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Preparative Electrochemical Reductive Methylation of Ortho-hydroxy-para-benzoquinones*

Bernardo A. Frontana, Jorge Cárdenas, Lydia Rodríguez-Hahn,** and Alejandro Baeza.‡

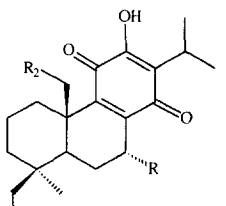
Instituto de Química de la Universidad Nacional Autónoma de México
Circuito Exterior, Ciudad Universitaria, Coyoacán 04510, México, D.F., México

‡Facultad de Química de la Universidad Nacional Autónoma de México
Circuito Escolar, Ciudad Universitaria, Coyoacán 04510, México, D.F., México

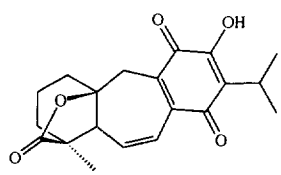
Abstract: An electrochemical methodology for the protection of the ortho-hydroxy-para-benzoquinone functionality has been developed, by a one step formation of the aromatic ethers of the reduced quinone function, improving the yields obtained for this reaction by the classical chemical methods.

INTRODUCTION

The ortho-hydroxy-para-benzoquinone is a functionality frequently found in natural products. A large number of abietane derivatives isolated from European and Asiatic *Salvia* sp. contain the C ring oxidized to an ortho-hydroxy-1,4-benzoquinone. Such is the case of royleanone **1a** and royleanone derivatives **1b-1d**.[1] Some American *Salvia* sp. are characterized by the presence of abietane quinones structurally related to royleanone **1a**, or icetexane derivatives with the C ring oxidized to an ortho-hydroxy-para-quinone and a variable degree of oxidation of the A and B rings, such as icetexone **2**.[2]



1a: R=R$_1$=R$_2$=H
1b: R=OH, R$_1$=R$_2$=H
1c: R=OAc, R$_1$=OH, R$_2$=H
1d: R=OAc, R$_1$=H, R$_2$=OH



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* Contribution No. 1472 From The Instituto de Química, UNAM.
** Author to whom correspondence should be addressed.

In synthetic or structure transformation studies, it becomes necessary to protect this functionality by reductive methylation in order to avoid undesirable reactions. This transformation has been shown to be troublesome and to proceed with low yields when performed by chemical reactions.[3] Recently we have undertaken a study to find the appropriate experimental conditions to achieve a one step reductive methylation of the ortho-hydroxy-1,4-benzoquinone functionality by an electrochemical process.

RESULTS AND DISCUSSION

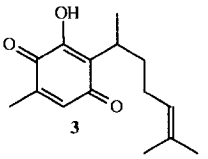
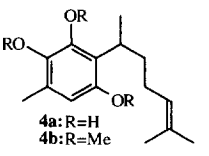
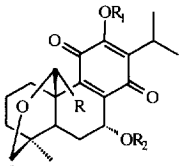
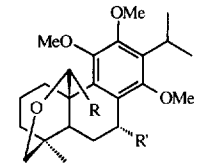
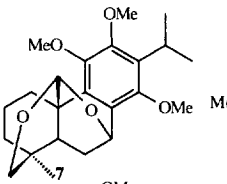
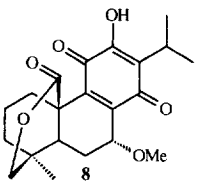
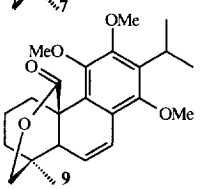
In order to find the best experimental conditions to achieve the electrochemical reductive methylation proposed, we investigated the reaction using 1,4-benzoquinone and 1,4-naphthoquinone as models. The electrochemical behaviour of quinonoid compounds in aqueous and non-aqueous solutions has been thoroughly studied,[4] but we have found only one report on the electrochemical reductive alkylation of a para-quinone, in which the authors studied the electrochemical ethylation of anthraquinone using ethyl bromide as the source of electrophile.[5] The low yields of the diethyl ether obtained (6-20%) were not very promising.

The electroanalytical studies performed using 1,4-benzoquinone and 1,4-naphthoquinone as models, showed that the use of a mercury electrode (HMDE) with TBAP 0.1M (tetrabutylammonium perchlorate) as the electrolyte in dry acetonitrile, were the conditions of choice for this study. The cyclic voltammetries of methyl iodide, ethyl bromide, methyl triflate and dimethyl sulfate in these conditions, showed that only dimethyl sulfate was not electroactive in the reductive range of the quinones, therefore it was chosen as the alkylating reagent. A cyclic voltammetry study of the of 1,4-benzoquinone and 1,4-naphthoquinone in the conditions mentioned (*vide supra*) in the presence of dimethyl sulfate, showed that both one electron reduction peaks of the quinones were displaced to more negative potentials in a two electron reduction peak, no oxidation peaks were observed in the reverse scan. This fact suggested that a chemical reaction had taken place after the electrochemical reduction and that the process was irreversible.

The preparative electrochemical reductive methylation of 1,4-benzoquinone and 1,4-naphthoquinone was performed at a controlled potential (-1.5V *vs.* Ref.) using a mercury electrode, a solution of TBAP 0.1 M as the supporting electrolyte in dry acetonitrile, in the presence of dimethyl sulfate as the alkylating agent. The starting material was totally consumed after passage of 3 F/mol. The dimethyl ethers of the dihydroderivatives of both products were obtained in 88 and 70 % yields, respectively.

We applied these experimental conditions to the reductive methylation of perezone **3**, a natural product isolated from the roots of *Perezia* sp., which contains an ortho-hydroxy-1,4-benzoquinone functionality.[6] The electrochemical reduction of perezone **3** in the same supporting electrolyte, in the presence of benzoic acid as a proton source, has been studied and found to proceed by a DISP1 mechanism.[7] Electrochemical reductive methylation of **3** in the conditions described for 1,4-benzoquinone at a controlled potential of -1.5V *vs.* Ref., yielded the trimethyl ether derivative **4b** in 71% yield.

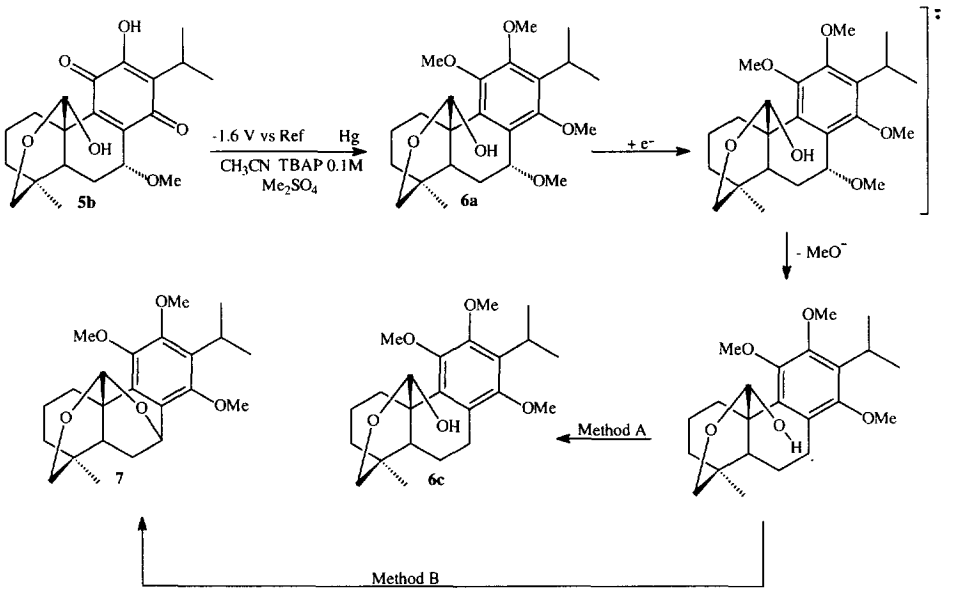
Table 1. Electrochemical reductive methylation of natural products containing hydroxy-benzoquinones

QUINONE	PRODUCTS	SUPPLIED ELECTRICITY F/mol	YIELD % (Isolated)
 3	 **4a:** R=H **4b:** R=Me	Method A: 3	**4b:** 71
 **5a:** R=OH, R_1=R_2=H **5b:** R=OH, R_1=H, R_2=Me	 **6a:** R=OH, R'=OMe **6b:** R=R'=OMe **6c:** R=OH, R'=H	Method A: 3	17 10.4 14
5b	 7	Method B: 6	75
 8	 9	Method B: 6	48.5

Conacytone **5a** is an abietane diterpenoid isolated from several Mexican *Salvia* species[8] in which the C ring is oxidized to an ortho-hydroxy-para-quinone. It also contains an α–axial hydroxy group bound to C-7 and a hemiacetal moiety whose hydroxyl has been found to be oriented towards ring B. The structure **5a** of this natural product, made it an interesting target to study the electrochemical reductive methylation conditions described, in a more complex molecule. To this purpose we utilized the 7-O-methyl ether derivative **5b.**

The electrochemical reductive methylation of **5b**, performed in the same conditions used for perezone **3** (Method A, see Experimental), yielded three products which were separated by column chromatography. Their structures **6a-6c** were deduced from spectral data. The expected tetramethyl derivative **6a** was obtained in 17% yield. It showed in the ^{1}H NMR three singlets at δ 3.74, 3.76 and 3.78 (3H each) assigned to the aromatic methyl ether groups. The aliphatic methyl ether bound to C-7 was observed at δ 3.41. A triplet (J=2.6 Hz) at 4.56 ppm (1H) was attributed to H-7. A singlet (1H) observed at 5.63 was ascribed to the hemiacetalic proton H-20. The second product obtained (10.4%) was shown to be the pentamethyl derivative **6b** as its ^{1}H NMR spectrum showed an additional methyl ether singlet at 3.15 ppm which was attributed to the acetalic methyl

ether bound to C-20, a singlet (1H) at δ 5.11 was attributed to its geminal proton. The formation of this product could be explained by the capability of donation of the proton of the hemiacetalic hydroxyl in the electrochemical conditions used.[9] The ^{1}H NMR of the third product obtained **6c** (14%) was very similar to that of **6a** but it lacked the singlet due to the methoxy group bound to C-7 and the signal assigned to H-7 in the resonance spectrum of **6a**. The hemiacetalic H-20 was observed as a broad doublet at 5.65 ppm. The cathodic cleavage of the benzylic ether has been previously described[10] and it is also a common reaction in catalytic reduction conditions.[11] The intramolecular participation of the hemiacetalic hydroxy group in this reductive process, could not be discarded. The overall yield of electroreductive methylation was 41%.

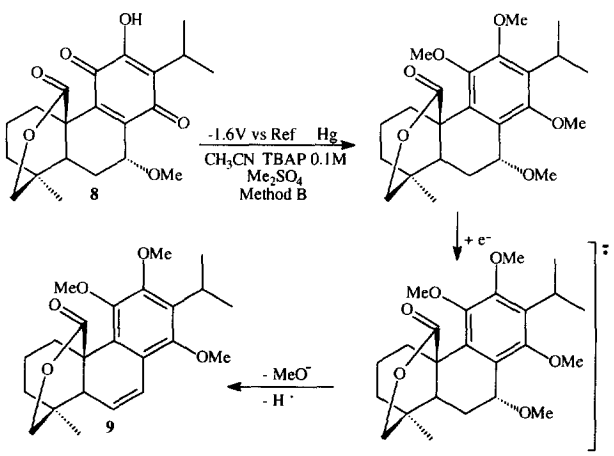


Scheme 1

In order to avoid the formation of many products, the electrochemical reaction was performed at high dilution conditions by a slow syringe-pump addition of the starting material **5b** to the electrochemical cell containing the TBAP and the dimethyl sulfate in dry acetonitrile (Method B, see Experimental). The electrochemical reduction was performed at an applied potential of -1.6V *vs.* Ref. as in the previous examples. In these conditions product **7** was obtained in 75% yield. The structure proposed was deduced by the analysis of the ^{1}H and ^{13}C NMR data. The ^{1}H NMR spectrum of **7** showed only the three aromatic methoxy singlets at δ 3.85, 3.75 and 3.72. One proton signal at 4.83 ppm (d, J=1.6 Hz) was assigned to the hemiacetalic H-20. The AB part of an ABCD system was observed at δ 4.05 (dd, J=12 and 3.2 Hz, H-19a) and 3.39 (dd, J=12 and 1.1 Hz, H-19b), it was due to the C-19 methylene protons. A double doublet at δ 5.23 (J=5 and 1.1 Hz) was

attributed to the ethereal geminal H-7. The chemical shift and coupling constants of this signal could be the result of a change in conformation of the B ring of the molecule to a *pseudo* boat. The Dreiding model of **7**, with the B ring in a boat conformation, suggested that H-7 was in the paramagnetic zone of the aromatic C ring and suffered the influence of the methoxy group bound to C-14. It also showed H-20 oriented towards the diamagnetic zone of the aromatic C ring, which could explain the chemical shift of 0.77 ppm to higher field of this proton. The ^{13}C NMR spectrum of **7** showed the signals due to six sp^3 carbon atoms bound to oxygen. The signals observed at δ 64.7 (d), 65.6 (t) and 98 (d) were unambiguously assigned to C-7, C-19 and C-20 respectively. The formation of product **7** could be the result of an intramolecular attack of the hemiacetalic hydroxyl to C-7, favored by the electrochemical cleavage of the benzylic methoxy group as shown in Scheme 1.

The lactone derivative **8** was obtained by oxidation of **5b** with Jones reagent. When the lactone **8** was submitted to the high dilution electrochemical reductive methylation conditions (Method B), product **9** was obtained in 48.5% yield. Its ^1H NMR spectrum showed two double doublets (1H each) at 6.84 (J=10 and 3 Hz) and 6.03 ppm (J=10 and 1.8 Hz) which were attributed to the vinylic H-7 and H-6 respectively. The signals of the methoxyl bound to C-7 and its geminal proton observed at 3.45 and 4.4 ppm respectively in the spectrum of **8**, were absent in the ^1H NMR of **9**. The formation of **9** confirmed the easy cathodic cleavage of the benzylic methoxy group, which in the case of the lactone derivative **8** is accompanied by the loss of H-6, as shown in Scheme 2.



Scheme 2

An analysis of the results obtained in this study, suggested that the cathodic cleavage of the methoxy group bound to C-7 occurred after the reductive methylation of the ring C quinone was completed. When the reaction was performed with the starting material present in the reaction vessel (Method A), the structure of the

products obtained **6a-6c**, point to a intermolecular mechanism (Scheme 1). At high dilution conditions (Method B) the reaction could proceed by an intramolecular stabilization of the radical generated at C-7, to produce the acetalic product **7** when the starting material **5b** contained an hydroxyl at C-20, or loss of H-6 in the absence of the C-20 hydroxy group (Schemes 1 and 2).

The present methodology provides a powerful tool in the selective protection of the ortho-hydroxy-para-benzoquinone functionality in the presence of other functions such as double bonds, lactones and hemiacetals. We observed the cathodic cleavage of the benzylic methoxy group in the reaction conditions used. Further mechanistic investigations are in progress.

EXPERIMENTAL

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. IR spectra were recorded on a Nicolet Magna-IR 750 spectrophotometer. ^{1}H and ^{13}C NMR spectra were determined for solutions in deuterochloroform with TMS as internal reference and obtained on a Varian Gemini 200 or Unity 300 spectrometers. Low resolution MS were obtained on a Jeol JMS AX505HA spectrometer. Thin-layer chromatography (TLC) was performed on aluminum sheets pre-coated with silica gel (Macherey-Nagel Alugram Sil G/UV^{254}). Column chromatography was performed on silica gel (Macherey-Nagel 230-400 mesh). Alkylating reagents and solvents were purchased from Aldrich Chemical Co. Milwaukee WI.

Electrochemical Instrumentation and Procedures

The experiments were carried out in dry CH_3CN with 0.1 M Bu_4NClO_4 electrochemical grade as supporting electrolyte in an inert atmosphere (N_2) at room temperature. The cyclic voltammetry and the preparative electrochemistry were performed with an EG&G PAR (Princeton Applied Research) potentiostat Model 273A. The analytical studies were carried out with a HMDE (Hanging Mercury Drop Electrode) EG&G PAR 303A as a working electrode. The analytical and preparative studies were carried out with a silver reference electrode ($Ag°/AgNO_3$ 0.1M CH_3CN //) and a platinum wire as auxiliary electrode. The preparative electrochemical experiments were performed in a EG&G PAR divided (vycor) cell model 377A at room temperature in an inert atmosphere. A Hg° electrode of 12.6 cm^2 was used as a working electrode.

Preparative electrochemistry. Method A. The starting material (100 mg, 0.3-1.0 mmol) was dissolved in a solution 0.1 M of TBAP (tetrabutylammonium perchlorate) in CH_3CN (50 ml) containing Me_2SO_4 (3-10 mmol). Nitrogen was bubbled through it for 40 min. The electrochemical reaction was performed at applied potential (-1.5 V *vs.* Ref.). The reaction was followed by TLC. On complete disappearance of the starting material (3 F/mol), the reaction mixture was poured into 10 % aq. KOH (10 ml) and stirred for 1h at room

temperature The organic solvent was removed under vacuum. Water was added and the reaction mixture extracted with methylene chloride. The organic fraction washed with brine, dried over $CaCl_2$ and the solvent removed. The addition of hexane produced the separation of the TBAP. The crude reaction products obtained, were separated by medium pressure column chromatography.

1,4-Dimethoxybenzene. The electroreduction of 1,4-benzoquinone (100mg) (method A) produced the 1,4-dimethoxybenzene, which was purified by column chromatography using hexane as eluent. Crystallization from CH_2Cl_2-MeOH gave the pure product, m.p. 56-58 °C (88% yield).

1,4-Dimethoxynaphthalene.-The electrochemical reduction of 1,4-naphthoquinone (150mg) (method A) yielded the 1,4-dimethoxynaphthalene which was purified by column chromatography using hexane as eluent. Crystallization from CH_2Cl_2-MeOH gave the pure product, m.p. 82-86 °C (70% yield).

Preparative electrochemistry. Method B. To the preparative electrochemical cell containing the supporting electrolyte solution (50 ml) and dimethyl sulfate (3 mmol), the starting material (0.15 mmol) dissolved in the supporting electrolyte solution (5 ml), was slowly added (3h, syringe pump). The electrochemical reaction was performed in an inert atmosphere at a controlled potential (-1.6 V *vs.* Ref.). On complete addition of the starting material (6 F/mol), the reaction mixture was poured into sat. aq. $NaHCO_3$ solution (10ml) and stirred for 1h at room temperature. The products of the reaction were isolated and purified as described for Method A.

Perezone (3). Perezone was previously isolated from *Perezia cuernavacana*.[6] and recrystallized from ethyl acetate-petroleum ether to constant melting point (yellow crystals, 102-104 °C). IR ($CHCl_3$): 3411, 3059, 1639 cm^{-1}; NMR ^1H ($CDCl_3$) δ ppm J Hz: 7.02 (s, 1H int. D_2O, -OH fenolic), 6.48 (c, 1H, J=1.6), 5.06 (th, 1H, J=6.8, 1.4) 3.05 (s, 1H, J=7) 2.06 (d, 3H, J=1.6), 1.64 (d, 3H, J=1.4), 1.53 (d, 3H, J=1.4), 1.2 (d, 3H, J=7); NMR ^{13}C ($CDCl_3$) δ ppm: 187.2, 183.7, 153.1, 140.9, 134.2, 130.3, 124.5, 123.5, 33.9, 28.7, 25.5, 26.4, 18.3, 17.4, 14.5; MS EI *m/z* (rel. int.): M^+ 248 (11.5), 234 (0.4), 219 (2), 191 (10), 186 (12), 176 (100), 151 (3). $C_{15}H_{20}O_3$ requires M^+ at 248.

1,3,4-O-trimethyl-leucoperezone (4b). After the electroreduction (method A) of perezone **3** (100 mg $4x10^{-4}$ mol) separation and purification by medium pressure column chromatography using hexane as eluent, the trimethyl derivative **4b** was obtained as a colorless oil (82 mg, 71 %): IR ($CHCl_3$): 3066, 2932, 1603, 1670, 1465, 1404, 1351, 1112, 1071, 1031 cm^{-1}; NMR ^1H ($CDCl_3$) δ ppm J Hz: 6.4 (d, 1H, J=1.6), 5.1 (t-hep, 1H, J=6.8, 1.4) 3.8 (s, 3H), 3.75 (s, 3H), 3.73 (s, 3H), 3.3 (hex, 1H, J=7), 2.2 (d, 3H, J=1.6), 1.65 (d, 3H, J=1.4), 1.53 (d, 3H, J=1.4), 1.25 (d, 3H, J=7); NMR ^{13}C ($CDCl_3$) δ ppm: 154.4, 152.0, 145.6, 130.8, 128.9,

126.9, 125.2, 108.5, 60.6, 60.0, 55.7, 35.5, 30.3, 27.1, 25.7, 19.6, 17.5, 15.9; MS EI *m/z* (rel. int.): M^+ 292 (47), 277 (1), 246 (2), 223 (5), 209 (86), 194 (51), 182 (100), 167 (28), 151 (21), 147 (11), 135 (13), 105 (11), 91 (22). $C_{18}H_{28}O_3$ requires M^+ at 292.

7α-O-methyl-conacytone (5b). The starting material **5a** was previously obtained from *Salvia candicans*[8b] and *Salvia anastomosans*.[8a] The treatment of **5a** with MeOH at room temperature yielded 7α-O-methyl-conacytone **5b**, which was recrystallized from ethyl acetate-petroleum ether to constant melting point (yellow crystals, 210-213 °C). IR ($CHCl_3$): 3595, 3393, 1639, 1150, 1110 cm^{-1}; NMR ^1H ($CDCl_3$) δ ppm; J Hz: 7.1 (s,1H, int D_2O, -OH enolic), 5.6 (d, 1H, J=2.6, H-20), 4.43 (dd, 1H, J=3.2, 2.2, H-7), 3.86 (dd, 1H, J=11, 2.4, H-19), 3.34 (dd, 1H, J=11, 1.4, H-19), 3.45 (s, 3H -OMe), 3.2 (hept., 1H, J=7, H-15), 1.25, 1.22 (d, 3H, J=7, Me-16 y Me-17), 0.825 (s, 3H, Me-18); NMR ^{13}C ($CDCl_3$) δ ppm: 186.1, 183.9, 150.8, 142.8, 142.5, 124.62, 94.65, 69.7, 65.6, 56.92, 41.7, 39.8, 39.8, 34.4, 32.1, 23.9, 23.1, 22.4, 20.89, 19.6, 19.5; MS EI *m/z* (rel. int.): M^+ 376 (1.2), 344 (100), 299 (33), 298 (91.7), 229 (31.7), 230 (35.7),.$C_{21}H_{28}O_6$ requires M^+ at 376.

Electrochemical reductive methylation of 7a-O-methyl-conacytone (5b).- The electrochemical reductive methylation of **5b** (100 mg, 2.6x10-4mol) using method A, produced the derivatives **6a**, **6b** and **6c** which were separated by medium pressure column chromatography.

7α,11,12,14-O-tetramethyl-9,12,14-trien-conacytone (6a). Obtained as a white crystalline product (19 mg, 17 %): mp 185-187 °C; IR ($CHCl_3$): 3389, 2945, 1454, 1410, 1114, 1050 cm^{-1}; NMR ^1H ($CDCl_3$) δ ppm J Hz: 5.63 (s, 1H, H-20), 4.56 (dd, 1H, J=2.6, 2.6, H-7), 3.78 (s, 3H, Ph-OMe), 3.76 (s, 3H, Ph-OMe), 3.74 (s, 3H, Ph-OMe), 3.41 (s, 3H -OMe), 3.35 (dd, 1H, J=11, 1.4, H-19), 1.33, 1.30 (d, 3H, J=7, Me-16 y Me-17), 0.81 (s, 3H, Me-18); NMR ^{13}C ($CDCl_3$) δ ppm: 96.7, 72.8, 66.6, 62,9, 59.8, 59.5, 55.8, 40.6, 40.3, 35.8, 26.3, 24.3, 22.4, 22.3, 22.07, 22.0.; MS EI *m/z* (rel. int.): M^+ 420 (51), 402 (42), 388 (100), 373 (28), 362 (24), 342 (27), 327 (24), 311 (28), 299 (27). $C_{24}H_{36}O_6$ requires M^+ at 420.

7α,11,12,14,20-O-pentamethyl-9,12,14-trien-conacytone (6b). This product was obtained as a white crystalline product (12 mg, 10.4 %): mp 163-165 °C; IR ($CHCl_3$): 2932, 1602, 1455, 1410, 1113, 1073, 1041 cm^{-1}; NMR ^1H ($CDCl_3$) δ ppm J Hz: 5.11 (s, 1H, H-20), 4.55 (dd, 1H, J=2.6, 2.6, H-7), 3.82 (s, 3H, Ph-OMe), 3.77 (s, 3H, Ph-OMe), 3.72 (s, 3H, Ph-OMe), 3.45 (s, 3H -OMe), 3.32 (dd, 1H, J=11, 1.4, H-19), 3.15 (s, 3H, -OMe), 1.32, 1.34 (d, 3H, J=7, Me-16 y Me-17), 0.81 (s, 3H, Me-18); MS EI *m/z* (rel. int.): M^+ 434 (27), 419 (1), 402 (22), 390 (11), 374 (29), 370 (16), 359 (5), 347 (48), 342 (100), 327 (27), 306 (46). $C_{25}H_{38}O_6$ requires M^+ at 434.

11,12,14-O-trimethyl-7α-demethoxy-9,12,14-trien-conacytone (6c). This product was isolated as a white crystalline product (15 mg, 14 %): mp 172-174 °C; NMR ^{1}H ($CDCl_3$) δ ppm J Hz: 5.55 (s, 1H, H-20), 3.98 (dd, 1H, J=14, 1.5, H-19), 3.87 (s, 3H Ph-OMe), 3.76 (s, 3H Ph-OMe), 3.62 (s, 3H Ph-OMe), 3.42 (hept., 1H, J= 7, H-15), 1.32, 1.31 (d, 3H, J=7, Me-16 y Me-17), 1.26 (s, 3H, Me-18).

11,12,14-O-trimethyl-(20→7)-oxo-7α-demethoxy-9,12,14-trien-conacytone (7). After the electroreduction (method B) of 7α-O-methyl-conacytone **5b** (50 mg $1.325x10^{-4}$ mol) and purification, the product **7** was obtained as a colorless oil (39 mg, 75 %): IR ($CHCl_3$) : 2935, 1599, 1457, 1337, 1117, 1103, 1045, 1050 cm^{-1}; NMR ^{1}H ($CDCl_3$) δ ppm J Hz: 5.23 (dd, 1H, J=5, 1.1, H-7), 4.83 (d, 1H, J=1.6, H-20), 4.05 (dd, 1H, J=12, 3.2, H-19), 3.85 (s, 3H, Ph-OMe), 3.75 (s, 3H, Ph-OMe), 3.72 (s, 3H, Ph-OMe), 3.4 (hept., 1H, J= 7, H-15), 3.39 (dd, 1H, J=12, 1.1, H-19), 1.34, 1.35 (d, 3H, J=7, Me-16 y Me-17), 0.78 (s, 3H, Me-18); NMR ^{13}C ($CDCl_3$) δ ppm: 130.9, 133.7, 98.6, 65.6, 64.7, 62.9, 60.7, 60.3, 40.2, 37.3, 33.4, 30.2, 29.6, 25.7, 24.1, 22.1, 21.3; MS EI *m/z* (rel. int.): M^+ 388 (100), 373 (11), 357 (3), 342 (15), 329 (16), 312 (7), 301 (9), 286 (10), 273 (11). $C_{23}H_{32}O_5$ requires M^+ at 388.

20-oxo-7α-O-methyl-conacytone (8). The oxidation of 7α-O-methyl-conacytone **5b** (130 mg) was performed with Jones reagent at 5 °C in the usual conditions. The crude product was separated by flash chromatography. The 20-oxo derivative **8** was obtained as a yellow crystalline product (110 mg, 85 %): mp 177-179 °C; IR ($CHCl_3$): 3382, 1723, 1656, 1153, 1084 cm^{-1}; NMR ^{1}H ($CDCl_3$) δ ppm J Hz: 7.3 (s, 1H, int D_2O, -OH enolic), 4.41 (s, 1H, H-7), 4.21 (s, 2H, H´s-19), 3.44 (s, 3H -OMe), 3.18 (hept., 1H, J= 7, H-15),2.3 (d, 1H, J=16 H-1), 2.01 (d, 1H, J=16, H-1), 1.21, 1.18 (d, 3H, J=7, Me-16 y Me-17), 0.98 (s, 3H, Me-18); NMR ^{13}C ($CDCl_3$) δ ppm: 185.6, 183.1, 171.2, 151.1, 143.1, 138.3, 124.6, 77.9, 68.7, 57.9, 48.9, 41.7, 40.6, 33.4, 32.5, 24.8, 24.3, 23.0, 21.0, 19.7, 19.6; MS EI *m/z* (rel. int.): M^+ 374 (100), 359 (32), 346 (65), 342 (85), 331 (76), 314 (53), 296 (34). $C_{21}H_{26}O_6$ requires M^+ at 374.

11,12,14-O-trimethyl-20-oxo-7α-demethoxy-6,9,12,14-tetraen-conacytone (9). After the electroreduction (method B) of 20-oxo-7α-O-methyl-conacytone **8** (50 mg $1.33x10^{-4}$ mol) and separation, the reduced derivative **9** was obtained as a colorless oil (25 mg, 48.5 %): IR ($CHCl_3$): 2933, 1724, 1602, 1338, 1143, 1041 cm^{-1}; NMR ^{1}H ($CDCl_3$) δ ppm J Hz: 6.84 (dd, 1H, J=10, 3, H-7), 6.03 (dd, 1H, J=10, 1.8 H-6), 4.35 (dd, 1H, J=11.7, 2.4, H-19), 4.15 (dd, 1H, J=11.7, 2, H-19), 3.87 (s, 3H, Ph-OMe), 3.85 (s, 3H, Ph-OMe), 3.66 (s, 3H, Ph-OMe), 3.39 (hept., 1H, J= 7, H-15), 2.45 (dd, 1H, J=3, 1.8 H-5), 1.32 (d, 6H, J=7, Me-16 y Me-17), 1.09 (s, 3H, Me-18); MS EI *m/z* (rel. int.): M^+ 386 (100), 371 (7), 358 (21), 343 (9), 327 (8), 315 (7), 299 (8), 285 (6), 271 (5). $C_{23}H_{30}O_5$ requires M^+ at 386.

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