Formal radical closure onto aromatic rings—a general route to carbocycles†

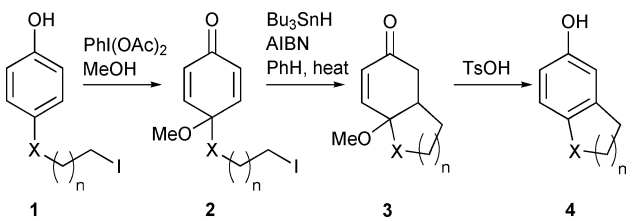
Derrick L. J. Clive,* Rajesh Sunasee and Zhenhua Chen

Received 26th February 2008, Accepted 2nd April 2008
First published as an Advance Article on the web 8th May 2008
DOI: 10.1039/b803308k

A general method is described for indirectly effecting radical carbocyclization of an alkyl chain onto an aromatic ring. Birch reductive-alkylation of aromatic *tert*-butyl esters with α,ω-dibromides, chromium(VI)-mediated oxidation of the resulting 1,4-dienes and Finkelstein displacement of Br^- with NaI gives cross-conjugated ketones that undergo radical cyclization. The products are easily aromatized to phenols by silylation, Saegusa oxidation and treatment with $BiCl_3.H_2O$. A special feature of the route is that it allows attachment of a substituent to the original aromatic ring in place of the phenolic oxygen of the normal product.

Introduction

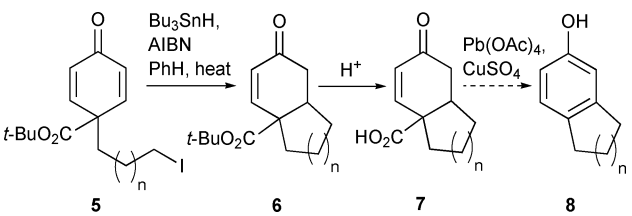
Previous publications[1] from this laboratory have described an indirect method for effecting radical cyclization onto a benzene ring, along the lines summarized in Scheme 1 (X = O, N). The essential steps of the method involve converting a phenol into a cross-conjugated ketone (**1**→**2**), which then undergoes stannane-mediated radical cyclization under standard conditions (**2**→**3**). Finally, exposure to TsOH causes rearomatization (**3**→**4**). In cases where X = O, the cross-conjugated ketone can be generated as shown, by oxidation in MeOH; alternatively, if the original benzene ring carries a MeO group *para* to the phenolic OH, then the oxidation must be done in the presence of an α,ω-iodoalcohol in order to generate the ketones **2**. When X = N, a route similar to that of Scheme 1 is followed,[1b,c] but with an additional step in which the nitrogen is protected as a carbamate before introduction of iodine and oxidation to the cross-conjugated ketone. Such cyclizations of *alkyl* radicals onto a benzene nucleus are generally difficult, but can be achieved in special cases, which we have summarized in other publications.[1] Application of the process summarized in Scheme 1 to an all-carbon case (**1**, X = C) could be a useful extension of the methodology.[2] However, we find that when X = C, oxidation in the sense **1**→**2** proceeds in poor yield. A few examples of such oxidation of *para* alkyl phenols have been reported to proceed efficiently, but these almost always involve *para* methyl substitution.[3] When the alkyl chain is longer than one carbon, our experiments show that the oxidation is usually inefficient, and such examples as we have found in the literature confirm this assessment.[3] The approaches we tried include use of $PhI(OAc)_2$ in water–MeOH;[3] $PhI(OCOCF_3)_2$ in water–MeCN or in MeOH;[4] *t*-BuOOH, $RuCl_2(PPh_3)_3$;[5] *t*-$Ph(Me_2)COOH$, $RuCl_2(PPh_3)_3$.



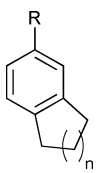
Scheme 1 General approach to radical closure onto aromatic rings. X = O, N.

Results and discussion

Our inability to extend the process of Scheme 1 directly to the all-carbon case caused us to consider alternatives to a MeO group that would still allow rearomatization, and the use of a *tert*-butyl ester, as in **5** (Scheme 2) appeared to be worthy of consideration. Such esters ought to be readily available by Birch reductive alkylation,[6] since preparation of the corresponding methyl esters had already been reported, together with studies on their radical cyclization.[7] We had anticipated that after radical cyclization (**5**→**6**), removal of the *tert*-butyl group (**6**→**7**) and oxidative decarboxylation[8] would give the desired rearomatized product (**7**→**8**). In the event, these speculations could not be fully implemented, as rearomatization along the intended lines was problematic; however, a modified version of the plan allowed us to effect the desired rearomatization.[9] We also investigated minor changes to the sequence, so as to expand the range of final products from phenols **8** to compounds of type **9** in which the phenolic OH of **8** is replaced by H, or an alkyl, allyl, propargyl, alkynyl, aryl or heteroaryl group.



Scheme 2 Cyclization of alkyl chains onto aromatic rings.



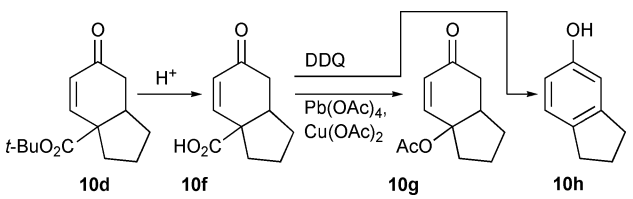
Chemistry Department, University of Alberta, Edmonton, Alberta, T6G 2G2, Canada. E-mail: derrick.clive@ualberta.ca

† Electronic supplementary information (ESI) available: Experimental procedures. See DOI: 10.1039/b803308k

Birch reductive alkylation of a number of aromatic *tert*-butyl esters (Table 1) with 1,3-dibromopropane, 1,4-dibromobutane or *o*-iodobenzyl bromide proceeded smoothly, giving in most cases yields of at least 80%. The second stage of the process requires oxidation of the resulting 1,4-diene system to a cross-conjugated ketone, and this was best achieved with CrO_3 in AcOH-Ac_2O.[10] In a few cases, better results were obtained under basic conditions with 3,5-dimethylpyrazole and CrO_3.[7,11] In one example (Table 1, entry 6), PDC-*t*-BuOOH was the best oxidant.[12] Formation of the cross-conjugated ketones is successful with benzenoid and naphthalenoid systems, and substituents such as methyl and methoxy groups can be present.

The bromides were converted into the corresponding iodides by Finkelstein reaction and in all cases the radical cyclization step (Table 2) was easily carried out by the standard method of slow addition (5 h) of a benzene solution of Bu_3SnH containing a catalytic amount of AIBN to a refluxing solution of the substrate in PhH.[7] At the end of the addition the mixtures were refluxed for an arbitrary period of 3–12 h. Attempts to use bromide **16b**, instead of the iodide, as a radical precursor gave a poor yield, presumably because bromides react with tributylstannyl radicals about 100 times more slowly than iodides.[7,13] Five- and six-membered rings are formed in 65–96% yield, but our attempts to generate a 7-membered ring (Table 2, entry 3) were unsuccessful. 7-*Exo*-trig cyclizations are not common, but a number are known[14] and it is not clear why the process is unsuccessful in the present case. We tried very slow addition of the stannane (over 10 h) in refluxing PhH or PhMe, or reactions at room temperature with Et_3B/air as initiator (in EtOAc), or at −78 °C with Et_3B/air (in PhMe), but always observed simple reduction (replacement of I by H) as by far the major product.

The next step of our planned sequence—the critical rearomatization—was initially troublesome and several approaches had to be tried. With **10d** as a test substrate (Scheme 3), we first removed the *tert*-butyl group in the standard way by treatment with CF_3CO_2H. Exposure of acid **10f** to the action of $Pb(OAc)_4$ in the presence of $Cu(OAc)_2$—conditions that had served us well in the past for the conversion of **18** into **19** (Scheme 4),[8] during a natural product synthesis—did not proceed as expected, but gave instead a compound tentatively identified as the acetate **10g**, which was itself resistant to elimination of AcOH under the influence of DBU in refluxing PhMe. When we used $PhI(OAc)_2$ for the attempted oxidative decarboxylation of **10f**, a complex mixture was obtained. Treatment of **10f** with DDQ in refluxing dioxane slowly produced the required aromatized product **10h**, but in poor yield (33%). These initial experiments prompted us to introduce a second double bond before attempting the decarboxylation. To this end, compound **10d** was subjected to Saegusa oxidation[15] by conversion into the corresponding silyl enol ether, followed by treatment with



Scheme 3 Decarboxylation and rearomatization.

Table 1 Formation of cross-conjugated ketones. Reductive alkylations were done by the general method given in the Experimental section. General method A was used for oxidations, except for entries 2 and 3, where method B was used, and entry 6, in which PDC-*t*-BuOOH was used

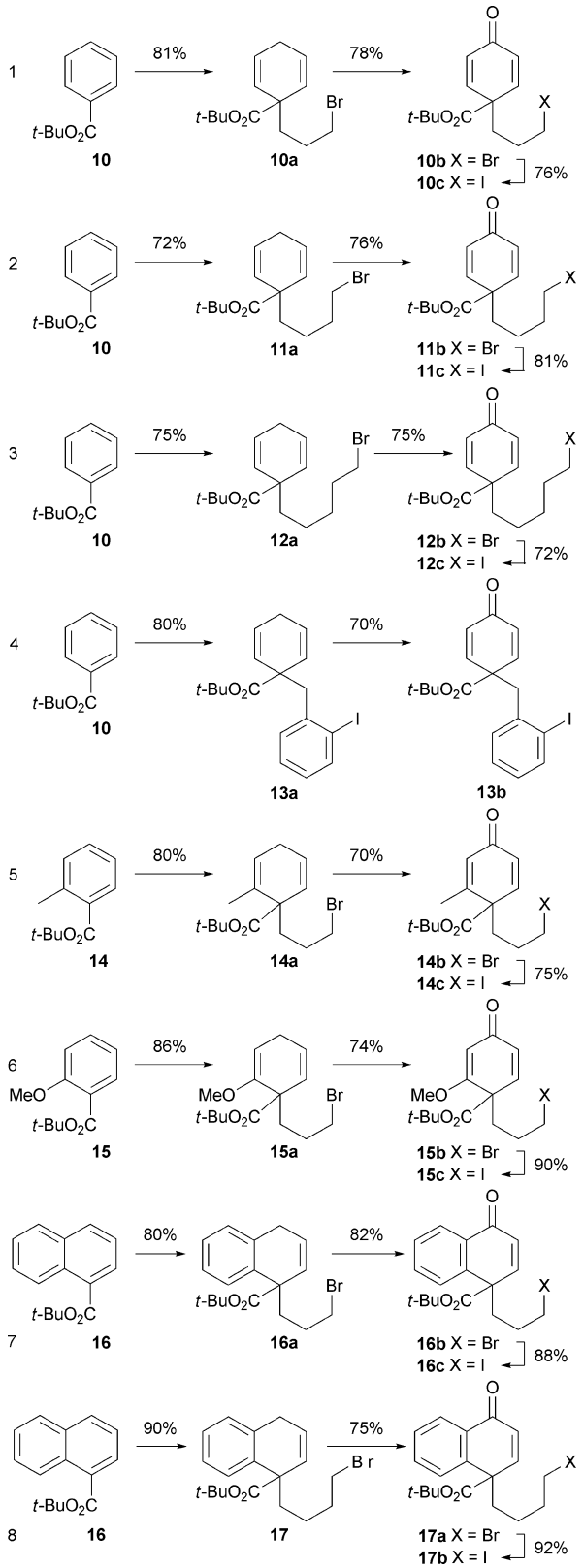
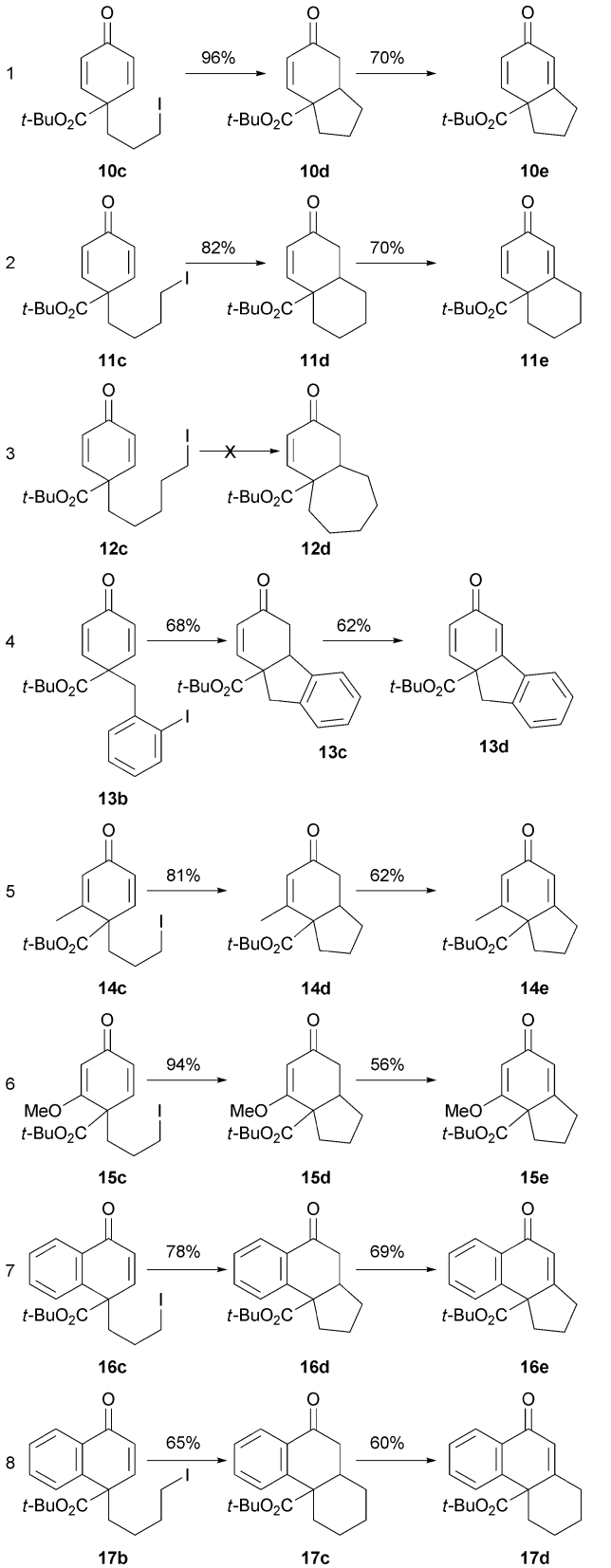
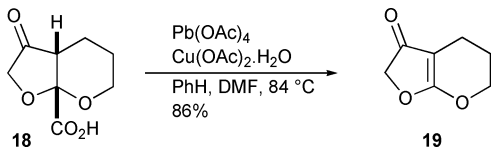


Table 2 Radical cyclization and reoxidation. Radical cyclization was done by the general method given in the Experimental section and Saegusa oxidation was used for desaturation of the ketones, except for entry 6, in which selenation and selenoxide fragmentation were used





Scheme 4 Oxidative decarboxylation.

$Pd(OAc)_2$ (Table 2, entry 1, **10d**→**10e**). This method of oxidation was applied to several other enones (Table 2) and in all but one case (entry 6) gave yields a little above 60%. In the case of **15d**, the silylation step, using either $Me_3SiOSO_2CF_3$ and 2,6-lutidine, or LDA and Me_3SiCl was unsuccessful, but these procedures were not examined exhaustively, since we found that phenylselenation (LDA, PhSeCl) and oxidation (H_2O_2) generated the required double bond, although only in modest yield (56%), presumably because just one of the two intermediate phenyl selenides had the appropriate stereochemistry for *syn* elimination.

The cross-conjugated ketone **10e** was treated with CF_3CO_2H to remove the *tert*-butyl group and, as expected, the resulting acid underwent spontaneous decarboxylation[16] to afford (55%) indanol **10h** (shown in Table 3) together with an unidentified byproduct. Addition of anisole to suppress formation of this byproduct was ineffective. We therefore turned our attention to the use of $BiCl_3.H_2O$ which had recently been reported to effect smooth removal of

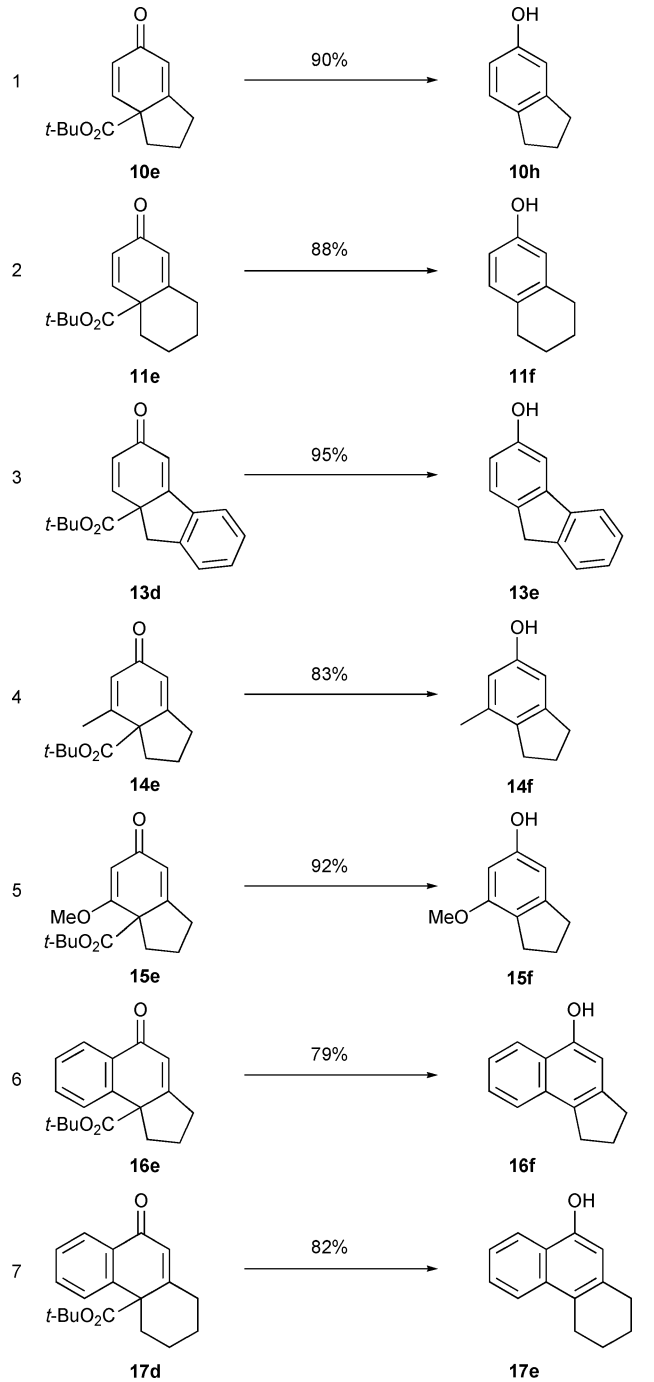
N-Boc groups from protected amino acids and peptides.[17] In these deprotections,[17] prolonged reaction times had to be avoided if the substrate also contained an ordinary *tert*-butyl ester, as cleavage of the latter then started to occur during reaction times longer than 1.5–2 h.[17] With our substrate **10e**, exposure to $BiCl_3.H_2O$ in aqueous MeCN at 65 °C resulted in efficient removal of the *tert*-butyl group as well as decarboxylation to give directly the desired aromatized product **10h** (90%, Table 3, entry 1). We did not establish if the decarboxylation occurred spontaneously or whether the bismuth reagent is involved. The removal of the *tert*-butyl group and decarboxylative aromatization are general and overall yields with our dienones were in the range 79–95% (Table 3). In no case did we notice the type of byproduct observed with **10e** when it was treated with CF_3CO_2H.

The intermediate ketones in our sequence can be modified by hydride reduction to the alcohol level or they can be converted into tertiary alcohols by reaction with a Grignard reagent or organolithium (Table 4). Decarboxylation and aromatization then gives the expected non-phenolic products. Simple alkyl and aryl groups can be introduced, as well as allylic, propargylic, acetylenic and heteroaromatic units (Table 4). When the intermediate ketone is modified in this way, either by hydride reduction or by carbanion addition, the rearomatization in the presence of $BiCl_3.H_2O$ still occurs efficiently but requires stoichiometric amounts of the reagent. In contrast, the cross-conjugated ketones themselves (Table 3) usually needed only 0.5 equivalents of $BiCl_3.H_2O$. Among all 23 examples we studied, using $BiCl_3.H_2O$, only that of Table 4, entry 14 took an unexpected course, giving the vinyl chloride **16n**.

Conclusions

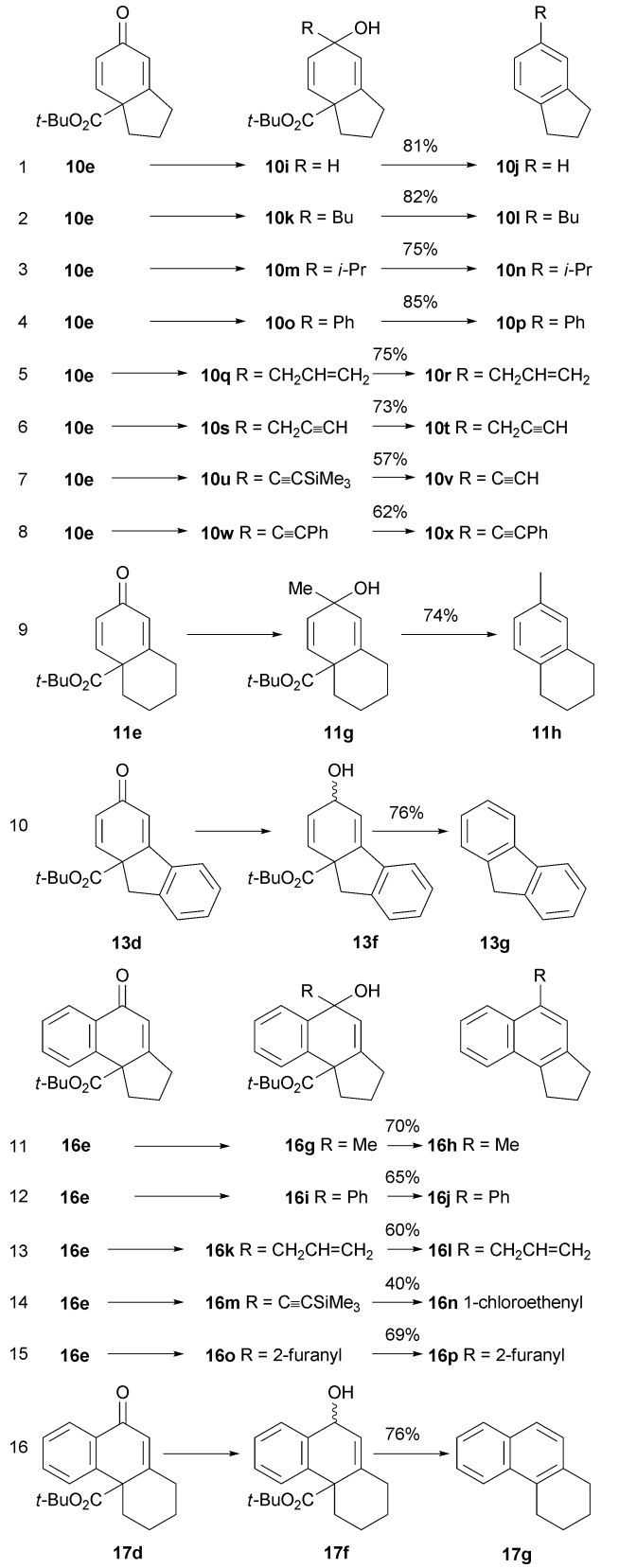
In summary, we have examined an indirect method for effecting radical cyclization of an all-carbon chain onto an aromatic ring and have shown that the process can be modified easily so that

Table 3 Formation of phenols. In all cases 0.5 equiv $BiCl_3.H_2O$ was used to effect rearomatization, except for entries 6 and 7, where 1 equiv was used



instead of the normal phenolic product one obtains compounds with H, alkyl, aryl, allyl, propargyl, alkynyl or heteroaryl groups in place of the phenolic OH. A key step in the sequence is the use of $BiCl_3.H_2O$ to deprotect the intermediate *tert*-butyl esters; the reagent is compatible with the presence of double and triple bonds as well as a furanyl unit. While many of our final products are expected to be available by transition metal catalyzed coupling processes, the present route avoids the

Table 4 Formation of alkylated aromatics. $NaBH_4$-$CeCl_3.7H_2O$, or appropriate Grignard reagent or organolithium were used to generate the secondary or tertiary alcohols. Rearomatization was effected with 1 equiv of $BiCl_3.H_2O$. Yields for rearomatization refer to two steps from the ketone



sometimes awkward synthesis of haloaromatics that would be required in order to apply such procedures.

Experimental

Experimental procedures not described below or in the Electronic Supplementary Information† are given in the supporting information for the preliminary communication.[9]

General procedure for reductive alkylation[7]

The apparatus consists of a three-necked round-bottomed flask fitted with a cold finger condenser fused onto one of the necks and containing a magnetic stirring bar. The exit of the condenser carried a drying tube filled $CaSO_4$. An external mark on the flask indicated the level corresponding to the desired volume of liquid ammonia. The central neck was closed by a septum carrying a nitrogen inlet. The flask was cooled in a dry ice-acetone bath and the cold finger condenser was charged with dry ice-acetone. Another round-bottomed flask was half-filled with liquid ammonia and several small pieces of Na were added, so as to form a permanently blue solution. This flask was connected *via* bent adaptors and dry Tygon tubing to the third neck of the other flask. A solution of the starting aromatic ester in a mixture of dry THF and *t*-BuOH (1–1.1 mole per mole ester) was injected into the three-necked flask, and liquid ammonia was condensed into the flask. Small pieces of Li wire (2–2.5 g-atom per mole ester) were added rapidly to the vigorously stirred solution, and stirring at −78 °C was continued for 10–15 min, to ensure that the dark blue color persisted. A solution of the alkyl halide in THF was then added dropwise from a syringe over *ca.* 2 min, and the resulting yellow solution was stirred for 1 h at −78 °C. Then the cooling bath was removed and the NH_3 was evaporated under a stream of N_2 (2–3 h). Water was added and the mixture was extracted with Et_2O (4 times). The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel gave the product.

General procedure A for oxidation[10]

A stirred solution of CrO_3 and Ac_2O in AcOH was cooled to 7 °C and diluted with dry PhH. A solution of the reductive alkylation product in PhH was added dropwise and stirring was continued for 1–3 h (TLC control) at 7 °C. The mixture was diluted with EtOAc and quenched carefully with saturated aqueous $NaHCO_3$, washed with water and brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel gave the cross-conjugated ketone as an oil.

General procedure B for oxidation[7,11]

3,5-Dimethylpyrazole was added in one portion to a stirred and cooled (−20 °C) suspension of dry CrO_3 in CH_2Cl_2. Stirring at −20 °C was continued for 10–20 min, and a solution of the reductive alkylation product in CH_2Cl_2 was then added at a fast dropwise rate. Stirring at −20 °C was continued for 30 min (TLC control). The mixture was transferred to an ice bath and aqueous NaOH (5 M) was added. Stirring at 0 °C was continued for 1 h, and the mixture was then partitioned between Et_2O and water. The aqueous phase was extracted with Et_2O and the combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel gave the cross-conjugated ketone as an oil.

General procedure for Finkelstein displacement

Acetone (distilled from $KMnO_4$ and dried over 4 Å molecular sieves) was added to a mixture of the bromide and anhydrous NaI. The mixture was stirred and refluxed for 16–20 h, cooled and partitioned between Et_2O and water. The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel gave the iodide as an oil.

General procedure A for radical cyclization

A solution of Bu_3SnH and AIBN in dry PhH was added over 5 h by syringe pump to a stirred and heated (85 °C) solution of the iodide in PhH. Heating was continued for several hours after the addition. Evaporation of the solvent and flash chromatography of the residue over KF-flash chromatography silica gel (10%w/w KF) afforded the cyclized product as an oil.

General procedure B for radical cyclization

Method A was followed, except that THF was used as the solvent.

General procedure for Saegusa oxidation[15]

2,6-Lutidine was added to a stirred and cooled (0 °C) solution of the enone in dry CH_2Cl_2. Neat $Me_3SiOSO_2CF_3$ was then added dropwise over 1 h. After the addition, stirring at 0 °C was continued for 1 h and then the mixture was quenched by addition of saturated aqueous $NaHCO_3$. The mixture was diluted with CH_2Cl_2 and the organic phase was dried ($MgSO_4$) and evaporated, first under waterpump vacuum and then under oilpump vacuum until all lutidine had been removed. The resulting enol silane was used directly without purification. Dry MeCN was added, followed by $Pd(OAc)_2$, and the mixture was stirred overnight (Ar atmosphere) and then filtered through a pad of Celite, using CH_2Cl_2. Evaporation of the filtrate and flash chromatography of the residue over silica gel gave the dienone.

General procedure A for rearomatization

$BiCl_3.H_2O$[17] was added to a solution of the dienone in a mixture of MeCN and water, and the mixture was stirred at 65–70 °C. An additional equal portion of $BiCl_3.H_2O$ was added after 1 h, and stirring at 65–70 °C was continued until the reaction was complete (TLC control). Solid $NaHCO_3$ was added and mixture was stirred at room temperature for 10 min, and then filtered through a pad of Celite, using CH_2Cl_2 as a rinse. The filtrate was washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel gave the aromatized product.

General procedure B for rearomatization

Method A was followed, except that 1 equiv of $BiCl_3.H_2O$ was added at the beginning of the reaction, and no further additions were made.

6-Hydroxy-6-phenyl-1,2,3,6-tetrahydroindene-3a-carboxylic acid *tert*-butyl ester (10o). PhMgCl (2 M in THF, 0.22 mL, 0.44 mmol) was added at a fast dropwise rate to a stirred and cooled (−78 °C) solution of **10e** (51 mg, 0.22 mmol) in Et_2O (5 mL). The cold bath was removed and stirring was continued for 1 h. The mixture was cooled to 0 °C, quenched by dropwise addition of saturated aqueous NH_4Cl, and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. The crude product (**10o**) was used directly in the next step.

5-Phenylindan (10p)[18]. General procedure B for rearomatization was followed, using $BiCl_3.H_2O$ (73 mg, 0.218 mmol), **10o** (total product from the previous step) in MeCN (5 mL) and water (0.1 mL), and an overnight reaction period. Flash chromatography of the crude product over silica gel, using hexane, gave **10p** (36 mg, 85%) as an oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.16 (apparent quintet, $J = 7.4$ Hz, 2 H), 2.89 (two overlapping apparent q, $J = 7.6$ Hz, 4 H), 7.34–7.63 (m, 8 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.6 (t), 32.6 (t), 32.9 (t), 123.2 (d), 124.6 (d), 125.2 (d), 126.8 (d), 127.2 (d), 128.7 (d), 139.5 (s), 141.8 (d), 143.4 (s), 144.9 (s); ν_{max} (microscope, $CDCl_3$ cast; cm^{-1}) 3058, 3030, 2950, 2842, 1599, 1480; exact mass m/z calcd for $C_{15}H_{14}$ 194.10956, found 194.10907.

7-Hydroxy-7-methyl-1,3,4,7-tetrahydro-2*H*-naphthalene-4a-carboxylic acid *tert*-butyl ester (11g). MeMgBr (3 M in THF, 0.20 mL, 0.60 mmol) was added at a fast dropwise rate to a stirred and cooled (−78 °C) solution of **11e** (100 mg, 0.40 mmol) in Et_2O (5 mL). The cold bath was removed and stirring was continued for 2 h. The mixture was cooled to 0 °C, quenched slowly with water, and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. The crude product (**11g**) was used directly in the next step.

6-Methyl-1,2,3,4-tetrahydronaphthalene (11h)[19]. General procedure B for rearomatization was followed, using $BiCl_3.H_2O$ (116.8 mg, 0.35 mmol), **11g** (total product from the previous step) in MeCN (5 mL) and water (0.1 mL), and a reaction time of 9 h. Flash chromatography of the crude product over silica gel (1.5 × 15 cm), using hexane, gave **11h** (38 mg, 74%) as an oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.78–1.83 (m, 4 H), 2.30 (s, 3 H), 2.73–2.77 (m, 4 H), 6.91 (s, 1 H), 6.94–6.97 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.8 (q), 23.2 (t), 23.3 (t), 28.9 (t), 29.3 (t), 126.1 (d), 128.9 (d), 129.6 (d), 133.9 (s), 134.7 (s), 136.8 (s); ν_{max} ($CHCl_3$ cast; cm^{-1}) 3000, 2925, 2857, 1505, 1449.

5-Allyl-5-hydroxy-1,2,3,5-tetrahydrocyclopenta[*a*]naphthalene-9b-carboxylic acid *tert*-butyl ester (16k). Allylmagnesium bromide (1 M in Et_2O, 0.24 mL, 0.24 mmol) was added at a fast dropwise rate to a stirred and cooled (−78 °C) solution of **16e** (46 mg, 0.16 mmol) in Et_2O (5 mL). The cold bath was removed and stirring was continued overnight. The mixture was cooled to 0 °C, quenched by dropwise addition of saturated aqueous NH_4Cl, and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. The crude product (**16k**) was used directly in the next step.

5-Allyl-2,3-dihydro-1*H*-cyclopenta[*a*]naphthalene (16l). General procedure B for rearomatization was followed, using $BiCl_3.H_2O$ (53 mg, 0.16 mmol), **16k** (total product from the previous step) in MeCN (5 mL) and water (0.1 mL), and an overnight reaction period. Flash chromatography of the crude product over silica gel, using hexane, gave **16l** (20 mg, 60%) as an oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.25 (apparent quintet, $J = 7.4$ Hz, 2 H), 3.11 (t, $J = 7.6$ Hz, 2 H), 3.27 (t, $J = 7.6$ Hz, 2 H), 3.84 (d, $J = 6.4$ Hz, 2 H), 5.10 (t, $J = 1.6$ Hz, 1 H), 5.12–5.15 (m, 1 H), 6.09–6.19 (m, 1 H), 7.30 (s, 1 H), 7.44–8.05 (m, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.5 (t), 31.2 (t), 33.9 (t), 37.5 (t), 115.9 (t), 123.8 (d), 124.6 (d), 124.7 (d), 125.0 (d), 125.5 (d), 130.8 (s), 130.9 (s), 134.7 (s), 137.4 (d), 138.1 (s), 140.7 (s); ν_{max} (microscope, $CDCl_3$ cast; cm^{-1}) 3074, 2950, 2844, 1638, 1439; exact mass m/z calcd for $C_{16}H_{16}$ 208.12520, found 208.12512.

5-Furan-2-yl-5-hydroxy-1,2,3,5-tetrahydrocyclopenta[*a*]naphthalene-9b-carboxylic acid tert-butyl ester (16o). *n*-BuLi (1.6 M in hexane, 3.125 mL, 5 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of furan (0.363 mL, 5 mmol) and TMEDA (0.748 mL, 5 mmol) in Et_2O (1.8 mL). The cooling bath was replaced by an ice bath and stirring was continued for 45 min. The resulting furanyllithium (0.46 mL) was taken up into a syringe and added at a fast dropwise rate to a stirred and cooled (−78 °C) solution of **16e** (65 mg, 0.23 mmol) in Et_2O (5 mL). The cold bath was replaced by an ice bath and stirring was continued overnight. The mixture was cooled to 0 °C, quenched by dropwise addition of saturated aqueous NH_4Cl, and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. The crude product (**16o**) was used directly in the next step.

2-(2,3-Dihydro-1*H*-cyclopenta[*a*]naphthalen-5-yl)furan (16p). General procedure B for rearomatization was followed, using $BiCl_3.H_2O$ (77 mg, 0.23 mmol), **16o** (total product from previous step) in MeCN (5 mL) and water (0.1 mL), and an overnight reaction period. Flash chromatography of the crude product over silica gel, using hexane, gave **16p** (37 mg, 69%) as an oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.29 (apparent quintet, $J = 7.5$ Hz, 2 H), 3.15 (t, $J = 7.8$ Hz, 2 H), 3.30 (t, $J = 7.8$ Hz, 2 H), 6.57–6.59 (m, 1 H), 6.66–6.67 (m, 1 H), 7.47–8.38 (m, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.4 (t), 31.3 (t), 33.7 (t), 108.6 (d), 111.1 (d), 123.6 (d), 124.7 (d), 125.2 (d), 125.8 (d), 126.1 (d), 127.3 (s), 129.6 (s), 130.7 (s), 140.2(s), 140.4 (s), 142.0 (s), 153.4 (s); ν_{max} (microscope, $CDCl_3$ cast; cm^{-1}) 3063, 2952, 2844, 1579, 1514, 1498, 1457; exact mass m/z calcd for $C_{17}H_{14}O$ 234.10446, found 234.10441.

1-(4-Bromobutyl)-1,4-dihydronaphthalene-1-carboxylic acid *tert*-butyl ester (17). The general procedure for reductive alkylation was followed, using **16** (1.79 g, 7.85 mmol) in dry THF (20 mL), *t*-BuOH (0.83 mL, 8.70 mmol), liquid NH_3 (70 mL), Li (0.12 g, 16.60 mmol), and 1,4-dibromobutane (2.40 mL, 19.80 mmol) in THF (20 mL). Flash chromatography of the crude product over silica gel (4 × 38 cm), using first hexane and then 1 : 9 EtOAc-hexane, gave **17** (2.56 g, 90%) as an oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.97–1.02 (m, 1 H), 1.31–1.33 (m, 1 H), 1.36 (s, 9 H), 1.75–1.83 (m, 2 H), 1.90–1.96 (m, 1 H), 2.09–2.16 (m, 1 H), 3.28–3.33 (m, 2 H), 3.40–3.44 (m, 2 H), 5.70 (ddd, $J = 10.1$, 2.2, 2.2 Hz, 1 H), 6.10 (ddd, $J = 10.1$, 3.7, 3.7 Hz, 1 H), 7.14–7.17 (m, 3 H), 7.20–7.32 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.0 (t), 27.7 (q), 29.7 (t), 33.0 (t), 33.3 (t), 38.1 (t), 51.6 (s), 80.7 (s), 125.7 (d), 126.1 (d), 126.3 (d), 126.4 (d), 128.2 (d), 128.4 (d), 134.1 (s), 135.5 (s), 173.7 (s); ν_{max} (CH_2Cl_2 cast; cm^{-1}) 2977, 2933, 1722,

1454, 1367, 1246; exact mass m/z calcd for $C_{19}H_{25}{}^{79}BrNaO_2$ (M + Na) 387.09301, found 387.09299.

1-(4-Bromobutyl)-4-oxo-1,4-dihydronaphthalene-1-carboxylic acid *tert*-butyl ester (17a). General procedure A for oxidation was followed, using CrO_3 (3.48 g, 34.80 mmol), Ac_2O (6.10 mL), AcOH (10.0 mL), PhH (10 mL), **17** (2.54 g, 6.96 mmol) in PhH (30 mL), and a reaction time of 3 h. Flash chromatography of the crude product over silica gel (4 × 36 cm), using first hexane and then EtOAc-hexane mixtures up to 3 : 7 EtOAc-hexane, gave **17a** (1.98 mg, 75%) as an oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.82–0.88 (m, 1 H), 1.22–1.25 (m, 1 H), 1.30 (s, 9 H), 1.68–1.70 (m, 2 H), 2.15 (ddd, J = 13.6, 12.2, 4.6 Hz, 1 H), 2.30 (ddd, J = 13.6, 12.3, 4.9 Hz, 1 H), 3.20–3.28 (m, 2 H), 6.56 (d, J = 10.3 Hz, 1 H), 6.92 (d, J = 10.3 Hz, 1 H), 7.41–7.46 (m, 1 H), 7.51–7.60 (m, 2 H), 8.16 (ddd, J = 7.9, 1.5, 0.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.6 (t), 27.7 (q), 32.6 (t), 32.8 (t), 37.7 (t), 53.5 (s), 82.5 (s), 126.2 (d), 126.7 (d), 127.7 (d), 129.6 (d), 131.8 (s), 132.6 (d), 141.7 (s), 148.2 (d), 170.2 (s), 184.4 (s); ν_{max} (CH_2Cl_2 cast; cm^{-1}) 2977, 2933, 1729, 1667, 1456, 1244; exact mass m/z calcd for $C_{19}H_{23}{}^{79}BrNaO_3$ (M + Na) 401.07228, found 401.07211.

1-(4-Iodobutyl)-4-oxo-1,4-dihydronaphthalene-1-carboxylic acid *tert*-butyl ester (17b). The general procedure for Finkelstein displacement was followed, using acetone (25 mL), **17a** (1.81 g, 4.75 mmol), anhydrous NaI (2.49 g, 16.6 mmol), and a reaction time of 17 h. Flash chromatography of the crude product over silica gel (2 × 20 cm), using 10% EtOAc-hexane, gave **17b** (1.86 g, 92%) as an oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81–0.83 (m, 1 H), 1.15–1.20 (m, 1 H), 1.31 (s, 9 H), 1.70–1.75 (m, 2 H), 2.14–2.18 (m, 1 H), 2.25–2.30 (m, 1 H), 3.00–3.05 (m, 2 H), 6.57 (d, J = 11.3 Hz, 1 H), 6.94 (d, J = 11.3 Hz, 1 H), 7.42–7.47 (m, 1 H), 7.52–7.60 (m, 2 H), 8.19 (d, J = 7.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 5.6 (t), 24.7 (t), 27.5 (q), 33.2 (t), 37.3 (t), 53.4 (s), 82.4 (s), 126.3 (d), 126.7 (d), 127.7 (d), 129.6 (d), 131.8 (s), 132.7 (d), 141.7 (s), 148.2 (d), 170.2 (s), 184.4 (s); ν_{max} (CH_2Cl_2 cast; cm^{-1}) 2925, 2853, 1727, 1665, 1600, 1242; exact mass m/z calcd for $C_{19}H_{23}INaO_3$ (M + Na) 449.05842, found 449.05835.

9-Oxo-1,3,4,9,10,10a-hexahydro-2*H*-phenanthrene-4a-carboxylic acid *tert*-butyl ester (17c). The general procedure for radical cyclization was followed, using Bu_3SnH (0.21 mL, 0.77 mmol) and AIBN (10.6 mg, 0.06 mmol) in PhH (5 mL), and **17b** (275 mg, 0.65 mmol) in PhH (10 mL). Heating was continued for 12 h after the addition. Flash chromatography of the crude product over KF-flash chromatography silica gel (10%$^w/_w$ KF) (1.5 × 17 cm), using EtOAc-hexane mixtures, gave **17c** (126 mg, 65%) as an oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.24–1.34 (m, 1 H), 1.36 (s, 9 H), 1.39–1.43 (m, 2 H), 1.57–1.61 (m, 3 H), 2.01–2.04 (m, 1 H), 2.22–2.30 (m, 1 H), 2.61 (dd, J = 18.2, 7.9 Hz, 1 H), 2.77–2.81 (m, 2 H), 7.34 (ddd, J = 7.8, 7.2, 1.2 Hz, 1 H), 7.39–7.41 (m, 1 H), 7.53 (ddd, J = 7.9, 7.2, 1.5 Hz, 1 H), 7.81 (ddd, J = 7.9, 1.5, 0.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.8 (t), 23.1 (t), 27.8 (q), 28.5 (t), 33.0 (t), 37.5 (d), 41.7 (t), 51.4 (s), 81.3 (s), 127.0 (d), 127.1 (d), 127.6 (d), 131.9 (s), 133.7 (d), 143.4 (s), 173.6 (s), 197.8 (s); ν_{max} (CH_2Cl_2 cast; cm^{-1}) 2934, 2862, 1721, 1692, 1599, 1246; exact mass m/z calcd for $C_{19}H_{24}NaO_3$ (M + Na) 323.16177, found 323.16166.

9-Oxo-1,3,4,9-tetrahydro-2*H*-phenanthrene-4a-carboxylic acid *tert*-butyl ester (17d). The general procedure for Saegusa oxidation was followed, using 2,6-lutidine (0.96 mL, 8.23 mmol), **17c** (705 mg, 2.35 mmol), CH_2Cl_2 (15 mL), $Me_3SiOSO_2CF_3$ (1.3 mL, 7.05 mmol), $Pd(OAc)_2$ (522 mg, 2.33 mmol) and MeCN (10 mL). Flash chromatography of the crude product over silica gel (2.5 × 25 cm), using 10% EtOAc-hexane, gave **17d** (434 mg, 60%) as an oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.28 (s, 9 H), 1.37–1.42 (m, 2 H), 1.81–1.86 (m, 2 H), 2.00–2.60 (m, 1 H), 2.28–2.29 (m, 1 H), 2.60–2.71 (m, 1 H), 2.92–2.97 (m, 1 H), 6.42 (s, 1 H), 7.43–7.59 (m, 1 H), 7.54–7.59 (m, 2 H), 8.21–8.23 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.4 (t), 27.4 (q), 27.7 (t), 35.3 (t), 39.6 (t), 53.9 (s), 81.9 (s), 124.9 (d), 125.5 (d), 126.5 (d), 127.6 (d), 130.3 (s), 132.3 (d), 143.8 (s), 161.8 (s), 169.8 (s), 184.9 (s); ν_{max} (CH_2Cl_2 cast; cm^{-1}) 2935, 2861, 1727, 1663, 1560, 1254; exact mass m/z calcd for $C_{19}H_{22}NaO_3$ (M + Na) 321.14612, found 321.14608.

1,2,3,4-Tetrahydrophenanthren-9-ol (17e)[20]. General procedure B for rearomatization was followed, using $BiCl_3.H_2O$ (386 mg, 1.16 mmol), **17d** (345 mg, 1.16 mmol) in MeCN (5 mL) and water (0.1 mL), and a reaction time of 12 h. Flash chromatography of the crude product over silica gel (1.5 × 15 cm), using 10% EtOAc-hexane, gave **17e** (188 mg, 82%) as an oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.87–1.90 (m, 2 H), 1.97–1.99 (m, 2 H), 2.83 (t, J = 6.1 Hz, 2 H), 3.06 (t, J = 6.3 Hz, 2 H), 5.40 (s, 1 H), 6.52 (s, 1 H), 7.46–7.51 (m, 1 H), 7.52–7.60 (m, 1 H), 7.97 (d, J = 8.4 Hz, 1 H), 8.23 (t, J = 8.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.9 (t), 23.3 (t), 25.2 (t), 30.4 (t), 110.5 (d), 121.8 (d), 122.8 (s), 123.4 (s), 124.1 (d), 125.1 (s), 126.3 (d), 133.6 (s), 134.4 (s), 149.0 (s); ν_{max} ($CDCl_3$ cast; cm^{-1}) 3408, 2929, 2859, 1626, 1599; exact mass m/z calcd for $C_{14}H_{14}O$ 198.10446, found 198.10438.

Acknowledgements

We thank the Natural Sciences and Engineering Research Council of Canada for financial support.

References

1 (*a*) D. L. J. Clive, S. P. Fletcher and D. Liu, *J. Org. Chem.*, 2004, **69**, 3282–3293; (*b*) S. P. Fletcher, D. L. J. Clive, J. Peng and D. A. Wingert, *Org. Lett.*, 2005, **7**, 23–26; (*c*) D. L. J. Clive, J. Peng, S. P. Fletcher, V. E. Ziffle and D. Wingert, *J. Org. Chem.*, 2008, **73**, 2330–2344.

2 For an example of a mechanistically related process involving quinone ketals, see: F. Villar, T. Kolly-Kovac, O. Equey and P. Renaud, *Chem.–Eur. J.*, 2003, **9**, 1566–1577.

3 (*a*) A. Pelter and S. Elgendy, *Tetrahedron Lett.*, 1988, **29**, 677–680; (*b*) A. Pelter, R. S. Ward and A. Abd-El-Ghani, *J. Chem. Soc., Perkin Trans. 1*, 1992, 2249–2251; (*c*) A. McKillop, L. McLaren and R. J. K. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1994, 2047–2048; (*d*) D. M. Goldstein and P. Wipf, *Tetrahedron Lett.*, 1996, **37**, 739–742; (*e*) A. McKillop, L. McLaren, R. J. K. Taylor, R. J. Watson and N. J. Lewis, *J. Chem. Soc., Perkin Trans. 1*, 1996, 1385–1393; (*f*) O. Karam, A. Martin, M.-P. Jouannetaud and J.-C. Jacquesy, *Tetrahedron Lett.*, 1999, **40**, 4183–4186; (*g*) P. Camps, A. González, D. Muñoz-Torrero, M. Simon, A. Zúñiga, M. A. Martins, M. Font-Bardia and X. Solan, *Tetrahedron*, 2000, **56**, 8141–8151; (*h*) R. W. Van De Water, C. Hoarau and T. R. R. Pettus, *Tetrahedron Lett.*, 2003, **44**, 5109–5113; (*i*) Q. Liu and T. Rovis, *J. Am. Chem. Soc.*, 2006, **128**, 2552–2553; (*j*) M. C. Carreño, M. González-López and A. Urbano, *Angew. Chem., Int. Ed.*, 2006, **45**, 2737–2741; (*k*) Oxidation of trimethylsilyl ethers of *para-aryl* phenols gives yields in the range 66–82%: F.-X. Felpin, *Tetrahedron Lett.*, 2007, **48**, 409–412. We found that the triisopropylsilyl ether of *p*-propylphenol did not react with $PhI(OCOCF_3)_2$; (*l*) N. T. Vo, R. D. M. Pace, F. O'Hara and M. J. Gaunt, *J. Am. Chem. Soc.*, 2008, **130**, 404–405.

4 Y. Kita, H. Tohma, K. Kikuchi, M. Inagaki and T. Yakura, *J. Org. Chem.*, 1991, **56**, 435–438.

5 (*a*) S.-I. Murahashi, T. Naota, N. Miyaguchi and S. Noda, *J. Am. Chem. Soc.*, 1996, **118**, 2509–2510; (*b*) M. Ochiai, A. Nakanishi and A. Yamada, *Tetrahedron Lett.*, 1997, **38**, 3927–2930.
6 *Cf.* (*a*) M. D. Bachi, J. W. Epstein, Y. Herzberg-Minzly and H. J. E. Loewenthal, *J. Org. Chem.*, 1969, **34**, 126–135; (*b*) H. Van Bekkum, C. B. Van den Bosch, G. Van Minnen-Pathuis, J. C. De Mos and A. M. Van Wijk, *Recl. Trav. Chim. Pays-Bas*, 1971, **90**, 137–149; (*c*) D. F. Taber, *J. Org. Chem.*, 1976, **41**, 2649–2650; (*d*) A. J. Birch and J. Slobbe, *Aust. J. Chem.*, 1977, **30**, 1045–1049; (*e*) J. M. Hook and L. N. Mander, *J. Org. Chem.*, 1980, **45**, 1722–1724; (*f*) A. G. Schultz, J. P. Dittami, F. P. Lavieri, C. Salowey, P. Sundararaman and M. B. Szymula, *J. Org. Chem.*, 1984, **49**, 4429–4440.
7 A. L. J. Beckwith and D. H. Roberts, *J. Am. Chem. Soc.*, 1986, **108**, 5893–5901.
8 D. L. J. Clive and Minaruzzaman, *Org. Lett.*, 2007, **9**, 5315–5317.
9 Preliminary communication: D. L. J. Clive and R. Sunasee, *Org. Lett.*, 2007, **9**, 2677–2680.
10 A. G. Schultz, F. P. Lavieri, M. Macielag and M. Plummer, *J. Am. Chem. Soc.*, 1987, **109**, 3991–4000.
11 W. G. Salmond, M. A. Barta and J. L. Havens, *J. Org. Chem.*, 1978, **43**, 2057–2059.
12 A. G. Schultz, A. G. Taveras and R. E. Harrington, *Tetrahedron Lett.*, 1988, **29**, 3907–3910.
13 K. U. Ingold, J. Lusztyk and J. C. Scaiano, *J. Am. Chem. Soc.*, 1984, **106**, 343–384.
14 For examples, of radical 7-*exo* trigonal cyclizations, see: (*a*) C. J. Moody and C. L. Norton, *Tetrahedron Lett.*, 1995, **36**, 9051–9052; (*b*) Y. Yuasa, W. Sato and S. Shibuya, *Synth. Commun.*, 1997, **27**, 573–585; (*c*) J. Marco-Contelles and E. de Opazo, *J. Org. Chem.*, 2002, **67**, 3705–3717; (*d*) P. A. Evans and T. Manangan, *Tetrahedron Lett.*, 1997, **38**, 8165–8168; (*e*) A. L. J. Beckwith and G. Moad, *J. Chem. Soc., Chem. Commun.*, 1974, 472–473; (*f*) For attempted 7-*exo* closure, see: J. Marco-Contelles and E. de Opazo, *Tetrahedron Lett.*, 2000, **41**, 5341–5345.
15 *Cf.* A. G. M. Barrett, F. Blaney, A. D. Campbell, D. Hamprecht, T. Meyer, A. J. P. White, D. Witty and D. J. Williams, *J. Org. Chem.*, 2002, **67**, 2735–2750.
16 For decarboxylative aromatization of methyl esters, see: A. G. Schultz, R. E. Harrington, M. Macielag, P. G. Mehta and A. G. Taveras, *J. Org. Chem.*, 1987, **52**, 5482–5484.
17 R. S. Navath, K. B. Pabbisetty and L. Hu, *Tetrahedron Lett.*, 2006, **47**, 389–393.
18 R. L. Hillard III and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, 1977, **99**, 4058–4069.
19 M. Adamczyk, D. S. Watt and D. A. Netzel, *J. Org. Chem.*, 1984, **49**, 4226–4237.
20 R. T. Arnold, J. S. Buckley Jr. and R. M. Dodson, *J. Am. Chem. Soc.*, 1950, **72**, 3153–3155.