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HYDROXYACETOPHENONE DERIVATIVES AND CHROMENE - EUPARIN DIMERS FROM ENCELIA PALMERI

Taha M. Sarg, Sameeh I. El-Dahmy, Hosny Abd El-Fattah* and Mahmoud Abd El-Aal*

Pharmacognosy Department, Faculty of Pharmacy, Zagazig University, Egypt.

** Pharmacognosy Department, Faculty of Pharmacy, Al-Fateh University, Tripoli, Libya.*

ABSTRACT

Investigation of the petroleum ether-ether extract of Encelia palmeri afforded four mixed dimers of euparin and encecalin. Further, derivatives of euparin, encecalin, ß-sitosterol, stigmasterol and ß-farnesene were also isolated. The structure of these compounds was elucidated on basis of spectral methods and direct comparison of their spectral data with those of authentic compounds (co-TLC and m.p.).

INTRODUCTION

The genus Encelia (Compositae, Tribe Heliantheae) is classified in the larger subtribe Ecliptinae[1]. Many species from the genus have been studied for their chemical constituents[2-8], indicated the presence of serveral hydroxyacetophenone derivatives. This class of compounds has demonstrated different biological activities. The benzofuran derivatives showed bacteriostatic and antitumor activity. It also implicated as the causative agents of milk sickness and toxic principles to goldfish[9].

In a recent study[9], the encealin and eurparin derivatives were found to be phototoxic to several fungi and bacteria. In addition, precocenes I and II proved to act as anti-juvenile hormones against certain types of insects. Currently, no records have been found on the phytochemical investigations of this species. Thus, it was deemed of interest to investigate this plant in order to isolate and identify the available constituents, which might have potential activity or chemical importance as well.

EXPERIMENTAL

Material and methods :

The plant material was collected from Mexico (March, 1989) and kindly authenticated by Prof. D.H. Robinson and Dr. R. King, Smithonian Institution, Washington, USA. ^{1}Hnmr spectra were recorded (in $CDCl_3$) with Bruker WM400. Mass spectra were recorded on Varian-Mat 335, at 70 ev, by direct inlet technique. Infrared spectra were recorded on Perkin Elmer infrared spectrophotomer 720 ($C Cl_4$).

Extraction and isolation :

The air-dried plant material (aerial part, 600 g) was exhaustively extracted with ether-petroleum ether (1:2). The resulting extract was concentrated under reduced pressure. The obtained residue (8.2 g) was fractionated on column chromatography (silicic acid) into four major fractions:

Fraction I: eluted with petroleum ether (100%) to yield 0.985 g.

Fraction II: eluted with petroleum ether-ether (9 : 1) to yield 1.2 g.

Fraction III: eluted with petroleum ether-ether (7.5 : 2.5) to yield 2.3 g.

Fraction IV: elued with petroleum ether-ether (1 : 1) to yield 1.5 g.

Constituents of fraction I and II: through PTLC, (SiO_2, PF_{245}), using petroleum ether 100% afforded 105 mg of ß-farnesene (co-tlc, nmr.).

Constituents of fraction III: by flash chromatography using SiO_2, 80 µ, 3 bar, with petroleum ether-ether 3:1 gave three fractions. Fraction **IIIa,** through PTLC (SiO_2, petroleum ether-ether 3:1) gave 10 mg of compound **3.** Fraction **III b,** gave by PTLC (SiO_2, petroleum ether-ether, 2:1,2 runs) gave 6 mg of compound **2.** Fraction **III c,** by using PTLC (SiO_2, petroleum ether-ether, 2:1, 2 runs) afforded 20 mg of mixture of **5** and **6.** By repeated PTLC (SiO_2, benzene-ether 9:1) gave 5 mg of **5** and 9 mg of **6.**

Constituents of fraction IV: by using flash chromatography (SiO_2, 80 µ, 3 bar, petroleum ether-ether 1:1) afforded three fractions. Fraction **IV a,** by using PTLC (SiO_2, petroleum ether-ether, 1:1, 2 runs) gave 11 mg of **4** and 2 mg **1.** Fraction **IV b,** by PTLC (SiO_2, petroleum ether-ether 1:1) gave mixture of ß-sitosterol and stigmasterol. Fraction **IV c,** by PTLC (SiO_2, petroleum ether-ether (1:2) gave 15 mg of compound **1** and 35 mg of mixture of **7** and **8.**

RESULTS AND DISCUSSION

The ethereal extract of aerial parts of Encelia palmeri Vasey & N by using different methods of chromatography afforded ß-sitosterol, stigmasterol, ß-farnesene and several hydroxy acetophenone derivatives; eurparin **1,** chromones **2-4** and the dimeric compounds **5-8.**The structure of compounds **1** and **2** was deduced from the ^{1}Hnmr spectral data (Table 1) through comparison with reported data of euparin and encecalin[4,6].

Table (1): ^{1}Hnmr spectral data of compounds 1-4 (400 MHz, $CDCl_3$, TMS as internal standard).

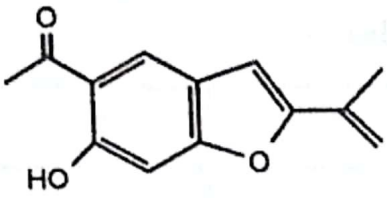
H	1	2	3	4
H-3	5.55 s	5.42 d	5.46 d	5.44 d
H-4	7.91 s	6.26 d	6.28 d	6.28 d
H-5	--------	6.95 s	7.06 s	7.84 s
H-7	6.98 brs	--------	--------	-------
H-8	--------	6.12 s	6.34 s	6.87 s
H-9	2.70 s	4.10 q	6.92 dd	-------
H-10	--------		5.11 dd	
H-10'	--------	1.46 d	5.57 dd	2.65 s
H-11	5.76 brs			
H-11'	5.19 brs	1.41 s	1.42 s	1.39 s
H-12	2.10 brs	1.41 s	1.42 s	1.39 s
Meo	--------	3.81 s	3.8 s	-------

J (Hz): Compound (1) : 4.6 = 3; 11, 11' = 2.5
Compound (2-4) : 3,4 = 10; 9,10 = 7.0
Compound (3) : 3,4 = 10; 9,10 = 11; 9,10' = 18; 10,10' = 2.0

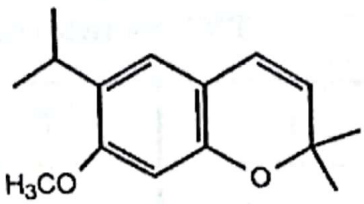
Table (2): ^{1}Hnmr spectral data of compounds 5-8 (400 MHz, $CDCl_3$, TMS as internal standard).

H	5	6	7	8
H-3	6.44 brs	6.72 brs	6.44 brs	6.16 brs
H-4	7.85 s	7.91 s	7.86 s	7.72 s
H-7	6.85 d	6.98 d	6.96 d	6.72 d
H-9	2.66 s	2.70 s	2.69 s	2.65 s
H-10	4.16 dq	3.40 ddq	3.10 ddq	3.35 ddq
H-11 a	6.42 dd	2.37 dd	2.17 dd	2.07 dd
H-11 b		2.77 dd	2.27 dd	2.39 dd
H-12	1.36 d	1.25 d	1.08 d	1.23 d
H-3'	5.45 d	5.46 d	5.24 d	5.28 d
H-4'	6.28 d	6.29 d	6.18 d	6.02 d
H-5'	6.88 s	6.81 s	6.71 s	6.60 s
H-8'	6.35 s	6.39 s	6.26 s	6.03 s
H-10'	2.02 d	5.13 brs	1.54 s	1.52 s
H-10''		5.81 brs		
H-11'	1.41 s	1.44 s	1.39 s	1.11 s
H-12'	1.42 s	1.43 s	1.37 s	1.29 s
Meo	3.81 s	3.81 s	3.73 s	3.77 s

J (Hz) : Compounds **(5-8)** 3.4' = 10; 10,12 = 7; 11_a, 11_b = 14.
Compound **(5)**: 10,11_a = 9; 10, 11_b = 1.
Compound **(6)**: 10, 11_a = 5; 10,11_b = 9.
Compound **(7)**: 3,7 = 1; 10,11_a = 5; 10,11_b = 8.
Compound **(8)**: 3,7 = 1; 10,11_a = 4,5; 10,11_b = 10.2



1



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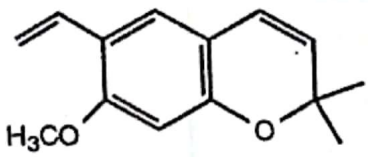

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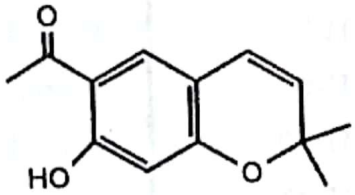

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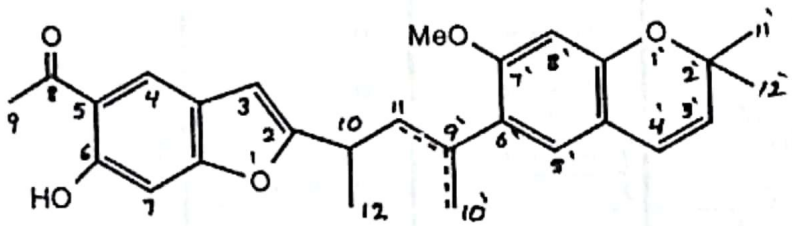
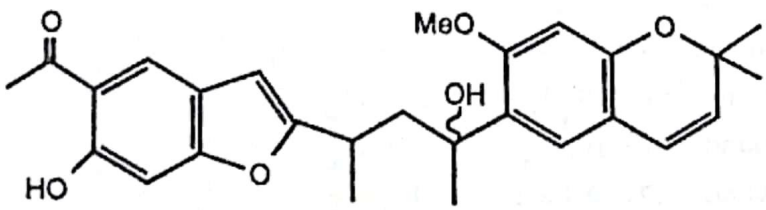


5: R = Δ 9', 11

6: R = Δ 9', 11'



7 : α Me, ß OH

8 : ß Me, α OH

The ^{1}Hnmr spectrum of compound **3** (Table 1) was close to compound **2.** The disappearance of the singlet at δ 1.46 (H-10) and the appearance of three doublets at δ 5.67 (H-10), δ 5.11 (H-10) and δ 6.92 (H-9) indicated the presence of a methylene group attached to C -8[6,8].

The ^{1}Hnmr spectrum of compound **4** (Table 1), suggested that this compound is 2,2-dimethyl-6-acetyl-7-hydroxy chromene. This assumption was deduced from the disappearance of the singlet at δ 3.81 (-OMe) and the down field shift of (H-10) to δ 2.65[8].

Concerning compound **7** and **8,** the IR spectra showed the same signals, 3480 (OH), 3600, 2600, 1640 for (o-hydroxyphenyl ketone), 1615 (C = C)[7,10].

Moreover, CIMS suggested a molecular formula $C_{27}H_{30}O_6$, while the EIMS confirmed the proposed molecular formula, besides the following fragments: m/z 450 (M^+, $C_{27}H_{30}O_6$); 422 (10%), 217 (100%, $C_{13}H_{13}O_3$). The base peak is formed by cleavage of the C_{11}-C_9 linkage which is in agreement with the reported data[7]. Together with the ^{1}Hnmr spectra (Table 2) these data clearly showed the structure of these compounds as: encecanescol **7** and 9-epi-encecanescol **8**[7].

The ^{1}Hnmr spectra (Table 2) showed that compound **5** and **6** are similar to compound **7** and **8,** with the difference only in the extra H_2O molecule in compound **7** and **8.** The ms spectra of these compounds confirmed the above assumption. The molecular ion peak at m/z 432 (for $C_{27}H_{28}O_5$) and the base peak at m/z 217, confirmed that compound **5** and **6** are formed after elimination of H_2O from compound **7** and **8.** The ^{1}Hnmr signals of compound **5** at δ 6.42 (dd, H-11) indicated the olefinic protons on the double bond between C_9-C_{11} [7], while the ^{1}Hnmr signals of compound **6** at δ 2.40 (dd, H-11a), 2.77 (dd, H-11b), 5.13 (br s, H-10') and 5.81 (br s, H-10") indicated that the position of the double bond between C9'-C10' [7] (Table 2).

Thus, the dimeric structure of compounds **5, 6, 7** and **8** has been confirmed.

To our knowledge, compounds **1-8** are isolated for the first time from this plants.

The identification[5] of ß-sitosterol, stigmasterol and ß-farnesene was confirmed by high field ^{1}Hnmr,ms, and co-tlc.

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مشتقات هيدروكسى أسيتوفينون ومشتقات اليوبارين والكرومين من نبات الإنسوليا بلميرى

طه مصطفى سرج - سميح إبراهيم الدهمى

حسنى عبد الفتاح* - ومحمود عبد العال*

قسم العقاقير - كلية الصيدلة - جامعة الزقازيق - مصر

** قسم العقاقير - كلية الصيدلة - جامعة الفاتح - لبيبا*

يتبع نبات الإنسوليا بلميرى العائلة المركبة ويشتهر هذا النبات بأحتوا ءة على مشتقات الهيدروكسى أسيتوفينون والايبارين والكرومين وهذه المركبات تمتاز بأن لها نشاطات حيوية هامة ومختلفة.

وقام الباحثون بفصل عدد من المركبات المشتقة من الهيدروكسى أسيتوفينون بالإضافة إلى مركبات مزدوجة من الايبارين والكرومين.

وتم التعرف على التركيب الكميانى لهذه المركبات بدراسة الصفات الطبيعية والكيميائية والطيفية لها.