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# Total synthesis of HM-1 and HM-2, aromatic sesquiterpenes isolated from the phytopathogenic fungus *Helicobasidium mompa*. Structure revision of HM-2

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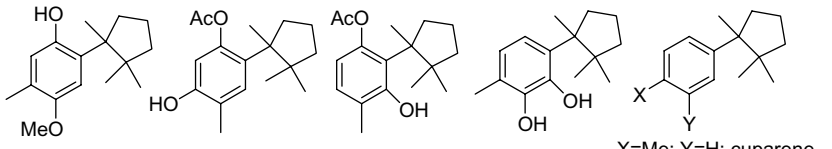
**Abstract**—The structure assigned to the sesquiterpene HM-2 was found to be incorrect by total synthesis. A ring-closing metathesis based strategy was developed for the total synthesis of the aromatic sesquiterpene HM-1, which on functional group transformation established the structure of HM-2 as **23**, a cuparene derivative.


The phytopathogenic fungus *Helicobasidium mompa* TANAKA is responsible for the violet root rot against mulberry and several other fruit trees. In the course of a study on the mechanism of violet root rot, Nohara and co-workers have investigated the fungus, and reported the isolation and structural elucidation of four aromatic sesquiterpenes from the methanolic extract of the mycelium grown with *H. mompa*, which was obtained from infected mulberry roots.[1] Of the four sesquiterpenes, two, HM-1 (**1**) and HM-4 (**4**), were found to belong to the cuparene class, whereas the structures of the remaining two, HM-2 (**2**) and HM-3 (**3**), were assigned as herbertanes on the basis of 1 and 2D NMR spectroscopy. Based on preliminary observations, it was speculated that all compounds **1**–**4** possessed antioxidant as well as antibiotic activities similar to those of the higher oxygenated analogues, the lagopodins.[1] Since herbertanes are considered as chemical markers of the liverworts belonging to the genus *Herberta*,[2] and as there was no report on the synthesis of compounds **1**–**4**,[3] in order to establish the structure of HM-2 as a herbertene, we carried out the total synthesis of HM-2, which established that the putative structure **2** is incorrect. Herein, we describe our studies on the synthesis of the compound having structure **2** and the assignment of a new structure for HM-2 via total synthesis of the natural products HM-1 and HM-2.



**1** (HM-1) **2** (HM-2) **3** (HM-3) **4** (HM-4)

For the synthesis of the putative structure **2** of HM-2 and HM-1 **1**, a ring-closing metathesis (RCM) reaction was envisaged (Scheme 1). It was contemplated that the RCM reaction of the diene ester **5** followed by alkylation and functional group manipulation of the resultant cyclopentenes **6** would lead to the target molecules. Claisen rearrangement of the allyl alcohol **7** followed by allylation of the pentenoate **8** was conceived for the generation of the diene ester **5**. Accordingly, the sequence was started with the appropriate acetophenone

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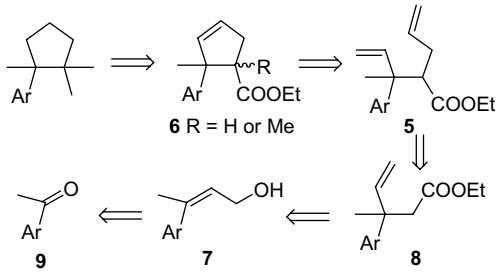
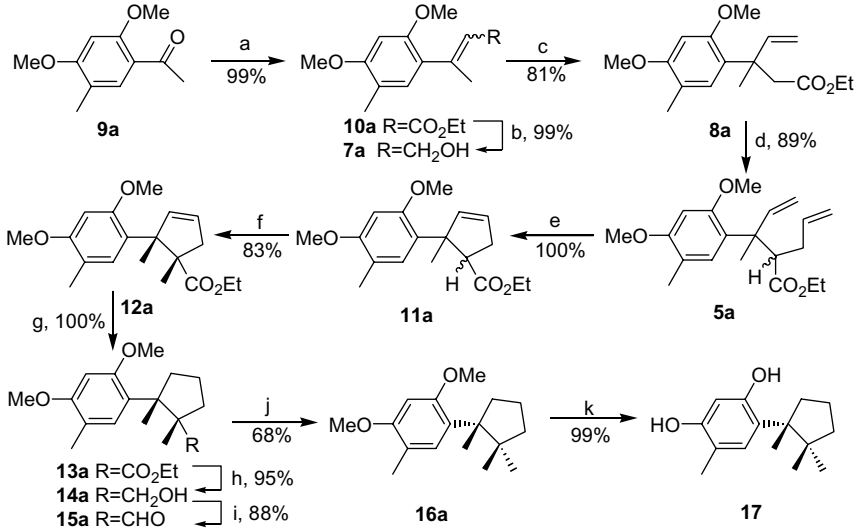
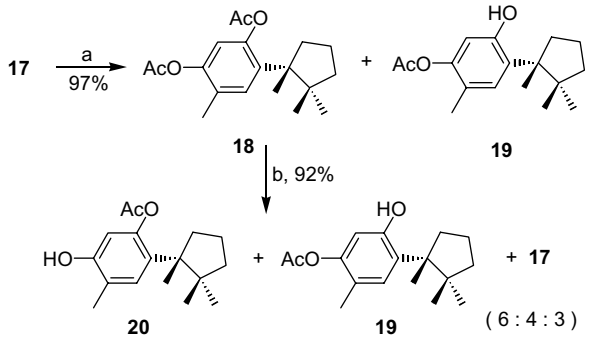



**Scheme 1.**

**9a** (Scheme 2). Thus, Horner–Wadsworth–Emmons reaction of 2,4-dimethoxy-5-methylacetophenone[4] **9a** with triethyl phosphonoacetate and sodium hydride followed by low temperature reduction of the resultant cinnamate **10a** with lithium aluminium hydride (LAH) furnished the cinnamyl alcohol **7a** in excellent yield. Johnson et al's orthoester variant[5] of the Claisen rearrangement was employed for the generation of the γ,δ-unsaturated ester containing the first quaternary carbon. Thermal activation of the cinnamyl alcohol **7a** with triethyl orthoacetate and a catalytic amount of propionic acid in a sealed tube furnished the pentenoate **8a** in 81% yield. Generation of the lithium enolate of the ester **8a** with lithium diisopropylamide (LDA) followed by treatment with allyl bromide furnished a 2:1 diastereomeric mixture of the diene ester **5a** in 89% yield. Since both diastereomers would be converged at a later stage via the enolates, no attempt was made to separate the diastereomers. RCM reaction of the diene ester **5a** in methylene chloride with 5 mol% of Grubbs' first generation catalyst[6] generated the cyclopentenecarboxylate **11a** in almost quantitative yield. Generation of the enolate of the ester **11a** with LDA in THF and HMPA followed by treatment with methyl iodide created the second quaternary carbon in a highly stereoselective manner via the approach of the electrophile from the less hindered face of the enolate to give ester **12a** in 83% yield.[13] Hydrogenation of the olefin **12a** with 10% palladium on carbon as the catalyst quantitatively furnished the ester **13a**. A three-step protocol was employed for the conversion of the ester into a methyl group. Thus, reduction of the ester **13a** with LAH followed by oxidation of the resultant primary alcohol **14a** with pyridinium chlorochromate (PCC) and silica gel in methylene chloride furnished the aldehyde **15a**. Huang–Minlon reduction of the aldehyde with hydrazine hydrate and potassium hydroxide in digol transformed the aldehyde **15a** into herbertene-1,3-diol dimethyl ether **16a**. Boron tribromide mediated cleavage of the methyl ethers in **16a**, however, failed to generate the herbertenediol **17**, and produced only the cleaved product, 4-methylresorcinol. Hence, demethylation was carried out using a Grignard reagent. Thus, refluxing a xylene solution of the dimethyl ether **16a** with methylmagnesium iodide quantitatively furnished herbertene-1,3-diol **17**. Since the acetate moiety is on the relatively hindered hydroxy group in compound **2**, diacetylation followed by partial hydrolysis was explored (Scheme 3). Thus, reaction of the diol **17** with pyridine and acetic anhydride in methylene chloride for 4 h furnished an easily separable 8:1 mixture of the diacetate **18** and the monoacetate **19**. On the other hand longer reaction times exclusively furnished the diacetate **18**.[13] Partial cleavage of the diacetate **18** with LAH furnished a 6:4:3 mixture of the monoacetates[13] **20** and **19** and the diol **17**, which were separated by column chromatography on silica gel. The $^1$H NMR spectra of the two monoacetates **19** and **20**, however, were found to be different from that reported[7] for HM-2, which clearly established that the proposed structure needed to be revised.




**Scheme 2.** Reagents and conditions: (a) $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF, reflux, 8 h; (b) LAH, $Et_2O$, −70 → −40 °C, 2 h; (c) $CH_3C(OEt)_3$, $EtCO_2H$, sealed tube, 180 °C, 48 h; (d) LDA, THF; allyl bromide, −70 °C → rt, 8 h; (e) 5 mol% $PhCH{=}Ru(Cl)_2(PCy_3)_2$, $CH_2Cl_2$, rt, 4 h; (f) LDA, THF–HMPA, $CH_3I$, −30 °C → rt, 8 h; (g) $H_2$, 10% Pd–C, EtOH, 3 h; (h) LAH, $Et_2O$, 0 °C, 0.5 h; (i) PCC, silica gel, $CH_2Cl_2$, rt, 1 h; (j) $NH_2NH_2{\cdot}H_2O$, KOH, digol, 190 °C, 12 h; (k) MeMgI, xylene, reflux, 12 h.

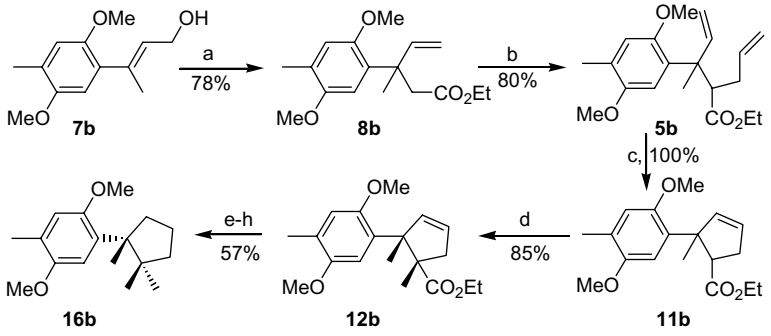



**Scheme 3.** Reagents and conditions: (a) $Ac_2O$, py, $CH_2Cl_2$, 4 h, rt, **18**:**19** 8:1; 12 h, only **18**; (b) LAH (2.3 M), THF, 0 °C, 5 min.

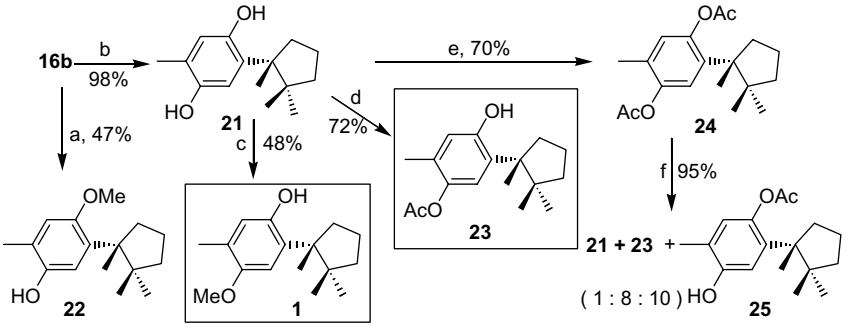
It was reasoned that HM-2 might be a derivative of cuparene like HM-1 and HM-4 and an acetate analogue of HM-1 was considered as a possibility. To test the validity of this hypothesis, synthesis of cuparene-1,4-diol **21** and its conversion to monomethyl ethers (for HM-1) and monoacetates (for HM-2) was undertaken (Schemes 4 and 5). Thus, orthoester Claisen rearrangement of the cinnamyl alcohol[8] **7b** followed by allylation of the resultant pentenoate **8b** furnished the diene ester **5b**. RCM reaction of **5b** followed by methylation of the resultant cyclopentenecarboxylate **11b** generated the ester **12b**. Catalytic hydrogenation of **12b** followed by a three-step conversion of the ester into a methyl group generated the HM-1 methyl ether[3] **16b**.

Cleavage of the methyl ethers in **16b** with boron tribromide furnished cuparene-1,4-diol[9,13] **21**. On the other hand selective cleavage of the less hindered methyl ether with 1 equiv of boron tribromide transformed **16b** into the monomethyl ether **22**,[13] which is isomeric to HM-1. Controlled methylation of the less hindered alcohol in cuparenediol **21** with potassium carbonate and methyl iodide in acetone furnished HM-1 **1**.[10] In contrast, acetylation of diol **21** with equiv of acetic anhydride and pyridine in methylene chloride furnished the monoacetate **23**,[13] whereas with an excess of $Ac_2O$ diacetate **24** was obtained.[10,13] Controlled cleavage of **24** with LAH furnished the monoacetate **25**,[13] along with the diol **21** and the monoacetate **23**. Synthetic HM-1 exhibited $^1$H NMR spectral data identical to that reported[1] for the natural product. The $^1$H NMR spectral data of the monoacetate **23** was found to be identical to that reported for HM-2,[1] which established the structure of the natural product HM-2 as cuparene derivative **23**.

In summary, we have accomplished an efficient total synthesis of the putative structure **2** of HM-2 and proved that the structure needs revision. We reasoned it to be a cuparene derivative. To substantiate further, the total synthesis of cuparene-1,4-diol **21** and its conversion to a monomethyl ether and several monoacetates was accomplished. This established the structure of HM-2 as **23**, and confirmed the structure of HM-1 as **1**.[12] A combination of a Claisen rearrangement, a RCM reaction and an alkylation was strategically




**Scheme 4.** Reagents and conditions: (a) $CH_3C(OEt)_3$, $EtCO_2H$, sealed tube, 180 °C, 48 h; (b) LDA, THF, allyl bromide, −70 °C → rt, 8 h; (c) 5 mol% $PhCH{=}Ru(Cl)_2(PCy_3)_2$, $CH_2Cl_2$, rt, 5 h; (d) LDA, THF–HMPA, $CH_3I$, −30 °C → rt, 12 h; (e) $H_2$, 10% Pd–C, EtOH, 3 h; (f) LAH, $Et_2O$, 0 °C, 20 min; (g) PCC, silica gel, $CH_2Cl_2$, rt, 1 h; (h) $NH_2NH_2{\cdot}H_2O$, KOH, digol, sealed tube 190 °C, 12 h.




**Scheme 5.** Reagents and conditions: (a) $BBr_3$ (1 equiv), $CH_2Cl_2$, −70 °C → rt, 2 h; (b) $BBr_3$ (excess), $CH_2Cl_2$, −70 °C → rt, 2 h; (c) $K_2CO_3$, acetone, MeI, rt, 6 h;[10] (d) $Ac_2O$ (1 equiv), py, $CH_2Cl_2$, rt, 8 h;[10] (e) $Ac_2O$ (excess), py, $CH_2Cl_2$, rt, 8 h;[10] (f) LAH, THF, 0 °C, 5 min.

employed for the construction of cyclopentanes containing two vicinal quaternary carbon atoms. Extension of this methodology for the synthesis of HM-3, HM-4 and oxygenated lagopodin analogues, for evaluating their biological potential, is currently in progress.

## Acknowledgement

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## References and notes

1. Kajimoto, T.; Yamashita, M.; Imamura, Y.; Nohara, T.; Shibata, M. *Chem. Lett.* **1989**, 527–530.
2. Irita, H.; Hashimoto, T.; Fukuyama, Y.; Asakawa, Y. *Phytochemistry* **2000**, *55*, 247–253.
3. To the best of our knowledge there is no report on the syntheses of HM-1 to 4. Synthesis of HM-1 methyl ether has been reported, but its conversion to HM-1 was not described, hence, the structure of HM-1 was also not confirmed until now. See: Paul, T.; Pal, A.; Gupta, P. D.; Mukherjee, D. *Tetrahedron Lett.* **2003**, *44*, 737–740; Srikrishna, A.; Rao, M. S. *Synlett* **2004**, 374–376.
4. Singh, C.; Kachru, C. N. *Indian J. Appl. Chem.* **1971**, *34*, 273–276.
5. Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T. T.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741–743.
6. (a) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450; (b) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3013–3043; (c) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29.
7. Even though signals due to methyl groups in the monoacetate **19** are in close agreement with those of HM-2, considerable difference is present for the signals due to aromatic protons, for example, for the two aromatic protons $\Delta\delta$ reported for HM-2 is 0.36; $\Delta\delta$ found in **19** is 0.69.
8. Fuganti, C.; Serra, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3758–3764.
9. Toyota, M.; Koyama, H.; Asakawa, Y. *Phytochemistry* **1997**, *46*, 145–150.
10. The cuparene-1,4-diol **21** was found to be very sensitive and readily undergoes oxidation to cuparene-1,4-quinone.[9,11] As a result, a significant amount (≈30%) of cuparene-1,4-quinone formation was observed in the acetylation and methylation reactions of cuparene-1,4-diol **21**.
11. Asakawa, Y.; Kondo, K.; Tori, M. *Phytochemistry* **1991**, *30*, 325–328.
12. Revision of the structure of HM-2 as a cuparene derivative, raises doubts about the structure of HM-3 as herbertene. It may also be a cuparene, such as the monoacetate of HM-4.
13. Yields refer to isolated and chromatographically pure compounds. All the compounds exhibited spectral data (IR, $^1$H and $^{13}$C NMR and mass) consistent with their structures. Selected spectral data for ethyl *cis*-1,2-dimethyl-2-(2,4-dimethoxy-5-methylphenyl)cyclopent-3-enecarboxylate **12a**: IR (neat): $\nu_{max}/cm^{-1}$ 1722, 1611, 1586; $^1$H NMR (300 MHz, $CDCl_3$+$CCl_4$): $\delta$ 6.88 (1H, s), 6.31 (1H, s), 5.77 (1H, dt, *J* 5.7 and 2.4 Hz), 5.71 (1H, dt, *J* 5.7 and 2.1 Hz), 3.77 (6H, s), 3.42 and 3.33 (2H, q of AB q, *J* 11.7 and 6.9 Hz), 2.99 (1H, dt, *J* 16.5 and 2.4 Hz), 2.24 (1H, dt, *J* 16.5 and 2.1 Hz), 2.06 (3H, s), 1.48 (3H, s), 1.46 (3H, s), 0.82 (3H, t, *J* 6.9 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$+$CCl_4$): $\delta$ 176.4 (C), 157.7 (C), 156.8 (C), 139.6 (CH), 130.9 (CH), 126.6 (CH), 125.0 (C), 116.5 (C), 95.6 (CH), 59.6 ($CH_2$), 58.3 (C), 55.6 (C), 55.2 ($CH_3$), 55.1 ($CH_3$), 46.0 ($CH_2$), 23.5 ($CH_3$), 21.3 ($CH_3$), 15.3 ($CH_3$), 13.6 ($CH_3$); HRMS: *m*/*z* calcd for $C_{19}H_{26}O_4Na$ (M+Na): 341.1729. Found: 341.1747. 3-Acetyloxy-6-methyl-4-(1,2,2-trimethylcyclopentyl)phenyl acetate **18**: IR (neat): $\nu_{max}/cm^{-1}$ 1764; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.21 (1H, s), 6.67 (1H, s), 2.60–2.47 (1H, m), 2.27 (3H, s), 2.26 (3H, s), 2.14 (3H, s), 1.80–1.47 (5H, m), 1.28 (3H, s), 1.13 (3H, s), 0.73 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 168.7 (C), 168.0 (C), 147.3 (C), 147.1 (C), 135.8 (C), 131.3 (CH), 126.2 (C), 117.8 (CH), 50.9 (C), 45.3 (C), 40.5 ($CH_2$), 38.9 ($CH_2$), 26.7 ($CH_3$), 25.2 ($CH_3$), 23.4 ($CH_3$), 21.8 ($CH_3$), 20.8 ($CH_3$), 20.2 ($CH_2$), 16.4 ($CH_3$); Mass: *m*/*z* 318 ($M^+$, 12%), 276 (40), 234 (65), 219 (12), 206 (18), 193 (11), 177 (21), 164 (100), 151 (67), 137 (11), 110 (23); HRMS: *m*/*z* calcd for $C_{19}H_{26}O_4Na$ (M+Na): 341.1729. Found: 341.1730. 5-Acetyloxy-4-methyl-2-(1,2,2-trimethylcyclopentyl)phenol **19**: IR (neat): $\nu_{max}/cm^{-1}$ 3336, 1721, 1609, 1515; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.10 (1H, s), 6.41 (1H, s), 4.91 (1H, s), 2.62–2.51 (1H, m), 2.29 (3H, s), 2.08 (3H, s), 1.82–1.45 (5H, m), 1.38 (3H, s), 1.16 (3H, s), 0.75 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 169.3 (C), 153.0 (C), 147.2 (C), 131.5 (CH), 131.2 (C), 120.4 (C), 110.2 (CH), 50.7 (C), 44.7 (C), 41.1 ($CH_2$), 39.5 ($CH_2$), 26.9 ($CH_3$), 25.5 ($CH_3$), 22.8 ($CH_3$), 20.9 ($CH_3$), 20.3($CH_2$), 15.7 ($CH_3$). 5-Acetyloxy-2-methyl-4-(1,2,2-trimethylcyclopentyl)phenol **20**: IR (neat): $\nu_{max}/cm^{-1}$ 3293, 1723; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.14 (1H, s), 6.40 (1H, s), 4.92 (1H, br s), 2.60–2.45 (1H, m), 2.29 (3H, s), 2.19 (3H, s), 1.82–1.45 (5H, m), 1.26 (3H, s), 1.11 (3H, s), 0.71 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 170.2 (C), 151.9 (C), 147.4 (C), 131.6 (CH), 130.1 (C), 120.8 (C), 110.4 (CH), 50.4 (C), 45.1 (C), 40.2 ($CH_2$), 38.7 ($CH_2$), 26.4 ($CH_3$), 24.9 ($CH_3$), 23.4 ($CH_3$), 21.8 ($CH_3$), 20.0 ($CH_2$), 15.7 ($CH_3$). 5-Methyl-2-(1,2,2-trimethylcyclopentyl)benzene-1,4-diol **21**: IR (neat): $\nu_{max}/cm^{-1}$ 3386; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 6.74 (1H, s), 6.46 (1H, s), 4.49 (1H, s), 4.41 (1H, s), 2.60–2.45 (1H, m), 2.15 (3H, s), 1.80–1.50 (5H, m), 1.38 (3H, s), 1.16 (3H, s), 0.76 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 148.2 (C), 146.8 (C), 132 (C), 121.9 (C), 119.1 (CH), 116.2 (CH), 50.8 (C), 44.7 (C), 41.1 ($CH_2$), 39.4 ($CH_2$), 26.9 ($CH_3$), 25.4 ($CH_3$), 22.9 ($CH_3$), 20.2 ($CH_2$), 15.1 ($CH_3$); Mass: *m*/*z* 234 ($M^+$, 30%), 164 (58), 151 (100), 137 (14). 4-Acetoxy-5-methyl-2-(1,2,2-trimethylcyclopentyl)phenyl acetate **24**: IR (neat): $\nu_{max}/cm^{-1}$ 1762; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.06 (1H, s), 6.82 (1H, s), 2.54–2.40 (1H, m), 2.30 (3H, s), 2.29 (3H, s), 2.12 (3H, s), 1.80–1.45 (5H, m), 1.28 (3H, s), 1.12 (3H, s), 0.74 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 169.7 (C), 169.1 (C), 146.5 (C), 146.1 (C), 137.2 (C), 128.4 (C), 126.0 (CH), 122.9 (CH), 50.8 (C), 45.2 (C), 40.1 ($CH_2$), 38.5 ($CH_2$), 26.3 ($CH_3$), 24.8 ($CH_3$), 23.2 ($CH_3$), 21.8 ($CH_3$), 20.8 ($CH_3$), 19.9 ($CH_2$), 15.6 ($CH_3$); Mass: *m*/*z* 318 ($M^+$, 10%), 276 (24), 234 (100), 220 (14), 206 (9), 178 (13), 164 (61), 151 (45); HRMS: *m*/*z* calcd for $C_{19}H_{26}O_4Na$ (M+Na): 341.1729. Found: 341.1729. 4-Acetoxy-5-methyl-2-(1,2,2-trimethylcyclopentyl)phenol **23** (revised HM-2): IR (neat): $\nu_{max}/cm^{-1}$ 3461, 1731; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 6.89 (1H, s), 6.52 (1H, s), 4.76 (1H, s), 2.60–2.40 (1H, m), 2.29 (3H, s), 2.07 (3H, s), 1.85–1.45 (5H, m), 1.39 (3H, s), 1.15 (3H, s), 0.76 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 169.7 (C), 152.0 (C), 142.3 (C), 131.9 (C), 128.1 (C), 122.6 (CH),118.8 (CH), 50.8 (C), 44.8 (C), 41.0 ($CH_2$), 39.3 ($CH_2$), 26.8 ($CH_3$), 25.4 ($CH_3$), 22.7 ($CH_3$), 20.8 ($CH_3$), 20.2 ($CH_2$), 15.5 ($CH_3$); Mass: *m*/*z* 276 ($M^+$, 23%), 234 (100), 177 (18),

164 (74), 163 (25), 152 (25), 151 (82); HRMS: *m*/*z* calcd for $C_{17}H_{24}O_3Na$ (M+Na): 299.1623. Found: 299.1628. 4-Acetoxy-2-methyl-5-(1,2,2-trimethylcyclopentyl)phenol **25**: IR (neat): $\nu_{max}/cm^{-1}$ 3430, 1729; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 6.84 (1H, s), 6.70 (1H, s), 4.64 (1H, s), 2.55–2.40 (1H, m), 2.28 (3H, s), 2.17 (3H, s), 1.80–1.45 (5H, m) 1.26 (3H, s), 1.12 (3H, s), 0.73 (3H, s); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 170.4 (C), 150.7 (C), 142.5 (C), 137.2 (C), 125.9 (CH), 122.1 (C), 115.8 (CH), 50.8 (C), 45.1 (C), 40.2 ($CH_2$), 38.6 ($CH_2$), 26.4 ($CH_3$), 24.9 ($CH_3$), 23.2 ($CH_3$), 21.8 ($CH_3$), 20.0 ($CH_2$), 15.2 ($CH_3$); Mass: *m*/*z* 276 ($M^+$, 19%), 234 (100), 217 (34), 164 (59), 151 (79), 137 (19); HRMS: *m*/*z* calcd for $C_{17}H_{24}O_3Na$ (M+Na): 299.1623. Found: 299.1616. 4-Methoxy-5-methyl-2-(1,2,2-trimethylcyclopentyl)phenol **1** (HM-1): IR (neat): $\nu_{max}/cm^{-1}$ 3356; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 6.80 (1H, s), 6.49 (1H, s), 4.42 (1H, s), 3.78 (3H, s), 2.66–2.50 (1H, m), 2.14 (3H, s), 1.84–1.50 (5H, m), 1.41 (3H, s), 1.18 (3H, s), 0.78 (3H, s); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 151.1 (C), 148.0 (C), 130.9 (C), 125.1 (C), 119.4 (CH), 112.5 (CH), 56.2 ($CH_3$), 51.1 (C), 44.8 (C), 40.9 ($CH_2$), 39.4 ($CH_2$), 26.8 ($CH_3$), 25.4 ($CH_3$), 23.0 ($CH_3$), 20.3 ($CH_2$), 15.3 ($CH_3$); Mass: *m*/*z* 248 ($M^+$, 62%), 178 (48), 165 (100), 151 (25), 91 (34). 4-Methoxy-2-methyl-5-(1,2,2-trimethylcyclopentyl)phenol **22**: IR (neat): $\nu_{max}/cm^{-1}$ 3372; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 6.77 (1H, s), 6.62 (1H, s), 4.25 (1H, s), 3.72 (3H, s), 2.55–2.40 (1H, m), 2.21 (3H, s), 1.80–1.45 (5H, m), 1.33 (3H, s), 1.12 (3H, s), 0.69 (3H, s); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 152.8 (C), 146.7 (C), 135.1 (C), 121.0 (C), 116.1 (CH), 114.6 (CH), 55.5 ($CH_3$), 51.0 (C), 44.2 (C), 41.8 ($CH_2$), 39.8 ($CH_2$), 27.4 ($CH_3$), 25.7 ($CH_3$), 23.0 ($CH_3$), 20.4 ($CH_2$), 15.5 ($CH_3$); Mass: *m*/*z* 248 ($M^+$, 76%), 191 (24), 178 (51), 166 (40), 165 (100), 163 (50), 151 (34), 138 (29), 91 (31).