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Novel synthetic strategy toward abietane and podocarpane-type diterpenes from (−)-sclareol: synthesis of the antitumor (+)-7-deoxynimbidiol

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Abstract—A new route to abietane and podocarpane-type terpenoids from labdane diterpenes is reported. The key step is the transformation of β-ketoester **9** into the corresponding *O*-acetylsalicylate ester **18**, via a manganese(III)-based oxidative free-radical cyclization carried out in Ac_2O. Utilizing this, the synthesis of the antitumor (+)-7-deoxynimbidiol (**5**) from (−)-sclareol (**11**) has been achieved. (+)-Nimbidiol (**6**) and the natural terpenoid **20** have also been synthesized.

Abietane and biosynthetically related polycyclic diterpenes constitute an important group of C ring aromatic diterpenes.[1] Abietane diterpenes show a wide range of biological activities, for example, antibiotic,[2] antiviral,[2a,3] antimalaria,[4] antioxidant,[5] cytotoxic,[6] and antileishmanial.[7] Noteworthy among these, because of their remarkable activities, are a number of variously oxidized compounds. Representative examples of these are taxodione (**1**),[6a] active against methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE), the cytotoxic xanthanthusin (**2**), recently isolated from *Coleus xanthanthus*,[8] and ferruginol (**3**), the gastroprotective[9] and antibacterial[10] activity of which has recently been reported. Podocarpane diterpenes are interesting metabolites from a biosynthetic point of view, as they do not occur extensively in nature. During recent years, some biologically active podocarpane phenols have been isolated; aminophenol **4**, a potent 5-lypoxygenase inhibitor is an example.[11] Very recently, a novel podocarpic diterpene (+)-7-deoxynimbidiol (**5**), a possible probe molecule because of its antitumor activity, has been isolated from *Calastrus hypoleucus*.[12] Different strategies have been utilized to achieve the racemic synthesis of this type of compound, including polyene cascade cyclizations promoted by sulfenium ions,[13] acid catalyzed cyclialkylations,[14] and domino acylation–cycloalkylation processes.[15] Enantioselective syntheses of these compounds have also been reported. In most cases, abietic acid[16] or podocarpic acid derivatives[17] have been utilized as starting materials. Two routes to podocarpane-type terpenoids from labdane diterpene have recently been described;[18,19] thus, a formal synthesis of (+)-nimbidiol (**6**)[20] from manool involving a Diels–Alder cycloaddition has been achieved (see Fig. 1).[18]

Continuing our research into the synthesis of bioactive compounds starting from natural diterpenes, we are interested in developing a new route to abietane and podocarpane-type terpenoids starting from (−)-sclareol (**11**), a labdane diterpene that is very abundant in the cultivable vegetal species *Salvia sclarea*. We focused on (+)-7-deoxynimbidiol (**5**), whose racemic synthesis through the acid catalyzed cyclialkylation of a

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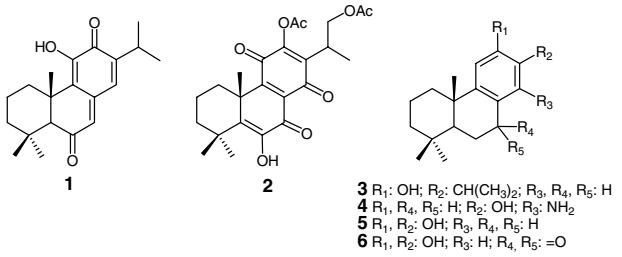


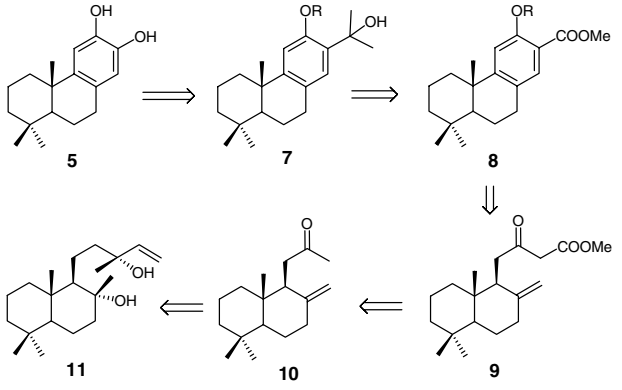
Figure 1.

homocyclogeranylcatechol has been recently reported[12] and (+)-nimbidiol (**6**), whose synthesis has been more extensively studied.[13–15,18]

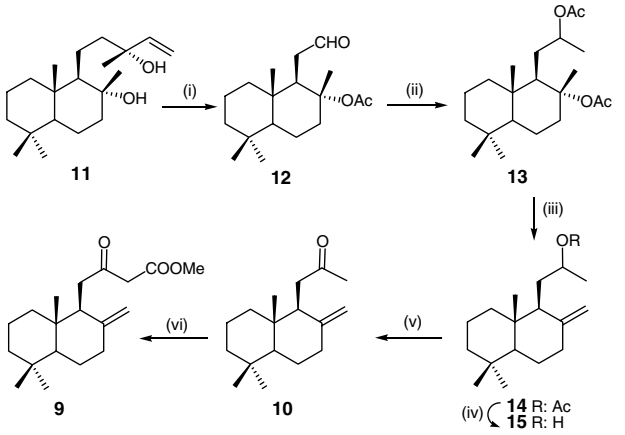
Our planned synthetic strategy is shown in Scheme 1. The key step is the transformation of β-ketoester **9**, obtained from **11**, into the aromatic ester **8**, through an oxidative free-radical cyclization.[21] The ester group of compound **8** will allow the introduction of the isopropyl group, providing the abietane skeleton of phenol **7**. The removal of the 15-hydroxy group in this intermediate, via cationic reduction or dehydration–hydrogenation processes, will allow the obtention of different abietane derivatives. Alternatively, the 15-hydroperoxide rearrangement will furnish the corresponding podocarpane derivatives, such as catechol **5**.

Scheme 2 shows the synthesis of β-ketoester **9** from (−)-sclareol (**11**). Treatment of acetoxyaldehyde **12**, which is obtained in high yield from **11** utilizing a modification of our previously reported procedure,[22] with MeMgBr gave the corresponding acetoxyalcohol, which after acetylation of the tertiary hydroxyl group led to diacetate **13**. The exocyclic acetoxyalkene **14**, together with a small quantity of the trisubstituted regioisomer (ratio 10:1), was obtained when compound **13** was refluxed with collidine, which was then hydrolyzed to alcohol **15**. The oxidation of alcohol **15**, obtained after hydrolysis of acetate **14**, and the further treatment of the resulting ketone **10** with Me_2CO_3 and NaH[23] led to ketoester **9**.

Next, the elaboration of the aromatic C ring of the target compounds, starting from β-ketoester **9**, was



Scheme 1.



Scheme 2. Reagents and conditions: (i) 0.2% OsO_4, $NaIO_4$, *t*-BuOH, 45 °C, 3 h (90%); (ii) (a) MeMgBr, OEt_2, 0 °C, 30 min (92%); (b) CH_3COCl, dimethylaniline, rt, 14 h, (92%); (iii) Collidine, reflux, 15 h (94%); (iv) KOH, MeOH, rt, 1 h (98%); (v) Jones, acetone, 0 °C, 15 min (90%); (vi) Me_2CO_3, NaH, benzene, reflux, 4 h (87%).

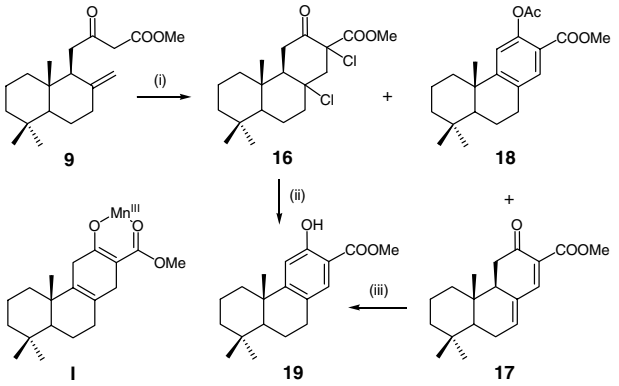
undertaken. The manganese(III)-based oxidative free-radical cyclization of unsaturated β-ketoesters, such as compound **9**, has been described as being suitable to synthesize the corresponding alkyl salicylates, such as intermediate **8** postulated in our retrosynthetic scheme (Scheme 1); the use of $Mn(OAc)_3{\cdot}2H_2O$ and LiCl in acetic acid has been described to minimize the overoxidation of cyclization products, thereby improving the yield of the resulting salicylates.[21] First, we studied the behavior of ketoester **9** under these oxidation conditions at different temperatures and utilizing different proportions of reagents: in all cases, a complex mixture of compounds, including small quantities of the desired methyl salicylate, was obtained.

In view of these results, the oxidation was essayed utilizing Ac_2O as the reaction medium; this could protect the phenolic hydroxyl group, preventing the overoxidation side reactions. The most representative experiments are shown in Table 1 (see Scheme 3).

Treatment of β-ketoester **9** with $Mn(OAc)_3{\cdot}2H_2O$ (4 equiv) and LiCl (3 equiv) in Ac_2O at room temperature for 12 h gave a complex mixture of compounds, including salicylate **18** in low yield (entry 1). When the reaction was carried out at 80–90 °C for 4 h, dichloro derivative **16** (10%), the conjugated diene-ketoester **17** (12%) and the methyl *O*-acetyl salicylate **18** (52%) were obtained (entry 2). Isolation of dichloro derivatives, such as compound **16**, has been described for the oxidation with $Mn(OAc)_3{\cdot}2H_2O$ and LiCl in acetic acid;[21]

Table 1. Treatment of β-ketoester **9** with $Mn(OAc)_3{\cdot}2H_2O$ (4 equiv) and LiCl (3 equiv) in Ac_2O

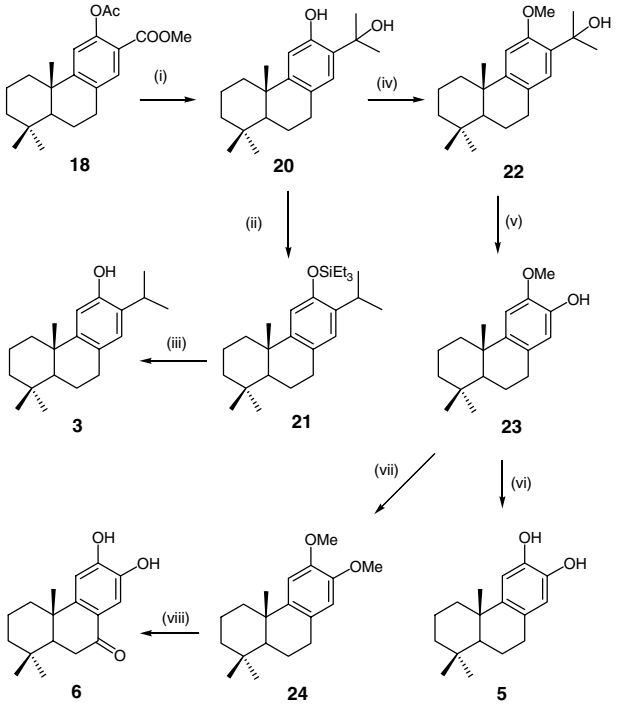
Entry	Temperature (°C)	Time (h)	Products (%)
1	rt	12	**16** (51), **18** (9), **19** (8)
2	80–90	4	**16** (10), **17** (12), **18** (8)
3	120	12	**18** (75)



Scheme 3. Reagents and conditions: (i) $Mn(OAc)_3{\cdot}2H_2O$ (4 equiv), LiCl (3 equiv), Ac_2O (see Table 1); (ii) DBU, toluene, reflux, 12 h (quant.); (iii) cat. H_2SO_4, AcOH, reflux, 3 h (87%).

as has also been reported, the conversion of this type of dihalo compounds into the corresponding salicylates by heating in acetic acid was not feasible, requiring the presence of LiCl. We also observed that compound **16** remained unaltered after refluxing with *p*-toluenesulfonic acid in toluene; nevertheless, as could be expected, this dichloro derivative was quantitatively transformed into methyl salicylate **19** by refluxing with DBU in toluene. Isolation of diene-ketoesters, such as **17**, is not very common, which is attributed to the easy polymerization of this type of compounds; this process would be more difficult for the most hindered tricyclic compound **17**. Ketoester **17** was transformed in high yield into methyl salicylate **19** after treatment with cat. H_2SO_4 in acetic acid under reflux. When the treatment of ketoester **9** with $Mn(OAc)_3{\cdot}2H_2O$ (4 equiv) and LiCl (3 equiv) was carried out in Ac_2O at 120 °C for 12 h we obtained only *O*-acetyl salicylate **18** in 75% yield (entry 3). It should be emphasized that this transformation involves the use of Ac_2O as a solvent for the first time in this type of reaction; the increased reaction yield utilizing this solvent could be attributed to the obtention of an *O*-acetylphenol which prevents the oxidation and polymerization side reactions of phenolic compounds. This *O*-acetyl derivative could be formed through the acetylation of a manganese(III) enolate intermediate, like **I**,[21] which takes place at high temperature; the unsatisfactory course of reaction at room temperature seems to support this supposition.

The transformation of salicylate **18** into ferruginol (**3**), 7-deoxynimbidiol (**5**) and nimbidiol (**6**) is depicted in Scheme 4. Treatment of compound **18** with an excess of MeMgBr afforded 15-hydroxyferruginol (**20**), an abietane diterpene isolated from *Chamaecyparis pisifera*.[24] Treatment of this phenol with Et_3SiH and CF_3COOH gave silyl ether **21**, which after treatment with TBAF in THF was converted into ferruginol (**3**). Alternatively, methyl ether **22** was treated with H_2O_2 in the presence of $BF_3{\cdot}OEt_2$ to give podocarpane **23**, a precursor of (+)-7-deoxynimbidiol (**5**). The spectroscopic properties of compound **5** were identical to those reported in the literature ($[\alpha]_D^{25}$ +36.5, *c* 0.4, MeOH; lit.:[12] $[\alpha]_D^{20}$ +49.4, *c* 0.1, MeOH). Methylation of phenol



Scheme 4. Reagents and conditions: (i) MeMgBr exc., Et_2O, 0 °C, 15 min; dil HCl (89%); (ii) Et_3SiH, CF_3COOH, CH_2Cl_2, −40 °C, 30 min (91%); (iii) TBAF, THF, rt, 15 min (97%); (iv) MeI, K_2CO_3, acetone, reflux, 12 h (93%); (v) 30% H_2O_2; $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C–rt, 3 h (84%); (vi) BBr_3, CH_2Cl_2, 0 °C, 1 h (93%); (vii) MeI, K_2CO_3, acetone, reflux, 18 h (90%); (viii) Ref. 14c.

23 afforded the dimethyl derivative **24**, whose transformation into (+)-nimbidiol (**6**) has been reported previously.[14c]

In summary, a new route to abietane and podocarpane-type terpenoids from labdane diterpenes is reported. The key step is the transformation of an unsaturated β-ketoester into the corresponding *O*-acetylsalicylate ester, via a manganese(III)-based oxidative free-radical cyclization carried out in Ac_2O. Utilizing this, the synthesis of the antitumor (+)-7-deoxynimbidiol (**5**),[25] starting from (−)-sclareol (**11**), has been accomplished (28% overall yield from **11**). (+)-Nimbidiol (**6**) and the natural 15-hydroxyferruginol (**20**) have also been synthesized (14% and 37% overall yields from **11**, respectively).

Acknowledgments

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25. Spectroscopic properties of natural terpenoids were identical to those reported in the literature. The spectroscopic data of compound **20** have been revised. All new compounds were fully characterized spectroscopically and had satisfactory high resolution mass spectroscopy data. Selected data:
Compound **5**: $[\alpha]_D^{25}$ +36.5 (*c* 0.4, MeOH) [lit.:[12] +49.44 (*c* 0.1, MeOH)]. ^{1}H NMR (500 MHz, $CDCl_3$,) δ: 0.91 (3H, s), 0.94 (3H, s), 1.15 (3H, s), 1.28 (1H, dd, $J = 12.4$, 2.4 Hz), 1.35 (1H, ddd, $J = 13.2$, 13.2, 3.5 Hz), 1.47 (1H, br d, $J = 13.2$ Hz), 1.52–1.78 (5H, m), 1.83 (1H, m), 2.15 (1H, br d, $J = 12.6$ Hz), 2.73 (1H, ddd, $J = 16.8$, 11.2, 7.3 Hz), 2.80 (1H, ddd, $J = 16.8$, 6.9, 1.5 Hz), 5.05 (1H, br s), 6.52 (1H, s), 6.75 (1H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.3 (CH_2), 19.5 (CH_2), 21.8 (CH_3), 25.1 (CH_3), 30.0 (CH_2), 33.5 (CH_3), 33.6 (C), 37.6 (C), 39.3 (CH_2), 41.9 (CH_2), 50.7 (CH), 111.7 (CH), 115.4 (CH), 128.2 (C), 141.3 (C), 141.6 (C), 143.5 (C). HRMS (FAB) *m*/*z* calcd for $C_{17}H_{24}NaO_2$, 283.1674; found, 283.1681.
Compound **6**: $[\alpha]_D^{25}$ +5.2 (*c* 1.0, $CHCl_3$) [lit.:[20] +3.4 ($CHCl_3$)]. ^{1}H NMR (500 MHz, $CDCl_3$,) δ: 0.92 (3H, s), 0.98 (3H, s), 1.20 (3H, s), 1.26 (1H, m), 1.46–1.56 (2H, m), 1.66 (1H, m), 1.75 (1H, m), 1.86 (1H, dd, $J = 13.3$, 4.0 Hz), 2.22 (1H, br d, $J = 13.6$ Hz), 2.60 (1H, dd, $J = 18.2$, 13.6 Hz), 2.68 (1H, dd, $J = 18.2$, 4.1 Hz), 6.35 (1H, br s), 6.87 (1H, s), 7.50 (1H, br s), 7.70 (1H, s). ^{13}C NMR (125 MHz, $CDCl_3$,) δ: 19.1 (CH_2), 21.5 (CH_3), 23.4 (CH_3), 32.7 (CH_3), 33.4 (C), 36.2 (CH_2), 38.1 (C), 38.2 (CH_2), 41.6 (CH_2), 50.0 (CH), 110.3 (CH), 113.7 (CH), 124.2 (C), 142.1 (C), 151.1(C), 152.6 (C), 200.1 (C). HRMS (FAB) *m*/*z* calcd for $C_{17}H_{22}NaO_3$, 297.1467; found, 297.1458.
Compound **9**: $[\alpha]_D^{25}$ −16.9 (*c* 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.69 (3H, s), 0.80 (3H, s), 0.88 (3H, s), 1.07 (1H, ddd, $J = 12.7$, 12.7, 4.1 Hz), 1.10–1.25 (3H, m), 1.31 (1H, dd, $J = 12.7$, 4.1 Hz), 1.40 (1H, br d,$J = 13.1$ Hz), 1.43–1.62 (3H, m), 1.74 (1H, m), 2.09 (1H, ddd, $J = 12.9$, 12.9, 5.1 Hz), 2.39 (1H, m), 2.60 (1H, dd, $J = 17.4$, 3.7 Hz), 2.69 (1H, dd, $J = 17.4$, 10.0 Hz), 3.43 (1H, d, $J = 15.3$ Hz), 3.48 (1H, d, $J = 15.4$ Hz), 3.72 (3H, s), 4.33 (1H, br s), 4.74 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 39.3 (C-1), 19.3 (C-2), 42.1 (C-3), 33.5 (C-4), 51.4 (C-5), 24.0 (C-6), 37.6 (C-7), 148.8 (C-8), 55.2 (C-9), 39.0 (C-10), 39.6 (C-11), 202.4 (C-12), 49.1 (C-13), 106.7 (C-14), 33.6 (C-15), 21.7 (C-16), 14.6 (C-17), 167.8 (*C*OOMe), 52.5 (COO*CH*$_3$). HRMS (FAB) *m*/*z* calcd for $C_{19}H_{30}NaO_3$, 329.2093; found, 329.2102.
Compound **16**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.75 (3H, s), 0.79 (3H, s), 0.91 (3H, s), 1.04 (1H, ddd, $J = 14.3$, 14.3, 3.9 Hz), 1.29–1.70 (8H, m), 2.17 (1H, d, $J = 14.5$ Hz), 2.24 (1H, dt, $J = 13.6$, 2.7 Hz), 2.60 (1H, dd, $J = 14.0$, 2.7 Hz), 2.90 (1H, t, $J = 14.0$ Hz), 3.23 (1H, d, $J = 14.5$ Hz), 3.73 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 15.3 (CH_3), 18.0 (CH_2), 18.2 (CH_2), 21.7 (CH_3), 33.5 (C), 33.6 (CH_3), 38.3 (CH_2), 38.6 (C), 39.3 (CH_2), 41.8 (CH_2), 43.5 (CH_2), 53.9 (CH_3), 55.9 (CH), 56.5 (CH_2), 58.2 (CH), 71.5 (C), 72.9 (C), 168.7 (C), 198.5 (C). HRMS (FAB) *m*/*z* calcd for $C_{19}H_{28}Cl_2NaO_3$, 397.1313; found, 397.1310.
Compound **17**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.82 (3H, s), 0.90 (3H, s), 0.93 (3H, s), 1.03 (1H, ddd, $J = 12.7$, 12.7, 4.0 Hz), 1.19 (1H, ddd, $J = 13.1$, 13.1, 3.9 Hz), 1.27 (1H, dd, $J = 12.3$, 4.7 Hz), 1.32–1.60 (4H, m), 1.74 (1H, br d, $J = 14.5$ Hz), 2.15 (1H, m), 2.39 (1H, m), 2.48 (2H, m), 3.79 (3H, s), 6.49 (1H, br s), 7.66 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1 (CH_3), 18.7 (CH_2), 21.8 (CH_3), 25.9 (CH_2), 33.0 (C), 33.4 (CH_3), 35.4 (C), 38.7 (CH_2), 38.7 (CH_2), 42.1 (CH_2), 48.6 (CH), 52.3 (CH_3),

133.6 (C), 143.1 (CH), 153.6 (CH), 165.3 (C), 196.1 (C). HRMS (FAB) *m/z* calcd for $C_{19}H_{26}NaO_3$, 325.1780; found, 325.1772.

Compound **18**: $[\alpha]_D^{25}$ +21.2 (*c* 0.9, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ: 0.92 (3H, s), 0.95 (3H, s), 1.17 (3H, s), 1.21 (1H, ddd, $J = 13.3$, 13.3, 3.9 Hz), 1.30 (1H, dd, $J = 12.5$, 2.1 Hz), 1.41 (1H, ddd, $J = 13.2$, 13.2, 3.8 Hz), 1.51 (1H, br d, $J = 15.4$ Hz), 1.62 (1H, m), 1.66–1.80 (2H, m), 1.90 (1H, m), 2.18 (1H, m), 2.32 (3H, s), 2.84 (1H, ddd, $J = 17.3$, 11.1, 7.7 Hz), 2.96 (1H, dd, $J = 17.3$, 6.7 Hz), 3.83 (3H, s), 6.94 (1H, s), 7.68 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 38.7 (C-1), 19.0 (C-2), 41.7 (C-3), 33.7 (C-4), 49.8 (C-5), 19.3 (C-6), 29.8 (C-7), 133.5 (C-8), 148.7 (C-9), 38.4 (C-10), 119.7 (C-11), 157.0 (C-12), 119.8 (C-13), 132.6 (C-14), 170.2 (C-15, *C*OOMe), 33.4 (C-16), 24.7 (C-17), 21.8 (C-20), 52.1 (COO*CH*$_3$), 21.2 (OCO*CH*$_3$), 165.3 (O*C*OCH$_3$). HRMS (FAB) *m/z* calcd for $C_{21}H_{28}NaO_4$, 367.1885; found, 367.1877.

Compound **19**: $[\alpha]_D^{25}$ +27.5 (*c* 0.8, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ: 0.92 (3H, s), 0.95 (3H, s), 1.17 (3H, s), 1.29 (1H, dd, $J = 12.4$, 2.2 Hz) 1.39 (1H, ddd, $J = 12.9$, 12.9, 3.6 Hz), 1.48 (1H, br d, $J = 13.2$ Hz), 1.57–1.79 (2H, m), 1.87 (1H, m), 2.22 (1H, br d, $J = 12.6$ Hz), 2.76 (1H, ddd, $J = 16.6$, 11.3, 7.8 Hz), 2.89 (1H, dd, $J = 16.6$, 6.5 Hz), 3.91 (3H, s), 6.87 (1H, s), 7.49 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 38.6 (C-1), 19.0 (C-2), 41.5 (C-3), 33.6 (C-4), 49.8 (C-5), 19.2 (C-6), 29.2 (C-7), 126.4 (C-8), 159.1 (C-9), 38.5 (C-10), 112.8 (C-11), 159.3 (C-12), 109.9 (C-13), 128.9 (C-14), 170.4 (C-15, *C*OOMe), 33.2 (C-16), 24.3 (C-17), 21.7 (C-20), 52.0 (COO*CH*$_3$). HRMS (FAB) *m/z* calcd for $C_{19}H_{26}NaO_3$, 325.1780; found, 325.1779.

Compound **20**: $[\alpha]_D^{25}$ +26.5 (*c* 0.4, $CHCl_3$); lit.:[23] $[\alpha]_D^{25}$ −8.2 (*c* 0.73, MeOH). ^1H NMR (400 MHz, $CDCl_3$) δ: 0.92 (3H, s), 0.94 (3H, s), 1.17 (3H, s), 1.20 (1H, ddd, $J = 13.4$, 13.4, 3.7 Hz), 1.30 (1H, dd, $J = 12.4$, 2.2 Hz), 1.38 (1H, ddd, $J = 12.9$, 12.9, 3.7 Hz), 1.47 (1H, br d, $J = 12.2$ Hz), 1.60 (1H, m), 1.63 (3H, s), 1.66 (3H, s), 1.54–1.77 (2H, m), 1.85 (1H, m), 2.20 (1H, br s), 2.22 (1H, br d, $J = 12.7$ Hz), 2.74 (1H, ddd, $J = 16.5$, 11.2, 7.5 Hz), 2.83 (1H, dd, $J = 16.5$, 6.2 Hz), 6.73 (1H, s), 6.77 (1H, s), 8.50 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 38.9 (C-1), 19.4 (C-2), 41.9 (C-3), 33.7 (C-4), 50.5 (C-5), 19.5 (C-6), 30.0 (C-7), 128.5 (C-8), 151.4 (C-9), 37.9 (C-10), 113.3 (C-11), 153.6 (C-12), 126.2 (C-13), 125.8 (C-14), 76.0 (C-15), 30.4 (C-16), 30.5 (C-17), 33.5 (C-18), 24.8 (C-19), 21.8 (C-20). HRMS (FAB) *m/z* calcd for $C_{20}H_{30}NaO_2$, 325.2143; found, 325.2151.

Compound **21**: $[\alpha]_D^{25}$ +34.7 (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ: 0.78 (6H, q, $J = 8.0$ Hz), 0.92 (3H, s), 0.95 (3H, s), 1.01 (9H, t, $J = 8.0$ Hz), 1.17 (3H, d, $J = 6.9$ Hz), 1.18 (3H, d, $J = 6.9$ Hz), 1.18 (3H, s), 1.23 (1H, ddd, $J = 13.4$, 13.4, 3.9 Hz), 1.34 (1H, dd, $J = 12.4$, 1.7 Hz), 1.38 (1H, ddd, $J = 13.0$, 13.0, 3.6 Hz), 1.48 (1H, br d, $J = 13.1$ Hz), 1.57–1.81 (3H, m), 1.86 (1H, m), 2.14 (1H, br d, $J = 12.6$ Hz), 2.77 (1H, ddd, $J = 16.2$, 11.4, 7.2 Hz), 2.86 (1H, dd, $J = 16.2$, 6.3 Hz), 3.21 (1H, h, $J = 6.9$ Hz), 6.66 (1H, s), 6.83 (1H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 39.1 (C-1), 19.5 (C-2), 41.9 (C-3), 33.6 (C-4), 50.6 (C-5), 19.6 (C-6), 31.1 (C-7), 135.8 (C-8), 148.2 (C-9), 37.7 (C-10), 114.0 (C-11), 151.0 (C-12), 127.4 (C-13), 126.5 (C-14), 26.9 (C-15), 23.0 (C-16), 23.1 (C-17), 33.5 (C-18), 25.1 (C-19), 21.8 (C-20), 5.7 (Si*CH*$_2$CH$_3$), 7.0 (SiCH$_2$*CH*$_3$). HRMS (FAB) *m/z* calcd for $C_{26}H_{44}NaOSi$, 423.3059; found, 423.3063.

Compound **23**: $[\alpha]_D^{25}$ +49.8 (*c* 0.7, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ: 0.92 (3H, s), 0.95 (3H, s), 1.18 (3H, s), 1.07 (1H, ddd, $J = 13.5$, 13.5, 4.1 Hz), 1.32 (1H, dd, $J = 12.4$, 2.2 Hz), 1.39 (1H, ddd, $J = 13.0$, 13.0, 3.7 Hz), 1.48 (1H, br d, $J = 13.2$ Hz), 1.61 (1H, m), 1.67 (1H, m), 1.75 (1H, dt, $J = 13.8$, 3.4 Hz), 1.84 (1H, m), 2.21 (1H, br d, $J = 12.5$ Hz), 2.75 (1H, ddd, $J = 16.9$, 11.3, 7.2 Hz), 2.82 (1H, ddd, $J = 16.9$, 7.0, 1.7 Hz), 3.85 (3H, s), 5.37 (1H, s), 6.58 (1H, s), 6.74 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 39.4 (C-1), 19.3 (C-2), 41.9 (C-3), 33.6 (C-4), 50.8 (C-5), 19.6 (C-6), 30.1 (C-7), 128.4 (C-8), 142.1 (C-9), 37.8 (C-10), 107.2 (C-11), 143.4 (C-12), 144.9 (C-13), 114.4 (C-14), 33.5 (C-15), 25.1 (C-16), 21.8 (C-17), 56.3 (O*CH*$_3$). HRMS (FAB) *m/z* calcd for $C_{18}H_{26}NaO_2$, 297.1830; found, 297.1838.