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The Synthesis of Benzo[*f*]isoindole-1,3-dicarboxylates via an I_2-Induced 1,3-Dipolar Cycloaddition Reaction

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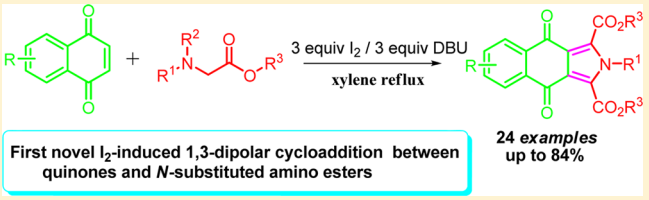
Supporting Information

ABSTRACT: An I_2-induced 1,3-dipolar cycloaddition reaction has been developed for the synthesis of benzo[*f*]-isoindole-1,3-dicarboxylates from quinones and N-substituted amino esters. The reaction proceeds in good to excellent yields in one step from 3 equiv of amino ester to react with the quinone structure. The utility of this transformation has been highlighted by its use for the construction of benzo[*f*]-isoindole-1,3-dicarboxylates, which have been identified in natural products exhibiting important biological activities.



INTRODUCTION

Pyrroles and their derivatives are an important class of heterocyclic compounds that can be found in a wide range of natural products and bioactive molecules.[1] The benzo[*f*]-isoindole framework is the core structure in a large number of natural products exhibiting important biological activities, such as azamonosporascone,[2] Reniera isoindole alkaloid,[3] GR30921 X,[4] and bhimamycin C and D,[1c,5] which show activities against *Monosporascus cannonballus*, bacteria, solid tumors, and human ovarian cancer cell lines, respectively (Figure 1). Furthermore, the benzo[*f*]isoindole framework frequently appears in a number of other anticancer compounds.[5b]

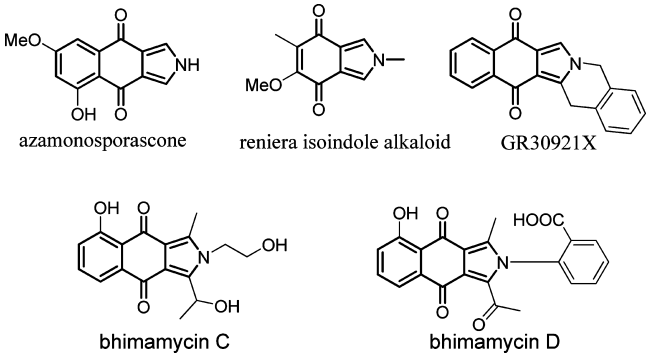


Figure 1. Representative examples of natural products.

Interest in the chemistry of benzo[*f*]isoindoles has continued unabated for many years because of their wide range of potential applications as biologically active agents and their role as important intermediates in organic synthesis.[6] The 1,3-dipolar cycloaddition is a powerful tool for the construction of five-membered heterocycles.[7] Since it was first reported by Huisgen in the 1960s,[7a] the chemistry of the 1,3-dipolar cycloaddition has evolved considerably, and a variety of different 1,3-dipoles have been discovered. Major advances in this area of synthetic chemistry include the Prato reaction,[7b,8] click chemistry established by Sharpless,[9] 1,3-dipolar cycloadditions of diazo compounds for the preparation of pyrazoles,[10] and the reactions of nitrones with alkenes.[11] Because of their prevalence in a large number of natural alkaloids, pharmaceuticals, and biologically active compounds, a variety of interesting compounds containing the isoindole structure have been constructed. Wang and co-workers[12] recently reported a highly efficient approach for the synthesis of pyrrolo[2,1-*a*]isoquinolines using a copper(II)-based catalyst. More recently, Xiao[13] published a photocatalytic strategy for the construction of pyrrolo[2,1-*a*]isoquinolines. Furthermore, a method for the orthogonal synthesis of isoindole and isoquinoline derivatives from organic azides has recently been developed.[14]

As part of our continued interest in developing methods for the functionalization of quinone structures,[15] we herein report an efficient one-pot method for the synthesis of novel benzo[*f*]isoindole-1,3-dicarboxylates via the 1,3-dipolar cycloaddition reaction of quinones and N-substituted amino esters. The resulting products contain two ester groups, which could be used as handles for the introduction of a variety of different functional groups and the construction of a range of useful building blocks. To the best of our knowledge, there have been no previous reports concerning the reaction of quinones with N-substituted amino esters for the direct construction of isoindole structures, and this report represents the first thorough investigation of this reaction.

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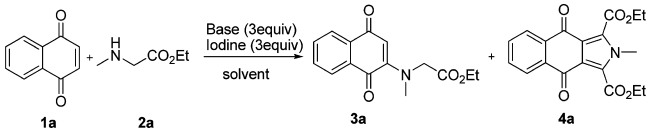
RESULTS AND DISCUSSION

Our initial investigations were focused on examining the feasibility of the addition reaction of sarcosine ethyl ester (**2a**) to 1,4-naphthoquinone (**1a**) in the presence of molecular iodine, with the aim of optimizing the reaction conditions to the extent that they could subsequently be applied to a variety of different amino esters. During the optimization process, benzo[*f*]isoindole-1,3-dicarboxylate (**4a**) was detected by GC−MS and NMR as an unexpected product, albeit in low yield, when an excess of iodine (3 equiv) was used in the reaction (Table 1, entry 1). The occurrence of compound **4a** prompted us to further investigate the reaction between quinones and *N*-alkylamino esters to elucidate the mechanism for the formation of this unexpected product. Subsequent experimentation revealed that the yield of **4a** could be increased to 18% when **1a** was added to the reaction following the premixing of **2a**, $NaHCO_3$, and iodine over a 1 h period (Table 1, entry 2). To further improve the yield of the desired product and make the reaction synthetically valuable, we proceeded to optimize some of the reaction conditions, including the solvent, base, and ratio of reactants. As shown in Table 1, although **4a** was obtained in 20% yield in the presence of $NaHCO_3$, the yield increased to 35% when DBU was used as the base in refluxing toluene (Table 1, entry 3). Some other common iodine-addition initiation systems were also investigated, including I_2/*t*-BuOCl and I_2/AgOAc, but these systems did not provide any improvement over molecular iodine only (Table 1, entries 4 and 5). A variety of different solvents were also screened for their effect on the production of compound **4a**. The results of these screening experiments revealed that refluxing solutions of CH_2Cl_2, $CHCl_3$, dichloroethane, tetrachloroethane (120 °C), and tetrachloroethane (146 °C) gave **4a** in yields of 8, 28, 67, 87, and 94%, respectively. Pleasingly, the yield of **4a** was also high when the reaction was conducted in refluxing xylene (Table 1, entry 12). When the reaction temperature was lowered to 80 or even 100 °C in this solvent, the yield of **4a** was reduced to 20 or 28%, respectively (Table 1, entries 13 and 14). On the basis of these results, it was clear that both solvent and temperature were key factors for this reaction and that the use of a nonpolar solvent and a high reaction temperature favored a higher yield of **4a**. Thus, the yield of the isolated product had been significantly optimized to 84% by changing the reaction conditions. However, the yield of **4a** dropped to 7% without iodine under the optimal conditions (Table 1, entry 15) and also decreased to 75% under nitrogen conditions (Table 1, entry 16).

Table 1. Optimization of the Reaction Conditions



				yield (%)[g]	
entry[a]	base	solvent	*T* (°C)	**3a**	**4a**
1[b]	$NaHCO_3$	CH_3CN	80	50	3
2	$NaHCO_3$	CH_3CN	80	20	18
3	DBU	toluene	110	15	35
4[c]	$NaHCO_3$	toluene	110	9	14
5[d]	$NaHCO_3$	toluene	110	0	0
6	DBU	CH_2Cl_2	40	40	8
7	DBU	$CHCl_3$	60	16	28
8	DBU	CH_3CN	80	20	36
9	DBU	dichloroethane	83	5	67
10	DBU	tetrachloroethane	120	0	87
11	DBU	tetrachloroethane	146	0	94
12	DBU	xylene	140	0	93
13	DBU	xylene	80	47	20
14	DBU	xylene	100	38	28
15[e]	DBU	xylene	140	42	7
16[f]	DBU	xylene	140	0	75

[a]Reaction conditions: the mixture of **2a** (3.0 mmol), base (3.0 mmol), and iodine (3.0 mmol) in solvent (5.0 mL) was stirred for 1 h at room temperature under air conditions; **1a** (1.0 mmol) was then added, and the mixture was stirred for 8 h at refluxing temperature. [b]All of the raw materials were added together. [c]3 equiv of *t*-BuOCl was added. [d]3 equiv of AgOAc was added. [e]Without iodine. [f]Under nitrogen conditions. [g]HPLC yields.

With the optimized conditions in hand, we then proceeded to evaluate the scope of the reaction using a wide range of *N*-alkylamino esters and quinones (Table 2). The desired benzo[*f*]isoindole-1,3-dicarboxylate products **4** were formed successfully in good to excellent yields in all cases. Furthermore, when *N*-alkylamino esters **2a−h** were employed in the reaction, the yield of **4** was reduced as the size of the substituent group on the N atom increased, indicating that steric repulsion at the N atom had an impact on the progress of the reaction (Table 2, entries 1−4 and 9−12). Interestingly, analysis of the reaction mixture by GC−MS revealed the presence of methylamine, indicating that a deamination process was involved in the formation of **4**, and it was proposed that the reduction in the yield of **4** that occurred as the size of the substituent group on the N atom increased in **2a−h** was related to the difficulty associated with the removal of the amine as the size of the group increased. It is noteworthy that although the ethyl, propyl, isopropyl, butyl, and isoamyl esters investigated in the current study all gave the corresponding products, the yields were slightly reduced in the isopropyl and isoamyl esters because of steric hindrance (Table 2, entries 5−8 and 13−16). The naphthoquinone derivatives 1,4-anthraquinone (**1b**) and 5-nitro-1,4-naphthoquinone (**1c**) were also subjected to the optimized cyclization reaction conditions using the *N*-alkylamino esters and gave the corresponding benzo[*f*]-isoindole-1,3-dicarboxylate products **4i−t** in good yield (Table 2, entries 9−20).

The presence of a hydroxyl substituent is invariably described as being critical to the activities of the bioactive benzo[*f*]-isoindole-4,9-dione molecules reported in the literature.[1c,5] With this in mind, we investigated the application of the current methodology to 5-hydroxy-1,4-naphthoquinone (**1d**) with a range of different N-substituted amino esters (**2a−d**). The reactions gave the desired products **4u−x** in yields ranging from 10 to 25% (Table 2, entries 21−24). Different reaction conditions using higher temperatures (150 °C, 160 °C), other solvents (DMSO, DMF), 4 equiv of amino ester, or different bases were tried, but the results were not better. Additionally, the quinones were entirely consumed and several byproducts were formed, such as the addition product of quinone and amino ester.

The N,N-disubstituted amino ester **2i** reacted with 1,4-naphthoquinone **1a** and 1,4-anthraquinone **1b** in a similar manner to the N-substituted amino esters, giving products **4a** and **4i** in yields of 46 and 34%, respectively (Table 2, entries 25 and 26).

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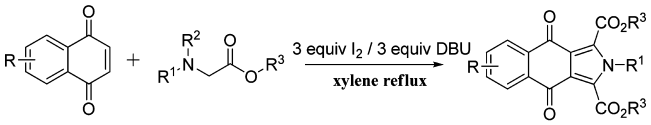
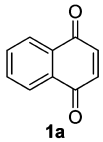
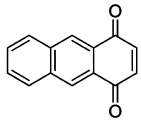
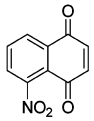
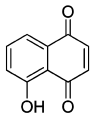
Table 2. Substrate Scope



1 2 4

entry	1	2	R^1	R^2	R^3	4	yield %[a]
1		**2a**	Me	H	Et	**4a**	84
2		**2b**	Et	H	Et	**4b**	60
3		**2c**	n-Pr	H	Et	**4c**	51
4		**2d**	n-Bu	H	Et	**4d**	32
5		**2e**	Me	H	n-Pr	**4e**	73
6	**1a**	**2f**	Me	H	i-Pr	**4f**	42
7		**2g**	Me	H	n-Bu	**4g**	60
8		**2h**	Me	H	Isoamyl	**4h**	44
9		**2a**	Me	H	Et	**4i**	73
10		**2b**	Et	H	Et	**4j**	63
11		**2c**	n-Pr	H	Et	**4k**	57
12		**2d**	n-Bu	H	Et	**4l**	48
13		**2e**	Me	H	n-Pr	**4m**	74
14	**1b**	**2f**	Me	H	i-Pr	**4n**	52
15		**2g**	Me	H	n-Bu	**4o**	47
16		**2h**	Me	H	Isoamyl	**4p**	40
17		**2a**	Me	H	Et	**4q**	55
18		**2b**	Et	H	Et	**4r**	46
19		**2c**	n-Pr	H	Et	**4s**	40
20	**1c**	**2d**	n-Bu	H	Et	**4t**	35
21		**2a**	Me	H	Et	**4u**	25
22		**2b**	Et	H	Et	**4v**	21
23		**2c**	n-Pr	H	Et	**4w**	16
24	**1d**	**2d**	n-Bu	H	Et	**4x**	10
25	**1a**	**2i**	Me	Me	Et	**4a**	46
26	**1b**	**2i**	Me	Me	Et	**4i**	34
27	**1a**	**2j**	Phenyl	H	Et	**4y**	-
28	**1a**	**2k**	Benzyl	H	Et	**4z**	Trace

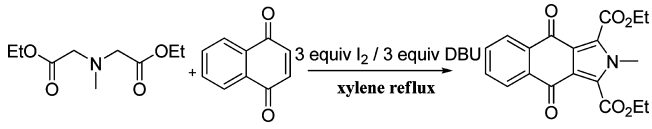
[a]Isolated yields.

Unfortunately, however, the reaction did not proceed as expected when *N*-phenylglycine ethyl ester (**2j**) was used in the reaction (Table 2, entry 27), and the desired benzo[*f*]-isoindole-1,3-dicarboxylate product **4y** was not observed. When *N*-benzylglycine ethyl ester (**2k**) was employed in the reaction (Table 2, entry 28), only a trace amount of the desired product **4z** was observed by GC−MS. Furthermore, several byproducts were formed, which could not be separated and characterized.

The structure of **4i** was unequivocally determined by single-crystal X-ray crystallographic analysis.[16]

Additionally, we formed diethyl 2,2′-(methylazanediyl)-diacetate (**2l**) and successfully reacted it with 1,4-naphthoquinone to obtain **4a** in 86% yield under the optimal conditions (Scheme 1).

Scheme 1. Reaction of 1,4-Naphthoquinone with Diethyl 2,2′-(Methylazanediyl)diacetate (2l)



2l **1a** **4a 86%**

On the basis of the results of the current study as well as reports from the literature, we have proposed a mechanism to account for the products observed in the current reaction (Scheme 2). Sarcosine ethyl ester (**2a**) reacts with I_2 to afford the intermediate α-iodosarcosine ethyl ester **5**.[17] Subsequent addition of **2a** to **5** in the presence of DBU gives rise to the dimeric species **6** with the loss of hydrogen iodide. Intermediate **6**, together with the HI generated from the reaction, then gives ammonium salt **7**,[18] which is converted to 1,3-dipole **8** through the loss of methylamine and HI. The subsequent reaction of **8** with naphthoquinone **1a** through a 1,3-dipolar cycloaddition reaction gives rise to intermediate **9** together with its isomer **10** through aromatization. The final product **4a** is obtained through O_2-mediated oxidation in the presence of I_2. In our reaction system, intermediate **5** is an active intermediate, and addition of **2a** to **5** gives **6**, which is then converted to **4a**. There is no need for **2a** to be completely converted to **5**, so the formation of cycloadduct **9** needs 1 equiv of **1a**, 2 equiv of **2a**, and 1 equiv of iodine. The residual 2 equiv of iodine could oxidize molecules **9** and **10** to give the target **4a**. Additionally, oxygen has a role to play in oxidizing molecules **9** and **10** to give the target **4a**. Thus, 3 equiv of iodine is enough and a little excess in order to get a good yield. GC−MS analysis of the reaction mixture of **2a** with a stoichiometric amount of I_2 revealed the formation of the dimeric species **6** (molecular ion peak at m/z 231.3 $[M - H]^+$), as well as the 1,3-dipole **8** (molecular ion peak at m/z 200.3 $[M - H]^+$). The mechanism was also subsequently supported by the successful capture of methylamine (see the Supporting Information).

CONCLUSION

In summary, we have developed a novel one-pot protocol for the synthesis of benzo[*f*]isoindole-1,3-dicarboxylates via the 1,3-dipolar cycloaddition reaction of quinones with 3 equiv of N-substituted amino esters induced by iodine in refluxing xylene. We believe these results will be of importance for the development of new reactions involving the use of N-substituted amino esters. The method incorporating a 1,3-dipolar cycloaddition provides a novel strategy for the synthesis of interesting isoindoles that could potentially be used as building blocks for natural products. Studies toward clarifying the reaction mechanism and developing further applications of this transformation are currently underway in our laboratory.

EXPERIMENTAL SECTION

General Information. All solvents were purified and dried using standard methods prior to use. Commercially available reagents were used without further purification. ^{1}H NMR spectra were recorded on an NMR instrument operated at 500 MHz. Chemical shifts are reported in parts per million with the solvent resonance as the internal standard ($CDCl_3$, δ 7.26). ^{13}C NMR spectra were recorded on an

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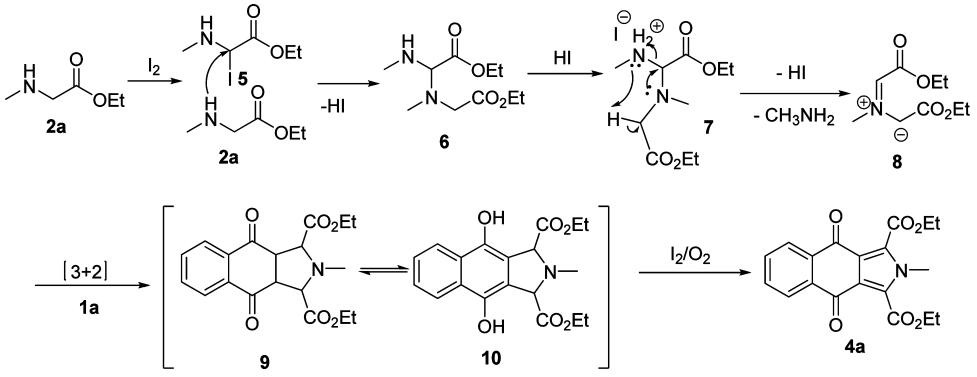
Scheme 2. Possible Reaction Mechanism



NMR instrument operated at 125 MHz with complete proton decoupling. Chemical shifts are reported in parts per million with the solvent resonance as the internal standard ($CDCl_3$, δ 77.1). MS and HRMS were measured in EI or ESI mode, and the mass analyzer of the HRMS was TOF. Thin-layer chromatography was performed on precoated glass-back plates and visualized with UV light at 254 nm. Flash column chromatography was performed on silica gel.

General Procedure for the Synthesis of 4. DBU (3.0 mmol, 3.0 equiv) and iodine (3.0 mmol, 3.0 equiv) were added sequentially to a solution of amino ester **2** (3.0 mmol, 3.0 equiv) in xylene (5.0 mL), and the resulting mixture was stirred for 1 h at ambient temperature in air. Quinone **1** (1.0 mmol, 1.0 equiv) was then added to the reaction, and the resulting mixture was stirred for 8 h at reflux. The reaction was followed by GC−MS and TLC. Upon completion of the reaction, the solvent was removed under vacuum, and the resulting crude product was purified by chromatography on silica gel eluted with CH_2Cl_2 to obtain **4** as a yellow solid.

Diethyl 2-Methyl-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4a). Yield 84% (0.298 g); mp 122−123 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (dd, J_1 = 3.0 Hz, J_2 = 7.5 Hz, 2H), 7.73 (dd, J_1 = 3.5 Hz, J_2 = 7.5 Hz, 2H), 4.55 (q, J = 7.5 Hz, 4H), 3.93 (s, 3H), 1.50 (t, J = 6.5 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.7 (2C), 160.8 (2C), 134.8 (2C), 133.4 (2C), 128.2 (2C), 127.1 (2C), 121.8 (2C), 62.7 (2C), 34.7, 14.0 (2C). IR (KBr): 2985, 1720, 1706, 1667, 1594, 1548, 1517, 1474, 1466, 1147, 1025, 1008, 800, 744, 703 cm^{-1}. GC−MS m/z: 355.1 $[M]^+$, 356.0, 310.3, 296.6, 237.5, 210.5, 206.6. HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{18}NO_6$ $[M + H]^+$ 356.1129, found 356.1131.

Diethyl 2-Ethyl-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4b). Yield 60% (0.222 g); mp 109−110 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (dd, J_1 = 3.5 Hz, J_2 = 7.5 Hz, 2H), 7.69 (dd, J_1 = 3.5 Hz, J_2 = 7.0 Hz, 2H), 4.52 (q, J = 6.5 Hz, 4H), 4.33 (q, J = 7.0 Hz, 2H), 1.48−1.44 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.8 (2C), 161.0 (2C), 134.9 (2C), 133.3 (2C), 127.5 (2C), 126.9 (2C), 121.7 (2C), 62.5 (2C), 43.0, 16.5, 13.8 (2C). IR (KBr): 2985, 1716, 1678, 1594, 1546, 1505, 1436, 1280, 1145, 1044, 1014, 743, 709 cm^{-1}. GC−MS m/z: 370 $[M + H]^+$, 369.0 $[M]^+$, 342.2, 297.3, 296.2, 268.3, 197.3, 76.1. HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{19}NO_6Na$ $[M + Na]^+$ 392.1104, found 392.1112.

Diethyl 2-Propyl-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4c). Yield 51% (0.192 g); mp 104−105 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (dd, J_1 = 4.0 Hz, J_2 = 7.0 Hz, 2H), 7.71 (dd, J_1 = 3.5 Hz, J_2 = 6.0 Hz, 2H), 4.54 (q, J = 7.5 Hz, 4H), 4.28 (t, J = 8.0 Hz, 2H), 1.87−1.81 (m, 2H), 1.48 (t, J = 7.5 Hz, 6H), 0.94 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.8 (2C), 161.0 (2C), 134.9 (2C), 133.5 (2C), 127.7 (2C), 127.1 (2C), 121.8 (2C), 62.6 (2C), 49.0, 24.6, 13.8 (2C), 10.8. IR (KBr): 2968, 1728, 1668, 1594, 1512, 1471, 1421, 1317, 1264, 1225, 1143, 1005, 798, 743, 713 cm^{-1}. GC−MS m/z: 384.1 $[M + H]^+$, 383.0 $[M]^+$, 325.3, 311.5, 211.3. HRMS (ESI-TOF) m/z: calcd for $C_{21}H_{21}NO_6Na$ $[M + Na]^+$ 406.1261, found 406.1265.

Diethyl 2-Butyl-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4d). Yield 32% (0.127 g); mp 99−100 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (dd, J_1 = 3.0 Hz, J_2 = 6.0 Hz, 2H), 7.72 (dd, J_1 = 3.0 Hz, J_2 = 5.5 Hz, 2H), 4.54 (q, J = 6.5 Hz, 4H), 4.31 (t, J = 8.0 Hz, 2H), 1.81−1.75 (m, 2H), 1.49 (t, J = 6.5 Hz, 6H), 1.38−1.32 (m, 2H), 0.94 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.9 (2C), 161.1 (2C), 134.9 (2C), 133.4 (2C), 127.7 (2C), 127.1 (2C), 121.7 (2C), 62.7 (2C), 47.6, 33.5, 19.8, 14.0 (2C), 13.5. IR (KBr): 2927, 1728, 1673, 1467, 1368, 1261, 1227, 1201, 1097, 1017, 800 cm^{-1}. GC−MS m/z: 398.5 $[M + H]^+$, 397.4 $[M]^+$, 352.5, 325.5, 324.5 (100%), 296.8, 282.7, 254.7, 224.5. HRMS (ESI-TOF) m/z: calcd for $C_{22}H_{23}NO_6Na$ $[M + Na]^+$ 420.1423, found 420.1427.

Dipropyl 2-Methyl-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4e). Yield 73% (0.280 g); mp 100−101 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (dd, J_1 = 3.5 Hz, J_2 = 5.5 Hz, 2H), 7.71 (dd, J_1 = 3.5 Hz, J_2 = 6.0 Hz, 2H), 4.43 (q, J = 7.0 Hz, 4H), 3.91 (s, 3H), 1.90−1.86 (m, 4H), 1.07 (t, J = 14.5 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.6 (2C), 161.1 (2C), 135.0 (2C), 133.4 (2C), 128.2 (2C), 127.1 (2C), 121.8 (2C), 68.2 (2C), 34.6, 21.7 (2C), 10.2 (2C). IR (KBr): 2965, 1725, 1674, 1619, 1505, 1448, 1281, 1182, 1035, 918, 760 cm^{-1}. GC−MS m/z: 383.0 $[M]^+$, 325.3, 311.4, 299.3, 269.3, 238.3, 211.3. HRMS (ESI-TOF) z: calcd for $C_{21}H_{22}NO_6$ $[M + H]^+$ 384.1442, found 384.1445.

Diisopropyl 2-Methyl-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4f). Yield 42% (0.161 g); mp 116−117 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (dd, J_1 = 3.0 Hz, J_2 = 5.5 Hz, 2H), 7.71 (dd, J_1 = 3.5 Hz, J_2 = 6.0 Hz, 2H), 5.42−5.37 (m, 2H), 3.90 (s, 3H), 1.48 (d, J = 6.0 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.6 (2C), 160.4 (2C), 135.0 (2C), 133.3 (2C), 128.4 (2C), 127.1 (2C), 121.4 (2C), 70.8 (2C), 34.4, 21.5 (4C). IR (KBr): 2980, 1732, 1716, 1678, 1668, 1558, 1523, 1455, 1283, 1263, 1095, 1004, 796, 705 cm^{-1}. GC−MS m/z: 384.2 $[M + H]^+$, 383.2 $[M]^+$, 325.2, 299.3, 269.5, 239.3, 211.3, 43.2. HRMS (ESI-TOF) m/z: calcd for $C_{21}H_{22}NO_6$ $[M + H]^+$ 384.1442, found 384.1444.

Dibutyl 2-Methyl-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4g). Yield 60% (0.247 g); mp 91−92 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (dd, J_1 = 3.0 Hz, J_2 = 5.0 Hz, 2H), 7.73 (dd, J_1 = 3.0 Hz, J_2 = 5.5 Hz, 2H), 4.48 (t, J = 7.0 Hz, 4H), 3.92 (s, 3H), 1.87−1.81 (m, 4H), 1.55−1.47 (m, 4H), 1.01 (t, J = 8.0 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.8 (2C), 161.0 (2C), 134.9 (2C), 133.4 (2C), 127.7 (2C), 127.0 (2C), 121.7 (2C), 66.6 (2C), 47.6, 33.5 (2C), 19.7 (2C), 14.0, 13.5. IR (KBr): 2926, 1728, 1642, 1578, 1466, 1443, 1322, 1289, 1241, 1204, 1155, 602 cm^{-1}. GC−MS m/z: 412.3 $[M + H]^+$, 411.3 $[M]^+$, 367.3, 339.3, 338.5 (100%), 325.5, 238.3, 41.2. HRMS (ESI-TOF) m/z: calcd for $C_{23}H_{26}NO_6$ $[M + H]^+$ 412.1755, found 412.1757.

Diisopentyl 2-Methyl-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4h). Yield 44% (0.193 g); mp 80−81 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (dd, J_1 = 3.5 Hz, J_2 = 5.5 Hz, 2H), 7.70 (dd, J_1 = 3.5 Hz, J_2 = 6.0 Hz, 2H), 4.50 (t, J = 7.0 Hz, 4H), 3.91 (s, 3H), 1.84−1.79 (m, 2H), 1.78−1.72 (m, 4H), 0.99 (d, J = 6.5 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.7 (2C), 161.0 (2C), 134.8 (2C), 133.5 (2C), 128.1 (2C), 127.0 (2C), 121.8 (2C), 71.3 (2C), 65.4 (2C), 37.0, 24.9 (2C), 22.4 (4C). IR (KBr): 2960, 1727, 1674, 1596, 1465, 1308, 1263, 1227, 1147, 1005, 707 cm^{-1}. GC−MS m/z:

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440.4 $[M + H]^+$, 439.4 $[M]^+$, 370.7, 353.7, 352.8 (100%), 300.5, 282.5, 238.3, 41.2. HRMS (ESI-TOF) m/z: calcd for $C_{25}H_{29}NO_6Na$ $[M + Na]^+$ 462.1887, found 462.1891.

Diethyl 2-Methyl-2*H*-naphtho[2,3-*f*]isoindole-4,11-dione-1,3-dicarboxylate (4i). Yield 73% (0.296 g); mp 176−177 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): 8.73 (s, 2H), 8.04 (dd, J_1 = 3.0 Hz, J_2 = 6.5 Hz 2H), 7.65 (dd, J_1 =3.5 Hz, J_2 = 6.0 Hz, 2H), 4.57 (q, J = 7.0 Hz, 4H), 3.93 (s, 3H), 1.52 (t, J = 7.5 Hz, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) 178.6 (2C), 161.0 (2C), 134.8 (2C), 131.3 (2C), 130.0 (2C), 129.3 (2C), 129.2 (2C), 128.3 (2C), 122.6 (2C), 62.7 (2C), 34.7 (1C), 14.1 (2C). IR (KBr): 2927, 1720, 1705, 1674, 1621, 1513, 1472, 1293, 1242, 1208, 1186, 1107, 1038, 1022, 762, 747 cm^{-1}. GC−MS m/z: 405.9 $[M + H]^+$, 361.2, 333.2, 289.3, 288.4, 262.3, 261.3. Anal. Calcd for $C_{23}H_{19}NO_6$: C, 68.14; H, 4.72; N, 3.46. Found: C, 68.04; H, 4.88; N, 3.26.

Diethyl 2-Ethyl-2*H*-naphtho[2,3-*f*]isoindole-4,11-dione-1,3-dicarboxylate (4j). Yield 63% (0.264 g); mp 134−135 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73 (s, 2H), 8.03 (dd, J_1 = 3.5 Hz, J_2 = 6.0 Hz, 2H), 7.64 (dd, J_1 = 3.5 Hz, J_2 = 6.5 Hz, 2H), 4.57 (q, J = 6.5 Hz, 4H), 4.36 (q, J = 7.5 Hz, 2H), 1.53−1.49 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.7 (2C), 161.2 (2C), 134.8 (2C), 131.3 (2C), 130.0 (2C), 129.2 (2C), 129.1 (2C), 127.5 (2C), 122.6 (2C), 62.6 (2C), 43.1, 16.8, 14.0 (2C). IR (KBr): 2978, 1725, 1674, 1619, 1437, 1281, 1234, 1185, 1038, 1015, 862, 759 cm^{-1}. GC−MS m/z: 419.9 $[M + H]^+$, 419.0 $[M]^+$, 390.2, 375.1, 346.2, 318.3, 300.2, 274.4. HRMS (ESI-TOF) m/z: calcd for $C_{24}H_{22}NO_6$ $[M + H]^+$ 420.1442, found 420.1449.

Diethyl 2-Propyl-2*H*-naphtho[2,3-*f*]isoindole-4,11-dione-1,3-dicarboxylate (4k). Yield 57% (0.247 g); mp 110−111 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.67 (s, 2H), 7.99 (dd, J_1 = 3.0 Hz, J_2 = 6.5 Hz, 2H), 7.60 (dd, J_1 = 3.0 Hz, J_2 = 6.5 Hz, 2H), 4.56 (q, J = 7.0 Hz, 4H), 4.28 (q, J = 7.5 Hz, 2H), 1.88−1.81 (m, 2H), 1.50 (q, J = 7.5 Hz, 6H), 0.95 (q, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.6 (2C), 161.1 (2C), 134.7 (2C), 131.2 (2C), 129.9 (2C), 129.2 (2C), 129.1 (4C), 127.8 (2C), 122.5 (2C), 62.7 (2C), 49.2, 24.7, 14.0 (2C), 10.9. IR (KBr): 2965, 1736, 1670, 1602, 1501, 1440, 1282, 1187, 1041, 1011, 917, 761 cm^{-1}. GC−MS: m/z: 433.8 $[M + H]^+$, 432.9 $[M]^+$, 404.2, 388.3, 347.2, 346.3, 300.2, 41.0. HRMS (ESI-TOF) m/z: calcd for $C_{25}H_{24}NO_6$ $[M + H]^+$ 434.1598, found 434.1606.

Diethyl 2-Butyl-2*H*-naphtho[2,3-*f*]isoindole-4,11-dione-1,3-dicarboxylate (4l). Yield 48% (0.215 g); mp 100−101 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.69 (s, 2H), 8.00 (dd, J_1 = 3.0 Hz, J_2 = 6.0 Hz, 2H), 7.61 (dd, J_1 = 3.0 Hz, J_2 = 6.5 Hz, 2H), 4.56 (q, J = 7.5 Hz, 4H), 4.30 (q, J = 8.0 Hz, 2H), 1.82−1.76 (m, 2H), 1.51 (q, J = 7.0 Hz, 6H), 1.38−1.31 (m, 2H), 0.94 (q, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.6 (2C), 161.1 (2C), 134.67 (2C), 131.2 (2C), 129.9 (2C), 129.1 (4C), 127.7 (2C), 122.5 (2C), 62.7 (2C), 47.5, 33.4, 19.7, 14.0 (2C), 13.5. IR (KBr): 2961, 1735, 1705, 1677, 1619, 1435, 1305, 1273, 1236, 1182, 1033, 1020, 753 cm^{-1}. GC−MS m/z: 448.0 $[M + H]^+$, 446.9 $[M]^+$, 418.0, 402.1, 375.1, 374.3 (100%), 304.3, 41.0. HRMS (ESI-TOF) m/z: calcd for $C_{26}H_{26}NO_6$ $[M + H]^+$ 448.1755, found 448.1750.

Dipropyl 2-Methyl-2*H*-naphtho[2,3-*f*]isoindole-4,11-dione-1,3-dicarboxylate (4m). Yield 74% (0.321 g); mp 140−141 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.68 (s, 2H), 8.00 (dd, J_1 = 3.5 Hz, J_2 = 6.5 Hz, 2H), 7.61 (dd, J_1 = 3.5 Hz, J_2 = 6.5 Hz, 2H), 4.45 (q, J = 6.5 Hz, 4H), 3.91 (s, 3H), 1.94−1.87 (m, 4H), 1.09 (q, J = 7.5 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.4 (2C), 161.0 (2C), 134.7 (2C), 131.2 (2C), 129.9 (2C), 129.1 (4C), 128.2 (2C), 122.5 (2C), 68.2 (2C), 34.7, 21.9 (2C), 10.4 (2C). IR (KBr): 2967, 1728, 1675, 1619, 1509, 1466, 1421, 1281, 1232, 1182, 1034, 918, 759 cm^{-1}. GC−MS m/z: 433.2 $[M]^+$, 432.4, 403.8, 387.8, 345.2, 285.7, 185.7, 41.5. HRMS (ESI-TOF) m/z: calcd for $C_{25}H_{24}NO_6$ $[M + H]^+$ 434.1598, found 434.1597.

Diisopropyl 2-Methyl-2*H*-naphtho[2,3-*f*]isoindole-4,11-dione-1,3-dicarboxylate (4n). Yield 52% (0.225 g); mp 159−160 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (s, 2H), 8.04 (dd, J_1 = 3.0 Hz, J_2 = 6.0 Hz, 2H), 7.65 (dd, J_1 = 3.5 Hz, J_2 = 7.0 Hz, 2H), 5.45−5.40 (m, 2H), 3.91 (s, 3H), 1.51 (d, J = 7.0 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.6 (2C), 160.6 (2C), 134.8 (2C), 131.4 (2C), 130.0 (2C), 129.2 (2C), 129.1 (2C), 128.6 (2C), 122.3 (2C), 70.9 (2C), 34.5, 21.7 (4C). IR (KBr): 2979, 1727, 1676, 1620, 1450, 1420, 1280, 1233, 1181, 1099, 1034, 917, 760, 748 cm^{-1}. GC−MS: m/z: 434.3 $[M + H]^+$, 433.4, 375.5, 319.5, 289.5, 362.5, 361.5, 41.2. HRMS (ESI-TOF) m/z: calcd for $C_{25}H_{23}NO_6Na$ $[M + Na]^+$ 456.1417, found 456.1426.

Dibutyl 2-Methyl-2*H*-naphtho[2,3-*f*]isoindole-4,11-dione-1,3-dicarboxylate (4o). Yield 47% (0.217 g); mp 99−100 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.75 (s, 2H), 8.06 (dd, J_1 = 3.5 Hz, J_2 = 6.5 Hz, 2H), 7.67 (dd, J_1 = 3.5 Hz, J_2 = 6.5 Hz, 2H), 4.51 (t, J = 7.0 Hz, 4H), 3.93 (s, 3H), 1.90−1.84 (m, 4H), 1.57−1.49 (m, 4H), 1.03 (t, J = 7.0 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.6 (2C), 161.1 (2C), 134.8 (2C), 131.4 (2C), 130.0 (2C), 129.3 (2C), 129.2 (2C), 128.3 (2C), 122.7 (2C), 66.6, 65.9, 34.8, 30.5 (2C), 19.2 (2C), 13.8 (2C). IR (KBr): 2958, 1731, 1702, 1678, 1619, 1466, 1452, 1281, 1234, 1202, 1180, 1034, 919, 760 cm^{-1}. GC−MS m/z: 463.1 $[M + H]^+$, 462.2, 418.2, 407.1, 390.2, 389.2, 376.2, 208.5. HRMS (ESI-TOF) m/z: calcd for $C_{27}H_{28}NO_6$ $[M + H]^+$ 462.1911, found 462.1920.

Diisopentyl 2-Methyl-2*H*-naphtho[2,3-*f*]isoindole-4,11-dione-1,3-dicarboxylate (4p). Yield 40% (0.196 g); mp 90−91 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (s, 2H), 8.54 (dd, J_1 = 3.0 Hz, J_2 = 5.5 Hz, 2H), 7.66 (dd, J_1 = 3.0 Hz, J_2 = 6.0 Hz, 2H), 4.50 (t, J = 7.0 Hz, 4H), 3.93 (s, 3H), 1.87−1.82 (m, 2H), 1.80−1.76 (m, 4H), 1.02 (d, J = 6.5 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.6 (2C), 161.1 (2C), 134.9 (2C), 131.4 (2C), 130.0 (2C), 129.2 (4C), 128.3 (2C), 122.7 (2C), 71.4 (2C), 65.5 (2C), 37.1 (2C), 25.2, 22.5 (4C). IR (KBr): 2959, 1726, 1676, 1619, 1551, 1459, 1424, 1283, 1181, 1112, 1035, 918, 759 cm^{-1}. GC−MS m/z: 489.5 $[M]^+$, 433.2, 375.2, 319.2, 261.4, 207.3, 126.3, 41.2. HRMS (ESI-TOF) m/z: calcd for $C_{29}H_{32}NO_6$ $[M + H]^+$ 490.2224, found 490.2227.

Diethyl 2-Methyl-5-nitro-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4q). Yield 55% (0.220 g); mp 85−86 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40 (dd, J_1 = 1.0 Hz, J_2 = 7.5 Hz, 1H), 7.83 (t, J = 7.5 Hz, 1H), 7.70 (dd, J_1 = 1.0 Hz, J_2 = 8.0 Hz, 1H), 4.54 (q, J = 7.0 Hz, 2H), 4.47 (q, J = 7.0 Hz, 2H), 3.96 (s, 3H), 1.49 (t, J = 7.0 Hz, 3H), 1.43 (t, J = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.2, 175.2, 160.3, 160.1, 149.4, 136.0, 133.8, 129.6, 128.7, 128.5, 127.4, 126.8, 121.6, 120.7, 62.9, 62.9, 35.0, 14.0, 13.7. IR (KBr): 2983, 1723, 1676, 1593, 1544, 1509, 1375, 1306, 1252, 1226, 1144, 1026, 912, 798, 712 cm^{-1}. GC−MS m/z: 400.8 $[M]^+$, 399.8, 384.2, 356.2, 339.3, 309.1, 284.1, 256.1. HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{16}N_2O_8Na$ $[M + Na]^+$ 423.0799, found 423.0807.

Diethyl 2-Ethyl-5-nitro-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4r). Yield 46% (0.191 g); mp 75−76 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (dd, J_1 = 0.5 Hz, J_2 = 7.0 Hz, 1H), 7.82 (t, J = 8.0 Hz, 1H), 7.70 (dd, J_1 = 1.5 Hz, J_2 = 8.5 Hz, 1H), 4.54 (q, J = 7.5 Hz, 2H), 4.47 (q, J = 7.5 Hz, 2H), 4.40 (q, J = 7.0 Hz, 2H), 3.96 (s, 3H), 1.48 (t, J = 7.0 Hz, 6H), 1.43 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.2, 175.3, 160.4, 160.2, 149.4, 136.0, 133.8, 129.5, 128.0, 127.8, 127.3, 126.8, 121.8, 120.7, 62.9 (2C), 43.4, 16.8, 13.9, 13.7. IR (KBr): 2982, 1730, 1681, 1531, 1440, 1309, 1233, 1141, 1018, 798, 711 cm^{-1}. GC−MS m/z: 414.8 $[M]^+$, 413.8, 396.0, 386.0, 369.2, 342.3, 325.3, 295.1. HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{18}N_2O_8Na$ $[M + Na]^+$ 437.0955, found 437.0958.

Diethyl 2-Propyl-5-nitro-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4s). Yield 40% (0.171 g); mp 70−71 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40 (dd, J_1 = 1.0 Hz, J_2 = 8.0 Hz, 1H), 7.83 (t, J = 8.0 Hz, 1H), 7.70 (dd, J_1 = 0.5 Hz, J_2 = 7.5 Hz, 1H), 4.54 (q, J = 7.5 Hz, 2H), 4.48 (q, J = 7.0 Hz, 2H), 4.37 (t, J = 7.5 Hz, 2H), 4.31−4.26 (m, 2H), 1.80−1.74 (m, 2H), 1.48 (t, J = 7.5 Hz, 3H), 1.43 (t, J = 7.0 Hz, 3H), 0.94 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.3, 175.3, 160.5, 160.3, 149.5, 136.1, 133.78, 129.6, 128.3, 128.1, 127.3, 126.9, 121.7, 120.7, 62.9, 62.9, 49.3, 24.8, 14.0, 13.7, 10.9. IR (KBr): 2977, 1734, 1682, 1532, 1438, 1367, 1315, 1227, 1142, 1018, 797, 712 cm^{-1}. GC−MS m/z: 429.1 $[M + H]^+$, 428.1, 400.2, 383.3, 342.3, 341.3, 295.4, 206.4. HRMS (ESI-TOF) m/z: calcd for $C_{21}H_{21}N_2O_8$ $[M + H]^+$ 429.1293, found 429.1321.

Diethyl 2-Butyl-5-nitro-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4t). Yield 35% (0.155 g); mp 65−66 °C. ^{1}H NMR

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(500 MHz, $CDCl_3$): δ 8.40 (dd, J_1 = 1.0 Hz, J_2 = 7.5 Hz, 1H), 7.83 (t, J = 7.5 Hz, 1H), 7.70 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H), 4.54 (q, J = 7.0 Hz, 2H), 4.48 (q, J = 7.0 Hz, 2H), 4.34 (t, J = 7.5 Hz, 2H), 1.85−1.79 (m, 2H), 1.49 (t, J = 7.5 Hz, 3H), 1.43 (t, J = 7.0 Hz, 3H), 0.94 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.3, 175.3, 160.5, 160.2, 149.5, 136.1, 133.7, 129.5, 128.3, 128.1, 127.3, 126.8, 121.7, 120.7, 62.9, 62.8, 47.7, 33.5, 19.7, 13.9, 13.7, 13.5. IR (KBr): 2966, 1740, 1620, 1544, 1445, 1373, 1220, 1018, 800, 711 cm^{-1}. GC−MS m/z: 443.1 $[M + H]^+$, 412.3, 397.2, 370.2, 369.2 (100%), 297.5, 269.3. HRMS (ESI-TOF) m/z: calcd for $C_{22}H_{23}N_2O_8$ $[M + H]^+$ 443.1449, found 443.1461.

Diethyl 2-Methyl-5-hydroxy-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4u). Yield 25% (0.093 g); mp 133−134 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.65 (s, 1H), 7.73 (dd, J_1 = 1.0 Hz, J_2 = 7.5 Hz, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.22 (dd, J_1 = 1.0 Hz, J_2 = 8.5 Hz, 1H), 4.56−4.51 (m, 4H), 3.91 (s, 3H), 1.50−1.47 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 184.8, 177.9, 162.7, 160.6, 160.6, 136.0, 135.2, 128.7, 128.2, 124.0, 121.8, 120.9, 119.4, 117.0, 62.8, 62.7, 34.8, 14.0 (2C). IR (KBr): 2964, 1705, 1669, 1634, 1455, 1262, 1082, 1021, 802, 695 cm^{-1}. GC−MS m/z: 372.2 $[M + H]^+$, 371.3, 326.4, 325.5, 299.5, 253.5, 225.5, 63.1. HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{17}NO_7Na$ $[M + Na]^+$ 394.0907, found 394.0897.

Diethyl 2-Ethyl-5-hydroxy-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4v). Yield 21% (0.081 g); mp 100−101 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.67 (s, 1H), 7.73 (dd, J_1 = 1.5 Hz, J_2 = 7.5 Hz, 1H), 7.59 (t, J = 8.5 Hz, 1H), 7.22 (dd, J_1 = 1.0 Hz, J_2 = 8.5 Hz, 1H), 4.56−4.52 (m, 4H), 4.34 (q, J = 6.5 Hz, 2H), 1.50−1.46 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 184.9, 178.0, 162.7, 160.8, 160.8, 136.0, 135.2, 128.1, 127.6, 124.0, 62.9, 62.8, 43.3, 16.73, 14.0 (2C). IR (KBr): 2977, 1735, 1705, 1674, 1633, 1555, 1365, 1350, 1263, 1226, 1075, 801, 715 cm^{-1}. GC−MS m/z: 386.3 $[M + H]^+$, 385.5 (100%), 339.6, 312.5, 266.5, 239.3, 183.2, 155.5. HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{20}NO_7$ $[M + H]^+$ 386.1235, found 386.1250.

Diethyl 2-Propyl-5-hydroxy-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4w). Yield 15% (0.060 g); mp 100−101 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.67 (s, 1H), 7.73 (dd, J_1 = 1.5 Hz, J_2 = 7.5 Hz, 1H), 7.59 (t, J = 8.5 Hz, 1H), 7.22 (dd, J_1 = 1.0 Hz, J_2 = 8.5 Hz, 1H), 4.56−4.51 (m, 4H), 4.26 (q, J = 8.5 Hz, 2H), 1.92−1.80 (m, 2H), 1.48 (t, J = 7.0 Hz, 3H), 0.95 (t, J = 7.5 Hz, 3H), 0.94 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 184.9, 178.1, 162.8, 160.9, 160.8, 136.0, 135.2, 128.3, 127.8, 124.0, 121.7, 120.8, 119.4, 117.0, 62.9 (2C), 49.3, 24.8, 14.0 (2C), 10.9. IR (KBr): 2974, 1732, 1637, 1618, 1557, 1509, 1444, 1356, 1342, 1268, 1218, 1081, 1010, 834, 748 cm^{-1}. GC−MS m/z: 400.1 $[M + H]^+$, 399.3, 370.3, 353.5, 312.3, 266.2, 254.3, 41.1. HRMS (ESI-TOF) m/z: calcd for $C_{21}H_{21}NO_7Na$ $[M + Na]^+$ 422.1210, found 422.1218.

Diethyl 2-Butyl-5-hydroxy-2*H*-benzo[*f*]isoindole-4,9-dione-1,3-dicarboxylate (4x). Yield 10% (0.041 g); mp 85−86 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.67 (s, 1H), 7.73 (dd, J_1 = 1.0 Hz, J_2 = 7.5 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.22 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H), 4.56−4.51 (m, 4H), 4.29 (t, J = 7.5 Hz, 2H), 1.81−1.75 (m, 2H), 1.48 (t, J = 7.0 Hz, 6H), 1.40−1.32 (m, 2H), 0.95 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 183.9, 177.0, 161.7, 159.8, 159.8, 135.0, 134.2, 127.3, 126.8, 122.948, 120.7, 119.8, 118.3, 116.0, 61.8, 61.7, 46.7, 32.4, 18.8, 13.0 (2C), 12.5. IR (KBr): 2964, 1712, 1671, 1632, 1560, 1511, 1439, 1367, 1349, 1262, 1204, 1079, 1019, 801 cm^{-1}. GC−MS m/z: 414.1 $[M + H]^+$, 413.2, 384.2, 368.2, 340.2, 312.2, 298.2, 270.2. HRMS (ESI-TOF) m/z: calcd for $C_{22}H_{23}NO_7Na$ $[M + Na]^+$ 436.1367, found 436.1376.

Procedure for the Synthesis of 3a. 1,4-Naphthoquinone (**1a**) (1.0 mmol, 1.0 equiv), $NaHCO_3$ (3.0 mmol, 3.0 equiv), and iodine (3.0 mmol, 3.0 equiv) were added sequentially to a solution of sarcosine ethyl ester (**2a**) (3.0 mmol, 3.0 equiv) in CH_3CN (5.0 mL), and the resulting mixture was stirred for 8 h at reflux. The reaction was followed by GC−MS and TLC. Upon completion of the reaction, the solvent was removed under vacuum, and the resulting crude product was purified by chromatography on silica gel eluted with CH_2Cl_2 to obtain **3a** in 50% yield as a red solid.

Ethyl 2-((1,4-Dioxo-1,4-dihydronaphthalen-2-yl)(methyl)-amino)acetate (3a). Yield 50% (0.136 g); red solid, mp 99−100 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.99 (dd, J_1 = 1.0 Hz, J_2 = 1.5 Hz, 1H), 7.92 (dd, J_1 = 1.0 Hz, J_2 = 1.0 Hz, 1H), 7.66−7.63 (m, 1H), 7.58−7.55 (m, 1H), 5.89 (s, 1H), 4.44 (s, 2H), 4.20 (q, J = 7.5 Hz, 2H), 3.08 (s, 3H), 1.26 (t, J = 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 183.2, 183.1, 169.4, 151.0, 133.9, 132.2, 132.1, 126.5, 125.3, 108.4, 61.3, 55.8, 42.3, 14.1. IR (KBr): 2984, 1737, 1668, 1642, 1633, 1592, 1556, 1304, 1247, 1215, 1131, 1037, 1024, 1012, 969, 845, 774, 720 cm^{-1}. EI-MS m/z: 273.01 $[M]^+$, 200.1, 172.1, 115.1, 75.1. HRMS (ESI-TOF) m/z: calcd for $C_{15}H_{15}NO_4Na$ $[M + Na]^+$ 296.0899, found 296.0901.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

X-ray structural data (CIF) for compound **4i** and copies of ^{1}H and ^{13}C NMR spectra of the products **3a** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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