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PARRYIN, A DITERPENE WITH A TRICYCLIC 6-7-5-RING SYSTEM FROM *SALVIA PARRYI**

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Key Word Index—*Salvia parryi*; Lamiaceae; roots; parryin; isopimara-6,8(14),15-triene; isopimara-8(14),15-dien-7-one; isopimara-8,15-dien-7-one; diterpenes.

Abstract—Parryin and six other pimarane-type diterpenes were isolated from the acetone extract of roots of *Salvia parryi*. Parryin represents the first example of a biogenetically new type of tricyclic 6-7-5-ring diterpenes. Isopimara-6,8(14),15-triene, isopimara-8(14),15-dien-7-one and isopimara-8,15-dien-7-one have been isolated from a natural source for the first time. The structures were determined by spectroscopic studies. © 1997 Elsevier Science Ltd. All rights reserved

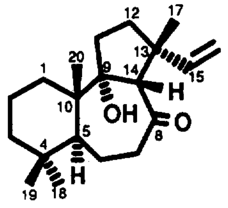
INTRODUCTION

Salvia represents the genus which comprises the largest number of plant species within the family Lamiaceae. *Salvia* species grow around the globe [2]. However, they are particularly numerous in Southern and Central America; and there are around 300 different *Salvia* species known to occur in México [3–6]. Quite a number of *Salvia* species have to be regarded as medicinal plants and they are utilized in folk medicine against various diseases [7, 8]. *Salvia parryi* is endemic in Northern México and in Arizona. Local people use its aqueous root extract to cure stomach disorders [9].

Since there are no reports on the chemical constituents of this medicinal plant, we started a phytochemical investigation.

RESULTS AND DISCUSSION

Chromatographic separation of an acetone extract from the root yielded **1** besides the known pimaranes **2**–**7**.



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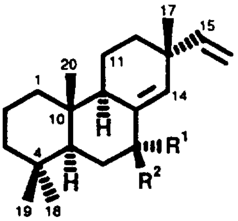
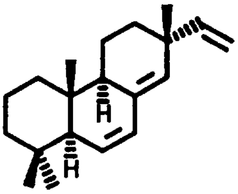
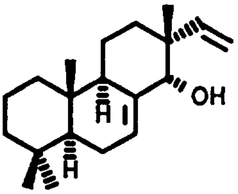




3

$\mathbf{2}$: $R^1 = R^2 = H$
$\mathbf{5}$: $R^1 = OH$; $R^2 = H$
$\mathbf{6}$: $R^1, R^2 = O$



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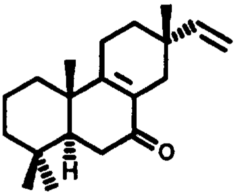

7

Compound **1** ($[M]^+$ by HR-EI mass spectrometry: $C_{20}H_{32}O_2$) exhibited ^1H NMR signals attributable to four methyl groups all bound to quaternary carbon atoms, one vinyl group, one alcoholic hydroxyl group and a singlet (1H) for a methine proton without any neighbouring protons. In addition, the ^{13}C NMR data (Table 1) gave evidence for a ketone group and one carbon–carbon double bond.

HMQC and HMBC (Fig. 1) measurements revealed the substituted tricyclic 6-7-5-ring system **1**, whose

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*Part 82 in the series 'Constituents of Tropical Medicinal Plants'. For part 81 see ref. [1].

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Table 1. ^{13}C NMR data of compounds **1**–**7** (δ [ppm], in $CDCl_3$)

C^{δ}	1	2	3	4	5	6	7
1	33.4	39.4	37.3	39.7	39.2	38.9	35.5*
2	18.8	19.1*	18.7*	18.8	19.0	19.0*	18.6
3	41.6	42.2	41.3	42.2	42.1	41.8	41.1
4	34.8	33.3	32.8	32.8	32.9	33.1	33.1
5	48.8	54.8	55.4	49.8	47.0	50.0	50.1
6	20.1	22.6	128.2	23.5	29.3	37.4	35.4*
7	45.2	36.0	130.3	127.7	73.4	200.8	200.1
8	212.2	137.3	135.6	137.2	139.6	135.4	128.8
9	88.5	50.7	50.5	47.0	46.2	51.1	166.0
10	43.9	38.3	37.3	35.1	38.5	36.0	39.8
11	37.9	18.8*	18.9*	19.4	18.3	18.7*	22.9
12	37.0	34.6	34.9	27.5	34.3	34.1	33.7
13	47.8	37.4	38.3	41.1	37.4	38.6	34.4
14	67.4	128.5	132.6	79.7	134.0	144.1	33.4
15	145.3	149.2	148.8	146.6	148.3	146.5	145.3
16	111.7	109.9	110.1	113.6	110.6	111.7	111.6
17	27.6	26.0	26.5	22.1	25.6	25.8	28.0
18	33.4	33.8	32.8	33.4	33.4	32.6	32.5
19	21.8	22.1	21.8	22.3	21.9	21.1	21.4
20	16.2	15.0	13.3	14.8	14.2	13.9	17.9

*Assignments may be interchangeable.

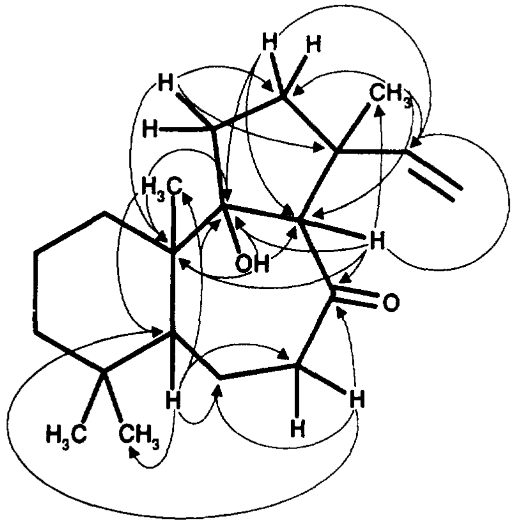


Fig. 1. Important long-range correlations in the HMBC of compound **1**.

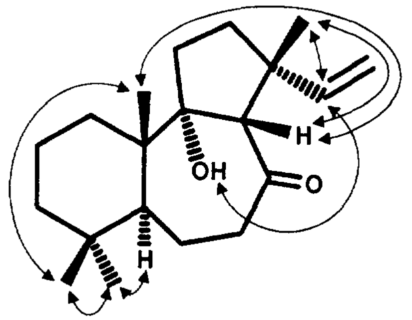


Fig. 2. Important NOEs observed in the ^{1}H NMR of compound **1**.

relative configuration was the result of NOE measurements (Fig. 2).

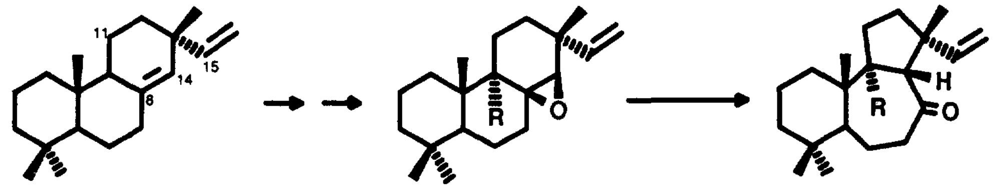
Parryin (**1**) with its 6-7-5-tricyclic skeleton represents a novel structural type among the diterpenes. Biogenetically, compound **1** might be generated by rearrangement of a pimarane-type precursor like **2** (Scheme 1).

All six compounds isolated from *S. parryi* besides parryin (**1**) are structurally related to **1**. Among these diterpenes, compounds **3**, **6** and **7** deserve special attention, since they came from natural sources for the first time. Until now they had only been reported as synthetic conversion products [10, 11].

Compound **3** represents the dehydration product of **5** and thus raises the question of whether it might be an artifact generated during the isolation procedure. However, we showed the presence of the triene **3** immediately in the root extract and, therefore, we regard **3** as a genuine natural product.

EXPERIMENTAL

General. Mps are uncorr. Unless otherwise stated, $[\alpha]_D$ and IR in $CHCl_3$; UV and CD in MeOH. $[\alpha]_D$ at 21°. Unless otherwise stated, ^{1}H NMR were run at 360 MHz, and ^{13}C NMR at 90 MHz with TMS as int. standard. EIMS were obtained at 70 eV; unless key ions, only ions are given with rel. intensities >10% and $m/z > 50$; HR-EIMS by peakmatching at $M/\Delta M$ *ca.* 10 000 on a Finnigan MAT 312. Analytical TLC was performed on precoated plates (HPTLC plates, silica gel 60 F_{254}, Merck) using the following solvent systems: S-1 = $CHCl_3$–cyclohexane (9 : 1), S-2 = $CHCl_3$–toluene (1 : 1), S-3 = petrol, S-4 = cyclohexane–Me_2CO (9 : 1), S-5 = $CHCl_3$, S-



2 1

Scheme 1. Hypothetical biosynthetic pathway to parryin (**1**), R = OH).

6 = toluene; detection by UV or anisaldehyde reagent [12].

Plant material. *Salvia parryi* Gray was collected in Los Chorros (Arteaga, Coahuila) near Saltillo, Coah., México. Botanical identification by Humberto Sánchez. A voucher specimen is held under No. 8716 in the ITESM herbarium in Monterrey.

Extraction and chromatography. The Me_2CO extract (prepared at 56°) of ground air dried roots (450 g) was subjected to MPLC (medium pressure liquid chromatography) on silica gel (cyclohexane with increasing amounts of EtOAc) to give 10 fractions, which were further separated by repeated CC or MPLC using the following systems: (a) silica gel 60 (Macherey-Nagel) with petrol or cyclohexane or cyclohexane–$CHCl_3$, cyclohexane–EtOAc, cyclohexane–Me_2CO, $CHCl_3$, CH_2Cl_2; (b) LiGhroprep® RP 18 (40–60 μm, Merck) with $MeOH–H_2O$ (4 : 1) → MeOH (100%); (c) Fractogel® PVA 500 (Merck) with $MeOH–CHCl_3$ (7 : 3). These procedures yielded the pure compounds **1**–**7**.

Parryin (**1**). Viscous oil (2 mg). TLC: R_f 0.37 (S-1); R_f 0.20 (S-2); anisaldehyde: yellow. $[\alpha]_D$ +40° (*c* 0.14). CD λ_{max} nm ($\Delta\varepsilon$): 244 (+0.02), 294 (+0.89). IR ν_{max} cm^{-1}: 3545, 3083, 2931, 2872, 2856, 1697, 1633, 1466, 1404, 1368, 994, 921. ^1H NMR ($CDCl_3$): δ 0.85–1.67 (*ca*. 24H) including 0.85 (3H, *s*, Me-19), 0.92 (3H, *s*, Me-18), 1.03 (3H, *s*, Me-20) and 1.22 (3H, *s*, Me-17), 2.03 (1H, *ddd*, $J_1 = 13$, $J_2 = 8$, $J_3 = 2.5$ Hz, H-12_α), 2.32 (1H, *m*, H-11_β), 2.37 (1H, *m*, H-7_A), 2.49 (1H, *m*, H-7_B), 2.93 (1H, *s*, H-14), 5.06 (1H, *dd*, $J_1 = 11$, $J_2 = 1.5$ Hz, H-16_A), 5.11 (1H, *dd*, $J_1 = 18$, $J_2 = 1.5$ Hz, H-16_B), 6.75 (1H, *ddd*, $J_1 = 18$, $J_2 = 11$, $J_3 = 1$ Hz, H-15). ^1H NMR (C_6D_6): δ 0.73–1.72 (*ca*. 23H) including 0.73 (3H, *s*, Me-20), 0.75 (3H, *s*, Me-19), 0.78 (3H, *s*, Me-18) and 1.31 (3H, *s*, Me-17), 1.74 (1H, *dd*, $J_1 = 9$, $J_2 = 1$ Hz, H-5), 1.81 (1H, *ddd*, $J_1 = 13$, $J_2 = 8$, $J_3 = 2.5$ Hz, H-12_α), 2.01 (1H, *ddd*, $J_1 = 14.5$, $J_2 = 9.5$, $J_3 = 2.5$ Hz, H-11_β), 2.40 (2H, *m*, H-7), 2.68 (1H, *s*, H-14), 4.95 (1H, *dd*, $J_1 = 11$, $J_2 = 1.5$ Hz, H-16_A), 4.99 (1H, *dd*, $J_1 = 18$, $J_2 = 1.5$ Hz, H-16_B), 7.07 (1H, *ddd*, $J_1 = 18$, $J_2 = 11$, $J_3 = 1$ Hz, H-15). ^{13}C NMR: Table 1. EIMS *m*/*z* (rel. int.): 304 $[M]^+$ (8), 286 (12), 271 (10), 236 (17), 179 (69), 166 (73), 151 (41), 137 (37), 123 (45), 109 (57), 95 (57), 81 (62), 69 (84), 55 (100); HR-EIMS *m*/*z*: 304.2410 $[M]^+$ (calcd for $C_{20}H_{32}O_2$: 304.2402).

(−)-*Isopimara*-8(14),15-*diene* (**2**). Amorphous (727 mg). Mp 40° (from cyclohexane) (ref. [13] mp 38–39° (from MeOH)). TLC: R_f 0.51 (S-3); anisaldehyde: violet. $[\alpha]_D$ −13° (*c* 0.55) (ref. [13] $[\alpha]_D^{20}$ −10° (*c* 2.36)). IR, ^1H NMR, MS in agreement with published data [13–16].

Isopimara-6,8(14),15-*triene* (**3**). Viscous oil of low chemical stability (14 mg). TLC: R_f 0.42 (S-3); anisaldehyde: violet. $[\alpha]_D$ *ca*. −40° (*c* 1.00). IR, UV, ^1H NMR, MS in agreement with published data [10].

14α-*Hydroxyisopimara*-7,15-*diene* (**4**). Crystalline (8 mg). Mp 54° (from Me_2CO) (ref. [17] mp 56–57° (from hexane)). TLC: R_f 0.39 (S-4); anisaldehyde: violet. $[\alpha]_D$ −53° (*c* 0.72). IR, ^1H NMR, MS in agreement with published data [17]. ^{13}C NMR in agreement with a compound of a comparable substructure [18].

7α-*Hydroxyisopimara*-8(14),15-*diene* (**5**). Crystalline (35 mg). Mp 82° (from Me_2CO) (ref. [17] mp 83–85° (from hexane)). TLC: R_f 0.30 (S-5); anisaldehyde: violet. $[\alpha]_D$ −67° (*c* 0.35) (ref. [19] $[\alpha]_{589}^{24}$ −69° (*c* 2.37)). IR, ^1H NMR, ^{13}C NMR, MS correlates well with the published data [10, 17, 19].

Isopimara-8(14),15-*dien*-7-*one* (**6**). Crystalline (23 mg). Mp 108° (from Me_2CO). TLC: R_f 0.22 (S-6); anisaldehyde: violet. $[\alpha]_D$ −36° (*c* 1.23). ^1H NMR ($CDCl_3$): δ 0.84–1.85 (*ca*. 23H) including 0.84 (3H, *s*, Me-20), 0.86 (3H, *s*, Me-18), 0.90 (3H, *s*, Me-19), 1.10 (3H, *s*, Me-17) and 1.49 (1H, *dd*, $J_1 = 14$, $J_2 = 5$ Hz, H-5), 2.06 (1H, *m*, H-9), 2.27 (1H, *dd*, $J_1 = 18.5$, $J_2 = 14$ Hz, H-6_{ax}), 2.55 (1H, *dd*, $J_1 = 18.5$, $J_2 = 5$ Hz, H-6_{eq}), 4.97 (1H, *dd*, $J_1 = 11$, $J_2 = 1$ Hz, H-16_A), 5.00 (1H, *dd*, $J_1 = 17.5$, $J_2 = 1$ Hz, H-16_B), 5.81 (1H, *dd*, $J_1 = 17.5$, $J_2 = 11$ Hz, H-15), 6.71 (1H, *dd*, $J_1 = 2.5$, $J_2 = 1.5$ Hz, H-14). IR, UV, MS in agreement with published data [11, 20].

Isopimara-8,15-*dien*-7-*one* (**7**). Amorphous (3mg). TLC: R_f 0.47 (S-1); anisaldehyde: violet. $[\alpha]_D$ +103° (*c* 0.3). IR, UV. ^1H NMR, ^{13}C NMR, MS in agreement with published data [11, 16, 20, 21].

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REFERENCES

1. Achenbach, H. and Benirschke, M., *Phytochemistry*, 1997, **44**, 1387.
2. Standley, P. and Williams, L., *Fieldiana Botany*, 1973, **24**, 237.
3. Epling, C., *Repertorium specierum novarum regni vegetabilis*. Beihefte, 1938, **110**, 1.

4. Rodríguez-Hahn, L., Esquivel, B., Sánchez, A. A., Sánchez, C., Cárdenas, J. and Ramamoorthy, T. P., *Revista Latinoamericana de Quimica*, 1989, **20**, 105.
5. Rodríguez-Hahn, L., Esquivel, B., Cárdenas, J. and Ramamoorthy, T. P., in *Advances in Labiatae Science*, ed. R. M. Harley and T. Reynolds. The Royal Botanic Garden, Kew, Surrey, 1992, p. 335.
6. Ramamoorthy, T. P. and Elliott, M., in *Biological Diversity of Mexico: Origins and Distribution*, ed. T. P. Ramamoorthy, R. Bye, A. Lot and J. Fa, Oxford University Press, New York, 1993, p. 513.
7. Usher, G., *A Dictionary of Plants Used by Man*, Constable, London, 1974, p. 520.
8. Morton, J. F., *Atlas of Medicinal Plants of Middle America*, Charles C. Thomas, Springfield, IL, 1981, p. 778.
9. Domínguez, X. A. and Abularach, T. D., personal communication.
10. Blunt, J. W., Boyd, G. S., Hartshorn, M. P. and Munro, M. H. G., *Australian Journal of Chemistry*, 1976, **29**, 987.
11. Pinto, A. C., Silva, A. J. R., Mayer, L. M. U. and Braz, F. R., *Phytochemistry*, 1979, **18**, 2036.
12. Stahl, E. and Kaltenbach, U., *Journal of Chromatography*, 1961, **5**, 351.
13. Corbett, R. E. and Smith, R. A. J., *Journal of the Chemical Society (C)*, 1967, 300.
14. Audier, H. E., Bory, S., Fétizon, M. and Anh, N. T., *Bulletin de la Société Chimique de France*, 1966, 4002.
15. Wenkert, E., Alfonso, A., Beak, P., Carney, R. W. J., Jeffs, P. W. and McChesney, J. D., *Journal of Organic Chemistry*, 1965, **30**, 713.
16. Chu, M. and Coates, R. M. *Journal of Organic Chemistry*, 1992, **57**, 4590.
17. Bheemasankara Rao, Ch., Suseela, K. and Subba Raju, G. V., *Indian Journal of Chemistry, Section B*, 1984, **23**, 177.
18. Bruno, M., Savona, G., Fernánez-Gadea, F. and Rodríguez, B., *Phytochemistry*, 1986, **25**, 475.
19. Bohlmann, F. and Lonitz, M., *Chemische Berichte*, 1978, **111**, 843.
20. Patitucci, M. L., da Silva, R. S., Valente, L. M. M., Epifanio, R. de A. and Pinto, A. C., *Quimica Nova*, 1990, **13**, 273.
21. Pinto, A. C., da Silva, R. S. and Valente, L. M. M., *Phytochemistry*, 1988, **27**, 3909.