SESQUITERPENE LACTONES OF *Centaurea nicaensis*

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Plants of the *Centaureae* genus (*Asteraceae*) are interesting not only for the variety of chemical compounds in them but also for their biological activity [1].

The *Centaurea* genus contains more than 700 species [2]. It is represented by 45 in Algeria [3].

In continuation of our examination of plants of the *Centaurea* genus [4–7], we investigated the aerial parts of *Centaurea nicaensis* All ssp.Q et S.

Previously isolated constituents were cnicin, onopordopicrin, dihydroamarin, amarin, 11β,13-dihydrocnicin, and lappaol A. [8].

Aerial parts were collected during flowering in eastern Algeria (june 1999) and authenticated by Dr. Mohamed Kaabache from the Department of Biology (University of Setif, Algeria). A voucher specimen is deposited in the herbarium of the Department of Botany, University of Constantine under n°5/1999/CCN15.

Air-dried and powdered aerial parts (1087g) were soaked in MeOH (3 × 7 L). The MeOH extract was concentrated and the residue dissolved in H_2O (400 ml). The solution was treated with $Pb(OAc)_2$ under stirring and filtered. The filtrate was successively treated with chloroform (3 × 220 ml) and ethylacetate (3 × 220 ml). The solvents were removed to afford chloroform (8 g) and ethylacetate (8.6 g) fractions.

Crude syrup of the chloroform fraction was chromatographed on silicagel (200–400 mesh) using solvent mixtures (*n*-hexane-EtOAc) with increasing polarities, 100 ml fractions being collected as follows. Fractions 1–4 (*n*-hexane), fractions 5–56 (*n*-hexane-EtOAc, 3:1), fractions 57–94 (*n*-hexane-EtOAc, 7:3), fractions 95–157 (*n*-hexane-EtOAc, 1:1), fractions 158–174 (*n*-hexane-EtOAc, 1:2), fractions 175–179 (EtOAc).

Fractions 158–174 upon dissolution in MeOH and refrigeration gave **1**. Rechromatography of fractions 95–98 (silicagel, *n*-hexane-EtOAc, 1:1) gave **2**, rechromatography of fractions 99–108 (sigel, $CHCl_3$–MeOH, 49:1) gave **3**, and rechromatography of fractions 145–157 (sigel, *n*-hexane-EtOAc, 1:1) gave **4**.

The structures of these compounds were elucidated by ^1H and ^{13}C NMR spectra analyzed with DEPT 90 and 135, ^1H–^1H correlations (Cosy 45°), ^1H–^{13}C correlations (HMQC, HMBC), mass spectrometry and comparisons with literature data.

11β(H),13-Dihydrocnicin (1). PMR (250 MHz, $CDCl_3$, δ, ppm, J/Hz)**:** 4.90 (1H, t, J = 8.6, H-1), 2.24 (1H, m, H-2), 2.2 (1H, m, H-2′), 2.55 (1H, m, H-3), 1.9 (1H, m, H-3′), 4.70 (1H, d, J = 9.7, H-5), 5.1 (1H, t, J = 9.5, H-6), 2.3 (1H, m, H-7), 5.20 (1H, dt, J_1=9.3, J_2=2.9, H-8), 2.50 (1H, m, H-9), 2.40 (1H, m, H-9′), 2.60 (1H, m, H-11), 1.30 (3H, d, J = 6.9, H-13), 1.48 (3H, s, H-14), 4.20 (1H, d, J = 14.2, H-15), 3.98 (1H, d, J = 14, H-15′), 6.3 (1H, s, H-18), 6.1(1H, s, H-18′), 4.55 (1H, dd, J_1= 6.7, J_2 = 3.1, H-19), 3.75 (1H, dd, J_1= 11.3, J_2=3.3, H-20), 3.48 (1H, dd, J_1= 11.3, J_2= 6.9, H-20′).

^{13}C NMR (62.9 MHz, $CDCl_3$, δ, ppm): 129.5 (C-1), 25.9 (C-2), 34.5 (C-3), 143.5 (C-4), 128.4 (C-5), 77 (C-6), 58.2 (C-7), 73.5 (C-8), 49 (C-9), 132.5 (C-10), 41.1 (C-11), 178.9 (C-12), 16.4 (C-13), 16.8 (C-14), 60.1 (C-15), 165.2 (C-16), 139.6 (C-17), 126.8 (C-18), 70.7 (C-19), 65.7 (C-20).

Mass spectrum (EI, 70 ev), *m/z*: 380$[M]^+$, $C_{20}H_{18}O_7$ [9].

8,15-Dihydroxyelema-1,3-dien-12,6-olide (Melitensin) (2). PMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz)**:** 5.75(1H, dd, J_1= 17, J_2 =11, H-1), 5.05 (1H, d, J = 11, H-2), 5.01 (1H, d, J = 1, H-2′), 5.38 (1H, s, H-3), 4.95 (1H, s, H-3′), 2,40 (1H, d, J = 11, H-5), 4.15 (1H, t, J = 11, H-6), 1.85 (1H, m, H-7), 3.95 (1H, brddd, J_1 = 10.5, J_2 = 5.3, H-8), 1.80 (1H, m, H-9), 1.62

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(1H, d, J = 12, H-9′), 2.62 (1H, dq, J_1 = 12, J_2 = 7, H-11), 1.41 (3H, d, J = 7, H-13), 1.11 (3H, s, H-14), 4.08 (1H, d, J = 14, H-15), 3.98 (1H, d, J = 14, H-15′).

^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm)**:** 146.3 (C-1), 112.5 (C-2), 114.5 (C-3), 144.4 (C-4), 50.4 (C-5), 78.7 (C-6), 58.4 (C-7), 68.8 (C-8), 49.4 (C-9), 41.7 (C-10), 41.5 (C-11), 178.6 (C-12), 14.3 (C-13), 18.9 (C-14), 67.3 (C-15).

Mass spectrum (DCI/NH_3), *m/z*:284 $[M+NH_4]^+$, $C_{15}H_{22}O_4$ [10].

11β(H),13-Dihydrosalonitenolide (3). PMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 4.85 (1H, td, J = 10, H-1), 1.85–2.20 (4H, m, H-2, H-2′, H-3, H-3′), 4.65 (1H, d, J = 10, H-5), 4.85 (1H, t, J = 10, H-6), 1.90 (1H, m, H-7), 3.85 (1H, m, H-8), 2.50 (1H, m, H-9), 2.30 (1H, brd, J = 12, H-9′), 2.75 (1H, dq, J_1 = 11, J_2 = 7, H-11), 1.38 (3H, d, J = 7, H-13), 1.30 (3H, s, H-14), 4.18 (1H, d, J = 14, H-15), 3.89 (1H, d, J = 14, H-15′).

^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 128.2 (C-1), 25.9 (C-2), 34.7 (C-3), 142.6 (C-4), 129.3 (C-5), 76.6 (C-6), 59.9 (C-7), 71.4 (C-8), 52.2 (C-9), 133.9 (C-10), 40.6 (C-11), 180.3 (C-12), 17.3 (C-13), 16.8 (C-14), 60.4 (C-15). Mass spectrum (DCI/NH_3), *m/z*:284$[M+NH_4]^+$, $C_{15}H_{22}O_4$ [11].

5α,6β,7α,8β,11β(H)-15-Hydroxy-8-(1′,2′-dihydroxyethyl)-acryloelema-1,3-dien-6,12-olide (4). PMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 5.77 (1H, dd, J_1= 17, J_2= 11, H-1), 5.07 (1H, d, J = 11, H-2), 5.01 (1H, d, J = 1, H-2′), 5.41 (1H, s, H-3), 4.99 (1H, s, H-3′), 2.48 (1H, d, J = 11, H-5), 4.28 (1H, t, J = 11, H-6), 2.02 (1H, m, H-7), 5.28 (1H, dt, J_1= 11, J_2 = 4, H-8), 1.95 (1H, dd, J_1 = 13, J_2 = 4, H-9), 1.73 (1H, m, H-9′), 2.65 (1H, dq, J_1 = 12, J_2 = 7, H-11), 1.25 (3H, d, J = 7, H-13), 1.19 (3H, s, H-14), 4.10 (1H, d, J = 14, H-15), 3.99 (1H, d, J = 14, H-15′), 6.38 (1H, s, H-18), 6.08 (1H, s, H-18′), 4.62 (1H, m, H-19), 3.85 (1H, dd, J_1 = 11, J_2 = 4, H-20), 3.60 (1H, dd, J_1 = 11, J_2 = 7, H-20′).

^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 145.8 (C-1), 113.0 (C-2), 114.8 (C-3), 144.1 (C-4), 50.3 (C-5), 78.4 (C-6), 56.0 (C-7), 70.7 (C-8), 44.9 (C-9), 41.6 (C-10), 41.0 (C-11), 177.8 (C-12), 14.1 (C-13), 18.7 (C-14), 67.2 (C-15), 165.3 (C-16), 139.0 (C-17), 127.4 (C-18), 71.1 (C-19), 65.7 (C-20) [8].

The ^{13}C NMR data of **4** is given for the first time.

Compounds **2** and **3** have been reported previously from another species of *Centaurea* [12, 13] and from *C. nicaensis* for the first time.

REFERENCES

1. H. Skaltsa, D. Lazari, C. Panagouleas, E. Georgiadou, B. Garcia, and M. Sokovic, *Phytochemistry*, **55**, 903 (2000)
2. D. J. Mabberley, *The Plant Book*, Combridge University Press, (1987).
3. P. Quezel and S. Santa, *Nouvelle Flore de l'Algerie et des Regions Desertiques Meridionales*, Edition CNRS, Paris (1963), Tome II..
4. K. Medjroubi, F. Banayache, S. Benayache, S. Akkal, M. Kaabache, F. Tillequin, and E.Seguin, *Phytochemistry*, **49,** 2425 (1998).
5. S. Akkal, F. Banayache, S. Benayache, K. Medjroubi, M. Jay, F. Tillequin, and E. Seguin, *Fitoterapia*, **70**, 368(1999).
6. J. Gonzalez-Platas, C. Ruiz-Perez, A. G. Gonzalez, J. Bermejo, and K. Medjroubi, *Acta Cryst.*, C55, 1837 (1999).
7. S. Akkal, F. Banayache, A. Bentamene, K. Medjroubi, E. Seguin, and F. Tillequin, *Chemistry of Natural Compounds*, **39**(2), 219 (2003).
8. M. Bruno, M. Pia Paternostro, T. E. Gedris, and W. Herz, *Phytochemistry*, **41**, 335(1996).
9. F. Banayache, S. Benayache, K. Medjroubi, G. Massiot, P. Aclinou, B. Drodz, and G. Novak, *Phytochemistry*, **31**, 4359 (1992).
10. A. Tortajada, M. T. Picher, M. M. Reventos, and J. M. Amigo, *Phytochemistry*, **27**, 3549(1988).
11. J. A. Marco, J. F. Sanz, F. Sancenon, A. Susanna, A. Rustaiyan, and M. Saberi, *Phytochemistry*, **31**, 3527(1992).
12. M. T. Picher, E. Seoane, and A. Tortajada, *Phytochemistry*, **23**, 1995 (1984).
13. I. Fernandez, J. R. Pedro, and E. Palo, *Phytochemistry*, **38**, 655 (1995).