

## A New Irregular Diterpenoid of Biogenetic Interest from the Flowers of *Magydaris tomentosa* (Desf.) DC. (Apiaceae)

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A new irregular acyclic diterpene, magytomol acetate (**2**), has been isolated from the light petroleum extract of the flowers of *Magydaris tomentosa* (Desf.) DC. (Apiaceae) and its structure has been elucidated by means of extensive spectroscopic experiments. The new compound can be considered the acetyl derivative of the biogenetic precursor of other irregular diterpenes isolated from other species belonging to the family Apiaceae.

**Keywords:** Apiaceae, *Magydaris tomentosa*, irregular diterpene, biogenesis.

Diterpenoids are generally biosynthesized via head-to-tail dimerisation of geranyl diphosphate, whereas a head-to-head dimerisation of prenyl diphosphate is generally confined to the biosynthesis of triterpenoids and tetraterpenoids [1]. Several years ago, a phytochemical study of *Magydaris panacifolia* (Vahl) Lange (Apiaceae) [2] allowed the isolation of a new monocyclic diterpene, magydaridiendiol, whose structure was later revised by us and shown to be identical to bonandioliol (**1**), an irregular monocyclic diterpene, isolated from *Bonannia graeca* (L.) Halacsy (Apiaceae) [3], that should arise from a pseudo head-to-head dimerisation of geranyl diphosphate. Some years later the structure of magydaridiendiol (bonandioliol) was confirmed by synthesis [4,5].

*Magydaris tomentosa* (Desf.) DC. [syn. *M. pastinacea* (Lam.) Paol.] belongs to the Apiaceae family and is a rare species which grows in the mountains of Sicily [6]. The plant, from 1 to 2 m in height, is characterized by a striated, sulcate, thick stalk, with very large leaves, and umbels with 40-50 pedicels, with white flowers, and which causes skin irritations, as we could confirm after collecting the

plant material. Here we report the isolation and structural elucidation of a new irregular acyclic diterpene (**2**) from the light petroleum extract of the flowers of *M. tomentosa*; this compound is, in our opinion, the acetyl derivative of the biogenetic precursor of bonandioliol (**1**) and of other known diterpenes with this acyclic irregular skeleton [7,8]. Extraction of the fresh flowers of *M. tomentosa* allowed us to isolate, after chromatographic purification, this compound in a large yield. However, it was unstable since, even when stored at -20°C, it completely decomposed after three days.

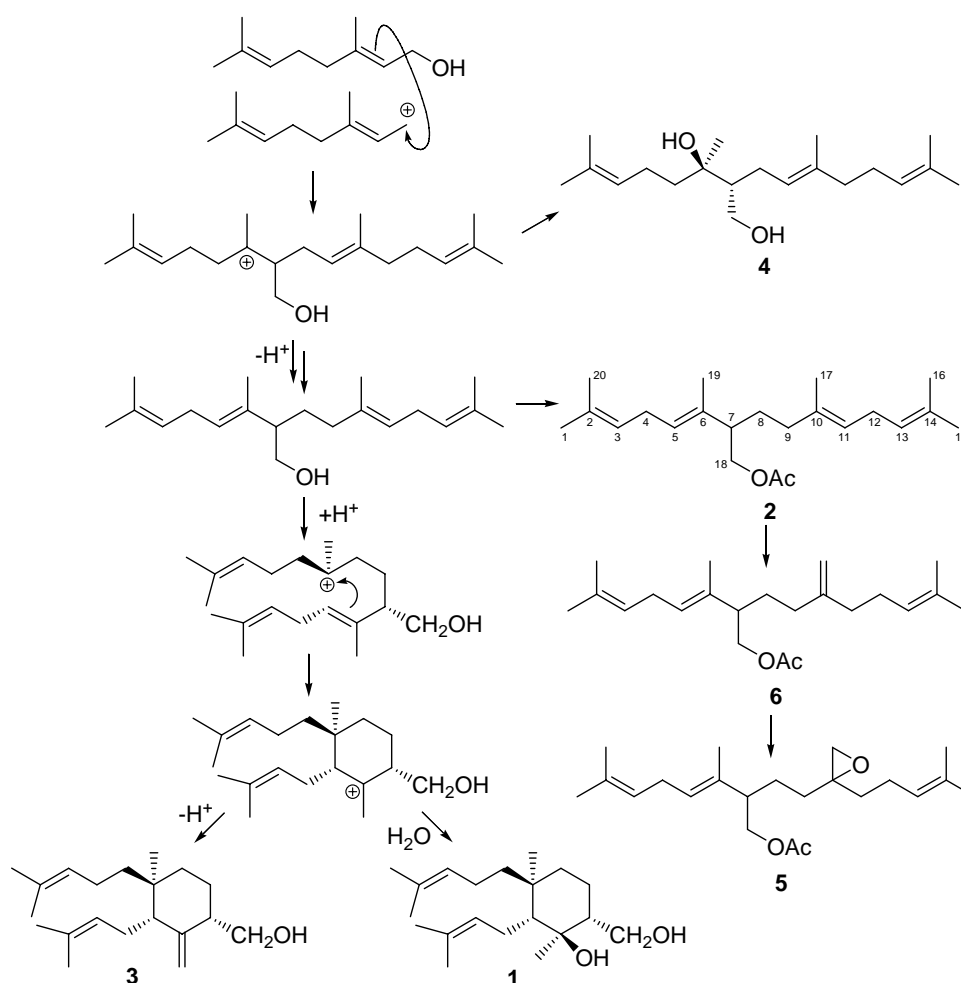
The elemental analysis and ESI-MS of the new compound were in agreement with a formula of C<sub>22</sub>H<sub>36</sub>O<sub>2</sub> and its IR spectrum showed the presence of an ester group (1743, 1230 cm<sup>-1</sup>) and double bonds (1696 cm<sup>-1</sup>). The <sup>1</sup>H and <sup>13</sup>C NMR spectra showed signals for an acetyl group (δ<sub>H</sub> 2.04, s, 3H; δ<sub>C</sub> 171.1 C and δ<sub>C</sub> 21.0 CH<sub>3</sub>), for a methylene bearing an oxygenated function (δ<sub>H</sub> 4.03, dd, 1H and δ<sub>H</sub> 3.99, dd, 1H; δ<sub>C</sub> 66.6, CH<sub>2</sub>, C-18) coupling with the allylic proton at δ<sub>H</sub> 2.30 m (δ<sub>C</sub> 47.2, CH, C-7), for four trisubstituted double bonds (δ<sub>H</sub> 5.26, t, 1H, H-5 and δ<sub>H</sub> 5.19, m, 3H, H-3, H-11 and H-13; δ<sub>C</sub> 126.8 CH,

123.4 CH, 123.3 CH, 123.0 CH, 131.5 C, 133.1 C, 134.6 C and 131.3 C), for six vinylic methyl groups, for an allylic methylene at  $\delta_{\text{H}}$  1.93 m ( $\delta_{\text{C}}$  37.0 CH<sub>2</sub>, C-9) and for two double allylic methylenes at  $\delta_{\text{H}}$  2.70 m ( $\delta_{\text{C}}$  27.0 CH<sub>2</sub> and 26.9 CH<sub>2</sub>, C-4 and C-12, respectively) coupling with all the four olefinic protons, as clearly indicated by the correlations observed in the <sup>1</sup>H-<sup>1</sup>H COSY spectrum. The HSQC and HMBC spectra allowed us to unequivocally identify all the carbons and protons (Table 1) and the NOESY correlations between H-11 and protons H-9, and between H-5 and H-7 clearly indicated an *E* geometry of the two double bonds C-5/C-6 and C-10/C-11. Consequently, to compound **2** was assigned the relative structure depicted in the formula and the trivial name of magytomol acetate.

Apart from bonandiol (**1**) and its dehydroderivative, magydatrienol (**3**) [3, 5], only very few other diterpenoids can be considered arising from a pseudo

head-to-head dimerisation of geranyl diphosphate. They comprise the acyclic diterpenoids peucedanediol (**4**), isolated from *Peucedanum oreoselinum* [7] and later synthesized [9], peucedalenoxide acetate (**5**) and 7-acetoxymethyl-10-methylidene-2,6,14-trimethylpentadeca-2,5*E*,13-triene (**6**), isolated from *Opopanax chironium* [8], and the bicyclic anisotomenoic acid, isolated from *Anisotome flexuosa* [10].

It is worth noting that irregular diterpenes seem to be restricted to the Apiaceae. Magytomol acetate (**2**) can be considered as the acetyl derivative of the biogenetic precursor of all these irregular diterpenes, as shown in Scheme 1. The dimerization of the geranyl units could involve a similar biogenetic pathway to those observed in the monoterpenoid series for lavandulol, with an analogous carbon skeleton [11], or an analogue precursor of the accepted biosynthesis of triterpenes [12].



Scheme 1: Biosynthetic pathway proposed for the irregular diterpenoids 1-6.

**Table 1:** Spectroscopic data of magytomol acetate (**2**) in CDCl<sub>3</sub>.

	$\delta_{\text{H}}$ J(Hz)	$\delta_{\text{C}}$	HMBC
1	1.72 s	25.7 C	Me-20
2		131.5 C <sup>a</sup>	H-4, Me-1, Me-20
3	5.19 o.s.	123.4 CH <sup>b</sup>	H-5, H-4, Me-1, Me-20
4	2.70 o.s.	27.0 CH <sub>2</sub>	H-5, H-3
5	5.26 t (7)	126.8 CH	H-4, H-7, Me-19
6		133.1 C	H-18, H-4, H-7, Me-19
7	2.30 m	47.2 CH	H-5, H-18, H-9, Me-19, H-8
8	1.48 m	27.5 CH <sub>2</sub>	H-18, H-7, H-9
9	1.93 m	37.0 CH <sub>2</sub>	H-11, Me-17, H-8
10		134.6 C	H-12, H-9, Me-17
11	5.19 o.s.	123.0 CH	H-9, H-12, Me-17
12	2.70 o.s.	26.9 CH <sub>2</sub>	H-11, H-13
13	5.09 o.s.	123.3 CH <sup>b</sup>	H-12, Me-15, Me-16
14		131.3 C <sup>a</sup>	H-12, Me-15, Me-16
15	1.72 s	25.6 CH <sub>3</sub>	Me-16
16	1.65 s	17.7 CH <sub>3</sub>	Me-15
17	1.63 s	15.9 CH <sub>3</sub>	H-11, H-9
18	4.03 dd (11,6); 3.99 dd (11,8)	66.6 CH <sub>2</sub>	H-7, H-8
19	1.57 s	12.5 CH <sub>3</sub>	H-5, H-7
20	1.65 s	17.7 CH <sub>3</sub>	Me-1
Ac	-	171.1 C	H-18
	2.04 s	21.0 CH <sub>3</sub>	

o.s. = overlapped signals. <sup>a,b</sup> Signals with the same letters can be interchanged.

## Experimental

**General experimental procedures:** Optical rotations were determined on a JASCO P-1010 digital polarimeter. <sup>1</sup>H and <sup>13</sup>C NMR, spectra were recorded on a Bruker AC 250 E MHz NMR spectrometer, using the residual solvent signal ( $\delta$  7.27 in <sup>1</sup>H and  $\delta$  77.00 in <sup>13</sup>C for CDCl<sub>3</sub>) as reference. <sup>13</sup>C NMR spectral assignments were determined from DEPT spectra. ESI-MS was obtained with an Applied Biosystem API-2000 mass spectrometer. Elemental analysis was carried out with a Perkin-Elmer 240 apparatus. The IR spectrum was run on a Shimadzu FTIR-8300 spectrophotometer. Merck Silica gel (70-230 mesh), deactivated with 15% H<sub>2</sub>O, was used for column chromatography.

## References

- [1] Bramley PM. (1997) Isoprenoid metabolism. In *Plant Biochemistry*. Dey PM, Harborne JB (Ed). Academic Press, San Diego USA. 417-437.
- [2] de Pascual Teresa J, Grande C, Grande M. (1978) Chemical components of Umbelliferae. Magydaridiol, diterpenoid with a new skeleton from *Magydaris panacifolia* (Umbelliferae). *Tetrahedron Letters*, **19**, 4563-4566.
- [3] Bruno M, Lamartina L, Lentini F, Pascual C, Savona G. (1984) Bonandiol: a new irregular, monocyclic diterpene from *Bonannia greca* (L.) Halacsy (Umbelliferae). *Tetrahedron Letters*, **25**, 4287-4290.
- [4] Nagano H, Masunaga, Y, Matsuo Y, Shiota M. (1987) Synthesis of 2,6-dimethyl-6-(8-methyl-4-methylene-7-nonyl)-2-cyclohexene-1-methanols from  $\alpha$ -santonin. *Bulletin of the Chemical Society of Japan*, **60**, 707-711.
- [5] de Pascual Teresa J, Rodriguez Moran J, Blanco Lopez JJ, Fernandez Mateos A, Grande Benito M. (1986) Synthesis of the new diterpene alcohols ( $\pm$ )-magydaridenediol and ( $\pm$ )-magydartrienol. *Anales de Quimica*, **82**, 183-186.

**Plant material:** The flowers of *Magydaris tomentosa* were collected in June 2005 near Godrano (Palermo) in Sicily, Italy and voucher specimens (PAL 05-608) were deposited in the Herbarium of the Botanical Garden of Palermo, Italy.

**Extraction and isolation:** Fresh and finely minced flowers (250 g) of *M. tomentosa* were extracted with light petroleum at room temperature for two days. After filtration, the solvent was evaporated to give a gum (3 g) that was chromatographed on a silica gel (Merck No. 7734, deactivated with 15% H<sub>2</sub>O, 400 g) column eluting with light petroleum and light petroleum-EtOAc. Fractions (100 mL) were collected as follows: 1-20, light petroleum; 21-40, light petroleum-EtOAc (19:1); 41-60, light petroleum-EtOAc (9:1); 61-80 light petroleum-EtOAc (4:1); and 81-100 light petroleum-EtOAc (1:1). Fractions 21-40 were re-chromatographed on a silica gel column. Elution with *n*-hexane-EtOAc (19:1) gave magytomol acetate (**2**, 500 mg):

## 7-Acetoxyethyl-2,6,10,14-tetramethylpentadeca-2,5E,10E,13-tetraene (magytomol acetate, **2**)

Oil.

$[\alpha]_{\text{D}}^{20}$ : +6.6° (*c* 3.0, CHCl<sub>3</sub>).

Rf : 0.9 (Light Petroleum -AcOEt, 19:1).

IR (film)  $\nu_{\text{max}}$ : 2925, 2854, 1743, 1696, 1451, 1376, 1230, 1107, 1036, 983 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): Table 1.

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz): Table 1.

ESIMS *m/z* (%) (positive mode): 371 [M+K]<sup>+</sup> (12), 355 [M+Na]<sup>+</sup> (100), 333 [M+H]<sup>+</sup> (4).

Anal. Calcd for C<sub>22</sub>H<sub>36</sub>O<sub>2</sub>: C, 79.46; H, 10.91. Found C, 79.50; H, 10.93.

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- [6] Pignatti S. (1982) *Flora d'Italia*, Edagricole, Bologna, vol II, pp. 221.
- [7] Lemmich E. (1979) Peuclinendiol, a new acyclic diterpenoid from *Peucedanum oreoselinum*. *Phytochemistry*, **18**, 1195-1197.
- [8] Muckenstrurm B, Boulanger A, Ouahabi S, Reduron J-P. (2005) A new irregular diterpenoid from *Opopanax chironium*. *Fitoterapia*, **76**, 768-770.
- [9] Rodriguez Moran J, Alcazar V, Grande M. (1988) Synthesis and structure of the diterpenoid peuclinendiol. *Bulletin of the Chemical Society of Japan*, **61**, 4435-4437.
- [10] van Klink JW, Barlow AJ, Perry NB, Weavers RT. (1999) A new irregular diterpene skeleton from *Anisotome flexuosa*. *Tetrahedron Letters*, **40**, 1409-1412.
- [11] Banthorpe DV, Doonan S, Gutowski JA. (1977) Biosynthesis of irregular monoterpenes in extracts from higher plants. *Phytochemistry*, **16**, 85-92.
- [12] Dewick PM. (1997) *Medicinal Natural Products: a Biosynthetic Approach*. Wiley, Chichester UK.