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Electroreductive Coupling of Phthalic Anhydrides with α,β-Unsaturated Carbonyl Compounds: Synthesis of 1,4-Dihydroxynaphthalenes

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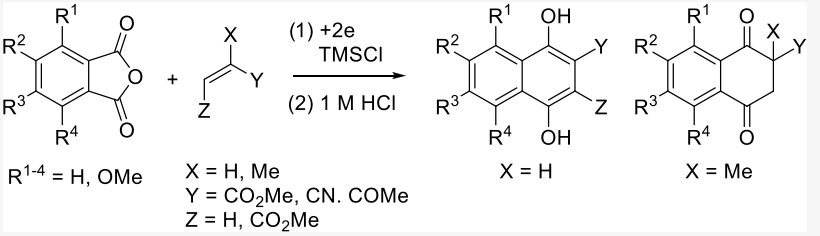
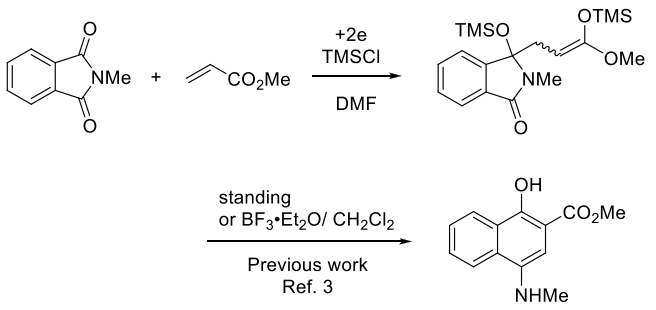


ABSTRACT: Electroreductive coupling of phthalic anhydrides with α,β-unsaturated carbonyl compounds in the presence of TMSCl and subsequent treatment with 1 M HCl gave 1,4-dihydroxynaphthalenes and 2-methyl-2,3-dihydronaphthalene-1,4-diones.

INTRODUCTION

Phthalic anhydrides have been used as a building block for the synthesis of a variety of aromatic compounds.[1] Recently, we reported the reductive coupling of phthalic anhydrides with aliphatic ketones by low-valent titanium:[2] this is the first report of the reductive cross-coupling of phthalic anhydrides with carbonyl compounds. In this context, we report herein the electroreductive coupling of phthalic anhydrides with α,β-unsaturated carbonyl compounds. In our previous work, the electroreductive coupling of *N*-methylphthalimide with methyl acrylate gave a silyl ketene acetal, and it was rearranged to methyl 1-hydroxy-4-(methylamino)-2-naphthoate by standing for 24 h (Scheme 1).[3] In this paper, we disclosed the electroreductive coupling of phthalic anhydrides with α,β-unsaturated carbonyl compounds and subsequent treatment with 1 M HCl gave 1,4-dihydroxynaphthalenes and 2-methyl-2,3-dihydronaphthalene-1,4-diones (Scheme 2). 1,4-Dihydroxynaphthalenes have been utilized as a building block for the total synthesis of biologically and pharmaceutically important compounds.[4] For the synthetic method of 1,4-dihydroxynaphthalenes, Hauser annulation is well known (Scheme 2).[5] This method, however, needs three-substituted phthalides as substrates, a strong base, and low-temperature conditions. On the contrary, the present method provides a new alternative synthetic route to 1,4-dihydroxynaphthalenes from phthalic anhydrides without using a strong base at room temperature. Reaction mechanisms of the electroreductive coupling and subsequent acid-catalyzed rearrangement were also discussed. It was presumed that 1,4-dihydroxynaphthalenes were obtained by acid-catalyzed rearrangement of silyl ketene acetals produced by electroreductive coupling.

Scheme 1. Electroreductive Coupling of *N*-Methylphthalimide with Methyl Acrylate (Previous Work)



RESULTS AND DISCUSSION

According to our reported method,[3] the electroreduction of phthalic anhydride (**1a**) with methyl acrylate (**2a**) was carried out in 0.3 M Et_4NOTs/dimethylformamide (DMF) in the presence of TMSCl at 0.1 A (2 F/mol). After usual workup, the formation of silyl ketene acetal **3a** was confirmed by ^1H NMR analysis of the crude product. In contrast to the electroreductive coupling of *N*-methylphthalimide with **2a**

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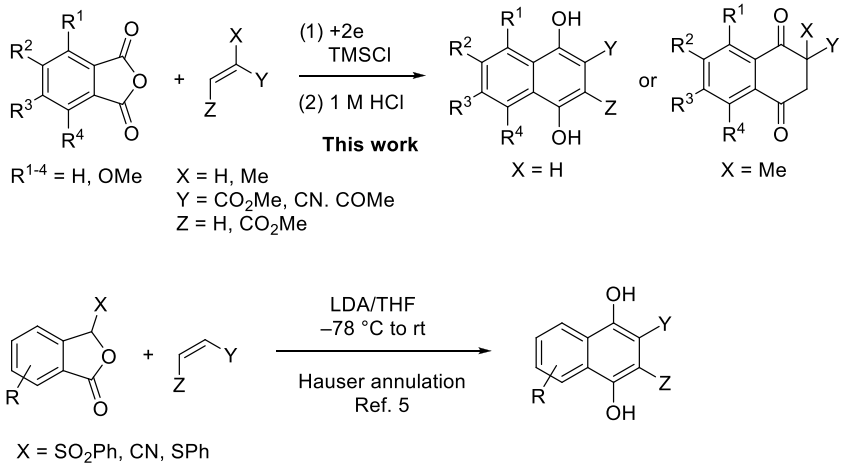
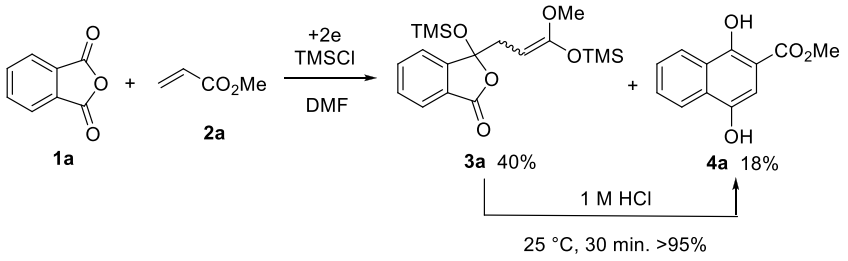
Scheme 2. Electroreductive Coupling of Phthalic Anhydrides with α,β-Unsaturated Carbonyl Compounds (This Work) and Hauser Annulation



Scheme 3. Electroreductive Coupling of Phthalic Anhydride with Methyl Acrylate and Transformation of 3a to 4a by Treatment with 1 M HCl



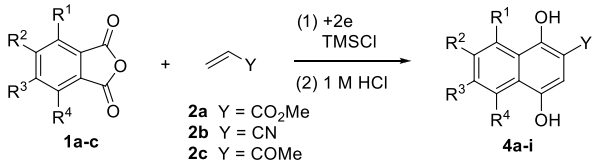
(Scheme 1),[3] **3a** could be isolated by column chromatography on silica gel, although a small amount of methyl 1,4-dihydroxy-2-naphthoate (**4a**) was formed during separation (Scheme 3). Since the isolated **3a** gradually rearranged to **4a** on standing exposed to air at 25 °C (completed within a week), **3a** was treated with 1 M HCl and dioxane (1:1) at 25 °C for 30 min to give **4a** quantitatively (Scheme 3). Therefore, the catholyte after the electroreduction of phthalic anhydrides **1** with α,β-unsaturated carbonyl compounds **2** was treated with 1 M HCl successively to obtain 1,4-dihydroxynaphthalenes **4** as the sole products. The results of the electroreductive coupling and subsequent treatment with 1 M HCl using **1a**, 5,6-dimethoxyphthalic anhydride (**1b**), and 4,7-dimethoxyphthalic anhydride (**1c**) with **2a**, acrylonitrile (**2b**), and methyl vinyl ketone (**2c**) are summarized in Table 1. The corresponding 1,4-dihydroxynaphthalenes **4a–i** were formed in moderate to good yields. In particular, dimethoxyphthalic anhydrides **1b** and **1c** gave products **4d–i** in better yields (runs 4–9) than did **1a** with products **4a–c** (runs 1–3).

The reaction of 4,5-dimethoxyphthalic anhydride (**1d**) with **2a–c** under the same conditions as above afforded 1,4-dihydroxynaphthalenes as mixtures of two regioisomers **4j–l** (major) and **4′j–l** (minor) in about 2:1 ratios (Scheme 4). The structures of minor isomers **4′j** and **4′l** were confirmed to be 7,8-dimethoxy-1,4-dihydroxynaphthalenes by their X-ray crystallographic analysis. Therefore, major isomers **4j–l** were identified to be 5,6-dimethoxy-1,4-dihydroxynaphthalenes.

Electroreduction and following workup with 1 M HCl were applied to **1a–d** with dimethyl maleate (**2d**) and dimethyl fumarate (**2e**), and the results are summarized in Table 2. In general, **2d** gave higher yields of diethyl 1,4-dihydroxynaphthalene-2,3-dicarboxylates **4m–p** (runs, 1, 3, 5, and 7) than **2e** did (runs 2, 4, 6, and 8). These results can be explained by the less negative reduction potential of **2e** than that of **2d** (vide infra). Although **1a** gave **4m** in low yield (32%) even using **2d** as an accepter (run 1), the reaction of dimethoxy-substituted phthalic anhydrides **1b–d** with **2d** produced **4n–p** in moderate to good yields (runs 3, 5, and 7).

On the other hand, the reaction of **1a–d** with methyl methacrylate (**2f**) and methacrylonitrile (**2g**) produced 2-methyl-2,3-dihydronaphthalene-1,4-diones **5a–h**, as shown in Table 3 and Scheme 5. Similarly to the results in Scheme 4,

Table 1. Electroreductive Coupling of 1a–c with 2a–c



run	1	R¹, R⁴	R², R³	2	Y	4	yield (%)[a]
1	**1a**	H	H	**2a**	CO_2Me	**4a**	54
2	**1a**	H	H	**2b**	CN	**4b**	65
3	**1a**	H	H	**2c**	COMe	**4c**	46
4	**1b**	H	MeO	**2a**	CO_2Me	**4d**	74
5	**1b**	H	MeO	**2b**	CN	**4e**	69
6	**1b**	H	MeO	**2c**	COMe	**4f**	52
7	**1c**	MeO	H	**2a**	CO_2Me	**4g**	79
8	**1c**	MeO	H	**2b**	CN	**4h**	83
9	**1c**	MeO	H	**2c**	COMe	**4i**	61

[a]Isolated yields.

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Scheme 4. Electroreductive Coupling of 1d with 2a−c

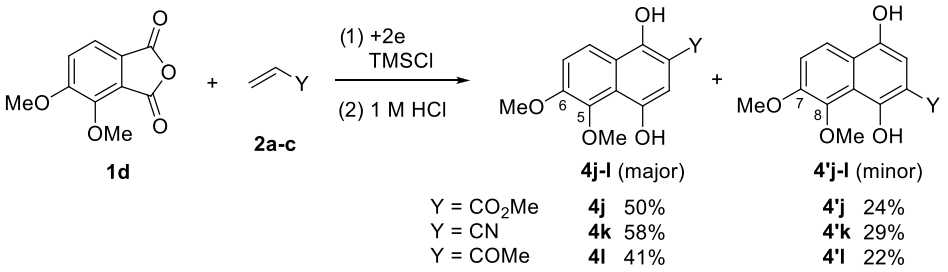
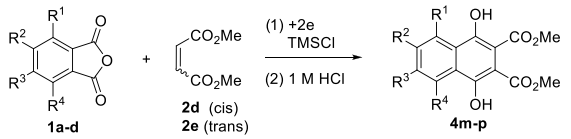


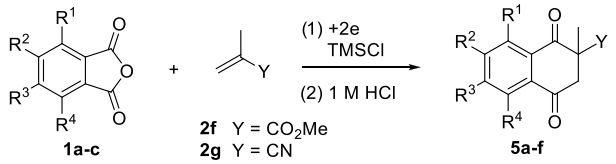
Table 2. Electroreductive Coupling of 1a−d with 2d,e



run	1	R^1	R^2	R^3	R^4	2	4	yield (%)[a]
1	**1a**	H	H	H	H	**2d**	**4m**	32
2	**1a**	H	H	H	H	**2e**	**4m**	14
3	**1b**	H	MeO	MeO	H	**2d**	**4n**	46
4	**1b**	H	MeO	MeO	H	**2e**	**4n**	20
5	**1c**	MeO	H	H	MeO	**2d**	**4o**	52
6	**1c**	MeO	H	H	MeO	**2e**	**4o**	28
7	**1d**	MeO	MeO	H	H	**2d**	**4p**	61
8	**1d**	MeO	MeO	H	H	**2e**	**4p**	43

[a]Isolated yields.

Table 3. Electroreductive Coupling of 1a−c with 2d,e



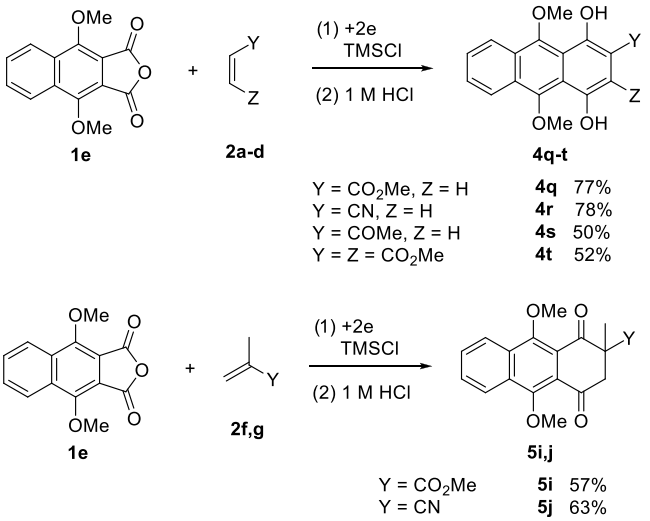
run	1	R^1, R^4	R^2, R^3	2	Y	5	yield (%)[a]
1	**1a**	H	H	**2f**	CO_2Me	**5a**	26
2	**1a**	H	H	**2g**	CN	**5b**	35
3	**1b**	H	MeO	**2f**	CO_2Me	**5c**	31
4	**1b**	H	MeO	**2g**	CN	**5d**	47
5	**1c**	MeO	H	**2f**	CO_2Me	**5e**	47
6	**1c**	MeO	H	**2g**	CN	**5f**	67

[a]Isolated yields.

two regioisomers **5g,h** and **5′g,h** were produced from the reaction of **1d** with **2f,g** (Scheme 5). The major isomers **5g,h** were identified to be 5,6-dimethoxy-2-methyl-2,3-dihydronaphthalene-1,4-diones, since the structure of **5h** was determined by X-ray crystallography.

From the results described above (Tables 1−3), it is found that 4,7-dimethoxyphthalic anhydride (**1c**) gave better results than **1a** and **1b**. Therefore, 4,9-dimethoxynaphtho[2,3-*c*]furan-1,3-dione (**1e**) was employed as the substrate (Scheme 6). Expectedly, 9,10-dimethoxyanthracene-1,4-diols

Scheme 6. Electroreductive Coupling of 1e with 2a−d and 2f,g



4q−t and 9,10-dimethoxy-2-methyl-2,3-dihydroanthracene-1,4-diones **5i,j** were obtained from the reaction of **1e** with **2a−d** and **2f,g**, respectively, in moderate to good yields.

The E_p values of **1a−e** and **2d,e** observed from cyclic voltammetry (CV) are summarized in Table 4. Other accepters **2a−c** and **2f,g** revealed no reduction peak from 0 to −2.00 V vs SCE. These results suggest that phthalic anhydrides **1a−e** are more reducible than **2a−d** and **2f,g**. On the contrary, the E_p value of **2e** is less negative than that of **2d** and almost same as those of **1b**, **1d**, and **1e**. It seems that the less negative potential of **2e** brought about poor results in the electroreductive coupling of **1a−d** with **2e** (Table 2). From

Scheme 5. Electroreductive Coupling of 1d with 2f,g

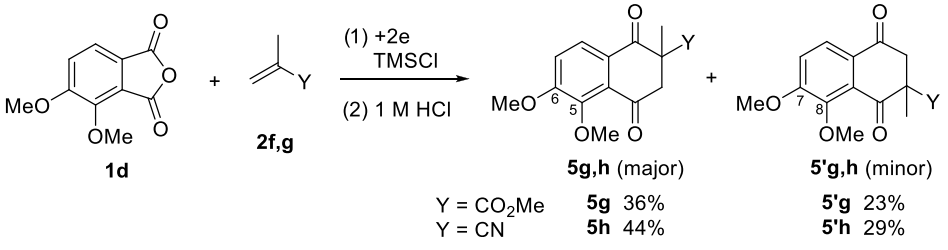


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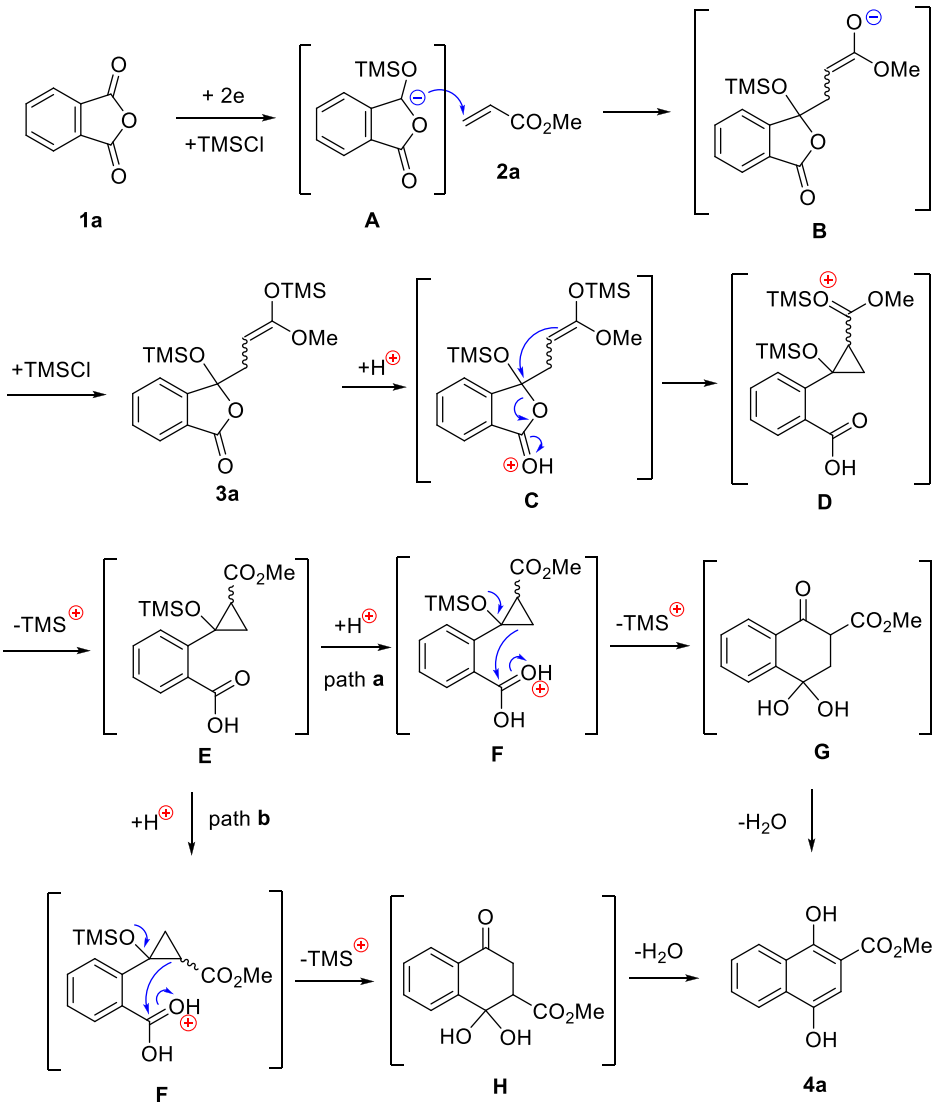
Table 4. E_p Values of 1a−e and 2d,e Derived from CV

	E_p[a]		E_p[a]		E_p[a]
1a	−1.31	**1d**	−1.47	**2d**	−1.70
1b	−1.47	**1e**	−1.49	**2e**	−1.48
1c	−1.32				

[a]First reduction peak (V vs SCE) in CV of 3 mM solution in 0.03 M TBAP/DMF at a Pt cathode at 0.1 V/s and 25 °C.

these CV data and our previously reported results of the electroreductive coupling of *N*-methylphthalimide with **2a**,[3] the reaction mechanism of the electroreductive coupling of **1a** with **2a** and the following rearrangement of **3a** to **4a** by treatment with 1 M HCl can be presumed, as illustrated in Scheme 7. First, carbanion **A** is formed by the two-electron transfer to **1a** and *O*-silylation with TMSCl. The nucleophilic addition of **A** to **2a** and the subsequent *O*-silylation of the resultant enolate anion **B** give silyl ketene acetal **3a** as the electroreductively coupled product. It seems that the substitution of two methoxy groups to the aromatic ring of **A** activates the anion in **A** from the results that dimethoxy-substituted **1b−d** constantly afforded better results than **1a**, as described above. Next, acid-catalyzed electrophilic addition of acetal moiety to silyl ketene acetal moiety in protonated **3a** (**C**) and subsequent desilylation of resultant **D** generate cyclopropane **E**. Successively, acid-catalyzed ring expansion of the cyclopropane ring in **E** forms methyl 4,4-dihydroxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**G**) through **F**. Finally, acid-catalyzed dehydration of **G** gives **4a** (path **a**). In the rearrangement of silyl ketene acetal derived from *N*-methylphthalimide and methyl acrylate (Scheme 1),[3] methyl 1-hydroxy-4-(methylamino)-2-naphthoate was selectively produced by the mechanism like path **a**. However, another path may be possible for the ring expansion of **F** to give methyl 1,1-dihydroxy-4-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**H**), which also produces **4a** after dehydration (path **b**). The reaction mechanism of the rearrangement from **3a** to **4a** shown in Scheme 7 is supported by the DFT calculations of **3a**, **E**, **G** (**H**), and **4a** at the B3LYP/6-311+G(2d,p) level in H_2O at 298 K. The energy profile exhibited in Scheme 8 indicates that the energies of **3a**, **E**, **G** (**H**), and **4a** decrease in this order. These results are consistent with the rapid

Scheme 7. Presumed Reaction Mechanism of Electroreductive Coupling of 1a with 2a and Subsequent Rearrangement of 3a to 4a by Treatment with 1 M HCl



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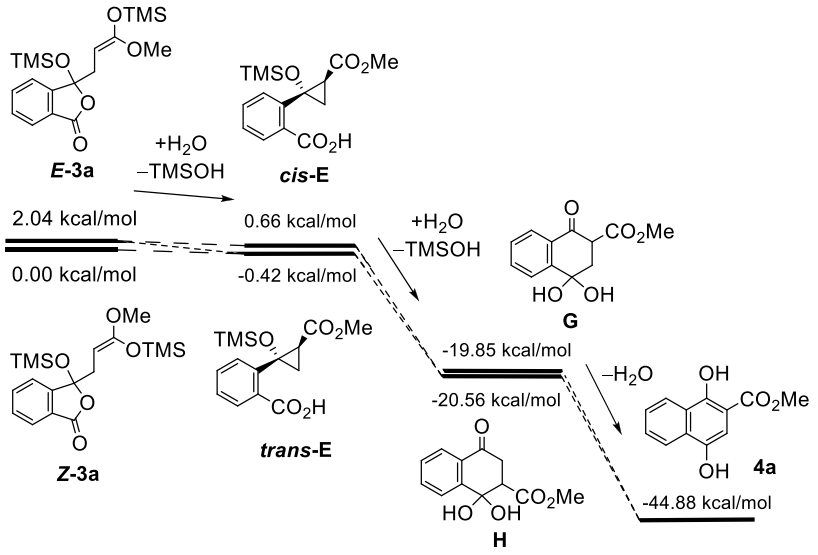
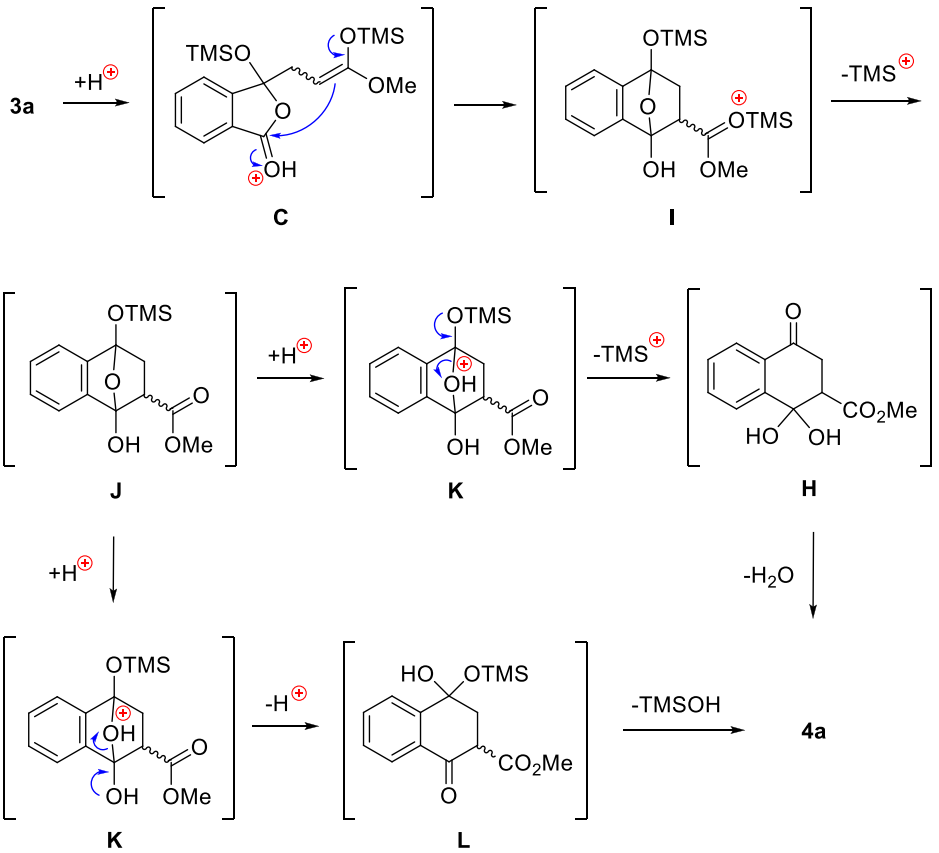
Scheme 8. Energy Profile for the Rearrangement from 3a to 4a Calculated by the B3LYP/6-311+G(2d,p)/IEFPCM(H_2O) Method at 298 K



Scheme 9. Alternative Presumed Reaction Mechanism of Rearrangement of 3a to 4a



formation of **4a** from **3a** under the acidic conditions. Since the intermediate **H** is slightly lower in energy than **G** (0.71 kcal/mol), path **b** may be more preferential than path **a** in Scheme 7.

An alternative reaction mechanism might be presumed for the rearrangement of **3a** to **4a**, as depicted in Scheme 9, similarly to the Hauser annulation mechanism.[5] The ketene silyl acetal moiety in **C** attacks the protonated lactone carbonyl group to form a 7-oxabicyclo[2.2.1]heptane ring, and the following desilylation of resultant **I** affords **J**. Subsequent acid-catalyzed ring opening of **J** forms **H** or **L** through **K**, and then dehydration of **H** or elimination of trimethylsilanol from **L** produces **4a**. However, the mechanism exhibited in Scheme 7 is more plausible, since the DFT calculations suggested that the intermediates ***exo*-J** and ***endo*-J** are 2.93 and 4.47 kcal/mol higher in energy than ***trans*-E** (Scheme 8), respectively, as shown in Scheme 10.

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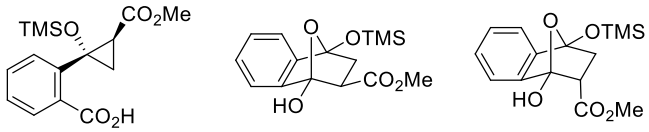
Scheme 10. Relative Energies of *trans*-E, *exo*-J, and *endo*-J against Z-3a Calculated by the B3LYP/6-311+G(2d,p)/IEFPCM(H_2O) Method at 298 K



***trans*-E** -0.42 kcal/mol | ***exo*-J** 2.51 kcal/mol | ***endo*-J** 4.05 kcal/mol

CONCLUSIONS

Electroreduction of phthalic anhydride (**1a**) with methyl acrylate (**2a**) in the presence of TMSCl gave a mixture of ketene silyl acetal **3a** and 1,4-dihydroxynaphthalene **4a**, and treatment of **3a** with 1 M HCl afforded **4a** quantitatively. Therefore, electroreduction of phthalic anhydrides **1a−d** with α,β-unsaturated compounds **2a−d** and subsequent treatment with 1 M HCl gave 1,4-dihydroxynaphthalenes **4a−p**. Using the same method, 2-methyl-2,3-dihydronaphthalene-1,4-diones **5a−h** were obtained from the reaction of phthalic anhydrides **1a−d** with methyl methacrylate (**2f**) and methacrylonitrile (**2g**). Similarly, 9,10-dimethoxyanthracene-1,4-diols **4q−t** and 9,10-dimethoxy-2-methyl-2,3-dihydroanthracene-1,4-diones **5i,j** were produced by the reaction of 4,9-dimethoxynaphtho[2,3-*c*]furan-1,3-dione (**1e**) with α,β-unsaturated compounds **2a−d** and **2f,g**, respectively.

EXPERIMENTAL SECTION

General Information. The ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were measured on a JEOL GMX-500 spectrometer with tetramethylsilane (TMS) or the residual signals of protonated solvents as an internal standard: $CDCl_3$ (δ = 77.0 in ^{13}C NMR); DMSO-d_6 (δ = 2.49 in ^{1}H NMR, δ = 39.5 in ^{13}C NMR). IR spectra were recorded on a Shimadzu IRAffinity-1 infrared spectrometer. HRMS spectra were measured on a Thermo Scientic Exactive FTMS spectrometer. Melting points were uncorrected. Column chromatography was performed on silica gel 60. TMSCl, TEA, and DMF were distilled from CaH_2. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl.

Starting Materials. 5,6-, 4,7-, and 4,5-Dimethoxyisobenzofuran-1,3-diones (**1b**,[6] **1c**,[7] and **1d**,[8] respectively) and 4,9-dimethoxynaphtho[2,3-*c*]furan-1,3-dione (**1e**)[9] were prepared by the reported methods.

*5,6-Dimethoxyisobenzofuran-1,3-dione (**1b**).* White solid; mp 175 °C (recryst. from chloroform; Lit.[6] 178 °C); R_f 0.5 (hexanes−ethyl acetate, 2:1); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37 (s, 2H), 4.05 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 163.1 (s), 155.7 (s), 124.9 (s), 106.1 (d), 56.9 (q).

*4,7-Dimethoxyisobenzofuran-1,3-dione (**1c**).* White solid; mp 272−274 °C (recryst. from chloroform; Lit.[7] 256−258 °C); R_f 0.35 (hexanes−ethyl acetate, 1:2); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.60 (s, 2H), 3.93 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 160.4 (s), 151.3 (s), 122.7 (s), 116.8 (d), 56.7 (q).

*4,5-Dimethoxyisobenzofuran-1,3-dione (**1d**).* White solid; mp 166−167 °C (recryst. from chloroform; Lit.[8] 166−167 °C); R_f 0.35 (hexanes−ethyl acetate, 2:1); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.68 (d, 1H, J = 8.3 Hz), 7.28 (d, 1H, J = 8.3 Hz), 4.22 (s, 3H), 4.01 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 162.4 (s), 160.6 (s), 158.6 (s), 148.5 (s), 122.9 (s), 121.5 (d), 120.5 (s), 118.2 (d), 62.6 (q), 56.9 (q).

*4,9-Dimethoxynaphtho[2,3-c]furan-1,3-dione (**1e**).* White solid; mp 210 °C (recryst. from chloroform; Lit.[9] 203−204 °C); R_f 0.5 (hexanes−ethyl acetate, 5:1); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.45−8.41 (m, 2H), 7.82−7.77 (m, 2H), 4.39 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 161.0 (s), 153.7 (s), 132.8 (s), 130.5 (d), 124.9 (d), 110.9 (s), 63.8 (q).

Typical Procedures for Electroreduction in the Presence of TMSCl (Table 1, Run 1). A 0.3 M solution of Et_4NOTS in DMF (15 mL) was placed in the cathodic chamber of a divided cell (40 mL beaker, 3 cm diameter, 6 cm height) equipped with a platinum cathode (5 × 5 cm^2), a platinum anode (2 × 1 cm^2), and a ceramic cylindrical diaphragm (1.5 cm diameter). A 0.3 M solution of Et_4NOTs in DMF (4 mL) was placed in the anodic chamber (inside the diaphragm). Phthalic anhydride (**1a**) (148 mg, 1.0 mmol), methyl acrylate (**2a**) (258 mg, 3.0 mmol), TMSCl (0.64 mL, 5 mmol), and TEA (0.70 mL, 5 mmol) were added to the cathodic chamber. After 200C of electricity was passed at a constant current of 100 mA at room temperature, the catholyte was transferred to an Erlenmeyer flask (100 mL). To the catholyte was added 1 M HCl (20 mL), and the mixture was stirred at room temperature for 30 min. The mixture was diluted with sat. NaCl aq (20 mL) and extracted with ethyl acetate (20 mL × 3), and the organic layer was washed with sat. NaCl aq, dried with $MgSO_4$, and filtered. After removal of the solvent in vacuo, the residue was purified by column chromatography on silica gel (hexanes−EtOAc) to give 118 mg of **4a**[10] in 54% yield.

Gram-Scale Synthesis of (4a). A 0.3 M solution of Et_4NOTS in DMF (50 mL) was placed in the cathodic chamber of a divided cell (100 mL beaker, 5 cm diameter, 7 cm height) equipped with a platinum cathode (5 × 10 cm^2), a platinum anode (2 × 2 cm^2), and a ceramic cylindrical diaphragm (2.5 cm diameter). A 0.3 M solution of Et_4NOTs in DMF (15 mL) was placed in the anodic chamber (inside the diaphragm). Phthalic anhydride (**1a**) (1.48 g, 10.0 mmol), methyl acrylate (**2a**) (2.58 g, 30.0 mmol), TMSCl (6.4 mL, 50 mmol), and TEA (7.0 mL, 50 mmol) were added to the cathodic chamber. After 2000C of electricity was passed at a constant current of 200 mA (2.78 h) at room temperature (in water bath), the catholyte was transferred to an Erlenmeyer flask (300 mL). To the catholyte was added 1 M HCl (80 mL), and the mixture was stirred at room temperature for 1 h. The mixture was diluted with sat. NaCl aq (80 mL) and extracted with ethyl acetate (80 mL × 3), and the organic layer was washed with sat. NaCl aq, dried with $MgSO_4$, and filtered. After removal of the solvent in vacuo, the residue was purified by column chromatography on silica gel (hexanes−EtOAc) to give 1.05 g of **4a** in 48% yield.

*3-(3-Methoxy-3-((trimethylsilyl)oxy)allyl)-3-((trimethylsilyl)oxy)-isobenzofuran-1(3H)-one (2:1 Mixture of Geometric Isomers) (**3a**).* Colorless paste (152 mg, 40%); R_f 0.45, 0.5 (hexanes−ethyl acetate, 10:1); IR (ATR) 1740, 1668, 1636, 1601 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.31−7.18 (m, 4H), 3.77 (s, 1H), 3.48 (s, 2H), 3.30 (dd, 0.67H, J = 4.6, 10.9 Hz), 2.82 (dd, 0.33H, J = 4.6, 8.2 Hz), 2.56 (dd, 0.33H, J = 4.6, 11.6 Hz), 2.35 (dd, 0.67H, J = 10.9, 12.0 Hz), 2.11 (dd, 0.67H, J = 4.6, 12.0 Hz), 1.93 (dd, 0.33H, J = 8.2, 11.6 Hz), 0.25 (s, 3H), 0.20 (s, 6H), 0.19 (s, 6H), 0.13 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 172.0 (s), 171.2 (s), 146.2 (s), 145.12 (s), 145.07 (s), 142.3 (s), 127.7 (d), 127.5 (d), 127.2 (d), 127.0 (d), 119.5 (d), 118.2 (d), 118.1 (d), 118.0 (d), 104.9 (s), 104.8 (s), 104.3 (s), 104.1 (s), 53.2 (d), 52.1 (d), 51.7 (q), 51.6 (q), 40.64 (t), 40.62 (t), 1.4 (q), 1.3 (q), 1.1 (q); HRMS (ESI) m/z: [M + H]$^+$ calcd. for $C_{18}H_{29}O_5Si_2$ 381.1554; found 381.1556.

*Methyl 1,4-Dihydroxy-2-naphthoate (**4a**).* Yellow solid (118 mg, 54%); R_f 0.6 (hexanes−ethyl acetate, 2:1); mp 197 °C (recryst. from hexanes−ethyl acetate, 1:1; Lit.[10] 191−193 °C); IR (ATR) 3379 (br), 1647, 1634, 1599, 1584 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.30 (brs, 1H), 9.96 (brs, 1H), 8.22 (d, 1H, J = 8.3 Hz), 8.09 (d, 1H, J = 8.5 Hz), 7.67−7.62 (m, 1H), 7.60−7.54 (m, 1H), 7.07 (s, 1H), 3.90 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 170.8 (s) 153.0 (s), 145.3 (s), 129.3 (s), 129.1 (d), 126.7 (d), 125.1 (s), 123.5 (d), 122.4 (d), 105.0 (s), 104.0 (d), 52.8 (q).

*1,4-Dihydroxy-2-naphthonitrile (**4b**).* Yellow solid (120 mg, 65%); R_f 0.4 (hexanes−ethyl acetate, 2:1); mp 220 °C (recryst. from hexanes−ethyl acetate, 1:1); IR (ATR) 3389 (br). 3198 (br), 2226, 1628, 1601, 1582 cm^{-1}; ^{1}H NMR ($CDCl_3$−DMSO-d_6, 500 MHz): δ 9.44 (brs, 1H), 9.21 (brs, 1H), 8.27 (d, 1H, J = 8.2 Hz),

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8.20 (d, 1H, J = 7.7 Hz), 7.60−7.51 (m, 2H), 6.78 (s, 1H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 125 MHz): δ 151.5 (s), 147.0 (s), 128.5 (d and s), 127.1 (d), 126.3 (s), 123.3 (d), 122.9 (d), 118.5 (s), 106.7 (d), 93.8 (s); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{11}H_8NO_2$ 186.0555; found 186.0550.

*1-(1,4-Dihydroxynaphthalen-2-yl)ethan-1-one (**4c**).* Yellow solid (93 mg, 46%); R_f 0.4 (hexanes−ethyl acetate, 2:1); mp 220−221 °C (recryst. from hexanes−ethyl acetate, 1:1; Lit.[11] 205−207 °C); IR (ATR) 3242 (br), 1636, 1614, 1595, 1574, 1520 cm^{-1}; ^1H NMR ($CDCl_3$-DMSO-d_6, 500 MHz): δ 13.52 (brs, 1H), 8.98 (brs, 1H), 8.39 (d, 1H, J = 8.6 Hz), 8.19 (d, 1H, J = 8.0 Hz), 7.65−7.61 (m, 1H), 7.55−7.51 (m, 1H), 7.05 (s, 1H), 2.63 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$-DMSO-d_6, 125 MHz): δ 203.6 (s), 155.6 (s), 144.3 (s), 129.8 (s), 128.8 (d), 125.7 (d), 125.4 (s), 123.8 (d), 121.9 (d), 112.1 (s), 104.8 (d), 26.6 (q).

*Methyl 1,4-Dihydroxy-6,7-dimethoxy-2-naphthoate (**4d**).* White solid (206 mg, 74%); R_f 0.3 (hexanes−ethyl acetate, 2:1); mp 192 °C (recryst. from hexanes−ethyl acetate, 2:1); IR (ATR) 3295 (br), 1774, 1663, 1636, 1609, 1589, 1518 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ, 11.51 (brs, 1H) 7.66 (s, 1H), 7.43 (s, 1H), 7.00 (s, 1H), 5.02 (brs, 1H), 4.04 (s, 6H), 3.96 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 171.2 (s), 154.4 (s), 151.8 (s), 149.5 (s), 142.4 (s), 125.0 (s), 120.5 (s), 104.1 (d), 103.3 (s), 102.9 (d), 101.2 (d), 56.0 (q), 52.1 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{15}O_6$ 279.0869; found 279.0863.

*1,4-Dihydroxy-6,7-dimethoxy-2-naphthonitrile (**4e**).* White solid (169 mg, 69%); R_f 0.4 (hexanes−ethyl acetate, 1:1); mp 230 °C (recryst. from hexanes−ethyl acetate, 1:5); IR (ATR) 3294 (br), 2228, 1620, 1589, 1528 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.48 (brs, 1H), 9.24 (brs, 1H), 7.60 (s, 1H), 7.49 (s, 1H), 6.69 (s, 1H), 4.02 (s, 3H), 4.00 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 150.5 (s), 150.2 (s), 149.3 (s), 145.3 (s), 124.1 (s), 121.0 (s), 118.6 (s), 105.5 (d), 102.2 (d), 101.5 (d), 91.2 (s), 55.70 (q), 55.65 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{13}H_{12}NO_4$ 246.0766; found 246.0757.

*1-(1,4-Dihydroxy-6,7-dimethoxynaphthalen-2-yl)ethan-1-one (**4f**).* Yellow solid (136 mg, 52%); R_f 0.35 (hexanes−ethyl acetate, 2:1); mp 236−238 °C (recryst. from hexanes−ethyl acetate, 2:1); IR (ATR) 3294 (br), 1603, 1582 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): δ 13.48 (brs, 1H), 9.66 (brs, 1H), 7.52 (s, 1H), 7.40 (s, 1H), 6.35 (s, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 2.60 (s, 3H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 125 MHz): δ 204.2 (s), 153.5 (s), 151.8 (s), 149.3 (s), 143.7 (s), 125.7 (s), 119.6 (s), 111.6 (s), 103.9 (d), 102.6 (d), 101.6 (d), 55.5 (q), 55.4 (q), 26.8 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{15}O_5$ 263.0919; found 263.0913.

*Methyl 1,4-Dihydroxy-5,8-dimethoxy-2-naphthoate (**4g**).* Yellow solid (220 mg, 79%); R_f 0.3 (hexanes−ethyl acetate, 2:1); mp 174−175 °C (recryst. from hexanes−ethyl acetate, 1:1); IR (ATR) 3339 (br), 1670, 1638, 1611, 1570, 1516 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 11.76 (brs, 1H), 9.20 (brs, 1H), 7.25 (s, 1H), 6.89 (d, 1H, J = 8.6 Hz), 6.78 (d, 1H, J = 8.6 Hz), 4.01 (s, 3H), 3.98 (s, 3H), 3.96 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 170.2 (s), 153.7 (s), 153.4 (s), 149.7 (s), 145.7 (s), 120.4 (s), 117.8 (s), 109.2 (d), 108.2 (d), 106.3 (d), 56.9 (q), 56.6 (q), 52.2 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{15}O_6$ 279.0869; found 279.0860.

*1,4-Dihydroxy-5,8-dimethoxy-2-naphthonitrile (**4h**).* White solid (203 mg, 83%); R_f 0.45 (hexanes−ethyl acetate, 1:2); mp 214−215 °C (recryst. from hexanes−ethyl acetate, 1:5); IR (ATR) 3354 (br), 3302 (brs), 2214, 1616, 1516 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.93 (brs, 1H), 9.14 (brs, 1H), 6.83 (s, 1H), 6.82 (d, 1H, J = 8.7 Hz), 6.77 (d, 1H, J = 8.7 Hz), 4.04 (s, 3H), 4.03 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$-DMSO-d_6, 125 MHz): δ 151.4 (s), 150.5 (s), 150.2 (s), 146.4 (s), 118.5 (s), 116.2 (s), 115.4 (s), 110.7 (d), 107.3 (d), 105.5 (d), 94.4 (s), 56.4 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{13}H_{12}NO_4$ 246.0766; found 246.0758.

*1-(1,4-Dihydroxy-5,8-dimethoxynaphthalen-2-yl)ethan-1-one (**4i**).* Yellow solid (160 mg, 61%); R_f 0.3 (hexanes−ethyl acetate, 2:1); mp 154−155 °C (recryst. from hexanes−ethyl acetate, 1:2); IR (ATR) 3362 (br), 1622, 1607, 1582, 1558, 1516 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 13.44 (brs, 1H), 9.19 (brs, 1H), 7.11 (s, 1H), 6.92 (d, 1H, J = 8.7 Hz), 6.79 (d, 1H, J = 8.7 Hz), 4.02 (s, 3H), 3.98 (s, 3H), 2.67 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 203.1 (s), 155.6 (s), 154.2 (s), 149.7 (s), 145.4 (s), 120.8 (s), 118.1 (s), 115.4 (s), 109.1 (d), 106.4 (d), 56.8 (q), 56.7 (q), 28.3 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{15}O_5$ 263.0919; found 263.0917.

*Methyl 1,4-Dihydroxy-5,6-dimethoxy-2-naphthoate (**4j**).* Yellow solid (139 mg, 50%); R_f 0.6 (hexanes−ethyl acetate, 2:1); mp 130 °C (recryst. from hexanes−ethyl acetate, 2:1); IR (ATR) 3356 (br), 1643, 1611, 1506 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 11.52 (s, 1H), 9.08 (s, 1H), 8.21 (d, 1H, J = 9.2 Hz), 7.28 (d, 1H, J = 9.2 Hz), 7.10 (s, 1H), 4.06 (s, 3H), 4.03 (s, 3H), 3.97 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 171.0 (s), 153.8 (s), 150.6 (s), 144.5 (s), 142.1 (s), 122.3 (s), 121.7 (d), 121.0 (s), 113.3 (d), 106.1 (d), 103.8 (s), 61.9 (q), 56.2 (q), 52.1 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{15}O_6$ 279.0869; found 279.0867.

*Methyl 1,4-Dihydroxy-7,8-dimethoxy-2-naphthoate (**4′j**).* Yellow solid (67 mg, 24%); R_f 0.3 (hexanes−ethyl acetate, 2:1); mp 201 °C (recryst. from hexanes−ethyl acetate, 1:2); IR (ATR) 3389 (br), 1665, 1638, 1601, 1578, 1526 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 11.94 (brs, 1H), 7.94 (d, 1H, J = 9.2 Hz), 7.40 (d, 1H, J = 9.2 Hz), 7.00 (s, 1H), 5.04 (brs, 1H), 4.00 (s, 3H), 3.96 (s, 3H), 3.95 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$-DMSO-d_6, 125 MHz): δ 170.6 (s), 153.7 (s), 150.0 (s), 145.1 (s), 144.1 (s), 125.5 (s), 120.3 (s), 118.6 (d), 116.0 (d), 105.2 (s), 102.4 (d), 61.3 (q), 56.2 (q), 51.6 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{15}O_6$ 279.0869; found 279.0869.

*1,4-Dihydroxy-5,6-dimethoxy-2-naphthonitrile (**4k**) and 1,4-Dihydroxy-7,8-dimethoxy-2-naphthonitrile (**4′k**) (2:1 Mixture).* White solid (213 mg, 87%); R_f 0.5 (hexanes−ethyl acetate, 1:1); ^1H NMR ($CDCl_3$, 500 MHz): δ 10.24 (brs, 0.33H), 9.36 (brs, 0.67H), 8.06 (d, 0.67H, J = 9.6 Hz), 7.98 (d, 0.33H, J = 9.5 Hz), 7.39 (d, 0.33H, J = 9.5 Hz), 7.34 (d, 0.67H, J = 9.6 Hz), 6.68 (s, 0.67H), 6.62 (s, 0.33H), 6.05 (brs, 0.67H), 5.23 (brs, 0.33H), 4.12 (s, 1H), 4.08 (s, 2H), 4.04 (s, 2H), 4.02 (s, 1H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 125 MHz): δ 151.34 (s), 151.31 (s), 151.1 (s), 149.1 (s), 146.3 (s), 146.2 (s), 142.8 (s), 142.7 (s), 123.8 (s), 122.1 (s), 122.0 (s), 120.8 (d), 119.9 (d), 118.1 (s), 118.0 (s), 117.8 (s), 117.2 (d), 115.2 (d), 108.1 (d), 104.5 (d), 92.2 (s), 92.0 (s), 62.2 (q), 61.9 (q), 56.7 (q), 56.5 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{13}H_{12}NO_4$ 246.0766; found 246.0756.

*1,4-Dihydroxy-5,6-dimethoxy-2-naphthonitrile (**4k**).* White solid; R_f 0.5 (hexanes−ethyl acetate, 1:1); mp > 300 °C (decomp.; recryst. from ethyl acetate); IR (ATR) 3347 (br), 3273 (br), 2224, 1636, 1609, 1582, 1508 cm^{-1}; ^1H NMR ($CDCl_3$-DMSO-d_6, 500 MHz): δ 10.10 (brs, 1H), 9.25 (s, 1H), 8.11 (d, 1H, J = 9.3 Hz), 7.35 (d, 1H, J = 9.3 Hz), 6.62 (s, 1H), 4.05 (s, 3H), 4.02 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$-DMSO-d_6, 125 MHz): δ 150.8 (s), 149.8 (s), 145.7 (s), 142.0 (s), 121.6 (s), 120.9 (s), 120.7 (d), 117.4 (s), 113.9 (d), 107.6 (d), 91.6 (s), 61.5 (q), 55.9 (q).

*1-(1,4-Dihydroxy-5,6-dimethoxynaphthalen-2-yl)ethan-1-one (**4l**).* Yellow solid (107 mg, 41%); R_f 0.6 (hexanes−ethyl acetate, 2:1); mp 170−172 °C (recryst. from hexanes−ethyl acetate, 1:1); IR (ATR) 3350 (br), 1607, 1576, 1504 cm^{-1}; ^1H NMR ($CDCl_3$-DMSO-d_6, 500 MHz): δ 13.58 (brs, 1H), 9.08 (brs, 1H), 8.25 (d, 1H, J = 9.3 Hz), 7.27 (d, 1H, J = 9.3 Hz), 6.96 (s, 1H), 4.07 (s, 3H), 4.03 (s, 3H), 2.62 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$-DMSO-d_6, 125 MHz): δ 203.0 (s), 154.6 (s), 151.1 (s), 143.7 (s), 141.9 (s), 122.3 (s), 121.5 (d), 120.6 (s), 113.6 (d), 111.0 (s), 106.1 (d), 61.4 (q), 55.9 (q), 26.2 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{15}O_5$ 263.0919; found 263.0914.

*1-(1,4-Dihydroxy-7,8-dimethoxynaphthalen-2-yl)ethan-1-one (**4′l**).* Yellow solid (58 mg, 22%); R_f 0.3 (hexanes−ethyl acetate, 2:1); mp 235−236 °C (recryst. from hexanes−ethyl acetate, 1:5); IR (ATR) 3393 (br), 1618, 1597, 1568, 1524 cm^{-1}; ^1H NMR ($CDCl_3$-DMSO-d_6, 500 MHz): δ 13.63 (brs, 1H), 8.99 (brs, 1H), 7.99 (d, 1H, J = 9.2 Hz), 7.40 (d, 1H, J = 9.2 Hz), 6.95 (s, 1H), 3.99 (s, 3H), 3.96 (s, 3H), 2.65 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$-DMSO-d_6, 125 MHz): δ 202.2 (s), 154.9 (s), 149.9 (s), 145.9 (s), 144.0 (s), 125.8 (s), 120.3 (s), 118.5 (d), 116.9 (d), 113.6 (s), 103.1 (d), 61.0 (q),

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56.3 (q), 27.5 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{15}O_5$ 263.0919; found 263.0912.

*Dimethyl 1,4-Dihydroxynaphthalene-2,3-dicarboxylate (**4m**).* White solid (88 mg, 32%); R_f 0.5 (hexanes−ethyl acetate, 5:1); mp 111−112 °C (recryst. from hexanes−ethyl acetate, 5:1; Lit.[12] 112−113 °C); IR (ATR) 1655, 1584 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.36 (s, 2H), 8.37−8.32 (m, 2H), 7.71−7.67 (m, 2H), 3.92 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 170.6 (s), 152.3 (s), 129.4 (d), 127.7 (s), 123.9 (d), 103.2 (s), 52.5 (q).

*Dimethyl 1,4-Dihydroxy-6,7-dimethoxynaphthalene-2,3-dicarboxylate (**4n**).* White solid (155 mg, 46%); R_f 0.5 (hexanes−ethyl acetate, 2:1); mp 200 °C (recryst. from hexanes−ethyl acetate, 1:1); IR (ATR) 1655, 1614, 1593, 1516 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.38 (brs, 2H), 7.62 (s, 2H), 4.05 (s, 6H), 3.91 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 170.8 (s), 151.7 (s), 151.4 (s), 123.1 (s), 103.3 (d), 102.2 (s), 56.2 (q), 52.4 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{16}H_{17}O_8$ ($M + H^+$) 337.0923; found 337.0915.

*Dimethyl 1,4-Dihydroxy-5,8-dimethoxynaphthalene-2,3-dicarboxylate (**4o**).* Yellow solid (175 mg, 52%); R_f 0.4 (hexanes−ethyl acetate, 1:2); mp 180−181 °C (recryst. from hexanes−ethyl acetate, 1:2); IR (ATR) 3319 (br), 3291 (br), 1728, 1653, 1616, 1591, 1506 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ, 10.52 (brs, 2H), 6.88 (s, 2H), 4.00 (s, 6H), 3.93 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 167.8 (s), 151.1 (s), 147.4 (s), 117.8 (s), 111.6 (s), 107.8 (d), 56.6 (q), 52.4 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{16}H_{17}O_8$ 337.0923; found 337.0915.

*Dimethyl 1,4-Dihydroxy-5,6-dimethoxynaphthalene-2,3-dicarboxylate (**4p**).* Yellow solid (205 mg, 61%); R_f 0.35 (hexanes−ethyl acetate, 2:1); mp 133 °C (recryst. from hexanes−ethyl acetate, 2:1); IR (ATR) 3289 (br), 3225 (br), 1724, 1651, 1636, 1607, 1504 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 11.88 (brs, 1H), 9.57 (brs, 1H), 8.22 (d, 1H, J = 9.2 Hz), 7.32 (d, 1H, J = 9.2 Hz), 4.07 (s, 3H), 4.03 (s, 3H), 3.96 (s, 3H), 3.94 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 169.7 (s), 168.0 (s), 154.3 (s), 151.1 (s), 142.3 (s), 142.2 (s), 121.6 (d), 121.0 (s), 120.5 (s), 114.0 (d), 111.9 (s), 100.3 (s), 61.8 (q), 55.8 (q), 52.4 (q), 52.1 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{16}H_{17}O_8$ 337.0923; found 337.0922.

*Methyl 1,4-Dihydroxy-9,10-dimethoxyanthracene-2-carboxylate (**4q**).* Yellow solid (253 mg, 77%); R_f 0.4 (hexanes−ethyl acetate, 5:1); mp 209−211 °C (recryst. from hexanes−ethyl acetate, 1:2); IR (ATR) 3335 (br), 1653, 1645, 1616, 1558 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 12.51 (brs, 1H), 9.48 (brs, 1H), 8.43 (d, 1H, J = 8.6 Hz), 8.17 (d, 1H, J = 8.6 Hz), 7.65−7.61 (m, 1H), 7.58−7.54 (m, 1H), 7.10 (s, 1H), 4.10 (s, 3H), 4.09 (s, 3H), 4.00 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 171.6 (s), 156.2 (s), 153.5 (s), 147.0 (s), 144.5 (s), 127.9 (d), 126.9 (s), 126.7 (s), 126.2 (d), 124.0 (d), 121.3 (d), 119.5 (s), 117.8 (s), 104.4 (d), 104.2 (s), 64.3 (q), 64.1 (q), 52.4 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{18}H_{17}O_6$ 329.1025; found 329.1016.

*1,4-Dihydroxy-9,10-dimethoxyanthracene-2-carbonitrile (**4r**).* Yellow solid (230 mg, 78%); R_f 0.4 (hexanes−ethyl acetate, 2:1); mp 202−204 °C (recryst. from hexanes−ethyl acetate, 1:5); IR (ATR) 3347 (br), 3244 (br), 2220, 1641, 1616 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.37 (brs, 1H), 9.40 (brs, 1H), 8.23−8.19 (m, 2H), 7.67−7.61 (m, 2H), 6.74 (s, 1H), 4.16 (s, 3H), 4.12 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 152.2 (s), 149.5 (s), 148.6 (s), 145.7 (s), 127.8 (d), 127.2 (d), 126.1 (s), 124.7 (s), 122.0 (d), 121.9 (d), 117.4 (s), 116.9 (s), 115.1 (s), 106.4 (d), 91.7 (s), 64.9 (q), 64.6 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{17}H_{14}NO_4$ ($M + H^+$) 296.0923; found 296.0916.

*1-(1,4-Dihydroxy-9,10-dimethoxyanthracen-2-yl)ethan-1-one (**4s**).* Yellow solid (156 mg, 50%); R_f 0.25 (hexanes−ethyl acetate, 5:1); mp 200−202 °C (recryst. from hexanes−ethyl acetate, 1:1); IR (ATR) 3387 (br), 1682, 1639, 1616, 1584, 1558, 1539 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 14.91 (brs, 1H), 9.49 (brs, 1H), 8.44 (d, 1H, J = 8.6 Hz), 8.18 (d, 1H, J = 8.6 Hz), 7.68−7.63 (m, 1H), 7.60−7.56 (m, 1H), 6.95 (s, 1H), 4.11 (s, 3H), 4.10 (s, 3H), 2.68 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 203.4 (s), 158.9 (s), 154.7 (s), 146.9 (s), 143.9 (s), 128.2 (d), 127.2 (s), 127.0 (s), 126.2 (d), 124.0 (d), 121.2 (d), 119.4 (s), 117.9 (s), 114.4 (s), 104.6 (d), 64.3 (q), 63.9 (q), 27.2 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{18}H_{17}O_5$ 313.1076; found 313.1065.

*Dimethyl 1,4-Dihydroxy-9,10-dimethoxyanthracene-2,3-dicarboxylate (**4t**).* Yellow solid (212 mg, 52%); R_f 0.4 (hexanes−ethyl acetate, 2:1); mp 211−213 °C (recryst. from hexanes−ethyl acetate, 1:1); IR (ATR) 3341 (br), 1730, 1717, 1663, 1622 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 11.38 (brs, 2H), 8.33−8.28 (m, 2H), 7.66−7.62 (m, 2H), 4.10 (s, 6H), 3.97 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 169.4 (s), 150.8 (s), 150.1 (s), 127.7 (d), 127.6 (s), 122.7 (d), 117.7 (s), 105.6 (s), 64.4 (q), 52.6 (q); HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{20}H_{18}O_8Na$ 409.0899; found 409.0894.

*Methyl 2-Methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**5a**).* Colorless paste (60 mg, 26%); R_f 0.55 (hexanes−ethyl acetate, 2:1); IR (ATR) 1734, 1695, 1593 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.10−8.03 (m, 2H), 7.78−7.74 (m, 2H), 3.65 (s, 3H), 3.50 (d, 1H, J = 16.2 Hz), 2.91 (d, 1H, J = 16.2 Hz), 1.61 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 193.8 (s), 193.3 (s), 171.2 (s), 134.8 (s), 134.4 (d), 134.3 (d), 133.9 (s), 127.5 (d), 126.5 (d), 56.9 (s), 53.1 (q), 47.6 (t), 20.7 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{13}H_{13}O_4$ 233.0814; found 233.0814.

*2-Methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (**5b**).* Colorless paste (70 mg, 35%); R_f 0.45 (hexanes−ethyl acetate, 2:1); IR (ATR) 2247, 1734, 1690, 1587 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.14−8.08 (m, 2H), 7.87−7.82 (m, 2H), 3.50 (d, 1H, J = 16.5 Hz), 3.20 (d, 1H, J = 16.5 Hz), 1.75 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 190.8 (s), 189.6 (s), 135.4 (d), 135.2 (d), 134.0 (s), 132.0 (d), 128.3 (d), 127.0 (d), 118.5 (s), 47.8 (t), 45.4 (s), 22.9 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{12}H_{10}NO_2$ 200.0712; found 200.0702.

*Methyl 6,7-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**5c**).* White solid (91 mg, 31%); R_f 0.35 (hexanes−ethyl acetate, 2:1); mp 176 °C (recryst. from hexanes−ethyl acetate, 1:1); IR (ATR) 1734, 1678, 1578, 1510 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.49 (s, 1H), 7.45 (s, 1H), 4.018 (s, 3H), 4.015 (s, 3H), 3.66 (s, 3H), 3.46 (d, 1H, J = 16.2 Hz), 2.88 (d, 1H, J = 16.2 Hz), 1.60 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 193.0 (s), 192.7 (s), 171.4 (s), 153.9 (s), 153.7 (s), 129.7 (s), 128.5 (s), 108.0 (d), 107.2 (d), 56.7 (s), 56.33 (q), 56.29 (q), 53.0 (q), 47.3 (t), 20.8 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{15}H_{17}O_6$ 293.1025; found 293.1017.

*6,7-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (**5d**).* White solid (122 mg, 47%); R_f 0.35 (hexanes−ethyl acetate, 2:1); mp 155 °C (recryst. from hexanes−ethyl acetate, 1:1); IR (ATR) 2247, 1697, 1686, 1585, 1508 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.49 (s, 1H), 7.48 (s, 1H), 4.04 (s, 6H), 3.47 (d, 1H, J = 16.1 Hz), 3.15 (d, 1H, J = 16.1 Hz), 1.74 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 190.1 (s), 188.9 (s), 154.8 (s), 154.5 (s), 129.1 (s), 126.6 (s), 118.9 (s), 108.8 (d), 107.6 (d), 56.6 (q), 47.7 (t), 45.3 (s), 23.4 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{14}NO_4$ 260.0923; found 260.0915.

*Methyl 5,8-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**5e**).* Yellow paste (137 mg, 47%); R_f 0.3 (hexanes−ethyl acetate, 2:1); IR (ATR) 1732, 1686, 1568, 1504 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.25 (d, 1H, J = 9.3 Hz), 7.22 (d, 1H, J = 9.3 Hz), 3.91 (s, 3H), 3.90 (s, 3H), 3.62 (s, 3H), 3.47 (d, 1H, J = 16.6 Hz), 2.74 (d, 1H, J = 16.6 Hz), 1.52 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 192.6 (s), 192.0 (s), 171.5 (s), 152.5 (s), 151.8 (s), 124.4 (s), 123.4 (s), 119.6 (d), 118.9 (d), 56.8 (s), 56.7 (q), 56.4 (q), 52.5 (q), 48.1 (t), 19.6 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{15}H_{17}O_6$ 293.1025; found 293.1017.

*5,8-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (**5f**).* Yellow solid (174 mg, 67%); R_f 0.3 (hexanes−ethyl acetate, 2:1); mp 140−141 °C (recryst. from ethyl acetate); IR (ATR) 2230, 1790, 1773, 1694, 1566, 1506 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.32 (s, 2H), 3.94 (s, 3H), 3.93 (s, 3H), 3.36 (d, 1H, J = 16.2 Hz), 2.98 (d, 1H, J = 16.2 Hz), 1.67 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 189.4 (s), 188.1 (s), 153.0 (s), 152.7 (s), 122.7 (s), 122.2 (s), 120.24 (d), 120.22 (d), 118.9 (s), 56.8 (q), 56.6 (q), 49.1 (t), 46.1 (s), 21.0 (q); HRMS

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(ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{14}NO_4$ 260.0923; found 260.0916.

*Methyl 5,6-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**5g**) and Methyl 7,8-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**5′g**) (2:1 Mixture).* Colorless paste (172 mg, 59%); R_f 0.3 (hexanes−ethyl acetate, 2:1); IR (ATR) 1734, 1697, 1686, 1574 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.91 (d, 0.67H, J = 8.6 Hz), 7.89 (d, 0.33H, J = 8.5 Hz), 7.23 (d, 0.67H, J = 8.6 Hz), 7.22 (d, 0.33H, J = 8.5 Hz), 3.98 (s, 3H), 3.929 (s, 1H), 3.927 (s, 2H), 3.69 (s, 2H), 3.61 (s, 1H), 3.45 (d, 0.33H, J = 17.2 Hz), 3.43 (d, 0.67H, J = 15.2 Hz), 2.90 (d, 0.67H, J = 15.2 Hz), 2.76 (d, 0.33H, J = 17.2 Hz), 1.57 (s, 2H), 1.55 (s, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ, 192.49 (s), 192.46 (s), 192.4 (s), 191.7 (s), 171.5 (s), 171.0 (s), 158.7 (s), 158.3 (s), 147.3 (s), 147.2 (s), 129.0 (s), 128.6 (s), 127.5 (s), 126.6 (s), 125.1 (d), 124.0 (d), 115.9 (d), 115.8 (d), 61.33 (q), 61.29 (q), 57.5 (s), 56.00 (s), 55.97 (q), 55.9 (q), 52.6 (q), 49.3 (t), 46.8 (t), 20.4 (q), 19.6 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{15}H_{17}O_6$ 293.1025; found 293.1014.

*5,6-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (**5h**) and 7,8-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (**5′h**) (2:1 Mixture).* White solid (189 mg, 73%); R_f 0.3 (hexanes−ethyl acetate, 2:1); IR (ATR) 2247, 2236, 1686, 1572 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.96 (d, 0.67H, J = 8.7 Hz), 7.93 (d, 0.33H, J = 8.7 Hz), 7.29 (d, 0.33H, J = 8.7 Hz), 7.28 (d, 0.67H, J = 8.7 Hz), 4.01 (s, 1H), 4.00 (s, 2H), 3.95 (s, 1H), 3.93 (s, 2H), 3.47 (d, 0.67H, J = 14.5 Hz), 3.37 (d, 0.33H, J = 16.6 Hz), 3.12 (d, 0.67H, J = 14.5 Hz), 3.06 (d, 0.33H, J = 16.6 Hz), 1.72 (s, 2H), 1.70 (s, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 190.0 (s), 189.2 (s), 188.3 (s), 188.2 (s), 159.5 (s), 159.0 (s), 148.3 (s), 147.6 (s), 128.0 (s), 126.8 (s), 126.7 (s), 126.2 (d), 124.6 (d), 124.4 (s), 118.7 (s), 118.6 (s), 116.7 (d), 116.5 (d), 61.7 (q), 61.5 (q), 56.20 (q), 56.18 (q), 49.5 (t), 47.6 (t), 46.6 (s), 44.9 (s), 22.5 (q), 21.2 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{14}H_{14}NO_4$ 260.0923; found 260.0916.

*5,6-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (**5h**).* White solid; R_f 0.3 (hexanes−ethyl acetate, 2:1); mp 169 °C (recryst. from hexanes−ethyl acetate, 1:1); IR (ATR) 2253, 1678, 1570 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.98 (d, 1H, J = 8.7 Hz), 7.27 (d, 1H, J = 8.7 Hz), 4.00 (s, 3H), 3.94 (s, 3H), 3.46 (d, 1H, J = 14.6 Hz), 3.11 (d, 1H, J = 14.6 Hz), 1.72 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 190.1 (s), 188.4 (s), 159.8 (s), 148.1 (s), 128.3 (s), 126.5 (d), 124.7 (s), 118.7 (s), 116.6 (d), 61.9 (q), 56.4 (q), 49.9 (t), 45.2 (s), 22.8 (q).

*Methyl 9,10-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydroanthracene-2-carboxylate (**5i**).* White solid (195 mg, 57%); R_f 0.5 (hexanes−ethyl acetate, 2:1); mp 162 °C; IR (ATR) 1734, 1690, 1611 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.42−8.38 (m, 1H), 8.36−8.32 (m, 1H), 7.76−7.70 (m, 2H), 4.06 (s, 3H), 4.04 (s, 3H), 3.59 (s, 3H), 3.49 (d, 1H, J = 16.8 Hz), 2.82 (d, 1H, J = 16.8 Hz), 1.58 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 192.5 (s), 192.1 (s), 171.8 (s), 154.6 (s), 153.5 (s), 132.3 (s), 132.2 (s), 129.7 (d), 129.5 (d), 124.7 (d), 124.3 (d), 121.7 (s), 120.9 (s), 63.5 (q), 63.1 (q), 56.9 (s), 52.8 (q), 48.0 (t), 19.9 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{19}H_{19}O_6$ 343.1182; found 343.1174.

*9,10-Dimethoxy-2-methyl-1,4-dioxo-1,2,3,4-tetrahydroanthracene-2-carbonitrile (**5j**).* Yellow solid (195 mg, 63%); R_f 0.5 (hexanes−ethyl acetate, 2:1); mp 134−135 °C (recryst. from hexanes−ethyl acetate, 1:1); IR (ATR) 2234, 1690, 1611, 1572 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.42−8.38 (m, 1H), 8.36−8.32 (m, 1H), 7.80−7.75 (m, 2H), 4.07 (s, 3H), 4.06 (s, 3H), 3.41 (d, 1H, J = 16.6 Hz), 3.09 (d, 1H, J = 16.6 Hz), 1.72 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 189.4 (s), 188.0 (s), 155.1 (s), 155.0 (s), 132.6 (s), 132.3 (s), 130.2 (d), 130.1 (d), 124.7 (d), 124.4 (d), 120.0 (s), 119.5 (s), 118.9 (s), 63.8 (q), 63.4 (q), 48.8 (t), 45.8 (s), 21.0 (q); HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{18}H_{16}NO_4$ 310.1079; found 310.1070.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02000.

Copies of ^1H and ^{13}C NMR spectra for all synthesized compounds; X-ray crystallographic data (ortep) of **4′j**, **4′l**, **4n**, **4p**, **5h**, and **5i**; CV data of **1a−e** and **2d,e**; and DFT calculation data of **3a**, **E**, **G**, and **4a** (PDF)

CIF files (TXT)

Crystallographic data for **4′j**, **4′l**, **4n**, **4p**, **5h**, and **5i** (CIF)

FAIR data, including the primary NMR FID files, for compounds **1b−e**, **3a**, **4a−t**, **4′j**, **4′k**, **4′l**, **5a−j**, **5′g**, and **5′h** (ZIP)

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Notes

The authors declare no competing financial interest.

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