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# Light Induced C−C Coupling of 2-Chlorobenzazoles with Carbamates, Alcohols, and Ethers

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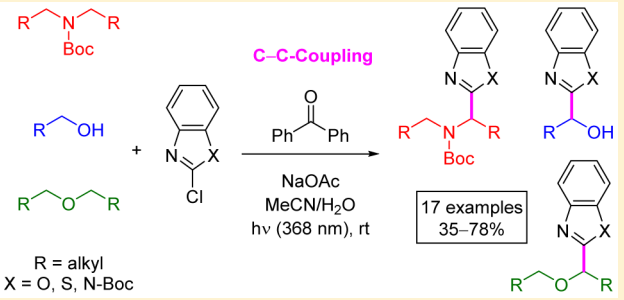
Supporting Information

**ABSTRACT:** A light induced, transition-metal-free C−C coupling reaction of 2-chlorobenzazoles with aliphatic carbamates, alcohols, and ethers is presented. Inexpensive reagents, namely sodium acetate, benzophenone, water, and acetonitrile, are employed in a simple reaction protocol using a cheap and widely available 25 W energy saving UV-A lamp at ambient temperature.




Benzimidazoles,[1−4] benzothiazoles,[5−8] and benzoxazoles[9−11] represent prominent structural motifs in a wide range of biologically active molecules and are attractive target structures in medicinal chemistry. The benzoxazole moiety occurs in various compounds with antimicrobial,[12] antitumor,[13] herbicidal,[14] antiretroviral,[15] or protein inhibitory[16] properties and is found in numerous ligands for biochemical receptors.[17,18] Furthermore, it was shown to be a valuable activating and directing group for the C($sp^3$)−H $\alpha$-alkylation of amines.[19] Therefore, methodologies for the synthesis of substituted benzazoles are attractive for various areas of chemical research.

For the functionalization of (benz)azoles, a variety of transition-metal-catalyzed C−C and C−N coupling reactions have been developed including for example the copper, nickel, or palladium catalyzed arylation,[20] benzylation,[20,21] allylation,[21] alkylation,[22] alkenylation,[20,23] alkynylation,[24] amination,[25] or amidation[26] at the C-2 position. MacMillan and co-workers recently reported the $\alpha$-arylation of tertiary arylamines with various chlorinated heteroarenes including 2-chlorobenzoxazole, 2-chlorobenzothiazole, and Boc-protected 2-chloro-1*H*-benzimidazole via an iridium-catalyzed photoredox reaction.[27] Weaver and co-workers also used an iridium-catalyzed photoredox approach for the $\alpha$-arylation of tertiary, sterically hindered (non-nucleophilic) amines with 2-chloro-(benz)azoles.[28] However, only very few metal-free systems for the C-2 functionalization of benzazoles were reported which are particularly attractive in view of the very expensive transition metal catalysts and ligands. For example, Nachtsheim and co-workers used a combination of catalytic tetrabutylammonium iodide (TBAI) and $H_2O_2$ or *tert*-butyl hydroperoxide (TBHP) as co-oxidants and HOAc as an additive to achieve the first metal-free direct C-2 amination of various benzoxazoles.[29] Simultaneously, He et al. developed a metal-free alkylation of benzazoles with alcohols and ethers (reacting adjacent to the heteroatom) using excess TBHP at 120 °C to access the corresponding C−C coupled products via a radical recombination mechanism.[30] These authors reacted ethers with benzoxazoles, benzimidazoles, and benzothiazoles whereas the use of alcohols as alkylating agents was only demonstrated with benzothiazoles. Recently, Ji and co-workers disclosed a protocol for the light induced amidation and alkylation of heteroarenes including benzothiazoles and benzimidazoles with formaldehyde, amides, or ethers (Scheme 1).[31] The C−C coupled products were accessed using ammonium persulfate, stoichiometric quantities of benzaldehyde, and an excess of the corresponding substrate. The authors proposed a radical mechanism based on a peroxodisulfate decomposition mediated by photoexcited benzaldehyde. However, benzoxazoles turned out to be incompatible with the reaction protocol.

Secondary amines (protected as carbamates) and alcohols would represent highly attractive coupling components since the resulting C−C coupled products could be further incorporated into other building blocks via esterification or reductive amination (for applications of these two reactions in the formation of sophisticated structures see for example refs 32−34). Therefore, this study aimed to develop a safe procedure for the mild and metal-free C−C coupling of benzazoles with carbamates, alcohols, and ethers. To avoid the use of aggressive and harmful stoichiometric oxidants, the process should be redox neutral. To the best of our knowledge, a coupling reaction with these characteristics has not been previously reported.

It is well-known that photoexcited benzophenone readily abstracts H atoms from substrate molecules to form ketyl radicals.[35−37] The potential use of benzophenone as a photosensitizer[38−40] for radical reactions has for example been studied by Inoue and co-workers.[41−43] Carbamates are

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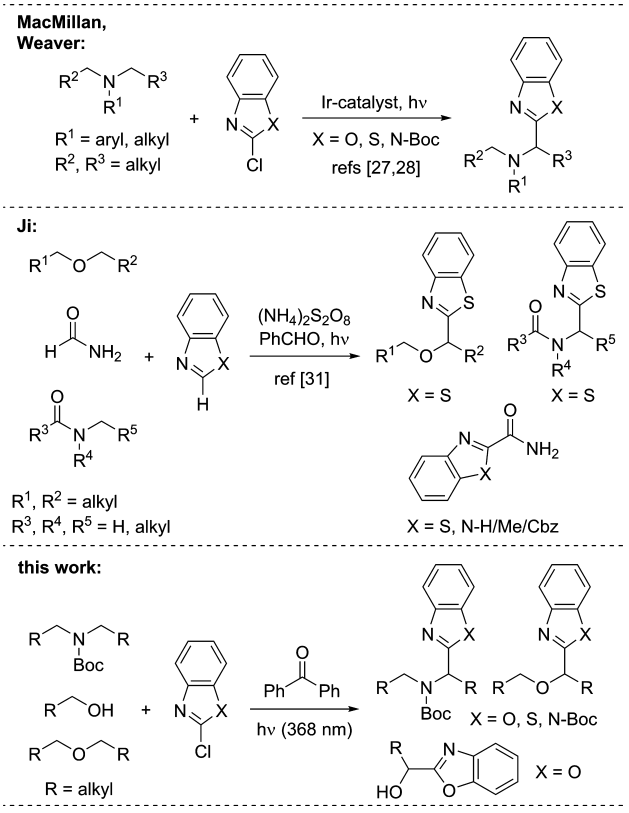
**Scheme 1. Selected Previous and Current Photoredox C−C Coupling Approaches to the C-2 Functionalization of Benzazoles**



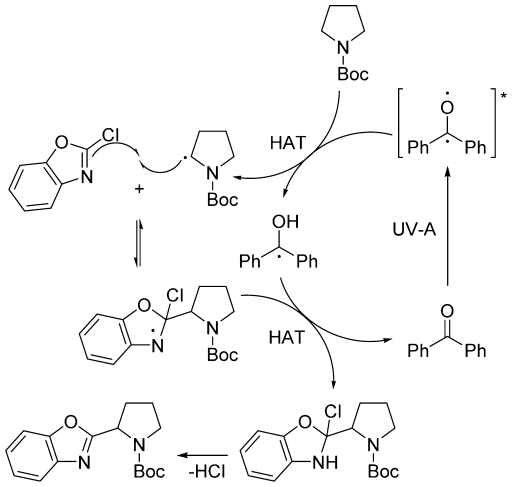

much less susceptible to oxidations via a single electron transfer (SET) process than tertiary amines due to the adjacent alkoxycarbonyl group. Therefore, an electron transfer mechanism including the oxidation of a carbamate (which typically have oxidation potentials above 1.70 V)[44,45] by the excited state of benzophenone (whose reduction potential can be approximated[46] based on the ground-state reduction potential $E_{red}(BP/BP^{-1})$ and the triplet energy $E_T$ as $E_{red}(BP^*/BP^{-1}) = E_{red}(BP/BP^{-1}) + E_T = -1.83$ V[37,47,48] + 3.00 V[37,48] = 1.17 V) is not feasible. Nevertheless, benzophenone mediated H-abstraction in $\alpha$-position to carbamate nitrogens can generate the corresponding $\alpha$-amino radicals.[41,42]

Our working hypothesis, deduced from a mechanistic proposal for the iridium-catalyzed photoredox $\alpha$-arylation of tertiary arylamines with chlorinated heteroarenes,[27] is that the reaction proceeds via a radical substitution pathway (Scheme 2).

A detailed screening of reaction conditions using 2-chlorobenzoxazole and either Boc-pyrrolidine or ethanol as a model system was initially undertaken (see Supporting Information, Tables S1 and S2). It was decided to employ the inexpensive and effective combination of benzophenone and sodium acetate in acetonitrile/water mixtures as the standard conditions for the coupling of 2-chlorobenzazoles with aliphatic carbamates, alcohols, or ethers. Using this reaction protocol, a series of C−C coupled products were prepared (Table 1).

As anticipated, cyclic carbamates reacted readily with 2-chlorobenzoxazole to produce the C−C coupled products **1a**−**1c** in high yields. To determine whether an increase in the intensity of the UV-A irradiation would allow the reaction times

**Scheme 2. Hypothetical Mechanism for the Photoinduced C−C Coupling**




to be shortened, Boc-piperidine was subjected to the standard reaction protocol using a 400 W UV-A lamp and a reduced reaction time of 14 h. However, the yield was lower than in the case of the simple and inexpensive 25 W energy saving UV-A bulb (**1b**). The reaction of Boc-pyrrolidine and Boc-azepane with Boc-protected 2-chloro-1*H*-benzimidazole provided the corresponding cross-coupled products **1d** and **1f** in appreciable yields, whereas Boc-piperidine was repeatedly found to furnish only trace amounts of product **1e**. This unexpected result is particularly surprising because the formation of compound **1b** indicates that H-abstraction from the Boc-piperidine core is feasible. Since NMR-analysis suggested that most of the carbamate remained unreacted, the formed amino radical might be able to reabstract a hydrogen atom instead of reacting with *tert*-butyl 2-chloro-1*H*-benzimidazole-1-carboxylate which appears to be an electronically or sterically unfavorable process. The coupling of 2-chlorobenzothiazole proceeded very slowly yielding only 11% of compound **1g** after 24 h. An increase of the reaction time to 120 h was required to obtain the C−C coupled product **1g** in moderate yield. The reaction protocol also proved suitable for the $\alpha$-functionalization of open-chain carbamates (**1h**), but the benzylic position in Boc-protected 1,2,3,4-tetrahydroisoquinoline turned out to be inaccessible for the developed coupling reaction (**1i**).

Next, the utility of this method for alcohols and ethers as coupling partners was investigated. Open-chain aliphatic alcohols such as ethanol, *n*-propanol, or *n*-butanol reacted with 2-chlorobenzoxazole to furnish the desired products **2a**−**2c** in appreciable yields. However, further increasing the chain length to *n*-octanol led to a decrease in the yield (**2d**). Interestingly, ethanol did not react with 2-chlorobenzothiazole and only trace amounts of the product were formed. This is in line with previous findings for carbamates (**1g**) which also showed significantly reduced reactivity toward the benzothiazole compared to the benzoxazole moiety. This is particularly noteworthy in view of the complementary selectivity of the thermal TBHP mediated radical recombination route employing alcohols to alkylate benzothiazoles but not benzoxazoles.[30] The developed reaction protocol is also suitable for cyclic alcohols providing the C−C coupled product of cyclohexanol and 2-chlorobenzoxazole in 61% yield (**2e**). Furthermore, the method could be extended to cyclic and open-chain ethers. THF reacted smoothly to give the desired cross-coupled


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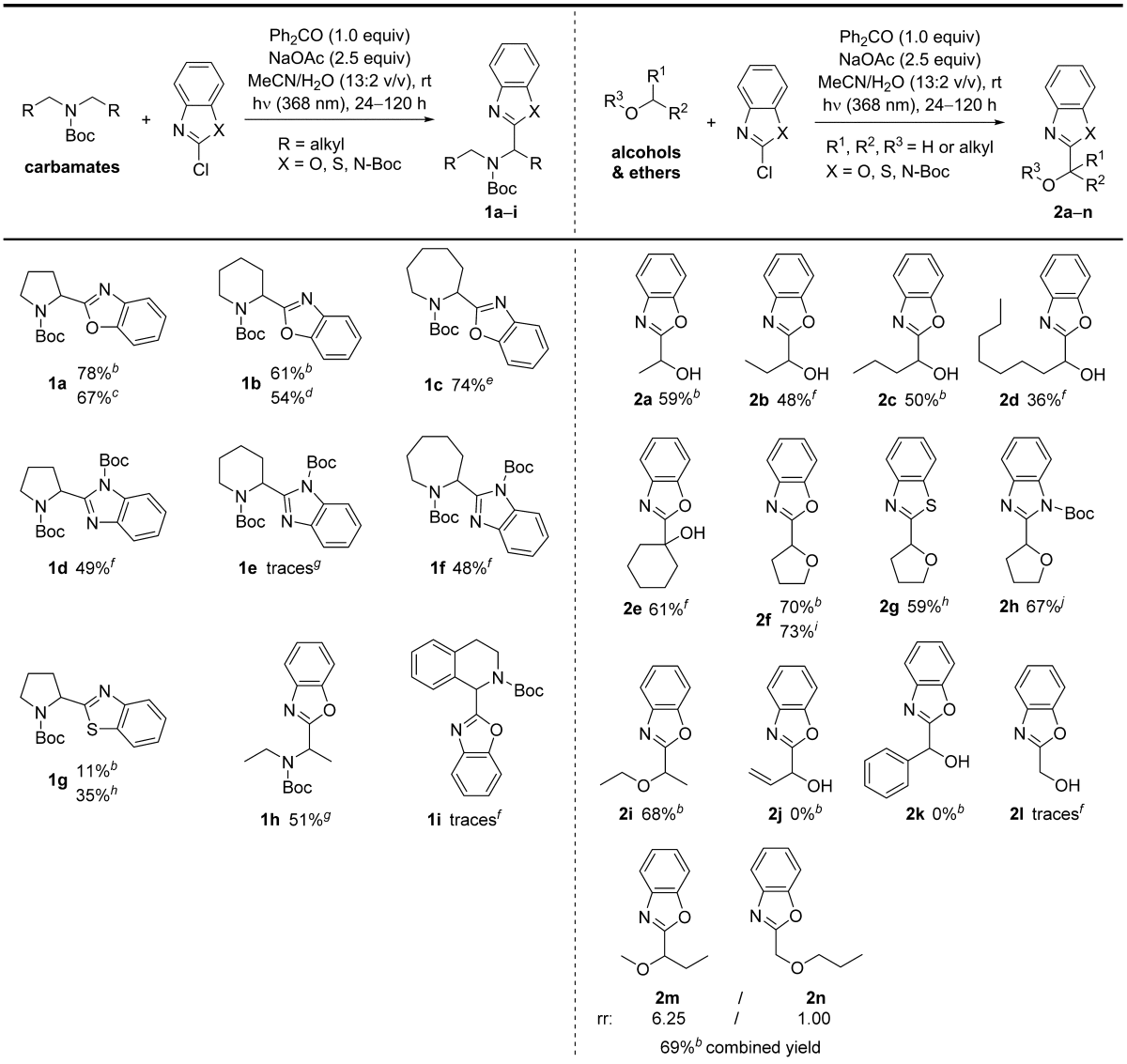
**Table 1. Scope of the Presented C−C Coupling Reaction**[a]




[a]For all reactions: 2-chlorobenzazole (0.90 mmol, 1.0 equiv), benzophenone (0.90 mmol, 1.0 equiv, unless stated otherwise), 15 mL of degassed solvent and either 2.0 equiv of carbamate or 50 equiv of alcohol/ether, 25 W UV-A lamp. Isolated yields after chromatographic purification. [b]24 h irradiation. [c]$K_2CO_3$, 24 h irradiation. [d]400 W UV-A lamp, 14 h irradiation. [e]0.50 equiv of benzophenone and 36 h irradiation. [f]36 h irradiation. [g]72 h irradiation. [h]120 h irradiation. [i]Multigram scale using 18 mmol of 2-chlorobenzoxazole and 50 equiv of THF, 60 h irradiation (see Experimental Section). [j]48 h irradiation.

products of all three tested 2-chlorobenzazoles in high yields (**2f−h**). A multigram scale reaction of THF with 2-chlorobenzoxazole proceeded equally well furnishing the desired product **2f** in high yield by simply irradiating the reaction mixture with two inexpensive 25 W energy saving UV-A lamps (Table 1). While diethyl ether smoothly reacted with 2-chlorobenzoxazole to **2i** in high yield, allyl alcohol and benzyl alcohol could not be transformed to the C−C cross-coupled products **2j** and **2k**. This finding is in line with the lacking formation of the arylated benzylic carbamate **1i** and might be attributable to the low reactivity of the involved well-stabilized radicals in the C−C bond formation. A similar inaccessibility of allylic and benzylic positions has been observed by He et al. in their thermal TBHP mediated procedure.[30] In contrast to primary alcohols, methanol failed to give the respective coupling product **2l**. The regioselectivity of the $\alpha$-arylation of methyl propyl ether which provided a regioisomeric mixture with a ratio of 6.25/1.00 in favor of the internal product in 69% combined yield (**2m**, **2n**) provides further evidence that primary radicals are less suitable intermediates in the process.

As in other photochemical H-abstractions,[41,42] stoichiometric amounts of benzophenone are employed. Although this cheap reagent is no cost factor, reduction of the loading of the sensitizer was investigated. Ethanol and 2-chlorobenzoxazole were chosen as model substrates. Even though the best results were obtained with 1.0 equiv of benzophenone, a reduction to 25 mol % still afforded appreciable yields (55% instead of 57%) while a loading of 1 mol % only resulted in a moderate turnover (22% under identical conditions; see Supporting Information, Table S3). The benzophenone loading of 25 mol % was successfully applied to the preparative C−C coupling reaction with Boc-azepane, ethanol, and THF (Table 2).

The addition of increasing amounts of the radical scavenger 2,6-bis(1,1-dimethylethyl)-4-methylphenol (butylated hydrox-



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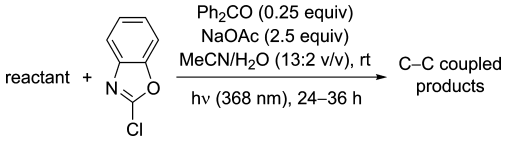
**Table 2. C−C Coupling with Reduced Benzophenone Loading**[a]




| reactant | product | time (h) | yield (%)[b] |
|---|---|---|---|
| ethanol | **2a** | 24 | 52 |
| THF | **2f** | 24 | 65 |
| Boc-azepane | **1c** | 36 | 51 |

[a]For all reactions: 2-chlorobenzoxazole (0.90 mmol, 1.0 equiv), benzophenone (0.225 mmol, 0.25 equiv), 15 mL of degassed solvent and either 2.0 equiv of carbamate or 50 equiv of alcohol/ether, 25 W UV-A lamp. [b]Isolated yields after chromatographic purification.

ytoluene, BHT) led to a dramatic decrease in the yield, underlining the key role of radical intermediates in the reaction mechanism (see Supporting Information, Table S3).

In summary, a mild, transition-metal-free and scalable photochemical, redox-neutral C−C coupling of ethers, alcohols, and carbamates with 2-chlorobenzazoles at ambient temperature has been developed. The inexpensive reagents sodium acetate, benzophenone, water, and acetonitrile were employed in combination with UV-A light from cheap and widely available energy saving lamps.

## EXPERIMENTAL SECTION

All reagents and solvents were received from commercial suppliers and used without further purification unless stated otherwise. Diethyl ether and THF were freshly distilled from sodium/potassium. Acetonitrile (HPLC grade) and deionized water were used without further purification. When used as solvents for cross-coupling reactions, acetonitrile and water were degassed by argon bubbling during ultrasonication (20 min). Flash chromatography was performed on silica gel (35−70 $\mu$m) using the specified eluent mixtures given as a volumetric ratio of components. NMR spectra were recorded on a 300 MHz (300 MHz $^1$H NMR, 75.5 MHz $^{13}$C NMR), 400 MHz (400 MHz $^1$H NMR, 100.6 MHz $^{13}$C NMR), or 600 MHz (600 MHz $^1$H NMR, 151 MHz $^{13}$C NMR) spectrometer. All $^{13}$C NMR spectra were broad-band $^1$H-decoupled. The chemical shifts are reported in ppm and are referenced to the residual solvent (e.g., for $CDCl_3$: $\delta$ = 7.26 ppm for $^1$H and $\delta$ = 77.16 ppm for $^{13}$C NMR spectra). Coupling constants ($J$) are given in Hz using the conventional abbreviations (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and combinations thereof). FT-IR spectra were recorded using a diamond ATR unit and are reported in terms of frequency of absorption $\nu$ [cm$^{-1}$]. Melting points were determined in open capillary tubes using a digital electrothermal apparatus. HPLC-ESI-MS measurements were performed on an HPLC system with a UV diode array detector coupled with an ion trap mass spectrometer using acetonitrile/water (with 0.1% v/v formic acid) mixtures as eluent. High-resolution masses were recorded on an ESI/QTOF-instrument with a suitable external calibrant. *tert*-Butyl pyrrolidine-1-carboxylate, *tert*-butyl piperidine-1-carboxylate, *tert*-butyl azepane-1-carboxylate, *tert*-butyl diethylcarbamate, and *tert*-butyl 3,4-dihydroisoquinoline-2(1*H*)-carboxylate were prepared according to known procedures.[49−51]

**General Procedure for the Preparation of Cross-Coupled Products (Table 1).** Acetonitrile and deionized water were degassed as described above. Under an argon atmosphere, benzophenone (164 mg, 0.900 mmol, 1.0 equiv), sodium acetate (185 mg, 2.26 mmol, 2.5 equiv), the required 2-chlorobenzazole (0.900 mmol, 1.0 equiv), acetonitrile (13 mL), deionized water (2 mL), and either the corresponding carbamate (1.80 mmol, 2.0 equiv) or the alcohol/ether (45.0 mmol, 50 equiv) were combined in a 25 mL Schlenk flask. The sealed reaction mixture was stirred and irradiated with a 25 W UV-A lamp for the indicated amount of time (lamp−sample distance approximately 6 cm; see further specifications in the Supporting Information). The volatiles were removed under reduced pressure, and the residue was redissolved in chloroform (50 mL), dried over sodium sulfate, and filtered. After the removal of the solvent under reduced pressure, the crude product was purified by flash chromatography on silica using eluent mixtures composed of cyclohexane and ethyl acetate.

As expected, all reported cross-coupled products with Boc-protected amines were obtained as mixtures of rotamers which can be distinguished by NMR spectroscopy.

**Multigram Scale Experiment (Compound 2f, Table 1).** Under an argon atmosphere, benzophenone (3.28 g, 18.0 mmol, 1.0 equiv), sodium acetate (3.69 g, 45.0 mmol, 2.5 equiv), THF (64.9 g, 900 mmol, 50 equiv), acetonitrile (260 mL), and deionized water (40 mL) were combined in a 500 mL Schlenk flask. The mixture was degassed by bubbling a stream of argon through the stirred reaction medium for 10 min. 2-Chlorobenzoxazole (2.76 g, 18.0 mmol, 1.0 equiv) was added to the vessel in an argon counterflow. The vessel was sealed, and the mixture was stirred and irradiated for 60 h with two 25 W UV-A lamps (lamps placed at opposite sides of the reaction vessel in order to increase the irradiated surface; lamp−sample distance approximately 6 cm; see specifications in the Supporting Information). A solution of sodium metabisulfite (5% in water, 50 mL, recommended in order to destroy peroxides (if formed) in ether multigram scale experiments) was added before THF and acetonitrile were removed under reduced pressure. The remaining aqueous layer was extracted with ethyl acetate (3 × 100 mL). The combined organic phases were dried over sodium sulfate and filtered. After removal of the solvent under reduced pressure, the crude mixture was purified by flash chromatography on silica ($^c$Hex/EtOAc = 10/1). The pure product was obtained as an orange oil (2.48 g, 13.1 mmol, 73%). Characterization data as given for **2f**.

*(±)-tert-Butyl 2-Chloro-1H-benzimidazole-1-carboxylate.* To a solution of di-*tert*-butyl-dicarbonate (2.71 g, 12.4 mmol, 1.1 equiv) in acetonitrile (50 mL), 2-chloro-1*H*-benzimidazole (1.70 g, 11.1 mmol, 1.0 equiv) and 4-dimethylaminopyridine (DMAP, 150 mg, 1.23 mmol, 0.11 equiv) were added at 0 °C. The reaction mixture was stirred for 14 h at room temperature. Water (50 mL) and ethyl acetate (50 mL) were added, the phases were separated, and the organic layer was washed with brine (50 mL), dried over sodium sulfate, and filtered. The volatiles were removed under reduced pressure, and the obtained crude product was purified by flash chromatography ($^c$Hex/EtOAc = 12/1) furnishing the title compound as a colorless solid (2.65 g, 10.5 mmol, 95%). Mp 65.0−66.5 °C. $R_f$ = 0.33 ($SiO_2$, $^c$Hex/EtOAc 12:1). IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 2982, 1761, 1494, 1449, 1346, 1327, 1151, 1116, 1081, 759. $^1$H NMR, COSY (300 MHz, $CDCl_3$): $\delta$/ppm = 7.94−7.86 (m, 1H, H−Ar), 7.70−7.61 (m, 1H, H−Ar), 7.40−7.30 (m, 2H, 2 × H−Ar), 1.72 (s, 9H, C($CH_3$)$_3$). $^{13}$C NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): $\delta$/ppm = 147.3 ($CO_2{}^tBu$), 141.1 ($C_q$−Ar), 139.8 (C-2), 133.5 ($C_q$−Ar), 125.2 (CH−Ar), 124.8 (CH−Ar), 119.7 (CH−Ar), 114.9 (CH−Ar), 86.8 (C($CH_3$)$_3$), 28.2 (C($CH_3$)$_3$). ESI-MS: $m/z$ (%) = 152.9 (100) [M − Boc + H]$^+$, 169.6 (31) [M − $^t$Bu + H]$^+$. ESI-HRMS: calcd for [$C_{12}ClH_{13}N_2NaO_2$]$^+$, $m/z$ = 275.0563; found, 275.0562.

*(±)-tert-Butyl 2-(1,3-Benzoxazol-2-yl)pyrrolidine-1-carboxylate (1a).* Prepared according to the general procedure using Boc-pyrrolidine (308 mg, 1.80 mmol, 2.0 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv) and a reaction time of 24 h. After purification by flash chromatography ($^c$Hex/EtOAc = 5/1) the title compound was obtained as a colorless solid (202 mg, 0.701 mmol, 78%). Mixture of rotamers with A/B = 0.36/0.64. Mp 91.0−93.0 °C (Lit.:[52] 65−70 °C). $R_f$ = 0.23 ($SiO_2$, $^c$Hex/EtOAc 4:1). IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 2977, 2932, 2880, 1698, 1455, 1392, 1367, 1242, 1163, 748. $^1$H NMR, COSY, NOESY (600 MHz, $CDCl_3$): **A**, $\delta$/ppm = 7.71−7.65 (m, 1H, H−Ar), 7.51−7.45 (m, 1H, H−Ar), 7.35−7.25 (m, 2H, 2 × H−Ar), 5.15 (br d, $J$ = 7.9 Hz, 1H, H-2), 3.77−3.66 (m, 1H, $H_a$-5), 3.53−3.44 (m, 1H, $H_b$-5), 2.44−2.26 (m, 1H, $H_a$-3), 2.22−2.07 (m, 2H, $H_b$-3, $H_a$-4), 2.02−1.92 (m, 1H, $H_b$-4), 1.44 (br s, 9H, C($CH_3$)$_3$);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**B**, $\delta$/ppm = 7.71−7.65 (m, 1H, H−Ar), 7.51−7.45 (m, 1H, H−Ar), 7.35−7.25 (m, 2H, 2 × H−Ar), 5.01 (dd, $J$ = 8.2, 4.4 Hz, 1H, H-2), 3.76−3.66 (m, 1H, $H_a$-5), 3.58 (dt, $J$ = 10.5, 7.1 Hz, 1H, $H_b$-5), 2.44−2.26 (m, 1H, $H_a$-3), 2.22−2.07 (m, 2H, $H_b$-3, $H_a$-4), 2.02−1.92 (m, 1H, $H_b$-4), 1.19 (br s, 9H, C($CH_3$)$_3$). $^{13}$C NMR, HSQC, HMBC (151 MHz, $CDCl_3$): **A**, $\delta$/ppm = 167.2 (C-2′), 154.5 ($CO_2{}^t$Bu), 150.8 ($C_q$−Ar), 141.3 ($C_q$−Ar), 124.7 (CH−Ar), 124.2 (CH−Ar), 120.2 (CH−Ar), 110.8 (CH−Ar), 80.1 ($C$(CH$_3$)$_3$), 55.1 (C-2), 46.9 (C-5), 31.6 (C-3), 28.5 (C($CH_3$)$_3$), 24.5 (C-4); **B**, $\delta$/ppm = 167.5 (C-2′), 154.0 ($CO_2{}^t$Bu), 150.5 ($C_q$−Ar), 141.2 ($C_q$−Ar), 124.9 (CH−Ar), 124.4 (CH−Ar), 120.0 (CH−Ar), 110.6 (CH−Ar), 80.1 ($C$(CH$_3$)$_3$), 55.5 (C-2), 46.6 (C-5), 32.7 (C-3), 28.2 (C($CH_3$)$_3$), 23.9 (C-4). ESI-MS: $m/z$ (%) = 189.3 (21) [M − Boc + H]$^+$, 233.1 (100) [M − $^t$Bu + H]$^+$, 289.1 (37) [M + H]$^+$. ESI-HRMS: calcd for [$C_{16}H_{20}N_2NaO_3$]$^+$, $m/z$ = 311.1372; found, 311.1382. The spectroscopic data are in accordance with those reported in the literature.[52]

*(±)-tert-Butyl 2-(1,3-Benzoxazol-2-yl)piperidine-1-carboxylate (**1b**).* Prepared according to the general procedure using Boc-piperidine (334 mg, 1.80 mmol, 2.0 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 24 h. After purification by flash chromatography ($^c$Hex/EtOAc = 20/1) the title compound was obtained as a colorless solid (165 mg, 0.546 mmol, 61%). Mixture of rotamers with A/B ≈ 1/1. Mp 139.0−141.0 °C. $R_f$ = 0.17 ($SiO_2$, $^c$Hex/EtOAc 15:1). IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 3004, 2974, 2862, 1695, 1455, 1409, 1242, 1122, 745. $^1$H NMR, COSY (600 MHz, $CDCl_3$): $\delta$/ppm = 7.74−7.68 (m, 1H, H−Ar), 7.51−7.47 (m, 1H, H−Ar), 7.34−7.28 (m, 2H, 2 × H−Ar), 5.89−5.36 (m, 1H, H-2), 4.11 (br s, 1H, $H_a$-6), 3.15−2.78 (m, 1H, $H_b$-6), 2.50−2.44 (m, 1H, $H_a$-3), 1.96−1.87 (m, 1H, $H_b$-3), 1.79−1.57 (m, 2H, $H_a$-4, $H_a$-5), 1.58−1.38 (m, 11H, $H_b$-4, $H_b$-5, C($CH_3$)$_3$). $^{13}$C NMR, HSQC, HMBC (151 MHz, $CDCl_3$): $\delta$/ppm = 165.7 (C-2′), 155.5 ($CO_2{}^t$Bu), 151.0 ($C_q$−Ar), 141.4 ($C_q$−Ar), 124.9 (CH−Ar), 124.3 (CH−Ar), 120.1 (CH−Ar), 110.7 (CH−Ar), 80.4 ($C$(CH$_3$)$_3$), 50.9 and 49.5 (C-2, rotamers A and B), 42.1 and 41.0 (C-6, rotamers A and B), 28.5 (C($CH_3$)$_3$), 27.6 (C-3), 25.1 ($CH_2$), 20.3 ($CH_2$). ESI-MS: $m/z$ (%) = 203.2 (91) [M − Boc + H]$^+$, 247.2 (100) [M − $^t$Bu + H]$^+$, 303.2 (51) [M + H]$^+$, 325.2 (49) [M + Na]$^+$. ESI-HRMS: calcd for [$C_{17}H_{22}N_2NaO_3$]$^+$, $m/z$ = 325.1528; found, 325.1539.

*(±)-tert-Butyl 2-(1,3-Benzoxazol-2-yl)azepane-1-carboxylate (**1c**).* Prepared according to the general procedure using Boc-azepane (359 mg, 1.80 mmol, 2.0 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), benzophenone (82 mg, 0.45 mmol, 0.50 equiv), and a reaction time of 36 h. After purification by flash chromatography ($^c$Hex/EtOAc = 15/1) the title compound was obtained as a colorless solid (211 mg, 0.667 mmol, 74%). Mixture of rotamers with A/B = 0.43/0.57. Mp 94.5−96.5 °C. $R_f$ = 0.34 ($SiO_2$, $^c$Hex/EtOAc 15:1). IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 2975, 2930, 2856, 1694, 1455, 1407, 1227, 1162, 749. $^1$H NMR, COSY (300 MHz, $CDCl_3$): **A**, $\delta$/ppm = 7.73−7.66 (m, 1H, H−Ar), 7.53−7.45 (m, 1H, H−Ar), 7.35−7.27 (m, 2H, 2 × H−Ar), 5.22 (dd, $J$ = 11.7, 6.2 Hz, 1H, H-2), 4.08−3.95 (m, 1H, $H_a$-7), 3.16 (ddd, $J$ = 14.7, 11.1, 1.6 Hz, 1H, $H_b$-7), 2.58−2.36 (m, 1H, $H_a$-3), 2.12−1.20 (m, 7H, $H_b$-3, H-4, H-5, H-6), 1.37 (br s, 9H, C($CH_3$)$_3$); **B**, $\delta$/ppm = 7.73−7.66 (m, 1H, H−Ar), 7.53−7.45 (m, 1H, H−Ar), 7.35−7.27 (m, 2H, 2 × H−Ar), 5.53 (dd, $J$ = 11.7, 6.9 Hz, 1H, H-2), 3.92−3.79 (m, 1H, $H_a$-7), 3.05 (ddd, $J$ = 14.8, 11.6, 1.8 Hz, 1H, $H_b$-7), 2.58−2.36 (m, 1H, $H_a$-3), 2.12−1.20 (m, 7H, $H_b$-3, H-4, H-5, H-6), 1.49 (br s, 9H, C($CH_3$)$_3$). $^{13}$C NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): **A**, $\delta$/ppm = 167.4 (C-2′), 155.3 ($CO_2{}^t$Bu), 150.6 ($C_q$−Ar), 141.2 ($C_q$−Ar), 124.9 (CH−Ar), 124.4 (CH−Ar), 120.1 (CH−Ar), 110.6 (CH−Ar), 80.4 ($C$(CH$_3$)$_3$), 54.9 (C-2), 43.5 (C-7), 32.6 (C-3), 29.5 ($CH_2$), 29.4 ($CH_2$), 28.4 (C($CH_3$)$_3$), 25.7 ($CH_2$); **B** , $\delta$/ppm = 167.1 (C-2′), 156.1 ($CO_2{}^t$Bu), 150.9 ($C_q$−Ar), 141.2 ($C_q$−Ar), 124.9 (CH−Ar), 124.3 (CH−Ar), 120.1 (CH−Ar), 110.9 (CH−Ar), 80.2 ($C$(CH$_3$)$_3$), 52.9 (C-2), 43.7 (C-7), 32.3 (C-3), 29.7 ($CH_2$), 29.3 ($CH_2$), 28.6 (C($CH_3$)$_3$), 25.0 ($CH_2$). ESI-MS: $m/z$ (%) = 217.2 (28) [M − Boc + H]$^+$, 261.2 (100) [M − $^t$Bu + H]$^+$, 317.2 (65) [M + H]$^+$, 339.2 (17) [M + Na]$^+$. ESI-HRMS: calcd for [$C_{18}H_{24}N_2NaO_3$]$^+$, $m/z$ = 339.1685; found, 339.1684.

*(±)-tert-Butyl 2-(tert-Butyl 1,3-benzimidazol-1-carboxylate-2-yl)-pyrrolidine-1-carboxylate (**1d**).* Prepared according to the general procedure using Boc-pyrrolidine (308 mg, 1.80 mmol, 2.0 equiv), *tert*-butyl 2-chloro-1*H*-benzimidazole-1-carboxylate (227 mg, 0.898 mmol, 1.0 equiv), and a reaction time of 36 h. After purification by flash chromatography ($^c$Hex/EtOAc = 12.5/1 → 8.33/1 → 7.14/1) the title compound was obtained as a yellowish oil (171 mg, 0.441 mmol, 49%). Mixture of rotamers with A/B = 0.49/0.51. $R_f$ = 0.13 ($SiO_2$, $^c$Hex/EtOAc 6:1). IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 2977, 2933, 2879, 1745, 1699, 1453, 1393, 1350, 1153, 1119. $^1$H NMR, COSY, NOESY (600 MHz, $CDCl_3$): **A**, $\delta$/ppm = 7.91−7.85 (m, 1H, H−Ar), 7.73−7.68 (m, 1H, H−Ar), 7.33−7.29 (m, 1H, H−Ar), 7.29−7.25 (m, 1H, H−Ar), 5.70 (dd, $J$ = 8.5, 1.9 Hz, 1H, H-2), 3.89−3.82 (m, 1H, $H_a$-5), 3.60−3.45 (m, 1H, $H_b$-5), 2.47−2.34 (m, 1H, $H_a$-3), 2.16−1.97 (m, 2H, $H_b$-3, $H_a$-4), 1.95−1.88 (m, 1H, $H_b$-4), 1.69 (br s, 9H, C′(C′$H_3$)$_3$), 1.45 (br s, 9H, C($CH_3$)$_3$); **B**, $\delta$/ppm = 7.91−7.85 (m, 1H, H−Ar), 7.73−7.68 (m, 1H, H−Ar), 7.33−7.29 (m, 1H, H−Ar), 7.29−7.25 (m, 1H, H−Ar), 5.61 (dd, $J$ = 8.3, 3.3 Hz, 1H, H-2), 3.89−3.82 (m, 1H, $H_a$-5), 3.60−3.45 (m, 1H, $H_b$-5), 2.47−2.34 (m, 1H, $H_a$-3), 2.16−1.97 (m, 2H, $H_b$-3, $H_a$-4), 1.95−1.88 (m, 1H, $H_b$-4), 1.71 (br s, 9H, C′(C′$H_3$)$_3$), 1.14 (br s, 9H, C($CH_3$)$_3$). $^{13}$C NMR, HSQC, HMBC (151 MHz, $CDCl_3$): **A**, $\delta$/ppm = 157.1 (C-2′), 154.6 ($CO_2{}^t$Bu), 148.9 (C′$O_2{}^t$Bu), 142.3 ($C_q$−Ar), 132.9 ($C_q$−Ar), 124.3 (CH−Ar), 124.0 (CH−Ar), 120.1 (CH−Ar), 115.0 (CH−Ar), 85.6 (C′(C′$H_3$)$_3$), 79.6 ($C$(CH$_3$)$_3$), 56.7 (C-2), 47.1 (C-5), 32.1 (C-3), 28.7 (C($CH_3$)$_3$), 28.2 (C′(C′$H_3$)$_3$), 23.5 (C-4); **B**, $\delta$/ppm = 158.2 (C-2′), 154.1 ($CO_2{}^t$Bu), 149.0 (C′$O_2{}^t$Bu), 142.3 ($C_q$−Ar), 133.5 ($C_q$−Ar), 124.4 (CH−Ar), 124.3 (CH−Ar), 120.1 (CH−Ar), 114.8 (CH−Ar), 85.8 (C′(C′$H_3$)$_3$), 79.2 ($C$(CH$_3$)$_3$), 56.3 (C-2), 46.7 (C-5), 32.9 (C-3), 23.2 (C-4), 28.2 (C($CH_3$)$_3$) and C′(C′$H_3$)$_3$). ESI-MS: $m/z$ (%) = 232.1 (10) [M − Boc − $^t$Bu + H]$^+$, 282.2 (100) [M − Boc + H]$^+$, 388.1 (86) [M + H]$^+$. ESI-HRMS: calcd for [$C_{21}H_{30}N_3O_4$]$^+$, $m/z$ = 388.2236; found, 388.2251.

*(±)-tert-Butyl 2-(tert-Butyl 1,3-Benzimidazol-1-carboxylate-2-yl)-azepane-1-carboxylate (**1f**).* Prepared according to the general procedure using Boc-azepane (359 mg, 1.80 mmol, 2.0 equiv), *tert*-butyl 2-chloro-1*H*-benzimidazole-1-carboxylate (227 mg, 0.898 mmol, 1.0 equiv), and a reaction time of 36 h. After purification by flash chromatography ($^c$Hex/EtOAc = 12/1) the title compound was obtained as a yellowish and highly viscous oil (180 mg, 0.433 mmol, 48%). Mixture of rotamers with A/B = 0.42/0.58. $R_f$ = 0.13 ($SiO_2$, $^c$Hex/EtOAc 12:1). IR (ATR): $\tilde{\nu}$ [cm$^{-1}$] = 2976, 2929, 2854, 1744, 1690, 1452, 1320, 1151, 1118. $^1$H NMR, COSY (400 MHz, $CDCl_3$): **A**, $\delta$/ppm = 7.92−7.84 (m, 1H, H−Ar), 7.72−7.66 (m, 1H, H−Ar), 7.34−7.24 (m, 2H, 2 × H−Ar), 5.98 (dd, $J$ = 11.9, 5.9 Hz, 1H, H-2), 4.11−4.02 (m, 1H, $H_a$-7), 3.55−3.42 (m, 1H, $H_b$-7), 2.53 (ddd, $J$ = 14.3, 8.4, 5.9 Hz, 1H, $H_a$-3), 2.05−1.25 (m, 7H, $H_b$-3, H-4, H-5, H-6), 1.71 (br s, 9H, C′(C′$H_3$)$_3$), 1.44 (br s, 9H, C($CH_3$)$_3$); **B**, $\delta$/ppm = 7.92−7.84 (m, 1H, H−Ar), 7.72−7.66 (m, 1H, H−Ar), 7.34−7.24 (m, 2H, 2 × H−Ar), 5.72 (dd, $J$ = 12.0, 5.2 Hz, 1H, H-2), 4.32−4.21 (m, 1H, $H_a$-7), 3.55−3.42 (m, 1H, $H_b$-7), 2.42 (ddd, $J$ = 14.1, 8.5, 5.2 Hz, 1H, $H_a$-3), 2.05−1.25 (m, 7H, $H_b$-3, H-4, H-5, H-6), 1.71 (br s, 9H, C′(C′$H_3$)$_3$), 1.22 (br s, 9H, C($CH_3$)$_3$). $^{13}$C NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): **A**, $\delta$/ppm = 158.8 (C-2′), 156.1 ($CO_2{}^t$Bu), 148.8 (C′$O_2{}^t$Bu), 142.5 ($C_q$−Ar), 133.1 ($C_q$−Ar), 124.0 (2C, 2 × CH−Ar), 119.9 (CH−Ar), 115.0 (CH−Ar), 85.7 (C′(C′$H_3$)$_3$), 79.5 ($C$(CH$_3$)$_3$), 54.6 (C-2), 44.4 (C-7), 33.3 (C-3), 30.0 ($CH_2$), 29.6 ($CH_2$), 28.6 (C($CH_3$)$_3$), 28.2 (C′(C′$H_3$)$_3$), 26.0 ($CH_2$); **B**, $\delta$/ppm = 159.7 (C-2′), 155.5 ($CO_2{}^t$Bu), 148.9 (C′$O_2{}^t$Bu), 142.5 ($C_q$−Ar), 132.6 ($C_q$−Ar), 124.3 (2C, 2 × CH−Ar), 120.1 (CH−Ar), 114.9 (CH−Ar), 85.7 (C′(C′$H_3$)$_3$), 79.5 ($C$(CH$_3$)$_3$), 56.2 (C-2), 44.0 (C-7), 33.3 (C-3), 30.4 ($CH_2$), 29.5 ($CH_2$), 28.4 (C($CH_3$)$_3$), 28.2 (C′(C′$H_3$)$_3$), 26.8 ($CH_2$). ESI-MS: $m/z$ (%) = 260.1 (8) [M − Boc − $^t$Bu + H]$^+$, 316.2 (77) [M − Boc + H]$^+$, 416.2 (100) [M + H]$^+$. ESI-HRMS: calcd for [$C_{23}H_{33}N_3NaO_4$]$^+$, $m/z$ = 438.2369; found, 438.2360.

*(±)-tert-Butyl 2-(1,3-Benzothiazol-2-yl)pyrrolidine-1-carboxylate (**1g**).* Prepared according to the general procedure using Boc-pyrrolidine (308 mg, 1.80 mmol, 2.0 equiv), 2-chlorobenzothiazole (153 mg, 0.902 mmol, 1.0 equiv), and a reaction time of 120 h. After purification by flash chromatography ($^c$Hex/EtOAc = 6/1) the title compound was obtained as a colorless solid (97 mg, 0.32 mmol, 35%). Mixture of rotamers with A/B = 0.35/0.65. Mp 97.0−99.0 °C. $R_f$ =


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0.18 ($SiO_2$, $^c$Hex/EtOAc 6:1). IR (ATR): $\bar{\nu}$ [$cm^{-1}$] = 2976, 2879, 1699, 1437, 1386, 1367, 1244, 1166, 1112, 760. $^1$H NMR, COSY (600 MHz, $CDCl_3$): **A**, $\delta$/ppm = 7.96 (d, $J$ = 8.1 Hz, 1H, H−Ar), 7.89−7.80 (m, 1H, H−Ar), 7.50−7.39 (m, 1H, H−Ar), 7.39−7.30 (m, 1H, H−Ar), 5.36−5.30 (m, 1H, H-2), 3.71−3.61 (m, 1H, $H_a$-5), 3.53−3.44 (m, 1H, $H_b$-5), 2.47−2.22 (m, 2H, H-3), 2.06−1.92 (m, 2H, H-4), 1.49 (br s, 9H, $C(CH_3)_3$); **B**, $\delta$/ppm = 7.96 (d, $J$ = 8.1 Hz, 1H, H−Ar), 7.89−7.80 (m, 1H, H−Ar), 7.50−7.39 (m, 1H, H−Ar), 7.39−7.30 (m, 1H, H−Ar), 5.22 (dd, $J$ = 8.3, 3.2 Hz, 1H, H-2), 3.71−3.61 (m, 1H, $H_a$-5), 3.61−3.53 (m, 1H, $H_b$-5), 2.47−2.22 (m, 2H, H-3), 2.06−1.92 (m, 2H, H-4), 1.30 (br s, 9H, $C(CH_3)_3$). $^{13}$C NMR, HSQC, HMBC (151 MHz, $CDCl_3$): **A**, $\delta$/ppm = 176.3 (C-2′), 154.9 ($CO_2{}^t$Bu), 153.9 ($C_q$−Ar), 135.1 ($C_q$−Ar), 125.9 (CH−Ar), 124.8 (CH−Ar), 123.0 (CH−Ar), 121.7 (CH−Ar), 80.3 ($C(CH_3)_3$), 59.6 (C-2), 47.2 (C-5), 33.1 (C-3), 28.6 ($C(CH_3)_3$), 24.2 (C-4); **B**, $\delta$/ppm = 177.1 (C-2′), 154.4 ($CO_2{}^t$Bu), 153.6 ($C_q$−Ar), 134.7 ($C_q$−Ar), 126.1 (CH−Ar), 124.9 (CH−Ar), 122.9 (CH−Ar), 121.8 (CH−Ar), 80.5 ($C(CH_3)_3$), 60.1 (C-2), 46.8 (C-5), 34.3 (C-3), 28.4 ($C(CH_3)_3$), 23.5 (C-4). ESI-MS: $m/z$ (%) = 205.4 (16) [M − Boc + H]$^+$, 249.2 (99) [M − $^t$Bu + H]$^+$, 305.1 (100) [M + H]$^+$. ESI-HRMS: calcd for $[C_{16}H_{20}N_2NaO_2S]^+$, $m/z$ = 327.1143; found, 327.1156.

*(±)-tert-Butyl (1-(1,3-Benzoxazol-2-yl)ethyl)ethylcarbamate (**1h**).* Prepared according to the general procedure using *tert*-butyl diethylcarbamate (312 mg, 1.80 mmol, 2.0 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 72 h. After purification by flash chromatography ($^c$Hex/EtOAc = 15/1) the title compound was obtained as a colorless solid (134 mg, 0.461 mmol, 51%). Mixture of rotamers with A/B = 0.44/0.56. Mp 53.0−54.5 °C. $R_f$ = 0.14 ($SiO_2$, $^c$Hex/EtOAc 15:1). IR (ATR): $\bar{\nu}$ [$cm^{-1}$] = 2976, 2936, 1690, 1455, 1407, 1378, 1288, 1149, 765, 743. $^1$H NMR, COSY (600 MHz, $CDCl_3$): **A**, $\delta$/ppm = 7.74−7.68 (m, 1H, H−Ar), 7.53−7.46 (m, 1H, H−Ar), 7.35−7.28 (m, 2H, 2 × H−Ar), 5.01 (br s, 1H, NC*H*$CH_3$), 3.56−2.95 (m, 2H, NC$H_2CH_3$), 1.81−1.63 (m, 3H, NCHC$H_3$), 1.62−1.20 (m, 9H, $C(CH_3)_3$), 1.19−0.89 (m, 3H, $NCH_2CH_3$); **B**, $\delta$/ppm = 7.74−7.68 (m, 1H, H−Ar), 7.53−7.46 (m, 1H, H−Ar), 7.35−7.28 (m, 2H, 2 × H−Ar), 5.68 (br s, 1H, NC*H*$CH_3$), 3.56−2.95 (m, 2H, NC$H_2CH_3$), 1.81−1.63 (br s, 3H, NCHC$H_3$), 1.62−1.20 (m, 9H, $C(CH_3)_3$), 1.19−0.89 (m, 3H, $NCH_2CH_3$). $^{13}$C NMR, HSQC, HMBC (151 MHz, $CDCl_3$): **A**, $\delta$/ppm = 166.3 (C-2′), 154.6 ($CO_2{}^t$Bu), 150.9 ($C_q$−Ar), 141.1 ($C_q$−Ar), 125.2 (CH−Ar), 124.4 (CH−Ar), 120.1 (CH−Ar), 110.8 (CH−Ar), 80.3 ($C(CH_3)_3$), 51.0 ($NCHCH_3$), 41.0 ($NCH_2CH_3$), 28.5 ($C(CH_3)_3$), 17.1 ($NCHCH_3$), 14.5 ($NCH_2CH_3$); **B**, $\delta$/ppm = 166.6 (C-2′), 155.6 ($CO_2{}^t$Bu), 150.9 ($C_q$−Ar), 141.1 ($C_q$−Ar), 125.2 (CH−Ar), 124.4 (CH−Ar), 120.1 (CH−Ar), 110.8 (CH−Ar), 80.3 ($C(CH_3)_3$), 48.9 ($NCHCH_3$), 38.8 ($NCH_2CH_3$), 28.5 ($C(CH_3)_3$), 16.7 ($NCHCH_3$), 15.3 ($NCH_2CH_3$). ESI-MS: $m/z$ (%) = 191.0 (44) [M − Boc + H]$^+$, 235.0 (100) [M − $^t$Bu + H]$^+$, 291.1 (48) [M + H]$^+$, 313.1 (15) [M + Na]$^+$. ESI-HRMS: calcd for $[C_{16}H_{22}N_2NaO_3]^+$, $m/z$ = 313.1528; found, 313.1524.

*(±)-1-(1,3-Benzoxazol-2-yl)ethan-1-ol (**2a**).* Prepared according to the general procedure using ethanol (2.07 g, 44.9 mmol, 50 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 24 h. After purification by flash chromatography ($^c$Hex/EtOAc = 6/1 → 7/3) the title compound was obtained as a yellowish oil which slowly crystallized to provide a colorless solid (87 mg, 0.53 mmol, 59%). Mp 33.0−34.5 °C (Lit.:[53] 29.0−31.0 °C). $R_f$ = 0.23 ($SiO_2$, $^c$Hex/EtOAc 7:3). IR (ATR): $\bar{\nu}$ [$cm^{-1}$] = 3327, 2985, 1613, 1569, 1456, 1243, 1121, 1100, 817, 748. $^1$H NMR, COSY (400 MHz, $CDCl_3$): $\delta$/ppm = 7.71−7.64 (m, 1H, H−Ar), 7.50−7.44 (m, 1H, H−Ar), 7.34−7.27 (m, 2H, 2 × H−Ar), 5.14 (q, $J$ = 6.7 Hz, 1H, $CH_3CHOH$), 4.75 (br s, 1H, O*H*), 1.71 (d, $J$ = 6.7 Hz, 3H, $CH_3CHOH$). $^{13}$C NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): $\delta$/ppm = 168.7 (C-2′), 150.8 ($C_q$−Ar), 140.4 ($C_q$−Ar), 125.3 (CH−Ar), 124.6 (CH−Ar), 120.0 (CH−Ar), 110.8 (CH−Ar), 64.1 ($CH_3CHOH$), 21.5 ($CH_3CHOH$). ESI-MS: $m/z$ (%) = 146.0 (28) [M − OH]$^+$, 164.0 (100) [M + H]$^+$, 185.9 (4) [M + Na]$^+$. ESI-HRMS: calcd for $[C_9H_9NNaO_2]^+$, $m/z$ = 186.0531; found, 186.0535. The analytical data are in accordance with those reported in the literature.[53]

*(±)-1-(1,3-Benzoxazol-2-yl)propan-1-ol (**2b**).* Prepared according to the general procedure using *n*-propanol (2.70 g, 44.9 mmol, 50 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 36 h. After purification by flash chromatography ($^c$Hex/EtOAc = 8/1 → 6/1) the title compound was obtained as a yellow oil (77 mg, 0.43 mmol, 48%). $R_f$ = 0.10 ($SiO_2$, $^c$Hex/EtOAc 6:1). IR (ATR): $\bar{\nu}$ [$cm^{-1}$] = 3316, 2969, 2936, 2879, 1613, 1568, 1455, 1242, 1125, 1103, 840, 744. $^1$H NMR, COSY (400 MHz, $CDCl_3$): $\delta$/ppm = 7.71−7.65 (m, 1H, H−Ar), 7.51−7.45 (m, 1H, H−Ar), 7.34−7.27 (m, 2H, 2 × H−Ar), 4.96−4.88 (m, 1H, $CH_2CHOH$), 4.47 (br s, 1H, CHO*H*), 2.15−1.93 (m, 2H, $CH_2CHOH$), 1.04 (t, $J$ = 7.4 Hz, 3H, $CH_3CH_2$). $^{13}$C NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): $\delta$/ppm = 168.1 (C-2′), 150.8 ($C_q$−Ar), 140.4 ($C_q$−Ar), 125.2 (CH−Ar), 124.6 (CH−Ar), 120.0 (CH−Ar), 110.8 (CH−Ar), 69.2 (CHOH), 28.8 ($CH_2CHOH$), 9.6 ($CH_3CH_2$). ESI-MS: $m/z$ (%) = 160.1 (74) [M − OH]$^+$, 178.0 (100) [M + H]$^+$. ESI-HRMS: calcd for $[C_{10}H_{11}NNaO_2]^+$, $m/z$ = 200.0687; found, 200.0679. This compound has been described in the literature,[54] but detailed analytical data are not available.

*(±)-1-(1,3-Benzoxazol-2-yl)butan-1-ol (**2c**).* Prepared according to the general procedure using *n*-butanol (3.34 g, 45.1 mmol, 50 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 24 h. After purification by flash chromatography ($^c$Hex/EtOAc = 10/1 → 6/1) the title compound was obtained as an orange oil (86 mg, 0.45 mmol, 50%). $R_f$ = 0.14 ($SiO_2$, $^c$Hex/EtOAc 6:1). IR (ATR): $\bar{\nu}$ [$cm^{-1}$] = 3328, 2961, 2935, 2874, 1612, 1568, 1456, 1243, 1128, 746. $^1$H NMR, COSY (400 MHz, $CDCl_3$): $\delta$/ppm = 7.71−7.64 (m, 1H, H−Ar), 7.51−7.45 (m, 1H, H−Ar), 7.34−7.28 (m, 2H, 2 × H−Ar), 5.02−4.94 (m, 1H, $CH_2CHOH$), 4.31 (d, $J$ = 6.0 Hz, 1H, CHO*H*), 2.07−1.90 (m, 2H, $CH_2CHOH$), 1.59−1.43 (m, 2H, $CH_3CH_2$), 0.96 (t, $J$ = 7.4 Hz, 3H, $CH_3CH_2$). $^{13}$C NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): $\delta$/ppm = 168.3 (C-2′), 150.8 ($C_q$−Ar), 140.4 ($C_q$−Ar), 125.2 (CH−Ar), 124.6 (CH−Ar), 120.0 (CH−Ar), 110.9 (CH−Ar), 67.8 (CHOH), 37.7 ($CH_2CHOH$), 18.5 ($CH_3CH_2$), 13.9 ($CH_3CH_2$). ESI-MS: $m/z$ (%) = 174.0 (23) [M − OH]$^+$, 192.0 (100) [M + H]$^+$. ESI-HRMS: calcd for $[C_{11}H_{14}NO_2]^+$, $m/z$ = 192.1025; found, 192.1033.

*(±)-1-(1,3-Benzoxazol-2-yl)octan-1-ol (**2d**).* Prepared according to the general procedure using *n*-octanol (5.86 g, 45.0 mmol, 50 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv) and a reaction time of 36 h. After removal of excess *n*-octanol in fine vacuum and subsequent purification by flash chromatography ($^c$Hex/EtOAc = 10/1 → 6/1) the title compound was obtained as a yellow oil (78 mg, 0.32 mmol, 36%). $R_f$ = 0.20 ($SiO_2$, $^c$Hex/EtOAc 6:1). IR (ATR): $\bar{\nu}$ [$cm^{-1}$] = 3329, 2925, 2856, 1613, 1568, 1456, 1243, 1105, 745. $^1$H NMR, COSY (300 MHz, $CDCl_3$): $\delta$/ppm = 7.74−7.62 (m, 1H, H−Ar), 7.59−7.47 (m, 1H, H−Ar), 7.36−7.28 (m, 2H, 2 × H−Ar), 5.00 (br s, 1H, $CH_2CHOH$), 3.61 (br s, 1H, CHO*H*), 2.15−1.88 (m, 2H, $CH_2CHOH$), 1.57−1.41 (m, 2H, $CH_2CH_2CHOH$), 1.39−1.16 (m, 8H, 4 × $CH_2$), 0.86 (t, $J$ = 7.0 Hz, 3H, $CH_3$). $^{13}$C NMR, HSQC, HMBC (151 MHz, $CDCl_3$): $\delta$/ppm = 168.1 (C-2′), 151.0 ($C_q$−Ar), 140.6 ($C_q$−Ar), 125.3 (CH−Ar), 124.6 (CH−Ar), 120.1 (CH−Ar), 110.9 (CH−Ar), 68.1 (CHOH), 35.8 ($CH_2CHOH$), 31.9 ($CH_2$), 29.4 ($CH_2$), 29.3 ($CH_2$), 25.2 ($CH_2$), 22.8 ($CH_3CH_2$), 14.2 ($CH_3$). ESI-MS: $m/z$ (%) = 230.0 (10) [M − OH]$^+$, 248.1 (100) [M + H]$^+$, 270.1 (4) [M + Na]$^+$. ESI-HRMS: calcd for $[C_{15}H_{21}NNaO_2]^+$, $m/z$ = 270.1470; found, 270.1477.

*(±)-1-(1,3-Benzoxazol-2-yl)cyclohexan-1-ol (**2e**).* Prepared according to the general procedure using cyclohexanol (4.51 g, 45.0 mmol, 50 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 36 h. After purification by flash chromatography ($^c$Hex/EtOAc = 20/1 → 10/1) the title compound was obtained as a colorless solid (120 mg, 0.552 mmol, 61%). $R_f$ = 0.18 ($SiO_2$, $^c$Hex/EtOAc 6:1). Mp 88.0−90.0 °C. IR (ATR): $\bar{\nu}$ [$cm^{-1}$] = 3377, 2936, 2858, 1562, 1455, 1244, 1152, 1040, 749. $^1$H NMR, COSY (400 MHz, $CDCl_3$): $\delta$/ppm = 7.74−7.68 (m, 1H, H−Ar), 7.55−7.48 (m, 1H, H−Ar), 7.36−7.30 (m, 2H, 2 × H−Ar), 2.96 (br s, 1H, O*H*), 2.21−2.08 (m, 2H, $H_a$-2, $H_a$-6), 2.00−1.90 (m, 2H, $H_b$-2, $H_b$-6), 1.90−1.76 (m, 2H, $H_a$-3, $H_a$-5), 1.72−1.57 (m, 3H, $H_b$-3, $H_a$-4, $H_b$-5), 1.47−1.35 (m, 1H, $H_b$-4). $^{13}$C NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): $\delta$/ppm =


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170.6 (C-2′), 150.9 ($C_q$–Ar), 140.8 ($C_q$–Ar), 125.2 (CH–Ar), 124.5 (CH–Ar), 120.2 (CH–Ar), 110.9 (CH–Ar), 71.3 (COH), 36.5 (2C, C-2 and C-6), 25.3 (C-4), 21.7 (2C, C-3 and C-5). ESI-MS: *m*/*z* (%) = 200.1 (44) $[M - OH]^+$, 218.0 (100) $[M + H]^+$, 240.4 (4) $[M + Na]^+$. ESI-HRMS: calcd for $[C_{13}H_{15}NNaO_2]^+$, *m*/*z* = 240.1000; found, 240.1002.

*(±)-2-(Oxolan-2-yl)-1,3-benzoxazole* ***(2f)***. Prepared according to the general procedure using THF (3.24 g, 44.9 mmol, 50 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 24 h. After purification by flash chromatography ($^c$Hex/EtOAc = 10/1) the title compound was obtained as an orange oil (119 mg, 0.629 mmol, 70%). $R_f$ = 0.20 ($SiO_2$, $^c$Hex/EtOAc 6:1). IR (ATR): $\tilde{\nu}$ [$cm^{-1}$] = 3059, 2980, 2955, 2875, 1614, 1569, 1455, 1242, 1059, 748. $^1$H NMR, COSY (400 MHz, $CDCl_3$): $\delta$/ppm = 7.73–7.66 (m, 1H, H–Ar), 7.54–7.47 (m, 1H, H–Ar), 7.35–7.27 (m, 2H, 2 × H–Ar), 5.19 (t, *J* = 6.8 Hz, 1H, H-2′), 4.11 (ddd, *J* = 8.3, 7.2, 6.4 Hz, 1H, $H_a$-5′), 3.99 (ddd, *J* = 8.3, 7.3, 6.1 Hz, 1H, $H_b$-5′), 2.42–2.34 (m, 2H, H-3′), 2.22–1.98 (m, 2H, H-4′). $^{13}$C NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): $\delta$/ppm = 166.3 (C-2), 150.9 ($C_q$–Ar), 140.9 ($C_q$–Ar), 125.2 (CH–Ar), 124.4 (CH–Ar), 120.2 (CH–Ar), 110.8 (CH–Ar), 74.0 (C-2′), 69.4 (C-5′), 30.8 (C-3′), 25.8 (C-4′). ESI-MS: *m*/*z* (%) = 190.1 (100) $[M + H]^+$, 212.0 (16) $[M + Na]^+$. ESI-HRMS: calcd for $[C_{11}H_{11}NNaO_2]^+$, *m*/*z* = 212.0687; found, 212.0678. The obtained spectroscopic data are in accordance with those reported in the literature.[55]

*(±)-2-(Oxolan-2-yl)-1,3-benzothiazole* ***(2g)***. Prepared according to the general procedure using THF (3.24 g, 44.9 mmol, 50 equiv), 2-chlorobenzothiazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 120 h. After purification by flash chromatography ($^c$Hex/EtOAc = 12/1 → 11/1) the title compound was obtained as a yellow oil (109 mg, 0.531 mmol, 59%). $R_f$ = 0.27 ($SiO_2$, $^c$Hex/EtOAc 6:1). IR (ATR): $\tilde{\nu}$ [$cm^{-1}$] = 3061, 2978, 2950, 2873, 1520, 1456, 1437, 1312, 1063, 760, 731. $^1$H NMR, COSY (300 MHz, $CDCl_3$): $\delta$/ppm = 7.99–7.94 (m, 1H, H–Ar), 7.90–7.85 (m, 1H, H–Ar), 7.48–7.41 (m, 1H, H–Ar), 7.38–7.31 (m, 1H, H–Ar), 5.34 (dd, *J* = 7.8, 5.3 Hz, 1H, H-2′), 4.15 (dt, *J* = 8.3, 6.5 Hz, 1H, $H_a$-5′), 3.99 (dt, *J* = 8.3, 7.0 Hz, 1H, $H_b$-5′), 2.58–2.43 (m, 1H, $H_a$-3′), 2.33–2.19 (m, 1H, $H_b$-3′), 2.08–1.96 (m, 2H, H-4′). $^{13}$C NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): $\delta$/ppm = 176.4 (C-2), 153.8 ($C_q$–Ar), 134.8 ($C_q$–Ar), 126.0 (CH–Ar), 124.9 (CH–Ar), 122.9 (CH–Ar), 121.9 (CH–Ar), 78.9 (C-2′), 69.9 (C-5′), 33.5 (C-3′), 25.8 (C-4′). ESI-MS: *m*/*z* (%) = 206.1 (100) $[M + H]^+$, 228.0 (3) $[M + Na]^+$. ESI-HRMS: calcd for $[C_{11}H_{12}NOS]^+$, *m*/*z* = 206.0640; found, 206.0635. The obtained spectroscopic data are in accordance with the literature.[30]

*(±)-tert-Butyl 2-(oxolan-2-yl)-1H-benzimidazole-1-carboxylate* ***(2h)***. Prepared according to the general procedure using THF (3.24 g, 44.9 mmol, 50 equiv), *tert*-butyl 2-chloro-1*H*-benzimidazole-1-carboxylate (227 mg, 0.898 mmol, 1.0 equiv), and a reaction time of 48 h. After purification by flash chromatography ($^c$Hex/EtOAc = 6/1) the title compound was obtained as a yellow oil (173 mg, 0.600 mmol, 67%). $R_f$ = 0.15 ($SiO_2$, $^c$Hex/EtOAc 6:1). IR (ATR): $\tilde{\nu}$ [$cm^{-1}$] = 2978, 2874, 1744, 1453, 1370, 1350, 1154, 1121, 767. $^1$H NMR, COSY (400 MHz, $CDCl_3$): $\delta$/ppm = 7.93–7.87 (m, 1H, H–Ar), 7.78–7.72 (m, 1H, H–Ar), 7.35–7.28 (m, 2H, 2 × H–Ar), 5.71 (dd, *J* = 7.8, 5.1 Hz, 1H, H-2′), 4.25–4.17 (m, 1H, $H_a$-5′), 4.04–3.96 (m, 1H, $H_b$-5′), 2.51–2.40 (m, 1H, $H_a$-3′), 2.34–2.23 (m, 1H, $H_b$-3′), 2.15–1.94 (m, 2H, H-4′), 1.70 (br s, 9H, $OC(CH_3)_3$). $^{13}$C NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): $\delta$/ppm = 156.7 (C-2), 148.8 ($CO_2{}^tBu$), 142.1 ($C_q$–Ar), 133.3 ($C_q$–Ar), 124.7 (CH–Ar), 124.3 (CH–Ar), 120.4 (CH–Ar), 114.9 (CH–Ar), 85.8 ($C(CH_3)_3$), 75.3 (C-2′), 69.2 (C-5′), 31.5 (C-3′), 28.2 ($C(CH_3)_3$), 25.5 (C-4′). ESI-MS: *m*/*z* (%) = 189.0 (100) $[M - Boc + H]^+$, 233.0 (28) $[M - {}^tBu + H]^+$, 289.1 (27) $[M + H]^+$. ESI-HRMS: calcd for $[C_{16}H_{20}N_2NaO_3]^+$, *m*/*z* = 311.1372; found, 311.1382.

*(±)-2-(1-Ethoxyethyl)-1,3-benzoxazole* ***(2i)***. Prepared according to the general procedure using diethyl ether (3.34 g, 45.1 mmol, 50 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 24 h. After purification by flash chromatography ($^c$Hex/EtOAc = 30/1) the title compound was obtained as a pale yellow oil (117 mg, 0.612 mmol, 68%). $R_f$ = 0.19 ($SiO_2$, $^c$Hex/EtOAc 15:1). IR (ATR): $\tilde{\nu}$ [$cm^{-1}$] = 3059, 2980, 2936, 2896, 2872, 1568, 1455, 1320, 1241, 1179, 1114, 751. $^1$H NMR, COSY (300 MHz, $CDCl_3$): $\delta$/ppm = 7.76–7.68 (m, 1H, H–Ar), 7.58–7.50 (m, 1H, H–Ar), 7.38–7.29 (m, 2H, 2 × H–Ar), 4.76 (q, *J* = 6.7 Hz, 1H, $OCHCH_3$), 3.58 (qd, *J* = 7.0, 0.9 Hz, 2H, $OCH_2CH_3$), 1.67 (d, *J* = 6.7 Hz, 3H, $OCHCH_3$), 1.23 (t, *J* = 7.0 Hz, 3H, $OCH_2CH_3$). $^{13}$C NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): $\delta$/ppm = 166.4 (C-2), 150.9 ($C_q$–Ar), 140.9 ($C_q$–Ar), 125.3 (CH–Ar), 124.5 (CH–Ar), 120.4 (CH–Ar), 111.0 (CH–Ar), 71.5 ($OCHCH_3$), 65.5 ($OCH_2CH_3$), 19.8 ($OCHCH_3$), 15.4 ($OCH_2CH_3$). ESI-MS: *m*/*z* (%) = 146.0 (48) $[M - EtO]^+$, 192.0 (100) $[M + H]^+$, 214.0 (3) $[M + Na]^+$. The obtained spectroscopic data are in accordance with those reported in the literature.[55]

*(±)-2-(1-Methoxypropyl)-1,3-benzoxazole* ***(2m)***. Prepared according to the general procedure using methyl propyl ether (3.34 g, 45.1 mmol, 50 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 24 h. After purification by flash chromatography ($^c$Hex/EtOAc = 25/1) the title compound and its regioisomer **2n** were obtained as a pale orange oil (119 mg, 0.622 mmol, 69%) with a regioisomeric ratio of 6.25/1.00 in favor of **2m**. $R_f$ = 0.38 ($SiO_2$, $^c$Hex/EtOAc 6:1). IR (ATR): $\tilde{\nu}$ [$cm^{-1}$] = 2970, 2936, 2879, 2827, 1568, 1455, 1242, 1130, 1097, 839, 749. $^1$H NMR, COSY (300 MHz, $CDCl_3$): $\delta$/ppm = 7.77–7.69 (m, 1H, H–Ar), 7.58–7.50 (m, 1H, H–Ar), 7.38–7.29 (m, 2H, 2 × H–Ar), 4.42 (t, *J* = 6.7 Hz, 1H, $OCHCH_2$), 3.41 (s, 3H, $OCH_3$), 2.13–1.92 (m, 2H, $OCHCH_2CH_3$), 0.98 (t, *J* = 7.5 Hz, 3H, $OCHCH_2CH_3$). $^{13}$C NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): $\delta$/ppm = 165.5 (C-2), 150.9 ($C_q$–Ar), 140.8 ($C_q$–Ar), 125.3 (CH–Ar), 124.5 (CH–Ar), 120.3 (CH–Ar), 111.0 (CH–Ar), 78.8 ($OCHCH_2$), 57.9 ($OCH_3$), 27.1 ($OCHCH_2$), 9.7 ($OCHCH_2CH_3$). ESI-HRMS: calcd for $[C_{11}H_{13}NNaO_2]$, *m*/*z* = 214.0844; found, 214.0835.

*(±)-2-(Propoxymethyl)-1,3-benzoxazole* ***(2n)***. Prepared according to the general procedure using methyl propyl ether (3.34 g, 45.1 mmol, 50 equiv), 2-chlorobenzoxazole (138 mg, 0.900 mmol, 1.0 equiv), and a reaction time of 24 h. After purification by flash chromatography ($^c$Hex/EtOAc = 25/1) the title compound and its regioisomer **2m** were obtained as a pale orange oil (119 mg, 0.622 mmol, 69%) with a regioisomeric ratio of 6.25/1.00 in favor of **2m**. $R_f$ = 0.38 ($SiO_2$, $^c$Hex/EtOAc 6:1). IR (ATR): $\tilde{\nu}$ [$cm^{-1}$] = 2970, 2936, 2879, 2827, 1568, 1455, 1242, 1130, 1097, 839, 749. $^1$H NMR, COSY (300 MHz, $CDCl_3$): $\delta$/ppm = 7.77–7.69 (m, 1H, H–Ar), 7.58–7.50 (m, 1H, H–Ar), 7.38–7.29 (m, 2H, 2 × H–Ar), 4.74 (s, 2H, $OCH_2$-Azol), 3.57 (t, *J* = 6.7 Hz, 2H, $OCH_2CH_2CH_3$), 1.75–1.59 (m, 2H, $OCH_2CH_2CH_3$), 0.94 (t, *J* = 7.4 Hz, 3H, $OCH_2CH_2CH_3$). $^{13}$C NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): $\delta$/ppm = 163.1 (C-2), 151.0 ($C_q$–Ar), 141.0 ($C_q$–Ar), 125.4 (CH–Ar), 124.5 (CH–Ar), 120.3 (CH–Ar), 111.0 (CH–Ar), 73.5 ($OCH_2CH_2$), 66.5 ($OCH_2$-Azol), 22.9 ($OCH_2CH_2$), 10.5 ($OCH_2CH_2CH_3$). ESI-HRMS: calcd for $[C_{11}H_{13}NNaO_2]$: *m*/*z* = 214.0844; found, 214.0835.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00715.

NMR spectra of all compounds, detailed reports of the performed screening reactions, loading experiments and radical scavenger studies as well as precise descriptions of the used light sources. (PDF)

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### Notes

The authors declare no competing financial interest.



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