Reaction of carbon nucleophiles with alkylideneindazolium and alkylideneindolium ions generated from their 3-(1-arylsulfonylalkyl) indazole and indole precursors

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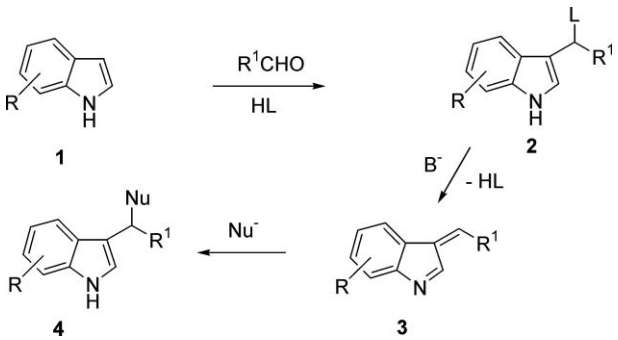
Lewis acid promoted elimination of *p*-toluenesulfinc acid from sulfonyl indazoles and sulfonyl indoles generates the corresponding iminium ion that reacts with allyltin reagents, silyl enol ethers, silyl ketene acetals and electron-rich aromatics leading to functionalized indazole and indole derivatives.

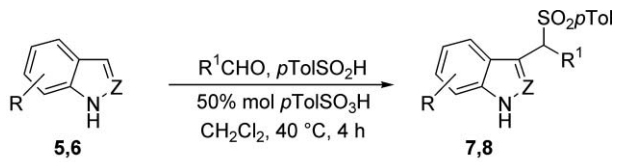
Introduction

Functionalization of benzofused azole derivatives is a recurrent synthetic process aimed at the preparation of complex structural entities endowed with practical interest. The indole ring is included in a large number of products isolated from natural sources that are often recognized for their powerful biological activities.[1] Conversely, the indazole nucleus is hardly found in natural products, but its presence in many synthetically prepared compounds is able to confer them a prominent pharmacological profile.[2] In electron-rich systems such as those featured by the indole ring, this goal may be attained exploiting a Friedel–Crafts process that involves reaction with electron-poor alkenes or other carbon electrophiles under acid catalysis.[3] However, this procedure is hardly achievable with indazoles that, because of their reduced electronic density at the pyrazole ring, are rather reluctant in the reaction with carbon electrophiles. A complementary approach for the introduction of carbon frameworks at 3 position in indoles consists in the utilization of derivatives of type **2** having a good leaving group at benzylic position (Scheme 1). Compounds **2** are obtained by a Friedel–Crafts reaction involving a three component coupling of an indole, an aldehyde and a protonated nucleophile HL. Reaction of **2** with a base causes an elimination of HL thus generating an alkylideneindolenine intermediate **3** that upon reaction with a nucleophilic reagent provides the corresponding addition product **4**. The success of this strategy is strongly affected by a series of factors such as the ease of formation of compound **2**, its stability and the aptitude of the leaving group L to be eliminated under mild and controlled conditions. For a long time, gramines [**2**, L=N(R_2)$_2$] have been the only substrates used for this purpose, but recently other procedures involving different leaving groups have been devised.[4] Particularly, sulfonyl indoles (**2**, L=SO_2Ar) can be easily obtained coupling indoles, aldehydes and arenesulfinc acids.[5] Rather surprisingly, this procedure is also effective for indazoles thus representing an unprecedented example of an intermolecular Friedel–Crafts reaction on this heterocycle (Scheme 2).

Reaction of sulfonyl indoles **8** with a large number of nucleophiles including Grignard and organozinc reagents, methylene active compounds and heteronucleophiles under basic conditions is by now a well established protocol for the preparation of substituted indoles **4**.[6] Conversely, sulfonyl indazoles **7** display a poor reactivity under the same conditions and the only useful transformation evidenced on them is a reductive desulfonylation leading to 3-alkyl indazole derivatives.[7] It has been demonstrated that removal of the arenesulfonyl group can be also pursued in the presence of Lewis acids, when stable oxonium or iminium ions are formed as intermediates.[8] These highly electrophilic species are able to react with faint nucleophiles such as enol ethers or allyltin reagents leading to the corresponding functionalized adducts.[9] In this paper we demonstrate that upon reaction with Lewis acids, sulfonyl indazoles **7** can be easily converted into alkylideneindazolium salts. These reactive electrophilic intermediates are able to react with different nucleophiles leading to the corresponding adducts. The same process can be successfully applied to sulfonyl indoles **8** with comparable results.[10]



Scheme 1 General synthetic strategy for indole functionalization.



5,7 Z= N **6,8** Z= CH

Scheme 2 Synthesis of sulfonyl indazoles and sulfonyl indoles.

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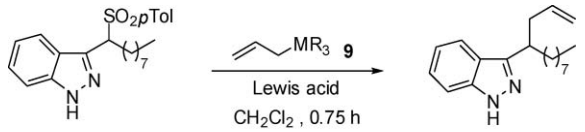
Table 1 Optimization studies for allylation of sulfonyl indazoles



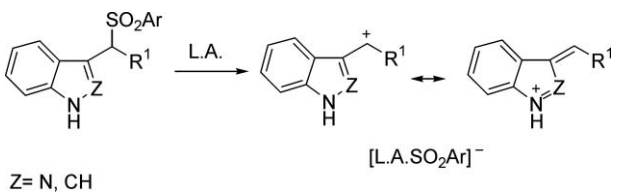
Entry	Lewis Acid (equiv.)	T/°C	MR_3 (equiv.)	Yield (%)[a]
1	$TiCl_4$ (2)	–78	$SnBu_3$ (2)	33
2	$SnCl_4$ (2)	–40	$SnBu_3$ (2)	10[b]
3	$AlCl_3$ (2)	–40	$SnBu_3$ (2)	50
4	$AlEtCl_2$ (2)	–15	$SnBu_3$ (2)	83
5	$AlEtCl_2$ (1.5)	–15	$SnBu_3$ (2)	70
6	$AlEtCl_2$ (2)	–15	$SnBu_3$ (1.5)	81
7	$AlEtCl_2$ (2)	–15	$SiMe_3$ (2)	20
8	$AlEtCl_2$ (2)	–15	$Si(allyl)_3$ (2)	Trace

[a] Yield of pure isolated product. [b] Reaction time 2.5 h.

Results and discussion

A preliminary evaluation of the reactivity of our systems toward allylation has been made on sulfonyl indazole **7a** under different reaction conditions (Table 1).

Allyltributyltin was initially selected for trial experiments because of its superior nucleophilicity over silane derivatives.[11] Among classical Lewis acids tested, $AlCl_3$ gave a promising result at –40 °C, while a temperature increase or prolonged reaction times were ineffective in improving the chemical yield (Table 1, entry 3). It is known that the strength of aluminium based Lewis acids may be suitably tuned introducing alkyl substituents on the metal.[12] The utilization of two equivalents of $AlEtCl_2$ consistently improved our process when carried out at –15 °C. A reduction of the acid amount to 1.5 eq. was however unfavorable for the efficiency of the process (Table 1, entries 4,5). Conversely, a lowering of the allyltin reagent until 1.5 eq. did not produce a significant decrease in the yield of the allyl indazole and this aspect is particularly important considering the safety troubles associated with the utilization of tin compounds (Table 1, entry 6).[13] Finally, allyltrimethylsilane and tetraallylsilane were used for the same purpose with disappointing results that once again testify the superior reactivity of allyltin reagents in many reactions involving electrophilic systems (Table 1, entries 7,8). The mechanistic aspects of this process seem to be related to the formation of a stabilized vinylogous iminium ion generated by interaction of the sulfonyl group with the Lewis acid. This ion could present an enhanced carbocationic character that preserves the aromaticity of the indazole core so that its direct involvement in the allylation reaction may be also conceived (Scheme 3).[14]



Scheme 3 Formation of iminium ions from sulfonyl derivatives.

The optimized conditions found in test experiments were then adopted for allylation of sulfonyl indazoles **7** (Table 2). The process

Table 2 Allylation of sulfonyl indazoles and indoles

7 Z = N
8 Z= CR

10 Z = N
11 Z= CR

7a R^1= H; R^2 = *n*-C_8H_{17}
7b R^1= H; R^2 = Et
7c R^1= H; R^2 = *n*-C_5H_{11}
7d R^1= H; R^2 = $Cl(CH_2)_5$
7e R^1= H; R^2 = $Ph(CH_2)_2$

9a R^3= H
9b R^3= Me

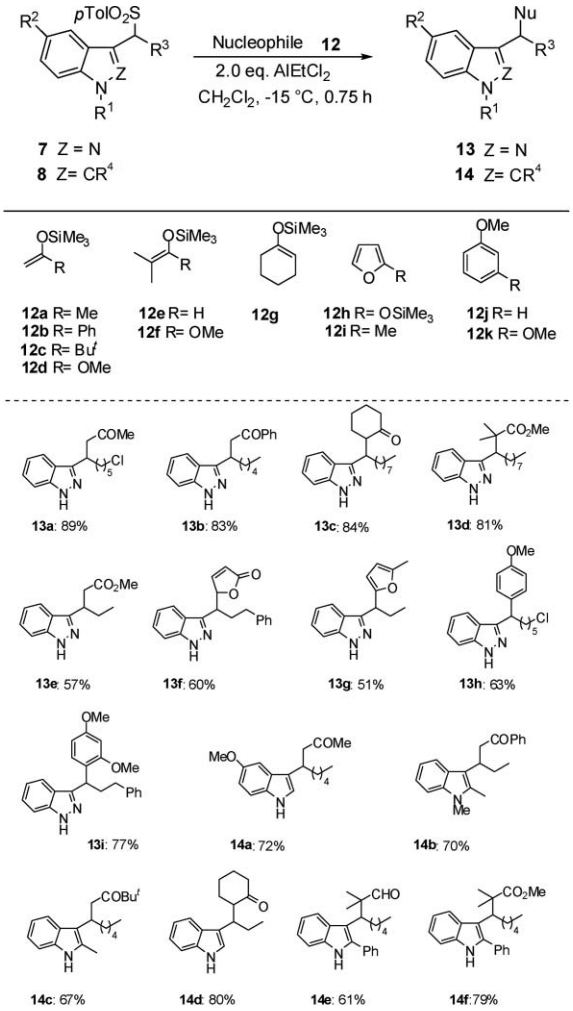
8a Z = CH; R^1= H; R^2 = Et
8b Z = CH; R^1= H; R^2 = *n*-C_5H_{11}
8c Z = CMe; R^1= H; R^2 = Ph
8d Z = CMe; R^1= H; R^2 = 4-MeOPh
8e Z = CMe; R^1= H; R^2 = (*Z*)-$CH_3(CH_2)_4CH{=}CH(CH_2)_2$
8f Z = CMe; R^1= Me; R^2 = Me
8g Z = CPh; R^1= H; R^2 = *n*-C_5H_{11}
8h Z = CPh; R^1= H; R^2 = Et

Entry	Substrate	Allyltin	Product	Yield (%)[a]
1	**7a**	**9a**	**10a**	81
2	**7b**	**9a**	**10b**	76
3	**7c**	**9a**	**10c**	71
4	**7d**	**9a**	**10d**	58
5	**7e**	**9a**	**10e**	83
6	**7e**	**9b**	**10f**	46
7	**8a**	**9a**	**11a**	72
8	**8b**	**9a**	**11b**	70
9	**8c**	**9a**	**11c**	86
10	**8d**	**9a**	**11d**	78
11	**8e**	**9a**	**11e**	77
12	**8f**	**9a**	**11f**	62
13	**8g**	**9a**	**11g**	77
14	**8h**	**9a**	**11h**	57
15	**8b**	**9b**	**11i**	63

[a] Yield of pure isolated product.

shows a satisfactory degree of efficiency for simple allylation using allyltributyltin as reagent. The utilization of crotyltributyltin is more problematic since the addition is less efficient, although a complete regioselectivity in favor of the gamma adduct is observed (Table 2, entry 6). The same reaction conditions when applied to sulfonyl indoles **8** lead to allylated indoles **11** in good yield. The generality of the procedure is evidenced by the large variety of substituted sulfonyl derivatives that can be used for the reaction. Aryl substituents as well as functionalized alkyl chains may be present in the substrate. Particularly, the acid-sensitive *Z* double bond in sulfonyl indole **8e** is preserved after allylation in compound **11e** (Table 2, entry 11). The introduction of substituents at the 2-position in indoles **8** does not seem to alter the reactivity of the intermediate iminium ion being the corresponding allylated products obtained in satisfactory yields. As a matter of fact, even sulfonyl indole **8f** bearing a tertiary carbon atom properly reacts with the allylating reagent leading to the formation of a quaternary center in compound **11f** (Table 2, entry 12). The reaction conditions proved to be successful for the allylation of compounds **7** and **8** were also employed using other nucleophilic reagents with the aim of introducing functionalized frameworks on the side chain of 3-substituted indazoles and indoles. Representative silyl enol ethers **12a–c**,**e**,**g** and silyl ketene acetals **12d**,**f** can be efficiently added to sulfonyl indazoles leading

Table 3 Reaction of sulfonyl indazoles and indoles with enol ethers and electron-rich aromatics[a]



[a] Yield of pure isolated products

to the corresponding ketones **13a–c** and esters **13d**,**e** (Table 3). An interesting result is obtained using 2-trimethylsilyloxy furan **12h**, a well-known reagent allowing the introduction of butenolide groups into substrates endowed of electrophilic character (Table 3, **13f**).[15] Electron-rich aromatic compounds are particularly prone to Friedel–Crafts reaction provided that a sufficiently strong reagent is used as electrophile. The iminium ion generated from sulfonyl indazoles **7** is enough reactive to attack some typical activated aromatic compounds **12i–k** in a regioselective fashion. Similarly, sulfonyl indoles **8** are able to react under the same conditions with silyl enol ethers and silyl ketene acetals leading to the corresponding adducts **14a–f**. In this context it is worth to note that in principle compounds **14a–c** could also be prepared by a direct Friedel–Crafts reaction involving enones and the parent 3-unsubstituted indole (Table 3). However, the same consideration does not apply for the synthesis of compounds **14e**,**f** since the presence of a quaternary carbon atom makes these derivatives unavailable by a direct Friedel–Crafts process. Furthermore, synthesis of cyclohexanone **14d** would involve the utilization of 2-alkylidenecyclohexanones that are poorly reactive in the same process.

Conclusions

In conclusion, sulfonyl indazoles and sulfonyl indoles are able to generate reactive vinylogous iminium ions upon reaction with Lewis acids. These highly electrophilic species react with allyltin reagents, enol ethers and electron-rich aromatics leading to functionalized indazole and indole derivatives. Since functionalization of the indazole ring is extremely difficult by ordinary substitutions involving carbon electrophiles, the present procedure represents a viable method to obtain 3-substituted indazole derivatives.

Experimental

General experimental

^{1}H NMR were recorded at 400 MHz on a Varian Mercury Plus 400.^{13}C NMR were recorded at 100 MHz. Microanalyses were performed with a CHNS–O analyzer Model EA 1108 from Fisons Instruments. Mass spectra were performed with a GC MS^{-1} system Agilent Technologies 6850 II/5973 Inert by means of the EI technique (70 eV). IR spectra were recorded with a Perkin-Elmer Paragon 500 FT-IR. All chemical used were commercial. Sulfonyl indazoles and indoles **7** and **8** were prepared as previously described.[5,7]

General procedure for the allylation of sulfonyl derivatives 7 and 8

To a stirred solution of the appropriate sulfonyl derivative **7** or **8** (1 mmol) in dry CH_2Cl_2 (14 mL) kept under nitrogen atmosphere at −15 °C, allyl tributiltin (1.5 mmol) and $AlEtCl_2$ (2 mmol) were subsequently added under stirring. After 0.75 h to the reaction mixture was added 2 N HCl (12 mL) and the aqueous phase extracted with CH_2Cl_2 (3 × 10 mL). After the evaporation of the solvent, the obtained residue was dissolved in Et_2O (10 mL), treated with 10% aq. KF (40 mL) and stirred for 1 h. The heterogeneous solution was then filtered through a short pad of celite, washed with Et_2O (30 mL) and after separation, the organic phase was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave the crude product that was purified by flash chromatography (hexanes–ethyl acetate 95 : 5).

10a. Yield 81%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 738, 908, 1426, 1465, 1615, 1643, 3063. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.84 (t, 3H, J = 6.8 Hz), 0.93–1.06 (m, 1H), 1.07–1.36 (m, 11H), 1.82–1.95 (m, 1H), 2.07–2.20 (m, 1H), 2.57–2.68 (m, 1H), 2.76–2.88 (m, 1H), 4.45–4.56 (m, 1H), 4.84–4.91 (m, 1H), 4.95–5.03 (m, 1H), 5.50–5.63 (m, 1H), 7.10–7.15 (m, 1H), 7.31–7.38 (m, 1H), 7.41 (d, 1H, J = 8.6 Hz), 7.72 (dt, 1H, J = 0.9, 8.1 Hz), 8.04 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 22.8, 26.5, 29.4, 29.5, 29.6, 32.0, 35.0, 40.0, 59.4, 109.2, 117.5, 120.5, 121.3, 123.8, 126.1, 133.2, 134.9, 140.3. MS (EI) m/z: 284 [M$^+$], 243 (100), 171, 144, 131, 119, 55, 41, 29. Anal. calcd. for $C_{19}H_{28}N_2$ (284.44): C, 80.23; H, 9.92; N, 9.85. Found: C, 80.34; H, 10.03; N, 9.72.

10b. Yield 76%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 740, 751, 908, 1426, 1463, 1616, 1643, 3063. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.73 (t, 3H, J = 7.3 Hz), 1.89–2.02 (m, 1H), 2.07-2.21 (m, 1H), 2.59–2.69 (m, 1H), 2.78–2.89 (m, 1H), 4.38–4.48 (m, 1H), 4.85–4.91 (m, 1H), 4.96–5.03 (m, 1H), 5.51–5.64 (m, 1H), 7.10–7.15

(m, 1H), 7.32–7.38 (m, 1H), 7.40–7.44 (m, 1H), 7.72 (dt, 1H, J = 0.9, 8.1 Hz), 8.05 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.1, 28.2, 39.7, 60.9, 109.2, 117.5, 120.5, 121.3, 123.8, 126.1, 133.2, 134.8, 140.5. MS (EI) m/z: 200 [M$^+$], 159 (100), 144, 132, 118, 91, 77, 41. Anal. calcd. for $C_{13}H_{16}N_2$ (200.28): C, 77.96; H, 8.05; N, 13.99. Found: C, 78.19; H, 8.16, 14.14.

10c. Yield 71%. Colorless oil. IR (neat) ν: 739, 908, 1426, 1464, 1616, 1642, 3063 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.79 (t, 3H, J = 6.8 Hz), 0.93–1.07 (m, 1H), 1.08–1.31 (m, 5H), 1.18–1.94 (m, 1H), 2.07–2.20 (m, 1H), 2.57–2.68 (m, 1H), 2.76–2.88 (m, 1H), 4.46-4.56 (m, 1H), 4.84–4.90 (m, 1H), 4.95–5.02 (m, 1H), 5.49–5.63 (m, 1H), 7.10–7.15 (m, 1H), 7.32–7.37 (m, 1H), 7.41 (dd, 1H, J = 0.9, 8.6 Hz), 7.72 (dt, 1H, J = 0.9, 8.1 Hz), 8.04 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 22.6, 26.1, 31.7, 34.9, 40.0, 59.3, 109.2, 117.5, 120.5, 121.3, 123.8, 126.1, 133.2, 134.8, 140.3. MS (EI) m/z: 242 [M$^+$], 201 (100), 171, 144, 131, 119, 91, 77, 55, 41, 29. Anal. calcd. for $C_{16}H_{22}N_2$ (242.36): C, 79.29; H, 9.15; N, 11.56. Found: C, 79.01; H, 9.06; N, 11.47.

10d. Yield 58%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 751, 768, 908, 1006, 1189, 1426, 1463, 1616, 1642, 3062. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.93–1.08 (m, 1H), 1.10–1.24 (m, 1H), 1.28–1.51 (m, 2H), 1.57–1.75 (m, 2H), 1.83–1.97 (m, 1H), 2.11–2.26 (m, 1H), 2.56–2.68 (m, 1H), 2.76–2.88 (m, 1H), 3.42 (t, 2H, J = 6.8 Hz), 4.46–4.57 (m, 1H), 4.85–4.93 (m, 1H), 4.95–5.04 (m, 1H), 5.50–5.63 (m, 1H), 7.13 (t, 1H, J = 7.3 Hz), 7.32–7.44 (m, 2H), 7.72 (d, 1H, J = 8.1 Hz), 8.04 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.8, 26.7, 32.5, 34.7, 40.1, 45.1, 59.2, 109.2, 117.7, 120.6, 121.3, 123.9, 126.2, 133.4, 134.7, 140.4. MS (EI) m/z: 278 [M+2$^+$], 276 [M$^+$], 235 (100), 171, 144, 131, 119, 91, 77, 55, 41, 29. Anal. calcd. for $C_{16}H_{21}ClN_2$ (276.80): C, 69.42; H, 7.65; N, 12.81. Found: C, 69.58; H, 7.57; N, 18.70.

10e. Yield 83%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 741, 908, 1426, 1465, 1618, 1641, 3059. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.17–2.28 (m, 1H), 2.31–2.49 (m, 2H), 2.52–2.68 (m, 2H), 2.76–2.87 (m, 1H), 4.46–4.56 (m, 1H), 4.85–4.90 (m, 1H), 4.93–5.01 (m, 1H), 5.48–5.61 (m, 1H), 7.01–7.06 (m, 2H), 7.12–7.21 (m, 2H), 7.21–7.31 (m, 3H), 7.32–7.39 (m, 1H), 7.75 (dt, 1H, J = 0.9, 8.1 Hz), 8.10 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 32.5, 36.3, 40.2, 58.2, 109.3, 117.7, 120.6, 121.3, 123.9, 126.1, 128.5, 128.7, 133.5, 134.6, 140.4, 141.4. (EI) m/z: 276 [M$^+$], 235, 172, 131, 119, 117, 91 (100), 77, 65. Anal. calcd. for $C_{19}H_{20}N_2$ (276.38): C, 82.57; H, 7.29; N, 10.14. Found: C, 82.73; H, 7.41; N, 10.29.

10f. Diastereomeric mixture d.r. 68 : 32. Yield 46%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 739, 907, 1426, 1466, 1616, 1641, 3061. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.61 (d, 2.04H, J = 6.8 Hz), 0.99 (d, 0.96H, J = 6.8 Hz), 2.12–2.38 (m, 3H), 2.44–2.65 (m, 1H), 2.70–2.91 (m, 1H), 4.10–4.18 (m, 0.68H), 4.23–4.30 (m, 0.32H), 4.76 (dd, 0.32H, J = 1.3, 10.3 Hz), 4.84 (dt, 0.32H, J = 1.3, 17.1 Hz), 5.03 (dd, 0.68H, J = 1.3, 10.3 Hz), 5.07–5.14 (m, 0.68H), 5.54–5.76 (m, 1H), 6.92–6.99 (m, 2H), 7.07–7.22 (m, 4H), 7.23–7.34 (m, 2H), 7.68–7.74 (m, 1H), 8.05 (s, 0.32H), 8.07 (s, 0.68H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 17.5, 17.9, 32.6, 33.7, 34.6, 43.6, 43.7, 62.4, 62.6, 109.5, 109.6, 115.2, 116.0, 120.5, 120.7, 121.2, 121.3, 123.7, 126.0, 126.1, 126.2, 128.4, 128.5, 128.6, 128.7, 133.3, 133.6, 140.4, 141.1, 141.2, 141.5. MS (EI) m/z: 290 [M$^+$], 235, 117, 91 (100), 77, 65. Anal. calcd. for $C_{20}H_{22}N_2$ (290.40): C, 82.72; H, 7.64; N, 9.65. Found: C, 82.51; H, 7.70; H, 9.79.

11a. Yield 72%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 741, 1456, 1618, 3058, 3419. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, 3H, J = 7.3 Hz), 1.69–1.89 (m, 2H), 2.45–2.59 (m, 2H), 2.89–2.98 (m, 1H), 4.92–4.97 (m, 1H), 4.99–5.06 (m, 1H), 5.73–5.86 (m, 1H), 6.96 (d, 1H, J = 2.6 Hz), 7.09–7.15 (m, 1H), 7.17–7.23 (m, 1H), 7.36 (d, 1H, J = 8.1 Hz), 7.67 (d, 1H, J = 8.1 Hz), 7.92 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.2, 28.0, 38.4, 39.9, 111.3, 115.6, 119.1, 119.7, 120.0, 121.1, 121.9, 127.4, 136.7, 138.0. MS (EI) m/z: 199 [M$^+$], 158 (100), 143, 130, 117, 89, 77. Anal. calcd. for $C_{14}H_{17}N$ (199.29): C, 84.37; H, 8.60; N, 7.03. Found: C, 84.58; H, 8.76; N, 7.18.

11b. Yield 70%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 740, 910, 1456, 1618, 1638, 3058, 3420. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.81–0.89 (m, 3H), 1.20–1.33 (m, 6H), 1.69–1.79 (m, 2H), 2.44–2.58 (m, 2H), 2.94–3.03 (m, 1H), 4.91–4.96 (m, 1H), 4.98–5.07 (m, 1H), 5.72–5.84 (m, 1H), 6.95 (d, 1H, J = 2.1 Hz), 7.09–7.14 (m, 1H), 7.17–7.22 (m, 1H), 7.36 (d, 1H, J = 8.1 Hz), 7.66 (d, 1H, J = 8.1 Hz), 7.91 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 22.8, 27.4, 32.2, 35.3, 36.8, 40.5, 111.3, 115.6, 119.1, 119.7, 120.4, 121.0, 121.9, 127.3, 136.6, 138.0. MS (EI) m/z: 241 [M$^+$], 200, 170, 143,130 (100), 115, 41. Anal. calcd. for $C_{17}H_{23}N$ (241.37): C, 84.59; H, 9.60; N, 5.80. Found: C, 84.88; 9.73; N, 5.66.

11c. Yield 86%. Yellow solid, m.p. 83-85 °C. IR (nujol) ν_{max}/cm^{-1}: 707, 737, 904, 1460, 1615, 1642, 3061, 3394. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.38 (s, 3H), 3.02–3.08 (m, 2H), 4.30 (t, 1H, J = 7.7 Hz), 4.90–4.96 (m, 1H), 5.06 (d, 1H, J = 17.1 Hz), 5.72–5.85 (m, 1H), 7.03 (t, 1H, J = 7.7 Hz), 7.11 (t, 1H, J = 7.7 Hz), 7.14–7.20 (m, 1H), 7.23–7.30 (m, 3H), 7.39 (d, 2H, J = 7.7 Hz), 7.53 (d, 1H, J = 7.7 Hz), 7.70 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.7, 39.0, 42.5, 110.5, 114.1, 115.9, 119.3, 119.6, 121.0, 126.0, 128.0, 128.1, 128.4, 131.5, 135.6, 137.9, 145.1. MS (EI) m/z: 261 [M$^+$], 220 (100), 218, 204, 178, 115, 102, 77, 41. Anal. calcd. for $C_{19}H_{19}N$ (261.36): C, 87.31; H, 7.33; N, 5.36. Found: C, 87.19; H, 7.48; N, 5.23.

11d. Yield 78%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 742, 828, 914, 1035, 1178, 1244, 1460, 1610, 1639, 3029, 3058, 3406. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.37 (s, 3H), 2.96–3.02 (m, 2H), 3.76 (s, 3H), 4.23 (t, 1H, J = 7.7 Hz), 4.88–4.93 (m, 1H), 5.00–5.07 (m, 1H), 5.70–5.82 (m, 1H), 6.81 (d, 2H, J = 9.0 Hz), 7.00 (dt, 1H, J = 1.3, 8.1 Hz), 7.08 (dt, 1H, J = 1.3, 7.3 Hz), 7.22–7.31 (m, 3H), 7.49 (d, 1H, J = 8.1 Hz), 7.73 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.6, 39.1, 41.5, 55.4, 110.4, 113.7, 114.4, 115.8, 119.2, 119.6, 120.9, 128.0, 128.8, 131.3, 135.5, 137.2, 138.0, 157.7. MS (EI) m/z: 291 [M$^+$], 250 (100), 235, 206, 125, 102. Anal. calcd. for $C_{20}H_{21}NO$ (291.39): C, 82.44; H, 7.26; N, 4.81. Found: C, 82.71; H, 7.43; N, 5.02.

11e. Yield 77%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 740, 910, 1461, 1620, 1639, 3003, 3058, 3409. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.86 (t, 3H, J = 7.3 Hz), 1.12–1.35 (m, 6H), 1.76–2.02 (m, 6H), 2.34 (s, 3H), 2.45–2.65 (m, 2H), 2.80–2.91 (m, 1H), 4.83–4.88 (m, 1H), 4.92–4.99 (m, 1H), 5.29–5.35 (m, 2H), 5.63–5.76 (m, 1H), 7.02 (dt, 1H, J = 1.3, 8.1 Hz), 7.08 (dt, 1H, J = 1.3, 7.3 Hz), 7.26 (d, 1H, J = 7.7 Hz), 7.60 (d, 1H, J = 7.7 Hz), 7.90 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.5, 14.3, 22.8, 25.9, 27.4, 29.6, 31.7, 35.1, 37.2, 40.3, 110.5, 114.0, 115.3, 118.8, 119.6, 120.6, 127.8, 130.0, 130.3, 131.4, 135.8, 138.4. MS (EI) m/z: 309 [M$^+$], 268 (100), 184, 158, 144, 130, 69, 55, 41. Anal. calcd. for $C_{22}H_{31}N$ (309.49): C, 85.38; H, 10.10; N, 4.53. Found: C, 85.21; H, 10.01, N, 4.36.

11f. Yield 62%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 741, 911, 1066, 1459,1618, 1638, 3069, 3408. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.52 (s, 6H), 2.51 (s, 3H), 2.62 (dt, 2H, J = 1.3, 7.3 Hz), 4.89–5.01

(m, 2H), 5.55–5.67 (m, 1H), 7.03 (dt, 1H, J = 1.3, 8.1 Hz), 7.09 (dt, 1H, J = 1.3, 6.8 Hz), 7.25 (d, 1H, J = 7.7 Hz), 7.58 (bs, 1H), 7.79 (d, 1H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 15.9, 29.9, 36.7, 47.8, 110.4, 116.4, 117.8, 118.8, 120.6, 121.4, 128.3, 129.9, 135.4, 136.7. MS (EI) m/z: 213 [M$^+$], 172 (100), 157, 144, 130, 115, 77, 39. Anal. calcd. for $C_{15}H_{19}N$ (213.32): C, 84.46; H, 8.98; N, 6.57. Found: C, 86.65; H, 9.13; N, 6.41.

11g. Yield 77%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 699, 741, 764, 911, 1456, 1605, 1640, 3061, 3409. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.76 (t, 3H, J = 7.3 Hz), 1.03–1.22 (m, 6H), 1.69–1.82 (m, 1H), 1.88–2.00 (m, 1H), 2.53–2.63 (m, 1H), 2.67–2.78 (m, 1H), 3.03–3.14 (m, 1H), 4.87–4.93 (m, 1H), 4.94–5.02 (m, 1H), 5.70–5.82 (m, 1H), 7.09–7.15 (m, 1H), 7.18–7.23 (m, 1H), 7.36–7.42 (m, 2H), 7.44–7.50 (m, 2H), 7.51–7.56 (m, 2H), 7.79 (d, 1H, J = 8.1 Hz), 7.92 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 22.8, 27.9, 32.0, 35.1, 37.1, 40.5, 111.1, 115.4, 116.1, 119.3, 121.1, 121.9, 127.6, 127.9, 128.8, 129.2, 133.9, 135.6, 136.5, 138.4. MS (EI) m/z: 317 [M$^+$], 276 (100), 246, 218, 206, 178. Anal. calcd. for $C_{23}H_{27}N$ (317.47): C, 87.02; H, 8.57; N, 4.41. Found: C, 87.31; H, 8.69; N, 4.55.

11h. Yield 57%. Waxy solid. IR (neat) ν_{max}/cm^{-1}: 738, 910, 1377, 1457, 1605, 1639, 3408. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.77 (t, 3H, J = 7.7 Hz), 1.73–2.04 (m, 2H), 2.52–2.79 (m, 2H), 2.94–3.07 (m, 1H), 4.83–5.04 (m, 2H), 5.65–5.83 (m, 1H), 7.12 (dt, 1H, J = 1.3, 8.1 Hz), 7.21 (dt, 1H, J = 1.3, 8.1 Hz), 7.33-7.59 (m, 5H), 7.79 (d, 1H, J = 8.1 Hz), 7.92 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.0, 28.1, 39.1, 40.3, 111.2, 115.4, 115.8, 119.3, 121.1, 122.0, 127.6, 127.9, 128.8, 129.3, 133.9, 135.8, 136.5, 138.4. MS (EI) m/z: 275 [M$^+$], 234 (100), 218, 204, 193, 103, 32. Anal. calcd. for $C_{20}H_{21}N$ (275.39): C, 87.23; H, 7.69; N, 5.09. Found: C, 87.05; H, 7.51; N, 5.27.

11i. Diastereomeric mixture d.r. 85 : 15. Yield 63%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 910, 996, 1011, 1456, 1618, 1639, 3059, 3419. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.77–0.87 (m, 3H), 0.90 (d, 2.55H, J = 6.8 Hz), 0.98 (d, 0.45H, J = 6.8 Hz), 1.08–1.31 (m, 6H), 1.61–1.86 (m, 2H), 2.49–2.63 (m, 1H), 2.67–2.76 (m, 0.85H), 2.91–2.99 (m, 0.15H), 4.93–5.07 (m, 2H), 5.72–5.89 (m, 1H), 6.93 (d, 0.15H, J = 2.6 Hz), 6.95 (d, 0.85H, J = 2.6 Hz), 7.08–7.14 (m, 1H), 7.19 (t, 1H, J = 7.7 Hz), 7.36 (d, 1H, J = 8.1 Hz), 7.63–7.70 (m, 1H), 7.94 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.4, 17.8, 19.1, 22.9, 27.9, 28.0, 32.3, 32.4, 32.5, 33.4, 41.9, 42.6, 42.8, 43.9, 111.2, 111.3, 113.6, 113.7, 118.9, 119.1, 119.9, 120.0, 121.8, 127.9, 128.4, 136.4, 136.7, 143.4, 144.6. MS (EI) m/z: 255 [M$^+$], 200, 143, 130 (100), 115, 55. Anal. calcd. for $C_{18}H_{25}N$ (255.40): C, 84.65; H, 9.87; N, 5.48. Found: C, 84.90; H, 9.99; 5.61.

General procedure for the reaction of sulfonyl derivatives 7 and 8 with enol ethers and aromatics

To a stirred solution of the appropriate sulfonyl derivative **7** or **8** (1 mmol) in dry CH_2Cl_2 (14 mL) kept under nitrogen atmosphere at −15 °C, the nucleophile (1.5 mmol) and $AlEtCl_2$ (2 mmol) were subsequently added under stirring. After 0.75 h to the reaction mixture was added 2 N HCl (12 mL) and the aqueous phase extracted with CH_2Cl_2 (3 × 10 mL). The organic phase was dried over Na_2SO_4 and after evaporation of the solvent under reduced pressure, the crude product that was purified by flash chromatography (hexanes-ethyl acetate 95 : 5).

13a. Yield 89%. Colorless oil. IR (neat) ν_{max}/cm^{-1}: 752, 907, 1161, 1363, 1427, 1463, 1616, 1717, 3061. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.86–1.00 (m, 1H), 1.07–1.21 (m, 1H), 1.26–1.47 (m, 2H), 1.53–1.70 (m, 2H), 1.76–1.89 (m, 1H), 2.01–2.16 (m, 1H), 2.03 (s, 3H), 2.95 (dd, 1H, J = 5.6, 17.5 Hz), 3.34 (dd, 1H, J = 7.7, 17.5 Hz), 3.40 (t, 2H, J = 6.8 Hz), 5.01–5.11 (m, 1H), 7.10–7.16 (m, 1H), 7.35–7.41 (m, 1H), 7.53 (dd, 1H, J = 0.9, 8.6 Hz), 7.69 (d, 1H, J = 8.1 Hz), 8.01 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.5, 26.6, 30.8, 32.4, 35.3, 45.0, 48.7, 53.8, 109.5, 120.8, 121.0, 123.6, 126.5, 133.7, 140.3, 206.5 MS (EI) m/z: 292 [M$^+$], 257, 235, 187, 145 (100), 131, 118, 91, 77, 43. Anal. calcd. for $C_{16}H_{21}ClN_2O$ (292.80): C, 65.63; H, 7.23; N, 9.57. Found: C, 65.88; H, 7.35; N, 9.71.

13b. Yield 83%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 739, 915, 1462, 1628, 1701, 3062. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.79 (t, 3H, J = 7.3 Hz), 0.91–1.05 (m, 1H), 1.11–1.32 (m, 5H), 1.86–1.98 (m, 1H), 2.12–2.46 (m, 1H), 3.47 (dd, 1H, J = 5.6, 17.5 Hz), 3.90 (dd, 1H, J = 7.3, 17.5 Hz), 5.25–5.35 (m, 1H), 7.11 (t, 1H, J = 7.3 Hz), 7.36–7.44 (m, 3H), 7.49–7.54 (m, 1H), 7.61 (d, 1H, J = 8.5 Hz), 7.68 (d, 1H, J = 8.1 Hz), 7.87–7.92 (m, 2H), 8.01 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 22.6, 26.0, 31.5, 35.7, 44.1, 54.2, 109.6, 120.7, 121.0, 123.6, 126.4, 128.3, 128.7, 133.4, 133.6, 136.8, 140.4, 197.9. MS (EI) m/z: 320 [M$^+$], 249, 215, 201, 145, 131, 118, 105 (105), 77, 55, 41, 29. Anal. calcd. for $C_{21}H_{24}N_2O$ (320.43): C, 78.71; H, 7.55; N, 8.74. Found: C, 78.96; H, 7.44; N, 8.87.

13c. Diastereomeric mixture 50 : 50. Yield 84%. Colorless oil. IR (neat) ν_{max}/cm^{-1}: 752, 908, 1130, 1424, 1464, 1616, 1709, 3060. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.79–0.86 (m, 3H), 0.98–1.32 (m, 13H), 1.47–1.81 (m, 4H), 1.88–2.20 (m, 3H), 2.21–2.51 (m, 2H), 2.99–3.15 (m, 1H), 4.76–4.84 (m, 0.5H), 5.03–5.11 (m, 0.5H), 7.08–7.17 (m, 1H), 7.32–7.41 (m, 1H), 7.45 (d, 0.5H, J = 8.6 Hz), 7.55 (d, 0.5H, J = 8.6 Hz), 7.67–7.75 (m, 1H), 7.98 (s, 0.5H), 8.06 (s, 0.5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 14.3, 22.7, 22.8, 25.2, 25.4, 26.3, 26.5, 28.2, 29.1, 29.3, 29.4, 29.5, 29.6, 30.4, 31.0, 31.8, 32.0, 33.4, 34.5, 42.6, 43.3, 55.5, 56.1, 56.7, 57.7, 109.3, 109.9, 120.6, 120.7, 121.0, 121.2, 123.4, 123.6, 126.2, 126.5, 133.2, 133.8, 140.5, 141.5, 211.4, 212.5. MS (EI) m/z: 340 [M$^+$], 243 (100), 228, 118, 81, 55. Anal. calcd. for $C_{22}H_{32}N_2O$ (340.50): C, 77.60; H, 9.47; N, 8.23. Found: C, 77.44; H, 9.36; N, 8.29.

13d. Yield 81%. Colorless oil. IR (neat) ν_{max}/cm^{-1}: 741, 752, 908, 1137, 1262, 1465, 1615, 1727, 3062. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.71–0.86 (m, 1H), 0.82 (t, 3H, J = 7.3 Hz), 0.88–1.01 (m, 1H), 1.03–1.27 (m, 10H), 1.06 (s, 3H), 1.41 (s, 3H), 1.58–1.69 (m, 1H), 2.35–2.48 (m, 1H), 3.60 (s, 3H), 4.82 (dd, 1H, J = 2.6, 11.5 Hz), 7.09–7.15 (m, 1H), 7.33–7.39 (m, 1H), 7.48 (d, 1H, J = 8.5 Hz), 7.70 (d, 1H, J = 8.1 Hz), 8.04 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 20.9, 22.8, 23.8, 26.6, 29.3, 23.4, 29.5, 30.3, 32.0, 48.5, 52.3, 63.7, 109.6, 120.7, 121.1, 123.4, 126.3, 133.6, 141.9, 177.3. MS (EI) m/z: 344 [M$^+$], 313, 243 (100), 171, 157, 144, 131, 118, 69, 55, 41. Anal. calcd. for $C_{21}H_{32}N_2O_2$ (344.49): C, 73.22; H, 9.36; N, 8.13. Found: C, 73.31; H, 9.48, N, 8.22.

13e. Yield 57%. Colorless oil. IR (neat) ν_{max}/cm^{-1}: 741, 908, 1171, 1203, 1436, 1464, 1616, 1737, 3061. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.71 (t, 3H, J = 7.3 Hz), 1.86–1.99 (m, 1H), 2.06–2.20 (m, 1H), 2.90 (dd, 1H, J = 5.1, 15.8 Hz), 3.14 (dd, 1H, J = 8.5, 16.2 Hz), 3.51 (s, 3H), 4.88–4.97 (m, 1H), 7.09–7.15 (m, 1H), 7.34–7.40 (m, 1H), 7.51 (dd, 1H, J = 0.9, 8.5 Hz), 7.70 (dt, 1H, J = 1.3, 8.1 Hz), 8.03 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.0, 28.6, 39.8, 52.0, 56.8, 109.4, 120.8, 121.2, 123.8, 126.4, 133.8, 140.6,

171.9. MS (EI) *m/z*: 232 [M$^+$], 203, 171, 159 (100), 144, 131, 118, 85, 77, 63, 55. Anal. calcd. for $C_{13}H_{16}N_2O_2$ (232.28): C, 67.22; H, 6.94; N, 12.06. Found: C, 67.14; H, 7.06; N, 12.18.

13f. Diastereomeric mixture 60 : 40, Yield 60%. **13fa**. Yield 36%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 752, 908, 1160, 1465, 1616, 1654, 1758, 3027, 3062, 3086. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.28–2.43 (m, 1H), 2.49–2.61 (m, 2H), 2.77–2.93 (m, 1H), 4.43–4.51 (m, 1H), 5.42 (dt, 1H, J = 1.7, 7.3 Hz), 5.96 (dd, 1H, J = 1.7, 5.6 Hz), 6.96–7.01 (m, 3H), 7.15–7.26 (m, 5H), 7.36–7.41 (m, 1H), 7.73–7.77 (m, 1H), 8.10 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.9, 33.3, 59.7, 85.0, 109.2, 121.5, 121.6, 122.5, 124.0, 126.5, 127.2, 128.7, 134.9, 140.3, 140.8, 154.0, 172.3. MS (EI) *m/z*: 318 [M$^+$], 235, 200, 117, 91 (100), 65, 39. Anal. calcd. for $C_{20}H_{18}N_2O_2$ (318.37): C, 75.45; H, 5.70; N, 8.80. Found: C, 75.55; H, 5.81; 8.97. **13fb**. Yield 24%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 751, 908, 1159, 1467, 1614, 1654, 1786, 3025, 3060, 3085. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.07–2.18 (m, 1H), 2.25–2.37 (m, 1H), 2.43–2.53 (m, 1H), 2.54–2.67 (m, 1H), 4.79–4.86 (m, 1H), 5.25 (dt, 1H, J = 1.7, 4.7 Hz), 6.11 (dd, 1H, J = 1.7, 5.6 Hz), 6.95–7.00 (m, 2H), 7.14–7.28 (m, 4H), 7.32 (dd, 1H, J = 0.9, 8.5 Hz), 7.38–7.45 (m, 1H), 7.69 (dd, 1H, J = 1.7, 5.6 Hz), 7.76 (dt, 1H, J = 0.9, 8.1 Hz), 8.11 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.4, 31.9, 58.6, 84.5, 109.2, 121.5, 123.0, 124.2, 126.5, 127.1, 128.6, 128.7, 128.8, 130.0, 134.8, 140.3, 154.1, 172.4. MS (EI) *m/z*: 318 [M$^+$], 235, 200, 117, 91 (100), 65, 39. Anal. calcd. for $C_{20}H_{18}N_2O_2$ (318.37): C, 75.45; H, 5.70; N, 8.80. Found: C, 75.68; H, 5.64; N, 8.91.

13g. Yield 51%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 741, 785, 912, 1022, 1173, 1219, 1421, 1464, 1616, 3061, 3102 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.87 (t, 3H, J = 7.7 Hz), 2.20 (s, 3H), 2.31–2.57 (m, 2H), 5.55 (dd, 1H, J = 6.0, 9.4 Hz), 5.87–5.90 (m, 1H), 6.17 (d, 1H, J = 3.0 Hz), 7.11–7.16 (m, 1H), 7.32–7.37 (m, 1H), 7.48 (dd, 1H, J = 0.9, 8.5 Hz), 7.71–7.43 (m, 1H), 8.04 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.2, 13.8, 26.1, 58.9, 106.4, 108.1, 109.7, 120.7, 121.3, 124.4, 126.2, 133.4, 139.7, 151.6, 152.0. (EI) *m/z*: 240 [M$^+$], 211, 123 (100), 107, 95, 77, 43. Anal. calcd. for $C_{15}H_{16}N_2O$ (240.30): C, 74.97; H, 6.71; N, 11.66. Found: 74.85; H, 6.84, N, 11.79.

13h. Yield 63%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 738, 1045, 1112, 1158, 1375, 1460, 1619, 1731. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.12–1.31 (m, 2H), 1.37–1.48 (m, 2H), 1.60–1.71 (m, 2H), 2.15–2.27 (m, 1H), 2.52–2.65 (m, 1H), 3.40 (t, 2H, J = 6.8 Hz), 3.67 (s, 3H), 5.45 (dd, 1H, J = 6.0, 9.4 Hz), 6.73 (d, 2H, J = 9.0 Hz), 7.01–7.07 (m, 1H), 7.20 (d, 2H, J = 9.0 Hz), 7.21–7.27 (m, 1H), 7.32 (d, 1H, J = 8.5 Hz), 7.64 (d, 1H, J = 8.1 Hz), 7.98 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.0, 26.5, 32.3, 35.0, 45.0, 55.2, 62.0, 109.3, 113.9, 120.6, 121.1, 124.2, 126.1, 127.9, 133.0, 133.3, 139.5, 159.0. (EI) *m/z*: 344 [M+2$^+$], 342 [M$^+$], 237, 225, 121 (100), 91, 77, 41. Anal. calcd. for $C_{20}H_{23}ClN_2O$ (342.86): C, 70.06; H, 6.76; N, 8.17. Found: C, 70.30; H, 6.89; N, 8.02.

13i. Yield 77%. Colorless waxy solid. IR (neat) ν_{max}/cm^{-1}: 740, 1040, 1116, 1157, 1377, 1462, 1616, 1732. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.45–2.68 (m, 3H), 2.92–3.04 (m, 1H), 3.74 (s, 3H), 3.79 (s, 3H), 6.02 (dd, 1H, J = 5.1, 10.3 Hz), 6.41 (s, 1H), 7.08–7.14 (m, 3H), 7.15–7.21 (m, 1H), 7.22–7.35 (m, 5H), 7.40 (d, 1H, J = 8.5 Hz), 7.71 (d, 1H, J = 8.1 Hz), 8.09 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 33.0, 36.3, 53.8, 55.5, 55.6, 98.4, 104.6, 109.9, 120.6, 120.9, 122.3, 124.0, 125.9, 126.0, 128.2, 128.4, 128.7, 133.3, 140.1, 141.7, 157.3, 160.3. (EI) *m/z*: 372 [M$^+$], 267, 255, 151 (100), 121, 91, 77, 65. Anal. calcd. for $C_{24}H_{24}N_2O_2$ (372.46): C, 77.39; H, 6.49; N, 7.52. Found: C, 77.25; H, 6.59; N, 7.71.

14a. Yield 72%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 752, 923, 1034, 1173, 1215, 1484, 1582, 1624, 1707, 3409. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.83 (t, 3H, J = 7.3 Hz), 1.16–1.32 (m, 6H), 1.60–1.82 (m, 2H), 2.03 (s, 3H), 2.74–2.91 (m, 2H), 3.37–3.48 (m, 1H), 3.88 (s, 3H), 6.85 (dd, 1H, J = 2.6, 8.6 Hz), 6.93 (s, 1H), 7.09 (d, 1H, J = 2.6 Hz), 7.23 (d, 1H, J = 9.0 Hz), 8.00 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 22.8, 27.4, 30.7, 32.0, 32.9, 35.9, 50.3, 56.2, 101.6, 111.9, 112.1, 118.9, 122.2, 127.2, 131.9, 153.8, 209.3. MS (EI) *m/z*: 287 [M$^+$], 244, 230, 216, 174, 160 (100), 130, 43. Anal. calcd. for $C_{18}H_{25}NO_2$ (287.40): C, 75.22; H, 8.77; N, 4.87. Found: C, 75.31; H, 8.69; N, 4.95.

14b. Yield 70%. Yellow solid, m.p. 84-87 °C. IR (nujol) ν_{max}/cm^{-1}: 740, 918, 1208, 1463, 1635, 1679. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.80 (t, 3H, J = 7.3 Hz), 1.81–2.04 (m, 2H), 2.37 (s, 3H), 3.40 (dd, 1H, J = 6.0, 15.4 Hz), 3.45–3.54 (m, 1H), 3.58 (dd, 1H, J = 6.4, 15.4 Hz), 3.61 (s, 3H), 7.03–7.08 (m, 1H), 7.10–7.16 (m, 1H), 7.23 (d, 1H, J = 8.1 Hz), 7.37 (t, 2H, J = 7.7 Hz), 7.44–7.51 (m, 1H), 7.67 (d, 1H, J = 7.7 Hz), 7.83–7.87 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.6, 12.9, 28.4, 29.7, 35.2, 44.8, 109.0, 112.9, 118.5, 119.2, 120.3, 127.8, 128.2, 128.5, 129.9, 132.8,136.7, 137.2, 200.3. MS (EI) *m/z*: 305 [M$^+$], 276, 186 (100), 171, 105, 77. Anal. calcd. for $C_{21}H_{23}NO$ (305.41): C, 82.58; H, 7.59; N, 4.59. Found: C, 82.36; H, 7.74; N, 5.51.

14c. Yield 67%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 1377, 1460, 1698, 3361. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.81 (t, 3H, J = 6.8 Hz), 0.97 (s, 9H), 1.07–1.33 (m, 6H), 1.60–1.75 (m, 1H), 1.81–1.96 (m 1H), 2.39 (s, 3H), 2.86 (dd, 1H, J = 6.4, 16.7 Hz), 3.11 (dd, 1H, J = 7.7, 17.1 Hz), 3.39–3.50 (m, 1H), 7.01–7.13 (m, 2H), 7.25 (d, 1H, J = 8.6 Hz), 7.61 (d, 1H, J = 7.3 Hz), 7.74 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.2, 14.3, 22.8, 26.3, 28.0, 32.0, 32.4, 35.0, 42.7, 44.4, 110.6, 114.0, 118.9, 119.3, 120.6, 127.4, 131.7, 135.8, 215.7. MS (EI) *m/z*: 313 [M$^+$], 242, 214 (100), 157, 144, 130, 85, 57, 41, 29. Anal. calcd. for $C_{21}H_{31}NO$ (313.48): C, 80.46; H, 9.97; N, 4.47. Found: C, 80.65; H, 10.11; N, 4.61.

14d. Diastereomeric mixture 50 : 50. Yield 80%. Colorless oil. IR (neat) ν_{max}/cm^{-1}: 738, 1377, 1458, 1618, 1700, 3411. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.75 (t, 1.5H, J = 7.7 Hz), 0.87 (t, 1.5H, J = 7.7 Hz), 1.28–2.08 (m, 8H), 2.15–2.27 (m, 0.5H), 2.31–2.53 (m, 1.5H), 2.61–2.70 (m, 0.5H), 2.74–2.85 (m, 0.5H), 3.17–3.27 (m, 0.5H), 3.53–3.61 (m, 0.5H), 6.99 (d, 0.5H, J = 2.1 Hz), 7.01 (d, 0.5H, J = 2.1 Hz), 7.07–7.14 (m, 1H), 7.15–7.22 (m, 1H), 7.33–7.40 (m, 1H), 7.58 (d, 0.5H, J = 7.7 Hz), 7.66 (d, 0.5H, J = 7.7 Hz), 8.05 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.8, 12.9, 24.0, 24.2, 24.7, 27.3, 27.9, 29.0, 29.1, 32.8, 36.3, 38.8, 42.3, 42.4, 55.5, 56.6, 111.4, 111.5, 117.0, 117.9, 119.1, 119.3, 119.4, 120.0, 122.0, 122.2, 122.8, 127.5, 127.8, 136.5, 136.8, 213.1, 214.9. MS (EI) *m/z*: 255 [M$^+$], 158 (100), 130, 115, 77. Anal. calcd. for $C_{17}H_{21}NO$ (255.35): C, 79.96; H, 8.29; N, 5.49. Found: C, 80.18; H,8.41; N, 5.57.

14e. Yield 61%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 771, 917, 1377, 1459, 1718, 3327. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.78 (s, 3H), 0.82 (t, 3H, J = 7.3 Hz), 1.08 (s, 3H), 1.17–1.39 (m, 6H), 1.51–1.63 (m, 1H), 2.20–2.34 (m, 1H), 3.34 (dd, 1H, J = 3.4, 12.4 Hz), 7.08–7.14 (m, 1H), 7.16–7.22 (m, 1H), 7.36 (d, 1H, J = 8.1 Hz), 7.39–7.51 (m, 5H), 7.72 (d, 1H, J = 8.1 Hz), 8.10 (bs, 1H), 9.32 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.9, 21.5, 22.7, 28.7, 29.2, 32.4, 42.4, 52.1, 111.1, 111.2, 119.7, 122.0, 122.2, 128.0, 128.4, 129.0, 129.8, 133.9, 136.4, 138.0, 207.5. MS (EI) *m/z*: 347 [M$^+$], 276, 217,

206, 44, 32 (100). Anal. calcd. for $C_{24}H_{29}NO$ (347.49): C, 82.95; H, 8.41; N, 4.03. Found: C, 83.09; H, 8.54; N, 3.91.

14f. Yield 79%. White solid, m.p. 165-167 °C. IR (nujol) ν_{max}/cm^{-1}: 736, 771, 869, 1121, 1259, 1618, 1715, 3369. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.78–0.88 (m, 3H), 0.84 (s, 3H), 1.16–1.35 (m, 6H), 1.19 (s, 3H), 1.47–1.59 (m, 1H), 2.28–2.44 (m, 1H), 3.51 (s, 3H), 3.57 (dd, 1H, $J = 3.4$, 12.0 Hz), 7.09 (t, 1H, $J = 7.7$ Hz), 7.17 (t, 1H, $J = 7.7$ Hz), 7.32–7.43 (m, 2H), 7.44–7.54 (m, 4H), 7.75 (d, 1H, $J = 8.1$ Hz), 8.08 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 22.1, 22.8, 26.0, 28.8, 29.7, 32.4, 44.5, 48.8, 51.8, 111.0, 111.6, 119.5, 121.7, 122.5, 128.1, 128.3, 128.8, 129.7, 134.3, 136.3, 138.4, 179.0. MS (EI) m/z: 377 [M^+], 276 (100), 232, 206, 179, 128, 73, 41. Anal. calcd. for $C_{25}H_{31}NO_2$ (377.52): C, 79.54; H, 8.28; N, 3.71. Found: C, 79.68; H, 8.39; N, 3.87.

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