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THE ABSOLUTE CONFIGURATION OF SALVILEUCOLIDE METHYL ESTER, A SESTERTERPENE FROM IRANIAN *SALVIA* SPECIES

ANTHONY LINDEN, MATHIAS JUCH, FIROUZ MATLOUBI MOGHADDAM,* BEHZAD ZAYNIZADEH* and PETER RÜEDI†

Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland; *Sharif University of Technology, Department of Chemistry, P.O. Box 11365-9516, Tehran, Iran

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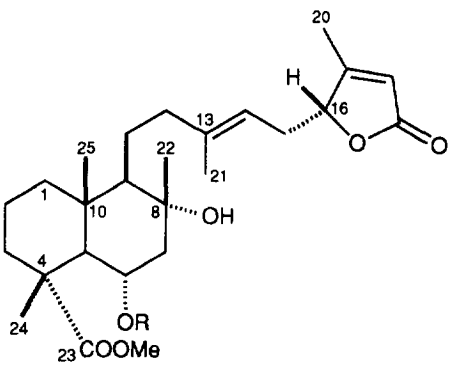
Key Word Index—*Salvia*; labiatae; sesterterpenoid; X-ray analysis; absolute configuration.

Abstract—The absolute configuration of the sesterterpenoid salvileucolide methyl ester, which has been isolated from the aerial parts of two Iranian *Salvia* species, was established by X-ray diffraction analysis. The compound was shown to belong to the normal series (10*R*) and the configuration at C-16 was determined to be *R*.

INTRODUCTION

The compound **1a** has been isolated as the major constituent from aerial parts of *Salvia hypoleuca* [1] and *S. sahendica* [2], both species being endemic to Iran. In previous papers the constitution of **1a** was assigned by spectroscopic methods, especially by extensive ^1H and ^{13}C NMR experiments. However, the relative configuration at C-16 and the absolute configuration of the molecule remained undetermined.

As the absolute configuration constitutes an essential feature of a natural product, we decided to determine it unequivocally. Chemical transformation of **1a** to an established reference compound (e.g. a suitable labdane derivative) and comparison of the chiroptical data would quite easily provide the absolute configuration of the skeleton. However, the unambiguous determination of the stereochemistry at C-16 (e.g. by degradation of **1a** to a 3-hydroxypentanoic acid derivative) was not expected to be without difficulties, probably resulting from racemization. This fact prompted us to undertake an X-ray analysis of the 6-*O*-*p*-bromobenzoyl ester **1b** where the Br atom greatly facilitates the direct determination of the absolute configuration. In this brief note we report the X-ray analysis of **1b**, which establishes the structure of **1a**.



	R
1a	H
1b	*p*-Br-benzoyl

RESULTS AND DISCUSSION

The structure of **1b** ($C_{33}H_{43}BrO_7$) was solved by direct methods using SHELXS86 [3] and DIRDIF92 [4]. The absolute configuration was determined by measuring the Friedel mates of all unique reflections and refining the enantiopole parameter [5, 6] with the CRYSTALS program [7]. This parameter refined to $-0.02(1)$, which confidently confirmed that the configuration of the molecule depicted in the Fig. 1 represents the true absolute configuration. As previously assumed [1, 2], the natural product belongs to the normal cyclic sesterterpenoid series (10*R* for **1a**) and has *R*-configuration at C-16. Full details of the X-ray determination will be published in *Acta Cryst. Sect. C*.

EXPERIMENTAL

General. The diffraction data were collected at 173 ± 1 K on a Rigaku AFC5R diffractometer with graphite-monochromated MoK_α radiation ($\lambda = 0.71069$ Å) and a 12 kW rotating anode generator. All calculations were performed using the TEXSAN crystallographic software package [8].

†Author to whom correspondence should be addressed.

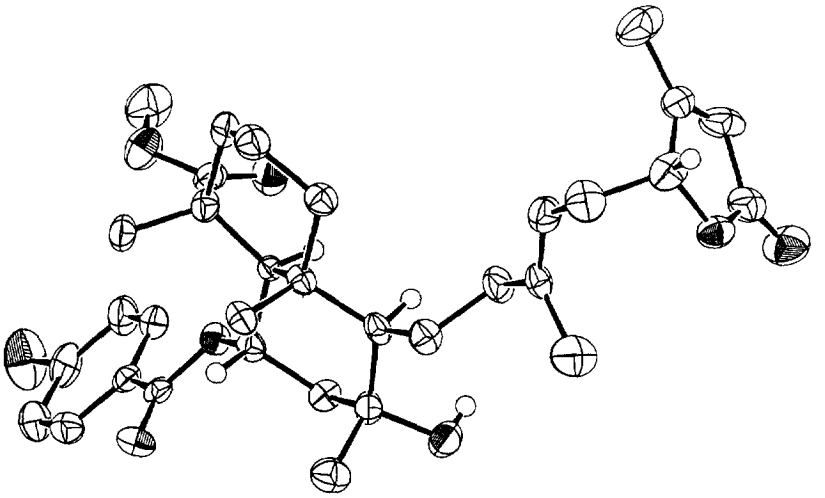


Fig. 1. ORTEP diagram (50% probability ellipsoids) showing the structure and solid-state conformation of **1b**. The H atoms, except for those at the chiral centres and of the hydroxyl group, are omitted.

Preparation of 6-O-*p-bromobenzoyl-salvileucolide-methyl ester* (**1b**). A soln of **1a** (13 mg, 0.029 mmol) and *p*-bromobenzoyl chloride (40 mg, 0.18 mmol) in pyridine (1 ml) was stirred at 70° overnight. CC (silica gel, hexane–Me_2CO 9:1 → 6:1) of the crude reaction product yielded **1b** (18.5 mg, 100%). Recrystallization from hexane–Et_2O followed by hexane–Me_2CO (diffusion method) yielded crystals that were suitable for the X-ray analysis: colourless plates, $C_{33}H_{43}BrO_7$ (M_r 631.62), mp 58–59° (uncorr.); $[\alpha]_D$ +39.6 (EtOH, *c* 0.58).

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