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Intramolecular Heck reaction strategy for the synthesis of functionalised tetrahydroanthracenes: a facile formal total synthesis of the linear abietane diterpene, umbrosone

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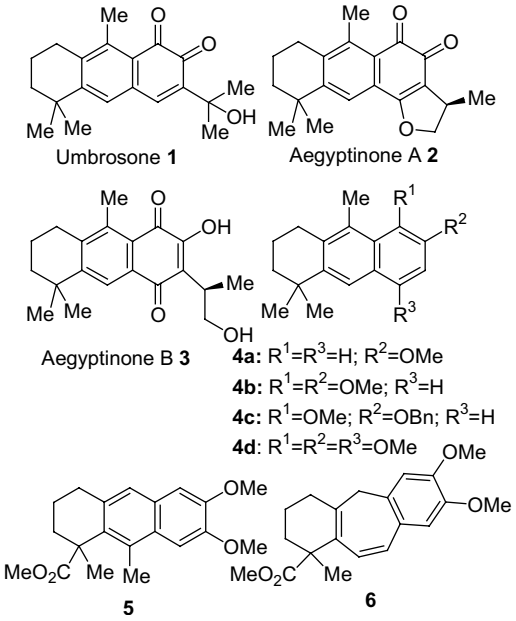
Abstract—Rapid annulation employing an intramolecular Heck reaction yielded the functionalised 1,1,10-trimethyl-6-methoxy-1,2,3,4-tetrahydroanthracene **4a**, a key intermediate for the linear diterpenoid quinone umbrosone (**1**), and the related compounds **4b–d**. A similar strategy was also successfully adopted for the synthesis of the 9-methyl tetrahydroanthracene ester **5** and the tetrahydrodibenzo[*a*,*d*]cycloheptene ester **6**.

The unusual rearranged linear abietane diterpenoid *o*-quinone umbrosone (**1**), isolated from the roots of *Hyptis umbrosa* Slazm (Lamiaceae) by Monache et al.,[1] shows significant activity against Gram-positive bacteria.[1] Several other new bioactive diterpenoid anthraquinone derivatives such as aegyptinone A (**2**) and aegyptinone B (**3**) were also isolated[2] and characterised from a number of traditional medicinal plants. The first total synthesis of umbrosone, reported by Ghosh and Ghatak,[3] utilised the key intermediate tetrahydroanthracene **4a** and was carried out through a lengthy sequence of classical reactions. The synthesis of aegyptinones A and B was achieved by Danheiser et al.[4] in 1994, based upon a 'new photochemical aromatic annulation'. So far, three other multi-step formal syntheses of **1** have been recorded involving skeletal rearrangements of the ring-C-aromatic diterpenoids (+)-dehyroabietic acid[5a] and (+)-podocarpic acid[5b] as well as through a naphthalene derivative[6] to the established intermediate **4a**.

We describe herein a short and flexible convergent route for the construction of **4a**, the key intermediate[3] for umbrosone, and of a variety of other tetrahydroanthracene analogues **4b–d**. All these products, which incorporate the aryl core structure as well as the appropriate methyl substituents of the natural anthraquinones, were prepared by employing a highly efficient intramolecular Heck reaction.[7] A similar strategy has also been successfully extended for the synthesis of the methyl tetrahydroanthracene **5** and the dibenzo[*a*,*d*]cycloheptene



Keywords: Heck reaction; Tetrahydroanthracene; Umbrosone; Suzuki coupling; 7-*endo* Heck cyclisation; Benzocycloheptadiene.
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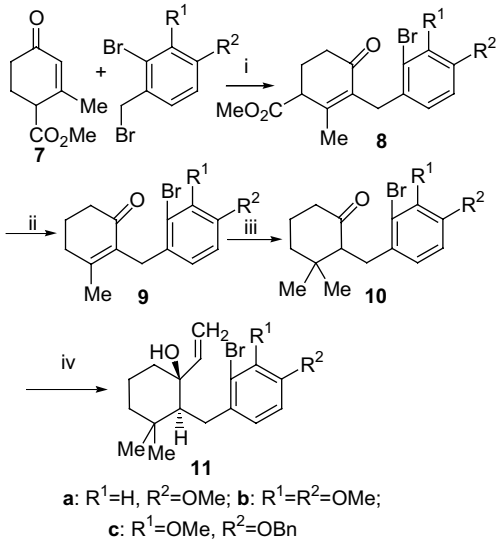
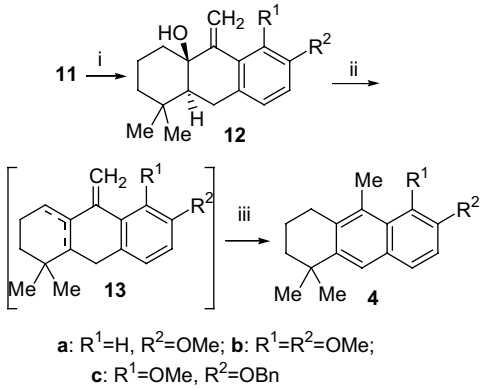
derivative **6** incorporating a *gem*-carboxymethyl–methyl functionality.

The desired vinyl alcohol substrates **11a–c** for the intramolecular Heck reaction were derived from the methyl ester analogue **7**[8] of Hagemann's ester. We initially converted **7** to the 2-(*o*-bromobenzyl)cyclohexanones **10a**[9a] and **10b** by adopting a modification of an established route[9a] recently reported[9b] from this laboratory for **10c**. The ketones **10a–c** were then condensed with vinyl lithium, generated in situ, to give only the corresponding trans diastereoisomers **11a–c**, as assigned by analogy,[10] in excellent yields (Scheme 1).

For the intramolecular Heck reactions of **11a–c**, we attempted several literature procedures; the best results were obtained by using Ma and Ni's method[11] [$Pd(OAc)_2$, K_2CO_3 and PPh_3 in acetonitrile under reflux for ca. 48 h]. The reactions proceeded exclusively in the 6-*exo*-mode, affording the respective crystalline tricyclic alcohols **12a–c**[12] in excellent yields (Scheme 2). Refluxing the alcohols **12a–c** with *p*-TsOH in toluene gave mixtures of the corresponding dehydration products **13a–c** retaining the *exo*-methylene group, as deduced from the ^1H NMR spectra. While **13a** and **13b** underwent smooth aromatisation to the respective anthracenes **4a** and **4b** in over 85% yields[13] by treatment with an excess of potassium *tert*-butoxide in DMSO[14] at room temperature for 72 h, the *O*-benzyl analogue **13c** gave a mixture of the expected product **4c**[13] with significant amounts of the debenzylated derivative. To our satisfaction, the desired product **4c** could be obtained pure in 70% yield when the reaction was carried out under slightly altered conditions using smaller amounts of potassium *tert*-butoxide for a shorter period (Scheme 2).



Scheme 1. Reagents and conditions: (i) KO^{t}Bu, ^{t}BuOH, NaI, reflux, 6 h, **8a** (88%), **8b** (86%), **8c** (92%); (ii) LiOH, MeOH, H_2O, rt, 24 h, then H^+, **9a** (80%), **9b** (70%), **9c** (64%); (iii) Me_2CuLi (3.5 equiv), $BF_3{\cdot}Et_2O$ (4 equiv), −30 to 0 °C, **10a** (90%), **10b** (87%), **10c** (94%); (iv) tri-*n*-butyl vinyl tin (3.7 equiv), MeLi (1.2 M, 3.5 equiv), −78 °C, 5 h, **11a** (97%), **11b** (84%), **11c** (89%).

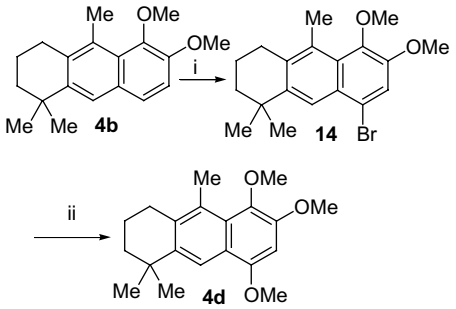


Scheme 2. Reagents and conditions: (i) $Pd(OAc)_2$ (10 mol %), PPh_3 (40 mol %), K_2CO_3 (6 equiv), CH_3CN, reflux, 48 h, **12a** (86%), **12b** (85%), **12c** (84%); (ii) *p*-TsOH, toluene, reflux, 4 h; (iii) for **13a** and **13b**: KO^{t}Bu (3 equiv), DMSO, rt, 72 h, **4a** (85%), **4b** (88%); for **13c**: KO^{t}Bu (1 equiv), DMSO, rt, 3 h, 70%.

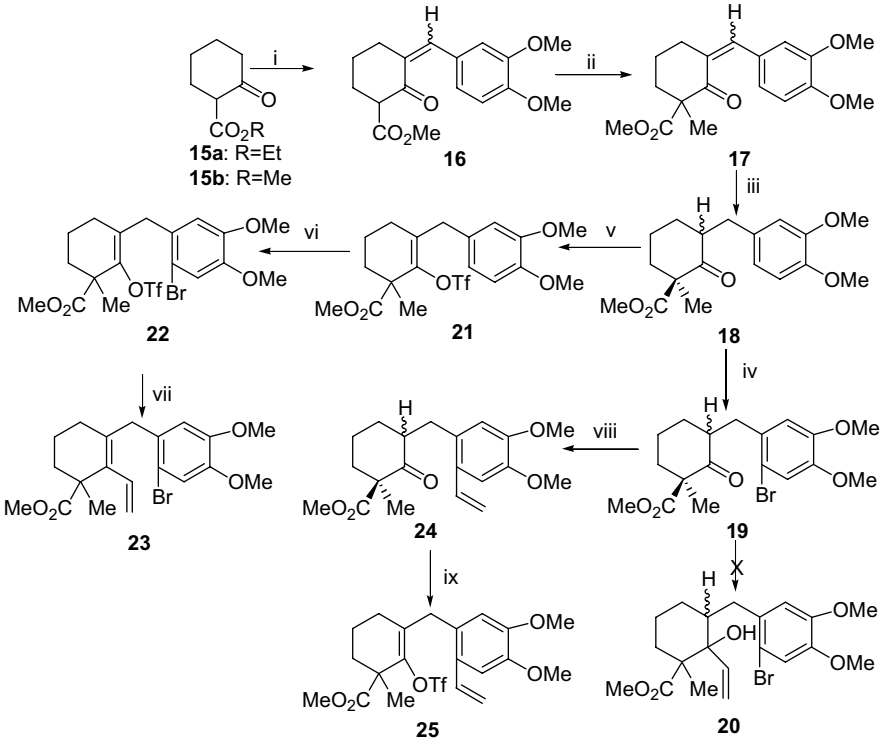
Finally, the trimethoxy derivative **4d** could be smoothly prepared from the dimethoxy anthracene **4b** by selective bromination with NBS in CH_3CN followed by heating the bromo derivative **14** with sodium methoxide in methanol and DMF in the presence of CuI[15] (Scheme 3).

In order to study the feasibility of the intramolecular Heck reaction for the synthesis of functionalised tetrahydroanthracene derivatives carrying other substituents, we decided to attempt it on substrates having *gem*-carboxymethyl–methyl grouping. The 3-(*o*-bromobenzyl)-cyclohexanone carboxylate ester **19** was considered as a suitable substrate for this task (Scheme 4). Towards this objective, ethyl 2-cyclohexanone carboxylate **15a** was treated with veratraldehyde in the presence of DBU[16] in refluxing MeOH to afford only the unsaturated keto methyl ester **16** in moderate yield, obviously arising through transesterification. Repeating the reaction with methyl ester **15b** gave **16** in marginally improved yield. Methylation of **16** with MeI in the presence of K_2CO_3[17] led to the alkylated product **17**, which on catalytic hydrogenation gave the corresponding saturated ketoester **18**.

Bromination of **18** with *N*-bromosuccinimide in acetonitrile afforded the bromoketoester **19** in very good yield.



Scheme 3. Reagents and conditions: (i) NBS (1.1 equiv), CH_3CN, −20 °C, 2 h, 90%; (ii) NaOMe (5 equiv), CuI (3 equiv), DMF, MeOH, reflux, 20 h, 60%.

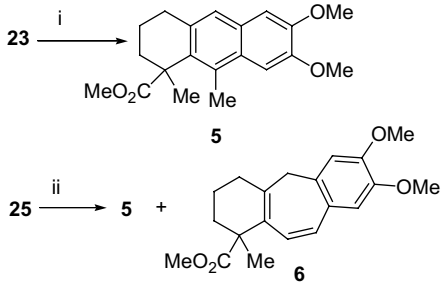


Scheme 4. Reagents and conditions: (i) veratraldehyde (1 equiv), DBU (1.1 equiv), MeOH, reflux, 48 h, (30% from **15a**, 40% from **15b**); (ii) MeI (5 equiv), K_2CO_3 (5 equiv), acetone, reflux, 14 h, 82%; (iii) H_2, Pd/C (10%), MeOH, 24 h, 95%; (iv) NBS (1.1 equiv), CH_3CN, −30 °C, 1.5 h, then rt, 24 h, 85%; (v) LDA (1.35 equiv), *N*-phenyltriflimide (1.2 equiv), THF, −78 to 0 °C, 6 h, then rt, 8 h, 60%; (vi) NBS (1.2 equiv), CH_3CN, −30 °C, 1.5 h, then rt, 24 h, 89%; (vii) $PdCl_2(CH_3CN)_2$ (10 mol %), LiCl (5 equiv), tri-*n*-butylvinyltin (1.2 equiv), DMF, rt, 24 h, 65%; (viii) $Pd(PPh_3)_4$ (10 mol %), K_2CO_3 (1.2 equiv), 2,4,6-trivinylcyclotriboroxane–pyridine complex (1.1 equiv), DME:H_2O (3:1), reflux, 24 h, 70%; (ix) LDA (1.5 equiv), *N*-phenyltriflimide (1.4 equiv), THF, −78 to 0 °C, 6 h, then rt, 8 h, 65%.

Unfortunately, attempted conversion of **19** to the desired vinyl alcohol **20** employing various reaction conditions failed. We therefore, modified the scheme to prepare the bromodiene **23** or a styrenoid enol triflate **25** to be used as substrates for the cyclisation.

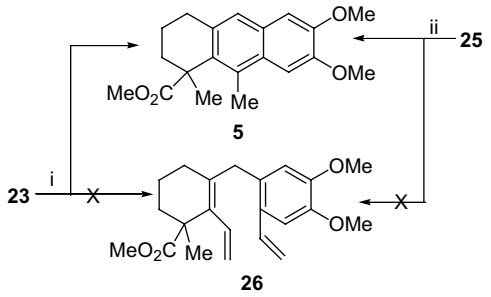
The preparation of the target substrates **23** and **25** from the common intermediate **18** is described in Scheme 4. Treatment of **18** with LDA followed by *N*-phenyltriflimide[18] furnished the enol triflate **21**, which on bromination with *N*-bromosuccinimide in acetonitrile gave the bromo triflate **22** in excellent yield. Selective olefination of the enol triflate **22** with vinyl tin in the presence of $PdCl_2(MeCN)_2$[19] produced the bromodiene **23** in good yield.[20] For the preparation of **25**, the bromoaryl keto-ester **19** was subjected to Suzuki coupling with 2,4,6-trivinylcyclotriboroxane pyridine complex[21] using tetrakis(triphenylphosphine) palladium(0) and K_2CO_3 in DME/water 3:1 under reflux for 24 h to afford the styrene **24** in good yield. The styrene **24** was transformed to the corresponding enol triflate **25**[20] as before (Scheme 4).

The intramolecular Heck reactions of **23** and **25** produced interesting results (Scheme 5). The cyclisation studies were initially carried out with the relatively more stable diene ester **23**. With $Pd(OAc)_2$, K_2CO_3 and PPh_3 in refluxing acetonitrile[11] under the conditions described previously for the vinyl alcohols **11a**–**c**, the bromo diene **23** furnished the fully aromatised 6-*exo* cyclic ester **5** in



Scheme 5. Reagents and conditions: (i) $Pd(OAc)_2$ (10 mol %), PPh_3 (40 mol %), K_2CO_3 (6 equiv), CH_3CN, reflux, 48 h, 86%; (ii) (a) $Pd(OAc)_2$ (10 mol %), Bu_4NH_4Br (2 equiv), NaOAc (6 equiv), DMF, 80 °C, 24 h, **5**:**6**, 88:12 (GLC); (b) $Pd(OAc)_2$ (1 mol %), PPh_3 (1 mol %), DMA:DMF:Et_3N, 7:1:1, 110 °C, 30 min, **5**:**6**, 43:57 (GLC).

excellent yield.[22] The other substrate, the unstable styrenoid ester **25**, gave intractable materials due to decomposition under the same conditions. However, carrying out the reaction under Jeffery's conditions[23] [using $Pd(OAc)_2$, Bu_4NBr, NaOAc in DMF at 80 °C], the 6-*exo* and the rare 7-*endo* products **5** and **6**[22] were obtained from **25** in a ratio of 88:12 (GLC). As functionalised 6-7-6 carbocyclic ring systems such as **6** form the core structures of a number of rearranged diterpenoids having potential bioactivity,[24] we turned our attention to the exploration of more selective 7-*endo* Heck



Scheme 6. Reagents and conditions: (i) tri-*n*-butylvinyltin (2 equiv), $Pd(PPh_3)_4$ (5 mol %), dioxane, reflux, 24 h, 90%; (ii) $PdCl_2(CH_3CN)_2$ (10 mol %), LiCl (5 equiv), tri-*n*-butylvinyltin (1.2 equiv), DMF, rt, 24 h, 80%.

cyclisation conditions, which has very little precedent.[7] Amongst a number of variations studied, the best result was realised by following a modification of the solvent concentration of a recently recorded intermolecular Heck coupling.[25] Thus, treatment of **25** with $Pd(OAc)_2$ and PPh_3 in DMA-DMF at 110 °C in the presence of Et_3N as base produced a mixture of the 6-*exo*- and the 7-*endo* products **5** and **6** in a ratio of 43:57 (GLC). In contrast, the diene ester **23** was mostly recovered unchanged when subjected to the same reaction conditions.

For a more direct synthetic entry to the desired 6-7-6 tricyclic compound **6** as the exclusive or major product through ring closing metathesis (RCM),[26] we focussed our interest on the preparation of the divinyl ester **26** (Scheme 6). Interestingly, an attempted Echaverren and Stille[27] vinylation reaction of **23** in the presence of $Pd(PPh_3)_4$ and tributyl vinyl tin in refluxing dioxane for 24 h, furnished only the Heck cyclisation product **5**, while under the same reaction conditions **25** remained unreacted. Attempted vinylation of styrenoid enol-triflate **25**, under the conditions successfully applied[19] for the conversion of **22** to **23** (cf. Scheme 4), surprisingly led to the tetrahydroanthracene **5** in 80% yield as the sole isolable product.

In summary, a rapid generalised synthesis of substituted tetrahydroanthracene core structures, including the advanced intermediate **4a** for the diterpenoid quinone umbrosone **1**, constituting a formal total synthesis of **1**, has been achieved employing an intramolecular Heck reaction as the key step. Heck reaction of the styrenoid enol triflate ester **24** producing the rare 7-*endo*-product **6** could be of interest in the synthesis of dibenzo-[*a,d*]cycloheptenes as potential intermediates towards the related bioactive 9(10 → 20)-*abeo*-abieta-8,11,13-triene diterpenoids.

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12. Spectral data for the new compounds: **12a**: mp 112 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.96 (3H, s), 1.12 (3H, s), 1.22–1.31 (1H, m), 1.48–1.63 (4H, m), 1.67–1.77 (1H, m), 1.86–1.99 (1H, m), 2.11–2.16 (1H, m), 2.78 (1H, dd, *J* 5.2, 16.5 Hz), 2.93 (1H, dd, *J* 12.2, 16.4 Hz), 3.81 (3H, s), 5.28 (1H, s), 5.49 (1H, s), 6.82 (1H, dd, *J* 2.6, 8.4 Hz), 7.06–7.09 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.19 (CH_2), 22.17 (CH_3), 25.72 (CH_2), 31.70 (CH_3), 33.36 (C), 36.58 (CH_2), 42.01 (CH_2), 48.44 (CH), 55.13 (CH_3), 71.06 (C), 107.35 (CH_2), 109.59 (CH), 114.31 (CH), 129.02 (C), 129.63 (CH), 133.83 (C), 150.87 (C), 157.69 (C); EIMS: *m/z*: 272 (M^+). Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37%, H, 8.88%. Found C, 79.51%, H, 8.97%. Compound **12b**: mp 90 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94 (3H, s), 1.11 (3H, s), 1.14 (1H, br s), 1.21–1.31 (2H, m), 1.49–1.63 (2H, m), 1.72–1.82 (1H, m), 1.87–1.97 (1H, m), 2.01–2.08 (1H, m), 2.77–2.94 (2H, m), 3.69 (3H, s), 3.85 (3H, s), 5.54 (1H, s), 6.08 (1H, s), 6.81 (1H, d, *J* 8.4 Hz), 6.88 (1H, d, *J* 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.20 (CH_2), 21.83 (CH_3), 26.33 (CH_2), 31.49 (CH_3), 33.43 (C), 36.24 (CH_2), 41.93 (CH_2), 48.53 (CH), 55.84 (CH_3), 59.64 (CH_3), 71.91 (C), 111.67 (CH), 112.64 (CH_2), 123.59 (CH), 127.53 (C), 130.52 (C), 147.24 (C), 147.79 (C), 151.07 (C); EIMS: *m/z*: 302 (M^+). Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.46%, H, 8.67%. Found C, 75.31%, H, 8.59%. Compound **12c**: mp 88 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (3H, s), 1.10 (3H, s), 1.16 (1H, br s), 1.17—1.30 (2H, m), 1.49–1.64 (2H, m), 1.73–1.82 (1H, m), 1.91–2.01 (1H, m), 2.04–2.08 (1H, m), 2.79–2.94 (2H, m), 3.74 (3H, s), 5.08, 5.14 (2H, 2 × d, *J* 12.0 Hz), 5.54 (1H, s), 6.09 (1H, s), 6.83 (2H, s), 7.26–7.46 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.39 (CH_2), 21.99 (CH_3), 26.59 (CH_2), 31.66 (CH_3), 33.66 (C), 36.45 (CH_2), 42.10 (CH_2), 48.68 (CH), 60.02 (CH_3), 71.22 (CH_2), 72.22 (C), 112.91 (CH_2), 114.26 (CH), 123.79 (CH), 127.27 (2 × CH), 127.78 (CH), 127.90 (C), 128.50 (2 × CH), 131.34 (C), 137.41 (C), 147.41 (C), 148.72 (C), 150.43 (C); EIMS: *m/z*: 378 (M^+).

Anal. Calcd for $C_{25}H_{30}O_3$: C, 79.33%, H, 7.99%. Found C, 79.58%, H, 7.83%.

13. Spectral data for the new compounds: **4a**: mp 110 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.38 (6H, s), 1.68–1.72 (2H, m), 1.87–1.93 (2H, m), 2.51 (3H, s), 2.90 (2H, t, *J* 6.5 Hz), 3.93 (3H, s), 7.06 (1H, dd, *J* 2.3, 8.9 Hz), 7.23 (1H, d, *J* 2.0 Hz), 7.65 (1H, s and 1H, d, *J* 8.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.44 (CH_3), 19.73 (CH_2), 29.05 (CH_2), 32.51 ($2\times CH_3$), 34.23 (C), 38.77 (CH_2), 55.22 (CH_3), 102.18 (CH), 117.02 (CH), 123.25 (CH), 127.63 (C), 129.46 (C), 129.65 (CH), 131.69 (C), 133.39 (C), 142.38 (C), 157.16 (C); EIMS: *m*/*z*: 254 (M^+). Anal. Calcd for $C_{18}H_{22}O$: C, 84.99%, H, 8.72%. Found C, 84.72%, H, 8.84%. Compound **4b**: mp 99 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.38 (6H, s), 1.67–1.71 (2H, m), 1.86–1.92 (2H, m), 2.81 (3H, s), 2.82–2.88 (2H, m), 3.83 (3H, s), 3.96 (3H, s), 7.19 (1H, d, *J* 8.9 Hz), 7.49 (1H, d, *J* 8.9 Hz), 7.61 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.64 (CH_3), 19.78 (CH_2), 29.19 (CH_2), 32.40 ($2\times CH_3$), 34.13 (C), 38.56 (CH_2), 56.90 (CH_3), 60.86 (CH_3), 113.93 (CH), 123.62 (CH), 124.71 (CH), 126.45 (C), 129.59 (C), 130.14 (C), 134.70 (C), 142.72 (CH), 144.87 (C), 149.37 (C); EIMS: *m*/*z*: 284 (M^+). Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24%, H, 8.51%. Found C, 80.54%, H, 8.35%. Compound **4c**: mp 92 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37 (6H, s), 1.67–1.70 (2H, m), 1.86–1.92 (2H, m), 2.83 (3H, s), 2.83–2.88 (2H, m), 3.88 (3H, s), 5.22 (2H, s), 7.18 (1H, d, *J* 8.9 Hz), 7.31–7.51 (6H, m), 7.61 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.76 (CH_3), 19.84 (CH_2), 29.25 (CH_2), 32.47 ($2\times CH_3$), 34.23 (C), 38.61 (CH_2), 61.06 (CH_3), 72.30 (CH_2), 116.44 (CH), 123.70 (CH), 124.69 (CH), 126.64 (C), 127.46 ($2\times CH$), 127.77 (CH), 128.47 ($2\times CH$), 130.08 (C), 130.46 (C), 134.79 (C), 137.68 (C), 143.11 (C), 146.06 (C), 148.61 (C); EIMS: *m*/*z*: 360 (M^+). Anal. Calcd for $C_{25}H_{28}O_2$: C, 83.29%, H, 7.83%. Found C, 83.07%, H, 7.98%. Compound **4d**: mp 146 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.39 (6H, s), 1.66–1.70 (2H, m), 1.86–1.94 (2H, m), 2.79 (3H, s), 2.82–2.86 (2H, m), 3.76 (3H, s), 3.97 (6H, s), 6.57 (1H, s), 8.09 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.60 (CH_3), 19.83 (CH_2), 29.23 (CH_2), 32.61 ($2\times CH_3$), 34.44 (C), 38.73 (CH_2), 55.68 (CH_3), 57.58 (CH_3), 61.02 (CH_3), 94.67 (CH), 117.17 (CH), 121.28 (C), 126.68 (C), 130.11 (C), 135.54 (C). 139.09 (C), 142.32 (C), 149.05 (C), 152.08 (C); EIMS: *m*/*z*: 314 (M^+). Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40%, H, 8.33%. Found C, 76.11%, H, 8.49%.
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20. Spectral data for the new compounds: **23**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (3H, s), 1.65–1.70 (3H, m), 1.99–2.16 (3H, m), 3.49, 3.59 (2H, $2\times$d, *J* 16 Hz), 3.67 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 4.97–5.10 (2H, m), 6.36 (1H, dd, *J* 12 and 18 Hz), 6.74 (1H, s), 7.02 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.74 (CH_2), 23.89 (CH_3), 30.34 (CH_2), 36.33 (CH_2), 39.19 (CH_2), 45.92 (C), 51.87 (CH_3), 55.85 (CH_3), 56.09 (CH_3), 111.93 (CH), 114.61 (C), 115.29 (CH), 115.77 (CH_2), 131.14 (C), 133.63 (CH), 134.91 (C), 135.22 (C), 147.67 (C), 148.43 (C), 177.92 (C); EIMS: *m*/*z*: 410 (M^+ for Br^{81}), 408 (M^+ for Br^{79}). Anal. Calcd for $C_{20}H_{25}BrO_4$: C, 58.69%, H, 6.16%. Found C, 58.48%, H, 6.25%. Compound **25**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.48 (3H, s), 1.58–1.66 (2H, m), 1.80–1.99 (2H, m), 2.03–2.12 (2H, m), 3.50 (1H, d, *J* 15 Hz), 3.72 (1H, d, *J* 15 Hz), 3.75 (3H, s), 3.88 (3H, s), 3.90 (3H, s), 5.22 (1H, d, *J* 11 Hz), 5.53 (1H, d, *J* 17 Hz), 6.69 (1H, s), 6.80 (1H, dd, *J* 11 and 17 Hz), 6.99 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.32 (CH_2), 22.14 (CH_3), 28.71 (CH_2), 33.57 (CH_2), 37.33 (CH_2), 47.67 (C), 52.29 (CH_3), 55.74 (CH_3), 55.77 (CH_3), 108.45 (CH), 112.09 (CH), 112.89 (CH_2), 126.88 (C), 129.30 (C), 129.49 (C), 132.22 (C), 133.61 (CH), 143.13 (C), 147.83 (C), 148.68 (C), 174.15 (C); EIMS: *m*/*z*: 478 (M^+). Anal. Calcd for $C_{21}H_{25}F_3O_7S$: C, 52.71%, H, 5.27%. Found C, 52.96%, H, 5.40%.
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22. Spectral data for the new compounds: **5**: mp 130 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.62 (3H, s), 1.88–1.99 (3H, m), 2.07–2.11 (1H, m), 2.42 (3H, s), 2.98–3.00 (2H, m), 3.68 (3H, s), 3.97 (3H, s), 3.99 (3H, s), 6.99 (1H, s), 7.17 (1H, s), 7.35 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.26 (CH_3), 19.15 (CH_2), 25.73 (CH_3), 31.60 (CH_2), 38.79 (CH_2), 47.02 (C), 52.27 (CH_3), 55.76 (CH_3), 55.78 (CH_3), 102.95 (CH), 105.90 (CH), 125.07 (CH), 127.74 (C), 127.96 (C), 130.30 (C), 132.76 (C), 134.61 (C), 148.92 (C), 149.22 (C), 180.20 (C); EIMS: *m*/*z*: 328 (M^+). Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15%, H, 7.37%. Found C, 73.43%, H, 7.27%. Compound **6**: mp 138 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (3H, s), 1.42–1.71 (3H, m), 1.97–2.02 (1H, m), 2.34–2.43 (2H, m), 2.90 (2H, s), 3.68 (3H, s), 3.87 (3H, s), 3.90 (3H, s), 6.24 (1H, d, *J* 12 Hz), 6.63 (1H, s), 6.79 (1H, s), 6.88 (1H, d, *J* 12 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.20 (CH_2), 24.84 (CH_3), 31.53 (CH_2), 34.79 (CH_2), 40.66 (CH_2), 46.18 (C), 51.92 (CH_3), 55.89 (CH_3), 55.95 (CH_3), 109.89 (CH), 110.45 (CH), 128.49 (C), 128.98 (CH), 129.60 (C), 130.16 (C), 131.10 (CH), 133.33 (C), 146.94 (C), 149.55 (C), 177.90 (C); EIMS: *m*/*z*: 328 (M^+). Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15%, H, 7.37%. Found C, 73.32%, H, 7.29%.
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