

SUPPLEMENTARY MATERIAL

Antifungal Activity of Phenolic Monoterpenes and Structure-related Compounds against Plant Pathogenic Fungi

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The aim of this work is to explore the possibility of using the phenolic monoterpenes (PMs) as leading compounds with antifungal activity against plant disease. The *in vitro* antifungal activities of carvacrol and thymol against 7 kinds of plant pathogenic fungi were evaluated on mycelium growth rate method, and the results showed that carvacrol and thymol exhibited broad spectrum antifungal activity. Structure requirement for the antifungal activity of PMs was also investigated. The preliminary conclusion was that phenolic hydroxyl and monoterpene were basic structures for the antifungal activity of PMs, and the position of phenolic hydroxyl showed less effect. Ester derivatives of carvacrol and thymol were more effective than carvacrol and thymol against plant pathogenic fungi. We suggested that carvacrol, thymol and their ester derivatives could potentially be used as new fungicide leading compounds.

¹ These authors contributed equally to this work.

Characterization and Spectroscopy data for synthetic compounds

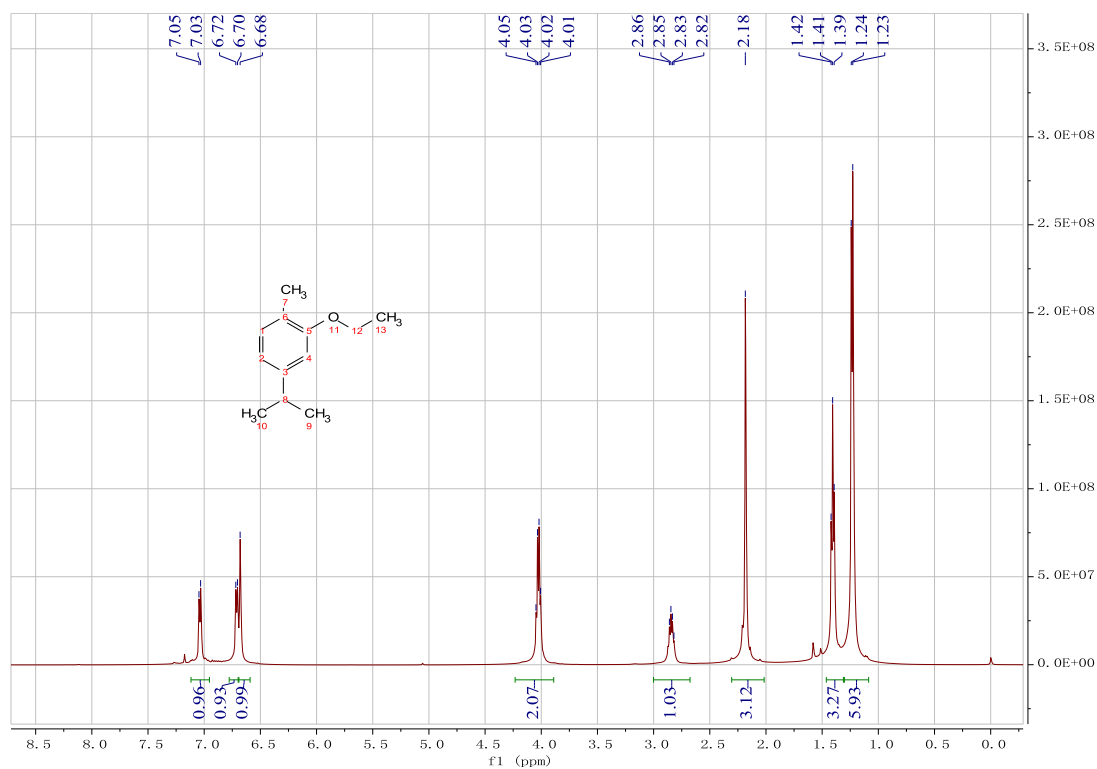
5-isopropyl-2-methylphenyl acetate (1a). Colorless oil. $^1\text{H-NMR}$ (500 MHz, CDCl_3): 7.13 (d, $J = 7.8$ Hz, 1 arom. H), 7.01 (d, $J = 7.7$ Hz, 1 arom. H), 6.86 (s, 1 arom. H), 2.87 (m, H-C(8)), 2.30 (s, $\text{CH}_3(13)$), 2.13 (s, $\text{CH}_3(7)$), 1.22 (d, $J = 6.9$ Hz, $\text{CH}_3(9, 10)$). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): 169.3 (C(12)); 149.3 (C(5)); 148.1 (C(3)); 130.9 (C(1)); 127.2 (C(6)); 124.2(C(2)); 119.8 (C(4)); 33.6 (C(8)); 23.9 (C(9, 10)); 20.8 (C(13)) 15.8 (C(7)). HR-ESI-MS: 193.1226 ($[\text{M}+\text{H}]^+$, $\text{C}_{12}\text{H}_{17}\text{O}_2^+$; calc. 193.1223).

2-ethoxy-4-isopropyl-1-methylbenzene (2a). Colorless oil. $^1\text{H-NMR}$ (500 MHz, CDCl_3): 7.04 (d, $J = 7.3$ Hz, 1 arom. H), 6.71 (d, $J = 7.4$ Hz, 1 arom. H), 6.68 (s, 1 arom. H), 4.03 (q, $J = 13.7, 6.8$ Hz, $\text{CH}_2(12)$), 2.84 (m, H-C(8)), 2.18 (s, $\text{CH}_3(7)$), 1.41 (t, $J = 6.9$ Hz, $\text{CH}_3(13)$), 1.23 (d, $J = 6.9$ Hz, $\text{CH}_3(9,10)$). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): 157.2 (C(5)); 147.9 (C(3)); 130.4 (C(1)); 124.2 (C(6)); 118.0 (C(2)); 109.7 (C(4)); 63.5 (C(12)); 34.2 (C(8)); 24.2 (C(9, 10)); 15.9 (C(7)); 15.1 (C(13)). HR-ESI-MS: 179.1429 ($[\text{M}+\text{H}]^+$, $\text{C}_{12}\text{H}_{19}\text{O}^+$; calc. 179.1430).

Synthesis of 2-isopropyl-5-methylphenyl acetate (1b). Colorless oil. $^1\text{H-NMR}$ (500 MHz, CDCl_3): 7.19 (d, $J = 7.9$ Hz, 1 arom. H), 7.02 (d, $J = 7.9$ Hz, 1 arom. H), 6.80 (s, 1 arom. H), 2.97 (m, H-C(7)), 2.31 (s, $\text{CH}_3(8, 11)$), 1.19 (d, $J = 6.9$ Hz, $\text{CH}_3(13, 14)$). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): 169.8 (C(10)); 147.9 (C(5)); 137.0 (C(6)); 136.6 (C(3)); 127.2 (C(2)); 126.5(C(1)); 122.8 (C(4)); 27.2 (C(7)); 23.1 (C(13, 14)); 21.0 (C(8)); 20.8 (C(11)). HR-ESI-MS: 193.1227 ($[\text{M}+\text{H}]^+$, $\text{C}_{12}\text{H}_{17}\text{O}_2^+$; calc. 193.1223).

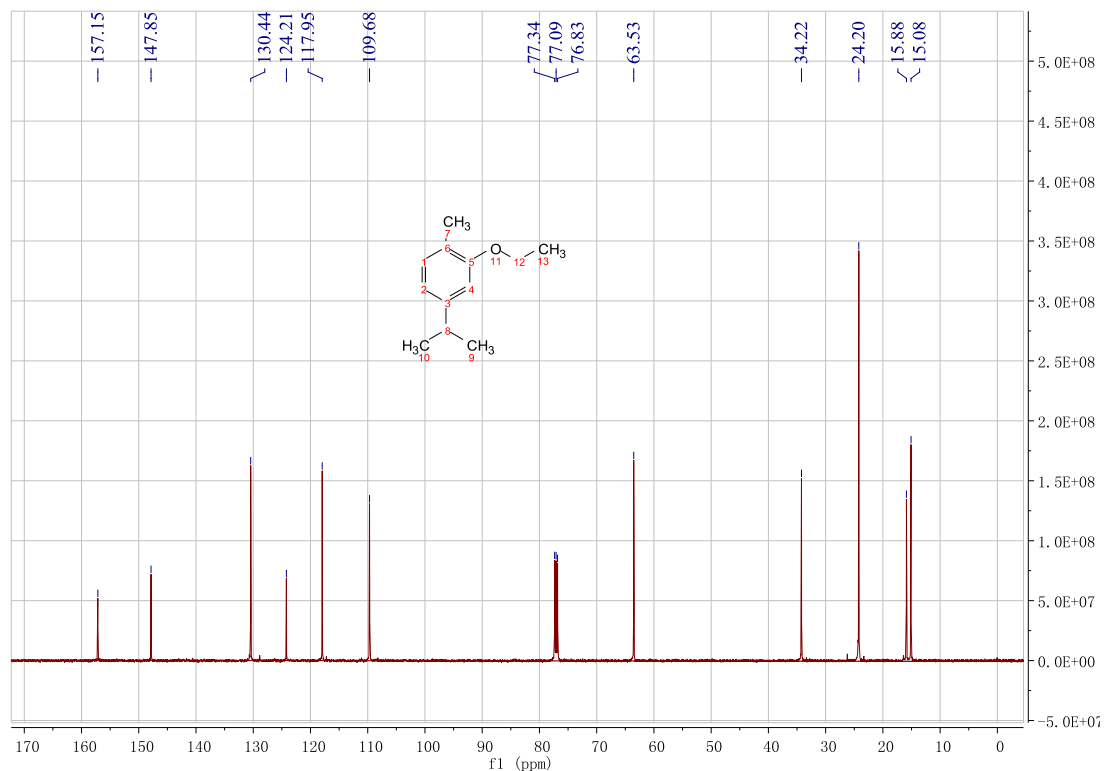
Synthesis of 4-ethoxy-2-isopropyl-1-methylbenzene (2b). Colorless oil. $^1\text{H-NMR}$ (500 MHz, CDCl_3): 7.08 (d, $J = 7.6$ Hz, 1 arom. H), 6.72 (d, $J = 7.6$ Hz, 1 arom. H), 6.65 (s, 1 arom. H), 4.01 (q, $J = 6.9$ Hz, $\text{CH}_2(10)$), 3.29 (m, H-C(7)), 2.31 (s, $\text{CH}_3(8)$), 1.41 (t, $J = 6.9$ Hz, $\text{CH}_3(11)$), 1.20 (d, $J = 6.9$ Hz, $\text{CH}_3(12, 13)$). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): 156.1 (C(5)); 136.2 (C(3)); 134.2 (C(6)); 125.9 (C(1)); 121.0 (C(2)); 112.5 (C(4)); 63.6 (C(10)); 26.7 (C(7)); 22.8 (C(12, 13)); 21.4 (C(8)); 15.1 (C(11)). HR-ESI-MS: 179.1438 ($[\text{M}+\text{H}]^+$, $\text{C}_{12}\text{H}_{19}\text{O}^+$; calc. 179.1430).

Figure S1. ^1H NMR of compound **2a**



^1H NMR (500 MHz, CDCl_3) δ 7.04 (d, $J = 7.3$ Hz, 1 arom. H), 6.71 (d, $J = 7.4$ Hz, 1 arom. H), 6.68 (s, 1 arom. H), 4.03 (q, $J = 13.7, 6.8$ Hz, $\text{CH}_2(12)$), 2.84 (m, H-C(8)), 2.18 (s, $\text{CH}_3(7)$), 1.41 (t, $J = 6.9$ Hz, $\text{CH}_3(13)$), 1.23 (d, $J = 6.9$ Hz, $\text{CH}_3(9,10)$).

Figure S2. ^{13}C NMR of compound **2a**



^{13}C NMR (125 MHz, CDCl_3): 157.2 (C(5)); 147.9 (C(3)); 130.4 (C(1)); 124.2 (C(6)); 118.0 (C(2)); 109.7 (C(4)); 63.5 (C(12)); 34.2 (C(8)); 24.2 (C(C9, C10)); 15.9 (C(7)); 15.1 (C(13))

Figure S3. HR-ESI-MS of compound 2a

08 #89 RT: 5.96 Av: 1 NL: 1.13E4
F: FIMS + c ESI Full ms [170.00-350.00]

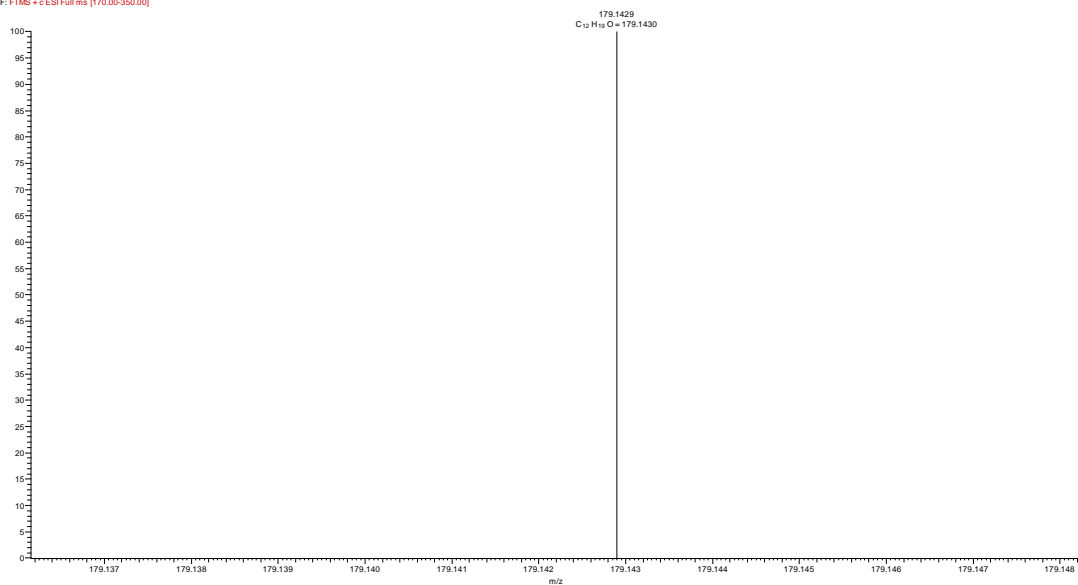
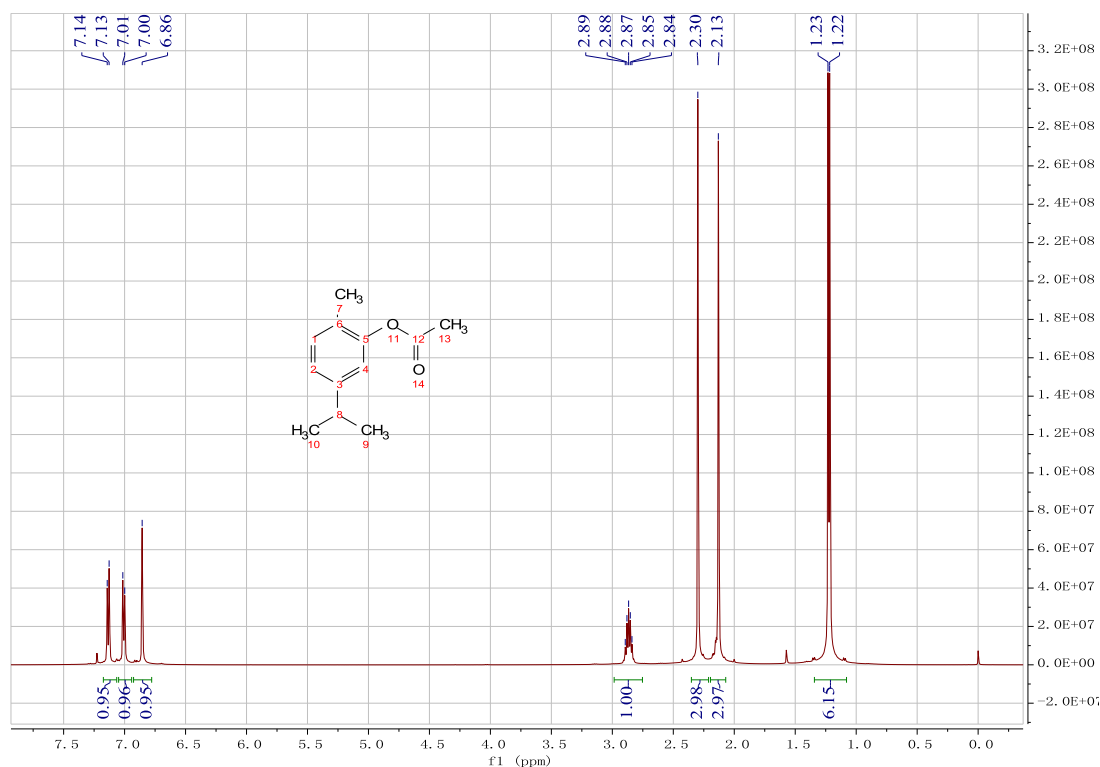
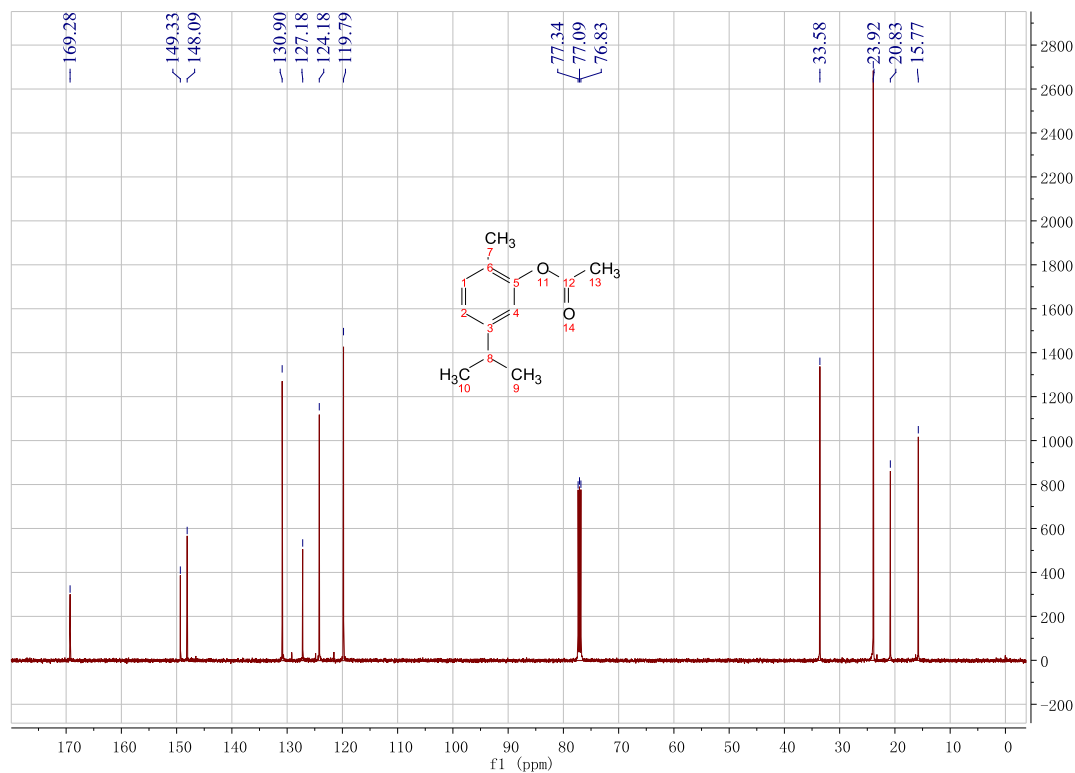


Figure S4. ^1H NMR of compound **1a**



^1H NMR (500 MHz, CDCl_3) δ 7.13 (d, $J = 7.8$ Hz, 1 arom. H), 7.01 (d, $J = 7.7$ Hz, 1 arom. H), 6.86 (s, 1 arom. H), 2.87 (m, H-C(8)), 2.30 (s, CH_3 (13)), 2.13 (s, CH_3 (7)), 1.22 (d, $J = 6.9$ Hz, CH_3 (9, 10)).

Figure S5. ^{13}C NMR of compound **1a**



^{13}C NMR (125 MHz, CDCl_3): 169.3 (C(12)); 149.3 (C(5)); 148.1 (C(3)); 130.9 (C(1)); 127.2 (C(6)); 124.2 (C(2)); 119.8 (C(4)); 33.6 (C(8)); 23.9 (C(C9, C10)); 20.8 (C(13)) 15.8 (C(7))

Figure S6. HR-ESI-MS of compound **1a**

09 #87 RT: 5.82 Av: 1 NL: 3.56E3
F: FTMS + e ESI Full ms [170.00-350.00]

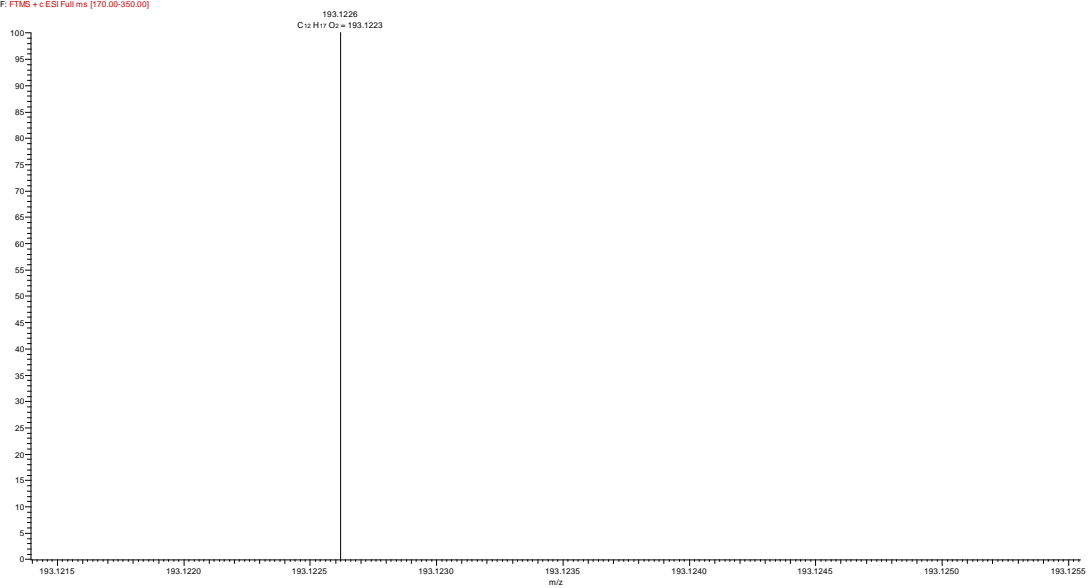
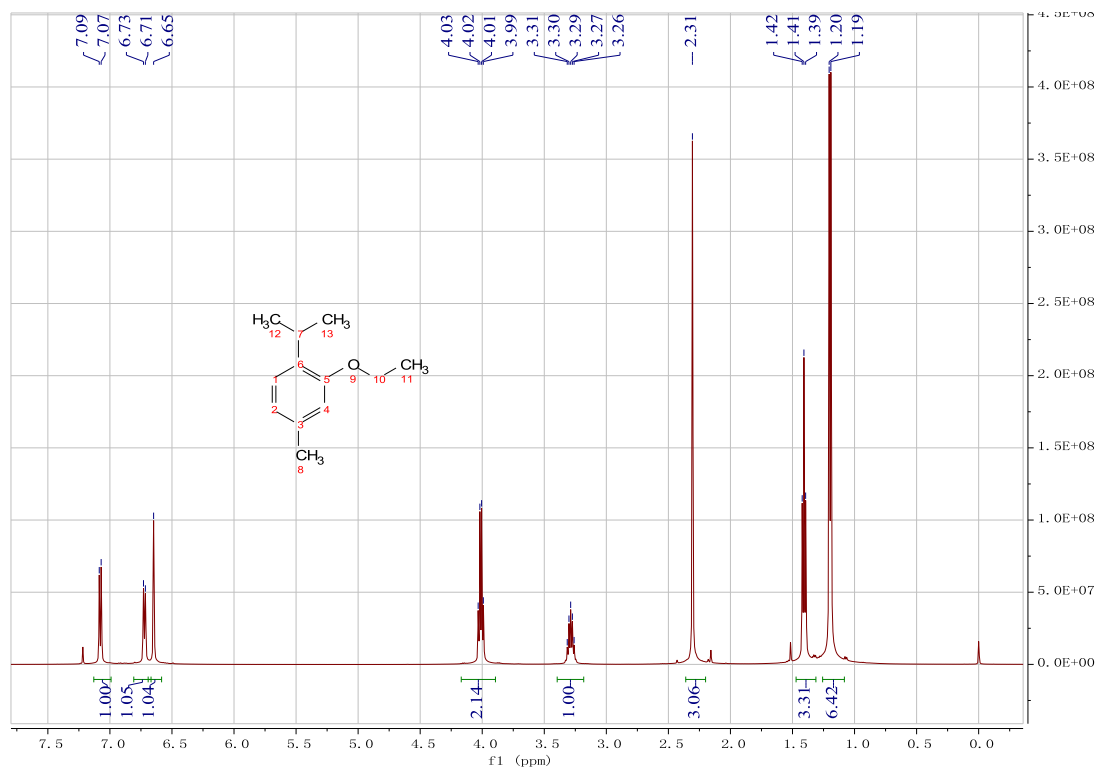
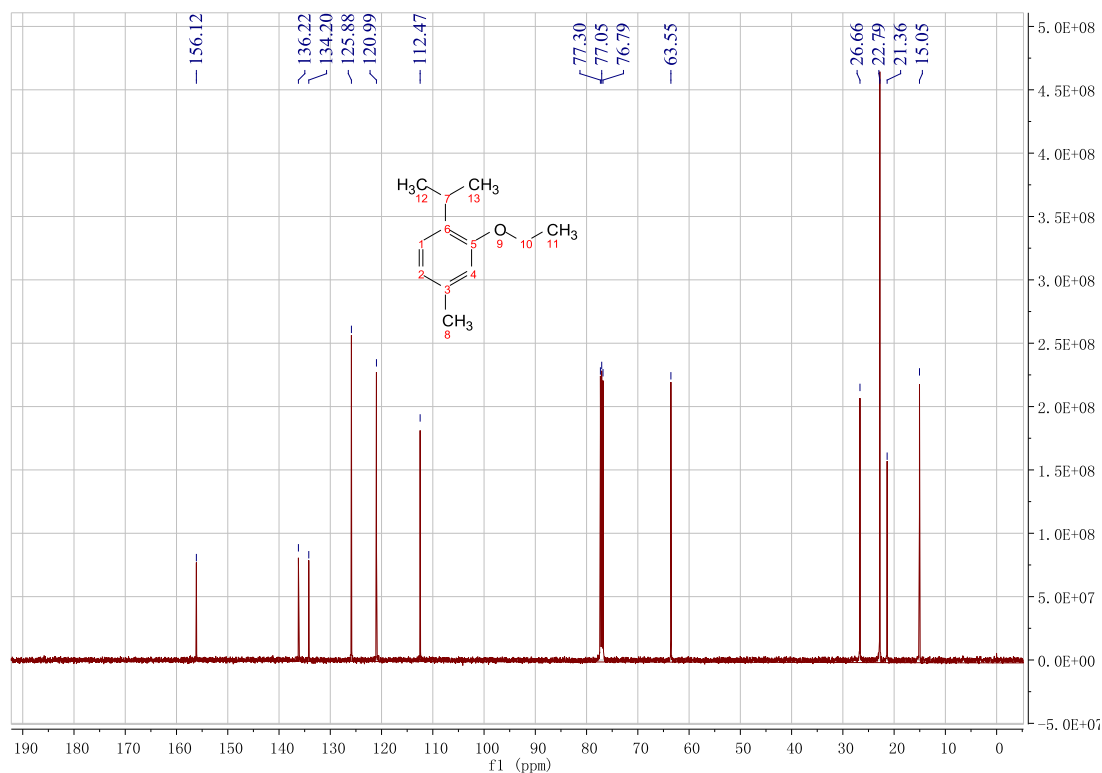


Figure S7. ^1H NMR of compound **2b**



^1H NMR (500 MHz, CDCl_3) δ 7.08 (d, $J = 7.6$ Hz, 1 arom. H), 6.72 (d, $J = 7.6$ Hz, 1 arom. H), 6.65 (s, 1 arom. H), 4.01 (q, $J = 6.9$ Hz, $\text{CH}_2(10)$), 3.29 (m, H-C(7)), 2.31 (s, $\text{CH}_3(8)$), 1.41 (t, $J = 6.9$ Hz, $\text{CH}_3(11)$), 1.20 (d, $J = 6.9$ Hz, $\text{CH}_3(12, 13)$).

Figure S8. ^{13}C NMR of compound **2b**



^{13}C NMR (125 MHz, CDCl_3): 156.1 (C(5)); 136.2 (C(3)); 134.2 (C(6)); 125.9 (C(1)); 121.0 (C(2)); 112.5 (C(4)); 63.6 (C(10)); 26.7 (C(7)); 22.8 (C(C12, C13)); 21.4 (C(8)); 15.1 (C(11))

Figure S9. HR-ESI-MS of compound **2b**

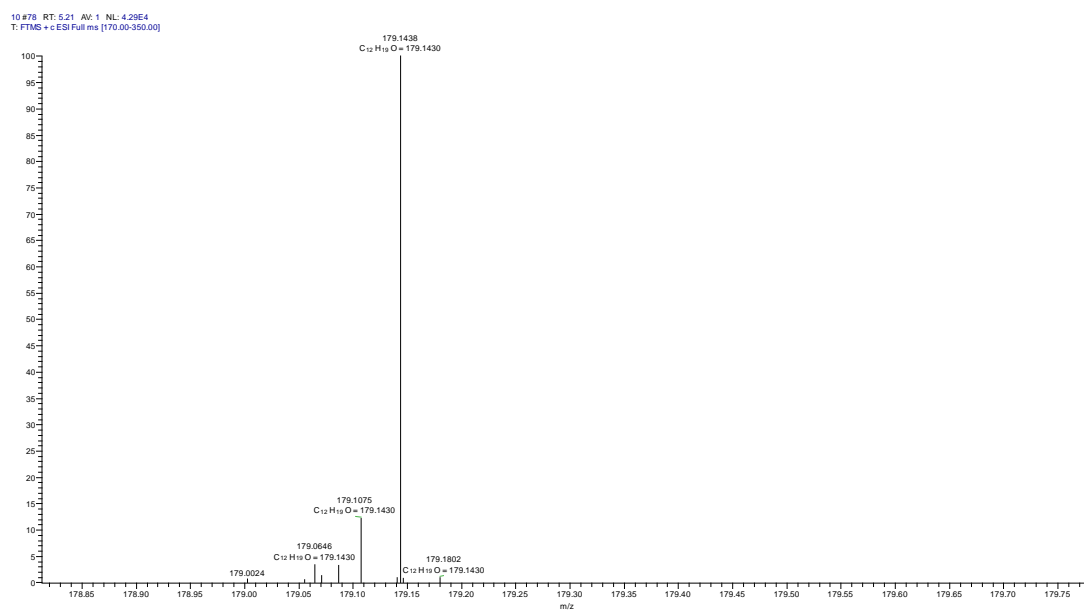
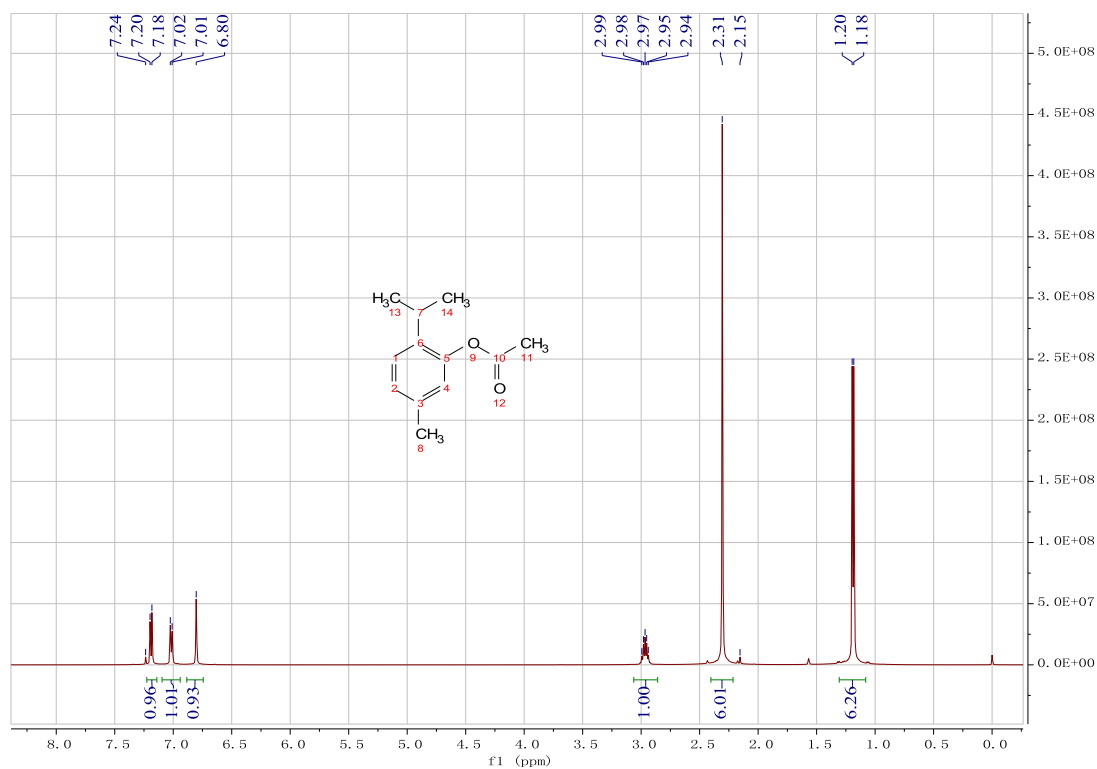
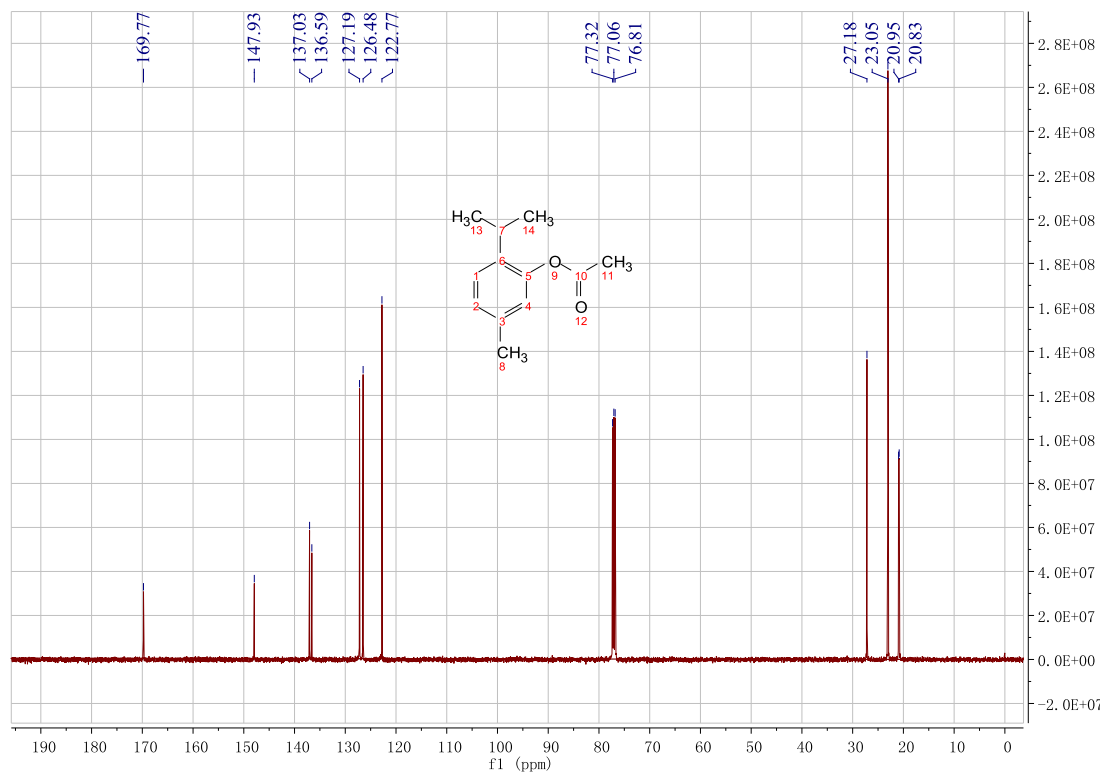


Figure S10. ^1H NMR of compound **1b**



^1H NMR (500 MHz, CDCl_3) δ 7.19 (d, $J = 7.9$ Hz, 1 arom. H), 7.02 (d, $J = 7.9$ Hz, 1 arom. H), 6.80 (s, 1 arom. H), 2.97 (m, H-C(7)), 2.31 (s, CH_3 (8, 11)), 1.19 (d, $J = 6.9$ Hz, CH_3 (13, 14)).

Figure S11. ^{13}C NMR of compound **1b**



^{13}C NMR (125 MHz, CDCl_3): 169.8 (C(10)); 147.9 (C(5)); 137.0 (C(6)); 136.6 (C(3)); 127.2 (C(2)); 126.5 (C(1)); 122.8 (C(4)); 27.2 (C(7)); 23.1 (C(C13, C14)); 21.0 (C(8)); 20.8 (C(11))

Figure S12. HR-ESI-MS of compound **1b**

