Supporting Information

A New Strategy Toward Indole Alkaloids Involving an Intramolecular Cycloaddition/Rearrangement Cascade

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Supporting Information Available: Spectroscopic and experimental procedures for compounds **20**, **21**, **31**, **38**, **45** and **46**. ¹H and ¹³C-NMR spectra for new compounds lacking elemental analyses. This material is available free of charge via the Internet at <http://pubs.acs.org>.

General Experimental Section Paragraph: Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70eV. Unless otherwise noted, all reactions were performed in flame dried glassware under an atmosphere of dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator and the residue was chromatographed on a silica gel column using an ethyl acetate-hexane mixture as the eluent unless specified otherwise.

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1-192-60c

expi stdln

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1-195-60C

expi stdh

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pentacyclic product-cd3cn-60c
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exp1 std1h

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ct 16
gain not used
flags not used
ll n
in n
dp n
hs y
nm cdc ph 100.000

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wp 3681.9
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sc 0
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th 20

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3wq-290--50C
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SAMPLE DEC. 8 VT
date Jan 5 2004 dfrq 599.746
solvent cdcl3 dn H1
file ACQUISITION exp dpr
sfrq 599.747 dm 0
tn H1 nmh

24

Supplementary Material

A New Strategy Toward Indole Alkaloids Involving an Intramolecular Cycloaddition/Rearrangement Cascade

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Supporting Information Available: Spectroscopic and experimental procedures for compounds **20**, **21**, **31**, **38**, **45** and **46**. ¹H and ¹³C-NMR spectra for new compounds lacking elemental analyses. This material is available free of charge via the Internet at <http://pubs.acs.org>.

Supplemental Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70eV. Unless otherwise noted, all reactions were performed in flame dried glassware under an atmosphere of dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator and the residue was chromatographed on a silica gel column using an ethyl acetate-hexane mixture as the eluent unless specified otherwise.

1-(1-Acetyl-1*H*-indol-3-yl)-2-bromoethanone. To a solution of 1.0 g (5.0 mmol) of 1-(3-acetylindol-1-yl)ethanone¹ in 25 mL of THF was added 1.9 g (5.0 mmol) of phenyltrimethyl ammonium tribromide. The reaction mixture was stirred at room temperature for 1 h then quenched with H₂O and extracted with EtOAc. The combined organic layers were dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residue was triturated with cold Et₂O to afford 0.85 g (62%) of the titled compound as a white solid: mp 150-151°C; IR (neat) 1726, 1680, 1547, 1449, and 1224 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 2.71 (s, 3H), 4.32 (s, 2H), 7.37-7.44 (m, 2H), 8.13 (s, 1H), 8.26-8.28 (m, 1H), and 8.33-8.35 (m, 1H); ¹³C-NMR (CDCl₃, 100 MHz) 24.3, 31.7, 116.4, 118.5, 122.6, 125.6, 126.8, 127.3, 132.1, 136.0, 168.7, and 187.4; Anal. Calcd. for C₁₂H₁₀NO₂Br: C, 51.45; H, 3.60; N, 5.00. Found: C, 51.58; H, 3.64; N, 5.02.

[2-(1-Acetyl-1*H*-indol-3-yl)-2-oxo-ethyl]furan-2-yl-carbamic Acid Ethyl Ester (20).

To a solution of 0.27 g (1.7 mmol) of furanyl-2-ylcarbamic acid ethyl ester in 8 mL of DMF was added 0.08 g (1.9 mmol) of NaH (60% dispersion in mineral oil). The reaction mixture was stirred at room temperature for 20 min and then a solution of 0.45 g (1.6 mmol) of the above bromide in 2 mL of DMF was added dropwise. The mixture was stirred at room temperature for an additional 30 min then quenched with H₂O and extracted with EtOAc. The combined organic layers were washed with H₂O, dried over anhydrous MgSO₄, and concentrated under reduced pressure. The

residue was subjected to flash silica gel chromatography to afford 0.25 g (45%) of **20** as a white solid: mp 62-64°C; IR (neat) 1725, 1706, 1680, 1603, 1547, and 1214 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 1.24 (brs, 3H), 2.63 (s, 3H), 4.20 (q, 2H, *J* = 9.6 Hz), 4.89 (s, 2H), 6.17 (brs, 1H), 6.33 (dd, 1H, *J* = 4.0 and 2.8 Hz), 7.15 (brs, 1H), 7.25-7.31 (m, 2H), 8.12 (s, 1H), and 8.14-8.22 (m, 2H); ¹³C-NMR (CDCl₃, 100 MHz) 14.5, 23.9, 55.5, 63.0, 102.3, 111.4, 116.2, 118.6, 122.1, 125.3, 126.4, 127.0, 131.1, 135.7, 138.6, 147.9, 155.5, 168.9, and 189.7; Anal. Calcd. for C₁₉H₁₈N₂O₅: C, 64.40; H, 5.12; N, 7.91. Found: C, 64.19; H, 5.18; N, 7.75.

(1-Benzenesulfonyl-1*H*-indol-3-yl)oxoacetic Acid Methyl Ester. To a solution of 1.0 g (4.9 mmol) of methyl indolyl-3-glyoxylate² in 30 mL of DMF at room temperature was added 0.2 g (5.4 mmol) of NaH (60% dispersion in mineral oil). The reaction mixture was stirred at room temperature for 30 min and 0.7 mL (5.4 mmol) of benzenesulfonyl chloride was added dropwise and stirring was continued for 30 min. The reaction was quenched with H₂O and extracted with EtOAc. The combined organics were washed with H₂O, dried over MgSO₄, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to afford 1.4 g (84%) of the titled compound as a white solid: mp 124-125°C; IR (neat) 1736, 1669, 1526, 1449, 1378, and 1132 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 3.98 (s, 3H), 7.34-7.42 (m, 2H), 7.48-7.52 (m, 2H), 7.60 (t, 1H, *J* = 7.6 Hz), 7.95-8.00 (m, 3H), 8.35 (d, 1H, *J* = 8.4 Hz), and 8.88 (s, 1H); ¹³C-NMR (CDCl₃, 100 MHz) 53.3, 113.3, 117.2, 123.1, 125.5, 126.5, 127.4, 127.8, 129.9, 134.6, 135.0, 137.0, 137.4, 162.1, and 178.4; Anal. Calcd. for C₁₇H₁₃NO₅S: C, 59.47; H, 3.82; N, 4.08. Found: C, 59.28; H, 3.98; N, 4.08.

(1-Benzenesulfonyl-1*H*-indol-3-yl)oxoacetic Acid. To a solution of 1.4 g (4.0 mmol) of the above indole in 30 mL of THF was added 0.6 g (4.0 mmol) of KOTMS (90%). The reaction mixture was stirred at room temperature for 1 h and the solvent was removed under reduced pressure. The residue was dissolved in 30 mL of H₂O,

acidified with 10% HCl, and extracted with CH_2Cl_2 . The combined organic layer was dried over anhydrous MgSO_4 and concentrated under reduced pressure. The residue was triturated with cold Et_2O to afford 1.1 g (83%) of the titled compound as a white solid: mp 166-167°C; IR (neat) 3329 (br), 1772, 1731, 1654, 1531, and 1449 cm^{-1} ; ^1H -NMR (CDCl_3 , 400 MHz) 7.40-7.47 (m, 2H), 7.52-7.56 (m, 2H), 7.62-7.66 (m, 1H), 8.00-8.04 (m, 3H), 8.30-8.32 (m, 1H), and 9.37 (s, 1H); ^{13}C -NMR (CDCl_3 , 100 MHz) 113.6, 115.2, 123.0, 125.9, 126.9, 127.6, 127.7, 130.1, 134.6, 135.3, 137.3, 139.8, 159.6, and 178.0; Anal. Calcd. for $\text{C}_{16}\text{H}_{11}\text{NO}_5\text{S}$: C, 58.35; H, 3.37; N, 4.25. Found: C, 58.32; H, 3.33; N, 4.22.

[2-(1-Benzenesulfonyl-1H-indol-3-yl)-2-oxo-acetyl]-furan-2-yl-carbamic acid

ethyl ester (21). To a solution of 0.6 g (1.8 mmol) of the above carboxylic acid in 10 mL of CH_2Cl_2 was added 0.2 mL (2.2 mmol) of oxalyl chloride followed by 1 drop of DMF. The reaction mixture was stirred at room temperature for 1 h and concentrated under reduced pressure. The crude residue was dissolved in 6 mL of THF and added dropwise to a solution of 0.18 g (1.2 mmol) of furanyl-2-ylcarbamic acid ethyl ester, 0.9 mL (6.0 mmol) of Et_3N , and 0.01 g (0.1 mmol) of 4-dimethylaminopyridine in 6 mL of THF. The reaction mixture was stirred at room temperature for 1 h then diluted with Et_2O and quenched with H_2O . The aqueous layer was extracted with EtOAc and then the combined organic layers were washed with saturated NaHCO_3 solution, dried over anhydrous MgSO_4 , and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to afford 0.3 g (53%) of the titled compound as a yellow oil: IR (neat) 1757, 1721, 1669, 1541, and 1265 cm^{-1} ; ^1H -NMR (CDCl_3 , 400 MHz) 1.12 (t, 3H, $J = 7.0$ Hz), 4.20 (q, 2H, $J = 7.0$ Hz), 6.45 (dd, 1H, $J = 3.2$ and 0.8 Hz), 6.53 (dd, 1H, $J = 3.2$ and 2.0 Hz), 7.37-7.44 (m, 2H), 7.46 (dd, 1H, $J = 2.0$ and 0.8 Hz), 7.47-7.52 (m, 2H), 7.58-7.62 (m, 1H), 7.96-7.99 (m, 3H), 8.28-8.30 (m, 1H), and 8.31 (s, 1H); ^{13}C -NMR (CDCl_3 , 100 MHz) 13.9, 64.9, 107.8, 111.8, 113.6, 113.4, 117.1, 122.8, 125.5, 126.5, 127.2, 127.4, 129.9, 134.8,

135.0, 135.1, 137.3, 140.5, 142.0, 152.6, 167.9, and 181.6; HRMS Calcd. for $C_{23}H_{18}N_2O_7S$: 466.0835. Found: 466.0841.

2-(1-Acetyl-1*H*-indol-3-yl)-*N*-methyl-*N*-furan-2-ylacetamide (31). To a solution of 0.18 g (0.6 mmol) of indole **29** in 3 mL of DMF was added 0.03 g (0.7 mmol) of NaH (60% dispersion in mineral oil). The reaction mixture was stirred at room temperature for 30 min and 0.06 mL (1.0 mmol) of methyl iodide was added dropwise. After an additional 30 min of stirring at room temperature, the reaction was quenched with H_2O and extracted with EtOAc. The organic layer was washed with H_2O , dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to provide 0.16 g (82%) of **31** as a pale yellow oil: IR (neat) 1700, 1680, 1610, 1451, and 1385 cm^{-1} ; 1H -NMR ($CDCl_3$, 400 MHz) 2.54 (s, 3H), 3.22 (s, 3H), 3.60 (s, 2H), 6.09 (d, 1H, $J = 3.2$ Hz), 6.40 (dd, 1H, $J = 3.2$ and 2.0 Hz), 7.21-7.33 (m, 4H), 7.38 (d, 1H, $J = 7.6$ Hz), and 8.39 (d, 1H, $J = 7.6$ Hz); ^{13}C -NMR ($CDCl_3$, 100 MHz) 24.2, 30.5, 36.6, 104.1, 111.5, 115.8, 116.8, 119.0, 123.7, 123.8, 125.5, 130.3, 135.8, 140.1, 149.7, 168.6, and 171.5; HRMS Calcd. for $C_{17}H_{16}N_2O_3$: 296.1161. Found: 296.1173.

Furan-2-yl[2-(1-methyl-1*H*-indol-3-yl)acetyl]carbamic Acid *tert*-Butyl Ester. To a solution of 1.0 g (5.5 mmol) of furan-2-yl carbamic acid *tert*-butyl ester (**82**) in 16 mL of THF at 0°C was added dropwise 4.0 mL (6.0 mmol) of *n*-BuLi (1.5 M in hexane). The reaction mixture was stirred at 0°C for 20 min. In a separate flask, 1.0 g (5.5 mmol) of 1-methyl-3-indoleacetic acid was dissolved in 20 mL of THF at 0°C and 0.6 mL (5.5 mmol) of 4-methylmorpholine, and 0.7 mL (5.5 mmol) of isobutyl chloroformate were added dropwise. After 5 min the white precipitate was removed *via* filtration and washed with 5 mL of THF. The filtrate was cooled to 0°C and the preformed lithiate was added dropwise *via* syringe. After stirring at 0°C for an additional 20 min, the reaction was quenched with H_2O and extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$,

and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to afford 1.4 g (72%) of the titled compound as a white solid: mp 86-87°C; IR (neat) 1782, 1746, 1716, 1603, 1255, and 1147 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) 1.46 (s, 9H), 3.76 (s, 3H), 4.31 (s, 2H), 6.14 (dd, 1H, $J = 3.2$ and 1.2 Hz), 6.43 (dd, 1H, $J = 3.2$ and 2.0 Hz), 7.10 (s, 1H), 7.13-7.17 (m, 1H), 7.24-7.28 (m, 1H), 7.32 (d, 1H, $J = 8.0$ Hz), 7.35 (dd, 1H, $J = 2.0$ and 1.2 Hz), and 7.63 (d, 1H, $J = 8.0$ Hz); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) 27.9, 32.8, 33.9, 83.9, 106.1, 106.6, 109.3, 111.4, 119.2, 121.7, 128.0, 128.4, 136.9, 140.6, 144.1, 151.7, and 173.4; Anal. Calcd. for $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_4$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.56; H, 6.28; N, 7.74.

N-Furan-2-yl-2-(1-methyl-1H-indol-3-yl)acetamide. To a solution of 1.3 g (3.7 mmol) of the above indole in 30 mL of CH_3CN was added 0.09 g (0.4 mmol) of magnesium perchlorate. The solution was heated to 45°C for 1.5 h then cooled to room temperature and the solvent was evaporated under reduced pressure. The residue was subjected to flash silica gel chromatography to afford 0.6 g (63%) of the titled compound as a white solid: mp 129-130°C; IR (neat) 3257, 1669, 1536, 1449, and 1388 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) 3.80 (s, 3H), 3.87 (s, 2H), 6.32-6.34 (m, 2H), 6.95 (t, 1H, $J = 1.6$ Hz), 7.05 (s, 1H), 7.18 (td, 1H, $J = 7.2$ and 1.2 Hz), 7.30 (td, 1H, $J = 7.2$ and 1.2 Hz), 7.37 (d, 1H, $J = 8.0$ Hz), 7.59 (dd, 1H, $J = 8.0$ and 0.8 Hz), and 7.89 (brs, 1H); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) 33.0, 33.5, 95.4, 106.6, 109.8, 111.6, 118.9, 120.1, 122.6, 127.5, 128.8, 135.4, 137.4, 145.4, and 168.3; Anal. Calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.83; H, 5.65; N, 10.93.

N-Allyl-N-furan-2-yl-2-(1-methyl-1H-indol-3-yl)acetamide (38). To a solution of 0.18 g (0.72 mmol) of the above compound in 3 mL of DMF was added 0.03 g (0.8 mmol) of NaH (60% dispersion in mineral oil). The reaction mixture was stirred at room temperature for 30 min and 0.08 mL (0.9 mmol) of allyl iodide was added dropwise. After an additional 30 min of stirring at room temperature, the reaction was

quenched with H₂O and extracted with EtOAc. The organic layer was washed with H₂O, dried over MgSO₄, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to provide 0.11 g (52%) of **38** as a pale yellow oil: IR (neat) 1685, 1603, 1372, 1147, and 737 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 3.70 (s, 2H), 3.74 (s, 3H), 4.28 (d, 2H, *J* = 6.0 Hz), 5.15-5.20 (m, 2H), 5.83-5.93 (m, 1H), 6.11 (d, 1H, *J* = 3.2 Hz), 6.43 (dd, 1H, *J* = 3.2 and 2.4 Hz), 6.95 (s, 1H), 7.13 (t, 1H, *J* = 7.6 Hz), 7.24 (t, 1H, *J* = 7.6 Hz), 7.30 (d, 1H, *J* = 8.0 Hz), 7.33 (s, 1H), and 7.51 (d, 1H, *J* = 8.0 Hz); ¹³C-NMR (CDCl₃, 100 MHz) 30.8, 32.7, 51.2, 105.1, 107.5, 109.2, 111.3, 117.9, 119.0, 121.6, 127.7, 127.8, 132.9, 136.9, 140.1, 148.7, and 172.3; HRMS Calcd. for C₁₈H₁₈N₂O₂: 294.1368. Found: 294.1375.

3-Ethylfuran-2-carboxylic Acid Methyl Ester. A modification of the procedure of Burness³ was used to prepare this furan. To a mixture containing 23 g (156 mmol) of 1,1-dimethoxy-3-pentanone⁴, 22 mL (250 mmol) of methyl chloroacetate, and 125 mL of dry Et₂O at -10°C was added 13.5 g (250 mmol) of freshly prepared powdered NaOMe in small portions over 30 min maintaining an internal temperature below -5°C. The reaction mixture was stirred an additional 2 h at -10°C and then warmed to room temperature overnight. The slurry was cooled to 0°C, quenched by the slow addition of a solution of 3 mL of AcOH in 50 mL of H₂O, and the aqueous layer was extracted with Et₂O. The combined organic layers were washed with dilute NaHCO₃ solution and brine, then dried over anhydrous MgSO₄ and concentrated under reduced pressure. The crude residue was transferred to a flask equipped with a 5 inch vigreux column and distillation head and heated at 170°C until MeOH distillation ceased. The mixture was cooled to room temperature and distilled under reduced pressure to afford 11.7 g (49%) of the titled compound as a colorless oil: bp 80-95°C (15 mm); IR (neat) 1716, 1598, 1490, 1434, 1301, and 1198 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 1.18 (t, 3H, *J* = 7.6 Hz), 2.81 (q, 2H, *J* = 7.6 Hz), 3.87 (s, 3H), 6.40 (d, 1H, *J* = 1.6 Hz), and 7.43 (d, 1H, *J* = 1.6 Hz); ¹³C-NMR (CDCl₃, 100 MHz)

14.3, 19.1, 51.7, 113.5, 137.8, 139.5, 145.2, and 160.1; HRMS Calcd. for $C_8H_{10}O_3$: 154.0630. Found: 154.0631.

3-Ethylfuran-2-carboxylic Acid. A suspension of 4.0 g (25.9 mmol) of the above ester in 30 mL of 10% aqueous NaOH was heated at reflux for 2 h. The homogeneous reaction mixture was cooled to 0°C and slowly acidified with conc. HCl. The resultant white precipitate was collected *via* filtration, washed with several portions of cold H_2O , and dried under high-vacuum to afford 3.4 g (94%) of the titled compound as a white solid: mp 106-107°C; IR (neat) 3139 (br), 1675, 1593, 1490, and 1285 cm^{-1} ; 1H -NMR ($CDCl_3$, 400 MHz) 1.22 (t, 3H, $J = 7.6$ Hz), 2.85 (q, 2H, $J = 7.6$ Hz), 6.46 (d, 1H, $J = 1.6$ Hz), 7.52 (d, 1H, $J = 1.6$ Hz), and 12.31 (brs, 1H); ^{13}C -NMR ($CDCl_3$, 100 MHz) 14.2, 19.4, 113.9, 138.9, 140.3, 146.5, and 165.0; Anal. Calcd. for $C_7H_8O_3$: C, 59.99; H, 5.75. Found: C, 59.82; H, 5.74.

(3-Ethyl-furan-2-yl)carbamic Acid *tert*-Butyl Ester. To a solution of 2.0 g (14.3 mmol) of the above carboxylic acid in 60 mL of CH_2Cl_2 were added 1.5 mL (17 mmol) of oxalyl chloride and 1 drop of DMF. The reaction mixture was stirred at rt for 1 h then concentrated under reduced pressure. The crude residue was dissolved in 40 mL of Et_2O and a solution of 1.1 g (17 mmol) of NaN_3 in 20 mL of H_2O was added. The biphasic reaction mixture was stirred vigorously for 3 h, then the organic layer was separated, dried over $MgSO_4$, and concentrated under reduced pressure. The crude residue was dissolved in 40 mL of *t*-BuOH and heated at reflux for 12 h. The reaction mixture was cooled to rt and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to afford 1.6 g (52 %) of the titled compound as a pale yellow oil: IR (neat) 3313, 1716, 1644, 1511, 1244, and 1157 cm^{-1} ; 1H -NMR ($CDCl_3$, 400 MHz) 1.13 (t, 3H, $J = 7.6$ Hz), 1.46 (s, 9H), 2.34 (q, 2H, $J = 7.6$ Hz), 6.09 (brs, 1H), 6.25 (d, 1H, $J = 2.0$ Hz), and 7.13 (d, 1H, $J = 2.0$ Hz); ^{13}C -NMR ($CDCl_3$, 100 MHz) 14.2, 17.7, 28.3, 81.2, 111.8, 119.2, 138.9, 139.3, and 154.0; HRMS Calcd. for $C_{11}H_{17}NO_3$: 211.1208. Found: 211.1215.

(3-Ethylfuran-2-yl)-(2-1*H*-indol-3-yl-acetyl)carbamic Acid *tert*-Butyl Ester. To a solution of 0.86 g (4.1 mmol) of the above furan in 15 mL of THF at 0°C was added dropwise 3.0 mL (4.5 mmol) of *n*-BuLi (1.5 M in hexane). The reaction mixture was stirred at 0°C for 20 min. In a separate flask, 0.71 g (4.1 mmol) of indole-3-acetic acid was dissolved in 15 mL of THF at 0°C and 0.45 mL (4.1 mmol) of 4-methylmorpholine, and 0.53 mL (4.1 mmol) of isobutyl chloroformate were added dropwise. After 5 min the white precipitate was removed *via* filtration and washed with 5 mL of THF. The filtrate was cooled to 0°C and the preformed lithiate was added dropwise *via* syringe. After stirring at 0°C for an additional 20 min, the reaction was quenched with H₂O and extracted with EtOAc. The organic layer was washed with saturated aqueous NaHCO₃, dried over MgSO₄, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to afford 0.97 g (65%) of the titled compound as a pale yellow oil: IR (neat) 3380, 1777, 1746, 1280, and 1152 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 1.00 (t, 3H, *J* = 7.6 Hz), 1.42 (s, 9H), 2.10 (q, 2H, *J* = 7.6 Hz), 4.22 (s, 2H), 6.29 (d, 1H, *J* = 2.0 Hz), 7.07-7.11 (m, 2H), 7.14-7.18 (m, 1H), 7.25 (d, 1H, *J* = 2.0 Hz), 7.29 (d, 1H, *J* = 8.0 Hz), 7.55 (d, 1H, *J* = 8.0 Hz), and 8.20 (brs, 1H); ¹³C-NMR (CDCl₃, 100 MHz) 13.6, 17.4, 27.9, 34.0, 83.7, 108.2, 111.3, 112.0, 119.1, 119.6, 120.8, 122.1, 123.8, 127.6, 136.2, 139.6, 140.0, 151.7, and 173.5; HRMS Calcd. for C₂₁H₂₄N₂O₄: 368.1736. Found: 368.1745.

2-(1-Acetyl-1*H*-indol-3-yl)acetyl[(3-ethylfuran-2-yl)carbamic Acid *tert*-Butyl Ester. To a solution of 0.89 g (2.4 mmol) of the above indole in 20 mL of CH₂Cl₂ at 0°C was added 0.08 g (0.24 mmol) of tetrabutylammonium hydrogensulfate followed by 0.48 g (12.0 mmol) of freshly powdered NaOH. After 5 min, 0.45 mL (6.0 mmol) of acetyl chloride was slowly added and the reaction mixture was stirred at 0°C for 15 min and then at room temperature for 15 min. The reaction was quenched with H₂O and the aqueous layer was extracted with CH₂Cl₂. The combined organic layer was dried over MgSO₄, and concentrated under reduced pressure. The residue was

subjected to flash silica gel chromatography to afford 0.84 g (84%) of the titled compound as a white solid: mp 128-129°C; IR (neat) 1782, 1741, 1710, 1449, 1367 and 1147 cm^{-1} ; ^1H -NMR (CDCl_3 , 400 MHz) 1.04 (t, 3H, $J = 7.6$ Hz), 1.42 (s, 9H), 2.16 (q, 2H, $J = 7.6$ Hz), 2.59 (s, 3H), 4.23 (s, 2H), 6.32 (d, 1H, $J = 2.4$ Hz) 7.25-7.29 (m, 1H), 7.26 (d, 1H, $J = 2.4$ Hz), 7.33-7.36 (m, 1H), 7.48-7.50 (m, 2H), and 8.43 (d, 1H, $J = 8.0$ Hz); ^{13}C -NMR (CDCl_3 , 100 MHz) 13.7, 17.5, 24.1, 27.9, 33.7, 84.1, 112.0, 115.0, 116.8, 119.1, 120.9, 123.8, 124.4, 125.5, 130.5, 135.7, 139.2, 140.1, 151.7, 168.7, and 172.2; Anal. Calcd. for $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_5$: C, 67.30; H, 6.38; N, 6.82. Found: C, 67.33; H, 6.49; N, 6.78.

2-(1-Acetyl-1*H*-indol-3-yl)-*N*-(3-ethylfuran-2-yl)acetamide. To a solution of 0.74 g (1.8 mmol) of the above indole in 30 mL of CH_3CN was added 0.04 g (0.2 mmol) of magnesium perchlorate. The solution was heated to 45°C for 1.5 h then cooled to rt and the solvent was evaporated under reduced pressure. The residue was subjected to flash silica gel chromatography to provide 0.44 g (78%) of the titled compound as a white solid: mp 128-129°C; IR (neat) 3257, 1705, 1680, 1511, 1454, and 1383 cm^{-1} ; ^1H -NMR (CDCl_3 , 400 MHz) (rotational isomer A) 1.07 (t, 3H, $J = 7.6$ Hz), 2.25 (q, 2H, $J = 7.6$ Hz), 2.60 (s, 3H), 3.81 (s, 2H), 6.26 (d, 1H, $J = 2.0$ Hz), 7.13 (d, 1H, $J = 2.0$), 7.21-7.27 (m, 1H), 7.32-7.36 (m, 1H), 7.39-7.43 (m, 1H), 7.49 (s, 1H), 7.57 (d, 1H, $J = 8.0$ Hz), and 8.44 (d, 1H, $J = 8.0$ Hz); (rotational isomer B) 1.07 (t, 3H, $J = 7.6$ Hz), 2.25 (q, 2H, $J = 7.6$ Hz), 2.57 (s, 3H), 3.56 (s, 2H), 6.33 (d, 1H, $J = 2.0$ Hz), 6.99 (brs, 1H), 7.21-7.27 (m, 2H), 7.32-7.36 (m, 1H), 7.39-7.43 (m, 1H), 7.39 (d, 1H, $J = 8.0$ Hz), and 8.39 (d, 1H, $J = 8.0$ Hz); ^{13}C -NMR (CDCl_3 , 100 MHz) (rotational isomer A) 14.1, 17.8, 24.2, 33.2, 112.1, 115.2, 117.1, 119.0, 123.8, 124.3, 124.7, 125.6, 126.2, 129.8, 136.1, 139.4, 168.7, and 169.8; (rotational isomer B) 14.1, 17.6, 24.2, 29.6, 112.2, 115.0, 116.9, 118.9, 123.9, 124.3, 124.7, 125.6, 126.2, 135.8, 138.1, 139.9, 171.7, and 173.5; Anal. Calcd. for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 67.37; H, 5.86; N, 8.97.

2-(1-Acetyl-1*H*-indol-3-yl)-*N*-allyl-*N*-(3-ethylfuran-2-yl)acetamide (45). To a solution of 0.20 g (0.64 mmol) of the above compound in 3 mL of DMF was added 0.03 g (0.70 mmol) of NaH (60% dispersion in mineral oil). The reaction mixture was stirred at room temperature for 30 min and 0.08 mL (0.83 mmol) of allyl iodide was added dropwise. After an additional 30 min of stirring at room temperature, the reaction was quenched with H₂O and extracted with EtOAc. The organic layer was washed with H₂O, dried over MgSO₄, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to provide 0.14 g (62%) of the titled compound as a pale yellow oil: IR (neat) 1705, 1680, 1639, 1454, and 1378 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 1.09 (t, 3H, *J* = 7.6 Hz), 2.23 (q, 2H, *J* = 7.6 Hz), 2.56 (s, 3H), 3.52 (s, 2H), 4.22 (d, 2H, *J* = 6.4 Hz), 5.10-5.18 (m, 2H), 5.79-5.89 (m, 1H), 6.34 (d, 1H, *J* = 2.0 Hz), 7.22-7.34 (m, 4H), 7.36 (d, 1H, *J* = 7.6 Hz), and 8.40 (d, 1H, *J* = 7.6 Hz); ¹³C-NMR (CDCl₃, 100 MHz) 14.2, 17.7, 24.2, 30.6, 51.4, 112.0, 115.7, 116.8, 118.7, 119.0, 120.8, 123.7, 123.9, 125.5, 130.4, 132.8, 135.8, 140.0, 143.7, 168.7, and 171.7; HRMS Calcd. for C₂₁H₂₂N₂O₃: 350.1630. Found: 350.1626.

3-Bromofuran-2-yl)carbamic Acid *tert*-Butyl Ester. To a suspension of 1.0 g (5.2 mmol) of 3-bromofuroic acid⁵ in 20 mL of *t*-BuOH were added 1.2 mL (5.7 mmol) of diphenylphosphoryl azide and 0.9 mL (6.3 mmol) of Et₃N. The reaction mixture was heated at reflux for 1.5 h then cooled to room temperature and poured into 40 mL of saturated aqueous NaHCO₃. The aqueous layer was extracted with EtOAc and the combined organic phases were dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to afford 1.10 g (80%) of the titled compound as a beige solid: mp 64-66°C; IR (neat) 3283, 1716, 1629, 1372, 1250, and 1137 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 1.48 (s, 9H), 6.21 (brs, 1H), 6.40 (d, 1H, *J* = 2.0 Hz), and 7.20 (d, 1H, *J* = 2.0 Hz); ¹³C-NMR (CDCl₃, 100 MHz) 28.3, 82.0, 93.6, 114.3, 139.8, 142.0, and

153.0; Anal Calcd. for $C_9H_{12}NO_3Br$: C, 41.24; H, 4.61; N, 5.34. Found: C, 41.03; H, 4.58; N, 5.48.

(3-Bromofuran-2-yl)-(2-1*H*-indol-3-yl-acetyl)carbamic Acid *tert*-Butyl Ester. To a solution of 0.26 g (1.0 mmol) of the above furan in 4 mL of THF at 0°C was added 0.04 g (1.1 mmol) of NaH (60% dispersion in mineral oil). The reaction mixture was stirred at room temperature for 20 min. In a separate flask, 0.19 g (1.1 mmol) of indole-3-acetic acid was dissolved in 5 mL of THF at 0°C and 0.12 mL (1.1 mmol) of 4-methylmorpholine, and 0.14 mL (1.1 mmol) of isobutyl chloroformate were added dropwise. After 5 min the white precipitate that formed was removed *via* filtration and washed with 2 mL of THF. The filtrate was cooled to 0°C and the furan was added dropwise *via* syringe. After stirring at 0°C for an additional 20 min, the reaction was quenched with H_2O and extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to afford 0.28 g (67%) of the titled compound as a pale yellow oil: IR (neat) 3400, 1787, 1746, 1618, 1291, and 1244 cm^{-1} ; 1H -NMR ($CDCl_3$, 400 MHz) 1.47 (s, 9H), 4.34 (s, 2H), 6.48 (d, 1H, $J = 2.0$ Hz), 7.03 (s, 1H), 7.11-7.20 (m, 2H), 7.26 (d, 1H, $J = 7.6$ Hz), 7.30 (d, 1H, $J = 2.0$ Hz), 7.61 (d, 1H, $J = 7.6$ Hz), and 8.22 (brs, 1H); ^{13}C -NMR ($CDCl_3$, 100 MHz) 27.9, 34.0, 84.5, 96.8, 107.6, 111.4, 114.5, 119.0, 119.6, 122.0, 124.0, 127.5, 136.2, 141.1, 142.4, 150.6, and 173.0; HRMS Calcd. for $C_{19}H_{19}N_2O_4Br$: 418.0528. Found: 418.0521.

[2-(1-Acetyl-1*H*-indol-3-yl)acetyl](3-bromofuran-2-yl)carbamic Acid *tert*-Butyl Ester. To a solution of 0.2 g (0.47 mmol) of the above indole in 5 mL of CH_2Cl_2 at 0°C were added 0.02 g (0.05 mmol) of tetrabutylammonium hydrogensulfate and 0.09 g (2.4 mmol) of freshly powdered NaOH. After 5 min, 0.08 mL (1.2 mmol) of acetyl chloride was slowly added and the reaction mixture was stirred at 0°C for 15 min and then at room temperature for 15 min. The reaction was quenched with H_2O and the

aqueous layer was extracted with CH₂Cl₂. The combined organic layer was dried over MgSO₄, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to afford 0.16 g (75%) of the titled compound as a white solid: mp 132-133°C; IR (neat) 1787, 1751, 1710, 1618, 1449, and 1372 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 1.45 (s, 9H), 2.59 (s, 3H), 4.33 (s, 2H), 6.49 (d, 1H, *J* = 2.0 Hz) 7.27-7.31 (m, 1H), 7.32 (d, 1H, *J* = 2.0 Hz), 7.34-7.38 (m, 1H), 7.51 (s, 1H), 7.54 (d, 1H, *J* = 8.0 Hz), and 8.44 (d, 1H, *J* = 8.0 Hz); ¹³C-NMR (CDCl₃, 100 MHz) 24.1, 27.9, 33.7, 84.8, 96.8, 114.6, 114.8, 116.8, 119.2, 123.8, 124.5, 125.5, 130.5, 135.7, 141.2, 142.0, 150.6, 168.7, and 171.7; Anal. Calcd. for C₂₁H₂₁N₂O₅Br: C, 54.68; H, 4.59; N, 6.07. Found: C, 54.72; H, 4.57; N, 6.03.

2-(1-Acetyl-1*H*-indol-3-yl)-*N*-(3-bromofuran-2-yl)acetamide. To a solution of 0.36 g (0.8 mmol) of the above indole in 10 mL of CH₃CN was added 0.02 g (0.1 mmol) of magnesium perchlorate. The solution was heated to 45°C for 1.5 h then cooled to rt and the solvent was evaporated under reduced pressure. The residue was subjected to flash silica gel chromatography to provide 0.2 g (72%) of the titled compound as a pale yellow solid: mp 147-148°C; IR (neat) 3262, 1697, 1622, 1451, and 1386 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 2.61 (s, 3H), 3.85 (s, 2H), 6.42 (s, 1H), 7.22 (s, 1H), 7.28 (brs, 1H), 7.35 (t, 1H, *J* = 7.6 Hz), 7.42 (t, 1H, *J* = 7.6 Hz), 7.52 (s, 1H), 7.49 (s, 1H), 7.61 (d, 1H, *J* = 8.0 Hz), and 8.45 (d, 1H, *J* = 8.0 Hz); ¹³C-NMR (CDCl₃, 100 MHz) 24.2, 33.2, 114.6, 114.9, 117.1, 119.2, 124.4, 124.8, 125.7, 126.3, 129.7, 136.1, 140.5, 141.0, 168.7, and 169.4; Anal. Calcd. for C₁₆H₁₃N₂O₃Br: C, 53.21; H, 3.63; N, 7.76. Found: C, 53.11; H, 3.61; N, 7.54.

2-(1-Acetyl-1*H*-indol-3-yl)-*N*-allyl-*N*-(3-bromofuran-2-yl)acetamide (46). To a solution of 0.1 g (0.27 mmol) of the above compound in 2.5 mL of DMF was added 0.01 g (0.3 mmol) of NaH (60% dispersion in mineral oil). The reaction mixture was stirred at room temperature for 30 min and 0.04 mL (0.4 mmol) of allyl iodide was added dropwise. After an additional 30 min of stirring at room temperature, the

reaction was quenched with H₂O and extracted with EtOAc. The organic layer was washed with H₂O, dried over MgSO₄, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to provide 0.07 g (63%) of **46** as a pale yellow oil: IR (neat) 1698, 1613, 1451, 1383, and 1214 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) 2.58 (s, 3H), 3.59 (s, 2H), 4.27 (d, 2H, *J* = 6.4 Hz), 5.12-5.21 (m, 2H), 5.79-5.89 (m, 1H), 6.50 (d, 1H, *J* = 2.4 Hz), 7.23-7.26 (m, 2H), 7.27 (d, 1H, *J* = 2.4 Hz), 7.32-7.36 (m, 1H), 7.41 (d, 1H, *J* = 7.6 Hz), and 8.40 (d, 1H, *J* = 7.6 Hz); ¹³C-NMR (CDCl₃, 100 MHz) 24.2, 30.9, 50.7, 96.9, 114.8, 115.3, 116.8, 119.0, 119.1, 123.7, 124.0, 125.5, 130.3, 132.3, 135.8, 141.0, 146.0, 168.6, and 170.8; HRMS Calcd. for C₁₉H₁₇N₂O₃Br: 400.0423. Found: 400.0428.

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