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Synthesis of complex dispirocyclopentanebisoxindoles via cycloaddition reactions of 4-dimethylamino-1-alkoxycarbonylmethylpyridinium bromides with 2-oxoindolin-3-ylidene derivatives

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ABSTRACT

The cycloaddition reactions of 4-dimethylamino-1-alkoxycarbonylmethylpyridinium bromides with various 2-oxoindolin-3-ylidene derivatives in ethanol in the presence of triethylamine afforded the unprecedented dispirocyclopentanebisoxindole derivatives in good yields and in high diastereoselectivity. Under similar reaction conditions, the reactions of 1-alkoxycarbonylmethylpyridinium bromides with 3-phenacylideneoxindoles only resulted in 4-oxo-3-(2-oxoindolin-3-ylidene)-4-arylbutanoates. The stereochemistry of the complex spirooxindoles was established by ^{1}H NMR data and single crystal structures.

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1. Introduction

The spirooxindole unit is a privileged heterocyclic motif that forms the core structure of a large family of natural alkaloids and many pharmacological agents with important bioactivity and interesting structural properties.[1,2] The unique structures and the highly pronounced pharmacological activity displayed by the spirooxindoles have made them attractive synthetic targets.[3,4] In versatile synthetic methods of spirooxindole system, the 1,3-dipolar cycloaddition of azomethine ylides with isatin and its functionalized derivatives might be the most convenient procedure.[5–9] However, there have been few reports about the synthesis of spirooxindole system by 1,3-cycloaddition of heteroaromatic *N*-ylides with functionalized oxindole derivatives. As one kind of reactive azomethine ylides, heteroaromatic *N*-ylides such as pyridinium, quinolinium, and isoquinolinium methylides are readily available from the alkylations of aza-aromatic heterocycles and sequential deprotonation reactions. The heteroaromatic *N*-ylides have been used extensively in cycloadditions for the synthesis of the various nitrogen-containing heterocycles.[10–13] L. Töke and co-workers reported the 1,3-cycloadditions of dihydroisoquinolinium salts with 2-oxoindolin-3-ylidene derivatives.[14] A.B. Serov and co-workers successfully developed the reactions of *N*-phenacylquinolinium ylides with 2-oxoindolin-3-ylidene derivatives.[15] The formation of spiro[cyclopropane-1,3′-indolines] by the reactions of *N*-phenacylpyridinium salts with phenacylideneoxindoles was also briefly reported.[16] Recently, we found that the reactions of *N*-benzylbenzimidazolium salts, isatylidene malononitrile gave a series of the novel zwitterionic salts.[17] We also reported that the 1,3-cycloaddition reactions of 3-phenacylideneoxindoles with aza-aromatic *N*-ylides generated from isoquinolinium, *N*-phenacylquinolinium, and 1,10-phenanthrolinium salts afforded a series of polycyclic system such as spiro[indoline-3,3′-pyrrolo[1,2-*a*]quinolines], spiro[indoline-3,1′-pyrrolo[2,1-*a*]isoquinolines] and spiro[benzo[*h*]pyrrolo[1,2-*a*]quinoline-3,3′-indolines].[18] On the other hand, the similar cycloaddition reactions of pyridinium salts and 4-dimethylamino pyridinium salts with 3-phenacylideneoxindoles produced the functionalized spiro[cyclopropane-1,3′-indolines], and 3-(furan-3(2*H*)-ylidene)indolin-2-ones depending upon the structures of the pyridinium salts and reaction conditions.[19] Thus, the very interesting molecular diversity of the cycloaddition of heteroaromatic *N*-ylides with 3-phenacylideneoxindoles so far promoted us to examine the reactivity of other pyridinium salts in this reaction. Here we wish to report the cycloaddition reactions of 4-dimethylamino-1-alkoxycarbonylmethylpyridinium bromides with 3-phenacylideneoxindoles for the efficient synthesis of the complex dispirocyclopentanebisoxindole derivatives.

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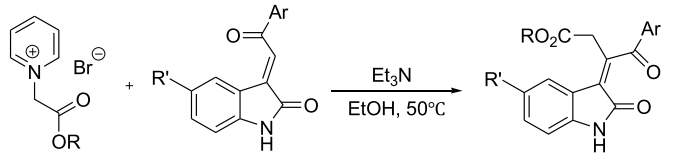
2. Results and discussion

According to the previously established reaction conditions for the cycloaddition of *N*-phenacylpyridinium bromide with 3-phenacyclideneoxindoles,[19] a mixture of slightly excess of *N*-ethoxycarbonylmethylpyridinium bromide (**1a**) and 3-phenacylideneoxindoles **2** in ethanol with triethylamine as base catalyst was stirred at 50–60 °C for several hours. After workup, instead of isolating the expected spiro[cyclopropane-1,3′-indolines], the reaction afforded a series of 3-(2-oxoindolin-3-ylidene)butanoates (**3a**–**f**) in satisfactory yields (Table 1, entries 1–6). It looks likely that this kind of products come from the substitution reaction of ethoxycarbonylmethyl group at the exocyclic carbon atom of 3-phenacylideneoxindoles. To determine the scope and limits of this reaction, the reactions of *N*-*tert*-butoxycarbonylmethylpyridinium bromide (**1b**) with 3-phenacylideneoxindoles under same conditions were also examined. All reactions proceeded smoothly to give the corresponding substituted products (**3g**–**j**) in high yields (Table 1, entries 7–10). The structures of the prepared 3-(2-oxoindolin-3-ylidene)butanoates (**3a**–**j**) were characterized by ^{1}H and ^{13}C NMR, MS, IR spectra and were further confirmed by single crystal X-ray diffraction performed for the representative compound **3a** (Fig. 1). ^{1}H NMR spectra of compounds **3a**–**f** indicated that a mixture of major isomer and minor isomer existed in the most samples. For examples, the *Z*/*E* isomers with about 4:1 molecular ratio existed in compound **3a** and the *Z*/*E* isomers with ratio of 25:1 existed in compound **3d**. From the crystal structure of compound **3a**, it can be seen that the benzoyl group and phenyl group of oxindole moiety existed in trans-configuration, which also suggested that the *Z*-isomer of compounds **3a**–**j** was the major isomer. ^{1}H NMR spectra of compounds **3g**–**j** clearly indicated only one diastereoisomer exists in these samples, which might be due to the large steric hindrance of *tert*-butyl group in molecule. It should be pointed out that there is one exocyclic C=C double bond in the 3-(2-oxoindolin-3-ylidene) butanoates **3a**–**j**, which is very similar to the structure of starting 3-phencaylideneoxindole. No further cycloadditions of 3-(2-oxoindolin-3-ylidene)butanoates **3a**–**j** were observed by using more than 2 M pyridinium bromides **1a** or **1b** in the experiments.

Table 1
Synthesis of 3-(2-oxoindolin-3-ylidene)butanoates **3a**–**j**[a]



1a-b 2 3a-j

Entry	Compd	R	R′	Ar	Yield[b] (%, *Z*/*E* ratio)
1	**3a**	C_2H_5	H	*p*-ClC_6H_4	88 (4:1)
2	**3b**	C_2H_5	CH_3	C_6H_5	71 (6:1)
3	**3c**	C_2H_5	CH_3	*p*-$CH_3C_6H_4$	89
4	**3d**	C_2H_5	CH_3	*p*-ClC_6H_4	80 (25:1)
5	**3e**	C_2H_5	F	C_6H_5	65 (10:3)
6	**3f**	C_2H_5	F	*p*-ClC_6H_4	74 (5:1)
7	**3g**	$C(CH_3)_3$	H	C_6H_5	70
8	**3h**	$C(CH_3)_3$	CH_3	*p*-$CH_3C_6H_4$	82
9	**3i**	$C(CH_3)_3$	Cl	*p*-ClC_6H_4	76
10	**3j**	$C(CH_3)_3$	F	C_6H_5	80

[a] Reaction conditions: pyridinium salts (1.1 mmol), 3-phenacylideneoxindole (1.0 mmol), triethylamine (0.2 mmol), EtOH (15 mL), 50–60 °C, 6 h.
[b] Isolated yields.

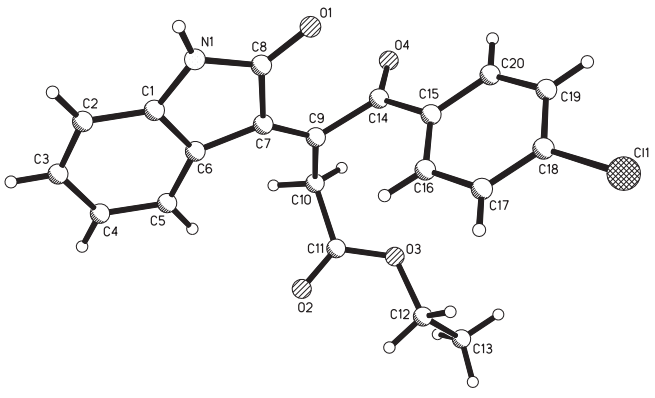
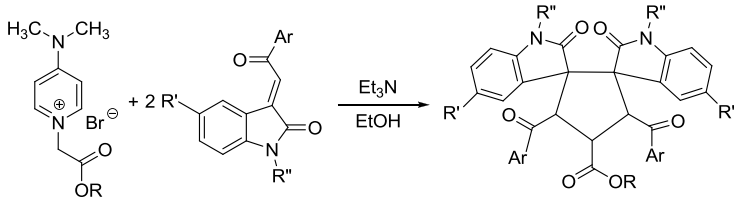


Fig. 1. Molecular structure of compound **3a**.

In order to develop the scope of this reaction, the reaction of 3-phenacylideneoxindoles with 4-dimethylamino-1-ethoxy carbonylmethylpyridinium bromide (**1c**) was examined under same reaction condition. To our surprise, the reaction resulted in a complex dispirocyclopentanebisoxindole derivative (**4a**) in 53% yield. The structure of the compound **4a** is very interesting, in which the two oxindole units exist in 1,2-positions of the newly formed cyclopentyl ring. A literature survey indicated there are only very few known examples of dispirocyclopentanebisoxindoles with two oxindole units in 1,2-positions of cylcopentyl ring,[20] while the similar dispirocyclopentanebisoxindoles with two oxindole units in 1,3-positions of cylcopentyl ring are more popular.[21] Due to two molecules of 3-phenacylideneoxindole took part in the reaction, the yield of the compound **4a** increased to 80% by using two equal 3-phenacylideneoxindoles in the reaction. Then, the similar reactions of other 3-phenacylideneoxindoles with 4-dimethylamino-1-alkoxy carbonylmethylpyridinium bromide (**1c**: R=Et; **1d**: R=*t*-Bu) also gave a series of functionalized dispirocyclopentanebisoxindoles (**4a**–**k**) in very good yields. The substituent on the 3-phena cylideneoxindoles did not show very important role in the reaction. On the other hand, the bulky *tert*-butyl group also did not affect the yields of products (Table 2, entries 5–11).

The structures of the prepared dispirocyclopentane bisoxindoles (**4a**–**k**) were characterized with spectroscopic methods. Because there are two oxindole moieties, two benzoyl groups, and one esteric group in the newly formed cyclopentyl ring in dispirocyclopentanebisoxindoles **4a**–**k**, a couple of diastereoisomers could exist for each product. In ^{1}H NMR spectra of spiro compounds **4a**–**d**, the one CH unit connecting ethoxycarbonyl group and the two CH units connecting phenacyl groups in the newly formed cyclopentyl ring usually displays different absorption patterns. Thus, it is difficult to determine the diastereochemistry of these complex dispiro compounds barely with ^{1}H NMR spectra. On the other hand, in the ^{1}H NMR spectra of spiro compounds **4e**–**k**, the CH unit connecting *tert*-butoxycarbonyl group always displays one triplet at about 5.20 ppm and the two CH units connecting benzoyl groups displays one doublet at about 5.10 ppm. The other characteristic groups also show only one set of absorption peaks. This fact strongly indicated that a high symmetric stereoisomer exists in each sample of the compounds **4e**–**k**. The single crystal structures of compounds **4b**, **4e** and **4h** were determined by X-ray diffraction (Figs. 2–4). In the molecule structure of **4b** (Fig. 2) it can be seen that the two oxindole moieties exist in opposite orientation and the two benzoyl groups also exist in trans-configuration. Thus, we can tentatively suggest that compounds **4a**–**d** all exist in this unsymmetrical isomer based on the NMR data and single crystal determination. On the other hand, the two oxindole moieties exist in cis-orientation and the two benzoyl groups exist in cis-configuration in the molecule structure of **4e** and **4h** (Figs. 3 and 4). The *tert*-butoxycarbonyl group is in the trans-position to the two neighboring benzoyl groups. There is one C_{2v} symmetric plane in the molecules of **4e** and **4h**, which is concordance

Table 2
Synthesis of dispirocyclopentanebisoxindoles **4a**–**k**[a] via cycloaddition reaction



Entry	Comp	R	R′	R″	Ar	Yield[b] (%)
1	**4a**	CH_2CH_3	H	Bn	C_6H_5	85
2	**4b**	CH_2CH_3	H	Bn	p-$CH_3C_6H_4$	80
3	**4c**	CH_2CH_3	Cl	H	p-$CH_3C_6H_4$	82
4	**4d**	CH_2CH_3	Cl	H	p-ClC_6H_4	58
5	**4e**	$C(CH_3)_3$	F	H	p-ClC_6H_4	49
6	**4f**	$C(CH_3)_3$	Cl	H	p-$CH_3C_6H_4$	80
7	**4g**	$C(CH_3)_3$	Cl	H	C_6H_5	65
8	**4h**	$C(CH_3)_3$	F	H	C_6H_5	71
9	**4i**	$C(CH_3)_3$	H	H	p-ClC_6H_4	74
10	**4j**	$C(CH_3)_3$	F	H	p-$CH_3C_6H_4$	78
11	**4k**	$C(CH_3)_3$	H	Bn	C_6H_5	79

[a] Reaction conditions: pyridinium salts (1.1 mmol), 3-phenacylideneoxindole (2.0 mmol), triethylamine (0.2 mmol), EtOH (15.0 mL), 50–60 °C, 12 h.
[b] Isolated yields.

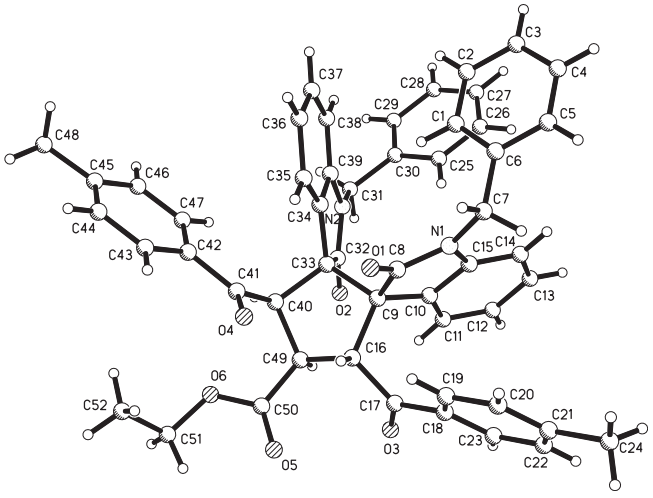


Fig. 2. Molecular structure of compound **4b**.

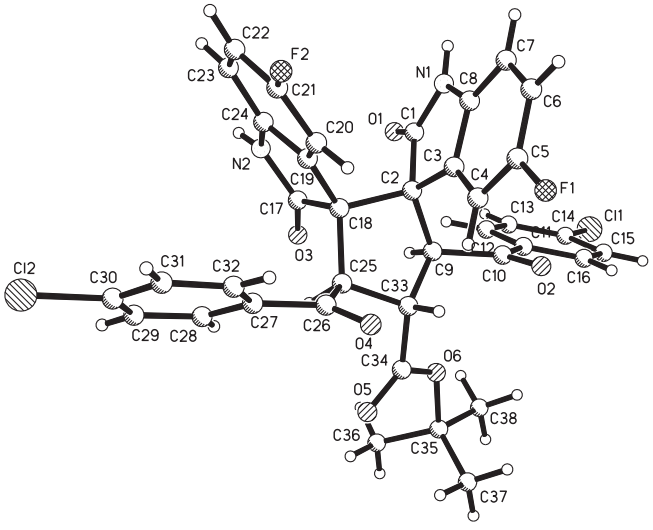


Fig. 3. Molecular structure of compound **4e**.

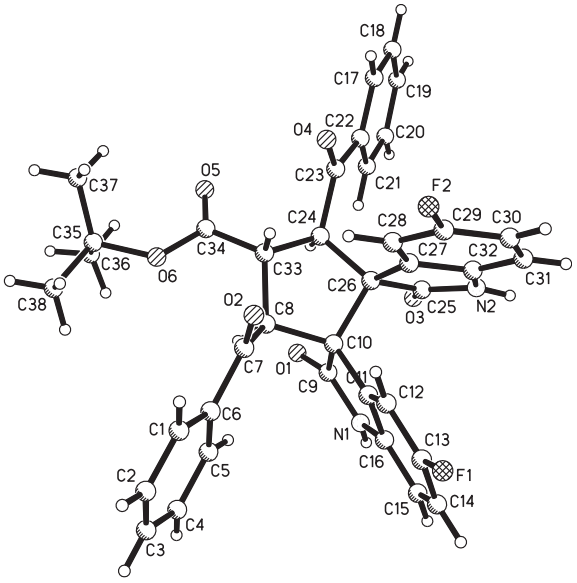
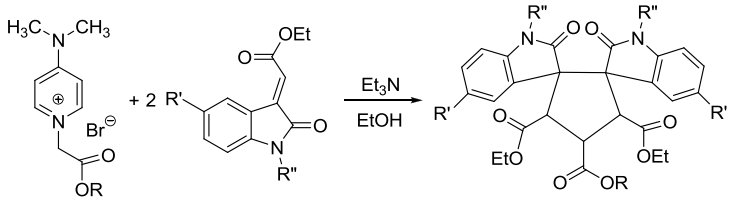


Fig. 4. Molecular structure of compound **4h**.

with the analytical result of ^{1}H NMR data. Thus, we can get a conclusion that compounds **4e**–**k** are in this kind of symmetric isomer. It is known that the benzoyl group and the aryl group of the oxindole moiety exist in the cis-position in the starting 3-phenacylideneoxindoles.[21] Thus, even this cis-configuration is retained in all compounds **4a**–**k**, two different isomers were obtained in the reactions due to the two moieties of 3-phenacylideneoxindoles connecting with each other in opposite direction.

In order to further develop the applicability of this reaction, another typical 3-methyleneoxindoles, ethyl (2-oxo-1,2-dihydro-indol-3-ylidene)acetates were also used to react with 4-dimethylamino-1-alkoxycarbonylmethylpyridinium bromides. The results are summarized in Table 3. It can be seen that the expected dispirocyclcopentanebisoxindoles **5a**–**j** were successfully obtained in good yields. Their structures have also been fully determined by the spectroscopic methods. ^{1}H NMR spectra of compounds **5a**–**j** clearly indicated one set of absorptions for the

Table 3
Synthesis of dispirocyclopentanebisoxindoles **5a**–**5j**[a]



1c-d 2 5a-j

Entry	Product	R	R′	R″	Yield[b] (%)
1	**5a**	CH_2CH_3	CH_3	H	70
2	**5b**	CH_2CH_3	F	H	80
3	**5c**	CH_2CH_3	H	H	65
4	**5d**	CH_2CH_3	F	Bn	71
5	**5e**	CH_2CH_3	Cl	Bn	55
6	**5f**	$C(CH_3)_3$	CH_3	H	95
7	**5g**	$C(CH_3)_3$	F	H	93
8	**5h**	$C(CH_3)_3$	H	H	91
9	**5i**	$C(CH_3)_3$	Cl	H	75
10	**5j**	$C(CH_3)_3$	F	Bn	75

[a] Reaction conditions: pyridinium salts (1.1 mmol), 3-phenacylideneoxindole (2.0 mmol), triethylamine (0.2 mmol), EtOH (15.0 mL), 50–60 °C, 12 h.
[b] Isolated yields.

characterized groups, which suggested only one diastereoisomer existing in each sample. For examples, in the ^{1}H NMR spectrum of **5a** the three CH units in cyclopentyl ring display one singlet at 4.58 ppm and one doublet at 3.94 ppm. The three ethyl groups also show two quartets at 4.17, and 3.79 ppm for CH_2 units and two triplets at 1.19, and 0.68 ppm for methyl group, which clearly indicates the molecule has high symmetry. ^{1}H NMR spectra of **5g** displays one triplet at 4.42 ppm for the CH unit connecting *tert*-butoxycarbonyl group, and one doublet at 3.93 ppm for the two CH units connecting ethoxycarbonyl groups. The *tert*-butyl group shows one singlet at 1.42 ppm and the two ethyl groups also display one set of signs at 3.87–3.82 ppm for methylene units and 0.76 ppm for methyl groups, which cleanly indicated this compound has very high symmetry. The single crystal determination of compounds **5e** and **5g** clearly indicated that the two oxindole moieties exist in same orientation and the two ethoxycarbonyl groups also exist in cis-configuration, while the ethoxycarbonyl or *tert*-butoxycarbonyl group oriented in the trans-position to the two neighboring two ethoxycarbonyl groups (Fig. 5). Thus, compounds **5a**–**j** all exist in the same symmetric isomer as the spiro compounds **4e**–**k** based on the ^{1}H NMR data and single crystal determination (Fig. 6).

In order to explain the reaction mechanism, a plausible mechanism for the formation of the two kinds of products is proposed in

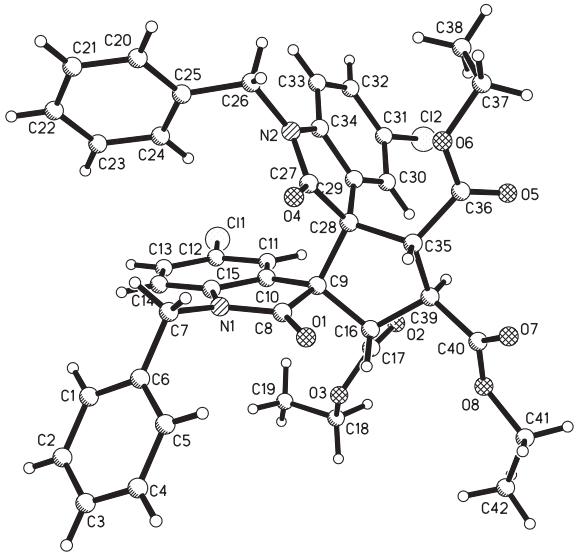


Fig. 5. Molecular structure of compound **5e**.

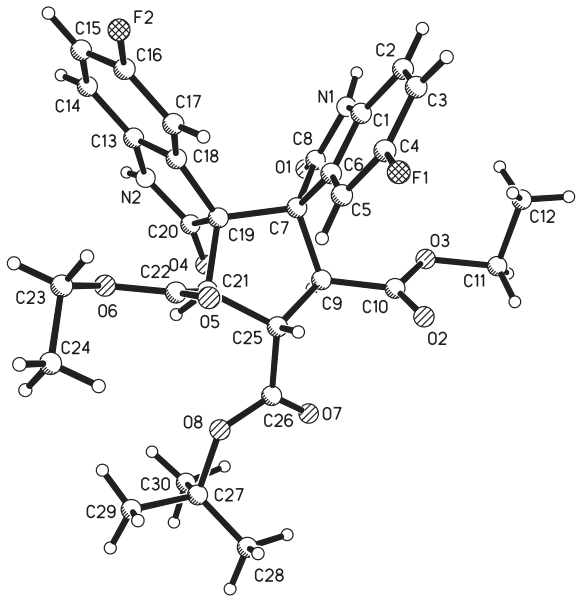
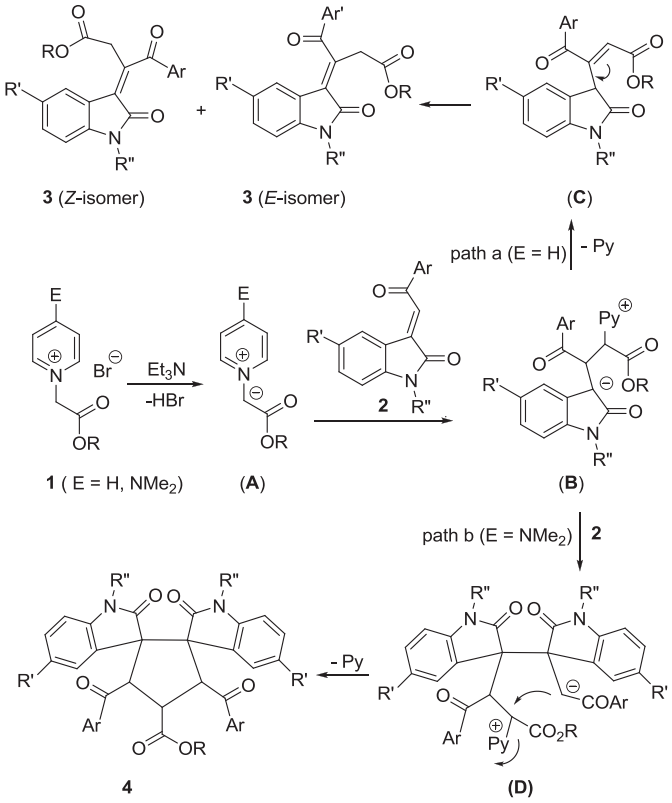


Fig. 6. Molecular structure of compound **5g**.

Scheme 1 based on the similar cycloaddition reactions of aza-aromatic nitrogen ylides. Firstly, deprotonation of pyridinium salt **1** with triethylamine afforded the desired pyridinium ylide (**A**). Secondly, Michael addition of pyridinium ylide (**A**) to the exocyclic carbon atom of 3-phenacylideneoxindole **2** gives addition intermediate (**B**). Two reactions existed for the further reaction depending on the properties of the pyridinium salts. In the path a, the elimination of pyridine and rearrangement of carbonium ion resulted a alkene intermediate (**C**), which is similar to our recently reported reactions of *N*-phenacylidenepyridinium ylide.[19] Then 1,3-H shift in the alkene (**C**) gave the *Z*/*E* isomers of compound **3** as final



Scheme 1. The proposed formation mechanism of compounds **3** and **4**.

product. The ratio of *Z*/*E* isomers was clearly affected by the effect of the nuleophiles. Thus, the reaction of *N*-ethoxycarbonylmethyl pyridinium bromide (**1a**) usually afforded a mixture of major isomer and minor isomer, whiles the bulky *N*-*tert*-buyoxycarbonylmethylpyridinium bromide (**1b**) predominately resulted in one isomer. When 4-dimethylamino-1-alkoxycarbonylmethyl pyridinium bromides (**1c**,**d**) were used in the reaction, the corresponding 4-dimethylaminopyridnium ylide is much more stable due the stronger electron-donating effect of dimethylamino group.[22] The further reaction was outlined in path b. The carbanion of the intermediate (**B**) added to the second molecular 3-phenacylideneoxindole to gave a double addition adduct (**D**). The intramolecular nucleophilic substitution in intermediate (**D**) produced the dispirocyclopentanebisoxindoles **4**. The formation process for the dispirocyclopentanebisoxindoles **4** is very similar to the base promoted dimerization reactions between two molecules of 3-phenacylideneoxindoles to give the dispirocyclopentane-1,3-bisoxindoles,[21b] in which the two oxindole moieties exist in 1,3-position of the newly formed cyclopentyl ring. Because the formation of dispirocyclcopentanebisoxindoles **4** contains several equilibrium reaction processes, the most thermodynamically stable diastereoisomer would be preferentially formed in this sequential reaction. The different reactivity of the pyridinium ylides plays key role on the reaction path and the steric effect of the substituents greatly affects the stereochemistry of the reaction.

3. Conclusion

In summary, we systematically investigated the cycloaddition reactions of alkoxycarbonylmethylpyridinium bromides with 3-phenacylideneoxindoles and ethyl (2-oxo-1,2-dihydro-indol-3-ylidene)acetates. An efficient synthetic protocol for the unprecedented dispirocyclopentanebisoxindole derivatives in good yields and with high diastereoselectivity was successfully developed. The stereochemistry of reaction and the reaction mechanism were briefly discussed. It is interesting to find that the dimethylamino group significantly affects the reactivity of pyridinium ylides, which would be found high potential applications in organic and medical synthesis. Further expansion of the reaction scope and synthetic applications of this methodology are in progress in our laboratory.

4. Experimental section

4.1. General procedure for the preparation of 3-(2-oxoindolin-3-ylidene)butanoates 3a–j from the reactions of *N*-alkoxycarbonylmethylpyridinium salts with 3-phenacylideneoxindoles

A mixture of *N*-ethoxycarbonylmethylpyridinium bromide or *N*-*tert*-butoxycarbonylmethylpyridinium chloride (1.1 mmol), 3-phenacylideneoxindoles (1.0 mmol), and triethylamine (0.2 mmol) in ethanol (15.0 mL) was stirred at about 50–60 °C for 6 h. The resulting precipitates were collected by filtration, which were recrystallized in a mixture of chloroform and ethanol to give pure product for analysis.

*4.1.1. Ethyl 4-(4-chlorophenyl)-4-oxo-3-(2-oxoindolin-3-ylidene)butanoate (**3a**).* Yellow solid, yield: 88%. Mp 146–148 °C. IR (KBr): 3224, 2979, 1736, 1707, 1668, 1614, 1586, 1464, 1397, 1342, 1270, 1232, 1185, 1092, 1035, 966. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): *Z*-isomer: 8.56 (s, 1H, NH), 7.98 (d, *J*=7.8 Hz, 2H, ArH), 7.57 (d, *J*=7.8 Hz, 1H, ArH), 7.40 (d, *J*=8.4 Hz, 2H, ArH), 7.29 (t, *J*=7.8 Hz, 1H, ArH), 7.07 (t, *J*=7.8 Hz, 1H, ArH), 6.72–6.67 (m, 1H, ArH), 4.15–4.07 (m, 2H, CH_2), 3.89 (s, 2H, CH_2), 1.14 (t, *J*=7.2 Hz, 3H, CH_3). *E*-isomer: 8.08 (d, *J*=8.4 Hz, 2H, ArH), 7.45 (d, *J*=8.4 Hz, 2H, ArH), 7.12 (t, *J*=7.2 Hz, 1H, ArH), 4.27 (s, 2H, CH_2), 1.19 (t, *J*=7.2 Hz, 3H, CH_3); ratio *Z*/*E*=4:1. ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 196.9, 168.1, 167.7, 142.9, 140.3, 139.6, 134.4, 130.9, 130.3, 128.8, 124.3, 122.4, 121.1, 110.9, 61.8, 38.4, 13.9. HRMS (ESI) calcd for $C_{20}H_{16}ClNNaO_4$ ([M+Na]$^+$): 392.0660. Found: 392.0667.

*4.1.2. Ethyl 3-(5-methyl-2-oxoindolin-3-ylidene)-4-oxo-4-phenylbutanoate (**3b**).* Yellow solid, yield: 71%. Mp 144 °C. IR (KBr): 3445, 3179, 3070, 2984, 1733, 1702, 1668, 1619, 1483, 1445, 1321, 1275, 1219, 1190, 1153, 1097, 1031, 952, 813. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): *Z*-isomer: 8.21 (s, 1H, NH), 8.02 (d, *J*=7.2 Hz, 2H, ArH), 7.54 (t, *J*=7.2 Hz, 1H, ArH), 7.43 (t, *J*=7.2 Hz, 2H, ArH), 7.41 (s, 1H, ArH), 7.08 (d, *J*=7.2 Hz, 1H, ArH), 6.62 (d, *J*=7.2 Hz, 1H, ArH), 4.11–4.08 (m, 2H, CH_2), 3.88 (s, 2H, CH_2), 2.36 (s, 3H, CH_3), 1.11 (t, *J*=7.2 Hz, 3H, CH_3). *E*-isomer: 8.13 (d, *J*=7.2 Hz, 2H, ArH), 7.61 (t, *J*=7.2 Hz, 1H, ArH), 7.48 (t, *J*=7.2 Hz, 2H, ArH), 6.54 (s, 1H, ArH), 6.89 (d, *J*=7.8 Hz, 1H, ArH), 6.57 (d, *J*=7.8 Hz, 1H, ArH), 4.27 (s, 2H, CH_2), 1.98 (s, 3H, CH_3), 1.18 (t, *J*=7.2 Hz, 3H, CH_3); ratio *Z*/*E*=6:1. ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 198.0, 168.0, 167.8, 140.7, 140.5, 135.9, 133.2, 131.6, 131.1, 130.2, 128.9, 128.4, 124.9, 121.3, 110.6, 61.7, 38.5, 21.3, 13.9. HRMS (ESI) calcd for $C_{21}H_{19}NNaO_4$ ([M+Na]$^+$): 372.1220. Found: 372.1216.

*4.1.3. Ethyl 3-(5-methyl-2-oxoindolin-3-ylidene)-4-oxo-4-p-tolylbutanoate (**3c**).* Yellow solid, yield: 89%. Mp 150–152 °C. IR (KBr): 3445, 2990, 2921, 1733, 1704, 1654, 1608, 1485, 1407, 1317, 1182, 1034, 811. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.03 (d, *J*=7.8 Hz, 2H, ArH), 7.29 (d, *J*=7.8 Hz, 2H, ArH), 6.92 (d, *J*=7.8 Hz, 1H, ArH), 6.69 (d, *J*=7.8 Hz, 1H, ArH), 6.61 (s, 1H, ArH), 4.25 (s, 2H, CH_2), 4.11 (q, *J*=7.2 Hz, 2H, CH_2), 2.42 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 1.20 (t, *J*=7.2 Hz, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 196.9, 169.2, 169.1, 145.7, 142.4, 138.5, 132.0, 131.3, 130.5, 130.0, 129.8,

127.2, 125.4, 120.9, 109.6, 61.1, 36.1. 21.9, 21.0, 14.1. HRMS (ESI) calcd for $C_{22}H_{21}NNaO_4$ ([M+Na]$^+$): 386.1376. Found: 386.1379.

*4.1.4. Ethyl 4-(4-chlorophenyl)-3-(5-methyl-2-oxoindolin-3-ylidene)-4-oxobutanoate (**3d**).* Yellow solid, yield: 80%. Mp 162–164 °C. IR (KBr): 3233, 2977, 1734, 1701, 1665, 1622, 1586, 1486, 1394, 1326, 1269, 1214, 1179, 1091, 1035, 951, 858. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): *Z* isomer: 7.98 (d, *J*=8.4 Hz, 2H, ArH), 7.40 (d, *J*=8.4 Hz, 2H, ArH), 7.39 (s, 1H, ArH), 7.11 (d, *J*=7.8 Hz, 1H, ArH), 6.62 (d, *J*=7.8 Hz, 1H, ArH), 4.12–4.09 (m, 2H, CH_2), 3.89 (s, 2H, CH_2), 2.37 (s, 3H, CH_3), 1.15 (t, *J*=7.2 Hz, 3H, CH_3); *E* isomer: 7.95 (d, *J*=8.4 Hz, 2H, ArH), 7.46 (d, *J*=8.4 Hz, 2H, ArH), 6.93 (d, *J*=7.8 Hz, 1H, ArH), 6.59 (d, *J*=7.8 Hz, 1H, ArH), 6.51 (s, 1H, ArH), 4.26 (s, 2H, CH_2), 2.01 (s, 3H, CH_3), 1.20 (t, *J*=7.2 Hz, 3H, CH_3); *Z*/*E* ratio=25:1. ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 197.0, 168.1, 167.6, 140.2, 140.1, 139.7, 134.5, 131.9, 131.4, 130.3, 130.2, 128.8, 125.1, 121.2, 110.4, 61.8, 38.5, 21.3, 14.0. HRMS (ESI) calcd for $C_{21}H_{18}ClNNaO_4$ ([M+Na]$^+$): 406.0817. Found: 406.0819.

*4.1.5. Ethyl 3-(5-fluoro-2-oxoindolin-3-ylidene)-4-oxo-4-phenylbutanoate (**3e**).* Yellow solid, yield: 65%. Mp 138 °C. IR (KBr): 3185, 3079, 2986, 2874, 1705, 1672, 1628, 1476, 1467, 1313, 1270, 1193, 1159, 1114, 1033, 1001, 953, 818. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): *Z* isomer: 8.48 (s, 1H, NH), 8.01 (d, *J*=7.8 Hz, 2H, ArH), 7.56 (t, *J*=7.2 Hz, 1H, ArH), 7.44 (t, *J*=7.2 Hz, 2H, ArH), 7.35 (dd, J_1=8.4 Hz, J_2=3.6 Hz, 1H, ArH), 6.70 (td, J_1=8.4 Hz, J_2=3.6 Hz, 1H, ArH), 6.65 (dd, J_1=8.4 Hz, J_2=4.2 Hz, 1H, ArH), 4.14–4.09 (m, 2H, CH_2), 3.83 (s, 2H, CH_2), 1.13 (t, *J*=7.2 Hz, 3H, CH_3). *E* isomer: 8.40 (s, 1H, NH), 8.11 (d, *J*=7.2 Hz, 2H, ArH), 7.65 (t, *J*=7.2 Hz, 1H, ArH), 7.51 (t, *J*=7.8 Hz, 2H, ArH), 6.48 (dd, J_1=8.4 Hz, J_2=3.6 Hz, 1H, ArH), 6.82 (t, *J*=8.4 Hz, 1H, ArH), 6.61 (dd, J_1=8.4 Hz, J_2=4.2 Hz, 1H, ArH), 4.26 (s, 2H, CH_2), 1.18 (t, *J*=7.2 Hz, 3H, CH_3); ratio Z/*E*=10:3. ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 197.5, 167.7, 167.6, 158.7 (d, *J*=238.2 Hz), 142.7, 138.6, 135.4, 133.6, 129.6, 128.9, 128.6, 122.0 (d, *J*=8.7 Hz), 117.0 (d, *J*=23.5 Hz), 111.8 (d, *J*=25.8 Hz), 111.3 (d, *J*=7.8 Hz), 61.9, 38.3, 13.9. HRMS (ESI) calcd for $C_{20}H_{16}FNNaO_4$ ([M+Na]$^+$): 376.0969. Found: 376.0967.

*4.1.6. Ethyl 4-(4-chlorophenyl)-3-(5-fluoro-2-oxoindolin-3-ylidene)-4-oxobutanoate (**3f**).* Yellow solid, yield: 74%. Mp 158–160 °C. IR (KBr): 3462, 3081, 2982, 1708, 1663, 1630, 1588, 1749, 1396, 1307, 1273, 1192, 1161, 1092, 1033, 1006, 953, 821. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): *Z* isomer: 8.58 (br s, 1H, NH), 7.96 (d, *J*=8.4 Hz, 2H, ArH), 7.41 (d, *J*=8.4 Hz, 2H, ArH), 7.32 (d, *J*=9.0 Hz, 1H, ArH), 7.02 (t, *J*=9.0 Hz, 1H, ArH), 6.63–6.61 (m, 1H, ArH), 4.14–4.09 (m, 2H, CH_2), 3.84 (s, 2H, CH_2), 1.67 (t, *J*=7.2 Hz, 3H, CH_3); *E* isomer: 8.07 (d, *J*=8.4 Hz, 2H, ArH), 7.48 (d, *J*=8.4 Hz, 1H, ArH), 6.44 (d, *J*=9.0 Hz, 1H, ArH), 6.85 (d, *J*=9.0 Hz, 1H, ArH), 4.25 (s, 2H, CH_2), 1.20 (t, *J*=7.2 Hz, 3H, CH_3); ratio Z/*E*=5:1. ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 196.4, 168.9, 167.6, 158.7 (d, *J*=238.2 Hz), 142.1, 140.0, 138.6, 134.0, 131.2, 130.2, 128.9, 121.8 (d, *J*=8.6 Hz), 117.2 (d, *J*=23.7 Hz), 111.9 (d, *J*=26.1 Hz), 111.3 (d, *J*=7.95 Hz), 62.0, 38.3, 14.0. HRMS (ESI) calcd for $C_{20}H_{15}FClNNaO_4$ ([M+Na]$^+$): 410.0566. Found: 410.0568.

*4.1.7. tert-Butyl 4-oxo-3-(2-oxoindolin-3-ylidene)-4-phenylbutanoate (**3g**).* Yellow solid, yield: 70%. Mp 130–132 °C. IR (KBr): 3446, 3077, 3022, 1733, 1703, 1657, 1615, 1464, 1318, 1276, 1156, 983, 794. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.41 (s, 1H, NH), 8.13 (d, *J*=6.0 Hz, 2H, ArH), 7.62 (br s, 1H, ArH), 7.49 (br s, 2H, ArH), 7.12 (br s, 1H, ArH), 6.82 (d, *J*=6.6 Hz, 1H, ArH), 6.79 (d, *J*=6.6 Hz, 1H, ArH), 6.68 (br s, 1H, ArH), 4.20 (s, 2H, CH_2), 1.37 (s, 9H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 197.2, 169.2, 168.0, 143.2, 141.0, 134.6, 134.4, 129.9, 129.2, 127.1, 124.5, 122.0, 120.9, 110.1, 81.8, 37.4, 28.0, 27.8. HRMS (ESI) calcd for $C_{22}H_{21}NNaO_4$ ([M+Na]$^+$): 386.1376. Found: 386.1375.

*4.1.8. tert-Butyl 3-(5-methyl-2-oxoindolin-3-ylidene)-4-oxo-4-p-tolylbutanoate (**3h**).* Yellow solid, yield: 82%. Mp 176–178 °C. IR (KBr): 3448, 1730, 1699, 1664, 1627, 1484, 1416, 1317, 1249, 1195, 1170, 1125, 816. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.11 (s, 1H, NH), 8.02 (d, *J*=7.2 Hz, 2H, ArH), 7.28 (d, *J*=7.2 Hz, 2H, ArH), 6.91 (d, *J*=7.2 Hz, 1H, ArH), 6.69 (d, *J*=7.2 Hz, 1H, ArH), 6.61 (s, 1H, ArH), 4.16 (s, 2H, CH_2), 2.42 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 1.38 (s, 9H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 196.9, 169.4, 168.1, 145.6, 143.0, 138.6, 132.1, 131.2, 130.4, 130.0, 129.8, 127.1, 125.2, 121.0, 109.7, 81.6, 37.5, 28.0, 27.8, 21.9, 21.0. HRMS (ESI) calcd for $C_{24}H_{25}NNaO_4$ ([M+Na]$^+$): 414.1676. Found: 414.1682.

*4.1.9. tert-Butyl 3-(5-chloro-2-oxoindolin-3-ylidene)-4-(4-chlorophenyl)-4-oxobutanoate (**3i**).* Yellow solid, yield: 76%. Mp 192–194 °C. IR (KBr): 3446, 2977, 1719, 1647, 1588, 1470, 1444, 1306, 1196, 1148, 1088, 1015, 982, 821. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.48 (s, 1H, NH), 7.97 (d, *J*=8.4 Hz, 2H, ArH), 7.58 (s, 1H, ArH), 7.41 (d, *J*=8.4 Hz, 2H, ArH), 7.26 (d, *J*=8.4 Hz, 1H, ArH), 6.59 (d, *J*=8.4 Hz, 1H, ArH), 3.76 (s, 2H, CH_2), 1.40 (s, 9H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 196.5, 167.5, 166.6, 143.1, 140.8, 140.0, 133.9, 130.4, 129.2, 129.0, 127.8, 124.5, 122.5, 111.7, 83.3, 39.6, 28.0, 27.9. HRMS (ESI) calcd for $C_{22}H_{19}Cl_2NNaO_4$ ([M+Na]$^+$): 454.0583. Found: 454.0586.

*4.1.10. tert-Butyl 3-(5-fluoro-2-oxoindolin-3-ylidene)-4-oxo-4-phenylbutanoate (**3j**).* Yellow solid, yield: 80%. Mp 124–126 °C. IR (KBr): 3193, 3079, 2980, 1735, 1708, 1664, 1626, 1477, 1368, 1299, 1230, 1154, 1008, 951, 860. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.62 (s, 1H, NH), 8.12 (d, *J*=8.4 Hz, 2H, ArH), 7.65 (t, *J*=7.2 Hz, 1H, ArH), 6.84 (td, J_1=8.4 Hz, J_2=1.8 Hz, 1H, ArH), 6.76 (dd, J_1=8.4 Hz, J_2=4.2 Hz, 1H, ArH), 6.52 (dd, J_1=9.0 Hz, J_2=3.6 Hz, 1H, ArH), 4.19 (s, 2H, CH_2), 1.38 (s, 9H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 196.6, 169.3, 167.8, 158.3 (d, *J*=237.5 Hz), 144.9, 137.1, 134.9, 134.1, 129.9, 129.3, 127.0, 121.7 (d, *J*=8.7 Hz), 116.5 (d, *J*=23.9 Hz), 111.8 (d, *J*=26.1 Hz), 110.7 (d, *J*=8.1 Hz), 82.0, 28.0, 27.9. HRMS (ESI) calcd for $C_{22}H_{20}FNNaO_4$ ([M+Na]$^+$): 404.1269. Found: 404.1269.

4.2. General procedure for the preparation of dispirocyclopentanebisoxindoles 4a–k and 5a–j from the reactions of 4-dimethylamino-1-alkoxycarbonylmethylpyridinium salts with 3-phenacylideneoxindoles or ethyl (2-oxo-1,2-dihydro-indol-3-ylidene)acetates

A mixture of 4-dimethylamino-1-alkoxycarbonylmethyl pyridinium bromide (1.1 mmol), 3-phenacylideneoxindoles or ethyl (2-oxo-1,2-dihydro-indol-3-ylidene)acetates (2.0 mmol), and triethylamine (0.2 mmol) in ethanol (15 mL) was stirred at about 50–60 °C for 12 h. The resulting precipitates were collected by filtration, which were recrystallized in a mixture of chloroform and ethanol to give pure product for analysis.

*4.2.1. Compound **4a**.* White solid, yield: 85%. Mp 288 °C, IR (KBr) ν: 3401, 3055, 2981, 1739, 1704, 1606, 1490, 1459, 1356, 1299, 1174, 1079, 1005, 982, 857, 754 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.05 (d, *J*=7.2 Hz, 2H, ArH), 7.60 (d, *J*=7.2 Hz, 1H, ArH), 7.52 (t, *J*=7.2 Hz, 1H, ArH), 7.46 (t, *J*=7.8 Hz, 2H, ArH), 7.43 (t, *J*=7.8 Hz, 2H, ArH) 7.27 (br s, 1H, ArH), 7.25 (m, 5H, ArH), 7.19–7.14 (m, 4H, ArH), 7.05 (t, *J*=7.8 Hz, 2H, ArH), 6.95 (t, *J*=7.8 Hz, 1H, ArH), 6.90 (t, *J*=7.8 Hz, 1H, ArH), 6.87 (d, *J*=7.2 Hz, 2H, ArH), 6.77 (t, *J*=7.8 Hz, 1H, ArH), 6.63 (t, *J*=7.8 Hz, 1H, ArH), 6.41 (d, *J*=7.8 Hz, 1H, ArH), 5.91 (d, *J*=11.4 Hz, 1H, CH), 5.81 (d, *J*=6.6 Hz, 1H, CH), 5.17–5.14 (m, 1H, CH), 5.07 (d, *J*=15.6 Hz, 1H, CH), 4.94 (d, *J*=16.2 Hz, 1H, CH), 4.74 (d, *J*=16.2 Hz, 1H, CH), 4.20 (d, *J*=15.6 Hz, 1H, CH), 3.93 (q, *J*=7.2 Hz, 2H, CH_2), 6.77 (d, *J*=7.2 Hz, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 197.9, 195.3, 177.5, 175.3, 171.5, 144.2, 143.2, 137.4, 136.9, 135.8, 134.9, 132.8, 132.6, 129.2, 129.0, 128.6, 128.3, 128.1, 127.7, 127.5, 127.3, 127.2, 125.5, 125.0, 123.7, 122.8, 122.3, 109.3, 109.1, 61.2,

61.1, 61.0, 56.8, 54.6, 46.6, 44.3, 43.8, 13.7. HRMS (ESI) calcd for $C_{50}H_{40}N_2NaO_6$ ([M+Na]$^+$): 787.2779. Found: 787.2777.

4.2.2. Compound ***4b***. White solid, yield: 80%. Mp 251 °C, IR (KBr) ν: 3450, 1716, 1677, 1641, 1612, 1490, 1462, 1413, 1361, 1303, 1181, 1089, 1032, 833, 752 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.50–7.46 (m, 5H, ArH), 7.20 (d, J=7.8 Hz, 1H, ArH), 7.06 (t, J=7.8 Hz, 1H, ArH), 7.00 (t, J=7.2 Hz, 1H, ArH), 6.96 (d, J=7.8 Hz, 4H, ArH), 6.94 (t, J=7.2 Hz, 2H, ArH), 6.89–6.81 (m, 5H, ArH), 6.50 (t, J=7.8 Hz, 1H, ArH), 6.45 (d, J=7.8 Hz, 2H, ArH), 6.29 (t, J=7.8 Hz, 3H, ArH), 6.00–5.95 (m, 2H, ArH, CH), 5.45–5.14 (m, 1H, CH), 4.98–4.95 (m, 2H, CH), 4.72 (d, J=15.6 Hz, 1H, CH), 4.31 (d, J=15.6 Hz, 1H, CH), 4.12–4.06 (m, 2H, CH_2), 3.83 (d, J=16.2 Hz, 1H, CH), 2.28 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 1.04 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 196.8, 196.7, 176.2, 175.8, 171.6, 143.6, 143.0, 142.6, 142.5, 135.2, 134.9, 134.7, 129.7, 129.6, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 127.1, 126.4, 125.3, 124.0, 122.2, 121.9, 108.5, 108.1, 63.8, 62.9, 60.7, 55.4, 53.0, 49.1, 43.6, 43.4, 21.5, 13.9. HRMS (ESI) calcd for $C_{52}H_{44}N_2NaO_6$ ([M+Na]$^+$): 815.3092. Found: 815.3090.

4.2.3. Compound ***4c***. Yellow solid, yield: 82%. Mp 210 °C, IR (KBr) ν: 3423, 1735, 1679, 1606, 1479, 1411, 1352, 1303, 1281, 1233, 1186, 1120, 816. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.62 (s, 2H, NH), 7.50 (d, J=7.8 Hz, 4H, ArH), 7.17 (d, J=7.8 Hz, 4H, ArH), 7.03 (d, J=8.4 Hz, 2H, ArH), 6.85 (s, 2H, ArH), 6.49 (d, J=8.4 Hz, 2H, ArH), 5.30 (t, J=9.6 Hz, 1H, CH), 5.10 (d, J=10.2 Hz, 2H, CH), 4.03 (q, J=7.2 Hz, 2H, CH_2), 2.18 (s, 6H, $2CH_3$), 0.97 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 195.8, 175.7, 171.4, 144.3, 140.8, 133.6, 129.2, 128.9, 128.0, 127.2, 125.6, 124.6, 110.6, 63.4, 61.0, 51.4, 46.8, 21.0, 13.8. HRMS (ESI) calcd for $C_{38}H_{30}Cl_2N_2O_6$ ([M+Na]$^+$): 681.1554. Found: 681.1553.

4.2.4. Compound ***4d***. Yellow solid, yield: 58%. Mp 212 °C, IR (KBr) ν: 3440, 1728, 1686, 1622, 1591, 1478, 1402, 1385, 1218, 1183, 1092, 1044, 1015, 818 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.51 (s, 1H, NH), 10.23 (s, 1H, NH), 8.07 (d, J=7.8 Hz, 2H, ArH), 7.81 (s, 1H, ArH), 7.61 (d, J=7.2 Hz, 2H, ArH), 7.46 (d, J=7.8 Hz, 2H, ArH), 7.40 (d, J=7.2 Hz, 2H, ArH), 7.26 (d, J=7.8 Hz, 1H, ArH), 7.03 (d, J=7.8 Hz, 1H, ArH), 6.69 (d, J=7.8 Hz, 1H, ArH), 6.43 (d, J=7.8 Hz, 1H, ArH), 5.99 (s, 1H, ArH), 5.59 (d, J=6.0 Hz, 1H, CH), 5.17–5.14 (m, 1H, CH), 4.97 (d, J=10.8 Hz, 1H, CH), 3.96–3.94 (m, 1H, CH), 3.84–3.81 (m, 1H, CH), 0.92 (t, J=6.6 Hz, 3H, CH_3). HRMS (ESI) calcd for $C_{36}H_{24}Cl_4N_2NaO_6$ ([M+Na]$^+$): 721.0448. Found: 721.0461.

4.2.5. Compound ***4e***. Yellow solid, yield: 49%. Mp 240 °C, IR (KBr) ν: 3447, 1740, 1702, 1635, 1489, 1406, 1387, 1231, 1154, 1094, 1047, 1010, 817. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.55 (s, 1.84H, NH), 7.60 (br s, 4H, ArH), 7.47 (br s, 4H, ArH), 6.88 (br s, 2H, ArH), 6.61 (br s, 2H, ArH), 6.53 (br s, 2H, ArH), 5.21 (br s, 1H, CH), 5.11 (d, J=6.0 Hz, 2H, CH), 1.24 (s, 9H, $3CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 196.1, 176.2, 171.0, 157.8, 156.3, 139.4, 138.8, 135.1, 130.2, 129.4, 125.6, 116.5 (d, J=5.1 Hz), 116.3, 115.0, 114.8, 110.9 (d, J=4.2 Hz), 82.1, 63.9, 52.2, 48.3, 27.8. HRMS (ESI) calcd for $C_{38}H_{28}Cl_2F_2N_2NaO_6$ ([M+Na]$^+$): 739.1171. Found: 739.1185.

4.2.6. Compound ***4f***. Yellow solid, yield: 80%. Mp 270–271 °C. IR (KBr) ν: 3434, 1740, 1709, 1683, 1609, 1479, 1441, 1388, 1296, 1237, 1185, 1156, 1123, 1013, 815. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.60 (s, 2H, NH), 7.52 (d, J=7.8 Hz, 4H, ArH), 7.19 (d, J=8.4 Hz, 4H, ArH), 7.04–7.03 (m, 2H, ArH), 6.90 (s, 2H, ArH), 6.50 (d, J=8.4 Hz, 2H, ArH), 5.20 (t, J=10.2 Hz, 1H, CH), 5.07 (d, J=9.6 Hz, 2H, CH), 2.28 (s, 6H, $2CH_3$), 1.20 (s, 9H, $3CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 195.9, 175.8, 170.9, 144.3, 140.8, 133.7, 129.2, 128,9, 128.0, 127.3, 125.7, 124.6, 110.6, 81.3, 63.5, 56.0, 51.4, 48.3, 27.4, 21.0, 18.5. HRMS (ESI) calcd for $C_{40}H_{34}Cl_2N_2NaO_6$ ([M+Na]$^+$): 731.1686. Found: 731.1704.

4.2.7. Compound ***4g***. Yellow solid, yield: 65%. Mp 272 °C. IR (KBr) ν: 3421, 1726, 1690, 1621, 1597, 1478, 1449, 1392, 1234, 1188, 1155, 1085, 1008, 843 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.59 (s, 2H, NH), 7.61 (s, 4H, ArH), 7.53 (s, 2H, ArH), 7.38 (s, 4H, ArH), 7.04 (s, 2H, ArH), 6.86 (s, 2H, ArH), 6.50 (s, 2H, ArH), 5.23 (s, 1H, CH), 5.14 (s, 2H, CH), 1.22 (s, 9H, $3CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 196.5, 175.6, 170.6, 156.0, 140.8, 136.1, 133.8, 129.0, 128.7, 127.8, 127.1, 125.6, 124.6, 110.7, 81.4, 63.4, 51.5, 48.0, 27.3. HRMS (ESI) calcd for $C_{38}H_{30}Cl_2N_2NaO_6$ ([M+Na]$^+$): 703.1317. Found: 703.1385.

4.2.8. Compound ***4h***. Yellow solid, yield: 71%. Mp 241 °C. IR (KBr) ν: 3420, 1724, 1690, 1633, 1600, 1487, 1452, 1235, 1190, 1157, 1111, 1049, 1004, 816 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.50 (s, 2H, NH), 7.62 (d, J=7.2 Hz, 4H, ArH), 7.53 (t, J=6.6 Hz, 2H, ArH), 7.38 (t, J=7.2 Hz, 4H, ArH), 6.84 (t, J=8.4 Hz, 2H, ArH), 6.67 (d, J=8.4 Hz, 2H, ArH), 6.51–6.49 (m, 2H, ArH), 5.24 (t, J=9.6 Hz, 1H, CH), 5.15 (d, J=9.0 Hz, 2H, CH), 1.22 (s, 9H, $3CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 196.6, 175.9, 170.7, 156.5 (d, J=234.6 Hz), 138.3, 136.1, 133.8, 128.6, 127.8, 125.3 (d, J=7.5 Hz), 115.7 (d, J=22.5 Hz), 114.5 (d, J=25.6 Hz), 110.1 (d, J=5.7 Hz), 81.4, 63.3, 51.6, 48.0, 27.3. HRMS (ESI) calcd for $C_{38}H_{30}F_2N_2NaO_6$ ([M+Na]$^+$).

4.2.9. Compound ***4i***. Yellow solid, yield: 74%. Mp 245 °C, IR (KBr) ν: 3432, 3288, 1739, 1709, 1620, 1590, 1475, 1401, 1232, 1156, 1115, 1091, 1003, 841, 756 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.39 (s, 2H, NH), 7.54 (d, J=6.6 Hz, 4H, ArH), 7.42 (d, J=6.6 Hz, 4H, ArH), 6.94 (br s, 2H, ArH), 6.81 (d, J=5.4 Hz, 2H, ArH), 6.56 (br s, 2H, ArH), 6.47 (d, J=6.0 Hz, 2H, ArH), 5.30 (t, J=8.4 Hz, 1H, CH), 5.07 (d, J=9.0 Hz, 2H, CH), 1.24 (s, 9H, $3CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 195.7, 176.3, 170.9, 141.9, 138.4, 135.0, 129.6, 129.1, 128.6, 127.0, 124.0, 120.3, 109.3, 81.2, 63.3, 52.1, 47.6, 27.4. HRMS (ESI) calcd for $C_{38}H_{30}Cl_2N_2NaO_6$ ([M+Na]$^+$): 703.1373. Found: 703.1381.

4.2.10. Compound ***4j***. Yellow solid, yield: 78%. Mp 234–235 °C. IR (KBr) ν: 3437, 1725, 1685, 1632, 1607, 1487, 1412, 1237, 1188, 1156, 1115, 1047, 1013, 844 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.49 (s, 2H, NH), 7.52 (d, J=8.4 Hz, 4H, ArH), 7.18 (d, J=8.4 Hz, 4H, ArH), 6.84 (td, J_1=8.4 Hz, J_2=2.4 Hz, 2H, ArH), 6.71 (d, J=8.4 Hz, 2H, ArH), 6.50–6.48 (m, 2H, ArH), 5.21 (t, J=9.6 Hz, 1H, CH), 5.10 (d, J=9.6 Hz, 2H, CH), 2.28 (s, 6H, $2CH_3$), 1.20 (s, 9H, $3CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 195.9, 176.0, 170.8, 156.5 (d, J=234.3 Hz), 144.3, 138.3, 133.7, 129.2, 128.0, 125.4 (d, J=8.3 Hz), 115.6 (d, J=23.1 Hz), 114.6 (d, J=26.1 Hz), 110.0 (d, J=8.6 Hz), 81.2, 63.6, 56.0, 51.4, 48.1, 27.4, 21.0, 18.5. HRMS (ESI) calcd for $C_{40}H_{34}F_2N_2NaO_6$ ([M+Na]$^+$): 699.2277. Found: 699.2288.

4.2.11. Compound ***4k***. White solid, yield: 79%. Mp 218 °C, IR (KBr) ν: 3448, 2978, 1708, 1642, 1461, 1366, 1271, 1229, 1162, 1085, 1002, 847, 757 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.04 (d, J=7.8 Hz, 2H, ArH), 7.61 (d, J=7.8 Hz, 1H, ArH), 7.53 (d, J=7.8 Hz, 2H, ArH), 7.50 (d, J=7.2 Hz, 1H, ArH), 7.44 (t, J=7.2 Hz, 2H, ArH) 7.28–7.27 (m, 4H, ArH), 7.26–7.24 (m, 2H, ArH), 7.20–7.16 (m, 4H, ArH), 7.10 (t, J=7.8 Hz, 2H, ArH), 6.96–6.93 (m, 3H, ArH), 6.90 (t, J=7.8 Hz, 1H, ArH), 6.76 (t, J=7.8 Hz, 1H, ArH), 6.63 (t, J=7.8 Hz, 1H, ArH), 6.41 (d, J=7.8 Hz, 1H, ArH), 6.11 (d, J=7.8 Hz, 1H, ArH), 5.98 (d, J=7.2 Hz, 1H, CH), 5.88 (d, J=11.4 Hz, 1H, CH), 5.08 (d, J=16.2 Hz, 1H, CH), 5.04–5.01 (m, 1H, CH), 4.98 (d, J=16.2 Hz, 1H, CH), 4.79 (d, J=15.6 Hz, 1H, CH), 4.35 (d, J=15.6 Hz, 1H, CH), 1.04 (s, 9H, $3CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 198.2, 195.0, 177.3, 175.4, 170.3, 144.2, 143.2, 137.2, 137.1, 136.0, 135.0, 132.8, 132.6, 129.0, 128.8, 128,6, 128.4, 127.8, 127.5, 127.4, 127.2, 125.4, 125.1, 124.8, 123.8,

122.6, 122.2, 109.1, 109.0, 82.2, 61.0, 60.8, 56.2, 55.3, 47.8, 44.2. HRMS (ESI) calcd for $C_{52}H_{44}N_2NaO_6$ ([M+Na]$^+$): 815.3092. Found: 815.3089.

4.2.12. Compound ***5a***. White solid, yield: 70%. Mp 270 °C, IR (KBr) ν: 3443, 2986, 1738, 1627, 1548, 1495, 1374, 1319, 1218, 1171, 1094, 1027, 858, 818 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.30 (s, 2H, NH), 6.93 (d, J=7.8 Hz, 2H, ArH), 6.67 (s, 2H, ArH), 6.53 (d, J=7.8 Hz, 2H, ArH), 4.58 (t, J=9.6 Hz, 1H, CH), 4.17 (q, J=7.2 Hz, 2H, CH_2), 3.94 (d, J=9.6 Hz, 2H, 2CH), 3.79 (q, J=7.2 Hz, 4H, $2CH_2$), 2.06 (s, 6H, $2CH_3$), 1.19 (t, J=7.2 Hz, 3H, CH_3), 0.68 (t, J=7.2 Hz, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 176.2, 171.3, 169.9, 140.0, 129.1, 128.9, 126.7, 124.9, 108.9, 62.0, 60.9, 60.6, 51.0, 46.4, 20.6, 14.0, 13.2. HRMS (ESI) calcd for $C_{30}H_{32}N_2NaO_8$ ([M+Na]$^+$): 571.2051. Found: 571.2050.

4.2.13. Compound ***5b***. White solid, yield: 80%. Mp 235 °C, IR (KBr) ν: 3444, 3086, 2986, 2880, 1702, 1635, 1492, 1399, 1375, 1295, 1170, 1094, 1021, 927, 868, 772 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.59 (s, 2H, NH), 7.08–7.05 (m, 2H, ArH), 6.73–6.71 (m, 2H, ArH), 6.67–6.66 (m, 2H, ArH), 4.50 (t, J=9.6 Hz, 1H, CH), 4.18 (q, J=7.2 Hz, 2H, CH_2), 3.99 (d, J=9.6 Hz, 2H, 2CH), 3.85 (q, J=7.2 Hz, 4H, $2CH_2$), 1.19 (t, J=7.2 Hz, 3H, CH_3), 0.74 (t, J=7.2 Hz, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 175.7, 170.8, 169.8, 157.5, 156.0, 138.9, 127.8 (d, J=8.1 Hz), 116.0 (d, J=23.0 Hz), 113.2 (d, J=26.0 Hz), 110.4 (d, J=8.1 Hz), 62.1, 61.1, 61.0, 51.0, 46.4, 13.9, 13.2. HRMS (ESI) calcd for $C_{28}H_{26}F_2N_2NaO_8$ ([M+Na]$^+$): 579.1549. Found: 579.1547.

4.2.14. Compound ***5c***. White solid, yield: 65%. Mp 230 °C, IR (KBr) ν: 3456, 2988, 1737, 1692, 1623, 1474, 1373, 1339, 1295, 1222, 1173, 1096, 1022, 858, 748 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.44 (s, 2H, NH), 7.12 (t, J=7.8 Hz, 2H, ArH), 6.87 (d, J=7.2 Hz, 2H, ArH), 6.73 (t, J=7.2 Hz, 2H, ArH), 6.66 (d, J=7.8 Hz, 2H, ArH), 4.57 (t, J=9.6 Hz, 1H, CH), 4.17 (q, J=7.2 Hz, 2H, CH_2), 3.96 (d, J=9.6 Hz, 2H, 2CH), 3.80–3.73 (m, 4H, $2CH_2$), 1.18 (t, J=7.2 Hz, 3H, CH_3), 0.67 (t, J=7.2 Hz, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 176.2, 171.2, 169.8, 142.5, 129.2, 125.7, 124.8, 120.4, 109.3, 61.8, 61.0, 60.6, 51.2, 46.4, 13.9, 13.2. HRMS (ESI) calcd for $C_{28}H_{28}N_2NaO_8$ ([M+Na]$^+$): 543.1738. Found: 543.1738.

4.2.15. Compound ***5d***. White solid, yield: 71%. Mp 167 °C, IR (KBr) ν: 3071, 2984, 2934, 1742, 1606, 1492, 1450, 1370, 1271, 1178, 1023, 941, 887 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 7.17–7.15 (m, 4H, ArH), 7.10 (t, J=7.2 Hz, 4H, ArH), 6.92 (d, J=7.2 Hz, 4H, ArH), 6.75–6.72 (m, 4H, ArH), 4.99 (d, J=16.2 Hz, 2H, 2CHPh), 4.65 (d, J=16.2 Hz, 2H, 2CHPh), 4.60 (t, J=9.6 Hz, 1H, CH), 4.22 (q, J=6.6 Hz, 2H, OCH_2), 4.18 (d, J=9.6 Hz, 2H, 2CH), 3.83 (q, J=6.6 Hz, 4H, $2OCH_2$), 1.21 (t, J=6.6 Hz, 3H, CH_3), 0.68 (t, J=6.6 Hz, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 174.2, 170.7, 169.4, 158.1, 156.6, 139.4, 135.0, 128.3, 127.2, 126.6, 125.1 (d, J=8.1 Hz), 116.2 (d, J=23.1 Hz), 113.2 (d, J=26.4 Hz), 110.6 (d, J=7.6 Hz), 61.6, 61.3, 61.1, 51.6, 46.5, 43.0, 13.9, 13.2. HRMS (ESI) calcd for $C_{42}H_{38}F_2N_2NaO_8$ ([M+Na]$^+$): 759.2488. Found: 759.2504.

4.2.16. Compound ***5e***. White solid, yield: 55%. Mp 188 °C, IR (KBr) ν: 3065, 2981, 2932, 1744, 1729, 1608, 1485, 1367, 1344, 1216, 1177, 1023, 889, 854 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 7.36 (d, J=7.2 Hz, 2H, ArH), 7.14–7.11 (m, 6H, ArH), 6.90 (br s, 6H, ArH), 6.76 (d, J=7.2 Hz, 2H, ArH), 4.98 (d, J=15.6 Hz, 2H, 2CHPh), 4.65 (d, J=15.6 Hz, 2H, 2CHPh), 4.61 (t, J=8.4 Hz, 1H, CH), 4.22 (br s, 2H, OCH_2), 4.16 (d, J=8.4 Hz, 2H, 2CH), 3.85–3.84 (m, 4H, $2OCH_2$), 1.22 (br s, 3H, CH_3), 0.69 (br s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 173.9, 170.6, 169.4, 141.9, 134.8, 129.6, 128.3, 127.2, 126.6, 125.9, 125.6, 125.3, 111.1, 61.5, 61.3, 61.2, 51.5, 46.5, 43.0, 40.1, 13.9, 13.2. HRMS (ESI) calcd for $C_{42}H_{38}Cl_2N_2NaO_8$ ([M+Na]$^+$): 791.1897. Found: 791.1890.

4.2.17. Compound ***5f***. White solid, yield: 95%. Mp 239 °C, IR (KBr) ν: 3451, 3249, 3038, 2979, 1739, 1691, 1627, 1496, 1457, 1371, 1294, 1177, 1096, 960, 853, 760 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.27 (s, 2H, NH), 6.92 (d, J=7.8 Hz, 2H, ArH), 6.71 (s, 2H, ArH), 6.51 (d, J=7.8 Hz, 2H, ArH), 4.50 (t, J=9.6 Hz, 1H, CH), 3.89 (d, J=9.6 Hz, 2H, 2CH), 3.79 (q, J=7.2 Hz, 4H, $2OCH_2$), 2.06 (s, 6H, $2CH_3$), 1.42 (s, 9H, $3CH_3$), 0.71 (t, J=7.8 Hz, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 176.2, 170.5, 170.0, 140.0, 129.0, 128.8, 126.8, 125.0, 108.8, 80.9, 61.9, 60.4, 51.2, 47.4, 20.6, 13.3. HRMS (ESI) calcd for $C_{32}H_{36}N_2NaO_8$ ([M+Na]$^+$): 599.2364. Found: 599.2362.

4.2.18. Compound ***5g***. White solid, yield: 93%. Mp 265 °C. IR (KBr) ν: 3449, 3085, 2979, 1738, 1696, 1632, 1489, 1456, 1372, 1283, 1217, 1158, 1095, 921, 871, 760 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.56 (s, 2H, NH), 6.72–6.69 (m, 4H, ArH), 4.42 (t, J=9.6 Hz, 1H, CH), 3.93 (d, J=10.2 Hz, 2H, 2CH), 3.87–3.82 (m, 4H, $2OCH_2$), 1.42 (s, 9H, $3CH_3$), 0.76 (t, J=7.2 Hz, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 175.8, 170.0, 169.8, 156.5, 156.0, 138.9, 125.8 (d, J=8.1 Hz), 115.9 (d, J=23.0 Hz), 113.2 (d, J=26.0 Hz), 110.4 (d, J=8.0 Hz), 81.3, 62.0, 60.8, 51.2, 47.4, 27.4, 13.3. HRMS (ESI) calcd for $C_{30}H_{30}F_2N_2NaO_8$ ([M+Na]$^+$): 607.1862. Found: 607.1856.

4.2.19. Compound ***5h***. White solid, yield: 91%. Mp 246 °C. IR (KBr) ν: 3450, 3095, 2978, 1730, 1694, 1620, 1473, 1397, 1373, 1288, 1156, 1095, 1024, 903, 848, 751 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.42 (s, 2H, NH), 7.11 (t, J=7.8 Hz, 2H, ArH), 6.90 (d, J=7.8 Hz, 2H, ArH), 6.73 (t, J=7.8 Hz, 2H, ArH), 6.65 (d, J=7.8 Hz, 2H, ArH), 4.50 (t, J=10.2 Hz, 1H, CH), 3.91 (d, J=7.8 Hz, 2H, 2CH), 3.80–3.72 (m, 4H, $2OCH_2$), 1.41 (s, 9H, $3CH_3$), 0.70 (t, J=7.2 Hz, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 176.3, 170.4, 170.0, 142.4, 129.2, 125.8, 124.8, 120.3, 109.3, 81.0, 61.8, 60.5, 51.4, 47.4, 27.5, 13.3. HRMS (ESI) calcd for $C_{30}H_{32}N_2NaO_8$ ([M+Na]$^+$): 571.2051. Found: 571.2047.

4.2.20. Compound ***5i***. White solid, yield: 75%. Mp 235 °C, IR (KBr) ν: 3467, 3120, 2982, 2900, 2728, 1734, 1620, 1479, 1395, 1371, 1220, 1161, 1090, 1022, 892, 802, 736 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 10.70 (s, 2H, NH), 7.26 (br s, 1H, ArH), 7.25 (br s, 1H, ArH), 6.88 (br s, 2H, ArH), 6.72 (d, J=8.4 Hz, 2H, ArH), 4.43 (t, J=9.6 Hz, 1H, CH), 3.92 (d, J=9.6 Hz, 2H, 2CH), 3.88–3.83 (m, 4H, $2OCH_2$), 1.42 (s, 9H, $3CH_3$), 0.77 (t, J=7.2 Hz, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 175.5, 169.7, 141.4, 129.3, 126.2, 125.8, 124.7, 110.9, 81.4, 61.9, 60.9, 51.5, 47.4, 27.5, 13.4. HRMS (ESI) calcd for $C_{30}H_{30}Cl_2N_2NaO_8$ ([M+Na]$^+$): 639.1271. Found: 639.1267.

4.2.21. Compound 5j. White solid, yield: 75%. Mp 169 °C, IR (KBr) ν: 2977, 2931, 1738, 1724, 1606, 1494, 1451, 1369, 1344, 1282, 1176, 1090, 941, 887 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 7.17–7.12 (m, 4H, ArH), 7.09 (t, J=7.2 Hz, 4H, ArH), 6.92 (d, J=7.2 Hz, 4H, ArH), 6.76–6.73 (m, 4H, ArH), 5.01 (d, J=15.6 Hz, 2H, 2CHPh), 4.64 (d, J=16.2 Hz, 2H, 2CHPh), 4.54 (t, J=9.6 Hz, 1H, CH), 4.11 (d, J=9.6 Hz, 2H, 2CH), 3.83 (q, J=6.6 Hz, 4H, $2OCH_2$), 1.44 (s, 9H, $3CH_3$), 0.70 (t, J=7.2 Hz, 6H, $2CH_3$). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 174.2, 169.9, 169.6, 158.1, 156.5, 139.4, 135.0, 128.3, 127.2, 126.6, 125.0 (d, J=8.2 Hz), 116.2 (d, J=22.4 Hz), 113.2 (d, J=26.8 Hz), 110.6 (d, J=7.6 Hz), 81.6, 61.6, 61.0, 51.7, 47.5, 43.0, 27.5, 13.3. HRMS (ESI) calcd for $C_{44}H_{42}F_2N_2NaO_8$ ([M+Na]$^+$): 787.2801. Found: 787.2817.

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Supplementary data

Crystallographic data **3a** (CCDC 904922), **4b** (CCDC 971841), **4e** (CCDC 971842), **4h** (CCDC 971843), **5e** (CCDC 983652), and **5g** (CCDC 971844) have been deposited at the Cambridge Crystallographic Database Centre. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.02.050.

References and notes

1. (a) Koch, M. A.; Schuffenhauer, A.; Scheck, M.; Wetzel, S.; Casaulta, M.; Odermatt, A.; Ertl, P.; Waldmann, H. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 17272–17277; (b) Ashimori, A.; Bachand, B.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 6477–6487.
2. (a) Sebahar, P. R.; Williams, R. M. *J. Am. Chem. Soc.* **2000**, *122*, 5666–5667; (b) Abdel-Rahman, A. H.; Keshk, E. M.; Hanna, M. A.; El-Bady, Sh. M. *Bioorg. Med. Chem.* **2004**, *12*, 2483–2488.
3. (a) iKotha, S. B.; Deb, A. C.; Lahiri, K.; Manivannan, E. *Synthesis* **2009**, 165–193; (b) Singh, G. S.; Desta, Z. Y. *Chem. Rev.* **2012**, *112*, 6104–6155; (c) Liu, Y. Y.; Wang, H.; Wan, J. P. *Asian J. Org. Chem.* **2013**, *2*, 374–386.
4. (a) Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, 3003–3025; (b) Ball-Jones, N. R.; Badillo, J. J.; Franz, A. K. *Org. Biomol. Chem.* **2012**, *10*, 5165–5181; (c) Hong, L.; Wang, R. *Adv. Synth. Catal.* **2013**, *355*, 1023–1052.
5. (a) Bazgir, A.; Tisseh, T. Z.; Mirzaei, P. *Tetrahedron Lett.* **2008**, *49*, 5165–5168; (b) Jadidi, K.; Ghahremanzadeh, R.; Bazgir, A. *Tetrahedron* **2009**, *65*, 2005–2009; (c) Dabiri, M.; Azimi, S. C.; Khavasi, H. R.; Bazgir, A. *Tetrahedron* **2008**, *64*, 7307–7311; (d) Jadidi, K.; Ghahremanzadeh, R.; Bazgir, A. *J. Comb. Chem.* **2009**, *11*, 341–344.
6. (a) Gao, S. J.; Tsai, C. H.; Tseng, C.; Yao, C. F. *Tetrahedron* **2008**, *64*, 9143–9149; (b) Litvinov, Y. M.; Mortikov, V. Y.; Shestopalov, A. M. *J. Comb. Chem.* **2008**, *10*, 741–745; (c) Liang, B.; Kalidindi, S.; Porco, J. A., Jr.; Stephenson, C. R. J. *Org. Lett.* **2010**, *12*, 572–575; (d) Chen, W. B.; Wu, Z. J.; Pei, Q. L.; Cun, N. F.; Zhang, X. M.; Yuan, W. C. *Org. Lett.* **2010**, *12*, 3132–3135.
7. (a) Liu, H.; Dou, D. L.; Shi, D. Q. *J. Comb. Chem.* **2010**, *12*, 633–637; (b) Liu, H.; Dou, G. L.; Shi, D. Q. *J. Comb. Chem.* **2010**, *12*, 292–294; (c) Li, Y. L.; Chen, H.; Shi, C. L.; Shi, D. Q.; Ji, S. J. *J. Comb. Chem.* **2010**, *12*, 231–237.
8. (a) Shanmugam, P.; Viswambharan, B.; Madhavan, S. *Org. Lett.* **2007**, *9*, 4095–4098; (b) Lakshmi, N. V.; Thirumurugan, P.; Perumal, P. T. *Tetrahedron Lett.* **2010**, *51*, 1064–1068; (c) Badillo, J. J.; Arevalo, G. E.; Fettinger, J. C.; Franz, A. K. *Org. Lett.* **2011**, *13*, 418–421.
9. (a) Lanka, S.; Thennarasu, S.; Perumal, P. T. *Tetrahedron Lett.* **2012**, *53*, 7052–7055; (b) Rao, J. N. S.; Raghunathan, R. *Tetrahedron Lett.* **2013**, *54*, 6568–6573; (c) Purushothaman, S.; Prasanna, R.; Lavanya, S.; Raghunathan, R. *Tetrahedron Lett.* **2013**, *54*, 5744–5747; (d) Singh, S. N.; Regati, S.; Paul, A. K.; Layek, M.; Jayaprakash, S.; Reddy, K. V.; Deora, G. S.; Mukherjee, S.; Pal, M. *Tetrahedron Lett.* **2013**, *54*, 5448–5452.
10. (a) Kröhnke, F.; Zecher, W. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 626–632; (b) Kröhnke, F. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 225–238.
11. (a) Yan, C. G.; Cai, X. M.; Wang, Q. F.; Wang, T. Y.; Zheng, M. *Org. Biomol. Chem.* **2007**, *5*, 945–951; (b) Yan, C. G.; Song, X. K.; Wang, Q. F.; Sun, J.; Siemeling, U.; Bruhn, C. *Chem. Commun.* **2008**, 1440–1442; (c) Wang, Q. F.; Song, X. K.; Chen, J.; Yan, C. G. *J. Comb. Chem.* **2009**, *11*, 1007–1010; (d) Wang, Q. F.; Hou, H.; Hui, L.; Yan, C. G. *J. Org. Chem.* **2009**, *74*, 7403–7406; (e) Yan, C. G.; Wang, Q. F.; Song, X. K.; Sun, J. *J. Org. Chem.* **2009**, *74*, 710–718.
12. (a) Wang, Q. F.; Hui, L.; Hou, H.; Yan, C. G. *J. Comb. Chem.* **2010**, *12*, 260–265; (b) Han, Y.; Chen, J.; Hui, L.; Yan, C. G. *Tetrahedron* **2010**, *66*, 7743–7748; (c) Hou, H.; Zhang, Y.; Yan, C. G. *Chem. Commun.* **2012**, 4492–4494.
13. Jacobs, J.; Van Hende, E.; Claessens, S.; De Kimpe, N. *Curr. Org. Chem.* **2011**, *15*, 1340–1362.
14. (a) Nyerges, M.; Gajdics, L.; Szöllösy, A.; Töke, L. *Synlett* **1999**, 111–113; (b) Fejes, I.; Töke, L.; Nyerges, M.; Pak, C. S. *Tetrahedron* **2000**, *56*, 639–644; (c) Fejes, I.; Nyerges, M.; Szollosy, A.; Blasko, G.; Töke, L. *Tetrahedron* **2001**, *57*, 1129–1137.
15. (a) Serov, A. B.; kartsev, V. G.; Aleksandrov, A. Yu; Dolgushin, F. M. *Russ. Chem. Bull.* **2005**, *54*, 2432–2436; (b) Velikorodov, A. V.; Imasheva, N. M.; Kuanchalieva, A. K.; Poddubnyi, O. Yu *Russ. J. Org. Chem.* **2010**, *46*, 971–975.
16. El-Ahl, A. A. S. *Pol. J. Chem.* **1997**, *71*, 27–31.
17. Hui, L.; Li, H. Y.; Yan, C. G. *Eur. J. Org. Chem.* **2012**, 3157–3164.
18. Wu, L.; Sun, J.; Yan, C. G. *Org. Biomol. Chem.* **2012**, *10*, 9452–9463.
19. Fu, Q.; Yan, C. G. *Tetrahedron* **2013**, *69*, 5841–5849.
20. (a) Basavaiah, D.; Reddy, K. R. *Org. Lett.* **2007**, *9*, 57–60; (b) Shanthi, G.; Perumal, P. T. *Tetrahedron Lett.* **2008**, *49*, 7139–7142; (c) Lingam, K.; Shanmugam, P.; Selvakumar, K. *Synlett* **2012**, 278–284.
21. (a) Tan, B.; Candeias, N. R.; Barbas, C. F., III. *Nat. Chem.* **2011**, *3*, 473–477; (b) Sun, J.; Xie, Y. J.; Yan, C. G. *J. Org. Chem.* **2013**, *78*, 8354–8365; (c) Wu, H.; Zhang, L. L.; Tian, Z. Q.; Huang, Y. D.; Wang, Y. M. *Chem.—Eur. J.* **2013**, *19*, 1747–1753.
22. Sarkunam, K.; Nallu, M. *J. Heterocycl. Chem.* **2005**, *42*, 5–11.