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Improved synthesis of 4-phenylphenalenones: the case of isoanigorufone and structural analogs

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ABSTRACT

2-Hydroxy-4-phenyl-1*H*-phenalen-1-one (isoanigorufone, **1**), a phytoalexin exclusive of Musaceae, was synthesized starting from 3-(2-hydroxynaphthalen-1-yl)propanenitrile in nine steps in an overall yield of 10%. Hydrolysis of ethyl 3-(2-phenylnaphthalen-1-yl)propanoate obtained from Suzuki–Miyaura coupling between the parent triflate and phenylboronic acid afforded the corresponding propionic acid which, after Friedel–Crafts acylation and bromine-mediated dehydrogenation, was subjected to Yang–Finnegan epoxidation to furnish **1**. The preparation of analogs using this procedure is also discussed.

Musa acuminata plants (bananas) exposed to chemical or biotic stress accumulate phenylphenalenones, which can be roughly divided into three types: 9-phenylphenalenones, 4-phenylphenalenones, and phenylnaphthalic anhydrides.[1] Similar or even identical compounds have been isolated from Haemodoraceae and Pontederiaceae plants as well; however, 4-phenylphenalenones remain exclusive to *Musa*.[2] Bioassay studies have suggested the involvement of a photooxidation component in the mode of action of phenalenones against *Fusarium oxysporum* and *Mycosphaerella fijiensis*.[3] Interestingly, these and other in vitro experiments have shown that the phenalenone isomer with a substitution at position C-4 is generally more active than corresponding phenalenones without a substitution in this position.[3,4] This fact can be partially rationalized in terms of the superior quantum yield of singlet oxygen production displayed by 4-phenylphenalenones in comparison with their 9-phenyl counterparts.[4a]

In spite of these results, no systematic study has been reported addressing structure–activity relationships among 4-phenylphenalenones, in part because only minute amounts can be isolated from natural sources with a minimum of structural variability.[1] In addition, there is only one report on the synthesis of 4-phenylphenalenones based on 9-phenylphenalenone carbonyl transposition via reduction–oxidation that leads to an isomeric mixture that is difficult to purify.[5] Moreover, the synthesis of 9-heterocyclic phenalenones, which can serve as educts for carbonyl transposition, is of limited success.[4c] Therefore, the development of other versatile and experimentally simpler synthetic routes for 4-phenylphenalenones is desirable.

Previously, we stated the plausibility of synthesizing 4-phenylphenalenones from 4-methoxyperinaphthenone via cross-coupling reactions.[6a] This strategy, however, is not free from pitfalls, as it implies the activation of 4-hydroxyperinaphthenone, a process that can afford a mixture of isomers due to the presence of its 7-hydroxyperinaphthenone tautomer.[6b] Here, we report the synthesis of 2-hydroxy-4-phenyl-1*H*-phenalen-1-one (isoanigorufone, **1**)[7] using a tactical variant in which the phenyl substituent was introduced prior to the formation of the perinaphthenone moiety in order to avoid the problem of tautomerism.

The general features of the isoanigorufone synthesis are outlined retrosynthetically in Scheme 1.

The Hardman[8] synthesis of 3-(2-hydroxynaphthalen-1-yl)propanenitrile (**9**) by means of refluxing acrylonitrile with a basic solution of 2-naphthol in benzene provided, after purification by flash column chromatography, the starting point for the synthesis of **1** in sufficient quantities (40 g) (Scheme 2).[8] Aqueous alkaline hydrolysis of **9**,[9] followed by Fisher esterification with ethanol according to the method of Nudelman, afforded ethyl 3-(2-hydroxynaphthalen-1-yl)propanoate (**7**) in 90% overall yield.[10] The treatment of **7** with trifluoromethanesulfonic anhydride in pyridine generated the corresponding triflate (**6**) in 62% (70% brsm) as a solid that can be chromatographed and set the stage for the cross-coupling reaction.[11] Coupling trimethyl(phenyl)tin and triflate **6**

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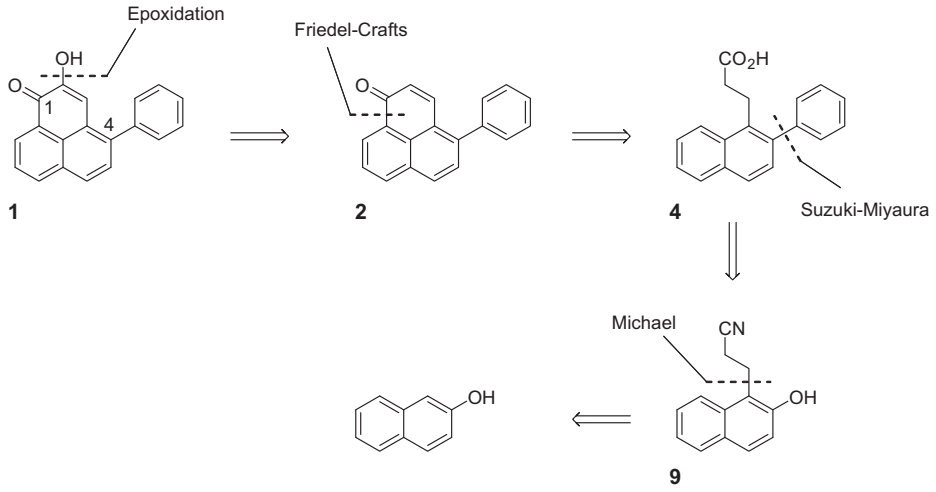
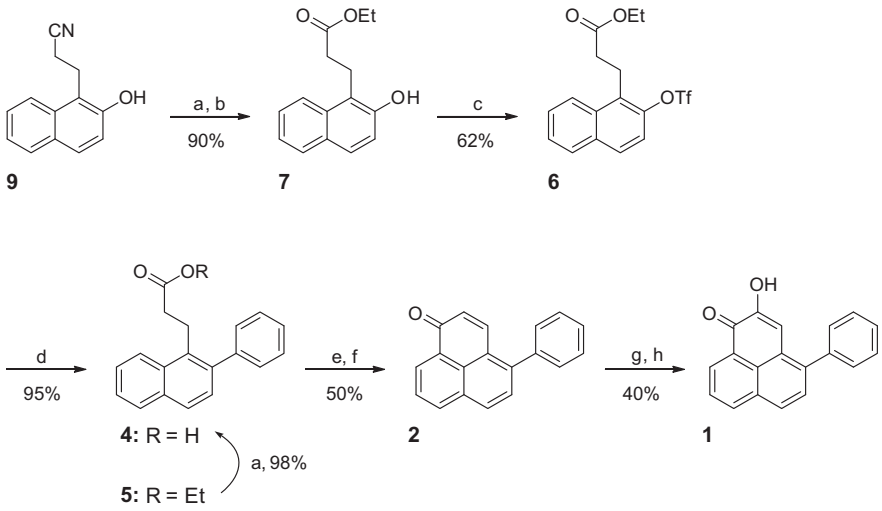


Scheme 1. Retrosynthetic analysis of isoanigorufone (**1**).[7]



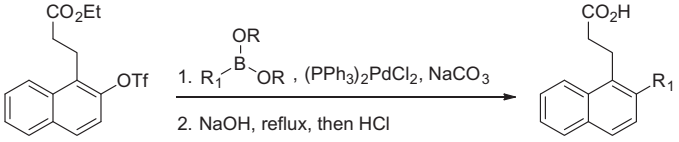
Scheme 2. Reagents and conditions: (a) NaOH 30%, 5 h reflux, then HCl until pH ~1; (b) EtOH, CH_3COCl (25 mol %), 4 h reflux; (c) Tf_2O (1.5 equiv), pyridine, 0 °C, 30 min, then 25 °C, 2.5 h; (d) $(PPh_3)_2PdCl_2$ (5 mol %), $PhB(OH)_2$ (1.5 equiv), $Na_2CO_{3(aq)}$ (2 M), dioxane, 22 h reflux; (e) $SOCl_2$, 30 °C until dryness, then CH_2Cl_2, $AlCl_3$ (3 equiv) 10 min; (f) NBS (1.2 equiv), CCl_4, 3 h reflux under irradiation (170 W UHE lamp, 1800 lumens); (g) *t*-BuOOH (80%), triton B, benzene, 0 °C, 5 min, then 25 °C, 18 h; (h) *p*-TSA, CH_2Cl_2, 25 °C, 1 h.

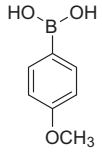
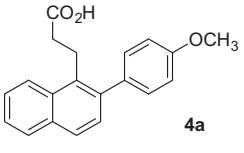
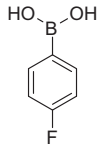
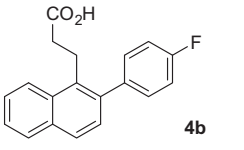
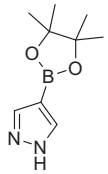
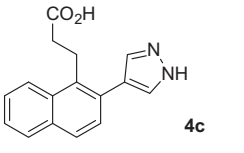
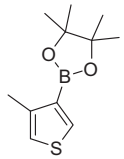
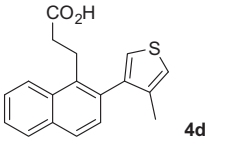
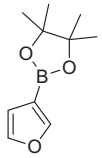
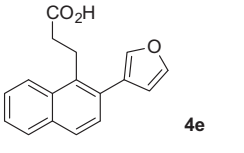
by means of the Stille reaction under a slight modification of Papadopoulos conditions proved successful after 20 h reflux (50% isolated yield).[12] However, superior yields were achieved using the Suzuki–Miyaura coupling under less demanding experimental conditions and without the use of additives.[12] Thus, the reaction of triflate **6** and phenylboronic acid mediated by bis(triphenylphosphine)palladium(II)chloride and Na_2CO_3 in dioxane–water afforded ethyl 3-(2-phenylnaphthalen-1-yl)propanoate (**5**) in a sufficiently pure, gratifying yield of 95% after 22 h reflux for the next step (Scheme 2).[12] Hydrolysis of **5** generated 3-(2-phenylnaphthalen-1-yl)propanoic acid (**4**) (98% yield) of sufficient purity for the anticipated regioselective Friedel–Crafts acylation.[13] Unfortunately, the reaction of **4** with thionyl chloride, followed by treatment with $AlCl_3$ and 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in dichloromethane according to our previously reported one-pot procedure,[6] afforded 4-phenyl-1*H*-phenalen-1-one (**2**) in a disappointing 15% yield after many tedious purification steps. Stepwise execution of this methodology allowed the preparation of 4-phenyl-2,3-dihydro-1*H*-phenalen-1-one (**3**) in 80% yield and identified the DDQ-mediated dehydrogenation as the problematic step.[14] Similar dehydrogenation processes have been performed by means of benzylic bromination–dehydrobromination sequences. Therefore, it was hoped that the combination of *N*-bromosuccinimide (NBS) and white-light catalysis according to the method of Mills could afford the desired 4-phenyl-1*H*-phenalen-1-one (**2**) directly.[15]

Fortunately, this proved to be the case and compound **2** was obtained in 62% yield after flash chromatography. The Yang–Finnegan epoxidation of **2** (Scheme 2) went on to produce the epoxide which was treated with *p*-toluenesulfonic acid to afford 2-hydroxy-4-phenyl-1*H*-phenalen-1-one (isoanigorufone, **1**) in 40% combined yield.[16] The spectroscopic data of **1** were identical with those of the natural compound.[7a]

In order to check the diversification possibilities offered by the synthetic route, steps d–f (Scheme 2) were repeated using five different boronic acid derivatives under the same conditions (Tables 1 and 2). Table 1 illustrates some generality in the Suzuki–Miyaura coupling protocol developed for **1** independent of the electronic nature of the aromatic partner (all yields Y_1 between 88% and 97%). Execution of the Friedel–Crafts reaction on these propanoic

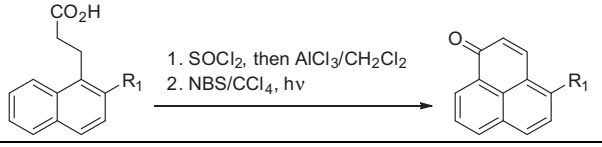
Table 1
Synthesis of 3-(naphthalene-1-yl)propanoic acid analogs using conditions developed for the synthesis of isoanigorufone

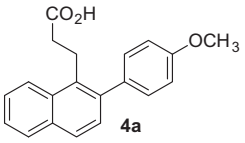
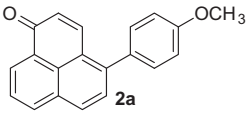
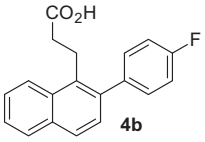
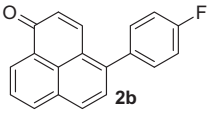
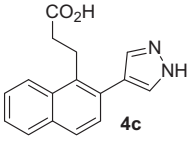
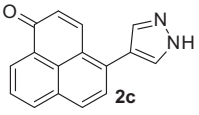
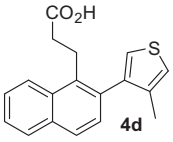
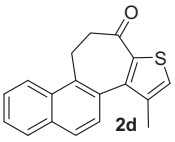
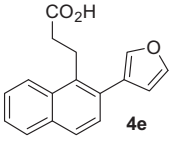
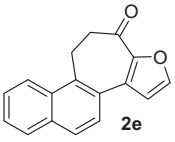


Entry	Boronic acid derivative	Product	Yield (%) Y_1, Y_2
1		 **4a**	97, 97
2		 **4b**	88, 96
3		 **4c**	95, 97
4		 **4d**	94, 80
5		 **4e**	97, 98

Y_1 = yield for step 1.
Y_2 = yield for step 2.
Experimental details can be found in Supplementary data.

Table 2
Synthesis of 4-phenylphenalenone analogs using conditions developed for the synthesis of isoanigorufone



Entry	Educt	Product	Yield (%) Y_1, Y_2
1	 **4a**	 **2a**	94, 43 58[a]
2	 **4b**	 **2b**	97, 56
3	 **4c**	 **2c**	66, 38[a]
4	 **4d**	 **2d**	68[b]
5	 **4e**	 **2e**	72[b]

Y_1 = yield for step 1.
Y_2 = yield for step 2.
NBS = *N*-bromosuccinimide.
[a] NBS/light replaced by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).
[b] Step 2 omitted. Experimental details can be found in Supplementary data.

acid substrates (Table 2) proved to be regioselective with preference for the six-member cyclization mode (Table 2, entries 1–3). However, electron rich five-member heterocycles displayed a tendency for a seven-member ring formation to give the 1,2-dihydro-3*H*-naphtho[2′,1′:3,4]cyclohepta[1,2-*b*]heterocyclic-3-one (Table 2, entries 4 and 5). This rather unexpected result represents the first synthetic entry to this type of nuclei but renders the synthesis unsuitable for the preparation of electron rich five-member heterocyclic analogs. It also shows the important influence the electron-density distribution of the lateral ring can exert on the ring size of the final product. Interestingly, execution of the Friedel–Crafts and DDQ mediated dehydrogenation as a one-pot procedure on substrate **4d** allowed the isolation of 4-(4-methylthiophen-3-yl)-1*H*-phenalen-1-one as a minor compound (4% yield, see Supplementary data). No phenalenone could be detected in the case of educt **4e**. Dehydrogenation of the Friedel–Crafts products using NBS/light (Table 2, entries 1–3) went as expected for the cases of phenyl analogs. However, no dehydrogenation occurred when this procedure was applied to the pyrazole derivative. This situation was partially remediated by the use of DDQ (Table 2, entry 3) albeit in low yield (38%, 44% brsm). Substrates **2d**–**2e** proved recalcitrant to the dehydrogenating conditions employed on the other substrates, probably due to the angular strain that would be introduced.

In conclusion, we have developed an operationally simple nine-step synthesis of 2-hydroxy-4-phenyl-1*H*-phenalen-1-one (isoanigorufone, **1**) starting from 3-(2-hydroxynaphthalen-1-yl)propanenitrile in a 10% global yield using the Suzuki–Miyaura and Friedel–Crafts reactions as key steps. The synthesis can be extrapolated to the preparation of 4-phenylphenalenone analogs with confidence.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.11.118.

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6. (a) Nanclares, J.; Gil, J.; Rojano, B.; Saez, J.; Schneider, B.; Otálvaro, F. *Tetrahedron Lett.* **2008**, *49*, 3844–3847; (b) In fact, triflation of 4-hydroxyperinaphthenone (prepared as described in Ref. 3b) afforded a 60:22:18 mixture of 1,1-dioxo-1*H*,1′*H*-[2,2′-biphenalene]-4,4′-diyl bis(trifluoromethanesulfonate), 1-oxo-1*H*-phenalen-7-yl trifluoromethanesulfonate, and 1-oxo-1*H*-phenalen-4-yl trifluoromethanesulfonate, respectively (for experimental details see Supplementary data).
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8. (a) Hardman, A. F. *J. Am. Chem. Soc.* **1948**, *70*, 2119–2120; (b) Duque, L.; Restrepo, C.; Sáez, J.; Gil, J.; Schneider, B.; Otálvaro, F. *Tetrahedron Lett.* **2010**, *51*, 4640–4643.
9. Hydrolysis of **9** (32 g) was performed according to Ref. 8a using aqueous NaOH (30%, 100 mL, 5 h reflux) to obtain 38 g of crude 3-(2-hydroxynaphthalen-1-yl)propanoic acid (**8**) as a white solid after acidic workup. ^{1}H NMR (C_3D_6O, 500.13 MHz) δ 7.95 (d, J = 8.1 Hz, H-5′), 7.92 (d, J = 8.5 Hz, H-8′), 7.67 (d, J = 8.9 Hz, H-4′), 7.44 (ddd, J = 8.5, 6.9, 1.2 Hz, H-7′), 7.26 (ddd, J = 8.1, 6.9, 1.2 Hz, H-6′), 7.18 (d, J = 8.9 Hz, H-3′), 3.31 (t, J = 7.5 Hz, H-3), 2.66 (t, J = 7.5 Hz, H-2); ^{13}C NMR (C_3D_6O, 125.75 MHz) δ 177.4 C-1), 153.6 (C-2′), 131.7 (C-8a′), 130.0 (C-4a′), 129.3 (C-5′), 128.7 (C-4′), 127.1 (C-7′), 123.3 (C-6′), 123.2 (C-8′), 119.9 (C-1′), 119.7 (C-3′), 35.2 (C-2), 21.3 (C-3). HREIMS: m/z 216.07904 (calcd for $C_{13}H_{12}O_3$, 216.07864).
10. Nudelman, A.; Bechor, Y.; Falb, E.; Fischer, B.; Wexler, B.A.; Nudelman, A. *Synth. Commun.* **1998**, *28*, 471–474. *Experimental procedure*: 3-(2-Hydroxynaphthalen-1-yl)propanoic acid (**8**) (38.0 g, 0.2 mol), dissolved in 200 mL of distilled EtOH (not anhydrous), was treated with 3 mL of acetyl chloride and refluxed. Addition of acetyl chloride (1 mL) was repeated after 2 h and the mixture was kept under reflux for another 2 h. Evaporation of the reaction mixture and purification by column chromatography (CH_2Cl_2) afforded 35 g (90% from **9**) of ethyl 3-(2-hydroxynaphthalen-1-yl)propanoate (**7**) as a yellow oil. ^{1}H NMR (C_3D_6O, 500.13 MHz) δ 7.95 (d, J = 8.1 Hz, H-5′), 7.78 (d, J = 8.5 Hz, H-8′), 7.67 (d, J = 8.9 Hz, H-4′), 7.47 (ddd, J = 8.5, 6.9, 1.2 Hz, H-7′), 7.29 (ddd, J = 8.1, 6.9, 1.2 Hz, H-6′), 7.20 (d, J = 8.9 Hz, H-3′), 4.10 (q, J = 7.1 Hz, –OCH_2CH_3), 3.36 (t, J = 7.7 Hz, H-3), 2.63 (t, J = 7.7 Hz, H-2), 1.19 (t, J = 7.1 Hz, –OCH_2CH_3); ^{13}C NMR (C_3D_6O, 125.75 MHz) δ 174.1 C-1), 153.1 (C-2′), 134.2 (C-8a′), 130.2 (C-4a′), 129.5 (C-5′), 128.9 (C-4′), 127.3 (C-7′), 123.5 (C-6′), 123.3 (C-8′), 119.2 (C-1′), 119.0 (C-3′), 60.9 (–OCH_2CH_3), 34.7 (C-2), 21.2 (C-3), 14.5 (–OCH_2CH_3). HREIMS: m/z 244.10888 (calcd for $C_{15}H_{16}O_3$, 244.10994).
11. *Experimental procedure*: A solution of **7** (12.87 g, 56.4 mmol) in pyridine (10 mL) was cooled to −10 °C and treated with triflic anhydride (18.8 mL, 112.8 mmol, 20 min addition). The reaction mixture was allowed to warm (room temperature) and stirred for an additional 2.5 h. The crude mixture was partitioned between saturated aqueous $CuSO_4$ and ethyl acetate, and the organic fraction was dried (Na_2SO_4), concentrated and submitted to column chromatography (AcOEt–*n*-hexane (1:9)) to give 13.2 g (62%) of ethyl 3-(2-(((trifluoromethyl)sulfonyl)oxy)naphthalene-1-yl)propanoate (**6**) as a white solid. ^{1}H NMR (C_3D_6O, 500.13 MHz) δ 8.25 (d, J = 8.5 Hz, H-8′), 8.05 (d, J = 8.1 Hz, H-5′), 8.02 (d, J = 9.1 Hz, H-4′), 7.72 (ddd, J = 8.3, 6.9, 1.4 Hz, H-7′), 7.65 (ddd, J = 8.1, 6.9, 1.2 Hz, H-6′), 7.50 (d, J = 9.1 Hz, H-3′), 4.11 (q, J = 7.1 Hz, –OCH_2CH_3), 3.53 (t, J = 7.7 Hz, H-3), 2.71 (t, J = 7.7 Hz, H-2), 1.20 (t, J = 7.1 Hz, –OCH_2CH_3); ^{13}C NMR (C_3D_6O, 125.75 MHz) δ 172.3 C-1), 146.0 (C-2′), 134.0 (C-4a′), 133.2 (C-8a′), 130.1 (C-1′), 130.7 (C-4′), 130.0 (C-5′), 128.9 (C-7′), 128.1 (C-6′), 125.4 (C-8′), 120.9 (q, J_{C-F} = 319.3 Hz, –SO_3CF_3), 120.3 (C-3′), 61.1 (–OCH_2CH_3), 34.8 (C-2), 22.3 (C-3), 14.5 (–OCH_2CH_3). HREIMS: m/z 376.06340 (calcd for $C_{16}H_{15}F_3O_6S$, 376.05923).
12. *The Stille reaction was performed as described in* Crisp, G.T.; Papadopoulus, S. *Aust. J. Chem.* **1988**, *41*, 1711–1715, using tris(dibenzylideneacetone) dipalladium instead of bis(dibenzylideneacetone)palladium. *Experimental procedure for the Suzuki–Miyaura reaction*: Compound **6** (3.08 g, 8.0 mmol), phenylboronic acid (1.94 g, 16.0 mmol), and bis(triphenylphosphine) palladium(II)chloride (281 mg, 5 mol %) were dissolved in dioxane (50 mL), mixed with a Na_2CO_3 solution (12 mL, 2 M) and refluxed for 22 h. Liquid partition with AcOEt/H_2O, dryness (Na_2SO_4) and concentration of the organic phase afforded 2.3 g (95%) of ethyl 3-(2-phenylnaphthalen-1-yl)propanoate (**5**). ^{1}H NMR (C_3D_6O, 500.13 MHz) δ 8.16 (d, J = 8.5 Hz, H-8′), 7.95 (d, J = 8.1 Hz, H-5′), 7.82 (d, J = 8.5 Hz, H-4′), 7.61 (ddd, J = 8.5, 6.9, 1.2 Hz, H-7′), 7.55 (ddd, J = 8.1, 6.9, 1.2 Hz, H-6′), 7.37–7.47 (m, H-2″–H-6″), 7.32 (d, J = 8.5 Hz, H-3′), 4.03 (q, J = 7.1 Hz, –OCH_2CH_3), 3.33 (t, J = 7.7 Hz, H-3), 2.73 (t, J = 7.7 Hz, H-2), 1.15 (t, J = 7.1 Hz, –OCH_2CH_3); ^{13}C NMR (C_3D_6O, 125.75 MHz) δ 172.8 C-1), 143.4 (C-1″), 140.6 (C-2′), 134.5 (C-4a′), 134.4 (C-1′), 132.7 (C-8a′), 130.1 (C-2″/6″), 129.8 (C-5′), 129.2 (C-3″/5″), 129.0 (C-3′), 128.0 (C-4″), 127.6 (C-7′), 127.6 (C-4′), 126.5 (C-6′), 125.0 (C-8′), 60.8 (–OCH_2CH_3), 37.0 (C-2), 28.7 (C-3), 14.5 (–OCH_2CH_3). HREIMS: m/z 304.14510 (calcd for $C_{21}H_{20}O_2$, 304.14633).
13. Hydrolysis of **5** (2.3 g, 7.6 mmol) was performed using aqueous NaOH (30%, 50 mL, 5 h reflux) to obtain 2.0 g (98%) of crude 3-(2-phenylnaphthalen-1-yl)propanoic acid (**4**) as a white solid after acidic workup. ^{1}H NMR (C_3D_6O, 500.13 MHz) δ 8.24 (d, J = 8.5 Hz, H-8′), 7.87 (d, J = 8.1 Hz, H-5′), 7.73 (d, J = 8.5 Hz, H-4′), 7.56 (ddd, J = 8.5, 6.9, 1.2 Hz, H-7′), 7.48 (ddd, J = 8.1, 6.9, 1.2 Hz, H-6′), 7.36-7.44 (m, H-2″–H-6″), 7.28 (d, J = 8.5 Hz, H-3′), 3.29 (t, J = 7.7 Hz, H-3), 2.46 (t, J = 7.7 Hz, H-2); ^{13}C NMR (C_3D_6O, 125.75 MHz) δ 181.7 (C-1), 144.2 (C-1″), 140.5 (C-2′), 136.4 (C-1′), 134.8 (C-4a′), 133.2 (C-8a′), 130.4 (C-2″/6″), 129.7 (C-5′), 129.3 (C-3′), 129.3 (C-3″/5″), 127.9 (C-4″), 127.4 (C-4′), 127.1 (C-7′), 126.5 (C-6′), 125.6 (C-8′), 40.4 (C-2), 27.4 (C-3). HREIMS: m/z 276.11528 (calcd for $C_{19}H_{16}O_2$, 276.11503).
14. *Experimental procedure*: Compound **4** (1.4 g, 5.0 mmol) was treated with 1 mL of $SOCl_2$ and the flask was air-dried after gas evolution. This process was repeated four times. The product was dissolved in CH_2Cl_2 (15 mL) and $AlCl_3$ (2.0 g, 15.0 mmol) was added in one portion (the solution turns red). After 10 min, the reaction mixture was dried and immediately submitted to column chromatography using CH_2Cl_2 as eluent to give 1.0 g (80%) of 4-phenyl-2,3-dihydro-1*H*-phenalen-1-one (**3**) as a pale yellow oil. Compound **3** decomposes rapidly upon exposure to open air. ^{1}H NMR (C_3D_6O, 500.13 MHz) δ 8.19 (dd, J = 8.1, 1.1 Hz, H-9), 8.14 (dd, J = 7.2, 1.1 Hz, H-7), 7.92 (d, J = 8.4 Hz, H-6), 7.65 (dd, J = 8.1, 7.2 Hz, H-8), 7.48 (d, J = 8.4 Hz, H-5), 7.42–7.50 (m, H-2″–H-6″), 3.34 (t, J = 6.8 Hz, H-3), 2.81 (t, J = 6.8 Hz, H-2); ^{13}C NMR (C_3D_6O, 125.75 MHz) δ 198.8 C-1), 142.9 (C-1′), 140.8 (C-4), 135.7 (C-9), 134.8 (C-6a), 133.6 (C-9b), 132.1 (C-9a), 132.0 (C-3a), 131.1 (C-2′/6′), 130.6 (C-5), 130.2 (C-3′/5′), 129.1 (C-4′), 128.1 (C-6), 127.4 (C-8), 126.8 (C-7), 39.8 (C-2), 28.3 (C-3). HREIMS: m/z 258.10515 (calcd for $C_{19}H_{14}O$, 258.10447).
15. Mills, F.D. *J. Org. Chem.* **1981**, *46*, 2389–2393. *Experimental procedure*: To a refluxing solution (PYREX® glassware) of compound **3** (450 mg, 1.7 mmol) in CCl_4 (15 mL) irradiated with an EPSON Powerlite S4 video beam (170 W UHE lamp, 1800 lumens) were added 3 mg of benzoyl peroxide and 100 mg of *N*-bromosuccinimide (NBS). NBS addition was repeated twice over 30 min intervals (1.7 mmol total). The mixture was refluxed for another hour (a change in color to intense yellow was noticed). Evaporation of the solvent and purification by column chromatography (CH_2Cl_2–*n*-hexane (1:1)) afforded 270 mg (62%) of 4-phenyl-1*H*-phenalen-1-one (**2**) as a yellow solid. ^{1}H NMR (C_3D_6O, 500.13 MHz) δ 8.57 (dd, J = 7.5, 1.3 Hz, H-9), 8.39 (dd, J = 8.0, 1.3 Hz, H-7), 8.23 (d, J = 8.5 Hz, H-6), 7.87 (dd, J = 7.9, 7.5 Hz, H-8), 7.83 (d, J = 10.1 Hz, H-3), 7.66 (d, J = 8.5 Hz, H-5), 7.53–7.58 (m, H-2″–H-6″), 6.60 (d, J = 10.1 Hz, H-2); ^{13}C NMR (C_3D_6O, 125.75 MHz) δ 184.9 C-1), 145.7 (C-4), 140.2 (C-3), 140.1 (C-1′), 135.9 (C-7), 132.8 (C-6), 132.8 (C-6a), 131.3 (C-2′/6′), 131.0 (C-9), 130.6 (C-9a), 130.3 (C-5), 129.6 (C-2), 129.5 (C-3′/5′), 129.2 (C-4′), 128.8 (C-9b), 128.0 (C-8), 125.1 (C-3a). HREIMS: m/z 256.08960 (calcd for $C_{19}H_{12}O$, 256.08882).
16. *Experimental procedure*: A solution of compound **2** (68 mg, 0.3 mmol) in benzene (4 mL) was treated with benzyltrimethylammonium hydroxide (40 μL of a 40% triton B solution in MeOH) and *t*-BuOOH (40 μL of an 80% solution in water) at 0 °C. The mixture was allowed to warm to room temperature, after which the same addition of triton B and *t*-BuOOH was repeated twice at intervals of 50 min and the reaction was stirred for additional 2 h. The crude mixture was submitted to flash column chromatography (CH_2Cl_2–*n*-hexane (1:4)). This last step was found to ameliorate complications in the purification of isoanigorufone (**1**) if the epoxide was treated in the same flask with *p*-toluenesulfonic acid (*p*-TSA). 1-Phenyl-7a,8a-dihydro-7*H*-phenaleno[1,2-*b*]oxiren-7-one: ^{1}H NMR (C_3D_6O, 500.13 MHz) δ 8.40 (dd, J = 7.3, 1.2 Hz, H-6), 8.37 (dd, J = 8.2, 1.2 Hz, H-4), 8.17 (d, J = 8.5 Hz, H-3), 7.79 (dd, J = 8.2, 7.3 Hz, H-5), 7.66 (d, J = 8.5 Hz, H-2), 7.53–7.64 (m, H-2″–H-6″), 4.61 (d, J = 3.9 Hz, H-7a), 4.05 (d, J = 3.9 Hz, H-8a); ^{13}C NMR (C_3D_6O, 125.75 MHz) δ 193.4 C-7), 145.7 (C-1), 141.1 (C-1′), 137.0 (C-4), 134.5 (C-3a), 131.8 (C-2′/6′), 131.4 (C-3), 131.3 (C-8c), 130.7 (C-2), 130.5 (C-3′/5′), 130.1 (C-6), 129.9 (C-4′), 129.0 (C-6a), 128.3 (C-5), 126.2 (C-8b), 58.6 (C-8a), 56.7 (C-7a). HREIMS: m/z 272.08198 (calcd for $C_{19}H_{12}O_2$, 272.08373). The purified product (epoxide) was dissolved in CH_2Cl_2 (10 mL) and treated with *p*-TSA (5 mg) under stirring (30 min) at room temperature to give 33 mg (40% from **2**) of 2-hydroxy-4-phenyl-1*H*-phenalen-1-one (isoanigorufone, **1**). HREIMS: m/z 272.08308 (calcd for $C_{19}H_{12}O_2$, 272.08373). Other spectroscopic data were identical with those of the natural compound.[7a]