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Base-mediated hydrolytic cleavage with chain migration of 1-chloromethyl-tetrahydropyrano[3,4-*b*]indoles: an unusual pathway to 2-succinoyl tryptophols

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Abstract—An unusual hydrolytic cleavage with 1,2-alkyl chain migration of 1-chloromethyl-tetrahydropyrano[3,4-*b*]indoles by heating with a limited amount of water and base in DMF is reported. A mechanism for the formation of 1,2-alkyl chain migration products, 2-succinoyl tryptophols, and the ring-expansion products, dihydro-oxepine fused indoles, is reported. No comparable 1,2-chain migration from a structurally related 1-chloromethyl-isochroman is observed.

Chain migration reactions, such as the Beckman rearrangement, pinacol–pinacolone rearrangement, and the alkaline hydrolysis of benzil to benzilic acid, represent an important class of reactions, which has continued to attract the attention of organic chemists. The driving force of such reactions can be explained by the co-existence of neighboring electrophilic- and nucleophilic centers during the chain migration. Many studies have reported the 1,2-alkyl migration of heterocyclic compounds, such as trialkyl(4-pyrodyl)-borates,[1] trialkyl-(1-methoxy methylindol-2-yl)-borates,[1] benzazepines, and piperidines.[2,3] Many related migrations, such as 1,2-sulfur migration,[4] 1,2-germyl group migration,[5] transannular benzoate migration,[6] nitro group migration,[7] the halogen-dance reaction,[8] phenyl group migration,[9] and phenylsulfanyl migration,[10] have also been reported. A theoretical analysis of [1,2] shifts in carbanions was recently reported.[11] Based on molecular orbital considerations, chain migration processes that involve unsaturated groups have been claimed to be favored, since the energy barrier in the transition state is low.[12] Previous accounts from this laboratory have revealed a class of indole ring-assisted ring expansion (1,2-oxygen migration) as well as chain migration reactions during cyanide substitution of tetrahydropyrano[3,4-*b*]indoles (Fig. 1).[13,14] This investigation reports the extension of this work to an anomalous hydrolysis reaction. The 1-chloromethyl-tetrahydropyrano[3,4-*b*]indole **1**, prepared by the Oxa-Pictet-Spengler cyclization reaction,[15] was utilized as the pilot molecule for this investigation. Heating of **1** in DMF that contains a limited amount of H_2O (~300 mol %, ~1.0 % in DMF) and potassium carbonate (~120 mol %) at 105–110 °C provided a chain migration product **2** as the major product, accompanied by a ring-expansion product as the minor product (Scheme 1). Four triplet methylene protons at 3.96, 3.36, 3.33, and 2.80, in the ^{1}H NMR spectrum of **2** indicated the presence of a hydroxyethyl and a succinoyl group. Oxime adducts **4** (or **5**), prepared by heating **2** with excessive amounts (~1200 mol %) of hydroxylamine (or methoxylamine), and confirmed the structure of **2**. Unexpectedly, a minor amount of the dihydrocarboline **5a** was formed as a side product.[16] The ring-expansion side product **3** was characterized by two methylene protons at 3.13 (t) and 4.40 (t) and an olefinic proton at 5.56

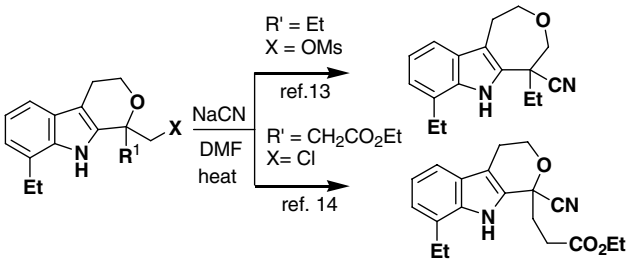

Figure 1. Unusual cynation of the tetrahydropyrano[3,4-*b*]indole derivative.

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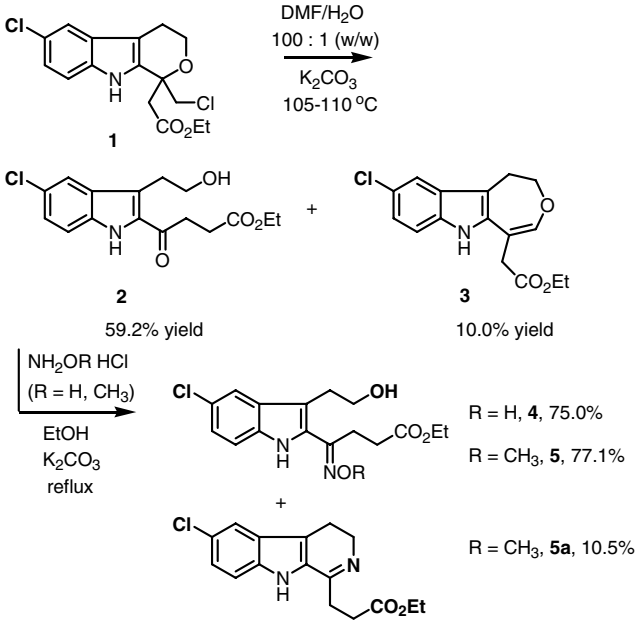
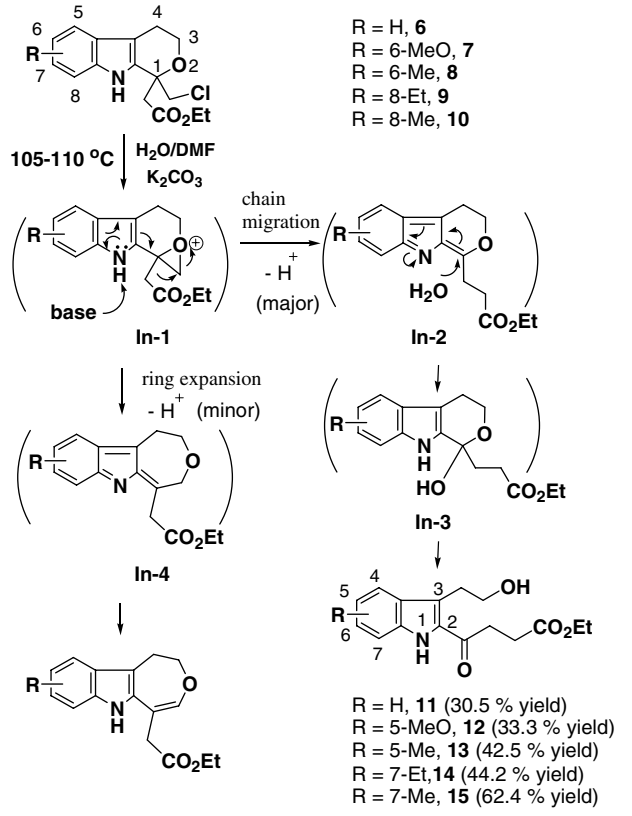


Scheme 1. Hydrolytic cleavage of the 1-chloromethyl-tetrahydropyrano[3,4-*b*]indole **1**.

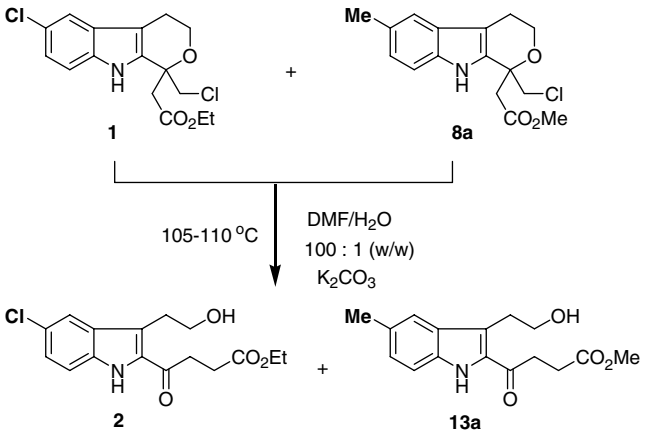
(s) in the ^{1}H NMR spectrum, indicating the presence of dihydro-oxepine ring system. Various nuclear-substituted analogs (**6**–**10**) of **1** were prepared to extend the scope of the reaction.[15] Hydrolysis of these compounds under comparable conditions yielded the corresponding chain migration products (**11**–**15**) as the major products.[17] As presented in Scheme 2, the experimental results can be explained by assuming the initial formation of the strained oxonium ion intermediate **In-1**, followed by a base-assisted migration of $-CH_2CO_2Et$ to provide intermediate **In-2**. Interception of **In-2** by H_2O gave the hemiketal intermediate **In-3**, which spontaneously yielded the 2-succinoyl tryptophols. However deprotonation and isomerization of **In-1** to the strained intermediate **In-4**, which spontaneously yielded the ring-expansion product.

Notably, the base (K_2CO_3) plays an important role in the chain migration reaction, because the reaction does not proceed in the absence of the base. Additionally, a comparison with the ring-expansion pathway (Fig. 1) shows that the chain migration involves the electron withdrawing property of its ester group, which stabilizes the partial negative charge generated during 1,2-alkyl chain migration.

A nonpolar solvent is employed to educe the extent of 1,2-chain migration and improve the yield of the ring-expansion product. Accordingly, heating of the pyranoindole **1** with 200 mol % of DBU in refluxing toluene improved the yield of the ring-expansion product **3** but no 1,2-chain migration product **2** was isolated; however, the yield is low (< 20.0%). The ring expansion does not proceed under a weak basic medium, such as in a refluxing mixture of toluene and pyridine at 110 °C. A crossover experiment supported the intramolecular 1,2-chain migration. As presented in Scheme 3, starting from an



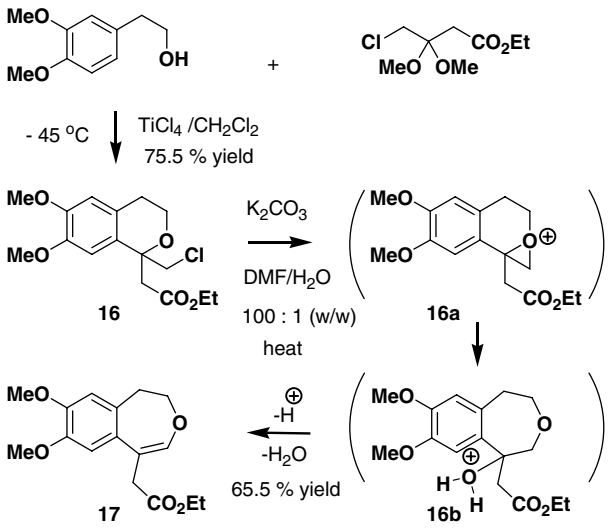
Scheme 2. Proposed mechanism for the chain migration and ring-expansion reactions of 1-chloromethyl-tetrahydropyrano[3,4-*b*]indoles **6**–**10**.



Scheme 3. The crossover experiment for compounds **1** and **8a**.

equal molar mixture of ethyl ester **1** and methyl ester **8a**, the reaction gave the corresponding intramolecular 1,2-chain migration products **2** and **13a**,[18] with no crossover products isolated.

A structurally related 1-chloromethyl-isochroman **16** was synthesized to serve as a control experiment to clarify the role of the indole ring in the chain migration reaction. Hence, the condensation of 3,4-dimethoxyphenethyl alcohol with 4-chloro-3,3-dimethoxy-butyric acid ethyl ester in dichloromethane in the presence of



Scheme 4. Synthesis and hydrolytic cleavage of 1-chloromethyl-isochroman **16**.

$TiCl_4$ afforded **16** in 75.5% yield. Compound **16** was then hydrolyzed under the same conditions as in the indole analogs (Scheme 4). However this reaction only provides ring-expansion product **17** in 65.5% yield,[19] without the formation of the 1,2-alkyl chain migration product. Therefore, the indole ring is critical in chain migration. Possibly, the indole ring is a nucleophilic heterocycle, and with an acidic indolyl NH proton when electron deficiency occurs in its neighborhood, these factors are favorable for chain migration process. In the case of isochroman **16**, there are no such factors as in the case of the tetrahydropyrano[3,4-*b*]indoles. Accordingly, the addition of H_2O to the strained oxonium intermediate **16a** generated the ring-expansion intermediate **16b**, which was dehydrated to form the ring-expansion product **17**.

In conclusion, this investigation demonstrated a novel chain migration reaction of 1-chloromethyl-tetrahydropyrano[3,4-*b*]indoles using a limited amount of water and base in DMF and characterized a plausible mechanism that involves the indole ring. These results were supported by a comparative study.

Acknowledgments

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15. The synthesis of **1** and structurally related 1-chloromethyl-tetrahydropyrano[3,4-*b*]indoles (**6**–**10**) has been described in our earlier article, see Ref. 14.
16. Compound **5a** might be formed by condensation of **5** with in situ generated ammonia formed from decomposition of NH_2OMe or an other pathway, the mechanism is to be verified in the future.
Compound **4**, a white powder, mp 160–161 °C (ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.27 (t, $J = 7.1$ Hz, 3H), 2.91–2.94 (m, 2H), 2.99 (t, $J = 6.7$ Hz, 2H), 3.13 (t, $J = 5.2$ Hz, 2H), 3.99 (t, $J = 5.2$ Hz, 2H), 4.20 (q, $J = 7.1$ Hz, 2H), 7.18 (dd, $J = 8.6$, 1.8 Hz, 1H), 7.37 (d, $J = 8.6$ Hz, 1H), 7.50 (s, 1H), 10.40 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.5 (q), 24.3 (t), 27.2 (t), 30.6 (t), 61.9 (t), 63.7 (t), 113.1 (s), 113.2 (d), 118.8 (d), 123.9 (d), 125.7 (s), 129.4 (s), 133.7 (s), 135.1 (s), 151.3 (s), 176.0 (s); MS (esp) 339.0/341.0 (3/1) (M^++1); Anal. Calcd for $C_{16}H_{19}ClN_2O_4$: C, 56.72; H, 5.65; N, 8.27. Found: C, 56.65; H, 5.79; N, 8.43.
Compound **5**, a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.20 (t, $J = 7.2$ Hz, 3H), 2.81 (t, $J = 6.8$ Hz, 2H), 2.85 (t, $J = 6.8$ Hz, 2H), 3.06 (t, $J = 5.7$ Hz, 2H), 3.86 (t, $J = 5.7$ Hz, 2H), 3.95 (s, 3H), 4.11 (q, $J = 7.2$ Hz, 2H), 7.08 (dd, $J = 8.6$, 1.8 Hz, 1H), 7.24 (d, $J = 8.6$ Hz, 1H), 7.45 (s, 1H), 10.07 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.1 (q), 24.0 (t), 27.7 (t), 30.7 (t), 61.5 (t), 62.5 (q), 63.5 (t), 112.7 (d), 113.5 (s), 118.7 (d), 123.7 (d), 125.3 (s), 129.3 (s), 131.9 (s), 134.7 (s), 151.7 (s), 174.9 (s); MS (esp) 352.0/354.0 (3/1) (M^+), 351.0/353.0 (3/1) (M^+–l); Anal. Calcd for $C_{17}H_{21}ClN_2O_4$: C, 57.87; H, 6.00; N, 7.94. Found: C, 57.75; H, 5.89; N, 7.75.
Compound **5a**, a white powder, mp 164–166 °C (ethyl acetate). ^{1}H NMR (500 MHz, acetone-d_6) δ: 1.21 (t, $J = 7.1$ Hz, 3H), 2.73 (t, $J = 6.2$ Hz, 2H), 3.35 (t, $J = 6.8$ Hz, 2H), 3.39 (t, $J = 6.5$ Hz, 2H), 3.82 (t, $J = 6.2$ Hz, 2H), 4.09 (q, $J = 7.1$ Hz, 2H), 7.27 (dd, $J = 8.7$, 1.8 Hz, 1H), 7.50 (d, $J = 8.7$ Hz, 1H), 7.78 (s, 1H), 10.90 (br s, 1H); ^{13}C NMR (125 MHz, acetone-d_6) δ: 14.9 (q), 28.9 (t), 29.8 (t), 36.3 (t), 61.2 (t), 63.5 (t), 115.2 (d), 120.5 (s), 121.6 (d), 126.3 (s), 127.0 (d), 130.8 (s), 134.7 (s), 136.2 (s), 173.5 (s), 192.7 (s); MS (esp) 305.5/307.5 (3/1) (M^++1); HRMS calcd for $C_{16}H_{18}ClN_2O_2$ (M^++1) 305.1057, found 305.1054; Anal. Calcd for $C_{16}H_{17}ClN_2O_2$: C, 63.05; H, 5.62; N, 9.19. Found: C, 63.34; H, 5.72; N, 9.42.
17. Representative procedure for hydrolytic cleavage of the 1-chloromethyl-tetrahydropyrano[3,4-*b*]indole derivative **1** to yield the chain migration product **2** and the ring-expansion product **3**: To a solution of **1** (1.0 g, 2.9 mmol) in DMF (15.0 g) and H_2O (0.15 g, 8.3 mmol) was added potassium carbonate (0.5 g, 3.6 mmol). The mixture was stirred at 100–110 °C for 2 h. The re-cooled mixture was diluted with an equal volume of ethyl acetate and filtered from Celite. The filtrate was evaporated under vacuum at

below 50 °C to remove solvents. The residue was diluted with ethyl acetate and washed twice with water. The separated organic layer was dried and evaporated. Purification by silica gel column chromatography using 1:4 (v/v) ethyl acetate–hexane provided (3-chloro-5,10-dihydro-6*H*-7-oxa-10-aza-benzo[*a*]azulen-9-yl)-acetic acid ethyl ester **3** (0.09 g, 10.0%) and 4-[5-chloro-3(2-hydroxyethyl)-1*H*-indol-2-yl]-4-oxo-butyric acid ethyl ester **2** (0.57 g, 59.2%).

Compound **3**, a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.29 (t, $J = 7.1$ Hz, 3H), 3.13 (t, $J = 4.7$ Hz, 2H), 3.26 (s, 2H), 4.20 (q, $J = 7.1$ Hz, 2H), 4.40 (t, $J = 4.5$ Hz, 2H), 5.56 (s, 1H), 7.06 (dd, $J = 8.5$, 1.8 Hz, 1H), 7.18 (d, $J = 8.5$ Hz, 1H), 7.39 (s, 1H), 9.13 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.2 (q), 27.6 (t), 42.2 (t), 61.1 (t), 70.1 (t), 98.6 (d), 111.4 (d), 111.7 (s), 117.1 (d), 121.7 (d), 125.2 (d), 129.8 (s), 132.3 (s), 133.5 (s), 153.9 (s), 170.1 (s); MS (esp): 305.5/307.5 (3/1) (M^+); Anal. Calcd for $C_{16}H_{16}ClNO_3$: C, 62.85; H, 5.27; N, 4.58. Found: C, 62.93; H, 5.39; N, 4.55.

Compound **2**, an off-white solid, mp 165–166 °C (ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.28 (t, $J = 7.1$ Hz, 3H), 2.80 (t, $J = 6.4$ Hz, 2H), 3.33 (t, $J = 6.4$ Hz, 2H), 3.36 (t, $J = 6.3$ Hz, 2H), 3.96 (t, $J = 6.3$ Hz, 2H), 4.17 (q, $J = 7.1$ Hz, 2H), 7.30 (dd, $J = 8.6$, 1.7 Hz, 1H), 7.32 (d, $J = 8.7$ Hz, 1H), 7.67 (s, 1H), 9.10 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.6 (q), 28.6 (t), 29.1 (t), 35.5 (t), 61.3 (t), 63.4 (t), 113.7 (d), 119.4 (s), 120.8 (d), 126.6 (s), 127.4 (d), 129.7 (s), 133.9 (s), 134.8 (s), 173.5 (s), 192.1 (s); MS (esp): 324.0/326.0 (3/1) (M^+), 306.0/308.0 (3/1) (M^+-H_2O); Anal. Calcd for $C_{16}H_{18}ClNO_4$: C, 59.35; H, 5.60; N, 4.33. Found: C, 59.53; H, 5.78; N, 4.32.

The *O*-acetate derivative of **2** was prepared in a usual manner (Ac_2O/CH_2Cl_2, pyridine), white powder, mp 152–153 °C (ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.28 (t, $J = 7.2$ Hz, 3H), 2.03 (s, 3H), 2.82 (t, $J = 6.5$ Hz, 2H), 3.33 (t, $J = 6.5$ Hz, 2H), 3.42 (t, $J = 7.2$ Hz, 2H), 4.18 (q, $J = 7.2$ Hz, 2H), 4.34 (t, $J = 7.0$ Hz, 2H), 7.28–7.30 (m, 1H), 7.31–7.33 (m, 1H), 7.69 (s, 1H), 9.08 (br s, 1H); MS (esp) 366.0/368.0 (3/1) (M^++1); Anal. Calcd for $C_{18}H_{20}ClNO_5$: C, 59.10; H, 5.51; N, 3.83. Found: C, 59.08; H, 5.47; N, 3.65. Other related chain migration products (**11**–**15**) were prepared by the representative procedure.

Compound **11**, an off-white solid, mp 117–118 °C (1/2 ethyl acetate–hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.27 (t, $J = 7.2$ Hz, 3H), 2.76 (t, $J = 6.1$ Hz, 2H), 3.31 (t, $J = 6.1$ Hz, 2H), 3.39 (t, $J = 5.9$ Hz, 2H), 3.96 (t, $J = 5.8$ Hz, 2H), 4.16 (q, $J = 7.1$ Hz, 2H), 7.14–7.17 (m, 1H), 7.34 (d, $J = 8.0$ Hz, 1H), 7.35–7.40 (m, 1H), 7.69 (d, $J = 8.1$ Hz, 1H), 9.17 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.5 (q), 28.4 (t), 29.1 (t), 35.4 (t), 61.2 (t), 63.5 (t), 112.6 (d), 120.3 (s), 120.8 (d), 121.4 (d), 126.8 (d), 128.6 (s), 132.7 (s), 136.8 (s), 173.6 (s), 192.2 (s); MS (esp): 290.0 (M^++1), 272.0 (M^+-H_2O); Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.47; H, 6.58; N, 4.79.

Compound **12**, an off-white solid, mp 154–155 °C (1/2 ethyl acetate–hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.27 (t, $J = 7.1$ Hz, 3H), 2.76 (t, $J = 6.5$ Hz, 2H), 3.29 (t, $J = 6.5$ Hz, 2H), 3.35 (t, $J = 6.4$ Hz, 2H), 3.86 (s, 3H), 3.95 (t, $J = 6.4$ Hz, 2H), 4.16 (q, $J = 7.1$ Hz, 2H), 7.01–7.02 (m, 1H), 7.03–7.04 (m, 1H), 7.28 (d, $J = 7.7$ Hz, 1H), 9.09 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.6 (q), 28.6 (t), 29.2 (t), 35.3 (t), 56.1 (q), 61.2 (t), 63.5 (t), 101.2 (d), 113.6 (d), 118.8 (d), 119.5 (s), 129.0 (s), 132.1 (s), 133.2 (s), 155.0 (s), 173.5 (s), 191.8 (s); MS (esp): 302.0 (M^++1), 302.0 (M^+-H_2O); Anal. Calcd for $C_{17}H_{21}NO_5$: C, 63.94; H, 6.63; N, 4.39. Found: C, 66.87; H, 6.59; N, 4.69.

Compound **13**, an off-white solid, mp 138–139 °C (1/2 ethyl acetate–hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.27 (t, $J = 7.2$ Hz, 3H), 2.45 (s, 3H), 2.79 (t, $J = 6.4$ Hz, 2H), 3.33 (t, $J = 6.5$ Hz, 2H), 3.39 (t, $J = 6.4$ Hz, 2H), 3.97 (t, $J = 6.4$ Hz, 2H), 4.17 (q, $J = 7.1$ Hz, 2H), 7.19 (d, $J = 8.6$ Hz, 1H), 7.28 (d, $J = 8.4$ Hz, 1H), 7.47 (s, 1H), 8.95 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.6 (q), 21.9 (q), 28.5 (t), 29.1 (t), 35.3 (t), 61.2 (t), 63.6 (t), 112.4 (d), 119.8 (s), 120.6 (d), 128.8 (s), 128.9 (d), 130.2 (s), 132.9 (s), 135.3 (s), 173.6 (s), 192.1 (s); MS (esp): 326.0 (M^++Na); Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.45; H, 6.79; N, 4.65.

Compound **14**, a yellow oil. ^{1}H NMR (500 MHz, acetone-d_6) δ: 1.26 (t, $J = 6.9$ Hz, 3H), 1.34 (t, $J = 7.6$ Hz, 3H), 2.77 (t, $J = 6.4$ Hz, 2H), 2.84 (q, $J = 7.5$ Hz, 2H), 3.35 (t, $J = 6.5$ Hz, 2H), 3.39 (d, $J = 6.5$ Hz, 2H), 3.95 (t, $J = 6.4$ Hz, 2H), 4.15 (q, $J = 7.0$ Hz, 2H), 7.08–7.11 (m, 1H), 7.16 (d, $J = 7.0$ Hz, 1H), 7.53 (d, $J = 8.0$ Hz, 1H), 9.08 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.1 (q), 14.6 (q), 24.2 (t), 28.6 (t), 29.5 (t), 35.5 (t), 61.2 (t), 63.5 (t), 119.1 (d), 120.7 (s), 121.3 (d), 125.1 (d), 128.1 (s), 128.6 (s), 132.7 (s), 135.8 (s), 173.7 (s), 192.2 (s); MS (esp): 318.5 (M^++1); Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 68.24; H, 7.42; N, 4.62.

Compound **15**, an off-white solid, mp 114–116 °C (1/2 ethyl acetate–hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.28 (t, $J = 7.1$ Hz, 3H), 2.49 (s, 3H), 2.80 (t, $J = 6.4$ Hz, 2H), 3.36 (t, $J = 6.4$ Hz, 2H), 3.41 (t, $J = 6.4$ Hz, 2H), 3.97 (t, $J = 6.4$ Hz, 2H), 4.17 (q, $J = 7.1$ Hz, 2H), 7.06–7.09 (m, 1H), 7.15 (d, $J = 6.9$ Hz, 1H), 7.54 (d, $J = 8.1$ Hz, 1H), 9.00 (br s, 1H); ^{13}C NMR (125 MHz, acetone-d_6) δ: 15.0 (q), 17.5 (q), 29.0 (t), 30.7 (t), 36.3 (t), 61.3 (t), 63.7 (t), 119.8 (d), 121.5 (s), 121.6 (d), 123.1 (s), 127.3 (d), 129.5 (s), 133.6 (s), 137.6 (s), 173.8 (s), 192.7 (s); MS (esp): 326.0 (M^++Na); Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H; 6.98, N, 4.62. Found: C, 67.48; H, 6.85; N, 4.57.

18. Compound **13a**, an off-white solid, mp 126–127 °C (1/2 ethyl acetate–hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.45 (s, 3H), 2.80 (t, $J = 6.5$ Hz, 2H), 3.34 (t, $J = 6.5$ Hz, 2H), 3.39 (t, $J = 6.4$ Hz, 2H), 3.72 (s, 3H), 3.97 (t, $J = 6.4$ Hz, 2H), 7.19 (d, $J = 8.4$ Hz, 1H), 7.28 (d, $J = 8.4$ Hz, 1H), 7.47 (s, 1H), 8.94 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.9 (q), 28.2 (t), 29.1 (t), 35.3 (t), 52.3 (q), 63.6 (t), 112.3 (d), 119.8 (s), 120.6 (d), 128.8 (s), 129.0 (d), 130.3 (s), 132.9 (s), 135.2 (s), 174.0 (s), 191.9 (s); LC/MS (esp): 290.5 (M^++1); Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.51; H, 6.78; N, 4.79.
19. Compound **16**, a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.19 (t, $J = 7.2$ Hz, 3H), 2.77, 2.99 (ABq, $J = 4.9$ Hz, 2H), 3.84 (s, 3H), 3.86 (s, 3H), 3.93–3.98 (m, 2H), 3.98–4.03 (m, 2H), 4.06 (q, $J = 7.2$ Hz, 2H), 6.61 (s, 1H), 6.63 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.5 (q), 28.9 (t), 43.8 (t), 51.1 (t), 56.2 (q), 56.5 (q), 60.9 (t), 66.2 (s), 76.7 (t), 108.8 (d), 111.8 (d), 127.6 (s), 128.4 (s), 147.9 (s), 148.7 (s), 170.1 (s); MS (esp): 329.0/331.0 (3/1) (M^++1); Anal. Calcd for $C_{16}H_{21}ClO_5$: C, 58.45; H, 6.44. Found: C, 58.61; H, 6.62.

Compound **17**, a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.27 (t, $J = 7.1$ Hz, 3H), 3.07 (t, $J = 4.1$ Hz, 2H), 3.21 (s, 2H), 3.84 (s, 3H), 3.85 (s, 3H), 4.19 (q, $J = 7.1$ Hz, 2H), 4.30 (t, $J = 4.1$ Hz, 2H), 5.40 (s, 1H), 6.56 (s, 1H), 6.60 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.3 (q), 38.2 (t), 43.0 (t), 56.0 (q), 56.1 (q), 61.0 (t), 69.9 (t), 105.2 (d), 112.4 (d), 112.9 (d), 127.3 (s), 131.5 (s), 146.6 (s), 147.2 (s), 149.2 (s), 170.7 (s); MS (esp): 293.3 (M^++1); Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.71; H, 6.82.