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Synthesis of functionalized chromeno[2,3-*b*]pyrrole-2,3-dicarboxylate *via* Zn(OTf)$_2$-catalyzed annulation of 2-amino-4*H*-chromen-4-one and electron-deficient acetylenes

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A Zn(OTf)$_2$-mediated annulation of 2-amino-4*H*-chromen-4-one with diethyl acetylenedicarboxylate (DEAD) has been investigated to provide access to functionalized chromeno[2,3-*b*]pyrrole-2,3-dicarboxylate in excellent yields with good functional group tolerance. Furthermore, this method has also been used to synthesize a variety of novel annulated chromeno[2,3-b]pyrroles **3a-n** through a plausible new mechanism.

Keywords: Zn(OTf)$_2$-catalyzed, chromeno[2,3-*b*]pyrroles , 2-aminochromen-4-one, annulation, cycloaddition

The functionalized chromeno[2,3-*b*]pyrrole is widely found in many biologically active molecules and plays an important role in medicinal chemistry due to its unique fusion of the chromene and pyrrole ring systems. Among these compounds, the chromeno [2,3-b]pyrrole scaffold is a key structure present in various biological applications, including antioxidant, antibiotic, antitumor, antimalarial activities, and the treatment of Alzheimer's disease[1-5]. For example, pyralomycins are well-known chromenopyrroles with biologically active compounds that exhibit antitumor activity (Fig. 1). Additionally, pyralomycins show remarkable optoelectronic properties and have been used in material chemistry[6,7]. These compounds, including chromeno[2,3-*b*]pyrroles like pyralomycins, were isolated from the soil bacterium *Nonomuraea spiralis* by Takeuchi and colleagues in 1996 (Ref. 8) As a result, the preparation of chromeno [2,3-*b*]pyrroles has garnered significant interest, and numerous efficient synthetic methods have been developed[9-12]. The synthesis of these compounds and their derivatives continues to inspire organic chemists. Consequently, due to the broad utility of chromenopyrroles, significant attention has been given to the efficient construction of their synthesis. Various methods have been reported[13-16], most of which focus on constructing the pyrrole moiety from functionalized chromenones in metal-catalyzed reactions, optimizing reaction conditions in terms of solvents, time, and yield[17-20]. Recently, one strategy was developed based on substituted glycine substrates and 3-formylchromones to construct the chromone unit[21]. Another important strategy involves using functionalized chromenones as substrates to construct pyridine rings[22,23]. Drawing inspiration from these approaches and based on our experience in organic chemistry, particularly in developing new catalytic reactions[24], we aimed to synthesize a new chromeno[2,3-*b*]pyrrole-2,3-dicarboxylate *via* a one-pot, three-component catalytic reaction, incorporating electron-donating and electron-withdrawing substituents on the chromeno ring under reflux conditions.

Experimental Details

Metarials and methods

Proton (^{1}H NMR, 400 MHz) and Carbon (^{13}C NMR, 100 MHz) spectra were performed on a

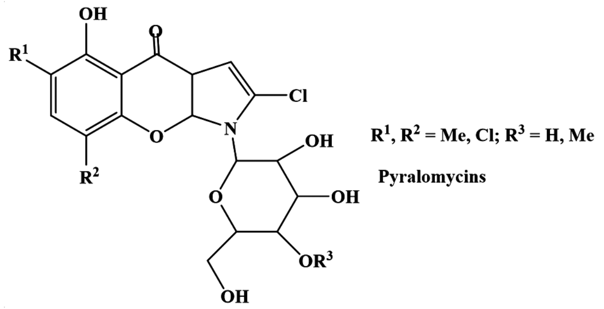


Fig. 1 — Examples of chromonopyrrole-containing biological active compounds

Bruker instrument DPX-400 MHz High-Performance Digital FT-NMR spectrometer $CDCl_3$ to tetramethylsilane (TMS) as the international standard at 25°C. Chemical shifts were reported in parts per million (ppm). Thin-layer chromatography was performed using commercially prepared 100-mesh silica gel plates (silica gel60 F254). All solvents were dried and distilled according to the standard methods before use. IR spectra were recorded as KBr pellets using a Mattson 1000 FT-IR Spectrometer. Melting points were determined in capillary tubes on a Gallenkamp apparatus and are uncorrected.

Representative general method for the synthesis of 3a-n

General procedure for the synthesis of functionalized chromeno[2,3-*b*]pyrrole-2,3-dicarboxylates **(3a-n)**: Substituted 2-amino-4*H*-chromen-4-one (1a-n) were prepared according to literature procedures and purified with EtOH (Ref. 30,31). A mixture of substituted 2-amino-4*H*-chromen-4-one (1a-n) (1.0 mmol), DEAD (4.0 mmol), and $Zn(OTf)_2$ (30 mol%) in 20 mL of MeOH was heated under reflux in an oil bath for 3-6 hours under a nitrogen atmosphere. The reaction was monitored by TLC (CH_2Cl_2/EtOAc, 4/1, silica gel); once the reaction was complete, the mixture was cooled to RT. The solvent was removed by reduced-pressure distillation, and the residue was extracted with EtOAc (3 × 1 mL). The combined organic phase was then washed with water (10 mL) and dried over anhydrous sodium sulfate to give the desired products **3a-n**.

Diethyl 4-oxo-1,4-dihydrochromeno[2,3-*b*]pyrrole-2,3-dicarboxylate, 3a: The product was obtained as a white solid. Yield 91%. m.p.283-285°C. R_f = 0.55 (EtOAc); IR (KBr): 3321, 3071, 2978, 2914, 1668, 1661 1628 1584, 1461, 1432, 1210 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.81 (s, 1H), 8.11 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.81-7.78 (m, 1H), 7.69 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.41 (dd, *J* = 8.1, 1.2 Hz, 1H), 4.43-4.31 (m, 4H), 1.42-1.34 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176. 5, 164.2, 161.11, 154.8, 153.4, 132.7, 126.9, 125.5, 123.1, 118.3, 116.2, 107.8, 105.3, 61.8, 61.3, 13.8, 13.3; HRMS-ESI: *m/z* Calcd for $C_{17}H_{15}NO_6$ $[M+H]^+$: 329.0914. Found: 329.0918.

Diethyl 6-methyl-4-oxo-1,4-dihydrochromeno[2,3-*b*]pyrrole-2,3-dicarboxylate, 3b: The product was obtained as a white solid. Yield 86%. m.p.269-171°C. R_f = 0.63 (EtOAc); IR (KBr): 3365, 3011, 2966, 2924, 1677, 1664, 1612, 1523, 1443, 1415, 1224 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.93 (s, 1H), 7.91 d (d, *J* = 8.1, 0.8 Hz, 1H), 7.61 (dd, *J* = 8.3, 21.2 Hz), 1H), 7.53 d (d, *J* = 8.6 Hz, 1H), 4.34-4.27 (m, 4H), 2.44 (s, 3H), 1.31-1.26 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4, 165.7,162.1, 153.4, 152.2, 133.4, 134.0, 126.6, 122.2, 119.4, 116.3, 107.6, 60.8, 60.2, 22.2, 21.3, 14.5, 14.2; HRMS-ESI: *m/z* Calcd for $C_{18}H_{17}NO_6$ $[M+H]^+$: 343.1167. Found: 343.1163.

Diethyl 6-ethyl-4-oxo-1,4-dihydrochromeno[2,3-*b*]pyrrole-2,3-dicarboxylate, 3c: The product was obtained as a yellow solid. Yield 97%. m.p.243-245°C. R_f = 0.48 (EtOAc); IR (KBr): 3224, 2978, 2945, 1656, 1648, 1610, 1525, 1473, 1431, 1204, 1185 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.83 (s, 1H), 7.65 (d, 1H, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.51 d (d, *J* = 8.6 Hz, 1H), 4.32-4.25 (m, 4H), 2.65 q (q, *J* = 7.5 Hz, 2H), 1.37-1.31 (m, 6H), 1.27 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.3, 164.4, 162.7, 151.5, 151.0, 141.2, 133.7, 125.1, 123.6, 118.7, 117.5, 107.5, 106.3, 62.4, 61.2, 26.3, 15.2 14.8, 14.2; HRMS-ESI: *m/z* Calcd for $C_{19}H_{19}NO_6$ $[M+H]^+$: 357.1234. Found: 357.1229.

Diethyl 6-methoxy-4-oxo-1,4-dihydrochromeno [2,3-*b*]pyrrole-2,3-dicarboxylate, 3d: The product was obtained as a white solid. Yield 96%. m.p. 230-232°C. R_f= 0.42 (EtOAc); IR (KBr): 3073, 2981, 1710, 1691, 1612, 1543, 1493, 1451, 1271 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.12 (s, 1H), 8.22 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.48 (d *J* = 2.8 Hz, 1H), 7.32 (dd, *J* = 9.0, 2.6 Hz, 1H), 4.25-3.92 (m, 4H), 3.73 (s, 3H), 1.41-1.37 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 163.7, 160.3, 154.2, 128.1, 125.8, 123.7, 117.0, 116.3, 114.7, 113.2, 112.7, 106.1, 62.9, 62.3, 55.7, 14.7, 14.2; HRMS-ESI: *m/z* Calcd for $C_{18}H_{17}NO_7$ $[M+H]^+$:359.1021. Found: 359.1026.

Diethyl 6-fluoro-4-oxo-1,4-dihydrochromeno [2,3-*b*]pyrrole-2,3-dicarboxylate, 3e: The product was obtained as off-white. Yield 91%. m.p. 248-250°C. R_f = 0.52 (EtOAc); IR (KBr): 3193, 2958, 1713, 1631, 1611, 1558, 1543, 1454, 1437, 1273, 1241; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 1H), 8.34 (d, *J* = 8.2 Hz, 1H), 7.63 (t, J = 8.2 Hz, 1H), 7.43 (d, *J* = 8.5 Hz, 1H), 4.18-3.91 (m, 4H), 1.38-1.29 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 162.2, 155.3, 152.5, 132.5, 131.8, 128.2, 124.1, 122.7, 121.7, 118.4, 114.2, 108.8, 62.3, 61.4, 14.4, 14.0; HRMS-ESI: *m/z* Calcd for $C_{17}H_{14}FNO_6$ $[M+H]^+$: 347.0828. Found: 347.0824.

Diethyl 6-chloro-4-oxo-1,4-dihydrochromeno [2,3-*b*]pyrrole-2,3-dicarboxylate, 3f: The product was obtained as a white solid. Yield 84%. m.p. 216-218°C. R_f = 0.58 (EtOAc); IR (KBr): 3061, 2985, 1703, 1631, 1623, 1562, 15151, 1452, 1431, 1273 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 10.02 s (1H), 8.25 dd (1H, *J* = 8.1, 1.5 Hz), 7.68 dd (1H, *J* = 8.3, 1.3 Hz), 7.46 d (1H, *J* = 8.4 Hz), 4.28-3.96 m (4H), 1.27-1.21 m (6H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 178.7, 163.3, 162.2, 153.4, 151.4, 134.2, 131.9, 129.3, 126.1, 123.7, 117.5, 115.9, 107.1, 64.4, 61.3, 14.1, 13.9. HRMS-ESI: *m/z* Calcd for $C_{17}H_{14}ClNO_6$ $[M+H]^+$: 363.0534. Found: 218.0628.

Diethyl 6-bromo-4-oxo-1,4-dihydrochromeno [2,3-*b*]pyrrole-2,3-dicarboxylate, 3g: The product was obtained as a white solid. Yield 77%. m.p. 233-235°C. R_f = 0.61 (EtOAc); IR (KBr): 3061, 2983, 1702, 1680.2, 1631, 1563, 1521, 1452, 1434, 1275, 1194 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 11.18 (s, 1H), 8.21 (dd, *J* = 7.5, 1.4 Hz,1H), 7.62 (d, *J* = 7.3 Hz, 1H), 7.61 (dd, 1H, *J* = 8.2, 1.3 Hz, 1H), 4.33-3.94 (m, 4H), 1.31-1.28 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 175.7, 165.4, 160.3, 153.4, 151.4, 138.5, 132.3, 129.4, 127.2, 126.7, 125.0, 124.4, 123.7, 106.9, 61.3, 13.7, 13.1; HRMS-ESI: *m/z* Calcd for $C_{17}H_{14}BrNO_{6\ 3}$ $[M+H]^+$: 407.0034. Found: 218.0028.

Diethyl 6-nitro-4-oxo-1,4-dihydrochromeno[2,3-*b*]pyrrole-2,3-dicarboxylate, 3h: The product was obtained as a white solid. Yield 51%. m.p. 267-269°C. R_f = 0.45 (EtOAc); IR (KBr): 3223, 2922, 1733, 1664, 1617, 1561, 1522, 1441, 1424, 1286, 1211 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 9.89 (s, 1H), 8.33 (dd, *J* = 8.2, 1.6 Hz, 1H), 8.20 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 4.38-4.32 (m, 4H), 1.29-1.18 (m, H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 173.8, 163.3, 160.8, 159.7, 151.4, 143.5, 135.5, 132.8, 128.2, 122.5, 116.5, 114.2, 107.2, 63.6, 61.8, 14.7, 14.1; HRMS-ESI: *m/z* Calcd for $C_{17}H_{114}N_2O_8$ $[M+H]^+$:374.0834. Found: 218.0628.

Diethyl 7-methyl-4-oxo-1,4-dihydrochromeno [2,3-*b*]pyrrole-2,3-dicarboxylate, 3i: The product was obtained as a gray white solid. Yield 81%. m.p. 195-197°C. R_f = 0.52 (EtOAc); IR (KBr): 3223, 2921, 1728, 1663, 1648, 1562, 1521, 1440, 1242, 1283 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 10.12 (s, 1H), 7.43 (d, *J* = 8.2 Hz, 1H),7.21 (d, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 1H), 4.46-4.39 (m, 4H), 2.63 (s, 3H), 1.18-1.12 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 176.9, 164.6, 162.3, 152.1, 147.7, 143.5, 132.9, 127.8, 123.9, 122.7, 116.3, 113.8, 107.4, 63.2, 61.1, 21.6, 14.1, 13.8; HRMS-ESI: *m/z* Calcd for $C_{17}H_{114}N_2O_8$ $[M+H]^+$:374.0834. Found: 218.0628.

Diethyl 7-ethyl-4-oxo-1,4-dihydrochromeno[2,3-*b*]pyrrole-2,3-dicarboxylate, 3j: The product was obtained as a yellow solid. Yield 93%. m.p. 181-183°C. R_f = 0.38 (EtOAc); IR (KBr): 3041, 2926, 1712, 1634, 1612, 1563, 1532, 1516, 1473, 1432, 1270, cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 11.23 (s, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.42 (s, 1H), 7.28 (dd, *J* = 8.3, 2.2 Hz, 1H), 4.34-4.27 (m, 4H), 2.23 (q, *J* = 7.4 Hz, 2H), 1.21 (t, J = 7.4 Hz, 3H), 1.28-1.21 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 173.2, 164.3, 169.5, 152.4, 145.6, 124.8, 123.5, 123.3, 121.9, 119.3, 115.4, 107.3. 106.6, 63.2, 60.4, 28.7, 14.8, 14.1, 13.9; HRMS-ESI: *m/z* Calcd for $C_{18}H_{17}NO_6$ $[M+H]^+$: 343.1332. Found: 218.1339.

Diethyl 7-methoxy-4-oxo-1,4-dihydrochromeno [2,3-*b*]pyrrole-2,3-dicarboxylate, 3k: The product was obtained as a yellow solid. Yield 92%. m.p. 205-207°C. R_f = 0.68 (EtOAc); IR (KBr): 3208, 2923, 1705, 1656, 1618, 1583, 1534, 1442, 1430, 1266, 1172 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 11.4 (s, 1H), 8.02 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.21 (dd, *J* = 73.6, 2.4 Hz, 1H), 7.14 (d, *J* = 2.7 Hz, 1H), 4.30-4.22 (m, 4H), 3.87 (s, 3H), 1.28-1.24 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 177.5, 164.2, 163.4, 161.2, 154.1, 148.8, 137.7, 128.7, 119.4, 114.2, 109.4, 64.2, 61.3, 57.5, 63.5, 60.1, 13.7, 13.4; HRMS-ESI: *m/z* Calcd for $C_{18}H_{17}NO_7$ $[M+H]^+$: 359.1341. Found: 218.1336.

Diethyl 7-fluoro-4-oxo-1,4-dihydrochromeno[2,3-*b*]pyrrole-2,3-dicarboxylate, 3l: The product was obtained as a yellow solid. Yield 61%. m.p. 252-254°C. R_f = 054 (EtOAc); IR (KBr): 3234, 2961, 1716, 1638, 1611, 1514, 1522, 1458, 1429, 1277, 1246 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 11.32 (s, 1H), 8.14 (dd, *J* = 8.5, 6.3 Hz, 1H), 7.56 (dd, *J* = 9.3, 2.1 Hz, 1H) , 7.32 (td, *J* = 8.5, 2.4 Hz, 1H), 4.46-4.27 (m, 4H), 1.26-1.19 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 174.2, 165.4, 163.5, 160.2, 153.7,152.5, 142.3, 127.8, 118.5, 118.1, 113.9 107.4, 106.3, 63.5, 60.2, 14.1, 13.6; HRMS-ESI: *m/z* Calcd for $C_{17}H_{14}FNO_6$ $[M+H]^+$: 347.3045. Found: 347.3051.

Diethyl 7-nitro-4-oxo-1,4-dihydrochromeno[2,3-*b*]pyrrole-2,3-dicarboxylate, 3m: The product was obtained as white solid. Yield 55%. m.p. 263-265°C. R_f= 0.45 (EtOAc); IR (KBr): 3232, 2956, 1726, 1661, 1622, 1558, 1534, 1439, 1418, 1278, 1206 cm^{-1};

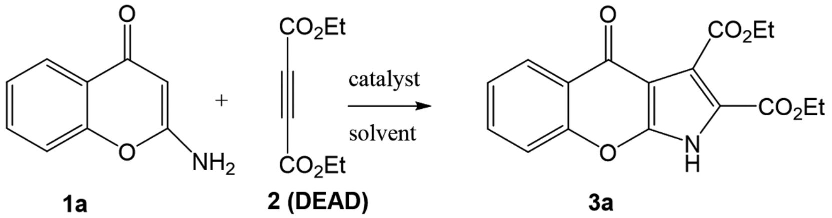
^{1}H NMR (400 MHz, $CDCl_3$): δ 10.02 (s, 1H), 8.56 (dd, *J* = 8.3, 2.2 Hz, 1H), 8.14 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.88 (d, J = 7.6 Hz, 1H), 4.24-4.16 (m, 4H), 1.17-1.09 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 164.5, 162.7, 156.4, 150.2, 144.2, 134.3, 131.2, 127.5, 121.1, 117.3, 115.58, 108.3, 64.2, 60.3, 13.8, 13.4; HRMS-ESI: *m/z* Calcd for $C_{17}H_{14}N_2O_8$ $[M+H]^+$: 374.3218. Found: 374.3211.

Diethyl 4-oxo-6-phenyl-1,4-dihydrochromeno [2,3-*b*]pyrrole-2,3-dicarboxylate, 3n: The product was obtained as white solid. Yield 73%. m.p. 218-220°C. R_f = 0.39 (EtOAc); IR (KBr): 3022, 2985, 1693, 1627, 1553, 1532, 1522, 1450, 1433, 1281 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.13 (s, 1H) 8.32–8.24 (m, 2H), 7.69–7.61 (m, 2H), 7.57–7.43 (m, 2H), 7.44–7.32 (m, 2H), 4.33–4.25 (m, 4H), 1.27–1.13 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 163.5, 161.2, 153.3, 151.7, 139.2, 138.3, 137.4, 133.4, 129.5, 128.5, 128.2, 126.6, 125.2, 123.6, 119.8, 119.2, 118.3, 108.4, 107.7, 65.3, 62.5, 14.3, 13.8; HRMS-ESI: *m/z* Calcd for $C_{23}H_{19}NO$ $[M+H]^+$: 405.4113. Found: 405.4119.

Results and Discussion

Recently, our group developed a new synthetic pathway for heterocyclic compounds and various catalysts, providing efficient and convenient methodologies for synthesizing heterocycles such as isocoumarin, isoxazole, methanoazocino[4,3-b]indole, nitriles, and chromeno[2,3-b]pyridine[25-30]. Our investigation began with an attempt to establish the optimized reaction conditions. First, we tested the reaction of 2-amino-4*H*-chromen-4-one **1a** with DEAD (**2**) under reflux with various triflate catalysts in a variety of solvents, including CH_3CN, THF, DMF, EtOH, 1,4-dioxane, CH_2Cl_2, and benzene. All of these reactions proceeded with relatively poor efficiency compared to the initial reaction in MeOH (Entry 7, Table 1), establishing MeOH as the solvent of choice for annulation reactions with $Zn(OTf)_2$. Next, we studied the effect of reaction temperature on the annulation reactions. A decrease in reaction temperature led to a significant drop in yield (Entry 8, Table 1). The $Zn(OTf)_2$-catalyzed reaction successfully produced the desired annulated product in CH_3CN under reflux conditions, affording **3a** in 91% yield. Following the optimization of reaction conditions, we examined the generality of the method for the synthesis of new 2,3-disubstituted 1,4-dihydrochromeno[2,3-b]pyrroles, using 2-amino-4*H*-chromen-4-ones in annulation reactions with DEAD under the optimized conditions (Table 1). We are pleased to report that the

Table 1 — Optimization of the reaction conditions for **3a**[a]



Compd	Catalyst	Solvent	Temp. (°C)	Yield (%)[a]
1	$Cu(OTf)_2$	CH_3CN	reflux	35
2	$Yb(OTf)_2$	CH_3CN	reflux	10
3	AgOTf	CH_3CN	reflux	61
4	$Zn(OTf)_2$	CH_3CN	reflux	81
5	$Zn(OTf)_2$	DMF	reflux	53
6	$Zn(OTf)_2$	THF	reflux	44
7	$Zn(OTf)_2$	MeOH	Reflux	91
8	$Zn(OTf)_2$	MeOH	RT	5
9	$Zn(OTf)_2$	EtOH	reflux	78
10	$Zn(OTf)_2$	1,4-dioxane	reflux	66
11	$Zn(OTf)_2$	CH_2Cl_2	reflux	20
12	$Zn(OTf)_2$	benzene	reflux	56

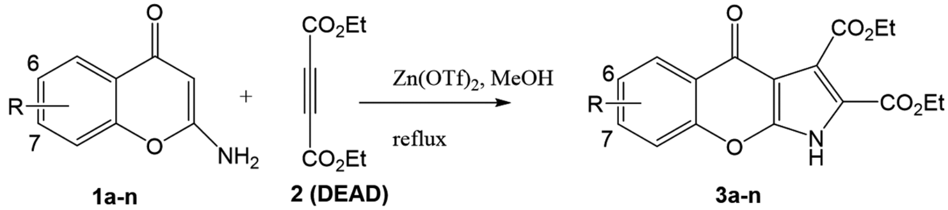
[a] Reaction were carried out 1.0 mmol 2-amino-4*H*-chromen-4-one (**1a**) using 4.0 mmol DEAD and catalyst (30 mol %) in solvent (20 mL) at refluxed.

[b] Refers to isolated yields after column chromathogrophic purificiation

Zn(OTf)$_2$-catalyzed annulation reaction between 1a and DEAD produced chromeno[2,3-*b*]pyrrole-2,3-dicarboxylate **3a** in good yields. Notably, reactions with 2-amino-4*H*-chromen-4-ones bearing electron-donating groups (such as methyl and methoxy) or electron-withdrawing groups (such as chloro, bromo, and nitro) on the aromatic ring afforded moderate yields (Table 2). Similarly, substrates with electron-donating groups, such as CH_3O, provided their respective products in yields ranging from 86% to 96%. Substituents at the C-6 and C-7 positions on the benzene ring were tolerated under the reaction conditions, although their effect on the reaction was noticeable. Chromeno[2,3-*b*]pyrrole 1a afforded slightly higher yields than substituted chromeno[2,3-*b*]pyrroles at the C-7 position. Additionally, halogen-containing substrates (**1e-g**) were well tolerated, with the annulated products (**3e-g**) obtained in good yields (77-91%). Likewise, 2-amino-4*H*-chromen-4-ones (**1c, 1n**) bearing 6-Et and 7-C_6H_5 groups efficiently cyclized into the corresponding products (**3c, 3n**) in yields of 97% and 73%, respectively. The slightly lower yields for substrates at C-6 and C-7 (**1h** and **1m**) may be attributed to electron-withdrawing effects. In general, we investigated the effect of various substituents on 2-amino-4*H*-chromen-4-one in this transformation. Furthermore, the structures of **3a-n** were well characterized by various spectroscopic techniques, including ^{1}H and ^{13}C NMR, and HRMS. We also propose a plausible mechanism for the formation of functionalized chromeno[2,3-*b*]pyrrole-2,3-dicarboxylates **3a-n**, as illustrated in Scheme 1[32].

In summary, we have developed a novel Zn(OTf)$_2$-catalyzed annulation reaction of 2-amino-4*H*-chromen-

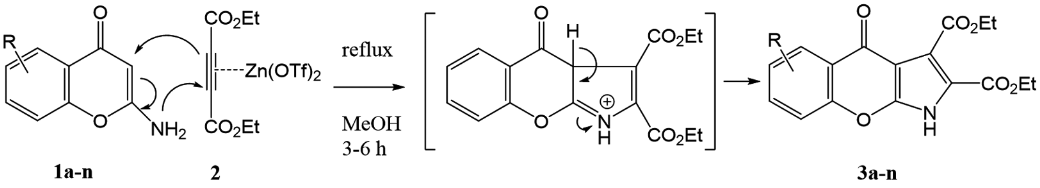
Table 2 — The reaction of 2-amino-4*H*-chromen-4-ones with DEAD



Product **3**	R	Reaction Time (h)	Yield (%)
3a	Ph	4	91
3b	6-Me	3	86
3c	6-Et	3	97
3d	6-MeO	3	96
3e	6-F	5	91
3f	6-Cl	5	84
3g	6-Br	5	77
3h	6-NO_2	6	51
3i	7-Me	5	81
3j	7-Et	4	93
3k	7-MeO	5	92
3l	7-F	5	61
3m	7-NO_2	6	55
3n	7-C_6H_5	5	73

[a] Reaction were carried out 1.0 mmol 2-amino-4*H*-chromen-4-one (**1a-n**) using 4 mmol DEAD and catalyst (30 mol %) in MeOH (20 mL) at refluxed.

[b] Refers to isolated yields after column chromathogrophic purificiation.



Scheme 1 — Reagents condition and mechanism: Zn(OTf)$_2$, MeOH, refluxing 3-6 h

4-one. This reaction represents an extremely effective, practical, and efficient method for constructing chromeno[2,3-b]pyrrole-2,3-dicarboxylates[33-37].

Conclusions

As a conclusion, We have successfully demonstrated the feasibility of annulation reactions for tricyclic chromeno[2,3-*b*]pyrrole derivatives as a new and different method. This methodology is appealing due to the readily accessible starting materials, and the simplicity and application of this transformation are being investigated in our laboratory. Moreover, the methodology for the annulation reaction is the first example of reactions between 2-amino-4*H*-chromen-4-one and electron-deficient acetylenes. This annulation reaction may find applications in drug discovery and natural product synthesis.

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Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

Conflicts of interest

There are no conflicts of interest to declare

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