Chemistry of Natural Compounds, Vol. 35, No. 5, 1999

MODIFICATION OF THE C-NOR, D-HOMOSTEROIDAL ALKALOID IMPERIALIN

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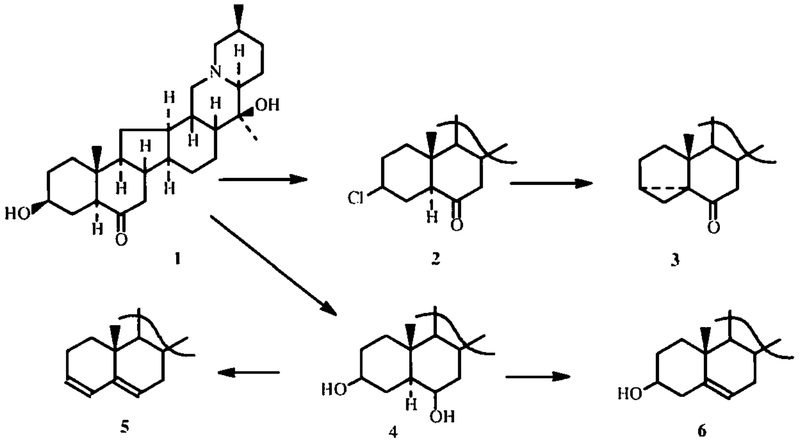
UDC. 547.944/945

Three new compounds, the structures of which are confirmed using chemical and spectral data, are prepared by modification of imperialin.

Imperialin (**1**) is the main component in *Petilium eduardi* and *P. raddeana* [1]. Esters and halide-containing derivatives of imperialin exhibit high M_2-choline blocking activity [2-4]. Three new compounds (**3**, **5**, **6**) (Scheme 1) were synthesized from **1** in order to produce more physiologically active compounds and to study the nature of their activity.



Chlorination of **1** produced 3β-chloroimperialin (**2**) [4]. Heating **2** in alkaline alcohol with subsequent purification gave $C_{27}H_{41}NO_2$ (**3**), which differs from **1** by 18 amu, i.e., by a water molecule. This suggests that a double bond has been introduced into imperialin. However, the PMR spectrum of **3** shows no signal for an olefinic proton. The chemical shift of the 19-methyl protons appears at weaker field (0.92 ppm) whereas those of the methyl protons of C-21 and C-27 are the same as in **1** [5] at 1.02 and 1.01 ppm, respectively. There is no proton geminal to the hydroxy group on C-3.

A comparison of the conditions under which **3** was prepared from 3β-chloroimperialin and 3α,5-cyclocholestan-6-one was prepared from 3β-chorocholestan-6-one [6] in addition to the NMR data suggests that **3** is 3α,5α-cyclocevanin-20β-ol-6-one. The fact that acid hydrolysis converts **3** to imperialin confirms this.

Heating dihydroimperialin (**4**) [7], prepared from **1**, produced $C_{27}H_{41}NO$ (**5**) and $C_{27}H_{43}NO_2$ (**6**). The PMR spectrum of **5** contains signals at 0.94 (s, 19-CH_3), 1.05 (d, J = 6.5 Hz, 27-CH_3), 5.39 (olefin H-6, dd, $^3J_1$ = 5.4, $^3J_2$ = 2.6 Hz), 5.60 (olefin H-3, m, ΣJ = 17 Hz), 5.98 (olefin H-4, dd, ^3J = 9.9, ^4J = 2.7 Hz), and 3.5 ppm (s, OH on C-20). The spectral data indicate that **5** is $\Delta^{3,5}$-cevanindien-20β-ol.

The PMR spectrum of **6** contains signals at 0.90 (s, 19-CH_3), 1.00 (s, 21-CH_3), 0.99 (d, 27-CH_3, J = 6.5 Hz), 3.44 (m, 3-CH–OH), and 5.30 ppm (olefin 6-H, m). The weak-field shift by 22 Hz of the signal for the 19-CH_3 protons compared with those in imperialin prove that the double bond occurs at C5–C6. The spectral data indicate that **6** is Δ^5-cevaninen-3β,20β-diol.

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0009-3130/99/3505-0554$22.00

EXPERIMENTAL

IR spectra were recorded on a Perkin—Elmer model 2000 Fourier-IR spectrometer. ^{1}H NMR spectra were obtained from Tesla BS-567A (100 MHz, $CDCl_3$, HMDS internal standard, δ) (compounds **3** and **6**) and UNITY Plus 400 MHz ($CDCl_3$, δ ppm, 0 = TMS) (compound **5**) instruments. Mass spectra were measured in an MX-1310 instrument (60-70 eV ionization potential, 100-190°C).

Preparation of 3α,5α-Cyclocevanin-20β-ol-6-one (3). 3β-Cl-Imperialin (**2**, 0.6 g) [4] was dissolved in ethanol containing KOH (5%), heated for 6 h, and left to stand at room temperature for 2 d. The solvent was distilled. The product was transfered from the aqueous layer into $CHCl_3$. The $CHCl_3$ was removed. The solid was separated on a silica-gel column using pure $CHCl_3$ as eluent. The initial fractions yielded 3α,5α-cyclocevanin-20β-ol-6-one (0.06 g), mp 143-145°C (methanol). Mass spectrum: M^+ 411. IR spectrum (KBr, ν, cm^{-1}): 3497-3692 (OH), 2845-2952 (*trans*-quinolizidine), 1709 (C=O).

Hydrolysis of 3α,5α-Cyclocevanin-20β-ol-6-one. Compound **3** (0.05 g) was dissolved in a mixture of 5% H_2SO_4 (2 ml) and acetic acid diluted with water (1:3). The mixture was heated for 3 h and then cooled. The acidic solution was made basic with ammonia. The product was extracted with $CHCl_3$. The $CHCl_3$ was removed. The dry solid was treated with methanol to give crystals with mp 251-253°C, identical to imperialin.

Preparation of $\Delta^{3,5}$-Cevanindien-20β-ol (5) and Δ^5-Cevaninen-3β,20β-diol (6). Dihydroimperialin (**4**, 2 g) [7] was dissolved in 5% H_2SO_4 (50 ml), heated for 3 h, and then cooled. The mixture was made basic with ammonia (pH 8-9) and extracted with $CHCl_3$. The concentrated $CHCl_3$ extract was passed over a silica-gel column and eluted with pure $CHCl_3$. The three initial fractions contained $\Delta^{3,5}$-cevanindien-20β-ol (**5**, 0.15 g, mp 198-200°C) (methanol). Mass spectrum: M^+ 395. IR spectrum (KBr, ν, cm^{-1}): 3715-3754 (OH), 2849 (*trans*-quinolizidine), 2901-2967 ($-CH_2$, $-CH_3$).

The next five fractions contained Δ^5-cevaninen-3β,20β-diol (**6**, 0.08 g, mp 235-236°C) (methanol). Mass spectrum: M^+ 413. IR spectrum (KBr, ν, cm^{-1}): 3417 (OH), 2949 (*trans*-quinolizidine), 2906-2936 ($-CH_3$, $-CH_3$).

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