added the heteroarene **1** (0.40 mmol, 1.0 equiv), 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol, 3.0 equiv), K_2HPO_4 (209 mg, 1.20 mmol, 3.0 equiv), 9-mesityl-10-methylacridinium perchlorate (8.2 mg, 5.0 mol%), and [Co(dmgH)(dmgH$_2$)Cl$_2$] (11.6 mg, 8.0 mol%). After the vial was capped with a septum, it was evacuated and refilled with N_2 for three times before DCE (1.5 mL) and H_2O (0.5 mL) were added sequentially. If the heterocyclic substrate **1** was a liquid, it was added at this point. The mixture was degassed and stirred for 24 h under visible light irradiation (Kessil A360N, see Figure S-1 in the Supporting Information). After 24 h, the mixture was diluted with CH_2Cl_2 (10 mL) and H_2O (10 mL), and the phases were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), the combined organic phases were dried (Na_2SO_4), and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (*n*-pentane or *n*-hexane/Et_2O 20:1 to 2:1) affording the corresponding product **3**.

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]benzo[*d*]thiazole (3a)

The general procedure was followed using benzothiazole (**1a**; 54.1 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 30:1) afforded **3a**; yield: 89.3 mg (331 µmol, 83%); white solid; mp 103–104 °C.

IR (ATR): 2898, 2845, 1506, 1434, 1168, 999, 963, 754, 725, 680 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (ddd, *J* = 8.2, 1.2, 0.7 Hz, 1 H), 7.86 (ddd, *J* = 7.2, 1.2, 0.7 Hz, 1 H), 7.44 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1 H), 7.32 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1 H), 2.18–2.12 (m, 9 H), 1.86–1.81 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.3 (C_q), 153.3 (C_q), 134.5 (C_q), 125.8 (CH), 124.5 (CH), 122.8 (CH), 121.7 (CH), 43.1 (CH_2), 40.3 (C_q), 36.7 (CH_2), 28.7 (CH).

MS (ESI): *m*/*z* (%) = 270 ([M + H]$^+$, 100).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{20}NS^+$ [M + H]$^+$: 270.1311; found: 270.1313.

The analytical data are in accordance with those reported in the literature.[10c]

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-6-methylbenzo[*d*]thiazole (3b)

The general procedure was followed using benzothiazole **1b** (59.7 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 30:1) afforded **3b**; yield: 60.6 mg (214 µmol, 53%); white solid; mp 132–133 °C.

IR (ATR): 2899, 2845, 1510, 1449, 1164, 1000, 835, 812, 679, 569 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.3 Hz, 1 H), 7.65–7.62 (m, 1 H), 7.24 (ddd, *J* = 8.2, 1.7, 0.6 Hz, 1 H), 2.46 (s, 3 H), 2.16–2.11 (m, 9 H), 1.83–1.80 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 181.2 (C_q), 151.4 (C_q), 134.6 (C_q), 134.5 (C_q), 127.3 (CH), 122.2 (CH), 121.4 (CH), 43.1 (CH_2), 40.2 (C_q), 36.7 (CH_2), 28.7 (CH), 21.6 (CH_3).

MS (ESI): *m*/*z* (%) = 284 ([M + H]$^+$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{22}NS^+$ [M + H]$^+$: 284.1467; found: 284.1471.

The analytical data are in accordance with those reported in the literature.[22]

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-6-methoxylbenzo[*d*]thiazole (3c)

The general procedure was followed using benzothiazole **1c** (66.1 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 25:1) afforded **3c**; yield: 70.2 mg (234 µmol, 59%); white solid; mp 118–119 °C.

IR (neat): 2904, 1467, 1450, 1435, 1261, 1223, 1028, 1000, 834, 827 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 8.9, 0.4 Hz, 1 H), 7.31 (d, *J* = 2.5 Hz, 1 H), 7.03 (dd, *J* = 8.9, 2.5 Hz, 1 H), 3.85 (s, 3 H), 2.15–2.11 (m, 9 H), 1.82–1.79 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.8 (C_q), 157.3 (C_q), 147.8 (C_q), 135.7 (C_q), 123.2 (CH), 114.9 (CH), 104.4 (CH), 55.9 (CH_3), 43.1 (CH_2), 40.1 (C_q), 36.7 (CH_2), 28.7 (CH).

MS (ESI): *m*/*z* (%) = 300 ([M + H]$^+$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{22}NOS^+$ [M + H]$^+$: 300.1417; found: 300.1419.

The analytical data are in accordance with those reported in the literature.[22]

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-6-(trifluoromethyl)benzo[*d*]thiazole (3d)

The general procedure was followed using benzothiazole **1d** (81.3 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 30:1) afforded **3d**; yield: 96.3 mg (285 µmol, 71%); white solid; mp 183–184 °C.

IR (ATR): 2911, 1317, 1278, 1163, 1112, 1085, 1001, 880, 829, 681 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (dq, *J* = 1.8, 0.7 Hz, 1 H), 8.07 (dt, *J* = 8.6, 0.7 Hz, 1 H), 7.68 (ddd, *J* = 8.6, 1.8, 0.7 Hz, 1 H), 2.19–2.14 (m, 9 H), 1.87–1.80 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 185.7 (C_q), 155.4 (C_q), 134.7 (C_q), 126.8 (q, $^2J_{C,F}$ = 32.7 Hz, C_q), 124.4 (q, $^1J_{C,F}$ = 272.0 Hz, C_q) 123.1 (CH), 122.8 (q, $^3J_{C,F}$ = 3.5 Hz, CH), 119.2 (q, $^3J_{C,F}$ = 4.2 Hz, CH) 43.1 (CH_2), 40.7 (C_q), 36.6 (CH_2), 28.7 (CH).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –61.3 (s).

MS (ESI): *m*/*z* (%) = 338 ([M + H]$^+$, 13), 300 (100).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{19}F_3NS^+$ [M + H]$^+$: 338.1185; found: 338.1188.

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-6-fluorobenzo[*d*]thiazole (3e)

The general procedure was followed using benzothiazole **1e** (61.3 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 30:1) afforded **3e**; yield: 62.1 mg (216 µmol, 54%); white solid; mp 107–108 °C.

IR (ATR): 2911, 2889, 1454, 1245, 1161, 1001, 915, 836, 800, 791 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (ddd, *J* = 8.9, 4.8, 0.4 Hz, 1 H), 7.52 (ddd, *J* = 8.2, 2.6, 0.4 Hz, 1 H), 7.16 (ddd, *J* = 8.9, 8.2, 2.6 Hz, 1 H), 2.16–2.12 (m, 9 H), 1.83–1.79 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.0 (d, $^5J_{C,F}$ = 3.1 Hz, C_q), 160.2 (d, $^1J_{C,F}$ = 244.2 Hz, Cq), 149.9 (d, $^4J_{C,F}$ = 1.6 Hz, C_q), 135.5 (d, $^3J_{C,F}$ = 11.2 Hz, C_q), 123.6 (d, $^3J_{C,F}$ = 9.4 Hz, CH), 114.3 (d, $^2J_{C,F}$ = 24.6 Hz, CH), 107.8 (d, $^3J_{C,F}$ = 26.4 Hz, CH), 43.1 (CH_2), 40.4 (C_q), 36.6 (CH_2), 28.7 (CH).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –117.4 (s).

MS (ESI): *m*/*z* (%) = 288 ([M + H]$^+$, 100).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{19}NSF^+$ [M + H]$^+$: 288.1217; found: 288.1219.

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-6-chlorobenzo[*d*]thiazole (3f)

The general procedure was followed using benzothiazole **1f** (67.9 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 30:1) afforded **3f**; yield: 71.8 mg (236 µmol, 59%); white solid; mp 145–146 °C.

IR (ATR): 2898, 2844, 1514, 1435, 1259, 1097, 999, 802, 768, 680 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 8.7, 0.4 Hz, 1 H), 7.81 (dd, *J* = 2.1, 0.4 Hz, 1 H), 7.38 (dd, *J* = 8.7, 2.1 Hz, 1 H), 2.16–2.11 (m, 9 H), 1.84–1.79 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.8 (C_q), 151.9 (C_q), 135.8 (C_q), 130.4 (C_q), 126.6 (CH), 123.5 (CH), 121.3 (CH), 43.1 (CH_2), 40.4 (C_q), 36.6 (CH_2), 28.7 (CH).

MS (ESI): *m*/*z* (%) = 304 ([M + H]$^+$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{19}ClNS^+$ [M + H]$^+$: 304.0921; found: 304.0924.

The analytical data are in accordance with those reported in the literature.[22]

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-6-bromobenzo[*d*]thiazole (3g)

The general procedure was followed using benzothiazole **1g** (85.6 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 30:1) afforded **3g**; yield: 75.1 mg (216 µmol, 54%); white solid; mp 182–183 °C.

IR (ATR): 2907, 2847, 1438, 1269, 1086, 1000, 860, 814, 804, 682 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (dd, *J* = 2.0, 0.4 Hz, 1 H), 7.82 (dd, *J* = 8.7, 0.4 Hz, 1 H), 7.52 (dd, *J* = 8.7, 2.0 Hz, 1 H), 2.16–2.11 (m, 9 H), 1.83–1.78 (m, 6 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 182.9 (C_q), 152.2 (C_q), 136.3 (C_q), 129.2 (CH), 124.2 (CH), 123.9 (CH), 118.0 (C_q), 43.0 (CH_2), 40.4 (C_q), 36.6 (CH_2), 28.6 (CH).

MS (ESI): *m*/*z* (%) = 348 ([M + H]$^+$, 100; ^{79}Br).

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{19}{}^{79}BrNS^+$ [M + H]$^+$: 348.0416; found: 348.0420.

Ethyl 2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]benzo[*d*]thiazole-6-carboxylate (3h)

The general procedure was followed using benzothiazole **1h** (82.9 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 48 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 15:1) afforded **3h**; yield: 60.0 mg (176 µmol, 44%); white solid; mp 131–133 °C.

IR (ATR): 2899, 1707, 1272, 1231, 1106, 1001, 850, 772, 730, 681 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (dd, *J* = 1.7, 0.6 Hz, 1 H), 8.12 (dd, *J* = 8.6, 1.7 Hz, 1 H), 8.00 (dd, *J* = 8.6, 0.6 Hz, 1 H), 4.41 (q, *J* = 7.1 Hz, 2 H), 2.16–2.12 (m, 9 H), 1.84–1.80 (m, 6 H), 1.41 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.0 (C_q), 166.4 (C_q), 156.3 (C_q), 134.4 (C_q), 127.1 (CH), 126.7 (C_q), 123.9 (CH), 122.4 (CH), 61.3 (CH_2), 43.0 (CH_2), 40.7 (C_q), 36.6 (CH_2), 28.6 (CH), 14.5 (CH_3).

MS (ESI): *m*/*z* (%) = 342 [M + H]$^+$ (100).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{24}NO_2S^+$ [M + H]$^+$: 342.1522; found: 342.1524.

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]benzo[*d*]oxazole (3i)

The general procedure was followed using benzoxazole **1i** (48.0 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-hexane/EtOAc 10:1) afforded **3i**; yield: 56.0 mg (221 µmol, 55%); white solid; mp 99–100 °C.

IR (ATR): 2907, 2852, 1560, 1455, 1264, 1240, 1044, 736, 704 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70–7.56 (m, 1 H), 7.46–7.35 (m, 1 H), 7.28–7.13 (m, 2 H), 2.15–1.97 (m, 9 H), 1.74 (t, *J* = 3.0 Hz, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9 (C_q), 150.5 (C_q), 141.2 (C_q), 124.2 (CH), 123.9 (CH), 119.7 (CH), 110.3 (CH), 40.2 (CH_2), 36.5 (CH_2), 36.0 (C_q), 27.9 (CH).

MS (ESI): *m*/*z* (%) = 254 ([M + H]$^+$, 100), 276 ([M + Na]$^+$, 15).

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{20}NO^+$ [M + H]$^+$: 254.1539; found: 254.1540.

The analytical data are in accordance with those reported in the literature.[10b]

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-5-methylbenzo[*d*]oxazole (3j)

The general procedure was followed using 5-methylbenzoxazole **1j** (53.3 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-hexane/EtOAc 10:1) afforded **3j**; yield: 61.0 mg (228 µmol, 57%); white solid; mp 94–96 °C.

IR (ATR): 2902, 2849, 1561, 1452, 1261, 1181, 1044, 923, 796 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.48–7.42 (m, 1 H), 7.32 (d, *J* = 8.2 Hz, 1 H), 7.06 (dd, *J* = 8.2, 1.7 Hz, 1 H), 2.43 (s, 3 H), 2.15–2.09 (m, 9 H), 1.79 (t, *J* = 3.2 Hz, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.9 (C_q), 148.6 (C_q), 141.4 (C_q), 133.5 (C_q), 125.2 (CH), 119.6 (CH), 109.6 (CH), 40.3 (CH_2), 36.6 (CH_2), 36.1 (C_q), 28.1 (CH), 21.5 (CH_3).

MS (EI) *m*/*z* (%) = 267 ([M]$^+$, 100), 135 (60).

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{22}NO^+$ [M + H]$^+$: 268.1696; found: 268.1702.

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-5-chlorobenzo[*d*]oxazole (3k)

The general procedure was followed using 5-chlorobenzoxazole **1k** (61.4 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-hexane/EtOAc 10:1) afforded **3k**; yield: 68.0 mg (236 µmol, 59%); white solid; mp 115–116 °C.

IR (ATR): 2906, 2851, 1557, 1451, 1264, 1044, 801, 739, 704 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 2.1 Hz, 1 H), 7.37 (d, *J* = 8.6 Hz, 1 H), 7.23 (dd, *J* = 8.6, 2.1 Hz, 1 H), 2.19–2.08 (m, 9 H), 1.83–1.76 (m, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 174.3 (C_q), 149.0 (C_q), 142.3 (C_q), 129.3 (C_q), 124.5 (CH), 119.7 (CH), 110.9 (CH), 40.2 (CH_2), 36.5 (CH_2), 36.3 (C_q), 28.0 (CH).

MS (EI): *m*/*z* (%) = 287 ([M]$^+$, 100), 135 (90).

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{19}ClNO^+$ [M + H]$^+$: 288.1150; found: 288.1155.

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-5-(*tert*-butyl)benzo[*d*]oxazole (3l)

The general procedure was followed using benzoxazole **1l** (66.1 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 48 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 20:1) afforded **3l**; yield: 56.0 mg (182 µmol, 45%); white solid; mp 159–160 °C.

IR (ATR): 2906, 2849, 1561, 1480, 1452, 1272, 1041, 924, 800 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.74 (dd, *J* = 2.0, 0.6 Hz, 1 H), 7.39 (dd, *J* = 8.6, 0.6 Hz, 1 H), 7.34 (dd, *J* = 8.6, 2.0 Hz, 1 H), 2.15–2.13 (m, 6 H), 2.12–2.10 (m, 3 H), 1.81 (t, *J* = 2.9 Hz, 6 H), 1.36 (s, 9 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.2 (C_q), 148.5 (C_q), 147.5 (C_q), 141.2 (C_q), 121.9 (CH), 116.4 (CH), 109.5 (CH), 40.5 (CH_2), 36.7 (CH_2), 36.3 (C_q), 35.0 (C_q), 32.0 (CH_3), 28.2 (CH).

MS (ESI): *m*/*z* (%) = 332 ([M + Na]$^+$, 2), 310 ([M + H]$^+$, 100).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{28}NO$ [M + H]$^+$: 310.2165; found: 310.2168.

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-5-bromobenzo[*d*]oxazole (3m)

The general procedure was followed using benzoxazole **1m** (79.2 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol). After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 20:1) afforded **3m**; yield: 56.1 mg (169 µmol, 42%); white solid; mp 135–136 °C.

IR (ATR): 2905, 2849, 1555, 1444, 1253, 1040, 907, 871, 798, 682 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 1.9 Hz, 1 H), 7.38 (dd, *J* = 8.4, 1.9 Hz, 1 H), 7.34 (d, *J* = 8.4 Hz, 1 H), 2.14–2.11 (m, 9 H), 1.84–1.77 (m, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 174.2 (C_q), 150.0 (C_q), 143.0 (C_q), 127.3 (CH), 122.8 (CH), 116.7 (C_q), 111.6 (CH), 40.3 (CH_2), 36.6 (CH_2), 36.4 (C_q), 28.1 (CH).

MS (ESI): *m*/*z* (%) = 334 ([M + H]$^+$, 97; ^{81}Br), 332 ([M + H]$^+$, 100; ^{79}Br).

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{19}{}^{79}BrNO^+$ [M + H]$^+$: 332.0645; found: 332.0648.

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-6-methylbenzo[*d*]oxazole (3n)

The general procedure was followed using benzoxazole **1n** (53.3 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 48 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 20:1) afforded **3n**; yield: 53.0 mg (198 µmol, 50%); white solid; mp 112–114 °C.

IR (ATR): 2908, 2849, 1566, 1451, 1263, 1234, 1040, 919, 809, 602 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.1 Hz, 1 H), 7.29–7.27 (m, 1 H), 7.11–7.08 (m, 1 H), 2.46 (s, 3 H), 2.16–2.10 (m, 9 H), 1.83–1.79 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.6 (C_q), 150.9 (C_q), 139.1 (C_q), 134.7 (C_q), 125.2 (CH), 119.1 (CH), 110.7 (CH), 40.4 (CH_2), 36.6 (CH_2), 36.2 (C_q), 28.1 (CH), 21.8 (CH_3).

MS (ESI): *m*/*z* (%) = 290 ([M + Na]$^+$, 9), 268 ([M + H]$^+$, 100).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{22}NO$ [M + H]$^+$: 268.1696; found: 268.1697.

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-6-chlorobenzo[*d*]oxazole (3o)

The general procedure was followed using benzoxazole **1o** (50.2.1 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 48 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 10:1) afforded **3o**; yield: 52.5 mg (182 µmol, 46%); white solid; mp 150–152 °C.

IR (ATR): 2915, 2851, 1609, 1564, 1460, 1039, 819, 800, 702, 599 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (dd, *J* = 8.5, 0.4 Hz, 1 H), 7.50–7.46 (m, 1 H), 7.26 (dd, *J* = 8.5, 2.0 Hz, 1 H), 2.16–2.10 (m, 9 H), 1.84–1.78 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.8 (C_q), 150.9 (C_q), 140.2 (C_q), 130.0 (C_q), 124.7 (CH), 120.3 (CH), 111.2 (CH), 40.3 (CH_2), 36.6 (CH_2), 36.3 (C_q), 28.0 (CH).

MS (ESI): *m*/*z* (%) = 288 ([M + H]$^+$, 60).

HR MS (EI): *m*/*z* calcd for $C_{17}H_{19}ClNO$ [M + H]$^+$: 288.1150; found: 288.1153.

tert-Butyl 2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]benzo[*d*]oxazole-6-carboxylate (3p)

The general procedure was followed using benzoxazole **1p** (87.7 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 48 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 10:1) afforded **3p**; yield: 52.8 mg (161 µmol, 40%); white solid; mp 116–118 °C.

IR (ATR): 2904, 1710, 1291, 1268, 1244, 1154, 1044, 943, 777 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (dd, *J* = 1.5, 0.6 Hz, 1 H), 7.98 (dd, *J* = 8.3, 1.5 Hz, 1 H), 7.67 (dd, *J* = 8.3, 0.6 Hz, 1 H), 2.17–2.10 (m, 9 H), 1.83–1.79 (m, 6 H), 1.60 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 175.6 (C_q), 165.5 (C_q), 150.3 (C_q), 145.0 (C_q), 128.6 (C_q), 125.8 (CH), 119.1 (CH), 112.0 (CH), 81.3 (C_q), 40.2 (CH_2), 36.5 (CH_2), 36.5 (C_q), 28.4 (CH_3), 28.0 (CH).

MS (ESI): *m*/*z* (%) = 354 ([M + H]$^+$, 100), 298 (14).

HR-MS (EI): *m*/*z* calcd for $C_{22}H_{28}NO_3$ [M + H]$^+$: 354.2064; found: 354.2064.

2-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-1-phenyl-1*H*-benzo[*d*]imidazole (3q)

The general procedure was followed using 1-phenylbenzimidazole **1q** (78.0 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) for 48 h. After aqueous workup, purification by column chromatography on silica gel (*n*-hexane/EtOAc 10:2) afforded **3q**; yield: 80.0 mg (244 µmol, 61%); white solid; mp 185–187 °C.

IR (ATR): 2904, 2850, 1498, 1454, 1375, 1264, 737, 700 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.78 (dt, *J* = 8.0, 0.9 Hz, 1 H), 7.55–7.51 (m, 3 H), 7.37–7.33 (m, 2 H), 7.21 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1 H), 7.10 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1 H), 6.71 (dt, *J* = 8.0, 0.9 Hz, 1 H), 2.05 (d, *J* = 2.9 Hz, 6 H), 2.00–1.89 (m, 3 H), 1.69–1.54 (m, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 161.1 (C_q), 141.2 (C_q), 140.0 (C_q), 138.2 (C_q), 129.3 (CH), 129.3 (CH), 129.2 (CH), 122.3 (CH), 121.9 (CH), 119.0 (CH), 109.9 (CH), 41.4 (CH_2), 37.7 (C_q), 36.5 (CH_2), 28.4 (CH).

MS (EI) *m*/*z* (%) = 328 ([M]$^+$, 70), 327 (100), 271 (30).

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{25}N_2^+$ [M + H]$^+$: 329.2012; found: 329.2018.

8-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-1,3,7-trimethyl-3,7-dihydro-1*H*-purine-2,6-dione (3r)

The general procedure was followed using caffeine (**1r**; 77.6 mg, 0.40 mmol) and 1-adamantanecarboxylic acid (**2**; 180 mg, 1.20 mmol) for 48 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 1:1) afforded **3r**; yield: 80.4 mg (245 µmol, 61%); white solid; mp 263–264 °C.

IR (ATR): 2895, 1700, 1660, 1539, 1426, 1361, 1223, 982, 743 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.15 (s, 3 H), 3.54 (s, 3 H), 3.37 (s, 3 H), 2.16–2.08 (m, 9 H), 1.81–1.74 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.6 (C_q), 155.8 (C_q), 151.9 (C_q), 147.2 (C_q), 108.2 (C_q), 40.0 (CH_2), 36.9 (C_q), 36.6 (CH_2), 34.5 (CH_3), 29.7 (CH_3), 28.3 (CH), 28.0 (CH_3).

MS (ESI): *m*/*z* (%) = 329 ([M + H]$^+$, 100).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{25}N_4O_2^+$ [M + H]$^+$: 329.1972; found: 329.1969.

The analytical data are in accordance with those reported in the literature.[23]

8-[(3*R*,5*R*,7*R*)-Adamantan-1-yl]-7-[2-(methoxymethoxy)propyl]-1,3-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (3s)

The general procedure was followed using substrate **1s** (85.0 mg, 0.30 mmol) and 1-adamantanecarboxylic acid (**2**; 162 mg, 0.90 mmol) for 48 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 10:1) afforded **3s**; yield: 53.5 mg (129 µmol, 43%); white solid; mp 147–148 °C.

IR (ATR): 2890, 1165, 1536, 1426, 1382, 1137, 1105, 1035, 743 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.55–4.46 (m, 2 H), 4.41 (dd, *J* = 14.0, 3.6 Hz, 1 H), 4.28–4.22 (m, 2 H), 3.56 (s, 3 H), 3.38 (s, 3 H), 3.01 (s, 3 H), 2.25–2.06 (m, 9 H), 1.80–1.75 (m, 6 H), 1.27 (d, *J* = 6.3 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.8 (C_q), 155.4 (C_q), 151.9 (C_q), 147.8 (C_q), 107.6 (C_q), 95.3 (CH_2), 73.1 (CH), 55.2 (CH_3), 52.4 (CH_2), 41.4 (CH_2), 37.6 (C_q), 36.6 (CH_2), 29.7 (CH_3), 28.5 (CH), 28.1 (CH_3), 18.4 (CH_3).

MS (ESI): *m*/*z* (%) = 439 ([M + Na]$^+$, 100), 417 ([M + H]$^+$, 99).

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{32}N_4O_4Na^+$ [M + Na]$^+$: 439.2316; found: 439.2319.

Competition Experiment

The general procedure was followed using benzothiazoles **1e** (61.3 mg, 0.40 mmol) and **1b** (59.7 mg, 0.40 mmol) as well as 1-adamantanecarboxylic acid (**2**; 72.0 mg, 0.40 mmol). After aqueous workup and removal of the remaining solvent, the crude mixture was analyzed by ^{1}H/^{19}F NMR spectroscopy using 4-fluoroanisole as internal standard (14.5 mg, 0.115 mmol).

Reaction in the Presence of Radical Scavengers

The general procedure was followed using benzothiazole (**1a**; 54.1 mg, 0.40 mmol), 1-adamantanecarboxylic acid (**2**; 216 mg, 1.20 mmol) and radical scavengers (1–3 equiv) for 24 h. After aqueous workup, purification by column chromatography on silica gel (*n*-pentane/Et_2O 10:1) yielded **3a**.

On/Off Plot

According to the general procedure, five independent reactions were set up and placed in front of the blue LEDs. The reaction mixtures were sequentially stirred under visible light irradiation and in the absence of light. Every 2 h a reaction vial was removed from the setup and workup was performed according to the general procedure. After a total of 10 h, the obtained isolated yields were plotted with respect to the reaction time.

Fluorescence Quenching Experiments

Sample solutions were prepared in DCE with [Acr-Mes]$^+$(ClO_4)$^-$ concentration of $c = 1.6 \times 10^{-7}$ M and varying concentrations of the respective quencher (added to each sample from a stock solution). The sample solutions were degassed prior to measurement by sparging with N_2. Stern–Volmer experiments were conducted with a fixed excitation wavelength of 430 nm and detection at 518 nm (emission maximum). Plotting of the I_0/I value against the concentration of the potential quencher resulted in the graphs (Figures 2b–d).

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1611633.

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