Monatsh Chem (2011) 142:501–506
DOI 10.1007/s00706-011-0480-z

ORIGINAL PAPER

First Lewis acid catalyzed [4+2] cycloaddition reaction of 1,3,3-trimethyl-2-vinyl-1-cyclohexene with chromones: a new entry to analogues of the puupehenone group of marine diterpenoids and kampanols

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Received: 4 August 2010 / Accepted: 24 February 2011 / Published online: 22 March 2011

Abstract A rapid assembly of the tetracyclic core of marine diterpenoids related to puupehenone and kampanols featuring a Lewis acid catalyzed [4+2] cycloaddition reaction of 1,3,3-trimethyl-2-vinyl-1-cyclohexene and chromone dienophiles is described.

Keywords Cycloaddition · Chromones · Lewis acid · Regioselectivity · Stereoselectivity · Terpenoids

Introduction

The Diels-Alder reaction [1] has been extensively applied for the synthesis of a wide variety of natural products. It constitutes one of the most frequently employed synthetic methods for pericyclic 6-electron processes resulting in the highly regio-, diastereo-, and enantioselective construction of polycyclic ring systems of fundamental interest in organic chemistry. In view of the outstanding importance of the method for the preparation of natural products, and hence also of physiologically active molecules, increasing interest has been placed in recent years on the development of $[4\pi + 2\pi]$ cycloadditions.

Diels-Alder reaction of 1,3,3-trimethyl-2-vinyl-1-cyclohexene with dienophiles like dimethyl acetylenedicarboxylate [2–4], unsymmetrical *p*-benzoquinones [5], 2-carbomethoxy-4,4-dimethyl-2-cyclohexenone [6], 1,4-benzoquinone [7], substituted 1,4-benzoquinones [8], 3-[(*E*)-3-(methoxycarbonyl)propenoyl]-1,3-oxazolidin-2-one [9], acetylenedicarbaldehyde [10], (*S*)-3-hydroxy-2-isopropyl-5-*tert*-butylsulfinyl-*p*-benzoquinone [11], and conjugated ketones [12] are reported. There have been very few reports on [4+2] cycloaddition reactions using chromones as dienophiles, and in all these cases an activating functionality like -CHO, -COR, -COOR, -CN, -Ar, etc., at position 3 has been utilized [13–15]. Only one Diels-Alder reaction of 1,3,3-trimethyl-2-vinyl-1-cyclohexene with 6-bromo-3-cyanochromone having an activating group at position 3 is reported in the literature [13]. Lewis acids are known to catalyze Diels-Alder reactions [1, 12, 13].

(+)-Puupehenone (**1**) [16–21], (+)-puupehedione (**2**) [19], (−)-15-oxopuupehenol (**3**) [20], (+)-15-cyanopuupehenone (**4**) [19, 20], (−)-8-epichromazonarol (**5**) [22], (−)-15-cyanopuupehenol (**6**) [20, 23], chloropuupehenone (**7**) [16], and cyclospongiaquinone-1 (**8**) [24] (Fig. 1) are an important group of biologically active marine terpenoids [25]. They are based on a mixed biogenetic origin involving a sesquiterpene unit with a quinol or quinone, and consist of a multiplicity of prenyl units uncommon in terrestrial organisms. They were isolated from sponges and possess a wide range of potent biological properties such as cytotoxic [19, 20], antiviral [19, 20], antimicrobial [16], antifungal [19], immunomodulatory [19, 20], antitumor [18, 26], antimalarial [20], antibiotic [27], antituberculosis [28], antioxidant [29], and insecticidal [30].

The characteristic structural features, namely a tetracyclic framework, four quaternary methyl groups, a benzopyran ring, a trimethyl cyclohexane moiety, four stereogenic centers at AB and BC ring junctions having *trans*- and *cis*- configurations, respectively, and an additional chiral center at C-15 of ring C are present in puupehenones and kampanols. These tetracyclic diterpenes and their biological activities encouraged chemists to develop methods for their synthesis. Kampanols A–C

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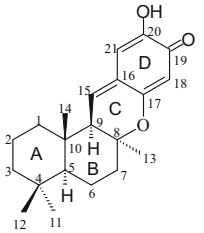
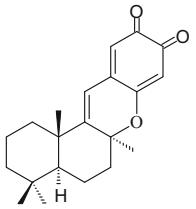
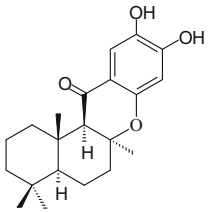
Fig. 1 Puupehenone group of marine diterpenoids (**1–8**) and kampanols (**9–11**)



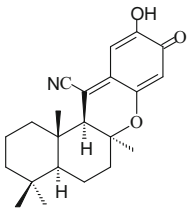
(+)-Puupehenone **1**



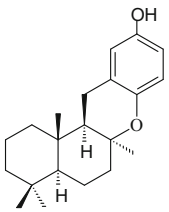
(+)-Puupehedione **2**



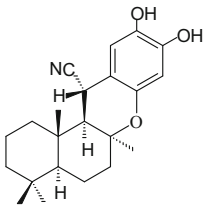
(-)-15-Oxopuupehenol **3**



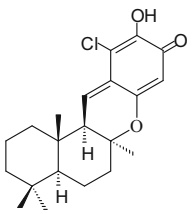
(+)-15-Cyanopuupehenone **4**



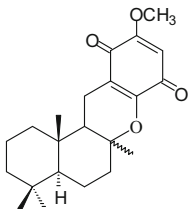
(-)-8-Epichromazonarol **5**



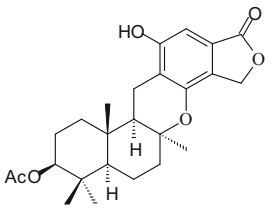
(-)-15-Cyanopuupehenol **6**



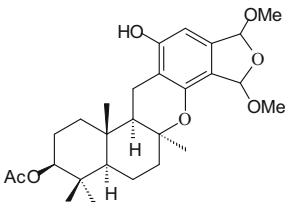
Chloropuupehenone **7**



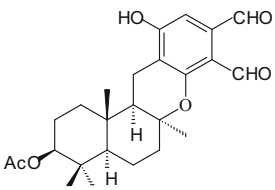
Cyclospongiaquinone-1 **8**



Kampanol A **9**



Kampanol B **10**



Kampanol C **11**

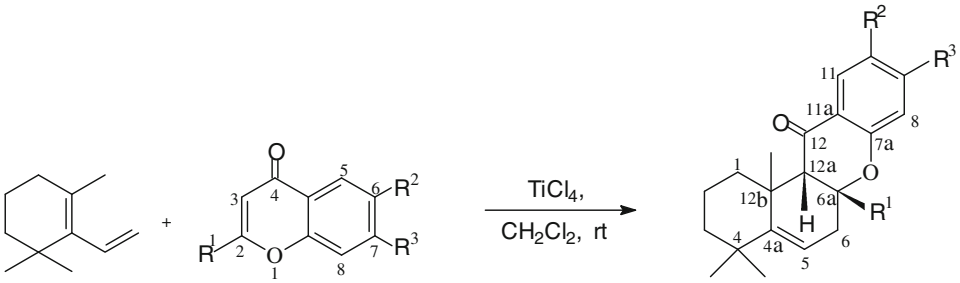
(**9–11**) (Fig. 1) are polycyclic natural products having similar structural features as puupehenone and were isolated from the fungal culture broth of *Stachybotrys kampalensis*; they are novel and specific inhibitors of farnesyl-protein transferase [31].

Our interest in the synthesis of natural products [32] and absence of reports on Diels-Alder reaction of 1,3,3-trimethyl-2-vinyl-1-cyclohexene with chromones not having an activating group on the enone double bond led us to explore the synthetic potential of chromones such as 6,7-dimethoxy-2-methylchromone (**12**) [33], 6-methoxy-2-methylchromone (**13**) [34], 6,7-methylenedioxy-2-methylchromone (**14**) [35], 6-nitro-2-methylchromone (**15**) [36], 2-methylchromone (**16**) [37], flavone (**17**) [38], and chromone (**18**) [39] as dienophiles in [4+2] cycloaddition reactions. We envisaged that if the diene 1,3,3-trimethyl-2-vinyl-1-cyclohexene (**19**) [3] could be used, then such a cycloaddition would lead to a convergent approach for the construction of the tetracyclic core of puupehenone and kampanol analogues.

Results and discussion

We now report for the first time a successful Diels-Alder reaction of 1,3,3-trimethyl-2-vinyl-1-cyclohexene (**19**) with chromones **12–18** not having an activating group at position 3 in the presence of a Lewis acid (Scheme 1).

Scheme 1



19 **12-18** **20-26**

The reaction of **12** with electron-rich diene **19** proceeded at room temperature with constant stirring for 7 days in the presence of a Lewis acid, $TiCl_4$, to give the cycloadduct **20** in moderate yield. The reaction was found to be regioselective as indicated by ^{1}H NMR data, which exhibited a singlet at $\delta = 2.71$ ppm for the C-12a proton, whereas the C-6a proton signal was absent. The diastereotopic protons at C-1 appeared at 2.18 and 1.65 ppm. These data indicate the formation of the regioisomer **20** (Fig. 2).

The reaction was also stereoselective as indicated by ^{1}H NMR, which showed a singlet for C-6a methyl protons at $\delta = 1.39$ ppm and C-12b methyl protons at 1.21 ppm.

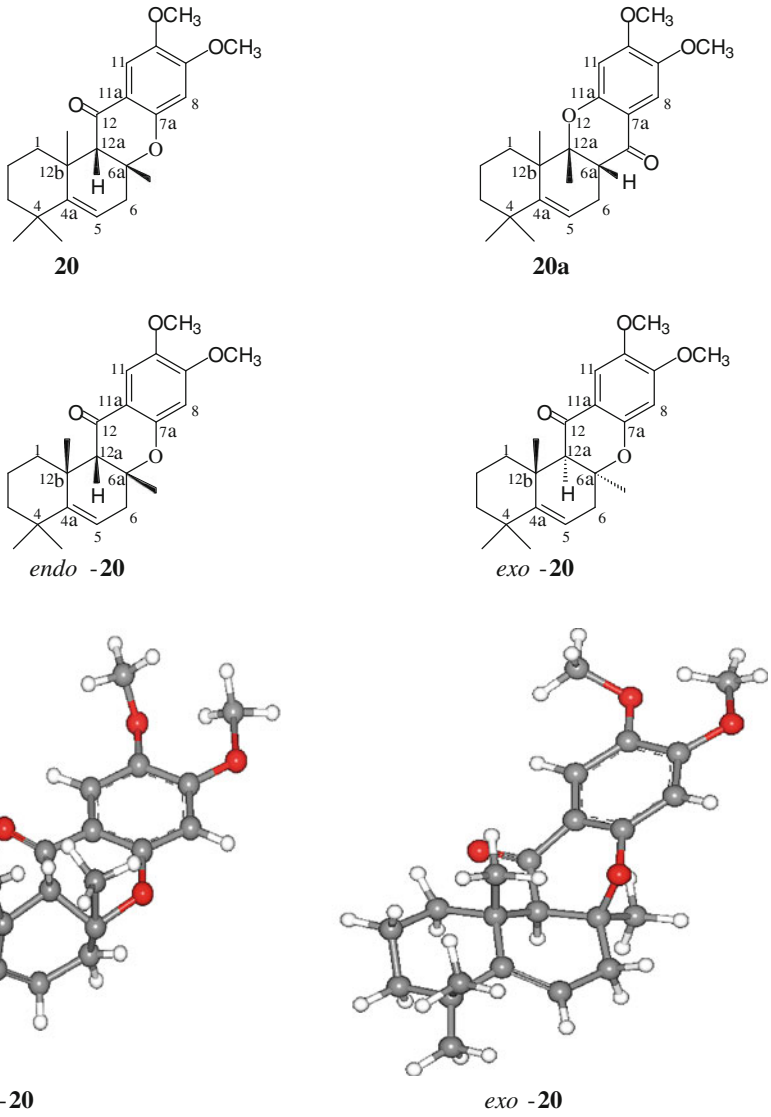


Fig. 2 Regioisomers **20**, **20a**, *endo-exo* conformations, and Ball-Stick models [41] of **20**

The C-6a methyl carbon exhibited a signal in ^{13}C NMR at $\delta = 34.2$ ppm, and C-12b methyl carbon exhibited a signal at 23.8 ppm.

These high δ values suggest the formation of the *endo*-configured product (Fig. 2). Recently, Wallace et al. [40] reported the synthesis of the *exo*-(±)-1,2,3,4,6,6a,12a,12b-octahydro-9,10-dimethoxy-4,4,6a,12b-tetramethylbenzo[*a*]-xanthen-12-one, which had lower δ values for 12a, 6a-Me, and 12b-Me protons. Furthermore, this compound has a melting point of 165 °C, whereas **20** has a melting point of 102 °C. Moreover, *exo*-(±)-1,2,3,4,6,6a,12a,12b-octahydro-4,4,6a,12b-tetramethylbenzo[*a*]xanthen-12-one is an oil [40], but our compound **24** is a solid with a melting point of 60 °C. Compound **24** also has higher δ values for 12a, 6a-Me, and 12b-Me protons. All this evidence suggests the formation of the *endo*-product. This represents the first example of a highly stereoselective [4+2] Lewis acid catalyzed cycloaddition reaction involving easily available chromone dienophiles.

Similar results were obtained with the other chromones **13**–**18** (Table 1). In all these cases, it led to the generation of the tetracyclic core as present in puupehenone **1** and related marine terpenoids and kampanols. Further, the catalytic hydrogenation of the C4a–C5 double bond could lead to a *trans*-fused AB ring [7, 8], which is present in these natural products.

In conclusion, we have accomplished the first highly stereoselective Lewis acid catalyzed [4+2] cycloaddition reaction using chromones as dienophiles and demonstrated the potential of this reaction in constructing the tetracyclic core of the marine diterpenoids related to puupehenone analogues **1**–**8** and kampanols **9**–**11** in a convergent manner.

Experimental

All purchased solvents and chemicals were of analytical grade and used without further purification. IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrophotometer in KBr discs. Elemental analyses for C, H, and N were performed using a Euro-Vector EA 3000 elemental analyzer, and the results agreed favorably with calculated values. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker Avance instrument using $CDCl_3$ as solvent and TMS as an internal standard at 300 and 75 MHz, respectively. Electron impact mass spectra were obtained using a 3200 Q TRAP LC-MS-MS System MDS SCI EX Shimadzu Prominence LC and Varian 500-MS (Model 210) LC-MS IT mass spectrometer. Boiling point of petroleum ether used was in the range of 60–80 °C. Silica gel (60–120 mesh, S.D. Fine Chemicals, Ltd.) was used in column chromatography.

Table 1 Reaction of 1,3,3-trimethyl-2-vinyl-1-cyclohexene (19) with chromones **12**–**18**

Entry	Chromone	R^1	R^2	R^3	Product	Time (d)	Yield (%)[a]
1	**12**	Me	OMe	OMe	**20**	7	56
2	**13**	Me	OMe	H	**21**	7	54
3	**14**	Me	–OCH_2O–		**22**	10	57
4	**15**	Me	NO_2	H	**23**	8	57
5	**16**	Me	H	H	**24**	7	54
6	**17**	Ph	H	H	**25**	9	52
7	**18**	H	H	H	**26**	8	56

[a] Isolated yields

General procedure for preparation of cycloadducts ***20–26***

1,3,3-Trimethyl-2-vinyl-1-cyclohexene **19** (900 mg, 6 mmol) and **12**–**18** (0.6 mmol) were dissolved in 25 cm^3 dry CH_2Cl_2, and then 0.5 cm^3 $TiCl_4$ was added. The reaction mixture was stirred at room temperature for 7–10 days. The reaction mixture was concentrated in vacuo at 40 °C temperature on a water bath. The brown-colored residue thus obtained was purified by column chromatography (silica gel) eluting with petroleum ether/$CHCl_3$ to afford the corresponding cycloadducts **20**–**26** (Table 1).

Endo-(±)-1,2,3,4,6,6a,12a,12b-Octahydro-9,10-dimethoxy-4,4,6a,12b-tetramethyl-12H-benzo[a]-xanthen-12-one (**20**, $C_{23}H_{30}O_4$)

Colorless solid; yield 56%; m.p.: 101–102 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.11$ (s, 3H, CH_{3ax}-4), 1.13 (s, 3H, CH_{3eq}-4), 1.21 (s, 3H, CH_3-12b), 1.39 (s, 3H, CH_3-6a), 1.43, 1.18 (m, 2H, H-3), 1.72, 1.61 (m, 2H, H-2), 2.18, 1.65 (m, 2H, H-1), 2.53 (dd, 1H, $J = 9.0$, 18.0 Hz, H-6), 2.61 (dd, 1H, $J = 9.0$, 18.0 Hz, H-6), 2.71 (s, 1H, H-12a), 3.86 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 5.58 (t, 1H, $J = 3.9$ Hz, H-5), 7.01 (s, 1H, H-8), 7.14 (s, 1H, H-11) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 17.5$ (C-2), 20.6 (C-3), 22.7 (CH_{3ax}-4), 23.8 (CH_3-12b), 32.0 (C-6), 32.6 (C-4), 33.5 (CH_{3eq}-4), 34.2 (CH_3-6a), 37.1 (C-12b), 37.5 (C-1), 56.2 (OCH_3), 56.6 (OCH_3), 64.2 (C-12a), 78.6 (C-6a), 121.2 (C-5), 130.5 (C-8), 132.1 (C-11), 137.3 (C-11a), 140.8 (C-4a), 154.2 (C-10), 154.4 (C-7a), 155.2 (C-9), 199.5 (C=O) ppm; IR (KBr): $\bar{\nu} = 2{,}924$, 1,678 (C=O), 1,474, 1,266, 1,063 cm^{-1}; EI-MS: m/z (%) = 370 (M^+, 11).

Endo-(±)-1,2,3,4,6,6a,12a,12b-Octahydro-10-methoxy-4,4,6a,12b-tetramethyl-12H-benzo[a]xan-then-12-one (**21**, $C_{22}H_{28}O_3$)

Colorless solid; yield 54%; m.p.: 110–111 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.12$ (s, 3H, CH_{3ax}-4), 1.14 (s, 3H, CH_{3eq}-4), 1.22 (s, 3H, CH_3-12b), 1.38 (s, 3H, CH_3-6a),

1.42, 1.19 (m, 2H, H-3), 1.71, 1.60 (m, 2H, H-2), 2.16, 1.64 (m, 2H, H-1), 2.51 (dd, 1H, J = 9.0, 18.1 Hz, H-6), 2.59 (dd, 1H, J = 9.0, 18.1 Hz, H-6), 2.80 (s, 1H, H-12a), 3.88 (s, 3H, OCH_3), 5.59 (t, 1H, J = 3.8 Hz, H-5), 6.99 (d, 1H, J = 8.9 Hz, H-8), 7.09 (d, 1H, J = 8.9 Hz, H-9), 7.19 (s, 1H, H-11) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.0 (C-2), 20.4 (C-3), 22.4 (CH_{3ax}-4), 23.2 (CH_3-12b), 31.8 (C-6), 32.2 (C-4), 32.8 (CH_{3eq}-4), 33.9 (CH_3-6a), 36.9 (C-1), 37.2 (C-12b), 55.9 (OCH_3), 64.1 (C-12a), 78.3 (C-6a), 121.0 (C-5), 126.2 (C-8), 130.9 (C-9), 131.7 (C-11), 137.5 (C-11a), 141.2 (C-4a), 153.2 (C-10), 154.1 (C-7a), 199.1 (C = O) ppm; IR (KBr): $\bar{\nu}$ = 3,061, 2,924, 1,676 (C=O), 1,483, 1,239, 1,028 cm^{-1}; EI-MS: *m/z* (%) = 340 (M^+, 5), 191 (100), 149 (17), 135 (18).

6,7-Methylenedioxy-2-methyl-4H-1-benzopyran-4-one (**14**, $C_{11}H_8O_4$)

This compound was prepared utilizing the general procedure reported for synthesis of chromone [35]. Faint yellow crystals; yield 98%; m.p.: 101–102 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.52 (s, 3H), 5.98 (s, 1H), 6.44 (s, 2H), 7.05 (s, 1H), 7.27 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.4, 101.7, 128.4, 129.8, 132.3, 138.1, 140.4, 154.4, 154.9, 155.2, 201.9 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 2,922, 1,632 (C=O), 1,484, 1,035, 922 cm^{-1}; EI–MS: *m/z* (%) = 204 (M^+, 21), 148 (54), 118 (83), 116 (100).

Endo-(±)-1,2,3,4,6,6a,12a,12b-Octahydro-4,4,6a,12b-tetramethyl-9,10-methylenedioxy–12H-benzo[a]xanthen-12-one (**22**, $C_{22}H_{26}O_4$)

Colorless solid; yield 57%; m.p.: 96–98 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 3H, CH_{3ax}-4), 1.15 (s, 3H, CH_{3eq}-4), 1.20 (s, 3H, CH_3-12b), 1.39 (s, 3H, CH_3-6a), 1.42, 1.18 (m, 2H, H-3), 1.69, 1.62 (m, 2H, H-2), 2.19, 1.67 (m, 2H, H-1), 2.55 (dd, 1H, J = 9.2, 18.2 Hz, H-6), 2.64 (dd, 1H, J = 9.2, 18.2 Hz, H-6), 2.69 (s, 1H, H-12a), 5.60 (t, 1H, J = 3.9 Hz, H-5), 5.97 (s, 2H, OCH_2O), 7.03 (s, 1H, H-8), 7.10 (s, 1H, H-11) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.8 (C-2), 20.5 (C-3), 22.8 (CH_{3ax}-4), 23.5 (CH_3-12b), 32.2 (C-6), 32.5 (C-4), 32.9 (CH_{3eq}-4), 34.1 (CH_3-6a), 37.2 (C-1), 37.5 (C-12b), 63.8 (C-12a), 78.7 (C-6a), 101.1 (OCH_2O), 121.4 (C-5), 130.2 (C-8), 132.5 (C-11), 137.5 (C-11a), 140.5 (C-4a), 154.1 (C-10), 154.5 (C-7a), 154.8 (C-9), 199.4 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 2,924, 1,680 (C=O), 1,484, 1,035, 923 cm^{-1}; EI–MS: *m/z* (%) = 354 (M^+, 4), 352 (100), 236 (10), 220 (40), 205 (21).

Endo-(±)-1,2,3,4,6,6a,12a,12b-Octahydro-4,4,6a,12b-tetramethyl-10-nitro-12H-benzo[a]xanthen-12-one (**23**, $C_{21}H_{25}NO_4$)

Colorless solid; yield 57%; m.p.: 170–171 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 3H, CH_{3ax}-4), 1.16 (s, 3H, CH_{3eq}-4), 1.24 (s, 3H, CH_3-12b), 1.39 (s, 3H, CH_3-6a), 1.42, 1.19 (m, 2H, H-3), 1.71, 1.64 (m, 2H, H-2), 2.20, 1.68 (m, 2H, H-1), 2.54 (dd, 1H, J = 8.9, 18.0 Hz, H-6), 2.62 (dd, 1H, J = 8.9, 18.0 Hz, H-6), 2.78 (s, 1H, H-12a), 5.55 (t, 1H, J = 3.9 Hz, H-5), 7.54 (d, 1H, J = 9.2 Hz, H-8), 8.46 (d, 1H, J = 9.2 Hz, H-9), 9.03 (s, 1H, H-11) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.7 (C-2), 20.8 (C-3), 22.3 (CH_{3ax}-4), 23.1 (CH_3-12b), 31.7 (C-6), 32.7 (C-4), 33.7 (CH_{3eq}-4), 34.3 (CH_3-6a), 37.1 (C-1), 37.5 (C-12b), 64.1 (C-12a), 78.5 (C-6a), 120.5 (C-5), 127.8 (C-8), 138.1 (C-11a), 140.4 (C-4a), 144.6 (C-9), 148.5 (C-11), 154.8 (C-7a), 159.2 (C-10), 199.8 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,063, 2,925, 1,679 (C=O), 1,531, 1,467 cm^{-1}; EI–MS: *m/z* (%) = 355 (M^+, 8), 327 (23), 206 (100), 160 (31), 143 (10).

Endo-(±)-1,2,3,4,6,6a,12a,12b-Octahydro-4,4,6a,12b-tetramethyl-12H-benzo[a]xanthen-12-one (**24**, $C_{21}H_{26}O_2$)

Colorless solid; yield 54%; m.p.: 59–60 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (s, 3H, CH_{3ax}-4), 1.13 (s, 3H, CH_{3eq}-4), 1.23 (s, 3H, CH_3-12b), 1.39 (s, 3H, CH_3-6a), 1.44, 1.17 (m, 2H, H-3), 1.69, 1.60 (m, 2H, H-2), 2.19, 1.66 (m, 2H, H-1), 2.52 (dd, 1H, J = 9.1, 18.1 Hz, H-6), 2.60 (dd, 1H, J = 9.1, 18.1 Hz, H-6), 2.75 (s, 1H, H-12a), 5.58 (t, 1H, J = 3.7 Hz, H-5), 6.90 (t, 1H, J = 8.5 Hz, H-10), 6.93 (t, 1H, J = 8.6 Hz, H-9), 6.97 (d, 1H, J = 8.5 Hz, H-8), 7.04 (d, 1H, J = 8.5 Hz, H-11) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.4 (C-2), 21.0 (C-3), 21.9 (CH_{3ax}-4), 23.5 (CH_3-12b), 32.2 (C-4), 32.4 (C-6), 33.4 (CH_{3eq}-4), 34.0 (CH_3-6a), 37.4 (C-1), 37.2 (C-12b), 64.5 (C-12a), 78.2 (C-6a), 120.8 (C-5), 121.2 (C-10), 121.4 (C-9), 126.5 (C-8), 128.2 (C-11), 137.7 (C-11a), 140.1 (C-4a), 155.1 (C-7a), 199.2 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1,676 (C=O), 1,478 cm^{-1}; EI–MS: *m/z* (%) = 310 (M^+, 4), 191 (100), 161 (96).

Endo-(±)-1,2,3,4,6,6a,12a,12b-Octahydro-4,4,12b-trimethyl-6a-phenyl-12H-benzo[a]xanthen-12-one (**25**, $C_{26}H_{28}O_2$)

Colorless solid; yield 52%; m.p.: 105–106 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (s, 3H, CH_{3ax}-4), 1.16 (s, 3H, CH_{3eq}-4), 1.24 (s, 3H, CH_3-12b), 1.40, 1.19 (m, 2H, H-3), 1.69, 1.60 (m, 2H, H-2), 2.20, 1.66 (m, 2H, H-1), 2.56 (dd, 1H, J = 9.0, 18.1 Hz, H-6), 2.63 (dd, 1H, J = 9.0, 18.1 Hz, H-6), 2.91 (s, 1H, H-12a), 5.73 (t, 1H, J = 3.8 Hz, H-5), 6.83–7.10 (m, 9-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.5 (C-2), 20.9 (C-3), 22.4 (CH_{3ax}-4), 24.0 (CH_3-12b), 31.2 (C-6), 32.1 (C-4), 33.2 (CH_{3eq}-4), 37.2 (C-1), 37.5 (C-12b), 66.5 (C-12a), 80.4 (C-6a), 115.5, 119.8, 119.8, 120.8 (C-10), 121.1 (C-9), 121.7 (C-5), 122.8, 122.8, 126.4 (C-8), 127.3, 128.5 (C-11), 137.3 (C-11a), 140.9 (C-4a), 155.5 (C-7a), 199.1 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,070, 2,924, 1,678 (C=O), 1,495 cm^{-1}; EI-MS: *m/z* (%) = 372 (M^+, 8), 344 (48), 223 (100), 121 (58), 77 (11).

Endo-(±)-1,2,3,4,6,6a,12a,12b-Octahydro-4,4,12b-trimethyl-12H-benzo[a]xanthen-12-one (**26**, $C_{20}H_{24}O_2$) Colorless solid; yield 56%; m.p.: 53–55 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.12$ (s, 3H, CH_{3ax}-4), 1.15 (s, 3H, CH_{3eq}-4), 1.22 (s, 3H, CH_3-12b), 1.42, 1.18 (m, 2H, H-3), 1.71, 1.63 (m, 2H, H-2), 2.16, 1.68 (m, 2H, H-1), 2.20 (ddd, 1H, $J = 5.2$, 8.9 Hz, H-6), 2.41 (ddd, 1H, $J = 5.2$, 8.9 Hz, H-6), 2.79 (d, 1H, $J = 4.8$ Hz, H-12a), 3.43 (ddd, 1H, $J = 5.2$, 8.9 Hz, H-6a), 5.56 (t, 1H, $J = 3.9$ Hz, H-5), 6.89 (t, 1H, $J = 5.1$ Hz, H-10), 6.92 (t, 1H, $J = 5.2$ Hz, H-9), 6.99 (d, 1H, $J = 5.0$ Hz, H-8), 7.03 (d, 1H, $J = 5.0$ Hz, H-11) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 17.2$ (C-2), 21.1 (C-3), 22.1 (CH_{3ax}-4), 23.9 (CH_3-12b), 31.5 (C-6), 32.7 (C-4), 33.8 (CH_{3eq}-4), 36.8 (C-1), 37.2 (C-12b), 63.8 (C-12a), 79.2 (C-6a), 120.9 (C-10), 121.2 (C-9), 121.5 (C-5), 126.2 (C-8), 128.3 (C-11), 137.2 (C-11a), 140.2 (C-4a), 155.2 (C-7a), 199.4 (C=O) ppm; IR (KBr): $\bar{\nu} = 3{,}085$, 2,925, 1,677 (C=O), 1,474 cm^{-1}; EI–MS: m/z (%) = 296 (M^+, 12), 147 (100), 105 (12), 91 (58), 77 (72).

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