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Clerodane and Aromatic Seco-Clerodane Diterpenoids from *Salvia rhyacophila*.

María del Carmen Fernández, Baldomero Esquivel, Jorge Cárdenas, Ana Adela Sánchez, Ruben Alfredo Toscano and Lydia Rodríguez-Hahn**.

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

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Abstract.- The known clerodane diterpenes salviarin **1** and 6β-hydroxy-7,8-dehydrobacchatricunaetin **2**, were isolated from *Salvia rhyacophila* together with five new clerodane diterpenoids **3-6** and **12** The structures of diterpenes **3-6** were established on spectral evidence and chemical transformations Rhyacophiline is an aromatic seco-clerodane diterpenoid whose structure **12** was established by spectral means and X-ray diffraction analysis

Introduction

The *Salvia spp* of México and Central and South America have been classified[1] in the *Calosphace* subgenus Our systematic chemotaxonomic study of the Mexican *Salvia* species revealed an interesting relationship between the diterpenoid content of the species studied and the Section to which it belongs [2,3] Most of the diterpenoids isolated from *Salvia* species, Subgenus *Calosphace*, are *neo*-clerodane diterpenoids or can be biogenetically derived from a clerodane precursor [4]

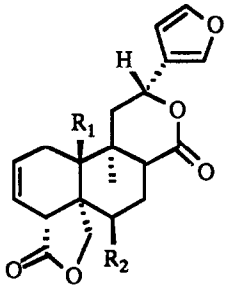
Following our systematic study of Mexican *Salvia* spp we have analysed the aerial parts of *S rhyacophila*, a species endemic to the States of México, Morelos and Guerrero *S rhyacophila* has been classified[1] in Section *Angulatae* (Subsection *Tiliaefoliae*) Recently we described[5] the unusual diterpenoid constituents isolated from *S tiliaefolia*, a species considered[1] representative of this Section

Results and Discussion

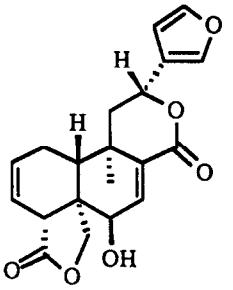
From the polar fraction of the aerial parts of *S. rhyacophila*, salviarin **1** was isolated as the major (0 08 % dry wt) diterpene component Salviarin had been previously found in *S. splendens*, [6] a species endemic to Brazil, which has been classified[1] in Section *Secundae* (*Salvia*, Subgenus *Calosphace*) The known 6β-hydroxy-7,8-dehydrobacchatricunaetin **2**, previously obtained[7] from *Aster alpinus* (*Compositae*)was also isolated from *S rhyacophila* together with five new clerodane diterpenoids

*Contribution No 1057 from the Instituto de Química

** Author to whom correspondence should be addressed



	1	3	5	6
R_1	H	H	H	OAc
R_2	H	OH	OAc	H



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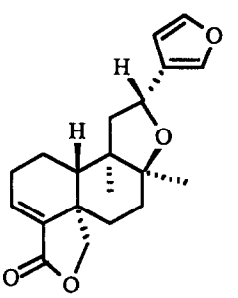
6β-Hydroxy-salviarin **3** had a molecular formula $C_{20}H_{22}O_6$ Its IR spectrum showed a strong hydroxyl absorption at 3600 cm^{-1} The carbonyl bands at 1770 and 1724 cm^{-1} were assigned to γ and δ lactones, respectively It also showed the characteristic[5,6] absorption due to a β substituted furan ring at 1505 and 875 cm^{-1} Its ^1H NMR spectrum (Table 1) indicated the presence of a 2,3 double bond as in salviarin, but the signal due to H-4 (t, J = 2 Hz) was shifted downfield to δ 3 7, whereas in salviarin it appeared at δ 2 78 A broad doublet (1H, J = 2 Hz) at δ 3 90 was assigned to H-6 gem to the hydroxyl group present in the molecule. Addition of TAI (trichloroacetyl isocyanate) moved this signal to δ 4 95 and the H-4 triplet upfield to δ 3.4 This result, together with the deshielding effect on H-4 in **3**, suggested a β-*axial* orientation for the hydroxyl group bound to C-6

Product **4**, showed a molecular formula $C_{20}H_{24}O_4$ Its IR spectrum exhibited bands at 1765 and 1660 cm^{-1} due to an α,β-unsaturated γ-lactone attached at ring A and the absorption at 1505 and 875 cm^{-1} due to a β substituted furan ring Its ^1H NMR spectrum (Table 1) was very similar to the spectrum exhibited by kerlin, a clerodane dilactone previously isolated from *S keerlii* [8] which has a β-butenolide bound to C-12 in place of the furan ring Therefore **4** could be named dehydrokerlin



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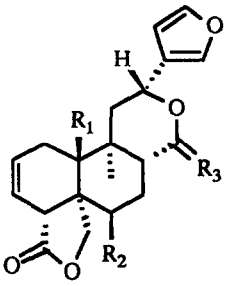
The diterpenes **5** and **6** were obtained as a mixture which showed M^+ at m/z 400 in the mass spectrum and peaks at m/z 358 (M-42) and 340 (M-60) which suggested the presence of an acetate residue in one or both products The IR spectrum of the mixture (1770, 1747, 1732, 1660, 1505, 875 cm^{-1}) was in agreement with the structures proposed for the diterpenes **5** and **6** The presence of an acetate group in both products was confirmed by the ^1H NMR spectrum of the mixture which showed two singlets at δ 2 03 and 2 05 Attempts to obtain the

Table 1 ^{1}H NMR data for compounds **1**, **3**,**4** and **7-12**

Compound	1*	3*	4*	7**	8**	9**	10**	11*	12*
H-1									7 50 m
H-2	6 0 m	6 0 m		5 95 m	6 00 m	6 00 m	6 0 m	6 0 m	7 50 m
H-3	5 60 br d (10)	5 65 br d (10)	6 80 dd (6, 4)	5 60 br d (10)	5 65 br d (10)	5 63 m	5 7 br d (10)	5 60 br d (10)	7 80 dd (9, 4)
H-4	2 78 m	3 70 t (2)	-	3 60 m	3 05 m	3 05 q (3)	3 0 t (3)	2 75 t (4)	-
H-6		3 90 br d (2)		3 80 t (2)	2 60 m	5 07 t (4)			1 40 d (6)
H-7									4 0 dq (10, 6)
H-8	2 45 m		-	3 30 dd (11, 5)		2 95 dd (12, 5)	3 62 dd (11, 4)	2 60 dd (11, 4)	2 0 dq (10, 7)
H-10	2 45 m	2 70 dd (10, 6)		2 60 m	-		-		-
H-11 a									2 30 dd (11, 12)
H-11 b									2 85 dd (12, 5)
H-12	5 33 dd (12, 4)	5 45 dd (12, 4)	5 0 dd (10, 8)	5 40 dd (11, 7)	3 75 dd (11, 5)	5 35 dd (11, 7)	5 35 dd (11, 7)	5 32 dd (11, 7)	5 17 dd (11, 5)
H-14	6 40 m	6 40 dd (2, 1)	6 35 t (2)	6 40 dd (2, 1)	6 38 m	6 38 dd (2, 1)	6 40 dd (2, 1)	6 37 t (1 5)	6 40 dd (2, 1)
H-15	7 43 m	7 40 t (2)	7 40 d (2)	7 40 m	7 35 d (2)	7 42 m	7 43 m	7 40 m	7 40 m
H-16	7 43 m	7 45 br d (1)	7 40 d (2)	7 40 m	7 35 d (2)	7 42 m	7 43 m	7 40 m	7 40 m
H-17	-	-	1 24 s***	-	5 13 d (8)	-	-	-	1 15 d*** (7)
H-19 pro-S	4 23 s	4 12 d (9)	3 90 dd (8, 2)	4 00 d (9)	4 15 d (9)	4 05 d (10)	4 12 d (9)	4 15 s	5 43 s
H-19 pro-R	4 23 s	4 30 d (9)	4 30 d (8)	4 25 d (9)	4 50 d (9)	4 28 d (10)	4 40 d (9)	4 15 s	5 43 s
H-20***	1 02 s	1 0 s	0 88 s	0 89 s	0 90 s	0 90 s	0 85 s	0 88 s	5 97 s

* $CDCl_3$ ** $CDCl_3$ + DMSO-d_6 *** Three protons intensity

diterpenes **5** and **6** as pure products by chromatographic methods were unsuccessful. In order to achieve an adequate separation of **5** and **6**, the mixture was treated with $NaBH_4$ (THF,MeOH,r.t.). Flash chromatography of the products obtained, led to the isolation of **7** and **8** as pure compounds Their structures and relative stereochemistry were deduced from spectral data. Product **7** showed a molecular ion at m/z 358 which is consistent with a molecular formula $C_{20}H_{22}O_6$. Its IR spectrum showed a strong absoption at 3440 cm^{-1} due to the presence of an hydroxyl group in the molecule. It also showed bands at 1770 and 1733 cm^{-1} which were assigned to the γ and δ lactone functions In its ^1H NMR spectrum (Table l) a triplet (1H,J=2Hz) at δ 3 80 was assigned to H-6 gem to the hydroxyl group which must be β-axially oriented in order to explain the deshielding effect on H-4, which appeared at δ3.60 (1H,t,J = 3 Hz) A double doublet (lH, J=5 and 11 Hz) at δ 3 30 was attributed to H-8 by comparison with similar structures,[10] therefore H-8 must be β-*axial* in **7** as a result of epimerisation at C-8. Acetylation of **7** gave the monoacetylated derivative **9** in which H-4 and H-8 were observed at a higher field in the ^1H NMR spectrum (Table 1), H-6 appeared at δ 5 07 (t, J = 4 Hz)



	7	8	9	10	11
R_1	H	OH	H	OH	H
R_2	OH	H	OAc	H	H
R_3	O	αH βOH	O	O	O

The second product obtained on sodium borohydride reduction of the mixture of diterpenes **5** and **6** was proved to be the lactol **8** as deduced from the spectral data (see Experimental) In the ^1H NMR spectrum (Table 1) a doublet (1H, J =10 Hz) at δ 5 13 was assigned to the hemiketalic proton 17 and a double doublet at δ 3 75 (1H, J=5 and 11Hz) to H-12 Jones oxidation of **8** yielded the dilactone **10** This product has been described as the sodium borohydride reduction product of salviacoccin,[10] a diterpenoid obtained from *S coccinea* (*Salvia*, Subgenus *Calosphace*) The structure and stereochemistry assigned to dihydrosalviacoccin were deduced on spectral evidence

From the data presented we can infer that the natural products isolated from *S. rhyacophila* are the 6β-acetoxy salvianin **5** and the l0β-acetoxy salvianin **6**, which suffer an epimerisation at C-8 and saponification of the ester group on sodium borohydride treatment. Saponification of the mixture of diterpenes **5** and **6**, yielded **7** and **10** as expected When salvianin **1** was submited to the same treatment, 8-episalvianin **11** was obtained (see Experimental)

Rhyacophiline, $C_{20}H_{20}O_5$ (EIMS) showed in the IR spectrum a band at 1763 cm^{-1} which was assigned to the α,β-unsaturated γ lactone, absorption at 1504 and 875 cm^{-1} due to a β-substituted furan ring and aromatic absorption at 1603 cm^{-1} The ^1HNMR (Table 1) and ^{13}CNMR (Table 2) spectra were in agreement with structure **12**. A double doublet (J=9 and 4Hz) at δ 7 80 was assigned to the aromatic H-3. The signals due to H-1 and H-2 appeared in the same region as the furan protons H-15 and H-16 A singlet (1H) at δ 5 97 was attributed to a ketalic proton The absence of the C-20 methyl group, which appears as a singlet in clerodanc diterpenoids, suggested that it was oxidized and this signal was assigned to H-20 A doublet at δ 112 28 in the ^{13}CNMR spectrum

of **12** (Table 2) was attributed to the ketalic C-20 The C-19 methylene was observed as a singlet (2H) at δ 5 43, in agreement with the phtalide nature of the γ-lactone function. A double doublet at δ 5.17 (J=11 and 5Hz) was attributed to H-12 and was shown to be coupled with signals at δ 2 30 (dd, J=11 and 12Hz) and 2.85 (dd,J=12 and 5Hz) which were assigned to H-11*ax* and H-11*eq*. Irradiation at δ 5 17 transformed the signals at δ 2 30 and 2 85 into an AB system (J=12Hz) A complex signal at δ 4.0 (dq, J=10 and 6Hz) was attributed to H-7 geminal to an ethereal oxygen Irradiation of this signal transformed the doublet (J=6Hz) observed at δ 1 40 (3H) to a singlet which could be thus assigned to the C-6 methyl group It also transformed a double quartet observed at δ 2 0 (J=10 and 7Hz) to a quartet (J=7Hz) which allowed the assignment of this signal to H-8 The 17 methyl group was responsible for a doublet (3H,J=7Hz) observed at δ 1 15 The ^{13}C NMR spectrum (Table 2) was in agreement with the structure **12** proposed for rhyacophiline SFORD experiments established the presence of three aromatic carbon atoms bearing hydrogens and three substituted aromatic carbon atoms All the assignments were in agreement with resonances observed in related structures [11]

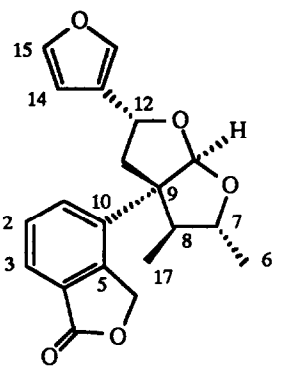


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Table 2 ^{13}C NMR SPECTRAL DATA FOR COMPOUND **12** ($CDCl_3$, 20 MHZ)

C	δ	C	δ
1	129 62 (d)	11	40 40 (t)
2	131 65 (d)	12	75 76 (d)
3	124 32 (d)	13	125 53 (s)
4	127 24 (s)	14	108 42 (d)
5	142 07 (s)	15	143 63 (d)
6	19 18 (q)	16	139 54 (d)
7	82 89 (d)	17	11 62 (q)
8	52 14 (d)	18	170 75 (s)
9	62 33 (s)	19	69.94 (t)
10	143 32 (s)	20	112 28 (d)

SFORD Multiplicities are in parenthesis

The chirality at C-9, C-8 and C-12 was deduced on biogenetic grounds In order to prove the structure and relative stereochemistry proposed for rhyacophiline an X-ray diffraction analysis was conducted on a single crystal Fig 1 shows the molecular structure and stereochemistry relative to 12-R. Both phenyl and furan rings are planar within experimental error. The γ-lactone ring is also fairly planar [maximum deviation C(19) 0 015 A], while the remainder two five-membered rings [C(7)-C(8)-C(9)-C(20)-0(1) and C(9)-C(11)-C(12)-O(2)-C(20)] adopt twist-chair conformations Methyl groups at C(7) and C(8) hold a synclinal [τ=79 4(5)°] relation .

Rhyacophiline is, therefore, a 5,6-seco clerodane diterpenoid with an aromatic A ring, a skeleton which we have named **rhyacophane.**[11] Compounds with this skeleton have been isolated from *Salvia reptans* and a 2nd population of *S rhyacophila* (Ortega et al Instituto de Química, personal communication)

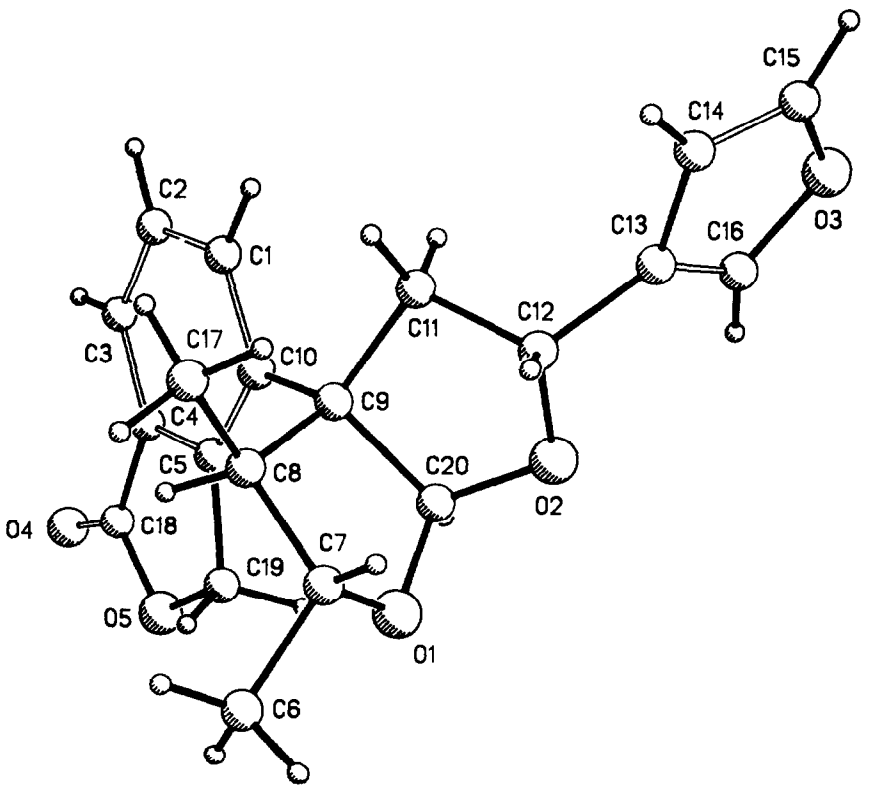

Figure 1 Computer generated perspective drawing of rhyacophiline **12**

EXPERIMENTAL

General Experimental Procedures. ^1H and ^{13}C NMR spectra were performed at 80 and 20 MHz respectively, using TMS as int standard, coupling constants are in Hz.Mps: uncorr. MS were obtained at 70 eV by direct inlet. Plant material was collected in November 1985 in the State of Guerrero (México). Voucher specimen (TPR 4822a) was deposited at the Herbarium of the Instituto de Biología, UNAM.

Isolation of the constituents from *S rhyacophila* Dried and powdered aerial parts of *S rhyacophila* (2.30 Kg) were extracted twice with Me_2CO at room temp. for 5 days. The solvent was removed under red. pres to yield 76.60 g of gummy residue This extract was partitioned between petrol-benzene (1 1) and MeOH-H_2O (4.1) The less polar extract (29 g) was subjected to vacuum chromatography over silica gel Mixtures of petrol-EtOAc of increasing polarity were used as eluents. From the fractions eluted with petrol-EtOAC (9.1), 511 mg of a mixture of oleanolic and ursolic acids were isolated.

The polar extract was subjected to a second partition, between EtOAc and H_2O. The solvent was removed from the organic layer under red pres , 39 g of crude extract were obtained which, was treated as above using the same eluent system. From the fractions eluted with petrol-EtOAc (8:2) an additional crop (360 mg) of oleanolic and ursolic acids was obtained From the mothers liquors, compounds **4** (25 mg, 0.001% dry wt) and **12** (120 mg, 0 0052 % dry wt) were isolated by flash chromatography (petrol-Me_2CO 9.3·0.7). Further elution with petrol-EtOAc (8 2) yielded 1 8 g (0.08 % dry wt) of salviarin (1) Physical data are in agreement with those described in literature [6]

Some fractions (9 10 g) eluted with petrol-EtOAc (1 1) were rechromatographed over silica gel (260 g) using mixtures of petrol-EtOAc of increasing polarity as eluents Elution with petrol-EtOAc (1:1) yield 1.4 g (0 06 % dry wt) of a crystalline mixture of compounds **5** and **6** Attempts to separate this mixture by chromatographic methods were unsuccessful The structure of the components of this mixture was established indirectly by chemical methods (see Discussion) From other fractions eluted with the same polarity, 40 mg (0.0017% dry wt) of compound **3** were isolated. Some fractions (320 mg) eluted with petrol-EtOAc (6:4) afforded 6 mg (0.0003% dry wt) of compound **2** after flash chromatography (Benzene-MeOH, 9.75:0 25) Compound **2** was identified as 6β-hydroxy-7,8-dehydrobacchatricuneatin, a diterpenoid previously isolated from *Aster alpinus* .The flavone cirsiliol, was isolated from some fractions eluted with petrol-EtOAc This compound was previously isolated from *Salvia officinalis* and recently from several Mexican *Salvia spp.*

6β-hydroxy-salviarin (3) Mp 188-192° (hexane-EtOAc), $[\alpha]_D$= -84 (MeOH, 0 11), UV λ^{MeOH} nm (ε) = 203 (7316), IR ν^{CHCl_3} cm-1· 3598, 1769, 1724, 1600, 1505, 875, ^1H NMR see Table 1 ; MS m/z (rel. int) 358 (43), 257 (8), 201 (7), 177 (10), 157 (15), 147 (12), 143 (18), 131 (14), 129 (21), 121 (18), 111 (36), 105 (18), 95 (62 1), 94 (100), 91 (49 4), 81 (31), 77 (31), 67 (12) $C_{20}H_{22}O_6$ requires M^+ at m/z 358

8,12R:15,16-diepoxy-*ent*-clerodan-3,13(16),14-trien-18:19-olide (4) Mp. 172 -173° (EtOAc); $[\alpha]_D$ = -77.33 ($CHCl_3$, c 0 15), UV $\lambda^{MeOH\ nm}$ (ε): 205 (10142); IR ν^{CHCl_3} cm^{-1}. 1765, 1660, 1500, 870; ^1H NMR see Table 1, MS m/z (rel int.): 328 (22.6), 313 (47.4), 164 (42), 121 (100), 94 (30), 91 (50.5), 81 (37), 67 (13). $C_{20}H_{24}O_4$ requires M+ at m/z 328.

Treatment of the mixture of 5 and 6 with $NaBH_4$. A solution of compounds **5** and **6** (200 mg) in THF-MeOH (1:1, 6 ml) was treated with 200 mg of $NaBH_4$ for 4 hours. After the usual work-up, 180 mg of the crude mixture of **7** and **8** were obtained and subjected to flash chromatography (Benzene-MeOH, 9.9:0.1) to yield 40 mg of **7** and 60 mg of **8.**

Compound 7 (6β-hydroxy-8-*epi*-salviarin). Mp. 260-262° (MeOH); IR ν^{nujol} cm^{-1} : 3440, 1770, 1733, 1600, 1502, 872; ^1H NMR see Table 1; MS m/z (rel int). 358 (18), 234 (7), 220 (7), 121 (13), 94 (100), 91 (46 3), 81 (29), 77 (30). $C_{20}H_{22}O_6$ requires M^+ at m/z 358.

Compound 8. Mp. 204-206° (MeOH), IR ν^{nujol} cm^{-1} · 3600-3200, 1740, 1615, 1505, 875, ^1H NMR see Table 1, MS m/z (rel. int.): 360 (0.7), 342 (17), 327 (18), 314 (8), 217 (7), 203 (10), 175 (42), 157 (23), 143 (30), 129 (41), 121 (45), 117 (37), 105 (55), 95 (19 1), 94 (100), 91 (19.9), 81 (74), 77 (13 6), 67 (54). $C_{20}H_{24}O_6$ requires M^+ at m/z 360

Acetylation of compound 7. A solution of 14 mg of **7** in 0.5 ml of pyridine was treated with 0.5 ml of Ac_2O at room temp for 4 h. After the usual work-up compound **9** (14.4 mg) was isolated as a crystalline product. Mp 249-251° (EtOAc-MeOH), IR ν^{nujol} cm^{-1} 1768, 1755, 1730, 1600, 1500, 870, ^1H NMR see Table 1; MS m/z (rel int). 400 (15.4), 358 (9), 340 (12), 245 (17), 157 (32), 148 (56 3), 129 (29), 121 (30), 94 (73), 91 (71 5), 81 (35), 77 (27), 67 (14), 43 (100). $C_{22}H_{24}O_7$, requires M^+ at m/z 400.

Treatment of 8 with Jones reagent. Compound **8** (50 mg) in Me_2CO (10 ml) at 5° was treated with Jones reagent. After the usual work-up crystalline compound **10** (31 mg) was obtained Mp. 230-233° (Me_2CO-MeOH), IR ν^{nujol} cm^{-1} 3440, 1765, 1720, 1600, 1500, 870, ^1H NMR see Table 1, MS m/z (rel int.) 358 (6.1), 314 (12), 247 (37), 220 (19), 213 (24), 201 (12), 175 (11), 153 (17), 145 (15), 131 (15), 121 (19), 109 (50 5), 95 (67.7), 94 (44.4), 91,(100), 81 (33), 77 (35), 66 (26). $C_{20}H_{22}O_6$ requires M^+ at m/z 358

Saponification of the mixture of 5 and 6 with $KHCO_3$. A solution of **5** and **6** (100 mg) in THF-MeOH (1:1, 10 ml) at room temp. was treated with an aqueous solution of $KHCO_3$ (50 mg in 0.5 ml H_2O). The mixture was stirred for 72 h After the usual work-up and flash chromatography (CH_2Cl_2 -MeOH, 99 5.0.5) of the crude reaction mixture, compounds **7** (27 mg) and **10** (20 mg) were isolated

Epimerization of Salviarin (1). Compound 1 (50 mg) in THF-MeOH (1:1, 8 ml), was treated with an aqueous solution of $KHCO_3$ (30 mg in 0.5 ml H_2O). The mixture was stirred for 72 h. After the usual work-up, compound 11 (8-*epi*-salviarin) (28 mg) was isolated as a crystalline product. Mp 233-235° (hexane-EtOAc) $[\alpha]_D$ = -48 ($CHCl_3$, c 0.1); IR ν^{CHCl_3} cm^{-1}: 1765, 1748, 1600, 1500, 875; ^1H NMR see Table 1; MS m/z (rel. int) 342 (12.8), 231 (6), 159 (8), 145 (15), 131 (22), 121 (27), 117 (27), 105 (21), 95 (41 6), 94 (84 1), 91 (100), 81 (22), 77 (32), 67 (20). $C_{20}H_{22}O_5$ requires M^+ at m/z 342.

Rhyacophiline (12). Mp. 125-126° (hexane- EtOAc), $[\alpha]_D$ = -12 (MeOH, C 0.1); UV λ^{MeOH} nm (ε) 203 (47468), 275 (1816), 282 (1816), IR $\nu^{CHCl_3}cm^{-1}$ .1763, 1602, 1504, 1484, 1019, 875, ^1H NMR see Table 1, ^{13}C NMR see Table 2, MS m/z (rel. int) 340 (3 9), 294 (45.8), 239 (100), 195 (39 4), 94 (32), 91 (17), 81 (56 3) $C_{20}H_{20}O_5$ requires M^+ at m/z 340

X-ray structure determination of Rhyacophiline. Crystals of rhyacophiline (12) were obtained by slow evaporation of CH_2Cl_2-MeOH soln The crystals are orthorhombic, space group $P2_12_12_1$. Unit cell dimensions were obtained by a least-squares fit to the angular settings of 25 centered reflections with $8.5 < 2\theta < 26.3°$ on a Nicolet P3F diffractometer using Ni-filtered CuKα radiation (λ = 1.54178 Å). Crystal data: $C_{20}H_{20}O_5$, Mr = 340 4, a= 7 939 (1), b= 14.502 (2), c= 14 923 (2) Å, V= 1718 1 (4) $Å^3$, d_{calc} = 1.32 g cm^{-3}, F (000)= 720, Z= 4 and μ (CuKα) = 7.36 cm^{-1} The crystal chosen for intensity measurement had dimensions 0.24 X 0.26 X 0 18 mm One octant of the reciprocal space, with an index range of h 0 to 8, k: 0 to 15, l: 0 to 15 ($110° < 2\theta$) was measured by 2θ-θ scan technique, the rate of scanning being varied from 4 0 to 29.3 deg min^{-1}, two standards (200, 103) monitored every 50 measurements show no significant fluctuation. 1269 unique reflections were collected of which 1202 were considered observed [Fo > 3σ(Fo)] and corrected by Lorentz and polarization effects, but not absorption The crystal structure was solved by direct methods using SHELXTL[12] and the model refined by block-diagonal least-squares with anisotropic thermal parameters for non-H atoms H-atoms were assigned on idealized positions with a fixed isotropic U= 0 06 $Å^2$. In final refinement cycle, R= 0.039 and wR = 0 051 for observed reflections, where $w = [\sigma^2(Fo) + 0\ 0035\ Fo^2]^{-1}$, function minimized $\Sigma w(\Delta F)^2$, S= 1 05, max. and minimum heights in last $\Delta\rho$ map were 0.14 and -0.19 $eÅ^{-3}$, isotropic extinction parameter X= 0.008(2), complex scattering factors from International Tables for X-ray Crystallography [13] All computations on a Nova 4S computer [14]

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