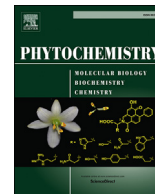




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Bioactive constituents from transformed root cultures of *Nepeta teydea*

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ABSTRACT

A phytochemical study of an extract from transformed root cultures of *Nepeta teydea*, induced by *Agrobacterium rhizogenes*, led to the isolation of the following new compounds: the sesquiterpene (-)-cinalbicol, the diterpene teydeadione (6,11,14-trihydroxy-12-methoxy-abieta-5,8,11,13,15-penten-7-one), a degraded C₂₃-triterpene (teydealdehyde) and three fatty acid esters of lanosta-7,24-dien-3 β -ol. The propyl ester of rosmarinic acid was also isolated for the first time from a natural source. In addition, two dehydroabietane diterpenes, eight triterpenes and eighteen known phenolic compounds were obtained. The antifeedant, cytotoxic and phytotoxic activities of the isolated compounds have also been investigated.

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1. Introduction

The *Nepeta* genus (Lamiaceae) is globally constituted by about 300 species. In the Canary Islands it is represented by *Nepeta teydea* Webb et Berth., an endemic herbaceous perennial plant growing at altitude between 1900 and 2100 m in the islands of Tenerife and La Palma. This plant has been used in traditional medicine as an anti-catarhal, diuretic, hypoglycemic and aphrodisiac agent (Pérez de Paz and Hernández Padrón, 1999). Phytochemically, the aerial parts of *N. teydea* are characterized by containing abietane and dehydroabietane diterpenes (Bretón et al., 1969a, 1970; González et al., 1973a, 1973b; Fraga et al., 1994, 1998), triterpenic acids (Bretón et al., 1970), spirostanic compounds (González et al., 1974) and essential oils (Velasco-Negueruela et al., 1989; Lawrence, 1992).

We have previously reported on the isolation of teydealdehyde

(5), a novel C₂₃ degraded triterpene, from *in vitro* cultures of transformed roots of *N. teydea* induced by *Agrobacterium rhizogenes* (Fraga et al., 2013). Now, in this full paper, we report on the isolation of the hitherto undescribed eremophilane sesquiterpene (-) cinalbicol (1) and the new diterpene teydeadione (4). Three new fatty acid esters of lanosta-7,24-dien-3 β -ol (6–8) have also been identified, whilst the propyl ester of rosmarinic acid (32) has been obtained for the first time from a natural source. A number of known compounds: two dehydroabietane diterpenes, eight triterpenes and eighteen phenolic compounds were also isolated. We also describe here the antifeedant, cytotoxic and phytotoxic activities of these products.

2. Results and discussion

The ¹H NMR spectrum of a constituent (1) isolated from the transformed root cultures of *N. teydea* was identical with that of the sesquiterpene (+)-cinalbicol, obtained from several species of the *Cineraria* genus (Bohlmann and Abraham, 1978; Gonser et al.,

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Table 1
¹³C NMR data of 1–4.

Position	1	2	3	3 ^c	4
1	22.7	29.9	27.0	26.9	26.8
2	16.4	17.7	33.0	32.7	33.0
3	29.7	36.3	214.3	211.5	214.2
4	29.5	36.6	48.7	48.5	48.7
5	142.3	145.5	141.5	141.4	141.7
6	120.9	141.9	140.4	140.4	140.3
7	146.7	183.7	183.9	183.9	183.5
8	111.6	109.1	109.4	109.7	108.6
9	150.9	135.8	131.5	131.8	132.2
10	124.2	41.5	40.4	40.3	40.5
11	142.7	138.4	138.9	138.8	138.7
12	114.3	151.3	151.5	151.2	151.5
13	24.7	125.7	126.7	126.7	122.1
14	14.6	156.1	156.6	156.5	154.3
15	20.5	26.0	26.1	26.2	137.3
16		20.3 ^a	20.3	20.2	118.6
17		20.4 ^a	20.3	20.2	23.1
18		27.1 ^b	24.3	24.0	24.3
19		27.4 ^b	21.1	21.1	21.1
20		28.0	20.0	19.6	19.9
21		62.2	62.3	61.3	61.2

^a, ^b These values can be interchanged.^c Solvent: C₆D₆.

1990).^{27,28} However, the optical rotations of both compounds were of opposite signs indicating that our product is the undescribed enantiomer (-)-cinalbicol. We have now confirmed its structure by using 2D NMR data and assigning its ¹³C NMR spectrum (Table 1).

The high resolution MS of compound **3**, with a molecular ion at *m/z* 374.1743, was in accordance with the molecular formula C₂₁H₂₆O₆. The ¹H NMR spectrum displayed signals of three angular methyls and an isopropyl group. Other signals observed in this spectrum were two coupled methylenes, a methoxy group, and three singlets of hydroxyl groups at δ 5.83, 6.91 and 12.5. The ¹³C NMR spectrum (Table 1) confirmed the presence of these

groups in the molecule, indicating a dehydroabietane diterpene structure for this compound. A 2D NMR study permitted the location of the hydroxyl and methoxy groups. Thus, in the HMBC experiment correlations were observed of HO-6 with C-5 and C-7; of HO-11 with C-9, C-11 and C-12; of HO-14 with C-8, C-13 and C-14; and of MeO-12 with C-12. The low field shift of the hydroxylic proton at C-14 (δ 13.0) was due to the hydrogen bond of this proton with the oxo group at C-7. Thus, the structure of **3** was determined as 6,11,14-trihydroxy-12-methoxy-abieta-5,8,11,13-tetraen-3,7-dione and confirmed by X-ray diffraction analysis (Fig. 1). This diterpene had only been previously isolated from *Lycopodium deuterodensum* and named licopodabietane A (Fuchino et al., 1998).

Teydeadione is a new diterpene to which the structure of 6,11,14-trihydroxy-12-methoxy-abieta-5,8,11,13,15-penten-3,7-dione (**4**) has been assigned, on the basis of the following considerations: Its HRMS displayed the molecular ion at *m/z* 372.1577 (C₂₁H₂₄O₆). Absorptions of alcoholic and carbonyl groups were observed in the IR spectrum. One at 1659 cm⁻¹ was characteristic of an oxo group conjugated with a double bond. The ¹H NMR spectrum, in comparison with that of **3**, showed the disappearance of a methyl and the methine of the isopropyl group and the presence of a methylenic double bond resonating as two singlets at δ 5.12 and 5.45, which were due to the two H-16. In addition, one of the methyl groups (δ 2.16, H-17) appears situated over a double bond. The location of the methylenic double bond was confirmed in the HMBC spectrum with crosspeaks of H-16 with C-13 (δ 122.1), C-15 (δ 137.3) and C-17 (δ 23.1). This experiment was also useful in the assignment of the 3-oxo group (δ 214.2), which showed correlations with H-1, H-2, H-18 and H-19.

Coleon U 12-methyl ether (**2**) was another abietane diterpene isolated in this work. This compound had been previously obtained from the aerial parts of *Plectranthus myrianthus* (Miyase et al., 1977) and from the roots of *N. leucophylla* (Mathela et al., 1991).

From the transformed roots of *N. teydea* we have isolated a C₂₃ degraded triterpene with a new carbon skeleton, teydealdehyde

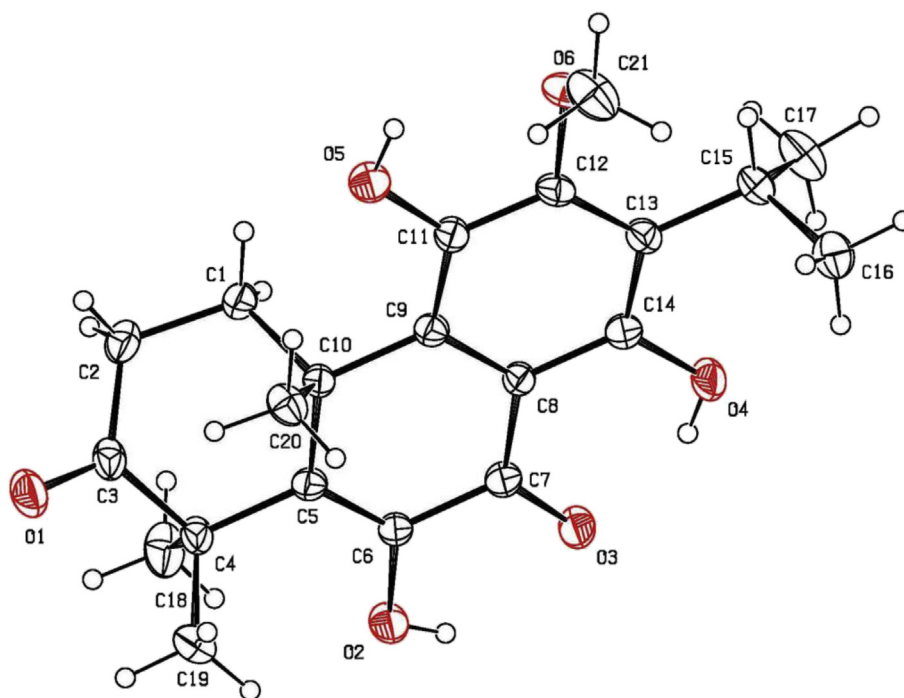


Fig. 1. A view of the structure of one of the two independent molecules of the compound **3**. The ellipsoids are drawn at the 30% probability level and H-atoms are shown as spheres of arbitrary radii.

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