Pergamon

Tetrahedron 57 (2001) 319–329

TETRAHEDRON

2-Alkoxyarenol-derived orthoquinols in carbon–oxygen, carbon–nitrogen and carbon–carbon bond-forming reactions

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Received 3 May 2000; revised 30 May 2000; accepted 12 July 2000

Abstract—Silylated oxygen- and nitrogen-tethered orthoquinol acetates, generated by phenyliodine(III) diacetoxy-mediated oxidative acetoxylation of 2-alkoxyphenols in CH_2Cl_2 can be used to furnish regioselectively benzannulated heterocycles. Oxidative activation of 2-alkoxynaphthols with non-nucleophilic phenyliodine(III) bis(trifluoroacetoxy) in the presence of carbon nucleophiles, including oxidation sensitive silyl enol ethers, constitute a potentially valuable route to naturally occurring vicinally oxygenated benz[*a*]anthracene motifs.
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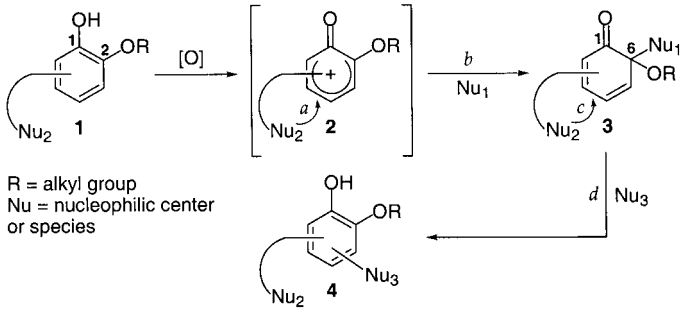
1. Introduction

Dearomatization of phenolic compounds, i.e. arenols, is a valuable tactic for rapid elaboration of functionalized cyclic polyolefins in organic synthesis. Two of the most critical issues that must be solved in order to ensure the success of such a transformation are the activation of the normally stable arenol entity and the prevention of rearomatization events. Transition metal-mediated activation,[1–4] sigmatropic rearrangements[5–8] and Birch reduction–alkylation combinations[9–11] directed toward already substituted positions are possible solutions that have been successfully implemented on various arenes to effect their dearomatization in a regiochemically controlled manner. Another solution offers itself to arenols since they can be subjected to phenol oxidation processes. In this context, 2-alkoxyphenols **1** constitute ideal free arenols for the preparation of cyclohexa-2,4-dienones derivatives, which are generally considered as potentially versatile synthetic intermediates because of their polyfunctionality.[10,12] We have recently embarked on a program aimed at exploring novel uses of orthoquinone monoketals and orthoquinol variants in organic synthesis.[12] These 6-oxocyclohexa-2,4-dien-1-one derivatives such as **3** in Scheme 1 exhibit valuable structural and reactivity features that can be exploited to construct various carbo- and heterocyclic skeleta for natural product synthesis. The conjugated dienone system and the two oxygen functionalities on vicinal carbon centers are the two key motifs that validate the choice of utilizing these electrophilic synthons. Dearomatization of 2-alkoxyphenols



Scheme 1.

Keywords: phenol oxidation; arenol; dearomatization; orthoquinone monoketals; orthoquinol acetates; oxidative nucleophilic substitution; cyclohexa-2,4-dienones; heterocyclization; diaryl ether; hypervalent iodine.
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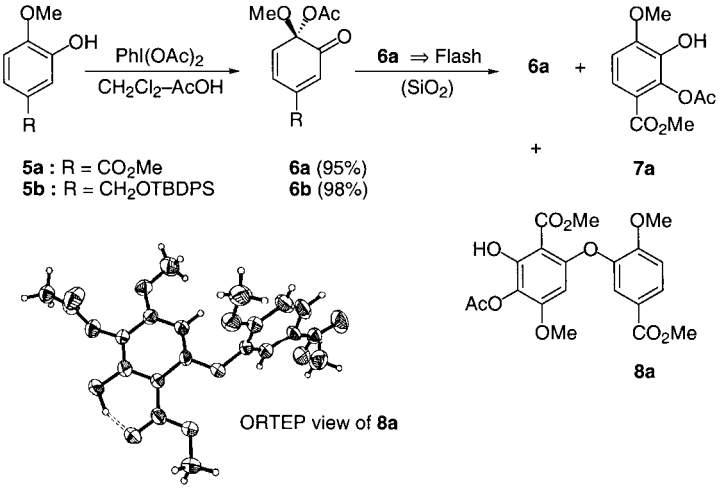


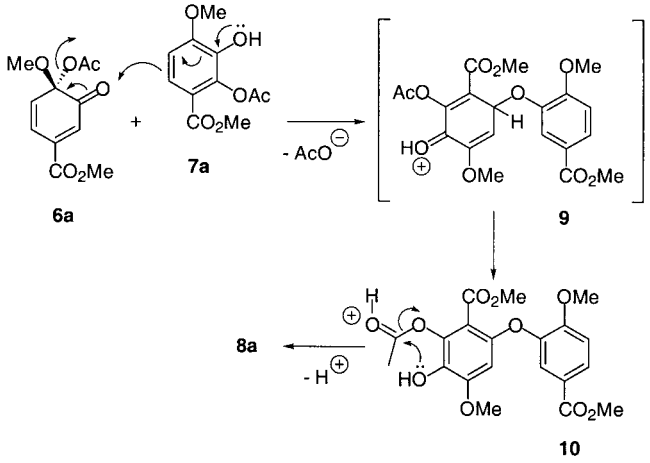
Scheme 2.

1 into 6-oxocyclohexa-2,4-dien-1-ones **3** via phenol oxidation is most conveniently accomplished by oxidative nucleophilic substitution.[12,13]

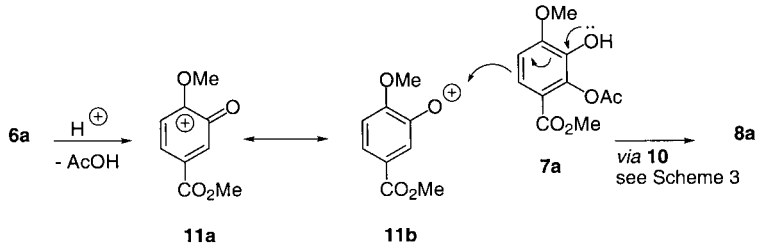
Orthoquinols **3** are formed when a nucleophilic species traps the oxidized phenol intermediate **2** at its alkoxylated position (path *b*), a reaction which generally exhibits a surprisingly high level of regioselectivity. The reactivity of these monoprotected versions of orthoquinones essentially relies on their electrophilic character and hence they can be further transformed by intramolecular (path *c*) and intermolecular (path *d*) nucleophilic processes. Internal nucleophilic centers (i.e. Nu_2) usually need to be protected to allow for efficient formation of **3** by preventing competitive intramolecular addition (path *a*, e.g. **17** in Scheme 6), and then deprotected when annulation via path *c* is desired. Numerous oxidizing systems based on either chemical or electrochemical methods are available to mediate the required two-electron oxidation of **1** into **2** or its equivalent.[12] Hypervalent iodine reagents are frequently used today to carry out this task because of their non-toxicity,[14–16] but anodic oxidation remains an attractive alternative.[17–24] Here we wish to report on our current investigations on iodine(III)-mediated oxidative acetoxylation and alkylation of 2-alkoxyphenols into orthoquinol acetates and ethers of type **3** (Scheme 1).

2. Results and discussion

Our interest in the oxidative transformation of 2-alkoxyphenols into 6-oxocyclohexa-2,4-dienone derivatives began with an evaluation of the methods available to prepare isolable orthoquinone monoketals that could be used in a controlled manner according to the different synthetic scenarii of Scheme 1. It is well known that certain 6,6-dioxocyclohexa-2,4-dienones such as 6,6-dimethoxy derivatives readily undergo Diels–Alder dimerization unless appropriately substituted.[25] These derivatives, which are conveniently prepared by oxidative methoxylation (Scheme 1, path *b*) under Wessely[26–28] or Pelter[14–16] oxidation reaction conditions [lead tetraacetate or phenyliodine(III) diacetoxy (PIDA), respectively, in MeOH], are often exploited in in situ reactions with either dienes or dienophiles in [4π+2π] cycloadditions.[12] As observed by Wessely in his seminal work on the reactivity of



Scheme 3.



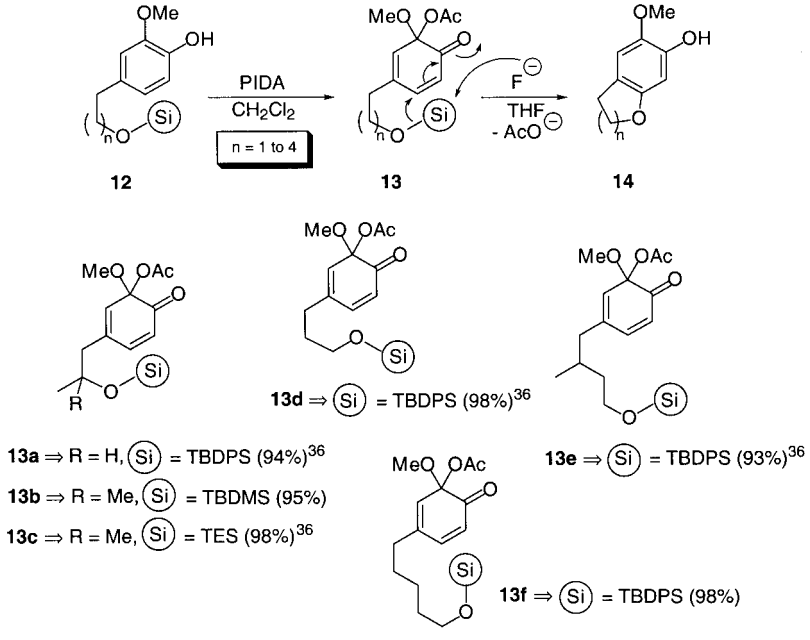
Scheme 4.

orthoquinols,[28,29] 6-acetoxy derivatives are less prone to participate in Diels–Alder reactions than 6,6-dimethoxy compounds.

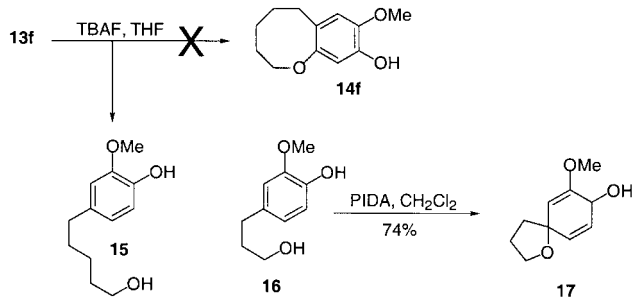
We recently confirmed these observations during our investigations on orthoquinol acetate sigmatropic rearrangements.[30] The non-dimerizing 6-acetoxy-6-methoxycyclohexa-2,4-dienones **6a** and **6b** are rapidly obtained from **5a**[30] and **5b** in excellent yields by an improved oxidative acetoxylation protocol which relies on the use of PIDA in CH_2Cl_2–AcOH (3:1) followed by standard workup under mildly acidic conditions (Scheme 2). No further purification is needed prior use of these orthoquinols, but silica gel chromatography of **6a**, eluting with hexanes–EtOAc (1:1), led to the formation of ca. 9:1 mixtures of **6a** and the 1,3-acetoxy migration product **7a** in yields ranging from 13% to 45%.[30] The other major fraction readily crystallized from CH_2Cl_2–Et_2O to furnish **8a** as small white needles in yields up to 18%. The structure of **8a** was confirmed by X-ray crystallographic analysis (Scheme 2). The formation of this diaryl ether from the orthoquinol acetate **6a** is somewhat intriguing. Its mechanistic description cannot simply rely on the addition of a phenolic oxygen of either **5a** or **7a** onto a carbon center of a two-electron oxidized phenol intermediate such as the phenoxenium ion **11** (see Scheme 4) or product such as **6a**. We propose that the formation of **8a** proceeds through the oxophilic addition of **7a**, also formed upon exposure to silica gel,[30] onto **6a** with concomitant departure of the acetate group of **6a** (Scheme 3).

This reaction can be viewed as an acid-catalyzed nucleophilic bimolecular substitution (SN_2'-like) of an acetate leaving group by a phenolic carbon nucleophile with oxoallylic rearrangement. A similarly unusual 1,6-addition reaction was recently proposed by Heathcock[31] as a possibly biomimetic key step in the synthesis of the naturally occurring naphthalenediol-derived spiroacetals preussomerins. One can also speculate that an unimolecular reaction path relying on the formation of a phenoxenium ion intermediate **11a/11b** is operative (Scheme 4). Phenoxenium ions are often invoked to rationalize the formation of phenol-derived biaryl species,[32–34] but their participation in C–O diaryl coupling cannot be disregarded on any ground. In any event, the aromatic phenoxonium ion **11b** might be the major contributing hybrid form of the resonance-stabilized ion **11** that is responsible for the observed C–O coupling. This two-electron oxidation channel to oxonium species could conceivably constitute an operative biosynthetic pathway to naturally occurring phenol-based diaryl ethers.

The migration of the acetyl group within the diaryl ether intermediate **10** to its adjacent phenolic position furnished



Scheme 5.



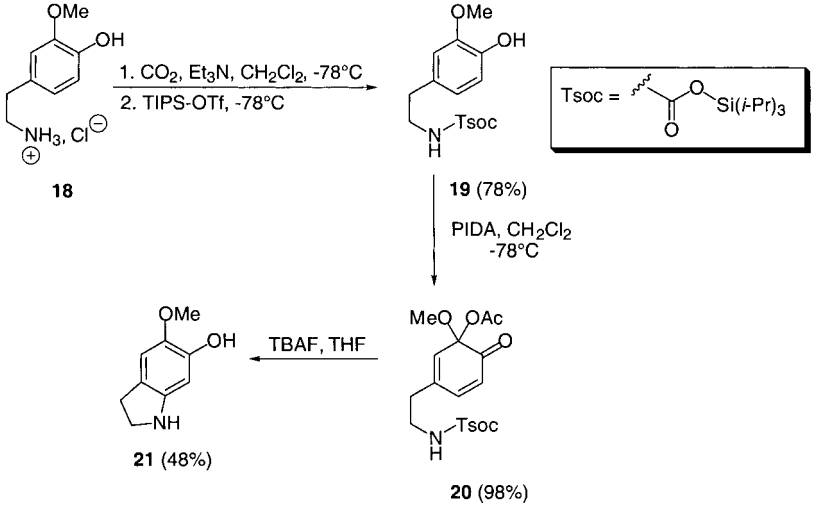
Scheme 6.

the diaryl ether product **8a**. This acetyl migration is often observed with orthoquinol acetates in strongly acidic media.[12,35] Of particular note is the fact that **7a** did not undergo such a regioisomerization when it was exposed to a suspension of silica gel in CH_2Cl_2 at room temperature for an extended period of time (>24 h).[30] Nonetheless, under the silica gel flash chromatography conditions used here, the nucleophilic phenolic oxygen of **10**, which is *meta*-positioned vis-à-vis the electron-withdrawing ester group, is capable of mediating an intramolecular nucleophilic acyl substitution which leads to **8a** wherein the phenolic group is hence further stabilized by resonance to an *ortho*-ester group; no diaryl ether ($10-H^+$) was isolated.

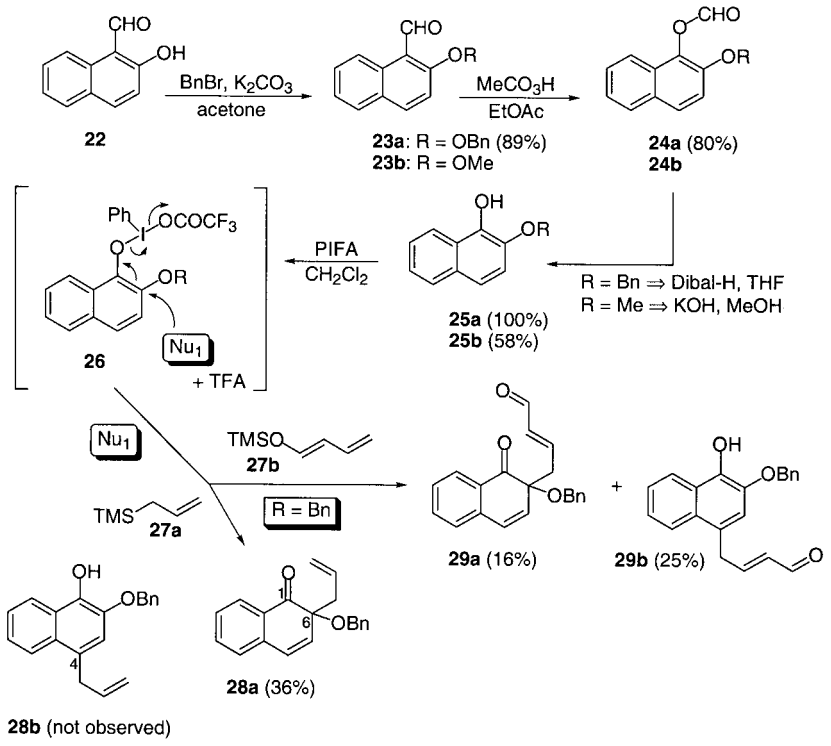
These preliminary observations on the rearrangement and substitution chemistry of these orthoquinol acetates prompted us to probe further the synthetic potential of these relatively stable orthoquinone monoketal variants that do not systematically dimerize via [4π+2π] cycloaddition processes. Furthermore, the use of PIDA in CH_2Cl_2 provided us with a convenient and efficient alternative to the use of toxic metal-based oxidants. This oxidative acetoxylation methodology was then exploited to prepare a series of silyloxyalkyl-bearing orthoquinol acetates **13** as substrates for cyclization (Scheme 1, path *c*) into benzannulated medium-sized oxygen rings **14** (Scheme 5).[36] The yields were all good to excellent, even though all orthoquinol products did not behave with equal efficacy in their role of ether ring precursors.

Cyclization was induced by fluoride ion-mediated desilylation of a silyloxyalkyl tether. The released alkoxide intramolecularly added to the electrophilic orthoquinol unit in a regioselective manner.[36] The *tert*-butyldiphenylsilyl (TBDPS) group was used to protect primary and secondary alkoxy groups such as in **13a** and **13d–f**. However, TBDPS-Cl was not reactive enough to silylate tertiary alkoxy groups and was replaced by *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBDMS-OTf). The TBDMS group was thus efficiently placed on tertiary alkoxy groups (i.e. **13b**), but could not be removed to induce the cyclization to **14b**. A satisfactory compromise was found by using triethylsilyl trifluoromethanesulfonate (TES-OTf).[36] Heterocyclization of orthoquinol **13f** into the eight-membered ether ring **14f** failed probably because the topology of the saturated six-atom tether is not well adapted to promote intramolecular bond formation. The only observed product was the alcohol **15** (14%) (Scheme 6), so desilylation did partially occur but the orthoquinol acetate unit was converted back into a phenol by an unknown reducing source before undergoing any ring-forming process. As alluded to in Scheme 1 (path *a*), protection of the alkoxy group before PIDA-mediated oxidation is a necessary preliminary step to prevent intramolecular attack at the *para*-position of the oxidized phenol unit. The resulting spirocyclization was, for example, observed on the one hand with alcohol **16** which furnished the cyclohexa-2,5-dienone **17** in good yield. On the other hand, adequately silylated precursors of 5- to 7-membered benzannulated ether rings met our expectations.[36]

The success of this orthoquinol acetate-based heterocyclization strategy prompted us to exploit similarly the inherent nucleophilicity of a nitrogen-tethered orthoquinol acetate to effect nitrogen heterocyclization in a regiochemically-controlled manner. We were particularly eager to check such a possibility because of our interest in developing alternative routes to the synthesis of lycorine-type *Amaryllidaceae* alkaloids.[37] Our initial attempts with various amine substrates all met with failure essentially related to the choice of the nitrogen protecting group and to the fact that nitrogen ring closure is apparently characterized by much slower kinetics than its oxygen analogue. Carbamate- and sulfonamide-based protections were tried by using, for



Scheme 7.



Scheme 8.

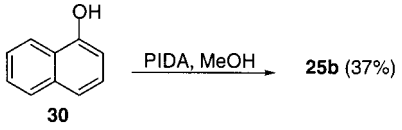
example, the Teoc [$C(O)OCH_2CH_2TMS$][38] or the SES ($SO_2CH_2CH_2TMS$)[39,40] group. These silylated groups were selected to resist PIDA oxidation in an acidic medium and, again, to take advantage of chemoselective fluoride-mediated deprotection. Unfortunately, these groups were also surprisingly resistant to a variety of fluoride-mediated desilylation conditions (e.g. TBAF in THF or DMF, CsF in CH_3CN or DMF, Et_3N–3HF in THF, TAS-F in CH_3CN).

A solution to this problem was found by using the triisopropylsilyloxycarbonyl (Tsoc) group, recently proposed by Lipshutz et al. as a novel carbamate protecting group for amines.[41] This group was easily installed on 3-*O*-methyl dopamine hydrochloride **18** to afford the *N*-Tsoc derivative **19** (Scheme 7). This starting phenol was chosen with the aim of modeling a nitrogen ring closure later applicable to the synthesis of lycorane 5/6-membered nitrogen-containing fused ring systems. Phenol **19** was then submitted to the same oxidative acetoxylation conditions developed for the phenols **12**. The orthoquinol acetate **20** was thus formed in good yield and the desired TBAF-mediated desilylation–cyclization domino event took place to furnish the 2,3-dihydroindole **21** in 48% yield (not optimized). Work is now in progress to extend this transformation to other models and lycorine-type precursors.

The synthetic value of 2-alkoxyphenol-derived orthoquinol acetates in oxygen and nitrogen heterocyclizations has thus so far been demonstrated in these investigations, but another aspect of the chemistry of oxidized 2-alkoxyphenol intermediates needed to be explored. At this point, it was clear that an acetate oxygen nucleophile, delivered from the oxidizing agent itself or from the reaction solvent, is quite efficient at trapping a phenoxenium-type intermediate (e.g. **2** in Scheme 1) or an equivalent transient species. We logically wondered if a *carbon* nucleophile could also intercept such a two-electron oxidation product, and if such an oxidative nucleophilic substitution could be effected regioselectively at the alkoxy-bearing carbon center (i.e. path *b*, Scheme 1, Nu_1 = carbon Nu). Similar oxidative transformations have been accomplished intramolecularly,[24,42–47] but intermolecular examples are rare[48,49] or directed toward unsubstituted arenol 2-positions to give rearomatized products,[17,22,50] and not cyclohexa-2,4-dienone species. Alternative carbon–carbon bond-forming reactions offering access to cyclohexa-2,4-dienones comprise direct addition of a carbon nucleophile to an orthoquinone carbonyl,[7,13,51] carbon alkylation of alkali metal salts of phenols,[52–54] reductive alkylation of phenol ethers,[10,11] and acid-catalyzed cyclization of phenolic diazoketones.[55] Introducing carbon appendages onto the alkoxylated carbon centers of 2-alkoxyarenols is a useful synthetic operation since it can deliver highly functionalized orthoquinol ethers. These vicinally oxygenated synthons are extremely valuable for natural product synthesis.

In particular, we are interested in the preparation of carbon-tethered naphthalene-based and anthracene-based cyclohexa-2,4-dienones as possible intermediates in the synthesis of natural benz[*a*]anthracene products bearing vicinal oxygens such as the angucyclines and the angucyclinones.[56,57] We recently reported examples of such transformations in which 2-methoxynaphthol (**25b**) was converted into naphthoid cyclohexa-2,4-dienones bearing a propene or a butenal motif at their 6-methoxylated position.[58] These transformations were accomplished by using a non-nucleophilic iodine(III)-based oxidizing agent [phenyliodine bis(trifluoroacetoxy), PIFA][59,60] in the presence of allyltrimethylsilane (**27a**) or 1-trimethylsilyloxybuta-1,3-diene (**27b**) at ambient temperature. We here report additional

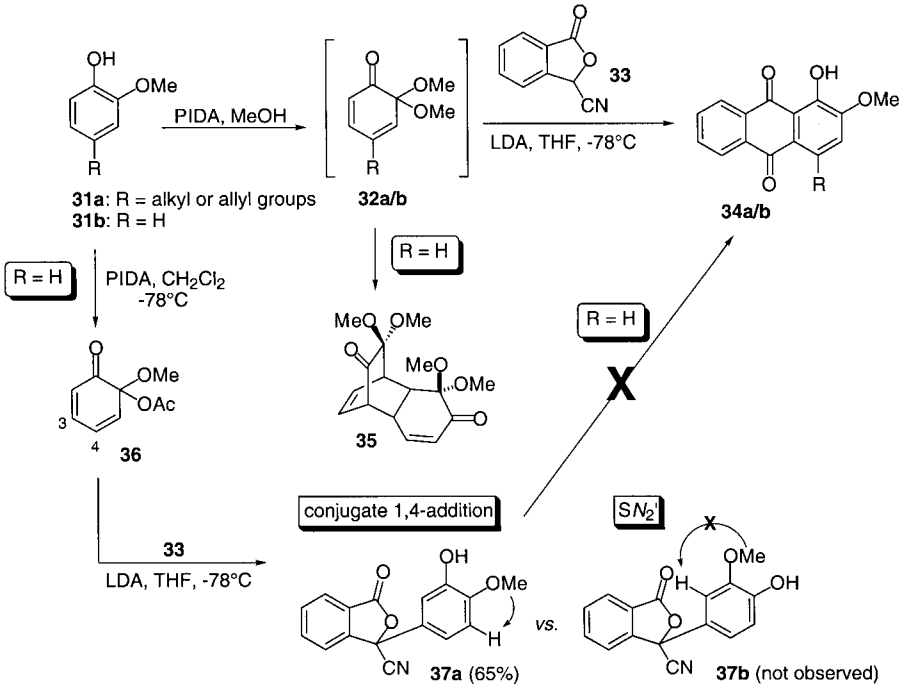
examples using 2-benzyloxynaphthol (**25a**) (Scheme 8); the benzyl group will be a priori preferred to the methoxy group in synthetic applications because its removal should be effected under milder conditions.[61,62] Yields of **28a** and **29a** were not as good as for the methoxylated versions.[58] Direct attack of the silane **27a** at the 4-position of **25a** or an acid-catalyzed Cope rearrangement of **28a** into **28b**[7] is apparently not responsible for this decrease of yield since phenol **28b** was not observed. However, in the case of substitution with the silyl enol ether **27b**, both the C-2 (**29a**) and the C-4 (**29b**) adducts were obtained in moderate yield. We are pursuing investigations to rationalize these intriguing regiochemical aspects and to improve the yields of these reactions. The starting naphthols **25a** and **25b** were prepared from their corresponding 2-alkoxynaphthaldehydes **23a** and **23b** via Baeyer–Villiger oxidation followed by alkaline hydrolysis[63–65] of the resulting formates **24a** and **24b**. Of particular note is the higher reproducibility and good yield obtained upon Dibal-H reduction instead of standard hydrolysis of **24a**. More interestingly, the naphthol **25b** was also obtained, albeit in moderate yield (37%), when 1-naphthol (**30**) was reacted with PIDA in MeOH (Scheme 9).



Scheme 9.

Finally, addition of a carbon nucleophile onto an orthoquinol acetate was also tested in the context of the synthesis of anthranoid derivatives. Mitchell and Russell[66,67] recently proposed a novel annulation route to anthraquinones **34a** which encompasses the conjugate addition of the anion of the phthalide **33**[68] to non-dimerizing C-4 substituted orthoquinone monoketals **32a** (Scheme 10). These intermediates were generated by PIDA-mediated oxidative methoxylation in MeOH. We attempted to intercept the orthoquinone monoketal **32b** derived from guaiacol (**31b**) by the same procedure, but the 6,6-dimethoxy derivative **32b** spontaneously dimerized in situ to form the Diels–Alder adduct **35**.[69] The orthoquinol acetate **36**, generated via PIDA-mediated oxidative acetoxylation of **31b** in CH_2Cl_2, did not dimerize. Its formation was verified by ^1H NMR analysis of the reaction mixture prior to addition of the phthalide **33** anion solution in THF. This experiment provides additional evidence of the much greater stability of orthoquinol acetates vis-à-vis their 6,6-dimethoxy orthoquinone monoketal analogues.[12,13] Unfortunately, annulation to the anthraquinone **34b** could not be completed, probably because of the greater nucleofugacity of the acetate as compared to the methanolate leaving group. Thus, only one C–C bond was formed to give rise, after rearomatizing departure of AcOH, to the nitrile **37** in 65% yield. Initial attempts to induce cyclization of phenol **37** by base treatment were to no avail, which led us to question the regiochemistry of **37**, since the alternative regioisomer **37b** is not suited for the desired cyclization. Indeed, although carbon nucleophiles usually add to orthoquinone monoketals to their 3-position via conjugate 1,4-addition,[35] here leading to **37a**, one cannot fully disregard the possibility of an SN_2'-like reaction at the 4-position with concomitant departure of the allylic acetate group to furnish **37b**, especially since the 4-position of **36** is unsubstituted in contrast to orthoquinone monoketals **32a** derived from **31a**.

The regiochemistry of **37** was thus unambiguously determined by a delayed ^1H–^1H COSY analysis (see Experimental)[70] which permitted the observation of a 5-bond correlation between the methoxy protons resonating at



Scheme 10.

3.92 ppm and the aromatic ^3J doublet at 6.88 ppm for **37a**; nitrile **37b** would have exhibited an analogous correlation but with an aromatic ^4J doublet resonance. It thus remains to identify reaction conditions that will enable complete annulation of **37a** into **34a** (R=H).

In conclusion, the results presented in this report demonstrate several facets of the synthetic value of two-electron oxidized 2-alkoxyarenol intermediates. Hypervalent iodine-based reagents again emerged as powerful tools for oxidative activation of arenols that can hence be converted into isolable orthoquinol acetates via oxidative acetoxylation. These non-dimerizing orthoquinone monoketal variants can then be exploited in a variety of C–C, C–N and C–O bond-forming reactions, including heterocycle constructions useful for the purpose of natural product synthesis. Carbon-based nucleophiles can also be used to intercept oxidized 2-alkoxyarenol intermediates and this process gives rise to orthoquinol ether precursors of naturally occurring vicinally oxygenated benz[*a*]anthracene motifs. Synthetic applications of these orthoquinonoid synthons are in progress, and will be reported in due course.

3. Experimental

3.1. General

Tetrahydrofuran (THF) and diethyl ether (Et_2O) were purified by distillation from sodium/benzophenone under Ar immediately before use. CH_2Cl_2 was distilled from CaH_2 prior to use. Light petroleum refers to the fraction boiling in the 40–60°C range. Moisture and oxygen sensitive reactions were carried out in flame-dried glassware under Ar. Evaporations were conducted under reduced pressure at temperatures less than 45°C unless otherwise noted. Column chromatography was carried out under positive Ar pressure using 40–63 μm silica gel (Merck) and the indicated solvents. Melting points are uncorrected. NMR spectra of samples in the indicated solvent were run at 300 MHz unless otherwise noted. Carbon multiplicities were determined by DEPT135 experiments.[71]Diagnostic correlation information was obtained with a delayed ^1H–^1H correlative experiment[70] using a fixed delay of 250 ms. Electron impact mass spectra (EIMS) were obtained at 50–70 eV. Electron impact and liquid secondary ion mass spectrometry low and high resolution mass spectrometric analyses (EIMS, and LSIMS, HRMS) were obtained from the mass spectrometry laboratory at the CESAMO, Bordeaux I University. Chemical ionization low and high resolutions mass spectrometric analyses (CIMS, HRMS) were obtained from the mass spectrometry laboratory at the University of Texas at Austin. Combustion analyses were performed by Desert Analytics, Tucson, AZ, or by Laboratoires Wolff, Clichy, France. The X-ray crystallographic analysis was performed at the University of Houston, Texas.

3.1.1. Methyl 3-hydroxy-4-methoxybenzoate (5a). This ester was prepared from the commercially available parent acid (5.35 g, 31.9 mmol) by stirring overnight with MeOH/HCl produced by adding 5 mL of acetyl chloride to 50 mL of MeOH,[72] and crystallized from EtOAc–light petroleum as white crystals (2.90 g, 50%): mp 56–57°C; IR (KBr) 3416, 1699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.85 (s, 3H), 3.91 (s, 3H), 5.74 (s, 1H), 6.84 (d, J=8.2 Hz, 1H), 7.58 (m, 1H), 7.60 (d, J=2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 166.8, 150.4, 145.2, 123.4, 122.8, 115.6, 109.8, 56.0, 51.9; EIMS *m/z* (relative intensity) 182 (M^+, 100), 167 (33), 120 (8).

3.1.2. 5-*tert*-Butyldiphenylsilyloxymethyl-2-methoxyphenol (5b). To a stirring ice-cold suspension of 4-methoxy-3-hydroxybenzyl alcohol (500 mg, 3.25 mmol) in dry CH_2Cl_2 (10 mL) was added triethylamine (994 μL, 7.14 mmol) and DMAP (871 mg, 7.14 mmol). The mixture was stirred for 10 min, after which time TBDPSCl (846 μL, 3.25 mmol) was added. After 30 min, the cooling ice bath was removed and the mixture was stirred for 3 h at room temperature. The solution was diluted with 20 mL of CH_2Cl_2, washed with 1 M H_3PO_4 (3×10 mL), and brine (3×10 mL). The organic layer was dried over $MgSO_4$, filtered and evaporated to give **5b** as a colorless oil (1.02 g, 80%): IR (NaCl) 3530 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (s, 9H), 3.88 (s, 3H), 4.68 (s, 2H), 5.61 (s, 1H), 6.81 (bs, 2H), 6.96 (bs, 1H), 7.34–7.43 (m, 6H), 7.68–7.72 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 145.5, 135.6, 134.5, 133.7, 129.6, 127.7, 117.6, 112.7, 110.5, 65.2, 56.0, 26.8, 19.3; EIMS *m/z* (relative intensity) 392 (M^+, 0.7), 335 (100), 199 (6); Anal. Calcd for $C_{24}H_{28}O_3Si$: C, 73.43; H, 7.19. Found: C, 73.69; H, 7.25.

3.1.3. Orthoquinol acetate 6b. This orthoquinol acetate was prepared as a yellow oil in 98% yield according to the PIDA-mediated oxidative acetoxylation method we previously described[30]: IR (NaCl) 1745, 1681 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.10 (s, 9H), 2.14 (s, 3H), 3.50 (s, 3H), 4.38 (bt, J=1.7 Hz, 2H), 6.11 (dd, J=1.2, 10.2 Hz, 1H), 6.25 (d, J=10.2 Hz, 1H), 6.44 (d, J=1.2 Hz, 1H), 7.29–7.77 (m, 10H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 191.2, 169.4, 153.6, 135.4, 134.7, 132.5, 130.2, 129.5, 127.6, 127.5, 125.3, 119.9, 93.2, 64.3, 51.4, 26.7, 19.2; EIMS *m/z* (relative intensity) 450 (M^+, 0.5), 393 (2), 335 (13), 199 (100); HRMS (EI) calcd for $C_{26}H_{30}O_5Si$ 450.1862, found 450.1858.

3.1.4. Diaryl ether 8a. White needles from CH_2Cl_2–Et_2O: mp 143–144°C; IR (KBr) 1760, 1721, 1663, 1604 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.33 (s, 3H), 3.66 (s, 3H), 3.77 (s, 3H), 3.83 (s, 3H), 3.91 (s, 3H), 5.92 (s, 1H), 7.00 (d, J=8.6 Hz, 1H), 7.45 (d, J=2.0 Hz, 1H), 7.83 (dd, J=8.6, 2.0 Hz, 1H), 11.82 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 170.5, 168.6, 166.2, 156.6, 156.3, 155.9, 154.3, 145.1, 126.8, 123.6, 123.1, 120.0, 111.7, 99.5, 94.4, 56,2, 56.0, 52.5, 52.1, 20.3; EIMS *m/z* (relative intensity) 420 (M^+, 58), 389 (29), 378 (100); Anal. Calcd for $C_{20}H_{20}O_{10}$: C, 57.14; H, 4.80. Found: C, 57.14; H, 4.99.

3.1.5. Orthoquinol acetate 13b. This orthoquinol acetate was prepared as a brownish red oil in 95% yield according to the PIDA-mediated oxidative acetoxylation method we previously described:[36] IR (NaCl) 1738, 1682 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.052 and 0.058 (2s, 6H), 0.84 (s, 9H), 1.22 (s, 3H), 1.23 (s, 3H), 2.07 (s, 3H), 2.32 (s, 2H), 3.43 (s, 3H), 5.91 (d, J=2.0 Hz, 1H), 6.00 (d, J=10.0 Hz, 1H), 6.97 (dd, J=2.0, 10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 191.9, 169.2, 145.1, 136.2, 132.4, 124.3, 93.0, 74.1, 51.3, 50.3, 29.8, 29.6, 25.9, 20.6, 18.0, −2.0;

EIMS *m/z* (relative intensity) 353 ($M-Me^+$, 1), 311 (12), 173 (100).

3.1.6. Orthoquinol acetate 13f. This orthoquinol acetate was prepared as a yellow oil in 98% yield according to the oxidative acetoxylation method we previously described:[36] IR (NaCl) 1737, 1684 cm^1; ^1H NMR ($CDCl_3$) δ 1.03 (s, 9H), 1.37–1.59 (m, 6H), 2.06 (s, 3H), 2.19 (bt, J=6.8 Hz, 2H), 3.43 (s, 3H), 3.65 (t, J=6.3 Hz, 2H), 5.86 (bs, 1H), 6.09 (d, J=10.0 Hz, 1H), 6.74 (dd, J=2.1, 10.0 Hz, 1H), 7.33–7.72 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 191.8, 169.3, 142.7, 138.7, 135.4, 134.0, 129.5, 128.7, 127.6, 125.7, 93.1, 63.7, 51.2, 34.9, 32.2, 27.5, 26.8, 25.2, 20.5, 19.2; EIMS *m/z* (relative intensity) 507 (MH^+, 8), 429 (12), 257 (79), 211 (100); HRMS (CI) calcd for $C_{30}H_{39}O_5Si$ 507.2566, found 507.2566.

3.1.7. Alcohol 15. Orthoquinol acetate **13f** (361 mg, 0.80 mmol) was treated with tetrabutylammonium fluoride (TBAF) according to the method we previously described.[36] Purification of the resulting dark oil by column chromatography, eluting with hexanes–EtOAc (9:1) followed by EtOAc, afforded **15** as a dark oil (24 mg, 14%): IR (NaCl) 3401 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.25–1.67 (m, 6H), 2.54 (bt, J=7.4 Hz, 2H), 3.64 (bt, J=6.4 Hz, 2H), 3.87 (s, 3H), 6.64–6.67 (m, 2H), 6.82 (dd, J=1.5, 8.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 146.2, 143.5, 134.5, 120.8, 114.1, 110.9, 62.9, 55.8, 35.5, 32.6, 31.5, 25.3; EIMS *m/z* (relative intensity) 211 (MH^+, 7), 210 (M^+, 52), 137 (100).

3.1.8. *O*-Spirocyclohexadienone tetrahydrofuran 17. Alcohol **16** (185 mg, 1.02 mmol) was submitted to the oxidative acetoxylation conditions we previously described[36] to furnish **17** (182 mg, 74%) as a yellow oil: IR (NaCl) 1675, 1644 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.00–2.19 (m, 4H), 3.63 (s, 3H), 3.98–4.09 (m, 2H), 5.67 (d, J=2.7 Hz, 1H), 6.09 (d, J=9.9 Hz, 1H), 6.77 (dd, J=2.7, 9.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 180.9, 150.1, 149.7, 126.1, 116.6, 79.3, 68.8, 54.8, 37.6, 26.8; EIMS *m/z* (relative intensity) 181 (MH^+, 10), 180 (M^+, 79), 137 (100); Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.64; H, 6.72. Found: C, 66.26; H, 6.69.

3.1.9. *N*-Tsoc-4-hydroxy-3-methoxyphenylethylamine (19). A stirring solution of 3-*O*-methyl dopamine hydrochloride **18** (500 mg, 2.45 mmol) and triethylamine (1.02 mL, 7.36 mmol) in dry CH_2Cl_2 (20 mL) was cooled at −78°C. Dry ice (5.4 g, ca. 50 equiv.) was added in one portion. After stirring at −78°C for 1 h, TIPS-OTf (659 μL, 2.45 mmol) was added dropwise via syringe. After 5 min, the mixture was allowed to warm up to room temperature, and was stirred for 30 min. The mixture was then poured in a separatory funnel containing H_2O (20 mL). After separation, the aqueous phase was extracted with CH_2Cl_2 (2×20 mL); the combined organic layers were washed with saturated $NaHCO_3$ (20 mL), brine (2×20 mL), and dried over $MgSO_4$. Evaporation of the solvent afforded 907 mg of an orange oil which was purified by column chromatography, eluting with hexanes–Et_2O (1:1), to give **19** as white crystals (703 mg, 78%): mp 60–61°C; IR (KBr) 3378, 3264, 1671 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.07 (d, J=7.1 Hz, 18H), 1.27 (h, J=7.1 Hz, 3H), 2.69–2.77 (m, 2H), 3.30–3.41 (m, 2H), 3.86 (s, 3H), 4.80 (bs, 1H), 5.62 (bs, 1H), 6.65–6.69 (m, 2H), 6.84 (d, J=7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 154.9, 146.5, 144.1, 130.7, 121.4, 114.3, 111.2, 55.8, 42.5, 35.8, 17.7, 12.0; EIMS *m/z* (relative intensity) 367 (M^+, 3), 324 (100); Anal. Calcd for $C_{19}H_{33}NO_4Si$: C, 62.09; H, 9.06; N, 3.81. Found: C, 62.01; H, 9.03; N, 3.87.

3.1.10. Orthoquinol acetate (20). A solution of phenol **19** (400 mg, 1.09 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise to a stirring solution of oxidizing agent (LTA, 1.1 equiv, or PIDA, 1.0 equiv.) in 5 mL of dry CH_2Cl_2 at −78°C. The reaction mixture immediately became bright yellow. After 1 h, TLC monitoring [hexanes–Et_2O (1:1)] indicated complete consumption of the starting material. The mixture was poured into ice-cold saturated aqueous $NaHCO_3$ (10 mL), extracted with CH_2Cl_2 (2×20 mL), washed with brine (10 mL), dried over Na_2SO_4, filtered and evaporated at room temperature. The residue was further dried under high vacuum for a couple of hours to give the orthoquinol acetate **20** as a bright yellow oil (454 mg, 98%). This oil was used without further purification: IR (NaCl) 3394, 1750, 1672, 1682 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.03 (d, J=6.7 Hz, 18H), 1.25 (h, J=6.7 Hz, 3H), 2.05 (s, 3H), 2.37–2.43 (m, 2H), 3.03–3.19 (m, 1H), 3.33–3.50 (m, 1H), 3.41 (s, 3H), 4.94–5.00 (m, 1H), 5.93 (bs, 1H), 6.10 (d, J=9.9 Hz, 1H), 6.76 (dd, J=2.2, 9.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 191.5, 169.6, 154.8, 141.9, 135.5, 131.0, 126.3, 92.8, 51.2, 38.9, 35.2, 20.5, 17.7, 11.9; EIMS *m/z* (relative intensity) 425 (M^+, 1), 382 (16), 324 (100), 137 (56); HRMS (EI) calcd for $C_{21}H_{35}NO_6Si$ 425.2234, found 425.2230.

3.1.11. 2,3-Dihydroindole (21). To a stirring ice-cold solution of **20** (380 mg, 0.89 mmol) in dry THF (8 mL) was added dropwise a commercial solution of TBAF (1 M in THF, 1.1 equiv.). The reaction mixture immediately became darker. After 15 min, the ice bath was removed, and the reaction was stirred at room temperature for 2.5 h. Progression of the reaction was monitored by the disappearance of the orthoquinol acetate, as indicated by TLC [hexanes–Et_2O (1:1), and then CH_2Cl_2–MeOH (20:1)]. The mixture was diluted with EtOAc (50 mL), poured into ice-cold water (15 mL), extracted with EtOAc (2×20 mL), washed with brine (2×20 mL), dried over Na_2SO_4, filtered and evaporated at room temperature. The resulting dark oily residue was purified by column chromatography, eluting with CH_2Cl_2–MeOH (40:1), to afford **21** as an orange oil (70.8 mg, 48%): IR (NaCl) 3432 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.96 (t, J=8.2 Hz, 2H), 3.53 (t, J=8.2 Hz, 2H), 3.81 (s, 3H), 6.39 (s, 1H), 6.72 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 145.3, 144.7, 140.5, 120.2, 109.0, 98.4, 57.1, 47.8, 29.9; EIMS *m/z* (relative intensity) 167 (3), 166 (MH^+, 6), 165 (M^+, 61), 150 (100); HRMS (EI) calcd for $C_9H_{11}NO_2$ 165.0790, found 165.0785.

3.1.12. 2-Benzyloxy-1-naphthaldehyde (23a). To a stirring solution of commercially available 2-hydroxy-1-naphthaldehyde **22** (2 g, 11.6 mmol) in acetone (50 mL) was added potassium carbonate (1.77 g, 12.8 mmol) and benzyl bromide (1.38 mL, 11.6 mmol), and the mixture was refluxed for 3 h. The solution was filtered through celite and the solvent removed in vacuo. The residue was dissolved with Et_2O (75 mL), washed with 1 M NaOH (50 mL), brine

(2×50 mL), and dried over Na_2SO_4. Evaporation of the solvent afforded crude **23a** as a yellow powder (2.7 g, 89%): mp 119°C; IR (KBr) 1666 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 5.33 (s, 2H), 7.32–7.49 (m, 7H), 7.60–7.67 (m, 1H), 7.77 (d, J=7.3 Hz, 1H), 8.03 (d, J=7.3 Hz, 1H), 9.30 (d, J=7.3 Hz, 1H), 10.98 (s, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 191.9, 163.1, 137.4, 135.9, 131.5, 129.8, 128.7, 128.6, 128.3, 128.2, 127.3, 125.0, 124.9, 117.3, 113.9, 71.5; LSIMS *m/z* (relative intensity) 285 (MNa^+, 32), 263 (MH^+, 100), 262 (M^+, 78).

3.1.13. 2-Benzyloxynaphthalen-1-yl formate (24a). To a stirring ice-cold solution of 2-benzyloxy-1-naphthaldehyde **23a** (800 mg, 3.05 mmol) in EtOAc (30 mL) was added dropwise peracetic acid (5.7 mL, 30.5 mmol), and then the mixture was stirred at room temperature overnight. The green solution was poured over water (40 mL), washed with 1 M aqueous sodium thiosulfate (20 mL) and brine (3×30 mL). The organic layer was dried over Na_2SO_4 and evaporated to give a solid which was submitted to column chromatography, eluting with hexanes–Et_2O (4:1) to afford **24a** as beige crystals (679 mg, 80%): mp 70°C; IR (KBr) 1740, 1266 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 5.25 (s, 2H), 7.32–7.57 (m, 8H), 7.73–7.91 (m, 3H), 8.47 (s, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 159.4, 146.5, 136.4, 133.0, 129.3, 128.6, 128.4, 128.3, 128.1, 127.8, 127.3, 127.2, 124.6, 120.2, 115.5, 71.6; EIMS *m/z* (relative intensity) 278 (M^+, 8), 250 (17), 159 (27), 91 (100), 77 (6); Anal. Calcd for $C_{18}H_{14}O_3$: C, 77.67; H, 5.07. Found: C, 77.64; H, 5.16.

3.1.14. 2-Benzyloxy-1-naphthol (25a). To a stirring ice-cold solution of 2-benzyloxy naphthalen-1-yl formate **24a** (100 mg, 0.36 mmol) in THF (8 mL) was slowly added DIBAL-H (1 M in toluene, 3.0 equiv.) via syringe. After stirring for 1 h at 0°C, the mixture was poured over ice-cold water (3 mL) and 1 M H_3PO_4 (5 mL), extracted with Et_2O (3×10 mL), and washed with brine (20 mL) to give **25a** (90 mg, 100%). This crude brownish solid was used without any further purification: mp 50–52°C (lit.[63] mp 76°C); IR (KBr) 3528, 1265 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 5.24 (s, 2H), 6.18 (s, 1H), 7.31–7.55 (m, 9H), 7.81 (d, J=7.9 Hz, 1H), 8.25 (d, J=7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz)[63] δ 140.3, 136.7, 129.8, 128.7, 128.3, 127.9, 127.7, 127.4, 125.3, 124.4, 124.1, 121.3, 119.5, 114.9, 72.4; EIMS *m/z* (relative intensity) 250 (M^+, 36), 159 (46), 91 (100).

3.1.15. 2-Methoxy-1-naphthol (25b). *Procedure A*. To a stirring ice-cold solution of commercially available 2-methoxy-1-naphthaldehyde **23b** (2.3 g, 12 mmol) in EtOAc (30 mL) was added dropwise peracetic acid[64,65] (3.4 mL, 18 mmol), and then the mixture was stirred at room temperature overnight. The green solution was poured over water (30 mL), washed with saturated aqueous $NaHCO_3$ (15 mL) and brine (3×15 mL). The organic layer was dried over Na_2SO_4 and concentrated. The residue (i.e. crude **24b**) was diluted with 25 mL of MeOH and treated with 83% KOH (0.8 g, 12 mmol) for 45 min. The mixture was diluted with water (25 mL) and extracted with Et_2O after acidification with 10% HCl. The organic layer was dried over Na_2SO_4 and evaporated to furnish a solid residue which was purified by column chromatography, eluting with hexanes–Et_2O (1:1), to afford **25b** as a colorless solid (1.2 g, 58%). *Procedure B*. To a stirring ice-cold solution of 1-naphthol **30** (569 mg, 3.95 mmol) in MeOH at rt was added PIDA (1.27 g, 3.95 mmol) as a solid. The mixture was stirred at rt for 1 h after which time MeOH was partially evaporated, and the residue was diluted with CH_2Cl_2, washed three times with 1 M HCl, and twice with brine. The organic layer was dried over $MgSO_4$ and concentrated to afford crude **25b**, which was purified by column chromatography, eluting with hexanes-Et_2O (1:1), to afford pure **25b** (253 mg, 37%): mp 52–53°C (lit.[73,74] mp 54–56°C); IR (KBr) 3392, 1269, 798 cm^{-1}; ^1H NMR ($CDCl_3$)[63] δ 3.97 (s, 3H), 6.09 (bs, 1H), 7.25 (d, J=8.9 Hz, 1H), 7.34–7.49 (m, 3H), 7.76 (d, J=8.2 Hz, 1H), 8.18 (d, J=8.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 141.2, 139.7, 129.5, 127.4, 125.3, 124.2, 123.9, 121.2, 119.5, 113.2, 57.1; EIMS *m/z* (relative intensity) 175 (MH^+, 40), 174 (M^+, 100), 159 (100).

3.1.16. 1,2-Dihydro-2-(prop-2-enyl)-2-benzyloxy-1-oxo-naphthalene (28a). To a stirring ice-cold solution of 2-benzyloxy-1-naphthol **25a** (200 mg, 0.8 mmol) in CH_2Cl_2 (14 mL) was added PIFA (516 mg, 1.2 mmol) as a solid, in one portion. The mixture became immediately dark purple, and then the allylsilane **27a** (355 μL, 2.24 mmol) was added dropwise. The mixture was allowed to warm up to room temperature over 2 h, after which time it was diluted with CH_2Cl_2 (40 mL), washed with 1 M H_3PO_4 (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL). The reddish organic layer was dried over Na_2SO_4 and evaporated at room temperature. The residue was purified by column chromatography, eluting with hexanes–Et_2O (4:1), to furnish **28a** as a light brown gum (82 mg, 36%): IR (NaCl) 1688 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.56–2.64 (m, 2H), 4.35 (s, 1H), 4.96–5.08 (m, 2H), 5.65–5.82 (m, 1H), 6.24 (d, J=10.0 Hz, 1H), 6.78 (d, J=10.0 Hz, 1H), 7.22–7.45 (m, 9H), 7.56–7.64 (m, 1H), 8.02–8.09 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 200.3, 138.3, 135.9, 134.9, 134.7, 133.4, 131.1, 128.8, 128.3, 128.2, 127.7, 127.5, 126.9, 119.2, 82.0, 68.2, 44.5; LSIMS *m/z* (relative intensity) 313 (MNa^+, 15), 291 (MH^+, 40), 223 (100); HRMS (LSIMS) calcd for $C_{20}H_{19}O_2$ 291.1385, found 291.1374.

3.1.17. 1,2-Dihydro-2-[(*E*)-3-formylprop-2-enyl]-2-benzyloxy-1-oxo-naphthalene (29a) and 4-[(*E*)-3-formylprop-2-enyl]-2-benzyloxy-1-naphthol (29b). To a stirring ice-cold solution of 2-benzyloxy-1-naphthol **25a** (100 mg, 0.4 mmol) in CH_2Cl_2 (5 mL) was added PIFA (258 mg, 0.6 mmol) as a solid, in one portion. The mixture became straight away dark purple, and then the silyl enol ether 27b (549 μL, 3.14 mmol) in solution in CH_2Cl_2 (4 mL) was added dropwise. The mixture was allowed to warm up to room temperature over 3 h, after which time it was diluted with CH_2Cl_2 (30 mL), washed with 1 M H_3PO_4 (10 mL), saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL), dried over Na_2SO_4, and evaporated at room temperature. The resulting brownish oil (160 mg) was purified by column chromatography, eluting with hexanes–Et_2O (4:1), to furnish a 2:3 mixture of **29a** and **29b** (52 mg, 41%) as a light brown gum, and 7 mg of recovered starting material. **29a**: IR (KBr) 1685 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.80–2.84 (m, 2H), 4.38 (s, 2H), 6.05 (ddt, J=1.5, 7.9, 15.5 Hz, 1H), 6.23 (d, J=10.0 Hz, 1H), 6.82 (d, J=10.0 Hz,

1H), 6.90 (dt, *J*=7.6, 15.5 Hz, 1H), 7.28–7.51 (m, 7H), 7.63 (td, *J*=7.5, 1.5 Hz, 1H), 8.05 (d, *J*=7.5 Hz, 1H), 9.43 (d, *J*=7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 199.0, 193.7, 156.4, 136.8, 135.8, 135.3, 134.9, 129.7, 129.5, 128.7, 128.6, 128.4, 128.3, 127.8, 127.7, 127.1, 81.1, 72.4, 42.4. **29b**: IR (KBr) 3424 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.00 (dd, *J*=1.5, 6.2 Hz, 2H), 5.20 (s, 2H), 6.05 (ddt, *J*=1.5, 7.9, 15.5 Hz, 1H), 6.14 (s, 1H), 7.03 (dt, *J*=6.2, 15.5 Hz, 1H), 7.14 (bs, 1H), 7.28–7.51 (m, 7H), 7.76 (dd, *J*=1.8, 7.9 Hz, 1H), 8.22 (dd, *J*=1.8, 7.9 Hz, 1H), 9.50 (d, *J*=7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 193.5, 150.8, 139.9, 139.7, 133.5, 128.2, 128.1, 127.9, 127.7, 127.6, 125.3, 124.9, 124.8, 124.6, 123.2, 122.2, 116.4, 72.5, 35.9; LSIMS *m/z* (relative intensity) 341 (MNa^+, 28), 318 (M^+, 100); HRMS (LSIMS) calcd for $C_{21}H_{18}O_3$ 318.1256, found 318.1257.

3.1.18. Nitrile 37a. A solution of commercially available guaiacol **31b** (100 mg, 0.805 mmol) in CH_2Cl_2 (2 mL) was added to a stirring solution of PIDA (390 mg, 1.208 mmol) in CH_2Cl_2 (5 mL) cooled at −78°C. After 1 h, the mixture was diluted with cold water (10 mL), saturated aqueous $NaHCO_3$ (5 mL) and extracted with CH_2Cl_2 (3×15 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, and evaporated in vacuo to afford the crude orthoquinol acetate **36**, which was used without any further purification. A solution of lithium diisopropylamine was prepared from the dropwise addition of *n*-butyllithium (2.5 M in hexanes, 1.05 equiv.) over a solution of diisopropylamine (123 μL, 0.885 mmol) in THF (2 mL) at −78°C. After 30 min, the mixture was allowed to warm up to room temperature for 15 min, and then was cooled again at −78°C. A solution of isobenzofuran-1-(3*H*)-one-3-carbonitrile **33**[68] (128.1 mg, 0.805 mmol) in THF (4 mL) was added dropwise while stirring. A solution of **36** in THF (4 mL) was then added via syringe and maintained under stirring at −78°C. After 1 h, the cooling bath was removed and the reaction was allowed to warm up to rt. The reaction was then diluted with 10% aqueous HCl (25 mL) and extracted with $CHCl_3$ (3×25 mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated. Purification by column chromatography, eluting with hexanes–Et_2O (2:1), furnished **37a** as a colorless gum (131 mg, 65%): IR (KBr) 3448, 2266, 1798 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.92 (s, 3H), 5.74 (s, 1H), 6.84 (d, *J*=2.1 Hz, 1H), 6.88 (d, *J*=8.5 Hz, 1H), 7.11 (dd, *J*=2.1, 8.5 Hz, 1H), 7.55 (d, *J*=7.6 Hz, 1H), 7.70 (td, *J*=7.6, 1.3 Hz, 1H), 7.80 (td, *J*=7.6, 1.3 Hz, 1H), 7.99–8.02 (m, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 167.3, 148.5, 146.7, 146.3, 135.7, 131.3, 126.4, 126.3, 124.3, 123.3, 118.5, 115.9, 112.2, 110.8, 79.6, 56.0; EIMS *m/z* (relative intensity) 282 (MH^+, 20), 281 (M^+, 100), 177 (70); HRMS (EI) calcd for $C_{16}H_{11}NO_4$ 281.0688, found 281.0688.

Acknowledgements

The support of the Délégation Régionale à la Recherche et à la Technologie pour l'Aquitaine (FEDER Grant n° Z0131), the Conseil Régional d'Aquitaine (Grant n° 990209003), and the Robert A. Welch Foundation (Grant D-1365) is gratefully acknowledged. The authors also wish to thank Anne-Marie Lamidey and Delphine Faure from Bordeaux I University, and Eva Maria León Pastor from the Universidad de Salamanca for their contribution to this work, as well as Simon G. Bott at the University of Houston, Texas, for the X-ray crystallographic analysis of **8a**.

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