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Construction of dispirocyclohexyl-3,3'-bisoxindole and dispirocyclopentyl-3,3'-bisoxindole via domino cycloaddition reactions of *N*-benzylbenzimidazolium salts with 2-(2-oxoindolin-3-ylidene)acetates

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Abstract: The cycloaddition reaction of *N*-benzyl-*N*-phenacylbenzimidazolium salts with two molecules of 2-(2-oxoindolin-3-ylidene)acetate in ethanol in the presence of triethylamine as base afforded functionalized dispirocyclohexyl-3,3'-bisoxindoles in good yields. Alternatively, the similar reactions of *N*-benzyl-*N*-(alkoxycarbonylmethyl)benzimidazolium salts with two molecules of 2-(2-oxoindolin-3-ylidene)acetates resulted in dispirocyclopentyl-3,3'-bisoxindole derivatives in good yields and with high diastereoselectivity.

Keywords: cycloaddition reaction; domino reaction; spirooxindole; nitrogen ylide; benzimidazole.

Introduction

Among the various classes of heterocyclic compounds, spirooxindoles, a class of nitrogen-containing spiroheterocycles, form an important component of many natural alkaloids and pharmacologically active compounds.[1,2] Hence, the synthesis of spirooxindole derivatives is currently of significant field in organic synthesis. Even through a number of elegant synthetic methods have been applied for the preparation of the diversely structured spirocyclic oxindoles.[3-5] The development of more convenient and efficient protocols for these useful compounds is still an active research area in current synthetic and medicinal chemistry.[6,7] On the other hand, the

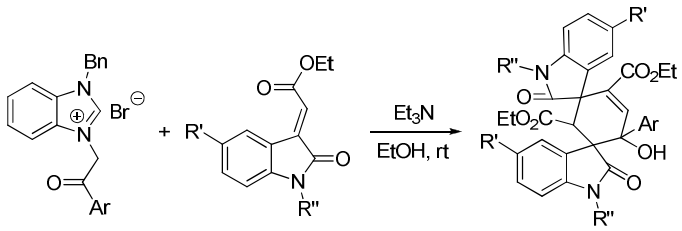
heterocyclic ammonium salts such as pyridinium, quinolinium, isoquinolinium and benzimidazolim salts can be easily obtained from the alkylation of azaaromatic heterocycles with active alkyl halides and are readily accessible and versatile reagents.[8,9] They could undergo various reactions such as 1,3-dipolar cycloaddition, Michael addition, cyclopropanation and have been widely used as for the synthesis of versatile carbocyclic and heterocylic heterocycles. Therefore, it is very nature to witness many applications on construction of spirooxindole systems with the cycloaddition reactions of the heterocyclic ammonium salts with various functionalized isatins and 3-methyleneoxindoles.[10,11] In the past few years, we have successfully developed some domino and multicomponent reactions by using the very easily *in situ* formed heterocyclic ammonium salts as key component of the reactions.[12] Recently, we found that the cycloaddition reaction of heterocyclic ammonium salts with 3-methyleneoxindole derivatives has very interesting molecular diversity, from which, functionalized isatinyl zwitterionates, spiro[cyclopropane-1,3'-indolines], 3-furan-3(2H)-ylidene)indolin-2-ones, 3-(2-oxoindolin-3-ylidene)butanoates, spiro[indoline-3,3'-pyrrolo[1,2-a]quinolines], and dispirocyclopentyl-3,3'-bisoxindoles have been selectively obtained depending on the structures of substrates and reaction conditions.[13] In order to further explore the potential applications of this methodology and with the aim of expanding our previous studies on the synthesis of spirooxindoles, herein we wish to report the selective construction of dispirocyclohexyl-3,3'-bisoxindole and dispirocyclopentyl-3,3'-bisoxindole via domino cycloaddition reactions of *N*-benzylbenzimidazolium salts with two molecules of 2-(2-oxoindolin-3-ylidene)acetates.

Results and discussions

According to the previously established reaction conditions for the reaction of benzimidazolium salts with benzalidene Meldrum acid,[12g] or isatinyl malononitrile,[13a] a mixture of *N*-benzyl-*N'*-phenacylbenzimidazolium salts[14] (**1a**) and a equivalent amount of 2-(2-oxoindolin-3-ylidene)acetates (**2a**) was carried out in ethanol in the presence of triethylamine at room temperature. After workup, we were pleased to find that a main product (**3a**) can be obtained in about 30% yield. Structural analysis showed that the obtained product **3a** was constructed by one phenacyl group and two moieties 2-(2-oxoindolin-3-ylidene)acetates oxindoles, while the moiety of benzimidazole was incorporated in the molecule. When two equivalent 2-(2-oxoindolin-3-ylidene)acetates were used in the reaction, the yield of the product **3a** can be increased to 62%. If the reaction was carried out at elevated temperature, the yield of product **3a** was sharply decreased with the formation of complicate mixtures. Thus, the simple reaction conditions for this domino reaction is using one equivalent *N*-benzyl-*N'*-phenacylbenzimidazolium bromide and slightly less two equivalent 2-(2-oxoindolin-3-ylidene)acetates with triethylamine as base in ethanol at room temperature. Under the chosen reaction conditions, the reactions of various *N*-benzyl-*N'*-phenacylbenzimidazolium salts and 2-(2-oxoindolin-3-ylidene)acetates proceeded smoothly to give desired dispirocyclohexyl-3,3'-bisoxindole derivatives **3a-3m** in good yields (**Table 1**). The substituents on the both substrates showed marginal effect. The structures of compounds **3a-3m** were deduced by IR, HRMS, ^{1}H and ^{13}C NMR spectroscopy. Due to four diastereoisomeric carbon atoms in the newly-formed cyclohexene ring, a couple of diastereoisomers might exist in the obtained products. ^{1}H NMR spectra of the compounds **3a-3m** usually display one set of absorptions for the characteristic groups in the molecule. This result

clearly indicated only one diastereoisomer existing in the products. Unambiguous evidence for the proposed structure was finally obtained by single crystal determination of compound **3f** (**Fig. 1**). It can be sent that the ring of cyclohexene exists in *half-chair* conformation and the two oxindole moieties stand in opposite direction. Thus, we assigned all dispirocyclohexyl-3,3'-bisoxindole derivatives **3a-3m** have this kind of configuration.

Table 1 Synthesis of dispirocyclohexyl-3,3'-bisoxindoles 3a-3m[a]



1a **2** **3a-3h**

Entry	Comp	Ar	R'	R"	Yield (%)[b]
1	**3a**	C_6H_5	F	Bn	62
2	**3b**	C_6H_5	Cl	Bn	70
3	**3c**	C_6H_5	Cl	n-C_4H_9	65
4	**3d**	*p*-ClC_6H_4	CH_3	Bn	58
5	**3e**	*p*-ClC_6H_4	F	Bn	62
6	**3f**	*p*-ClC_6H_4	Cl	Bn	71
7	**3g**	*p*-ClC_6H_4	Cl	n-C_4H_9	68
8	**3h**	*p*-FC_6H_4	F	Bn	74
9	**3i**	*p*-FC_6H_4	Cl	Bn	73
10	**3j**	*p*-$CH_3C_6H_4$	F	Bn	60
11	**3k**	*p*-$CH_3C_6H_4$	Cl	Bn	65
12	**3l**	*p*-$CH_3OC_6H_4$	F	Bn	75
13	**3m**	*p*-$CH_3OC_6H_4$	Cl	Bn	71

a. Reaction condition: *N*-benzyl-*N'*-phenacylbenzimidazolium bromide (0.6 mmol), ethyl 2-(2-oxoindolin-3-ylidene)acetate (1.0 mmol), Et_3N (0.5 mmol) in EtOH (10.0 mL), rt, 12 hrs;

b. Isolated yield.

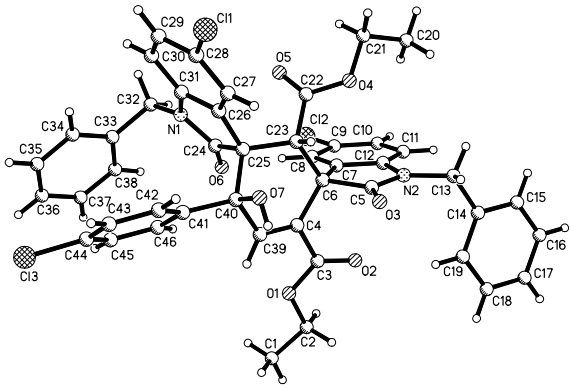
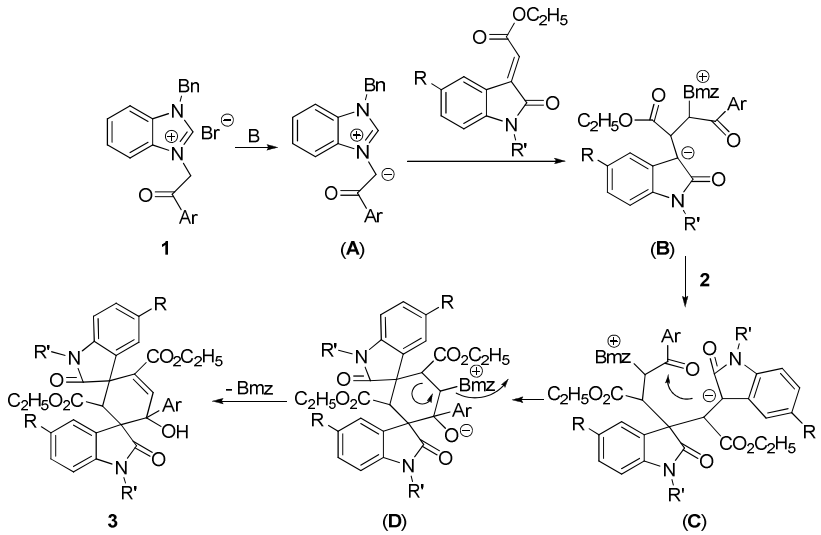


Fig. 1 Molecular structure of compound 3f

Although the precise mechanism is not very clear at present time, for explaining the formation mechanism of dispirocyclohexyl-3,3'-bisoxindoles, we proposed a plausible reaction course, which is illustrated in **Scheme 1**. At first, *N*-benzyl-*N'*-phenacylbenzimidazolium bromide (**1**) was deprotonated by triethylamine to give the benzimidazolium ylide (**A**). Secondly, Michael addition of the benzimidazolium ylide (**A**) to 2-(2-oxoindolin-3-ylidene)acetate (**2**) resulted in the adduct (**B**). Thirdly, further addition of carbanion (**B**) to second molecular 2-(2-oxoindolin-3-ylidene)acetate afforded another intermediate (**C**). Then, the intramolecular

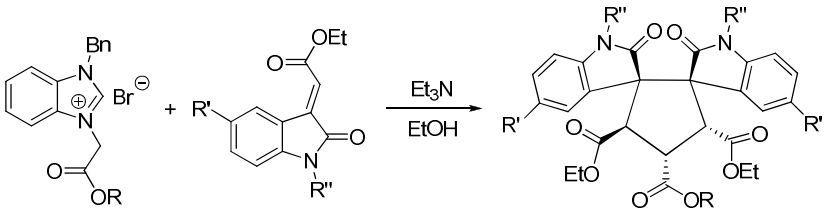


Scheme 1 proposed formation mechanism for dispirocyclohexyl-3,3'-bisoxindoles.

nucleophilic addition of carbanion to carbonyl group produced a cyclic intermediate (**D**). Finally, the substituted dispirocyclohexyl-3,3'-bisoxindole **3** was formed through the splitting off *N*-benzylbenzimidazole and protonation process. Because all reactions were in retro-equilibrium, the most stable thermodynamic isomer would be preferably formed as the main product in this domino reaction process.

In order to develop the scope of this reaction, *N*-benzyl-*N'*-(alkoxycarbonylmethyl)benzimidazolium salts (**1b**) were also utilized to react with 2-(2-oxoindolin-3-ylidene)acetates (**2**) under same reaction conditions. However, instead of giving dispirocyclohexyl-3,3'-bisoxindoles, the reaction afforded functionalized dispirocyclopentyl-3,3'-bisoxindoles **4a-4g** with two oxindole moieties at 1,2-positions of newly-formed cyclopentyl ring (**Table 2**). A literature survey indicated that there are very few reports about the synthesis of kind of dispirocyclopentyl-3,3'-bisoxindoles.[15] We have recently prepared this kind of dispirocyclopentyl-3,3'-bisoxindoles by the base prompted cycloaddition reactions of 1-(alkoxycarbonylmethyl)-4-dimethylaminopyridinium salts with 3-phenacylideneoxindoles.[13d] Here, the formation of two kinds of dispirooxindole systems is attribute to the different structures of *N*-benzyl-*N'*-phenacylbenzimidazolium salts (**1a**) and *N*-benzyl-*N'*-(alkoxycarbonylmethyl)benzimidazolium salts (**1b**). There is one active carbonyl groups in the salts **1a**, which can underwent the intramolecular nucleophilic addition of carbanion to carbonyl group to produce a six-memebred cyclic intermediate (**D**) in **Scheme 1**. Alternatively, there is only the ester group in salts (**1b**), such a nucleophilic addition can not take place for relative unactive ester group. Thus, the sequential reaction procedded according to other way to afford functionalized dispirocyclopentyl-3,3'-bisoxindoles **4a-4f**. ^{1}H NMR

Table 2 Synthesis of dispirocyclopentyl-3,3'-bisoxindoles 4a-4h[a]



1b **2** **4a-4g**

Entry	Comp	R	R'	R"	Yield (%) [b]
1	**4a**	CH_3	H	Bn	63
2	**4b**	CH_3	CH_3	Bn	67
3	**4c**	CH_3	F	Bn	58
4	**4d**	CH_3	Cl	Bn	66
5	**4e**	C_2H_5	CH_3	Bn	52 (2.5:1) [c]
6	**4f**	C_2H_5	F	Bn	59 (2:1) [c]
7	**4g**	C_2H_5	Cl	Bn	48 (1.4:1) [c]

a Reaction condition: *N*-benzyl-*N'*-alkoxycarbonylmethylbenzimidazolium bromide (0.6 mmol), ethyl 2-(2-oxoindolin-3-ylidene)acetate (1.0 mmol), Et_3N (0.5 mmol) in EtOH (10.0 mL), rt, 12 hrs; b. Isolated yield; c. the ratio of isomers is determined by ^1H NMR spectra.

spectra indicated that one diastereoisomer was predominately prodcuced in the products **4a-4d** and a mixtue of diastereisomers were also obtained in the products **4e-4g**. The single crystal structures of compounds **4a** and **4d** were determined by X-ray diffraction (Fig. 2 and Fig. 3). It can be seen that the two neighboring oxindole units stand at *cis*-position in the newly-formed cyclopentyl ring, while the two ethoxycarbonyl groups exist at *trans*-position. The single crystal structure of one diastereoisomer of **4f** was also obtained, which has the same configuration to that of compounds **4a** and **4d**. On the basis of ^1H NMR spectra and single crystal structures we can assigned that dispirocyclopentyl-3,3'-bisoxindoles **4a-4g** exist mainly in this configuration. It should be also pointed out that the stereochemistry of the **4a-4g** is different to that of the previously obtained main diastereoisomer in the reactions of

1-(alkoxycarbonylmethyl)-4-dimethylaminopyridinium salts.[13d] This result reflected the different reactivity and steric effect of benzimidazolium salts to 4-dimethylaminopyridinium salts.

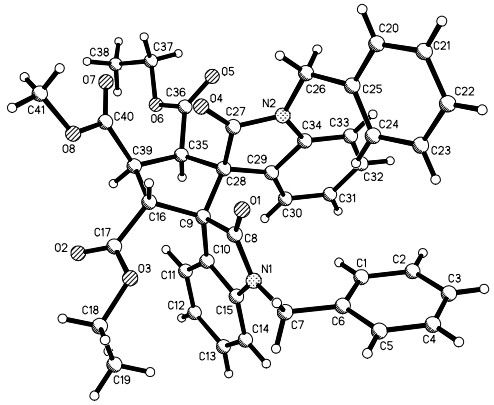


Fig. 2 Molecular structure of compound **4a**

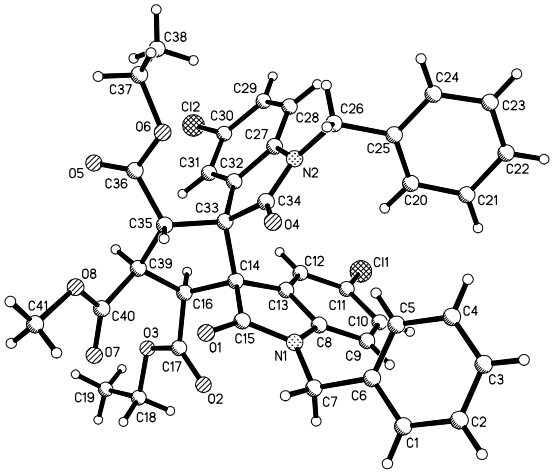


Fig. 3 Molecular structure of compound **4d**

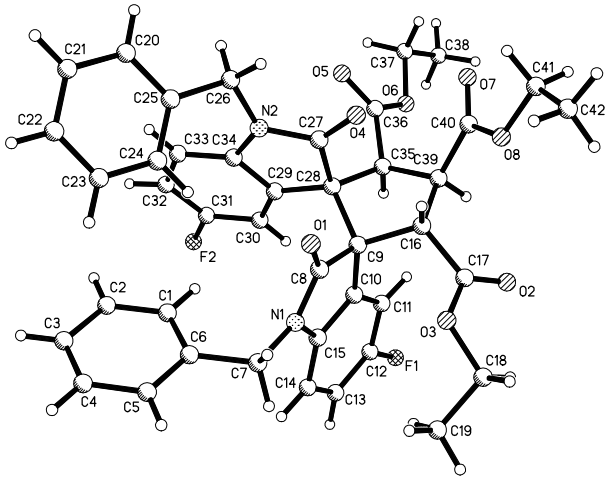
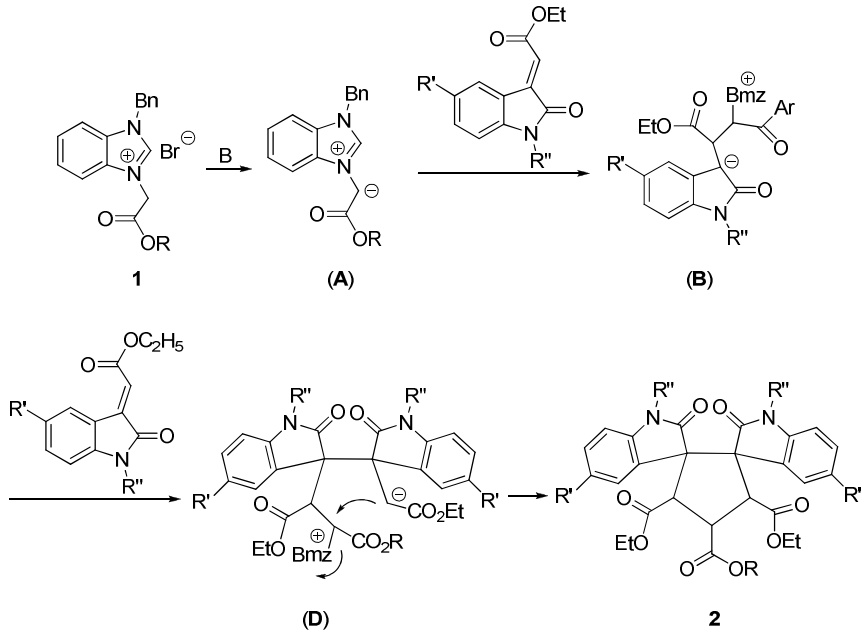


Fig. 4 Molecular structure of compound **4f**

A plausible reaction process is also proposed to rationalize the formation of dispirocyclopentyl-3,3'-bisoxindoles (Scheme 2). The first two steps are same to that in **Scheme 1**. In the third step, the addition of carbanion (**B**) to the C-3 position of second molecular 2-(2-oxoindolin-3-ylidene)acetate affords a double adduct (**E**). Because there is no carbonyl group in the double adduct (**E**), the intramolecular addition of carbanion to the carbonyl group in **Scheme 1** can not take place here. Alternatively, intramolecular nucleophilic substitution of carbanion to benzimidazolyl ring in the double adduct (**E**) gives dispirocyclopentyl-3,3'-bisoxindole **4**. Thus, the formation of two kinds of dispirooxindole systems is attribute to the different structures of *N*-benzyl-*N'*-phenacylbenzimidazolium salts and *N*-benzyl-*N'*-(alkoxycarbonylmethyl)benzimidazolium salts.



Scheme 2 Proposed formation mechanism of dispirocyclopentyl-3,3'-bisoxindoles

Conclusion

In summary, we have systematically investigated the domino cycloaddition reaction of benzimidazolium salts with two molecules of 2-(2-oxoindolin-3-ylidene)acetates. This reaction provided efficient synthetic protocols for selective synthesis of novel dispirocyclopentyl-3,3'-bisoxindole and dispirocyclohexyl-3,3'-bisoxindole derivatives. The reaction mechanism and stereochemistry of products were established on the careful analysis of molecular structures of the substrates, spectroscopic data and single crystal structures of the products. The advantages of this reaction are using readily available reagents, mild reaction conditions, easy purification of the products, good yields and high diasteresoselectiivty, which makes it a useful and attractive method for the synthesis of the complex spiroheterocycles in synthetic and medicinal chemistry.

Experimental section

1. **General procedure for the synthesis of dispirocyclohexyl-3,3'-bisoxindoles 3a-3m:** a mixture of *N*-benzyl-*N'*-phenacylbenzimidazolium bromide (0.6 mmol), ethyl 2-(2-oxoindolin-3-ylidene)acetate (1.0 mmol) and triethylamine (0.5 mmol) in 10.0 mL of ethanol was stirred at room temperature for about twelve hours. After removing the solvent by rotatory evaporation at reduced pressure, the residue was subjected to preparative thin-layer chromatography with a mixture of light petroleum and ethyl acetate (V/V = 3:1) as developing reagent to give the pure product for analysis.

Compound 3a: white solid, 62%, m.p. 145~147℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.71 (d, *J* = 7.8Hz, 1H, ArH), 7.66 (s, 1H, ArH), 7.52 (t, *J* = 7.2Hz, 3H, ArH), 7.37 (t, *J* = 7.2Hz, 2H, ArH), 7.30 (t, *J* = 7.2Hz, 1H, ArH), 7.21~7.14 (m, 6H, ArH), 7.10 (t, *J* = 7.2Hz, 2H, ArH), 6.86 (t, *J* = 7.8Hz, 1H, ArH), 6.82 (d, *J* = 4.2Hz, 2H, ArH), 6.73 (t, *J* = 8.4Hz, 1H, ArH), 6.68~6.66 (m, 1H, ArH), 6.12~6.10 (m, 1H, ArH), 5.15 (d, *J* = 15.6Hz, 1H, CH), 4.88 (d, *J* = 15.6Hz, 1H, CH), 4.61 (d, *J* = 16.2Hz, 1H, CH), 4.53 (d, *J* = 16.2Hz, 1H, CH), 4.50 (s, 1H, CH), 4.11~4.06 (m, 1H, CH), 3.94~3.88 (m, 1H, CH), 3.80 (s, 1H, CH), 3.36~3.31 (m, 1H, CH), 3.14~3.09 (m, 1H, CH), 1.05 (t, *J* = 7.2Hz, 3H, CH_3), 0.39 (t, *J* = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.9, 175.2, 167.7, 164.3, 143.7, 141.1, 139.7, 139.6, 135.3, 135.3, 134.1, 129.7, 128.8, 128.5, 127.9, 127.7, 127.4, 127.2, 127.0, 126.9, 116.2, 116.0, 115.0, 114.9, 114.8, 113.7, 113.5, 109.0, 109.0, 108.9, 73.1, 61.4, 61.0, 56.8, 53.4, 45.5, 44.3, 13.8, 13.1; IR (KBr) υ: 3343, 3068, 2979, 2936, 1738, 1717, 1695, 1620, 1490, 1451, 1350, 1263, 1185, 1138, 1045, 1024, 976, 931, 900, 866, 811, 770, 732 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{46}H_{38}F_2N_2O_7$ ($[M+H]^+$): 791.2539. Found: 791.255.

Compound 3b: white solid, 70%, m.p. 142~144℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.92 (d, *J* = 1.2Hz, 1H, ArH), 7.75 (d, *J* = 1.8Hz, 1H, ArH), 7.68 (s, 1H, ArH), 7.50 (d, *J* = 7.8Hz, 2H, ArH), 7.38 (t, *J* = 7.8Hz, 2H, ArH), 7.31 (t, *J* = 7.8Hz, 1H, ArH), 7.22~7.18 (m, 4H, ArH), 7.15~7.10 (m, 5H, ArH), 7.02 (dd, J_1 = 8.4Hz, J_2 = 1.8Hz, 1H, ArH), 6.83 (t, *J* = 3.6Hz, 2H, CH), 6.61 (d, *J* = 8.4Hz, 1H, CH), 6.15 (d, *J* = 8.4Hz, 1H, ArH), 5.13 (d, *J* = 15.6Hz, 1H, CH), 4.90 (d, *J* = 15.6Hz, 1H, CH), 4.55 (s, 2H, CH), 4.49 (s, 1H, CH), 4.13~4.07 (m, 1H, CH), 3.95~3.89 (m, 1H, CH), 3.80 (s, 1H, CH), 3.33~3.28 (m, 1H, CH), 3.12~3.07 (m, 1H, CH), 1.07 (t, *J* = 7.2Hz, 3H, CH), 0.37 (t, *J* = 7.2Hz, 3H, CH); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.5, 175.0, 174.9, 167.7, 167.6,

164.2, 143.2, 135.0, 134.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.2, 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, 127.3, 127.2, 127.0, 125.9, 109.6, 109.6, 72.7, 61.5, 61.5, 61.2, 56.4, 53.5, 52.5, 45.5, 44.3, 13.8, 13.1; IR (KBr) υ: 3432, 3081, 2981, 1714, 1657, 1608, 1481, 1456, 1430, 1369, 1343, 1262, 1176, 1116, 1094, 1018, 967, 909, 874, 843, 812, 782, 734 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{46}H_{38}Cl_2N_2NaO_7$ ($[M+H]^+$): 823.1948. Found: 823.1937.

Compound 3c: white solid, 65%, m.p. 171~173℃; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.87 (s, 1H, ArH), 7.68 (s, 1H, ArH), 7.61 (s, 1H, ArH), 7.24 (d, *J* = 8.4Hz, 1H, ArH), 7.13~7.08 (m, 6H, ArH), 6.78 (d, *J* = 8.4Hz, 1H, ArH), 6.32 (d, *J* = 7.8Hz, 1H, ArH), 4.35 (s, 1H, CH), 4.10~4.04 (m, 1H, CH), 3.98~3.92 (m, 1H, CH), 3.83~3.77 (m, 2H, CH), 3.72 (s, 1H, CH), 3.45~3.40 (m, 2H, CH), 3.22~3.15 (m, 2H, CH), 1.76~1.72 (m, 3H, CH), 1.54~1.48 (m, 2H, CH), 1.20~1.17 (m, 3H, CH), 1.10 (t, *J* = 7.2Hz, 3H, CH_3), 1.02 (t, *J* = 7.2Hz, 3H, CH_3), 0.87 (t, *J* = 6.3Hz, 3H, CH_3), 0.64 (t, *J* = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.2, 174.5, 167.6, 164.2, 144.0, 143.4, 142.5, 139.4, 134.0, 131.5, 129.9, 128.6, 128.3, 128.1, 127.7, 127.1, 126.9, 126.8, 125.7, 108.6, 108.2, 73.1, 61.2, 60.9, 56.3, 52.9, 52.3, 41.2, 40.0, 29.3, 29.0, 20.3, 20.2, 13.9, 13.7, 13.7, 13.3; IR (KBr) υ: 3818, 3747, 3616, 3388, 3078, 2961, 2869, 2368, 2342, 1737, 1718, 1696, 1656, 1606, 1559, 1543, 1484, 1461, 1427, 1365, 1306, 1264, 1211, 1185, 1147, 1113, 1051, 1020, 908, 869, 810, 780, 754 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{40}H_{42}Cl_2N_2NaO_7$ ($[M+H]^+$): 755.2261. Found: 755.2268.

Compound 3d: white solid, 58%, m.p. 108~110℃; ^1H NMR (600 MHz, $CDCl_3$) δ: 8.32 (d, *J* = 8.4Hz, 2H, ArH), 7.50 (d, *J* = 8.4Hz, 2H, ArH), 7.42 (s, 1H, ArH), 7.25 (s, 1H, ArH), 7.12 (q, J_1 = 15.6Hz, J_2 = 7.2Hz, 2H, ArH), 7.07~7.02 (m, 4H, ArH), 6.87 (d, *J* = 7.8Hz, 1H, ArH), 6.84 (d, *J* = 7.8Hz, 1H, ArH), 6.65 (q, J_1 = 16.2Hz, J_2 = 4.2Hz, 4H, ArH), 6.27 (q, J_1 = 7.2Hz, J_2 = 4.2Hz, 2H, ArH), 6.20 (t, *J* = 11.4Hz, 1H, ArH), 5.01 (d, *J* = 16.2Hz, 1H, CH), 4.98 (d, *J* = 16.2Hz, 1H, CH), 4.58~4.52 (m, 2H, CH), 4.40~4.36 (m, 2H, CH), 3.72 (q, J_1 = 7.2Hz, J_2 = 2.4Hz, 2H, CH), 3.64~3.59 (m, 1H, CH), 3.57~3.52 (m, 1H, CH), 2.13 (s, 3H, CH), 2.04 (s, 3H, CH), 0.63 (t, *J* = 7.2Hz, 3H, CH_3), 0.50 (t, *J* = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 199.5, 177.7, 176.4, 169.6, 169.4, 141.1, 139.7, 139.6, 136.0, 135.4, 135.0, 132.3, 132.2, 130.7, 129.3, 129.2, 128.8, 128.5, 128.4, 127.2, 127.1, 127.0, 126.5, 126.4, 126.3, 108.7, 108.6, 61.8, 61.0, 60.6, 55.8, 55.1, 46.7, 43.7, 43.5, 21.1, 20.9, 13.3, 13.2; IR (KBr) υ: 3819, 3747, 3616, 3032, 2981, 2369, 2347, 1737, 1712, 1617, 1544, 1495, 1454, 1435, 1403, 1366, 1267, 1222, 1196, 1093, 1015, 893,

852, 810, 734 cm^{-1}; MS (*m/z*): HRMS (ESI) Calcd. for $C_{48}H_{43}ClN_2NaO_7$ ($[M+H]^+$): 817.2651. Found: 817.2643.

Compound 3e: white solid, 62%, m.p. 139~141℃; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.67 (dd, J_1 = 8.4Hz, J_2 = 2.4Hz,1H,ArH), 7.57 (s, 1H, ArH), 7.52~7.50 (m, 3H, ArH), 7.38 (t, *J* = 7.5Hz, 2H, ArH), 7.32 (t, *J* = 7.2Hz, 1H, ArH), 7.26 (brs, 1H, ArH), 7.25~7.22 (m, 2H, ArH), 7.05 (q, 4H, ArH), 6.89~6.86 (m, 1H, ArH), 6.82~6.77 (m, 3H, ArH), 6.69~6.67 (m, 1H, ArH), 6.23~6.21 (m, 1H, ArH), 5.16 (d, *J* = 15.6Hz, 1H, CH), 4.87 (d, *J* = 15.6Hz, 1H, CH), 4.82(d, *J* = 16.2Hz, 1H, CH), 4.48 (d, *J* = 16.2Hz, 1H, CH), 4.45 (s, 1H, CH), 4.11~4.06 (m, 1H, CH), 3.93~3.88 (m, 2H, CH), 3.36~3.30 (m, 1H, CH), 3.14~3.09 (m, 1H, CH), 1.61 (s, 1H, CH), 1.05 (t, *J* = 7.2Hz, 3H, CH), 0.38 (t, *J* = 6.9Hz, 3H, CH); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.8, 179.7, 175.1, 167.6, 164.2, 160.1, 159.5, 158.5, 157.9, 143.2, 141.1, 139.7, 138.4, 135.3, 135.1, 134.3, 133.9, 131.3, 131.2, 129.4, 129.4, 128.8, 128.6, 128.5, 127.9, 127.6, 127.4, 127.1, 116.3, 116.1, 115.2, 115.1, 115.0, 114.9, 113.8, 113.6, 109.2, 109.1, 109.0, 109.0, 72.8, 61.4, 61.1, 56.6, 53.5, 52.7, 45.5, 44.4, 13.8, 13.1; IR (KBr) υ: 3454, 2978, 2025, 1738, 1717, 1700, 1624, 1489, 1450, 1336, 1259, 1185, 1136, 1092, 1042, 1020, 978, 933, 904, 861, 831, 808, 734 cm^{-1}; MS (*m/z*): HRMS (ESI) Calcd. for $C_{46}H_{37}ClF_2N_2NaO_7$ ($[M+H]^+$): 825.215. Found: 825.2152.

Compound 3f: white solid, 71%, m.p. 136~138℃; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.87 (s, 1H, ArH), 7.73 (s, 1H, ArH), 7.58 (s, 1H, ArH), 7.50 (d, *J* = 7.2Hz, 2H, ArH), 7.38 (d, *J* = 7.2Hz, 2H, ArH), 7.31 (d, *J* = 7.8Hz, 1H, ArH), 7.26 (brs, 1H, ArH), 7.24 (d, *J* = 10.2Hz, 2H, ArH), 7.15 (d, *J* = 8.4Hz, 1H, ArH), 7.06 (d, *J* = 14.4Hz, 5H, ArH), 6.83 (d, *J* = 7.2Hz, 2H, ArH), 6.68 (d, *J* = 8.4Hz, 1H, ArH), 6.25 (d, *J* = 7.8Hz, 1H, ArH), 5.13 (d, *J* = 15.6Hz, 1H, CH), 4.85 (d, *J* = 15.6Hz, 1H, CH), 4.76 (d, *J* = 16.2Hz, 1H, CH), 4.50 (d, *J* = 16.2Hz, 1H, CH), 4.45 (s, 1H, CH), 4.12~4.07 (m, 1H, CH), 3.94~3.90 (m, 2H, CH), 3.34~3.28 (s, 11H, CH), 3.13~3.08 (m, 1H, CH), 1.06 (t, *J* = 7.2Hz, 3H, CH), 0.38 (t, *J* = 7.2Hz, 3H, CH); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.6, 175.0, 167.7, 164.3, 143.8, 143.7, 142.2, 135.2, 134.0, 131.4, 129.7, 128.8, 128.7, 128.6, 128.5, 128.3, 128.0, 127.9, 127.8, 127.6, 127.4, 127.3, 127.2, 127.0, 125.8, 109.6, 109.4, 73.1, 61.5, 61.1, 56.6, 53.4, 52.5, 45.5, 44.2, 13.9, 13.1; IR (KBr) υ: 3432, 3065, 2981, 1715, 1609, 1482, 1453, 1429, 1368, 1344, 1260, 1176, 1117, 1080, 1020, 967, 909, 872, 811, 781, 750 cm^{-1}; MS (*m/z*): HRMS (ESI) Calcd. for $C_{46}H_{37}Cl_3N_2NaO_7$ ($[M+Na]^+$): 857.1559. Found: 857.1554.

Compound 3g: white solid, 68%, m.p. 205~207℃; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.83 (d, *J* =

2.4Hz, 1H, ArH), 7.65 (d, J = 1.8Hz, 1H, ArH), 7.52 (s, 1H, ArH), 7.25 (dd, J_1 = 8.4Hz, J_2 = 1.8Hz, 1H, ArH), 7.15 (dd, J_1 = 8.4Hz, J_2 = 1.8Hz, 1H, ArH), 7.07 (d, J = 8.4Hz, 2H, ArH), 7.03 (d, J = 9.0Hz, 2H, ArH), 6.78 (d, J = 8.4Hz, 1H, ArH), 6.38 (d, J = 8.4Hz, 1H, ArH), 4.32 (s, 1H, CH), 4.10~4.04 (m, 1H, CH), 3.98~3.93 (m, 1H, CH), 3.83~3.75 (m, 3H, CH), 3.52~3.48 (m, 1H, CH), 3.46~3.40 (m, 1H, CH), 3.24~3.20 (m, 1H, CH), 3.18~3.13 (m, 1H, CH), 1.78~1.73 (m, 2H, CH), 1.54~1.47 (m, 2H, CH), 1.25~1.20 (m, 3H, CH), 1.16~1.13 (m, 1H, CH), 1.09 (t, J = 7.2Hz, 3H, CH_3), 1.01 (t, J = 7.2Hz, 3H, CH_3), 0.91 (t, J = 6.6Hz, 3H, CH_3), 0.64 (t, J = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.1, 174.4, 167.5, 164.1, 143.9, 142.7, 142.4, 140.5, 138.2, 131.3, 134.2, 133.8, 131.4, 129.6, 128.8, 128.5, 128.3, 128.2, 127.2, 127.0, 125.8, 108.6, 108.4, 72.8, 61.3, 61.0, 56.2, 52.9, 52.3, 41.2, 40.1, 29.2, 29.1, 20.2, 13.8, 13.7, 13.2; IR (KBr) υ: 3746, 3463, 2962, 2933, 2871, 2366, 1744, 1714, 1691, 1641, 1610, 1543, 1484, 1429, 1356, 1270, 1213, 1184, 1146, 1112, 1053, 1026, 931, 908, 872, 853, 834, 811, 790, 737 cm^{-1}; MS (m/z): HRMS (ESI) Calcd. for $C_{40}H_{41}Cl_3N_2NaO_7$ ($[M+Na]^+$): 789.1872. Found: 789.1869.

Compound 3h: white solid, 74%, m.p. 212~214℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69~7.66 (m, 1H, ArH), 7.59 (s, 1H, ArH), 7.52~7.48 (m, 3H, ArH), 7.38~7.35 (m, 2H, ArH), 7.32~7.28 (m, 1H, ArH), 7.22~7.20 (m, 3H, ArH), 7.10~7.07 (m, 2H, ArH), 6.89~6.84 (m, 3H, ArH), 6.79~6.71 (m, 3H, ArH), 6.68~6.65 (m, 1H, ArH), 6.22~6.18 (m, 1H, ArH), 5.15 (d, J= 22.8Hz, 1H, CH), 4.86 (d, J = 23.4Hz, 1H, CH), 4.78 (d, J = 24.0Hz, 1H, CH), 4.52 (d, J = 24.0Hz, 1H, CH), 4.45~4.44 (m, 1H, CH), 4.10~4.04 (m, 1H, CH), 3.92~3.87 (m, 1H, CH), 3.35~3.28 (m, 1H, CH), 3.15~3.07 (m, 1H, CH), 1.04 (t, J = 10.8Hz, 3H, CH_3), 0.38 (t, J = 10.8Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.7, 175.1, 167.7, 164.2, 143.4, 141.0, 139.6, 135.6, 135.2, 135.2, 134.1, 128.9, 128.8, 128.7, 128.5, 127.9, 127.3, 127.0, 116.3, 116.0, 115.2, 115.0, 114.9, 114.8, 114.3, 114.1, 113.8, 113.5, 109.0, 109.0, 108.9, 72.7, 61.4, 61.0, 56.7, 53.3, 52.6, 45.5, 44.2, 13.8, 13.1; IR (KBr) υ: 3397, 3065, 2983, 1717, 1606, 1487, 1449, 1340, 1264, 1221, 1188, 1028, 924, 875, 839, 813, 742, cm^{-1}; MS (m/z): HRMS (ESI) Calcd. for $C_{46}H_{37}F_3N_2NaO_7$ ($[M+H]^+$): 809.2445. Found: 809.2447.

Compound 3i: white solid, 73%, m.p. 208~210℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 (d, J = 3.0Hz, 1H, ArH), 7.73 (d, J = 3.6Hz, 1H, ArH), 7.60 (s, 1H, ArH), 7.50 (d, J = 10.8Hz, 2H, ArH), 7.38 (t, J = 11.1Hz, 2H, ArH), 7.33~7.29 (m, 1H, ArH), 7.23~7.21 (m, 3H, ArH), 7.16~7.04 (m, 1H, ArH), 7.10~7.04 (m, 3H, ArH), 6.89~6.87 (m, 2H, ArH), 6.75 (t, J = 13.2Hz, 2H, ArH), 6.68 (d, J = 12.6Hz, 1H, ArH), 6.24 (d, J = 12.6Hz, 1H, ArH), 5.13 (d, J= 23.4Hz, 1H, CH), 4.88 (d, J

= 23.4Hz, 1H, CH), 4.64 (d, *J* = 24.0Hz, 1H, CH), 4.55 (d, *J* = 24.0Hz, 1H, CH), 4.45 (s, 1H, CH), 4.14~4.06 (m, 1H, CH), 3.96~3.90 (m, 1H, CH), 3.34~3.27 (m, 1H, CH), 3.14~3.06 (m, 1H, CH), 1.06 (t, *J* = 10.5Hz, 3H, CH_3), 0.38 (t, *J* = 10.5Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.5, 174.9, 167.5, 164.1, 161.1, 143.6, 143.3, 142.2, 135.1, 135.0, 134.1, 131.2, 129.5, 128.8, 128.8, 128.8, 128.7, 128.5, 128.1, 128.0, 127.8, 127.4, 127.3, 127.2, 125.8, 114.4, 114.2, 109.6, 109.4, 72.7, 61.5, 61.2, 56.6, 53.4, 52.4, 45.5, 44.2, 13.8, 13.0; IR (KBr) υ: 3474, 3074, 2984, 1714, 1609, 1482, 1429, 1345, 1263, 1222, 1176, 1114, 1016, 912, 844, 811, 740, 700 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{46}H_{37}Cl_2FN_2NaO_7$ ($[M+H]^+$): 841.1854. Found: 841.1852.

Compound 3j: white solid, 60%, m.p. 210~212℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (d, *J* = 12.6Hz, 2H, ArH), 7.65 (s, 1H, ArH), 7.54~7.50 (m, 3H, ArH), 7.39~7.35 (m, 2H, ArH), 7.32~7.28 (m, 1H, ArH), 7.22~7.17 (m, 3H, ArH), 7.02 (d, *J* = 11.4Hz, 2H, ArH), 6.92~6.84 (m, 3H, ArH), 6.81~6.72 (m, 3H, ArH), 6.67~6.66 (m, 1H, ArH), 6.14~6.12 (m, 1H, ArH), 5.16 (d, *J* = 23.4Hz, 1H, CH), 4.88 (d, *J* = 23.4Hz, 1H, CH), 4.78 (d, *J* = 24.0Hz, 1H, CH), 4.46 (d, *J* = 24.6Hz, 2H, CH), 4.12~4.04 (m, 1H, CH), 3.94~3.86 (m, 1H, CH), 3.37~3.29 (m, 1H, CH), 3.15~3.07 (m, 1H, CH), 2.30 (s, 3H, CH_3), 1.05 (t, *J* = 10.5Hz, 3H, CH_3), 0.39 (t, *J* = 10.5Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.8, 175.3, 167.8, 164.3, 144.1, 141.1, 139.7, 132.3, 136.8, 135.3, 135.3, 133.8, 131.3, 129.8, 129.7, 128.7, 128.3, 128.1, 127.9, 127.1, 126.9, 116.3, 116.0, 115.0, 114.7, 114.7, 113.7, 113.5, 108.9, 72.9, 61.3, 61.0, 56.7, 53.5, 45.5, 44.3, 21.1, 13.8, 13.1; IR (KBr) υ: 3419, 3067, 2981, 2926, 1719, 1619, 1488, 1451, 1347, 1262, 1183, 1033, 975, 937, 902, 873, 811, 735 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{47}H_{40}F_2N_2NaO_7$ ($[M+H]^+$): 805.2696. Found: 805.2693.

Compound 3k: white solid, 65%, m.p. 222~224℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (s, 1H, ArH), 7.75 (s, 1H, ArH), 7.66 (s, 1H, ArH), 7.50 (d, *J* = 11.4Hz, 2H, ArH), 7.37 (t, *J* = 11.4Hz, 2H, ArH), 7.32~7.29 (m, 1H, ArH), 7.22~7.13 (m, 4H, ArH), 7.04~7.00 (m, 3H, ArH), 6.92 (d, *J* = 12.0Hz, 2H, ArH), 6.83 (d, *J* = 9.6Hz, 2H, ArH), 6.67 (d, *J* = 12.0Hz, 1H, ArH), 6.17 (d, *J* = 12.0Hz, 1H, ArH), 5.15~5.11 (m, 1H, CH), 4.92~4.88 (m, 1H, CH), 4.73~4.69 (m, 1H, CH), 4.51~4.47 (m, 2H, CH), 4.14~4.06 (m, 1H, CH), 3.95~3.87 (m, 1H, CH), 3.62~3.58 (m, 1H, CH), 3.35~3.27 (m, 1H, CH), 3.14~3.06 (m, 1H, CH), 2.30 (s, 3H, CH_3), 1.06 (t, *J* = 10.5Hz, 3H, CH_3), 0.38 (t, *J* = 10.5Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.6, 175.0, 167.6, 164.2, 144.1, 143.7, 142.3, 137.4, 136.6, 135.2, 133.8, 131.3, 129.8, 128.8, 128.6, 128.6, 128.4, 128.4, 128.1,

127.9, 127.8, 127.2, 127.2, 127.1, 126.8, 125.8, 109.5, 109.4, 72.9, 61.4, 56.5, 53.5, 52.4, 45.5, 44.3, 21.1, 13.8, 13.1; IR (KBr) υ: 3423, 3068, 2980, 2925, 1721, 1610, 1484, 1430, 1347, 1261, 1179, 1116, 1079, 1023, 909, 816, 780, 732 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{47}H_{40}Cl_2N_2NaO_7$ ($[M+H]^+$): 837.2105. Found: 837.2106.

Compound 3l: white solid, 75%, m.p. 182~184℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.72~7.69 (m, 1H, ArH), 7.65 (s, 1H, ArH), 7.54~7.50 (m, 3H, ArH), 7.37 (t, *J* = 11.1Hz, 2H, ArH), 7.32~7.29 (m, 1H, ArH), 7.19~7.15 (m, 3H, ArH), 7.05 (d, *J* = 13.2Hz, 2H, ArH), 6.89~6.84 (m, 1H, ArH), 6.79~6.73 (m, 3H, ArH), 6.68~6.64 (m, 2H, ArH), 6.62 (s, 1H, ArH), 6.16~6.13 (m, 1H, ArH), 5.15 (d, *J* = 23.4Hz, 1H, CH), 4.88 (d, *J* = 23.4Hz, 1H, CH), 4.76 (d, *J* = 23.4Hz, 1H, CH), 4.49 (d, *J* = 24.0Hz, 2H, CH), 4.13~4.05 (m, 1H, CH), 3.94~3.86 (m, 1H, CH), 3.75 (s, 3H, OCH_3), 3.37~3.29 (m, 1H, CH), 3.16~3.08 (m, 1H, CH), 1.05 (t, *J* = 10.5Hz, 3H, CH_3), 0.39 (t, *J* = 10.5Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.8, 175.2, 167.7, 164.3, 159.1, 144.1, 141.1, 141.1, 139.7, 135.3, 135.2, 133.8, 131.8, 128.7, 128.4, 128.2, 127.9, 127.2, 127.0, 116.3, 116.0, 115.0, 114.9, 114.8, 113.7, 113.4, 112.8, 109.1, 109.0, 108.9, 108.8, 72.8, 61.3, 61.0, 56.8, 56.8, 55.1, 53.5, 45.5, 44.2, 13.8, 13.1; IR (KBr) υ: 3431, 3070, 2975, 1714, 1609, 1488, 1451, 1368, 1343, 1257, 1178, 1116, 1034, 904, 866, 837, 809, 733 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{47}H_{40}F_2N_2NaO_8$ ($[M+H]^+$): 821.2645. Found: 821.2644.

Compound 3m: white solid, 71%, m.p. 204~206℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.90 (s, 1H, ArH), 7.74 (s, 1H, ArH), 7.65 (s, 1H, ArH), 7.50 (d, *J* = 10.8Hz, 2H, ArH), 7.37 (t, *J* = 11.1Hz, 2H, ArH), 7.32~7.29 (m, 1H, ArH), 7.19~7.13 (m, 4H, ArH), 7.04 (d, *J* = 12.6Hz, 3H, ArH), 6.81 (d, *J* = 6.0Hz, 2H, ArH), 6.68~6.62 (m, 3H, ArH), 6.18 (d, *J* = 12.0Hz, 1H, ArH), 5.13 (d, *J* = 23.4Hz, 1H, CH), 4.89 (d, *J* = 23.4Hz, 1H, CH), 4.70 (d, *J* = 24.0Hz, 1H, CH), 4.54~4.47 (m, 2H, CH), 4.14~4.06 (m, 1H, CH), 3.96~3.89 (m, 1H, CH), 3.75 (s, 3H, OCH_3), 3.35~3.27 (m, 1H, CH), 3.14~3.06 (m, 1H, CH), 1.06 (t, *J* = 10.5Hz, 3H, CH_3), 0.38 (t, *J* = 10.5Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.5, 175.0, 167.6, 164.2, 159.2, 144.1, 143.7, 142.3, 135.2, 135.1, 133.8, 131.7, 129.8, 128.8, 128.6, 128.6, 128.4, 128.2, 127.9, 127.9, 127.3, 127.2, 127.1, 125.8, 112.8, 109.5, 72.8, 61.4, 61.1, 56.6, 55.1, 535.5, 52.4, 45.5, 44.1, 13.8, 13.1; IR (KBr) υ: 3400, 3067, 2979, 1719, 1609, 1483, 1429, 1345, 1252, 1180, 1118, 1081, 1024, 908, 811, 782, 736 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{47}H_{40}Cl_2N_2NaO_8$ ($[M+H]^+$): 853.2054. Found: 853.2047.

2. **General procedure for the synthesis of dispirocyclopentyl-3,3'-bisoxindoles 4a-3f:** a

mixture of *N*-benzyl-*N*'-alkoxymethoxymethylbenzimidazolium bromide (0.6 mmol), ethyl 2-(2-oxoindolin-3-ylidene)acetate (1.0 mmol) and triethylamine (0.5 mmol) in 10.0 mL of ethanol was stirred at room temperature for about twelve hours. After removing the solvent by rotatory evaporation at reduced pressure, the residue was subjected to preparative thin-layer chromatography with a mixture of light petroleum and ethyl acetate (V/V = 3:1) as developing reagent to give the pure product for analysis.

Compound 4a: white solid, 63%, m.p. 142~144℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43~7.40 (m, 3H, ArH), 7.21 (td, J_1 = 7.6Hz, J_2 = 0.8Hz, 1H, ArH) 7.15~7.09 (m, 4H, ArH), 7.05~7.00 (m, 2H, ArH), 6.94 (t, *J* = 7.6Hz, 2H, ArH), 6.49~6.42 (m, 5H, ArH), 5.86 (d, *J* = 7.2Hz, 1H, ArH), 5.34~5.30 (m, 1H, CH), 5.19~5.13 (m, 2H, CH), 4.64~4.55 (m, 2H, CH), 4.26~4.22 (m, 1H, CH), 4.18~4.14 (m, 2H, CH), 4.10~4.05 (m, 1H, CH), 3.87~3.81 (m, 4H, CH), 3.67~3.63 (m, 1H, CH), 1.18 (t, *J* = 7.2Hz, 3H, CH_3), 0.53 (t, *J* = 7.2Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ:175.0, 173.3, 171.0, 170.5, 168.7, 144.5, 143.7, 135.7, 134.8, 129.7, 129.1, 128.6, 128.4, 127.6, 127.1, 127.0, 126.9, 126.1, 124.6, 123.5, 123.0, 122.1, 121.3, 109.5, 109.3, 61.1, 60.7, 52.7, 51.6, 51.1, 44.6, 43.6, 13.9, 13.3; IR (KBr) υ: 3539, 3473, 3059, 3032, 2978, 2989, 1733, 1609, 1490, 1467, 1438, 1368, 1321, 1209, 1181, 1127, 1102, 1074, 1020, 989, 935, 884, 852, 792, 754, 732, 701 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{41}H_{38}N_2NaO_8$ ($[M+Na]^+$): 709.2534. Found: 709.2533.

Compound 4b: white solid, 67%, m.p. 132~134℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39 (brs, 2H, ArH), 7.21 (s, 1H, ArH), 7.11~6.95 (m, 7H, ArH), 6.82~6.81 (m, 1H, ArH), 6.40~6.31 (m, 4H, ArH), 5.60 (s, 1H, NH_2), 5.28~5.13 (m, 3H, CH), 4.66~4.54 (m, 2H, CH), 4.32~4.06 (m, 5H, CH), 3.84 (brs, 3H, OCH_3), 3.68~3.66 (m, 1H, CH), 2.42 (s, 3H, CH_3), 1.80 (s, 3H, CH_3), 1.24~1.19 (m, 3H, CH_3), 0.58~0.53 (m, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ:175.0, 173.2, 171.1, 170.6, 168.8, 142.0, 141.4, 135.9, 134.9, 131.6, 130.4, 129.7, 129.3, 128.4, 128.3, 127.6, 127.0, 126.1, 125.2, 124.1, 123.5, 109.1, 61.5, 61.2, 61.1, 61.0, 60.7, 52.7, 51.5, 50.9, 44.7, 44.4, 43.6, 21.3, 20.8, 13.9, 13.3; IR (KBr) υ: 3545, 3032, 2983, 2955, 2921, 1737, 1617, 1497, 1435, 1354, 1318, 1247, 1204, 1165, 1137, 1102, 1082, 990, 949, 878, 854, 823, 728 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{43}H_{42}N_2NaO_8$ ($[M+Na]^+$): 737.2833. Found: 737.2831.

Compound 4c: white solid, 58%, m.p. 138~140℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43~7.41 (m, 2H, ArH), 7.19~7.16 (m, 4H, ArH), 7.11~7.07 (m, 1H, ArH), 6.98 (t, *J* = 7.6Hz, 3H, ArH), 6.73 (td, J_1 = 8.8Hz, J_2 = 2.4Hz, 1H, ArH), 6.51 (d, *J* = 7.6Hz, 2H, ArH), 6.47~6.44 (m, 1H, ArH),

6.42~6.38 (m, 1H, ArH), 5.66 (dd, J_1 = 8.4Hz, J_2 = 2.4Hz, 1H, ArH), 5.32~5.28 (m, 1H, CH), 5.15~5.09 (m, 2H, CH), 4.62~4.58 (m, 1H, CH), 4.56~4.52 (m, 1H, CH), 4.29~4.25 (m, 1H, CH), 4.20~4.08 (m, 2H, CH), 4.02~3.89 (m, 1H, CH), 3.93~3.88 (m, 1H, CH), 3.86~3.83 (m, 3H, CH), 3.72~3.69 (m, 1H, CH), 1.23 (t, J = 6.8Hz, 3H, CH_3), 0.60 (t, J = 6.8Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ:174.5, 172.8, 170.7, 168.3, 159.6, 159.1, 157.2, 156.7, 140.5, 139.7, 135.4, 134.4, 128.6, 128.5, 127.6, 126.3, 124.9, 124.8, 116.4, 116.2, 115.7, 115.4, 113.0, 112.8, 111.3, 111.0, 110.1, 61.4, 61.0, 52.8, 51.6, 51.0, 44.6, 44.5, 43.9, 13.9, 13.4; IR (KBr) υ: 3486, 3082, 2984, 2955, 1741, 1617, 1492, 1452, 1354, 1274, 1212, 1178, 1129, 1099, 1026, 969, 888, 865, 819, 761, 729 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{41}H_{36}F_2N_2NaO_8$ ([M+Na]$^+$): 745.2332. Found: 745.2336.

Compound 4d: white solid, 66%, m.p. 132~134℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: major: 7.40~7.36 (m, 3H,ArH), 7.20~6.97 (m, 8H, ArH), 6.50 (d, J = 7.2Hz, 2H, ArH), 6.46 (d, J = 8.4Hz, 1H, ArH), 6.38 (d, J = 8.4Hz, 1H, ArH), 5.83 (d, J = 2.0Hz, 1H, ArH), 5.27~5.23 (m, 1H, CH), 5.12~5.04 (m, 2H, CH), 4.64~4.60 (m, 1H, CH), 4.56~4.50 (m, 1H, CH), 4.31~4.27 (m, 1H, CH), 4.21~4.08 (m, 2H, CH), 4.02~3.99 (m, 1H, CH), 3.96~3.88 (m, 1H, CH), 3.84(s, 3H, CH), 3.73~3.68 (m, 1H, CH), 1.25 (t, J = 7.2Hz, 3H, CH_3), 0.60 (t, J = 7.2Hz, 3H, CH_3); minor: 7.27 (d, J = 2.0Hz, 1H, ArH), 7.25 (d, J = 2.0Hz, 1H, ArH), 6.88 (d, J = 7.2Hz, 4H, ArH), 6.41 (d, J = 8.4Hz, 2H, ArH), 4.86 (t, J = 9.2Hz, 1H, CH), 4.42 (d, J = 9.2Hz, CH), 3.83 (s, 3H, CH), 0.80 (t, J = 7.2Hz, 3H, CH_3). major/minor = 2.5:1. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.7, 174.3, 172.6, 171.8, 170.6, 169.9, 169.7, 168.3, 143.0, 142.2, 141.8, 135.2, 134.4, 134.2, 129.9, 129.3, 129.2, 128.7, 128.6, 128.5, 128.3, 127.8, 127.6, 127.5, 127.5, 127.4, 127.4, 126.8, 126.6, 126.6, 126.2, 126.1, 124.9, 124.7, 123.5, 110.4, 110.1, 62.1, 61.4, 61.1, 61.0, 60.9, 58.4, 52.8, 52.0, 51.6, 50.9, 46.8, 44.6, 44.5, 44.1, 43.8, 18.4, 13.9, 13.6, 13.4; IR (KBr) υ: 3066, 2982, 2959, 1741, 1609, 1486, 1429, 1343, 1241, 1213, 1177, 1082, 1020, 874, 852, 823, 732, 700 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{41}H_{36}Cl_2N_2NaO_8$ ([M+H]$^+$): 777.1741. Found: 777.1744.

Compound 4e: white solid, 52%, m.p. 152~154℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40~7.39 (m, 2H, ArH), 7.21 (s, 1H, ArH), 7.11~7.04 (m, 4H, ArH), 7.01~6.94 (m, 3H, ArH), 6.81 (d, J = 11.4Hz, 1H, ArH), 6.39 (d, J = 10.8Hz, 2H, ArH), 6.32 (t, J = 8.7Hz, 2H, ArH), 5.60 (s, 1H, ArH), 5.25~5.11 (m, 3H, CH), 4.66~4.62 (m, 1H, CH), 4.57~4.52 (m, 1H, CH), 4.23~4.04 (m, 4H, CH), 3.89~3.84 (m, 1H, CH), 3.71~3.65 (m, 1H, CH), 2.42 (s, 3H, CH_3), 1.80 (s, 3H, CH_3), 1.32 (t, J =

10.8Hz, 3H, CH_3), 1.19 (t, *J* = 10.8Hz, 3H, CH_3), 0.56 (t, *J* = 10.2Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ:174.8, 173.2, 170.5, 168.8, 142.0, 141.4, 136.0, 135.0, 131.5, 130.3, 129.6, 129.2, 128.4, 128.3, 127.6, 127.1, 127.0, 126.1, 125.3, 124.1, 123.6, 109.0, 109.0, 61.5, 61.2, 61.0, 61.0, 60.6, 51.4, 51.0, 44.8, 44.4, 43.6, 21.3, 20.8, 14.1, 13.9, 13.3; IR (KBr) υ: 3474, 3067, 3032, 2988, 1731, 1617, 1497, 1436, 1352, 1317, 1247, 1202, 1165, 1136, 1102, 1082, 1028, 952, 822, 728 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{44}H_{44}N_2NaO_8$ ($[M+Na]^+$): 751.2990. Found: 751.2982.

Compound 4f: white solid, 59%, m.p. 146~148℃; ^1H NMR (400 MHz, $CDCl_3$) δ: major: 7.43~7.41 (m, 2H, ArH), 7.19~7.14 (m, 2H, ArH), 7.12~7.04 (m, 3H, ArH), 7.00~6.96 (m, 1H, ArH), 6.92~6.89 (m, 2H, ArH), 6.84 (t, *J* = 9.6Hz, 1H, ArH), 6.53~6.51 (m, 2H, ArH), 6.47~6.38 (m, 2H, ArH), 5.66 (d, *J* = 4.4Hz, 1H, ArH), 5.30~5.26 (m, 1H, CH), 5.14~5.09 (m, 2H, CH), 4.64~4.60 (m, 1H, CH), 4.54~4.48 (m, 1H, CH), 4.34~4.25 (m, 3H, CH), 4.18~4.10 (m, 2H, CH), 4.01~3.98 (m, 1H, CH), 3.74~3.71 (m, 1H, CH), 1.34~1.30 (m, 3H, CH_3), 1.23~1.20 (m, 3H, CH_3), 0.62 (t, *J* = 7.2Hz, 3H, CH_3); minor: 6.73 (t, *J* = 8.8Hz, 1H, ArH), 4.81 (t, *J* = 9.6 Hz, 1H, CH), 4.45 (d, *J* = 9.2Hz, 2H, CH), 0.80 (t, *J* = 7.2Hz, 6H, CH_3); major/minor = 2:1. ^{13}C NMR (100 MHz, $CDCl_3$) δ:175.0, 174.3, 172.8, 171.3, 170.1, 170.0, 169.8, 168.3, 159.6, 159.4, 159.0, 157.2, 157.0, 156.6, 140.6, 140.5, 139.7, 139.7, 139.4, 139.4, 135.4, 134.6, 134.5, 128.6, 128.6, 128.5, 127.6, 127.4, 127.4, 127.3, 126.8, 126.3, 116.4, 116.2, 115.9, 115.7, 115.6, 115.4, 114.5, 114.2, 113.0, 112.8, 111.2, 111.0, 110.1, 110.0, 110.0, 109.9, 109.7, 109.6, 62.2, 61.6, 61.3, 61.3, 61.2, 61.2, 60.9, 52.1, 51.5, 51.1, 47.1, 44.6, 44.5, 44.1, 43.8, 14.1, 13.9, 13.6, 13.4; IR (KBr) υ: 3457, 3076, 2987, 2934, 1740, 1618, 1492, 1451, 1371, 1344, 1272, 1214, 1179, 1127, 1096, 1024, 966, 888, 864, 822, 735, 702 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{42}H_{38}F_2N_2NaO_8$ ($[M+Na]^+$): 759.2488. Found: 759.2484.

Compound 4g: white solid, 48%, m.p. 180~182℃; ^1H NMR (400 MHz, $CDCl_3$) δ: major: 7.40~7.38 (m, 3H, ArH), 7.27 (brs, 1H, ArH), 7.18~7.15 (m, 3H, ArH), 7.13~7.06 (m, 4H, ArH), 6.50 (d, *J* = 7.6Hz, 2H, ArH), 6.46 (d, *J* = 8.4Hz, 1H, ArH), 6.37 (d, *J* = 8.4Hz, 1H, ArH), 5.83 (d, *J* = 1.2Hz, 1H, ArH), 5.24~5.20 (m, 1H, CH), 5.11~5.04 (m, 2H, CH), 4.66~4.62 (m, 1H, CH), 4.54~4.50 (m, 1H, CH), 4.34~4.27 (m, 3H, CH), 4.20~4.13 (m, 1H, CH), 4.12~4.06 (m, 1H, CH), 4.01~3.98 (m, 1H, CH), 3.94~3.88 (m, 1H, CH), 3.74~3.71 (m, 1H, CH), 1.24~1.29 (m, 3H, CH_3), 1.24~1.22 (m, 3H, CH_3), 0.62 (t, *J* = 7.2Hz, 3H, CH_3); minor: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.25 (brs, 1H, ArH), 7.02~6.98 (m, 4H, ArH), 6.89~6.88 (m, 4H, ArH), 6.41 (d, *J* = 8.4Hz, 2H, ArH),

4.84 (t, J = 8.4 Hz, 1H, CH), 4.42 (d, J = 9.2Hz, 2H, CH), 0.82 (t, J = 7.1Hz, 6H, CH_3). Major/minor = 1.4:1; ^{13}C NMR (100 MHz, $CDCl_3$) δ:174.7, 174.1, 172.6, 171.3, 170.1, 169.9, 169.7, 168.4, 143.0, 142.2, 141.8, 135.3, 134.3, 129.8, 129.2, 129.2, 128.7, 128.6, 128.5, 128.3, 127.7, 127.6, 127.5, 127.4, 127.3, 126.8, 126.6, 126.5, 126.2, 126.1, 125.0, 124.8, 123.5, 110.4, 110.3, 110.1, 62.1, 61.7, 61.3, 61.1, 61.0, 60.8, 52.0, 51.5, 51.0, 47.0, 44.6, 44.1, 43.8, 29.7, 14.1, 13.9, 13.6, 13.4; IR (KBr) υ: 3449, 3065, 2981, 2918, 2849, 1731, 1609, 1486, 1429, 1346, 1277, 1215, 1179, 1084, 1022, 954, 890, 852, 822, 741, 701 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{42}H_{38}Cl_2N_2NaO_8$ ($[M+Na]^+$): 791.1897. Found: 791.1892.

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Supporting Information: ^1H NMR and ^{13}C NMR spectra for all compounds are available. Crystallographic data **3f** (CCDC 1029433), **4a** (CCDC 1029434), **4d** (CCDC 1030434), and **4f** (CCDC 1036833) have been deposited vat the Cambridge Crystallographic Database Centre.

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Graphic abstract:

Construction of dispirocyclohexyl-3,3'-bisoxindole and dispirocyclopentyl-3,3'-bisoxindole via domino cycloaddition reactions of *N*-benzylbenzimidazolium salts with 2-(2-oxoindolin-3-ylidene)acetates

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