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Synthesis of Naphthalene Amino Esters by the Blaise Reaction of *o*-Alkynylarenenitriles

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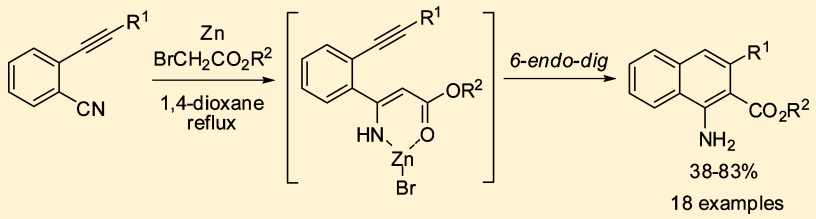
Supporting Information



ABSTRACT: The action of a Reformatsky reagent on *o*-alkynylarenenitriles provides a convenient access to naphthalene amino esters *via* tandem 6-*endo*-*dig* carbannulation of *in situ* generated Blaise reaction intermediates. The products are formed in moderate to good yields with high chemo- and regioselectivity.

The Blaise reaction, which involves the addition of a Reformatsky reagent to nitrile, is an important carbon−carbon bond forming reaction.[1] A zinc bromide complex of *β*-enaminoester is generated as an intermediate in the reaction, and the intermediate after acidic or basic workup gives *β*-ketoester or *β*-enaminoester (Scheme 1, eq 1). The reaction has been exploited in the synthesis of numerous heterocycles and natural products.[1,2] In recent years, the Blaise reaction intermediates have been trapped with suitable partners in a tandem manner, which has provided access to a variety of compounds. Thus, the trapping of the intermediates with acetic anhydride,[3] propiolates,[4] epoxides,[5] 1,4-benzoquinones,[6] 1,3-enynes,[7] nitriles,[8] isocyanates,[9] and nitroolefins[10] have yielded *α*-acyl-*β*-enaminoketoesters (subsequently, pyrazoles), 2-pyridones, *α*-aminomethylene-*γ*-butyrolactones, benzofuran-2-ones, pyridines, pyrimidin-4-ones, pyrimidin-2,4-diones, and pyrroles, respectively. A palladium-catalyzed intramolecular *N*-alkylative/arylative trapping of the intermediate has furnished indoles,[11] and a chemoselective intramolecular alkylation of the intermediate has afforded various *N*-fused heterocyclic compounds *via* *exo*-cyclic enamino esters.[12] An interesting addendum to the list is Lee's tandem alkenylation of the Blaise reaction intermediates with unactivated alkynes, which has resulted in various *α*-vinylated *β*-enaminoesters (Scheme 1, eq 2).[13,14] The work caused us to envisage that an intramolecular version of the reaction using *o*-alkynylarenenitriles as substrates would result in naphthalene amino esters through tandem 6-*endo*-*dig* carbannulation of *in situ* generated Blaise reaction intermediates (Scheme 1, eq 3).

Earlier methods reported for the synthesis of naphthalene amino esters include addition of *α*-lithio derivatives of 2-alkylbenzonitriles to *α*,*β*-unsaturated carboxylic acids or esters *via* tandem Michael addition/enolate coupling,[15] copper(I) cyanide-mediated cascade cyclization of 4-(2-bromoaryl)-2-butenoates,[16] and hypervalent iodine(III)-mediated benzannulation of *β*-enaminoesters with alkynes.[17] The development of new methods for the access of functionalized naphthalenes is actively pursued owing to the widespread applications of substituted naphthalenes in academia and industry and the occurrence of the naphthalene core in many natural products, pharmaceuticals, and functional materials.[18] In this context, the present method would be an interesting and useful addition to the existing methods.

To test our hypothesis, we required a variety of *o*-alkynylarenenitriles with various substitution patterns. They were prepared from appropriate *o*-haloarenenitriles and terminal acetylenes by a standard *Sonogashira* coupling procedure. The requisite *o*-haloarenenitriles were in turn prepared from the corresponding *o*-haloarenecarbaldehydes by heating with hydroxylamine hydrochloride and DMSO.[19] We began the study with the generation of methyl zincbromoacetate *in situ* from methyl bromoacetate and activated zinc and its addition to *o*-alkynylbenzonitrile **1a** in THF under reflux conditions. To our delight, the desired naphthalene amino ester **2a** was obtained in 65% isolated yield after 2 h. After several attempts, we found that the yield of **2a** could be improved to 81% when solvent was switched to 1,4-dioxane (under reflux) and 5 equiv of methyl bromoacetate and 7.5 equiv of zinc were used for the formation of the Reformatsky reagent (Table 1, entry 1). Under these optimized conditions, we investigated the scope of the reaction for various *o*-alkynylarenenitriles using different Reformatsky reagents (Table 1).[20] The reaction of **1a** with ethyl zincbromoacetate afforded the respective naphthalene amino ester **2b** in almost similar yield (83%) (entry 2). When *tert*-butyl zincbromoacetate was employed in the reaction, **1a** did not undergo any change even after 12 h (entry 3), probably due to the lower nucleophilicity of the

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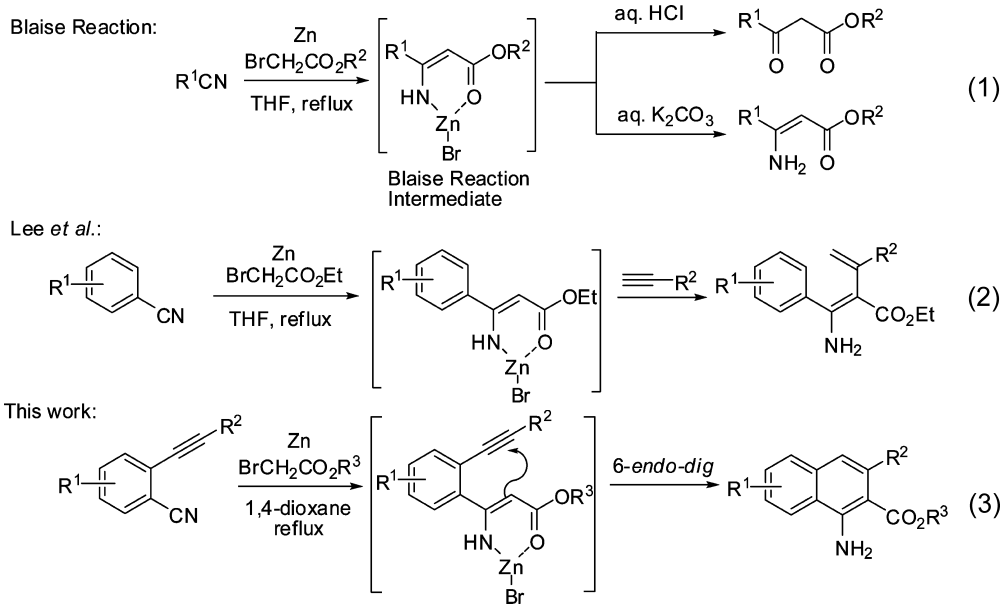
Scheme 1. Inter- and Intramolecular Tandem Alkenylation of Blaise Reaction Intermediates



reagent caused by the bulky *tert*-butyl group. Next, we tested the suitability of *o*-alkynylarenenitriles **1b**–**g** having different aromatic rings (R^1) attached to the yne unit. The presence of phenyl rings with electron-donating and halogen substituents was tolerated (entries 4–7) as well as the bulky naphthyl ring (entry 8) and the heteroaromatic thienyl ring, albeit in low yield in the latter case (entry 9). However, the reaction failed for a terminal acetylene **1h**, in which R^1 = H (entry 10), likely due to abstraction of the acidic terminal acetylenic hydrogen by the Reformatsky reagent.[21] We then examined *o*-alkynylbenzonitriles **1i**–**r** bearing one or two methoxy groups on the main aryl ring (entries 11–20). The yields were comparatively low and the reaction time was longer (6 h) when an alicyclic ring or aliphatic chain was linked to the yne unit (entries 12–14). The reaction did not take place when a *p*-nitrophenyl group was attached to the yne unit (entry 20). Except for these pitfalls, all other *o*-alkynylbenzonitriles furnished the corresponding naphthalene amino esters in moderate to good yields (entries 11 and 15–19). Finally, we tested the tetrahydrobenzothiophene-based *o*-alkynylarenenitrile **1s**, which also afforded the corresponding amino ester **2r** in 45% yield (entry 21). All the products were thoroughly characterized by various spectroscopic techniques, and for one of the products, **2i**, the structure was further confirmed by X-ray analysis.[22]

In all the successful reactions mentioned above, we obtained only naphthalene amino esters **2** as single or only isolable products. Obviously, the initially formed Blaise reaction intermediate has acted as a carbon nucleophile and attacked the triple bond in a tandem manner *via* 6-*endo*-*dig* cyclization mode producing the carbannulated product **2**. The high chemo- and regioselectivities of the reactions are noteworthy. We did not observe any products **3**–**5** arising from 5-*exo*-*dig* carbannulation or 6-*endo*-*dig*/5-*exo*-*dig* hydroamination (when the Blaise reaction intermediate acts as a *N*-nucleophile) (Scheme 2). It may be noted that Lee's alkenylation of Blaise reaction intermediates with alkynes (Scheme 1, eq 2) was applicable mainly to terminal alkynes and only one internal alkyne (methyl phenyl acetylene) has been successfully employed in the reaction.[13] In contrast, our intramolecular strategy is applicable only to internal diaryl or alkylaryl alkynes.

In summary, we have developed a convenient protocol for the synthesis of naphthalene amino esters from *o*-alkynylarenenitriles and Reformatsky reagents. The reaction proceeds in a highly chemo- and regioselective manner *via* tandem 6-*endo*-*dig* carbannulation of *in situ* formed Blaise reaction intermediates.

EXPERIMENTAL SECTION

General Remarks. Melting points were determined using an apparatus by the open capillary tube method and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz NMR spectrometer. HRMS (ESI) were recorded on Q-TOF mass spectrometers. Low resolution mass spectra (ESI) were recorded on LC-MS spectrometers. Elemental analyses were performed on a CHN analyzer. X-ray crystallographic data were collected on a CCD diffractometer using graphite-monochromated Mo Kα radiation. Thin layer chromatography (TLC) was performed on precoated alumina sheets and detected under UV light. Silica gel (100–200 mesh) was used for column chromatography.

General Procedures for the Synthesis of Naphthalene Amino Esters 2a–r. To a stirred suspension of zinc dust (3.75 mmol) in anhydrous 1,4-dioxane (5 mL) was added methanesulfonic acid (5 mol %) and heated to reflux. After 10 min, *o*-alkynylarenenitrile **1** (0.5 mmol) was added followed by slow addition (15 min) of alkyl bromoacetate (2.5 mmol) in 1,4-dioxane (1 mL). After 2 h (6 h for **1j**–**l**), the reaction mixture was cooled to room temperature, quenched with saturated NH_4Cl, and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (9.5/0.5) as eluent to obtain pure naphthalene amino ester **2**.

Methyl 1-Amino-3-phenyl-2-naphthoate (***2a***). Brown viscous liquid. Yield: 112 mg (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.56–7.52 (m, 1H), 7.49–7.45 (m, 1H), 7.39–7.36 (m, 4H), 7.33–7.30 (m, 1H), 7.13 (s, 1H), 6.02 (brs, 2H), 3.41 (s, 3H); ^{13}C NMR (100 MHz,$CDCl_3$): δ 170.5, 146.3, 143.7, 139.9, 134.9, 128.7, 128.4, 127.91, 127.85, 126.5, 125.5, 122.4, 121.4, 119.1, 107.7, 51.2 ppm; HRMS (ESI): $[M + H]^+$ Calcd for $C_{18}H_{16}NO_2$, 278.1181; found, 278.1165.

Ethyl 1-Amino-3-phenyl-2-naphthoate (***2b***).[15] Brown viscous liquid. Yield: 121 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.40–7.32 (m, 5H), 7.14 (s, 1H), 6.10 (brs,

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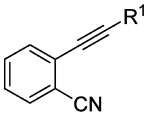
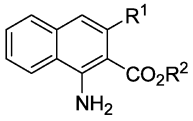
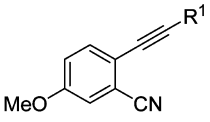
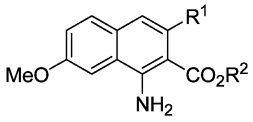
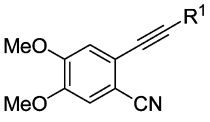
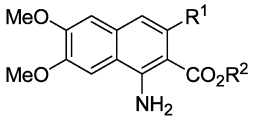
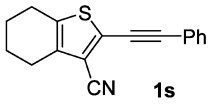
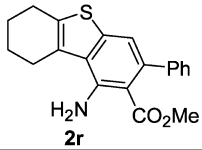
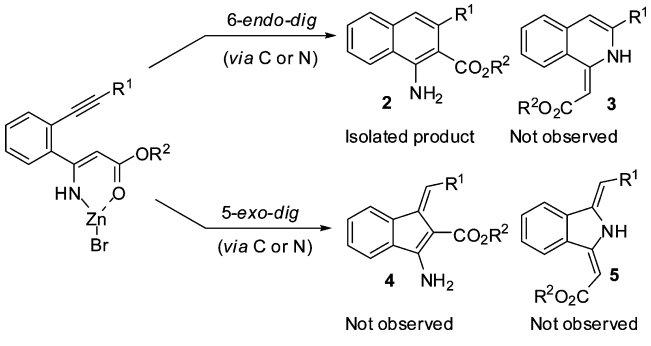
Table 1. Substrate Scope for the Tandem Carbannulation of Blaise Reaction Intermediates[a]

Entry	*o*-alkynylarenenitrile	$BrZnCH_2CO_2R^2$	Product	Yield (%)[b]
				
1	R^1 = Ph, **1a**	Me	**2a**	81
2	R^1 = Ph, **1a**	Et	**2b**	83
3	R^1 = Ph, **1a**	^{t}Bu	-	NR
4	R^1 = 4-MeC_6H_4, **1b**	Me	**2c**	79
5	R^1 = 2-MeC_6H_4, **1c**	Me	**2d**	75
6	R^1 = 4-$OMeC_6H_4$, **1d**	Me	**2e**	67
7	R^1 = 4-ClC_6H_4, **1e**	Me	**2f**	64
8	R^1 = 4-methoxy-1-naphthyl, **1f**	Me	**2g**	60
9	R^1 = 2-thienyl, **1g**	Et	**2h**	45
10	R^1 = H, **1h**	Et	-	NR
				
11	R^1 = Ph, **1i**	Et	**2i**	78
12	R^1 = cyclopropyl, **1j**	Et	**2j**	38[c]
13	R^1 = butyl, **1k**	Et	**2k**	48[c]
14	R^1 = heptyl, **1l**	Et	**2l**	43[c]
				
15	R^1 = Ph, **1m**	Et	**2m**	74
16	R^1 = 4-MeC_6H_4, **1n**	Et	**2n**	70
17	R^1 = 2-$OMeC_6H_4$, **1o**	Et	**2o**	62
18	R^1 = 4-ClC_6H_4, **1p**	Et	**2p**	64
19	R^1 = 4-methoxy-1-naphthyl, **1q**	Et	**2q**	54
20	R^1 = 4-$NO_2C_6H_4$, **1r**	Et	-	NR
21	 **1s**	Me	 **2r**	45

[a]Reaction conditions: nitrile (0.5 mmol), alkyl bromoester (2.5 mmol), zinc (3.75 mmol, preactivated with 5 mol % of methanesulfonic acid) in 1,4-dioxane (6 mL) at reflux for 2 h. [b]Isolated yield. [c]Reaction time was 6 h.

Scheme 2. Possible Tandem Carbannulation/ Hydroamination of the Blaise Reaction Intermediates



2H), 3.94 (q, J = 7.2 Hz, 2H), 0.73 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 146.5, 144.1, 140.1, 134.9, 128.7, 128.4, 128.1, 127.9, 126.5, 125.5, 122.5, 121.5, 119.1, 107.7, 60.4, 13.2 ppm; MS (ESI): m/z 292 $(M + H)^+$.

*Methyl 1-Amino-3-(4-methylphenyl)-2-naphthoate (**2c**).* Brown solid. Yield: 115 mg (79%). Mp 78−80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.53−7.49 (m, 1H), 7.45−7.41 (m, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.12 (s, 1H), 5.94 (brs, 2H), 3.44 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 146.1, 140.7, 139.8, 136.1, 135.0, 128.69, 128.68, 128.3, 127.8, 125.4, 122.4, 121.4, 119.1, 108.0, 51.3, 21.2 ppm; HRMS (ESI): $[M + H]^+$ Calcd for $C_{19}H_{18}NO_2$, 292.1338; found, 292.1321.

*Methyl 1-Amino-3-(2-methylphenyl)-2-naphthoate (**2d**).* Brown viscous liquid. Yield: 109 mg (75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.56−7.52 (m, 1H),

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7.49−7.45 (m, 1H), 7.21−7.13 (m, 4H), 6.97 (s, 1H), 6.29 (brs, 2H), 3.36 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 147.1, 143.8, 139.8, 135.2, 135.0, 129.2, 128.52, 128.51, 128.4, 126.5, 125.4, 125.1, 122.4, 121.5, 119.0, 107.5, 51.1, 20.1 ppm; HRMS (ESI): $[M + H]^+$ Calcd for $C_{19}H_{18}NO_2$, 292.1338; found, 292.1347.

*Methyl 1-Amino-3-(4-methoxyphenyl)-2-naphthoate (**2e**).* Orange liquid. Yield: 103 mg (67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.31 (d, J = 8.4 Hz, 2H), 7.12 (s, 1H), 6.94 (d, J = 8.8 Hz, 2H), 5.95 (brs, 2H), 3.86 (s, 3H), 3.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 158.5, 146.0, 139.4, 136.1, 134.9, 128.9, 128.6, 128.3, 125.3, 122.3, 121.4, 118.9, 113.5, 108.1, 55.3, 51.3 ppm; HRMS (ESI): $[M + H]^+$ Calcd for $C_{19}H_{18}NO_3$, 308.1287; found: 308.1278.

*Methyl 1-Amino-3-(4-chlorophenyl)-2-naphthoate (**2f**).* Pale yellow liquid. Yield: 100 mg (64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.50 (t, J = 7.0 Hz, 1H), 7.36 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.08 (s, 1H), 6.13 (brs, 2H), 3.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 146.8, 142.3, 138.7, 134.8, 132.4, 129.2, 128.7, 128.6, 128.0, 125.7, 122.5, 121.4, 119.1, 106.9, 51.2 ppm; MS (ESI): m/z 312 $(M + H)^+$. Anal. Calcd for $C_{18}H_{14}ClNO_2$: C, 69.35; H, 4.53; N, 4.49. Found: C, 69.55; H, 4.63; N 4.62.

*Methyl 4′-Amino-4-methoxy-1,2′-binaphthyl-3′-carboxylate (**2g**).* Orange oil. Yield: 107 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.59−7.49 (m, 2H), 7.46−7.36 (m, 2H), 7.29 (d, J = 7.6 Hz, 1H), 7.17 (s, 1H), 6.86 (d, J = 7.6 Hz, 1H), 6.27 (brs, 2H), 4.06 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 154.4, 146.8, 138.4, 135.1, 134.4, 133.1, 128.6, 128.4, 126.3, 125.6, 125.5, 125.4, 125.2, 124.8, 122.6, 121.9, 121.5, 120.4, 108.8, 103.2, 55.5, 51.0 ppm; HRMS (ESI): $[M + H]^+$ Calcd for $C_{23}H_{20}NO_3$, 358.1443; found, 358.1430.

*Ethyl 1-Amino-3-(thiophen-2-yl)-2-naphthoate (**2h**).* Brown viscous liquid. Yield: 67 mg (45%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.48 (t, J = 7.2 Hz, 1H), 7.41 (t, J = 7.2 Hz, 1H), 7.22 (d, J = 5.2 Hz, 1H), 7.19 (s, 1H), 6.98−6.92 (m, 2H), 5.87 (brs, 2H), 3.97 (q, J = 7.0 Hz, 2H), 0.84 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 145.9, 145.3, 134.6, 131.9, 128.7, 128.4, 126.9, 125.8, 125.1, 124.6, 122.8, 121.4, 119.9, 108.6, 60.7, 13.4 ppm; MS (ESI): m/z 320 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{15}NO_2S$: C, 68.66; H, 5.08, N, 4.71. Found: C, 68.75; H, 5.20; N, 4.90.

*Ethyl 1-Amino-7-methoxy-3-phenyl-2-naphthoate (**2i**).* Orange solid. Yield: 125 mg (78%). Mp 135−137 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 8.8 Hz, 1H), 7.39−7.35 (m, 4H), 7.33−7.28 (m, 1H), 7.23 (dd, J = 8.8, 2.4 Hz, 1H), 7.13 (d, J = 2.4 Hz, 1H), 7.11 (s, 1H), 5.81 (brs, 2H), 3.96 (s, 3H), 3.91 (q, J = 7.0 Hz, 2H), 0.71 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 157.7, 145.0, 144.0, 137.7, 130.3, 130.0, 128.1, 127.9, 126.3, 123.5, 120.1, 119.2, 108.9, 101.1, 60.4, 55.5, 13.1 ppm; MS (ESI): m/z 344 $(M + Na)^+$. Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.83; H, 6.02; N, 4.50. Single crystals suitable for X-ray studies were grown from a solution of **2i** in hexane/ethyl acetate (9.5:0.5).

*Ethyl 1-Amino-3-cyclopropyl-7-methoxy-2-naphthoate (**2j**).* Brown liquid. Yield: 54 mg (38%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 8.8 Hz, 1H), 7.16 (dd, J = 9.2, 2.2 Hz, 1H), 7.05 (d, J = 2.0 Hz, 1H), 6.96 (s, 1H), 5.58 (brs, 2H), 4.44 (q, J = 7.2 Hz, 2H), 3.92 (s, 3H), 2.39−2.32 (m, 1H), 1.42 (t, J = 7.0 Hz, 3H), 0.88−0.84 (m, 2H), 0.68−0.64 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 157.3, 143.9, 137.4, 130.2, 129.7, 123.1, 119.6, 116.7, 111.8, 100.93, 100.90, 60.8, 55.5, 16.3, 14.3, 7.1 ppm; HRMS (ESI): $[M + H]^+$ Calcd for $C_{17}H_{20}NO_3$, 286.1443; found, 286.1434.

*Ethyl 1-Amino-3-butyl-7-methoxy-2-naphthoate (**2k**).* Brown liquid. Yield: 72 mg (48%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 8.8 Hz, 1H), 7.16 (dd, J = 8.8, 2.4, Hz, 1H), 7.05 (d, J = 2.4 Hz, 1H), 6.97 (s, 1H), 5.68 (brs, 2H), 4.41 (q, J = 7.0 Hz, 2H), 3.90 (s, 3H), 2.90 (t, J = 7.8 Hz, 2H), 1.63−1.53 (m, 2H), 1.43−1.34 (m, 5H), 0.92 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 157.2, 144.8, 137.2, 130.3, 129.5, 123.0, 119.7, 118.5, 109.8, 100.9, 60.8, 55.4, 35.9, 34.0, 22.9, 14.2, 14.1 ppm; HRMS (ESI): $[M + H]^+$ Calcd for $C_{18}H_{24}NO_3$, 302.1756; found, 302.1750.

*Ethyl 1-Amino-3-heptyl-7-methoxy-2-naphthoate (**2l**).* Brown liquid. Yield: 74 mg (43%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 9.2 Hz, 1H), 7.17 (dd, J = 8.8, 2.4 Hz, 1H), 7.06 (d, J = 2.0 Hz, 1H), 6.98 (s, 1H), 5.67 (brs, 2H), 4.42 (q, J = 7.0 Hz, 2H), 3.92 (s, 3H), 2.89 (t, J = 8.0 Hz, 2H), 1.62−1.56 (m, 3H), 1.42 (t, J = 7.2 Hz, 3H), 1.33−1.26 (m, 7H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 157.2, 144.8, 137.3, 130.4, 129.5, 122.9, 119.7, 118.5, 109.8, 100.9, 60.8, 55.4, 36.2, 31.90, 31.87, 29.8, 29.3, 22.7, 14.3, 14.1 ppm; HRMS (ESI): $[M + H]^+$ Calcd for $C_{21}H_{30}NO_3$, 344.2226; found, 344.2218.

*Ethyl 1-Amino-6,7-dimethoxy-3-phenyl-2-naphthoate (**2m**).* Brown solid. Yield: 130 mg (74%). Mp 118−120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.35 (m, 4H), 7.34−7.28 (m, 1H), 7.10 (s, 1H), 7.05 (s, 1H), 7.03 (s, 1H), 5.83 (brs, 2H), 4.03 (s, 3H), 3.99 (s, 3H), 3.91 (q, J = 7.2 Hz, 2H), 0.70 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 151.2, 149.2, 145.2, 144.2, 138.8, 131.0, 128.1, 127.8, 126.3, 118.4, 117.3, 107.6, 107.4, 101.1, 60.3, 56.0, 55.9, 13.1 ppm; MS (ESI): m/z 352 $(M + H)^+$. Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 71.90; H, 6.21; N, 4.10.

*Ethyl 1-Amino-6,7-dimethoxy-3-(4-methylphenyl)-2-naphthoate (**2n**).* Pale yellow solid. Yield: 128 mg (70%). Mp 205−207 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, J = 8.8 Hz, 2H), 7.19 (s, 1H), 7.17 (s, 1H), 7.09 (s, 1H), 7.03 (d, J = 6.8 Hz, 2H), 5.77 (brs, 2H), 4.03 (s, 3H), 3.99 (3H), 3.93 (q, J = 7.0 Hz, 2H), 2.40 (s, 3H), 0.74 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 151.1, 149.1, 144.9, 141.1, 138.7, 135.9, 131.0, 128.5, 127.9, 118.3, 117.2, 107.9, 107.3, 101.0, 60.3, 56.0, 55.9, 21.1, 13.2 ppm; MS (ESI): m/z 388 (M + Na)$^+$. Anal. Calcd for $C_{22}H_{23}NO_4$: C, 72.31; H, 6.34; N, 3.83. Found: C, 72.56; H, 6.47; N, 3.96.

*Ethyl 1-Amino-6,7-dimethoxy-3-(2-methoxyphenyl)-2-naphthoate (**2o**).* Pale orange liquid. Yield: 118 mg (62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.27 (m, 2H), 7.10 (s, 1H), 7.03−6.98 (m, 3H), 6.87 (d, J = 8.0 Hz, 1H), 4.02 (s, 3H), 3.98 (s, 3H), 3.94−3.85 (m, 2H), 3.72 (s, 3H), 0.75 (t, J = 7.2 Hz, 3H); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.64 (s, 1H), 7.38−7.34 (m, 1H), 7.29 (d, J = 1.6 Hz, 1H), 7.27 (s, 1H), 7.07−7.01 (m, 2H), 6.96 (brs, 2H), 6.86 (s, 1H), 3.99 (s, 3H), 3.93 (s, 3H), 3.87−3.85 (m, 2H), 3.69 (s, 3H), 0.72 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 156.3, 151.0, 149.1, 145.1, 135.2, 133.6, 131.2, 129.8, 127.8, 120.6, 119.1, 117.8, 109.9, 108.0, 107.4, 101.2, 59.9, 56.0, 55.9, 55.4, 13.2 ppm; MS (ESI): m/z 382 $(M + H)^+$. Anal. Calcd for $C_{22}H_{23}NO_5$: C, 69.28; H, 6.08; N, 3.67. Found: C, 69.46; H, 6.17; N, 3.74.

*Ethyl 1-Amino-3-(4-chlorophenyl)-6,7-dimethoxy-2-naphthoate (**2p**).* Semibrown solid. Yield: 123 mg (64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7 10 (s, 1H), 7.04 (s, 1H), 6.96 (s, 1H), 5.94 (brs, 2H), 4.03 (s, 3H), 3.99 (s, 3H), 3.94 (q, J = 7.2 Hz, 2H), 0.78 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 151.4, 149.3, 145.7, 142.8, 137.6, 132.2, 130.9, 129.4, 127.9, 118.3, 117.4, 107.4, 106.8, 101.1, 60.3, 56.1, 55.9, 13.3 ppm; MS (ESI): m/z 385 $(M)^+$. Anal. Calcd for $C_{21}H_{20}ClNO_4$: C, 65.37; H, 5.22; N, 3.63. Found: C, 65.50; H, 5.34; N, 3.79.

*Ethyl 4′-Amino-4,6′,7′-trimethoxy-1,2′-binaphthyl-3′-carboxylate (**2q**).* Pale orange solid. Yield: 116 mg (54%). Mp 128−130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.45−7.41 (m, 1H), 7.38−7.36 (m, 1H), 7.27−7.25 (m, 1H), 7.16 (s, 1H), 7.04 (d, J = 7.6 Hz, 2H), 6.84 (d, J = 7.6 Hz, 1H), 6.11 (brs, 2H), 4.06 (s, 3H), 4.05 (s, 3H), 3.98 (s, 3H), 3.67−3.59 (m, 1H), 3.55−3.46 (m, 1H), 0.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 154.5, 151.3, 149.2, 145.8, 137.2, 135.0, 133.6, 131.2, 126.2, 126.0, 125.3, 124.8, 121.8, 119.7, 117.5, 108.5, 107.3, 103.2, 101.3, 59.8, 56.1, 55.9, 55.6, 12.7 ppm; MS (ESI): m/z 432 (M + H)$^+$. Anal. Calcd for $C_{26}H_{25}NO_5$: C, 72.37; H, 5.84; N, 3.25. Found: C, 72.50; H, 5.56; N, 3.38.

*Methyl 1-Amino-3-phenyl-6,7,8,9-tetrahydrodibenzo[b,d]thiophene-2-carboxylate (**2r**).* Pale yellow solid. Yield: 76 mg (45%). Mp 146−148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.28 (m, 5H), 7.05 (s, 1H), 5.76 (brs, 2H), 3.37 (s, 3H), 3.15 (d, J = 5.6 Hz, 2H), 2.82 (d, J = 4.0 Hz, 2H), 1.93−1.88 (m, 4H); ^{13}C NMR (100 MHz,

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$CDCl_3$): δ 170.7, 145.4, 143.4, 142.5, 139.1, 135.5, 129.1, 127.92, 127.85, 126.5, 126.3, 113.8, 109.1, 51.1, 27.3, 26.0, 22.9, 22.5 ppm; HRMS (ESI): $[M + H]^+$ Calcd for $C_{20}H_{20}NO_2S$, 338.1215; found, 338.1207.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and ^{13}C NMR spectra for all products and X-ray structural information of **2i** (CIF). 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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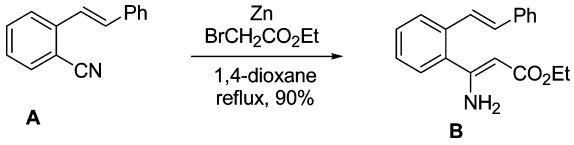

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