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Molecular Diversity of Three-Component Reactions of *N*-Benzylbenzimidazolium Salts, Isatin, and Malononitrile or Ethyl Cyanoacetate

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The three-component reactions of *N*-benzylbenzimidazolium salts, isatins, and malononitrile or ethyl cyanoacetate showed very interesting molecular diversity depending on the structures of the benzimidazolium salts. The reactions of *N*-benzyl-*N*′-*p*-nitrobenzylbenzimidazolium salts gave a series of zwitterionic salts in good yields. Under similar reaction conditions the reactions of *N*-benzyl-*N*′-phenacylbenzimidazolium salts resulted in the unexpected products with opening of the imidazole ring.

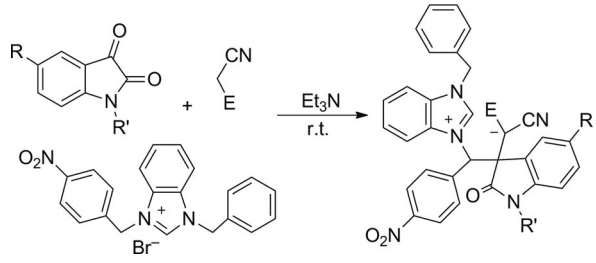
Introduction

Heterocyclic ammonium salts such as pyridinium, quinolinium, and isoquinolinium salts are readily available from the alkylation of azaaromatic heterocycles and have been used in a great variety of synthetic reactions for the synthesis of complex heterocycles.[1–6] Five-membered heterocyclic ammonium salts such as imidazolium salts have also attracted much attention[7–9] aside from their use as ionic liquids and precursors of N-heterocyclic carbenes. The reactivity and synthetic applications of the related benzimidazolium salts remain unexplored, although there are several reports of the use of their benzimidazolium ylide precursors in 1,3-dipolar cycloadditions for the preparation of pyrrolo[1,2-*a*]benzimidazoles.[10–13] Recently, we found that the one-pot reactions of *N*-benzylbenzimidazolium salts, aromatic aldehydes, and active methylene compounds gave a series of zwitterionic salts or functionalized pyrrolo[1,2-*a*]-benzimidazoles in good yields.[14] To evaluate the scope of this reaction, we investigated the three-component reaction of *N*-benzylbenzimidazolium salts with isatin and malononitrile or ethyl cyanoacetate. Here we wish to report the efficient synthesis of a new type of *N*-benzylbenzimidazolium zwitterionic salts and the unexpected products with opening of the imidazole ring.

Results and Discussion

According to previously established reaction conditions for the one-pot reaction of functionalized pyrrolo[1,2-*a*]-benzimidazoles,[14] a mixture of *N*-benzyl-*N*′-*p*-nitrobenzylbenzimidazolium bromide (**1a**), 5-methylisatin, and malononitrile with triethylamine as a base catalyst in methanol was stirred at room temperature for several hours. After workup, we unexpectedly found that instead of isolating the expected pyrrolo[1,2-*a*]benzimidazole, zwitterionic salt

Table 1. Synthesis of zwitterionic salts **2a**–**n** through a three-component reaction.[a]



Entry	Compound	R	R′	E	Yield [%]
1	**2a**	CH_3	H	CN	68
2	**2b**	Cl	H	CN	59
3	**2c**	CH_3	$CH_2C_6H_5$	CN	84
4	**2d**	Cl	$CH_2C_6H_5$	CN	70
5	**2e**	F	$CH_2C_6H_5$	CN	79
6	**2f**	CH_3	n-C_4H_9	CN	82
7	**2g**	Cl	n-C_4H_9	CN	90
8	**2h**	F	n-C_4H_9	CN	87
9	**2i**	CH_3	$CH_2C_6H_5$	$CO_2C_2H_5$	71
10	**2j**	Cl	$CH_2C_6H_5$	$CO_2C_2H_5$	68
11	**2k**	F	$CH_2C_6H_5$	$CO_2C_2H_5$	74
12	**2l**	CH_3	n-C_4H_9	$CO_2C_2H_5$	76
13	**2m**	Cl	n-C_4H_9	$CO_2C_2H_5$	58
14	**2n**	F	n-C_4H_9	$CO_2C_2H_5$	62

[a] Reactions were carried out at room temperature by using *N*-benzyl-*N*′-*p*-nitrophenylbenzimidazolium bromide (1.0 mmol), isatin (1.0 mmol), malononitrile or ethyl cyanoacetate (1.0 mmol), and triethylamine (1.0 mmol) in methanol (25 mL).

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2a was obtained in 68% yield. Under similar conditions, other substituted isatins reacted smoothly to afford the corresponding zwitterionic salt **2b**–**h** in satisfactory yields (59–90%; Table 1, Entries 2–8). It should be noted that isatins bearing 1-benzyl and 1-*n*-butyl groups gave relatively higher yields than those of other isatins due to the better solubility of the zwitterionic salts. Ethyl cyanoacetate was also successfully utilized in the three-component reaction to give the corresponding zwitterionic salts **2i**–**n**) in good yields (Table 1, Entries 9–14). The structures of prepared zwitterionic salts **2a**–**n** were fully confirmed by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy and HRMS and were further confirmed by single-crystal X-ray diffraction studies performed for compound **2e** (Figure 1). It should be noted that compounds **2** contains two chiral centers, which means that more than one diastereomer may exist.

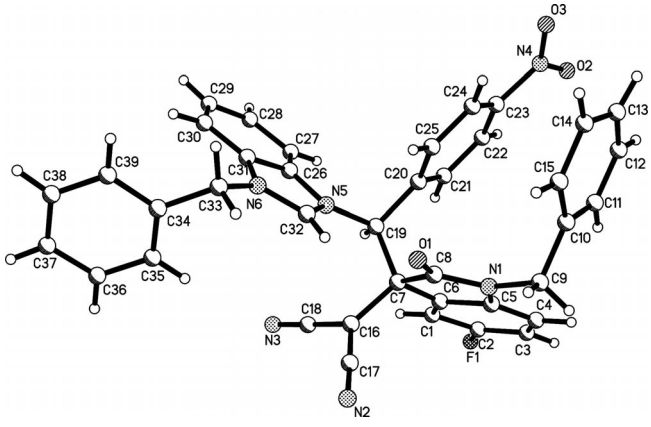
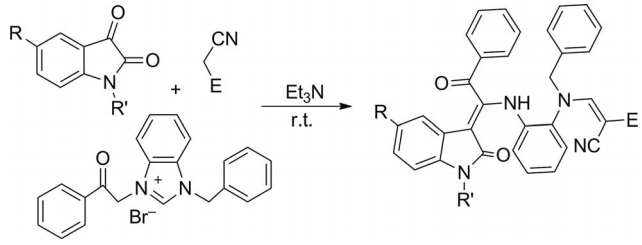


Figure 1. Molecular structure of zwitterionic salt **2e**.

At present we could not determine the major diastereomer or the ratio of the existing two diastereomers by ^{1}H NMR spectroscopy. On the basis of the structure of the zwitterionic salts, we could propose a rational mechanism for their formation. At first, isatin reacted with malononitrile to give the condensation isatylidene malononitrile product; secondly, Michael addition of the in situ formed benzimidazolium ylide to isatylidene malononitrile resulted in the zwitterionic salt. No further reactions and cyclization processes were observed if the length of the reaction was prolonged to several days at room temperature. Trying to carry out the reaction at elevated temperatures caused the formation of a very complicated mixture with decomposition of the zwitterion salts. The formation of the zwitterionic salts in the above reaction is very interesting. The reactions of isatylidene malononitrile usually gave cyclized spiro compounds,[15–18] and our previously reported three-component reaction of *N*-benzylbenzimidazolium salts, aromatic aldehydes, and malononitrile also yielded the functionalized pyrrolo[1,2-*a*]benzimidazoles.[14] The reason for no further cyclization is probably due to heavy steric hindrance of the substituents in the zwitterionic salts.

To extend the scope of this one-pot reaction, the reactivity of other *N*-benzylbenzimidazolium salts was also explored. Under similar reaction conditions, the three-component reaction of *N*-benzyl-*N*′-phenacylbenzimidazolium bromide (**1b**), isatins, and malononitrile with triethylamine as the base catalyst gave products **3a**–**g**, in which the imidazole ring is opened and the malononitrile unit is not connected to isatin (Table 2). Then, the reactions of ethyl cyanoacetate showed similar phenomena and produced the corresponding ring-opening products **3h**–**m** in satisfactory yields. Here, the formation of the ring-opening products is completely unexpected. The structures of **3a**–**m** were established on the basis of spectroscopic methods and were further confirmed by single-crystal determination of compounds **3e** (Figure 2) and **3f** (Supporting Information).

Table 2. Synthesis of ring-opening products **3a**–**m** through a three-component reaction.[a]



Entry	Compound	R	R′	E	Yield [%]
1	**3a**	Cl	H	CN	89
2	**3b**	CH_3	$CH_2C_6H_5$	CN	86
3	**3c**	Cl	$CH_2C_6H_5$	CN	77
4	**3d**	F	$CH_2C_6H_5$	CN	82
5	**3e**	CH_3	*n*-C_4H_9	CN	80
6	**3f**	Cl	*n*-C_4H_9	CN	67
7	**3g**	F	*n*-C_4H_9	CN	73
8	**3h**	CH_3	$CH_2C_6H_5$	$CO_2C_2H_5$	67
9	**3i**	Cl	$CH_2C_6H_5$	$CO_2C_2H_5$	60
10	**3j**	F	$CH_2C_6H_5$	$CO_2C_2H_5$	78
11	**3k**	CH_3	*n*-C_4H_9	$CO_2C_2H_5$	85
12	**3l**	Cl	*n*-C_4H_9	$CO_2C_2H_5$	63
13	**3m**	F	*n*-C_4H_9	$CO_2C_2H_5$	68

[a] Reactions were carried out at room temperature by using *N*-benzyl-*N*′-phenacylbenzimidazolium. bromide (1.0 mmol), isatin (1.0 mmol), malononitrile or ethyl cyanoacetate (1.0 mmol), and triethylamine (1.0 mmol) in methanol (25 mL).

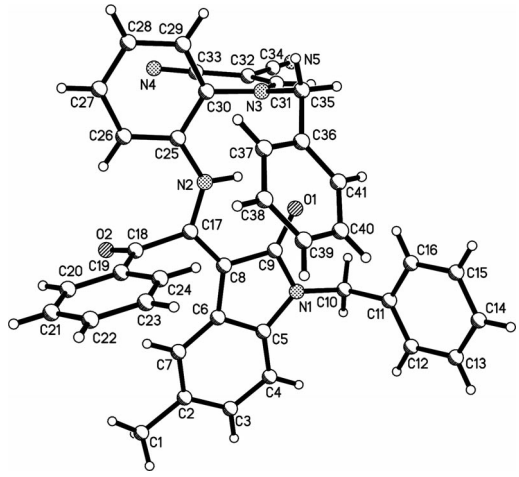
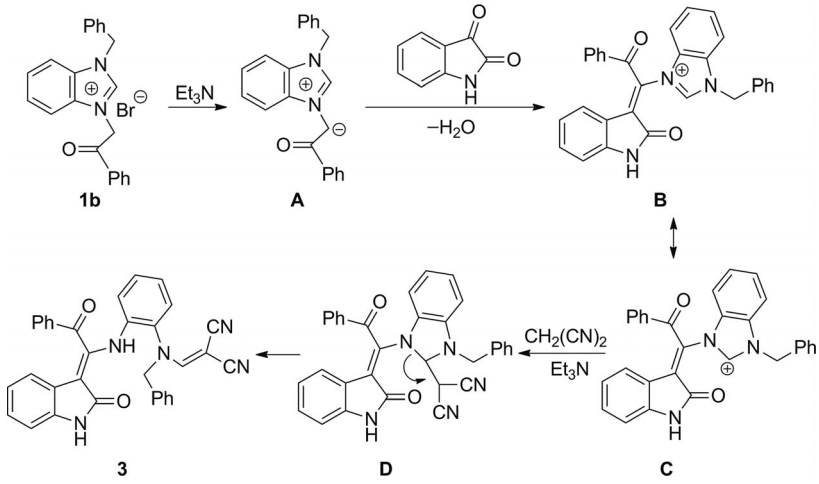


Figure 2. Molecular structure of zwitterionic salt **3b**.



Scheme 1. Proposed mechanism for the formation of compound **3**.

Even though at present the exact reason for the opening of the imidazole ring is not very clear, to explain the mechanism for the formation of the unexpected ring-opening products, we propose a plausible reaction course, which is illustrated in Scheme 1. At first, **1b** is deprotonated by triethylamine to give benzimidazolium ylide **A**. Secondly, ylide **A** attacks the carbonyl group at the 3-position of isatin to form condensation intermediate **B** with elimination of water. Intermediate **B** is a cyclic iminium ion, in which the positive charge can be delocalized to its resonance hybrid form **C**. Thirdly, the combination of the carbanion of malononitrile with carbocation **C** results in neutral product **D**. Possibly due to the lower stability of the dihydrobenzimidazole ring, intermediate **D** is transformed into final product **3** through opening of the imidazoline ring and formation of a C=C bond.

Conclusions

In conclusion we found that the three-component reaction of *N*-benzylbenzimidazolium salts with isatins and malononitrile or ethyl cyanoacetate show very interesting molecular diversity, from which the efficient synthesis of *N*-benzylbenzimidazolium zwitterionic salts was achieved, and in some cases, unexpected products resulting from opening of the imidazole ring were obtained. This protocol has the advantage of mild reaction conditions, easily accessible starting materials, and easy purification of the products, which makes it a useful and attractive method for the synthesis of complex N,O-containing heterocycles in synthetic and medicinal chemistry. Further expansion of the reaction scope and synthetic applications of this methodology are in progress in our laboratory.

Experimental Section

General Methods: All reagents and solvents were commercially available in analytical grade and were used as received. The evaporation of the organic solvents was carried out with a rotary evaporator in conjunction with a water aspirator. Melting points were taken with a hot-plate microscope apparatus. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AV-600 instrument. IR spectra were obtained with a Bruker Tensor 27 spectrometer (KBr disc). HRMS were measured with an AB 5800 MALDI-TOF/TOF instrument. *N*-Benzyl-*N*′-*p*-nitrobenzylbenzimidazolium bromide (**1a**) and *N*-benzyl-*N*′-phenacylbenzimidazolium bromide (**1b**) were prepared by heating *N*-benzylbenzimidazole with *p*-nitrobenzyl bromide or α-phenacyl bromide in toluene according to a published procedure.[14] X-ray data were collected with a Bruker Smart APEX-2 diffractometer. CCDC-870084 (for **2e**), -870085 (for **3d**), and -870086 (for **3f**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General Procedure for the Preparation of Zwitterionic Salts 2a–k through a Three-Component Reaction: A mixture of *N*-benzyl-*N*′-*p*-nitrobenzylbenzimidazolium bromide (1.0 mmol, 0.423 g), isatin (1.0 mmol), malononitrile or ethyl cyanoacetate (1.0 mmol), and triethylamine (1.0 mmol, 0.10 g) in methanol (25 mL) was stirred at room temperature for 2 d. The resulting precipitate was collected by filtration and then subjected to preparative thin-layer chromatography (ethyl acetate/light petroleum ether, 2:1) to give the pure product for analysis.

2a: Yield: 68%. Yellow solid, m.p. 144–146 °C. IR (KBr): $\tilde{\nu}$ = 3065 (w), 2857 (w), 2169 (s), 2100 (vs), 1700 (s), 1623 (w), 1606 (w), 1555 (w), 1525 (m), 1493 (m), 1442 (w), 1379 (w), 1348 (s), 1259 (w), 1193 (m), 1121 (w), 1014 (w), 973 (w), 861 (w) cm^{-1}. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 10.99 (s, 1 H, ArH), 10.55 (s, 1 H, NH), 8.23 (d, J = 7.2 Hz, 1 H, ArH), 8.00 (d, J = 7.8 Hz, 2 H, ArH), 7.88 (d, J = 7.8 Hz, 1 H, ArH), 7.68 (s, 1 H, ArH), 7.65 (d, J = 6.6 Hz, 2 H, ArH), 7.62 (d, J = 3.6 Hz, 1 H, ArH), 7.53 (d, J = 7.8 Hz, 3 H, ArH), 7.43 (t, J = 7.2 Hz, 2 H, ArH), 7.39 (d, J = 7.2 Hz, 1 H, ArH), 6.99 (d, J = 7.8 Hz, 1 H, ArH), 6.61 (s, 1 H, ArH), 6.53 (d, J = 7.8 Hz, 1 H, CH), 6.06 (d, J = 15.6 Hz, 1 H, CH$_2$), 5.89 (d, J = 15.6 Hz, 1 H, CH$_2$), 2.37 (s, 3 H, CH$_3$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ =: 176.3, 147.4, 144.6, 140.9, 137.6, 133.8, 132.3, 131.4, 130.7, 130.2, 129.7, 129.0, 128.8, 128.6, 128.1, 126.9, 126.8, 126.7, 125.1, 123.0, 114.1, 113.8, 109.1, 64.2, 55.8, 50.6, 21.0 ppm. HRMS (ESI): calcd. for C$_{33}$H$_{23}$N$_6$O$_3$ [M – H]$^-$ 551.1837; found 551.1826.

2b: Yield: 59%. Yellow solid, m.p. 144–146 °C. IR (KBr): $\tilde{\nu}$ = 3067 (w), 2165 (s), 2108 (vs), 1710 (s), 1662 (m), 1617 (m), 1555 (w),

1525 (m), 1478 (m), 1443 (w), 1384 (w), 1349 (m), 1255 (w), 1190 (m), 1116 (w), 1079 (w), 1013 (w), 861 (w), 821 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 10.94 (s, 1 H, ArH), 10.83 (s, 1 H, NH), 8.33 (d, J = 8.4 Hz, 1 H, ArH), 8.06 (d, J = 9.0 Hz, 2 H, ArH), 7.98 (s, 1 H, ArH), 7.88 (d, J = 8.4 Hz, 1 H, ArH), 7.68–7.64 (m, 3 H, ArH), 7.63–7.59 (m, 3 H, ArH), 7.42 (t, J = 7.2 Hz, 2 H, ArH), 7.38 (t, J = 7.2 Hz, 1 H, ArH), 7.24–7.22 (m, 1 H, ArH), 6.74 (s, 1 H, ArH), 6.67 (d, J = 8.4 Hz, 1 H, CH), 6.07 (d, J = 15.6 Hz, 1 H, CH_2), 5.89 (d, J = 15.6 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 176.0, 147.5, 144.7, 140.7, 138.9, 133.7, 133.1, 132.4, 130.1, 129.7, 129.0, 128.6, 128.4, 128.1, 126.9, 126.8, 126.5, 126.0, 124.7, 123.3, 114.2, 113.8, 110.9, 63.8, 55.9, 50.7, 18.7 ppm. HRMS (ESI): calcd. for $C_{32}H_{21}ClN_6O_3$ [M – H]$^-$ 571.1281; found 571.1270.

2c: Yield: 84%. Yellow solid, m.p. 126–128 °C. IR (KBr): $\tilde{\nu}$ = 3112 (w), 3063 (w), 2163 (s), 2109 (vs), 1692 (s), 1603 (s), 1553 (m), 1522 (s), 1496 (s), 1541 (m), 1375 (m), 1348 (s), 1288 (w), 1252 (w), 1188 (m), 1122 (w), 1080 (w), 1016 (w), 971 (w), 881 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 11.09 (s, 1 H, ArH), 8.25 (d, J = 7.8 Hz, 1 H, ArH), 7.89 (d, J = 8.4 Hz, 3 H, ArH), 7.82 (s, 1 H, ArH), 7.68 (d, J = 7.8 Hz, 2 H, ArH), 7.66–7.60 (m, 2 H, ArH), 7.45–7.40 (m, 4 H, ArH), 7.38 (d, J = 7.2 Hz, 1 H, ArH), 7.16 (t, J = 7.8 Hz, 1 H, ArH), 7.09 (t, J = 7.8 Hz, 2 H, ArH), 7.03 (d, J = 7.8 Hz, 2 H, ArH), 6.91 (d, J = 7.8 Hz, 2 H, ArH), 6.72 (s, 1 H, ArH), 6.64 (d, J = 7.8 Hz, 1 H, CH), 6.10 (d, J = 15.6 Hz, 1 H, CH_2), 5.93 (d, J = 15.6 Hz, 1 H, CH_2), 4.75 (d, J = 16.2 Hz, 1 H, CH_2), 4.68 (d, J = 15.6 Hz, 1 H, CH_2), 2.40 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ =: 174.3, 147.3, 144.9, 140.5, 138.2, 135.6, 133.8, 132.3, 131.8, 130.7, 130.1, 129.5, 129.0, 128.8, 128.6, 128.1, 128.0, 127.2, 127.1, 126.9, 126.8, 126.7, 125.0, 123.0, 114.1, 113.9, 109.0, 64.0, 55.9, 50.7, 42.8, 21.0, 19.3 ppm. HRMS (ESI): calcd. for $C_{40}H_{29}N_6O_3$ [M – H]$^-$ 641.2307; found 641.2220.

2d: Yield: 70%. Yellow solid, m.p. 146–148 °C. IR (KBr): $\tilde{\nu}$ = 3063 (w), 3036 (w), 2158 (s), 2107 (vs), 1689 (s), 1605 (m), 1555 (w), 1520 (s), 1486 (m), 1446 (w), 1430 (w), 1381 (w), 1348 (s), 1254 (w), 1182 (m), 1163 (m), 1119 (w), 1083 (w), 1052 (w), 1026 (m), 1009 (w), 983 (w), 872 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 11.02 (s, 1 H, ArH), 8.32 (d, J = 8.4 Hz, 1 H, ArH), 8.12 (s, 1 H, ArH), 7.94 (d, J = 9.0 Hz, 2 H, ArH), 7.89 (d, J = 8.4 Hz, 1 H, ArH), 7.67 (t, J = 7.2 Hz, 3 H, ArH), 7.62 (t, J = 7.8 Hz, 1 H, ArH), 7.49 (d, J = 9.0 Hz, 2 H, ArH), 7.43 (t, J = 7.2 Hz, 2 H, ArH), 7.39 (t, J = 7.8 Hz, 1 H, ArH), 7.31–7.29 (m, 1 H, ArH), 7.18 (t, J = 7.2 Hz, 1 H, ArH), 7.12 (t, J = 7.2 Hz, 2 H, ArH), 6.93 (d, J = 7.2 Hz, 2 H, ArH), 6.83 (s, 1 H, ArH), 6.82 (d, J = 8.4 Hz, 1 H, CH), 6.11 (d, J = 15.0 Hz, 1 H, CH_2), 5.92 (d, J = 15.6 Hz, 1 H, CH_2), 4.82 (d, J = 16.2 Hz, 1 H, CH_2), 4.75 (d, J = 15.6 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 174.0, 147.4, 140.3, 139.3, 135.2, 133.8, 132.3, 129.5, 129.0, 128.6, 128.5, 128.2, 127.4, 127.1, 127.0, 126.9, 126.8, 126.3, 123.3, 114.2, 110.8, 55.9, 50.7, 42.9, 19.1 ppm. HRMS (ESI): calcd. for $C_{39}H_{26}ClN_6O_3$ [M – H]$^-$ 661.1760; found 661.1744.

2e: Yield: 79%. Yellow solid, m.p. 124–126 °C. IR (KBr): $\tilde{\nu}$ = 3128 (w), 3067 (w), 2154 (s), 2105 (vs), 1703 (s), 1607 (m), 1556 (m), 1522 (s), 1493 (s), 1453 (s), 1343 (s), 1272 (m), 1237 (m), 1203 (m), 1174 (s), 1141 (w), 1077 (w), 1016 (w), 984 (w), 854 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 11.05 (s, 1 H, ArH), 8.32 (d, J = 8.4 Hz, 1 H, ArH), 7.96–7.92 (m, 3 H, ArH), 7.90 (d, J = 8.4 Hz, 1 H, ArH), 7.68 (t, J = 7.2 Hz, 3 H, ArH), 7.63 (t, J = 7.8 Hz, 1 H, ArH), 7.51 (d, J = 9.0 Hz, 2 H, ArH), 7.43 (t, J = 7.8 Hz, 2 H, ArH), 7.37 (t, J = 7.2 Hz, 1 H, ArH), 7.18 (t, J = 7.2 Hz, 1 H, ArH), 7.12 (t, J = 7.8 Hz, 2 H, ArH), 7.09–7.07 (m, 1 H, ArH), 6.94 (d, J = 7.2 Hz, 2 H, ArH), 6.81–6.79 (m, 2 H, ArH, CH), 6.10 (d, J = 15.6 Hz, 1 H, CH_2), 5.92 (d, J = 15.0 Hz, 1 H, CH_2), 4.82 (d, J = 16.2 Hz, 1 H, CH_2), 4.75 (d, J = 15.6 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 174.1, 157.6, 147.4, 144.9, 140.3, 136.7, 135.3, 133.7, 132.3, 130.1, 129.6, 129.0, 128.6, 128.2, 128.1, 127.4, 127.2, 127.0, 126.9, 126.4, 123.3, 114.8, 114.1, 113.9, 63.8, 56.0, 50.8, 42.9, 19.0 ppm. HRMS (ESI): calcd. for $C_{39}H_{26}FN_6O_3$ [M – H]$^-$ 645.2056; found 644.9788.

2f: Yield: 82%. Yellow solid, m.p. 114–116 °C. IR (KBr): $\tilde{\nu}$ = 3060 (w), 2958 (w), 2162 (s), 2107 (vs), 1692 (s), 1604 (m), 1554 (w), 1525 (s), 1496 (s), 1453 (m), 1378 (m), 1348 (s), 1288 (w), 1260 (w), 1193 (m), 1143 (w), 1107 (w), 1015 (w), 859 (w), 812 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 11.10 (s, 1 H, ArH), 7.98 (d, J = 9.0 Hz, 2 H, ArH), 7.90 (d, J = 7.8 Hz, 1 H, ArH), 7.78 (s, 1 H, ArH), 7.66 (d, J = 7.2 Hz, 2 H, ArH), 7.64–7.59 (m, 2 H, ArH), 7.43 (t, J = 7.8 Hz, 4 H, ArH), 7.38 (t, J = 7.2 Hz, 1 H, ArH), 7.34–7.30 (m, 1 H, ArH), 7.10 (d, J = 7.8 Hz, 1 H, ArH), 6.76 (d, J = 8.4 Hz, 1 H, ArH), 6.67 (s, 1 H, CH), 6.10 (d, J = 15.6 Hz, 1 H, CH_2), 5.93 (d, J = 15.6 Hz, 1 H, CH_2), 3.55–3.50 (m, 1 H, CH_2), 3.40–3.36 (m, 1 H, CH_2), 2.42 (s, 3 H, CH_3), 1.13–1.10 (m, 1 H, CH_2), 1.08–1.04 (m, 1 H, CH_2), 0.95–0.87 (m, 1 H, CH_2), 0.84–0.79 (m, 1 H, CH_2), 0.65 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 174.1, 147.3, 145.0, 144.2, 140.6, 138.7, 133.9, 132.2, 131.5, 130.8, 130.1, 129.6, 129.0, 128.9, 128.6, 128.1, 127.7, 127.3, 126.8, 126.7, 124.9, 122.9, 122.3, 121.5, 119.5, 114.0, 113.8, 110.7, 108.5, 64.1, 55.7, 50.7, 47.6, 28.9, 21.0, 19.3, 13.4 ppm. HRMS (ESI): calcd. for $C_{37}H_{31}N_6O_3$ [M – H]$^-$ 607.2453; found 607.2449.

2g: Yield: 90%. Yellow solid, m.p. 130–132 °C. IR (KBr): $\tilde{\nu}$ = 3062 (w), 2963 (w), 2165 (s), 2109 (vs), 1699 (s), 1606 (m), 1555 (w), 1525 (m), 1485 (m), 1446 (w), 1349 (s), 1278 (w), 1259 (w), 1194 (m), 1144 (w), 1110 (m), 1081 (w), 1046 (w), 1015 (w), 979 (w), 860 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 11.05 (s, 1 H, ArH), 8.29 (d, J = 8.4 Hz, 1 H, ArH), 8.08 (s, 1 H, ArH), 8.05 (d, J = 9.0 Hz, 2 H, ArH), 7.90 (d, J = 8.4 Hz, 1 H, ArH), 7.66 (t, J = 7.2 Hz, 3 H, ArH), 7.61 (t, J = 7.8 Hz, 1 H, ArH), 7.50 (d, J = 9.0 Hz, 2 H, ArH), 7.43 (t, J = 7.8 Hz, 2 H, ArH), 7.39 (d, J = 7.2 Hz, 1 H, ArH), 7.37–7.35 (m, 1 H, ArH), 6.95 (d, J = 8.4 Hz, 1 H, ArH), 6.81 (s, 1 H, CH), 6.12 (d, J = 15.6 Hz, 1 H, CH_2), 5.94 (d, J = 15.6 Hz, 1 H, CH_2), 3.60–3.55 (m, 1 H, CH_2), 3.47–3.42 (m, 1 H, CH_2), 1.18–1.14 (m, 1 H, CH_2), 1.13–1.08 (m, 1 H, CH_2), 0.96–0.90 (m, 1 H, CH_2), 0.85–0.79 (m, 1 H, CH_2), 0.67 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 173.9, 147.5, 145.0, 140.3, 139.9, 133.8, 132.5, 132.2, 130.1, 129.6, 129.0, 128.5, 128.1, 126.9, 126.8, 126.7, 126.4, 124.5, 123.2, 114.2, 113.9, 110.4, 63.7, 56.0, 55.8, 50.7, 28.8, 19.2, 13.4 ppm. HRMS (ESI): calcd. for $C_{36}H_{28}ClN_6O_3$ [M – H]$^-$ 627.1917; found 627.1912.

2h: Yield: 87%. Yellow solid, m.p. 126–128 °C. IR (KBr): $\tilde{\nu}$ = 3061 (w), 2963 (w), 2166 (s), 2109 (vs), 1698 (s), 1607 (m), 1555 (m), 1525 (s), 1492 (s), 1450 (s), 1379 (m), 1349 (s), 1263 (m), 1188 (s), 1145 (w), 1134 (w), 1046 (w), 1016 (w), 984 (w), 872 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 11.06 (s, 1 H, ArH), 8.28 (d, J = 7.8 Hz, 1 H, ArH), 8.04 (d, J = 9.0 Hz, 2 H, ArH), 7.89 (d, J = 7.8 Hz, 2 H, ArH), 7.67 (t, J = 7.8 Hz, 3 H, ArH), 7.62 (t, J = 7.8 Hz, 1 H, ArH), 7.51 (d, J = 8.4 Hz, 2 H, ArH), 7.43 (t, J = 7.8 Hz, 2 H, ArH), 7.38 (t, J = 7.2 Hz, 1 H, ArH), 7.17–7.13 (m, 1 H, ArH), 6.94–6.92 (m, 1 H, ArH), 6.75 (s, 1 H, CH), 6.10 (d, J = 15.6 Hz, 1 H, CH_2), 5.93 (d, J = 15.0 Hz, 1 H, CH_2), 3.60–3.56 (m, 1 H, CH_2), 3.47–3.42 (m, 1 H, CH_2), 1.20–1.14 (m, 1 H, CH_2), 1.13–1.08 (m, 1 H, CH_2), 0.95–0.89 (m, 1 H, CH_2), 0.86–0.79 (m, 1 H, CH_2), 0.67 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 174.0, 157.5, 147.4, 144.9, 140.4,

137.2, 133.8, 132.3, 130.1, 129.6, 129.0, 128.6, 128.1, 127.0 126.9, 126.5, 123.2, 115.0, 114.9, 114.1, 113.9, 109.9, 109.8, 63.8, 55.8, 50.7, 28.8, 19.3, 13.4 ppm. HRMS (ESI): calcd. for $C_{36}H_{28}FN_6O_3$ $[M - H]^-$ 611.2191; found 611.2208.

2i: Yield: 71%. Yellow solid, m.p. 150–152 °C. IR (KBr): $\tilde{\nu}$ = 3057 (w), 2938 (w), 2135 (s), 1750 (w), 1694 (s), 1626 (vs), 1549 (w), 1517 (m), 1494 (m), 1454 (w), 1435 (m), 1350 (s), 1262 (w), 1210 (w), 1186 (m), 1132 (w), 1108 (m), 1051 (w), 1016 (w), 971 (w), 878 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 10.36 (s, 1 H, ArH), 7.87 (d, J = 8.4 Hz, 2 H, ArH), 7.75 (s, 1 H, ArH), 7.64 (d, J = 7.8 Hz, 1 H, ArH), 7.51 (d, J = 7.2 Hz, 3 H, ArH), 7.42 (t, J = 7.2 Hz, 2 H, ArH), 7.40–7.36 (m, 2 H, ArH), 7.33 (t, J = 7.2 Hz, 1 H, ArH), 7.23 (d, J = 7.8 Hz, 2 H, ArH), 7.12 (t, J = 7.2 Hz, 1 H, ArH), 7.04 (t, J = 7.8 Hz, 2 H, ArH), 7.01 (d, J = 7.8 Hz, 1 H, ArH), 6.85 (d, J = 7.2 Hz, 2 H, ArH), 6.51 (d, J = 7.87 Hz, 1 H, CH), 5.88 (d, J = 15.6 Hz, 1 H, CH_2), 5.69 (d, J = 15.6 Hz, 1 H, CH_2), 4.61 (d, J = 16.2 Hz, 1 H, CH_2), 4.51 (d, J = 15.6 Hz, 1 H, CH_2), 3.22 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.7, 167.9, 147.3, 141.4, 139.8, 135.8, 134.9, 131.9, 131.8, 130.5, 129.2, 128.9, 128.8, 128.1, 127.9, 127.7, 127.5, 127.1, 127.0, 125.6, 125.1, 124.7, 122.8, 113.1, 112.3, 108.6, 65.1, 58.4, 50.5, 49.7, 43.1, 20.9 ppm. HRMS (ESI): calcd. for $C_{41}H_{32}N_5O_5$ $[M - H]^-$ 674.2409; found 674.2402.

2j: Yield: 68%. Yellow solid, m.p. 162–164 °C. IR (KBr): $\tilde{\nu}$ = 3042 (w), 3016 (w), 2138 (s), 1750 (w), 1698 (s), 1624 (vs), 1552 (s), 1518 (m), 1496 (m), 1438 (m), 1350 (s), 1262 (w), 1207 (w), 1190 (m), 1166 (m), 1127 (m), 1112 (m), 1080 (w), 1053 (w), 1017 (w), 967 (w), 886 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 10.89 (s, 1 H, ArH), 7.99 (s, 1 H, ArH), 7.89 (d, J = 9.0 Hz, 2 H, ArH), 7.84–7.79 (m, 2 H, ArH), 7.52 (t, J = 7.2 Hz, 2 H, ArH), 7.50 (d, J = 7.8 Hz, 1 H, ArH), 7.43 (t, J = 7.8 Hz, 2 H, ArH), 7.38 (t, J = 7.2 Hz, 1 H, ArH), 7.28 (d, J = 9.0 Hz, 2 H, ArH), 7.26–7.24 (m, 1 H, ArH), 7.13 (t, J = 7.2 Hz, 2 H, ArH), 7.06 (t, J = 7.8 Hz, 2 H, ArH), 6.87 (d, J = 7.2 Hz, 2 H, ArH), 6.63 (d, J = 7.8 Hz, 1 H, CH), 6.07 (d, J = 15.6 Hz, 1 H, CH_2), 5.90 (d, J = 15.0 Hz, 1 H, CH_2), 4.64 (d, J = 16.2 Hz, 1 H, CH_2), 4.55 (d, J = 16.2 Hz, 1 H, CH_2), 3.18 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 176.3, 168.7, 147.3, 140.8, 140.7, 135.5, 134.3, 129.4, 129.0, 128.4, 128.1, 127.9, 127.5, 127.2, 126.7, 126.3, 124.2, 122.8, 120.0, 110.0, 63.2, 57.9, 50.3, 49.1, 43.2 ppm. HRMS (ESI): calcd. for $C_{40}H_{29}ClN_5O_5$ $[M - H]^-$ 694.1863; found 694.1853.

2k: Yield: 74%. Yellow solid, m.p. 184–186 °C. IR (KBr): $\tilde{\nu}$ = 3043 (w), 3007 (w), 2139 (s), 1750 (w), 1697 (s), 1625 (vs), 1553 (w), 1520 (m), 1492 (s), 1441 (m), 1350 (s), 1263 (m), 1212 (w), 1178 (m), 1142 (m), 1120 (w), 1054 (w), 1016 (w), 967 (w), 882 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 10.83 (s, 1 H, ArH), 7.89 (d, J = 9.0 Hz, 2 H, ArH), 7.83 (d, J = 1.8 Hz, 1 H, ArH), 7.77 (d, J = 7.8 Hz, 2 H, ArH), 7.52 (d, J = 7.2 Hz, 2 H, ArH), 7.50–7.45 (m, 2 H, ArH), 7.42 (t, J = 7.2 Hz, 2 H, ArH), 7.38 (t, J = 7.2 Hz, 1 H, ArH), 7.30 (d, J = 8.4 Hz, 2 H, ArH), 7.13 (t, J = 7.2 Hz, 2 H, ArH), 7.06 (t, J = 7.8 Hz, 3 H, ArH), 6.88 (d, J = 7.2 Hz, 2 H, ArH), 6.63–6.61 (m, 1 H, CH), 6.04 (d, J = 15.6 Hz, 1 H, CH_2), 5.86 (d, J = 15.6 Hz, 1 H, CH_2), 4.65 (d, J = 15.6 Hz, 1 H, CH_2), 4.56 (d, J = 16.2 Hz, 1 H, CH_2), 3.17 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 176.2, 168.7, 159.3, 157.8, 147.3, 140.8, 138.1, 135.6, 134.4, 132.7, 129.4, 129.0, 128.9, 128.3, 127.9, 127.7, 127.5, 127.2, 127.1, 126.2, 126.1, 122.9, 122.8, 114.6, 113.7, 112.0, 109.5, 63.4, 58.2, 50.3, 49.2, 43.2 ppm. HRMS (ESI): calcd. for $C_{40}H_{29}FN_5O_5$ $[M - H]^-$ 678.2158; found 678.2156.

2l: Yield: 76%. Yellow solid, m.p. 172–174 °C. IR (KBr): $\tilde{\nu}$ = 3060 (w), 2934 (w), 2145 (w), 1752 (vs), 1701 (s), 1602 (m), 1522 (s), 1489 (s), 1453 (w), 1437 (w), 1350 (s), 1316 (w), 1252 (m), 1206 (m), 1142 (w), 1115 (w), 1073 (w), 1014 (w), 972 (w), 867 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 10.23 (s, 1 H, ArH), 7.97 (d, J = 9.0 Hz, 2 H, ArH), 7.71 (s, 1 H, ArH), 7.60 (d, J = 8.4 Hz, 1 H, ArH), 7.48 (d, J = 7.2 Hz, 3 H, ArH), 7.41 (t, J = 7.8 Hz, 2 H, ArH), 7.36 (t, J = 7.8 Hz, 2 H, ArH), 7.30 (t, J = 7.8 Hz, 1 H, ArH), 7.21 (d, J = 8.4 Hz, 2 H, ArH), 7.09 (d, J = 7.8 Hz, 1 H, ArH), 6.73 (s, 1 H, ArH), 6.68 (d, J = 7.8 Hz, 1 H, CH), 5.84 (d, J = 15.6 Hz, 1 H, CH_2), 5.65 (d, J = 15.6 Hz, 1 H, CH_2), 3.42–3.30 (m, 1 H, CH_2), 3.22–3.18 (m, 4 H, CH_2, CH_3), 2.39 (s, 3 H, CH_3), 1.01–0.97 (m, 1 H, CH_2), 0.92–0.83 (m, 2 H, CH_2), 0.79–0.74 (m, 1 H, CH_2), 0.61 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.2, 167.8, 147.3, 141.5, 140.2, 140.0, 135.0, 131.5, 129.2, 129.1, 128.9, 128.1, 127.5, 125.4, 124.7, 124.5, 122.7, 112.9, 108.1, 94.5, 50.5, 28.9, 20.9, 19.3, 13.4 ppm. HRMS (ESI): calcd. for $C_{38}H_{34}N_5O_5$ $[M - H]^-$ 640.2565; found 640.2551.

2m: Yield: 58%. Yellow solid, m.p. 158–160 °C. IR (KBr): $\tilde{\nu}$ = 3051 (w), 2931 (w), 2142 (s), 1750 (w), 1685 (s), 1600 (vs), 1556 (m), 1524 (m), 1486 (m), 1436 (m), 1344 (s), 1258 (w), 1206 (w), 1190 (w), 1052 (w), 1014 (w), 891 (w), 808 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 10.85 (s, 1 H, ArH), 8.00 (d, J = 9.0 Hz, 2 H, ArH), 7.96 (s, 1 H, ArH), 7.82–7.77 (m, 2 H, ArH), 7.50 (d, J = 7.8 Hz, 3 H, ArH), 7.47 (d, J = 8.4 Hz, 1 H, ArH), 7.42 (t, J = 7.2 Hz, 2 H, ArH), 7.38 (d, J = 6.6 Hz, 1 H, ArH), 7.29 (t, J = 8.4 Hz, 3 H, ArH), 7.09 (s, 1 H, ArH), 6.80 (d, J = 8.4 Hz, 1 H, CH), 6.05 (d, J = 15.6 Hz, 1 H, CH_2), 5.88 (d, J = 15.6 Hz, 1 H, CH_2), 3.45–3.41 (m, 1 H, CH_2), 3.26–3.22 (m, 1 H, CH_2), 3.14 (s, 3 H, CH_3), 1.04–0.97 (m, 1 H, CH_2), 0.92–0.87 (m, 2 H, CH_2), 0.78–0.76 (m, 1 H, CH_2), 0.63 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.9, 168.7, 147.4, 141.2, 140.8, 134.3, 132.6, 129.5, 129.0, 128.3, 128.2, 127.7, 127.5, 126.4, 126.2, 126.1, 124.2, 122.7, 113.8, 113.1, 109.6, 63.4, 57.7, 50.3, 49.1, 28.8, 19.3, 13.4 ppm. HRMS (ESI): calcd. for $C_{37}H_{31}ClN_5O_5$ $[M - H]^-$ 660.2019; found 660.2008.

2n: Yield: 62%. Yellow solid, m.p. 166–168 °C. IR (KBr): $\tilde{\nu}$ = 3047 (w), 2932 (w), 2134 (s), 1751 (w), 1694 (m), 1630 (vs), 1556 (w), 1524 (m), 1492 (s), 1439 (w), 1347 (m), 1261 (s), 1026 (m), 1183 (w), 1140 (m), 1118 (w), 1051 (w), 1015 (w), 978 (w), 854 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 10.77 (s, 1 H, ArH), 7.99 (d, J = 9.0 Hz, 2 H, ArH), 7.79–7.77 (m, 1 H, ArH), 7.75 (d, J = 7.8 Hz, 2 H, ArH), 7.50 (d, J = 7.2 Hz, 2 H, ArH), 7.48–7.44 (m, 2 H, ArH), 7.41 (t, J = 7.2 Hz, 2 H, ArH), 7.37 (t, J = 7.2 Hz, 1 H, ArH), 7.28 (d, J = 8.4 Hz, 2 H, ArH), 7.12–7.08 (m, 1 H, ArH), 7.07 (s, 1 H, ArH), 6.81–6.79 (m, 1 H, CH), 6.01 (d, J = 15.6 Hz, 1 H, CH_2), 5.84 (d, J = 15.6 Hz, 1 H, CH_2), 3.46–3.41 (m, 1 H, CH_2), 3.27–3.23 (m, 1 H, CH_2), 3.14 (s, 3 H, CH_3), 1.02–0.99 (m, 1 H, CH_2), 0.92–0.87 (m, 2 H, CH_2), 0.79–0.76 (m, 1 H, CH_2), 0.62 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.7, 168.8, 159.2, 157.6, 147.4, 141.0, 138.5, 134.4, 132.8, 129.4, 129.0, 128.3, 127.5, 126.1, 126.0, 122.7, 114.8, 114.6, 113.7, 113.0, 112.0, 111.8, 109.1, 109.0, 63.6, 58.1, 50.3, 49.2, 28.8, 19.3, 13.4 ppm. HRMS (ESI): calcd. for $C_{37}H_{31}FN_5O_5$ $[M - H]^-$ 644.2315; found 644.2290.

General Procedure for the Preparation of Products 3a–m through a Three-Component Reaction: A mixture of *N*-benzyl-*N*′-phenacylbenzimidazolium bromide (1.0 mmol, 0.407 g), isatin (1.0 mmol), malononitrile or ethyl cyanoacetate (1.0 mmol), and triethylamine (1.0 mmol, 0.10 g) in methanol (25 mL) was stirred at room temperature for 2 d. The resulting precipitate was collected by filtration and then subjected to preparative thin-layer chromatography (ethyl acetate/light petroleum ether, 1:3) to give the pure product for analysis.

3a: Yield: 89%. Yellow solid, m.p. 210–212 °C. IR (KBr): ṽ = 3338 (m), 2217 (m), 1659 (s), 1615 (vs), 1589 (s), 1513 (m), 1447 (m), 1362 (m), 1300 (m), 1216 (m), 1194 (m), 1116 (w), 1079 (w), 1017 (w), 900 (w), 812 (w) cm^{-1}. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 12.18 (s, 1 H, NH), 11.21 (s, 1 H, NH), 8.70 (s, 1 H, ArH), 8.17–8.02 (m, 1 H, ArH), 7.85 (s, 1 H, ArH), 7.78 (d, J = 6.6 Hz, 1 H, ArH), 7.76–7.57 (m, 2 H, ArH), 7.32–7.26 (m, 4 H, ArH), 7.20 (t, J = 8.4 Hz, 2 H, ArH), 7.08 (s, 1 H, ArH), 6.96 (d, J = 7.2 Hz,1 H, ArH), 6.92 (s, 2 H, ArH), 6.32–6.31 (m, 1 H, CH), 5.16 (d, J = 14.4 Hz,1 H, CH$_2$), 4.80 (d, J = 14.4 Hz,1 H, CH$_2$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 170.3, 136.4, 136.3, 133.9, 131.2, 130.2, 130.1, 129.5, 129.4, 129.2, 128.6, 128.5, 124.9, 122.8, 117.1, 111.9, 111.3, 62.2, 50.8 ppm. HRMS (ESI): calcd. for $C_{33}H_{21}ClN_5O_2$ [M – H]$^-$ 554.1380; found 554.1367.

3b: Yield: 86%. Yellow solid, m.p. 170–172 °C. IR (KBr): ṽ = 3031 (w), 2922 (w), 2190 (m), 1681 (s), 1653 (s), 1613 (vs), 1593 (s), 1511 (w), 1487 (w), 1451 (m), 1350 (s), 1275 (w), 1200 (w), 1189 (m), 1159 (w), 1129 (w), 1078 (w), 1047 (w), 1029 (w), 1002 (w), 962 (w), 869 (w) cm^{-1}. ^{1}H NMR (600 MHz, CDCl$_3$): δ = 12.32 (s, 1 H, NH), 8.19–8.00 (m, 2 H, ArH), 7.68 (s, 1 H, ArH), 7.56 (s, 3 H, ArH), 7.38 (s, 3 H, ArH), 7.35 (d, J = 3.6 Hz, 4 H, ArH), 7.29–7.27 (m, 4 H, ArH), 7.22–7.17 (m, 2 H, ArH), 7.06 (s, 1 H, ArH), 6.94 (t, J = 7.8 Hz, 1 H, ArH), 6.85–6.81 (m, 2 H, ArH), 6.68 (d, J = 7.8 Hz, 1 H, ArH), 6.56 (s, 1 H, CH), 5.15 (s, 1 H, CH$_2$), 5.06 (s, 2 H, CH$_2$), 4.71–4.69 (m, 1 H, CH$_2$), 2.08 (s, 3 H, CH$_3$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 168.5, 163.4, 136.2, 135.9, 135.2, 134.0, 132.2, 130.4, 130.0, 129.9, 129.8, 129.7, 129.3, 129.0, 128.8, 128.6, 128.4, 128.3, 128.1, 127.4, 127.2, 127.0, 120.6, 118.6, 109.0, 98.0, 52.9, 47.9, 20.9 ppm. HRMS (ESI): calcd. for $C_{41}H_{30}N_5O_2$ [M – H]$^-$ 624.2405; found 624.2302.

3c: Yield: 77%. Yellow solid, m.p. 194–196 °C. IR (KBr): ṽ = 3031 (m), 2205 (m), 1633 (s), 1593 (vs), 1574 (s), 1519 (m), 1495 (w), 1451 (m), 1421 (m), 1366 (s), 1336 (m), 1309 (w), 1252 (w), 1210 (w), 1182 (m), 1120 (w), 1080 (w), 1021 (w), 954 (w), 891 (w) cm^{-1}. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 12.05 (s, 1 H, NH), 8.78 (s, 1 H, ArH), 8.21–7.99 (m, 1 H, ArH), 7.78 (d, J = 4.2 Hz, 2 H, ArH), 7.65–7.58 (m, 2 H, ArH), 7.42 (s, 2 H, ArH), 7.39 (t, J = 7.2 Hz, 2 H, ArH), 7.30 (t, J = 7.2 Hz, 2 H, ArH), 7.26 (t, J = 6.6 Hz, 2 H, ArH), 7.22 (t, J = 7.8 Hz, 3 H, ArH), 7.11–7.01 (m, 4 H, ArH), 6.91 (s, 1 H, ArH), 6.60–6.36 (m, 1 H, CH), 5.18 (s, 3 H, CH$_2$), 4.91 (d, J = 7.2 Hz, 1 H, CH$_2$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 168.3, 136.6, 136.3, 133.8, 131.3, 130.2, 130.1, 129.4, 129.3, 128.7, 128.6, 128.5, 128.4, 127.5, 127.3, 122.1, 117.1, 111.9, 110.8, 50.9, 42.3 ppm. HRMS (ESI): calcd. for $C_{40}H_{27}ClN_5O_2$ [M – H]$^-$ 644.1845; found 644.1854.

3d: Yield: 82%. Yellow solid, m.p. 186–188 °C. IR (KBr): ṽ = 3032 (w), 2215 (m), 1656 (s), 1613 (vs), 1591 (s), 1513 (w), 1480 (m), 1452 (m), 1418 (w), 1357 (s), 1306 (w), 1217 (w), 1168 (m), 1114 (w), 967 (w), 851 (w) cm^{-1}. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 12.08 (s, 1 H, NH), 8.78 (s, 1 H, ArH), 8.32–8.00 (m, 1 H, ArH), 7.78 (d, J = 7.8 Hz, 2 H, ArH), 7.57 (s, 2 H, ArH), 7.43 (s, 2 H, ArH), 7.39 (t, J = 7.8 Hz, 2 H, ArH), 7.30 (t, J = 7.2 Hz, 2 H, ArH), 7.27 (t, J = 6.6 Hz, 2 H, ArH), 7.21 (t, J = 7.2 Hz, 3 H, ArH), 7.06–7.00 (m, 3 H, ArH), 6.91 (s, 2 H, ArH), 6.38–6.14 (m, 1 H, CH), 5.18 (s, 3 H, CH$_2$), 4.91 (s, 1 H, CH$_2$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 168.5, 136.5, 133.8, 131.3, 130.2, 130.0, 129.3, 128.7, 128.6, 128.5, 128.4, 128.3, 127.5, 127.3, 117.1, 111.9, 79.1, 59.7, 50.9, 42.6 ppm. HRMS (ESI): calcd. for $C_{40}H_{27}FN_5O_2$ [M – H]$^-$ 628.2144; found 628.2127.

3e: Yield: 80%. Yellow solid, m.p. 184–186 °C. IR (KBr): ṽ = 2948 (m), 2871 (w), 2206 (m), 1713 (m), 1654 (s), 1619 (vs), 1516 (m), 1487 (w), 1450 (m), 1352 (s), 1314 (w), 1277 (m), 1202 (m), 1186 (m), 1163 (w), 1124 (m), 1080 (w), 1003 (w), 950 (w), 804 (w) cm^{-1}. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 12.00 (s, 1 H, NH), 8.64 (s, 1 H, ArH), 8.32–7.99 (m, 1 H, ArH), 7.81–7.73 (m, 2 H, ArH), 7.54 (d, J = 7.2 Hz, 2 H, ArH), 7.27 (s, 4 H, ArH), 7.15 (t, J = 7.8 Hz, 2 H, ArH), 7.00–6.92 (m, 5 H, ArH), 6.52–6.25 (m, 1 H, ArH), 5.21 (s, 1 H, CH$_2$), 4.82 (d, J = 13.8 Hz, 1 H, CH$_2$), 3.69 (s, 2 H, CH$_2$), 2.03 (s, 3 H, CH$_3$), 1.66 (t, J = 6.0 Hz, 2 H, CH$_2$), 1.38–1.35 (m, 2 H, CH$_2$), 0.94 (t, J = 7.2 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 165.7, 135.4, 134.4, 130.6, 129.9, 129.8, 129.3, 129.2, 128.4, 128.3, 120.4, 113.8, 108.7, 72.8, 60.3, 51.7, 29.6, 20.9, 19.6, 13.6 ppm. HRMS (ESI): calcd. for $C_{38}H_{32}N_5O_2$ [M – H]$^-$ 590.2549; found 590.2532.

3f: Yield: 67%. Yellow solid, m.p. 196–198 °C. IR (KBr): ṽ = 2958 (w), 2871 (w), 2216 (m), 1656 (s), 1612 (vs), 1591 (w) 1513(s), 1476 (s), 1451 (w), 1419 (m), 1351 (m), 1311 (m), 1279 (m), 1250 (m), 1210 (w), 1192 (w), 1144 (w), 1124 (w), 1082 (w), 1049 (w), 1026 (w), 1002 (w), 948 (w), 875 (w) cm^{-1}. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 12.06 (s, 1 H, NH), 8.76 (s, 1 H, ArH), 8.18–7.98 (m, 1 H, ArH), 7.78 (s, 2 H, ArH), 7.68–7.56 (m, 2 H, ArH), 7.35–7.32 (m, 1 H, ArH), 7.27 (t, J = 6.6 Hz, 3 H, ArH), 7.20 (t, J = 7.2 Hz, 4 H, ArH), 7.07–6.98 (m, 2 H, ArH), 6.94–6.86 (m, 1 H, ArH), 6.60–6.33 (m, 1 H, CH), 5.13–5.12 (m, 1 H, CH$_2$), 4.86 (d, J = 14.4 Hz, 1 H, CH$_2$), 3.93 (s, 2 H, CH$_2$), 1.69 (s, 2 H, CH$_2$), 1.42–1.38 (m, 2 H, CH$_2$), 0.97 (t, J = 7.2 Hz, 3 H, CH$_3$) ppm. HRMS (ESI): calcd. for $C_{37}H_{29}ClN_5O_2$ [M – H]$^-$ 610.2015; found 610.2009.

3g: Yield: 73%. Yellow solid, m.p. 178–180 °C. IR (KBr): ṽ = 2932 (w), 2216 (m), 1655 (s), 1614 (vs), 1591 (s), 1514 (w), 1481 (m), 1453 (m), 1418 (w), 1353 (s), 1310 (w), 1281 (w), 1192 (m), 1137 (w), 953 (w), 852 (w) cm^{-1}. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 12.09 (s, 1 H, NH), 8.76–8.68 (m, 1 H, ArH), 8.18–7.97 (m, 1 H, ArH), 7.78 (s, 2 H, ArH), 7.65–7.55 (m, 2 H, ArH), 7.33 (d, J = 14.4 Hz, 1 H, ArH), 7.27 (s, 3 H, ArH), 7.19 (d, J = 7.8 Hz, 3 H, ArH), 7.03 (d, J = 6.0 Hz, 1 H, ArH), 6.97 (s, 2 H, ArH), 6.92–6.86 (m, 1 H, ArH), 6.37–6.12 (m, 1 H, CH), 5.14 (s, 1 H, CH$_2$), 4.88 (s, 1 H, CH$_2$), 3.92 (s, 2 H, CH$_2$), 1.69 (s, 2 H, CH$_2$), 1.40 (d, J = 6.6 Hz,2 H, CH$_2$), 0.96 (t, J = 7.2 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 168.3, 136.3, 136.2, 133.8, 131.2, 130.2, 130.1, 130.0, 129.9, 129.3, 129.2, 128.6, 128.4, 128.3, 128.2, 117.1, 111.9, 109.8, 109.7, 50.9, 29.6, 19.6, 13.7 ppm. HRMS (ESI): calcd. for $C_{37}H_{29}FN_5O_2$ [M – H]$^-$ 594.2284; found 594.2302.

3h: Yield: 67%. Yellow solid, m.p. 194–196 °C. IR (KBr): ṽ = 3031 (w), 2946 (w), 2206 (m), 1713 (m), 1653 (m), 1617 (vs), 1591 (s), 1568 (s), 1515 (w), 1486 (w), 1447 (m), 1358 (m), 1339 (m), 1311 (w), 1275 (m), 1250 (w), 1211 (w), 1188 (m), 1162 (w), 1124 (m), 1103 (w), 1079 (w), 1032 (w), 959 (w), 866 (w) cm^{-1}. ^{1}H NMR (600 MHz, CDCl$_3$): δ = 12.22 (s, 1 H, NH), 8.34 (s, 1 H, ArH), 8.19 (d, J = 1.8 Hz, 1 H, ArH), 8.05–7.85 (m, 1 H, ArH), 7.66–7.62 (m, 1 H, ArH), 7.53–7.46 (m, 2 H, ArH), 7.39 (s, 1 H, ArH), 7.33 (s, 6 H, ArH), 7.23 (s, 2 H, ArH), 7.12–7.01 (m, 2 H, ArH), 6.90 (t, J = 7.2 Hz, 1 H, ArH), 6.81–6.72 (m, 2 H, ArH), 6.65 (d, J = 7.8 Hz, 1 H, ArH), 6.59–6.51 (m, 1 H, CH), 5.09 (s, 3 H, CH$_2$), 4.74–4.72 (m, 1 H, CH$_2$), 4.24 (s, 2 H, CH$_2$), 2.09 (s, 3 H, CH$_3$), 1.29 (s, 3 H, CH$_3$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 168.4, 165.7, 136.7, 135.9, 135.3, 134.4, 130.6, 130.3, 130.2, 130.1, 130.0, 129.9, 129.8, 129.6, 129.5, 129.3, 129.2, 128.7, 128.6, 128.4, 127.4, 127.2, 120.5, 113.9, 109.1, 72.9, 60.3, 51.8, 42.4, 20.8, 14.3 ppm. HRMS (ESI): calcd. for $C_{43}H_{35}N_4O_4$ [M – H]$^-$ 671.2637; found 671.2656.

3i: Yield: 60%. Yellow solid, m.p. 198–200 °C. IR (KBr): ṽ = 3064 (w), 2929 (w), 2206 (m), 1710 (m), 1659 (s), 1615 (vs), 1570 (s), 1516 (w), 1496 (m), 1476 (m), 1450 (m), 1367 (m), 1340 (m), 1309

(w), 1274 (w), 1251 (w), 1206 (w), 1182 (w), 1124 (w), 1103 (w), 1081 (w), 1031 (w), 1004 (w), 958 (w), 893 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 12.04 (s, 1 H, NH), 8.64 (s, 1 H, ArH), 8.21–8.03 (m, 1 H, ArH), 7.93–7.76 (m, 2 H, ArH), 7.67–7.56 (m, 2 H, ArH), 7.38 (s, 4 H, ArH), 7.30 (d, J = 6.0 Hz, 4 H, ArH), 7.19 (t, J = 7.8 Hz, 3 H, ArH), 7.05 (s, 5 H, ArH), 6.61–6.29 (m, 1 H, CH), 5.12 (s, 3 H, CH$_2$), 4.88 (d, J = 14.4 Hz, 1 H, CH$_2$), 4.17–4.14 (m, 2 H, CH$_2$), 1.19 (t, J = 7.2 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 165.1, 136.4, 134.4, 130.7, 130.1, 129.4, 129.3, 128.7, 128.5, 127.5, 127.2, 124.9, 122.2, 60.4, 42.5, 14.3 ppm. HRMS (ESI): calcd. for $C_{42}H_{32}ClN_4O_4$ [M – H]$^-$ 691.2118; found 691.2111.

3j: Yield: 78%. Yellow solid, m.p. 194–196 °C. IR (KBr): $\tilde{\nu}$ = 2980 (w), 2207 (m), 1703 (s), 1657 (s), 1615 (vs), 1572 (s), 1514 (w), 1481 (m), 1451 (m), 1363 (m), 1275 (m), 1215 (w), 1168 (m), 1124 (w), 1101 (w), 1030 (w), 966 (w), 851 (w) cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 12.34 (s, 1 H, NH), 8.35 (s, 1 H, ArH), 8.17 (d, J = 5.4 Hz, 1 H, ArH), 8.03–7.85 (m, 1 H, ArH), 7.70–7.64 (m, 1 H, ArH), 7.56 (s, 2 H, ArH), 7.36 (d, J = 7.2 Hz, 1 H, ArH), 7.34 (s, 5 H, ArH), 7.28 (t, J = 6.6 Hz, 3 H, ArH), 7.13–7.02 (m, 3 H, ArH), 6.93 (t, J = 7.2 Hz, 1 H, ArH), 6.77 (s, 1 H, ArH), 6.65 (d, J = 4.2 Hz, 2 H, ArH), 6.51–6.40 (m, 1 H, CH), 5.11 (t, J = 14.4 Hz, 2 H, CH$_2$), 5.04 (d, J = 15.0 Hz, 1 H, CH$_2$), 4.72 (d, J = 13.2 Hz, 1 H, CH$_2$), 4.25 (s, 2 H, CH$_2$), 1.29 (s,3 H, CH$_3$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 165.1, 136.5, 135.0, 134.4, 130.6, 130.1, 130.0, 129.9, 129.3, 129.2, 128.7, 128.5, 127.5, 127.3, 113.8, 73.3, 60.3, 42.5, 14.3 ppm. HRMS (ESI): calcd. for $C_{42}H_{32}FN_4O_4$ [M – H]$^-$ 675.2413; found 675.2409.

3k: Yield: 85%. Yellow solid, m.p. 166–168 °C. IR (KBr): $\tilde{\nu}$ = 2951 (m), 2871 (w), 2209 (m), 1691 (s), 1654 (s), 1619 (vs), 1591 (s), 1517 (m), 1488 (w), 1451 (m), 1414 (w), 1354 (s), 1315 (w), 1276 (s), 1204 (m), 1165 (w), 1125 (m), 1102 (w), 1005 (w), 950 (w), 812 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 11.99 (s, 1 H, NH), 8.62 (s, 1 H, ArH), 8.17–7.99 (m, 1 H, ArH), 7.81–7.73 (m, 2 H, ArH), 7.64–7.55 (m, 2 H, ArH), 7.32 (s, 1 H, ArH), 7.28 (d, J = 6.0 Hz, 3 H, ArH), 7.15 (t, J = 7.8 Hz, 2 H, ArH), 7.00–6.97 (m, 2 H, ArH), 6.92 (s, 3 H, ArH), 6.52–6.24 (m, 1 H, CH), 5.20 (s, 1 H, CH$_2$), 4.81 (d, J = 14.4 Hz, 1 H, CH$_2$), 4.17–4.15 (m, 2 H, CH$_2$), 3.84 (t, J = 7.2 Hz, 2 H, CH$_2$), 2.07 (s, 3 H, CH$_3$), 1.66 (t, J = 6.6 Hz, 2 H, CH$_2$), 1.38–1.34 (m, 2 H, CH$_2$), 1.21 (t, J = 7.2 Hz, 3 H, CH$_3$), 0.94 (t, J = 7.8 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 165.2, 135.4, 134.4, 130.5, 130.0, 129.9, 129.8, 129.3, 128.4, 120.4, 113.9, 108.6, 73.1, 60.3, 29.6, 20.9, 19.6, 14.3, 13.6 ppm. HRMS (ESI): calcd. for $C_{40}H_{37}N_4O_4$ [M – H]$^-$ 637.2820; found 637.2819.

3l: Yield: 63%. Yellow solid, m.p. 208–210 °C. IR (KBr): $\tilde{\nu}$ = 3065 (w), 2930 (w), 2206 (m), 1707 (w), 1659 (s), 1617 (vs), 1573 (s), 1517 (w), 1478 (w), 1451 (m), 1351 (w), 1310 (s), 1277 (w), 1252 (m), 1208 (w), 1185 (w), 1123 (m), 1081 (m), 1047 (w), 1014 (w), 950 (w), 860 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 12.04 (s, 1 H, NH), 8.63 (s, 1 H, ArH), 8.26–7.98 (m, 1 H, ArH), 7.82 (s, 1 H, ArH), 7.75 (s, 1 H, ArH), 7.65 (s, 1 H, ArH), 7.56 (d, J = 7.8 Hz, 1 H, ArH), 7.33 (s, 1 H, ArH), 7.27 (s, 3 H, ArH), 7.17 (d, J = 7.2 Hz, 4 H, ArH), 7.01–6.95 (m, 3 H, ArH), 6.60–6.30 (m, 1 H, CH), 5.21 (s, 1 H, CH$_2$), 4.83 (d, J = 14.4 Hz, 1 H, CH$_2$), 4.17–4.16 (m, 1 H, CH$_2$), 3.88 (s, 2 H, CH$_2$), 3.69 (s, 1 H, CH$_2$), 1.66 (s, 2 H, CH$_2$), 1.36 (d, J = 6.6 Hz, 2 H, CH$_2$), 1.21 (t, J = 7.2 Hz, 3 H, CH$_3$), 0.94 (d, J = 7.2 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 168.1, 165.1, 136.3, 136.2, 135.0, 134.4, 130.6, 130.2, 130.1, 130.0, 129.9, 129.8, 129.3, 129.1, 128.6, 128.5, 128.4, 128.3, 128.2, 127.3, 125.3, 122.1, 120.9, 113.8, 73.3, 60.3, 51.8, 29.5, 19.5, 14.3, 13.6 ppm. HRMS (ESI): calcd. for $C_{39}H_{34}ClN_4O_4$ [M – H]$^-$ 657.2234; found 657.2266.

3m: Yield: 68%. Yellow solid, m.p. 196–198 °C. IR (KBr): $\tilde{\nu}$ = 2952 (w), 2929 (w), 2206 (m), 1658 (s), 1617 (vs), 1573 (s), 1516 (w), 1477 (w), 1451 (m), 1415 (w), 1351 (m), 1309 (w), 1277 (m), 1252 (w), 1208 (w), 1192 (m), 1123 (m), 1081 (w), 1047 (w), 1013 (w), 950 (w), 860 (w) cm^{-1}. ^1H NMR (600 MHz, [D$_6$]DMSO): δ = 12.07 (s, 1 H, NH), 8.63 (s, 1 H, ArH), 8.18–7.99 (m, 1 H, ArH), 7.82–7.75 (m, 2 H, ArH), 7.65–7.55 (m, 2 H, ArH), 7.33 (s, 1 H, ArH), 7.28 (d, J = 5.4 Hz, 3 H, ArH), 7.17 (t, J = 7.8 Hz, 3 H, ArH), 7.01–6.96 (m, 4 H, ArH), 6.38–6.07 (m, 1 H, CH), 5.21 (s, 1 H, CH$_2$), 4.84 (d, J = 14.4 Hz, 1 H, CH$_2$), 4.18–4.15 (m, 2 H, CH$_2$), 3.87 (t, J = 7.2 Hz, 2 H, CH$_2$), 1.66 (t, J = 6.6 Hz, 2 H, CH$_2$), 1.39–1.35 (m, 2 H, CH$_2$), 1.21 (t, J = 7.2 Hz, 3 H, CH$_3$), 0.95 (t, J = 7.2 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 168.3, 165.1, 136.2, 135.0, 134.4, 130.6, 130.1, 130.0, 129.9, 129.3, 128.4, 128.3, 121.6, 121.5, 113.8, 109.7, 73.3, 60.3, 29.5, 19.5, 14.3, 13.6 ppm. HRMS (ESI): calcd. for $C_{39}H_{34}FN_4O_4$ [M – H]$^-$ 641.2543; found 641.2564.

Supporting Information (see footnote on the first page of this article): Molecular structure of zwitterionic salt **3f**, general procedure for the preparation of products (**3a**–**m**) from three-component reactions, ^1H and ^{13}C NMR spectra.

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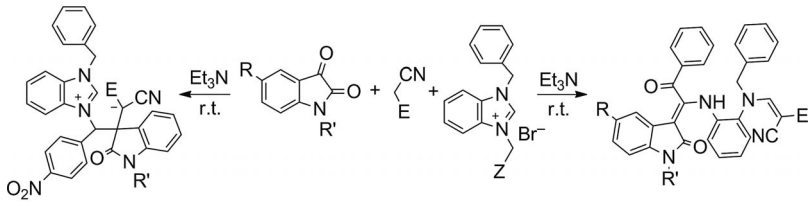

E = CN, CO_2Et; Z = *p*-$NO_2C_6H_4$

E = CN, CO_2Et; Z = C_6H_5CO

The three-component reactions of *N*-benzylbenzimidazolium salts, isatins, and malononitrile or ethyl cyanoacetate showed very interesting molecular diversity depending on the structures of the benzimidazolium salts: zwitterionic or ring-opened products were obtained.

Keywords: Multicomponent reactions / Zwitterions / Nitrogen heterocycles / Molecular diversity

