JOC The Journal of Organic Chemistry

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Transpositive Tandem Annulation of Phthalides with Allene Carboxylates: Regioselective Synthesis of Arylnaphthalene Lignans

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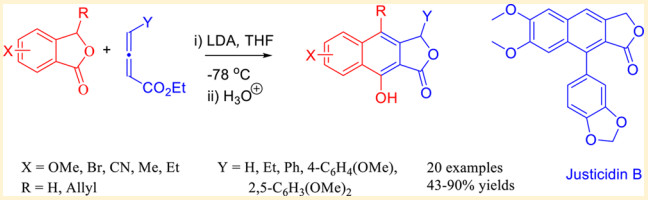
Supporting Information

ABSTRACT: Allene carboxylates, scarcely used as Michael acceptors, serve as acceptors in the annulation with phthalides in the presence of LDA and provide a one-pot synthesis of naphtho[*c*]furanones in very good yields. This tandem annulation is proposed to proceed via transposition of the hydroxy group resulting from the initial annulation.



INTRODUCTION

Annulations of phthalides, namely Hauser annulation[1] and Sammes annulation,[2] are established reactions for regiodefined synthesis of peri-oxygenated naphthalenes, anthracenes, and naphthacene derivatives. Their applications in the total synthesis of natural products have been well documented in the literature.[3] These annulations have been extensively studied with conjugated carboxylates, enones, unsaturated lactones, pyrones, benzyne precursors, sulfones, etc.[4] However, no report is available on the annulation reactivity of conjugated allene carboxylates, although they are expected to behave like an acrylate. More strikingly, there have been an insignificant number of reports on their Michael addition reactivity until 1992.[5] One of the earliest examples of Michael addition of an allene-1-carboxylate is the reaction of diethylacetamido malonate in the presence of sodium ethoxide in ethanol.[6] The phosphine-promoted Michael addition reactivity of activated allenes has, however, been extensively studied.[7a] Likewise, their [4 + 2] cycloaddition reactions with unsaturated compounds have been explored for the synthesis of six-membered-ring systems.[7] Kita et al. and Scheinmann et al. demonstrated heteroannulation reactivity of allene-1-carboxylates involving hetero-Michael additions.[8,9] However, their studies were confined to only one symmetrical acceptor.[10] These studies still revealed the possibilities of an annulation in two distinct steps forming six-membered carbocycles.

Prompted by these findings, we envisaged that the annulation of phthalides **1** with unsymmetrical allene acceptors **2** would generate 1,4-naphthols **4** and **5** (Scheme 1). If path I occurs, the reaction between **1** and **2** would produce Michael adduct **3**, which can further react to form naphthol **4**. Alternatively, **3** can form isomeric naphthol **5** via enolate isomerization, as in path II.

RESULTS AND DISCUSSION

With the background in mind, we initiated this study with racemic allene-1-carboxylates **2** toward the annulation. For the synthesis of allene carboxylates **8a**−**e**, we adopted the synthetic protocols[11] of Kwon et al. After several experimentations, we prepared **8a**−**e** in reasonable yields (Scheme 2). Freshly prepared acid chlorides **7a**−**e** were treated with phosphorane **6** in the presence of triethylamine in DCM at −20 °C to room temperature. The unknown allene esters **8d,e** were duly characterized. The yields of the allenes **8d,e** are delicately sensitive to reaction conditions. Some preparations required critical optimizations of the reaction conditions.

For the initial studies, 7-methoxyphthalide (**9**) was reacted with allene carboxylate **8a** in the presence of LDA in THF at −78 °C to room temperature. Routine workup of the reaction mixture followed by chromatographic purification afforded a white solid. The ^{1}H NMR spectrum of the product did not match the structure of the expected product (cf. **4** or **5**). A downfield $-CH_2$ group at δ 5.3 ppm and an exchangeable hydrogen in the spectrum led to the proposal of structure **10**. This structure was further supported by an IR band at 1750 cm^{-1}, characteristic of a five-membered lactone ring. Having confirmed the structure **10** by HRMS data, we optimized the reaction with bases such as LiO^{t}Bu, LiHMDS, NaH, KO^{t}Bu, and NaHMDS. From the results given in Table 1, it is apparent entry 5 is the best set of conditions for the reaction.

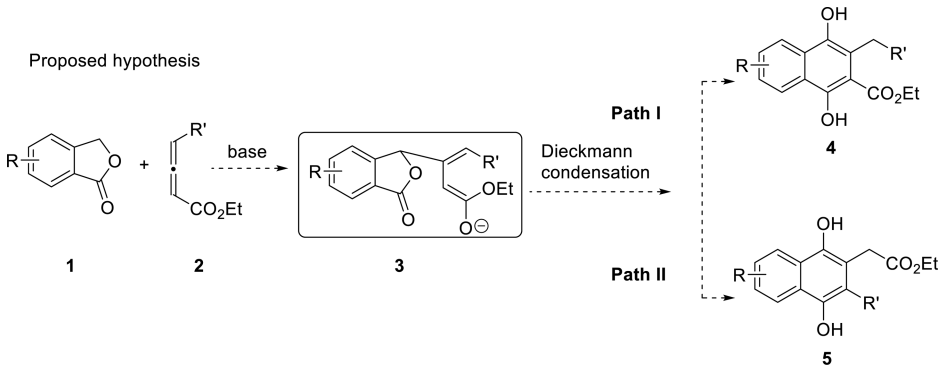
With the optimized conditions (Table 1, entry 5), a range of substituted phthalides **11** and allene carboxylates **8** were screened to establish the scope of this reaction. The reaction of simple phthalide **11a** with **8a** afforded naphthofuranone **13** in 73% yield. Next, we looked into the reactivity of the methoxy-substituted phthalides, since a great majority of aromatic polyketides feature methoxy substitutions. To this end, we prepared phthalide **11b**[13] following the literature method and then subjected it to reaction with allene carboxylate **8a**. When the phthalide **11b** was reacted with allene carboxylate **8a**, products **14a,b** were obtained in 45% and 35% yields, respectively.

Likewise, naphthalide **15** was obtained in 57% yield (over two steps), when the annulation of phthalide **11a** with allene

Received: September 21, 2016
Published: October 27, 2016

DOI: 10.1021/acs.joc.6b02313
J. Org. Chem. 2016, 81, 11857−11865

Scheme 1. Working Hypothesis for the Single-Step Synthesis of 1,4-Naphthoquinols 4 and 5 from Phthalides



Scheme 2. Synthesis of Allene Carboxylates 8[11]

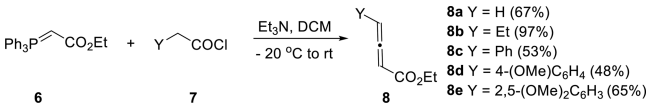
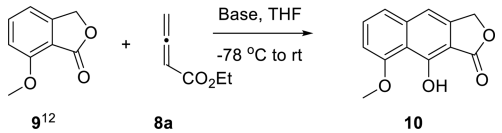
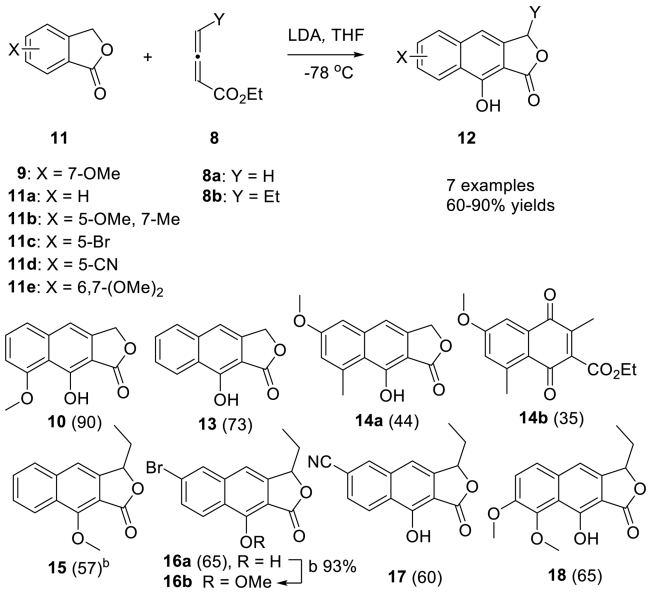


Table 1. Optimization of Reaction Conditions



entry	base (amt (equiv))/conditions	product	yield (%)
1	LiO^{t}Bu (3)/−78 °C to room temp	**10**	16
2	LiHMDS (3)/−78 °C to room temp	**10**	56
3	LDA (1)/−78 °C to room temp	**10**	48
4	LDA (2)/−78 °C to room temp	**10**	81
5	LDA (3)/−78 °C to room temp	**10**	90
6	NaH/0 °C to room temp		0
7	KO^{t}Bu/−78 °C to room temp	**10**	10
8	NaHMDS/−78 °C to room temp	**10**	25

Table 2. Scope of the Annulation Leading to 12[a]

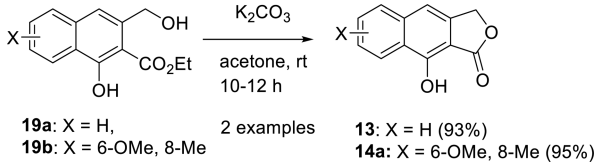


[a]Reaction conditions: (a) LDA (3 equiv), THF, −78 °C to room temperature, 6−7 h, quenched with 3 M HCl; (b) MeI, K_2CO_3, acetone, room temperature, 4−8 h.

carboxylate **8b** was conducted. The intermediate naphthalide **15a** (see the Experimental Section for details) was also isolated in ∼63% yield. Due to a purification problem, it was converted into **15** in 91% yield by treating with MeI and K_2CO_3. On the other hand, naphthol **16a** was formed in 65% yield when 5-bromophthalide **11c** was subjected to annulation with allene acceptor **8b**. Similarly, 5-cyanophthalide **11d** reacted smoothly with **8b** under same reaction conditions and gave the expected naphthol **17** in 60% yield. Naphtho[2,3-*c*]furan-1(3*H*)-one **18** was formed in 65% yield, when dimethoxyphthalide **11e** was reacted with **8b**. The structure of compound **18** was confirmed by a single-crystal structure analysis (see the Supporting Information for details). The results presented in Table 2 show that there is a great deal of flexibility in the choice of phthalides and allene esters to furnish the corresponding naphtho[2,3-*c*]furan-1(3*H*)-ones **12** in good to excellent yields, and various functional groups were tolerated.

The substituents in **11** could be bromo, cyano, methoxy, methyl, and ethyl. For substituents in **8**, it could be an alkyl group such as ethyl. These results indicate that this synthetic method is quite general for the preparation of naphthalides with diverse substitution patterns. In certain cases, intermediate naphthols, such as **19a,b**, accompanied the naphthalide products. These naphthols could, however, be further cyclized to the corresponding naphthalides by treating them with either mild acids or bases (Scheme 3).

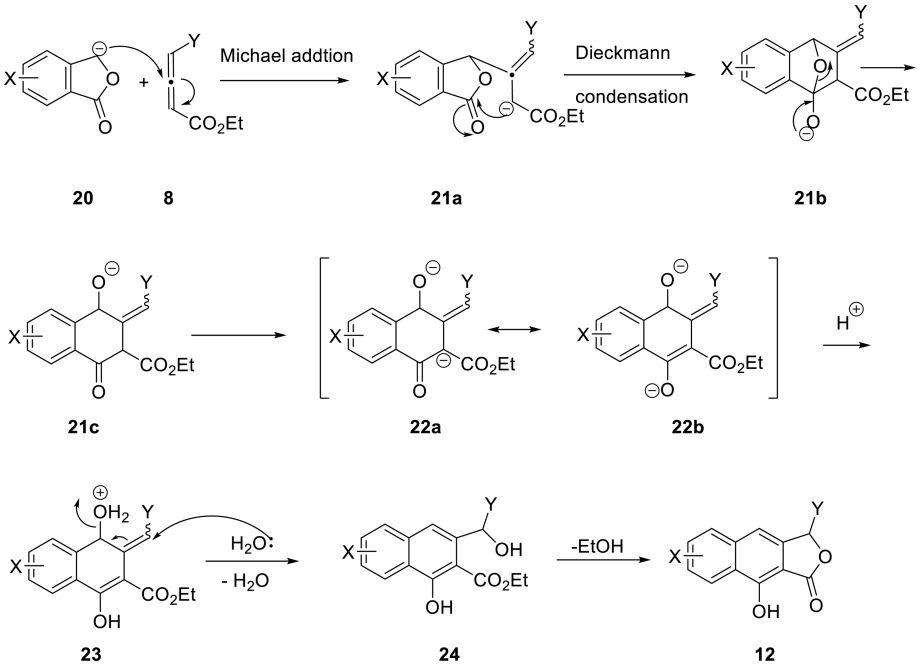
Scheme 3. Intramolecular Lactonization of 19 to Lactones 13 and 14a



The formation of naphtho[*c*]furanones **12** can be explained by the mechanism shown in Scheme 4. The annulation cascade is initiated by LDA-promoted generation of 3-lithiophthalides **20**, which undergo Michael addition to the central carbon of the allene carboxylate **8** to give **21a**. The Dieckmann condensation of **21a** leads to the formation of **21c** via tricyclic intermediate **21b**. With excess base, **21c** is further deprotonated to **22a,b**. During workup of the mixture, intermediates **22** combine with H^+ to give **23**. Attack of H_2O at the electron-deficient double bond of **23** forms naphthol **24**. Further

DOI: 10.1021/acs.joc.6b02313
J. Org. Chem. 2016, 81, 11857−11865

Scheme 4. Probable Mechanism for the Formation of Naphtho[*c*]furanones 12



cyclization of the naphthol **24** with mild bases gives desired naphtho[*c*]furanones **12**.

Having established the new tandem annulation, we proceeded to find its application in the synthesis of bioactive molecules. It is well-known that arylnaphthalene lactone lignans are widely distributed in plants.[14] Structurally, they occur in various levels of oxidation. They exhibit valuable medicinal properties such as antiviral, inhibition of calcium release from a fetal long-bone culture, antimicrobial ,and antiplatelet activities.[15] In particular, justicidin B (**25**) displays antifungal and antiproliferative properties.[16]

Keeping in mind the importance of lignans and structural complexity of saccharothrixones A−C,[17] viridicatumtoxin D (**27**), and viridicatumtoxin E (**28**)[18] (Figure 1), we planned to

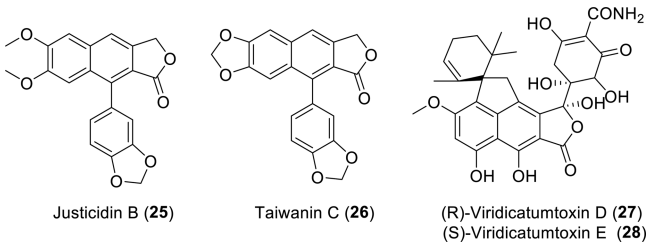


Figure 1. Biologically important naphtho[*c*]furanones.

apply the developed method for generation of analogues of arylnaphthalene lignans. As shown in Table 3, the annulation of phthalides **29** with dienoates **8c−e** give the arylnaphthalene lignan analogues **30**.

A range of the combination of substituted phthalides **29** and allene carboxylates **8** were screened to probe the scope of this reaction. The results displayed in Table 3 showed that the reaction is robustly general and furnished the corresponding arylnaphthofuranones **30** in good to excellent yields and various functional groups were well tolerated. In addition to the phthalides **9** and **11a,c−e**, phthalides **29a−e** were also reacted with the allene acceptors **8c−e**. 6-Ethyl-7-methoxyphthalide **29a**[19] was compatible with the annulation reaction with **8c**, forming the product **34** in 70% yield. Similarly, 4-methoxyphthalide **29b**[20] and 5-methoxyphthalide **29c**, upon annulation, afforded products **35** and **36** in 60% and 65% yields, respectively. We then considered 3-allylphthalide **29d**, to arrive at 4-substituted naphtho[*c*]furanones. Phthalide **29d**, prepared by the reported procedure,[21] was reacted with the acceptor **8c**, and naphthalide **39** was expectedly obtained in 43% yield. Next, we proceeded to check the reactivity of the angular phthalide **29e**, in view of its anomalous behavior[18] in the Hauser annulation. It was prepared by Yu lactonization.[12] As shown in Table 3, the phthalide **29e** was as efficient as the other donors and produced the expected product **40** in 72% yield. We then focused on changing the acceptors. To this end, we synthesized new acceptors **8d,e** in 48% and 65% yields, respectively, and these were reacted with the simple phthalide **11a**. The desired products **41** and **42** were obtained in 75% and 72% yields, respectively. No complication arose due to a nuclear lithiation/ortho lithiation. Thus, the substituents in **29** could be methoxy, bromo, cyano, methyl, ethyl, etc. and those in **8** could be phenyl, 4-methoxyphenyl, and 2,5-dimethoxyphenyl.

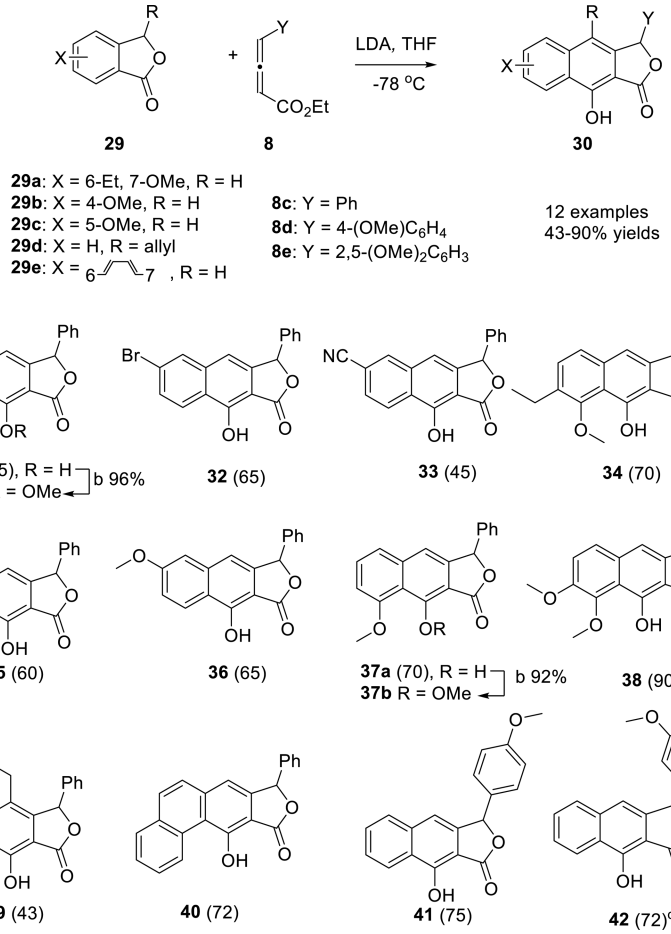
In order to demonstrate the utility of the annulation, we synthesized a natural product: namely, justicidin B (**25**). Phthalide **43**[2f] was reacted with **8a** in the presence of LDA to provide **44** in 59% yield. Naphtho[*c*]furanone **44** was converted to justicidin B (**25**) in two steps (Scheme 5).[15b]

CONCLUSION

In conclusion, we report an unprecedented anionic cascade reaction of 2,3-butenoates (allene carboxylates) with phthalides. It results in a regiodefined synthesis of naphtho[*c*]furanones. The regiochemical outcome of the reaction suggests that the first step is a Michael addition followed by Dieckmann condensation. The second crucial step, i.e. transposition of the newly generated hydroxy groups, leads to the formation of products. Extension of the reaction to arylallene carboxylates has led to an efficient and convenient synthesis of

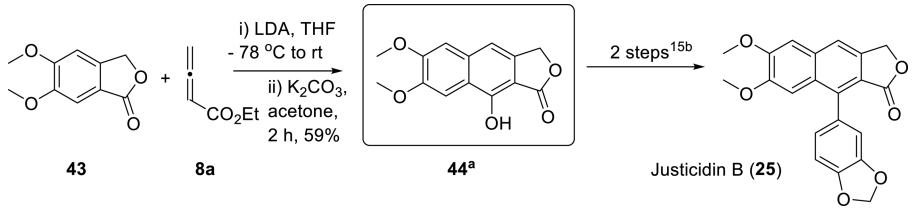
DOI: 10.1021/acs.joc.6b02313
J. Org. Chem. 2016, 81, 11857−11865

Table 3. Scope of the Annulation Leading to 30[a]



[a]Reaction conditions: (a) LDA (3 equiv), THF, −78 °C to room temperature, 6−7 h, quenched with 3 M HCl; (b) MeI, K_2CO_3, acetone, room temperature, 4−8 h; (c) crude product, K_2CO_3, acetone, room temperature, 3 days.

Scheme 5. Formal Synthesis of Justicidin B (25) from the Active Intermediate 44



[a]**44** was accompanied by 16% of ethyl 6,7-dimethoxy-3-methyl-1,4-dioxo-1,4-dihydronaphthalene-2-carboxylate (**44a**; see the Experimental Section for details).

arylnaphthalene lignan analogues. Its synthetic utility in the synthesis of lignans has briefly been demonstrated by the formal synthesis of justicidin B (**25**).

EXPERIMENTAL SECTION

General Procedures. Melting points were determined in open-end capillary tubes and are uncorrected. Solvents were dried and distilled following the standard procedures. TLC was carried out on precoated plates (silica gel 60, GF254), and the spots were visualized with UV and fluorescent lights. Column chromatography was performed on silica gel (60−120 or 230−400 mesh). ^{1}H NMR spectra for all the compounds were recorded at 400/600 MHz. Chemical shifts are quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for tetramethylsilane. The following abbreviations are used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, ddd = doublet of doublets of doublets, m = multiplet. Coupling constants, *J*, are reported in Hertz (Hz). ^{13}C NMR was recorded on 100 and 150 MHz instruments. The spectra were fully decoupled by broad band proton decoupling. IR spectra were recorded on an FT-IR instrument using a KBr pellet. The phrase "usual workup" or "worked up in the usual manner" refers to washing of the organic phase with water (2 × 1/3 the volume of the organic phase) and brine (1 × 1/4 the volume of the organic phase), drying (anhydrous Na_2SO_4), filtration, and concentration under reduced pressure.

General Procedure for the Preparation of Allene Carboxylates.[11] Et_3N (5.5 mmol, 1.1 equiv) was added to a stirred solution of (carbethoxymethylene)triphenylphosphorane (**6**; 5 mmol, 1 equiv) in CH_2Cl_2 (20 mL). After the mixture was stirred for 10 min, the required acyl chloride **7** (5 mmol, 1 equiv) was added dropwise over

DOI: 10.1021/acs.joc.6b02313
J. Org. Chem. 2016, 81, 11857−11865

10 min at −20 to 0 °C. After it was stirred overnight, the resulting mixture was poured unto a Büchner funnel packed with silica gel and was washed with CH_2Cl_2 several times. The combined filtrate was carefully concentrated, and the resulting crude oil was purified by flash column chromatography (hexane/EtOAc, 20/1) to provide the 4-substituted 2,3-butadienoates **8**.

*Ethyl Buta-2,3-dienoate (**8a**[22]).* Yield: 67%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.62 (t, J = 6.6 Hz, 1H), 5.21 (d, J = 6.6 Hz, 2H), 4.20 (q, J = 7.2 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 215.7, 165.7, 88.0, 79.2, 61.0, 14.2.

*Ethyl Hexa-2,3-dienoate (**8b**[23]).* Yield: 97%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.69−5.59 (m, 2H), 4.21−4.17 (m, 2H), 2.18−2.13 (m, 2H), 2.28 (m, 3H), 1.07 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.1, 166.3, 97.1, 88.9, 60.7, 20.8, 14.2, 13.0.

*Ethyl 4-Phenylbuta-2,3-dienoate (**8c**[24]).* Yield: 53%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.261 (m, 5H), 6.63 (d, J = 6.0 Hz, 1H), 6.02 (d, J = 6.4 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 1.27 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.8, 165.3, 131.3, 129.0, 128.3, 127.7, 98.8, 92.1, 61.3, 14.4.

*Ethyl 4-(4-Methoxyphenyl)buta-2,3-dienoate (**8d**[25]).* Yield: 48%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 6.59 (d, J = 6.4 Hz, 1H), 5.99 (d, J = 6.0 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 3.80 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.7, 165.4, 159.7, 128.9, 123.4, 114.5, 98.3, 92.0, 61.8, 55.5, 14.4.

*Ethyl 4-(2,5-Dimethoxyphenyl)buta-2,3-dienoate (**8e**).* According to the general procedure for the preparation of allene carboxylates, the reaction of triethylamine (0.8 mL, 5.5 mmol), (carbethoxymethylene)-triphenylphosphorane (1.8 g, 5.0 mmol), and 2,5-dimethoxyphenyl acetyl chloride (1.1 g, 5.0 mmol) gave ethyl 4-(2,5-dimethoxyphenyl)-buta-2,3-dienoate (**8e**) (805 mg, 65%) as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (d, J = 6.4 Hz, 1H), 6.86 (s, 1H), 6.80 (br s, 2H), 5.98 (d, J = 6.4 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 3.79 (s, 3 H), 3.75 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.5, 165.5, 153.9, 151.0, 120.7, 114.7, 113.9, 112.6, 93.2, 91.4, 61.2, 56.5, 55.9, 14.4. HRMS (ESI): calcd for $C_{14}H_{16}O_4$ $[M - C_2H_4 + H]^+$ 221.0814, found 221.0818.

Method A: General Annulation Procedure with LDA. In a flame-dried flask, LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere. After 30 min at −78 °C, an appropriate phthalide (1 mmol) in THF (5 mL) was added dropwise over 15 min. The reaction mixture was stirred at −78 °C for 30 min, and then a solution of the appropriate Michael acceptor (1.2 mmol) in THF (5 mL) was added dropwise over 15 min at −78 °C. The reaction mixture was further stirred for 1 h at the same temperature and warmed under ambient conditions to room temperature over 5−6 h. The solution was then quenched with 3 M HCl (15 mL) or saturated ammonium chloride solution (15 mL). The resulting mixture was concentrated under reduced pressure and the residue extracted with ethyl acetate (3 × 50 mL). The combined extracts were washed with brine (3 1/3 vol), dried (Na_2SO_4), and concentrated to obtain the crude product, which was purified by column chromatography on silica gel using ethyl acetate in petroleum ether to afford the pure products.

Method B: General Annulation Procedure with LiHMDS. To a stirred solution of lithium hexamethyldisilazide (3.2 mmol) in THF (10 mL) at −78 °C under an inert atmosphere was added a solution of phthalide (1 mmol) in THF (5 mL). The resulting yellow solution was stirred at −78 °C for 30 min, after which a solution of a Michael acceptor (1.2 mmol) in THF (5 mL) was added to it. The cooling bath was removed after about 1 h at −78 °C, and the reaction mixture was brought to room temperature over a period of 1 h and further stirred for 5−6 h. The reaction was then quenched with 3 M HCl (15 mL), and the resulting solution was concentrated under reduced pressure. The residue was diluted with ethyl acetate (3 × 50 mL), and the layers were separated. The combined extracts were washed with brine (3 × 1/3 vol), dried (Na_2SO_4), and concentrated to provide the crude product. The crude solid product was purified by column chromatography on silica gel using ethyl acetate in petroleum ether to obtain a pure product.

General Procedure for the Protection of an −OH Group by MeI and K_2CO_3. To a stirred solution of naphthol compound (1.0 mmol) in 10 mLof dry acetone was added K_2CO_3 (5.0 mmol) at 0 °C. After 30 min, MeI (5.0 mmol) was added. Then the reaction mixture was further stirred for another 6−10 h at room temperature. After completion of the reaction (checked by TLC), acetone was evaporated under reduced pressure. The reaction mixture was extracted with ethyl acetate, and the extracts were washed with brine (3 × 1/3 vol), dried (Na_2SO_4), and concentrated to provide the crude product. The crude solid product was purified by column chromatography on silica gel using ethyl acetate in petroleum ether to obtain a pure product.

*9-Hydroxy-8-methoxynaphtho[2,3-c]furan-1(3H)-one (**10**).* According to the general procedure for annulation (method A), the condensation of 7-methoxyphthalide **9** (164 mg, 1 mmol) with ethyl buta-2,3-dienoate **8a** (134.5 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **10** as a white solid (207 mg, 90%), mp 143−145 °C. ν_{max} (KBr, cm^{-1}): 3318, 1750, 1606, 1458, 1380, 1364, 1157o, 1080, 1034, 755, 626. ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.47 (s, 1H), 7.51 (t, J = 7.8 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.25 (s, 1H), 6.90 (d, J = 7.8 Hz, 1H), 5.35 (s, 2H), 4.12 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.5, 158.3, 156.8, 142.9, 140.3, 129.4, 121.8, 114.6, 110.8, 106.3, 104.9, 68.6, 56.6. HRMS (ESI): calcd for $C_{13}H_{10}O_4$ $[M + H]^+$ 231.0657, found 231.0649.

*9-Hydroxynaphtho[2,3-c]furan-1(3H)-one (**13**[15b]).* According to the general procedure for annulation, the condensation of simple phthalide **11a** (134 mg, 1 mmol) with ethyl buta-2,3-dienoate **8a** (134.5 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing a mixture of compound **13** (40.5%) and **19a** (35%); the mixture of the two compounds on treatment with K_2CO_3 in acetone produced **13** as a white solid (146 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.6 (s, 1H), 8.39 (d, J = 8.8 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 8.0 Hz, 1H), 7.56 (t, J = 7.2 Hz, 1H), 7.36 (s, 1H), 5.47 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 155.1, 139.0, 138.6, 129.8, 128.0, 125.8, 123.5, 111.8, 104.6, 70.7. HRMS (ESI): calcd for $C_{12}H_8O_3$ $[M + H]^+$ 201.0552, found 201.0546.

*9-Hydroxy-6-methoxy-8-methylnaphtho[2,3-c]furan-1(3H)-one (**14a**).* According to the general procedure for annulation, the condensation of phthalide **11b** (366.5 mg, 2 mmol) with ethyl buta-2,3-dienoate **8a** (269 mg, 2.4 mmol) in the presence of LDA (6.4 mmol) was prepared by adding *n*-BuLi (6.4 mmol, 1.6 M in hexane) to a solution of diisopropylamine (6.4 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **14a** as a white solid (97.72 mg, 20%), mp 146−148 °C. Compound **14a** was formed along with 35% of **14b** and 25% of **19b**. Compound **19b** was converted to **14a** in 95% yield on treatment with K_2CO_3 in acetone. The overall yield of **14a** is 44% (215 mg). ν_{max} (KBr, cm^{-1}): 3378, 2928, 1749, 1649, 1345, 1220, 760. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.10 (s, 1H), 7.16 (s, 1H), 5.12 (s, 2H), 5.39 (s, 2H), 3.92 (s, 3H), 2.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 159.9, 158.2, 142.9, 140.0, 139.8, 120.5, 118.1, 111.2, 104.7, 103.6, 70.2, 55.3, 24.2, 14.2. HRMS (ESI): calcd for $C_{14}H_{12}O_4$ $[M + H]^+$ 245.0814, found 245.0820.

*Ethyl 6-Methoxy-3,8-dimethyl-1,4-dioxo-1,4-dihydronaphthalene-2-carboxylate (**14b**).* According to the general procedure for annulation, the condensation of phthalide **11b** (366.5 mg, 2 mmol) with ethyl buta-2,3-dienoate **8a** (269 mg, 2.4 mmol) in the presence of LDA (6.4 mmol) was prepared by adding *n*-BuLi (6.4 mmol, 1.6 M in hexane) to a solution of diisopropylamine (6.4 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **14b** as a yellow solid (201.8 mg, 35%), mp 120−122 °C as a byproduct. ν_{max} (KBr, cm^{-1}): 2932, 1768, 1687, 1598, 1276, 1220, 773. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.52 (d, J = 3.0 Hz, 1H), 7.02 (d, J = 2.4 Hz, 1H), 4.46 (q, J = 7.2 Hz, 2H), 3.95 (s, 3H), 2.73 (s, 3H), 2.15

DOI: 10.1021/acs.joc.6b02313
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(s, 3H), 1.43 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 185.4, 182.4, 165.2, 162.9, 144.6, 141.3, 141.2, 135.3, 123.5, 122.8, 109.6, 62.0, 55.8, 22.9, 14.23, 13.4. HRMS (ESI): calcd for $C_{16}H_{16}O_5$ $[M + H]^+$ 289.1076, found 289.1063.

*Ethyl 1-Hydroxy-3-(1-hydroxypropyl)-2-naphthoate (**15a**).* According to the general procedure for annulation, the condensation of simple phthalide **11a** (134 mg, 1 mmol) with ethyl hexa-2,3-dienoate **8b** (168.2 mg, 1.2 mmol) in the presence of LDA (3.2 mmol), was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **15a** as a white solid (172.8 mg, 63%), mp 145−147 °C. ν_{max} (KBr, cm^{-1}): 3420, 2934, 1668, 1560, 1345, 1120. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.58 (s, 1H), 8.37 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.61 (s, 1H), 7.59−7.57 (m, 1H), 7.50−7.47 (m, 1H), 5.43−5.41 (m, 1H), 4.50−4.47 (m, 2H), 1.93−1.85 (m, 1H), 1.69−1.62 (m, 1H), 1.47 (t, J = 7.2 Hz, 3H), 1.06 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.0, 162.4, 142.1, 136.0,129.9, 127.6, 125.8, 124.1, 116.1, 104.5, 84.1, 73.1, 62.2, 32.3, 14.3, 10.9. HRMS (ESI): calcd for $C_{16}H_{18}O_4$ $[M - H_2O + H]^+$ 257.1177, found 257.1173.

*3-Ethyl-9-methoxynaphtho[2,3-c]furan-1(3H)-one (**15**).* According to the general procedure for the protection of an −OH group, in the reaction of compound **15a** (172.8 mg, 0.63 mmol) with K_2CO_3 (435 mg, 3.15 mmol) and MeI (0.20 mL, 3.15 mmol), **15** was obtained as a white solid (139.5 mg, 91%), mp 135−137 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, J = 8.4 Hz, 1H), 8.86 (d, J = 8.0 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 7.47 (s, 1H), 5.53−5.51 (m, 1H), 4.39 (s, 3H), 2.21−2.15 (m, 1H), 1.93−1.86 (m, 1H), 1.04 (t, J = 8.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5, 157.8, 145.1, 137.9, 129.6, 128.0, 127.9, 126.4, 124.4, 114.8, 111.6, 81.57, 64.0, 28.6, 8.9. HRMS (ESI): calcd for $C_{15}H_{14}O_3$ $[M + H]^+$ 243.1021, found 243.1026.

*6-Bromo-3-ethyl-9-hydroxynaphtho[2,3-c]furan-1(3H)-one (**16a**).* According to the general procedure for annulation, the condensation of 6-bromophthalide **11c** (319.5 mg, 1.5 mmol) with ethyl hexa-2,3-dienoate **8b** (252.3 mg, 1.8 mmol) in the presence of LDA (4.8 mmol) was prepared by adding *n*-BuLi (4.8 mmol, 1.6 M in hexane) to a solution of diisopropylamine (4.8 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **16a** as a white solid (300.0 mg, 65%), mp 152−154 °C. ν_{max} (KBr, cm^{-1}): 3345, 2928, 2851, 2340, 1758, 772. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (s, 1H), 8.23 (d, J = 8.8 Hz, 1H), 8.01 (s, 1H), 7.62 (dd, J = 1.6 Hz, 8.8 Hz, 1H), 7.19 (s, 1H), 5.60−5.59 (m, 1H), 2.20−2.13 (m, 1H), 1.97−1.89 (m, 1H), 1.05 (t, J = 7.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.5, 155.1, 144.2, 139.6, 130.4, 129.4, 125.3, 124.7, 122.2, 110.8, 105.8, 84.1, 28.2, 8.9. HRMS (ESI): calcd for $C_{14}H_{11}BrO_3$ $[M + H]^+$ 306.9970, found 306.9976.

*6-Bromo-3-ethyl-9-methoxynaphtho[2,3-c]furan-1(3H)-one (**16b**).* According to the general procedure for the protection of an −OH group, in a reaction of compound **16a** (300 mg, 0.98 mmol) with K_2CO_3 (675 mg, 4.9 mmol) and MeI (0.3 mL, 4.9 mmol), compound **16b** was obtained as a white solid (292.5 mg, 93%), mp 164−166 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.28 (d, J = 9.2 Hz, 1H), 8.02 (s, 1H), 7.62 (dd, J = 2.0 Hz, 9.2 Hz, 1H), 7.36 (s, 1H), 5.53−5.50 (m, 1H), 4.40 (s, 3H), 2.21−2.14 (m, 1H), 1.92 (m, 1H), 1.04 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1, 157.9, 146.6, 138.8, 129.9, 129.9, 126.6, 126.2, 124.5, 113.6, 111.6, 81.5, 64.2, 28.6, 8.9. HRMS (ESI): calcd for $C_{15}H_{13}BrO_3$ $[M + H]^+$ 321.0126, found 321.0121.

*3-Ethyl-9-hydroxy-1-oxo-1,3-dihydronaphtho[2,3-c]furan-6-carbonitrile (**17**).* According to the general procedure for annulation, the condensation of 6-cyanophthalide **11d** (159 mg, 1 mmol) with ethyl hexa-2,3-dienoate **8b** (168.2 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **17** as a pale yellow solid (151.8 mg, 60%), mp 149−151 °C. ν_{max} (KBr, cm^{-1}): 3324, 2925, 1756, 1588, 1455, 1219, 772. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.78 (s, 1H), 7.50 (d, J = 9.0 Hz, 1H), 8.25 (s, 1H), 7.71 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 7.39 (s, 1H), 5.68−5.66 (m, 1H), 2.24−2.20 (m, 1 H), 2.00−1.95 (m,1H), 1.09 (t, J = 7.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.1, 154.7, 144.8, 137.2, 134.1, 126.5, 125.1, 118.6, 113.3, 112.1, 107.9, 84.2, 28.2, 9.0. HRMS (ESI): calcd for $C_{15}H_{11}NO_3$ $[M + H]^+$ 254.0817, found 254.0813.

*3-Ethyl-9-hydroxy-7,8-dimethoxynaphtho[2,3-c]furan-1(3H)-one (**18**).* According to the general procedure for annulation, the condensation of 6,7-dimethoxy phthalide **11e** (194.2 mg, 1 mmol) with ethyl hexa-2,3-dienoate **8b** (168.2 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **18** as a pale yellow solid (187.4 mg, 65%), mp 145−147 °C. The structure of compound **18** was confirmed by a single-crystal structure analysis (see the Supporting Information for details). ν_{max} (KBr, cm^{-1}): 3342, 2934, 1752, 1634, 1460, 1102. ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.77 (s, 1H), 7.62 (d, J = 9.0 Hz, 1H), 7.43 (d, J = 9.6 Hz, 1H), 7.17 (s, 1H), 5.48−5.5.46 (m, 1H), 4.14 (s, 3H), 4.03 (s, 3H), 2.16−2.12 (m, 1H), 1.91−1.86 (m, 1H), 1.05 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.6, 155.6, 148.0, 145.2, 143.6, 134.4, 125.2, 118.5, 118.1, 110.7, 107.1, 81.5, 62.5, 57.2, 28.5, 8.9. HRMS (ESI): calcd for $C_{16}H_{16}O_5$ $[M + H]^+$ 289.1076, found 289.1075.

*Ethyl 1-Hydroxy-3-(hydroxymethyl)-2-naphthoate (**19a**).* According to the general procedure for annulation, the condensation of simple phthalide **11a** (134 mg, 1 mmol) with ethyl buta-2,3-dienoate **8a** (134.5 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **19a** as a white solid (98.5 mg, 35%), mp 143−145 °C. ν_{max} (KBr, cm^{-1}): 3411, 2850, 1735, 1630, 1498, 1320, 1182, 1072, 920, 765. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.82, 8.41 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.0, 1H), 7.65−7.61 (m, 1H), 7.56−7.53 (m, 1H), 7.35 (s, 1H), 5.05 (s, 2H), 4.54 (q, J = 7.2, 2H), 1.53 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 163.3, 135.5, 133.6, 130.2, 127.5, 126.7, 125.3, 124.3, 122.1, 104.5, 62.4, 48.1, 14.1. HRMS (ESI): calcd for $C_{14}H_{14}O_4$ $[M - H_2O + H]^+$ 229.0864, found 229.0869.

*Ethyl 1-Hydroxy-3-(hydroxymethyl)-6-methoxy-8-methyl-2-naphthoate (**19b**).* According to the general procedure for annulation, the condensation of phthalide **11b** (366.5 mg, 2 mmol) with ethyl buta-2,3-dienoate **8a** (269 mg, 2.4 mmol) in the presence of LDA (6.4 mmol) was prepared by adding *n*-BuLi (6.4 mmol, 1.6 M in hexane) to a solution of diisopropylamine (6.4 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **19b** as a white solid (145.2 mg, 25%), mp 132−134 °C. ν_{max} (KBr, cm^{-1}): 3448, 2989, 1733, 1654, 1596, 1384, 1314, 1247, 1222, 1338, 1065, 874, 722. ^{1}H NMR (600 MHz, $CDCl_3$): δ 13.34 (s, 1H), 7.19 (s, 1H), 6.91 (s, 1H), 6.86 (d, J = 1.2 Hz, 1H), 5.00 (s, 2H), 4.53 (q, J = 7.2 Hz, 2H), 3.92 (s, 3H), 2.93 (s, 3H), 1.52 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.1, 166.4, 160.1, 140.8, 139.4, 133.8, 121.8, 121.1, 119.5, 104.7, 102.8, 62.0, 55.3, 48.1, 25.1, 14.0. HRMS (ESI): calcd for $C_{16}H_{18}O_5$ $[M - H_2O + H]^+$ 273.1126, found 273.1124.

*9-Hydroxy-3-phenylnaphtho[2,3-c]furan-1(3H)-one (**31a**).* According to the general procedure for annulation, the condensation of simple phthalide **11a** (134 mg, 1 mmol) with ethyl 4-phenylbuta-2,3-dienoate **8c** (225.8 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **31a** as a colorless liquid (207 mg, 75%), mp 152−154 °C. ν_{max} (KBr, cm^{-1}): 3413, 2918, 2850, 1726, 1640, 1598, 1319, 1082, 1072, 910, 765. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.71 (s, 1H), 8.42 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.66 (t, J = 7.2 Hz, 1H), 7.58 (t, J = 7.8 Hz, 1H), 7.43−7.42 (m, 3H), 7.39−7.38 (m, 2H), 7.23 (s, 1H), 6.58 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.6, 154.9, 142.4, 138.6, 136.8, 129.8, 129.4, 129.0, 128.2, 127.2, 126.0, 123.6, 123.5, 113.0, 104.7, 84.1. HRMS (ESI): calcd for $C_{18}H_{12}O_3$ $[M + H]^+$ 277.0865, found 277.0862.

*9-Methoxy-3-phenylnaphtho[2,3-c]furan-1(3H)-one (**31b**).* According to the general procedure for the protection of an −OH group, in a reaction of **31a** (207 mg, 0.75 mmol), K_2CO_3 (517.5 mg, 3.75 mmol), and MeI (0.25 mL, 3.75 mmol), **31b** was obtained as a

DOI: 10.1021/acs.joc.6b02313
J. Org. Chem. 2016, 81, 11857−11865

white solid (209.0 mg, 96%), mp 159−161 °C. ν_{max} (KBr, cm^{-1}): 2924, 2852, 1759, 1630, 1583, 1458, 1336, 1290, 1088, 912, 764, 705. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.46 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.65−7.63 (m, 1H), 7.60−7.57 (m, 1H), 7.42−7.37 (m, 6H), 6.50 (s, 1H), 4.48 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.1, 157.8, 144.9, 137.9, 137.6, 129.6, 129.2, 129.0, 127.9, 127.1, 126.5, 124.3, 116.1, 110.5, 82.0, 64.0. HRMS (ESI): calcd for $C_{19}H_{14}O_3$ [M + H]$^+$ 291.1021, found 291.1035.

*6-Bromo-9-hydroxy-3-phenylnaphtho[2,3-c]furan-1(3H)-one (**32**).* According to the general procedure for annulation, the condensation of 6-bromophthalide **11c** (213 mg, 1 mmol) with ethyl 4-phenylbuta-2,3-dienoate **8c** (225.8 mg, 1.2 mmol) in the presence of LDA (4.8 mmol) was prepared by adding *n*-BuLi (4.8 mmol, 1.6 M in hexane) to a solution of diisopropylamine (4.8 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **32** as a light yellow solid (230.5 mg, 65%), mp 165−167 °C. ν_{max} (KBr, cm^{-1}): 3398, 1725, 1612, 1251, 1076, 991, 750. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.32 (br s, 1H), 7.28 (d, J = 8.8 Hz, 1H), 8.21 (d, J = 1.6 Hz, 1H), 7.67 (dd, J = 1.2 Hz, 8.8 Hz, 1H), 7.43−7.34 (m, 5H), 7.26 (s, 1H), 6.71 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.4, 154.9, 146.5, 139.7, 138.5, 130.6, 129.7, 129.6, 127.7, 126.5, 124.0, 112.1, 106.2, 81.7. HRMS (ESI): calcd for $C_{18}H_{11}BrO_3$ [M + H]$^+$ 354.9970, found 354.9974.

*9-Hydroxy-1-oxo-3-phenyl-1,3-dihydronaphtho[2,3-c]furan-6-carbonitrile (**33**).* According to the general procedure for annulation, the condensation of 6-cyanophthalide **11d** (159 mg, 1 mmol) with ethyl 4-phenylbuta-2,3-dienoate **8c** (225.8 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **33** as a pale yellow solid (135.5 mg, 45%), mp 168−170 °C. ν_{max} (KBr, cm^{-1}): 3368, 2936, 1734, 1653, 1127, 1075, 697. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (s, 1H), 8.50 (d, J = 8.8 Hz, 1H), 8.16 (s, 1H), 7.70 (d, J = 8.8 Hz, 1H), 7.43−7.34 (m, 5H), 7.28 (s, 1H), 6.60 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.9, 154.7, 144.6, 137.4, 136.1, 134.1, 129.9, 129.3, 127.2, 126.7, 125.2, 125.2, 118.5, 113.5, 113.5, 107.3, 84.3. HRMS (ESI): calcd for $C_{19}H_{11}NO_3$ [M + H]$^+$ 302.0817, found 302.0810.

*7-Ethyl-9-hydroxy-8-methoxy-3-phenylnaphtho[2,3-c]furan-1(3H)-one (**34**).* According to the general procedure for annulation, the condensation of 6-ethyl-7-methoxyisobenzofuran-1(3*H*)-one **29a** (97 mg, 0.5 mmol) with ethyl 4-phenylbuta-2,3-dienoate **8c** (113 mg, 0.6 mmol) in the presence of LDA (1.6 mmol) was prepared by adding *n*-BuLi (1.6 mmol, 1.6 M in hexane) to a solution of diisopropylamine (1.6 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **34** as a light red solid (117.1 mg, 70%), mp 158−160 °C. ν_{max} (KBr, cm^{-1}): 3378, 1735, 1632, 1231, 1046, 945, 730. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.60 (br s, 1H), 7.52−7.44 (m, 2H), 7.37−7.34 (m, 5H), 7.10 (s, 1H), 6.43 (s, 1H), 3.99 (s, 3H), 2.84 (q, J = 7.6 Hz, 2H), 1.32 (t, J = 7.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.9, 155.5, 155.0, 144.5, 139.1, 137.4, 133.0, 131.7, 129.1, 128.9, 127.0, 125.2, 117.4, 112.3, 106.1, 82.0, 63.5, 22.03, 15.0. HRMS (ESI): calcd for $C_{21}H_{18}O_4$ [M + H]$^+$ 335.1283, found 335.1286.

*9-Hydroxy-5-methoxy-3-phenylnaphtho[2,3-c]furan-1(3H)-one (**35**).* According to the general procedure for annulation, the condensation of 4-methoxyphthalide **29b** (164 mg, 1 mmol) with ethyl 4-phenylbuta-2,3-dienoate **8c** (225.8 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **35** as a white solid (183.6 mg, 60%), mp 150−152 °C. ν_{max} (KBr, cm^{-1}): 3408, 1728, 1615, 1232, 1026, 750. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.63 (s, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.67 (s, 1H), 7.49 (t, J = 7.8 Hz, 1H), 7.41−7.38 (m, 5H), 7.00 (d, J = 7.8 Hz, 1H), 6.57 (s, 1H), 3.98 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.7, 155.4, 154.5, 141.7, 136.9, 130.8, 129.4, 129.0, 127.3, 126.1, 124.6, 115.3, 107.7, 107.6, 105.2, 55.6. HRMS (ESI): calcd for $C_{19}H_{14}O_4$ [M + H]$^+$ 307.0970, found 307.0976.

*9-Hydroxy-6-methoxy-3-phenylnaphtho[2,3-c]furan-1(3H)-one (**36**).* According to the general procedure for annulation, the condensation of 6-methoxyphthalide **29c** (164 mg, 1 mmol) with ethyl 4-phenylbuta-2,3-dienoate **8c** (225.8 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **36** as a white solid (199 mg, 65%), mp 148−150 °C. ν_{max} (KBr, cm^{-1}): 3414, 2930, 1720, 1615, 1451, 1370, 1287, 1219, 1072, 1030, 755, 699. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.60 (s, 1H), 8.30 (d, J = 9.6 Hz, 1H), 7.41 (br s, 3H), 7.38 (br s, 2H), 7.21 (d, J = 9.0 Hz, 1H), 7.09 (s, 1H), 7.07 (s, 1H), 6.53 (s, 1H), 3.92 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.6, 160.8, 154.9, 143.7, 140.9, 136.9, 129.4, 129.0, 127.1, 125.1, 118.6, 118.5, 111.7, 106.5, 103.2, 83.8, 55.4. HRMS (ESI): calcd for $C_{19}H_{14}O_4$ [M + H]$^+$ 307.0970, found 307.0973.

*9-Hydroxy-8-methoxy-3-phenylnaphtho[2,3-c]furan-1(3H)-one (**37a**).* According to the general procedure for annulation, the condensation of 7-methoxyphthalide **9** (164 mg, 1 mmol) with ethyl 4-phenylbuta-2,3-dienoate **8c** (225.8 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **37a** as a white solid (214.2 mg, 70%), mp 155−157 °C. ν_{max} (KBr, cm^{-1}): 3442, 1752, 1613, 1363, 1268, 1198, 1066, 974, 716. ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.53 (s, 1H), 7.48−7.37 (m, 7H), 7.10 (s, 1H), 6.88 (d, J = 7.8 Hz, 1H), 6.43 (s, 1H), 4.15 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.9, 158.3, 156.7, 146.2, 140.4, 137.6, 129.4, 129.1, 128.9, 127.0, 122.0, 114.8, 11.9, 106.1, 105.0, 81.5, 56.6. HRMS (ESI): calcd for $C_{19}H_{14}O_4$ [M + H]$^+$ 307.0970, found 307.0969.

*8,9-Dimethoxy-3-phenylnaphtho[2,3-c]furan-1(3H)-one (**37b**).* According to the general procedure for the protection of an −OH group, in a reaction of compound **37a** (214.2 mg, 0.70 mmol), K_2CO_3 (483.0 mg, 3.5 mmol) and MeI (0.22 mL, 3.5 mmol), compound **37b** was obtained as a colorless oil (206.3 mg, 92%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.52 (t, J = 8.4 Hz, 1H), 7.43−7.28 (m, 7H), 6.92 (d, J = 7.2 Hz, 1H), 6.44 (s, 1H), 4.21 (s, 3H), 4.06 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 167.9, 158.5, 141.0, 137.5, 129.7, 129.2, 129.0, 127.0, 120.8, 120.7, 117.1, 113.9, 106.5, 81.21, 63.8, 56.4. HRMS (ESI): calcd for $C_{20}H_{16}O_4$ [M + H]$^+$ 321.1127, found 321.1124.

*9-Hydroxy-7,8-dimethoxy-3-phenylnaphtho[2,3-c]furan-1(3H)-one (**38**).* According to the general procedure for annulation, the condensation of 6,7-dimethoxy phthalide **11e** (194.2 mg, 1 mmol) with ethyl 4-phenylbuta-2,3-dienoate **8c** (225.8 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **38** as a pale yellow solid (302.4 mg, 90%), mp 156−158 °C. ν_{max} (KBr, cm^{-1}): 3447, 1750, 1617, 1373, 1278, 1198, 1115, 1066, 974, 706. ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.9 (s, 1H), 7.53 (d, J = 9.6 Hz, 1H), 7.40−7.37 (m, 6H), 7.39 (s, 1H), 6.41 (s, 1H), 4.16 (s, 3H), 4.02 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.2, 155.5, 148.0, 145.0, 143.4, 137.8, 134,3, 129.1, 128.9, 126.9, 125.2, 118.4, 118.0, 11.9, 106.1, 81.7, 62.4, 57.0. HRMS (ESI): calcd for $C_{20}H_{16}O_5$ [M + H]$^+$ 337.1076, found 337.1065.

*4-Allyl-9-hydroxy-3-phenylnaphtho[2,3-c]furan-1(3H)-one (**39**).* According to the general procedure for annulation, the condensation of 3-allyl phthalide **29d** (174.2 mg, 1 mmol) with ethyl 4-phenylbuta-2,3-dienoate **8c** (225.8 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **39** as a pale yellow solid (136 mg, 43%), mp 167−169 °C. ν_{max} (KBr, cm^{-1}): 3356, 1732, 1634, 1257, 1058, 723. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.73 (s, 1H), 8.49 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.69 (t, J = 7.2 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.41−7.38 (m, 3H), 7.30 (br s, 2H), 6.53 (s, 1H), 5.60−5.56 (m, 1H), 4.87 (d, J = 10.2 Hz, 1H), 4.72 (d, J = 17.4 Hz, 1H), 3.52 (dd, J = 4.8 Hz, 16.2 Hz, 1H), 3.37 (dd, J = 6.0 Hz, 16.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 154.0, 139.9, 137.6, 136.3, 134.6, 129.8, 129.2, 128.6, 125.8, 124.6, 124.2,

DOI: 10.1021/acs.joc.6b02313
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121.7, 116.3, 104.8, 84.7, 31.9. HRMS (ESI): calcd for $C_{21}H_{16}O_3$ $[M + H]^+$ 317.1178, found 317.1175.

*11-Hydroxy-8-phenylphenanthro[2,3-c]furan-10(8H)-one (**40**).* According to the general procedure for annulation, the condensation of angular phthalide **29e** (185 mg, 1 mmol) with ethyl 4-phenylbuta-2,3-dienoate **8c** (225.8 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **40** as a colorless liquid (235 mg, 72%). ν_{max} (KBr, cm^{-1}): 3411, 2928, 1736, 1630, 1578, 1309, 1182, 1052, 910, 745. ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.81 (s, 1H), 9.73 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 7.8 Hz, 1H), 7.89 (d, J = 9.0 Hz, 1H), 7.78 (t, J = 7.8 Hz, 1H), 7.70−7.66 (m, 2H), 7.45−7.39 (m, 5H), 7.32 (s, 1H), 6.61 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 173.6, 157.4, 144,32, 140.4, 136.4, 132.3, 131.8, 130.8, 129.7, 129.2, 128.6, 128.5, 128.0, 127.4, 127.0, 119.2, 114.1, 107.5, 84.0. HRMS (ESI): calcd for $C_{22}H_{14}O_3$ $[M + H]^+$ 327.1021, found 327.1031.

*9-Hydroxy-3-(4-methoxyphenyl)naphtho[2,3-c]furan-1(3H)-one (**41**).* According to the general procedure for annulation, the condensation of simple phthalide **11a** (134 mg, 1 mmol) with ethyl 4-(4-methoxyphenyl)buta-2,3-dienoate **8d** (261.6 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **41** as a white solid (230 mg, 75%), mp 156−158 °C. ν_{max} (KBr, cm^{-1}): 3320, 1751, 1610, 1438, 1345, 1215, 1137, 1040, 755. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.72 (s, 1H), 8.42 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.66 (t, J = 7.8 Hz, 1H), 7.59 (t, J = 7.8 Hz, 1H), 7.28 (d, J = 9.0 Hz, 2H), 7.21 (S, 1H), 6.93 (d, J = 9.0 Hz, 2H), 6.55 (s, 1H), 3.84 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.7, 160.7, 155.0, 142.7, 138.8, 129.9, 129.2, 128.8, 128.4, 126.1, 123.8, 123.6, 114.5, 113.2, 105.2, 84.3, 55.5. HRMS (ESI): calcd for $C_{19}H_{14}O_4$ $[M + Na]^+$ 329.0790, found 329.0776.

*3-(2,5-Dimethoxyphenyl)-9-hydroxynaphtho[2,3-c]furan-1(3H)-one (**42**).* According to the general procedure for annulation, the condensation of simple phthalide **11a** (134 mg, 1 mmol) with ethyl 4-(4-methoxyphenyl)buta-2,3-dienoate **8e** (298.0 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen; the crude product was immediately treated with approximately 5 equiv of K_2CO_3 in acetone, and the reaction mixture was stirred for 3 days at room temperature, producing compound **42** as a white solid (242 mg, 72%), mp 154−156 °C. ν_{max} (KBr, cm^{-1}): 3412, 1748, 1626, 1324, 1278, 1158, 1105, 1046, 954, 770. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.70 (s, 1H), 8.40 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.63 (t, J = 7.8 Hz, 1H), 7.56 (t, J = 7.8 Hz, 1H), 7.31 (s, 1H), 6.57 (s, 1H), 6.95 (d, J = 9.0 Hz, 1H), 6.89 (dd, J = 3.0 Hz, 9.0 Hz, 1H), 6.73 (d, J = 3.0 Hz, 1H), 3.92 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1, 154.9, 153.9, 151.5, 142.9, 138.8, 129.7, 128.4, 126.5, 125.9, 123.7, 123.6, 115.0, 113.2, 113.0, 112.5, 104.9, 56.4, 55.9. HRMS (ESI): calcd for $C_{20}H_{16}O_5$ $[M + Na]^+$ 359.0895, found 359.0880.

*9-Hydroxy-6,7-dimethoxynaphtho[2,3-c]furan-1(3H)-one (**44**[15b]).* According to the general procedure for annulation, the condensation of 5,6-dimethoxy phthalide **43** (194 mg, 1 mmol) with ethyl buta-2,3-dienoate **8a** (134.5 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere; after the usual workup we treated the crude reaction with K_2CO_3 in acetone and the reaction mixture was stirred for 2 h, producing compound **44** as a white solid (153.5 mg, 59%). Along with compound **44**, compound **44a** was formed in 14% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (br s, 1H), 7.59 (s, 1H), 7.20 (s, 1H), 7.11 (s, 1H), 5.42 (s, 2H), 4.06 (s, 3H), 4.04 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 173.4, 153.5, 152.5, 149.4, 138.2, 135.4, 118.4, 110.3, 106.5, 103.7, 101.6, 70.6, 56.1, 56.0.

*Ethyl 6,7-Dimethoxy-3-methyl-1,4-dioxo-1,4-dihydronaphthalene-2-carboxylate (**44a**).* According to the general procedure for annulation, the condensation of 5,6-dimethoxy phthalide **43** (194 mg, 1 mmol) with ethyl buta-2,3-dienoate **8a** (134.5 mg, 1.2 mmol) in the presence of LDA (3.2 mmol) was prepared by adding *n*-BuLi (3.2 mmol, 1.6 M in hexane) to a solution of diisopropylamine (3.2 mmol) in THF (10 mL) at −78 °C under a nitrogen atmosphere, producing compound **44a** as a bright yellow solid (48.7 mg, 16%), mp 121−123 °C. ν_{max} (KBr, cm^{-1}): 3443,1926, 1737, 1650, 1578, 1373, 1335, 1220, 1103, 1052, 1008. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.53 (s, 1H), 7.50 (s, 1H), 4.46 (q, J = 7.2 Hz, 2H), 4.04 (s, 3H), 4.03 (s, 3H), 2.18 (s, 3H), 1.42 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.4, 181.4, 164.9, 153.9, 153.8, 143.6, 139.3, 126.7, 126.4, 108.2, 107.9, 76.9, 62.2, 56.7, 14.4, 13.9. HRMS (ESI): calcd for $C_{16}H_{16}O_6$ $[M + H]^+$ 305.1025, found 305.1021.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02313.

^{1}H and ^{13}C NMR spectra of the synthesized compounds and X-ray crystallographic data (PDF)

X-ray crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the Council of Science & Industrial Research, New Delhi, India, for financial support. S.J. is thankful to IIT KHARAGPUR for her research fellowship and contingency grant. We are also thankful to the DST-FIST for financial support for establishing an NMR facility.

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DOI: 10.1021/acs.joc.6b02313
J. Org. Chem. 2016, 81, 11857−11865