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Construction of nitrogen-heterocyclic compounds through zirconium mediated intramolecular alkene-carbonyl coupling reaction of *N*-(*o*-alkenylaryl)carbamate derivatives

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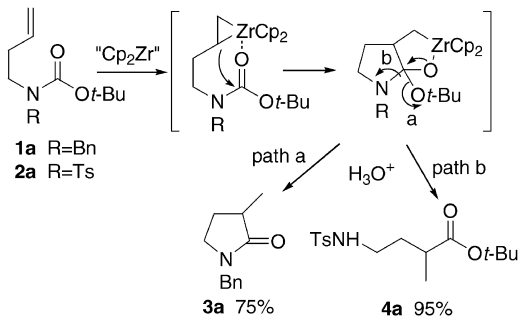
Abstract—Intramolecular alkene-carbonyl coupling reaction of *N*-benzyl-*N*-(*o*-alkenylaryl)carbamate derivative derived from *o*-aminostyrene, *o*-(aminomethyl)styrene and *o*-aminoallylbenzene smoothly proceeded by treating with zirconocene–butene complex to give the corresponding lactam derivative.

1. Introduction

Low valent zirconium-mediated intramolecular coupling reaction of unsaturated functional groups has been extensively developed as a powerful mean for the construction of cyclic compounds.[1] While such zirconium-mediated intramolecular coupling reactions were limited to the cases of alkene, alkyne and imine derivatives,[2,3] we have recently demonstrated successful examples of intramolecular alkene-carbonyl coupling reaction by using *N*-alkenyl-*N*-substituted *tert*-butyl carbamate derivatives as the substrates.[4] One of the characteristic features of the present reaction is the effect of the substituent on the nitrogen atom on the reaction course. That is, as shown in Scheme 1,



Scheme 1.

depending on the ability as a leaving group (–NBn vs –NTs vs O*t*-Bu), lactam derivative **3a** is formed from the substrate **1a** having an electron donating group such as benzyl group (path a), while γ-aminobutyric acid derivative **4a** is obtained from the substrate **2a** having an electron withdrawing group such as sulfonyl group (path b).

Furthermore, not only electronic nature of the substituent on the nitrogen atom, steric effect of carbamate moiety maybe influences the reactivity and the reaction pathway. For example, the coupling reaction of sterically bulky *tert*-butyl carbamate of *N*-4-pentenyl-*N*-tosylamide **2b** proceeded after migration of zirconium into the inner site resulting in the formation of γ-aminobutyric acid derivative **4b**, while the benzyl carbamate **2c** gave δ-aminopentanoic acid derivative **4c** (Scheme 2).[4,5]

Based on our findings mentioned above, we extended the present zirconium-mediated intramolecular coupling reaction to *N*-(*o*-alkenylaryl)carbamate derivatives **1c–m** (*N*-benzyl derivatives), **2d–g** (*N*-tosyl derivatives) to examine the substituent effect of the carbamate moiety on the reactivity as well as to develop an efficient method for the preparation of nitrogen-containing heterocyclic compounds (Chart 1).[6]

2. Results and discussion

Since *N*-tosyl *tert*-butyl carbamates are good substrates in the zirconium mediated intramolecular alkene-carbonyl coupling reaction as reported in our preliminary results,[4] *N*-Boc-*N*-tosyl substituted *o*-aminostyrene **2d** and

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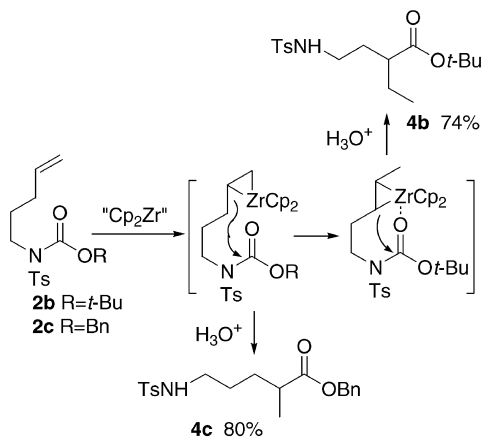


Scheme 2.

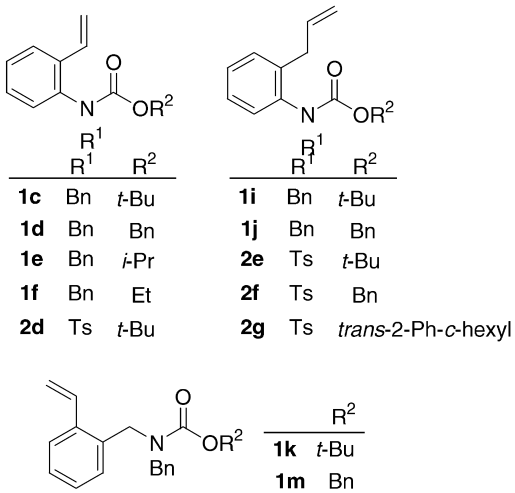
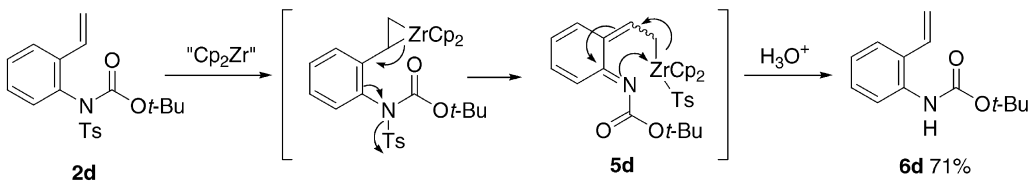


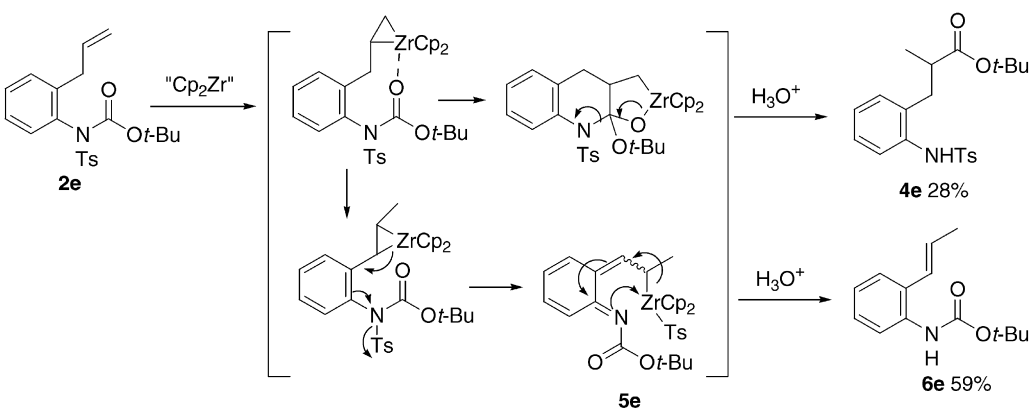
Chart 1.

o-aminoallylbenzene **2e** were chosen as a starting material. Reaction of *o*-aminostyrene derivative **2d** with zirconocene–butene complex[7] did not give the desired ester transfer product but exclusively afforded the desufonylated carbamate **6d** in 71% isolated yield. As shown in Scheme 3, the reaction pathway to the carbamate **6d** possibly involves the zirconium-promoted 1,4-elimination of sulfonyl group to form *o*-quinodimethane intermediate **5d** and the subsequent re-aromatization.[8] With one carbon elongated allylbenzene derivative **2e**, both alkene-carbonyl coupling reaction and desulfonylation reaction competitively proceeded. In this case, unlike the aliphatic substrate **2b** (Scheme 2), the alkene-carbonyl coupling reaction proceeded without migration of zirconium to give the α-methylated ester derivative **4e** as a minor product (28% yield) and the major product was the *E* isomer of desulfonylated compound **6e** (59% yield) derived after migration of zirconium (Scheme 4).

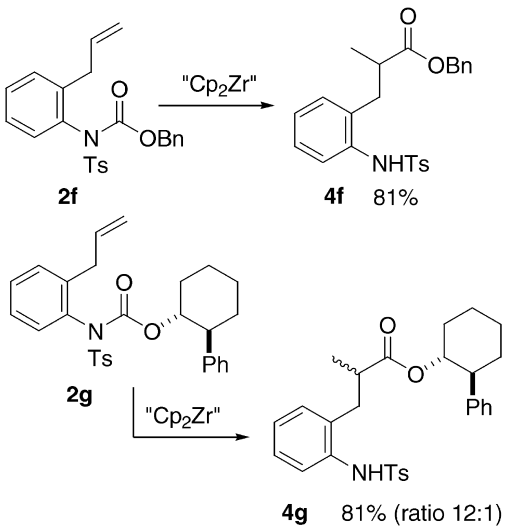
We found that in the case of allylbenzene derivatives, the desired alkene-carbonyl coupling reaction can be controlled to be a major reaction by using sterically less hindered carbamate by changing *tert*-butyl ester to primary or secondary alkyl ester such as benzyl carbamate **2f** and cyclohexyl carbamate **2g**. That is, with these substrates prior to migration of zirconium into the inner site (see Scheme 4), alkene-carbonyl coupling reaction smoothly occurred to give the ester transfer product **4f** and **4g** in good yields as shown in Scheme 5. It is also noted that reaction of *trans*-2-phenylcyclohexyl carbamate **2g** proceeded in a highly diastereoselective manner (isomer ratio 12:1) obtaining the α-methylated ester derivative **4g**, although the relative stereochemistry was not determined. In contrast to the allylbenzene derivatives mentioned above, desulfonylation was a major pathway in the reaction of benzyl carbamate of *o*-(tosylamino)styrene with zirconocene–butene complex.



Scheme 3.



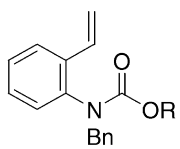
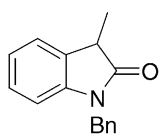
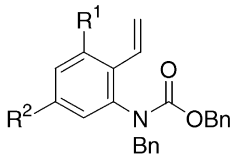
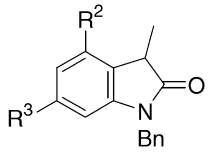
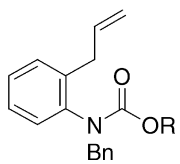
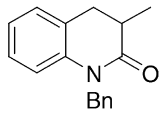
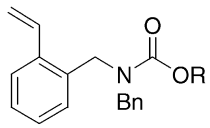
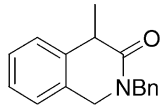
Scheme 4.



Scheme 5.

As mentioned above, since the present alkene-carbonyl coupling reaction cannot be applied to the *N*-sulfonyl carbamate of *o*-aminostyrene such as **2d** or the corresponding benzyl carbamate due to the facile desulfonylation reaction, *N*-benzyl derivatives were examined as substrates.

Table 1. 'Cp_2Zr' mediated coupling reaction of *N*-benzyl carbamate derivatives

Entry	Substrate	Product	Yield (%)
			
1	**1c** R=*t*-Bu	**3c**	51
2	**1d** R=Bn		59
3	**1e** R=*i*-Pr		48
4	**1f** R=Et		40
			
5	**1g** R^1=OMe R^2=H	**3g**	45
6	**1h** R^1=H R^2=OMe	**3h**	49
			
7	**1i** R=*t*-Bu	**3i**	69
8	**1j** R=Bn		88
			
9	**1k** R=*t*-Bu	**3k**	69
10	**1m** R=Bn		62

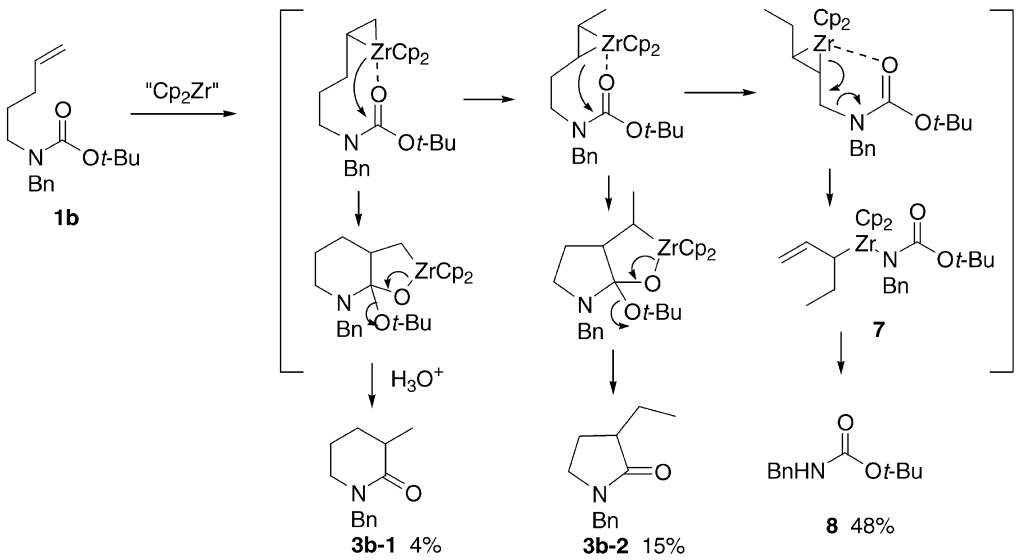
Thus, reaction of *N*-benzyl carbamates **1c**–**h** derived from *o*-aminostyrene, **1i**, **1j** from *o*-aminoallylbenzene and **1k**, **1m** from *o*-(aminomethyl)styrene with in situ generated zirconocene–butene complex were conducted and results are summarized in Table 1.

Contrary to the *N*-tosyl derivative **2d** (Scheme 3), *N*-benzyl derivative **1c** smoothly reacted with zirconocene–butene complex to give the intramolecular alkene-carbonyl coupling product **3c** in moderate yield (51%, entry 1, see also Scheme 7). Yield of the lactam derivative **3c** slightly varied by changing the steric demand of the ester part. Thus, the benzyl ester **1d** gave a higher yield of **3c** than either sterically hindered *tert*-butyl ester **1c** or less hindered ethyl ester **1f** (see entries 1, 2, 4). With the substrates **1g**, **1h** having an additional methoxyl group on the aromatic ring gave the corresponding 3-methylindoline derivatives **1g** and **1h**, respectively (entries 5, 6).

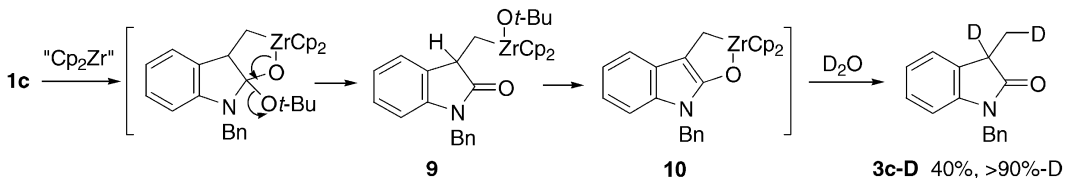
Six-membered ring forming reaction from *o*-aminoallylbenene derivatives **1i**, **1j** and *o*-(aminomethyl)styrene derivatives **1k**, **1m** proceeded much more effectively giving rise to the coupling product in good yields (entries 7–10). In the case of conversion into dihydroquinolone **3i**, benzyl ester **1j** gave a higher yield than *tert*-butyl ester **1i**, and in both cases 3-ethylindolinone derivative, possibly formed via migration of zirconium, was not detected (entries 7, 8). Efficient formation of these six-membered ring compounds **3i**, **3k** via alkene-carbonyl coupling reaction should be mainly due to *ortho*-substituted benzene structure of the substrate, because such an efficient cyclization reaction could not be achieved with the substrate of linear chain structure. For example, upon treating *N*-4-pentenyl benzyl carbamate **1b** with zirconocene–butene complex, two coupling products, piperidone **3b-1** (4%) and pyrrolidone **3b-2** (15%), were obtained in low yields along with the isolation of the pentenyl chain lacked *N*-benzyl carbamate **8** as a main product (48%). It is likely that formation of the dealkenylated product **8** involves the stepwise migration of zirconium leading to the intermediacy allylic zirconium species **7** (Scheme 6).[9]

To clarify the reaction pathway, deuterium oxide (D_2O) quenching of the reaction mixture was examined. After treatment of **1c** with zirconocene–butene complex under similar conditions as before (Table 1, entry 1), the reaction mixture was quenched with D_2O. High level (>90%) of deuterium incorporation was observed at both 3-position and at the methyl group of indoline derivative **3c-D** (Scheme 7). The reaction pathway possibly involves the intramolecular alkene-carbonyl coupling reaction followed by the formation of the lactam structure **9** having zirconated methyl substituent at the 3-position. In the next stage, it would be likely that zirconium *tert*-butoxide in the intermediate **9** acts as a base to deprotonate at the 3-position to form the five-membered zirconium enolate form **10**, which converted to the bisdeuterated indoline **3c-D**.

In the cases of six-membered ring forming reaction with the substrates **1j** and **1k**, deuterium incorporation was observed at the methyl group, giving rise to **3i-D** and **3k-D** in high yields (Scheme 8). When the reaction mixture was

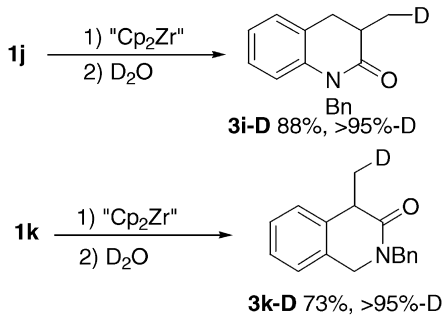


Scheme 6.

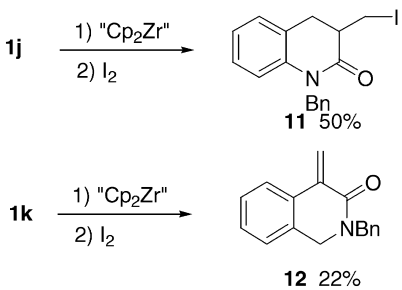


Scheme 7.

quenched by the addition of iodine instead of D_2O, iodomethyl derivative **11** was isolated in 50% yield in the case of **1j** and methylene derivative **12** was obtained in 22% yield in the case of **1k** (Scheme 9).



Scheme 8.



Scheme 9.

3. Conclusion

Zirconocene–butene complex mediated intramolecular alkene-carbonyl coupling reaction can be applied to *N*-benzyl carbamate derivatives derived from *o*-aminostyrene, *o*-aminoallylbenzene and *o*-(aminomethyl)styrene to give the corresponding nitrogen-heterocyclic compounds.

4. Experimental

4.1. General

Toluene (dehydrated), THF (dehydrated, no stabilizer) and zirconocene dichloride are available commercially. All reactions were conducted under an argon atmosphere. ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ and the chemical shifts are given in ppm using $CHCl_3$ (7.26 ppm) in $CDCl_3$ for ^1H NMR and $CDCl_3$ (77.01 ppm) for ^{13}C NMR as internal standard, respectively. Mass spectra and HRMS were recorded by electrospray ionization. Column chromatography was performed on silica gel (70–230 mesh). Medium-pressure liquid chromatography (MPLC) was performed on a 30 cm×2.2 cm i.d. prepacked column (silica gel, 50 μm) with a UV or RI detector.

4.2. Procedure for the preparation of the carbamate derivative 1 and 2

To a mixture of 2-vinylbenzoic acid (741 mg, 5 mmol), triethylamine (1.05 ml, 7.5 mmol) in benzene (50 ml) was

added diphenylphosphoryl azide (DPPA, 1.62 ml, 7.5 mmol) at room temperature. After being stirred for 1 h at the same temperature, 2-methyl-2-propanol (4.8 ml, 50 mmol) was added and the reaction mixture was heated at reflux. After being stirred for 3 h until gas evolution had ceased, the reaction mixture was poured into sat. $NaHCO_3$ and then extracted with ether. The organic layer was washed with brine, dried over $MgSO_4$, and then concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/AcOEt=20:1) to give *tert*-butyl 2-vinylphenylcarbamate **6d** (800 mg, 73% yield) whose ^{1}H NMR data were in good agreement with those described in the literature.[10] The above carbamate (439 mg, 2 mmol) dissolved in DMF was added dropwise to sodium hydride (96.0 mg, 2.4 mmol) in DMF (20 ml) at room temperature. After being stirred for 30 min at the same temperature, benzyl bromide (0.36 ml, 3 mmol) was added and the whole was stirred overnight. The reaction mixture was quenched by the addition of 1N HCl and extracted with ether. The organic layer was washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, and then concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/AcOEt=20:1) to give **1c** (616 mg, quantitative yield).

4.2.1. *tert*-Butyl benzyl(2-vinylphenyl)carbamate 1c. Colorless oil. IR (neat) ν; 1698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ; 7.58 (1H, d, J=7.6 Hz), 7.33–7.23 (6H, m), 7.18 (1H, t, J=7.2 Hz), 6.91 (1H, brs), 6.71(1H, dd, J=17.5, 11.1 Hz), 5.71 (1H, d, J=17.6 Hz), 5.29 (1H, d, J=11.0 Hz), 5.07 (1H, brs), 4.45 (1H, brs), 1.43 (9H, brs). ^{13}C NMR (100.6 MHz, $CDCl_3$, 50 °C) δ; 115.1, 140.1, 138.1, 135.7, 133.0, 129.1, 128.8, 128.3, 128.1, 127.3, 127.2, 125.9, 115.4, 80.2, 53.8, 28.3. MS m/z: 310 $(M+H)^+$. Anal. calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.51; H, 7.63; N, 4.45.

4.2.2. Benzyl benzyl(2-vinylphenyl)carbamate 1d. Colorless oil. IR (neat) ν; 1704 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ; 7.56 (1H, d, J=7.8 Hz), 7.26–7.21 (11H, m), 7.15 (1H, t, J=7.6 Hz), 6.86 (1H, brs), 6.63 (1H, dd, J=17.5, 11.1 Hz), 5.66 (1H, d, J=17.5 Hz), 5.22 (1H, d, J=11.1 Hz), 5.16 (1H, brs), 4.41 (1H, brs). ^{13}C NMR (100.6 MHz, $CDCl_3$, 50 °C) δ; 155.9, 139.2, 137.4, 136.8, 135.7, 132.4, 129.3, 129.0, 128.3, 128.3, 128.2, 127.8, 127.5, 126.2, 116.0, 67.3, 54.4. MS m/z: 366 $(M+Na)^+$. Anal. calcd for $C_{23}H_{21}NO_2$: C, 80.44; H, 6.16; N, 4.08. Found: C, 80.36; H, 6.33; N, 4.13.

4.2.3. Isopropyl benzyl(2-vinylphenyl)carbamate 1e. Colorless oil. IR (neat) ν; 1696 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ; 7.61 (1H, d, J=7.6 Hz), 7.34–7.26 (6H, m), 7.20 (1H, t, J=7.6 Hz), 6.92 (1H, brs), 6.70 (1H, dd, J=17.4, 11.1 Hz), 5.73 (1H, d, J=17.6 Hz), 5.30 (1H, d, J=11.0 Hz), 5.11–5.02 (2H, m), 4.47 (1H, brs), 1.22 (6H, brs). ^{13}C NMR (100.6 MHz, $CDCl_3$, 50 °C) δ; 155.7, 139.6, 137.4, 137.8, 135.7, 132.7, 129.2, 129.0, 128.3, 128.1, 127.5, 127.4, 126.1, 115.6, 69.2, 54.2, 22.0. MS m/z: 318 $(M+Na)^+$. Anal. calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.12; H, 7.30; N, 4.68.

4.2.4. Ethyl benzyl(2-vinylphenyl)carbamate 1f. Colorless oil. IR (neat) ν; 1702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ; 7.54 (1H, dd, J=7.8, 1.3 Hz), 7.28–7.18 (6H, m), 7.13 (1H, dd, J=7.6, 1.4 Hz), 6.84 (1H, d, J=7.4 Hz), 6.33 (1H, dd, J=17.5, 11.1 Hz), 5.65 (1H, dd, J=17.6, 0.9 Hz), 5.29 (1H, dd, J=11.0, 0.9 Hz), 5.05 (1H, brs), 4.40 (1H, brs), 4.14 (2H, brs), 1.14 (3H, brs). ^{13}C NMR (100.6 MHz, $CDCl_3$, 50 °C) δ; 156.1, 139.4, 137.6, 135.7, 132.6, 129.2, 129.0, 128.3, 128.2, 127.6, 127.5, 126.1, 115.8, 61.7, 54.3, 14.6. MS m/z: 304 $(M+Na)^+$. Anal. calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.84; H, 6.81; N, 4.83.

4.2.5. Benzyl benzyl(3-methoxy-2-vinylphenyl)carbamate 1g. White solid: mp 64.0–65.0 °C. IR (KBr) ν; 1697 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ; 7.39–7.14 (10H, m), 7.06 (1H, t, J=8.1 Hz), 6.83 (1H, d, J=8.2 Hz), 6.54 (1H, dd, J=17.9, 12.0 Hz), 6.48 (1H, brs), 5.79 (1H, dd, J=18.0, 2.2 Hz), 5.41 (1H, dd, J=6.0, 2.1 Hz), 5.17 (3H, brs), 4.23 (1H, d, J=14.0 Hz), 3.85 (3H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, 50 °C) δ; 158.6, 155.9, 140.5, 137.6, 136.9, 129.0, 128.8, 128.3, 127.7, 127.4, 124.7, 122.2, 119.9, 110.4, 67.3, 55.8, 54.2. MS m/z: 396 $(M+Na)^+$. Anal. calcd for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. Found: C, 77.19; H, 6.15; N, 3.73.

4.2.6. Benzyl benzyl(5-methoxy-2-vinylphenyl)carbamate 1h. Colorless oil. IR (neat) ν; 1703 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ; 7.48 (1H, d, J=8.7 Hz), 7.26–7.22 (10H, m), 6.82 (1H, dd, J=8.7, 2.5 Hz), 6.55 (1H, dd, J=17.8, 11.1 Hz), 6.33 (1H, brs), 5.55 (1H, d, J=17.5 Hz), 5.16 (3H, brs), 5.11 (1H, d, J=11.1 Hz), 4.35 (1H, brs), 3.61 (3H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, 50 °C) δ; 159.5, 155.8, 140.1, 137.5, 136.8, 131.9, 129.1, 128.3, 128.3, 127.8, 127.6, 127.0, 114.4, 114.3, 113.9, 67.4, 55.3, 54.3. MS m/z: 396 $(M+Na)^+$. Anal. calcd for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. Found: C, 77.30; H, 6.09; N, 3.79.

4.2.7. *tert*-Butyl 2-allylphenyl(benzyl)carbamate 1i. Colorless oil. IR (neat) ν; 1697 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ; 7.37–7.24 (7H, m), 7.18 (1H, t, J=6.8 Hz), 7.04–6.87 (1H, brs), 5.94–5.78 (1H, m), 5.13 (1H, d, J=10.0 Hz), 5.12 (1H, d, J=18.2 Hz), 5.02 (1H, d, J=14.6 Hz), 4.53 (1H, d, J=14.6 Hz), 3.40–3.12 (2H, m), 1.49 (9H, brs). ^{13}C NMR (100.6 MHz, $CDCl_3$, 50 °C) δ; 155.0, 140.8, 138.2, 138.0, 136.7, 129.8, 128.9, 128.3, 127.4, 127.3, 126.7, 116.1, 80.1, 54.1, 35.2, 28.4. MS m/z: 324 $(M+H)^+$. Anal. calcd for $C_{21}H_{25}NO_2$: C, 77.98; H, 7.79; N, 4.33. Found: C, 77.88; H, 7.79; N, 4.07.

4.2.8. Benzyl 2-allylphenyl(benzyl)carbamate 1j. Colorless oil. IR (neat) ν; 1703 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ; 7.33–7.15 (13H, m), 6.95 (1H, brs), 5.77 (1H, brs), 5.22 (2H, brs), 5.09 (1H, d, J=14.8 Hz), 5.06 (1H, d, J=8.3 Hz), 5.04 (1H, d, J=15.3 Hz), 4.55 (1H, d, J=14.5 Hz), 3.31–3.07 (2H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$, 50 °C) δ; 155.9, 139.9, 138.1, 137.5, 136.8, 136.4, 130.0, 129.1, 129.0, 128.4, 127.7, 127.6, 126.9, 116.2, 67.3, 54.5, 35.2. MS m/z: 380 $(M+Na)^+$. Anal. calcd for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.49; N, 3.92. Found: C, 80.53; H, 6.60; N, 3.84.

4.2.9. *tert*-Butyl benzyl(2-vinylbenzyl)carbamate 1k. Colorless oil. IR (neat) ν; 1703 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ; 7.48 (1H, d, J=7.5 Hz),

7.32–7.13 (8H, m), 6.91 (1H, dd, *J*=17.1, 11.1 Hz), 5.59 (1H, d, *J*=17.3 Hz), 5.26 (1H, d, *J*=11.0 Hz), 4.52 (2H, s), 4.33 (2H, s), 1.50 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, 50 °C) *δ*; 155.9, 138.2, 137.4, 134.9, 134.4, 128.5, 127.8, 127.6, 127.1, 126.3, 116.0, 80.1, 49.1, 47.1, 28.5. MS *m/z*: 346 $(M+Na)^+$. Anal. calcd for $C_{21}H_{25}NO_2$: C, 77.98; H, 7.79; N, 4.33. Found: C, 77.93; H, 7.99; N, 4.38.

4.2.10. Benzyl benzyl(2-vinylbenzyl)carbamate 1m. Colorless oil. IR (neat) *ν*; 1699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) *δ*; 7.48 (1H, d, *J*=7.3 Hz), 7.34–7.12 (14H, m), 6.86 (1H, brs), 5.57 (1H, d, *J*=17.1 Hz), 5.26 (1H, s) 5.22 (1H, d, *J*=10.9 Hz), 4.59 (2H, brs), 4.41 (2H, brs). ^{13}C NMR (100.6 MHz, $CDCl_3$, 50 °C) *δ*; 156.6, 137.5, 136.8, 134.2, 128.5, 128.5, 128.0, 127.8, 127.7, 127.3, 126.4, 116.4, 67.6, 49.1, 47.2. MS *m/z*: 380 $(M+Na)^+$. Anal. calcd for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.49; N, 3.92. Found: C, 80.70; H, 6.76; N, 3.90.

4.2.11. *tert*-Butyl (4-methylphenyl)sulfonyl(2-vinylphenyl)carbamate 2d. White solid: mp 85.0–86.0 °C. IR (KBr) *ν*; 1739 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*; 7.93 (2H, d, *J*=8.2 Hz), 7.67 (1H, d, *J*=7.8 Hz), 7.41–7.30 (4H, m), 7.18 (1H, d, *J*=7.8 Hz), 6.74 (1H, dd, *J*=17.4, 11.0 Hz), 5.79 (1H, d, *J*=17.4 Hz), 5.32 (1H, d, *J*=11.1 Hz), 2.47 (3H, s), 1.32 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ*; 150.6, 144.6, 137.4, 136.6, 134.3, 131.9, 130.0, 129.3, 129.3, 129.1, 128.4, 125.9, 116.9, 84.2, 27.8, 21.7. MS *m/z*: 396 $(M+Na)^+$. Anal. calcd for $C_{20}H_{23}NO_4S$: C, 64.32; H, 6.21; N, 3.75. Found: C, 64.36; H, 6.09; N, 3.78.

4.2.12. *tert*-Butyl 2-allylphenyl[(4-methylphenyl)sulfonyl]carbamate 2e. White solid: mp 92.0–93.0 °C. IR (KBr) *ν*; 1730 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*; 8.03 (2H, d, *J*=8.3 Hz), 7.46–7.44 (4H, m), 7.37–7.33 (1H, m), 7.16 (1H, d, *J*=7.7 Hz), 6.04 (1H, ddt, *J*=16.9, 10.2, 6.8 Hz), 5.27 (1H, ddd, *J*=17.4, 3.3, 1.6 Hz), 5.21(1H, ddd, *J*=10.0, 2.7, 1.2 Hz), 3.63 (1H, dd, *J*=15.8, 7.0 Hz), 3.53 (1H, dd, *J*=15.7, 6.5 Hz), 2.57 (3H, s), 1.44 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ*; 150.7, 144.6, 140.3, 136.8, 135.9, 135.4, 130.2, 129.3, 129.2, 128.9, 127.0, 116.8, 84.1, 35.7, 27.8, 21.7. MS *m/z*: 410 $(M+Na)^+$. Anal. calcd for $C_{21}H_{25}NO_4S$: C, 65.09; H, 6.50; N, 3.61. Found: C, 65.18; H, 6.46; N, 3.62.

4.2.13. Benzyl 2-allylphenyl[(4-methylphenyl)sulfonyl]carbamate 2f. White solid: mp 92.0–93.0 °C. IR (KBr) *ν*; 1736 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*; 8.04 (2H, d, *J*=8.3 Hz), 7.55–7.38 (8H, m), 7.25–7.20 (3H, m), 5.97 (1H, ddt, *J*=16.9, 10.2, 6.8 Hz), 5.26–5.15 (4H, m), 3.60 (1H, dd, *J*=16.1, 7.4 Hz), 3.54 (1H, dd, *J*=16.1, 6.9 Hz), 2.59 (3H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ*; 152.4, 145.3, 140.8, 136.5, 136.0, 135.3, 135.1, 130.8, 130.1, 129.8, 129.6, 129.6, 128.8, 128.7, 128.2, 127.5, 117.3, 69.0, 36.1, 22.1. MS *m/z*: 444 $(M+Na)^+$. Anal. calcd for $C_{24}H_{23}NO_4S$: C, 68.39; H, 5.50; N, 3.32. Found: C, 68.45; H, 5.47; N, 3.35.

4.2.14. *trans*-2-Phenylcyclohexyl 2-allylphenyl[(4-methylphenyl)sulfonyl]carbamate 2g. White solid: mp 128.5–129.5 °C. IR (KBr) *ν*;1732 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*; 7.87 (1H, d, *J*=8.2 Hz), 7.79 (1H, d, *J*=8.2 Hz), 7.34–7.02 (12H, m), 6.86–6.83 (3H, m), 6.78 (0.5H, d, *J*=7.8 Hz), 6.13 (1H, d, *J*=7.8 Hz), 5.88 (1H, ddt, *J*=16.9, 10.0, 6.9 Hz), 5.68–5.58 (0.5H, m), 5.16–4.99 (3H, m), 4.92–4.81 (1.5H, m), 3.44 (1H, dd, *J*=15.8, 7.1 Hz), 3.32 (1H, dd, *J*=15.7, 6.4 Hz), 3.07 (0.5H, dd, *J*=16.0, 6.2 Hz), 2.73 (0.5H, dd, *J*=16.0, 7.3 Hz), 2.50 (3H, s), 2.47 (1.5H, s), 2.44–2.31 (1.5H, m), 2.16–2.11 (1.5H, m), 1.82–1.78 (3H, m), 1.71–1.68 (1.5H, m), 1.49–1.16 (3H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ*; 151.4, 151.3, 144.5, 142.4, 142.3, 140.2, 136.2, 135.8, 135.8, 129.9, 129.3, 129.2, 129.2, 129.1, 129.0, 128.9, 128.3, 128.0, 127.5, 127.3, 126.9, 126.7, 126.5, 126.2, 116.8, 116.7, 79.8, 79.3, 49.6, 49.2, 35.7, 34.7, 34.1, 33.9, 32.0, 31.9, 25.5, 24.6, 24.5, 21.7, 15.3. HRMS calcd for $C_{29}H_{31}NO_4S$: 512.1883 $(M+Na)^+$. Found: 512.1872.

4.3. General procedure for zirconocene–butene complex mediated reaction of carbamate derivatives

A solution of *N*-benzyl-*N*-benzyloxycarbonyl 2-aminostyrene **1d** (172 mg, 0.5 mmol) in THF (2 ml) was added to a solution of 'Cp_2Zr', prepared from Cp_2ZrCl_2 (175 mg, 0.6 mmol) and *n*-BuLi (1.30 M in hexane 0.92 ml, 1.2 mmol) in THF (2 ml) at −78 °C. After being stirred for 2 h at room temperature, the reaction mixture was quenched by the addition of 1 N HCl and then extracted with ether. The organic extracts were washed with brine and dried over $MgSO_4$. Purification of the residue obtained by evaporation of the solvent, by silica gel column chromatography (hexane–AcOEt, 10:1) gave the indoline derivative **3c** (71 mg, 59% yield).

4.3.1. 1-Benzyl-3-methyl-1,3-dihydro-*2H*-indol-2-one 3c.[11] White solid: mp 117.0–118.0 °C. IR (KBr) *ν*; 1715 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*; 7.34–7.24 (6H, m), 7.16 (1H, t, *J*=7.3 Hz), 7.02 (1H, t, *J*=7.5 Hz), 6.72 (1H, d, *J*=7.8 Hz), 4.91 (2H, s), 3.54 (1H, q, *J*=7.6 Hz), 1.54 (3H, d, *J*=7.6 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ*; 178.7, 143.1, 136.0, 130.6, 128.7, 127.8, 127.5, 127.3, 123.5, 122.4, 108.9, 43.6, 40.5, 15.6. MS *m/z*: 238 $(M+H)^+$. HRMS calcd for $C_{16}H_{15}NO$: 238.1232 $(M+H)^+$. Found: 128.1222.

4.3.2. 1-Benzyl-4-methoxy-3-methyl-1,3-dihydro-*2H*-indol-2-one 3g. White solid: mp 88.0–89.0 °C. IR (KBr) *ν*; 1717 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*; 7.21–7.10 (5H, m), 7.00 (1H, t, *J*=8.2 Hz), 6.46 (1H, t, *J*=8.4 Hz), 6.27 (1H, d, *J*=7.8 Hz), 4.80 (1H, d, *J*=15.7 Hz), 4.74 (1H, d, *J*=15.7 Hz), 3.73 (3H, s), 3.46 (1H, q, *J*=7.5 Hz), 1.45 (3H, d, *J*=7.6 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ*; 179.5, 156.4, 144.7, 136.6, 129.4, 129.1, 127.9, 127.6, 117.0, 105.9, 102.8, 55.7, 44.2, 40.0, 14.9. MS *m/z*: 268 $(M+H)^+$. Anal. calcd for $C_{17}H_{17}NO_2$: C,76.38; H, 6.41; N, 5.24. Found: C, 76.22; H, 6.47; N, 5.14.

4.3.3. 1-Benzyl-6-methoxy-3-methyl-1,3-dihydro-*2H*-indol-2-one 3h. White solid: mp 76.0–77.0 °C. IR (KBr) *ν*; 1694 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*; 7.29–7.19 (5H, m), 7.08 (1H, dd, *J*=8.2, 0.8 Hz), 6.47 (1H, dd, *J*=8.1, 2.3 Hz), 6.27 (1H, d, *J*=2.2 Hz), 4.83 (2H, s), 3.68 (3H, s), 3.43 (1H, q, *J*=7.6 Hz), 1.46 (3H, d, *J*=7.6 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ*; 179.4, 159.8, 144.2, 135.9, 128.7, 127.6, 127.3, 124.0, 122.7, 106.0, 97.2, 55.4, 43.7, 40.0, 15.9. MS *m/z*: 268 $(M+H)^+$. Anal. calcd for $C_{17}H_{17}NO_2$:

C,76.38; H, 6.41; N, 5.24. Found: C, 76.20; H, 6.49; N, 5.16.

4.3.4. 1-Benzyl-3-methyl-3,4-dihydro-2(*1H*)-quinolinone 3i.[12] White solid: mp 79.5–80.5 °C. IR (KBr) ν; 1671 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ; 7.33–7.21 (5H, m), 7.17 (1H, d, J=7.3 Hz), 7.11 (1H, td, J=7.8, 1.2 Hz), 6.98 (1H, td, J=7.4, 0.6 Hz), 6.87 (1H, d, J=8.1 Hz), 5.28 (1H, d, J=16.2 Hz), 5.09 (1H, d, J=16.2 Hz), 3.06–2.98 (1H, m), 2.85–2.75 (2H, m), 1.35 (3H, d, J=6.5 Hz). ^{13}C NMR (100.6 Hz, $CDCl_3$) δ; 173.2, 139.7, 137.2, 128.7, 128.0, 127.3, 127.0, 126.3, 125.7, 122.8, 115.3, 46.4, 35.6, 33.4, 15.7. MS m/z: 252 $(M+H)^+$. Anal. calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.02; H, 6.79; N, 5.41.

4.3.5. 2-Benzyl-4-methyl-1,4-dihydro-3(*2H*)-isoquinolinone 3k. Pale yellow oil (unstable). IR (neat) ν; 1651 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ; 7.35–7.18 (8H, m), 7.07 (1H, d, J=7.5 Hz), 4.79 (1H, d, J=14.8 Hz), 4.54 (1H, d, J=14.9 Hz), 4.44 (1H, d, J=15.7 Hz), 4.29 (1H, d, J=15.7 Hz), 3.66 (1H, q, J=7.3 Hz), 1.55 (3H, d, J=7.4 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 172.3, 137.9, 136.8, 131.0, 128.7, 127.8, 127.7, 127.5, 126.4, 126.2, 125.2, 50.1, 49.6, 41.6, 18.1. MS m/z: 274 $(M+Na)^+$. HRMS calcd for $C_{17}H_{17}NO$: 274.1208 $(M+H)^+$. Found: 174.1205.

4.3.6. *tert*-Butyl 2-methyl-3-(2-{[(4-methylphenyl)sulfonyl]amino}phenyl)-propanoate 4e. White solid: mp 113.0–114.0 °C. IR (KBr) ν; 3263, 1704 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ; 7.92 (1H, brs), 7.62 (2H, d, J=8.3 Hz), 7.20 (2H, d, J=8.1 Hz), 7.16 (1H, td, J=7.6, 1.6 Hz), 7.10 (1H, td, J=7.4, 1.2 Hz), 7.04 (1H, dd, J=7.5, 1.6 Hz), 2.52–2.43 (2H, m), 2.38 (3H, s), 2.18–2.10 (2H, m), 1.32 (9H, s), 1.13 (3H, d, J=6.6 Hz). ^{13}C NMR (100.6 Hz, $CDCl_3$) δ; 176.7, 143.3, 137.3, 134.6, 133.6, 130.6, 129.4, 127.4, 127.1, 126.0, 125.6, 81.4, 42.6, 33.8, 27.9, 21.5, 18.5. MS m/z: 412 $(M+Na)^+$. Anal. calcd for $C_{21}H_{27}NO_4S$: C, 64.75; H, 6.99; N, 3.60. Found: C, 64.52; H, 6.88; N, 3.61.

4.3.7. *tert*-Butyl 2-[(*E*)-1-propenyl]phenylcarbamate 6e. Colorless oil. IR (KBr) ν; 3346, 1732 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ; 7.79 (1H, d, J=6.9 Hz), 7.30 (1H, d, J=7.7 Hz), 7.21 (1H, t, J=7.5 Hz), 7.03 (1H, t, J=7.5 Hz), 6.45 (1H, d, J=15.6 Hz), 6.40 (1H, brs), 6.11 (1H, dq, J=15.6, 6.6 Hz), 1.93 (3H, dd, J=6.6, 1.6 Hz), 1.53 (9H, s). ^{13}C NMR (100.6 Hz, $CDCl_3$) δ; 153.1, 134.7, 130.0, 129.2, 127.6, 127.1, 126.0, 123.8, 121.3, 80.5, 28.4, 18.9. MS m/z: 178 $(M+Na)^+$. Anal. calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 71.90; H, 8.45; N, 5.82.

4.3.8. Benzyl 2-methyl-3-(2-{[(4-methylphenyl)sulfonyl]-amino}phenyl)propanoate 4f. White solid: mp 52.0–53.0 °C. IR (KBr) ν; 3330, 1734 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ; 7.70 (1H, brs), 7.61 (2H, d, J=8.3 Hz), 7.36–7.29 (4H, m), 7.20–7.14 (5H, m), 7. 09 (1H, td, J=7.4, 1.3 Hz), 7.04 (1H, td, J=7.6, 1.7 Hz), 5.07 (1H, d, J=12.3 Hz), 5.01 (1H, d, J=12.3 Hz), 2.70–2.59 (2H, m), 2.37 (3H, s), 2.32–2.24 (1H, m), 1.19 (3H, d, J=6.7 Hz). ^{13}C NMR (100.6 Hz, $CDCl_3$) δ; 176.9, 143.4, 137.2, 135.5, 134.6, 133.5, 130.6, 129.5, 128.5, 128.2, 128.0, 127.5, 127.1, 126.2, 125.7, 66.7, 41.5, 33.8, 21.5, 18.3. MS m/z: 424 $(M+H)^+$. Anal. calcd for $C_{24}H_{25}NO_4S$: C, 68.06; H, 5.95; N, 3.31. Found: C, 67.93; H, 6.06; N, 3.31.

4.3.9. *trans*-2-Phenylcyclohexyl 2-methyl-3-(2-{[(4-methylphenyl)sulfonyl]amino} phenyl)propanoate 4g. White solid: mp 110.0–112.0 °C. IR (KBr) ν; 3263, 1704 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ; 7.86 (1H, brs), 7.59 (1H, d, J=8.3 Hz), 7.36 (2H, dd, J=8.0, 0.9 Hz), 7.23 (2H, d, J=7.0 Hz), 7.20–7.11 (6H, m), 7.04 (1H, dd, J=7.5, 1.2 Hz), 6.91(1H, dd, J=7.6, 1.4 Hz), 4.93 (1H, td, J=10.9, 4.2 Hz), 2.60 (1H, td, J=11.6, 3.4 Hz), 2.37 (3H, s), 2.31–2.24 (2H, m), 1.98 (1H, dd, J=13.1, 3.2 Hz), 1.94–1.88 (1H, m), 1.84–1.73 (3H, m), 1.53–1.16 (4H, m), 0.56 (3H, d, J=6.8 Hz). ^{13}C NMR (J=100.6 Hz, $CDCl_3$) δ; 176.6, 143.2, 142.9, 137.3, 134.5, 133.4, 130.5, 129.4, 128.3, 127.5, 127.3, 127.1, 126.5, 125.9, 125.4, 76.7, 49.4, 41.7, 34.0, 33.5, 32.1, 25.7, 24.7, 21.5, 17.8. MS m/z: 514 $(M+Na)^+$. Anal. calcd for $C_{29}H_{33}NO_4S$: C, 70.85; H, 6.77; N, 2.85. Found: C, 70.79; H, 6.84; N, 2.84.

4.4. Iodination reaction of the intermediate

After treating **1j** (179 mg, 0.5 mmol) with zirconocene–butene complex in THF as described in general procedure, to the reaction mixture was added iodine (508 mg, 2.0 mmol) dissolved in THF (2 ml), and then the whole was stirred for 1 h at −20 °C. Usual extractive work-up and purification of the crude material by silica gel column (hexane–AcOEt, 20:1) gave the iodide **11** in 50% yield.

4.4.1. 1-Benzyl-3-(iodomethyl)-3,4-dihydro-2(*1H*)-quinolinone 11. Light yellow solid: mp 92.0–93.0 °C. IR (KBr) ν; 1674 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ; 7.33–7.19 (6H, m), 7.14 (1H, t, J=7.8 Hz), 7.01 (1H, t, J=7.2 Hz), 6.89 (1H, d, J=8.1 Hz), 5.26 (1H, d, J=16.2 Hz), 5.09 (1H, d, J=16.2 Hz), 3.74 (1H, dd, J=10.1, 3.8 Hz), 3.38 (1H, dd, J=10.0, 8.8 Hz), 3.19 (1H, dd, J=15.3, 5.4 Hz), 3.01 (1H, dd, J=15.3, 11.3 Hz), 2.88 (1H, dddd, J=11.1, 8.9, 5.4, 3.6 Hz). ^{13}C NMR (100.6 Hz, $CDCl_3$) δ; 169.4, 139.2, 136.7, 128.8, 128.4, 127.8, 127.2, 126.3, 124.6, 123.3, 115.5, 46.6, 42.7, 32.1, 4.9. MS m/z: 400 $(M+Na)^+$. Anal. calcd for $C_{17}H_{16}INO$: C, 54.13; H, 4.28; N, 3.71. Found: C, 53.91; H, 4.53; N, 3.61.

4.4.2. Benzyl-4-methylene-1,4-dihydro-3(*2H*)-isoquinolinone 12. Pale yellow oil (unstable). IR (neat) ν; 1649 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ; 7.66 (1H, d, J=7.5 Hz), 7.34–7.24 (7H, m), 7.08 (1H, d, J=7.3 Hz), 6.53 (1H, s), 6.09 (1H, s), 4.85 (2H, s), 4.47 (2H, s). ^{13}C NMR (100.6 Hz, $CDCl_3$) δ; 163.9, 136.6, 134.6, 131.1, 129.5, 128.7, 128.2, 128.1, 127.7, 127.6, 125.6, 123.8, 119.6, 50.5, 49.7. MS m/z: 250 $(M+H)^+$. HRMS calcd for $C_{17}H_{15}NO$: 250.1232 $(M+H)^+$. Found: 250.1234.

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