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An unusual novel triterpenoid ether, multiflor-7-en-12,13-ether and a new multiflor-7-en-12α-ol from *Wattakaka volubilis*[†]

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Abstract—A new multiflor-7-en-12α-ol (**1**) and a novel multiflor-7-en-12,13-ether (**2**) triterpenoid were isolated from the leaves of *Wattakaka volubilis* and their structures were established by means of spectroscopic analysis. © 2002 Elsevier Science Ltd. All rights reserved.

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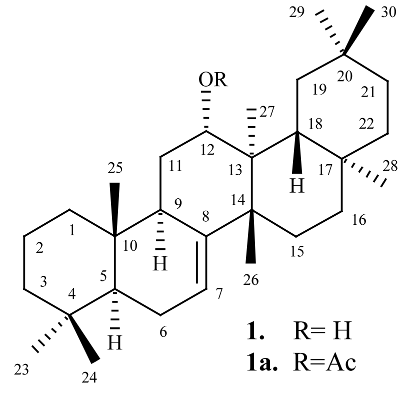
1. Introduction

The *Wattakaka* genus belongs to the Asclepiadaceae family. The alcoholic extract of the plant *Wattakaka volubilis* is widely used in India as a traditional medicine in the application for boils and abscesses.[1] During the course of our chemotaxonomic studies on medicinal plants of the Indian system of medicine (ISM),[2,3] a detailed chemical investigation of the *W. volubilis* Linn., afforded multiflor-7-en-12α-ol (**1**) and a novel triterpenoid, multiflor-7-en-12,13-ether (**2**) (Fig. 1).

Multiflor-7-en-12α-ol (**1**) was isolated as a solid and its molecular formula $C_{30}H_{50}O$ was established by High Resolution Electron Impact Mass Spectrum (HREIMS), m/z 426.3865 (calc. 426.3861), which requires six degrees of unsaturation. The IR spectrum showed a band at 3485 cm^{-1} due to the presence of a hydroxyl group, which formed a mono acetate (**1a**) on acetylation with Ac_2O/pyridine. The ^1H NMR spectrum of **1** displayed signals due to eight tertiary methyls at δ 0.82 (3H, s, H_3-23), 0.80 (3H, s, H_3-24), 0.95 (3H, s, H_3-25), 0.97 (3H, s, H_3-26), 1.09 (3H, s, H_3-27), 0.92 (3H, s, H_3-28) and 0.90 (6H, s, H_3-29 and H_3-30), a trisubstituted vinylic proton at δ 5.53 (1H, dd, J=3.1, 8.1 Hz, H-7) and an equatorial hydroxy methine proton at δ 3.19 (1H, dd, J=4.7, 11.2 Hz, H-12). The low-resolution mass spectrum showed diagnostic[4] peaks (Chart 1) at m/z 204 and m/z 218, suggesting that the compound has the multiflorene skeleton with a hydroxyl group located in the C-ring system of the molecule. The formation of base peak ions at m/z 204 is considered to



1. R= H
1a. R=Ac

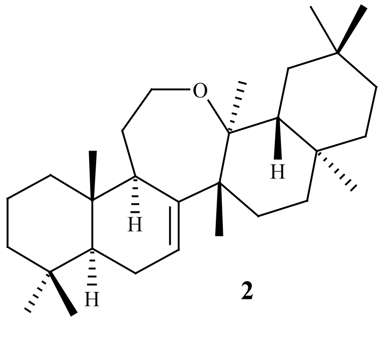


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Figure 1.

Keywords: Asclepiadaceae; multiflor-7-en-12α-ol; multiflor-7-en-12,13-ether; triterpenoids; *Wattakaka volubilis*.

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be formally initiated by cleavage[4] of the C(8)–C(14) and C(12)–C(13) bonds. Other significant fragment ions at *m*/*z* 302, 287 and 269 were observed in the Electron Impact Mass Spectrum (EIMS) and are shown in Chart 2.

The structure was also supported by a Total Correlation Spectroscopy (TOCSY) spectrum (Fig. 2), which showed the correlation of the C-12 methine proton at δ 3.19 with C-11 at δ 1.59 (2H, dd, $J=2.4$, 5.5 Hz), which in turn correlated with C-9 at δ 0.99 (1H, d, $J=3.3$ Hz). Further, the trisubstituted olefinic proton at C-7 (δ 5.53) showed a correlation with C-6 at δ 1.63 (2H, d, $J=5.9$ Hz), which in turn correlated with C-5 at δ 1.92 (1H, dd, $J=2.8$, 14.7 Hz). These spectroscopic data indicated that the hydroxyl group is located at C-12 and the double bond at C-7. The α orientation of the 12-hydroxyl group of **1** was also indicated by nuclear Overhauser effect spectroscopy (NOESY), due to the cross-peaks observed between H-12β (δ 3.19) and H-18β (δ 0.75); H-12β and H_3-26β (δ 0.97); and other cross-peaks observed between H_3-24β (δ 0.80) and H_3-25β (δ 0.95); H-5α (δ 1.92) and H-9α (δ 0.99); H_3-26β and H-18β and H_3-27α (δ 1.09) and H_3-28α (δ 0.92). Thus, compound **1** was established as multiflor-7-en-12α-ol.

The molecular formula of **2** was established as $C_{30}H_{50}O$ by HREIMS (M^+) at *m*/*z* 426.3855 (calc. 426.3861). In the IR spectrum no hydroxyl stretching bands were observed. Its ^{1}H NMR spectrum exhibited signals for eight tertiary methyl groups at δ 0.77 (3H, s, H_3-23), 0.80 (3H, s, H_3-24), 1.07 (3H, s, H_3-25), 0.95 (3H, s, H_3-26), 1.24 (3H, s, H_3-27), 0.94 (3H, s, H_3-28), 0.89 (3H, s, H_3-29) and 0.91 (3H, s, H_3-30), a trisubstituted vinylic proton at δ 5.5 (1H, dd, $J=2.8$, 7.9 Hz) and geminal protons for a –CH_2-O- grouping at δ 3.45 (1H, d, $J=5.3$ Hz, H_α-12), 3.09 (1H, dd, $J=6.6$, 14.5 Hz, H_β-12). The ^{13}C NMR spectrum exhibited 30 carbons, which included the presence of two oxygenated carbons at δ 77.08 (t) and 78.32 (s), and a trisubstituted double bond at δ 116.0 (d) and 157.57 (s), respectively. Com-

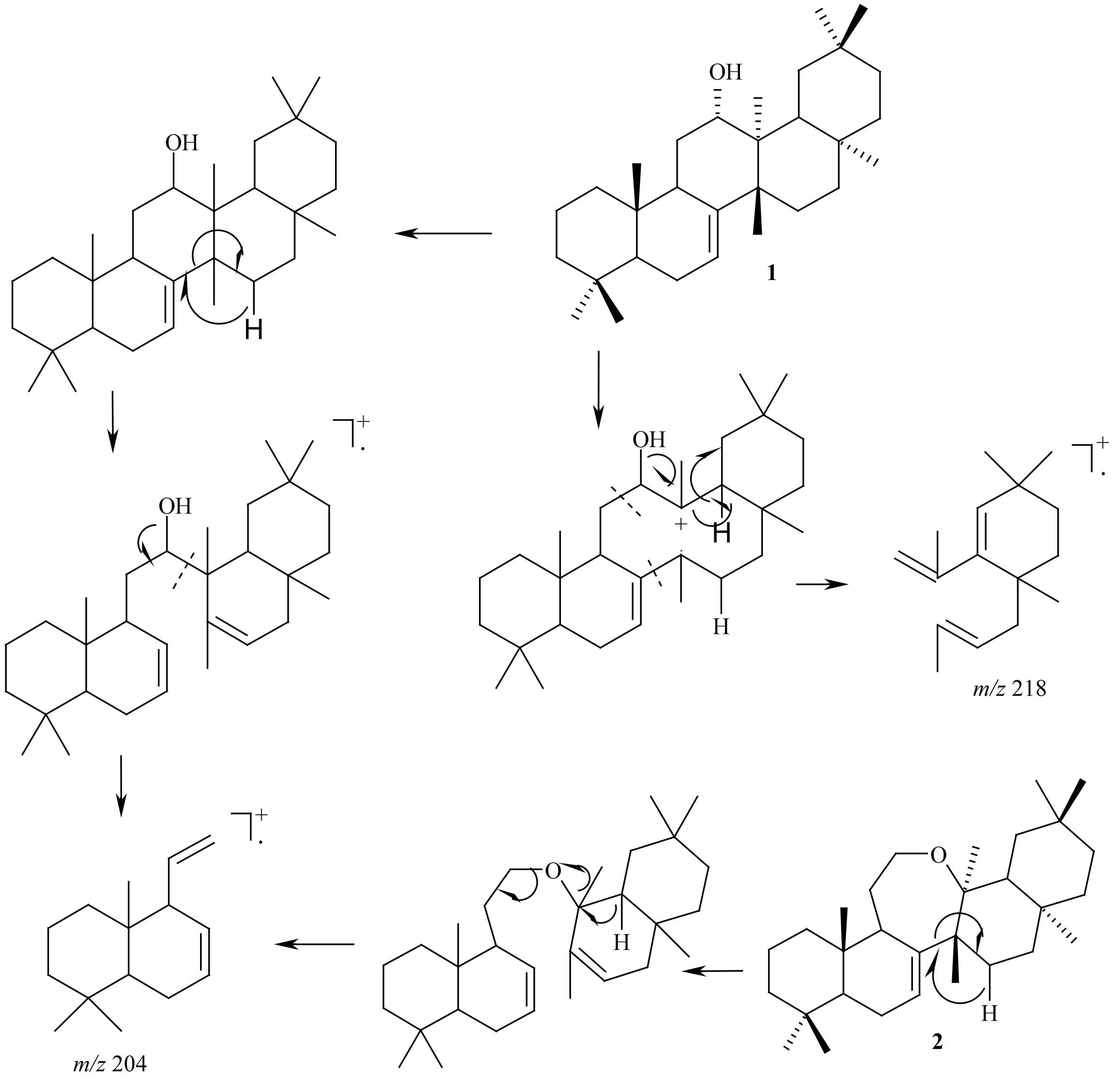


Chart 1.

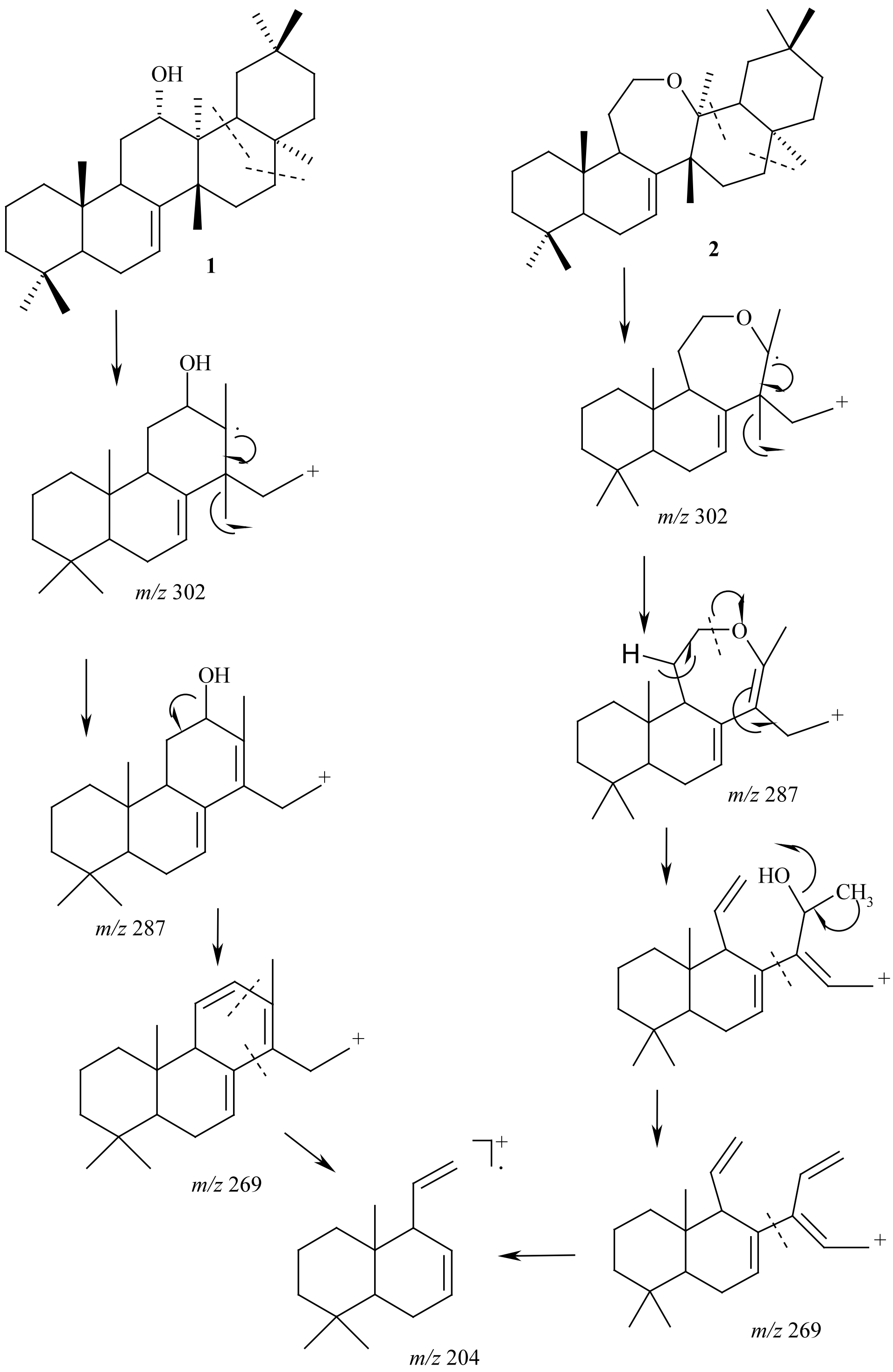
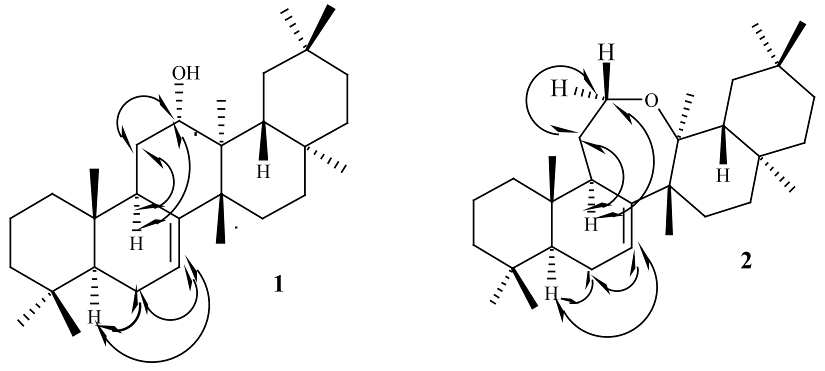
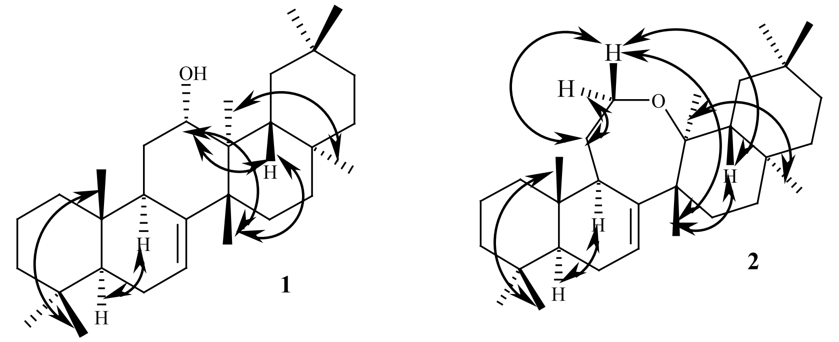


Chart 2.

pound **2** did not form an acetate (Ac_2O/Py), suggesting that the oxygen atom in the molecule could be in the ether form in any of the rings. In the TOCSY spectrum, the protons at δ 3.45 and 3.09 due to the C-12 methylene showed correlation with the C-11 methylene protons at δ 1.55 (2H, br s), which in turn showed correlation with the C-9 methine proton at δ 0.90 (1H, br s). Further, the trisubstituted olefinic proton at C-7 (δ 5.5) showed a correlation with C-6 at δ 1.61 (2H, d, $J=3.2$ Hz), which in turn showed a correlation with C-5 at δ 2.01 (1H, d, $J=12.6$, Hz). The low-resolution mass spectrum exhibited diagnostic[4] fragmentation for Δ^7 triterpenoids of multiflorene derivatives leading to the formation of a base peak (Chart 1) at m/z 204, suggesting that compound **2** belongs to the multiflorene skeleton with an ether group located in the C-ring system of the molecule. The formation of the base peak ion at m/z 204 is considered to be formally initiated by



Selected TOCSY Correlations of **1** and **2**



Selected NOESY Correlations of **1** and **2**

Figure 2.

cleavage[4] of the C(8)–C(14) bond as observed in **1** and other significant fragment ions at *m*/*z* 302, 287 and 269 were also observed in the EIMS, which is shown in Chart 2. These spectroscopic data indicated that the ether link is present between C-12 and C-13 and that a double bond is at C-7 in the molecule. The relative stereochemistry of multiflorene-ether **2** was established by its NOESY spectrum, which showed correlations between methyls, methylene and methine protons on the β-side (H_3-26–H-18; H_β-12–H_2-11; H_β-12–H_3-26; H_β-12–H-18; H_3-24–H_3-25) and on the α-side (H-5–H-9; H_α-12–H_2-11; H_3-27–H_3-28). Thus the structure of compound **2** was established as multiflor-7-en-12,13-ether.

2. Experimental

2.1. Plant material

The plant material *W. volubilis* Linn (Asclepiadaceae) was collected from Bhadrachalam forest, Andhra Pradesh, India, in December 2000 and identified by Prof. M. Prabhakar Rao, Department of Botany, Osmania University, Hyderabad, India. The voucher specimen (No. 006934) is kept in the herbarium of the Department of Botany, Osmania University.

2.2. Extraction and isolation

The shade-dried and powdered leaves (1.2 kg) of *W. volubilis* were successively extracted with hexane and acetone (3×5 L) at room temperature. The hexane extract (30 g) was subjected to silica gel chromatography, eluting with hexane through hexane/ethyl acetate mixtures to ethyl acetate and afforded 12α-hydroxymultiflorene (**1**) (240 mg) from the 20% EtOAc/hexane fraction. The acetone extract (68 g) was subjected to silica gel chromatography, eluting with hexane through hexane/ethyl acetate mixtures to ethyl acetate to afford multiflorene-ether **2** (110 mg) from the 50% EtOAc/hexane fraction.

2.3. Multiflor-7-en-12α-ol (1)

Colorless solid (240 mg), mp 276–278 °C, $[\alpha]_D^{25}$ +1.338° (*c* 0.25, $CHCl_3$). IR (KBr) ν_{max} 3485, 2933, 2860, 1639, 1471, 1381, 1132, 1036, 1000, 815, 689 cm^{-1}; ^1H NMR ($CDCl_3$ 400 MHz, δ): 5.53 (1H, dd, J=3.1, 8.1 Hz, H-7), 3.19 (1H, dd, J=4.7, 11.2 Hz, H-12), 1.63 (2H, d, J=5.9 Hz, H_2-6) 1.59 (2H, dd, J=2.4, 5.5 Hz, H_2-11), 1.92 (1H, dd, J=2.8, 14.7 Hz, H-5), 1.09 (3H, s, H_3-27), 0.99 (1H, d, J=3.3 Hz, H-9), 0.97 (3H, s, H_3-26), 0.95 (3H, s, H_3-25), 0.92 (3H, s, H_3-28), 0.90 (6H, s, H_3-29 and H_3-30), 0.82 (3H, s, H_3-23), 0.80 (3H, s, H_3-24), 0.75 (1H, d, J=2.2 Hz, H-18); ^{13}C NMR ($CDCl_3$ 50 MHz, δ): 36.04 (C-1), 27.55 (C-2), 40.74 (C-3), 38.37 (C-4), 55.0 (C-5), 25.35 (C-6), 116.15 (C-7), 157.52 (C-8), 48.63 (C-9), 36.93 (C-10), 26.56 (C-11), 77.82 (C-12), 38.19 (C-13), 37.38 (C-14), 33.10 (C-15), 29.37 (C-16), 35.17 (C-17), 48.10 (C-18), 37.21 (C-19), 28.20 (C-20), 32.79 (C-21), 37.09 (C-22), 14.85 (C-23), 15.12 (C-24), 16.87 (C-25), 20.71 (C-26), 18.21 (C-27), 29.26

(C-28), 34.49 (C-29), 32.48 (C-30); HRMS, obsd. *m*/*z* 426.3861 $C_{30}H_{50}O$ requires *m*/*z* 426.3865 [M^+]. EIMS obsd. *m*/*z* (%): 426, [M^+, 14], 411 (10), 302 (50), 287 (35), 269 (16), 257 (13), 231 (13), 218 (23), 204 (100), 189 (24), 175 (15), 161 (15), 147 (22), 135 (52), 121 (35), 107 (33), 95 (40), 81 (30), 69 (44), 55 (26).

2.4. Multiflor-7-en-12,13-ether (2)

Colorless solid (110 mg), mp 270–272 °C; $[\alpha]_D^{25}$ +0.571° (*c* 0.4, $CHCl_3$); IR (KBr) ν_{max}: 2932, 2852, 1638, 1471, 1449, 1417, 1381, 1314, 1129, 1035, 997 cm^{-1}. ^{1}H NMR ($CDCl_3$ 400 MHz, δ): 5.5 (1H, dd, *J*=2.8, 7.9 Hz, H-7), 3.45 (1H, d, *J*=5.3 Hz, H_α-12), 1.61 (2H, d, *J*=3.2 Hz, H_2-6), 1.55 (2H, br s, H-11), 3.09 (1H, dd, *J*=6.6, 14.5 Hz, H_β-12), 2.01 (1H, d, *J*=12.6 Hz, H-5), 1.24 (3H, s, H_3-27), 1.07 (3H, s, H_3-25), 0.95 (3H, s, H_3-26), 0.94 (3H, s, H_3-28), 0.91 (3H, s, H_3-30), 0.90 (1H, br s, H-9), 0.89 (3H, s, H_3-29), 0.80 (3H, s, H_3-24), 0.77 (3H, s, H_3-23), 0.73 (1H, br s, H-18); ^{13}C NMR ($CDCl_3$ 50 MHz, δ): 36.06 (C-1), 27.75 (C-2), 38.41 (C-3), 38.20 (C-4), 55.12 (C-5), 25.38 (C-6), 116.00 (C-7), 157.57 (C-8), 48.64 (C-9), 37.08 (C-10), 26.69 (C-11), 77.08 (C-12), 78.32 (C-13), 37.32 (C-14), 33.18 (C-15), 29.42 (C-16), 35.10 (C-17), 48.29 (C-18), 38.41 (C-19), 28.19 (C-20), 32.87 (C-21), 28.82 (C-22), 14.88 (C-23), 15.34 (C-24), 16.81 (C-25), 20.77 (C-26), 18.26 (C-27), 28.82 (C-28), 34.51 (C-29), 32.57 (C-30); HRMS, obsd. *m*/*z* 426.3861 $C_{30}H_{50}O$ requires *m*/*z* 426.3855 [M^+]. EIMS obsd. *m*/*z* (%): 426, [M^+, 11], 411 (15), 317 (8), 302 (49), 287 (35), 269 (15), 257 (15), 231 (10), 218 (22), 204 (100), 189 (23), 175 (13), 161 (13), 147 (21), 135 (55), 121 (32), 107 (30), 95 (35), 81 (30), 69 (50), 55 (26).

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