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Four-component reaction of *N*-alkylimidazoles (*N*-alkylbenzimidazoles), dialkyl but-2-ynedioate, *N*-alkylisatins and malononitrile

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Abstract: Under the catalyst-free conditions, four-component reaction of *N*-alkylimidazole, dialkyl but-2-ynedioate, *N*-alkylisatins and malononitrile in tetrahydrofuran at room temperature afforded the novel functionalized spiro[imidazo[1,2-a]pyridine-7,3'-indolines] in good yields. Otherwise, the similar four-component reaction containing *N*-alkylbenzimidazole usually resulted in a mixture of spiro[benzimidazo[1,2-a]pyridine-6,3'-indoline] and spiro[benzimidazo[1,2-a]pyridine-7,3'-indoline] derivatives, which is derived from two regioselective reaction modes of isatylidene malononitrile in cyclocondensation reaction. The structures and formation mechanism of the different products were clearly elucidated.

Keywords: multicomponent reaction; spirooxindole; imidazole; benzimidazole; electron-deficient alkyne; malononitrile.

1. Introduction

Spirooxindole is a privileged heterocyclic ring system that is featured in a large number of bioactive naturally occurring alkaloids and medicinally relevant compounds.[1,2] These potential properties have prompted many efforts toward the synthesis of various spirooxindole derivatives. As a consequence, a number of efficient synthetic methods have been developed for the preparation of the diversely structural spirocyclic oxindoles.[3-5] On the other hand, the chemistry of Huisgen's 1,4-dipoles has been attracted much attention in recent years. Huisgen's 1,4-dipoles can be easily generated from addition reaction of aromatic nitrogen heterocycles to electron-deficient

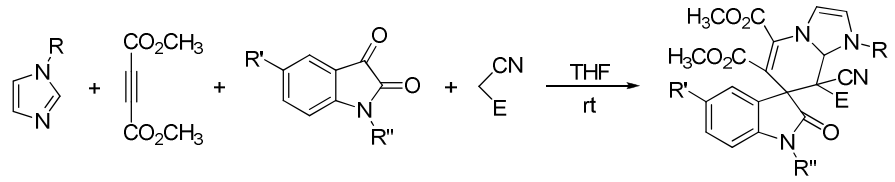
alkynes.[6,] Numerous convenient and efficient synthetic strategy for the versatile carbocyclic and heterocyclic systems have been developed by using Huisgen's 1,4-dipoles as the key reaction substrates.[7] Therefore, the 1,4-dipolar cycloaddition of Huisgen 1,4-dipoles with isatin and its 3-methylene derivatives has been developed as one of the convenient synthetic methodology for various spirooxindoles.[8,9] In this field, Nair and co-workers firstly reported the three-component reaction of pyridine, dimethyl acetylenedicarboxylate and *N*-benzylisatins to give spiro[indololine-3,2'-pyrido[2,1-b][1,3]oxazine].[10] Later Yavari[11] and Nair[12] reported the similar reactions of quinoline or isoquinoline with DMAD and isatins for the preparation of complex spirooxindole derivatives. Shi and co-workers found that the three-component reactions of pyridine, dimethyl acetylenedicarboxylate and *N*-substituted isatylidene derivatives affording spiro[indoline-3,2-quinolizine] in high yields and with good diastereoselectivity.[13] We also found that the reactions of various Huisgen 1,4-dipoles with 3-methyleneoxindoles afforded spiro[indoline-3,1'-quinolizines], spiro[indoline-3,4'-pyrido[1,2-a]quinolines], spiro[indoline-3,1'-pyrido[2,1-a]isoquinoline] and complex dispirooxindole-fused heterocycles.[14] In continuation of our efforts to explore the practical applications of Huisgen's *1,4*-dipoles in domino reactions,[15] herein we wish to report the convenient synthesis of novel spiro[imidazo[1,2-a]pyridine-7,3'-indoline] derivatives by four-component reaction of *N*-alkylimidazole and its benzo-derivatives, dialkyl but-2-ynedioate, *N*-alkylisatins and malononitrile.

2. Results and Discussions

According to the previously reported three-component reaction of *N*-benzylbenzylbenzimidazoles, dialkyl but-2-ynedioate and isatins for the synthesis of

benzimidazo[2,1-b][1,3]oxazine spirooxindoles,[16] a mixture of *N*-alkylimidazole, dimethyl but-2-ynedioate, isatin and malononitrile in tetrahydrofuran was stirred at room temperature for about six hours. Without adding other catalyst, the reaction proceeded smoothly to give the expected functionalized spiro[imidazo[1,2-a]pyridine-7,3'-indolines] **1a-1l** in good yields (**Table 1**). Imidazole with *N*-phenyl group, methyl and n-butyl groups and isatins with different substituents showed similar reactivity. When ethyl cyanoacetate was used to replace malononitrile in the reaction, a catalytic amount of triethylamine should be added. The reaction also finished at room temperature in six hours to give the spiro compounds **1m** and **1n** in moderate yields (**Table 1**, entries 14-15). This is due to the condensation of isatin with ethyl cyanoacetate needs much stronger basic conditions. The structures of the obtained spiro compounds **1a-1n** were fully characterized with IR, HRMS, ^{1}H and ^{13} NMR spectra. The single crystal structures of compounds **1a** and **1b** were determined by X-ray diffraction method (**Fig. 1**, **Fig. 2**). The ^{1}H NMR spectra of the spiro compounds **1a-1n** clearly display one set of absorptions for the characteristic groups in the molecule, which indicates that only one diastereosiomer exists in the obtained spiro compounds **1a-1n**. From **Fig. 1** and **Fig. 2**, it can be seen that the proton at C2-position and phenyl group of oxindole moiety exist at C4-position in *trans*-position in the newly-formed dihydropyridyl ring. Thus, we can get a conclusion that spiro compounds **1a-1n** are belonging to *trans*-diastereoisomer and this four-component reaction has high diastereoselectivity.

Table 1 Synthesis of spiro[imidazo[1,2-a]pyridine-7,3'-indolines] 1a-1n [a]



Entry	Compd	R	R'	R"	E	Yield [b]
1	**1a**	Ph	H	Bn	CN	67
2	**1b**	Ph	H	n-C_4H_9	CN	73
3	**1c**	Ph	CH_3	Bn	CN	70
4	**1d**	Ph	CH_3	n-C_4H_9	CN	80
5	**1e**	Ph	Cl	Bn	CN	76
6	**1f**	Ph	Cl	n-C_3H_7	CN	69
7	**1g**	Ph	F	Bn	CN	78
8	**1h**	Ph	F	n-C_4H_9	CN	71
9	**1i**	CH_3	CH_3	n-C_4H_9	CN	73
10	**1j**	CH_3	Cl	n-C_3H_7	CN	82
11	**1k**	CH_3	F	n-C_4H_9	CN	77
12	**1l**	n-C_4H_9	CH_3	Bn	CN	66
13	**1n**	Ph	H	Bn	$CO_2C_2H_5$	55[c]
14	**1o**	Ph	Cl	n-C_3H_7	$CO_2C_2H_5$	50[c]

a. Reaction conditions: isatin (1.0 mmol), *N*-alkylimidazole (1.2 mmol), malononitrile (1.2 mmol), dimethyl but-2-ynedioate (1.2 mmol) in dry THF (10.0 mL), rt, 6 hrs; b. Isolated yields; c. Et_3N (0.5 mmol) was added.

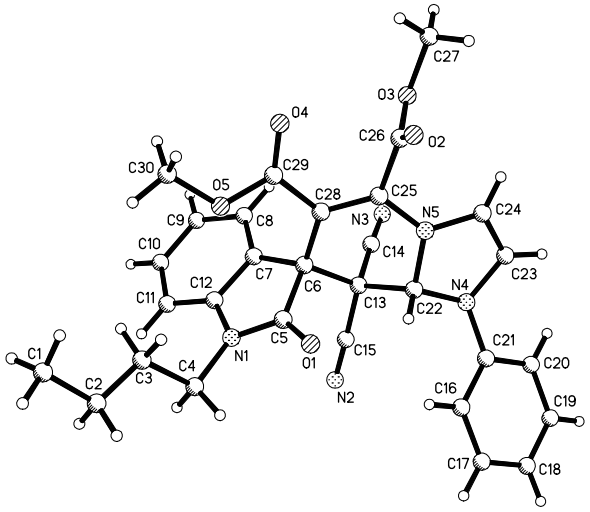


Fig. 1 Molecular structure of compound **1a**

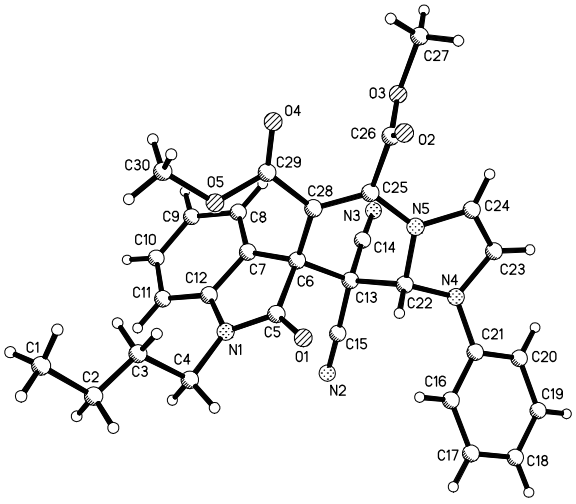
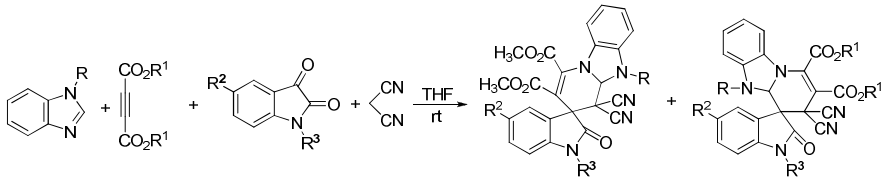


Fig. 2 Molecular structure of compound **1b**

In order to develop the scope of this reaction, *N*-benzylbenzimidazole was also utilized in the four component reaction. The four-component reaction also proceeded smoothly at room temperature in one day to give the expected spiro compounds. But ^{1}H NMR spectra clearly indicated that the obtained products contain two structural isomers with a wide variable molecular ratios (**Table 2**). In most cases these two isomers have nearly same polarity and cannot be separated by column or thin-layer chromatography. We assigned one series of isomers as **2a-2o** and another series of isomers as **2a'-2o'** by careful analysis of the ^{1}H NMR spectra and single crystal structures. From **Table 2**, it can be observed that ^{1}H NMR spectra showed that a mixture of isomers **2a-2j** and **2a'-2j'** were produced (**Table 2**, entries 1-10). But only one kind of isomers **2k**, **2l** and another kind of isomers **2m'**, **2n'**, **2o'** were detected by ^{1}H NMR spectra **(Table 2**, entries 11-15). The ^{1}H NMR spectra of pure isomers **2m'**, **2n'**, and **2o'** clearly display one singlet at about 6.10 ppm for the one proton at C-2 position of imidazole ring. Contrarily, this characteristic absorption is shifted to lower field and is overlapped with the absorptions of aromatic protons in

Table 2 Synthesis of two isomeric benzimidazo[1,2-a]pyridine spirooxindoles [a]



2a-n **2a-n'**

Entry	R	R^1	R^2	R^3	Compd	Yield (%) [b]	ratio of **2/2'** [c]
1	Bn	Me	H	Bn	**2a/2a'**	61	4:1
2	Bn	Me	Me	Bn	**2b/2b'**	53	5:1
4	Bn	Me	F	Bn	**2c/2c'**	65	1:1
5	Bn	Me	H	C_4H_9	**2d/2d'**	71	6:1
6	Bn	Et	H	Bn	**2e/2e'**	64	6:1
7	Bn	Et	Me	Bn	**2f/2f'**	52	1:1
12	Bn	Et	Cl	C_4H_9	**2g/2g'**	62	1:2
13	Bn	Et	F	C_4H_9	**2h/2h'**	66	3:1
14	C_4H_9	Me	H	Bn	**2i/2i'**	70	1:1
11	Bn	Et	Me	C_4H_9	**2j/2j'**	65	1:2
3	Bn	Me	Cl	Bn	**2k**	55	
15	C_4H_9	Me	F	Bn	**2l**	67	
8	Bn	Et	Cl	Bn	**2m'**	60	
9	Bn	Et	F	Bn	**2n'**	74	
10	Bn	Et	H	C_4H_9	**2o'**	61	

a. Reaction conditions: isatin (0.5 mmol), *N*-alkylbenzimidazole (0.5 mmol), malononitrile (0.5 mmol), dialky but-2-ynedioate (0.6 mmol) in dry THF (12.0 mL), rt, one day; b. Isolated yields; c. ratio was determined by ^{1}H NMR.

the pure isomers **2k** and **2l**. Furthermore, this characteristic peak is observed with the less than one proton integration in the ^{1}H NMR spectra of other mixtures of products. Additionally, the two sets of other characteristic absorptions are also clearly observed in the ^{1}H NMR spectra of the mixtures of products. Therefore, one kind of isomers **2a-2o** and another kind of **2a'-2o'** as well as their ratios were successfully assigned based on the analysis of ^{1}H NMR spectra. The assignation of real structures of isomers **2a-2o** and **2a'-2o'** can be done by determination of single crystal structures. At first, the single crystal structure of pure isomer **2m'** was successfully determined by X-ray diffraction (**Fig. 3**). It is observed that the moiety of benzimidazole is connected to moiety of oxindole in the molecule. Secondly, the single crystals are obtained from the samples

containing the mixtures of **2d/2d'** and **2e/2e'**. The molecular structures are showed in **Fig. 4** and **Fig. 5**. As shown in **Fig. 4**, the moiety of benzimidazole is also connected to moiety of oxindole in the molecule. It has the same structure to that of **2m'**. Thus, we assigned the series of isomers **2a'-2o'** have this kind of structure, in which the moiety of benzimidazole is connecting to moiety of oxindole. Thirdly, in the molecular structure showed in Fig. 5, it can be seen that the moiety of benzimidazole did not connected with moiety of oxindole, while linking with the moiety of malononitrile. Based on this fact, we assigned the series of isomers **2a-2o** have this kind of structure. Thus, the molecular structures of both isomers **2a-2o** and **2a'-2o'** were successfully determined. The compounds **2a-2o** and **2a'-2o'** are not diastereoisomers and are belonging to structural isomers. The formation of two structural isomers in the four-component reaction is obviously attributed to the different reaction processes. It is also worthy to mention the stereochemistry of the both compounds **2a-2o** and **2a'-2o'**. The three single crystal structures of **2d**', **2e** and **2m**' showed that the proton atom at C2 position exists to the *trans*-position of phenyl group of the oxindole moiety in the newly-formed dihydropyridyl ring. This result also indicated that both compounds **2a-2o** and **2a'-2o'** have the same *trans*-configuration to the above obtained spiro[imidazo[1,2-a]pyridine-7,3'-indolines] **1a-1n**.

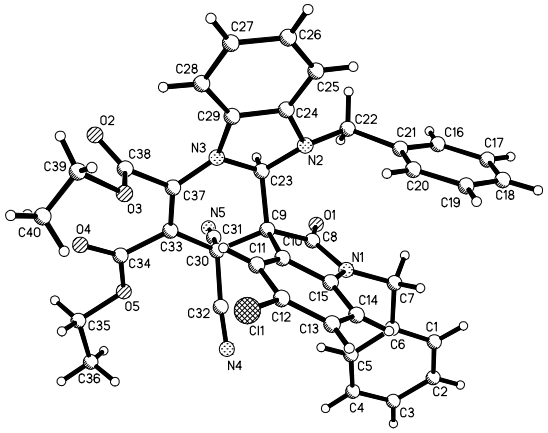


Fig. 3 Molecular structure of compound 2m'

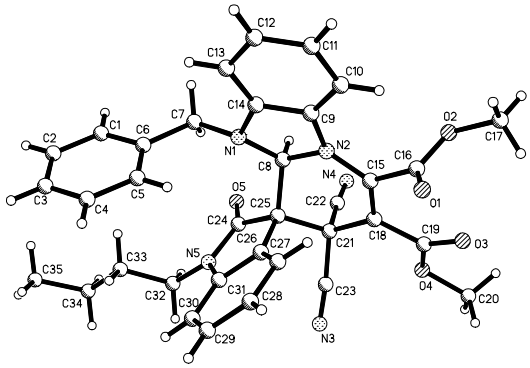


Fig. 4 Molecular structure of compound 2d'

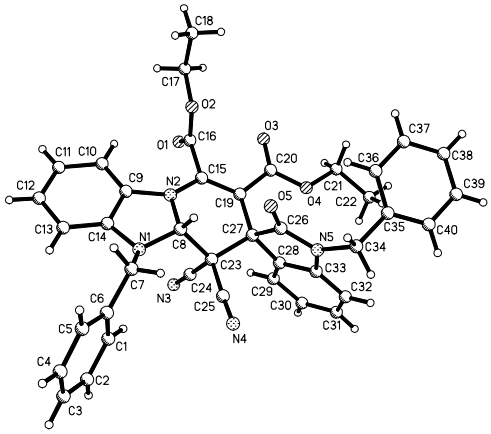
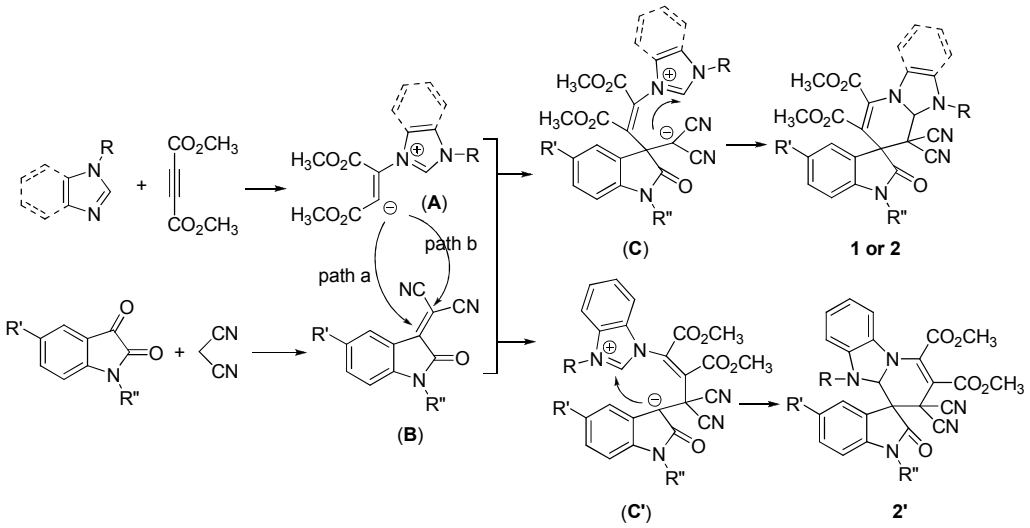


Fig. 5 Molecular structure of compound 2e

Although the precise mechanism is not very clear, a plausible reaction process is proposed to rationalize the formation of the different products (**Scheme 1**). Firstly, addition of *N*-alkylimidazole or *N*-alkylbenzimidazole to but-2-ynedioate gives the expected Huisgen's 1,4-dipole (**A**). In the meantime, condensation of isatin with malononitrile affords isatylidene malononitrile (**B**). Because isatylidene malononitrile is a special Michael acceptor with two cyano groups at one carbon atom and a carbonyl group at other carbon atom of C=C double band. Thus, nucleophilic addition of Huisgen's 1,4-dipole (**A**) to isatylidene malononitrile can proceeds with both path a or path b. Addition of Huisgen's 1,4-dipole (**A**) to the C-3 atom of oxindole in intermediate (**B**) gives a zwitterionic intermediate (**C**) according to the path a. On the other hand, addition of Huisgen's 1,4-dipole (**A**) to the exoccylic carbon atom of isatylidene malononitrile (**B**) gives a zwitterionic intermediate (**C'**) in the path b. Finally, the coupling of the negative charge with the positive charge in the two zwitterionic intermediates **C** and **C'** results in the obtained structural isomeric spirooxindoles **2** and **2'**. The reaction of *N*-alkylimidazole preceded on path a to give entirely spiro[imidazo[1,2-a]pyridine-4,3'-indolines] **1**. It might be due to the electronic effects and steric effect of *N*-alkylbenzimidazoles, the reaction with *N*-alkylbenzimidazole can proceed with two different paths to give a mixture of two isomers **2** and **2'** with wide range of molar ratio.



Scheme 1 Proposed mechanism for four-component reaction

Conclusion

In summary, we investigated four-component reactions of *N*-alkylimidazole or *N*-alkylbenzimidazole, dialkyl but-2-ynedioate, *N*-alkylisatins and malononitrile and found very interesting results. The four-component reaction containing *N*-alkylimidazole provided a convenient synthetic procedure for the novel spiro[imidazo[1,2-a]pyridine-4,3'-indoline] derivatives. Alternatively, the similar four-component reaction containing *N*-alkylbenzimidazole resulted in a mixture of isomeric spiro compounds without high regioselectivity. The reason for the formation of different products was explained by the analysis of the reaction mechanism. It is for the first time to observe the two kinds of addition modes of isatylidene malononitrile in cyclocondensation reaction. The interesting results obtained in this work will help to investigate the reactivity of Huisgen's 1,4-dipoles and to design the new multicomponent reactions for synthesis of diverse organic molecules.

Experimental section

1. General procedure for the synthesis of spiro compounds 1a-1n via four-component reaction: To a solution of isatin (1.0 mmol), *N*-alkylimidazole (1.2 mmol) and malononitrile (1.2 mmol) in dry tetrahydrofuran (10.0 mL) at room temperature was added a solution of dialkyl

acetylenedicarboxylate (1.2 mmol) in tetrahydrofuran (2.0 mL). Then, the mixture was stirred at room temperature for six hours. After removing the solvent by rotator evaporation, the residue was titrated with ethanol to give the crude product. Further recrystallization in a mixture of ethanol and acetone (V/V = 3:1 to 5:1) gives the pure product.

Dimethyl 1'-benzyl-8,8-dicyano-2'-oxo-1-phenyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1a): yellow solid, 67%, m.p. 170-172□; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55 (d, *J* = 7.6 Hz, 1H, ArH), 7.42-7.27 (m, 9H, ArH), 7.23 (d, *J* = 8.0 Hz, 2H, ArH), 7.13-7.08 (m, 2H, ArH), 6.83 (d, *J* = 8.0 Hz, 1H, CH), 6.54 (d, *J* = 2.4 Hz, 1H, CH), 6.20 (d, *J* = 2.4 Hz, 1H, CH), 5.25 (d, *J* = 15.6 Hz, 1H, CH), 4.82 (d, *J* = 16.0 Hz, 1H, CH), 3.97 (s, 3H, OCH_3), 3.17 (s, 3H, OCH_3); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 173.8, 163.6, 163.2, 143.5, 142.5, 141.5, 134.8, 130.5, 129.8, 128.8, 127.9, 127.6, 125.4, 124.1, 123.9, 123.8, 118.3, 113.1, 110.1, 97.1, 75.9, 53.6, 52.9, 51.6, 45.2, 42.3; IR(KBr) υ: 3135, 2950, 1753, 1712,1577, 1492, 1454, 1429, 1375,1328, 1287, 1260, 1229, 1192, 1146, 1079, 1036, 994, 947, 899, 831, 758 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{33}H_{26}N_5O_5$ ($[M+H]^+$): 572.1939, found: 572.1928.

Dimethyl 1'-butyl-8,8-dicyano-2'-oxo-1-phenyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1b): yellow solid, 73%, m.p. 169-171□; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54 (d, *J* = 7.6 Hz, 1H, ArH), 7.43-7.33 (m, 4H, ArH), 7.21 (d, *J* = 8.0 Hz, 2H, ArH), 7.14-7.08 (m, 2H, ArH), 6.95 (d, *J* = 8.0 Hz, 1H, CH), 6.53 (d, *J* = 2.4 Hz, 1H, CH), 6.19 (d, *J* = 2.8 Hz, 1H, CH), 3.96 (s, 3H, OCH_3), 3.86-3.77 (m, 2H, CH_2), 3.33 (s, 3H, OCH_3), 1.77-1.67 (m, 2H, CH_2), 1.51-1.42 (m, 2H, CH_2), 0.98 (t, *J* = 7.6 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.3, 163.5, 162.2, 143.8, 142.5, 141.3, 130.5, 129.8, 125.5, 124.0, 123.9, 123.5, 118., 113.1, 110.3, 109.2, 97.3, 75.7, 53.6, 52.7, 51.6, 42.4, 41.0, 29.1, 20.2, 13.7; IR(KBr) υ: 3141, 3048, 2955, 2870, 1755, 1710, 1589, 1488, 1465, 1426, 1365, 1326, 1292, 1258, 1233, 1201, 1150, 1079, 1028, 946, 898, 832, 757 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{30}H_{28}N_5O_5$ ($[M+H]^+$): 538.2100, found: 538.2085.

Dimethyl 1'-benzyl-8,8-dicyano-5'-methyl-2'-oxo-1-phenyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1c): yellow solid, 70%, m.p. 165-167□; ^{1}H NMR (400 MHz,

$CDCl_3$) δ: 7.45-7.27 (m, 9H, ArH), 7.23 (d, *J* = 8.0 Hz, 2H, ArH), 7.13-7.07 (m, 2H, ArH), 6.71 (d, *J* = 8.0 Hz, 1H, CH), 6.54 (d, *J* = 2.4 Hz, 1H, CH), 6.19 (d, *J* = 2.4 Hz, 1H, CH), 5.24 (d, *J* = 16.0 Hz, 1H, CH), 4.78 (d, *J* = 7.6 Hz , 1H, CH), 3.98(s, 3H, OCH_3), 3.19(s, 3H, OCH_3), 2.31(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.7, 163.7, 163.2, 142.6, 141.4, 135.0, 133.5, 130.8, 129.8, 128.8, 127.9, 125.3, 124.5, 124.1, 124.0, 118.2, 113.1, 109.8, 97.2, 75.8, 53.6, 53.0, 51.6, 45.1, 42.4, 21.2; IR(KBr) υ: 3142, 3016, 2954, 2869, 1751, 1704, 1588, 1496, 1426,1383, 1325, 1296, 1261, 1233, 1202, 1165, 1147, 1078, 1035, 946, 901, 816, 758, 729 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{34}H_{28}N_5O_5$ ($[M+H]^+$): 586.2076, found: 586.2085.

Dimethyl

1'-butyl-8,8-dicyano-5'-methyl-2'-oxo-1-phenyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1d): yellow solid, 80%, m.p. 206-208□; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.54-7.33 (m, 4H, ArH), 7.20 (d, *J* = 7.6 Hz, 3H, ArH), 7.09 (t, *J* = 7.2 Hz, 1H, ArH), 6.84 (d, *J* = 8.0 Hz, 1H, CH), 6.53 (d, *J* = 2.0 Hz, 1H, CH), 6.18 (d, *J* = 2.0 Hz, 1H, CH), 3.97 (s, 3H, OCH_3), 3.84-3.74 (m, 2H, CH_2), 3.35 (s, 3H, OCH_3), 2.35 (s, 3H, CH_3), 1.75-1.68 (m, 2H, CH_2), 1.50-1.41 (m, 2H, CH_2), 0.97 (t, *J* = 7.6 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.2, 163.6, 163.2, 142.5, 141.4, 133.2, 130.9, 129.7, 125.4, 124.6, 123.9, 118.1, 113.1, 110.3, 97.4, 75.7, 53.6, 52.7, 51.6, 42.4, 41.0, 29.2, 21.2, 20.2, 13.7; IR (KBr) υ: 3132, 3040, 2949, 1746, 1702, 1577, 1496, 1455, 1427, 1382, 1325, 1292, 1261, 1234, 1195, 1160, 1131, 1104, 1079, 1026, 938, 900, 815, 764, 729 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{31}H_{30}N_5O_5$ ($[M+H]^+$): 552.2238, found: 552.2241.

Dimethyl

1'-benzyl-5'-chloro-8,8-dicyano-2'-oxo-1-phenyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1e): yellow solid, 76%, m.p. 178-180□; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.53 (s, 1H, ArH), 7.38-7.24 (m, 9H, ArH), 7.23 (d, *J* = 8.0 Hz, 2H, ArH), 7.13 (t, *J* = 7.6 Hz, 1H, ArH), 6.74 (d, *J* = 8.4 Hz, 1H, CH), 6.55 (brs, 1H, CH), 6.19 (d, *J* = 2.4 Hz, 1H, CH), 5.24 (d, *J* = 15.6 Hz, 1H, CH), 4.80 (d, *J* = 15.6 Hz, 1H, CH),3.99 (s, 3H, OCH_3), 3.27 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ:173.5, 163.3, 163.0, 142.3, 142.1, 141.8, 134.4, 130.5, 129.8, 129.2, 128.9, 128.1, 127.6, 127.4, 124.6, 124.3, 124.2, 118.4, 113.0, 111.1, 96.4, 75.9, 53.7, 53.0, 51.8, 45.3, 42.1; IR(KBr) υ: 3130, 3032, 2951, 1748, 1715, 1573, 1496, 1454, 1427, 1386, 1332, 1289, 1258, 1232, 1190, 1172, 1148, 1129, 1078, 1029, 934, 902, 831, 819, 778, 759cm^{-1};

MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{33}H_{25}ClN_5O_5$ ($[M+H]^+$): 606.1533, found: 606.1539

Dimethyl

5'-chloro-8,8-dicyano-2'-oxo-1-phenyl-1'-propyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1f): yellow solid, 69%, m.p. 182-184□; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (s, 1H, ArH), 7.40-7.34 (m, 4H, ArH), 7.20 (d, *J* = 7.6 Hz, 2H, ArH), 7.11 (t, *J* = 6.8 Hz, 1H, ArH), 6.89 (d, *J* = 8.4 Hz, 1H, CH), 6.54 (s, 1H, CH), 6.18 (s, 1H, CH), 3.98 (s, 3H, OCH_3), 3.76 (t, *J* = 7.2 Hz, 2H, CH_2), 3.41 (s, 3H, OCH_3), 1.81-1.72 (m, 2H, CH_2), 1.02 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.1, 163.3, 163.0, 142.5, 142.3, 141.6, 130.6, 129.8, 128.9, 127.4, 124.5, 124.3, 124.2, 118.3, 113.0, 110.1, 96.6, 75.8, 53.7, 52.7, 51.8, 43.0, 42.2, 20.5, 11.5; IR(KBr) υ: 3143, 2951, 2879, 1756, 1711, 1582, 1484, 1426, 1380, 1323, 1290, 1262, 1231, 1203, 1149, 1076, 1034, 946, 897, 830, 759 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{29}H_{25}ClN_5O_5$ ($[M+H]^+$): 558.1540, found: 558.1539.

Dimethyl

1'-benzyl-8,8-dicyano-5'-fluoro-2'-oxo-1-phenyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1g): yellow solid, 78%, m.p. 168-170□; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40-7.28 (m, 10H, ArH), 7.23 (d, *J* = 8.0 Hz, 1H, ArH), 7.13 (t, *J* = 7.2 Hz, 1H, ArH), 7.02-6.97 (m, 1H, ArH), 6.75-6.72 (m, 1H, CH), 6.55 (s, 1H, CH), 6.20 (s, 1H, CH), 5.24 (d, *J* = 15.6 Hz, 1H, CH), 4.81 (d, *J* = 16.0 Hz, 1H, CH), 3.98 (s, 3H, OCH_3), 3.26 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.6, 163.4, 163.0, 160.6, 158.1, 142.3, 141.7, 139.5 (d, *J* = 1.8 Hz), 134.5, 129.6, 129.0, 128.1, 127.5, 124.4 (d, *J* = 19.6 Hz), 118.5, 116.9 (d, *J* = 23.3 Hz), 113.0, 112.4, 112.2 (d, *J* = 25.9 Hz), 110.7 (d, *J* = 8.0 Hz), 96.5, 75.9, 53.7, 53.1, 51.7, 45.3, 42.1; IR (KBr) υ: 3145, 3033, 2950, 1752, 1713, 1620, 1576, 1493, 1451, 1331, 1270, 1245, 1183, 1160, 1141, 1103, 1064, 1028, 946, 895, 836, 797, 760, 731 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{35}H_{25}FN_5O_5$ ($[M+H]^+$): 590.1842, found: 590.1834.

Dimethyl

1'-butyl-8,8-dicyano-5'-fluoro-2'-oxo-1-phenyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1h): yellow solid, 71%, m.p. 188-190□; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37-7.32 (m, 4H, ArH), 7.20 (d, *J* = 8.0 Hz, 2H, ArH), 7.14-7.09 (m, 2H, ArH), 6.91-6.88 (m, 1H, CH), 6.54 (d, *J* = 1.6 Hz, 1H, CH), 6.17 (d, *J* = 2.4 Hz, 1H, CH), 3.97 (s, 3H, OCH_3), 3.86-3.73 (m, 2H, CH_2), 3.39 (s, 3H, OCH_3), 1.75-1.67 (m, 2H, CH_2), 1.50-1.41 (m, 2H,

CH_2), 0.98 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.1, 163.3, 163.0, 160.4, 158.0, 142.3, 141.6, 139.8(d, J = 1.9 Hz), 129.8, 127.4 (d, J = 8.2 Hz), 124.3 (d, J = 20.5 Hz), 118.3, 116.9 (d, J = 23.4 Hz), 113.0, 122.3 (d, J = 26.0 Hz), 110.1, 109.8 (d, J = 8.0 Hz), 96.7, 75.8, 53.6, 52.8, 51.7, 42.2, 41.4, 29.1, 20.2, 13.7; IR(KBr) υ: 3143, 2956, 2871, 1758, 1710, 1587, 1490, 1448, 1382, 1325, 1293, 1264, 1234, 1202, 1163, 1143, 1028, 942, 900, 831, 815, 760, 728 cm^{-1}; MS (m/z): HRMS (ESI) Calcd. for $C_{30}H_{27}FN_5O_5$ ($[M+H]^+$): 556.2000, found: 556.1991.

Dimethyl

1'-butyl-8,8-dicyano-1,5'-dimethyl-2'-oxo-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1i): yellow solid, 73%, m.p. 162-164□; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.33 (s, 1H, ArH), 7.19 (d, J = 8.0 Hz, 1H, ArH), 6.84 (d, J = 8.0 Hz, 1H, ArH), 6.42 (s, 1H, CH), 5.99 (d, J = 2.4 Hz, 1H, CH), 5.97 (d, J = 2.8 Hz , 1H, CH), 3.94 (s, 3H, OCH_3), 3.76 (t, J = 7.6 Hz, 2H, CH_2), 3.32 (s, 3H, OCH_3), 2.95 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 1.75-1.67 (m, 2H, CH_2), 1.49-1.40 (m, 2H, CH_2), 0.97 (t, J = 7.6 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.4, 163.8, 163.2, 141.1, 140.8, 133.0, 130.7, 128.6, 126.0, 124.7, 111.8, 111.2, 108.8, 97.1, 82.9, 53.5, 52.7, 51.5, 41.9, 40.9, 40.5, 29.2, 21.2, 20.2, 13.7; IR(KBr) υ: 3143, 3107, 2958, 2872, 2164, 2104, 1730, 1695, 1637, 1613, 1580, 1549, 1494, 1441, 1351, 1330, 1286, 1202, 1164, 1110, 1049, 979, 956, 910, 837, 816, 753, 714 cm^{-1}; MS (m/z): HRMS (ESI) Calcd. for $C_{26}H_{28}N_5O_5$ ($[M+H]^+$): 490.2088, found: 490.2085.

Dimethyl

5'-chloro-8,8-dicyano-1-methyl-2'-oxo-1'-propyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (**1j**): yellow solid, 82%, m.p. 191-193□; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.50 (s, 1H, ArH), 7.37 (d, J = 6.8 Hz, 1H, ArH), 6.88 (d, J = 8.0 Hz, 1H, ArH), 6.45 (s, 1H, CH), 6.03 (d, J = 3.2 Hz, 2H, CH, CH), 3.94 (s, 3H, OCH_3), 3.80-3.65 (m, 2H, CH_2), 3.38 (s, 3H, OCH_3), 2.98 (s, 3H, CH_3), 1.80-1.71 (m, 2H, CH_2), 1.02 (t, J = 7.6 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.1, 163.5, 162.8, 142.1, 140.7, 130.3, 128.6, 124.4, 112.2, 111.4, 140.7, 130.3, 128,6, 124.4, 112.2, 111.4, 109.9, 98.0, 84.6, 53.6, 52.8, 51.7, 42.9, 40.9, 40.3, 20.5, 11.4; IR(KBr) υ: 3136, 3095, 2957, 2871, 2166, 2111, 1740, 1704, 1641, 1617, 1587, 1546, 1491, 1445, 1347, 1291, 1264, 1195, 1151, 1121, 1091, 979, 931, 874, 822, 772, 736 cm^{-1}; MS (m/z): HRMS (ESI) Calcd. for $C_{24}H_{23}ClN_5O_5$ ($[M+H]^+$): 496.1385, found: 496.1382.

Dimethyl

1'-butyl-8,8-dicyano-5'-fluoro-1-methyl-2'-oxo-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1k): yellow solid, 77%, m.p. 169-171□; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30 (s, 1H, ArH), 7.11 (t, *J* = 8.0 Hz, 1H, ArH), 6.90-6.87 (m, 1H, ArH), 6.47 (s, 1H, CH), 6.03 (d, *J* = 5.2 Hz, 2H, CH, CH), 3.93 (s, 3H, OCH_3), 3.79-3.74 (m, 2H, CH_2), 3.36 (s, 3H, OCH_3), 2.98 (s, 3H, CH_3), 1.74-1.67 (m, 2H, CH_2), 1.49-1.38 (m, 2H, CH_2), 0.97 (t, *J* = 7.6 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.2, 163.6, 162.8, 160.4, 157.9, 140.5, 139.5 (d, *J* = 2.2 Hz), 128.5, 116.6 (d, *J* = 23.1 Hz), 112.4, 111.6 (d, *J* = 1.5 Hz), 109.6 (d, *J* = 8.1 Hz), 98.6, 85.1, 53.6, 53.0, 51.6, 41.1, 40.7, 40.3, 29.1, 20.2, 13.7 ; IR(KBr) υ: 3135, 3098, 2965, 2878, 2163, 2110, 1740, 1703, 1655, 1605, 1542, 1483, 1430, 1378, 1345, 1290, 1257, 1203, 1176, 1147, 1121, 1071, 970, 929, 874, 822, 785, 754, 737 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{25}H_{25}FN_5O_5$ ($[M+H]^+$): 494.1839, found: 494.1834。

Dimethyl

1'-benzyl-1-butyl-8,8-dicyano-5'-methyl-2'-oxo-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6-dicarboxylate (1l): yellow solid, 66%, m.p. 144-146 □; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40 (d, *J* = 7.6 Hz, 2H, ArH), 7.34-7.27 (m, 4H, ArH), 7.05 (d, *J* = 7.2 Hz, 1H, ArH), 6.84 (s, 1H, ArH), 6.68 (d, *J* = 7.6 Hz, 1H, CH), 6.30 (d, *J* = 22.8 Hz , 1H, CH), 6.19 (s, 1H, CH), 5.10 (d, *J* = 16.0 Hz, 1H, CH_2), 4.83 (d, *J* = 16.0 Hz, 1H, CH_2), 3.94 (s, 3H, OCH_3), 3.29 (brs, 2H, CH_2), 3.20 (s, 3H, OCH_3), 2.30 (s, 3H, CH_3), 1.73-1.62 (m, 2H, CH_2), 1.43-1.36 (m, 2H, CH_2), 0.96 (t, *J* = 7.6 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.7, 164.0, 163.0, 140.4, 140.3, 139.3, 139.0, 133.2, 130.4, 130.3, 128.8, 127.8, 127.6, 125.7, 125.2, 124.7, 113.9, 113.4, 109.6, 63.2, 53.6, 52.4, 52.2, 51.6, 51.5, 45.0, 29.8, 21.2, 19.9, 13.8; IR(KBr) υ: 3130, 3091, 2959, 1872, 2167, 2110, 1741, 1707, 1641, 1602, 1547, 1496, 1438, 1376, 1346, 1284, 1260, 1190, 1131, 1107, 1069, 1028, 975, 864, 808, 777, 750 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{32}H_{32}N_5O_5$ ($[M+H]^+$): 566.2406, found: 566.2398.

8-Ethyl 5,6-dimethyl

1'-benzyl-8-cyano-2'-oxo-1-phenyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6,8-tricarboxylate (1m): yellow solid, 55%, m.p. 188-190 □; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (d, *J* = 7.6 Hz, 1H, ArH), 7.59 (s, 1H, ArH), 7.39 (d, *J* = 7.2 Hz, 2H, ArH), 7.33-7.26 (m, 5H, ArH), 7.16 (t, *J* = 7.6 Hz, 1H, ArH), 7.07 (d, *J* = 8.0 Hz, 2H, ArH), 7.04-6.95 (m, 2H, ArH), 6.64 (d, *J* = 8.0 Hz, 1H, CH), 6.44 (d, *J* = 2.8 Hz, 1H, CH), 6.12 (d, *J* = 2.8 Hz, 1H, CH), 5.27 (d,

J = 15.6 Hz , 1H, CH), 4.63 (d, *J* = 15.6 Hz , 1H, CH), 3.97 (s, 3H, OCH_3), 3.61-3.57 (m, 1H, CH), 3.33-3.29 (m, 1H, CH), 3.14 (s, 3H, OCH_3), 0.62 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.9, 164.2, 163.8, 162.6, 144.0, 142.1, 142.0, 135.6, 129.5, 129.4, 128.6, 127.6, 126.7, 123.8, 123.6, 122.7, 120.2, 119.0, 113.8, 112.2, 109.0, 97.1, 75.1, 63.5, 53.4, 52.2, 51.8, 51.2, 44.9, 13.0; IR(KBr) υ: 3141, 3057, 2988, 2947, 1739, 1716, 1637, 1611, 1577, 1494, 1468, 1435, 1356, 1331, 1270, 1226, 1185, 1116, 1077, 998, 932, 896, 854, 803, 752 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{35}H_{30}N_4NaO_7$ ($[M+Na]^+$): 641.2016, found: 641.2007.

8-Ethyl 5,6-dimethyl 5'-chloro-8-cyano-2'-oxo-1-phenyl-1'-propyl-8,8a-dihydro-1H-spiro[imidazo[1,2-a]pyridine-7,3'-indoline]-5,6,8-tricarboxylate (**1n**): yellow solid, 50%, m.p. 146-148 □; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 1.6 Hz, 1H, ArH), 7.53 (s, 1H, ArH), 7.27 (t, *J* = 8.0 Hz, 3H, ArH), 7.02 (t, *J* = 8.0 Hz, 3H, ArH), 6.72 (d, *J* = 8.4 Hz, 1H, CH), 6.45 (d, *J* = 2.8 Hz, 1H, CH), 6.10 (d, *J* = 2.8 Hz, 1H, CH), 3.97 (s, 3H, OCH_3), 3.79-3.73 (m, 1H, CH), 3.62-3.54 (m, 2H, CH_2), 3.36 (s, 3H, OCH_3), 3.33-3.28 (m, 1H, CH), 1.76-1.65 (m, 2H, CH_2), 1.00 (t, *J* = 7.6 Hz, 3H, CH_3), 0.66 (t, *J* = 7.6 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.2, 163.8, 163.6, 162.2, 143.2, 142.0, 129.5, 128.5, 127.7, 125.0, 124.2, 123.6, 120.2, 118.7, 113.5, 112.1, 108.9, 96.7, 74.9, 63.6, 53.4, 52.0, 51.7, 51.4, 42.7, 20.3, 13.0, 11.4; IR(KBr) υ: 3132, 3065, 2949, 2874, 1745, 1715, 1573, 1490, 1425, 1384, 1331, 1260, 1227, 1195, 1138, 1106, 1076, 1036, 1012, 947, 908, 894, 856, 828, 765 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{31}H_{29}ClN_4NaO_7$ ($[M+Na]^+$): 627.1650, found: 627.1655.

2. **General procedure for the synthesis of spiro compounds 2a-2n and 2a'-2n' via four-component reaction**: To a solution of isatin (0.5 mmol), *N*-alkylbenzimidazole (0.5 mmol) and malononitrile (0.5 mmol) in dry tetrahydrofuran (10.0 mL) at room temperature was added a solution of dialkyl but-2-ynedioate (0.6 mmol) in tetrahydrofuran (2.0 mL). Then, the mixture was stirred at room temperature for about one day. After removing the solvent by rotator evaporation, the residue was subjected to preparative thin-layer chromatography with a mixture of light petroleum and ethyl acetate (V/V = 3:1) to give the products.

Compounds 2a/2a': yellow solid, 61%, m.p. 216-218□; ^1H NMR (600 MHz, $CDCl_3$) δ: **2a**: 7.52 (s, 1H, ArH), 7.40-7.28 (m, 12H, ArH), 6.93 (t, *J* = 7.2Hz, 1H, ArH), 6.84-6.79 (m, 1H, ArH), 6.77-6.75 (m, 2H, ArH, CH), 6.69-6.65 (m, 1H, ArH), 6.61 (d, *J* = 7.8Hz, 1H, ArH), 5.16 (d, *J* =

15.6Hz, 1H, CH_2), 4.84-4.78 (m, 2H, CH_2), 4.60 (d, *J* = 16.2Hz, 1H, CH_2), 4.06 (s, 3H, OCH_3), 3.24 (s, 3H, OCH_3); 2a': 7.46 (d, *J* = 7.8Hz, 2H, ArH), 7.15-7.14 (m, 2H, ArH), 7.03 (t, *J* = 7.8Hz, 1H, ArH), 6.87 (d, *J* = 7.8Hz, 1H, ArH), 6.84-6.79 (m, 1H, ArH), 5.81 (s, 1H, CH), 5.07-4.99 (m, 2H, CH_2), 4.89 (d, *J* = 16.2Hz, 1H, CH_2), 4.52 (d, *J* = 16.2Hz, 1H, CH_2), 4.03 (s, 3H, OCH_3), 3.32 (s, 3H, OCH_3). **2a/2a' =** 4:1; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.5, 163.3, 163.0, 142.7, 142.1, 141.9, 141.8, 135.7, 134.5, 131.1, 130.5, 129.5, 129.2, 129.1, 128.9, 128.8, 128.5, 128.2, 128.1, 128.0, 127.8, 127.6, 127.4, 125.2, 125.0, 124.5, 121.4, 110.9(2C), 110.7, 110.5, 109.9, 109.8, 98.9, 88.1, 78.7, 54.9, 54.5, 53.6(2C), 53.1, 52.3, 51.9, 45.3, 44.6; IR(KBr) υ: 3469, 3062, 2957, 2870, 2374, 2341, 1743, 1713, 1609, 1575, 1494, 1435, 1357, 1317, 1284, 1230, 1183, 1154, 1122, 1075, 1025, 973, 938, 826, 777, 734, 701 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{38}H_{29}NaN_5O_5$ ($[M+Na]^+$): 658.2066, found: 658.2071.

Compounds 2b/2b': yellow solid, 53%, m.p. 186-188□; ^{1}H NMR (600 MHz, $CDCl_3$) δ: **2a**: 7.41 (d, *J* = 7.2Hz, 2H, ArH), 7.36-7.28 (m, 8H, ArH), 7.24-7.19 (m, 1H, ArH), 7.09 (d, *J* = 8.4Hz, 1H, ArH), 6.90 (t, *J* = 7.8Hz, 1H, ArH), 6.83-6.78 (m, 2H, ArH, CH), 6.73 (d, *J* = 7.8Hz, 1H, ArH), 6.68 (d, *J* = 7.8Hz, 1H, ArH), 6.58 (d, *J* = 7.8Hz, 1H, ArH), 5.16 (d, *J* = 15.6Hz, 1H, CH_2), 4.84-4.77 (m, 2H, CH_2), 4.60 (d, *J* = 16.2Hz, 1H, CH_2), 4.06 (s, 3H, OCH_3), 3.17 (s, 3H, OCH_3), 2.31 (s, 3H, CH_3); **2a'**: 7.14 (d, *J* = 7.8Hz, 2H, ArH), 7.05 (d, *J* = 8.4Hz, 1H, ArH), 6.83-6.78 (m, 1H, ArH), 6.71 (d, *J* = 4.2Hz, 2H, ArH), 6.44 (d, *J* = 7.8Hz, 1H, ArH), 6.25 (d, *J* = 7.8Hz, 1H, ArH), 6.08 (s, 1H, CH), 4.50 (d, *J* = 17.4Hz, 1H, CH_2), 4.24 (d, *J* = 17.4Hz, 1H, CH_2), 4.19 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3),3.28 (d, *J* = 16.2Hz, 1H, CH_2), 2.20 (s, 3H, CH_3). **2b/2b'** = 5:1; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.7, 163.6, 163.2, 142.7, 141.6, 141.0, 135.9, 135.1, 134.2, 133.5, 131.4, 131.3(2C), 130.8, 129.2, 129.0, 128.8, 128.7, 128.5, 128.2, 128.0, 127.9, 127.8(2C), 127.5, 127.3, 127.0, 126.8, 126.2, 125.8, 125.4, 124.7, 121.2(2C), 120.4, 110.7, 110.1(2C), 109.7, 109.3, 108.4, 99.6, 82.6, 78.8, 54.9, 54.4, 53.5, 53.1, 52.5, 51.7, 45.2, 45.0, 43.5,21.3, 21.2; IR(KBr) υ: 3443, 3059, 2951, 2865, 2374, 2343, 1747, 1710, 1571, 1497, 1437, 1416, 1351, 1313, 1281, 1237, 1199, 1165, 1074, 1027, 970, 817, 773, 737 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{39}H_{31}NaN_5O_5$($[M+Na]^+$): 672.2217, found: 672.2210.

Compounds 2c/2c': yellow solid, 65%, m.p. 190-192□; ^{1}H NMR (600 MHz, $CDCl_3$) δ: **2c**: 7.40-7.27 (m, 7H, ArH), 7.24-7.21 (m, 2H, ArH), 7.15-7.12 (m, 2H, ArH), 7.02-6.97 (m, 1H, ArH), 6.93 (t, *J* = 7.8Hz, 1H, ArH), 6.83-6.79 (m, 1H, ArH), 6.77-6.72 (m, 2H, ArH, CH), 6.68 (d, *J* =

7.8Hz, 1H, ArH), 6.60 (d, *J* = 7.8Hz, 1H, ArH), 5.16 (d, *J* = 15.6Hz, 1H, CH_2), 4.85-4.79 (m, 2H, CH_2), 4.61 (d, *J* = 16.2Hz, 1H, CH_2), 4.06 (s, 3H, OCH_3), 3.23 (s, 3H, OCH_3); **2c'**: 6.88 (t, *J* = 7.2Hz, 1H, ArH), 6.83-6.79 (m, 1H, ArH), 6.47-6.45 (m, 1H, ArH), 6.28 (d, *J* = 7.8Hz, 1H, ArH), 6.11 (s, 1H, CH), 4.49 (d, *J* = 17.4Hz, 1H, CH_2), 4.26 (d, *J* = 16.8Hz, 1H, CH_2), 4.19 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.19 (d, *J* = 15.6Hz, 1H, CH_2). **2c/2c' =** 1:1; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.6, 169.5, 163.3, 163.0, 162.9, 162.3, 160.2, 158.6, 143.8, 142.7, 142.0, 141.9, 140.1, 139.5, 137.2, 135.7, 134.6, 133.6, 131.1, 129.8, 129.1, 128.9(2C), 128.7, 128.6, 128.1(2C), 128.0(2C), 127.8, 127.6, 127.4, 127.2, 126.9, 126.1(2C), 125.0, 122.6 (d, *J* = 8.7Hz), 121.4, 120.8, 117.6 (d, *J* = 23.6Hz), 116.9 (d, *J* = 23.4Hz), 114.3 (d, *J* = 26.7Hz), 112.4 (d, *J* = 26.3Hz), 111.4, 111.3, 111.2, 110.9, 110.7 (d, *J* = 7.9Hz), 110.5, 110.4, 109.9, 109.4, 98.9, 92.2, 82.7, 78.7, 54.9, 54.5, 54.2, 53.6, 52.6, 51.9, 50.8, 45.3, 44.6, 43.7, 38.2, 29.7; IR(KBr) υ: 3341, 3101, 2961, 2870, 2374, 2343, 1743, 1715, 1607, 1571, 1494, 1447, 1338, 1311, 1267, 1179, 1137, 1099, 1026, 979, 866, 819, 772, 737 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{38}H_{28}FNaN_5O_5([M+Na]^+)$: 676.1967, found: 676.1957.

Compounds 2d/2d': yellow solid, 71%, m.p. 158-160□; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2d: 7.54 (d, *J* = 7.8Hz, 1H, ArH), 7.40 (t, *J* = 7.8Hz, 1H, ArH), 7.38-7.35 (m, 4H, ArH), 7.30-7.29 (m, 1H, ArH), 7.12 (t, *J* = 7.8Hz, 1H, ArH), 6.95 (d, *J* = 7.8Hz, 1H, ArH), 6.89 (t, *J* = 7.8Hz, 1H, ArH), 6.82-6.77 (m, 1H, ArH), 6.74-6.73 (m, 1H, CH), 6.67 (d, *J* = 8.4Hz, 1H, ArH), 6.56 (d, *J* = 7.8Hz, 1H, ArH), 4.80 (d, *J* = 16.2Hz, 1H, CH_2), 4.59 (d, *J* = 16.2Hz, 1H, CH_2), 4.04 (s, 3H, OCH_3), 3.80-3.75 (m, 2H, CH_2), 3.33 (s, 3H, OCH_3), 1.74-1.69 (m, 2H, CH_2), 1.49-1.38 (m, 2H, CH_2), 0.98 (t, *J* = 7.8Hz, 3H, CH_3); 2d': 7.20-7.16 (m, 3H, ArH), 7.04 (t, *J* = 7.2Hz, 1H, ArH), 6.74-6.73 (m, 1H, ArH), 6.70 (d, *J* = 4.2Hz, 2H, ArH), 6.20 (d, *J* = 7.8Hz, 1H, ArH), 6.07 (s, 1H, CH), 4.47 (d, *J* = 17.4Hz, 1H, CH_2), 4.23 (d, *J* = 17.4Hz, 1H, CH_2), 4.18 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.40-3.36 (m, 1H, CH_2), 2.61-2.55 (m, 1H, CH_2), 1.29-1.27 (m, 2H, CH_2), 0.85 (t, *J* = 7.2Hz, 3H, CH_3). **2d/2d'** = 6:1. ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.4, 163.5, 163.2, 148.0, 143.8, 142.7, 141.5, 135.9, 131.3, 131.0, 130.5, 129.2, 129.0, 128.5, 128.4, 128.0, 127.5, 127.2, 125.9, 125.6, 124.7, 124.2, 123.5, 121.2, 120.3, 110.7, 110.5, 110.3, 110.2, 109.7, 109.6, 109.1, 99.7, 92.4, 82.4, 78.7, 54.9, 54.2, 54.0, 53.5, 52.9, 52.5, 52.1, 51.7, 44.9, 40.9, 39.8, 29.2, 28.8, 20.3, 20.0, 18.4, 13.7, 13.5; IR(KBr) υ: 3454, 3061, 2954, 2868, 2374, 2342, 1751, 1709, 1610, 1568, 1495, 1461, 1441, 1360, 1255, 1200, 1142, 1086, 1027, 929, 878, 829, 747 cm^{-1}; MS (*m*/*z*): HRMS (ESI)

Calcd. for $C_{35}H_{31}NaN_5O_5$([M+Na]$^+$): 624.2217, found: 624.2211.

Compounds 2e/2e': yellow solid, 64%, m.p. 180-182□; ^{1}H NMR (600 MHz, $CDCl_3$) δ: **2e**: 7.56 (d, *J* = 7.8Hz, 1H, ArH), 7.44 (d, *J* = 7.8Hz, 2H, ArH), 7.39-7.29 (m, 9H, ArH), 7.10 (t, *J* = 7.8Hz, 1H, ArH), 6.90 (t, *J* = 7.2Hz, 1H, ArH), 6.85 (d, *J* = 8.4Hz, 1H, ArH), 6.80-6.76 (m, 3H, ArH, CH), 6.57 (d, *J* = 7.8Hz, 1H, ArH), 5.06 (d, *J* = 15.6Hz, 1H, CH_2), 4.90 (d, *J* = 15.0Hz, 1H, CH_2), 4.84-4.79 (m, 1H, CH_2), 4.62-4.57 (m, 1H, CH_2), 4.56-4.47 (m, 2H, CH_2), 3.92-3.87 (m, 1H, CH_2), 3.53-3.48 (m, 1H, CH_2), 1.44 (t, *J* = 7.2Hz, 3H, CH_3), 0.50 (t, *J* = 7.2Hz, 3H, CH_3); **2e'**: 7.21 (d, *J* = 7.2Hz, 1H, ArH), 7.14 (d, *J* = 7.2Hz, 2H, ArH), 7.01 (t, *J* = 7.8Hz, 1H, ArH), 6.80-6.76 (m, 1H, ArH), 6.71 (d, *J* = 7.8Hz, 1H, ArH), 6.54 (d, *J* = 7.8Hz, 1H, ArH), 6.23 (d, *J* = 7.8Hz, 1H, ArH), 6.11 (s, 1H, CH), 4.67-4.63 (m, 2H, CH_2), 4.25 (d, *J* = 16.8Hz, 1H, CH_2), 3.25 (d, *J* = 16.2Hz, 1H, CH_2), 1.53 (t, *J* = 7.2Hz, 3H, CH_3), 1.38 (t, *J* = 7.2Hz, 3H, CH_3). **2e/2e'** = 6:1. ^{13}C NMR (150 MHz, $CDCl_3$) δ: 174.0, 163.1, 162.8, 143.6, 142.7, 142.1, 135.9, 134.9, 134.0, 131.4, 130.9, 130.4, 129.2, 129.0, 128.8, 128.7, 128.4, 128.1, 127.9, 127.8, 127.5, 127.3, 126.9, 126.0, 125.8, 125.7, 124.6, 124.2, 123.7, 121.2, 120.3, 110.8, 110.7, 110.5, 110.1, 110.0, 92.2, 82.7, 78.7, 63.1, 62.1, 61.6, 60.6, 55.0, 53.1, 45.3, 44.8, 43.5, 43.4, 13.9, 13.8,13.7,13.2, 11.2; IR(KBr) υ: 3413, 3060, 2953, 2869, 2374, 2342, 1742, 1706, 1611, 1559, 1494, 1369, 1277, 1222, 1185, 1150, 1109, 1025, 862, 749 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{40}H_{33}NaN_5O_5$([M+Na]$^+$): 686.2374, found: 686.2366.

Compounds 2f/2f': yellow solid, 52%, m.p.160-162□; ^{1}H NMR (600 MHz, $CDCl_3$) δ: **2f**: 7.43 (d, *J* = 7.2Hz, 2H, ArH), 7.36-7.27 (m, 7H, ArH), 7.24-7.19 (m, 2H, ArH), 7.09 (d, *J* = 7.8Hz, 1H, ArH), 6.89 (t, *J* = 6.6Hz, 1H, ArH), 6.83-6.76 (m, 3H, ArH, CH), 6.73-6.68 (m, 1H, ArH), 6.56 (d, *J* = 7.8Hz, 1H, ArH), 5.03 (d, *J* = 15.6Hz, 1H, CH_2), 4.89-4.76 (m, 2H, CH_2), 4.70-4.47 (m, 3H, CH_2, CH_2), 3.93-3.88 (m, 1H, CH_2), 3.56-3.51 (m, 1H, CH_2), 2.31 (s, 3H, CH_3), 1.44 (t, *J* = 7.2Hz, 3H, CH_3), 0.54 (t, *J* = 7.2Hz, 3H, CH_3); **2f**: 7.14 (d, *J* = 7.8Hz, 2H, ArH), 7.04 (d, *J* = 8.4Hz, 1H, ArH), 6.83-6.76 (m, 1H, ArH), 6.43 (d, *J* = 7.8Hz, 1H, ArH), 6.23 (d, *J* = 7.8Hz, 1H, ArH), 6.08 (s, 1H, CH), 4.38-4.34 (m, 2H, CH_2), 4.24 (d, *J* = 16.8Hz, 1H, CH_2), 3.28 (d, *J* = 17.4Hz, 1H, CH_2), 2.19 (s, 3H, CH_3), 1.52 (t, *J* = 7.2Hz, 3H, CH_3), 1.38 (t, *J* = 7.2Hz, 3H, CH_3). **2f/2f' =** 1:1. ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.9, 169.7, 163.1, 162.8, 162.6, 143.9, 142.7, 141.5, 137.4, 136.0, 135.0, 134.2, 133.5, 131.3, 130.7, 130.2, 129.0, 128.8, 128.7, 127.9(2C), 127.7, 127.5, 127.3, 126.9(2C), 126.1, 125.6, 124.9, 124.6, 121.2, 121.1, 120.3, 111.7, 110.6, 110.2, 109.9, 109.7,

109.2, 82.7, 78.8, 63.7, 63.1, 62.1, 60.6, 55.0, 54.3, 53.1, 50.8, 45.3, 44.8, 43.4, 38.5, 21.2, 21.1, 13.9, 13.8, 13.7; IR(KBr) υ: 3559, 2062, 2956, 2869, 2377, 2346, 1754, 1710, 1616, 1566, 1497, 1430, 1364, 1276, 1175, 1136, 1108, 1025, 816, 738 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{41}H_{35}NaN_5O_5([M+Na]^+)$: 700.2530, found: 700.2521.

Compounds 2g/2g': yellow solid, 62%, m.p. 196-198□; ^1H NMR (600 MHz, $CDCl_3$) δ: **2g**: 7.41-7.30 (m, 1H, ArH), 7.21-7.20 (m, 1H, ArH), 6.65 (d, *J* = 8.4Hz, 1H, ArH), 6.24 (d, *J* = 7.8Hz, 1H, ArH), 6.06 (s, 1H, CH), 4.24 (d, *J* = 16.8Hz, 1H, CH_2), 3.86-3.75 (m, 1H, CH_2), 3.38-3.33 (m, 1H, CH_2), 2.54-2.49 (m, 1H, CH_2), 1.74-1.69 (m, 1H, CH_2), 1.52 (t, *J* = 7.8Hz, 3H, CH_3). **2g'**: 7.54 (s, 1H, ArH), 7.41-7.30 (m, 3H, ArH), 7.21-7.20 (m, 1H, ArH), 6.91-6.83 (m, 2H, ArH), 6.80-6.77 (m, 3H, ArH, CH), 6.75-6.70 (m, 2H, ArH), 6.56 (d, *J* = 7.8Hz, 1H, ArH), 4.79 (d, *J* = 16.2Hz, 1H, CH_2), 4.68-4.43 (m, 3H, CH_2, CH_2), 4.37-4.34 (m, 2H, CH_2), 3.95-3.89 (m, 1H, CH_2), 3.66-3.61 (m, 1H, CH_2), 1.47-1.34 (m, 5H, CH_2, CH_3), 1.29-1.22 (m, 2H, CH_2), 0.98 (t, *J* = 7.2Hz, 3H, CH_3), 0.86-0.81 (m, 3H, CH_3); **2g/2g'**= 1:2. ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.2, 169.1, 162.8, 162.6, 162.3, 143.8, 143.0, 142.6, 142.5, 142.2,(2C), 137.1, 135.8, 131.2, 131.0, 130.4, 129.9, 129.3, 129.0, 128.9, 128.6, 128.0, 127.8, 127.5, 127.3, 126.7, 126.0, 125.9. 124.8, 124.6, 123.0, 121.2, 120.6, 111.3(2C), 110.7, 110.6, 110.4, 110.0, 109.9, 109.3, 98.7, 91.9, 82.6, 78.7, 63.8, 63.2, 62.2, 60.8, 55.0, 54.4, 52.8, 50.5, 44.5, 41.2, 39.9, 38.5, 29.1, 28.8, 20.3, 19.9, 13.9, 13.8, 13.7(2C), 13.6, 13.5; IR(KBr) υ: 3394, 3058, 2952, 2866, 2374, 2343, 1747, 1709, 1610, 1567, 1498, 1428, 1367, 1277, 1187, 1147, 1107, 1027, 820, 737 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{37}H_{34}ClNaN_5O_5([M+Na]^+)$: 686.2141, found: 686.2129.

Compounds 2h/2h': yellow solid, 66%, m.p. 166-168□; ^1H NMR (600 MHz, $CDCl_3$) δ: **2h**: 7.37-7.33 (m, 4H, ArH), 7.30-7.29 (m, 1H, ArH), 7.2-7.17 (m, 1H, ArH), 7.13-7.09 (m, 1H, ArH), 6.91-6.83 (m, 2H, ArH), 6.80-6.71 (m, 3H, ArH, CH), 6.56 (d, *J* = 7.8Hz, 1H, ArH), 4.79 (d, *J* = 16.2Hz, 1H, CH_2), 4.66-4.44 (m, 3H, CH_2, CH_2), 3.93-3.88 (m, 1H, CH_2), 3.87-3.82 (m, 1H, CH_2), 3.80-3.75 (m, 1H, CH_2), 3.66-3.61 (m, 1H, CH_2), 1.75-1.70 (m, 2H, CH_2), 1.49-1.40 (m, 5H, CH_2, CH_3), 0.98 (t, *J* = 7.8Hz, 3H, CH_3), 0.81 (t, *J* = 7.2Hz, 3H, CH_3); **2h'**: 6.80-6.71 (m, 1H, ArH), 6.66-6.64 (m, 1H, ArH), 6.23 (d, *J* = 7.8Hz, 1H, ArH), 6.07 (s, 1H, CH), 4.37-4.33 (m, 2H, CH_2), 4.23 (d, *J* = 17.4Hz, 1H, CH_2), 3.40-3.35 (m, 1H, CH_2), 2.55-2.51 (m, 1H, CH_2), 1.51 (t, *J* = 7.2Hz, 3H, CH_3), 1.37 (t, *J* = 7.2Hz, 3H, CH_3), 1.29-1.24 (m, 2H, CH_2), 0.85 (t, *J* = 7.2Hz, 3H, CH_3). **2h/2h'** = 3:1. ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.3, 162.8, 162.6, 162.3, 160.1, 158.5, 143.8,

142.6, 142.4, 139.9, 137.1, 135.9, 131.7 (d, J = 6.6Hz), 131.3, 129.3, 129.0, 128.5, 128.0, 127.7, 127.5, 127.3, 125.9, 125.8, 124.7, 121.2, 120.6, 116.8 (d, J = 23.8Hz), 112.7 (d, J = 26.0Hz), 111.3 (d, J = 4.5Hz), 110.7, 110.6, 110.3, 110.1, 110.0, 109.6 (d, J = 7.9Hz), 109.2, 98.8, 91.9, 82.5, 78.7, 63.8, 63.2, 62.2, 60.8, 55.0, 54.3, 53.0, 44.6, 41.2, 39.9. 29.1, 28.7, 20.3, 20.0, 13.9, 13.8, 13.7(2C), 13.6; IR(KBr) υ: 3521, 3063, 2957, 2871, 2375, 2344, 1746, 1711, 1615, 1569, 1496, 1451, 1365, 1277, 1192, 1141, 1025, 819, 775, 736 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{37}H_{34}FNaN_5O_5([M+Na]^+)$: 670.2436, found: 670.2433.

Compounds 2i/2i': yellow solid, 70%, m.p. 178-180□; ^1H NMR (600 MHz, $CDCl_3$) δ: **2i**: 7.50 (d, J = 1.8Hz, 1H, ArH), 7.42-7.39 (m, 2H, ArH), 7.35 (t, J = 7.2Hz, 1H, ArH), 7.32-7.27 (m, 1H, ArH), 7.23-7.21 (m, 2H, ArH), 7.13-7.11 (m, 1H, ArH), 7.01 (t, J = 7.8Hz, 1H, ArH), 6.80-6.74 (m, 3H, ArH), 6.70-6.66 (m, 2H, ArH, CH), 5.21-5.15 (m, 1H, CH_2), 4.81 (d, J = 15.6Hz, 1H, CH_2), 4.07 (s, 3H, OCH_3), 3.55-3.44 (m, 1H, CH_2), 3.23 (s, 3H, OCH_3), 1.79-1.72 (m, 1H, CH_2), 1.67-1.62 (m, 1H, CH_2), 1.41-1.35 (m, 1H, CH_2), 1.19-1.12 (m, 1H, CH_2), 0.99-0.92 (m, 4H, CH_3, CH_2); **2i'**: 7.95 (d, J = 1.2Hz, 1H, ArH), 7.35 (t, J = 7.2Hz, 1H, ArH), 7.32-7.27 (m, 1H, ArH), 6.96 (t, J = 7.8Hz, 1H, ArH), 6.49 (d, J = 7.8Hz, 1H, ArH), 5.86 (s, 1H, CH), 4.57 (d, J = 16.2Hz, 1H, CH_2), 4.13 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 2.73-2.68 (m, 1H, CH_2), 2.44-2.39 (m, 1H, CH_2), 0.68 (t, J = 7.8Hz, 3H, CH_3), 0.48-0.42 (m, 1H, CH_2). **2i/2i'**: = 1:1; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.5, 168.4, 163.3, 163.2, 163.0, 162.7, 143.5, 143.4, 142.8, 142.2, 142.0, 141.9, 134.4, 134.1, 131.4, 131.1(2C), 130.5, 129.2, 128.9, 128.7, 128.2, 127.9, 127.7, 127.4, 126.4, 125.3, 125.0, 124.4, 122.7, 121.0, 120.8, 112.9, 111.6, 111.5, 110.9, 110.7(2C), 110.3, 109.8, 109.7(2C), 98.8, 91.3, 81.8, 78.5, 53.9, 53.6, 53.1, 52.6, 51.9, 50.5, 50.2, 45.3, 44.5, 44.3, 37.9, 28.8(2C), 20.1, 19.8, 13.8, 13.5; IR(KBr) υ: 3442, 3058, 2950, 2865, 2375, 2347, 1746, 1714, 1607, 1571, 1496, 1430, 1344, 1267, 1196, 1142, 1083, 1027, 972, 835, 776, 738 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{35}H_{31}NaN_5O_5([M+Na]^+)$: 624.2223, found: 624.2225.

Compounds 2j/2j': yellow solid, 65%, m.p. 174-176□; ^1H NMR (600 MHz, $CDCl_3$) δ: **2j**: 7.36-7.33 (m, 1H, ArH), 6.69 (t, J = 7.8Hz, 1H, ArH), 6.63 (d, J = 7.8Hz, 1H, ArH), 6.19 (d, J = 7.2Hz, 1H, ArH), 6.05 (s, 1H, CH), 4.22 (d, J = 17.4Hz, 1H, CH_2), 3.91-3.81 (m, 1H, CH_2), 3.36-3.31 (m, 1H, CH_2), 257-2.52 (m, 1H, CH_2), 2.23 (s, 3H, CH_3), 1.75-1.70 (m, 1H, CH_2), 1.52 (t, J = 7.2Hz, 3H, CH_3), 1.37 (t, J = 7.2Hz, 3H, CH_3), 0.85 (t, J = 7.2Hz, 3H, CH_3). **2j'**: 7.36-7.33 (m, 1H, ArH), 7.29 (brs, 1H, ArH), 7.21-7.16 (m, 5H, ArH), 6.88 (t, J = 7.2Hz, 1H,

ArH), 6.83-6.79 (m, 1H, ArH), 6.77-6.75 (m, 3H, ArH, CH), 6.54 (d, *J* = 7.8Hz, 1H, ArH), 4.79 (d, *J* = 16.2Hz, 1H, CH_2), 4.68-4.47 (m, 4H, CH_2, CH_2), 4.36-4.32 (m, 2H, CH_2), 3.75-3.70 (m, 1H, CH_2), 3.65-3.60 (m, 1H, CH_2), 2.35 (s, 3H, CH_3), 1.49-1.40 (m, 5H, CH_2, CH_3), 1.29-1.22 (m, 2H, CH_2), 0.97 (t, *J* = 7.2Hz, 3H, CH_3), 0.75 (t, *J* = 7.2Hz, 3H, CH_3); **2j/2j'** = 1:2; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.4, 169.3, 163.1, 162.9, 162.6, 144.0, 142.7, 141.8, 141.4, 137.2, 136.1, 133.2, 131.4, 131.3, 130.7, 130.1, 128.9, 128.5, 127.9, 127.4, 127.1, 127.0, 125.9(2C), 125.6, 124.9, 124.5, 121.1, 120.2, 111.6, 110.6, 110.2, 109.8, 109.2(2C), 108.8, 99.5, 92.3, 82.5, 78.8, 65.4, 63.6, 63.1, 62.1, 60.6, 59.5, 55.0, 54.3, 52.9, 50.4, 44.9, 41.0, 39.7, 38.7, 31.9, 29.7, 29.2, 28.9, 21.3, 21.2, 20.4, 20.0, 13.9, 13.8, 13.7, 13.6, 13.5; IR(KBr) υ: 3394, 3059, 2952, 2870, 2374, 2343, 1747, 1709, 1610, 1567, 1498, 1428, 1367, 1277, 1187, 1147, 1107, 1027, 820, 737 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{38}H_{37}NaN_5O_5$([M+Na]$^+$): 666.2687, found: 666.2677.

Compounds 2k: yellow solid, 55%, m.p. 196-198□; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.52 (s, 1H, ArH), 7.39-7.28 (m, 11H, ArH), 6.92 (t, *J* = 7.2Hz, 1H, ArH), 6.80 (t, *J* = 7.2Hz, 1H, ArH), 6.76-6.75 (m, 2H, ArH, CH), 6.68 (d, *J* = 7.8Hz, 1H, ArH), 6.61 (d, *J* = 7.2Hz, 1H, ArH), 5.16 (d, *J* = 15.6Hz, 1H, CH_2), 4.81 (t, *J* = 15.6Hz, 2H, CH_2), 4.60 (d, *J* = 16.2Hz, 1H, CH_2), 4.06 (s, 3H, OCH_3), 3.24 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.4, 163.3, 163.0, 142.7, 142.0, 141.9, 135.7, 134.5, 131.1, 130.5, 129.2, 129.1, 128.9, 128.2, 128.1, 127.8, 127.6, 127.3, 125.0, 124.4, 121.4, 110.9, 110.8, 110.4, 109.9, 109.8, 98.8, 78.7, 54.9, 53.6, 53.1, 51.9, 45.3, 44.6; IR(KBr) υ: 3494, 3061, 2953, 2869, 2373, 2342, 1745, 1715, 1608, 1575, 1495, 1435, 1418, 1359, 1315, 1285, 1251, 1229, 1183, 1155, 1125, 1075, 1026, 974, 941, 870, 828, 777, 733, 701 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{38}H_{28}NaClN_5O_5$([M+Na]$^+$): 692.1671, found: 692.1664.

Compound 2l: yellow solid, 67%, m.p. 128-130□; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41-7.27 (m, 6H, ArH), 6.70 (brs, 2H, ArH), 6.78-6.65 (m, 5H, ArH, CH), 5.19 (d, *J* = 17.4Hz, 1H, CH_2), 4.81 (d, *J* = 17.4Hz, 1H, CH_2), 4.05 (s, 3H, OCH_3), 3.52-3.45 (m, 2H, CH_2), 3.22 (s, 3H, OCH_3), 1.77-1.72 (m, 1H, CH_2), 1.67-1.61 (m, 1H, CH_2), 1.41-1.33 (m, 2H, CH_2), 0.95 (t, *J* = 9.0Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.7, 163.3, 163.0, 160.5, 158.1, 155.2, 142.2, 141.9, 139.4 (d, *J* = 3.4Hz), 134.6, 131.1, 128.9, 128.1, 127.7, 127.3 (d, *J* = 7.8Hz), 125.0, 120.8, 116.9 (d, *J* = 23.5Hz), 112.5 (d, *J* = 26.0Hz), 110.7, 110.3, 109.8, 109.7, 98.9, 78.5, 53.5, 53.2, 51.8, 50.2, 45.3, 44.5, 29.7, 28.8, 20.1, 13.8; IR(KBr) υ: 3561, 3065, 2958, 2871, 2375, 2343, 1744, 1710, 1573, 1495, 1451, 1344, 1271, 1238, 1196, 1138, 1026, 970, 884, 795, 741, 700 cm^{-1}; MS

(*m*/*z*): HRMS (ESI) Calcd. for $C_{35}H_{30}FNaN_5O_5$([M+Na]$^+$): 642.2123, found: 642.2122.

Compound 2m': yellow solid, 60%, m.p. 194-196□; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.42 (s, 1H, ArH), 7.33-7.27 (m, 4H, ArH), 7.24-7.21 (m, 3H, ArH), 7.12 (d, *J* = 7.2Hz, 2H, ArH), 6.88-6.83 (m, 3H, ArH), 6.80 (d, *J* = 7.8Hz, 1H, ArH), 6.74 (t, *J* = 7.8Hz, 1H, ArH), 6.44 (d, *J* = 8.4Hz, 1H, ArH), 6.28 (d, *J* = 7.8Hz, 1H, ArH), 6.10 (s, 1H, CH), 4.81 (d, *J* = 16.2Hz, 1H, CH_2), 4.71-4.59 (m, 2H, CH_2), 4.48 (d, *J* = 17.4Hz, 2H, CH_2), 4.39-4.36 (m, 2H, CH_2), 4.26 (d, *J* = 17.4Hz, 1H, CH_2), 3.16 (d, *J* = 15.6Hz, 1H, CH_2), 1.53 (t, *J* = 7.2Hz, 3H, CH_3), 1.39 (t, *J* = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 169.5, 162.3, 161.7, 143.9, 142.6, 142.3, 137.3, 133.6, 131.0, 130.0, 129.6, 128.9, 128.7, 128.0, 127.4, 126.9, 126.6, 126.1, 126.0, 122.9, 120.7, 111.6, 111.4, 111.3, 110.5, 109.4, 92.2, 82.8, 63.8, 62.2, 54.6, 50.9, 43.6, 38.3, 13.9, 13.7; IR(KBr) υ: 3448, 3059, 2952, 2866, 2375, 2343, 1750, 1716, 1651, 1609, 1567, 1493, 1433, 1369, 1346, 1308, 1279, 1242, 1190, 1137, 1097, 1021, 949, 865, 823, 771, 738 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{40}H_{32}ClNaN_5O_5$([M+Na]$^+$): 720.1984, found: 720.1969.

Compound 2n': yellow solid, 74%, m.p. 202-204□; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.32-7.27 (m, 4H, ArH), 7.24-7.19 (m, 3H, ArH), 7.12 (d, *J* = 7.8Hz, 2H, ArH), 6.97 (t, *J* = 8.4Hz, 1H, ArH), 6.86 (t, *J* = 7.2Hz, 1H, ArH), 6.83-6.79 (m, 3H, ArH), 6.74 (t, *J* = 7.8Hz, 1H, ArH), 6.45-6.43 (m, 1H, ArH), 6.27 (d, *J* = 7.8Hz, 1H, ArH), 6.11 (s, 1H, CH), 4.83 (d, *J* = 16.2Hz, 1H, CH_2), 4.68-4.62 (m, 2H, CH_2), 4.49 (d, *J* = 17.4Hz, 1H, CH_2), 4.39-4.35 (m, 2H, CH_2), 4.26 (d, *J* = 17.4Hz, 1H, CH_2), 3.16 (d, *J* = 15.6Hz, 1H, CH_2), 1.52 (t, *J* = 7.2Hz, 3H, CH_3), 1.38 (t, *J* = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 169.6, 162.3, 160.3, 143.8, 142.2, 140.1, 137.3, 133.7, 130.0, 128.9, 128.7, 127.9, 127.4, 126.9, 126.1, 125.9, 122.7 (d, *J* = 8.5Hz), 120.7, 117.5 (d, *J* = 23.1Hz), 114.5 (d, *J* = 26.6Hz), 111.6, 111.3, 111.2 (d, *J* = 8.1Hz), 110.6, 109.3, 92.2, 82.8, 63.9, 62.2, 54.5, 50.9, 43.7, 38.4, 13.9, 13.7; IR(KBr) υ: 3461, 3063, 2956, 2870, 2375, 2343, 1753, 1714, 1607, 1568, 1495, 1452, 1370, 1308, 1246, 1187, 1138, 1099, 1023, 865, 823, 771, 738 cm^{-1}; MS (*m*/*z*): HRMS (ESI) Calcd. for $C_{40}H_{32}FNaN_5O_5$([M+Na]$^+$): 704.2280, found: 704.2268.

Compound 2o': yellow solid, 61%, m.p. 214-216□; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.40-7.37 (m, 2H, ArH), 7.20-7.16 (m, 3H, ArH), 7.04 (t, *J* = 7.2Hz, 1H, ArH), 6.81 (t, *J* = 7.2Hz, 1H, ArH), 6.77-6.68 (m, 5H, ArH), 6.19 (d, *J* = 7.8Hz, 1H, ArH), 6.07 (s, 1H, CH), 4.66-4.62 (m, 2H, CH_2), 4.47 (d, *J* = 17.4Hz, 1H, CH_2), 4.36-4.32 (m, 2H, CH_2), 4.23 (d, *J* = 17.4Hz, 1H, CH_2), 3.39-3.34 (m, 1H, CH_2), 2.58-2.54 (m, 1H, CH_2), 1.52 (t, *J* = 7.2Hz, 3H, CH_3), 1.48-1.38 (m, 2H, CH_2), 1.36

(t, J = 7.2Hz, 3H, CH_3), 1.30-1.23 (m, 2H, CH_2), 0.85 (t, J = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 164.9, 162.5, 162.1, 144.3, 143.9, 142.2, 137.2, 130.9, 130.1, 128.5, 127.1, 126.1, 125.9, 125.6, 124.0, 121.6, 120.2, 111.6, 111.5, 110.4, 109.5, 109.1, 92.4, 82.5, 63.7, 62.1, 54.2, 50.4, 39.8, 38.7, 28.8, 20.0, 13.9, 13.7, 13.5; IR(KBr) υ: 3365, 3058, 2952, 2866, 2374, 2343, 1745, 1708, 1612, 1565, 1497, 1467, 1371, 1307, 1255, 1200, 1147, 1105, 1015, 864, 748 cm^{-1}; MS (m/z): HRMS (ESI) Calcd. for $C_{37}H_{35}NaN_5O_5$([M+Na]$^+$): 652.2530, found: 652.2521.

Acknowledgments: This work was financially supported by the National Natural Science Foundation of China (Grant No. 21172189) and the Priority Academic Program Development of Jiangsu Higher Education Institutions. We thanked Analysis and Test Center of Yangzhou University providing instruments for analysis.

Supporting Information: ^1H NMR and ^{13}C NMR spectra for all compounds are available. Crystallographic data **1a** (CCDC 1028708), **1b** (CCDC 1028709), **2d'** (CCDC 1028710), **2e** (CCDC 1028711) and **2l'** (CCDC 1028712) have been deposited vat the Cambridge Crystallographic Database Centre.

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Graphic abstract:

Four-component reaction of *N*-alkylimidazoles (*N*-alkylbenzimidazoles), dialkyl but-2-ynedioate, *N*-alkylisatins and malononitrile

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