An Example of the Co-Occurrence of Enantiomeric Labdane-Type Diterpenes in the Leaves of *Mimosa hostilis*[1)]

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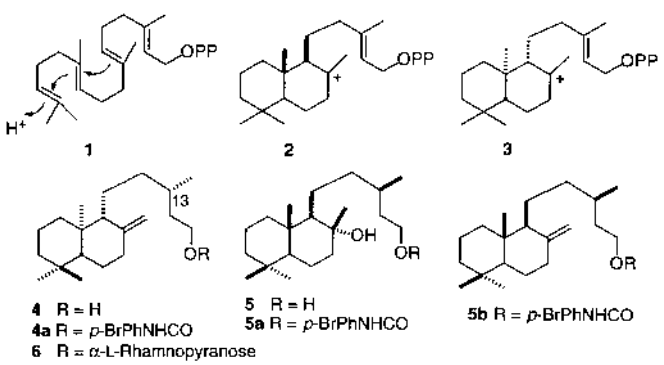
Two labdane-type diterpenes 4 and 5 isolated from the Brazilian medicinal plant *Mimosa hostilis* were confirmed to have absolute configurations in enantiomeric relation to each other by X-ray crystallographic analysis of *p*-bromophenyl carbamate derivative 5a and comparison between 4a and 5b, readily available from 5a.

Key words *Mimosa hostilis*; Leguminosae; 8,15-labdanediol; *ent*-8(17)-labden-15-ol; labdane-type diterpene; co-occurrence of enantiomers

The normal and antipodal bicyclic labdanoids are frequently isolated from plants.[2,3)] They are presumably biosynthesized from normal (**2**) and enantiomeric carbocation (**3**), respectively, which are converted from the achiral geranyl geranyl pyrophosphate (**1**). The first example of the co-occurrence of normal labdadienoic acid and antipodal dihydroeperutic acid in the same plant was reported in 1967.[4)] Since then, the surprising co-occurrence of both enantiomeric labdane series in a single plant species was subsequently observed.[5—9)] Thus a plant biosynthesizing normal labdane-type diterpenes *via* **2** could also produce enantiomeric congeners *via* **3**, and thererfore we should pay attention to the optical purity of all natural diterpenoids, especially, labdanoids.[10)]

In this communication, we report an additional example of the co-occurrence of normal labdandiol **5** and antipodal *ent*-labdenol **4** in the leaves of the Brazilian medicinal plant *Mimosa hostilis* (Leguminosae).

In course of structural studies on new diterpene rhamnoside **6** and its acetyl derivatives[11)] isolated from the leaves of *M. hostilis*, we were involved in making out the absolute configuration, including the C-13 chirality, of the aglycone part of **6**. Thus acid hydrolysis of **6** gave L-rhamnose and a labdenol **4**, $[\alpha]_D$ −22° (*c* 0.64, $CHCl_3$),[12)] as the sugar and diterpene parts, respectively. The same diterpene alcohol **4** was also isolated from *M. hostilis* simultaneously. The structure of **4** was identical except for the specific rotation (+25.2°) to that of 8(17)-labden-15-ol isolated from *Citrus palinhae*[13)] as well as that of a compound derived from manool,[14)] and thereby **4** was most likely the enantiomer of 8(17)-labden-15-ol cited in the literature. Hence we decided to unambiguously establish the absolute configuration, including the C-13 chirality, of **4** using the X-ray crystallographic method. To do this, **4** was converted to *p*-bromophenyl carbamate **4a**, $[\alpha]_D$ −13.7°. However, no single crystal was obtained. Fortunately, *p*-bromophenyl carbamate **5a** derived from ladbdan-8, 15-diol (**5**)[13,15)] which also co-occurred in *M. hostilis* gave a single crystal suitable for X-ray crystallographic analysis. ORTEP drawing[16)] as depicted in Fig. 1 indicates the normal absolute configuration including 13*R* for **5a**. With this unambiguous result, we compared all spectral data between **4a** and **5b**, which was derived from **5a**. Upon heating **5a** in Ac_2O–NaOAc,[17)] dehydration took place smoothly, giving rise a mixture of double bond isomers, followed by purification on $AgNO_3$ impregnated silica-gel chromatography to furnish **5b**, $[\alpha]_D$ +15.8°, which was identical in all respects except for the opposite specific rotation with **4a**. Thus the absolute configuration of **4a** is antipodal to that of **5b**. Subsequently, both labdanes **4** and **5** can be assigned as *ent*-(13*S*)-8(17)-labden-



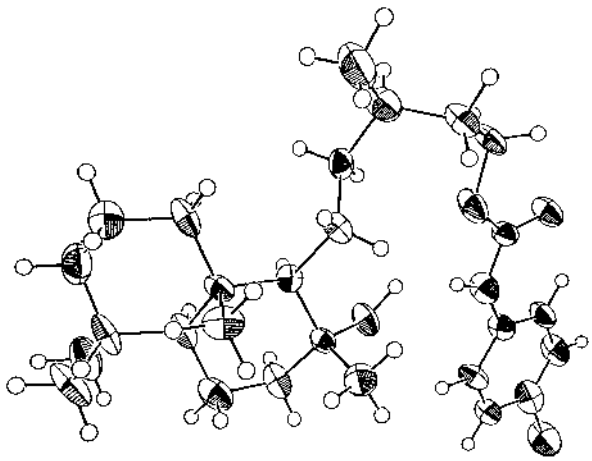


Fig. 1. ORTEP Drawing of **5a**

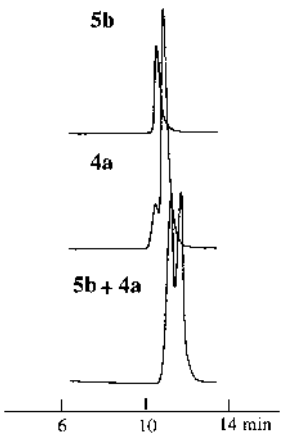


Fig. 2. HPLC Analyses of **4a** and **5b**

Column: CHIRALCEL OD ϕ 4.6×250 mm; solvent: hexane/2-propanol (9 : 1, 0.5 ml min^{-1}); det: 254 nm.

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15-ol and (13*R*)-labdan-8,15-diol, respectively. Additionally, the optical purities of **4** and **5** were determined to be 68% e.e. and 100% e.e. on the basis of HPLC analyses of **4a** and **5b** using a chiral column (Fig. 2).

Although **5b** was found to be optically pure, **4a** contained 12% enantiomer. This result indicates that the co-occurrence of the normal and antipodal diterpenoids in a single plant species is not rare but frequently encountered, so that care should be taken not only to determine the absolute structure but also the optical purity of all natural products, especially, those produced in the early stream of biosynthesis.

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REFERENCES AND NOTES

1) Dedicated to Professor Takashi Kubota on the occasion of his 90th birthday.
2) Cocker D. J., Halsall T. G., *J. Chem. Soc*., **1956**, 4262—4271.
3) Connoly J. D., Hill R. A., "Dictionary of Terpenoids", Vol. 2, Chapman & Hall, Tokyo, 1991, p. 677.
4) Ekong D. E. U., Okogun J. I., *Chem. Commun*., **1967**, 72—73.
5) Caputo R., Mangoni L., *Phytochemistry*, **13**, 467—470 (1974).
6) De Santis V., Medina J. D., *J. Nat. Prod*., **44**, 370—372 (1981).
7) Perry N. B., Weavers R. T., *Phytochemistry*, **24**, 2899—2904 (1985).
8) Zdero C., Bohlmann F., Niemeyer H. M., *Phytochemistry*, **29**, 326—329 (1990).
9) Zdero C., Bohlmann F., King R. M., *Phytochemistry*, **30**, 2991—3000 (1991).
10) Carman R. M., Duffield A. R., *Aust. J. Chem*., **46**, 1105—1114 (1993).
11) Fukuyama Y., Yokoyama R., Miyatake H., Minami H., Takahashi H., Ohsaki A., Abstracts of Papers, 42nd TEAC Symposium, October 1998, p. 215. A full account of the new diterpene rhamnosides will appear in due course. **6**. $[\alpha]_D$ −38.7° (*c* 0.78, $CHCl_3$); IR cm^{-1}: 3412 (OH), 1644 (C=C); EI-MS *m*/*z* (rel. int.): 438.3372 (M^+, 10) (calcd. 438.3345 for $C_{26}H_{46}O_5$), 291 (100), 137 (93); ^{1}H-NMR ($CDCl_3$): δ 0.68 (3H, s), 0.80 (3H, s), 0.89 (3H, s), 0.89 (3H, d, *J*=6.3 Hz), 1.31 (3H, d, *J*=6.3 Hz), 3.92 (1H, dd, *J*=3.4, 2.0 Hz), 4.48 (1H, br s), 4.75 (1H, d, *J*=2.0 Hz), 4.81 (1H, br s); ^{13}C-NMR ($CDCl_3$): δ 14.6 (C-20), 17.6 (rham. C-6), 19.5 (C-2), 19.7 (C-16), 21.0 (C-11), 21.8 (C-19), 24.6 (C-6), 30.5 (C-13), 33.7 (C-4), 33.7 (C-18), 36.1 (C-12), 36.8 (C-14), 38.5 (C-7), 39.2 (C-1), 39.8 (C-10), 42.3 (C-3), 55.6 (C-5), 57.3 (C-9), 66.2 (C-15), 67.8 (rham. C-5), 71.2 (rham. C-2), 71.9 (rham. C-3), 73.5 (rham. C-4), 99.7 (rham. C-1), 106.2 (C-17), 148.9 (C-8).
12) **4**. IR cm^{-1}: 3333 (OH), 1644 (C=C); EI-MS *m*/*z* (rel. int.): 292 (M^+, 64), 191 (41), 177 (52), 137 (100); ^{1}H-NMR ($CDCl_3$): δ 0.65 (3H, s), 0.78 (3H, s), 0.84 (3H, s), 0.88 (3H, d, *J*=6.8 Hz), 3.65 (2H, m), 4.47 (1H, s), 4.78 (1H, s); ^{13}C-NMR ($CDCl_3$): δ 14.6 (C-20), 19.5 (C-2), 19.6 (C-16), 21.0 (C-11), 21.8 (C-19), 24.6 (C-6), 30.1 (C-13), 33.7 (C-4), 33.7 (C-18), 36.3 (C-12), 38.5 (C-7), 39.2 (C-1), 39.3 (C-14), 39.8 (C-10), 42.3 (C-3), 55.6 (C-5), 57.2 (C-9), 61.3 (C-15), 106.2 (C-17), 148.9 (C-8).
13) Teresa J. D-P., Urones J. G., Marcos I. S., Nünez L., Basabe P., *Phytochemistry*, **22**, 2805—2808 (1983).
14) Grant P. K., Lai C. K., Prasad J. S., Yap T. M., *Aust. J. Chem*., **41**, 711—725 (1988).
15) **5**. $[\alpha]_D$ −3.9° (*c* 0.08, $CHCl_3$); IR cm^{-1}: 3362 (OH); EI-MS *m*/*z* (rel. int.): 310 (M^+, 10), 292 (68), 277 (80), 191 (100). ^{1}H-NMR ($CDCl_3$): δ 0.79 (6H, s), 0.87 (3H, s), 0.92 (3H, d, *J*=6.5 Hz), 1.15 (3H, s), 3.69 (2H, m).
16) Crystal data for **5a**: $C_{27}H_{42}O_3NBr$, Orthorhombic, $P2_12_12_1$, a=8.2380 (0) Å, b=11.2650 Å, c=28.7160 Å, V=2664.8999 (0) $Å^3$, Z=4, D_x= 1.530 Mg m^{-3}, D_m=1.500 Mg m^{-3}, R factor=0.050.
17) Tabacik C., Bard M., *Phytochemistry*, **10**, 3093—3109 (1971).