Pd(0)-catalyzed regio- and stereoselective cyclization of alkynes: Selective synthesis of (E)-4-(isobenzofuran-1(3H)-ylidene)-1,2,3,4-tetrahydroisoquinolines and aze/oxepinoindoles

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General Information:

Reagents and solvents purchased from commercial sources (Aldrich and Merck) were used without further purification unless otherwise noted. $^1$H NMR (500 MHz) and $^{13}$C (125 MHz) spectra were recorded in CDCl$_3$ solution with TMS as internal standard on a JEOL spectrometer and $^1$H NMR (500, 400 and 300 MHz) and $^{13}$C NMR (125, 100 and 75 MHz) spectra were recorded in CDCl$_3$ with TMS as an internal standard on a Bruker Spectrometer. Mass spectra were recorded using a Thermo Finnigan LCQ Advantage MAX 6000 ESI mass spectrometer and ESI/HRMS at 60000 resolution using Thermoscientific Exactive mass spectrometer. Column chromatography was performed on silica gel (100–200 mesh, SRL. India). Analytical TLC was performed on pre-coated aluminium sheets of silica gel 60F$_{254}$ of 0.2 mm thickness (Merck, Germany).

Synthesis of starting materials for the formation of $(E)$-4-(isobenzofuran-1(3H)-ylidene)-1,2,3,4-tetrahydroisoquinolines

Scheme 1. Synthesis of substituted propargylamines (2a-n)

General procedure for synthesis of substituted propargylamines (S-4a-m):

A mixture of CuI (15 mol %), amine S-1 (1 mmol), aldehyde S-2 (1.1 mmol) and methyl 2-ethynylbenzoate S-3 (1.5 mmol) in toluene (3mL) was heated at 100 °C for 3 h and the reaction mixture was filtered through Celite and washed with ethyl acetate. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to afford the compound S-4a–m in good yields (Scheme 1 and Table 1).

General procedure for synthesis of substituted 2-(ethynyl)benzyl alcohols (2a-m):

To a stirred suspension of LiBH$_4$ (1.5 mmol) in THF at rt was added the solution of substituted propargylamines S-4 (1 mmol) in THF, stirred at room temperature and was monitored by TLC until consumption of the starting materials. The resulting solution was quenched with 1N HCl and was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The resulting
residue was purified by column chromatography using petroleum ether/ethyl acetate as eluent to afford the compound 2a-m (Scheme 1 and Table 1).

Procedure for the synthesis of substituted 2-(ethynyl)benzyl alcohol 2n:

To a stirred solution of EtMgBr [2.2 mmol, prepared in anhydrous Et₂O (from 0.04 g of Mg (1.66 mmol) and 0.188 g of EtBr (2.4 mmol)] was added dropwise a solution of the alkynyl ester S-4k (1 mmol) in anhydrous benzene with cooling. The mixture was then refluxed with stirring for 1 h. After cooling, 1N HCl (10 ml) was slowly added with external cooling, followed by the addition of NH₄Cl solution and Et₂O Phases were separated, and the organic layer was washed with water, 5% NaHCO₃ and water again. After drying over anhydrous sodium sulfate, solvent was removed by rotary evaporation and the crude product purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to afford 2n was as a pale yellow oil (75 % yield) (Scheme 1 and Table 1).

Table 1 Synthesis of substituted propargylamines (2a-n)

<table>
<thead>
<tr>
<th>Entry</th>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
<th>Substrate 4 (Yield %)²</th>
<th>Substrate 2 (Yield %)²</th>
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<tr>
<td>1</td>
<td>4,5-OMe</td>
<td>4-Methylbenzyl</td>
<td>4-OMeC₆H₄</td>
<td>S-4a (84)</td>
<td>2a (95)</td>
</tr>
<tr>
<td>2</td>
<td>4,5-OMe</td>
<td>Benzyl(S-1b)</td>
<td>4-MeC₆H₄</td>
<td>S-4b (84)</td>
<td>2b (92)</td>
</tr>
<tr>
<td>3</td>
<td>4,5-OMe</td>
<td>Benzyl(S-1b)</td>
<td>4-OMeC₆H₄</td>
<td>S-4c (85)</td>
<td>2c (93)</td>
</tr>
<tr>
<td>4</td>
<td>4,5-OMe</td>
<td>Benzyl(S-1b)</td>
<td>4-ClC₆H₄</td>
<td>S-4c (80)</td>
<td>2d (90)</td>
</tr>
<tr>
<td>5</td>
<td>4,5-OMe</td>
<td>Benzyl(S-1b)</td>
<td>1-Naphthyl</td>
<td>S-4e (88)</td>
<td>2e (92)</td>
</tr>
<tr>
<td>6</td>
<td>4,5-OMe</td>
<td>Benzyl(S-1b)</td>
<td>2-Fluorenyl</td>
<td>S-4f (82)</td>
<td>2f (91)</td>
</tr>
<tr>
<td>7</td>
<td>H</td>
<td>Benzyl(S-1c)</td>
<td>4-MeC₆H₄</td>
<td>S-4h (83)</td>
<td>2h (95)</td>
</tr>
<tr>
<td>8</td>
<td>H</td>
<td>Benzyl(S-1c)</td>
<td>4-ClC₆H₄</td>
<td>S-4i (80)</td>
<td>2i (93)</td>
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<tr>
<td>9</td>
<td>H</td>
<td>Benzyl(S-1c)</td>
<td>9-Ethyl-9H-carbazol-3-yl</td>
<td>S-4j (76)</td>
<td>2j (89)</td>
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<tr>
<td>10</td>
<td>4,5-OMe</td>
<td>Benzyl(S-1b)</td>
<td>1,3,5-Trioxane</td>
<td>S-4k (88)</td>
<td>2k (96)</td>
</tr>
<tr>
<td>11</td>
<td>4,5-OMe</td>
<td>Benzyl(S-1b)</td>
<td>2-Thienyl</td>
<td>S-4l (75)</td>
<td>2l (87)</td>
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<tr>
<td>12</td>
<td>4,5-OMe</td>
<td>Benzyl(S-1b)</td>
<td>3-Furyl</td>
<td>S-4m (84)</td>
<td>2m (87)</td>
</tr>
<tr>
<td>13</td>
<td>4,5-OMe</td>
<td>Benzyl(S-1b)</td>
<td>1,3,5-Trioxane</td>
<td>S-4k (88)</td>
<td>2n (75)</td>
</tr>
</tbody>
</table>

²Isolated yields after column chromatography.
Scheme 2 Synthesis of substituted propargylamines (2o-q)

**General procedure for the synthesis of S-5a and S-5b:**

The terminal propargyl amine S-5a and S-5b were prepared by N-alkylation of S-1(b, c) (1 mmol) with propargyl bromide (1.5 mmol) using K₂CO₃ (2 mmol) as a base in DMF which was stirred under room temperature condition for 3h. The reaction mixture was quenched by the addition of water and extracted using EtOAc. The organic phases were separated, dried over MgSO₄, filtered and concentrated in vacuo. The residue was then purified by flash column chromatography on siliga gel using petroleum ether/ethyl acetate as eluent to afford the compound S-5a and S-5b in 88 % and 86 % yields respectively (scheme 2 and 3).

**General procedure for synthesis of S-7a and 2o-q:**

α-Iodobenzaldehyde S-6a (1 mmol), PdCl₂(PPh₃)₂ (3 mol% mol) and CuI (3 mol% ) were added to NEt₃ (4.0 mL) and the mixture was stirred under N₂ for 10 minutes. Then, N-benzyl-N-(2-bromo-4,5-dimethoxybenzyl)prop-2-yn-1-amine S-5a (1.1 mmol) in THF was added dropwise and the resulting reaction mixture was stirred for 3 h. After the consumption of starting materials (monitor by TLC), the resulting mixture was filtered through celite bed and washed with THF. Removal of the solvent under reduced pressure gave the crude product, which was further purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to afford pure product S-7a (Scheme 2).

To a stirred solution of RMgBr (1.1 mmol) (R = Ph (2o) or 4-MePh (2p) or Et (2q)) was added dropwise a solution of the alkynyl aldehyde S-7a (1 mmol) in anhydrous benzene with cooling. The mixture was then allowed for 1h. After cooling, 1N HCl (10 ml) was slowly added with external cooling. Et₂O Phases were separated, and the organic layer was washed with water, 5%
NaHCO$_3$ and water again. After drying over anhydrous sodium sulfate, solvent was removed by rotary evaporation and the crude product was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to afford the compound 2o-q (Scheme 2)$^2$.

**Scheme 3** Synthesis of substituted propargylamine 2r

**Preparation of compound S-7b and 2r:**

6-Bromoveratraldehyde (S-6b) (1.0 mmol), Pd(PPh$_3$)$_2$Cl$_2$ (2.5 mol%), CuI (5.2 mol%) and alkyne S-5b (1.3 mmol) were stirred in degassed NEt$_3$ at room temperature overnight. After purification by flash column chromatography (using ethyl acetate and petroleum ether as eluent) the compound S-7b was obtained as an oily liquid (Scheme 3)$^3$.

The compound S-7b (1 mmol) was reduced with NaBH$_4$ (1 mmol) using methanol as a solvent. The resulting solution was quenched with 1N HCl and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography to afford the corresponding (2-(3-(benzyl(2-bromobenzyl)amino)prop-1-ynyl)-4,5-dimethoxyphenyl)methanol 2r in 88 % yield (Scheme 3)$^2$. 

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Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Analytical data of propargylamines (S-4a-m, S-7a and S-7b):

**Methyl 2-(3-((bromo-4,5-dimethoxybenzyl)(4-methylbenzyl)amino)-3-((4-methoxyphenyl)prop-1-ynyl)benzoate (S-4a):** Yellow oily liquid; ^1^H NMR (400 MHz, CDCl$_3$): δ 2.32 (s, 3H, -CH$_3$), 3.60-3.66 (m, 2H, -CH$_2$), 3.76 (d, J = 14.00 Hz, 1H, -CH$_2$), 3.79 (s, 3H, -CH$_3$), 3.83 (s, 3H, -CH$_3$), 3.87-3.88 (m, 4H, -CH$_2$, -CH$_3$), 3.95 (s, 3H, -CH$_3$), 4.93 (s, 1H, -CH), 6.89 (d, J = 8.80 Hz, 2H, Ar-H), 6.94 (s, 1H, Ar-H), 7.12 (d, J = 8.00 Hz, 2H, Ar-H), 7.15 (s, 1H, Ar-H), 7.31 (d, J = 8.00 Hz, 2H, Ar-H), 7.41 (td, J = 1.20 Hz, J = 8.00 Hz, 1H, Ar-H), 7.52 (td, J = 1.20 Hz, J = 7.60 Hz, 1H, Ar-H), 7.66 (d, J = 8.40 Hz, 2H, Ar-H), 7.75 (d, J = 8.00 Hz, 1H, Ar-H), 7.98 (d, J = 7.60 Hz, 1H, Ar-H); ^13^C NMR (100 MHz, CDCl$_3$): δ 21.1, 52.3, 53.3, 54.5, 55.2, 55.8, 55.9, 56.1, 86.8, 90.8, 113.3, 113.4, 114.2, 115.0, 123.5, 127.8, 128.3, 148.3(2), 158.9, 166.9; MS (ESI) for C$_{35}$H$_{34}$BrNO$_5$; m/z 628 [M+H]$^+$, 630 [(M+H)+2]$^+$.  

**Methyl 2-(3-(benzyl(2-bromo-4,5-dimethoxybenzyl)amino)-3-p-tolylprop-1-ynyl)benzoate (S-4b):** Yellow oily liquid; ^1^H NMR (500 MHz, CDCl$_3$): δ 2.33 (s, 3H, -CH$_3$), 3.62 (d, J = 14.00 Hz, 1H, -CH$_2$), 3.69 (d, J = 12.50 Hz, 1H, -CH$_2$), 3.80 (d, J = 14.00 Hz, 1H, -CH$_2$), 3.83 (s, 3H, -CH$_3$), 3.88 (s, 3H, -CH$_3$), 3.94 (d, J = 12.00 Hz, 1H, -CH$_2$), 3.95 (s, 3H, -CH$_3$), 4.96 (s, 1H, -CH), 6.94 (s, 1H, Ar-H), 7.16-7.17 (m, 3H, Ar-H), 7.23-7.26 (m, 1H, Ar-H), 7.31 (t, J = 6.50 Hz, 2H, Ar-H), 7.41-7.43 (m, 3H, Ar-H), 7.53 (t, J = 7.50 Hz, 1H, Ar-H), 7.63 (d, J = 7.50 Hz, 2H, Ar-H), 7.75 (d, J = 7.50 Hz, 1H, Ar-H); ^13^C NMR (125 MHz, CDCl$_3$): δ 21.1, 52.4, 53.5, 54.8, 55.9, 56.1, 56.3, 86.9, 90.7, 113.3, 114.2, 115.0, 123.5, 127.0, 127.8, 128.2, 128.3, 128.8, 129.0, 130.3, 130.7, 131.6, 132.2, 134.7, 136.0, 137.0, 139.4, 148.3(2), 166.9; MS (ESI) for C$_{34}$H$_{32}$BrNO$_5$; m/z 598 [M+H]$^+$, 600 [(M+H)+2]$^+$.  

**Methyl 2-(3-(benzyl(2-bromo-4,5-dimethoxybenzyl)amino)-3-(4-methoxyphenyl)prop-1-ynyl)benzoate (S-4c):** Yellow oily liquid; ^1^H NMR (500 MHz, CDCl$_3$): δ 3.64 (d, J = 13.50 Hz, 1H, -CH$_2$), 3.69 (d, J = 14.00 Hz, 1H, -CH$_2$), 3.79 (s, 3H, -CH$_3$), 3.83 (s, 3H, -CH$_3$), 3.86-3.88 (m, 4H, -CH$_2$, -CH$_3$), 3.92-3.96 (m, 4H, -CH$_2$, -CH$_3$), 4.95 (s, 1H, -CH), 6.90 (d, J = 8.50 Hz, 2H, Ar-H), 6.94 (s, 1H, Ar-H), 7.14 (s, 1H, Ar-H), 7.23 (t, J = 8.00 Hz, 1H, Ar-H), 7.31 (t, J = 6.50 Hz, 2H, Ar-H), 7.39-7.43 (m, 3H, Ar-H), 7.52 (t, J = 7.50 Hz, 1H, Ar-H), 7.67 (d, J = 8.00 Hz, 2H, Ar-H), 7.73 (d, J = 7.50 Hz, 1H, Ar-H), 7.98 (d, J = 8.00 Hz, 1H, Ar-H); ^13^C NMR (125 MHz, CDCl$_3$): δ 52.3, 53.4, 54.7, 55.2, 55.9(2), 56.0, 86.9, 90.7, 113.3, 113.4, 114.2, 115.0, 123.5, 127.0, 127.8, 128.2, 128.9, 129.5, 130.3, 130.6, 131.0, 131.6, 132.1, 134.6, 139.4, 148.2, 148.3, 158.9, 166.8; MS (ESI) for C$_{34}$H$_{32}$BrNO$_5$; m/z 614 [M+H]$^+$, 616 [(M+H)+2]$^+$.  

Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
**Methyl 2-(3-(benzyl(2-bromo-4,5-dimethoxybenzyl)amino)-3-(4-chlorophenyl)prop-1-yny)benzoate (S-4d):** Yellow oily liquid; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 3.62 (d, \(J = 13.60\) Hz, 1H, -CH\(_2\)), 3.68 (d, \(J = 13.20\) Hz, 1H, -CH\(_2\)), 3.78 (d, \(J = 13.20\) Hz, 1H, -CH\(_2\)), 3.83 (s, 3H, -CH\(_3\)), 3.87 (s, 3H, -CH\(_3\)), 3.91-3.96 (m, 4H, -CH\(_2\), -CH\(_3\)), 4.94 (s, 1H, -CH), 6.95 (s, 1H, Ar-H), 7.10 (s, 1H, Ar-H), 7.22-7.26 (m, 1H, Ar-H), 7.30-7.34 (m, 4H, Ar-H), 7.41 (d, \(J = 8.00\) Hz, 3H, Ar-H), 7.51-7.55 (m, 1H, Ar-H), 7.71 (t, \(J = 8.00\) Hz, 2H, Ar-H), 7.76 (d, \(J = 7.60\) Hz, 1H, Ar-H), 7.99 (d, \(J = 6.80\) Hz, 1H, Ar-H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 52.3, 53.7, 54.9, 55.9, 56.1(2), 87.4, 89.8, 113.4, 114.4, 115.2, 123.3, 127.2, 128.0, 128.2(2), 129.0, 130.2, 130.3, 131.6, 132.1, 133.2, 134.6, 137.6, 139.1, 148.3, 148.5, 166.6; MS (ESI) for C\(_{33}\)H\(_{29}\)BrClNO\(_4\): \(m/z\) 618 [M+H]\(^+\), 620 [(M+H)+2]\(^+\), 622 [(M+H)+4]\(^+\).

**Methyl 2-(3-(benzyl(2-bromo-4,5-dimethoxybenzyl)amino)-3-(naphthalen-1-yl)prop-1-yny)benzoate (S-4e):** Yellow oily liquid; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 3.39 (s, 3H, -CH\(_3\)), 3.66 (d, \(J = 14.00\) Hz, 1H, -CH\(_2\)), 3.80 (s, 3H, -CH\(_3\)), 3.85 (d, \(J = 14.00\) Hz, 2H, -CH\(_2\)), 3.92 (d, \(J = 14.00\) Hz, 1H, -CH\(_2\)), 3.99 (s, 3H, -CH\(_3\)), 5.66 (s, 1H, -CH), 6.53 (s, 1H, Ar-H), 6.88 (s, 1H, Ar-H), 7.26-7.50 (m, 9H, Ar-H), 7.57 (t, \(J = 7.50\) Hz, 1H, Ar-H), 7.72 (d, \(J = 8.50\) Hz, 1H, Ar-H), 7.76 (d, \(J = 8.50\) Hz, 1H, Ar-H), 7.80 (d, \(J = 8.00\) Hz, 1H, Ar-H), 7.83 (d, \(J = 7.50\) Hz, 1H, Ar-H), 8.03 (d, \(J = 8.00\) Hz, 1H, Ar-H), 8.20 (d, \(J = 7.00\) Hz, 1H, Ar-H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 52.5, 53.2, 54.7, 55.4, 56.0(2), 87.6, 90.7, 113.7, 113.9, 114.5, 123.5, 124.9, 125.0, 125.2, 125.3, 127.4, 127.8, 128.0, 128.1, 128.4, 128.8, 130.2, 130.4, 130.8, 131.4, 131.7, 132.2, 133.9, 134.0, 134.7, 138.5, 148.0, 148.1, 166.9; MS (ESI) for C\(_{37}\)H\(_{32}\)BrNO\(_4\): \(m/z\) 634 [M+H]\(^+\), 636 [(M+H)+2]\(^+\).

**Methyl 2-(3-(benzyl(2-bromo-4,5-dimethoxybenzyl)amino)-3-(9-fluoren-3-yl)prop-1-yny)benzoate (S-4f):** Yellow oily liquid; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 3.66-3.79 (m, 2H, -CH\(_2\)), 3.82 (s, 3H, -CH\(_3\)), 3.85 (d, \(J = 13.00\) Hz, 1H, -CH\(_3\)), 3.89-3.93 (m, 4H, -CH\(_2\), -CH\(_3\)), 3.95-3.99 (m, 5H, -CH\(_2\), -CH\(_3\)), 5.07 (s, 1H, -CH), 6.94 (s, 1H, Ar-H), 7.18 (s, 1H, Ar-H), 7.24 (d, \(J = 6.50\) Hz, 1H, Ar-H), 7.27-7.38 (m, 4H, Ar-H), 7.42-7.45 (m, 3H, Ar-H), 7.53-7.57 (m, 2H, Ar-H), 7.76-8.0 (m, 4H, Ar-H), 7.95 (s, 1H, Ar-H), 8.01 (d, \(J = 7.50\) Hz, 1H, Ar-H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 36.9, 52.4, 53.6, 55.0, 55.9, 56.1, 56.8, 87.2, 90.7, 113.4, 114.3, 115.1, 119.3, 119.8, 125.0, 125.2, 126.6, 126.7, 127.1, 127.2, 127.9, 128.2, 129.1, 130.4, 130.5, 130.6, 131.6, 132.3, 134.7, 137.7, 139.4, 141.1, 141.4, 143.1, 143.4, 148.3, 148.4, 166.9; MS (ESI) for C\(_{40}\)H\(_{34}\)BrNO\(_4\): \(m/z\) 672 [M+H]\(^+\), 674 [(M+H)+2]\(^+\).

**Methyl 2-(3-(benzyl(2-bromo-4,5-dimethoxybenzyl)amino)-3-(9-ethyl-9H-carbazol-3-yl)prop-1-yny)benzoate (S-4g):** Yellow oily liquid; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 1.42 (t, \(J = 7.00\) Hz, 3H, -CH\(_3\)), 3.70-3.77 (m, 2H, -CH\(_2\)), 3.81 (s, 3H, -CH\(_3\)), 3.88-3.91 (m, 4H, -CH\(_2\), -CH\(_3\)), 3.95-
4.01 (m, 4H, -CH₂, -CH₃), 4.35 (q, J = 7.00 Hz, 2H, -CH₂), 5.20 (s, 1H, -CH), 6.93 (s, 1H, Ar-H), 7.20-7.24 (m, 3H, Ar-H), 7.32 (t, J = 7.50 Hz, 2H, Ar-H), 7.37-7.40 (m, 2H, Ar-H), 7.42-7.47 (m, 4H, Ar-H), 7.56 (t, J = 7.50 Hz, 1H, Ar-H), 7.82 (t, J = 7.50 Hz, 2H, Ar-H), 8.02 (d, J = 7.50 Hz, 1H, Ar-H), 8.17 (d, J = 7.50 Hz, 1H, Ar-H), 8.61 (s, 1H, Ar-H); ^13^C NMR (125 MHz, CDCl₃): δ 13.8, 37.6, 52.4, 53.4, 54.9, 55.8, 56.0, 56.8, 87.0, 91.3, 107.9, 108.4, 113.3, 114.2, 115.0, 118.7, 120.4, 120.7, 122.5, 122.9, 123.7, 125.5, 126.2, 127.0, 127.8, 128.2, 129.0, 129.4, 130.3, 130.8, 131.6, 132.3, 134.7, 139.4, 139.6, 140.2, 148.2, 167.0; MS (ESI) for C₄₁H₃₇BrN₂O₄: m/z 701 [M+H]^+, 703 [(M+H)+2]^+.

**Methyl 2-((benzyl)(2-bromobenzyl)amino)-3-p-tolyprop-1-ynyl)benzoate (S-4h):** ^1^H NMR (400 MHz, CDCl₃): Yellow oily liquid; δ 2.31 (s, 3H, -CH₃), 3.72 (d, J = 14.00 Hz, 2H, -CH₂), 3.83 (d, J = 13.60 Hz, 1H, -CH₂), 4.05 (d, J = 14.00 Hz, 1H, -CH₂), 4.98 (s, 1H, -CH), 7.03 (t, J = 7.60 Hz, 1H, Ar-H), 7.16 (d, J = 7.60 Hz, 2H, Ar-H), 7.20-7.23 (m, 1H, Ar-H), 7.26-7.32 (m, 3H, Ar-H), 7.36 (t, J = 7.60 Hz, 1H, Ar-H), 7.47 (d, J = 7.60 Hz, 4H, Ar-H), 7.67-7.75 (m, 4H, Ar-H), 7.97 (d, J = 7.60 Hz, 1H, Ar-H); ^1^C NMR (100 MHz, CDCl₃): δ 21.0, 52.3, 53.8, 54.8, 56.3, 87.0, 90.6, 123.4, 124.5, 127.0, 127.2, 127.8, 128.2(2), 128.3, 128.7, 128.9, 130.3, 130.6, 131.5, 132.2, 132.6, 134.6, 135.8, 138.5, 139.2, 166.8; MS (ESI) for C₃₂H₂₈BrNO₂: m/z 538 [M+H]^+, 540 [(M+H)+2]^+.

**Methyl 2-((benzyl)(2-bromobenzyl)amino)-3-(4-chlorophenyl)prop-1-ynyl)benzoate (S-4i):** Yellow oily liquid; ^1^H NMR (400 MHz, CDCl₃): δ 3.69 (d, J = 14.00 Hz, 2H, -CH₂), 3.80 (d, J = 13.60 Hz, 1H, -CH₂), 3.96 (s, 3H, -CH₃), 4.02 (d, J = 14.00 Hz, 1H, -CH₂), 4.95 (s, 1H, -CH), 7.09 (t, J = 7.60 Hz, 1H, Ar-H), 7.25-7.34 (m, 6H, Ar-H), 7.43-7.45 (m, 3H, Ar-H), 7.50-7.57 (m, 2H, Ar-H), 7.64-7.66 (m, 1H, Ar-H), 7.73-7.78 (m, 3H, Ar-H), 8.01 (d, J = 8.00 Hz, 1H, Ar-H); ^1^C NMR (100 MHz, CDCl₃): δ 52.4, 54.0, 55.0, 56.1, 87.6, 89.8, 123.3, 124.7, 127.2, 127.4, 128.0, 128.3(2), 128.5, 129.1, 129.5, 129.9, 130.4, 130.8, 131.7, 132.8, 133.3, 134.7, 137.6, 138.3, 139.0, 166.7; MS (ESI) for C₃₁H₂₃BrClNO₂: m/z 558 [M+H]^+, 560 [(M+H)+2]^+, 562 [(M+H)+4]^+.

**Methyl 2-((benzyl)(2-bromobenzyl)amino)-3-(9-ethyl-9H-carbazol-3-yl)prop-1-ynyl)benzoate (S-4j):** Yellow oily liquid; ^1^H NMR (400 MHz, CDCl₃): δ31.41 (t, J = 6.80 Hz, 3H, -CH₃), 3.73-3.82 (m, 2H, -CH₂), 3.89 (d, J = 13.60 Hz, 1H, -CH₂), 3.97 (s, 3H, -CH₃), 4.08 (d, J = 14.40 Hz, 1H, -CH₂), 4.35 (q, J = 7.20 Hz, 2H, -CH₂), 5.20 (s, 1H, -CH), 7.06 (t, J = 7.20 Hz, 1H, Ar-H), 7.20-7.23 (m, 2H, Ar-H), 7.30-7.32 (m, 3H, Ar-H), 7.37-7.39 (m, 2H, Ar-H), 7.42-7.50 (m, 5H, Ar-H), 7.56 (t, J = 7.20 Hz, 1H, Ar-H), 7.74 (d, J = 7.20 Hz, 1H, Ar-H), 7.82 (d, J = 7.60 Hz, 2H, Ar-H), 8.02 (d, J = 7.60 Hz, 1H, Ar-H), 8.20 (d, J = 7.60 Hz, 1H, Ar-H), 8.63 (s, 1H, Ar-H); ^1^C NMR (100 MHz, CDCl₃): δ 14.0, 37.7, 52.5,
54.1, 55.1, 57.0, 87.3, 91.5, 108.2, 108.6, 118.9, 120.7, 120.9, 122.7, 123.2, 123.9, 124.8, 125.6, 126.4, 127.1, 127.4, 128.0, 128.4, 129.2, 129.4, 130.5, 131.0, 131.8, 132.5, 132.8, 134.9, 138.9, 139.6(2), 140.3, 167.2; MS (ESI) for C_{39}H_{33}BrN_{2}O_{2}: m/z 641 [M+H]^+, 643 [(M+H)+2]^+.

**Methyl 2-(3-(benzyl(2-bromo-4,5-dimethoxybenzyl)amino)prop-1-ynyl)benzoate (S-4k):** Yellow oily liquid; ¹H NMR (400 MHz, CDCl₃): δ 3.55 (s, 2H, -CH₂), 3.83 (s, 2H, -CH₂), 3.86 (s, 3H, -CH₃), 3.88 (s, 5H, -CH₂, -CH₃), 3.93 (s, 3H, -CH₃), 7.02 (s, 1H, Ar-H), 7.21 (s, 1H, Ar-H), 7.24-7.27 (m, 1H, Ar-H), 7.31-7.39 (m, 3H, Ar-H), 7.44-7.50 (m, 3H, Ar-H), 7.62 (d, J = 7.60 Hz, 1H, Ar-H), 7.93 (d, J = 7.60 Hz, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 42.2, 52.2, 56.0, 56.1, 57.1, 57.4, 84.4, 90.3, 113.7, 114.7, 115.4, 123.7, 127.1, 127.6, 128.2, 129.1, 130.2, 131.6, 132.0, 134.5, 138.8, 148.3, 148.5, 166.6; MS (ESI) for C_{27}H_{26}BrNO₄: m/z 508 [M+H]^+, 510 [(M+H)+2]^+.

**Methyl 2-(3-(benzyl(2-bromo-4,5-dimethoxybenzyl)amino)-3-(thiopen-2-yl)prop-1-ynyl)benzoate (S-4l):** Yellow oily liquid; ¹H NMR (400 MHz, CDCl₃): δ 3.68-3.73 (m, 2H, -CH₂), 3.83 (s, 3H, -CH₃), 3.90-3.97 (m, 7H, -CH₂,-CH₃), 4.01 (d, J = 14.40 Hz, 1H, -CH₂), 5.12 (s, 1H, -CH), 6.95-6.98 (m, 2H, Ar-H), 7.21-7.28 (m, 2H, Ar-H), 7.30-7.34 (m, 2H, Ar-H), 7.39-7.45 (m, 3H, Ar-H), 7.50-7.53 (m, 3H, Ar-H), 7.74 (dd, J = 1.20 Hz, J = 8.00 Hz, 1H, Ar-H), 7.96-8.00 (m, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 52.3, 53.3, 53.4, 54.6, 56.0, 56.1, 85.8, 89.7, 112.8, 114.0, 115.1, 123.2, 125.4, 126.4, 126.7, 127.2, 128.0, 128.3, 128.7, 130.3, 130.4, 131.6, 132.3, 134.7, 139.1, 144.3, 148.4, 148.5, 166.7; MS (ESI) for C_{33}H_{28}BrNO_{4}S: m/z 590 [M+H]^+, 592 [(M+H)+2]^+.

**Methyl 2-(3-(benzyl(2-bromo-4,5-dimethoxybenzyl)amino)-3-(furan-3-yl)prop-1-ynyl)benzoate (S-4m):** Yellow oily liquid; ¹H NMR (400 MHz, CDCl₃): δ 3.65-3.72 (m, 2H, -CH₂), 3.84-3.86 (m, 4H, -CH₂, -CH₃), 3.88-3.90 (m, 4H, -CH₂,-CH₃), 3.94 (s, 3H, -CH₃), 4.83 (s, 1H, -CH), 6.56 (s, 1H, Ar-H), 6.96 (s, 1H, Ar-H), 7.18 (s, 1H, Ar-H), 7.21-7.25 (m, 1H, Ar-H), 7.31 (t, J = 7.60 Hz, 2H, Ar-H), 7.39-7.43 (m, 4H, Ar-H), 7.50-7.53 (m, 1H, Ar-H), 7.70 (d, J = 7.60 Hz, 1H, Ar-H), 7.77-7.78 (m, 1H, Ar-H), 7.95-7.98 (m, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 49.3, 52.3, 53.5, 54.7, 55.9, 56.1, 84.6, 90.6, 110.1, 113.1, 113.2, 114.2, 115.2, 124.8, 127.1, 128.0, 128.3, 128.8, 130.3, 130.6, 131.6, 132.2, 134.7, 139.4, 142.0, 143.2, 148.4(2), 166.6; MS (ESI) for C_{31}H_{28}BrNO_{5}: m/z 574 [M+H]^+, 576 [(M+H)+2]^+.

2-(3-(Benzyl(2-bromo-4,5-dimethoxybenzyl)amino)prop-1-ynyl)benzaldehyde (S-7a): Yellow oily liquid; ¹H NMR (400 MHz, CDCl₃): δ 3.58 (s, 2H, -CH₂), 3.80 (s, 2H, -CH₂), 3.86 (s, 5H, -CH₂, -CH₃), 3.89 (s, 3H, -CH₃), 7.02 (s, 1H, Ar-H), 7.12 (s, 1H, Ar-H), 7.27 (d, J = 8.40 Hz, 1H, Ar-H), 7.34 (t, J = 7.20 Hz, 2H, Ar-H), 7.41-7.47 (m, 3H, Ar-H), 7.56-7.63 (m, 2H, Ar-H), 7.94 (d, J = 8.00 Hz, 1H, Ar-H), 10.66 (s, 1H, -CHO); ¹³C NMR (125 MHz, CDCl₃): δ 42.1, 56.0, 56.1, 57.1, 57.5,
81.5, 92.2, 113.2, 114.5, 115.4, 126.8, 127.2, 127.3, 128.4(2), 128.9, 129.6, 133.6, 133.7, 136.0, 138.4, 148.3, 148.6, 191.6; MS (ESI) for C_{26}H_{34}BrNO_3: m/z 478 [M+H]^+, 480 [(M+H)+2]^+.

2-(3-(Benzyl(2-bromobenzyl)amino)prop-1-ynyl)-4,5-dimethoxybenzaldehyde (S-7b): Yellow oily liquid; ^1^H NMR (400 MHz, CDCl_3): δ 3.56 (s, 2H, -CH_2), 3.82 (s, 2H, -CH_2), 3.92 (s, 2H, -CH_2), 3.96 (s, 3H, -CH_3), 3.98 (s, 3H, -CH_3), 7.01 (s, 1H, Ar-H), 7.13 (dd, J = 1.20 Hz, J = 7.60 Hz, 1H, Ar-H), 7.25-7.30 (m, 2H, Ar-H), 7.32-7.36 (m, 3H, Ar-H), 7.42-7.44 (m, 2H, Ar-H), 7.57 (t, J = 7.80 Hz, 2H, Ar-H), 10.51 (s, 1H, -CHO); ^1^C NMR (100 MHz, CDCl_3): δ 42.0, 56.1, 56.3, 57.5, 57.9, 81.3, 90.6, 108.1, 114.7, 121.6, 124.8, 127.3(2), 128.4, 128.7, 128.9, 130.3, 130.8, 132.9, 137.7, 138.4, 149.6, 153.6, 190.4; MS (ESI) for C_{26}H_{34}BrNO_3: m/z 478 [M+H]^+, 480 [(M+H)+2]^+.

Analytical data of substituted 2-(ethynyl)benzyl alcohols (2a-r):

(2-(3-((2-Bromo-4,5-dimethoxybenzyl)(4-methylbenzyl)amino)-3-(4-methoxyphenyl)prop-1-ynyl)phenyl)methanol (2a): Orange solid; mp: 118-120 °C; ^1^H NMR (400 MHz, CDCl_3): δ 2.16 (brs, 1H, -OH), 2.32 (s, 3H, -CH_3), 3.55-3.62 (m, 2H, -CH_2), 3.79-3.81 (m, 5H, -CH_2, -CH_3), 3.83 (s, 3H, -CH_3), 3.88 (s, 3H, -CH_3), 4.93 (s, 1H, -CH), 5.02 (s, 2H, -CH_2), 6.88 (d, J = 8.80 Hz, 2H, Ar-H), 6.94 (d, J = 8.00 Hz, 2H, Ar-H), 7.12 (d, J = 8.00 Hz, 2H, Ar-H), 7.27-7.35 (m, 4H, Ar-H), 7.40 (td, J = 1.20 Hz, J = 7.60 Hz, 1H, Ar-H), 7.53 (d, J = 7.60 Hz, 1H, Ar-H), 7.58 (d, J = 8.40 Hz, 2H, Ar-H), 7.64 (dd, J = 0.80 Hz, J = 7.60 Hz, 1H, Ar-H); 13C NMR (100 MHz, CDCl_3): δ 21.1, 53.2, 54.6, 55.3, 55.8, 55.9, 56.1, 64.2, 85.7, 90.2, 113.1, 113.5, 113.9, 115.0, 121.3, 127.2, 127.5, 128.6, 128.8, 129.0, 129.3, 130.5, 130.9, 132.8, 136.0, 136.7, 142.5, 148.4(2), 159.0; MS (ESI) for C_{34}H_{34}BrNO_4: m/z 600 [M+H]^+, 602 [(M+H)+2]^+.

(2-(3-(Benzyl(2-bromo-4,5-dimethoxybenzyl)amino)-3-p-toly1prop-1-ynyl)phenyl)methanol (2b): Orange solid; mp: 83-85 °C; ^1^H NMR (500 MHz, CDCl_3): δ 2.33 (s, 3H, -CH_3), 3.60-3.63 (m, 2H, -CH_2), 3.80-3.83 (m, 4H, -CH_2, -CH_3), 3.88-3.91 (m, 4H, -CH_2, -CH_3), 4.95 (s, 1H, -CH), 5.02 (s, 2H, -CH_2), 6.94 (s, 1H, Ar-H), 7.12 (s, 1H, Ar-H), 7.15-7.17 (m, 3H, Ar-H), 7.24-7.25 (m, 2H, Ar-H), 7.30-7.34 (m, 2H, Ar-H), 7.40-7.41 (m, 2H, Ar-H), 7.53 (d, J = 7.50 Hz, 1H, Ar-H), 7.57 (d, J = 8.50 Hz, 2H, Ar-H), 7.64 (d, J = 7.50 Hz, 1H, Ar-H); 13C NMR (125 MHz, CDCl_3): δ 21.1, 53.4, 54.9, 55.9, 56.1, 56.2, 65.2, 85.8, 90.0, 113.1, 114.2, 115.0, 121.2, 127.0, 127.1(2), 127.4, 128.1, 128.3, 128.6, 128.9, 129.2, 130.4, 132.7, 137.3, 139.2, 142.5, 148.3, 148.4; MS (ESI) for C_{33}H_{32}BrNO_3: m/z 570 [M+H]^+, 572 [(M+H)+2]^+. 

(2-(3-(Benzyl(2-bromo-4,5-dimethoxybenzyl)amino)-3-(4-methoxyphenyl)prop-1-ynyl)phenyl)methanol (2c): Pale yellow solid; mp: 75-77 °C; ^1^H NMR (500 MHz, CDCl_3): δ 1.90
(brs, 1H, -OH), 3.59-3.63 (m, 2H, -CH₂), 3.79-3.83 (m, 7H, -CH₂, -CH₃), 3.88-3.90 (m, 4H, -CH₂, -CH₃), 4.94 (s, 1H, -CH), 5.03 (s, 2H, -CH₂), 6.89 (d, J = 8.50 Hz, 2H, Ar-H), 6.94 (s, 1H, Ar-H), 7.09 (s, 1H, Ar-H), 7.24 (t, J = 6.50 Hz, 1H, Ar-H), 7.30-7.34 (m, 3H, Ar-H), 7.39-7.42 (m, 3H, Ar-H), 7.54 (d, J = 7.50 Hz, 1H, Ar-H), 7.59 (d, J = 8.50 Hz, 2H, Ar-H), 7.64 (d, J = 7.50 Hz, 1H, Ar-H); ¹³C NMR (125 MHz, CDCl₃): δ 53.3, 54.9, 55.2, 55.9(2), 56.1, 64.2, 85.8, 90.1, 113.1, 113.5(2), 114.2, 115.0, 121.2, 127.2, 127.5, 128.3, 128.7, 128.9, 129.3, 130.4, 130.8, 132.7, 139.2, 142.5, 148.3, 148.4, 159.0; MS (ESI) for C₃H₂BrNO₄: m/z 586 [M+H]⁺, 588 [(M+H)+2]⁺.

(2-(3-(N-(2-Bromo-4,5-dimethoxybenzyl)-N-benzilamino)-3-(4-chlorophenyl)prop-1-ynyl)phenyl)methanol (2d): Pale yellow solid; mp: 62-64 °C; ¹H NMR (400 MHz, CDCl₃): δ 2.13 (bres, 1H, -OH), 3.57-3.61 (m, 2H, -CH₂), 3.79 (d, J = 13.60 Hz, 1H, -CH₂), 3.84 (s, 3H, -CH₃), 3.87-3.90 (m, 4H, -CH₂, -CH₃), 4.93 (s, 1H, -CH), 5.02 (s, 2H, -CH₂), 6.95 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H), 7.25 (t, J = 7.20 Hz, 1H, Ar-H), 7.29-7.35 (m, 5H, Ar-H), 7.37-7.43 (m, 3H, Ar-H), 7.55 (d, J = 7.60 Hz, 1H, Ar-H), 7.63 (t, J = 8.40 Hz, 3H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 53.6, 55.0, 55.9, 56.0, 56.1, 64.1, 86.4, 89.1, 113.1, 114.4, 115.1, 120.9, 127.2, 127.5, 128.3, 128.4, 128.9(2), 129.6, 129.9, 132.3, 133.4, 137.4, 138.8, 142.5, 148.4, 148.5; MS (ESI) for C₃₂H₂₉BrClNO₃: m/z 590 [M+H]⁺, 592 [(M+H)+2]⁺, 594 [(M+H)+4]⁺.

(2-(3-(N-(2-Bromo-4,5-dimethoxybenzyl)-N-benzilamino)-3-(naphthalen-1-yl)prop-1-ynyl)phenyl)methanol (2e): Pale yellow solid; mp: 52-54 °C; ¹H NMR (500 MHz, CDCl₃): δ 2.19 (bres, 1H, -OH), 3.37 (s, 3H, -CH₃), 3.65 (d, J = 14.00 Hz, 1H, -CH₂), 3.76-3.79 (m, 5H, -CH₂, -CH₃), 3.88 (d, J = 14.00 Hz, 1H, -CH₂), 5.11 (s, 2H, -CH₂), 5.66 (s, 1H, -CH), 6.46 (s, 1H, Ar-H), 6.87 (s, 1H, Ar-H), 7.25-7.31 (m, 3H, Ar-H), 7.34-7.39 (m, 5H, Ar-H), 7.40-7.44 (m, 2H, Ar-H), 7.58 (t, J = 8.00 Hz, 1H, Ar-H), 7.69 (d, J = 8.00 Hz, 1H, Ar-H), 7.72 (d, J = 7.50 Hz, 1H, Ar-H), 7.76 (d, J = 8.50 Hz, 1H, Ar-H), 7.80 (d, J = 8.50 Hz, 1H, Ar-H), 8.07 (d, J = 7.00 Hz, 1H, Ar-H); ¹³C NMR (125 MHz, CDCl₃): δ 53.2, 54.7, 55.4, 56.0, 56.2, 64.2, 86.6, 90.1, 113.5, 113.9, 114.5, 121.3, 124.8, 124.9, 125.3, 125.4, 127.2, 127.5(2), 127.6, 128.1, 128.4, 128.7, 128.9, 130.1, 130.5, 131.0, 131.3, 132.8, 133.8, 133.9, 138.2, 142.5, 148.1, 148.2; MS (ESI) for C₆₃H₄₃BrNO₅: m/z 606 [M+H]⁺, 608 [(M+H)+2]⁺.

(2-(3-(N-(2-Bromo-4,5-dimethoxybenzyl)-N-benzilamino)-3-(9H-fluoren-3-yl)prop-1-ynyl)phenyl)methanol (2f): Orange solid; mp: 58-60 °C; ¹H NMR (500 MHz, CDCl₃): δ 2.13 (bres, 1H, -OH), 3.66 (d, J = 14.50 Hz, 2H, -CH₂), 3.82-3.94 (m, 10H, -CH₂, -CH₃), 5.06 (s, 3H, -CH, -CH₂), 6.94 (s, 1H, Ar-H), 7.13 (s, 1H, Ar-H), 7.25-7.38 (m, 6H, Ar-H), 7.41-7.44 (m, 3H, Ar-H), 7.53-7.57 (m, 2H, Ar-H), 7.69 (d, J = 7.50 Hz,
2H, Ar-H), 7.76 (d, J = 8.50 Hz, 2H, Ar-H); 13C NMR (125 MHz, CDCl3): δ 36.9, 53.5, 55.1, 55.9, 56.1, 56.7, 65.2, 86.0, 90.1, 113.2, 114.3, 115.1, 119.5, 119.9, 121.3, 125.0(2), 126.7, 126.8, 127.1, 127.2, 127.5, 128.3, 128.7, 129.0, 130.3, 130.5, 132.8, 137.4, 139.2, 141.3, 142.6, 143.2, 143.4, 148.4, 148.5; MS (ESI) for C39H34BrNO3: m/z 644 [M+H]+, 646 [(M+H)+2]+.

(2-(3-(N-(2-Bromo-4,5-dimethoxy benzyl)-N-benzylamino)-3-(9-ethyl-9H-carbazol-3-yl)prop-1-ynyl)phenyl)methanol (2g): Orange solid; mp: 70-72 °C; 1H NMR (500 MHz, CDCl3): δ 1.42 (t, J = 6.50Hz, 3H, -CH3), 2.16 (brs, 1H, -OH), 3.68-3.72 (m, 2H, -CH2), 3.81 (s, 3H, -CH3), 3.87-3.96 (m, 5H, -CH2, -CH3), 4.36 (q, J = 7.00 Hz, 2H, -CH2), 5.10 (s, 2H, -CH2), 5.19 (s, 1H, -CH), 6.93 (s, 1H, Ar-H), 7.16 (s, 1H, Ar-H), 7.21-7.25 (m, 2H, Ar-H), 7.32 (t, J = 7.00 Hz, 2H, Ar-H), 7.35-7.42 (m, 3H, Ar-H), 7.42-7.47 (m, 4H, Ar-H), 7.57 (d, J = 7.50 Hz, 1H, Ar-H), 7.72 (d, J = 7.50 Hz, 1H, Ar-H), 7.76 (d, J = 9.50 Hz, 1H, Ar-H), 8.10 (d, J = 7.50 Hz, 1H, Ar-H), 8.43 (s, 1H, Ar-H); 13C NMR (125 MHz, CDCl3): δ 13.8, 37.6, 53.4, 55.0, 55.9, 56.1, 56.7, 64.3, 85.8, 90.7, 108.1, 108.5, 113.1, 114.2, 114.9, 118.8, 120.2, 121.5, 122.6, 122.8, 125.7, 126.0, 127.1, 127.3, 127.6, 128.3, 128.7, 129.0, 129.1, 130.6, 132.8, 139.4, 139.5, 140.2, 142.6, 148.3; MS (ESI) for C40H37BrNO3: m/z 673 [M+H]+, 675 [(M+H)+2]+.

(2-(3-(N-(2-Bromobenzyl)-N-benzylamino)-3-p-tolylprop-1-ynyl)phenyl)methanol (2h): Orange solid; mp: 113-115 °C; 1H NMR (400 MHz, CDCl3): δ 2.15 (brs, 1H, -OH), 2.33 (s, 3H, -CH3), 3.61 (d, J = 13.60 Hz, 1H, -CH2), 3.70 (d, J = 14.80 Hz, 1H, -CH2), 3.82 (d, J = 13.20 Hz, 1H, -CH2), 3.98 (d, J = 14.40 Hz, 1H, -CH2), 4.96 (s, 1H, -CH), 5.02 (s, 2H, -CH2), 7.07 (t, J = 7.60 Hz, 1H, Ar-H), 7.16 (d, J = 7.60 Hz, 2H, Ar-H), 7.23 (t, J = 7.20 Hz, 1H, Ar-H), 7.28-7.33 (m, 4H, Ar-H), 7.38 (d, J = 7.60 Hz, 1H, Ar-H), 7.43 (d, J = 7.20 Hz, 2H, Ar-H), 7.49 (d, J = 8.00 Hz, 1H, Ar-H), 7.53 (d, J = 7.20 Hz, 1H, Ar-H), 7.59 (d, J = 8.00 Hz, 2H, Ar-H), 7.63-7.68 (m, 2H, Ar-H); 13C NMR (100 MHz, CDCl3): δ 21.1, 53.8, 55.1, 56.3, 64.2, 85.9, 90.1, 121.3, 124.6, 127.1, 127.4(2), 128.1, 128.3(2), 128.6, 128.9(2), 130.5, 132.6, 132.8, 135.6, 137.3, 138.4, 139.0, 142.5; MS (ESI) for C31H28BrNO: m/z 510 [M+H]+, 512 [(M+H)+2]+.

(2-(3-(N-(2-Bromobenzyl)-N-benzylamino)-3-(4-chlorophenyl)prop-1-ynyl)phenyl)methanol (2i): Orange solid; mp: 103-105 °C; 1H NMR (400 MHz, CDCl3): δ 2.05 (brs, 1H, -OH), 3.60 (d, J = 13.60 Hz, 1H, -CH2), 3.67 (d, J = 14.40 Hz, 1H, -CH2), 3.80 (d, J = 13.20 Hz, 1H, -CH2), 3.96 (d, J = 14.40 Hz, 1H, -CH2), 4.93 (s, 1H, -CH), 5.02 (s, 2H, -CH2), 7.09 (t, J = 7.20 Hz, 1H, Ar-H), 7.29-7.36 (m, 7H, Ar-H), 7.40-7.44 (m, 3H, Ar-H), 7.51 (d, J = 8.00 Hz, 1H, Ar-H), 7.55 (d, J = 7.60 Hz, 1H, Ar-H), 7.60-7.65 (m, 4H, Ar-H); 13C NMR (100 MHz, CDCl3): δ
54.0, 55.2, 56.1, 64.2, 86.5, 89.1, 121.0, 124.6, 127.2, 127.3, 127.4, 127.5, 128.4(2), 128.5, 128.9, 129.0, 129.6, 130.6, 132.8(2), 133.4, 137.3, 138.0, 138.6, 142.5; MS (ESI) for C_{30}H_{25}BrClNO: m/z 530 [M+H]^+, 532 [(M+H)+2]^+, 534 [(M+H)+4]^+.

(2-(3-(N-(2-Bromobenzyl)-N-benzylamino)-3-(9-ethyl-9H-carbazol-3-yl)prop-1-ynyl)phenyl)methanol (2j): Orange solid; mp: 93-95 °C; ^1H NMR (400 MHz, CDCl_3): δ 1.42 (t, J = 6.80 Hz, 3H, -CH_3), 3.68 (d, J = 13.60 Hz, 1H, -CH_2), 3.79 (d, J = 10.40 Hz, 1H, -CH_2), 3.90 (d, J = 11.20 Hz, 1H, -CH_2), 4.03 (d, J = 14.80 Hz, 1H, -CH_2), 4.35 (q, J = 7.20 Hz, 2H, -CH_2), 5.09 (s, 2H, -CH_2), 5.19 (s, 1H, -CH), 7.05-7.14 (m, 2H, Ar-H), 7.20-7.50 (m, 11H, Ar-H), 7.56 (t, J = 7.60 Hz, 2H, Ar-H), 7.72 (d, J = 7.20 Hz, 2H, Ar-H), 7.78 (d, J = 8.40 Hz, 1H, Ar-H), 8.14 (d, J = 7.20 Hz, 1H, Ar-H), 8.45 (s, 1H, Ar-H); ^13C NMR (100 MHz, CDCl_3): δ 13.8, 37.6, 53.8, 55.1, 56.8, 64.3, 86.0, 90.7, 108.2, 108.5, 118.8, 120.3, 120.4, 122.6, 122.8, 125.6, 126.1, 127.1, 127.3(2), 127.5, 128.2, 128.3, 128.4, 128.6, 129.0, 130.4, 130.7, 132.6, 132.8, 132.9, 138.5, 139.2, 139.5, 140.2, 142.6; MS (ESI) for C_{38}H_{33}BrN_{2}O: m/z 613 [M+H]^+, 615 [(M+H)+2]^+.

(2-(3-(N-(2-Bromo-4,5-dimethoxybenzyl)-N-benzylamino)prop-1-ynyl)phenyl)methanol (2k): Orange solid; mp: 104-106 °C; ^1H NMR (500 MHz, CDCl_3): δ 2.22 (brs, 1H, -OH), 3.54 (s, 2H, -CH_2), 3.78 (s, 2H, -CH_2), 3.84 (s, 2H, -CH_2), 3.85(s, 3H, -CH_3), 3.88 (s, 3H, -CH_3), 4.91 (s, 2H, -CH_2), 7.01 (s, 1H, Ar-H), 7.13 (s, 1H, Ar-H), 7.25-7.29 (m, 2H, Ar-H), 7.31-7.36 (m, 3H, Ar-H), 7.42 (d, J = 8.00 Hz, 2H, Ar-H), 7.47 (d, J = 8.00 Hz, 1H, Ar-H), 7.51 (d, J = 8.00 Hz, 1H, Ar-H); ^13C NMR (125 MHz, CDCl_3): δ 42.1, 56.0, 56.1, 57.1, 57.3, 64.1, 83.2, 89.4, 113.2, 114.5, 115.3, 121.3, 127.1, 127.2, 127.4, 128.3, 128.4, 128.9, 129.8, 132.5, 138.5, 142.4, 148.3, 148.5; MS (ESI) for C_{26}H_{26}BrNO_{3}: m/z 480 [M+H]^+, 482 [(M+H)+2]^+.

(2-(3-(N-(2-Bromo-4,5-dimethoxybenzyl)-N-benzylamino)-3-(thiophen-2-yl)prop-1-ynyl)phenyl)methanol (2l): Yellow oily liquid; ^1H NMR (400 MHz, CDCl_3): δ 2.11 (brs, 1H, -OH), 3.62 (d, J = 13.60 Hz, 1H, -CH_2), 3.70 (d, J = 14.40 Hz, 1H, -CH_2), 3.84 (s, 3H, -CH_3), 3.91-3.98 (m, 5H, -CH_2,-CH_3), 5.01 (s, 2H, -CH_2), 5.12 (s, 1H, -CH), 6.95-6.97 (m, 2H, Ar-H), 7.23-7.28 (m, 2H, Ar-H), 7.30-7.32 (m, 3H, Ar-H), 7.34-7.35 (m, 2H, Ar-H), 7.41 (td, J = 1.20 Hz, J = 7.20 Hz, 1H, Ar-H), 7.48 (d, J = 7.20 Hz, 2H, Ar-H), 7.53 (d, J = 7.60 Hz, 1H, Ar-H), 7.63 (dd, J = 1.20 Hz, J = 7.60 Hz, 1H, Ar-H); ^13C NMR (100 MHz, CDCl_3): δ 53.2, 53.4, 54.7, 56.0, 56.1, 64.1, 84.7, 89.2, 112.6, 114.0, 115.1, 120.9, 125.6, 126.2, 126.5, 127.2, 127.3, 127.5, 128.4, 128.7, 128.9, 130.0, 132.8, 138.8, 142.7, 144.2, 148.5, 148.6; MS (ESI) for C_{30}H_{28}BrNO_{3}S: m/z 562 [M+H]^+, 564 [(M+H)+2]^+.

(2-(3-(N-(2-Bromo-4,5-dimethoxybenzyl)-N-benzylamino)-3-(furan-3-yl)prop-1-ynyl)phenyl)methanol (2m): Yellow oily liquid; ^1H NMR (400 MHz, CDCl_3): δ 2.13 (brs, 1H, -OH), 3.60 (d, J = 13.60 Hz, 1H, -CH_2), 3.70
(d, \( J = 14.40 \) Hz, 1H, -CH\(_2\), 3.84-3.86 (m, 4H, -CH\(_2\), -CH\(_3\)), 3.88-3.90 (m, 4H, -CH\(_2\), -CH\(_3\)), 4.83 (s, 1H, -CH), 4.97 (s, 2H, -CH\(_2\)), 6.54 (s, 1H, Ar-H), 6.96 (s, 1H, Ar-H), 7.15 (s, 1H, Ar-H), 7.22-7.26 (m, 1H, Ar-H), 7.30-7.33 (m, 3H, Ar-H), 7.37-7.41 (m, 4H, Ar-H), 7.51 (d, \( J = 7.60 \) Hz, 1H, Ar-H), 7.75 (d, \( J = 7.60 \) Hz, 1H, Ar-H), 7.62 (s, 1H, Ar-H); \( ^{13} \text{C} \) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 49.2, 53.4, 54.7, 55.9, 56.1, 64.1, 83.5, 89.9, 110.0, 112.9, 114.2, 115.2, 121.0, 124.8, 127.2, 127.5, 128.3, 128.7, 130.2, 132.7, 139.1, 141.5, 142.5, 143.5, 148.4(2); MS (ESI) for C\(_{30}\)H\(_{28}\)BrNO\(_4\): \( m/z \) 546 [M+H]\(^+\), 548 [([M+H]+2]+).

3-(2-(3-(N-(2-Bromo-4,5-dimethoxybenzyl)-N-benzylamino)prop-1-ynyl)phenyl)pentan-3-ol (2n):

Orange solid; mp: 50-52 °C; \(^1\text{H} \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 0.80 (t, \( J = 7.60 \) Hz, 6H, -CH\(_3\)), 1.92-2.01 (m, 2H, -CH\(_2\)), 2.40-2.49 (m, 2H, -CH\(_2\)), 2.66 (brs, 1H, -OH), 3.54 (s, 2H, -CH\(_2\)), 3.78 (s, 2H, -CH\(_2\)), 3.84 (s, 2H, -CH\(_2\)), 3.86 (s, 3H, -CH\(_3\)), 3.88 (s, 3H, -CH\(_3\)), 7.02 (s, 1H, Ar-H), 7.14 (s, 1H, Ar-H), 7.16-7.23 (m, 1H, Ar-H), 7.24-7.35 (m, 4H, Ar-H), 7.41 (d, \( J = 7.20 \) Hz, 2H, Ar-H), 7.54-7.56 (m, 2H, Ar-H); \(^{13} \text{C} \) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 8.1, 33.0, 42.3, 56.0, 56.2, 57.3, 57.5, 78.4, 85.9, 90.7, 113.3, 114.5, 115.5, 119.5, 126.3, 126.9, 127.2, 127.9, 128.3, 129.0, 130.0, 135.2, 138.7, 146.8, 148.4, 148.6; MS (ESI) for C\(_{30}\)H\(_{34}\)BrNO\(_3\): \( m/z \) 536 [M+H]\(^+\), 538 [([M+H]+2]+).

(2-(3-(N-(2-Bromo-4,5-dimethoxybenzyl)-N-benzylamino)prop-1-ynyl)phenyl)(phenyl)methanol (2o):

Yellow oily liquid; \(^1\text{H} \) NMR (500 MHz, CDCl\(_3\)): \( \delta \) 2.71 (brs, 1H, -OH), 3.50 (s, 2H, -CH\(_2\)), 3.67 (s, 2H, -CH\(_2\)), 3.76 (s, 2H, -CH\(_2\)), 3.83(s, 6H, -CH\(_3\)), 6.40 (s, 1H, -CH), 6.99 (s, 1H, Ar-H), 7.08 (s, 1H, Ar-H), 7.23-7.26 (m, 3H, Ar-H), 7.30 (t, \( J = 8.00 \) Hz, 4H, Ar-H), 7.33-7.35 (m, 3H, Ar-H), 7.42 (d, \( J = 8.00 \) Hz, 2H, Ar-H), 7.49 (d, \( J = 8.00 \) Hz, 1H, Ar-H), 7.51 (d, \( J = 7.50 \) Hz, 1H, Ar-H); \(^{13} \text{C} \) NMR (125 MHz, CDCl\(_3\)): \( \delta \) 42.1, 55.9, 56.0, 57.0, 57.3, 73.7, 83.8, 89.9, 113.2, 114.5, 115.3, 121.4, 126.5, 126.7, 127.1, 127.3, 127.4, 128.2, 128.3, 128.6, 128.9, 132.7, 138.5, 142.9, 145.3, 148.2, 148.4; MS (ESI): \( m/z \) 556 [M+H]\(^+\), 558 [([M+H]+2]+).

(2-(3-(N-(2-Bromo-4,5-dimethoxybenzyl)-N-benzylamino)prop-1-ynyl)phenyl)(p-tolyl)methanol (2p):

Yellow oily liquid; \(^1\text{H} \) NMR (500 MHz, CDCl\(_3\)): \( \delta \) 2.29 (s, 3H, -CH\(_3\)), 2.62 (brs, 1H, -OH), 3.50 (s, 2H, -CH\(_2\)), 3.67 (s, 2H, -CH\(_2\)), 3.76 (s, 2H, -CH\(_2\)), 3.83(s, 6H, -CH\(_3\)), 6.37 (s, 1H, -CH), 7.00 (s, 1H, Ar-H), 7.09 (s, 1H, Ar-H), 7.10 (d, \( J = 8.00 \) Hz, 2H, Ar-H), 7.23-7.26 (m, 2H, Ar-H), 7.28-7.32 (m, 4H, Ar-H), 7.34-7.35 (m, 3H, Ar-H), 7.50 (d, \( J = 8.00 \) Hz, 2H, Ar-H); \(^{13} \text{C} \) NMR (125 MHz, CDCl\(_3\)): \( \delta \) 21.0, 42.2, 55.9, 56.0, 57.0, 57.3, 73.7, 83.8, 89.9, 113.2, 114.5, 115.3, 121.4, 126.4, 126.5, 127.1, 127.2, 128.2, 128.5, 128.9, 129.0, 129.8, 132.7, 137.0, 138.6, 140.0, 145.4, 148.2, 148.4; MS (ESI) for C\(_{33}\)H\(_{32}\)BrNO\(_3\): \( m/z \) 570 [M+H]\(^+\), 572 [([M+H]+2]+).
1-(2-(3-(N-(2-Bromo-4,5-dimethoxybenzyl)-N-benzylamino)prop-1-ynyl)phenyl) propan-1-ol (2q): Yellow oily liquid; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 1.01 (t, \(J = 6.40\) Hz, 3H, -CH\(_3\)), 1.84-1.93 (m, 2H, -CH\(_2\)), 2.20 (brs, 1H, -OH), 3.54 (s, 2H, -CH\(_2\)), 3.77 (s, 2H, -CH\(_2\)), 3.83 (s, 2H, -CH\(_2\)), 3.85 (s, 3H, -CH\(_3\)), 3.88 (s, 3H, -CH\(_3\)), 5.19 (t, \(J = 5.60\) Hz, 1H, -CH), 7.01 (s, 1H, Ar-H), 7.13 (s, 1H, Ar-H), 7.22-7.27 (m, 2H, Ar-H), 7.31-7.36 (m, 3H, Ar-H), 7.41 (d, \(J = 6.00\) Hz, 2H, Ar-H), 7.48-7.52 (m, 2H, Ar-H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 10.3, 31.0, 42.1, 55.9, 56.1, 57.1, 57.3, 73.6, 83.6, 89.4, 113.1, 114.5, 115.3, 120.7, 125.4, 126.9, 127.2, 128.3, 128.4, 128.9, 129.8, 132.6, 138.6, 146.2, 148.2, 148.4; MS (ESI) for C\(_{28}\)H\(_{30}\)BrNO\(_3\): \(m/z\) 508 [M+H]+, 510 [(M+H)+2]⁺.

(2-(3-(BenzyI(2-bromobenzyl)amino)prop-1-ynyl)-4,5-dimethoxyphenyl)methanol (2r): Yellow solid; mp: 110-112 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 3.52 (s, 2H, -CH\(_2\)), 3.81 (s, 2H, -CH\(_2\)), 3.90 (s, 5H, -CH\(_2\), -CH\(_3\)), 3.92 (s, 3H, -CH\(_3\)), 4.87 (s, 2H, -CH\(_2\)), 6.99 (s, 1H, Ar-H), 7.00 (s, 1H, Ar-H), 7.13 (td, \(J = 1.20\) Hz, \(J = 7.80\) Hz, 1H, Ar-H), 7.26-7.33 (m, 4H, Ar-H), 7.44 (d, \(J = 7.20\) Hz, 2H, Ar-H), 7.56 (d, \(J = 7.60\) Hz, 1H, Ar-H), 7.60 (d, \(J = 7.20\) Hz, 1H, Ar-H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 41.9, 55.9, 56.0, 57.4, 57.7, 63.9, 83.3, 87.6, 110.5, 114.8, 124.8, 127.2, 127.3, 128.3, 128.6, 128.8, 130.0, 130.8, 132.9, 136.0, 137.9, 138.6, 147.9, 149.3; MS (ESI) for C\(_{26}\)H\(_{28}\)BrNO\(_3\): \(m/z\) 480 [M+H]+, 482 [(M+H)+2]⁺.

**General procedure for the synthesis of 1,2,3,4-tetrahydroisoquinolines (3a-r):**

Pd(PPh\(_3\))\(_4\) (10 mol\%) and K\(_2\)CO\(_3\) (5 mmol) were added into a two-neck round bottom flask. The flask was evacuated and flushed with nitrogen. Propargylamine (2) (1 mmol) dissolved in DMF was added to the flask and heated to 100 °C under \(\text{N}_2\) atmosphere until starting materials were consumed. After completion of the reaction, the reaction mixture was cooled to rt and quenched by the addition of saturated NH\(_4\)Cl (aq.) solution. The aqueous layer was extracted with EtOAc. The organic phase was washed with brine, dried (anhydrous Na\(_2\)SO\(_4\)) and concentrated under reduced pressure. The crude product was chromatographed using petroleum ether and ethyl acetate as an eluent to afford the compounds (3a-r).

**Spectral data of compounds (3a-r):**

(E)-4-(Isobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-3-(4-methoxyphenyl)-2-(4-methylbenzyl)-1,2,3,4-tetrahydroisoquinoline (3a): Yellow solid; mp: 97-99 °C; IR (KBr): 762, 821, 1028, 1251, 1456, 1509, 1607, 2836, 2928 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.27 (s, 3H, -CH\(_3\)), 3.47 (d, \(J = 17.20\) Hz, 1H, -CH\(_2\)), 3.74 (s, 3H, -CH\(_3\)), 3.78-3.84 (m, 6H, -CH\(_2\), -CH\(_3\)), 3.98 (s, 3H, -CH\(_3\)), 5.23 (s, 1H, -CH), 5.53 (ABq, \(J = 14.4\) Hz, 2H, -CH\(_2\)), 6.38 (s, 1H, Ar-H), 6.81 (d, \(J = 8.80\) Hz, 2H, Ar-H), 6.98 (d, \(J = 7.60\) Hz, 2H, Ar-H), 7.02-7.03 (m, 2H, Ar-H), 7.20-7.26 (m, 3H, Ar-H), 7.30 (t, \(J = 7.80\) Hz, 1H, Ar-H), 7.31-7.36 (m, 3H, Ar-H), 7.41 (d, \(J = 6.00\) Hz, 2H, Ar-H), 7.48-7.52 (m, 2H, Ar-H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 10.3, 31.0, 42.1, 55.9, 56.1, 57.1, 57.3, 73.6, 83.6, 89.4, 113.1, 114.5, 115.3, 120.7, 125.4, 126.9, 127.2, 128.3, 128.4, 128.9, 129.8, 132.6, 138.6, 146.2, 148.2, 148.4; MS (ESI) for C\(_{28}\)H\(_{30}\)BrNO\(_3\): \(m/z\) 508 [M+H]+, 510 [(M+H)+2]⁺.
7.60 Hz, 1H, Ar-H), 7.43 (d, J = 8.40 Hz, 2H, Ar-H), 8.25 (s, 1H, Ar-H); 13C NMR (100 MHz, CDCl₃): δ 21.0, 48.5, 55.1, 55.6, 55.9, 57.7, 60.2, 73.4, 104.1, 109.2, 110.8, 113.6, 120.9, 123.8, 124.8, 125.4, 127.8, 127.9, 128.7, 128.9, 129.4, 132.8, 133.9, 136.3, 136.5, 140.7, 146.9, 147.5, 153.2, 158.6; MS (ESI) for C₃₄H₃₃NO₄: m/z 520 [M+H]⁺; HRMS calculated for [C₃₄H₃₃NO₄⁺H]⁺: 520.2488, Found: 520.2457.

(E)-2-Benzyl-4-(isobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-3-p-tolyl-1,2,3,4-tetrahydroisoquinoline (3b): Yellow solid; mp: 91-93 °C; IR (KBr): 736, 800, 1010, 1252, 1443, 1511, 1627, 2883, 2921 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 2.28 (s, 3H, -CH₃), 3.49 (d, J = 16.50 Hz, 1H, -CH₂), 3.78 (s, 3H, -CH₃), 3.82-3.88 (m, 3H, -CH₂), 3.98 (s, 3H, -CH₃), 5.27 (s, 1H, -CH), 5.52 (ABq, J = 14.00 Hz, 2H, -CH₂), 6.37 (s, 1H, Ar-H), 7.00-7.03 (m, 2H, Ar-H), 7.07 (d, J = 7.50 Hz, 2H, Ar-H); 7.14-7.21 (m, 4H, Ar-H); 7.28 (d, J = 8.00 Hz, 1H, Ar-H), 7.34 (d, J = 7.00 Hz, 2H, Ar-H), 7.41 (d, J = 7.50 Hz, 2H, Ar-H), 8.26 (s, 1H, Ar-H); ¹³C NMR (125 MHz, CDCl₃): δ 21.0, 48.6, 55.5, 55.8, 58.1, 60.4, 73.4, 103.9, 109.1, 111.8, 120.8, 123.7, 124.7, 125.3, 126.7, 127.8, 127.9, 128.0, 128.2, 128.9, 129.0, 133.8, 136.5, 137.6, 139.6, 140.7, 146.9, 147.4, 153.2; MS (ESI) for C₃₃H₃₂NO₅: m/z 490 [M+H]⁺.

(E)-2-Benzyl-4-(isobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-3-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (3c): Yellow solid; mp: 89-91 °C; IR (KBr): 711, 819, 1022, 1250, 1468, 1512, 1619, 2897, 2923 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): 63.49 (d, J = 17.00 Hz, 1H, -CH₂), 3.74 (s, 3H, -CH₃), 3.80 (s, 3H, -CH₃), 3.83-3.86 (m, 3H, -CH₂), 3.98 (s, 3H, -CH₃), 5.24 (s, 1H, -CH), 5.53 (ABq, J = 14.50 Hz, 2H, -CH₂), 6.38 (s, 1H, Ar-H), 6.81 (d, J = 8.00 Hz, 2H, Ar-H), 7.02 (d, J = 4.00 Hz, 2H, Ar-H), 7.15-7.22 (m, 4H, Ar-H), 7.30 (d, J = 8.00 Hz, 1H, Ar-H), 7.33 (d, J = 7.00 Hz, 2H, Ar-H), 7.43 (d, J = 8.50 Hz, 2H, Ar-H), 8.27 (s, 1H, Ar-H); ¹³C NMR (125 MHz, CDCl₃): δ 48.6, 55.1, 55.6, 55.9, 58.0, 60.2, 73.4, 103.9, 109.1, 111.8, 113.6, 120.9, 123.7, 124.7, 125.3, 126.7, 127.9, 128.0(2), 128.9, 129.4, 132.7, 133.8, 139.6, 140.7, 146.9, 147.5, 153.2, 158.5; MS (ESI) for C₃₃H₃₂NO₅: m/z 506 [M+H]⁺.

(E)-2-Benzyl-3-(4-chlorophenyl)-4-(isobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (3d): Yellow solid; mp: 86-88 °C; IR (KBr): 710, 823, 1027, 1240, 1432, 1508, 1623, 2854, 2924 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 3.51 (d, J = 17.20 Hz, 1H, -CH₂), 3.81-3.84 (m, 6H, -CH₂, -CH₃), 3.98 (s, 3H, -CH₃), 5.24 (s, 1H, -CH), 5.54(ABq, J = 14.00 Hz, 2H, -CH₂), 6.38 (s, 1H, Ar-H), 6.92 (d, J = 8.00 Hz, 1H, Ar-H), 7.02 (t, J = 7.60 Hz, 1H, Ar-H), 7.17-7.20 (m, 3H, Ar-H), 7.22-7.25 (m, 3H, Ar-H), 7.31-7.33 (m, 3H, Ar-H), 7.47 (d, J = 8.40 Hz, 2H, Ar-H), 8.24 (s, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 48.7, 55.6, 55.9, 58.1, 60.1, 73.5, 103.1, 109.1, 111.8, 121.0, 123.5, 124.4, 125.0, 126.9, 127.9, 128.1, 128.2, 128.5, 128.9, 129.8, 132.7, 133.6, 139.4(2), 140.8, 147.0, 147.6, 153.5; MS (ESI) for C₃₂H₂₈ClNO₅: m/z 510 [M+H]⁺, 512 [(M+H)+2]⁺.
(E)-2-Benzyl-4-(isobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-3-(naphthalen-1-yl)-1,2,3,4-tetrahydroisoquinoline (3e): Orange solid; mp: 80-82 °C; IR (KBr): 719, 829, 1034, 1236, 1478, 1519, 1613, 2845, 2919 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 3.42 (d, J = 17.00 Hz, 1H, -CH₂), 3.67 (d, J = 17.00 Hz, 1H, -CH₂), 3.82 (s, 3H, -CH₃), 3.88 (d, J = 13.50 Hz, 1H, -CH₂), 4.01-4.04 (m, 4H, -CH₂, -CH₃), 5.52 (d, J = 14.00 Hz, 1H, -CH₂), 5.61 (d, J = 14.00 Hz, 1H, -CH₂), 5.93 (s, 1H, -CH), 6.39 (s, 1H, Ar-H), 6.87 (t, J = 7.50 Hz, 1H, Ar-H), 6.92 (d, J = 7.50 Hz, 1H, Ar-H), 7.16-7.23 (m, 5H, Ar-H), 7.28 (d, J = 7.00 Hz, 1H, Ar-H), 7.34-7.35 (m, 2H, Ar-H), 7.39 (d, J = 8.00 Hz, 1H, Ar-H), 7.51-7.54 (m, 2H, Ar-H), 7.71 (d, J = 8.50 Hz, 1H, Ar-H), 7.87 (d, J = 8.50 Hz, 1H, Ar-H), 8.29 (d, J = 8.50 Hz, 1H, Ar-H), 8.47 (s, 1H, Ar-H); ¹³C NMR (125 MHz, CDCl₃): δ 48.8, 55.8, 56.1, 58.3, 59.7, 73.7, 104.1, 109.7, 110.9, 121.1, 123.9, 124.9, 125.0, 125.2, 125.5, 125.6, 126.0, 126.1, 127.2, 128.2(2), 128.4, 128.9, 129.6, 132.1, 133.9, 134.4, 136.5, 139.4, 140.9, 147.3, 147.7, 153.8; MS (ESI) for C₃₆H₃₅NO₅: m/z 526 [M+H]⁺.

(E)-2-Benzyl-3-(9H-fluoren-3-yl)-4-(isobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (3f): Yellow solid; mp: 70-72 °C; IR (KBr): 783, 837, 1016, 1223, 1489, 1517, 1610, 2839, 2927 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 3.52 (d, J = 16.50 Hz, 1H, -CH₂), 3.80-3.82 (m, 4H, -CH₂, -CH₃), 3.88-3.94 (m, 3H, -CH₂), 4.00-4.05 (m, 4H, -CH₂, -CH₃), 5.35 (s, 1H, -CH), 5.56 (ABq, J = 14.50 Hz, 2H, -CH₂), 6.40 (s, 1H, Ar-H), 6.99-7.03 (m, 2H, Ar-H), 7.16-7.37 (m, 9H, Ar-H), 7.48 (d, J = 6.50 Hz, 1H, Ar-H), 7.55 (d, J = 8.50 Hz, 1H, Ar-H), 7.67-7.72 (m, 3H, Ar-H), 8.31 (s, 1H, Ar-H); ¹³C NMR (125 MHz, CDCl₃): δ 36.9, 48.8, 55.6, 55.9, 58.1, 60.9, 73.5, 103.8, 109.2, 111.8, 119.6, 120.9, 123.8, 124.8, 124.9(2), 125.3, 126.4, 126.6, 126.8, 127.1, 127.9, 128.0, 128.1, 128.2, 129.0, 129.1, 133.8, 139.5, 139.7, 140.7, 141.5, 143.4(2), 147.0, 147.5, 153.4; MS (ESI) for C₃₉H₃₅NO₅: m/z 564 [M+H]⁺.

(E)-3-(2-Benzyl-4-(isobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-3-yl)-9-ethyl-9H-carbazole (3g): Pale yellow solid; mp: 80-82 °C; IR (KBr): 742, 842, 1038, 1048, 1212, 1497, 1523, 1642, 2837, 2933, 3489 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.39 (t, J = 7.20 Hz, 3H, -CH₃), 3.51 (d, J = 16.80 Hz, 1H, -CH₂), 3.78 (s, 3H, -CH₃), 3.87-3.96 (m, 3H, -CH₂), 4.04 (s, 3H, -CH₃), 4.31 (q, J = 7.20 Hz, 2H, -CH₂), 5.48 (s, 1H, -CH), 5.57 (s, 2H, -CH₂), 6.37 (s, 1H, Ar-H), 6.96 (t, J = 7.60 Hz, 1H, Ar-H), 7.09 (d, J = 8.00 Hz, 1H, Ar-H), 7.14-7.23 (m, 5H, Ar-H), 7.29-7.36 (m, 3H, Ar-H), 7.38-7.42 (m, 3H, Ar-H), 7.66 (d, J = 8.40 Hz, 1H, Ar-H), 8.02 (d, J = 7.60 Hz, 1H, Ar-H), 8.18 (s, 1H, Ar-H), 8.36 (s, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 13.8, 37.5, 48.7, 55.6, 56.0, 58.1, 61.2, 73.5, 104.4, 108.2, 108.3, 109.3, 112.0, 118.5, 120.2, 120.5, 120.8, 122.8, 122.9, 124.0, 125.1, 125.4, 125.6, 126.4, 126.7, 127.9, 128.1, 129.1, 131.2, 133.9, 139.4, 139.8, 140.1, 140.7, 147.0, 147.5, 153.3; MS (ESI) for C₄₀H₃₆N₂O₃: m/z 593 [M+H]⁺.
(E)-2-Benzyl-4-(isobenzofuran-1(3H)-ylidene)-3-p-tolyl-1,2,3,4-tetrahydroisoquinoline (3h):

Yellow solid; mp: 60-62 °C; IR (KBr): 757, 857, 1005, 1219, 1440, 1526, 1637, 2826, 2947 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 2.28 (s, 3H, -CH₃), 3.56 (d, J = 16.50 Hz, 1H, -CH₂), 3.70 (ABq, J = 14.00 Hz, 2H, -CH₂), 3.92 (d, J = 16.50 Hz, 1H, -CH₂), 5.30 (s, 1H, -CH), 5.52 (ABq, J = 14.50 Hz, 2H, -CH₂), 6.88 (d, J = 7.50 Hz, 1H, Ar-H), 7.00-7.10 (m, 5H, Ar-H), 7.14-7.19 (m, 3H, Ar-H), 7.22-7.27 (m, 2H, Ar-H), 7.28-7.33 (m, 3H, Ar-H), 7.41 (d, J = 8.50 Hz, 2H, Ar-H), 8.60 (d, J = 8.50 Hz, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 21.1, 49.1, 58.2, 60.6, 73.5, 103.9, 120.9, 124.0, 125.8, 126.0, 126.7, 127.9, 128.0, 128.2(2), 128.7, 129.0, 129.1, 132.4, 132.5, 133.8, 136.5, 137.7, 139.6, 141.1, 154.7; MS (ESI) for C₃₁H₂₇NO: m/z 430 [M+H]+.

(E)-2-Benzyl-3-(4-chlorophenyl)-4-(isobenzofuran-1(3H)-ylidene)-1,2,3,4-tetrahydroisoquinoline (3i): Yellow solid; mp: 63-65 °C; IR (KBr): 762, 834, 1026, 1239, 1436, 1533, 1622, 2824, 2948 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 3.58 (d, J = 17.20 Hz, 1H, -CH₂), 3.83-3.91 (m, 3H, -CH₂), 5.27 (s, 1H, -CH), 5.54 (ABq, J = 14.80 Hz, 2H, -CH₂), 6.88-6.95 (m, 2H, Ar-H), 7.03 (t, J = 7.60 Hz, 1H, Ar-H), 7.11 (t, J = 7.20 Hz, 1H, Ar-H), 7.16-7.18 (m, 2H, Ar-H), 7.21-7.35 (m, 8H, Ar-H), 7.48 (d, J = 8.00 Hz, 2H, Ar-H), 8.60 (d, J = 8.00 Hz, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 49.0, 58.1, 60.1, 73.6, 102.9, 121.1, 123.8, 126.0, 126.2, 126.7, 126.9, 127.9, 128.1, 128.4, 128.5, 128.7, 129.0, 129.8, 132.0, 132.1, 132.7, 133.6, 139.2, 139.4, 141.2, 155.0; MS (ESI) for C₂₃H₂₃ClNO: m/z 450 [M+H]+, 452 [(M+H)+2]+.

(E)-3-(2-Benzyl-4-(isobenzofuran-1(3H)-ylidene)-1,2,3,4-tetrahydroisoquinolin-3-yl)-9-ethyl-9H-carbazole (3j): Yellow solid; mp: 77-79 °C; IR (KBr): 722, 829, 1049, 1247, 1439, 1567, 1632, 2820, 2917 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.36 (t, J = 6.80 Hz, 3H, -CH₃), 3.58 (d, J = 17.20 Hz, 1H, -CH₂), 3.91 (s, 2H, -CH₂), 3.96 (d, J = 17.20 Hz, 1H, -CH₂), 4.28 (q, J = 7.20 Hz, 2H, -CH₂), 5.52 (s, 1H, -CH), 5.55 (s, 2H, -CH₂), 6.87 (d, J = 7.60 Hz, 1H, Ar-H), 6.95 (t, J = 7.60 Hz, 1H, Ar-H), 7.07-7.21 (m, 7H, Ar-H), 7.28-7.33 (m, 4H, Ar-H), 7.38 (t, J = 6.00 Hz, 3H, Ar-H), 7.69 (d, J = 8.00 Hz, 1H, Ar-H), 8.01 (d, J = 8.00 Hz, 1H, Ar-H), 8.20 (s, 1H, Ar-H), 8.71 (d, J = 8.00 Hz, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 13.8, 37.5, 49.0, 58.1, 61.3, 73.5, 104.2, 108.3, 118.5, 120.2, 120.5, 120.8, 122.8, 124.2, 125.3, 125.8, 126.1, 126.3, 126.7, 126.8, 128.1, 128.2, 128.7, 129.1, 131.2, 132.5, 132.7, 133.9, 139.4, 139.7, 140.1, 141.1, 154.7; MS (ESI) for C₃₈H₃₂N₂O: m/z 533 [M+H]+.

(E)-2-Benzyl-4-(isobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (3k): Yellow solid; mp: 120-122 °C; IR (KBr): 715, 820, 1045, 1263, 1417, 1583, 1609, 2817, 2936 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 3.70 (s, 2H, -CH₂), 3.75 (s, 2H, -CH₂), 3.84 (s, 3H, -CH₃), 3.86 (s, 2H, -CH₂), 3.93 (s, 3H, -CH₃), 5.44 (s, 2H, -CH₂), 6.53 (s, 1H, Ar-H), 7.25-7.31 (m, 6H, Ar-H), 7.37 (t, J = 8.00 Hz, 3H, Ar-H), 8.16 (s, 1H, Ar-H); ¹³C NMR (125 MHz, CDCl₃): δ 53.0, 55.5, 55.6, 55.9, 61.1, 73.3, 104.8, 109.3, 111.9, 121.0, 123.8, 125.3, 127.0, 127.2, 127.7, 135.2; MS (ESI) for C₂₆H₂₂N₂O₂: m/z 426 [M+H]+, 428 [(M+H)+2]+.
127.8, 128.2, 129.3, 134.2, 137.8, 140.7, 146.9, 147.0, 150.8; MS (ESI) for C_{26}H_{25}NO_{3}: m/z 400 [M+H]^+.

**(E)-2-Benzyl-4-[(isobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-3-(thiophen-2-yl)-1,2,3,4-tetrahydroisoquinoline (3l):** Yellow solid; mp: 83-85 °C; IR (KBr): 723, 812, 1078, 1287, 1420, 1592, 1600, 2868, 2978 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 3.57 (d, J = 16.80 Hz, 1H, -CH₂), 3.80 (s, 3H, -CH₃), 3.84 (s, 2H, -CH₂), 3.96 (s, 3H, -CH₃), 4.09 (d, J = 16.80 Hz, 1H, -CH₂), 5.47 (s, 1H, -CH), 5.52 (ABq, J = 14.40 Hz, 2H, -CH₂), 6.41 (s, 1H, Ar-H), 6.81-6.84 (m, 1H, Ar-H), 6.88-6.89 (m, 1H, Ar-H), 7.04-7.11 (m, 2H, Ar-H), 7.16-7.25 (m, 5H, Ar-H), 7.29-7.31 (m, 1H, Ar-H), 7.34-7.36 (m, 2H, Ar-H), 8.24 (s, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 49.0, 55.6, 55.9, 57.7, 57.8, 73.5, 104.4, 109.1, 112.0, 120.9, 123.8, 124.1, 125.2(2), 125.8, 126.4, 126.8, 128.0, 128.1, 128.7, 133.5, 139.1, 140.7, 145.4, 147.0, 147.5, 153.2; MS (ESI) for C_{30}H_{27}NO_{3}S: m/z 482 [M+H]^+.

**(E)-2-Benzyl-3-(furan-3-yl)-4-(isobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (3m):** Yellow solid; mp: 75-77 °C; IR (KBr): 730, 819, 1043, 1278, 1452, 1560, 1603, 2877, 2989 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 3.56 (d, J = 16.40 Hz, 1H, -CH₂), 3.78-3.83 (m, 5H, -CH₂, -CH₃), 3.93-3.96 (m, 4H, -CH₂, -CH₃), 5.24 (s, 1H, -CH), 5.51 (ABq, J = 14.00 Hz, 2H, -CH₂), 6.44 (s, 1H, Ar-H), 6.50 (s, 1H, Ar-H), 7.13 (t, J = 7.20 Hz, 1H, Ar-H), 7.16-7.27 (m, 6H, Ar-H), 7.31-7.36 (m, 4H, Ar-H), 8.21 (s, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 49.2, 53.8, 55.6, 55.9, 57.7, 73.4, 105.1, 109.1, 110.7, 112.0, 121.0, 123.8, 124.5, 124.6, 125.4, 126.8, 127.9, 128.0, 128.1, 128.9, 133.7, 139.2, 140.8, 141.5, 143.0, 147.0, 147.5, 152.4; MS (ESI) for C_{30}H_{27}NO_{4}: m/z 466 [M+H]^+.

**(E)-2-Benzyl-4-(3,3-diethylisobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (3n):** Yellow solid; mp: 69-71 °C; IR (KBr): 733, 808, 1040, 1274, 1459, 1588, 1617, 2889, 2935 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 0.72 (t, J = 7.60 Hz, 6H, -CH₃), 1.76-1.85 (m, 2H, -CH₂), 1.90-1.99 (m, 2H, -CH₂), 3.58 (s, 2H, -CH₂), 3.67 (s, 2H, -CH₂), 3.73 (s, 2H, -CH₂), 3.83 (s, 3H, -CH₃), 3.87 (s, 3H, -CH₃), 6.58 (s, 1H, Ar-H), 7.09-7.15 (m, 2H, Ar-H), 7.26 (t, J = 6.80 Hz, 2H, Ar-H), 7.29-7.33 (m, 3H, Ar-H), 7.36-7.38 (m, 2H, Ar-H), 8.03 (d, J = 8.00 Hz, 1H, Ar-H); ¹³C NMR (100 MHz, CDCl₃): δ 7.7, 32.7, 53.5, 54.7, 55.9(2), 60.9, 91.0, 106.0, 109.9, 110.8, 121.2, 122.0, 125.1, 126.7, 126.9, 128.2(2), 128.7, 129.1, 134.1, 138.7, 146.5, 146.9, 147.4, 149.9; MS (ESI) for C_{30}H_{33}NO_{4}: m/z 456 [M+H]^+.

**(E)-2-Benzyl-6,7-dimethoxy-4-(3-phenylisobenzofuran-1(3H)-ylidene)-1,2,3,4-tetrahydroisoquinoline (3o):** Yellow solid; mp: 66-68 °C; IR (KBr): 713, 826, 1037, 1283, 1464, 1522, 1618, 2840, 2940 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 3.68 (s, 3H, -CH₃), 3.71 (s, 2H, -CH₂), 3.78 (s, 2H, -CH₂), 3.82-3.86 (m, 4H, -CH₂, -CH₃), 3.97 (d, J = 13.5 Hz, 1H, -CH₂), 6.50 (s, 1H, -CH), 6.52 (s, 1H,
Ar-H), 7.15 (d, J = 7.00 Hz, 1H, Ar-H), 7.22 (d, J = 8.00 Hz, 1H, Ar-H), 7.26 (t, J = 7.00 Hz, 2H, Ar-H), 7.31 (t, J = 7.00 Hz, 3H, Ar-H), 7.34-7.36 (m, 4H, Ar-H), 7.38-7.40 (m, 3H, Ar-H), 8.23 (s, 1H, Ar-H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 53.0, 55.5, 55.6, 55.7, 61.3, 85.6, 105.3, 109.2, 112.0, 122.3, 123.6, 125.3, 126.3, 127.2(2), 127.9, 128.2, 128.3(2), 128.6, 129.3, 134.0, 138.0, 140.4, 143.6, 146.9, 149.8; MS (ESI) for C$_3$H$_2$NO$_3$: m/z 476 [M+H]$^+$. 

(E)-2-Benzyl-6,7-dimethoxy-4-(3-p-tolylisobenzofuran-1(3H)-ylidene)-1,2,3,4-tetrahydroisoquinoline (3p): Yellow solid; mp: 120-122 °C; IR (KBr): 3171, 2818, 2940 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): δ 2.33 (s, 3H, -CH$_3$), 3.70 (s, 3H, -CH$_3$), 3.72 (s, 2H, -CH$_2$), 3.79 (s, 2H, -CH$_2$), 3.84-3.87 (m, 4H, -CH$_2$, -CH$_3$), 3.98 (d, J = 13.00 Hz, 1H, -CH$_2$), 6.48 (s, 1H, -CH), 6.53 (s, 1H, Ar-H), 7.15 (d, J = 8.00 Hz, 3H, Ar-H), 7.22-7.28 (m, 5H, Ar-H), 7.31 (t, J = 7.00 Hz, 2H, Ar-H), 7.38-7.40 (m, 3H, Ar-H), 8.22 (s, 1H, Ar-H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 21.2, 53.0, 55.5, 55.6, 55.7, 61.2, 85.6, 105.1, 109.3, 112.1, 122.3, 123.7, 125.4, 126.4, 127.0, 127.2, 128.0, 128.1, 128.3, 129.3, 129.4, 134.1, 137.5, 138.0, 138.2, 143.9, 147.0(2), 149.9; MS (ESI) for C$_3$H$_3$NO$_3$: m/z 490 [M+H]$^+$. 

(E)-2-Benzyl-4-(3-ethylisobenzofuran-1(3H)-ylidene)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (3q): Yellow solid; mp: 76-78 °C; IR (KBr): 714, 1037, 1283, 1460, 1524, 1617, 2838, 2942 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): δ 1.12 (t, J = 6.00 Hz, 3H, -CH$_3$), 1.72-1.78 (m, 1H, -CH$_2$), 2.00-2.05 (m, 1H, -CH$_2$), 3.67-3.73 (m, 2H, -CH$_2$), 3.76(s, 2H, -CH$_2$), 3.82-3.91 (m, 5H, -CH$_2$, -CH$_3$), 3.94 (s, 3H, -CH$_3$), 5.50-5.52 (m, 1H, -CH), 6.54 (s, 1H, Ar-H), 7.24-7.32 (m, 6H, Ar-H), 7.33-7.35 (m, 1H, Ar-H), 7.37-7.39 (m, 2H, Ar-H), 8.26 (s, 1H, Ar-H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 9.9, 29.5, 53.3, 55.8, 55.9, 61.3, 85.4, 104.6, 109.5, 111.9, 121.2, 124.0, 125.8, 127.1, 127.3, 127.9, 128.1, 128.4, 129.5, 134.7, 138.1, 144.2, 146.9, 147.2, 150.2; MS (ESI) for C$_{28}$H$_{29}$NO$_3$: m/z 428 [M+H]$^+$. 

(E)-2-Benzyl-4-(5,6-dimethoxyisobenzofuran-1(3H)-ylidene)-1,2,3,4-tetrahydroisoquinoline (3r): Yellow solid; mp: 79-81 °C; IR (KBr): 720, 823, 1048, 1265, 1415, 1580, 1611, 2818, 2940 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 3.70 (s, 3H,-CH$_3$), 3.76 (s, 2H, -CH$_2$), 3.79 (s, 2H, -CH$_2$), 3.80 (s, 2H, -CH$_2$), 3.90 (s, 3H, -CH$_3$), 5.37 (s, 2H, -CH$_2$), 6.79 (s, 1H, Ar-H), 6.80 (s, 1H, Ar-H), 7.04-7.11 (m, 2H, Ar-H), 7.22-7.29 (m, 4H, Ar-H), 7.37-7.39 (m, 2H, Ar-H), 8.45 (d, J = 8.00 Hz, 1H, Ar-H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 52.8, 56.0(2), 56.9, 61.6, 73.4, 102.7, 103.4, 106.8, 125.1, 126.4, 126.5(2), 127.2, 128.2, 128.3, 129.1, 133.2, 134.0, 134.2, 138.3, 148.8, 149.8, 152.7; MS (ESI) for C$_{26}$H$_{25}$NO$_3$: m/z 400 [M+H]$^+$. 

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Synthesis of starting materials for the formation of oxe/azepinoindoles

Table 2 Synthesis of substituted propargylamines (4a-d) and propargylethers (4e-g)

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>R¹(S-5)</th>
<th>R⁶(S-8)</th>
<th>Substrate S-9 (Yield %)ᵃ</th>
<th>Substrate 4 (Yield %)ᵃ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NBn</td>
<td>4,5-OMe (S-5b)</td>
<td>H (S-8a)</td>
<td>S-9a (82)</td>
<td>4a (75)</td>
</tr>
<tr>
<td>2</td>
<td>NBn</td>
<td>H (S-5c)</td>
<td>H (S-8a)</td>
<td>S-9b (80)</td>
<td>4b (73)</td>
</tr>
<tr>
<td>3</td>
<td>NBn</td>
<td>4,5-OMe (S-5b)</td>
<td>NO₂ (S-8b)</td>
<td>S-9c (83)</td>
<td>4c (77)</td>
</tr>
<tr>
<td>4</td>
<td>NBn</td>
<td>4,5-OMe (S-5b)</td>
<td>Cl (S-8c)</td>
<td>S-9d (81)</td>
<td>4d (72)</td>
</tr>
<tr>
<td>5</td>
<td>O</td>
<td>4,5-OMe (S-5d)</td>
<td>H (S-8a)</td>
<td>S-9e (81)</td>
<td>4e (71)</td>
</tr>
<tr>
<td>6</td>
<td>O</td>
<td>4,5-OMe (S-5d)</td>
<td>Me (S-8d)</td>
<td>S-9f (85)</td>
<td>4f (75)</td>
</tr>
<tr>
<td>7</td>
<td>O</td>
<td>4,5-OMe (S-5d)</td>
<td>NO₂ (S-8b)</td>
<td>S-9g (80)</td>
<td>4g (74)</td>
</tr>
</tbody>
</table>

ᵃIsolated yields after column chromatography.

General procedure for synthesis of substituted propargyl ether (S-5d):

The terminal propargyl ether S-5d was prepared by O-alkylation of (2-bromo-4,5-dimethoxyphenyl)methanol (1 mmol) with propargyl bromide (1.5 mmol) using NaH (1.5 mmol) as a base in THF as a solvent under nitrogen atmosphere and was stirred under room temperature condition for 6h. The reaction mixture was then quenched by the addition of methanol to quench excess sodium hydride and extracted using ethylacetate. The organic phase was washed with 1N HCl and twice with H₂O. The organic phases were separated, dried over MgSO₄, filtered and concentrated in vacuo. The residue was then purified by flash column chromatography technique (petroleum ether/ethyl acetate) to afford the compound S-5d in 86 % yield.

General procedure for sonagashira coupling of propargylamines and ethers with substituted 2-iodoanilines (S-9):

α-Iodoanilines S-8 (1mmol), Pd(PPh₃)₂Cl₂ (3 mol%) and CuI (3 mol%) were added to 5.0 mL of NEt₃ and the mixture was stirred under N₂ for 10 minutes. Then, terminal alkyne 6 (1.1 mmol) in
THF was added dropwise and the resulting reaction mixture was stirred for 3 h. After consumption of starting materials (monitor by TLC), the resulting mixture was filtered through celite bed and washed with THF. Removal of the solvent under reduced pressure gave the crude product, which was further purified by column chromatography on silica gel using petroleum ether and ethylacetate as eluent to afford pure product S-9.

General procedure for the preparation of 2-ethynyltrifluoroacetanilides (4a-g)\(^4\):

2-Alkynylanilines (S-9) (1 mmol) was dissolved in CH\(_2\)Cl\(_2\) (5 mL) and cooled to 0°C. To this mixture, pyridine (3 mmol) was added followed by the dropwise addition of trifluoroacetic anhydride (2 mmol). The reaction was stirred for 2h at rt and was quenched by the addition of 1N HCl. The mixture was extracted with CH\(_2\)Cl\(_2\), washed twice with water, brine and dried over MgSO\(_4\). It was then filtered and concentrated in vacuo. The crude residue was then purified by column chromatography (petroleum ether and ethylacetate as eluent) to afford 4.

N-(2-(3-(Benzy1(2-bromo-4,5-dimethoxyphenyl)amino)prop-1-ynyl)phenyl)-2,2,2-trifluoroacetamide (4a): White solid; mp: 93-95 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 3.62 (s, 2H, -CH\(_2\)), 3.78 (s, 2H, -CH\(_2\)), 3.83 (s, 2H, -CH\(_2\)), 3.86 (s, 3H, -CH\(_3\)), 3.88 (s, 3H, -CH\(_3\)), 7.02 (s, 1H, Ar-\(H\)), 7.09 (s, 1H, Ar-\(H\)), 7.21 (t, \(J = 7.60\) Hz, 1H, Ar-\(H\)), 7.28 (d, \(J = 7.20\) Hz, 1H, Ar-\(H\)), 7.34 (t, \(J = 7.60\) Hz, 2H, Ar-\(H\)), 7.40-7.43 (m, 3H, Ar-\(H\)), 7.55 (dd, \(J = 7.70\) Hz, 1.30 Hz, 1H, Ar-\(H\)), 8.37 (d, \(J = 8.40\) Hz, 1H, Ar-\(H\)), 8.74 (s, 1H, -NH, D\(_2\)O exchangeable); \(^1\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 42.2, 56.0, 56.1, 57.0, 57.5, 79.9, 93.5, 113.3, 113.4, 115.0, 115.5, 115.7 (q, \(J_{CF} = 287\) Hz), 119.7, 125.5, 127.4, 128.4, 128.9, 129.4, 129.6, 132.3, 136.2, 138.2, 148.5, 148.8, 154.5 (q, \(J_{CF} = 37\) Hz); MS (ESI) for C\(_{27}\)H\(_{23}\)BrF\(_3\)N\(_2\)O: \(m/z\) 561 [M+H]\(^+\), 563 [(M+H)+2]\(^+\).

N-(2-(3-(Benzy1(2-bromobenzyl)amino)prop-1-ynyl)phenyl)-2,2,2-trifluoroacetamide (4b): White solid; mp: 103-105 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 3.58 (s, 2H, -CH\(_2\)), 3.80 (s, 2H, -CH\(_2\)), 3.88 (s, 2H, -CH\(_2\)), 7.13 (t, \(J = 7.70\) Hz, 1H, Ar-\(H\)), 7.20 (t, \(J = 7.50\) Hz, 1H, Ar-\(H\)), 7.26-7.29 (m, 1H, Ar-\(H\)), 7.31-7.35 (m, 3H, Ar-\(H\)), 7.38-7.43 (m, 3H, Ar-\(H\)), 7.54-7.57 (m, 3H, Ar-\(H\)), 8.38 (d, \(J = 8.50\) Hz, 1H, Ar-\(H\)), 8.80 (s, 1H, -NH, D\(_2\)O exchangeable); \(^1\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 41.8, 57.3, 57.7, 79.9, 93.5, 113.3, 115.6 (q, \(J_{CF} = 287\) Hz), 119.6, 124.8, 125.5, 127.3, 127.4, 128.4, 128.9, 129.6, 130.7, 132.4, 133.0, 136.1, 137.5, 138.2, 139.1, 154.4 (q, \(J_{CF} = 37\) Hz); MS (ESI) for C\(_{25}\)H\(_{24}\)BrF\(_3\)N\(_2\)O: \(m/z\) 501 [M+H]\(^+\), 503 [(M+H)+2]\(^+\).

N-(2-(3-(Benzy1(2-bromo-4,5-dimethoxyphenyl)amino)prop-1-ynyl)-4-nitrophenyl)-2,2,2-trifluoroacetamide (4c): Yellow solid; mp: 120-122 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 3.67 (s, 2H, -CH\(_2\)), 3.80 (s, 2H, -CH\(_2\)), 3.85 (s, 2H, -CH\(_2\)), 3.87 (s, 3H, -CH\(_3\)), 3.89 (s, 3H, -CH\(_3\)), 7.02 (s, 1H, Ar-\(H\)), 7.08 (s, 1H, Ar-\(H\)), 7.26-7.31 (m, 1H, Ar-\(H\)), 7.36 (t, \(J = 7.5\) Hz, 2H, Ar-\(H\)), 7.41 (d, \(J = 7.4\) Hz, 2H, Ar-\(H\)), 8.27 (dd, \(J = 9.06\) Hz, 2.10 Hz, 1H, Ar-\(H\)), 8.41 (d, \(J = 2.04\) Hz, 1H, Ar-\(H\)), 7.4.
8.59 (d, \( J = 9.16 \) Hz, 1H, Ar-\( H \)), 8.99 (s, 1H, -NH, D\( _2 \)O exchangeable); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 42.1, 56.0, 56.1, 56.9, 57.6, 78.0, 96.5, 113.1, 114.3, 114.5, 115.3 (q, \( J_{CF} = 287 \) Hz), 115.4, 119.6, 124.9, 127.5, 127.6, 128.5, 128.8, 129.0, 137.8, 141.0, 144.3, 148.5, 148.8, 154.8 (q, \( J_{CF} = 37 \) Hz); MS (ESI) for C\(_{27}\)H\(_23\)BrF\(_3\)N\(_3\)O\(_5\): \( m/z \) 606 [M+H]+, 608 [(M+H)+2]+.

**N-(2-(3-(BenzyI(2-bromo-4,5-dimethoxybenzyl)amino)prop-1-ynyl)-4-chlorophenyl)-2,2,2-trifluoroacetamide (4d):** White solid; mp: 90-92 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 3.62 (s, 2H, -CH\(_2\)), 3.77 (s, 2H, -CH\(_2\)), 3.82 (s, 2H, -CH\(_2\)), 3.86 (s, 3H, -CH\(_3\)), 3.88 (s, 3H, -CH\(_3\)), 7.02 (s, 1H, Ar-\( H \)), 7.07 (s, 1H, Ar-\( H \)), 7.25-7.29 (m, 1H, Ar-\( H \)), 7.33-7.37 (m, 3H, Ar-\( H \)), 7.40 (d, \( J = 6.50 \) Hz, 2H, Ar-\( H \)), 7.51 (d, \( J = 2.50 \) Hz, 1H, Ar-\( H \)), 8.32 (d, \( J = 8.50 \) Hz, 1H, Ar-\( H \)), 8.72 (s, 1H, -NH, D\( _2 \)O exchangeable); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta \) 42.1, 56.0, 56.1, 56.9, 57.5, 78.7, 94.9, 113.1, 114.5, 115.4, 115.5 (q, \( J_{CF} = 287 \) Hz), 120.7, 127.4, 128.4, 128.8, 129.3, 129.7, 130.6, 131.8, 134.7, 138.1, 148.4, 148.7, 154.4 (q, \( J_{CF} = 37 \) Hz); MS (ESI) for C\(_{27}\)H\(_23\)BrClF\(_3\)N\(_3\)O\(_5\): \( m/z \) 595 [M+H]+, 597 [(M+H)+2]+, 599 [(M+H)+4]+.

**N-(2-(3-(2-Bromo-4,5-dimethoxybenzoxo)prop-1-ynyl)phenyl)-2,2,2-trifluoroacetamide (4e):** White solid; mp: 99-101 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 3.86 (s, 3H, -CH\(_3\)), 3.87 (s, 3H, -CH\(_3\)), 4.53 (s, 2H, -CH\(_2\)), 4.68 (s, 2H, -CH\(_2\)), 7.00 (s, 1H, Ar-\( H \)), 7.02 (s, 1H, Ar-\( H \)), 7.18 (dt, \( J = 7.6 \) Hz, 1 Hz, 1H, Ar-\( H \)), 7.40 (t, \( J = 8 \) Hz, 1H, Ar-\( H \)), 7.49 (dd, \( J = 7.7 \) Hz, 1.4 Hz, 1H, Ar-\( H \)), 8.32 (d, \( J = 8.2 \) Hz, 1H, Ar-\( H \)), 8.74 (s, 1H, -NH, D\( _2 \)O exchangeable); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta \) 55.9, 56.1, 58.0, 71.3, 80.4, 93.8, 112.3, 112.7, 113.3, 115.4, 115.6 (q, \( J_{CF} = 287 \) Hz), 119.7, 125.4, 128.4, 130.0, 132.1, 136.3, 148.5, 149.2, 154.4 (q, \( J_{CF} = 37 \) Hz); MS (ESI) for C\(_{20}\)H\(_{17}\)BrF\(_3\)NO\(_4\): \( m/z \) 472 [M+H]+, 474 [(M+H)+2]+.

**N-(2-(3-(2-Bromo-4,5-dimethoxybenzoxy)prop-1-ynyl)-4-methylphenyl)-2,2,2-trifluoroacetamide (4f):** White solid; mp: 140-142 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 2.33 (s, 3H, -CH\(_3\)), 3.87 (s, 3H, -CH\(_3\)), 3.89 (s, 3H, -CH\(_3\)), 4.53 (s, 2H, -CH\(_2\)), 4.68 (s, 2H, -CH\(_2\)), 6.99 (s, 1H, Ar-\( H \)), 7.01 (s, 1H, Ar-\( H \)), 7.21 (d, \( J = 8.4 \) Hz, 1H, Ar-\( H \)), 7.30 (s, 1H, Ar-\( H \)), 8.19 (d, \( J = 8.4 \) Hz, 1H, Ar-\( H \)), 8.66 (s, 1H, -NH, D\( _2 \)O exchangeable); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta \) 20.7, 56.0, 56.1, 58.1, 71.3, 80.7, 93.3, 112.1, 112.5, 113.3, 115.2, 115.6 (q, \( J_{CF} = 287 \) Hz), 119.6, 128.4, 130.8, 132.4, 133.9, 135.4, 148.4, 149.1, 154.3 (q, \( J_{CF} = 37 \) Hz); MS (ESI) for C\(_{20}\)H\(_{19}\)BrF\(_3\)NO\(_4\): \( m/z \) 486 [M+H]+, 488 [(M+H)+2]+.

**N-(2-(3-(2-Bromo-4,5-dimethoxybenzoxo)prop-1-ynyl)-4-nitrophenyl)-2,2,2-trifluoroacetamide (4g):** Yellow solid; mp: 132-134 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 3.88 (s, 3H, -CH\(_3\)), 3.89 (s, 3H, -CH\(_3\)), 4.56 (s, 2H, -CH\(_2\)), 4.70 (s, 2H, -CH\(_2\)), 6.99 (s, 1H, Ar-\( H \)), 7.03 (s, 1H, Ar-\( H \)), 8.28 (dd, \( J = 9.8 \) Hz, 2.5 Hz, 1H, Ar-\( H \)), 8.37 (d, \( J = 3 \) Hz, 1H, Ar-\( H \)), 8.58 (d, \( J = 9 \) Hz, 1H, Ar-\( H \)), 8.94 (s, 1H, -NH, D\( _2 \)O exchangeable); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta \) 56.0, 56.1, 57.8, 71.6, 78.4, 96.5,
Analytical data of compound 5a-g:

7-Benzyl-10,11-dimethoxy-5,6,7,8-tetrahydro indolo[2,3-c][2]benzazepine (5a): Brown solid; mp: 117-119 °C; IR (KBr): 824, 1083, 1283, 1312, 1606, 1749, 2886, 2999, 3328 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 3.61 (s, 2H, -CH₂), 3.74 (s, 3H, -OCH₃), 3.85 (s, 3H, -OCH₃), 7.10-7.16 (m, 2H, Ar-H), 7.23-7.25 (m, 2H, Ar-H), 7.75-7.80 (m, 4H, Ar-H), 7.85 (d, J = 7.4 Hz, 1H, Ar-H). MS (ESI) for C₂₅H₂₄N₂O₂: m/z 385 [M+H]⁺.

7-Benzyl-5,6,7,8-tetrahydro indolo[2,3-c][2]benzazepine (5b): Brown solid; mp: 122-124 °C; IR (KBr): 889, 1097, 1292, 1303, 1612, 1756, 2835, 2975, 3337 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 3.70 (s, 4H, -CH₂), 7.10-7.12 (m, 2H, Ar-H), 7.24-7.27 (m, 4H, Ar-H), 7.30-7.35 (m, 4H, Ar-H), 7.40 (t, J = 7.5 Hz, 1H, Ar-H), 7.49 (t, J = 7.5 Hz, 1H, Ar-H), 7.85 (d, J = 7.4 Hz, 1H, Ar-H). MS (ESI) for C₂₅H₂₄N₂O₂: m/z 337 [M+H]⁺.

7-Benzyl-5,6,7,8-tetrahydro indolo[2,3-c][2]benzazepine (5c): Yellow solid; mp: 114-116 °C; IR (KBr): 873, 1012, 1235, 1319, 1628, 1788, 2847, 2947, 3301 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 3.60 (s, 2H, -CH₂), 3.76 (s, 3H, -OCH₃), 3.79 (s, 3H, -OCH₃), 6.44 (s, 1H, Ar-H), 6.85 (s, 1H, Ar-H), 7.18-7.23 (m, 5H, Ar-H), 7.96 (d, J = 9 Hz, 1H, Ar-H). MS (ESI) for C₂₅H₂₄N₂O₂: m/z 325 [M+H]⁺.
113.9, 114.6, 115.6, 117.1, 117.2, 127.4, 127.8, 128.4, 129.0, 129.5, 138.1, 138.9, 140.3, 141.7, 148.3, 148.8; MS (ESI) for C_{25}H_{23}N_{3}O_{4}: m/z 430 [M+H]^+.

7-Benzyl-2-chloro-10,11-dimethoxy-5,6,7,8-tetrahydro indolo[2,3-c][2]benzazepine (5d):
Yellow solid; mp: 127-129 °C; IR (KBr): 857, 1010, 1274, 1329, 1619, 1733, 2815, 2983, 3356 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 3.65 (s, 2H, -CH\(_2\)), 3.66 (s, 2H, -CH\(_2\)), 3.73 (s, 2H, -CH\(_2\)), 3.83 (s, 3H, -CH\(_3\)), 3.84 (s, 3H, -CH\(_3\)), 6.95 (s, 1H, Ar-H), 6.97 (s, 1H, Ar-H), 7.07 (d, J = 8.5Hz, 1H, Ar-H), 7.21 (d, J = 8.68 Hz, 1H, Ar-H), 7.26-7.35 (m, 5H, Ar-H), 7.48 (s, 1H, Ar-H), 8.36 (s, 1H, -NH, D\(_2\)O exchangeable); \(^13\)C NMR (100 MHz, CDCl\(_3\)): δ 50.6, 56.1(2), 57.7, 58.3, 101.1, 111.5, 113.7, 114.5, 115.5, 119.4, 121.6, 125.2, 127.3, 128.4, 129.0, 129.5, 129.8, 134.2, 138.1, 138.3, 148.3, 148.6; MS (ESI) for C\(_{25}\)H\(_{23}\)ClN\(_2\)O\(_2\): m/z 418 [M+H]^+.

10,11-Dimethoxy-5,6,8-tri hydro indolo[2,3-c][2]benzoxepine (5e): Brown solid; mp: 110-112 °C; IR (KBr): 826, 1059, 1263, 1339, 1651, 1726, 2820, 2967, 3333 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 3.94 (s, 3H, -CH\(_3\)), 4.01 (s, 3H, -CH\(_3\)), 4.56 (s, 2H, -CH\(_2\)), 5.03 (s, 2H, -CH\(_2\)), 6.92 (s, 1H, Ar-H), 7.23 -7.29 (m, 2H, Ar-H), 7.41 (d, J = 7.50 Hz, 1H, Ar-H), 7.55 (s, 1H, Ar-H), 8.00 (d, J = 7.50 Hz, 1H, Ar-H), 8.18 (s, 1H, -NH, D\(_2\)O exchangeable); \(^13\)C NMR (75 MHz, CDCl\(_3\)): δ 56.1, 56.2, 66.5, 70.8, 110.8, 111.2, 112.8, 113.7, 119.4, 120.6, 122.6, 126.4, 128.1, 130.1, 134.5, 136.3, 146.6, 149.0; HRMS calculated for [C\(_{18}\)H\(_{17}\)NO\(_3\)+Na]^+: 318.1106. Found : 318.1102.

2-Methyl-10,11-dimethoxy-5,6,8-tri hydro indolo[2,3-c][2]benzoxepine (5f): Brown solid; mp: 130-132 °C; IR (KBr): 834, 1010, 1262, 1335, 1610, 1744, 2836, 2987, 3320 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 2.31 (s, 3H, Ar-H), 3.74 (s, 3H, -CH\(_3\)), 3.82 (s, 3H, -CH\(_3\)), 4.34 (s, 2H, -CH\(_2\)), 4.77 (s, 2H, -CH\(_2\)), 6.73 (s, 1H, Ar-H), 6.89 (d, J = 8.10 Hz, 1H, Ar-H), 7.09 (d, J = 8.40 Hz, 1H, Ar-H), 7.34 (s, 1H, Ar-H), 7.58 (s, 1H, Ar-H), 8.03 (s, 1H, -NH, D\(_2\)O exchangeable); \(^13\)C NMR (75 MHz, CDCl\(_3\)): δ 21.8, 56.1, 56.3, 66.2, 70.6, 110.9, 112.9, 113.3, 119.1, 124.1, 126.6, 128.4, 129.8, 130.0, 134.6, 134.7, 146.5, 149.0; MS (ESI) for C\(_{19}\)H\(_{19}\)NO\(_3\): m/z 310 [M+H]^+.

2-Nitro-10,11-dimethoxy-5,6,8-tri hydro indolo[2,3-c][2]benzoxepine (5g): Yellow solid; mp: 110-112 °C; IR (KBr): 802, 1099, 1259, 1326, 1612, 1738, 2848, 2924, 3303cm\(^{-1}\); \(^1\)H NMR(400 MHz, DMSO-d\(_6\)): δ 3.74 (s, 3H, -CH\(_3\)), 3.75 (s, 3H, -CH\(_3\)), 4.52 (s, 2H, -CH\(_2\)), 4.73 (s, 2H, -CH\(_2\)), 6.72 (s, 1H, Ar-H), 7.06 (s, 1H, Ar-H), 7.12 (s, 1H, Ar-H), 7.50 (d, J = 9.00 Hz, 1H, Ar-H), 7.98 (dd, J = 9.00 Hz, 2.10 Hz, 1H, Ar-H), 8.52 (s, 1H, -NH, D\(_2\)O exchangeable); \(^13\)C NMR (100 MHz, DMSO-d\(_6\)): δ 55.8, 56.0, 64.9, 71.0, 103.5, 111.7, 112.8, 113.3, 115.6, 116.8, 117.3, 127.1, 128.9, 139.8, 139.9, 140.8, 148.3, 149.1; MS (ESI) for C\(_{19}\)H\(_{16}\)N\(_2\)O\(_5\): m/z 341 [M+H]^+.

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References:


H NMR spectrum of compound 2a

$^{13}$C NMR spectrum of compound 2a
$^1$H NMR spectrum of compound 3a

$^{13}$C NMR spectrum of compound 3a
1D noe spectrum of compound 3a

1D noe spectrum of compound 3a
HSQC spectrum of compound 3a
HMBC spectrum of compound 3a

HRMS spectrum of compound 3a
$^1$H NMR spectrum of compound S-4b

$^{13}$C NMR spectrum of compound S-4b
$^1$H NMR spectrum of compound 2b

$^{13}$C NMR spectrum of compound 2b
1H NMR spectrum of compound 3b

13C NMR spectrum of compound 3b
\( ^1H \) NMR spectrum of compound S-4c

\( ^13C \) NMR spectrum of compound S-4c
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\[ ^1H \text{NMR spectrum of compound 2c} \]

\[ ^{13}\text{C NMR spectrum of compound 2c} \]
1H NMR spectrum of compound 3c

13C NMR spectrum of compound 3c
$^1$H NMR spectrum of compound S-4d

$^{13}$C NMR spectrum of compound S-4d
$^1$H NMR spectrum of compound 2d

$^{13}$C NMR spectrum of compound 2d
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**1H NMR spectrum of compound 3d**

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**13C NMR spectrum of compound 3d**
$^1$H NMR spectrum of compound S-4e

$^{13}$C NMR spectrum of compound S-4e
**H NMR spectrum of compound 2e**

**13C NMR spectrum of compound 2e**
\(^{1}\text{H} \) NMR spectrum of compound 3e

\(^{13}\text{C} \) NMR spectrum of compound 3e
$^1$H NMR spectrum of compound S-4f

$^{13}$C NMR spectrum of compound S-4f
$^1$H NMR spectrum of compound 2f

$^{13}$C NMR spectrum of compound 2f
\(^1\)H NMR spectrum of compound 3f

\(^{13}\)C NMR spectrum of compound 3f
$^1$H NMR spectrum of compound S-4g

$^{13}$CNMR spectrum of compound S-4g
$^1$H NMR spectrum of compound 2g

$^{13}$C NMR spectrum of compound 2g
H NMR spectrum of compound 3g

\[ \text{H NMR spectrum of compound 3g} \]

C NMR spectrum of compound 3g

\[ \text{C NMR spectrum of compound 3g} \]
1H NMR spectrum of compound S-4h

13C NMR spectrum of compound S-4h
$^1$H NMR spectrum of compound 2h

$^{13}$C NMR spectrum of compound 2h
$^1$H NMR spectrum of compound 3h

$^{13}$C NMR spectrum of compound 3h
**H NMR spectrum of compound S-4i**

**C NMR spectrum of compound S-4i**
$^1$H NMR spectrum of compound 2i

$^{13}$C NMR spectrum of compound 2i
$^1$H NMR spectrum of compound 3i

$^{13}$C NMR spectrum of compound 3i
H NMR spectrum of compound S-4j

13C NMR spectrum of compound S-4j
H NMR spectrum of compound 2j

$^{13}$C NMR spectrum of compound 2j
$^1$H NMR spectrum of compound 3j

$^{13}$C NMR spectrum of compound 3j
H NMR spectrum of compound S-4k

13C NMR spectrum of compound S-4k
$^1$H NMR spectrum of compound 2k

$^{13}$C NMR spectrum of compound 2k
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**1H NMR spectrum of compound 3k**

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**13C NMR spectrum of compound 3k**
\( ^1\text{H NMR spectrum of compound S-4l} \)

\( ^{13}\text{C NMR spectrum of compound S-4l} \)
$^1$H NMR spectrum of compound 2l

$^{13}$C NMR spectrum of compound 2l
$^1$H NMR spectrum of compound 3l

$^{13}$C NMR spectrum of compound 3l
\(^1\)H NMR spectrum of compound S-4m

\(^{13}\)C NMR spectrum of compound S-4m
$^1$H NMR spectrum of compound 2m

$^{13}$C NMR spectrum of compound 2m
$^1$H NMR spectrum of compound 3m

$^{13}$C NMR spectrum of compound 3m
H NMR spectrum of compound 2n

13C NMR spectrum of compound 2n
H NMR spectrum of compound 3n

13C NMR spectrum of compound 3n
$^1$H NMR spectrum of compound S-8a

$^{13}$C NMR spectrum of compound S-8a
$^1$H NMR spectrum of compound 2o

$^{13}$C NMR spectrum of compound 2o
$^1$H NMR spectrum of compound 3o

$^{13}$C NMR spectrum of compound 3o
**$^1$H NMR spectrum of compound 2p**

**$^{13}$C NMR spectrum of compound 2p**
$^1$H NMR spectrum of compound 3p

$^{13}$C NMR spectrum of compound 3p
$^1$H NMR spectrum of compound 2q

$^{13}$C NMR spectrum of compound 2q
$^1$H NMR spectrum of compound 3q

$^{13}$C NMR spectrum of compound 3q
**$^1$H NMR spectrum of compound S-8b**

**$^{13}$C NMR spectrum of compound S-8b**
H NMR spectrum of compound 2r

13C NMR spectrum of compound 2r
$^1$H NMR spectrum of compound $3r$

$^{13}$C NMR spectrum of compound $3r$
$^1$H NMR Spectrum of compound 4a

$^{13}$C NMR Spectrum of compound 4a
\textbf{H NMR spectrum of compound 5a}

\textbf{\textsuperscript{13}C NMR spectrum of compound 5a}
$^1$H NMR spectrum of compound 4b

$^{13}$C NMR spectrum of compound 4b
H NMR spectrum of compound 5b

$^1$C NMR spectrum of compound 5b
$^1$H NMR spectrum of compound 4c

$^{13}$C NMR spectrum of compound 4c
$^1$H NMR spectrum of compound 5c

$^{13}$C NMR spectrum of compound 5c
\(^1\)H NMR spectrum of compound 4d

\(^{13}\)C NMR spectrum of compound 4d
$^1$H NMR spectrum of compound 5d

$^{13}$C NMR spectrum of compound 5d
$^{1}H$ NMR spectrum of compound 4e

$^{13}C$ NMR spectrum of compound 4e
$^1$H NMR spectrum of compound 5e

$^{13}$C NMR spectrum of compound 5e
HRMS spectrum of compound 5e
$^1$H NMR spectrum of compound 4f

$^{13}$C NMR spectrum of compound 4f
**H NMR spectrum of compound 5f**

**13C NMR spectrum of compound 5f**
$^1$H NMR spectrum of compound 4g

$^{13}$C NMR spectrum of compound 4g
$^1$H NMR spectrum of compound 5g

$^{13}$C NMR spectrum of compound 5g
### Crystal data for 5e

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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<tbody>
<tr>
<td><strong>Identification code</strong></td>
<td>5e</td>
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<td><strong>Empirical formula</strong></td>
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<tr>
<td><strong>Formula weight</strong></td>
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<tr>
<td><strong>Temperature</strong></td>
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<td><strong>Wavelength</strong></td>
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<tr>
<td><strong>Crystal system, space group</strong></td>
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<tr>
<td><strong>Unit cell dimensions</strong></td>
<td>a = 9.3972(2) Å   alpha = 90 deg.</td>
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<tr>
<td></td>
<td>b = 16.1308(3) Å   beta = 90 deg.</td>
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<tr>
<td></td>
<td>c = 19.6022(3) Å   gamma = 90 deg.</td>
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<tr>
<td><strong>Volume</strong></td>
<td>2971.39(10) Å^3</td>
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<tr>
<td><strong>Z, Calculated density</strong></td>
<td>8, 1.320 Mg/m^3</td>
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<tr>
<td><strong>Absorption coefficient</strong></td>
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<tr>
<td><strong>F(000)</strong></td>
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<tr>
<td><strong>Crystal size</strong></td>
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<tr>
<td><strong>Theta range for data collection</strong></td>
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<tr>
<td><strong>Limiting indices</strong></td>
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<td><strong>Reflections collected / unique</strong></td>
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<td><strong>Max. and min. transmission</strong></td>
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<td><strong>Refinement method</strong></td>
<td>Full-matrix least-squares on F^2</td>
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<tr>
<td><strong>Data / restraints / parameters</strong></td>
<td>7154 / 0 / 401</td>
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<td><strong>Goodness-of-fit on F^2</strong></td>
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<td><strong>Final R indices [I&gt;2sigma(I)]</strong></td>
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<td><strong>R indices (all data)</strong></td>
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<td><strong>Absolute structure parameter</strong></td>
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<tr>
<td><strong>Largest diff. peak and hole</strong></td>
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</tbody>
</table>