A Highly α -Regioselective AgOTf-Catalyzed Nucleophilic Substitution of the Baylis-Hillman Acetates with Indoles

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Supporting Information

	Page
1. General Methods	S3
1.1. General Method	S3
1.2. General experimental procedure for the preparation of Baylis-Hillman acetates	S3
2. Typical Experimental Procedures	
2.1. Typical experimental procedure for nucleophilic substitution	S3
2.2. Typical experimental procedure for reductive cyclization	S4
3. Characterization data	S5
3.1 Characterization data of the Baylis-Hillman acetates	S5-S7
3.1.1 2-(Acetoxyphenylmethyl)-cyclohex-2-enone (2a)	
3.1.2 2-(Acetoxycyclohexylmethyl)-cyclohex-2-enone (2b)	
3.1.3 2-[2-Bromophenyl]acetoxymethyl)-cyclohex-2-enone (2c)	
3.1.4 2-[2-Nitrophenyl]acetoxymethyl)-cyclohex-2-enone (2d)	
3.1.5 2-[3-Methoxyphenyl]acetoxymethyl)-cyclohex-2-enone (2e)	
3.1.6 3-[Acetoxy(4-chlorophenyl)]-4- <i>H</i> -chromen-4-one (2f)	
3.1.7 3-[Acetoxy(2-fluorophenyl)]-4- <i>H</i> -chromen-4-one (2g)	

3.1.8 3-[Acetoxy(2-triflouromethylphenyl)]-4-*H*-chromen-4-one (**2h**)

3.2 Characterization data of the products

S7-S11

3.2.1 2-[(2-Methylindolyl)phenylmethyl]cyclohex-2-enone (**3a**)

3.2.2 2-[(Indolyl)phenylmethyl]cyclohex-2-enone (**3b**)

3.2.3 2-[(N-Methylindolyl)phenylmethyl]cyclohex-2-enone (**3c**)

3.2.4 2-[(2-Phenylindolyl)phenylmethyl]cyclohex-2-enone (**3d**)

3.2.5 2-[(5-Nitroindolyl)phenylmethyl]cyclohex-2-enone (**3e**)

3.2.6 2-[(2-Methylindolyl)-cyclohexylmethyl]cyclohex-2-enone (**3f**)

3.2.7 2-[(2-Methylindolyl)-*o*-bromophenylmethyl]cyclohex-2-enone (**3g**)

3.2.8 2-[(2-Methylindolyl)-*o*-nitrophenylmethyl]cyclohex-2-enone (**3h**)

3.2.9 2-[(2-Methylindolyl)-*m*-methoxyphenylmethyl]cyclohex-2-enone (**3i**)

3.2.10 3-[(2-Methy-4-nitrolindolyl)-*p*-nitrophenylmethyl]-4-*H*-chromen-4-one (**3j**)

3.2.11 3-[(2-Methy-4-nitrolindolyl)-*o*-flourophenylmethyl]-4-*H*-chromen-4-one (**3k**)

3.2.12 3-[(2-Methy-4-nitrolindolyl)-*o*-(triflouromethyl)phenylmethyl]-4-*H*-
chromen-4-one (**3l**)

3.2.13 (*E*)-2-Benzylidenecyclohex-3-enone (**2a'**)

3.2.14 2-Methyl-3-*p*-chlorophenyl-4-(2'-hydroxbenzoyl)-3,6-dihydro-1-*H*-
azepino-[4,3,2-*cd*]-indole (**4a**)

3.2.15 2-Methyl-3-*o*-flourophenyl-4-(2'-hydroxbenzoyl)-3,6-dihydro-1-*H*-
azepino-[4,3,2-*cd*]-indole (**4b**)

3.2.16 2-Methyl-3-*o*-(triflouromethyl)phenyl-4-(2'-hydroxbenzoyl)-3,6-dihydro-
1-*H*-azepino-[4,3,2-*cd*]-indole (**4c**)

4. ¹H and ¹³C NMR Spectra

S12-35

1. General Methods

1.1 General Method

The ^1H and ^{13}C NMR spectra were recorded on Bruker-AV 300 spectrometer and chemical shift reported in CDCl_3 or DMSO-d_6 with tetramethylsilane as an internal standard. IR spectra were recorded on a Bruker tensor 27 infrared spectrometer. HRMS spectra were recorded on GCT-Mass Micromass spectrometer. Melting points were measured on Beijing-Tiker X-4 apparatus without correction. All reactions were carried out in oven dried flasks. Common reagents were purchased from commercial sources and were used without further purification.

1.2 General Procedure for the preparation of Baylis-Hillman Acetates

The Baylis-Hillman adducts were prepared by reported procedures (Scheme 1)¹⁻³. To a stirred solution of B-H adduct (X= C, R = Phenyl) (1.0 g, 5 mmol) in dry CH₂Cl₂ (20 mL), pyridine (0.8 g, 10 mmol) and AcCl (0.79g, 10 mmol) were added dropwise at 0 °C. After 1 h, the mixture was treated with 2N HCl and extracted with diethyl ether (3 × 10 mL). The combined organic layer was dried over anhydrous Na₂SO₄, concentrated and the crude product was purified by flash chromatography on silica gel (eluent: EtOAc/petroleum ether = 1:20) to afford a colorless liquid **2a** (1.08 g, 89%).

Scheme 1

2 Typical Experimental Procedures

2.1 Typical Experimental procedure for nucleophilic substitution

To a stirred mixture of 2-methylindole (**1a**, 0.05 g, 0.4 mmol) and B-H acetate (**2a**, 0.1 g, 0.4 mmol) in CH₂Cl₂ (3 mL) at room temperature was added AgOTf (0.011g, 0.04 mmol) and the reaction mixture was refluxed for 5 h. Upon completion of the reaction as judged by TLC, the reaction was quenched with water and extracted with EtOAc (2 × 5 mL). The combined extract was dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (gradient eluent: EtOAc/petroleum ether) to afford a yellow solid **3a** (0.104 g, 80%).

2.2 Typical experimental procedure for reductive cyclization

To a solution of compound **3j** (0.15 g, 0.37 mmol) in MeOH (5 mL), 10% Pd/C (25 mg) was added, followed by hydrogenation with H₂ at atmospheric pressure for 2 h. The catalyst was removed by filtration through a pad of Celite and rinsed with methanol. Evaporation of the filtrates gave a residue, which was purified by flash chromatography on silica gel (eluent: EtOAc/petroleum ether = 1:15) to furnish a yellow solid **4a** (0.13 g, 93%).

References:

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3 Characterization data of the compounds

3.1 Characterization data of the Baylis-Hillman acetates

3.1.1 2-(Acetoxymethyl)-cyclohex-2-enone (2a)

2a: Colorless oil. IR (neat): $\nu_{\max}$ 2947, 2870, 1741, 1675, 1231, 1023 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 1.94-2.02 (m, 2H), 2.08 (s, 3H), 2.39-2.45 (m, 2H), 2.38-2.44 (m, 2H), 6.72 (s, 1H), 7.48 (t, 1H, $J = 3.6$ Hz), 7.25-7.36 (m, 5H); ^{13}C NMR (CDCl_3 , 75

MHz): δ 21.1, 22.4, 25.7, 38.3, 71.5, 138.8, 138.8, 146.1, 169.4, 196.9. MS (EI): m/z 244, 202(100), 185, 155, 128, 105, 91; HRMS: m/z calcd. for $\text{C}_{15}\text{H}_{16}\text{O}_3$ 244.1099, found 244.1097.

3.1.2 2-(Acetoxycyclohexylmethyl)-cyclohex-2-enone (2b)

2b: Colorless oil; IR (neat): $\nu_{\max}$ 2928, 2856, 1739, 1674, 1370, 1238, 1022 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 0.93-1.15 (m, 5H), 1.64-1.73 (m, 6H), 1.98-2.00 (m, 2H), 2.05 (s, 3H), 2.38-2.45 (m, 4H), 5.44 (d, 1H, $J = 6.2$ Hz), 6.81 (t, 1H, $J = 4.2$ Hz); ^{13}C

NMR (CDCl_3 , 75MHz): δ 21.0, 22.5, 25.7, 25.8, 26.0, 26.2, 27.9, 29.2, 38.4, 40.9, 74.6, 137.9, 145.9, 170.0, 197.4; EI MS m/z 250, 190(100), 161, 147, 125, 109, 81; HRMS m/z calcd. for $\text{C}_{15}\text{H}_{22}\text{O}_3$ 250.1569, found 250.1565.

3.1.3 2-[2-Bromophenyl)acetoxymethyl)-cyclohex-2-enone (2c)

2c: Colorless oil. IR (neat): $\nu_{\max}$ 2944, 2873, 1744, 1676, 1228, 1023 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 2.00-2.10 (m, 2H), 2.10 (s, 3H), 2.36-2.40 (m, 2H), 2.45-2.50 (m, 2H), 6.65 (t, 1H, $J = 4.2$ Hz), 6.95 (s, 1H), 7.12-7.18 (m, 1H), 7.26-7.32 (m, 2H),

7.54 (d, 1H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 75MHz): δ 20.9, 22.4, 25.9, 38.3, 71.0, 123.1, 127.3, 128.1, 129.3, 133.1, 137.0, 137.7, 148.7, 169.2, 196.7. MS (EI): m/z 279/281 ($\text{M}^+ - \text{COCH}_3$), 183 (100), 155, 123, 115; HRMS: m/z calcd. for $\text{C}_{13}\text{H}_{12}\text{O}_2^{81}\text{Br}$ ($\text{M} - \text{OCCH}_3$): 281.0000, found: 281.0001.

3.1.4 2-[2-Nitrophenyl)acetoxymethyl)-cyclohex-2-enone (2d)

2d: Light yellow solid, mp = 104-105 °C. IR (KBr): $\nu_{\max}$ 2945, 1746, 1676, 1528, 1360, 1228, 1024 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 1.98-2.05 (m, 2H), 2.11 (s, 3H), 2.35-2.40 (m, 2H), 2.45-2.50 (m, 2H), 6.64 (t, 1H, J = 4.2 Hz), 7.27 (s, 1H), 7.49 (t, 1H, J = 1.7, 6.7 Hz), 7.55-7.63 (m, 2H), 8.00 (dd, 1H, J = 1.2, 8.2 Hz); ^{13}C NMR (CDCl_3 , 75MHz): δ 20.8, 22.3, 25.8, 38.1, 67.9, 125.0, 128.6, 128.7, 133.1, 134.0, 137.3, 147.8, 148.0, 169.3, 196.4. EI MS m/z 243 (M^+ -COCH₃), 197, 180(100), 169, 141, 114; HRMS: m/z calcd. for $\text{C}_{15}\text{H}_{15}\text{O}_3$ (M-NO₂): 243.1021, found: 243.1023.

3.1.5 2-[3-Methoxyphenyl]acetoxymethyl)-cyclohex-2-enone (2e)

2e: Colorless oil. IR (neat): 2945, 2836, 1742, 1675, 1230, 1026 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 1.95-2.02 (m, 2H), 2.09 (s, 3H), 2.38-2.46 (m, 4H), 3.79 (s, 3H), 6.71 (s, 1H), 6.78-6.82 (m, 1H), 6.88-6.94 (m, 2H), 7.23 (t, 1H, J = 7.9 Hz);

^{13}C NMR (CDCl_3 , 75MHz): δ 21.1, 22.4, 25.7, 38.2, 55.2, 71.2, 112.9, 113.1, 119.3, 129.4, 138.7, 140., 146.3, 159.5, 169.4, 196.8. MS (EI): m/z 274, 231, 214(100), 183, 123, 115; HRMS: m/z calcd. for $\text{C}_{16}\text{H}_{18}\text{O}_4$ 274.1205, found 274.1203.

3.1.6 3-[Acetoxy(4-chlorophenyl)]-4-*H*-chromen-4-one (2f)

2f: White solid, mp = 113-114 °C. IR (KBr): $\nu_{\max}$ 2974, 1742, 1648, 1565, 1225, 1046 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 2.15 (s, 3H), 7.00 (s, 1H), 7.30-7.45 (m, 6H), 7.64-7.66 (m, 1H), 7.95 (s, 1H), 8.17 (dd, 1H, J = 1.5, 7.9 Hz); ^{13}C NMR

(CDCl_3 , 75MHz): δ 21.04, 69.5, 118.0, 123.7, 124.0, 125.4, 125.9, 128.4, 128.7, 133.9, 134.1, 136.8, 153.4, 156.2, 169.2, 175.5. MS (EI): m/z 328, 285(100), 270, 173, 149, 121; HRMS: m/z calcd. for $\text{C}_{18}\text{H}_{13}\text{O}_4\text{Cl}$ 328.0502, found 328.0501.

3.1.7 3-[Acetoxy(2-fluorophenyl)]-4-*H*-chromen-4-one (2g)

2g: White solid, mp = 130-131 °C. IR (KBr): $\nu_{\max}$ 3076, 1745, 1650, 1468, 1225, 1029 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 2.15 (s, 3H), 7.00-7.18 (m, 3H), 7.26-7.44 (m, 3H), 7.55-7.65 (m, 2H), 7.95 (s, 1H), 8.17 (dd, 1H, J = 1.6, 8.0 Hz); ^{13}C

NMR (CDCl_3 , 75MHz): δ 20.9, 65.9, 115.6, 115.9, 118.0, 122.4, 124.0, 124.0, 124.1, 125.3, 125.9, 129.2, 129.3, 130.0, 130.1, 133.8, 154.2, 154.2, 156.2, 169.3, 175.5. MS (EI): m/z 312, 269(100), 254, 233, 173, 133, 121; HRMS: m/z calcd. for $\text{C}_{18}\text{H}_{13}\text{O}_4\text{F}$ 312.0798, found 312.0795.

3.1.8 3-[Acetoxy(2-trifluoromethylphenyl)]-4-*H*-chromen-4-one (2h)

2h: White solid, mp = 156-157 °C. IR (KBr): $\nu_{\max}$ 3079, 1746, 1653, 1468, 1226, 1123, 1032 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 2.13 (s, 3H), 7.38-7.52 (m, 5H), 7.58-7.76 (m, 4H), 8.21 (dd, 1H, $J=1.1, 7.8$ Hz); ^{13}C NMR (CDCl_3 , 75MHz): δ

20.8, 66.7, 118.0, 123.0, 124.0, 125.4, 125.7, 126.0, 126.5, 126.6, 127.9, 128.5, 132.0, 133.9, 135.9, 135.0, 155.0, 156.2, 169.2, 175.5; EI MS m/z 362, 319(100), 299, 284, 183, 164, 120; HR MS calcd. for $\text{C}_{19}\text{H}_{13}\text{O}_4\text{F}_3$ 362.0766, found 362.0768.

3.2 Characterization data of the products

3.2.1 2-[(2-Methylindolyl)phenylmethyl]cyclohex-2-enone (3a)

3a: Yellow solid, mp = 165-167 °C. IR (KBr): $\nu_{\max}$ 3390, 3342, 2922, 1661, 1457, 1128 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 1.97-2.04 (m, 2H), 2.24 (s, 3H), 2.34-2.48 (m, 4H), 5.61 (s, 1H), 6.59 (t, 1H, $J = 4.2$ Hz), 6.86 (ddd, 1H, $J = 1.0, 7.0, 7.9$ Hz), 6.98 (ddd, 1H, $J = 1.0, 7.2, 8.1$ Hz), 7.08-7.18 (m, 7H), 7.72 (brs, 1H); ^{13}C NMR(CDCl_3 ,

75MHz): δ 12.2, 23.0, 26.1, 38.7, 40.5, 110.3, 111.6, 119.0, 119.3, 120.4, 125.9, 128.1, 128.5, 128.8, 132.6, 135.3, 141.8, 142.7, 147.7, 198.7. MS (EI): m/z 316, 315(100), 300, 220, 130, 115; HRMS (EI): m/z calcd. for $\text{C}_{22}\text{H}_{21}\text{NO}$ [M^+]: 315.1623, found 315.1621.

3.2.2 2-[(Indolyl)phenylmethyl]cyclohex-2-enone (3b)

3b: Brown solid, mp = 194-195 °C. IR (KBr) $\nu_{\max}$ 3408, 2952, 2860, 1729, 1665, 1455, 1276, 1129 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 2.02-2.06 (m, 2H), 2.35-2.39 (m, 2H), 2.49-2.54 (m, 2H), 5.70 (s, 1H), 6.57-6.61 (m, 2H), 7.07-7.40 (m, 9H), 8.01 (brs, 1H); ^{13}C NMR (CDCl_3 , 75MHz): δ 23.0, 26.1, 38.7, 41.0, 111.1, 118.6, 119.3, 119.7,

122.0, 123.9, 126.2, 126.7, 128.2, 128.5, 136.8, 141.4, 142.6, 147.2, 198.3. MS (EI) m/z 301(100), 272, 244, 206, 117; HRMS (EI): calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}$: 301.1467, found 301.1465.

3.2.3 2-[(N-Methylindolyl)phenylmethyl]cyclohex-2-enone (3c)

3c: Violet waxy solid. IR (neat): $\nu_{\max}$ 3026, 2928, 1671, 1470, 1205, 979 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 2.04-2.08 (m, 2H), 2.37-2.41 (m, 2H), 2.50-2.55 (m, 2H), 3.71 (s, 3H), 5.71 (s, 1H), 6.45 (d, 1H, $J = 0.7$ Hz), 6.64-6.65 (m, 1H), 7.08-7.11 (m, 1H), 7.24-7.39 (m, 7H), 7.39 (dd, 1H, $J = 0.8, 7.9$ Hz); ^{13}C NMR (CDCl_3 , 75MHz): δ

23.0, 26.1, 32.6, 38.8, 41.0, 109.1, 117.0, 118.8, 119.8, 121.6, 126.2, 127.1, 128.2, 128.5, 128.6, 137.5, 141.5, 142.8, 147.1, 198.2; EI MS m/z 315(100), 300, 286, 238, 220, 130; HRMS m/z calcd. for $\text{C}_{22}\text{H}_{21}\text{NO}$: 315.1623, found 315.1624.

3.2.4 2-[(2-Phenylindol-1-yl)methyl]cyclohex-2-en-1-one (3d)

3d: White solid, mp = 200-201 $^{\circ}\text{C}$. IR (KBr) $\nu_{\max}$ 3329, 2942, 2866, 1674, 1249, 1094 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 1.94-2.05 (m, 2H), 2.33-2.42 (m, 4H), 5.79 (s, 1H), 6.70 (t, 1H, $J = 3.5$ Hz), 6.97 (m, 1H), 7.13-7.46 (m, 13H), 8.19 (brs, 1H); ^{13}C NMR (CDCl_3 , 75MHz): δ 23.0, 26.2, 38.6, 41.4, 111.1, 112.6, 119.4, 120.7, 121.6, 125.9,

127.8, 128.2, 128.5, 128.7, 128.7, 128.9, 133.1, 135.9, 136.1, 142.0, 143.0, 147.7, 198.2. MS (EI) m/z 377, 300, 282 (100), 204, 193; HRMS m/z calcd. for $\text{C}_{27}\text{H}_{23}\text{NO}$: 377.1780, found 377.1783.

3.2.5 2-[(5-Nitroindol-1-yl)methyl]cyclohex-2-en-1-one (3e)

3e: Yellow solid, mp = 222-224 $^{\circ}\text{C}$. IR (KBr): $\nu_{\max}$ 3348, 2927, 1663, 1517, 1330, 1102 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 2.04-2.08 (m, 2H), 2.40-2.42 (m, 2H), 2.49-2.56 (m, 2H), 5.70 (s, 1H), 6.57 (t, 1H, $J = 4.2$ Hz), 6.78 (dd, 1H, $J = 0.9, 2.3$ Hz), 7.21-7.35 (m, 6H), 8.07 (dd, 1H, $J = 2.2, 9.0$ Hz), 8.34 (d, 1H, $J = 2.2$ Hz),

8.65 (brs, 1H); ^{13}C NMR (CDCl_3 , 75MHz): δ 22.9, 26.1, 38.7, 40.9, 111.2, 116.9, 117.8, 120.9, 126.1, 126.7, 126.8, 128.5, 128.5, 139.7, 141.2, 141.6, 147.7, 198.2. MS (EI): m/z 346, 329(100), 299, 251, 243, 204, 121; HRMS m/z calcd. for $\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}_3$: 346.1317, found 346.1316.

3.2.6 2-[(2-Methylindol-1-yl)methyl]cyclohex-2-en-1-one (3f)

3f: White crystalline solid, mp = 97-99 $^{\circ}\text{C}$. IR (KBr): $\nu_{\max}$ 3396, 3053, 2925, 2852, 1662, 1453, 1370, 1246, 909, 735 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 0.88-1.15 (m, 2H), 1.49-1.59 (m, 3H), 1.74-1.89 (m, 7H), 2.20-2.39 (m, 8H), 3.96 (d, 1H, $J = 11.3$ Hz), 6.97-7.04 (m, 2H), 7.08-7.20 (m, 2H), 7.60-7.62 (m, 1H), 7.76 (brs, 1H, NH); ^{13}C

NMR (CDCl₃, 75MHz) δ 12.2, 22.8, 26.1, 26.5, 26.6, 31.9, 32.1, 38.7, 39.4, 40.2, 110.4, 112.4, 118.8, 119.3, 120.2, 127.8, 132.5, 135.5, 141.6, 144.0, 199.4. MS (EI): m/z 321, 238(100), 220, 182, 130; HRMS m/z calcd. for C₂₂H₂₇NO: 321.2093, found 321.2090.

3.2.7 2-[(2-Methylindolyl)-*o*-bromophenylmethyl]cyclohex-2-enone (3g)

3g: Light pink solid, mp = 174-175 °C. IR (KBr): $\nu_{\max}$ 3393, 2932, 1667, 1458, 1227, 1021 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 1.95-2.04 (m, 2H), 2.23 (s, 3H), 2.35-2.46 (m, 4H), 5.80 (s, 1H), 6.51 (t, 1H, J = 3.8 Hz), 6.94 (t, 1H, J = 7.0 Hz), 7.03 (t, 2H, J = 7.4 Hz), 7.14 (ddd, 1H, J = 1.1, 6.7, 7.4 Hz), 7.19-7.23 (m, 1H), 7.26-7.32 (m, 2H), 7.52

(dd, 1H, J = 1.0, 7.8 Hz), 8.00 (brs, 1H); ¹³C NMR (CDCl₃, 75MHz): δ 12.3, 22.9, 26.2, 38.6, 41.6, 109.6, 110.5, 119.0, 119.0, 120.4, 125.0, 126.9, 127.8, 128.6, 130.5, 133.1, 133.2, 135.3, 140.6, 142.0, 146.6, 198.0; EI MS m/z 393/395, 378/380, 314(100), 298/300, 254/256, 218, 183, 130. HRMS (EI): m/z calcd. for C₂₂H₂₀NO⁷⁹Br: 393.0728, found 393.0727; for C₂₁H₁₈NO⁸¹Br: 395.0708, found 395.0705.

3.2.8 2-[(2-Methylindolyl)-*o*-nitrophenylmethyl]cyclohex-2-enone (3h)

3h: Yellow solid mp = 200-201 °C. IR (KBr): $\nu_{\max}$ 3388, 2934, 1667, 1524, 1457, 1354, 1243, 751 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 1.98-2.03 (m, 2H), 2.32 (s, 3H), 2.32-2.49 (m, 4H), 6.33 (s, 1H), 6.60 (t, 1H, J = 4.1 Hz), 6.93 (ddd, 1H, J = 0.9, 8.0, 8.0 Hz), 7.07-7.12 (m, 1H), 7.26 (d, 1H, J = 9.0 Hz), 7.34-7.46 (m, 3H), 7.80 (dd, 1H, J =

1.0, 7.9 Hz), 8.06 (brs, 1H, NH); ¹³C NMR (CDCl₃, 75 MHz): δ 12.0, 22.8, 26.0, 37.1, 38.4, 108.7, 110.6, 118.8, 119.2, 120.6, 124.7, 127.2, 128.1, 130.9, 132.1, 133.8, 135.4, 137.3, 140.3, 146.2, 149.6, 197.7. MS (EI): m/z 360, 308, 293(100), 269, 219, 180, 130; HRMS: m/z calcd. for C₂₂H₂₀N₂O 360.1474, found 360.1478.

3.2.9 2-[(2-Methylindolyl)-*m*-methoxyphenylmethyl]cyclohex-2-enone (3i)

3i: Brown waxy solid. IR (neat): $\nu_{\max}$ 3396, 2924, 1665, 1458, 1302, 1263, 1046 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 1.93-1.98 (m, 2H), 2.11 (s, 3H), 2.26-2.31 (m, 2H), 2.38-2.45 (m, 2H), 3.65 (s, 3H), 5.63 (s, 1H), 6.63-6.69 (m, 2H), 6.88-7.02 (m,

2H), 7.09-7.14 (m, 2H), 7.23 (d, 1H, J = 7.8 Hz), 8.00 (brs, 1H, NH); ¹³C NMR (CDCl₃, 75MHz): δ 12.1, 23.0, 26.1, 38.7, 40.6, 55.1, 110.4, 110.9, 111.4, 115.0, 119.0, 119.2, 120.4, 121.4, 128.5, 129.0, 132.7, 135.3, 141.6, 144.6, 147.6, 159.5, 198.8. MS (EI): m/z 345, 330, 250, 238, 130(100); HRMS: m/z calcd. for C₂₃H₂₀NO₂ 345.1729, found 345.1726.

3.2.10 3-[(2-Methy-4-nitrolindolyl)-*p*-chlorophenylmethyl]-4-*H*-chromen-4-one (3j)

3j: Orange solid, mp = 307-308 °C. IR (KBr): $\nu_{\max}$ 3269, 1636, 1509, 1465, 1341, 757 cm^{-1} . ^1H NMR (DMSO- d_6 , 300 MHz): δ 1.90 (s, 3H), 5.96 (s, 1H), 7.13-7.19 (m, 3H), 7.29-7.32 (m, 2H), 7.55-7.69 (m, 6H), 8.03-8.06 (m, 1H), 11.83 (brs, 1H, NH); ^{13}C NMR (DMSO- d_6 , 75MHz): δ 13.6, 37.7, 38.7, 108.2,

116.3, 116.4, 118.2, 118.9, 119.1, 122.9, 125.2, 125.3, 128.0, 130.3, 130.5, 134.0, 137.3, 139.3, 140.6, 142.2, 155.3, 155.8, 175.5. MS (EI): m/z 444, 396, 301, 289(100), 255, 173, 121. HRMS m/z calcd. for $\text{C}_{25}\text{H}_{17}\text{N}_2\text{O}_4\text{Cl}$ 444.0877, found 444.0871.

3.2.11 3-[(2-Methy-4-nitrolindolyl)-*o*-fluorophenylmethyl]-4-*H*-chromen-4-one (3k)

3k: Yellow solid, mp = > 300 °C (decompose). IR (KBr): $\nu_{\max}$ 3213, 1627, 1511, 1462, 1347, 1226, 1151, 757 cm^{-1} . ^1H NMR (DMSO- d_6 , 300 MHz): δ 1.91 (s, 3H), 5.72 (s, 1H), 7.02-7.30 (m, 5H), 7.45 (t, 1H, $J = 7.5$ Hz), 7.57 (t, 2H, $J = 7.5$ Hz), 7.67 (t, 1H, $J = 6.5$ Hz), 7.76 (t, 1H, $J = 7.3$ Hz), 8.04 (d, 1H, $J = 7.3$ Hz), 11.80

(brs, 1H, NH); ^{13}C NMR (DMSO- d_6 , 75MHz): δ 13.9, 33.0, 107.1, 115.8, 116.8, 116.9, 118.7, 119.3, 119.7, 123.4, 124.3, 124.9, 125.6, 125.8, 128.8, 128.8, 129.0, 130.2, 134.5, 137.7, 139.5, 142.7, 155.5, 156.3, 175.8. MS (EI): m/z 428, 394, 352, 289(100), 285, 239, 173, 121; HRMS: m/z calcd. for $\text{C}_{25}\text{H}_{17}\text{N}_2\text{O}_4\text{F}$ 428.1172, found 428.1175.

3.2.12 3-[(2-Methy-4-nitrolindolyl)-*o*-(trifluoromethyl)phenylmethyl]-4-*H*-chromen-4-one (3l)

3l: Orange solid, mp = 186-187 °C. IR (KBr): $\nu_{\max}$ 3296, 2971, 2892, 1631, 1514, 1467, 1310, 1116, 1051, 755 cm^{-1} . ^1H NMR (DMSO- d_6 , 300 MHz): δ 1.72 (s, 3H), 6.33 (s, 1H), 7.22 (t, 1H, $J = 7.95$ Hz), 7.52-7.86 (m, 10H), 8.06 (d, 1H, $J = 7.4$ Hz), 11.76 (s, 1H, NH); ^{13}C NMR (DMSO- d_6 , 75MHz): δ 13.2, 36.0, 39.9,

107.0, 116.1, 116.3, 118.3, 119.4, 122.7, 122.9, 125.0, 125.3, 126.3, 126.8, 127.3, 130.3, 130.4, 131.9, 134.1, 137.0, 138.9, 139.6, 142.4, 155.5, 155.8, 175.2. MS (EI): m/z 478, 461, 444, 430, 362, 341, 289(100), 286, 258, 173, 121; HRMS: m/z calcd. for $\text{C}_{26}\text{H}_{17}\text{N}_2\text{O}_4\text{F}_3$ 478.1140, found 478.1147.

3.2.13 2-Benzylidenecyclohex-3-enone (2a')

2a': Colorless oil. IR (neat): $\nu_{\max}$ 3046, 2931, 1693, 1584, 1260, 1135 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz): δ 2.56-2.61 (m, 2H), 2.65-2.70 (m, 2H), 6.13-6.16 (m, 1H), 6.90-6.94 (m, 1H), 7.25-7.44 (m, 6H); ^{13}C NMR (CDCl_3 , 75MHz): δ 24.1, 37.8, 124.8, 128.0, 128.1, 129.6, 130.6, 130.7, 131.6, 135.0, 199.9. MS (EI): m/z 184(100), 183, 155, 141, 115; HRMS m/z calcd. for $\text{C}_{13}\text{H}_{12}\text{O}$ 184.0888, found 184.0886.

3.2.14 2-Methyl-3-*p*-chlorophenyl-4-(2'-hydroxybenzoyl)-3,6-dihydro-1*H*-azepino[4,3,2-*cd*]-indole (4a)

4a: Yellow solid, mp = 157-159 $^{\circ}\text{C}$. IR (KBr): $\nu_{\max}$ 3357, 2927, 1581, 1523, 1481, 1353, 1277, 1212, 1091 cm^{-1} . ^1H NMR ($\text{DMSO}-d_6/\text{CDCl}_3$, 300 MHz): δ 2.29 (s, 3H), 5.50 (s, 1H), 6.57-6.59 (m, 1H), 6.78-6.94 (m, 5H), 7.09-7.19 (m, 6H), 9.60 (s, 1H, OH), 9.68 (d, 1H, J = 8.2 Hz), 10.93 (brs, 1H, NH); ^{13}C NMR ($\text{DMSO}-d_6/\text{CDCl}_3$, 75

MHz): δ 11.4, 38.7, 104.3, 105.8, 111.0, 115.8, 116.9, 118.1, 118.4, 120.4, 127.6, 128.1, 128.5, 128.9, 129.2, 129.7, 130.3, 132.6, 136.0, 144.8, 147.7, 154.4, 194.3. MS (EI) m/z 414, 396, 380, 293(100), 259, 145, 121; HRMS m/z calcd. for $\text{C}_{25}\text{H}_{19}\text{N}_2\text{O}_2\text{Cl}$: 414.1135, found 414.1137.

3.2.15 2-Methyl-3-*o*-fluorophenyl-4-(2'-hydroxybenzoyl)-3,6-dihydro-1*H*-azepino[4,3,2-*cd*]-indole (4b)

4b: Yellow solid, mp = 181-183 $^{\circ}\text{C}$. IR (KBr): $\nu_{\max}$ 399, 3296, 2923, 1693, 1522, 1139, 1000, 756 cm^{-1} . ^1H NMR (DMSO , 300 MHz) δ 2.35 (s, 3H), 5.78 (s, 1H), 6.61 (d, 1H, J = 6.8 Hz), 6.83-7.01 (m, 8H), 7.20-7.25 (m, 3H), 9.65 (s, 1H, OH), 9.77 (d, 1H, J = 8.25 Hz), 10.98 (s, 1H, NH); ^{13}C NMR (DMSO , 75 MHz): δ 11.2, 33.1, 104.1, 105.8, 110.7, 115.8, 116.7, 117.0, 118.5, 120.3, 123.9, 126.4, 128.2, 128.5, 129.8,

129.9, 130.0, 130.6, 132.6, 135.1, 135.2, 135.8, 144.9, 154.5, 194.4; EI MS m/z 398, 303, 277(100), 183, 145, 121; HRMS m/z calcd. for $\text{C}_{25}\text{H}_{19}\text{N}_2\text{O}_2\text{F}$: 398.1431, found 398.1429.

3.2.16 2-Methyl-3-*o*-(trifluoromethyl)phenyl-4-(2'-hydroxybenzoyl)-3,6-dihydro-1*H*-azepino[4,3,2-*cd*]-indole (4c)

4c: Orange solid, mp = 163-165 $^{\circ}\text{C}$; IR (KBr): $\nu_{\max}$ 3374, 3018, 2923, 1690, 1528, 1448, 1304, 1035 cm^{-1} . ^1H NMR ($\text{DMSO}-d_6$, 300 MHz): δ 2.28 (s, 3H), 6.05 (s, 1H),

6.66 (d, 1H, $J = 6.5$ Hz), 6.81-7.02 (m, 6H), 7.11-7.28 (m, 4H), 7.53 (d, 1H, $J = 8.0$, Hz), 9.76 (s, 1H, OH), 9.81 (d, 1H, $J = 8.3$ Hz), 11.05 (s, 1H, NH); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 11.4, 35.4, 104.1, 105.9, 111.4, 115.9, 117.3, 118.4, 120.5, 125.3, 125.7, 126.1, 127.5, 128.6, 130.2, 130.9, 131.6, 132.5, 135.9, 143.7, 147.1, 155.1, 194.5. MS (EI) m/z 448, 328, 327(100), 303, 183, 145, 121; HRMS: m/z calcd. for $\text{C}_{26}\text{H}_{19}\text{N}_2\text{O}_2\text{F}_3$: 448.1399, found 448.1396.

4. ^1H and ^{13}C NMR Spectra

4.1 Compound 2a

300MHz ¹H and 75.5MHz ¹³C NMR in CDCl₃ of 2-(Acetoxymethyl)-cyclohex-2-enone (2a)

4.2 Compound 2b

300MHz ^1H and 75.5MHz ^{13}C NMR in CDCl_3 of 2-(Acetoxycyclohexylmethyl)-cyclohex-2-enone (2b)

4.3 Compound 2c

300MHz ^1H and 75.5MHz ^{13}C NMR in CDCl_3 of 2-[2-Bromophenyl)acetoxymethyl)-cyclohex-2-enone (2c)

4.4 Compound 2d

300MHz ^1H and 75.5MHz ^{13}C NMR in CDCl_3 of 2-[2-Nitrophenyl]acetoxymethyl)-cyclohex-2-enone (2d)

4.5 Compound 2e

300MHz ^1H and 75.5MHz ^{13}C NMR in CDCl_3 of 2-[3-Methoxyphenyl]acetoxymethyl)-cyclohex-2-enone (2e)

4.6 Compound 2f

300MHz ¹H and 75.5MHz ¹³C NMR in CDCl₃ of 3-[Acetoxy(4-chlorophenyl)]-4-*H*-chromen-4-one (2f)

4.7 Compound 2g

300MHz ^1H and 75.5MHz ^{13}C NMR in CDCl_3 of 3-[Acetoxy(2-fluorophenyl)]-4-*H*-chromen-4-one (2g)

4.8 Compound 2h

300MHz ¹H and 75.5MHz ¹³C NMR in CDCl₃ of 3-[Acetoxy(2-trifluoromethylphenyl)]-4-*H*-chromen-4-one (2h)

4.9 Compound 3a

4.10 Compound 3b

300MHz ¹H and 75.5MHz ¹³C NMR in CDCl₃ of 2-[(Indolyl)phenylmethyl]cyclohex-2-enone (3b)

4.11 Compound 3c

300MHz ¹H and 75.5MHz ¹³C NMR in CDCl₃ of 2-[(N-Methylindolyl)phenylmethyl] cyclohex-2-enone (3c)

4.12 Compound 3d

300MHz ^1H and 75.5MHz ^{13}C NMR in CDCl_3 of 2-[(2-Phenylindolyl)phenylmethyl]cyclohex-2-enone (3d)

4.13 Compound 3e

300MHz ^1H and 75.5MHz ^{13}C NMR in CDCl_3 of 2-[(5-Nitroindolyl)phenylmethyl]cyclohex-2-enone (3e)

4.14 Compound 3f

300MHz ¹H and 75.5MHz ¹³C NMR in CDCl₃ of 2-[(2-Methylindolyl)-cyclohexylmethyl]cyclohex-2-enone (3f)

4.15 Compound 3g

300MHz ^1H and 75.5MHz ^{13}C NMR in CDCl_3 of 2-[(2-Methylindolyl)-*o*-bromophenylmethyl]cyclohex-2-enone (3g)

4.16 Compound 3h

300MHz ¹H and 75.5MHz ¹³C NMR in CDCl₃ of 2-[(2-Methylindolyl)-*o*-nitrophenylmethyl]cyclohex-2-enone (3h)

4.17 Compound 3i

300MHz ¹H and 75.5MHz ¹³C NMR in CDCl₃ of 2-[(2-Methylindolyl)-*m*-methoxyphenylmethyl]cyclohex-2-enone (3i)

4.18 Compound 3j

300MHz ^1H and 75.5MHz ^{13}C NMR in CDCl_3 of 3-[(2-Methy-4-nitroindolyl)-*p*-chlorophenylmethyl]-4-*H*-chromen-4-one (3j)

4.19 Compound 3k

300MHz ¹H and 75.5MHz ¹³C NMR in CDCl₃ of 3-[(2-Methy-4-nitroindolyl)-*o*-fluorophenylmethyl]-4-*H*-chromen-4-one (3k)

4.20 Compound 3l

300MHz ¹H and 75.5MHz ¹³C NMR in CDCl₃ of 3-[(2-Methy-4-nitroindolyl)-o-(triflouromethyl)phenylmethyl]-4-*H*-chromen-4-one (3I)

4.21 Compound 2a'

300MHz ^1H and 75.5MHz ^{13}C NMR in CDCl_3 of 2-Benzylidenecyclohex-3-enone (2a')

4.22 Compound 4a

300MHz ¹H and 75.5MHz ¹³C NMR & DEPT ¹³C NMR in DMSO/CDCl₃ of 2-Methyl-3-*p*-chlorophenyl-4-(2'-hydroxbenzoyl)-3,6-dihydro-1*H*-azepino-[4,3,2-*cd*]-indole (4a)

4.23 Compound 4b

300MHz ¹H and 75.5MHz ¹³C NMR in DMSO of 2-Methyl-3-*o*-fluorophenyl - 4-(2'-hydroxybenzoyl)-3,6-dihydro-1*H*-azepino-[4,3,2-*cd*]-indole (4b)

4.24 Compound 4c

300MHz ^1H and 75.5MHz ^{13}C NMR in DMSO of 2-Methyl-3-*o*-(trifluoromethyl)phenyl-4-(2'-hydroxybenzoyl)-3,6-dihydro-1*H*-azepino-[4,3,2-*cd*]-indole (4c)