Iridium-Catalyzed C-3 Allylation of Indoles with Allylic Alcohols Promoted by a Brønsted Acid

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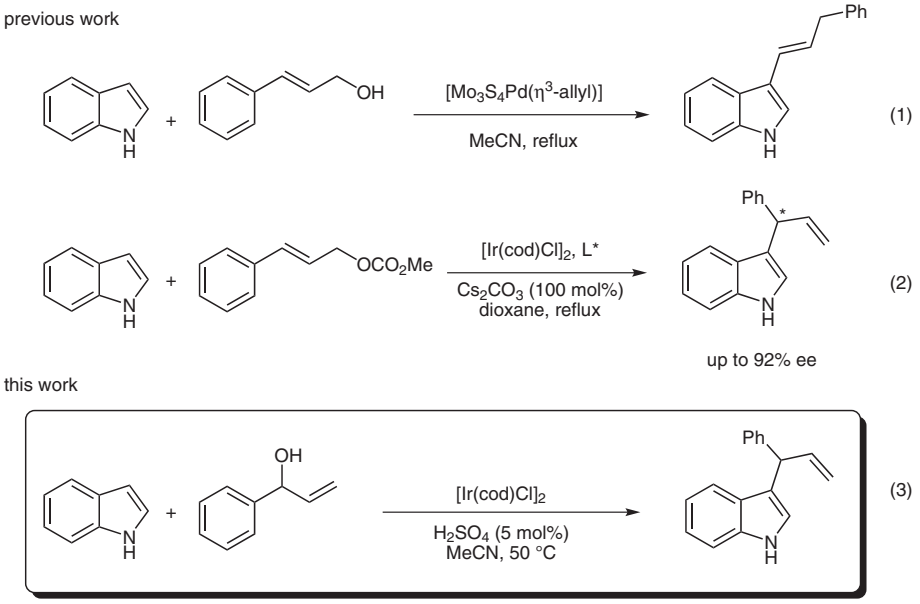
Abstract: A highly regioselective method has been developed for the allylation of indoles with an iridium catalyst. This regioselective procedure uses allylic alcohols directly as allylating agents in the presence of a catalytic amount of sulfuric acid. A wide range of indoles reacted smoothly with asymmetrical allylic alcohols to give the corresponding branched products in branched-to-linear ratios of up to 99:1 and yields as high as 92%. A series of inorganic and organic acids were tested in this approach, and it was shown that acids with pK_a values in acetonitrile of less than 15 are required in this iridium-catalyzed system.

Key words: iridium, allylations, indoles, regioselectivity, homogeneous catalysis

The indole nucleus is a versatile building block for the synthesis of a wide range of bioactive natural products and pharmaceutical agents,[1] such as the plant-growth hormone indole-3-acetic acid[2] and the nonsteroidal antiinflammatory drug indomethacin.[3] As a result, significant efforts have been devoted to the discovery of methods for the preparation of functional indoles.[4] Among these, allyl indoles represent an important group of organic intermediates, because the allyl group is capable of undergoing a range of transformations, such as hydrogenation, halogenation, or hydroformylation.[5] These useful characteristics have stimulated organic researchers to seek more efficient methods for the allylation of indoles.

In 1999, Kočovský and co-workers described the first allylation of indole with allyl acetates in the presence of a molybdenum(II) catalyst.[6] Since then, the transition-metal-catalyzed allylation of indoles has continued to attract considerable interest, and a series of protocols have been developed that use allyl carbonates or acetates in conjunction with transition-metal catalysts.[7] However, these reactions often require large amounts of base (more than one equivalent) and they involve wastage of the leaving group, the addition of which to the corresponding allylic alcohol entails an additional prior step. The direct use of allylic alcohols as allylating agents is therefore both more atom-economic and more environmentally friendly.

In 2005, Tamaru and co-workers described a palladium(0)-catalyzed C-3-selective allylation of indoles with allylic alcohols as allylating agents in the presence of tri-



Scheme 1 Regioselectivities of various transition-metal-catalyzed allylation reactions of indoles

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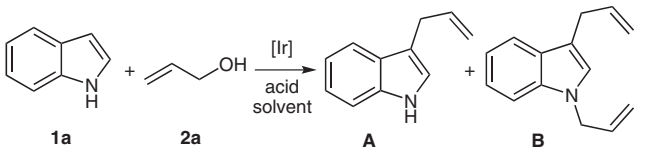
Table 1 Optimization of the Reaction Conditions



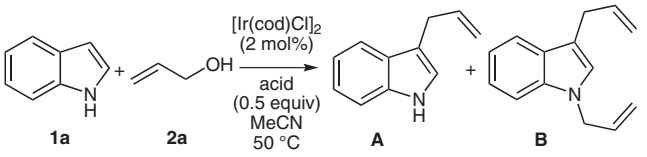
Entry[a]	Catalyst	Acid	Solvent	Yield[b] (%) of **A**	Yield[b] (%) of **B**
1	$[Ir(cod)Cl]_2$	BEt_3[c]	THF	n.d.[d]	n.d.
2	$[Ir(cod)Cl]_2$	$BF_3{\cdot}OEt_2$	THF	41	7
3	$[Ir(cod)Cl]_2$	TFA	toluene	35	8
4	$[Ir(cod)Cl]_2$	TFA	1,4-dioxane	5	0
5	$[Ir(cod)Cl]_2$	TFA	THF	16	0
6	$[Ir(cod)Cl]_2$	TFA	DMF	21	0
7	$[Ir(cod)Cl]_2$	TFA	MeCN	58	24
8[e]	$[Ir(cod)Cl]_2$	TFA	MeCN	0	93
9	$[Ir(cod)(OMe)]_2$	TFA	MeCN	53	17
10	$[Ir(cod)(OH)]_2$	TFA	MeCN	32	8
11	$IrCl_3{\cdot}H_2O$	TFA	MeCN	n.d.	n.d.
12	$[IrCp^*Cl_2]_2$[f]	TFA	MeCN	n.d.	n.d.
13	$[Ir(coe)_2Cl]_2$[f]	TFA	MeCN	7	0
14	$[Ir(cod)_2Cl]_2$	H_2SO_4[g]	MeCN	60	21
15	$[Ir(cod)_2Cl]_2$	–	MeCN	n.d.	n.d.
16	–	TFA	MeCN	n.d.	n.d.

[a] Reaction conditions: indole (**1a**; 0.2 mmol), allylic alcohol **2a** (0.2 mmol), Ir catalyst (2 mol%), acid (0.5 equiv), solvent (1 mL), 50 °C, 15 h.
[b] By GC.
[c] 1 M solution in THF.
[d] n.d. = not detected.
[e] 3 equiv of **2a** were used.
[f] Cp^* = 1,2,3,4,5-pentamethylcyclopenta-1,3-diene; coe = cyclooctene.
[g] 5 mol% H_2SO_4 (1 M in H_2O).

ethylborane (30 mol%).[8] In this protocol, triethylborane acts as a Lewis acid, coordinating to the hydroxy group to activate the allylic alcohol. Pregosin and co-workers have reported a series of ruthenium catalysts for the allylation of indoles with allylic alcohols as allylating agents.[9] In addition, enantioselective gold-catalyzed intramolecular allylic alkylations of indoles with alcohols have been reported by Bandini and co-workers.[10] Recently, You and co-workers developed a ruthenium-catalyzed intermolecular dearomatization reaction of indoles with allylic alcohols in the presence of *p*-toluenesulfonic acid monohydrate.[11] Relevant researches have concentrated mainly on the transition metals palladium, ruthenium, and gold.[12] In 2008, You and co-workers reported the first iridium-catalyzed regio- and enantioselective Friedel–Crafts-type allylic alkylation of indoles with allylic carbonates as the allylating agents and a chiral phosphoramidite as a ligand (Scheme 1, equation 2).[13] This catalytic system showed a high enantioselectivity (ee ≤ 92%) and a different regioselectivity from that obtained by the palladium-based approach (Scheme 1, equation 1).[14] However, there are few reports on iridium-catalyzed allylations of indoles with allylic alcohols as allylating agents.[15] Inspired by the pioneering work of Carreira and co-workers on iridium-catalyzed asymmetric allylic substitution reactions with branched allylic alcohols as allylic precursors,[16] we have developed a simple and highly regioselective method for the allylation of indoles with allylic alcohols in the presence of a catalytic amount of sulfuric acid (Scheme 1, equation 3).

We began by studying the reaction of indole (**1a**; 0.2 mmol) with allylic alcohol (**2a**; 0.2 mmol), as model substrates in tetrahydrofuran containing dichlorobis(cyclooctadiene)diiridium (2 mol%) and triethylborane (0.5 equiv) at 50 °C for 15 hours. Unfortunately, the triethylborane failed to activate the allylic alcohol in this iridium-catalyzed system, and no allylation product **A** or **B** was obtained (Table 1, entry 1). In the presence of the stronger Lewis acid boron trifluoride etherate ($BF_3{\cdot}Et_2O$), the reaction proceeded with a moderate yield (entry 2). When the reaction was performed in the presence of trifluoroacetic acid (0.5 equiv) in toluene at 50 °C for 15 hours, the allylation products **A** and **B** were obtained as a 35:8 mixture

Table 2 The Effect of the Acid on the Reaction



Entry[a]	Acid	pK_a[b]	Yield[c] (%) of **A** + **B**	**A**/**B**
1	H_2SO_4[d]	7.20	80	56:24
2	TsOH	8.45	78	55:23
3	HCl[d]	8.90	82	52:30
4	MsOH	9.97	77	59:18
5	TFA	12.65	81	58:23
6	oxalic acid dihydrate	14.50	71	57:14
7	$H_2OCCH_2CO_2H$	15.30	19	19:0
8	$2\text{-}HOC_6H_4CO_2H$	16.70	n.d.[e]	–
9	$2\text{-}ClC_6H_4CO_2H$	19.00	n.d.	-

[a] Reaction conditions: indole (**1a**; 0.2 mmol), allylic alcohol **2a** (0.2 mmol), $[Ir(cod)Cl]_2$ (2 mol%), acid (0.5 equiv), MeCN (1 mL), 50 °C, 5 h.
[b] In MeCN.[17]
[c] By GC.
[d] 1 M aq soln.
[e] n.d. = not detected.

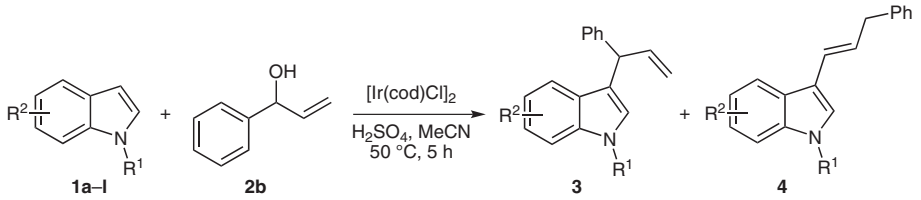
in a total yield of 43% (entry 3). Rapid screening of the solvent (entries 4–7) showed that acetonitrile was suitable for this reaction, giving the major product, the 3-substituted allylic compound **A**, in 58% yield, together with a 24% yield of the double allylation product **B** as a minor product (entry 7). By using an excess of the allylic alcohol **2a**, the double allylation product **B** was obtained exclusively in 93% yield (entry 8).

The allylation of indole (**1a**) with bis(cyclooctadiene)dimethoxyiridium as catalyst proceeded in a slightly low yield of 70% (entry 9), and this yield decreased further when bis(cyclooctadiene)dihydroxyiridium was used as the catalyst (entry 10). Neither allylation product **A** or **B** was formed when iridium(III) chloride monohydrate or tetrachlorobis(η^5-1,2,3,4,5-pentamethylcyclopenta-1,3-diene)diiridium was used as the catalyst (entries 11 and 12). dichlorobis(cyclooctene)iridium also showed a low catalytic activity in this reaction (entry 13). However, when the strong Brønsted acid sulfuric acid was used as a 1 M aqueous solution, a catalytic loading (5 mol%) was sufficient to obtain a satisfactory result (entry14). The allylation reaction failed to proceed in the absence of either the iridium catalyst or the acid (entries 15 and 16).

Next, we examined a series of acids to investigate their effect on the reaction, and we found that the yield of the reaction was related to the pK_a of the acid in acetonitrile (Table 2). When the pK_a value was more than 15, the yield decreased dramatically. In particular, the reaction proceeded smoothly and efficiently when an inorganic acid such as sulfuric acid or hydrochloric acid was used. We therefore inferred that the allylic alcohol is activated by protons dissociating from the Brønsted acid and subsequently coordinates with the metal to form an iridium π-allyl intermediate that participates in electrophilic substitution of the indole to form the products.

To test the regioselectivity of the protocol, we examined the reaction of the asymmetric allylic alcohol **2b** with indole (**1a**). The reaction regioselectively gave the branched products **3a** and **4a** in 90% yield and ratios as high as 99:1 (Table 3, entry 1). We then tested the generality of the reaction by treating a series of substituted indoles **1b**–**l** with allylic alcohol **2b** (entries 2–12). The protocol had a wide tolerance to various substituents; indoles carrying an electron-donating or electron-withdrawing substituent at the C-2, C-4, or C-5 position all reacted well with **2b** (entries 2–8). It was noteworthy that the iridium-catalyzed system was also active in allylation of the N-substituted indoles **1i**–**k**, giving the corresponding C-3 allylation product **3i**–**k** in 61–87% yield (entries 9–11). When the N-position of the indole was locked by a strongly electron-withdrawing tosyl substituent, the nucleophilic ability of the C-3

Table 3 Iridium-Catalyzed C-3 Allylation of Indoles **1a**–**l** with Allylic Alcohol **2b**



Entry[a]	R^1	R^2	Reactant	Product	Ratio[b] **3**/**4**	Yield[c] (%) of **3**
1	H	H	**1a**	**3a**	99:1	90
2	H	4-MeO	**1b**	**3b**	98:2	87
3	H	5-F	**1c**	**3c**	99:1	84
4	H	5-Br	**1d**	**3d**	99:1	92
5	H	5-MeO	**1e**	**3e**	97:3	85
6	H	5-Me	**1f**	**3f**	98:2	86
7	H	2-Me	**1g**	**3g**	97:3	83
8	H	2-Ph	**1h**	**3h**	99:1	86
9	Me	H	**1i**	**3i**	99:1	87
10	Ph	H	**1j**	**3j**	97:3	61
11	Bn	H	**1k**	**3k**	98:2	89
12	Ts	H	**1l**	**3l**	–	n.d.

[a] Reaction conditions: indole **1** (0.2 mmol), allylic alcohol **2b** (0.2 mmol), $[Ir(cod)Cl]_2$ (2 mol%), 1 M aq H_2SO_4 (5 mol%), MeCN (1 mL), 50 °C, 5 h.
[b] By ^{1}H NMR analysis of the crude mixture.
[c] Isolated yield.

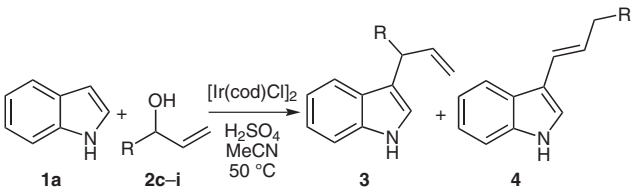
position appeared to be seriously weakened, and none of the desired product was formed (entry 12). These results show that the mechanism of this iridium-catalyzed reaction differs from that of many palladium/base-catalyzed allylation reactions, which frequently required the presence of a base to deprotonate the nitrogen atom to form a more nucleophilic anion.[7a]

Next, we conducted a series of experiments to investigate the scope of the reaction in relation to the allylic alcohol reactant (Table 4). The reactions of **1a** with α-aryl allylic alcohols bearing electron-donating or electron-withdrawing substituents on the aromatic ring gave the corresponding C-3 allylation indole products in moderate to good yields and high regioselectivities (entries 1–5). The reactions of allylic alcohols **2d** and **2e** required a higher catalyst loading (4 mol%), but gave the corresponding products **3n** and **3o** in 72% and 81% yield, respectively (entries 2 and 3). The 4-methyl-substituted α-aryl allylic alcohol **2g** was less reactive than the 4-trifluoromethyl derivative **2f**, giving **3p** in a moderate yield of 67% after a slightly longer reaction time (entry 5). The 1-naphthyl allylic alcohol **2h** proved to be good substrate for the reaction, giving the corresponding C-3 allylation indole **3r** in good yield and with excellent regioselectivity (entry 6). Furthermore, the aliphatic allylic alcohol **2i** was also tolerated by this system, and gave the corresponding product **3s** in a moderate yield of 53% (entry 7).

We also examined the application of the method in the asymmetric allylation of indole. We chose indole (**1a**; 0.2 mmol) and allylic alcohol **2b** (0.2 mmol) as model substrates. Initially, a chiral bisoxazoline ligand **L*** was added to the catalytic system (Scheme 2). When 5 mol% sulfuric acid was used as the additive, the alkylation product **3a** was obtained as a racemic mixture in 81% yield [Scheme 2 (a)]. Subsequently, we used the chiral Brønsted acid D-camphorsulfonic acid as the activator. The reaction gave the same product **3a** in a slightly lower yield, but the product was still racemic [Scheme 2 (b)]. These results showed that the bisoxazoline ligand is not suitable for asymmetric catalysis in this system. We are currently attempting to develop more-efficient chiral ligands for the asymmetric allylation of indoles.

In conclusion, we have developed a simple iridium-catalyzed system for the allylation of indoles. Our new approach uses used allylic alcohols directly as allylating agents, thereby avoiding the waste of a leaving group. The method tolerates a wide range of substrates. For various unsymmetrical allylic alcohols and substituted indoles, the reaction proceeded smoothly in moderate to good yields with excellent selectivity toward branched products. In addition, a series of inorganic and organic acids was tested in this approach, and it was shown that an acid with a pK_a value in acetonitrile of less than 15 is required in this iridium-catalyzed system.

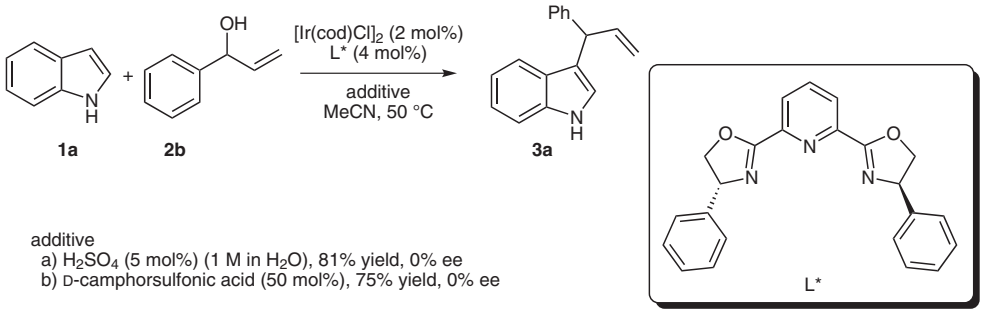
Table 4 Scope of the Reaction With Respect to the Allylic Alcohol Reactant



Entry[a]	Alcohol		Product	Ratio[b] **3**/**4**	Yield[c] (%) of **3**
1	**2c**	2-BrC_6H_4	**3m**	98:2	76
2[d]	**2d**	2-$F_3CC_6H_4$	**3n**	94:6	72
3[d]	**2e**	3-$F_3CC_6H_4$	**3o**	95:5	81
4	**2f**	4-$F_3CC_6H_4$	**3p**	97:3	87
5[e]	**2g**	4-Tol	**3q**	92:8	67
6	**2h**	1-naphthyl	**3r**	99:1	86
7	**2i**	$Ph(CH_2)_2$	**3s**	90:10	53

[a] Reaction conditions: indole (**1a**; 0.2 mmol), allylic alcohol **2** (0.2 mmol), $[Ir(cod)Cl]_2$ (2 mol%), 1 M aq H_2SO_4 (5 mol%), MeCN (1 mL), 50 °C, 5 h.
[b] By ^1H NMR analysis of the crude mixture.
[c] Isolated yield.
[d] 4 mol% $[Ir(cod)Cl]_2$ was used.
[e] Reaction time: 10 h.

All chemicals were purchased from commercial suppliers and used as received unless otherwise noted. TLC was performed on glass plates coated with silica gel; visualization was performed by UV irradiation (254 nm). Mass spectra were recorded on a Finnigan TSQ Quantum-MS instrument operated in the electrospray ionization (ESI) mode. IR spectra were recorded on a Thermo Scientific Nicolet iS10 instrument. ^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded in $CDCl_3$ on a Bruker AVANCE 500 spectrometer operat-



Scheme 2 Attempted asymmetric allylations of indole

ed at 500, 125, or 470 MHz, respectively. Chemical shifts are reported in ppm relative to TMS as an internal standard. Elemental analyses were performed on a Yanagimoto MT3CHN instrument. GC analysis were performed on an Agilent 7890A instrument (Column: Agilent 19091J-413, 30 m × 320 μm × 0.25 μm; carrier gas: H_2; FID detection).

Allylic Alcohols 2b–i; General Procedure[18]
An oven-dried round-bottomed flask was charged with a solution of the appropriate aldehyde (10 mmol, 1 equiv) in anhydrous THF (20 mL), and the mixture was stirred for 10 min under N_2 at 0 °C. A 1 M solution of vinylmagnesium bromide in THF (12 mmol, 1.2 equiv) was added slowly. After 15 min, the mixture was allowed to warm to r.t. and stirred for an additional 1–3 h. The reaction was quenched with sat. aq NH_4Cl, and the mixture was extracted with Et_2O (3 × 30 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated to give the crude allylic alcohol **2b–i**, which was used in the next step without further purification.

Allylindoles A, B, and 3a–s; General Procedure
MeCN (1 mL), allylic alcohol **2** (0.200 mmol), and 1 M aq H_2SO_4 (0.010 mmol) were successively added from a syringe to a N_2-purged flame-dried Schlenk tube containing indole **1** (0.200 mmol) and $[Ir(cod)Cl]_2$ (0.004 mmol), and the mixture was stirred at 50 °C for 5 h. When the reaction was complete, the solvent was removed under reduced pressure. The branched/linear ratio of regioisomers was then determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. Finally, the crude residue was purified by flash column chromatography [silica gel, PE–EtOAc (95:5 to 90:10)].

3-Allyl-1*H*-indole (A)[19]
Yellow oil; yield: 15.6 mg (50%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.93 (s, 1 H), 7.62 (d, *J* = 7.9 Hz, 1 H), 7.36 (d, *J* = 8.1 Hz, 1 H), 7.24–7.18 (m, 1 H), 7.16–7.10 (m, 1 H), 6.99 (s, 1 H), 6.09 (ddt, *J* = 16.6, 10.0, 6.5 Hz, 1 H), 5.18 (dq, *J* = 17.0, 1.7 Hz, 1 H), 5.09 (ddd, *J* = 10.0, 3.1, 1.4 Hz, 1 H), 3.54 (dd, *J* = 6.5, 1.1 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 136.31, 135.47, 126.47, 121.02, 120.64, 118.27, 118.11, 114.19, 113.57, 110.08, 28.83.

1,3-Diallyl-1*H*-indole (B)[19]
Yellow oil; yield: 33.8 mg (86%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64 (dd, *J* = 7.9, 3.2 Hz, 1 H), 7.37–7.29 (m, 1 H), 7.24 (ddd, *J* = 8.2, 3.1, 1.3 Hz, 1 H), 7.19–7.08 (m, 1 H), 6.99–6.86 (m, 1 H), 6.22–5.89 (m, 2 H), 5.31–5.00 (m, 4 H), 4.82–4.60 (m, 2 H), 3.68–3.42 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 136.46, 135.61, 132.70, 127.06, 124.46, 120.59, 118.26, 117.85, 116.16, 114.09, 112.39, 108.53, 47.69, 28.81.

3-(1-Phenylprop-2-en-1-yl)-1*H*-indole (3a)[13]
Yellow oil; yield: 41.8 mg (90%).

IR (neat): 3414, 3059, 1457, 917, 736, 702 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.98 (s, 1 H), 7.43 (d, *J* = 8.0 Hz, 1 H), 7.37 (d, *J* = 8.2 Hz, 1 H), 7.32 (d, *J* = 4.4 Hz, 4 H), 7.24 (dt, *J* = 8.7, 4.2 Hz, 1 H), 7.19 (t, *J* = 7.6 Hz, 1 H), 7.06 (t, *J* = 7.5 Hz, 1 H), 6.91–6.88 (m, 1 H), 6.38 (ddd, *J* = 17.1, 10.1, 7.1 Hz, 1 H), 5.22 (d, *J* = 10.1 Hz, 1 H), 5.10 (d, *J* = 17.1 Hz, 1 H), 4.99 (d, *J* = 7.1 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.22, 139.50, 135.68, 127.45, 127.36, 125.85, 125.31, 121.49, 121.09, 118.87, 118.36, 117.56, 114.48, 110.09, 45.99.

4-Methoxy-3-(1-phenylprop-2-en-1-yl)-1*H*-indole (3b)
Pale-yellow oil; yield: 45.8 mg (87%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.97 (s, 1 H), 7.28 (t, *J* = 3.9 Hz, 4 H), 7.18 (dt, *J* = 5.5, 4.1 Hz, 1 H), 7.08 (t, *J* = 8.0 Hz, 1 H), 6.96 (d, *J* = 7.9 Hz, 1 H), 6.81 (d, *J* = 2.0 Hz, 1 H), 6.45 (d, *J* = 7.7 Hz, 1 H), 6.39 (ddd, *J* = 17.0, 10.1, 6.8 Hz, 1 H), 5.42 (d, *J* = 6.8 Hz, 1 H), 5.16 (d, *J* = 10.1 Hz, 1 H), 4.98 (d, *J* = 17.1 Hz, 1 H), 3.75 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.89, 143.56, 140.84, 137.13, 127.55, 126.95, 124.70, 121.92, 120.11, 118.12, 116.10, 113.73, 103.33, 98.98, 54.02, 46.16.

MS (ESI): *m*/*z* = 264 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{17}NO$: C, 82.10; H, 6.51; N, 5.32. Found: C, 82.34; H, 6.39; N, 5.49.

5-Fluoro-3-(1-phenylprop-2-en-1-yl)-1*H*-indole (3c)
Pale-yellow oil; yield: 42.2 mg (84%).

IR (neat): 3427, 2980, 1483, 1452, 1166, 796, 698, 591 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (s, 1 H), 7.31–7.17 (m, 6 H), 7.00 (dd, *J* = 9.8, 2.0 Hz, 1 H), 6.91–6.83 (m, 2 H), 6.29 (ddd, *J* = 17.1, 10.1, 7.1 Hz, 1 H), 5.17 (d, *J* = 10.1 Hz, 1 H), 5.04 (d, *J* = 17.1 Hz, 1 H), 4.85 (d, *J* = 7.1 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.57 (d, $^1J_{C,F}$ = 233.4 Hz), 141.81, 139.11, 132.17, 127.44, 127.37, 126.18, 125.46, 123.25, 117.73, 114.71, 110.64 (d, $^3J_{C,F}$ = 9.0 Hz), 109.47 (d, $^2J_{C,F}$ = 26.4 Hz), 103.80 (d, $^2J_{C,F}$ = 23.5 Hz), 45.94.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –124.47.

MS (ESI): *m*/*z* = 252 $[M + H]^+$.

Anal. Calcd for $C_{17}H_{14}FN$: C, 81.25; H, 5.62; N, 5.57. Found: C, 81.04; H, 5.74; N, 5.70.

5-Bromo-3-(1-phenylprop-2-en-1-yl)-1*H*-indole (3d)
Pale-yellow oil; yield: 57.2 mg (92%).

IR (neat): 3421, 2922, 1453, 794, 698, 579 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.04 (s, 1 H), 7.56–7.52 (m, 1 H), 7.32 (dd, *J* = 10.0, 4.7 Hz, 2 H), 7.29–7.26 (m, 3 H), 7.23 (dd, *J* = 10.2, 3.4 Hz, 2 H), 6.88 (d, *J* = 1.7 Hz, 1 H), 6.32 (ddd, *J* = 17.1, 10.1, 7.0 Hz, 1 H), 5.22 (d, *J* = 10.1 Hz, 1 H), 5.06 (d, *J* = 17.1 Hz, 1 H), 4.91 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.68, 139.05, 134.26, 127.61, 127.45, 127.35, 125.49, 123.99, 122.73, 121.37, 117.33, 114.83, 111.69, 111.51, 45.69.

MS (ESI): *m*/*z* = 312 $[M + H]^+$.

Anal. Calcd for $C_{17}H_{14}BrN$: C, 65.40; H, 4.52; N, 4.49. Found: C, 65.56; H, 4.34; N, 4.38.

5-Methoxy-3-(1-phenylprop-2-en-1-yl)-1*H*-indole (3e)
Pale-yellow oil; yield: 44.7 mg (85%).

IR (neat): 3418, 2936, 1483, 1205, 1170, 915, 701 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.90 (s, 1 H), 7.33 (d, *J* = 4.4 Hz, 4 H), 7.26 (t, *J* = 2.0 Hz, 1 H), 7.24 (t, *J* = 2.1 Hz, 1 H), 6.91–6.81 (m, 3 H), 6.37 (ddd, *J* = 17.1, 10.1, 7.1 Hz, 1 H), 5.27–5.20 (m, 1 H), 5.11 (dt, *J* = 17.1, 1.5 Hz, 1 H), 4.94 (dd, *J* = 7.1, 0.8 Hz, 1 H), 3.77 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.78, 142.13, 139.39, 130.83, 127.46, 127.36, 126.28, 125.31, 122.33, 117.22, 114.46, 111.11, 110.74, 100.89, 54.84, 46.02.

MS (ESI): *m*/*z* = 264 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{17}NO$: C, 82.10; H, 6.51; N, 5.32. Found: C, 81.84; H, 6.37; N, 5.49.

5-Methyl-3-(1-phenylprop-2-en-1-yl)-1*H*-indole (3f)
Pale-yellow oil; yield: 42.5 mg (86%).

IR (neat): 3410, 2918, 912, 791, 703, 586 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (s, 1 H), 7.33 (d, *J* = 4.6 Hz, 4 H), 7.28–7.22 (m, 3 H), 7.03 (dd, *J* = 8.2, 1.3 Hz, 1 H), 6.84 (d, *J* = 1.8 Hz, 1 H), 6.38 (ddd, *J* = 17.1, 10.1, 7.1 Hz, 1 H), 5.25–5.20 (m, 1 H), 5.13–5.06 (m, 1 H), 4.97 (dd, *J* = 7.1, 0.7 Hz, 1 H), 2.42 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.29, 139.60, 133.99, 127.58, 127.46, 127.34, 126.10, 125.26, 122.73, 121.67, 118.37, 117.00, 114.41, 109.76, 45.88, 20.55.

MS (ESI): *m*/*z* = 248 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found: C, 87.54; H, 6.76; N, 5.78.

2-Methyl-3-(1-phenylprop-2-en-1-yl)-1*H*-indole (3g)
Pale-yellow oil; yield: 41.1 mg (83%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.80 (s, 1 H), 7.36 (d, *J* = 7.9 Hz, 1 H), 7.30 (dt, *J* = 8.2, 5.7 Hz, 5 H), 7.20 (t, *J* = 7.1 Hz, 1 H), 7.10 (t, *J* = 7.6 Hz, 1 H), 6.99 (t, *J* = 7.5 Hz, 1 H), 6.47 (ddd, *J* = 17.1, 10.1, 7.0 Hz, 1 H), 5.22 (d, *J* = 10.1 Hz, 1 H), 5.08 (d, *J* = 17.1 Hz, 1 H), 5.00 (d, *J* = 7.0 Hz, 1 H), 2.35 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.19, 138.96, 134.35, 130.51, 127.22, 127.17, 127.01, 124.99, 119.89, 118.43, 118.15, 114.53, 111.76, 109.22, 44.85, 11.35.

MS (ESI): *m*/*z* = 248 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found: C, 87.64; H, 6.77; N, 5.54.

2-Phenyl-3-(1-phenylprop-2-en-1-yl)-1*H*-indole (3h)
Pale-yellow oil; yield: 53.1 mg (86%).

IR (neat): 3405, 3054, 1447, 1243, 736, 697 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.10 (s, 1 H), 7.57–7.53 (m, 2 H), 7.50–7.39 (m, 5 H), 7.36 (d, *J* = 7.4 Hz, 2 H), 7.29 (t, *J* = 7.6 Hz, 2 H), 7.21 (dd, *J* = 15.4, 7.6 Hz, 2 H), 7.03 (t, *J* = 7.6 Hz, 1 H), 6.56 (ddd, *J* = 17.1, 10.1, 7.0 Hz, 1 H), 5.27 (d, *J* = 10.1 Hz, 1 H), 5.17 (d, *J* = 6.9 Hz, 1 H), 5.11 (d, *J* = 17.1 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.20, 139.08, 135.29, 134.56, 132.03, 127.83, 127.59, 127.27, 127.23, 127.03, 126.92, 125.04, 121.12, 120.36, 118.58, 115.15, 112.78, 109.94, 44.92.

MS (ESI): *m*/*z* = 310 $[M + H]^+$.

Anal. Calcd for $C_{23}H_{19}N$: C, 89.28; H, 6.19; N, 4.53. Found: C, 89.06; H, 6.41; N, 4.37.

1-Methyl-3-(1-phenylprop-2-en-1-yl)-1*H*-indole (3i)
Pale-yellow oil; yield: 42.8 mg (87%).

IR (neat): 2912, 1473, 1330, 1230, 913, 737, 698 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 8.0 Hz, 1 H), 7.38–7.33 (m, 5 H), 7.30–7.25 (m, 2 H), 7.09 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1 H), 6.78 (d, *J* = 0.5 Hz, 1 H), 6.42 (ddd, *J* = 17.1, 10.1, 7.1 Hz, 1 H), 5.28–5.23 (m, 1 H), 5.15 (dt, *J* = 17.0, 1.5 Hz, 1 H), 5.03 (dd, *J* = 7.1, 0.8 Hz, 1 H), 3.78 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.48, 139.75, 136.49, 127.50, 127.42, 126.32 (2 C), 125.34, 120.69, 118.99, 117.87, 116.00, 114.40, 108.25, 46.05, 31.72.

MS (ESI): *m*/*z* = 248 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found: C, 87.62; H, 7.07; N, 5.48.

1-Phenyl-3-(1-phenylprop-2-en-1-yl)-1*H*-indole (3j)
Yellow oil; yield: 37.7 mg (61%).

IR (neat): 3030, 1595, 1497, 1453, 1214, 737, 695 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 8.3 Hz, 1 H), 7.52 (d, *J* = 4.3 Hz, 4 H), 7.48 (d, *J* = 7.9 Hz, 1 H), 7.36 (ddd, *J* = 8.5, 5.4, 3.8 Hz, 5 H), 7.26–7.24 (m, 1 H), 7.22 (dd, *J* = 8.2, 1.1 Hz, 1 H), 7.13–7.09 (m, 1 H), 7.08 (d, *J* = 0.7 Hz, 1 H), 6.42 (ddd, *J* = 17.1, 10.1, 7.2 Hz, 1 H), 5.25 (d, *J* = 10.1 Hz, 1 H), 5.16 (d, *J* = 17.0 Hz, 1 H), 5.04 (d, *J* = 7.2 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.91, 139.31, 138.85, 135.47, 128.57, 127.47, 127.27, 125.42, 125.33, 125.19, 123.40, 123.20, 121.50, 119.19, 118.95, 118.52, 114.72, 109.55, 45.96.

MS (ESI): *m*/*z* = 310 $[M + H]^+$.

Anal. Calcd for $C_{23}H_{19}N$: C, 89.28; H, 6.19; N, 4.53. Found: C, 89.46; H, 6.28; N, 4.38.

1-Benzyl-3-(1-phenylprop-2-en-1-yl)-1*H*-indole (3k)
Pale-yellow oil; yield: 57.4 mg (89%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 7.9 Hz, 1 H), 7.33 (s, 2 H), 7.32 (s, 3 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 7.25 (dd, *J* = 8.4, 4.9 Hz, 2 H), 7.18–7.14 (m, 1 H), 7.12 (d, *J* = 6.9 Hz, 2 H), 7.06–7.02 (m, 1 H), 6.87 (s, 1 H), 6.38 (ddd, *J* = 17.1, 10.1, 7.1 Hz, 1 H), 5.31 (s, 2 H), 5.24–5.18 (m, 1 H), 5.10 (dt, *J* = 17.0, 1.5 Hz, 1 H), 5.01 (d, *J* = 7.1 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.26, 139.61, 136.75, 136.07, 127.74, 127.44, 127.35, 126.52, 125.73, 125.63, 125.27, 123.92, 120.82, 119.04, 118.06, 116.60, 114.41, 108.71, 49.01, 45.99.

MS (ESI): *m*/*z* = 324 $[M + H]^+$.

Anal. Calcd for $C_{24}H_{21}N$: C, 89.12; H, 6.54; N, 4.33. Found: C, 89.01; H, 6.36; N, 4.50.

3-[1-(2-Bromophenyl)prop-2-en-1-yl]-1*H*-indole (3m)
Yellow oil; yield: 47.3 mg (76%).

IR (neat): 3409, 2976, 915, 736 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.01 (s, 1 H), 7.66–7.59 (m, 1 H), 7.41 (d, *J* = 8.0 Hz, 1 H), 7.37 (d, *J* = 8.2 Hz, 1 H), 7.23–7.16 (m, 3 H), 7.13–7.03 (m, 2 H), 6.93 (d, *J* = 1.3 Hz, 1 H), 6.31 (ddd, *J* = 16.9, 10.2, 6.4 Hz, 1 H), 5.49 (dd, *J* = 6.3, 1.0 Hz, 1 H), 5.27 (d, *J* = 10.2 Hz, 1 H), 5.04 (d, *J* = 17.1 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.08, 137.87, 135.67, 131.91, 129.21, 126.93, 126.42, 125.83, 123.85, 121.79, 121.22, 118.76, 118.50, 116.67, 115.35, 110.09, 44.57.

MS (ESI): *m*/*z* = 312 $[M + H]^+$.

Anal. Calcd for $C_{17}H_{14}BrN$: C, 65.40; H, 4.52; N, 4.49. Found: C, 65.63; H, 4.66; N, 4.60.

3-{1-[2-(Trifluoromethyl)phenyl]prop-2-en-1-yl}-1*H*-indole (3n)
Pale-yellow oil; yield: 43.3 mg (72%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.91 (s, 1 H), 7.61 (d, *J* = 7.9 Hz, 1 H), 7.29 (dd, *J* = 14.1, 6.9 Hz, 2 H), 7.25–7.11 (m, 3 H), 7.10–7.02 (m, 1 H), 6.96–6.82 (m, 2 H), 6.21 (ddd, *J* = 16.9, 10.2, 6.6 Hz, 1 H), 5.31 (d, *J* = 6.5 Hz, 1 H), 5.13 (dd, *J* = 10.2, 1.2 Hz, 1 H), 4.86 (d, *J* = 17.1 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.98, 138.93, 135.72, 130.75, 129.74, 127.25 (q, $^1J_{C,F}$ = 29.3 Hz), 127.03, 125.56, 125.35, 124.84, 121.82, 121.22, 118.66, 118.54, 117.29, 115.14, 110.03, 41.16.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –58.50.

MS (ESI): *m*/*z* = 302 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{14}F_3N$: C, 71.75; H, 4.68; N, 4.65. Found: C, 71.91; H, 4.57; N, 4.74.

3-{1-[3-(Trifluoromethyl)phenyl]prop-2-en-1-yl}-1*H*-indole (3o)
Colorless oil; yield: 48.7 mg (81%).

IR (neat): 3419, 2982, 1327, 1118, 1071, 740, 701 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.02 (s, 1 H), 7.61 (s, 1 H), 7.49 (dd, *J* = 14.7, 7.7 Hz, 2 H), 7.45–7.35 (m, 3 H), 7.25–7.18 (m, 1 H), 7.12–7.03 (m, 1 H), 6.90 (d, *J* = 1.7 Hz, 1 H), 6.36 (ddd, *J* = 17.1,

10.1, 7.0 Hz, 1 H), 5.27 (d, *J* = 10.1 Hz, 1 H), 5.10 (d, *J* = 17.1 Hz, 1 H), 5.05 (d, *J* = 6.9 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.20, 138.62, 135.69, 130.87, 129.66 (q, $^1J_{C,F}$ = 31.8 Hz), 127.79, 125.59, 124.40, 124.20, 122.28, 121.58, 121.33, 118.58 (2 C), 116.68, 115.33, 110.22, 45.69.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –62.35.

MS (ESI): *m*/*z* = 302 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{14}F_3N$: C, 71.75; H, 4.68; N, 4.65, Found: C, 71.58; H, 4.89; N, 4.50.

3-{1-[4-(Trifluoromethyl)phenyl]prop-2-en-1-yl}-1*H*-indole (3p)[13]
Yellow oil; yield: 52.4 mg (87%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (s, 1 H), 7.56 (d, *J* = 8.2 Hz, 2 H), 7.45–7.33 (m, 4 H), 7.24–7.17 (m, 1 H), 7.05 (t, *J* = 7.5 Hz, 1 H), 6.93 (s, 1 H), 6.35 (ddd, *J* = 17.1, 10.1, 7.1 Hz, 1 H), 5.25 (d, *J* = 10.1 Hz, 1 H), 5.09 (d, *J* = 17.1 Hz, 1 H), 5.04 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 146.29, 138.60, 135.69, 127.73 (q, $J_{C,F}$ = 32.0 Hz), 127.77, 125.55, 124.30, 123.98, 122.26, 121.54, 121.32, 118.58, 116.60, 115.28, 110.22, 45.75.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –62.27.

3-[1-(4-Tolyl)prop-2-en-1-yl]-1*H*-indole (3q)
Yellow oil; yield: 33.0 mg (67%).

IR (neat): 3415, 2918, 1457, 737 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.87 (s, 1 H), 7.31 (d, *J* = 8.0 Hz, 1 H), 7.25 (d, *J* = 8.1 Hz, 1 H), 7.07 (ddd, *J* = 9.2, 6.2, 2.0 Hz, 3 H), 7.01 (d, *J* = 7.9 Hz, 2 H), 6.93 (dd, *J* = 11.1, 3.9 Hz, 1 H), 6.78 (d, *J* = 1.4 Hz, 1 H), 6.24 (ddd, *J* = 17.1, 10.1, 7.2 Hz, 1 H), 5.08 (d, *J* = 10.1 Hz, 1 H), 4.97 (d, *J* = 17.0 Hz, 1 H), 4.83 (d, *J* = 7.1 Hz, 1 H), 2.23 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.68, 139.19, 135.67, 134.75, 128.05, 127.28, 125.87, 121.40, 121.04, 118.89, 118.31, 117.74, 114.24, 110.05, 45.59, 20.06.

MS (ESI): *m*/*z* = 248 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found: C, 87.61; H, 6.77; N, 5.73.

3-[1-(1-Naphthyl)prop-2-en-1-yl]-1*H*-indole (3r)
Pale-yellow oil; yield: 48.7 mg (86%).

IR (neat): 3415, 2972, 781, 736 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.1 Hz, 1 H), 7.93 (s, 1 H), 7.91–7.88 (m, 1 H), 7.78 (dd, *J* = 6.7, 2.5 Hz, 1 H), 7.51–7.39 (m, 5 H), 7.37 (d, *J* = 8.1 Hz, 1 H), 7.21 (t, *J* = 7.5 Hz, 1 H), 7.07 (t, *J* = 7.5 Hz, 1 H), 6.75 (s, 1 H), 6.47 (ddd, *J* = 16.8, 10.1, 6.3 Hz, 1 H), 5.78 (d, *J* = 6.2 Hz, 1 H), 5.29 (d, *J* = 10.1 Hz, 1 H), 5.05 (d, *J* = 17.1 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.90, 137.92, 135.67, 133.04, 130.81, 127.75, 126.16, 126.00, 124.86 (2 C), 124.50, 124.39, 123.17, 122.38, 121.10, 118.71, 118.41, 117.29, 115.34, 110.12, 41.17.

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

Anal. Calcd for $C_{21}H_{17}N$: C, 89.01; H, 6.05; N, 4.94. Found: C, 89.15; H, 5.94; N, 5.13.

3-[1-(2-Phenylethyl)prop-2-en-1-yl]-1*H*-indole (3s)
Pale-yellow oil; yield: 27.6 mg (53%).

IR (neat): 3419, 2918, 1475, 912, 732, 698 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.96 (s, 1 H), 7.61 (d, *J* = 7.9 Hz, 1 H), 7.37 (d, *J* = 8.1 Hz, 1 H), 7.31–7.26 (m, 2 H), 7.22–7.16 (m, 4 H), 7.13–7.08 (m, 1 H), 7.00 (s, 1 H), 6.08–6.00 (m, 1 H), 5.20–5.12 (m, 1 H), 5.09 (ddd, *J* = 10.2, 1.7, 0.9 Hz, 1 H), 3.62 (q, *J* = 7.3 Hz, 1 H), 2.76–2.61 (m, 2 H), 2.23 (ddt, *J* = 13.2, 9.8, 6.5 Hz, 1 H), 2.11 (dddd, *J* = 13.6, 9.8, 7.8, 6.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.54, 140.86, 135.58, 127.55, 127.33, 125.80, 124.72, 121.02, 119.76, 118.58, 118.22, 117.79, 113.19, 110.18, 39.71, 35.38, 32.91.

MS (ESI): *m*/*z* = 262 $[M + H]^+$.

Anal. Calcd for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36. Found: C, 87.57; H, 7.43; N, 5.19.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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