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Alkenes with antioxidative activities from *Murraya koenigii* (L.) Spreng

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ABSTRACT

Four new alkenes (**1**–**4**), and six known alkenes (**5**–**12**) were isolated from *Murraya koenigii* (L.) Spreng. Their structures were elucidated on the basis of spectroscopic analyses and references. Compounds (**1**–**12**) were evaluated for antioxidative activities. Among them, compounds **1**, **2**, **4**, and **7** exhibited significant antioxidative activities using 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay with IC_{50} = 21.4–49.5 μM. The known compounds (**5**–**12**) were isolated from this plant for the first time.

Murraya koenigii (L.) Spreng has been known as a spice in Southeast Asia areas for a long time, which is mainly distributed the tropical and subtropical areas in the world. In fork, *M. koenigii* is not only used as condiment, but also herb. Previous phytochemical investigation of this plant reported the presence of various compounds such as alkaloids,[1] coumarins,[2,3] and volatile oils.[4–6] Modern pharmacology revealed that *M. koenigii* exhibited many pharmacological activities such as antidiarrhoeal,[7] antimicrobial,[8] hepatoprotective,[9] radical-scavenging,[10] hypoglycemic,[11] and immunomodulatory[12] activities. The biological importance of *M. koenigii* encouraged us to undertake a phytochemical study of this plant. According to references, the bioactivities of alkenes from *M. koenigii* were previously little chemically studied. Consequently, we described here the bio-guided isolation and structure elucidation of four new alkenes (**1**–**4**), together with six known alkenes (**5**–**12**) from the EtOAc-soluble fraction of *M. koenigii*. Meanwhile, all the compounds (**1**–**12**) (Fig. 1) were evaluated for their antioxidative activities, compounds **1**, **2**, **6**, and **7** exhibited significant antioxidative activities using 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay with IC_{50} = 21.4–49.5 μM (Table 3).

Compound **1** was isolated as a colorless amorphous powder and its molecular formula was determined to be $C_{21}H_{36}O_8$ by HR-ESI-MS data (*m*/*z* 439.2310 $[M+Na]^+$, calcd. for 439.2302) elucidating four degrees of unsaturation. The UV spectrum showed at λ_{max} 201, 233 nm. The IR spectrum indicated the presence of hydroxyl (3370.5 cm^{-1}), methyl (2921.5, 1376.5 cm^{-1}) functionalities.

The ^1H NMR spectrum of compound **1** exhibited a typical terminal double bond[13] at δ_H 6.00 (1H, dd, *J* = 17.1, 6.3 Hz, H-11), 5.23 (1H, d, *J* = 6.3 Hz, H-12a), 5.05 (1H, d, *J* = 17.1 Hz, H-12b), two trans double bonds at δ_H 5.77 (1H, t, *J* = 15.9, 6.3 Hz, H-4), 6.19 (1H, d, *J* = 15.9 Hz, H-5), and an alkene hydrogen at δ_H 5.59 (1H, m, H-7) in the low field. Furthermore, in the middle field of the ^1H NMR spectrum, there were four methyl signals according to the data of ^1H NMR and ^{13}C NMR (Table 1). In addition, a characteristic doublet at δ_H 4.45 (1H, d, *J* = 7.5 Hz, H-1′) was ascribed to the anomeric proton of the glucosyl unit, corresponding to δ_C 106.4 (C-1′) of the ^{13}C NMR and HSQC spectra, which indicated the presence of the glucose in compound **1** (Table 1). In the HMBC spectrum of **1**, correlations of H-3/C-1′, C-2; H-4/C-3, C-5; H-5/C-4, C-6; H-7/C-6, C-9; H-8/C-6; H-9/C-10; H-11/C-10; H-12/C-10, C-11; H-1′/C-3, C-3′ (Fig. 2) indicating the planar construction of **1**. Moreover, the relative configuration of compound **1** was determined by the 2D-NOESY correlations of H-1′/H-3; H-4/H-3, H-5 (Fig. 2).

According to the biosynthesis pathway and literature[14] of compound **1**, the absolute configuration of C-10 was identified as 10*R*. In addition, the absolute configuration of C-3 was determined by the CD method. The 10-OH of compound **1** was protected by *tert*-butyldimethylsilyl chloride (TBSCl),[15] and obtained ramification

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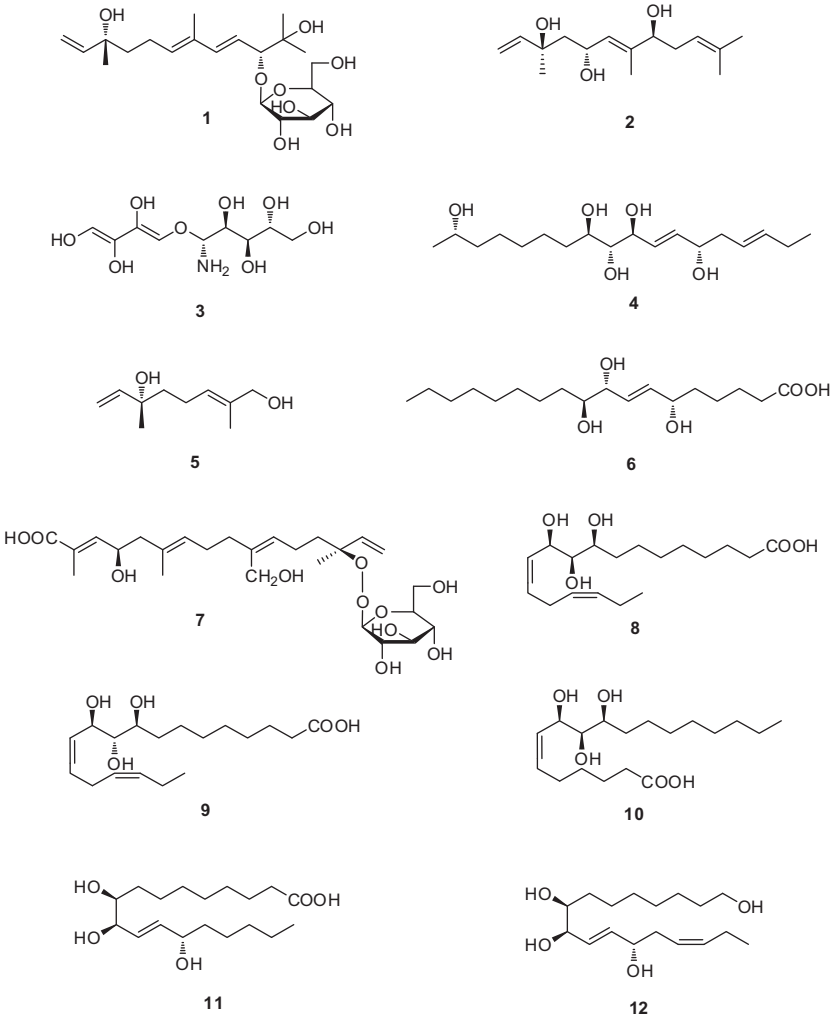

Figure 1. Structures of compounds (**1**–**12**).

1a. Compound **1a** was a TBS ether which its 10-OH was protected by TBSCl, then its CD spectrum was recorded on a JASCO J-815 CD spectrometer. From the CD spectrum of compound **1a**, it was found that the positive cotton effect at 285 ($\Delta\varepsilon$ +0.08) nm and the negative cotton effect at 228 ($\Delta\varepsilon$ −0.85) nm, which was induced by reagent of $MO_2(OAC)_4$. According to the spiral rule and literature,[13] compound **1** was identified as (3*S*,4*E*,6*E*,10*R*)-2,10-dihydroxy-2-hydroxy-2-methylethyl-6,10-di-methyl-4,6,11-sencolaninic-3-β-D-glucopyranoside.

Compound **2** was obtained as a colorless amorphous powder. Its molecular formula, $C_{15}H_{26}O_3$, with three degrees of unsaturation, was based on HR-ESI-MS data (*m*/*z* 277.1776 $[M+Na]^+$, calcd. for 277.1774). The UV spectrum showed at λ_{max} 202, 230 nm. The IR spectrum indicated the presence of hydroxyl (3423.3 cm^{-1}), methyl (2973.0, 1372.3 cm^{-1}) functionalities. The UV and IR data of compound **2** were similar to those of compound **1**. So, compounds 1 and 2 were both alkeno-derivatives.

The ^1H NMR spectrum of **2** (Table 1) revealed the presence of a typical terminal double bond[13] at δ_H 5.20 (1H, dd, *J* = 12.0, 2.0 Hz, H-1a), 4.96 (1H, dd, *J* = 6.0, 2.0 Hz, H-1b), 5.93 (1H, dd, *J* = 12.0, 2.0 Hz, H-2) and two protons of alkene at δ_H 5.21 (1H, d, *J* = 15.5 Hz, H-6), 5.66 (1H, m, H-10) in the middle field. Furthermore, four methyl signals were observed in the ^1H NMR and ^{13}C NMR spectra of compound **2** (Table 1). The planar construction of compound **2** was determined by the HMBC correlations of H-1/C-2, C-3; H-2/C-3; H-4/C-2, C-3, C-6; H-6/C-4, C-8; H-9/C-11; H-10/C-8, C-11 (Fig. 2). According to the correlations of H-2/3-CH_3; H-10/8-OH of 2D-NOESY spectrum, the relative configuration was identified. The 3-OH of compound **2** was protected by *tert*-butyldimethylsilyl chloride (TBSCl),[15] and obtained ramification **2a**. Compound **2a** was also a TBS ether which the 3-OH was protected by TBSCl. The ramification **2a** was measured by the CD method. The CD spectrum of compound **2a** showed that the positive cotton effect at 218 ($\Delta\varepsilon$ +0.56) nm, which was induced by reagent of $Rh_2(OCOCF_3)_4$. Consequently, compound **2** was identified as (3*R*,5*S*,6*E*,8*S*,10*E*)-3,7,11-trimethyl-1,6,10-dodecatriene-3,5,8-triol according to the spiral rule and reference.[13]

Compound **3** was isolated as a colorless powder, its molecular formula was determined to be $C_9H_{17}NO_8$ by HR-ESI-MS data (*m*/*z* 290.0853 $[M+Na]^+$, calcd. for 290.0846) with two degrees of unsaturation. The UV spectrum showed at λ_{max} 206, 260 nm. The IR absorption at 3332.3 cm^{-1} suggested the presence of amino group in compound **3**.

In the ^1H NMR spectrum of compound **3**, there were two single peaks of at δ_H 8.19 (1H, s, H-1), 8.32 (1H, s, H-4) in the aromatic field, it can be concluded two alkene hydrogens by the degrees of unsaturation of compound **3**. Moreover, a double-peak of single proton at δ_H 5.97 (1H, d, *J* = 6.3 Hz, H-5) in the middle field which indicated that the fragment of $-NH_2$ was in compound **3** according to Ref. 16. The ^{13}C NMR spectrum (Table 2) of compound **3** showed