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Direct sp^3 C–H Amination of Nitrogen-Containing Benzoheterocycles Mediated by Visible-Light-Photoredox Catalysts

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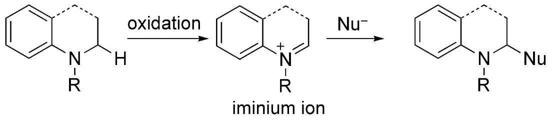
Abstract: Visible-light-mediated direct sp^3 C–H amination of benzocyclic amines via α-aminoalkyl radicals by using photoredox catalysts is described here. The obtained *N,N*-acetals were also successfully applied for carbon–carbon bond forming reactions with carbon nucleophiles. The procedure is suitable for a late-stage modification of C–H bonds to C–C bonds.

Keywords: amination • heterocycles • photocatalysts • redox chemistry

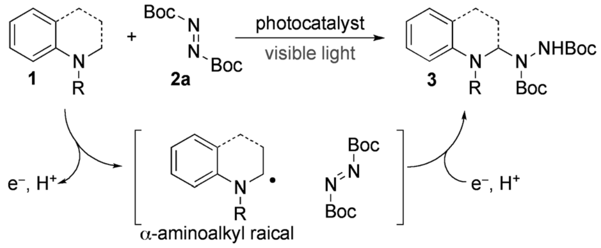
Introduction

Nitrogen-containing benzoheterocycles, such as 1,2,3,4-tetrahydroquinolines and indolines, are common and important structural motifs in biologically active natural compounds and pharmaceutical products,[1] and thus the development of efficient synthetic strategies to construct these skeletons is highly important. Direct functionalization of an sp^3 C–H bond adjacent to the nitrogen atom is expected to be a suitable route for a late-stage modification of nitrogen-containing benzoheterocycles. Consequently, the oxidation of amines to iminium ions and the subsequent addition of nucleophiles are extensively studied as an efficient method for C–H functionalization (Scheme 1).[2,3] In most of the reported systems that proceed via iminium ions,[2a] reactions of 1,2,3,4-tetrahydroisoquinolines, methylamines, and glycine derivatives that form non-enolizable iminium ions have been developed so far, but successful transformations of 1,2,3,4-tetrahydroquinolines and indolines are quite limited[4,5] because undesirable reactions such as tautomerization of iminium ions into enamines[6] and aromatization in the presence of stoichiometric oxidants[7] are considered to inhibit the reaction of iminium ions with nucleophiles.



Scheme 1. sp^3 C–H functionalization of benzocyclic amines by oxidation into an iminium ion.

Recently, we reported visible-light-mediated direct α-alkylation of amines[8] in which the formation of α-aminoalkyl radicals meditated by photoredox catalysts is a key step,[9–13] and this C–H functionalization via α-aminoalkyl radicals provides an alternative approach to routes via iminium ions. It is also worth noting that this reaction system is applicable to the α-alkylation of indolines.[8] As an extension of our study, we have now envisaged visible-light-mediated addition of α-aminoalkyl radicals to azodicarboxylate esters to give C–N bond formation at the α-position. In fact, we have succeeded in the direct α-C–H amination of 1,2,3,4-tetrahydroquinolines and indolines to give *N,N*-acetals, which were applied to further transformations to give functionalized benzocyclic amines (Scheme 2). To the best of our knowledge, there is no report of direct α-C–H amination of 1,2,3,4-tetrahydroquinolines and indolines, although the formation of C–C and C–O bonds at the α-position of these structures has been reported.[4,5] For decades it has been known that heating tertiary amines with azodicarboxylate esters gives α-aminated products via triazine intermediates, but applicable substrates are still limited and there is no report for diarylamines, including *N*-aryl-1,2,3,4-tetrahydroquinolines and *N*-arylindolines.[6b,14,15] Preliminary results are described herein.



Scheme 2. Photochemical sp^3 C–H amination of benzocyclic amines with azodicarboxylate esters (this work).

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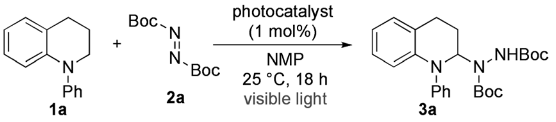
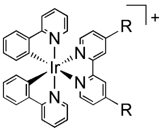
Results and Discussion

First, we investigated the reaction of *N*-phenyl-1,2,3,4-tetrahydroquinoline (**1a**) with di-*tert*-butyl azodicarboxylate (**2a**). When a solution of **1a** and two equivalents of **2a** in the presence of 1 mol% of [**4a**][BF$_4$] in *N*-methylpyrrolidone (NMP) was illuminated with a 14 W white LED at 25 °C for 18 h, *N*-phenyl-2-(1,2-di-*tert*-butoxycarbonylhydrazino)-1,2,3,4-tetrahydroquinoline (**3a**) was obtained in 45% yield (Table 1, entry 1). Use of a larger amount of **2a** increased the yield of **3a**, and the best result (85% yield) was obtained when four equivalents of **2a** was used (Table 1, entries 2 and 3). When other photocatalysts, such as [**4b**][BF$_4$], [**4c**][BF$_4$], and [Ru(bpy)$_3$][BF$_4$], were used in place of [**4a**][BF$_4$], **3a** was obtained in slightly lower yields (Table 1, entries 4–6), whereas the use of 9,10-dicyanoanthracene (DCA) dramatically decreased the yield of **3a** (Table 1, entry 7). The reaction did not proceed at all in the absence of photocatalyst or in the absence of light (Table 1, entries 8 and 9). Separately, we confirmed that the use of heating conditions (at 80 °C)[6b,15] was not effective for the reaction of **1a** with **2a** (Table 1, entry 10).

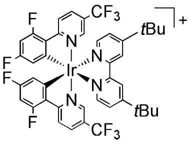
Table 1. Photochemical reactions of *N*-phenyl-1,2,3,4-tetrahydroquinoline (**1a**) with di-*tert*-butyl azodicarboxylate (**2a**).[a]



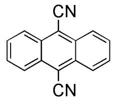
Entry	**2a** [equiv]	Photocatalyst	Yield of **3a** [%]
1	2	[**4a**][BF$_4$]	45
2	3	[**4a**][BF$_4$]	72
3	4	[**4a**][BF$_4$]	85
4	4	[**4b**][BF$_4$]	79
5	4	[**4c**][BF$_4$]	72
6	4	[Ru(bpy)$_3$][BF$_4$]	66
7	4	DCA	24
8	4	none	0
9[b]	4	[**4a**][BF$_4$]	0
10[b,c]	4	none	28



4a: R = *t*Bu
4b: R = H



4c

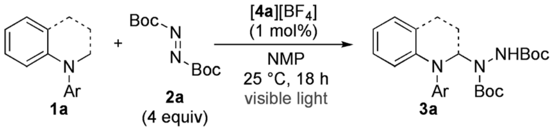


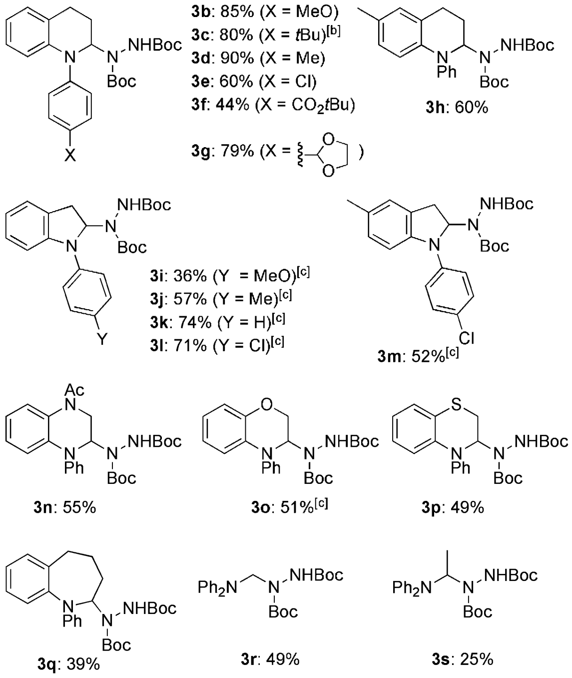
DCA

[a] All reactions of **1a** (0.25 mmol) with **2a** were carried out in the presence of photocatalyst (0.0025 mmol) in NMP (2.5 mL) with 14 W white LED illumination at 25 °C for 18 h. [b] In the absence of light. [c] At 80 °C.

Next we investigated reactions of various amines (**1**) with **2a** (Table 2). The introduction of a variety of functional groups at the *para*-position in the benzene ring of *N*-phenyl-1,2,3,4-tetrahydroquinoline was successful and the corresponding aminated products (**3b**–**h**) were obtained in good to high yields. A variety of indolines were also applicable to this reaction system, giving α-aminated indolines (**3i**–**m**) in good yields. Reactions of other six-membered benzocyclic amines, such as 1,2,3,4-tetrahydroquinoxaline, 3,4-dihydro-2*H*-1,4-benzoxazine, and 3,4-dihydro-2*H*-benzo-1,4-thiazine derivatives, proceeded smoothly to give **3n**–**p** in moderate yields. When seven-membered benzocyclic amine was used as a substrate, **3q** was also obtained in 39% yield. Unfortunately, reactions of acyclic amines were sluggish and the yields of **3r** and **3s** were relatively low.[16] On the other hand, in reactions of dialkyl amines, such as *N*-phenyl-1,2,3,4-tetrahydroisoquinoline, *N*-phenylmorphorine, and *N*-isopropyl-1,2,3,4-tetrahydroquinoline, only trace amounts of α-aminated products were observed. These results are in sharp contrast to reactions of dialkyl and trialkyl amines with azodicarboxylate esters under thermal conditions,[6b,15] and thus the photochemical reaction described here is considered to be a complementary method to the reported thermal reactions.

Table 2. Photochemical reactions of amines (**1a**) with di-*tert*-butyl azodicarboxylate (**2a**).[a]



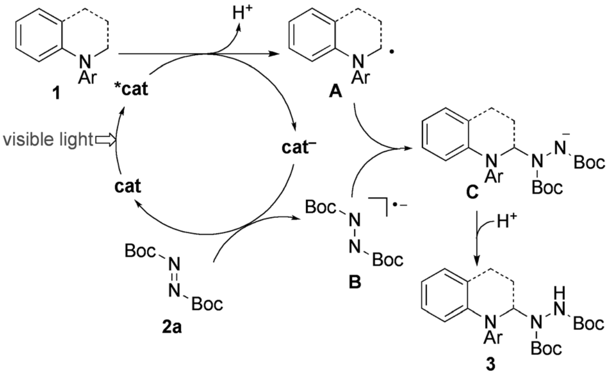


3b: 85% (X = MeO)
3c: 80% (X = *t*Bu)[b]
3d: 90% (X = Me)
3e: 60% (X = Cl)
3f: 44% (X = CO$_2$*t*Bu)
3g: 79% (X = 1,3-dioxolan-2-yl)
3h: 60%
3i: 36% (Y = MeO)[c]
3j: 57% (Y = Me)[c]
3k: 74% (Y = H)[c]
3l: 71% (Y = Cl)[c]
3m: 52%[c]
3n: 55%
3o: 51%[c]
3p: 49%
3q: 39%
3r: 49%
3s: 25%

[a] All reactions of **1a** (0.25 mmol) with **2a** (4 equiv) were carried out in the presence of photocatalyst) 0.0025 mmol) in NMP (2.5 mL) at 25 °C and under illumination with a 14 W white LED for 18 h. [b] 3 equiv of **2a** was used. [c] 5 equiv of **2a** was used.

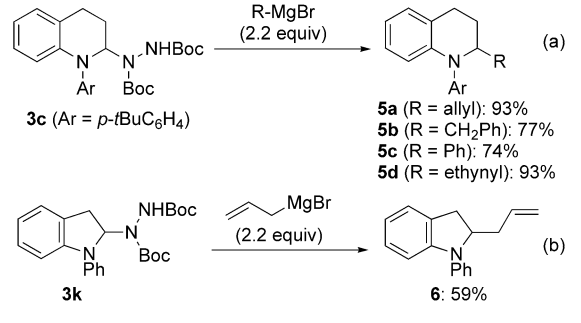
Considering the redox potential of amines[17] and azodicarboxylate esters,[18] both oxidation of amines and reduction of azodicarboxylate esters by excited photocatalyst[19] are possible. To obtain mechanistic insight into the electron-transfer process, we investigated fluorescence quenching studies of **4a** in the presence of **1a** or **2a** in NMP. The rate constants for **1a** and **2a** were estimated to be $9.07\times10^{8}\,\mathrm{M}^{-1}\mathrm{s}^{-1}$ and $6.35\times10^{8}\,\mathrm{M}^{-1}\mathrm{s}^{-1}$, respectively, by using the Stern–Volmer plot. These results indicate that both electron-transfer processes certainly occur and the oxidation of amines is slightly faster than the reduction of azodicarboxylate esters. Additionally, the quantum yield in the reaction of **1a** with **2a** was estimated to be 0.27, which is less than 1 and is within the usual range of molecular transformations by photoinduced electron transfer mediated by transition-metal polypyridyl complexes.[8,20]

Accordingly, a plausible reaction pathway is shown in Scheme 3. First, oxidation of amine (**1**) by the excited photocatalyst (***cat**) and deprotonation occur to give the reduced form of photocatalyst (**cat**$^-$) and α-aminoalkyl radical (**A**). Subsequent reduction of the azodicarboxylate ester (**2a**) by **cat**$^-$ affords radical anion (**B**). After the radical–radical coupling of **A** with **B** to give **C**,[10,21] protonation of **C** leads to the α-aminated product (**3**). On the other hand, the reaction pathway involving the direct addition of **A** to **2a**[15a,22] and subsequent reduction into **C**, similar to that described in our previous reports,[8] is also possible.

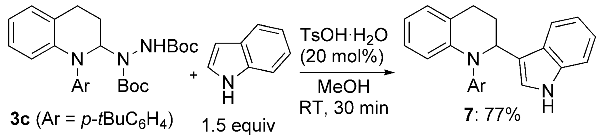


Scheme 3. A plausible reaction pathway.

N,*N*-Acetals are useful building blocks for nitrogen-containing compounds because of their high reactivity toward nucleophilic substitution reactions at the α-position.[14,23] We applied the obtained *N*,*N*-acetals **3** for nucleophilic substitution reactions with various carbon-centered nucleophiles (Schemes 4 and 5). A variety of Grignard reagents were applicable as nucleophiles (Scheme 4). The use of allyl-, benzyl-, phenyl- and ethynyl-magnesium bromides as sp^3-, sp^2-, and sp-carbon-centered nucleophiles gave **5a**–**d** in high yields (Scheme 4a). The reaction of indoline derivative **3k** with allylmagnesium bromide was also successful to give **6** in 59 % yield (Scheme 4b). It is worth noting that Grignard reagents were successfully applied as nucleophiles because Grignard reagents are usually difficult to use under oxidative reaction conditions. Interestingly, reaction of **3c** with indole in the presence of a catalytic amount of TsOH also proceeded smoothly to give **7** in 77 % yield (Scheme 5). On the other hand, when the reaction of *N*-(4-*tert*-butylphenyl)-1,2,3,4-tetrahydroquinoline (**1c**) with indole in the presence of a catalytic amount of CuBr was carried out under oxidative reaction conditions, unidentified products were observed without the formation of **7**.[24] This result is in sharp contrast to the reported reactions of tetrahydroisoquinolines, which form non-enolizable iminium ions with indoles to give the coupling products in high yields under similar conditions.[25] From these results, we believe that the obtained *N*,*N*-acetals from our procedure are useful building blocks for the synthesis of α-functionalized amines. In addition, the combination of photochemical sp^3 C–H amination of **1** (Tables 1 and 2) and the substitution reactions of **3** with carbon-centered nucleophiles (Schemes 4 and 5) is considered to be a formal transformation of the sp^3 C–H bond of amines into a C–C bond, and is an alternative method for oxidative transformations of amines via iminium ions (Scheme 1).



Scheme 4. Reactions of **3c** and **3k** with Grignard reagents.



Scheme 5. Reaction of **3c** with indole.

Conclusion

In summary, we have developed a visible-light-mediated direct sp^3 C–H amination of benzocyclic amines via α-aminoalkyl radicals, which is still a challenging task in synthetic organic chemistry.[26] The procedure of sp^3 C–H amination and nucleophilic substitution described in this article is suitable for a late-stage modification of nitrogen-containing heterocycles. Further applications of the method to the synthesis of nitrogen-containing organic compounds are now under investigation.

Experimental Section

General method: ^{1}H NMR (270 MHz) and ^{13}C NMR (67.8 MHz) spectra were recorded in a suitable solvent by using a JEOL Excalibur 270 spectrometer. Mass spectra were measured on a JEOL JMS-700 mass spectrometer. Absorption and emission spectra were recorded by using Shimadzu MultiSpec-1500 and Shimadzu RF-5300PC spectrometers, respectively. Excited-state lifetimes were measured by using a Hamamatsu Quantaurus-Tau C11367 instrument. All reactions were carried out under a dry nitrogen atmosphere. Solvents were dried by using general methods and degassed before use. Photoirradiation was carried out by using 14 W white LED. Amines (**1**) were prepared from the reaction of corresponding secondary amines with aryl halides.[27] Photocatalysts (**4a–c**) were prepared according to reported procedures.[8b] Note that only observed signals are described for ^{13}C NMR spectroscopic data because several signals are not observed due to significant broadening even at elevated temperature.

General procedure for photocatalytic reactions of amines (1) with azodicarboxylate esters (2a): A typical experimental procedure for the reaction of *N*-phenyl-1,2,3,4-tetrahydroquinoline (**1a**) with di-*tert*-butyl azodicarboxylate (**2a**) is described below. A mixture of [**4a**][BF_4] (2.1 mg, 0.0025 mmol), **2a** (229.8 mg, 0.998 mmol), and *N*-methylpyrrolidone (2.5 mL) was placed in a 20 mL Schlenk flask (diameter: 2.5 cm) under N_2, and then **1a** (52.2 mg, 0.249 mmol) was added. The reaction flask was placed in a water bath (25 °C) and illuminated by using a 14 W white LED (approximately 2 cm from the light source) for 18 h. The resulting mixture was purified by using column chromatography (SiO_2) with hexane/ethyl acetate (20:1 to 10:1) as the eluent to give *N*-phenyl-2-(1,2-di-*tert*-butoxycarbonylhydrazino)-1,2,3,4-tetrahydroquinoline (**3a**; 93.1 mg, 0.212 mmol, 85 % isolated yield).

Data for ***3a***: White solid. M.p.: 127.6–129.1 °C; ^{1}H NMR (C_6D_6, 70 °C): δ = 7.13–7.07 (m, 4H), 6.97–6.83 (m, 3H), 6.73–6.67 (m, 1H), 6.60–6.57 (m, 1H), 6.07 (brs, 1H), 5.90 (brs, 1H), 2.79 (brs, 1H), 2.64–2.54 (brm, 1H), 2.42 (brs, 1H), 2.18–2.06 (brm, 1H), 1.37 (s, 9H), 1.30 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 154.2, 129.8, 128.6, 126.9, 119.3, 80.8, 80.6, 28.2, 28.1, 25.3 ppm; HRMS (FAB): *m/z* calcd for $C_{25}H_{34}N_3O_4$: 440.2549 [M+H]; found: 440.2546.

Data for ***3b***: White solid (yield: 85 %). M.p.: 141.8–142.4 °C; ^{1}H NMR (C_6D_6, 70 °C): δ = 7.03–7.00 (m, 2H), 6.94–6.86 (m, 2H), 6.75–6.65 (m, 3H), 6.49–6.46 (m, 1H), 6.01 (brs, 2H), 3.37 (s, 3H), 2.92–2.81 (brm, 1H), 2.74–2.63 (brm, 1H), 2.54–2.45 (brm, 1H), 2.20–2.08 (brm, 1H), 1.41 (s, 9H), 1.27 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 154.3, 128.7, 127.0, 118.5, 115.5, 80.8, 80.6, 55.0, 28.3, 28.1, 27.7 ppm; elemental analysis calcd (%) for $C_{26}H_{35}N_3O_5$: C 66.50, H 7.51, N 8.95; found: C 66.30, H 7.64, N 8.74.

Data for ***3c***: White solid (yield: 80 %). M.p.: 180.6 °C (decomp.); ^{1}H NMR (CD_2Cl_2, 25 °C): δ = 7.44–7.41 (m, 2H), 7.17–7.14 (m, 2H), 7.03–7.00 (m, 1H), 6.90–6.85 (m, 1H), 6.68–6.63 (m, 1H), 6.36–5.70 (brm, 3H), 2.85 (brs, 2H), 2.38–2.01 (brm, 2H), 1.44 (s, 9H), 1.33 (s, 9H), 1.23 ppm (s, 9H); ^{13}C NMR (CD_2Cl_2, 25 °C): δ = 128.0, 126.4, 126.2, 34.1, 30.8, 27.6, 27.4, 22.3 ppm; HRMS (FAB): *m/z* calcd for $C_{29}H_{41}N_3O_4$: 495.3097 [M]; found: 495.3078.

Data for ***3d***: White solid (yield: 90 %). M.p.: 129.3–131.2 °C; ^{1}H NMR (C_6D_6, 70 °C): δ = 7.05–7.02 (brm, 2H), 6.94–6.84 (brm, 4H), 6.72–6.66 (m, 1H), 6.57–6.54 (brm, 1H), 6.05 (brs, 1H), 5.94 (brs, 1H), 2.89–2.78 (brm, 1H), 2.69–2.58 (brm, 1H), 2.50–2.43 (brm, 1H), 2.19–2.06 (brm, 1H), 2.11 (s, 3H), 1.38 (s, 9H), 1.28 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 154.2, 130.6, 128.7, 126.9, 118.9, 80.6, 28.2, 28.1, 20.8 ppm; HRMS (FAB); *m/z* calcd for $C_{26}H_{35}N_3O_4$: 453.2628 [M]; found: 453.2645.

Data for ***3e***: White solid (yield 60 %). M.p. 138.2–139.5 °C; ^{1}H NMR (C_6D_6, 70 °C): δ = 7.08–7.04 (m, 2H), 6.94–6.85 (brm, 4H), 6.74–6.68 (m, 1H), 6.53–6.51 (brm, 1H), 5.94 (brs, 1H), 5.81 (brs, 1H), 2.68 (brs, 1H), 2.57–2.27 (brm, 1H), 2.33 (brs, 1H), 2.13–2.00 (brm, 1H), 1.35 (s, 9H), 1.30 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 154.1, 129.9, 128.6, 127.0, 81.1, 80.7, 28.2, 28.1, 25.2 ppm; HRMS (FAB): *m/z* calcd for $C_{25}H_{32}N_3O_4Cl$: 473.2081 [M]; found: 473.2100.

Data for ***3f***: Viscous oil (yield: 44 %). ^{1}H NMR (C_6D_6, 70 °C): δ = 8.07–8.04 (brm, 2H), 7.20 (brs, 2H), 6.93–6.89 (brm, 3H), 6.80–6.74 (brm, 1H), 6.09 (brs, 1H), 5.77 (brs, 1H), 2.53 (brs, 1H), 2.42–2.06 (brm, 3H), 1.50 (s, 9H), 1.37 (s, 9H), 1.30 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 165.4, 155.5, 154.1, 131.3, 126.9, 121.5, 81.3, 80.5, 80.0, 28.3, 28.17, 28.16, 25.1 ppm; HRMS (FAB): *m/z* calcd for $C_{30}H_{42}N_3O_6$: 540.3074 [M+H]; found: 540.3065.

Data for ***3g***: Viscous oil (yield: 79 %). ^{1}H NMR (C_6D_6, 70 °C): δ = 7.47–7.42 (m, 2H), 7.17–7.15 (brm, 2H), 6.93–6.83 (m, 2H), 6.74–6.60 (brm, 2H), 6.06 (brs, 1H), 5.94 (brs, 1H), 5.74 (s, 1H), 3.75–3.63 (m, 2H), 3.59–3.51 (m, 2H), 2.73 (brs, 1H), 2.61–2.51 (brm, 1H), 2.39 (brs, 1H), 2.18–2.06 (brm, 1H), 1.36 (s, 9H), 1.31 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 128.2, 127.0, 103.8, 80.5, 65.2, 28.2, 28.1 ppm; HRMS (FAB): *m/z* calcd for $C_{28}H_{37}N_3O_6$: 511.2682 [M]; found: 511.2663.

Data for ***3h***: White solid (yield: 60 %). M.p.: 178.6 °C (decomp.); ^{1}H NMR (C_6D_6, 70 °C): δ = 7.16–7.08 (brm, 4H), 6.94–6.89 (brm, 1H), 6.73–6.69 (brm, 2H), 6.61–6.58 (brm, 1H), 6.09 (brs, 1H), 6.87 (brs, 1H), 2.70 (brs, 1H), 2.60–2.43 (brm, 2H), 2.21–2.11 (brm, 1H), 2.13 (s, 3H), 1.36 (s, 9H), 1.33 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 28.2, 28.1, 20.5 ppm; HRMS (FAB): *m/z* calcd for $C_{26}H_{36}N_3O_4$: 454.2706 [M+H]; found: 454.2689.

Data for ***3i***: Viscous oil (yield: 36 %). ^{1}H NMR (C_6D_6, 70 °C): δ = 7.24–7.15 (brm, 2H), 6.98–6.95 (brm, 2H), 6.93–6.66 (brm, 4H), 6.47 (brs, 1H), 5.91 (brs, 1H), 3.52–3.35 (brm, 1H), 3.38 (s, 3H), 3.21–3.11 (brm, 1H), 1.33 (s, 9H), 1.32 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 124.6, 119.0, 115.2, 107.9, 55.1, 28.13, 28.07 ppm; HRMS (FAB): *m/z* calcd for $C_{25}H_{33}N_3O_5$: 455.2420 [M]; found: 455.2437.

Data for ***3j***: Viscous oil (yield: 57 %). ^{1}H NMR (C_6D_6, 70 °C): δ = 7.22–7.16 (brm, 2H), 6.98–6.93 (brm, 4H), 6.83–6.80 (brm, 1H), 6.71–6.66 (brm, 1H), 6.50 (brs, 1H), 5.82 (brs, 1H), 3.52–3.45 (brm, 1H), 3.18–3.08 (brm, 1H), 2.13 (s, 3H), 1.34 (s, 9H), 1.30 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 130.2, 124.6, 119.3, 28.1, 20.8 ppm; HRMS (FAB): *m/z* calcd for $C_{25}H_{34}N_3O_4$: 440.2549 [M+H]; found: 440.2550.

Data for ***3k***: Viscous oil (yield: 74 %). ^{1}H NMR (C_6D_6, 70 °C): δ = 7.31–7.28 (brm, 2H), 7.18–7.12 (brm, 2H), 6.96–6.83 (brm, 4H), 6.72–6.66 (brm, 1H), 6.50 (brs, 1H), 5.78 (brs, 1H), 3.43 (brs, 1H), 3.16–3.06 (brm, 1H), 1.34 (s, 9H), 1.29 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 129.6, 127.2, 124.7, 119.6, 108.6, 28.11, 28.10 ppm; HRMS (FAB): *m/z* calcd for $C_{24}H_{32}N_3O_4$: 426.2393 [M+H]; found: 426.2414.

Data for ***3l***: Viscous oil (yield: 71 %). ^{1}H NMR (C_6D_6, 70 °C): δ = 7.16–6.91 (brm, 6H), 6.75–6.66 (brm, 2H), 6.36 (brs, 1H), 5.70 (brs, 1H), 3.36 (brs, 1H), 3.11–3.01 (brm, 1H), 1.33 (s, 9H), 1.28 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 129.6, 124.7, 119.9, 28.1 ppm; HRMS (FAB): *m/z* calcd for $C_{24}H_{31}N_3O_4Cl$: 460.2003 [M+H]; found: 460.1995.

Data for ***3m***: Viscous oil (yield: 52 %). ^{1}H NMR (C_6D_6, 70 °C): δ = 7.16–6.99 (brm, 4H), 6.78–6.72 (brm, 3H), 6.37 (brs, 1H), 5.70 (brs, 1H), 3.36 (brs, 1H), 3.12–3.02 (brm, 1H), 2.14 (s, 3H), 1.36 (s, 9H), 1.28 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 129.6, 129.1, 125.7, 28.11, 28.07 ppm; HRMS (FAB): *m/z* calcd for $C_{25}H_{32}N_3O_4Cl$: 473.2081 [M]; found: 473.2099.

Data for ***3n***: Viscous oil (yield: 55 %). ^{1}H NMR (C_6D_6, 70 °C): δ = 7.20–7.11 (brm, 5H), 7.01–6.96 (brm, 1H), 6.77–6.71 (brm, 1H), 6.64–6.59 (brm, 2H), 6.14 (brs, 1H), 6.05 (brs, 1H), 4.42 (brs, 1H), 3.71 (brs, 1H), 2.1 (s, 3H), 1.34 (s, 9H), 1.26 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 129.9, 28.2, 28.0 ppm; HRMS (FAB): *m/z* calcd for $C_{26}H_{35}N_4O_5$: 483.2607 [M+H]; found: 483.2603.

Data for ***3o***: White solid (yield: 51 %). M.p.: 110.9–112.3 °C; ^{1}H NMR (C_6D_6, 70 °C): δ = 7.20–7.08 (brm, 4H), 6.99–6.91 (brm, 2H), 6.70–6.61 (brm, 3H), 5.93 (brs, 2H), 4.48 (brs, 1H), 4.01 (brs, 1H), 1.35 (s, 9H), 1.31 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 129.8, 121.8, 112.0, 117.1, 28.2, 28.0 ppm; HRMS (FAB): *m/z* calcd for $C_{24}H_{31}N_3O_5$: 441.2264 [M]; found: 441.2260.

Data for ***3p***: White solid (yield: 49 %). M.p.: 130.1–131.8 °C; ^{1}H NMR (C_6D_6, 70 °C): δ = 7.16–7.05 (brm, 5H), 6.93–6.87 (brm, 1H), 6.77–6.72 (brm, 2H), 6.64–6.58 (brm, 1H), 6.27 (brs, 1H), 6.11 (brs, 1H), 3.27 (brs, 1H), 3.01 (brs, 1H), 1.35 (s, 9H), 1.32 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C): δ = 129.8, 126.3, 125.6, 124.9, 120.6, 81.3, 28.2, 28.1 ppm; HRMS (FAB): *m/z* calcd for $C_{24}H_{32}N_3O_4S$: 458.2114 [M+H]; found: 458.2124.

Data for ***3q***: Viscous oil (yield: 39 %). ^{1}H NMR (C_6D_6, 40 °C): δ = 7.16–6.74 (brm, 9H), 6.10 (brs, 1H), 5.76 (brs, 1H), 2.44 (brs, 1H), 2.24 (brs, 1H), 2.07 (brs, 1H), 1.62–1.27 ppm (brm, 21H); ^{13}C NMR (C_6D_6, 40 °C): δ = 28.4, 28.2 ppm; HRMS (FAB): *m/z* calcd for $C_{26}H_{35}N_3O_4$: 453.2628 [M]; found: 453.2619.

Data for ***3r***: White solid (yield: 49 %). M.p.: 141.1–143.1 °C; ^{1}H NMR (C_6D_6, 70 °C): δ = 7.14–7.06 (m, 8H), 6.88–6.81 (m, 2H), 5.87 (brs, 1H), 5.43 (brs, 2H), 1.38 (s, 9H), 1.32 ppm (s, 9H); ^{13}C NMR (C_6D_6, 50 °C):

$\delta = 147.7, 129.5, 122.3, 121.9, 28.2$ ppm; elemental analysis calcd (%) for $C_{23}H_{31}N_3O_4$: C 66.81, H 7.56, N 10.16; found: C 66.69, H 7.73, N 9.96. *Data for **3s***: Viscous oil (yield: 25%). ^{1}H NMR (C_6D_6, 70°C): $\delta = 7.15$–7.07 (m, 4H), 7.00–6.94 (brm, 4H), 6.90–6.84 (m, 2H), 6.47 (brs, 1H), 5.60 (brs, 1H), 1.45–1.27 ppm (brm, 21H); ^{13}C NMR (C_6D_6, 50°C): $\delta =$ 129.4, 123.7, 122.8, 28.3, 28.2 ppm; HRMS (FAB): m/z calcd for $C_{24}H_{33}N_3O_4$: 427.2471 [M]; found: 427.2461.

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