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ISOLEPIDOZENE, A DIASTEREOMER OF BICYCLOGERMACRENE, IN SOME LIVERWORTS

INGO H. HARDT, ANGELA RIECK, WILFRIED A. KÖNIG* and HERMANN MUHLE†

Institut für Organische Chemie, Universität Hamburg, D-20146 Hamburg, Germany; †Abteilung Spezielle Botanik, Universität Ulm, D-89091 Ulm, Germany

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Key Word Index—*Preissia quadrata*; *Frullania tamarisci*; *Scapania aequiloba*; Hepaticae; liverworts; essential oils; *trans*-bicyclo[8.1.0]undecane; (−)-isolepidozene.

Abstract—Isolepidozene, the diastereomer of the widespread sesquiterpene hydrocarbon, bicyclogermacrene, has been identified in several liverworts. This previously unknown sesquiterpene hydrocarbon is based on the rare *trans*-bicyclo[8.1.0]undecane skeleton.

INTRODUCTION

Bicyclogermacrene is a widespread sesquiterpene hydrocarbon, which was first isolated from the peel oil of the shrub, *Citrus junos* [1], and has since been identified as a constituent in a variety of other species. The (+)-enantiomer is found in some essential oils of higher plants, while (−)-bicyclogermacrene (**1**) has been identified as a constituent of many liverworts. The 4,5-double bond isomer, (+)-isobicyclogermacrene (**2**), is a thermal rearrangement product of (−)-bicyclogermacrene [2], but has not yet been identified as a natural product; only the 14-formyl derivative, (−)-isobicyclogermacrenal, was isolated from the liverwort, *Lepidozia vitrea* [3].

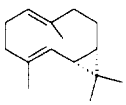
The diastereomer of (−)-isobicyclogermacrenal with a bicycloundecane system containing a *trans*-fused cyclopropane ring has been isolated from *L. vitrea* and called, (−)-lepidozenal [4]. The corresponding hydrocarbon, (−)-lepidozene (**3**), was prepared from the aldehyde for the first time. Meanwhile, the enantiomeric form, (+)-lepidozene, was isolated from the gorgonia, *Lophogorgia ruberrima* [5]; further hydroperoxylepidozenes were found in the actinia, *Anthopleura pacifica* [6]. The rare *trans*-bicyclo[8.1.0]undecane skeleton has previously only been found in a diterpenoid of the brown alga, *Dilophus prolificans* [7].

The fourth isomer, the diastereomer of bicyclogermacrene and the double-bond isomer of lepidozene, has so far not been identified as a natural product, although it has been synthesized by McMurry and Bosch, together with the three other isomers, and was called isolepidozene [8].

RESULTS AND DISCUSSION

During the analysis of the essential oil of the liverwort, *Preissia quadrata*, we observed that the main component (> 40%) had a mass spectrum almost identical with that of bicyclogermacrene, but this sesquiterpene hydrocarbon eluted before bicyclogermacrene on an apolar CpSil-5 capillary column. The sign of optical rotation of the unknown compound corresponded to **1**, which is a common constituent of liverworts. Although the ^{1}H NMR spectra of both compounds were quite similar, there were obvious differences in the chemical shifts of the ring-fused cyclopropane protons (1.29 and 0.61 ppm for bicyclogermacrene, and 0.81 and − 0.07 ppm for the unknown compound) and of the olefinic proton next to the cyclopropane group (4.35 and 4.58 ppm, respectively). Analysis of the coupling constants of the ring-fused cyclopropane protons suggested the presence of a *trans*-fused bicyclo[8.1.0]undecane system, as in (−)-isolepidozene (**4**), instead of the *cis*-fused system, as in **1**. Comparison of NMR spectral data for the new compound with the data reported by McMurry and Bosch [8] confirmed its identity as isolepidozene (**4**). The absolute stereochemistry of **4** has so far not been determined, but was tentatively assigned as illustrated in structure **4** by analogy to **3** from the liverwort, *L. vitrea*. Due to the strain in the cyclodecadiene ring, **3** decomposes in $CDCl_3$ solution in an NMR tube within one day when exposed to sunlight.

After the identification of isolepidozene in *P. quadrata*, this compound was also isolated from the essential oils of the liverworts *Frullania tamarisci* and *Scapania aequiloba*; it could also be detected by GC-mass spectrometry (MS) in several other liverworts. Our results may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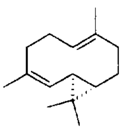
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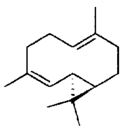
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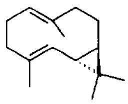
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*Author to whom correspondence should be addressed.

indicate that isolepidozene has so far been misinterpreted as bicyclogermacrene during the analysis of the essential oils of liverworts by GC-MS, although there are apparent differences in the relative intensities of the fragments between *m/z* 100 and 120 in their EI mass spectra.

Bicyclogermacrene has been suggested to be a biogenetic precursor of a number of other sesquiterpenes containing a *cis*-fused dimethylcyclopropane ring, such as maaliane, aristolane and aromodendrane derivatives. Consequently, isolepidozene may be a precursor of sesquiterpenes containing the *trans*-fused dimethylcyclopropane ring, which have so far not been identified or described.

EXPERIMENTAL

The liverworts, *P. quadrata* (Scop.) Nees, *F. tamarisci* (L.) Dum., and *S. aequiloba* (Schwaegr.) were collected in the Westalb and Allgäu, Germany, in October 1993. Essential oils were obtained by steam dist. of aq. homogenates of *ca* 50 g of green plants using *n*-hexane as collection solvent. Isolepidozene (**4**) was isolated by prep. GC using a 1.8 m × 4.3 mm column packed with 10% SE-30. The fr. obtained from *F. tamarisci* was only 50% pure.

(−)-*Isolepidozene* (**4**). $C_{15}H_{24}$. $[\alpha]_D$ − 50 (*ca* 0.05, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ0.07 (1H, *ddd*, $J = 9.6$, 5.0 and 1.0 Hz), 0.81 (1H, *dd*, $J = 10.2$ and 5.0 Hz), 1.00–1.10 (1H, *m*), 1.06 (3H, *s*), 1.13 (3H, *s*), 1.52 (3H, *s*), 1.63 (3H, *d*, $J = 1.0$ Hz), 1.92 (1H, *dt*, $J = 13.7$ and 3.0 Hz), 2.00 (1H, *td*, $J = 12.7$ and 4.0 Hz), 2.10–2.24 (3H, *m*), 2.29 (1H, *dt*, $J = 12.7$ and 3.0 Hz), 2.52 (1H, *m*), 4.58 (1H, *bd*, $J = 10.2$ Hz), 4.83 (1H, *dd*, $J = 11.7$ and 3.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ134.94, 132.08, 131.96, 127.19, 42.25, 41.14, 40.38, 36.24, 29.30, 24.92, 24.28, 23.03, 21.84, 17.26, 16.36. GC-MS (EI, 70 eV), *m/z* (rel. int.): 204 (12), 189 (8), 161 (15), 136 (24), 121 (100), 119 (22), 107 (81), 105 (26), 93 (67), 91 (38), 79 (41), 67 (25), 55 (31), 41 (68).

Bicyclogermacrene (**1**). GC-MS (EI, 70 eV) *m/z* (rel. int.): 204 (18), 189 (12), 161 (25), 136 (24), 121 (100), 119 (30), 107 (63), 105 (39), 93 (84), 91 (38), 79 (40), 67 (26), 5 (32), 41 (61).

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