

Thermal [3+2] Cycloaddition of Aromatic Azomethine Imines with Allenoates

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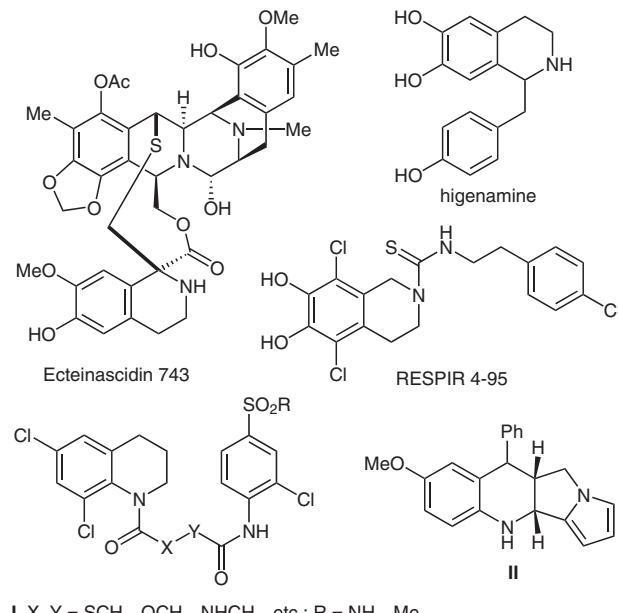
Abstract: The thermal [3+2] cycloadditions of two classes of aromatic azomethine imines with allenotes have been investigated. The reactions are operationally simple and proceed smoothly under mild reaction conditions to provide a variety of dinitrogen-fused heterocycles in moderate to excellent yields.

Key words: cycloaddition, azomethine imine, allenate, quinoline, isoquinoline

Quinoline, isoquinoline and structurally related heterocycles occur widely in nature and some have a broad range of clinical applications, exhibiting a wide range of biological activities such as antitumor, anti-HIV, antibiotic, antifungal, antivirus, anti-inflammatory, anticoagulation, and bronchodilation, and can also act on the central nervous system.¹ For example, Ecteinascidin 743 (Yondelis, trabectedin; Figure 1) is a new antitumor agent of marine origin discovered in the Caribbean tunicate Ecteinascidia turbinata for the treatment of soft tissue sarcoma and ovarian cancer.² Phase II trials with Yondelis are also being carried out for breast cancer, lung cancer, prostate cancer, and for paediatric tumors. Higenamine³ and RESPIR 4-95⁴ (Figure 1) display anticoagulation and bronchodilation activities, respectively. Compounds **I** (Figure 1) are potent nonnucleoside, allosteric inhibitors of reverse transcriptase, and could interact with retroviral targets relevant to anti-HIV therapy.⁵ The tetrahydroquinoline derivative **II** shows activity against antibacterial targets such as DNA gyrase.⁶ Accordingly, the synthesis of quinoline and isoquinoline derivatives has attracted much attention.⁷ However, although many synthetic methods have been developed,⁷ new procedures for their synthesis would still be highly desirable.

Azomethine imines have emerged as a versatile 1,3-dipole for various thermal, metal-catalyzed, and organocatalytic 1,3-dipolar cycloaddition reactions and have been extensively applied in organic synthesis because of their easy accessibility, stability and the potential applications of the corresponding cycloadducts.^{8,9} The range of azomethine imines available for the cycloaddition reactions has been expanded to include various imines such as 3-oxopyrazolidin-1-iium-2-ide derivatives and benzoyl(3,4-dihydroisoquinolin-2-iium-2-yl)amides, but research on aromatic azomethine imines is somewhat limited.^{9z,10} Recently, we successfully developed [3+2], [3+3], [4+3],

and [3+2+3] annulation reactions of azomethine imines with allenotes, affording facile access to dinitrogen-fused bicyclic or tricyclic heterocycles,¹¹ which are key units in or building blocks of many pharmaceuticals, agrochemicals, biologically active compounds, and other useful chemicals.¹² As part of our continuing efforts to develop the annulation reaction of azomethine imines,¹¹ we recently investigated the reactions of aromatic azomethine imines with allenotes. Herein, we present our results on the thermal [3+2] cycloaddition of aromatic azomethine imines with allenotes to furnish functionalized dinitrogen-fused tricyclic heterocycles.

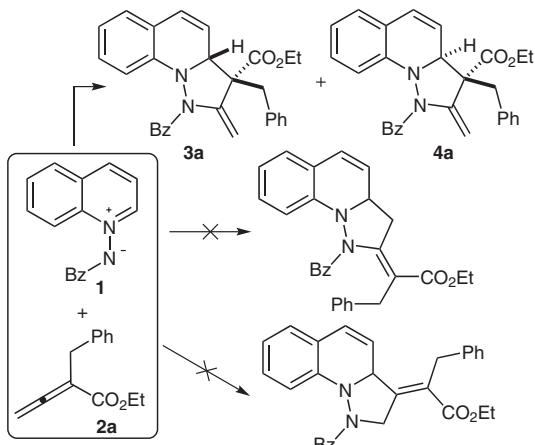


I, X-Y = SCH₂, OCH₂, NHCH₂, etc.; R = NH₂, Me

Figure 1 Pharmaceutically active quinoline and isoquinoline-related derivatives

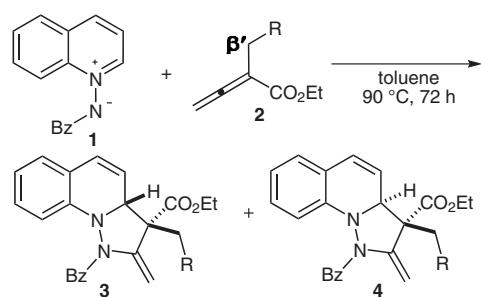
The azomethine imines **1**, **8** and **13** were easily prepared according to reported procedures.¹³ In initial attempts, azomethine imine **1** was treated with the allenate **2a** in dichloromethane at room temperature for 96 hours (Scheme 1). The reaction worked sluggishly, and two new products were isolated in total 20% yield. When the reaction was carried out in toluene at room temperature for 96 hours, the same two products were obtained in poor yield (5%) due to the poor solubility of azomethine imine **1** in toluene. To increase the yield, the reaction was carried out in refluxing toluene. Under these conditions the azomethine imine was completely converted in 72 hours to give the product in 70% yield. However, several side-

products were observed in small amounts. Decreasing the reaction temperature to 90 °C resulted in a clean reaction and improved yield (89%). The two products could be separated by silica gel chromatography, and were determined to be [3+2] cycloaddition products **3a** and **4a** (Scheme 1), on the basis of 2D NMR spectroscopic and X-ray crystallographic¹⁴ analyses (Figure 2). In principle, since both active double bonds in allenolate could undergo the cycloaddition reaction with azomethine imine, three kinds of cycloadducts could be produced in the reaction, but the reaction was highly regioselective and produced the *2-exo* methylene isomer as the sole regioisomer, which possessed two chiral carbons (Scheme 1). It is noteworthy that an interesting quaternary carbon center was incorporated into the molecular skeleton of the products **3a** and **4a**.



Scheme 1 The thermal cycloaddition of azomethine imine **1** with ethyl α -substituted allenate **2a**

Table 1 Thermal Cycloaddition of Azomethine Imine **1** with α -Substituted Allenotes **2**^a



Entry	R	Product	Yield (%) ^b	Ratio 3/4 ^c
1	Ph (2a)	3a + 4a	89	53:47
2	2-MeC ₆ H ₄ (2b)	3b + 4b	96	41:59
3	3-MeC ₆ H ₄ (2c)	3c + 4c	81	52:48
4	4-MeC ₆ H ₄ (2d)	3d + 4d	79	57:43
5	2-FC ₆ H ₄ (2e)	3e + 4e	94	49:51
6	3-FC ₆ H ₄ (2f)	3f + 4f	86	57:43
7	4-FC ₆ H ₄ (2g)	3g + 4g	82	52:48
8	2-ClC ₆ H ₄ (2h)	3h + 4h	91	40:60
9	3-ClC ₆ H ₄ (2i)	3i + 4i	68	40:60
10	4-ClC ₆ H ₄ (2j)	3j + 4j	65	60:40
11	2-BrC ₆ H ₄ (2k)	3k + 4k	73	45:55
12	3-BrC ₆ H ₄ (2l)	3l + 4l	70	53:47
13	CO ₂ Et (2m)	3m + 4m	86	74:26 ^d

^a 1.2 equivalent of allenate was used.

^b Isolated yields.

^c Based on isolated yield unless otherwise stated.

^d Based on integration of signals in the ¹H NMR spectrum.

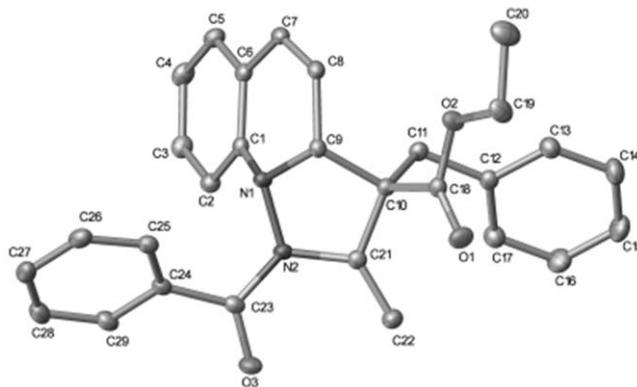
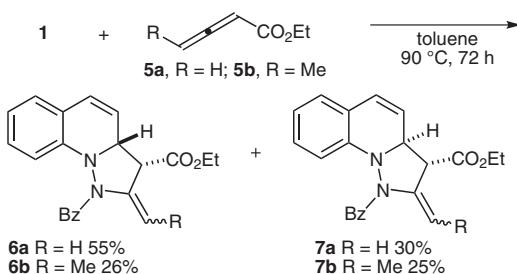


Figure 2 The X-ray crystal structure of **4a**

With the optimal reaction conditions in hand (toluene, 90 °C), azomethine imine **1** was treated with various substituted allenotes **2** in toluene for 72 hours, giving the functionalized dinitrogen-fused tricyclic heterocycles **3** and **4** in moderate to excellent yields, albeit with poor diastereoselectivity (Table 1, entries 1–13). Although poor

diastereoselectivities were obtained, both diastereomers could be separated, providing diverse heterocycles for medicinal chemistry. The allenotes with electron-withdrawing substituents in the aryl group worked as well as those allenotes with electron-donating substituents in the aryl group under otherwise identical conditions (entries 1–12), and the derivatives of ethyl 1-benzoyl-2-methylene-1,2,3,3a-tetrahydropyrazolo[1,5-*a*]quinoline-3-carboxylate could be obtained in 65–96% yield. The highest yield (96%) was achieved in the cycloaddition of β' -2-MeC₆H₄ substituted allenote (entry 2). Although the R substituent in allenote is some distance away from the active double bond, it seems that the position of R relative to the β' -position of allenote has an influence on the yield. In general, in comparison with allenotes with *meta*- and *para*-substituents in the aryl group, allenotes with *ortho*-substituents in the aryl group underwent the reaction in higher yields (entries 2, 5, 8, and 11). The β' -ethoxycarbonyl allenote was active and smoothly partic-

ipated in the cycloaddition to give the expected cycloadduct in 86% yield (entry 13), and ethyl buta-2,3-dienoate (**5a**) also worked efficiently to give the cycloadducts in 85% yield (Scheme 2). Unfortunately, the reaction with γ -substituted allenolate **5b** was more sluggish and afforded the cycloadduct in moderate yield (Scheme 2).



Scheme 2 Thermal cycloaddition of azomethine imine **1** with ethyl buta-2,3-dienoate (**5a**) and γ -substituted allenolate (**5b**)

Table 2 Thermal Cycloaddition of Azomethine Imine **8** with α -Substituted Allenoates **2^a**

Entry	R	Product	Yield (%) ^b	Ratio 9/10 ^c
1	Ph (2a)	9a + 10a	71	41:59
2	2-MeC ₆ H ₄ (2b)	9b + 10b	50	72:28 ^d
3	3-MeC ₆ H ₄ (2c)	9c + 10c	75	40:60 ^d
4	2-FC ₆ H ₄ (2e)	9e + 10e	98	52:48
5	3-FC ₆ H ₄ (2f)	9f + 10f	61	23:77
6	4-FC ₆ H ₄ (2g)	9g + 10g	71	32:68
7	2-ClC ₆ H ₄ (2h)	9h + 10h	72	51:49
8	3-ClC ₆ H ₄ (2i)	9i + 10i	66	35:65
9	3-BrC ₆ H ₄ (2l)	9l + 10l	76	41:59
10	CO ₂ Et (2m)	9m + 10m	86	37:63

^a 1.2 equivalent of allenolate was used.

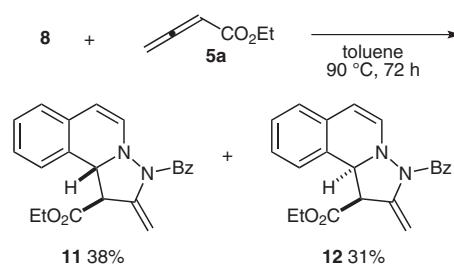
^b Isolated yield.

^c Based on isolated yield unless otherwise stated.

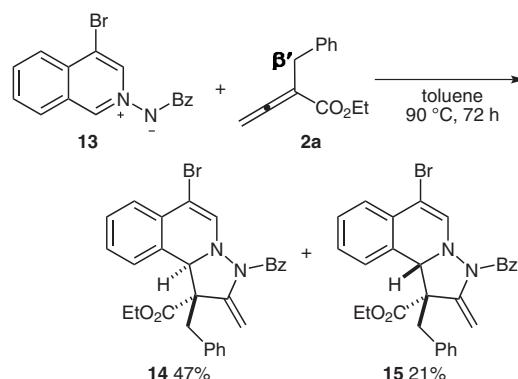
^d Based on integration of signals in the ¹H NMR spectrum.

Having investigated the reactions of aromatic azomethine imine **1**, based on the dihydroquinoline structure, with allenoates, we then explored the reaction of aromatic azomethine imine **8**, based on dihydroisoquinoline structure, with allenoates (Table 2). We were pleased to find that imine **8** was also active. A wide range of aryl groups with

electron-donating or withdrawing substituents at the β' -position of the allenolate could be tolerated in the cycloaddition. The reactions were carried out in toluene at 90 °C for 72 hours to afford derivatives of ethyl 3-benzoyl-2-methylene-1,2,3,10b-tetrahydropyrazolo[5,1-*a*]isoquinoline-1-carboxylate in 50–98% yields with moderate diastereoselectivities (entries 1–10). Fortunately, most diastereomeric mixtures could be separated by using flash column chromatography. However, the diastereomeric mixtures obtained from the reaction of imine **8** with either allenolate **2b** or **2c** could not be separated by flash column chromatography, and the diastereomeric ratios were determined by NMR spectroscopic analysis. In contrast to reactions with azomethine imine **1**, the influence of the position of the R substituent relative to the β' -position of the allenolate on the yields were not clear (entries 2, 3 vs 4–8). Ethyl buta-2,3-dienoate (**5a**) also smoothly underwent the cycloaddition reactions, affording the corresponding cycloadduct in good yield (Scheme 3). Azomethine imine **13**, which is an analogue of **8**, underwent the reaction to produce the desired product in 68% yield with a diastereomeric ratio of around 2:1 (Scheme 4).



Scheme 3 Thermal cycloaddition of azomethine imine **8** with ethyl buta-2,3-dienoate (**5a**)



Scheme 4 Thermal cycloaddition of azomethine imine **13** with ethyl 2-benzylbuta-2,3-dienoate (**2a**)

In summary, thermal [3+2] cycloaddition reactions of aromatic azomethine imines with allenoates have been developed; the reactions were performed in toluene at 90 °C to give the functionalized dinitrogen-fused tricyclic heterocycles, which are pharmaceutically important compounds. The desired products were obtained in moderate to excellent yields. The reaction is operationally simple

and works efficiently, thus it is a potentially useful protocol for the synthesis of biologically active molecules.

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Organic solutions were concentrated under reduced pressure using a rotary evaporator or oil pump. Reactions were monitored by thin-layer chromatography (TLC) on silica gel precoated glass plates; chromatograms were visualized by fluorescence quenching under UV light at 254 nm. Flash column chromatography was performed with Qingdao Haiyang flash silica gel (200–300 mesh). Infrared spectra were recorded with a Bruker Optics TENSOR 27 instrument. ¹H and ¹³C NMR spectra were recorded with a Bruker-300 spectrometer. Accurate mass measurements were performed with an Agilent instrument using the ESI-MS technique. X-ray crystallographic data were collected with a Bruker SMART CCD-based diffractometer equipped with a low-temperature apparatus operated at 100 K.

[3+2] Annulation of Azomethine Imines with Allenoates; General Procedure

A mixture of azomethine imine (0.125 mmol) and allenolate (0.15 mmol) in toluene (5 mL) was stirred at 90 °C for 72 h and then concentrated. The residue was purified by flash column chromatography (EtOAc–hexane) to afford the corresponding product. Some annulation products (**3m** and **4m** in Table 1; **9b** and **10b**, **9c** and **10c** in Table 2) were obtained as diastereomeric mixtures that could not be separated by flash silica gel column chromatography; in these cases the NMR spectra, the IR data, and HRMS data were collected for the diastereomeric mixture. Melting points are reported for crystalline solids but were not measured for amorphous solids.

Compound 3a

Yield: 26.7 mg (47%); white crystalline solid; mp 132.6–134.5 °C.

IR (film): 2979, 1722, 1666, 1599, 1484, 1454, 1339, 1292, 1261, 1222, 1187, 1095, 1079, 1043, 1009, 861, 773, 756, 738, 699, 653, 628 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.39–7.26 (m, 8 H), 7.20–7.18 (m, 2 H), 7.00–6.90 (m, 1 H), 6.78–6.70 (m, 1 H), 6.68–6.62 (m, 2 H), 6.32 (d, *J* = 9.8 Hz, 1 H), 6.06 (d, *J* = 1.4 Hz, 1 H), 5.42–5.40 (m, 1 H), 5.01 (d, *J* = 1.5 Hz, 1 H), 4.45–4.43 (m, 1 H), 3.88–3.83 (m, 1 H), 3.57–3.35 (m, 2 H), 3.24 (d, *J* = 14.3 Hz, 1 H), 0.60 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.3, 169.7, 143.8, 143.7, 135.8, 134.6, 130.8, 130.6, 129.5, 128.5, 127.7, 127.6, 127.40, 127.36, 126.8, 121.2, 120.9, 118.7, 111.8, 100.6, 64.6, 62.6, 61.3, 40.3, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₇N₂O₃: 451.2016; found: 451.2017.

Compound 3b

Yield: 22.83 mg (39%); white crystalline solid; mp 164.2–165.6 °C.

IR (film): 3122, 3031, 2963, 2934, 1720, 1673, 1645, 1599, 1578, 1485, 1456, 1447, 1403, 1368, 1335, 1294, 1263, 1233, 1217, 1191, 1179, 1159, 1109, 1088, 1074, 1018, 956, 931, 914, 883, 863, 835, 795, 779, 758, 726, 702, 661, 631, 601, 562, 531, 520, 462 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.55–7.43 (m, 1 H), 7.36–6.97 (m, 9 H), 6.79–6.77 (m, 1 H), 6.76–6.58 (m, 2 H), 6.33 (d, *J* = 10.0 Hz, 1 H), 6.05 (d, *J* = 1.4 Hz, 1 H), 5.56–5.53 (m, 1 H), 5.03 (d, *J* = 1.5 Hz, 1 H), 4.29–4.27 (m, 1 H), 3.91–3.86 (m, 1 H), 3.68 (d, *J* = 14.7 Hz, 1 H), 3.49–3.46 (m, 1 H), 3.22 (d, *J* = 14.7 Hz, 1 H), 2.39 (s, 3 H), 0.60 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.6, 169.6, 144.1, 143.8, 137.4, 134.6, 134.3, 130.54, 130.51, 130.3, 129.6, 127.7, 127.6, 127.3, 127.2, 126.8, 126.4, 121.2, 120.9, 119.2, 111.8, 101.2, 65.2, 62.7, 61.3, 35.9, 20.5, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₃₀H₂₉N₂O₃: 465.2173; found: 465.2184.

Compound 3c

Yield: 24.2 mg (42%); white solid.

IR (film): 3025, 2978, 2924, 1727, 1671, 1647, 1600, 1578, 1485, 1455, 1446, 1403, 1368, 1344, 1294, 1262, 1224, 1188, 1160, 1096, 1049, 1026, 1016, 862, 794, 785, 771, 751 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.37–7.26 (m, 3 H), 7.19–7.13 (m, 5 H), 7.12–6.93 (m, 2 H), 6.78–6.75 (m, 1 H), 6.74–6.57 (m, 2 H), 6.32 (d, *J* = 10.0 Hz, 1 H), 6.03 (d, *J* = 11.9 Hz, 1 H), 5.45–5.42 (m, 1 H), 5.03 (d, *J* = 1.5 Hz, 1 H), 4.45–4.43 (m, 1 H), 3.89–3.85 (m, 1 H), 3.56–3.35 (m, 2 H), 3.21 (d, *J* = 14.3 Hz, 1 H), 2.30 (s, 3 H), 0.60 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.3, 169.7, 143.8, 138.2, 135.7, 134.7, 131.3, 130.5, 129.5, 128.4, 128.1, 127.8, 127.7, 127.6, 127.3, 126.7, 121.2, 120.8, 118.8, 111.8, 100.5, 64.5, 62.5, 61.3, 40.2, 21.3, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₃₀H₂₉N₂O₃: 465.2173; found: 465.2174.

Compound 3d

Yield: 26 mg (45%); white crystalline solid; mp 163.4–165.4 °C.

IR (film): 3064, 3029, 2960, 2923, 1721, 1671, 1645, 1601, 1516, 1484, 1448, 1405, 1374, 1348, 1293, 1263, 1228, 1187, 1112, 1093, 1048, 1025, 1009, 874, 790, 772, 753, 694 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.39–7.15 (m, 7 H), 7.10 (d, *J* = 7.9 Hz, 2 H), 7.00 (m, 1 H), 6.78–6.76 (m, 1 H), 6.67–6.63 (m, 2 H), 6.31 (d, *J* = 10.0 Hz, 1 H), 6.13–5.95 (m, 1 H), 5.42–5.39 (m, 1 H), 5.01 (d, *J* = 4.2 Hz, 1 H), 4.46–4.45 (m, 1 H), 3.88–3.82 (m, 1 H), 3.59–3.34 (m, 2 H), 3.20 (d, *J* = 14.2 Hz, 1 H), 2.30 (s, 3 H), 0.60 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.3, 169.7, 143.8, 143.8, 136.9, 134.7, 132.6, 130.62, 130.57, 129.5, 129.1, 127.7, 127.6, 127.4, 126.7, 121.2, 120.8, 118.8, 111.8, 100.4, 64.6, 62.6, 61.2, 39.9, 21.0, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₃₀H₂₉N₂O₃: 465.2173; found: 465.2165.

Compound 3e

Yield: 27.3 mg (46%); white crystalline solid; mp 156.8–158.6 °C.

IR (film): 3070, 3029, 2980, 2936, 2902, 1726, 1674, 1644, 1601, 1484, 1453, 1401, 1351, 1315, 1291, 1263, 1227, 1186, 1176, 1168, 1152, 1110, 1092, 1046, 1020, 1006, 875, 793, 773, 753, 736, 697, 658, 527 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.48–7.46 (m, 1 H), 7.36–7.14 (m, 6 H), 7.14–6.94 (m, 3 H), 6.79–6.77 (m, 1 H), 6.68–6.62 (m, 2 H), 6.34 (d, *J* = 10.0 Hz, 1 H), 6.07 (d, *J* = 1.1 Hz, 1 H), 5.62–5.59 (m, 1 H), 5.09 (d, *J* = 1.5 Hz, 1 H), 4.35 (d, *J* = 4.9 Hz, 1 H), 3.90–3.85 (m, 1 H), 3.77 (d, *J* = 14.3 Hz, 1 H), 3.46–3.41 (m, 1 H), 3.03–3.01 (m, 1 H), 0.60 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.2, 169.7, 161.7 (d, *J* = 244.3 Hz), 143.8, 143.5, 134.6, 132.7 (d, *J* = 3.7 Hz), 130.6, 129.5, 129.2 (d, *J* = 8.3 Hz), 127.71, 127.66, 127.2, 126.8, 124.4 (d, *J* = 3.5 Hz), 122.7 (d, *J* = 14.5 Hz), 121.2, 120.9, 119.0, 115.1 (d, *J* = 23.0 Hz), 111.7, 100.3, 64.5, 62.5, 61.4, 31.7, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃: 469.1922; found: 469.1929.

Compound 3f

Yield: 28.8 mg (49%); white solid.

IR (film): 3065, 2964, 2927, 1726, 1671, 1646, 1600, 1577, 1485, 1471, 1455, 1446, 1401, 1367, 1345, 1310, 1292, 1261, 1225, 1187, 1092, 1027, 928, 876, 795, 757, 732, 699, 664, 655, 633, 527, 488, 463 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.64–7.50 (m, 2 H), 7.35–7.14 (m, 6 H), 7.10–7.09 (m, 1 H), 7.05–6.94 (m, 1 H), 6.79–6.77 (m, 1 H), 6.68–6.62 (m, 2 H), 6.31 (d, *J* = 10.0 Hz, 1 H), 6.09 (d, *J* = 1.3 Hz, 1 H), 5.73–5.70 (m, 1 H), 5.12 (d, *J* = 1.5 Hz, 1 H), 4.39–4.38 (m, 1 H), 4.04 (d, *J* = 14.5 Hz, 1 H), 3.93–3.70 (m, 1 H), 3.51–3.48 (m, 1 H), 3.26 (d, *J* = 14.6 Hz, 1 H), 0.60 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.2, 169.5, 144.1, 143.8, 135.5, 134.5, 132.9, 132.1, 130.6, 129.5, 129.0, 127.8, 127.7, 127.5, 127.2, 126.8, 121.3, 120.9, 119.7, 111.7, 101.0, 65.1, 62.1, 61.4, 38.8, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃⁺: 469.1922; found: 469.1914.

Compound 3g

Yield: 25.3 mg (43%); white crystalline solid; mp 134.0–135.5 °C.

IR (film): 2963, 2925, 1727, 1669, 1601, 1578, 1510, 1485, 1455, 1446, 1403, 1368, 1346, 1261, 1222, 1188, 1160, 1103, 1050, 1017, 862, 839, 828, 794, 751 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.47–7.38 (m, 2 H), 7.38–7.28 (m, 3 H), 7.28–7.16 (m, 2 H), 7.08–6.92 (m, 3 H), 6.86–6.59 (m, 3 H), 6.33 (d, *J* = 10.0 Hz, 1 H), 6.04 (d, *J* = 1.4 Hz, 1 H), 5.40–5.38 (m, 1 H), 4.95 (d, *J* = 1.5 Hz, 1 H), 4.41–4.40 (m, 1 H), 3.88–3.85 (m, 1 H), 3.54–3.35 (m, 2 H), 3.21 (d, *J* = 14.3 Hz, 1 H), 0.59 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.1, 169.6, 162.2 (d, *J* = 246.3 Hz), 143.7, 143.6, 134.4, 132.3 (d, *J* = 7.9 Hz), 131.5 (d, *J* = 3.3 Hz), 130.8, 129.6, 127.8, 127.6, 126.8, 121.2, 121.0, 118.6, 115.3 (d, *J* = 21.0 Hz), 111.9, 101.0, 64.6, 63.1, 61.3, 39.7, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃⁺: 469.1922; found: 469.1915.

Compound 3h

Yield: 22.1 mg (36%); white crystalline solid; mp 185.7–187.1 °C.

IR (film): 3071, 3030, 2964, 2928, 2899, 1725, 1670, 1643, 1601, 1483, 1473, 1447, 1401, 1373, 1351, 1311, 1291, 1263, 1225, 1186, 1155, 1110, 1094, 1081, 1046, 1018, 877, 827, 793, 775, 757, 733, 695, 657, 631, 463 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.63–7.61 (m, 1 H), 7.48–7.38 (m, 1 H), 7.35–7.24 (m, 1 H), 7.24–7.14 (m, 6 H), 7.07–6.94 (m, 1 H), 6.86–6.56 (m, 3 H), 6.32 (d, *J* = 10.0 Hz, 1 H), 6.09 (d, *J* = 1.2 Hz, 1 H), 5.70–5.68 (m, 1 H), 5.13 (d, *J* = 1.5 Hz, 1 H), 4.34–4.32 (m, 1 H), 4.03 (d, *J* = 14.5 Hz, 1 H), 3.92–3.89 (m, 1 H), 3.50–3.47 (m, 1 H), 3.18 (d, *J* = 14.5 Hz, 1 H), 0.60 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.2, 169.6, 143.9, 143.8, 135.8, 134.5, 133.6, 132.2, 130.5, 129.5, 129.4, 128.8, 127.7, 127.5, 127.2, 127.1, 126.7, 121.2, 120.9, 119.4, 111.7, 100.9, 65.0, 62.0, 61.4, 35.9, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1621.

Compound 3i

Yield: 16.2 mg (27%); white solid.

IR (film): 3058, 3024, 2978, 2964, 2933, 2902, 1726, 1669, 1599, 1575, 1485, 1455, 1446, 1402, 1368, 1344, 1312, 1295, 1262, 1225, 1188, 1095, 1049, 1017, 883, 863, 786, 751, 725, 695, 671, 662, 650, 638, 629, 617, 605 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.48–7.40 (m, 2 H), 7.40–7.17 (m, 7 H), 7.08–6.95 (m, 1 H), 6.81–6.79 (m, 1 H), 6.70–6.66 (m, 2 H), 6.35 (d, *J* = 10.0 Hz, 1 H), 6.03 (d, *J* = 1.5 Hz, 1 H), 5.41–5.38 (m, 1 H), 4.96 (d, *J* = 1.6 Hz, 1 H), 4.42–4.40 (m, 1 H), 3.89–3.86 (m, 1 H), 3.57–3.34 (m, 2 H), 3.21 (d, *J* = 14.2 Hz, 1 H), 0.61 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.0, 169.6, 143.7, 143.5, 137.9, 134.4, 134.3, 130.85, 130.79, 129.7, 129.6, 128.9, 127.9, 127.8,

127.6, 126.8, 121.2, 121.0, 118.5, 111.9, 101.1, 64.4, 63.2, 61.4, 40.2, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1624.

Compound 3j

Yield: 23.5 mg (39%); white crystalline solid; mp 155.9–157.2 °C.

IR (film): 2980, 2347, 1726, 1670, 1600, 1578, 1486, 1455, 1446, 1403, 1368, 1344, 1294, 1261, 1224, 1183, 1094, 1046, 1016, 909, 866, 840, 753, 697, 650, 528, 464 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.49–7.39 (m, 2 H), 7.39–7.18 (m, 7 H), 7.09–6.96 (m, 1 H), 6.80–6.77 (m, 1 H), 6.76–6.63 (m, 2 H), 6.34 (d, *J* = 10.0 Hz, 1 H), 6.04 (d, *J* = 1.5 Hz, 1 H), 5.40–5.38 (m, 1 H), 4.95 (d, *J* = 1.5 Hz, 1 H), 4.39–4.38 (m, 1 H), 3.88–3.85 (m, 1 H), 3.52–3.42 (m, 1 H), 3.38 (d, *J* = 14.2 Hz, 1 H), 3.21 (d, *J* = 14.2 Hz, 1 H), 0.59 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.0, 169.7, 143.7, 143.5, 134.33, 134.29, 133.4, 132.2, 130.8, 129.6, 128.6, 127.85, 127.81, 127.6, 126.8, 121.2, 121.0, 118.5, 111.9, 101.2, 64.5, 63.2, 61.4, 39.9, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1605.

Compound 3k

Yield: 21.72 mg (33%); white crystalline solid; mp 192.4–193.9 °C.

IR (film): 3064, 2984, 2936, 2902, 1727, 1673, 1645, 1600, 1578, 1485, 1471, 1455, 1446, 1401, 1368, 1345, 1310, 1292, 1261, 1224, 1187, 1110, 1090, 1044, 1027, 1010, 929, 909, 866, 827, 756, 732, 698, 655, 634 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.64–7.50 (m, 2 H), 7.34–7.15 (m, 6 H), 7.10–7.05 (m, 1 H), 7.01–7.00 (m, 1 H), 6.79–6.70 (m, 1 H), 6.68–6.62 (m, 2 H), 6.31 (d, *J* = 10.0 Hz, 1 H), 6.09 (d, *J* = 1.3 Hz, 1 H), 5.73–5.70 (m, 1 H), 5.12 (d, *J* = 1.5 Hz, 1 H), 4.39–4.37 (m, 1 H), 4.04 (d, *J* = 14.5 Hz, 1 H), 3.93–3.89 (m, 1 H), 3.51–3.48 (m, 1 H), 3.26 (d, *J* = 14.6 Hz, 1 H), 0.60 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.2, 169.5, 144.1, 143.8, 135.5, 134.5, 132.8, 132.1, 130.6, 129.5, 129.0, 127.8, 127.7, 127.5, 127.2, 126.8, 121.3, 120.9, 119.6, 111.7, 100.9, 65.1, 62.0, 61.4, 38.8, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆BrN₂O₃⁺: 529.1121; found: 529.1125.

Compound 3l

Yield: 24.8 mg (37%); white solid.

IR (film): 2979, 1726, 1669, 1600, 1567, 1485, 1455, 1446, 1426, 1402, 1368, 1343, 1294, 1261, 1224, 1188, 1074, 1045, 1011, 863, 753, 698, 671 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.52 (t, *J* = 1.7 Hz, 1 H), 7.48–7.37 (m, 3 H), 7.37–7.29 (m, 2 H), 7.29–7.20 (m, 2 H), 7.16 (t, *J* = 7.8 Hz, 1 H), 7.07–6.97 (m, 1 H), 6.80–6.75 (m, 1 H), 6.77–6.61 (m, 2 H), 6.34 (d, *J* = 10.0 Hz, 1 H), 6.03 (d, *J* = 1.5 Hz, 1 H), 5.41–5.39 (m, 1 H), 4.96 (d, *J* = 1.6 Hz, 1 H), 4.41–4.40 (m, 1 H), 3.88–3.86 (m, 1 H), 3.54–3.42 (m, 1 H), 3.43–3.33 (m, 1 H), 3.20 (d, *J* = 14.2 Hz, 1 H), 0.60 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 172.0, 169.6, 143.7, 143.5, 138.2, 134.4, 133.7, 130.8, 130.5, 130.0, 129.6, 129.4, 127.88, 127.82, 127.6, 126.8, 122.4, 121.2, 121.0, 118.5, 111.9, 101.2, 64.5, 63.2, 61.4, 40.1, 12.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆BrN₂O₃⁺: 529.1121; found: 529.1121.

Compounds 3m and 4m

Yield: 47.9 mg (86%); white solid.

IR (film): 3058, 2982, 2936, 1732, 1669, 1600, 1578, 1485, 1455, 1403, 1371, 1347, 1293, 1265, 1191, 1098, 1045, 1025, 981, 931, 871, 755, 698, 665, 529, 463 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.84–7.68 (m, 4 H), 7.44–7.27 (m, 6 H), 7.13–6.97 (m, 2 H), 6.94–6.64 (m, 6 H), 6.39 (t, J = 9.6 Hz, 2 H), 6.03–5.75 (m, 4 H), 5.33 (d, J = 1.5 Hz, 1 H), 5.17 (d, J = 5.5 Hz, 1 H), 5.08–4.91 (m, 2 H), 4.37–3.98 (m, 6 H), 3.98–3.76 (m, 1 H), 3.46–3.43 (m, 1 H), 3.09–2.79 (m, 3 H), 2.51 (d, J = 17.9 Hz, 1 H), 1.37–1.14 (m, 9 H), 0.62 (t, J = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.2, 170.7, 170.1, 169.8, 169.7, 169.2, 143.7, 143.5, 143.33, 143.27, 134.4, 133.9, 130.9, 130.8, 129.6, 129.4, 128.0, 127.8, 127.7, 127.6, 127.1, 126.9, 126.7, 122.1, 121.7, 121.4, 121.2, 120.9, 119.0, 112.3, 111.8, 101.2, 99.9, 64.5, 62.1, 61.8, 61.7, 61.3, 60.8, 60.5, 58.9, 40.1, 39.9, 14.0, 14.0, 13.8, 12.7.

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₆H₂₇N₂O₅⁺: 447.1914; found: 447.1915.

Compound 4a

Yield: 23.4 mg (42%); white crystalline solid; mp 152.3–153.6 °C.

IR (film): 2957, 2928, 2855, 2347, 1728, 1668, 1600, 1578, 1527, 1484, 1454, 1386, 1339, 1277, 1215, 1184, 1117, 1074, 820, 772, 751, 699, 660 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.79–7.67 (m, 2 H), 7.33–7.25 (m, 3 H), 7.21–7.04 (m, 4 H), 7.00–6.71 (m, 5 H), 6.54 (d, J = 10.0 Hz, 1 H), 6.04–5.94 (m, 1 H), 5.90–5.87 (m, 1 H), 4.78 (d, J = 5.2 Hz, 1 H), 4.35 (s, 1 H), 4.22–4.18 (m, 2 H), 3.43 (d, J = 13.9 Hz, 1 H), 2.72 (d, J = 13.9 Hz, 1 H), 1.27 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.9, 169.4, 143.6, 140.6, 136.0, 134.6, 130.74, 130.71, 129.6, 128.7, 128.0, 127.7, 127.4, 127.2, 126.6, 121.9, 121.8, 120.2, 111.8, 103.9, 65.0, 62.1, 61.6, 38.5, 13.9.

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₉H₂₇N₂O₃⁺: 451.2016; found: 451.2008.

Compound 4b

Yield: 32.85 mg (57%); white crystalline solid; mp 147.3–148.2 °C.

IR (film): 3058, 2964, 1739, 1665, 1600, 1578, 1484, 1455, 1401, 1349, 1278, 1221, 1181, 1113, 1058, 1044, 912, 879, 796, 754, 696, 662 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.79–7.68 (m, 2 H), 7.42–7.26 (m, 3 H), 7.15–6.86 (m, 6 H), 6.86–6.73 (m, 2 H), 6.58 (d, J = 10.0 Hz, 1 H), 6.04–5.92 (m, 1 H), 5.85 (s, 1 H), 4.72–4.70 (m, 1 H), 4.44–4.13 (m, 3 H), 3.37 (d, J = 14.3 Hz, 1 H), 2.94 (d, J = 14.3 Hz, 1 H), 1.69 (s, 3 H), 1.29 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.4, 169.5, 143.6, 140.2, 138.0, 134.7, 134.6, 130.8, 130.1, 129.8, 129.5, 128.7, 128.0, 127.8, 127.2, 126.7, 125.4, 121.94, 121.87, 120.4, 112.4, 103.8, 65.3, 62.0, 61.7, 34.5, 20.0, 14.0.

HRMS (ESI): m/z [M + H]⁺ calcd for C₃₀H₂₉N₂O₃⁺: 465.2173; found: 465.2166.

Compound 4c

Yield: 22.9 mg (39%); white crystalline solid; mp 141.1–142.3 °C.

IR (film): 3026, 2979, 2924, 1717, 1664, 1599, 1577, 1483, 1454, 1446, 1401, 1367, 1349, 1276, 1230, 1208, 1187, 1164, 1096, 1051, 1018, 796, 783, 771, 751, 696 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.73 (d, J = 6.9 Hz, 2 H), 7.32–7.25 (m, 3 H), 7.18–6.85 (m, 4 H), 6.80 (t, J = 7.4 Hz, 2 H), 6.68 (s, 2 H), 6.53 (d, J = 10.0 Hz, 1 H), 5.99 (s, 1 H), 5.90–5.87 (m, 1 H), 4.77 (d, J = 5.2 Hz, 1 H), 4.41 (s, 1 H), 4.35–4.09 (m, 2 H), 3.39 (d, J = 13.9 Hz, 1 H), 2.69 (d, J = 13.9 Hz, 1 H), 2.24 (s, 3 H), 1.27 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.1, 169.5, 143.7, 140.6, 136.9, 135.9, 134.6, 131.5, 130.8, 129.6, 128.7, 128.0, 127.8, 127.4, 127.2, 122.0, 121.8, 120.4, 111.9, 104.0, 65.0, 62.2, 61.6, 38.7, 21.3, 14.0.

HRMS (ESI): m/z [M + H]⁺ calcd for C₃₀H₂₉N₂O₃⁺: 465.2173; found: 465.2168.

Compound 4d

Yield: 20.1 mg (34%); white solid.

IR (film): 3054, 3023, 2981, 2924, 2414, 2379, 2358, 2344, 2324, 1727, 1667, 1600, 1578, 1515, 1484, 1455, 1447, 1402, 1368, 1349, 1276, 1230, 1209, 1186, 1165, 1113, 1096, 1072, 1050, 1017, 984, 972, 951, 939, 928, 907, 883, 861, 851, 838, 826, 817, 795, 771, 760, 727, 715, 695, 683 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.83–7.62 (m, 2 H), 7.44–7.22 (m, 3 H), 7.09–7.04 (m, 1 H), 7.03–6.86 (m, 3 H), 6.85–6.70 (m, 4 H), 6.53 (d, J = 10.1 Hz, 1 H), 5.98 (s, 1 H), 5.89–5.87 (m, 1 H), 4.76–4.75 (m, 1 H), 4.40 (d, J = 1.0 Hz, 1 H), 4.32–4.10 (m, 2 H), 3.39 (d, J = 13.9 Hz, 1 H), 2.68 (d, J = 13.9 Hz, 1 H), 2.27 (s, 3 H), 1.28 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.1, 169.5, 143.7, 140.6, 136.2, 134.6, 132.8, 130.8, 130.6, 129.6, 128.7, 128.2, 128.0, 127.8, 127.2, 122.0, 121.8, 120.4, 111.9, 104.0, 65.0, 62.2, 61.6, 38.3, 21.0, 14.0.

HRMS (ESI): m/z [M + H]⁺ calcd for C₃₀H₂₉N₂O₃⁺: 465.2173; found: 465.2163.

Compound 4e

Yield: 28 mg (48%); white crystalline solid; mp 143.9–145.6 °C.

IR (film): 2965, 2935, 1721, 1665, 1600, 1585, 1492, 1484, 1455, 1402, 1367, 1349, 1290, 1275, 1233, 1211, 1181, 1106, 1074, 1049, 1026, 930, 912, 884, 800, 755, 697, 662, 613, 526, 462 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.78–7.68 (m, 2 H), 7.41–7.26 (m, 3 H), 7.21–7.02 (m, 2 H), 7.00–6.84 (m, 4 H), 6.84–6.74 (m, 2 H), 6.59 (d, J = 10.0 Hz, 1 H), 5.97–5.93 (m, 2 H), 4.84–4.83 (m, 1 H), 4.37 (d, J = 1.1 Hz, 1 H), 4.28–4.15 (m, 2 H), 3.50–3.33 (m, 1 H), 2.90–2.73 (m, 1 H), 1.26 (t, J = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.8, 169.6, 161.7 (d, J = 246.2 Hz), 143.6, 140.1, 134.7, 132.9 (d, J = 4.2 Hz), 130.8, 129.7, 129.0, 128.6 (d, J = 8.2 Hz), 128.0, 127.8, 127.2, 123.2, 123.0 (d, J = 3.7 Hz), 121.7 (d, J = 1.2 Hz), 120.1, 114.8 (d, J = 22.4 Hz), 112.0, 103.4, 100.0, 64.9, 61.8, 61.1, 31.3, 13.8.

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃⁺: 469.1922; found: 469.1902.

Compound 4f

Yield: 21.9 mg (37%); white crystalline solid; mp 141.3–142.4 °C.

IR (film): 3058, 2964, 2929, 1720, 1666, 1600, 1577, 1484, 1472, 1455, 1446, 1401, 1349, 1264, 1210, 1050, 1022, 912, 880, 800, 752, 697, 663, 549, 458 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.80–7.66 (m, 2 H), 7.48–7.21 (m, 4 H), 7.21–6.96 (m, 4 H), 6.91–6.89 (m, 1 H), 6.85–6.71 (m, 2 H), 6.60 (d, J = 10.0 Hz, 1 H), 6.04–5.89 (m, 2 H), 4.82–4.80 (m, 1 H), 4.39 (d, J = 1.0 Hz, 1 H), 4.33–4.12 (m, 2 H), 3.60 (t, J = 14.3 Hz, 1 H), 3.10 (d, J = 14.2 Hz, 1 H), 1.25 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.0, 169.6, 143.5, 140.0, 135.9, 134.7, 132.6, 131.9, 130.8, 129.5, 129.0, 128.3, 128.0, 127.8, 127.3, 126.8, 126.5, 121.8, 121.7, 120.0, 112.7, 103.8, 65.1, 62.0, 61.3, 37.2, 13.9.

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃⁺: 469.1922; found: 469.1926.

Compound 4g

Yield: 22.8 mg (39%); white crystalline solid; mp 169.7–170.7 °C.

IR (film): 2964, 2346, 1736, 1661, 1600, 1509, 1483, 1454, 1351, 1221, 1192, 1160, 1098, 1051, 1017, 928, 881, 862, 838, 804, 759, 695, 683, 672, 660, 640, 628 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.83–7.62 (m, 2 H), 7.44–7.20 (m, 3 H), 7.10–7.07 (m, 1 H), 6.97–6.70 (m, 7 H), 6.55 (d, *J* = 10.0 Hz, 1 H), 5.98 (d, *J* = 5.2 Hz, 1 H), 5.88–5.86 (m, 1 H), 4.79–4.78 (m, 1 H), 4.31 (d, *J* = 1.1 Hz, 1 H), 4.22–4.19 (m, 2 H), 3.41 (d, *J* = 14.0 Hz, 1 H), 2.68 (d, *J* = 14.0 Hz, 1 H), 1.27 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.9, 169.5, 161.8 (d, *J* = 245.5 Hz), 143.6, 140.6, 134.6, 132.4 (d, *J* = 8.0 Hz), 131.7 (d, *J* = 3.3 Hz), 130.8, 129.8, 128.9, 128.0, 127.8, 127.3, 121.9, 121.8, 120.0, 114.3 (d, *J* = 21.2 Hz), 111.8, 103.8, 65.1, 62.2, 61.8, 37.5, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃⁺: 469.1922; found: 469.1916.

Compound 4h

Yield: 33.05 mg (55%); white solid.

IR (film): 3059, 2982, 2936, 1720, 1666, 1600, 1577, 1484, 1455, 1446, 1402, 1367, 1349, 1272, 1231, 1210, 1189, 1167, 1112, 1058, 1025, 972, 930, 912, 882, 786, 753, 697, 661, 621 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.79–7.66 (m, 2 H), 7.44–7.17 (m, 4 H), 7.18–6.97 (m, 4 H), 6.98–6.85 (m, 1 H), 6.79 (t, *J* = 7.4 Hz, 2 H), 6.61 (d, *J* = 10.0 Hz, 1 H), 6.06–5.87 (m, 2 H), 4.82–4.80 (m, 1 H), 4.37 (d, *J* = 1.0 Hz, 1 H), 4.30–4.13 (m, 2 H), 3.54 (d, *J* = 14.1 Hz, 1 H), 3.05 (d, *J* = 14.1 Hz, 1 H), 1.25 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.9, 169.6, 143.5, 139.9, 135.8, 134.6, 134.0, 132.1, 130.7, 129.5, 129.1, 129.0, 128.1, 127.9, 127.7, 127.2, 125.8, 121.7, 121.6, 120.0, 112.4, 103.6, 65.1, 61.9, 61.2, 34.6, 13.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1630.

Compound 4i

Yield: 25 mg (41%); white solid.

IR (film): 3059, 3023, 2981, 2935, 2903, 1725, 1666, 1599, 1575, 1483, 1455, 1446, 1433, 1402, 1368, 1349, 1310, 1268, 1231, 1211, 1187, 1166, 1096, 1081, 1049, 1018, 882, 793, 752, 728, 695, 671, 661, 650, 639, 626, 616, 606 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.78–7.67 (m, 2 H), 7.42–7.22 (m, 3 H), 7.11–7.08 (m, 3 H), 6.95–6.87 (m, 2 H), 6.86–6.71 (m, 3 H), 6.54 (d, *J* = 10.0 Hz, 1 H), 6.04–5.96 (m, 1 H), 5.87–5.84 (m, 1 H), 4.81–4.80 (m, 1 H), 4.38 (d, *J* = 1.3 Hz, 1 H), 4.33–4.11 (m, 2 H), 3.38 (d, *J* = 14.0 Hz, 1 H), 2.70 (d, *J* = 14.0 Hz, 1 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.8, 169.5, 143.6, 140.7, 138.2, 134.5, 133.3, 130.9, 129.8, 129.1, 129.0, 128.7, 128.0, 127.8, 127.3, 126.9, 121.9, 121.8, 121.0, 111.9, 103.7, 65.0, 62.1, 61.9, 38.1, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1634.

Compound 4j

Yield: 15.8 mg (26%); white crystalline solid; mp 177.8–179.0 °C.

IR (film): 2982, 2935, 2361, 2342, 1725, 1664, 1599, 1577, 1483, 1454, 1402, 1349, 1291, 1268, 1231, 1211, 1187, 1107, 1092, 1049, 1016, 928, 911, 881, 827, 785, 755, 697, 662, 521, 462 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.86–7.54 (m, 2 H), 7.49–7.19 (m, 3 H), 7.19–6.98 (m, 3 H), 6.90–6.87 (m, 1 H), 6.86–6.66 (m, 4 H), 6.54 (d, *J* = 10.0 Hz, 1 H), 6.07–5.93 (m, 1 H), 5.87–5.84 (m, 1 H), 4.81–4.80 (m, 1 H), 4.32 (d, *J* = 4.2 Hz, 1 H), 4.29–4.11 (m, 2 H), 3.40 (d, *J* = 14.0 Hz, 1 H), 2.68 (d, *J* = 14.0 Hz, 1 H), 1.28 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.8, 169.5, 143.6, 140.6, 134.6, 134.5, 132.6, 132.2, 130.9, 129.8, 129.0, 128.0, 127.8, 127.6, 127.3, 121.9, 120.0, 111.8, 103.8, 65.1, 62.2, 61.8, 37.7, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1622.

Compound 4k

Yield: 26.55 mg (40%); white crystalline solid; mp 136.3–138.2 °C.

IR (film): 2982, 1719, 1665, 1600, 1577, 1484, 1472, 1455, 1446, 1401, 1349, 1270, 1230, 1210, 1120, 1049, 1022, 912, 881, 784, 752, 697, 662 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.80–7.63 (m, 2 H), 7.44–7.21 (m, 3 H), 7.20–7.03 (m, 2 H), 6.98–6.72 (m, 4 H), 6.71–6.45 (m, 3 H), 5.98 (d, *J* = 4.0 Hz, 1 H), 5.87–5.84 (m, 1 H), 4.81–4.79 (m, 1 H), 4.36 (d, *J* = 1.3 Hz, 1 H), 4.34–4.13 (m, 2 H), 3.42 (d, *J* = 13.9 Hz, 1 H), 2.72 (d, *J* = 14.0 Hz, 1 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.9, 169.5, 143.6, 140.7, 134.5, 130.8, 129.8, 129.0, 128.9, 128.8, 128.0, 127.8, 127.3, 126.64, 126.61, 121.91, 121.88, 120.0, 117.8, 117.5, 113.7, 113.4, 111.9, 103.7, 65.1, 62.2, 61.8, 38.2, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆BrN₂O₃⁺: 529.1121; found: 529.1123.

Compound 4l

Yield: 21.7 mg (33%); white crystalline solid; mp 153.1–154.0 °C.

IR (film): 3059, 2980, 2935, 1724, 1666, 1598, 1569, 1483, 1455, 1446, 1402, 1348, 1309, 1267, 1233, 1211, 1186, 1095, 1074, 1048, 1019, 972, 867, 788, 753, 697, 662, 612 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.83–7.64 (m, 2 H), 7.43–7.23 (m, 4 H), 7.17–6.96 (m, 3 H), 6.91–6.82 (m, 1 H), 6.80–6.77 (m, 3 H), 6.53 (d, *J* = 10.0 Hz, 1 H), 6.05–5.94 (m, 1 H), 5.86–5.84 (m, 1 H), 4.91–4.71 (m, 1 H), 4.40 (d, *J* = 1.3 Hz, 1 H), 4.35–4.09 (m, 2 H), 3.37 (d, *J* = 14.0 Hz, 1 H), 2.70 (d, *J* = 14.0 Hz, 1 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.8, 169.5, 143.6, 140.7, 138.5, 134.5, 133.8, 130.9, 129.8, 129.6, 129.0, 128.0, 127.8, 127.3, 121.9, 121.8, 121.5, 120.0, 111.9, 103.7, 65.0, 62.1, 61.9, 38.1, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆BrN₂O₃⁺: 529.1121; found: 529.1099.

Compound 6a

Yield: 24.6 mg (55%); white solid.

IR (film): 3057, 2983, 2924, 1732, 1668, 1600, 1578, 1484, 1447, 1402, 1368, 1342, 1291, 1261, 1205, 1160, 1096, 1017, 900, 881, 862, 817, 793, 772, 759, 737, 716, 694, 683, 671 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.84–7.71 (m, 2 H), 7.48–7.27 (m, 3 H), 7.19–7.02 (m, 1 H), 7.00–6.70 (m, 3 H), 6.41 (d, *J* = 9.8 Hz, 1 H), 6.06–5.84 (m, 2 H), 5.19 (s, 1 H), 4.53–4.50 (m, 1 H), 4.40–4.12 (m, 2 H), 3.90–3.88 (m, 1 H), 1.32 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 169.2, 168.8, 143.1, 139.1, 134.3, 130.9, 129.6, 128.3, 127.8, 127.2, 126.9, 122.7, 122.5, 121.7, 114.2, 99.8, 61.6, 60.6, 54.1, 14.1.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₂H₂₁N₂O₃⁺: 361.1547; found: 361.1533.

Compound 6b

Yield: 12.1 mg (26%); white solid.

IR (film): 3058, 2963, 2925, 2859, 1732, 1651, 1600, 1577, 1485, 1453, 1404, 1378, 1337, 1308, 1259, 1211, 1156, 1115, 1044, 1015, 967, 891, 794, 760, 696, 663, 606 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.79–7.69 (m, 2 H), 7.45–7.28 (m, 3 H), 7.15 (td, *J* = 7.8, 1.7 Hz, 1 H), 7.02–6.93 (m, 1 H), 6.89–6.86 (m, 2 H), 6.42 (d, *J* = 9.9 Hz, 1 H), 6.15 (s, 1 H), 5.90–5.88 (m, 1 H), 4.41–4.38 (m, 1 H), 4.34–4.15 (m, 2 H), 3.82–3.80 (m, 1 H), 1.65–1.63 (m, 3 H), 1.31 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.2, 169.5, 142.8, 134.4, 133.9, 130.7, 129.8, 128.2, 127.7, 127.3, 126.6, 122.53, 122.49, 121.5, 115.9, 114.4, 63.2, 61.5, 54.3, 14.2, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₃H₂₃N₂O₃⁺: 375.1703; found: 375.1711.

Compound 7a

Yield: 13.3 mg (30%); white solid.

IR (film): 3059, 3027, 2962, 2933, 2902, 1727, 1665, 1600, 1578, 1485, 1455, 1447, 1403, 1370, 1346, 1292, 1261, 1223, 1176, 1158, 1102, 1071, 1020, 896, 872, 862, 802, 775, 752, 727, 697, 671, 652, 638, 628, 617, 606, 593 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.82–7.73 (m, 2 H), 7.44–7.26 (m, 3 H), 7.11–6.96 (m, 1 H), 6.83–6.78 (m, 1 H), 6.74–6.70 (m, 2 H), 6.43 (d, *J* = 10.0 Hz, 1 H), 6.09–5.98 (m, 1 H), 5.80–5.78 (m, 1 H), 5.09–4.94 (m, 1 H), 4.70–4.68 (m, 1 H), 3.89–3.84 (m, 2 H), 3.65–3.62 (m, 1 H), 0.76 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.0, 169.6, 143.4, 139.7, 134.4, 131.0, 129.6, 128.1, 127.9, 127.8, 126.8, 121.50, 121.47, 119.2, 112.6, 100.4, 61.1, 60.4, 57.2, 13.2.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₂H₂₁N₂O₃⁺: 361.1547; found: 361.1530.

Compound 7b

Yield: 11.9 mg (25%); white solid.

IR (film): 2979, 1725, 1648, 1600, 1577, 1484, 1455, 1404, 1376, 1322, 1291, 1260, 1216, 1176, 1156, 1114, 1071, 1047, 1022, 966, 888, 829, 796, 754, 706, 652 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.73–7.70 (m, 2 H), 7.46–7.20 (m, 3 H), 7.11–7.06 (m, 1 H), 6.95–6.67 (m, 3 H), 6.52–6.50 (m, 1 H), 6.43 (d, *J* = 10.0 Hz, 1 H), 5.81–5.78 (m, 1 H), 4.59–4.56 (m, 1 H), 4.00–3.81 (m, 2 H), 3.65–3.59 (m, 1 H), 1.71–1.68 (m, 3 H), 0.80 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.2, 169.9, 143.6, 134.7, 133.8, 130.7, 129.7, 128.0, 127.9, 127.8, 126.8, 121.7, 121.5, 119.5, 113.9, 112.9, 61.0, 60.6, 54.5, 14.6, 13.4.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₃H₂₃N₂O₃⁺: 375.1703; found: 375.1713.

Compound 9a

Yield: 16 mg (29%); white crystalline solid; mp 128.3–130.1 °C.

IR (film): 3029, 2964, 1725, 1661, 1631, 1494, 1454, 1409, 1368, 1340, 1262, 1237, 1200, 1084, 1042, 941, 872, 753, 700, 675, 655 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.71 (d, *J* = 6.4 Hz, 2 H), 7.51–7.30 (m, 3 H), 7.31–6.96 (m, 8 H), 6.93 (d, *J* = 7.4 Hz, 1 H), 6.10 (d, *J* = 7.7 Hz, 1 H), 5.96 (s, 1 H), 5.37 (d, *J* = 7.8 Hz, 1 H), 5.32 (s, 1 H), 4.47–4.21 (m, 2 H), 4.19 (s, 1 H), 3.16 (s, 2 H), 1.32 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.5, 167.7, 141.6, 137.2, 136.2, 134.9, 131.4, 131.3, 130.6, 129.0, 128.3, 128.00, 127.97, 127.4, 126.9, 126.8, 126.4, 125.2, 104.9, 102.0, 66.7, 64.5, 61.8, 38.0, 14.1.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₇N₂O₃⁺: 451.2016; found: 451.2017.

Compound 9b and 10b

Yield: 29 mg (50%); white crystalline solid; mp 152.1–153.7 °C.

IR (film): 3061, 3023, 2979, 1726, 1662, 1631, 1601, 1577, 1492, 1447, 1408, 1368, 1340, 1278, 1221, 1200, 1098, 1059, 1037, 940, 904, 872, 750, 699, 673, 567 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.75–7.65 (m, 2 H), 7.55–7.46 (m, 1 H), 7.46–7.27 (m, 5 H), 7.27–6.83 (m, 13 H), 6.13 (d, *J* = 7.8 Hz, 1 H), 5.98–5.97 (m, 1 H), 5.92 (d, *J* = 7.8 Hz, 1 H), 5.80 (d,

1.0 Hz, 1 H), 5.44 (d, *J* = 7.8 Hz, 1 H), 5.31 (d, *J* = 7.8 Hz, 1 H), 5.22 (s, 1 H), 4.82 (d, *J* = 10.4 Hz, 1 H), 4.61 (d, *J* = 1.3 Hz, 1 H), 4.40–4.19 (m, 2 H), 4.01 (d, *J* = 1.2 Hz, 1 H), 3.83–3.67 (m, 1 H), 3.58 (d, *J* = 14.7 Hz, 1 H), 3.34–3.33 (m, 1 H), 3.02 (d, *J* = 14.2 Hz, 1 H), 2.43 (s, 1 H), 2.14 (s, 3 H), 1.31 (t, *J* = 9.2, 5.1 Hz, 3 H), 0.92 (t, *J* = 7.1 Hz, 1 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.8, 171.6, 167.62, 167.57, 142.2, 141.1, 138.6, 137.8, 137.4, 137.1, 135.0, 134.8, 134.4, 131.3, 130.8, 130.59, 130.56, 130.51, 130.47, 130.0, 129.3, 129.0, 128.8, 128.2, 128.00, 127.95, 127.9, 127.6, 127.1, 127.0, 126.8, 126.5, 126.3, 126.1, 125.3, 125.2, 124.9, 104.8, 104.6, 101.8, 101.6, 67.3, 67.2, 64.8, 64.6, 61.8, 61.4, 37.7, 33.7, 21.1, 20.8, 14.0, 13.4.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₃₀H₂₉N₂O₃⁺: 465.2173; found: 465.2175.

Compound 9c and 10c

Yield: 43.4 mg (75%); white solid.

IR (film): 2963, 2926, 1727, 1667, 1634, 1603, 1491, 1447, 1408, 1368, 1340, 1260, 1227, 1203, 1097, 1047, 1026, 939, 905, 862, 755, 700, 667, 635, 561 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.71 (dd, *J* = 7.9, 1.6 Hz, 1 H), 7.52–7.31 (m, 3 H), 7.31–6.97 (m, 13 H), 6.93 (d, *J* = 7.3 Hz, 1 H), 6.87 (dd, *J* = 5.6, 2.1 Hz, 1 H), 6.76 (s, 1 H), 6.11 (t, *J* = 4.7 Hz, 1 H), 5.98 (s, 1 H), 5.89 (d, *J* = 7.8 Hz, 1 H), 5.44–5.18 (m, 2 H), 5.00 (d, *J* = 1.4 Hz, 1 H), 4.86 (s, 1 H), 4.42–4.19 (m, 1 H), 3.90–3.60 (m, 2 H), 3.51 (d, *J* = 14.4 Hz, 1 H), 3.34 (d, *J* = 14.4 Hz, 1 H), 3.14 (s, 1 H), 2.30 (s, 3 H), 2.23 (s, 1 H), 1.34 (t, *J* = 7.1 Hz, 2 H), 0.94 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.8, 171.6, 167.7, 143.1, 141.8, 138.2, 137.2, 136.9, 136.7, 136.0, 135.5, 134.9, 132.0, 131.5, 130.7, 130.6, 130.2, 128.9, 128.7, 128.4, 128.2, 128.1, 128.04, 127.97, 127.8, 127.7, 127.4, 127.2, 127.1, 126.9, 126.8, 126.7, 126.3, 125.1, 124.9, 105.0, 104.2, 102.0, 101.1, 66.5, 65.6, 64.4, 63.3, 61.8, 61.3, 41.4, 38.3, 21.3, 14.0, 13.5.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₃₀H₂₉N₂O₃⁺: 465.2173; found: 465.2167.

Compound 9e

Yield: 29.9 mg (51%); white crystalline solid; mp 140.3–141.6 °C.

IR (film): 3432, 2963, 1725, 1662, 1630, 1584, 1492, 1455, 1409, 1369, 1341, 1262, 1235, 1202, 1182, 1104, 1047, 942, 904, 861, 798, 758, 699, 674 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.72–7.69 (m, 2 H), 7.47–7.32 (m, 3 H), 7.33–7.06 (m, 5 H), 7.05–6.81 (m, 3 H), 6.14 (d, *J* = 7.8 Hz, 1 H), 5.88 (d, *J* = 1.3 Hz, 1 H), 5.48–5.28 (m, 2 H), 4.42–4.15 (m, 2 H), 4.04 (d, *J* = 1.3 Hz, 1 H), 3.45 (d, *J* = 14.1 Hz, 1 H), 2.91 (d, *J* = 14.1 Hz, 1 H), 1.31 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.4, 167.6, 162.3 (d, *J* = 245.7 Hz), 141.5, 137.4, 135.0, 132.7 (d, *J* = 4.1 Hz), 131.5, 130.6, 129.0, 128.4 (d, *J* = 8.4 Hz), 128.2, 128.0, 127.5, 126.8 (d, *J* = 2.4 Hz), 125.3, 123.9, 123.7, 123.1 (d, *J* = 3.4 Hz), 114.7 (d, *J* = 22.6 Hz), 104.3, 100.4, 66.6, 64.0, 61.9, 30.3, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃⁺: 469.1922; found: 469.1921.

Compound 9f

Yield: 8.4 mg (14%); white solid.

IR (film): 3066, 2981, 2935, 1726, 1662, 1630, 1616, 1588, 1524, 1489, 1448, 1409, 1368, 1340, 1254, 1201, 1144, 1122, 1099, 1080, 1047, 941, 904, 877, 753, 700, 674, 629 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.75–7.64 (m, 2 H), 7.47–7.31 (m, 3 H), 7.21–7.20 (m, 1 H), 7.09–7.07 (m, 3 H), 6.97–6.88 (m, 1 H), 6.87–6.69 (m, 3 H), 6.09 (d, *J* = 7.8 Hz, 1 H), 5.98 (d, *J* = 1.4 Hz, 1 H), 5.37 (d, *J* = 8.0 Hz, 2 H), 4.47–4.10 (m, 3 H), 3.16 (s, 2 H), 1.35 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.3, 167.9, 162.0 (d, J = 244.5 Hz), 141.7, 138.8 (d, J = 7.6 Hz), 137.0, 134.8, 131.3, 130.7, 129.1, 128.6 (d, J = 8.2 Hz), 128.2, 128.0, 127.8, 126.9 (d, J = 2.7 Hz), 126.83, 126.7, 125.3, 117.9 (d, J = 21.4 Hz), 113.3 (d, J = 20.9 Hz), 104.9, 101.6, 66.5, 64.4, 62.0, 37.8, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃⁺: 469.1922; found: 469.1931.

Compound 9g

Yield: 13.6 mg (23%); white solid.

IR (film): 3430, 2963, 1721, 1663, 1629, 1601, 1509, 1446, 1368, 1341, 1262, 1222, 1159, 1098, 1045, 798, 757, 699, 670 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.77–7.63 (m, 2 H), 7.50–7.30 (m, 3 H), 7.25–6.89 (m, 6 H), 6.87–6.73 (m, 2 H), 6.08 (d, J = 7.8 Hz, 1 H), 5.98 (d, J = 1.8 Hz, 1 H), 5.36 (d, J = 7.1 Hz, 2 H), 4.40–4.19 (m, 2 H), 4.15 (d, J = 9.7 Hz, 1 H), 3.13 (s, 2 H), 1.33 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.4, 167.7, 161.7 (d, J = 244.9 Hz), 141.6, 137.1, 134.8, 132.8 (d, J = 7.9 Hz), 131.8 (d, J = 3.1 Hz), 131.4, 130.7, 129.0, 128.3, 128.0, 127.8, 126.8 (d, J = 5.7 Hz), 125.3, 114.3, 114.0, 104.8, 101.7, 66.6, 64.5, 61.9, 37.0, 14.1.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃⁺: 469.1922; found: 469.1920.

Compound 9h

Yield: 22.4 mg (37%); white solid.

IR (film): 3066, 2964, 1724, 1662, 1630, 1572, 1493, 1475, 1446, 1409, 1369, 1341, 1263, 1238, 1201, 1099, 1056, 1028, 941, 904, 860, 756, 698, 668, 623, 564 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.71–7.69 (m, 2 H), 7.40–7.35 (m, 4 H), 7.31–7.02 (m, 6 H), 6.96 (d, J = 7.3 Hz, 1 H), 6.15 (d, J = 7.8 Hz, 1 H), 5.88 (s, 1 H), 5.50–5.16 (m, 2 H), 4.47–4.15 (m, 2 H), 4.02 (s, 1 H), 3.56 (d, J = 14.0 Hz, 1 H), 3.08 (d, J = 14.0 Hz, 1 H), 1.29 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.4, 167.5, 141.0, 137.6, 137.0, 135.0, 134.6, 132.5, 131.5, 130.6, 129.10, 129.04, 128.2, 128.0, 127.9, 127.6, 126.7, 126.6, 126.0, 125.3, 104.0, 100.8, 66.8, 64.5, 61.9, 34.0, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1614.

Compound 9i

Yield: 14.1 mg (23%); white solid.

IR (film): 3064, 2980, 1724, 1662, 1630, 1599, 1573, 1477, 1447, 1368, 1341, 1262, 1201, 1081, 1046, 940, 880, 771, 700, 671 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.77–7.63 (m, 2 H), 7.51–7.31 (m, 3 H), 7.21–7.20 (m, 1 H), 7.16–7.00 (m, 4 H), 7.00–6.88 (m, 3 H), 6.08 (d, J = 7.8 Hz, 1 H), 6.00 (d, J = 1.4 Hz, 1 H), 5.37 (s, 1 H), 5.35 (s, 1 H), 4.51–4.12 (m, 3 H), 3.14 (s, 2 H), 1.35 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.3, 167.7, 141.8, 138.3, 137.0, 134.8, 133.1, 131.33, 131.25, 130.7, 129.3, 129.1, 128.5, 128.3, 128.0, 127.8, 126.8, 126.7, 126.6, 125.3, 104.9, 101.6, 66.3, 64.4, 62.0, 37.9, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1604.

Compound 9l

Yield: 20.7 mg (31%); white solid.

IR (film): 3063, 2980, 1725, 1662, 1630, 1597, 1569, 1492, 1475, 1447, 1368, 1340, 1239, 1201, 1096, 1073, 1046, 941, 878, 769, 699, 664 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.73–7.66 (m, 2 H), 7.47–7.33 (m, 3 H), 7.28–7.17 (m, 2 H), 7.14–7.03 (m, 3 H), 7.03–6.89 (m, 3 H), 6.08 (d, J = 7.8 Hz, 1 H), 6.01 (d, J = 1.4 Hz, 1 H), 5.46–5.25 (m, 2 H), 4.46–4.15 (m, 3 H), 3.14 (s, 2 H), 1.35 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.3, 167.7, 141.8, 138.6, 137.0, 134.8, 134.1, 131.3, 130.7, 129.7, 129.5, 129.1, 128.8, 128.2, 128.0, 127.8, 126.8, 126.6, 125.3, 121.4, 104.9, 101.6, 66.3, 64.3, 62.0, 37.9, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆BrN₂O₃⁺: 529.1121; found: 529.1117.

Compound 9m

Yield: 18.2 mg (32%); white solid.

IR (film): 3064, 2982, 2936, 1732, 1667, 1631, 1601, 1579, 1492, 1447, 1408, 1370, 1344, 1261, 1226, 1182, 1093, 1059, 1028, 935, 907, 878, 755, 701, 649 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.69–7.50 (m, 2 H), 7.47–7.31 (m, 3 H), 7.30–7.23 (m, 1 H), 7.23–7.04 (m, 2 H), 6.90 (d, J = 7.4 Hz, 1 H), 6.04 (d, J = 7.8 Hz, 2 H), 5.50 (s, 1 H), 5.46 (d, J = 7.8 Hz, 1 H), 5.39 (d, J = 1.0 Hz, 1 H), 4.48–4.11 (m, 2 H), 3.75–3.41 (m, 2 H), 3.12–2.90 (m, 2 H), 1.35 (t, J = 7.1 Hz, 3 H), 0.98 (t, J = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.2, 169.3, 167.7, 143.8, 137.7, 134.5, 130.9, 130.8, 130.2, 129.0, 128.3, 128.0, 126.4, 126.2, 124.8, 106.3, 100.0, 63.4, 61.9, 60.5, 60.3, 40.4, 14.0, 13.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₆H₂₇N₂O₅⁺: 447.1914; found: 447.1916.

Compound 10a

Yield: 23.8 mg (42%); white crystalline solid; mp 173.5–174.8 °C.

IR (film): 3062, 3026, 2963, 1728, 1666, 1634, 1601, 1572, 1494, 1453, 1408, 1368, 1340, 1286, 1260, 1226, 1200, 1096, 1017, 939, 906, 862, 769, 700, 664, 635 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.47–7.38 (m, 2 H), 7.38–7.20 (m, 8 H), 7.20–7.11 (m, 3 H), 6.91–6.80 (m, 1 H), 6.12 (d, J = 1.4 Hz, 1 H), 5.89 (d, J = 7.8 Hz, 1 H), 5.27 (d, J = 7.8 Hz, 1 H), 4.97 (d, J = 1.4 Hz, 1 H), 4.84 (s, 1 H), 3.90–3.61 (m, 2 H), 3.53 (d, J = 14.3 Hz, 1 H), 3.36 (d, J = 14.4 Hz, 1 H), 0.93 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.8, 167.7, 142.9, 136.9, 135.6, 134.8, 130.9, 130.7, 130.3, 128.8, 128.5, 127.8, 127.6, 127.5, 127.4, 126.8, 126.3, 125.0, 104.3, 101.2, 65.5, 63.5, 61.4, 41.4, 13.4.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₇N₂O₃⁺: 451.2016; found: 451.2025.

Compound 10e

Yield: 28 mg (47%); white crystalline solid; mp 176.0–177.9 °C.

IR (film): 3064, 2963, 1729, 1668, 1636, 1601, 1581, 1491, 1453, 1407, 1368, 1339, 1288, 1260, 1227, 1179, 1097, 1046, 1016, 938, 907, 871, 792, 759, 699, 663, 634 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.54–7.40 (m, 1 H), 7.33–7.31 (m, 2 H), 7.28–7.18 (m, 3 H), 7.18–7.00 (m, 6 H), 6.86–6.85 (m, 1 H), 6.10 (d, J = 1.3 Hz, 1 H), 5.85 (d, J = 7.8 Hz, 1 H), 5.27 (d, J = 7.8 Hz, 1 H), 5.07 (d, J = 1.5 Hz, 1 H), 4.81 (s, 1 H), 3.91–3.57 (m, 3 H), 3.17 (d, J = 15.8 Hz, 1 H), 0.92 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.7, 167.3, 161.6 (d, J = 243.9 Hz), 143.2, 136.4, 134.7, 132.3 (d, J = 3.6 Hz), 130.6, 130.3, 129.2 (d, J = 8.4 Hz), 128.7, 127.8, 127.4, 127.0, 126.9 (d, J = 5.9 Hz), 124.9, 124.5 (d, J = 3.5 Hz), 122.5, 122.3, 115.3 (d, J = 23.4 Hz), 104.4, 100.8, 65.9, 63.38, 63.35, 61.4, 33.29, 33.26, 13.4.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃⁺: 469.1922; found: 469.1931.

Compound 10f

Yield: 27.5 mg (47%); white crystalline solid; mp 155.1–156.7 °C.
 IR (film): 3023, 2963, 2925, 1728, 1667, 1634, 1601, 1573, 1515, 1493, 1446, 1408, 1368, 1340, 1286, 1260, 1225, 1202, 1096, 1045, 1023, 939, 906, 863, 802, 769, 699, 665, 634 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.41–7.19 (m, 7 H), 7.20–7.05 (m, 5 H), 6.90–6.77 (m, 1 H), 6.11 (d, *J* = 1.3 Hz, 1 H), 5.88 (d, *J* = 7.8 Hz, 1 H), 5.26 (d, *J* = 7.8 Hz, 1 H), 4.96 (d, *J* = 1.4 Hz, 1 H), 4.84 (s, 1 H), 3.91–3.57 (m, 2 H), 3.49 (d, *J* = 14.4 Hz, 1 H), 3.31 (d, *J* = 14.4 Hz, 1 H), 0.92 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.8, 167.7, 142.9, 137.0, 136.9, 134.9, 132.4, 130.8, 130.7, 130.3, 129.2, 128.8, 127.8, 127.7, 127.6, 126.8, 126.3, 125.0, 104.3, 101.0, 65.5, 63.4, 61.4, 40.9, 20.9, 13.5.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1613.

Compound 10g

Yield: 27.9 mg (48%); white crystalline solid; mp 146.0–147.0 °C.
 IR (film): 3064, 2961, 2929, 1727, 1665, 1635, 1602, 1573, 1510, 1493, 1446, 1408, 1368, 1340, 1286, 1223, 1160, 1098, 1046, 1016, 939, 906, 863, 837, 756, 699, 664, 633 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.45–7.24 (m, 7 H), 7.24–7.09 (m, 3 H), 7.07–6.94 (m, 2 H), 6.88 (d, *J* = 6.6 Hz, 1 H), 6.11 (d, *J* = 1.4 Hz, 1 H), 5.91 (d, *J* = 7.8 Hz, 1 H), 5.30 (d, *J* = 7.8 Hz, 1 H), 4.90 (d, *J* = 1.4 Hz, 1 H), 4.77 (s, 1 H), 3.88–3.57 (m, 2 H), 3.51 (d, *J* = 14.4 Hz, 1 H), 3.29 (d, *J* = 14.4 Hz, 1 H), 0.93 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.6, 167.8, 162.2 (d, *J* = 246.3 Hz), 142.6, 136.9, 134.7, 132.5 (d, *J* = 7.8 Hz), 131.3 (d, *J* = 3.2 Hz), 130.6, 130.5, 128.9, 127.9, 127.7, 127.4, 126.8, 126.3, 125.1, 115.3 (d, *J* = 21.1 Hz), 104.6, 101.7, 65.4, 64.2, 61.4, 40.6, 13.5.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆FN₂O₃⁺: 469.1922; found: 469.1914.

Compound 10h

Yield: 21.2 mg (35%); white crystalline solid; mp 104.1–106.0 °C.
 IR (film): 3065, 2963, 2930, 1729, 1668, 1636, 1601, 1572, 1494, 1475, 1446, 1407, 1368, 1338, 1287, 1260, 1226, 1096, 1045, 1016, 936, 906, 865, 757, 699, 663, 635, 562, 462 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.62–7.60 (m, 1 H), 7.47–7.41 (m, 1 H), 7.40–7.21 (m, 6 H), 7.21–7.06 (m, 4 H), 6.85–6.83 (m, 1 H), 6.08 (d, *J* = 1.5 Hz, 1 H), 5.82 (d, *J* = 7.8 Hz, 1 H), 5.27 (d, *J* = 7.8 Hz, 1 H), 4.94 (d, *J* = 1.5 Hz, 2 H), 3.97 (d, *J* = 14.8 Hz, 1 H), 3.81–3.73 (m, 1 H), 3.68–3.59 (m, 1 H), 3.42 (d, *J* = 14.8 Hz, 1 H), 0.91 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.6, 167.1, 143.4, 136.5, 135.6, 134.7, 133.5, 131.8, 130.6, 130.4, 129.8, 128.74, 128.69, 127.9, 127.6, 127.5, 127.13, 127.09, 126.4, 124.9, 104.4, 100.9, 66.1, 64.1, 61.5, 37.8, 13.4.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1641.

Compound 10i

Yield: 26 mg (43%); white crystalline solid; mp 152.5–153.4 °C.
 IR (film): 3064, 3024, 2981, 2931, 1728, 1667, 1634, 1598, 1572, 1493, 1476, 1446, 1408, 1368, 1339, 1286, 1226, 1202, 1120, 1096, 1047, 1027, 940, 907, 865, 769, 699, 666, 645 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.46–7.08 (m, 12 H), 6.92–6.85 (m, 1 H), 6.10 (d, *J* = 1.2 Hz, 1 H), 5.93 (d, *J* = 7.8 Hz, 1 H), 5.31 (d, *J* = 7.8 Hz, 1 H), 4.89 (d, *J* = 1.3 Hz, 1 H), 4.77 (s, 1 H), 3.86–3.61 (m, 2 H), 3.52 (d, *J* = 14.3 Hz, 1 H), 3.27 (d, *J* = 14.3 Hz, 1 H), 0.94 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.4, 167.8, 142.5, 137.7, 136.9, 134.7, 134.3, 131.0, 130.6, 130.5, 129.7, 129.1, 129.0, 127.9, 127.7, 127.6, 127.3, 126.8, 126.4, 125.1, 104.6, 101.9, 65.3, 64.6, 61.5, 41.1, 13.5.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆ClN₂O₃⁺: 485.1626; found: 485.1613.

Compound 10l

Yield: 29.5 mg (45%); white crystalline solid; mp 162.0–164.0 °C.

IR (film): 2978, 1727, 1665, 1634, 1599, 1567, 1493, 1474, 1446, 1407, 1367, 1339, 1286, 1226, 1201, 1096, 1073, 1045, 939, 863, 783, 751, 698, 668 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.57 (s, 1 H), 7.44–7.26 (m, 7 H), 7.24–7.08 (m, 4 H), 6.91–6.84 (m, 1 H), 6.09 (d, *J* = 1.4 Hz, 1 H), 5.93 (d, *J* = 7.8 Hz, 1 H), 5.31 (d, *J* = 7.8 Hz, 1 H), 4.89 (d, *J* = 1.5 Hz, 1 H), 4.76 (s, 1 H), 3.90–3.60 (m, 2 H), 3.52 (d, *J* = 14.2 Hz, 1 H), 3.25 (d, *J* = 14.3 Hz, 1 H), 0.94 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.3, 167.8, 142.5, 138.0, 136.9, 134.7, 133.8, 130.58, 130.52, 130.46, 130.0, 129.6, 128.9, 127.9, 127.7, 127.3, 126.8, 126.4, 125.0, 122.5, 104.6, 101.9, 65.3, 64.6, 61.5, 41.1, 13.4.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆BrN₂O₃⁺: 529.1121; found: 529.1126.

Compound 10m

Yield: 30.2 mg (54%); white solid.

IR (film): 3063, 2982, 2937, 2905, 1732, 1666, 1633, 1602, 1579, 1492, 1447, 1409, 1370, 1343, 1261, 1189, 1097, 1071, 1026, 940, 910, 865, 773, 754, 701, 667, 646 cm⁻¹.

¹H NMR (75 MHz, CDCl₃): δ = 7.70–7.68 (m, 2 H), 7.46–7.30 (m, 3 H), 7.25–7.06 (m, 3 H), 6.90 (d, *J* = 7.3 Hz, 1 H), 6.14 (d, *J* = 1.6 Hz, 1 H), 5.95 (t, *J* = 8.1 Hz, 1 H), 5.28 (d, *J* = 7.9 Hz, 1 H), 5.28 (d, *J* = 7.9 Hz, 1 H), 5.21 (s, 1 H), 4.24–4.06 (m, 2 H), 3.84–3.62 (m, 2 H), 3.22–2.91 (m, 2 H), 1.26 (td, *J* = 7.1, 2.6 Hz, 3 H), 0.91 (t, *J* = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.8, 169.9, 167.9, 142.5, 137.3, 135.1, 130.6, 130.4, 129.1, 128.1, 127.9, 127.1, 126.9, 126.3, 125.0, 104.3, 98.8, 65.2, 61.5, 61.1, 61.0, 39.0, 14.1, 13.4.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₆H₂₇N₂O₅⁺: 447.1914; found: 447.1917.

Compound 11

Yield: 16.9 mg (38%); white solid.

IR (film): 2963, 1733, 1665, 1631, 1525, 1492, 1447, 1369, 1346, 1261, 1177, 1088, 1027, 930, 864, 798, 758, 700, 657 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.79–7.63 (m, 2 H), 7.50–7.31 (m, 3 H), 7.24–7.06 (m, 3 H), 6.96 (d, *J* = 7.5 Hz, 1 H), 6.00–5.95 (m, 1 H), 5.91 (d, *J* = 7.4 Hz, 1 H), 5.54 (d, *J* = 7.8 Hz, 1 H), 5.08–5.01 (m, 1 H), 4.95 (d, *J* = 10.5 Hz, 1 H), 4.42–4.12 (m, 3 H), 1.32 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 169.0, 167.8, 139.9, 137.4, 134.7, 130.7, 129.4, 129.0, 128.4, 127.9, 127.0, 126.9, 125.2, 107.2, 97.4, 62.5, 61.7, 54.4, 14.2.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₂H₂₁N₂O₃⁺: 361.1547; found: 361.1539.

Compound 12

Yield: 14.1 mg (31%); white solid.

IR (film): 3064, 2962, 2929, 2870, 1734, 1703, 1664, 1631, 1601, 1577, 1524, 1492, 1452, 1408, 1371, 1336, 1276, 1261, 1210, 1195, 1178, 1162, 1087, 1028, 968, 936, 899, 866, 797, 762, 700, 665, 644, 632 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.76–7.63 (m, 2 H), 7.46–7.32 (m, 3 H), 7.23–7.08 (m, 3 H), 6.90 (d, J = 6.8 Hz, 1 H), 6.13 (s, 1 H), 5.94 (d, J = 7.9 Hz, 1 H), 5.32 (d, J = 7.9 Hz, 1 H), 5.10 (d, J = 7.8 Hz, 1 H), 5.02–4.98 (m, 1 H), 4.03–3.88 (m, 1 H), 3.86–3.56 (m, 2 H), 0.82 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 170.3, 167.7, 139.1, 136.7, 134.8, 130.7, 130.4, 128.9, 128.3, 128.0, 127.7, 127.1, 126.4, 125.1, 105.0, 99.5, 62.0, 61.1, 57.7, 13.4.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₂H₂₁N₂O₃: 361.1547; found: 361.1542.

Compound 14

Yield: 31.3 mg (47%); white solid.

IR (film): 2979, 1729, 1671, 1523, 1486, 1449, 1381, 1355, 1278, 1225, 1086, 1018, 959, 802, 758, 702 cm⁻¹.

¹H NMR (300 MHz, DMSO-*d*₆): δ = 7.50–7.07 (m, 14 H), 6.26 (s, 1 H), 6.08 (d, J = 1.6 Hz, 1 H), 5.00 (d, J = 1.6 Hz, 1 H), 4.85 (s, 1 H), 3.85 (dq, J = 10.8, 7.2 Hz, 1 H), 3.67 (dq, J = 10.8, 7.1 Hz, 1 H), 3.52 (d, J = 14.4 Hz, 1 H), 3.36 (d, J = 14.4 Hz, 1 H), 0.98 (t, J = 7.2 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.4, 167.6, 142.8, 137.5, 135.3, 134.5, 130.9, 130.5, 129.6, 129.1, 128.6, 127.9, 127.7, 127.6, 127.53, 127.48, 126.5, 125.2, 101.3, 98.5, 65.5, 63.5, 61.7, 41.4, 13.6.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆BrN₂O₃: 529.1121; found: 529.1113.

Compound 15

Yield: 13.6 mg (21%); white solid.

IR (film): 3063, 2965, 1706, 1603, 1522, 1451, 1367, 1323, 1277, 1261, 1198, 1165, 1108, 1086, 1024, 861, 799, 756, 711 cm⁻¹.

¹H NMR (300 MHz, DMSO-*d*₆): δ = 7.72–7.62 (m, 2 H), 7.50–7.24 (m, 5 H), 7.22–7.05 (m, 5 H), 7.02–6.90 (m, 2 H), 6.48 (s, 1 H), 5.90 (d, J = 1.4 Hz, 1 H), 5.35 (s, 1 H), 4.41 (d, J = 1.5 Hz, 1 H), 4.37–4.22 (m, 2 H), 3.16 (s, 2 H), 1.33 (t, J = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 171.4, 167.8, 141.8, 137.7, 135.8, 134.5, 131.4, 130.9, 130.4, 129.3, 129.0, 128.2, 128.12, 128.09, 127.99, 127.5, 126.9, 126.6, 125.3, 102.4, 99.2, 66.6, 63.9, 62.0, 38.9, 14.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆BrN₂O₃: 529.1121; found: 529.1099.

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