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PII: S0040-4020(19)30419-3

DOI: https://doi.org/10.1016/j.tet.2019.04.020

Reference: TET 30265

To appear in: *Tetrahedron*

Received Date: 18 March 2019

Accepted Date: 6 April 2019

Please cite this article as: Singh S, Samineni R, Srihari P, Mehta G, Benzannulation of arynes with dimethylacetonedicarboxylates via an insertion-fragmentation-Dieckman-aromatization cascade: Expeditious entry to naphthoresorcinols and binaphthoresorcinols, *Tetrahedron* (2019), doi: https://doi.org/10.1016/j.tet.2019.04.020.

Graphical Abstract

Benzannulation of Arynes with Dimethylacetonedicarboxylates via an Insertion-Fragmentation-Dieckman Aromatization Cascade: Expeditious Entry to Naphthoresorcinols and Binaphthoresorcinols

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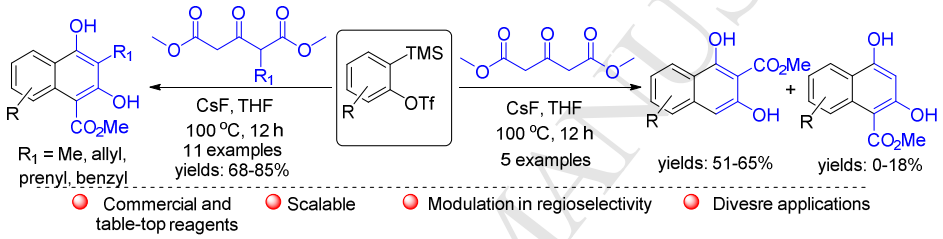

Tetrahedron
journal homepage: www.elsevier.com

Benzannulation of Arynes with Dimethylacetonedicarboxylates via an Insertion-Fragmentation-Dieckman-Aromatization Cascade: Expeditious Entry to Naphthoresorcinols and Binaphthoresorcinols

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Aryne, dimethylacetonedicarboxylates, natural products, naphthoresorcinols, binaphthols, nigerone.

ABSTRACT

Aryne insertions into 1,3,5-tricarbonyl bearing dimethylacetonedicarboxylate (DMAD) proceeds through a 4-step cascade process to eventuate in a versatile one pot synthesis of functionally embellished naphthoresorcinols. Functional group amplifications and transformations on these entities have been explored with the intent to apply them for natural products syntheses and to access other interesting scaffolds.

1. Introduction

The development of novel domino and cascade reactions play an important role in advancing organic synthesis since they not only conform to the atom and step economy criterion but also lead to rapid build-up of complexity, necessary for accessing challenging structural motifs, in a single-pot operation.[1] The cascade processes usually entail successive generation of reactive intermediates and sequential formation of multiple bonds [C–C, C–H and C–Het etc.] under the same reaction/reagent regime. In this context, arynes, now accessible through readily prepared or commercially available Kobayashi precursors,[2a] have shown considerable promise and their potential for the construction of complex structures and bioactive natural products through domino/cascade processes being explored with increasing frequency.[2b-h]

Among the various options to trigger a cascade process involving arynes and activated reaction partners, exposure to β–dicarbonyl compounds bearing an active methylene group has shown promise and drawn traction.[3] Danishefsky was the first to report the reaction of an aryne with diethylmalonate to furnish a homophthalate[3a] derivative through insertion-fragmentation steps enroute a total synthesis of dynemicin A,[3b] Scheme 1. More recently, groups of Stoltz,[3c] Yoshida[3d] and Okuma[3e] among others ~~have inve~~stigated the reaction of arynes with acetoacetic ester and acyl/benzoyl acetones to furnish products bearing 1,5-dicarbonyl moiety through an insertion-fragmentation cascade in which the aryne reaction partner is formally 'split and added' across the triple bond, Scheme 1. The resulting 1,5-dicarbonyl products are well poised for further manipulations and applications.[3e]

Taking a cue from these earlier observations[3] and motivation from our own recent efforts[4] on aryne insertion reactions with cyclic 1,3-diketones and oxindoles, leading to benzocarbocycles and dibenzoazepinones, respectively, we have ventured to investigate the reaction of arynes with homologous 1,3,5-tricarbonyl bearing reactant, dimethylacetonedicarboxylate (DMAD) which embodies not one but two active methylene sites. Drawing parallel from some recent studies,[3e,5] it was anticipated that the reaction between aryne and DMAD, after the initial insertion-fragmentation to a benzo-1,3,7-tricarbonyl product, could further unfold a deeper cascade process to eventuate in robust, fully aromatized end-products. Indeed, this expectation has been realized and the present communication discloses the reaction between diverse arynes **1** and various DMAD's **2** leading to regioisomeric naphthoresorcinols **3** and **4** in one pot operation involving a 4-step cascade process. In addition, the potential and utilitarian aspects of the resultant naphthoresorcinols have been demonstrated through potentially

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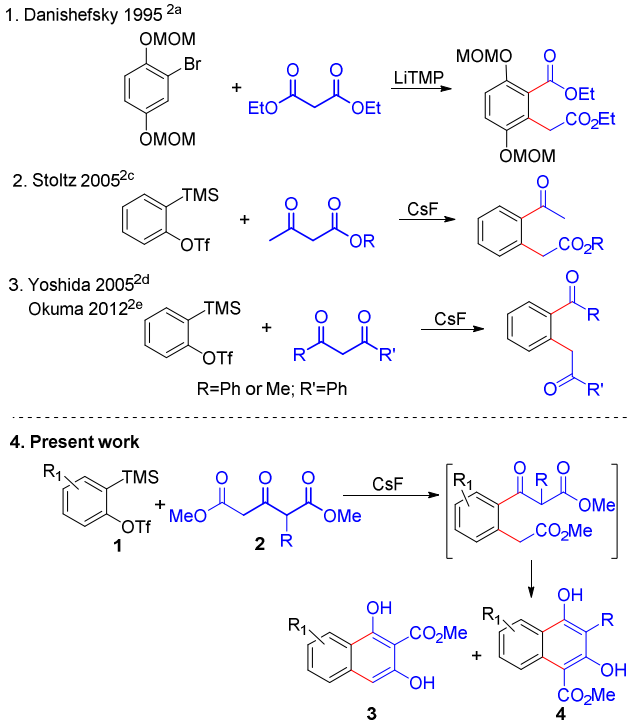
useful functional group elaborations and more notably their oxidative coupling to furnish dimeric binaphthoresorcinols.



Scheme 1: Reaction of arynes with β-dicarbonyl compounds

At this point, it may be contextual to recall that napthoresorcinol motif maps into many structurally embellished bioactive natural products displayed in Figure 1.[6] Napthoresorcinols also serve as useful precursors for the synthesis of functional materials and ligands and find application in several colorimetric detections and estimations.[7] In the context of the results reported here, it also needs to be mentioned here that when this paper was under review in another Journal, a report describing the reaction between arynes and DMAD appeared.[5d] While the work reported here is conceptually similar to the one reported concurrently,[5d] it differs markedly in its objectives and scope.

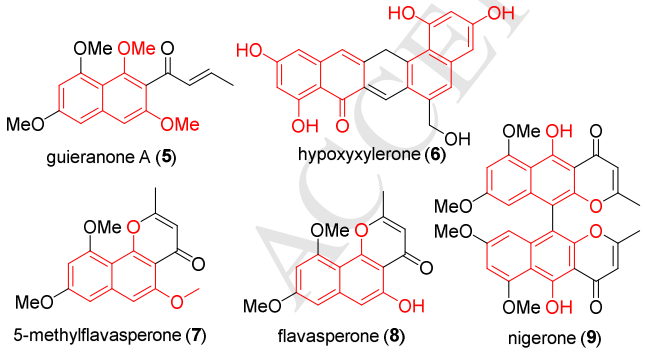


Figure 1: Natural products embodying naphthoresorcinol segment

2. Results and Discussions

As an exploratory foray, reaction of aryne precursor 2-(trimethylsilyl)phenyltrifluoromethanesulfonate (**1a**) with dimethylacetonedicarboxylate **2a** (DMAD) was investigated and after screening several reaction regimes (Table 1), it was found that under the optimized conditions (CsF, THF at 100 °C, 12 h; Table 1, Entry 6), the reaction afforded two regioisomeric napthoresorcinols **3a** (65%), **4a** (12%). Their structures were settled through spectral comparison with reported compounds either directly or through their derivatives.[8] To establish the generality of this new observation and to concurrently amplify the functionality pattern on the naphthoresorcinol framework, various substituted aryne precursors **1b-e** were reacted with DMAD, Scheme 2. In all the cases, both the napthoresorcinol regioisomers **3b-e** and **4b-e** were formed, with the former predominating, in decent yield, and were separated and characterized (except **4e** formed only in trace amounts). The pronounced and consistent deshielding of the peri-proton by the carbomethoxy group in **4a-e** (δ~7.5-9.0 *cf* 7.0-8.5 in **3a-e**) served as the structure differentiator between the napthoresorcinol regioisomers, Scheme 2. The small variation in regioselectivity during the formation of **3a-e** and **4a-e** can be attributed to the subtle tuning of stereoelectronic by the substituents on the arynes **1b-e** during the reaction with DMAD.

Reaction optimization using DMAD and aryne precursor:

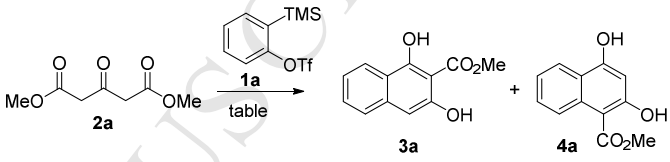
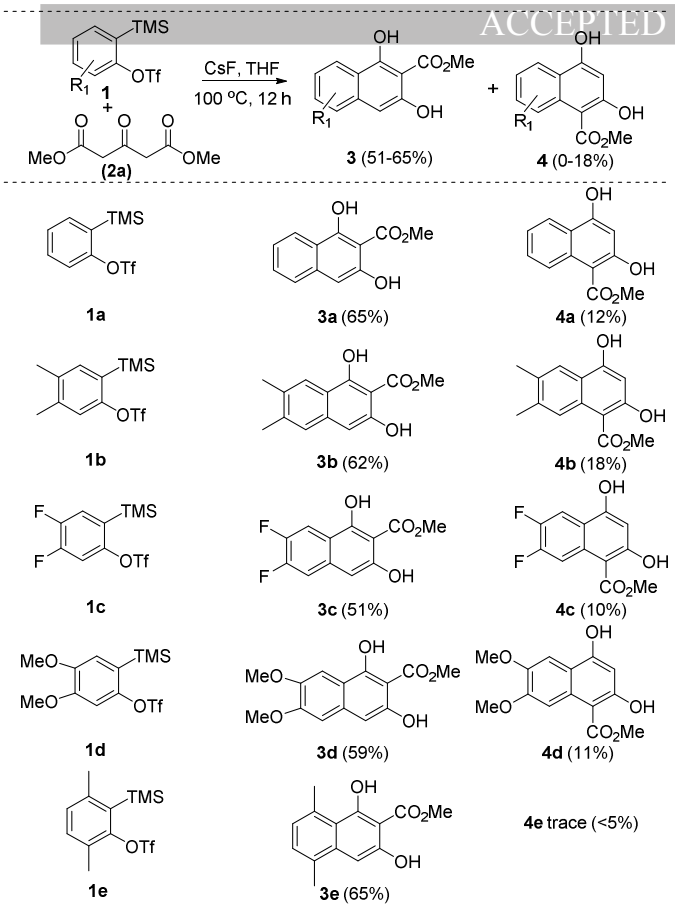


Table: Optimization of reaction conditions

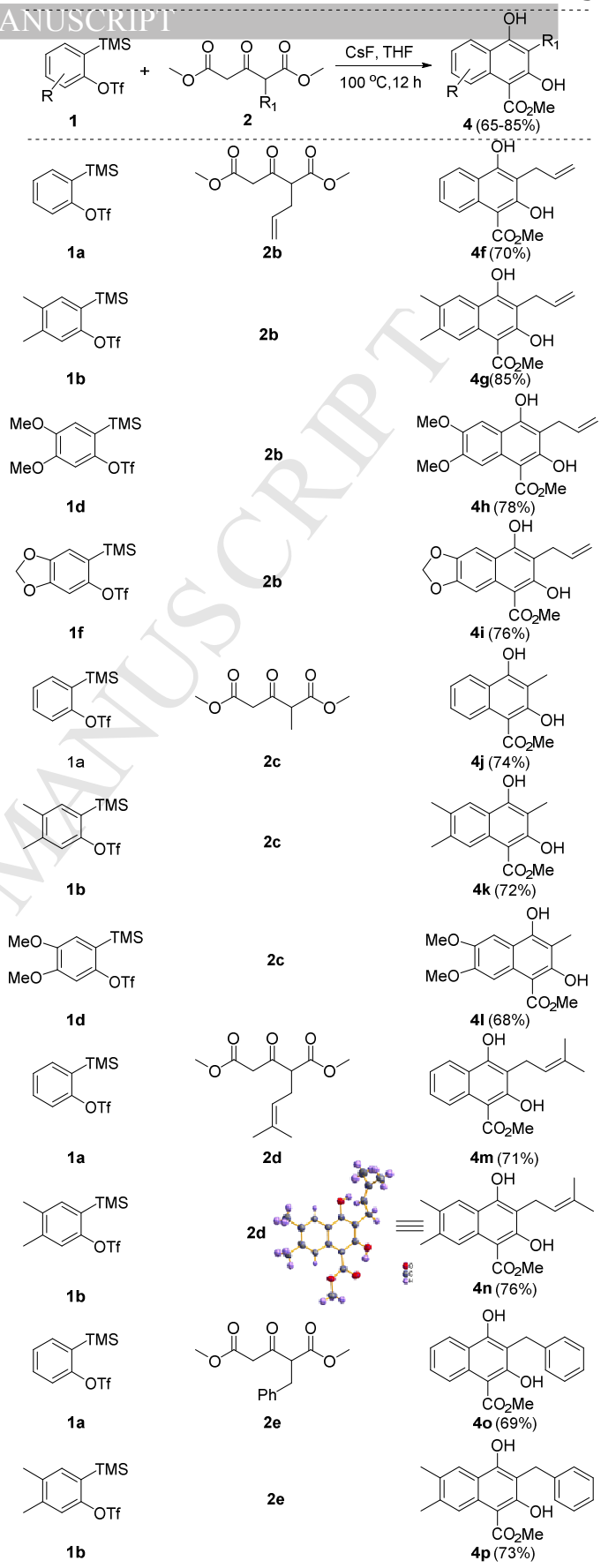
S.No	**1a** (equiv)	Fluoride (equiv) /solvent	Temp /time	**3a**/**4a** (%)[a]
1	1.1	CsF (2)/acetonitrile	rt/24 h	Complex mixture[b]
2	1.1	KF (2)/THF	rt/12h	Complex mixture[b]
3	1.1	KF (2)/THF, 18-C-6	rt/12 h	Complex mixture[b]
4	1.1	CsF (2)/THF	70 °C/12 h	50/7
5	1.1	CsF (2)/THF	70 °C/24 h	57/15
6	1.1	CsF (2)/THF	100 °C/12 h	65/12
7	1.1	CsF (2)/acetonitrile	100 °C/12 h	53/14
8	1.1	TBAF (2.5)/THF	rt/12 h	Complex mixture[b]

[a] isolate yields, [b] complex mixture: multiple spots in TLC with different ratios along with products



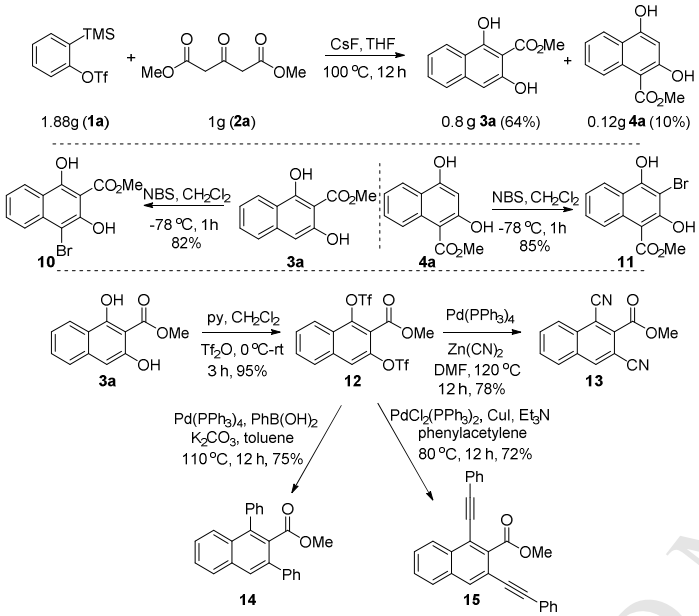
Scheme 2: Reaction between diverse arynes and DMAD

Having demonstrated the generality of the aryne-DMAD reaction, it was of interest to explore the scope of this new reaction employing substituted DMAD derivatives[9] **2b-e**, readily obtainable from **2a** *via* the enolate generation and capture with different halides (SI), as reaction partners with different arynes. Initial attempt was made with allyl substituted DMAD **2b** which was reacted with the aryne precursor (**1a**), following the optimized conditions to regioselectively furnish 1,2,3,4-tetrasubstituted naphthoresorcinol (**4f**) as a single product, Scheme 3. As expected, this maneuver became a handy tool to install an additional desired substituent on the naphthoresorcinol platform in a regioselective manner. Moreover, this tactic of DMAD substitution also led to a reversal of regioselectivity (*vide infra*). The reaction was further extended to three additional arynes generated from precursors (**1b**, **d**, **e**) to yield the corresponding tetrasubstituted naphthoresorcinols (**4g-i**). Additionally, methyl substituted DMAD (**2c**), prenyl substituted DMAD (**2d**) and benzyl substituted DMAD (**2e**) on reaction with appropriate aryne precursors afforded the corresponding naphthoresorcinols (**4j-p**), respectively, regioselectively and in good yield, Scheme 3. Structures of all the products were secured on the basis of internally consistent spectral profile and single crystal X-ray structure determination of **4n**, Scheme 3.



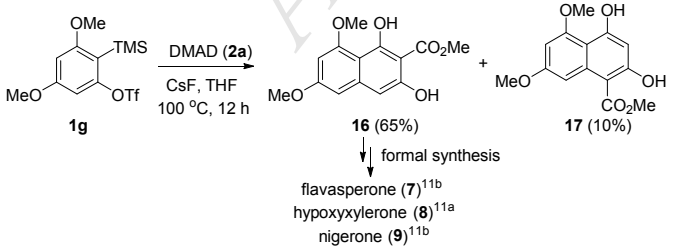
Scheme 3: Reaction between diverse arynes and substituted DMAD's

To gauge the appeal and utility of the naphthoresorcinols encountered here, the aryne-DMAD cascade reaction between **1a** with **2a** was implemented on a gram scale and the resulting regioisomeric naphthoresorcinols **3a** and **4a** were subjected to some classical functional group amplifications and alterations. These included NBS mediated regioselective bromination of **3a** & **4a** to furnish tetrasubstituted napthoresorcinols **10** & **11**, respectively; conversion of the major naphthoresorcinol **3a** to a bis-triflate **12** and its further Pd-mediated couplings[10] to deliver dicyanated **13**, diarylated **14** and dialkynated **15** products. Needless to add that these are just a few of the many possibilities that exist for the embellishment of the naphthalene framework through the replacement of the Ar C-O bonds with Ar C-C bonds, Scheme 4.



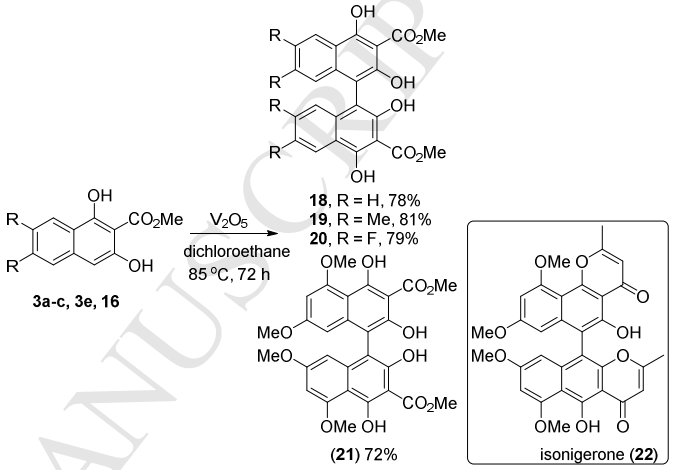
Scheme 4: Gram scale aryne reaction and selected transformations

In the backdrop of this versatile entry into diverse naphthoresorcinols, it was pertinent to make an initial assessment of their utilitarian value through a few examples. In this quest, unsymmetrical aryne precursor **1g** was reacted with DMAD to deliver pentasubstituted naphthoresorcinol **16** as the major product along with a minor regioisomers **17**, Scheme 5. Naphthoresorcinol **16** has served as an advanced intermediate for the total synthesis of natural products guieranone A (**5**), 5-methyl flavasperone (**6**), flavasperone (**7**) hypoxyxylerone (**8**) and nigerone (**9**) and was previously prepared in 5-7-steps.[11] Our methodology employing **1f** and table top DMAD, enables access to **16** in good yield and through one pot cascade process as delineated here, Scheme 5.



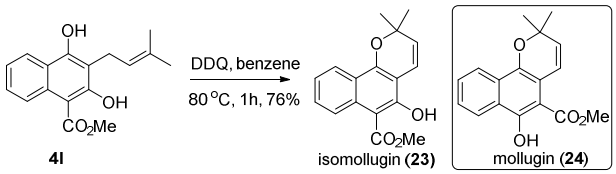
Scheme 5: Accessing a key intermediate for natural products synthesis

Next, we turned our attention to transform the functionally embellished naphthoresorcinols into the corresponding binaphthoresorcinols as that motif is present in many bioactive natural products, Scheme 1. As binaphthols are preeminent for their role as chiral auxiliaries[7] and in catalysis and therefore preparation of binaphthoresorcinols with additional binding domains was considered as an attractive proposition. Towards that end, it was observed that vanadium (V) mediated oxidative biaryl coupling[12] on our naphthoresorcinols **3a-c**, **3e**, **16** proceeded smoothly and efficiently to furnish corresponding binaphthoresorcinols (**18-21**), Scheme 6. Some of these biaryls, like **21** map directly into natural products nigerone **9**, isonigerone **22** and related natural products. It is quite significant that such highly functionalized binaphthoresorcinol entities are assembled in just two synthetic operations from commercially available aryne precursors.



Scheme 6: Synthesis of functionally embellished binaphthoresorcinols

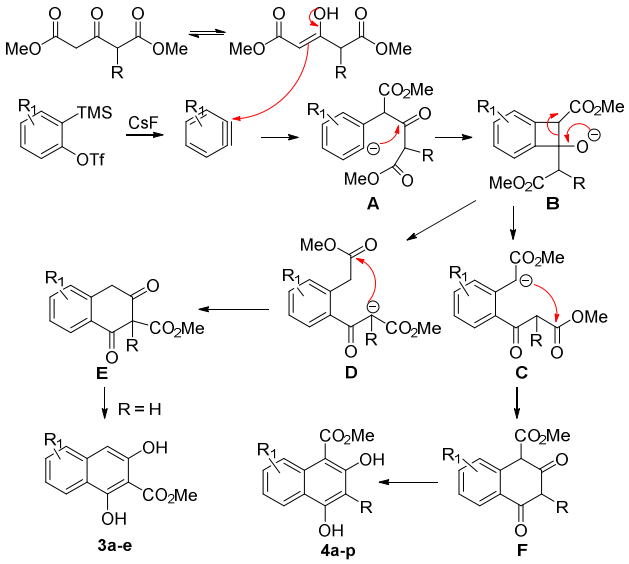
The last foray was to gain entry into a naphthopyran framework found in many naturally occurring oxa-heterocycles.[13] Prenylated naphthoresorcinol **4l** obtained from reaction between 1a and prenylated DMAD 2d on exposure to DDQ underwent oxidative oxa-cyclization to furnish an analogue **23** (isomollugin) of natural product mollugin incorporating a naphthopyran system, Scheme 7.



Scheme 7: Synthesis of an analogue (**23**) of naphthopyran natural product mollugin (**24**)

A possible reaction mechanism for the formation of napthoresorcinols from aryne and DMAD is depicted in Scheme 8. Accordingly, the initial nucleophilic attack of DMAD derived anion on aryne generates intermediate **A**. This anion intermediate undergoes a more commonly invoked pathway[3] involving a strained cyclobutane intermediate **B**, which fragments to **C** and/or **D**. A Dieckman-type cyclization and aromatization completes the 4-step cascade process and terminates in naphthoresorcinol products **3** and **4**. Observation of complete regioselectivity in the reaction between substituted DMAD's **2** (R = Me, allyl, prenyl and Bn) and arynes leading only to **4f-p** merits a comment and can be traced to the preference for cyclization via intermediate anion **C** owing to favorable stereoelectronic factors present as compared to **D**. It may also be

mentioned that the naphthoresorcinol products corresponding to **3** and **4** do not interconvert/equilibrate under the reaction conditions.



Scheme 8: Plausible reaction mechanism

3. Conclusion

In summary, we have unraveled a general reaction between arynes and dimethylacetonedicarboxylate and its derivatives (DMAD's) to furnish functionally enriched naphthoresorcinols through a cascade process. Substitution on DMAD has been employed to modulate the regioselectivity leading to naphthoresorcinols. Diversity and utility space around these new entities has been explored via functional group manipulations, ready conversion to bi-naphthoresorcinols and accession to potent building blocks for natural products.

4. Experimental Section

General methods: Unless otherwise mentioned, all reagents were used as received from commercial sources. All air and moisture sensitive reactions were conducted under a nitrogen or argon atmosphere in a glove box using flame-dried or oven-dried glassware with magnetic stirring. Anhydrous acetonitrile was prepared by stirring it with P_2O_5, distillation and storage over 3Å molecular sieves prior to use. Tetrahydrofuran (THF) was dried over Na, benzophenone and distilled prior to use. Toluene was freshly distilled from CaH_2 before usage. Reactions were monitored by thin-layer chromatography, carried out on silica plates (silica gel 60 F254, Merck) using UV-light, iodine and *p*-anisaldehyde for visualization. Column chromatography was performed using silica gel (60-120 mesh or 100- 200 mesh) packed in glass columns. Technical grade ethyl acetate and petroleum ether were used for column chromatography and were distilled prior to use. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ as a solvent on 300 MHz or 400 MHz or 500 MHz spectrometer at ambient temperature. The coupling constant *J* is given in Hz. The chemical shifts (δ) are reported in ppm on scale downfield from TMS using the residual solvent peak in $CDCl_3$ (H: δ = 7.26 and C: δ = 77.0 ppm) or TMS (δ = 0.0) as internal standard and signal patterns are indicated as follows: s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, q = quartet, qd = quartet of doublet, m = multiplet, br = broad, tt = triplet of triplet. IR spectra were recorded on a Bruker Infrared spectrophotometer and are reported as cm^{-1}. High-resolution mass spectra (HRMS) were recorded on a Waters-TOF spectrometer.

General procedure for the synthesis of arynes:[14,5d] The mixture of bromonaphthol (10 mmol, 1.0 equiv) and hexamethyldisilazide (HMDS) (11 mmol, 1.1 equiv) were combined in THF (25.0 mL) and refluxed for 3 h. The reaction was cooled to room temperature and volatiles were removed under vacuum. The resulting crude compound was directly used for next step. The crude compound was taken up in THF (30.0 mL) and cooled to –80 °C, *n*-Butyllithium (10 mmol, 1.0 equiv) was added slowly and stirred for 1 h, to this triflic anhydride (11 mmol, 1.1 equiv) was added drop wise at –80 °C and stirred for 1 h. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution (10.0 mL) and subsequently warmed to room temperature, diluted with H_2O (20.0 mL) and ethyl acetate (30.0 mL). Layers were separated and aqueous layer was extracted with ethyl acetate (3 x 30 mL), the combined organic extract was washed with brine (25 mL) and the organic layer was dried over Na_2SO_4, concentrated under vacuum and purified by flash chromatography (ethyl acetate/hexanes) to yield aryne precursors (**1a-g**).

Representative General Procedure for the preparation of naphthoresorcinols: (Note: All the reagents and solvents were added in an Ace pressure tube inside the glove box and it was sealed with cap before heating). An oven dried 15 mL Ace pressure tube (Sigma-Aldrich) was charged with aryne precursor silyl aryl triflate **1a** (0.33 mmol) and Dimethyl-1,3-acetonedicarboxylate **2a** (0.3 mmol) to which anhydrous THF (5 mL) and CsF (0.6 mmol) were added the tube was sealed with the cap and was placed in a pre-heated oil bath at 100 °C and was stirred for 12 h. The reaction mixture was cooled to room temperature and filtered through celite with the aid of EtOAc, volatile components were removed under reduced pressure using rotary evaporator and the resulted crude compound was purified by silica gel flash column chromatography to afford the substituted naphthoresorcinols **3a-e, 4a-e** and **16, 17**.

Methyl 2,4-dihydroxy-1-naphthoate (4a) and methyl 1,3-dihydroxy-2-naphthoate (3a): By following the general procedure **1** using aryne precursor (**1a**) and DMAD (**2a**), compound **4a** (7.8 mg, 12%), **3a** (42.5 mg, 65%) were prepared. **4a:** Pale yellow solid. R_f = 0.6 (20% EtOAc + Hexane); mp 171-173 °C {lit.[15] 172-174 °C}; ^{1}H NMR (500 MHz, Acetone-d_6) *δ* 12.65 (s, 1H), 10.26 (s, 1H), 8.79 (d, *J* = 8.8 Hz, 1H), 8.24 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.58 (ddd, *J* = 8.6, 6.8, 1.5 Hz, 1H), 7.37 (ddd, *J* = 8.1, 6.9, 1.0 Hz, 1H), 6.58 (s, 1H), 4.07 (s, 3H); ^{13}C NMR (126 MHz, Acetone-d_6) *δ* 172.8, 166.9, 160.2, 133.4, 129.1, 125.3, 122.8, 121.3, 100.1, 97.5, 51.6; IR (neat): υ_{max} 766, 836, 1236, 1342, 1433, 1591, 1636, 2957, 3349 cm^{-1}; HRMS (ESIMS) calcd for $C_{12}H_{11}O_4$ $[M+H]^+$: *m/z* 219.0657; found: 219.0664; **3a:** Pale yellow solid. R_f = 0.4 (20% EtOAc + Hexane); mp 77-78 °C {lit.[5d] 76-77 °C}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 11.35 (s, 1H), 8.92 (s, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.51 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 7.29 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 6.79 (s, 1H), 4.14 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 170.4, 161.8, 153.8, 137.9, 130.6, 126.0, 124.2, 123.1, 119.6, 102.6, 97.4, 53.1; IR (neat): υ_{max} 769, 1082, 1148, 1261, 1325, 1442, 1511, 1574, 1680, 2959, 3378, 3445 cm^{-1}; HRMS (ESIMS) calcd for $C_{12}H_{11}O_4$ $[M+H]^+$: *m/z* 219.0657; found: 219.0667.

Gram scale reaction: An oven dried 100 mL Ace pressure tube (Sigma-Aldrich) was charged with aryne precursor silyl aryl triflate **1a** (1.88 g, 6.32 mmol) and Dimethyl-1,3-acetonedicarboxylate **2a** (1 g, 5.74 mmol), to which anhydrous

THF (15 mL) and CsF (1.75 g, 11.49 mmol) were added, the tube was sealed with the cap and was placed in a pre-heated oil bath at 100 °C and was stirred for 12 h. The reaction mixture was cooled to room temperature and was filtered through celite with the aid of EtOAc, volatile components were removed under reduced pressure using rotary evaporator, the resulted crude compound was purified by silica gel flash column chromatography to afford the substituted naphthoresorcinols **3a** (0.80 g, 64%) and **4a** (0.12 g, 10%).

Methyl 1,3-dimethoxy-2-naphthoate (25): To a stirring solution of naphthoresorcinol **3a** (20.0 mg, 0.09 mmol) in anhydrous acetone (2.0 mL) were added K_2CO_3 (38.6 mg, 0.28 mmol) and Me_2SO_4 (25 □L, 0.23 mmol), the resulting reaction mixture was heated at 80 °C for 4 h. After completion of the reaction, it was filtered through a short plug of celite and the filtrate was concentrated in rotary evaporator to give the crude compound which was purified by silica gel column chromatography to yield the dimethoxy protected naphthalene as white crystalline solid **25** (21.4 mg, 95%). R_f = 0.6 (20% EtOAc + Hexane); mp 80-82 °C {lit.[16] 80-81 °C}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.2 Hz, 1H), 7.49 (ddd, J = 8.2, 6.9, 1.3 Hz, 1H), 7.39 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H), 6.95 (s, 1H), 4.02 (s, 3H), 3.99 (s, 3H), 3.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 154.6, 154.2, 135.5, 127.8, 127.0, 124.2, 123.1, 122.7, 117.3, 102.0, 63.2, 56.0, 52.6; IR (neat): υ_{max} 769, 1082, 1148, 1261, 1325, 1442, 1511, 1574, 1680, 2959, 3378, 3445 cm^{-1}; HRMS (ESIMS) calcd for $C_{14}H_{14}O_4Na$ $[M+Na]^+$: *m/z* 269.0790; found: 269.0791.

Methyl 2,4-dihydroxy-6,7-dimethyl-1-naphthoate (4b) and methyl 1,3-dihydroxy-6,7-dimethyl-2-naphthoate (3b): By following the general procedure **1** using aryne **1b** and DMAD **2a**, compounds **4b** (13.3 mg, 18%), **3b** (45.7 mg, 62%) were prepared;

4b: Pale yellow powder, R_f = 0.6 (20% EtOAc+Hexane); mp 152-153 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.62 (s, 1H), 8.50 (s, 1H), 7.89 (s, 1H), 6.42 (s, 1H), 6.31 (s, 1H), 4.07 (s, 3H), 2.44 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 165.8, 158.0, 139.1, 132.4, 132.0, 125.5, 122.2, 119.2, 100.3, 98.2, 52.0, 21.0, 19.8; IR (neat): υ_{max} 766, 833, 1097, 1236, 1351, 1442, 1636, 2956, 3340 cm^{-1}; HRMS (ESIMS) calcd for $C_{14}H_{15}O_4$ $[M+H]^+$: *m/z* 247.0970; found: 247.0972; **3b:** White powder, R_f = 0.4 (20% EtOAc + Hexane); mp 169-171 °C {lit.[5d] 168-170 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.31 (s, 1H), 8.83 (s, 1H), 7.97 (s, 1H), 7.31 (s, 1H), 6.67 (s, 1H), 4.11 (s, 3H), 2.37 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 161.2, 153.1, 141.1, 136.9, 132.8, 125.8, 123.5, 118.2, 101.7, 96.7, 52.9, 20.5, 20.0; IR (neat): υ_{max} 638, 764, 884, 1096, 1167, 1225, 1460, 1510, 1569, 1679, 2967, 3132, 3369 cm^{-1}; HRMS (ESIMS) calcd for $C_{14}H_{14}O_4Na$ $[M+Na]^+$: *m/z* 269.0790; found: 269.0791.

Methyl 6,7-difluoro-2,4-dihydroxy-1-naphthoate (4c) and methyl 6,7-difluoro-1,3-dihydroxy-2-naphthoate (3c): By following the general procedure **1** using aryne precursor **1c**, DMAD **2a**, compounds **4c** (7.6 mg, 10%) and **3c** (38.8 mg, 51%), were prepared.

4c: Yellow powder, R_f = 0.4 (20% EtOAc + Hexane); mp 152-154 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.67 (s, 1H), 8.58 (dd, J = 14.7, 8.0 Hz, 1H), 7.93 (dd, J = 11.3, 8.8 Hz, 1H), 6.94 (s, 1H), 6.50 (s, 1H), 4.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO): δ 170.3, 165.5, 158.4, 129.0, 128.92, 116.9, 116.8, 111.4, 111.1, 108.5, 108.3, 99.2, 95.5, 50.8; IR (neat): υ_{max} 762, 825, 898, 1164, 1210, 1312, 1447, 1513, 1603, 1738, 2855, 2920, 3350 cm^{-1}; HRMS (ESIMS) calcd for $C_{12}H_9O_4F_2$ $[M + H]^+$: *m/z* 255.0469; found: 255.0498. **3c:** Pale yellow powder, R_f = 0.2 (20% EtOAc + Hexane); mp 140-142 °C {lit.[5d] 138-139 °C}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.30 (s, 1H), 8.96 (s, 1H), 7.96 (dd, J = 11.2, 8.3 Hz, 1H), 7.27 (q, J = 7.7 Hz, 1H), 6.71 (s, 1H), 4.15 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 154.4, 154.3, 152.4, 152.2, 149.2, 149.0, 147.2, 147.1, 135.5, 135.4, 115.8, 115.7, 111.9, 111.8, 111.1, 110.9, 102.1, 102.1, 97.6, 53.3; IR (neat): υ_{max} 717, 788, 877, 1099, 1166, 1231, 1295, 1482, 1526, 1584, 1683, 3145, 3395 cm^{-1}; HRMS (ESIMS) calcd for $C_{12}H_9O_4F_2$ $[M+H]^+$: *m/z* 255.0469; found: 255.0466.

Methyl 1,3-dihydroxy-6,7-dimethoxy-2-naphthoate (3d) and methyl 2,4-dihydroxy-6,7-dimethoxy-1-naphthoate (4d): By following the general procedure 1 using aryne precursor **1d**, DMAD **2a**, compounds **3d** (49.2 mg, 59%), **4d** (9.2 mg, 11%) were prepared. **3d**: Pale yellow powder, R_f = 0.5 (30% EtOAc + Hexane); mp 178-180 °C {lit.[17] 176-177 °C}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.31 (s, 1H), 8.82 (s, 1H), 7.49 (s, 1H), 6.84 (s, 1H), 6.67 (s, 1H), 4.12 (s, 3H), 3.99 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 159.9, 153.4, 153.2, 147.5, 134.8, 113.9, 104.8, 102.7, 101.7, 96.0, 56.0 (2C), 52.9; IR (neat): υ_{max} 772, 1012, 1113, 1173, 1245, 1507, 1656, 2367, 3443, 3464 cm^{-1}; HRMS (ESIMS) calcd for $C_{14}H_{15}O_6$ $[M + H]^+$: *m/z* 279.0869; found: 279.0871; **4d:** R_f = 0.4 (30% EtOAc + Hexane); Semi-solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.40 (s, 1H), 8.26 (s, 1H), 7.49 (s, 1H), 6.40 (s, 1H), 5.92 (s, 1H), 4.07 (s, 3H), 4.02 (s, 3H), 4.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 165.2, 157.2, 151.5, 146.7, 129.4, 115.2, 106.1, 102.1, 99.6, 98.4, 55.80, 55.63, 52.12; IR (neat): υ_{max} 821, 1084, 1148, 1261, 1324, 1446, 1655, 2929, 2963, 3466 cm^{-1}; HRMS (ESIMS) calcd for $C_{14}H_{14}O_6Na$ $[M+Na]^+$: *m/z* 301.0688; found: 301.0686.

Methyl 1,3-dihydroxy-5,8-dimethyl-2-naphthoate (3e): By following the general procedure **1** using aryne precursor **1e** and DMAD **2a**, compound **3e** (47.0 mg, 65%) was prepared as white solid; R_f = 0.5 (20% EtOAc + Hexane); mp 109-111 °C{lit.[5d] 108-110 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.13 (s, 1H), 8.76 (s, 1H), 7.39 – 7.10 (m, 1H), 7.06 – 6.78 (m, 2H), 4.13 (s, 3H), 2.86 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 165.6, 153.0, 138.8, 136.4, 132.1, 130.7, 130.1, 126.0, 119.2, 100.0, 97.1, 53.0, 25.4, 19.8; IR (neat): υ_{max} 761, 827, 1042, 1233, 1320, 1469, 1630, 2908, 3329 cm^{-1}; HRMS (ESIMS) calcd for $C_{14}H_{15}O_4$ $[M+H]^+$: *m/z* 247.0970; found: 247.0970.

2. General Procedure for the Synthesis of Substituted DMAD's (2b-2e):[9] To a stirring solution of DMAD (5 mmol) in anhydrous THF (20.0 mL) at 0 °C was added 60% NaH (6.5 mmol) and the reaction was stirred for 15 min. To this stirred mixture, alkyl halide (6.0 mmol) was added and it was further stirred for 12 h, quenched with sat. NH_4Cl solution (5 mL) and diluted with 10 mL H_2O, layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic extract was washed with sat. NaCl solution and dried over Na_2SO_4, volatiles were removed under reduced pressure; the obtained crude compound was purified by silica gel column chromatography to give the substituted DMAD's **2b-2e**. The compounds **2b, 2c, 2e** are known and the spectral data was compared with the reported one.

Dimethyl 2-(3-methylbut-2-en-1-yl)-3-oxopentanedioate (2d): Keto+enol mixture, Pale yellow liquid, R_f = 0.4 (20% EtOAc + Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.05–4.98 (m, 1H), 3.75–3.70 (m, 6H), 3.67–3.56 (m, 3H), 2.57 (t, J = 7.3 Hz, 2H), 1.68 (d, J = 1.0 Hz, 3H), 1.63 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.4, 169.4, 167.0, 135.3, 119.3, 58.69, 52.55, 52.44, 48.28, 26.92, 25.77, 17.75; IR (neat): υ_{max} 765, 845, 944, 995, 1162, 1261, 1318, 1400, 1451, 1665, 2858, 2951, 3322 cm^{-1}; HRMS (ESIMS) calcd for $C_{12}H_{19}O_5$ $[M+H]^+$: *m/z* 243.1232; found: 243.1262.

3. Representative General Procedure (Note: All the reagents and solvents were added in an Ace pressure tube inside the glove box and it was sealed with cap before heating). An oven dried 15 mL Ace pressure tube (Sigma-Aldrich) was charged with aryne precursor silyl aryl triflate (0.22 mmol) and substituted DMAD (0.2 mmol) to which anhydrous THF (5 mL) and CsF (0.4 mmol) were added, the tube was sealed with the cap and was placed in a pre-heated oil bath at 100 ^{o}C and was stirred for 12 h. The reaction mixture was cooled to room temperature and was filtered through celite with the aid of EtOAc, volatile components were removed under reduced pressure using rotary evaporator and the resulted crude compound was purified by silica gel flash column chromatography to give the substituted naphthoresorcinols **4f-p**.

Methyl 3-allyl-2,4-dihydroxy-1-naphthoate (4f): By following the general procedure **3** using dimethyl 2-allyl-3-oxopentanedioate **2b** (allyl-DMAD) and aryne precursor **1a** , compound **4f** (36.1 mg, 70%) was prepared as a semi-solid; R_f = 0.5 (20% EtOAc + Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.19 (s, 1H), 8.72 (d, J = 8.8 Hz, 1H), 8.17 (dd, J = 8.3, 1.0 Hz, 1H), 7.53 (ddd, J = 8.6, 6.9, 1.5 Hz, 1H), 7.35 (ddd, J = 8.1, 6.9, 1.0 Hz, 1H), 6.25 (s, 1H), 6.05 (ddt, J = 16.2, 10.1, 6.1 Hz, 1H), 5.36–5.14 (m, 2H), 4.07 (s, 3H), 3.67 (dt, J = 6.1, 1.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 164.8, 156.8, 135.4, 131.9, 128.7, 125.1, 123.2, 122.3, 120.5, 117.1, 109.1, 98.5, 52.2, 27.7; IR (neat): υ_{max} 803, 855, 1029, 1095, 1171, 1238, 1440, 1464, 1518, 1635, 1713, 2855, 2927, 3390 cm^{-1}; HRMS (ESIMS) calcd for $C_{15}H_{15}O_4$ $[M+H]^+$: *m/z* 259.0970; found: 259.0981.

Methyl 3-allyl-2,4-dihydroxy-6,7-dimethyl-1-naphthoate (4g): By following the general procedure **3** using allyl-DMAD **2b** and aryne precursor **1b**, compound **4g** (48.6 mg, 85%) was prepared as semi-solid. R_f = 0.4 (20% EtOAc + Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.01 (s, 1H), 8.39 (s, 1H), 7.81 (s, 1H), 6.11 – 5.88 (m, 2H), 5.16 (ddd, J = 13.7, 11.6, 1.5 Hz, 2H), 3.99 (s, 3H), 3.57 (dt, J = 5.9, 1.4 Hz, 2H), 2.35 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 164.2, 156.4, 138.4, 135.6, 132.5, 130.5, 125.5, 121.9, 119.1, 116.8, 108.2, 97.9, 52.1, 27.6, 21.0, 19.8; IR (neat): υ_{max} 820, 877, 944, 1226, 1359, 1435, 1571, 1631, 2955, 3495 cm^{-1}; HRMS (ESIMS) calcd for $C_{17}H_{19}O_4$ $[M+H]^+$: *m/z* 287.1283; found: 287.1284.

Methyl 3-allyl-2,4-dihydroxy-6,7-dimethoxy-1-naphthoate (4h): By following the general procedure **3** using allyl-DMAD **2b** and aryne precursor **1d**, compound **4h** (49.6 mg, 78%) was prepared as a white solid. R_f = 0.5 (30% EtOAc + Hexane); mp 159-161 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.92 (s, 1H), 8.22 (s, 1H), 7.50 (s, 1H), 6.19 (s, 1H), 6.06 (ddd, J = 23.3, 11.1, 6.1 Hz, 1H), 5.35 – 5.19 (m, 2H), 4.08 (s, 3H), 4.01 (s, 3H), 3.99 (s, 3H), 3.67 (dt, J = 6.1, 1.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 163.4, 156.0, 151.1, 146.8, 135.8, 127.9, 117.0, 115.2, 107.3, 105.8, 101.9, 98.1, 55.8, 55.6, 52.2, 27.7; IR (neat): υ_{max} 796, 857, 989, 1180, 1260, 1324, 1438, 1517, 1632, 2955, 3006, 3472 cm^{-1}; HRMS (ESIMS) calcd for $C_{17}H_{19}O_6$ $[M+H]^+$: *m/z* 319.1182; found: 319.1179.

Methyl 7-allyl-6,8-dihydroxynaphtho[2,3-d][1,3]dioxole-5-carboxylate (4i): By following the general procedure **3** using allyl-DMAD **2b** and aryne precursor **1f**, compound **4i** (45.9 mg, 76%) was prepared as a pale yellow powder. R_f = 0.4 (30% EtOAc + Hexane); mp 168-170 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.92 (s, 1H), 8.16 (s, 1H), 7.51 (s, 1H), 6.13 (s, 1H), 6.08-6.00 (m, 1H), 6.04 (s, 2H), 5.48 – 5.07 (m, 2H), 4.05 (s, 3H), 3.64 (d, J = 6.0 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 163.3, 156.2, 149.9, 145.0, 135.7, 129.3, 117.1, 116.3, 107.6, 103.3, 101.2, 99.6, 99.0, 52.2, 27.7; IR (neat): υ_{max} 794, 861, 1186, 1269, 1343, 1483, 1571, 1623, 2959, 3011, 3465 cm^{-1}; HRMS (ESIMS) calcd for $C_{16}H_{15}O_6$ $[M+H]^+$: *m/z* 303.0869; found: 303.0874.

Methyl 2,4-dihydroxy-3-methyl-1-naphthoate (4j): By following the general procedure **3** using methyl-DMAD **2c** and aryne precursor **1a**, compound **4j** (34.3 mg, 74%) was prepared as white solid; R_f = 0.5 (20% EtOAc + Hexane); mp 112-114 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.15 (s, 1H), 8.73 (d, J = 8.8 Hz, 1H), 8.15 (d, J = 9.1 Hz, 1H), 7.53 (t, J = 8.5 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 5.75 (s, 1H), 4.08 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 165.4, 155.1, 131.3, 128.3, 125.2, 123.1, 121.9, 120.0, 107.7, 98.4, 52.2, 8.3; IR (neat): υ_{max} 705, 746, 1258, 1329, 1462, 1630, 2678, 3052, 3300 cm^{-1}; HRMS (ESIMS) calcd for $C_{13}H_{12}O_4Na$ $[M+Na]^+$: *m/z* 255.0269; found: 255.0257.

Methyl 2,4-dihydroxy-3,6,7-trimethyl-1-naphthoate (4k): By following the general procedure **3** using methyl-DMAD **2c** and aryne precursor **1b**, compound **4k** (37.4 mg, 72%) was prepared as a sticky pale yellow oil. R_f = 0.5 (20% EtOAc + Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.04 (s, 1H), 8.48 (s, 1H), 7.85 (s, 1H), 5.64 (s, 1H), 4.07 (s, 3H), 2.43 (s, 3H), 2.39 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 164.8, 154.7, 138.0, 132.4, 130.0, 125.3, 121.5, 118.6, 106.8, 97.8, 52.1, 21.0, 19.9, 8.3; IR (neat): υ_{max} 707, 751, 1025, 1247, 1325, 1666, 2330, 2981, 3082, 3410 cm^{-1}; HRMS (ESIMS) calcd for $C_{15}H_{17}O_4$ $[M+H]^+$: *m/z* 261.1127; found: 261.1126.

Methyl 2,4-dihydroxy-6,7-dimethoxy-3-methyl-1-naphthoate (4l): By following the general procedure **3** using methyl-DMAD **2c** and aryne precursor **1d**, compound **4l** (39.7 mg, 68%) was prepared as a white solid. R_f = 0.3 (20% EtOAc + Hexane); mp: 135-137 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.90 (s, 1H), 8.20 (s, 1H), 7.48 (s, 1H), 5.66 (s, 1H), 4.07 (s, 3H), 4.00 (s, 3H), 3.99 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 163.9, 154.4, 150.8, 146.7, 127.2, 114.7, 105.9, 105.8, 101.8, 98.0, 55.8, 55.6, 52.1, 8.2; IR (neat): υ_{max} 705, 764, 1176, 1285, 1368, 1560, 1652, 2932, 3426 cm^{-1}; HRMS (ESIMS) calcd for $C_{15}H_{17}O_6$ $[M+H]^+$: *m/z* 293.1025; found: 293.1025.

Methyl 2,4-dihydroxy-3-(3-methylbut-2-en-1-yl)-1-naphthoate (4m): By following the general procedure **3** using prenyl-DMAD **2d** and aryne precursor **1a**, compound **4m** (40.6 mg, 71%) was prepared as a white solid. R_f = 0.5 (20% EtOAc + Hexane); mp: 72-74 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.22 (s, 1H), 8.71 (d, J = 8.8 Hz, 1H), 8.15 (dd, J = 8.3, 0.8 Hz, 1H), 7.52 (ddd, J = 8.6, 6.9, 1.4 Hz, 1H), 7.38–7.29 (m, 1H), 6.74 (s, 1H), 5.36 (t, J = 7.2 Hz, 1H), 4.07 (s, 3H), 3.62 (d, J = 7.2 Hz, 2H), 1.89 (s, 3H), 1.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.4, 165.9, 158.0, 138.2, 132.6, 129.5, 126.0, 124.0, 123.2, 122.0, 121.6, 111.6, 99.2, 53.1, 26.9, 23.6, 19.0; IR (neat): υ_{max} 755, 1230, 1349, 1447, 1643, 2322, 2860, 2925, 3508, 3606 cm^{-1}; HRMS (ESIMS) calcd for $C_{17}H_{19}O_4$ $[M+H]^+$: *m/z* 287.1283; found: 287.1291.

Methyl 2,4-dihydroxy-6,7-dimethyl-3-(3-methylbut-2-en-1-yl)-1-naphthoate (4n): By following the general procedure **3** using prenyl-DMAD **2d** and aryne precursor **1b**, compound **4n** (47.7 mg, 76%) was prepared as a white solid. R_f = 0.5 (20% EtOAc + Hexane); mp: 101-103 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.10 (s, 1H), 8.45 (s, 1H), 7.87 (s, 1H), 6.64 (s, 1H), 5.45–5.27 (m, 1H), 4.06 (s, 3H), 3.59 (d, J = 7.2 Hz, 2H), 2.42 (s, 3H), 2.37 (s, 3H), 1.88 (s, 3H), 1.81 (d, J = 1.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 164.3, 156.6, 138.2, 136.9, 132.3, 130.3, 125.2, 121.9, 121.3, 119.2, 109.7, 97.6, 52.0, 25.9, 22.6, 21.0, 19.8, 18.0; IR (neat): υ_{max} 796, 1034, 1138, 1266, 1600, 1681, 2985, 3320 cm^{-1}; HRMS (ESIMS) calcd for $C_{19}H_{23}O_4$ $[M+H]^+$:

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m/z 315.1596; found: 315.1626. **X-Ray data for 4n:** (CCDC 1884238)

Methyl 3-benzyl-2,4-dihydroxy-1-naphthoate (4o): By following the general procedure **3** using benzyl-DMAD **2e** and aryne precursor **1a**, compound **4o** (42.5 mg, 69%) was prepared as pale yellow solid. R_f = 0.4 (20% EtOAc + Hexane); mp: 150-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.23 (s, 1H), 8.75 (d, *J* = 8.8 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 7.54 (ddd, *J* = 8.6, 6.9, 1.5 Hz, 1H), 7.37 – 7.26 (m, 5H), 7.26 – 7.18 (m, 1H), 5.79 (s, 1H), 4.25 (s, 2H), 4.08 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 165.1, 156.1, 138.5, 131.9, 129.0 (2C), 128.7, 128.3 (2C), 126.9, 125.2, 123.2, 122.0, 120.4, 111.4, 98.7, 52.3, 29.0; IR (neat): υ_{max} 736, 815, 1008, 1105, 1225, 1346, 1429, 1583, 1635, 2953, 3023, 3539 cm^{-1}; HRMS (ESIMS) calcd for $C_{19}H_{17}O_4$ $[M+H]^+$: *m/z* 309.1127; found: 309.1122.

Methyl 3-benzyl-2,4-dihydroxy-6,7-dimethyl-1-naphthoate (4p): By following the general procedure **3** using benzyl-DMAD **2e** and aryne precursor **1b**, compound **4p** (49.0 mg, 73%) was prepared as a viscous liquid. R_f = 0.5 (20% EtOAc + Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.09 (s, 1H), 8.50 (s, 1H), 7.81 (s, 1H), 7.28 (d, *J* = 4.4 Hz, 4H), 7.21 (dq, *J* = 8.7, 4.2 Hz, 1H), 5.71 (s, 1H), 4.22 (s, 2H), 4.07 (s, 3H), 2.43 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 164.5, 155.6, 138.8, 138.5, 132.5, 130.6, 128.9 (2C), 128.3 (2C), 126.7, 125.4, 121.6, 118.9, 110.5, 98.1, 52.3, 29.0, 21.0, 19.8; IR (neat): υ_{max} 706, 1008, 1150, 1200, 1392, 1710, 2952, 3385 cm^{-1}; HRMS (ESIMS) calcd for $C_{21}H_{21}O_4$ $[M+H]^+$: *m/z* 337.1440; found: 337.1433.

Methyl 4-bromo-1,3-dihydroxy-2-naphthoate (10): To a stirring solution of methyl 1,3-dihydroxy-2-naphthoate **3a** (22.0 mg, 0.1 mmol) in CH_2Cl_2 (2.0 mL) at -78 °C was added NBS (20.0 mg, 0.11 mmol) and the reaction was stirred for 5 min, after completion of the reaction (monitored by TLC) it was diluted with CH_2Cl_2 (5 mL) and H_2O (5 mL). Layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL), the combined organic extract was dried over Na_2SO_4, volatiles were removed under reduced pressure and the resulted crude compound was purified by silica gel column chromatography to afford the *o*-bromo naphthol **10** as pale yellow solid (24.6 mg, 82%). R_f = 0.5 (20% EtOAc + Hexane); mp 123-125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.25 (s, 1H), 9.79 (s, 1H), 8.39 – 8.22 (m, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.67 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.39 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 4.18 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 161.1, 150.3, 136.0, 131.9, 125.6, 124.6, 124.0, 120.5, 97.6, 96.8, 53.5; IR (neat): υ_{max} 761, 867, 1086, 1148, 1233, 1318, 1444, 1505, 1571, 1641, 1676, 2925, 3413 cm^{-1}; HRMS (ESIMS) calcd for $C_{12}H_{10}O_4Br$ $[M+H]^+$: *m/z* 296.9762; found: 296.9780.

Methyl 3-bromo-2,4-dihydroxy-1-naphthoate (11): To a stirring solution of methyl 2,4-dihydroxy-1-naphthoate **4a** (22.0 mg, 0.1 mmol) in CH_2Cl_2 (2.0 mL) at -78 °C was added NBS (20.0 mg, 0.11 mmol) and the reaction was stirred for 15 min, after completion of the reaction (monitored by TLC) it was diluted with CH_2Cl_2 (5 mL) and H_2O (5 mL). Layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL), the combined organic extract was dried over Na_2SO_4, volatiles were removed under reduced pressure and the resulted crude compound was purified by silica gel column chromatography to give the bromo naphthoresorcinol **11** as pale yellow solid (25.5 mg, 85%). R_f = 0.3 (10% EtOAc + Hexane); mp 95-97 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.50 (s, 1H), 8.75 (d, *J* = 8.8 Hz, 1H), 8.26 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.60 (ddd, *J* = 8.6, 6.9, 1.5 Hz, 1H), 7.40 (ddd, *J* = 8.1, 6.9, 1.0 Hz, 1H), 6.63 (s, 1H), 4.11 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 161.9, 155.1, 131.6, 129.6, 125.3, 123.9, 123.1, 119.6, 99.5, 97.5, 52.6; IR (neat): υ_{max} 651, 757, 844, 1227, 1270, 1339, 1442, 1580, 1626, 2957, 3432, 3589 cm^{-1}; HRMS (ESIMS) calcd for $C_{12}H_{10}O_4Br$ $[M+H]^+$: *m/z* 296.9762; found: 296.9771.

Methyl 1,3-bis(((trifluoromethyl)sulfonyl)oxy)-2-naphthoate (12): To a stirring solution of naphthoresorcinol (100.0 mg, 0.46 mmol) in dichloromethane (5 .0 mL) at 0 °C were added Et_3N (0.19 mL, 1.38 mmol) and Tf_2O (0.19 mL, 1.15 mmol), the reaction was warmed to room temperature and was allowed to stir for additional 2 h. After completion of the reaction (monitored by TLC) it was diluted with dichloromethane (5.0 mL), quenched by the addition of sat.aq. $NaHCO_3$ (1.0 mL), H_2O (5.0 mL), layers were separated and the aqueous layer was extracted with dichloromethane (2 x 5 mL). The combined organic extract was dried over Na_2SO_4 and the volatiles were removed under reduced pressure to give the crude compound, which was purified by silica gel column chromatography to yield the ditriflate compound **12** as pale yellow solid (210 mg, 95%). R_f = 0.5 (20% EtOAc + Hexane); mp 84-86 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.8 Hz, 1H), 7.96 (dd, *J* = 4.6, 2.1 Hz, 1H), 7.87 (s, 1H), 7.85 – 7.69 (m, 2H), 4.03 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.6, 143.7, 142.6, 133.9, 130.5, 129.7, 128.3, 125.8, 122.5, 121.0, 119.9, 119.8, 119.5, 117.3, 117.2, 114.8, 114.7, 53.5; IR (neat): υ_{max} 760, 813, 1008, 1142, 1226, 1434, 1749, 2321, 2861, 2924 cm^{-1}; HRMS (ESIMS) calcd for $C_{14}H_9O_8S_2F_6$ $[M+H]^+$: *m/z* 482.9643; found: 482.9672.

Methyl 1,3-dicyano-2-naphthoate (13): To a stirring solution of ditriflate **12** (24.1 mg, 0.05 mmol) in DMF (2.0 mL) were added $Pd(PPh_3)_4$ (12.0 mg) and $Zn(CN)_2$ (18.0 mg, 0.15 mmol), the reaction mixture was heated at 120 °C for 12 h. After completion of the reaction, solids were filtered, the filtrate was diluted with cold H_2O and was extracted with EtOAc (3 x 5 mL), the combined organic extract was dried over Na_2SO_4 and volatiles were removed under reduced pressure to give the crude compound, which was purified by silica gel column chromatography to afford the dicyano compound **13** as a crystalline white solid (9.1 mg, 78%). R_f = 0.3 (20% EtOAc + Hexane); mp 149-151 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.50 (d, *J* = 8.4 Hz, 1H), 8.07 (d, *J* = 8.1 Hz, 1H), 7.92 (dt, *J* = 15.1, 7.2 Hz, 2H), 4.17 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.3, 140.2, 133.8, 133.3, 132.7, 132.6, 130.9, 129.1, 126.9, 116.2, 114.4, 113.2, 109.0, 53.8; IR (neat): υ_{max} 759, 1160, 1299, 1448, 1733, 2320, 2365, 2859, 2926 cm^{-1}; HRMS (ESIMS) calcd for $C_{14}H_9N_2O_2$ $[M+H]^+$: *m/z* 237.0664; found: 237.0693.

Methyl 1,3-diphenyl-2-naphthoate (14): To a stirring solution of ditriflate **12** (24.1 mg, 0.05 mmol) and phenylboronicacid (18.3 mg, 0.15 mmol) in toluene (2.0 mL), were added $Pd(PPh_3)_4$ (12.0 mg) and K_2CO_3 (20.7 mg, 0.15 mmol) and the reaction mixture was heated at 110 °C for 12 h. After completion of the reaction it was diluted with H_2O (5 mL) and was extracted with EtOAc (3 x 5 mL), the combined organic extract was dried over Na_2SO_4 and volatiles were removed under reduced pressure to give crude compound, which was purified by silica gel column chromatography to afford the diphenyl compound **14** as sticky liquid (12.6 mg, 75%). R_f = 0.6 (10% EtOAc + Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.2 Hz, 1H), 7.88 (s, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.57–7.35 (m, 12H), 3.30 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 140.8, 138.4, 137.8, 136.7, 133.5, 131.9, 131.2, 130.2, 128.6, 128.5, 128.4, 128.1, 128.0, 127.8, 127.5, 127.2, 126.9, 126.7, 51.7; IR (neat): υ_{max} 706, 761, 1109, 1272, 1447, 1495, 1735, 2334, 2949 cm^{-1}; HRMS (ESIMS) calcd for $C_{24}H_{19}O_2$ $[M+H]^+$: *m/z* 339.1385; found: 339.1415.

Methyl 1,3-bis(phenylethynyl)-2-naphthoate (15): To a stirring solution of ditriflate **12** (24.1 mg, 0.05 mmol) and

phenylacetylene (17 μL, 0.15 mmol) in Et_3N (2.0 mL), were added $PdCl_2(PPh_3)_2$ (8.0 mg) and CuI (4.0 mg) and the reaction mixture was heated at 80 °C for 12 h. After completion of the reaction it was diluted with H_2O (5 mL) and extracted with EtOAc (3 x 5 mL), the combined organic extract was dried over Na_2SO_4 and volatiles were removed under reduced pressure to give the crude compound, which was purified by silica gel column chromatography to afford the dialkyne compound **15** as pale-yellow liquid (13.8 mg, 72%). R_f = 0.5 (10% EtOAc + Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50–8.41 (m, 1H), 8.08 (s, 1H), 7.89–7.79 (m, 1H), 7.69–7.51 (m, 6H), 7.46–7.33 (m, 6H), 4.08 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 136.5, 132.9, 132.4, 132.1, 131.8, 131.7, 129.0, 128.7, 128.5, 128.4, 128.3, 128.1, 126.9, 122.9, 122.8, 119.6, 117.9, 98.8, 92.9, 86.6, 84.3, 52.7; IR (neat): υ_{max} 759, 1144, 1229, 1447, 1736, 2210, 2315, 2922 cm^{-1}; HRMS (ESIMS) calcd for $C_{28}H_{19}O_2$ $[M+H]^+$: *m/z* 387.1385; found: 387.1416.

Methyl 1,3-dihydroxy-6,8-dimethoxy-2-naphthoate (16) and Methyl 2,4-dihydroxy-5,7-dimethoxy-1-naphthoate (17): By following the general procedure **1** using DMAD **2a** and aryne precursor **1g**, compound **16** (54.2 mg, 65%) and **17** (8.3 mg, 10%) were synthesized.

16: pale yellow powder, R_f = 0.3 (20% EtOAc + Hexane); mp 161-163 °C {lit.[11] 162-164 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.11 (s, 1H), 10.70 (s, 1H), 6.61 (s, 1H), 6.46 (s, 1H), 6.26 (s, 1H), 4.03 (s, 3H), 4.00 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 160.9, 160.9, 159.0, 157.8, 141.3, 105.3, 102.1, 98.0, 97.6, 96.0, 56.3, 55.4, 52.5; IR (neat): υ_{max} 765, 860, 1107, 1169, 1244, 1334, 1442, 1503, 1581, 1658, 2858, 3460 cm^{-1}; HRMS (ESIMS) calcd for $C_{14}H_{15}O_6$ $[M+H]^+$: *m/z* 279.0869; found: 279.0869. **17:** semi-solid, R_f = 0.2 (20% EtOAc + Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.46 (s, 1H), 10.03 (s, 1H), 7.95 (d, *J* = 2.2 Hz, 1H), 6.42 (d, *J* = 2.2 Hz, 1H), 6.38 (s, 1H), 4.04 (s, 3H), 4.04 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 167.6, 161.9, 160.1, 157.9, 137.4, 106.2, 100.6, 99.8, 97.6, 95.6, 56.4, 55.2, 52.1; IR (neat): υ_{max} 831, 1041, 1230, 1332, 1438, 1610, 2845, 2954, 3371 cm^{-1}; HRMS (ESIMS) calcd for $C_{14}H_{15}O_6$ $[M+H]^+$: *m/z* 279.0869; found: 279.0898.

General procedure for V_2O_5 catalyzed oxidative dimerization:[12] To a stirring solution of naphthoresorcinol (0.1 mmol) in 1,2-dichloroethane (2 mL) was added V_2O_5 (20 mol%) and 2 drops of conc. HCl (pH 3.00) and the reaction mixture was heated at 85 °C for 12 h. After completion of the reaction as monitored by TLC, the reaction mixture was filtered through a short plug of celite with the aid of EtOAc, volatiles were removed under reduced pressure to give the crude compound which was purified by silica gel column chromatography.

Dimethyl-2,2',4,4'-tetrahydroxy-[1,1'-binaphthalene]-3,3'-dicarboxylate (18): By following the general procedure **4** using naphthoresorcinol **3a**, binaphthoresorcinol **18** was prepared as yellow semi-solid (17.0 mg, 78%); R_f = 0.4 (40% EtOAc + Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.47 (s, 2H), 9.08 (s, 2H), 8.44–8.14 (m, 2H), 7.32–7.22 (m, 4H), 7.05 (dd, *J* = 7.7, 0.8 Hz, 2H), 4.04 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6 (2C), 161.9 (2C), 151.2 (2C), 137.7 (2C), 130.9 (2C), 124.5 (2C), 124.3 (2C), 123.2 (2C), 120.0 (2C), 107.5 (2C), 97.4 (2C), 53.1 (2C); IR (neat): υ_{max} 642, 767, 1089, 1153, 1222, 1307, 1444, 1572, 1625, 1679, 3112, 3378 cm^{-1}; HRMS (ESIMS) calcd for $C_{24}H_{19}O_8$ $[M+H]^+$: *m/z* 435.1080; found: 435.1087.

Dimethyl-2,2',4,4'-tetrahydroxy-6,6',7,7'-tetramethyl-[1,1'-binaphthalene]-3,3'-dicarboxylate (19): By following the general procedure **4** using naphthoresorcinol **3b**, binaphthoresorcinol **19** (20 mg, 81%) was prepared as white solid. R_f = 0.4 (40% EtOAc + Hexane); mp 180-181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.52 (s, 2H), 8.99 (s, 2H), 8.13 (s, 2H), 6.88 (s, 2H), 4.08 (s, 6H), 2.37 (s, 6H), 2.19 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7 (2C), 161.2 (2C), 150.4 (2C), 141.3 (2C), 136.7 (2C), 132.9 (2C), 124.0 (2C), 123.9 (2C), 118.7 (2C), 107.1 (2C), 96.8 (2C), 52.8 (2C), 20.7 (2C), 19.9 (2C); IR (neat): υ_{max} 760, 971, 1099, 1151, 1225, 1302, 1383, 1449, 1631, 1669, 2959, 3185, 3418 cm^{-1}; HRMS (ESIMS) calcd for $C_{28}H_{27}O_8$ $[M+H]^+$: *m/z* 491.1706; found: 491.1709.

Dimethyl-6,6',7,7'-tetrafluoro-2,2',4,4'-tetrahydroxy-[1,1'-binaphthalene]-3,3'-dicarboxylate (20): By following the general procedure **4** using naphthoresorcinol **3c**, binaphthoresorcinol **20** (20.1 mg, 79%) was prepared as pale yellow semi-solid. R_f = 0.3 (40% EtOAc + Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.40 (s, 2H), 9.30 (s, 2H), 8.12 (dd, *J* = 11.2, 8.3 Hz, 2H), 6.79 (dd, *J* = 12.0, 7.7 Hz, 2H), 4.14 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2 (2C), 160.8 (2C), 152.1 (2C), 135.4 (2C), 135.3 (2C), 116.4 (2C), 111.6, 111.4, 110.7, 110.5, 106.7 (2C), 97.8 (2C), 53.4 (2C); IR (neat): υ_{max} 763, 801, 1098, 1159, 1251, 1464, 1516, 1678, 3078, 3399 cm^{-1}; HRMS (ESIMS) calcd for $C_{24}H_{15}O_8F_4$ $[M+H]^+$: *m/z* 507.0703; found: 507.0726.

Dimethyl 2,2',4,4'-tetrahydroxy-5,5',7,7'-tetramethoxy-[1,1'-binaphthalene]-3,3'-dicarboxylate (21): By following the general procedure **4** using naphthoresorcinol **16**, binaphthoresorcinols **21** (20 mg, 72%) were prepared as white solid. R_f = 0.3 (40% EtOAc + Hexane); mp 158-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.34 (s, 2H), 10.93 (s, 2H), 6.31 (d, *J* = 2.2 Hz, 2H), 6.09 (d, *J* = 2.2 Hz, 2H), 4.04 (s, 6H), 4.03 (s, 6H), 3.54 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.7 (2C), 161.1 (2C), 160.8 (2C), 159.5 (2C), 155.6 (2C), 140.8 (2C), 107.5 (2C), 105.7 (2C), 97.8 (2C), 96.9 (2C), 96.1 (2C), 56.5 (2C), 55.2 (2C), 52.7 (2C); IR (neat): υ_{max} 756, 824, 1124, 1213, 1272, 1317, 1385, 1442, 1610, 1657, 2948, 3298 cm^{-1}; HRMS (ESIMS) calcd for $C_{28}H_{27}O_{12}$ $[M + H]^+$: *m/z* 555.1503; found: 555.1534.

Methyl 5-hydroxy-2,2-dimethyl-2H-benzo[h]chromene-6-carboxylate (23, isomollugin): To a stirred solution of dihydroxyprenyl compound **4l** (20.0 mg, 0.07 mmol) in benzene (2.0 mL) was added recrystallized DDQ (31.8 mg, 0.14 mmol) and the reaction was refluxed at 80 °C for 1 h. After completion of the reaction, solids were filtered and volatiles were removed under reduced pressure, the resulted crude compound was purified by silica gel column chromatography to give **23** as a white powder (15.1 mg, 76%). R_f = 0.5 (5% EtOAc + Hexane); mp 86-88 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.02 (s, 1H), 8.69 (d, *J* = 8.8 Hz, 1H), 8.19 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.51 (ddd, *J* = 8.6, 6.9, 1.4 Hz, 1H), 7.36–7.27 (m, 1H), 6.84 (d, *J* = 10.0 Hz, 1H), 5.65 (d, *J* = 10.0 Hz, 1H), 4.06 (s, 3H), 1.54 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 162.4, 154.8, 132.5, 128.9, 127.7, 125.2, 123.1, 122.6, 121.0, 116.7, 107.1, 97.8, 78.3, 52.1, 28.3 (2C); IR (neat): υ_{max} 784, 1008, 1258, 1342, 1449, 1645, 2925, 3407 cm^{-1}; HRMS (ESIMS) calcd for $C_{17}H_{17}O_4$ $[M+H]^+$: *m/z* 285.1127; found: 285.1156.

5. Acknowledgments

This research was carried out under the Indo-French "Joint Laboratory for Natural Products and Synthesis towards Affordable Health (NPSAH)", supported by the Council of Scientific and Industrial Research (CSIR) and Department of Science and Technology (DST), New Delhi (project code GAP-584). SS thanks UGC for D. S. Kothari Postdoctoral fellowship. GM wishes to thank Dr. Reddy's Laboratory (DRL) for the

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award of Dr. Kallam Anji Reddy Chair Professorship and University of Hyderabad for their extended support. IICT communication no. IICT/Pub/2018/381.

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Supplementary Material

The Supporting Information is available free of charge on the ACS Publications website. Detailed experimental procedures and spectral data (^{1}H, ^{13}C, IR and HRMS) for all new compounds are provided (PDF)

Crystallographic data for compound **4n** (CIF)