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NOESY Spectra of 1-Acetoxy-6-aryl-2-aryloxy-3,7-dioxabicyclo[3.3.0]-octanes. Revision of the Absolute Configuration of (+)-Phrymarolin I

Eiji TANIGUCHI* and Fumito ISHIBASHI
Department of Agricultural Chemistry, Faculty of Agriculture,
Kyushu University, Hakozaki 6-10-1, Higashiku, Fukuoka 812

The absolute configuration of (+)-phrymarolin I was revised as (1S,2R,5R,6S) on the basis of its relative configuration established by comparison of the NOESY spectra of the stereoisomers.

A stereocontrolled synthesis of 1-acetoxy-2-(2-methoxy-4,5-methylenedioxyphenoxy)-6-(2-methoxy-4,5-methylenedioxyphenyl)-3,7-dioxabicyclo[3.3.0]octane starting from (+)-S-β-vinylbutyrolactone as chiral synthon furnished the natural lignan, (+)-phrymarolin I (1) along with its 2-epimer, (-)-isophrymarolin I (2).[1,2] The chirality of the synthon strictly induced 5S-configuration of the 3,7-dioxabicyclo[3.3.0]octane backbone of those molecules to facilitate assignment of their absolute configuration as (1S,2S,5R,6S) for 1 and (1S,2R,5R,6S) for 2, respectively, on the basis of the relative configuration ($1S^*,2S^*,5R^*,6S^*$) of 1. The $2S^*$-configuration had been assigned from the acetylation shift behavior of 2-H (0.52 ppm downfield) of 1.[3,4] However, the large acetylation shift of 2-H of 1α-acetoxy-6-aryl-2-aryloxy-3,7-dioxabicyclo[3.3.0]-octane has been found to be not relevant to assignment of its relative configuration in haedoxan A (4).[5] The 2β-H showing an evident cross peak to 8β-H in the NOESY spectrum of 4 was deshielded, as much as 0.58 ppm, similar to 2-H of 1, by acetylation of the 1α-hydroxyl group. The cis protons to 1α-hydroxyl group, 5α-H and 8α-H of 4, also showed similar acetylation shift (0.28 and 0.35 ppm, respectively) to those of 1 (5α-H, 0.33 ppm; 8α-H, 0.31 ppm).

In this paper, the stereochemistry of 1-acetoxy-6-aryl-2-aryloxy-3,7-dioxabicyclo[3.3.0]octane has been comparatively investigated by means of NOESY experiments focusing on the relative configuration of 2-H in 1[6)] and its 2-epimer, 2.[7)] The latter epimer was prepared by acetylation of (-)-desacetyl isophrymarolin I (3). The epimer was obtained as the major product in the acetalization reaction of 2-fluoro-1α-[(TBDMS)oxy]-6α-(2-methoxy-4,5-methylenedioxyphenyl)-3,7-dioxabicyclo[3.3.0]octane with 2-methoxy-4,5-methylenedioxyphenol by preferential β-side attack of the phenol due to steric hindrance of 1α-(t-butyldimethylsilyl)oxyl group.[1,2)] The relative configuration of 3 was verified by a stereo-

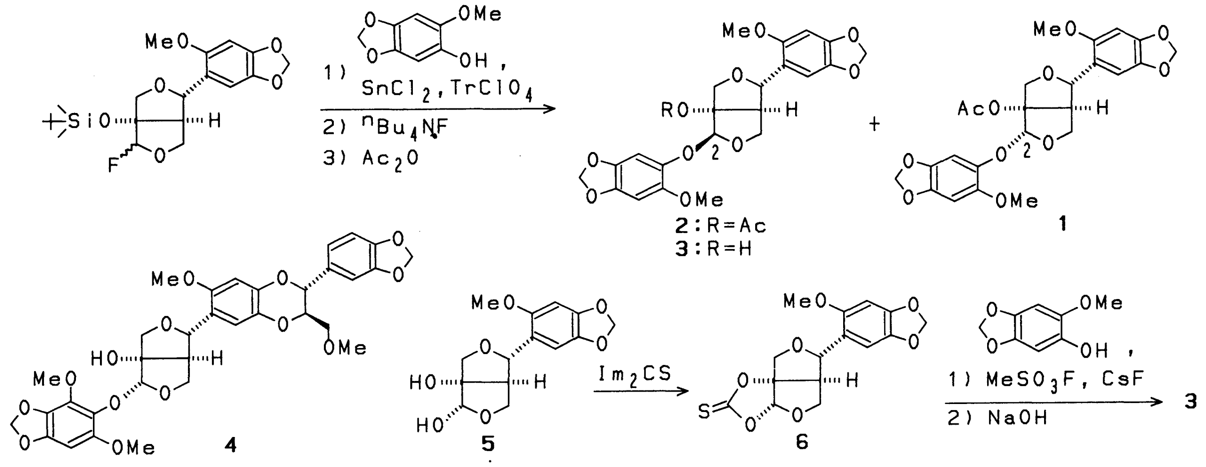


Fig. 1.

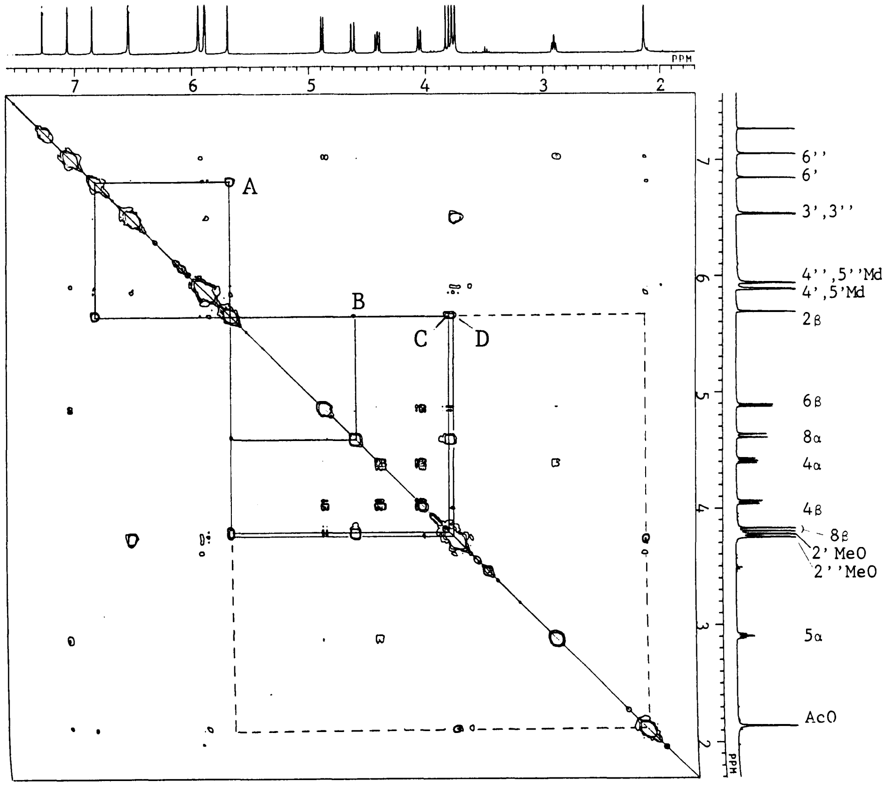
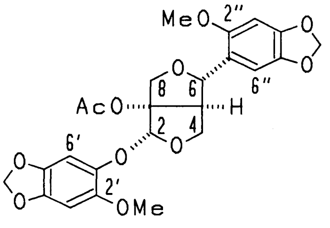


Fig. 2.
NOESY Spectrum of (+)-phrymarolin I.

A (2β,6')
B (2β,8α)
C (2β,8β)
D (2β,2'MeO)



selective synthesis of its racemate (Fig. 1) from (±)-1α,2α-dihydroxy-6α-(2-methoxy-4,5-methylenedioxyphenyl)-3,7-dioxabicyclo[3.3.0]octane-1,2-thiocarbonate (6)[8] (5, 1,1'-thiocarbonyldiimidazole, dichloromethane, 0 °C, 9 h, 90%) and 2-methoxy-4,5-methylenedioxyphenol ($MeSO_3F$, CsF, dichloroethane, 50-60 °C, 5 h, then aq. NaOH, MeOH, rt, 35%) by applying a method for highly stereocontrolled synthesis of β-furanosides.[9] The evident cross peak (C in Fig. 2) between 2-H (5.66 ppm) and 8β-H (4.96 ppm) in the 400 MHz NOESY spectrum of 1 ($CDCl_3$; τ_m, 1739 ms) revealed that the 2-H located on the β-side of the 3,7-dioxabicyclo[3.3.0]octane ring. In the NOESY spectrum of 2 ($CDCl_3$; τ_m, 3188 ms) was not observed any cross peak between 2-H (5.66 ppm) and 8β-H (4.15 ppm), while a cross peak (E in Fig. 3) between 1α-acetoxyl group and 2-H, which was absent in the NOESY spectrum of 1, was evident to indicate α-arrangement of 2-H. Therefore, the β-configuration previously assigned[3] for the 2-aryloxyl group of 1 has been revised to α-configuration.

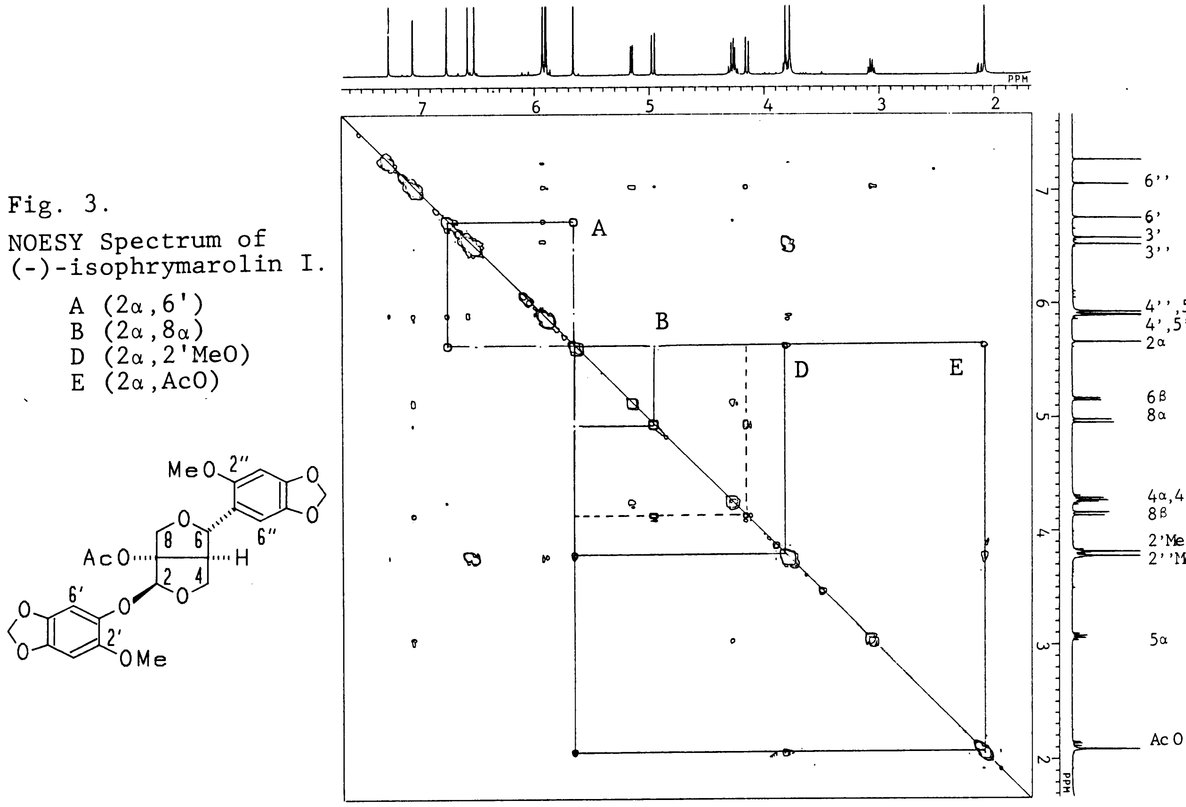


Fig. 3.
NOESY Spectrum of (-)-isophrymarolin I.
A (2α,6')
B (2α,8α)
D (2α,2'MeO)
E (2α,AcO)

The fact that the acetylation shift (0.52 ppm) of the proton locating at trans-position to 1α-acetoxyl group (2β-H of 1) exceeds that (0.36 ppm) of the cis-proton (2α-H of 2) is supposed to be attributable to a twisted conformation of the dioxabicyclooctane ring due to repulsion between the 2α-(2-methoxy-4,5-methylenedioxyphenoxyl) and 1α-acetoxyl groups of 1. Since the absolute configuration at 1-, 5-,and 6-position of 1 was unequivocally determined as S, R, and S, respectively, the absolute configuration of 1, reported as (1S,2S,5R,6S) in the literature,1,2) has to be revised as (1S,2R,5R,6S).

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References

1) F. Ishibashi and E. Taniguchi, Chem. Lett., 1986, 1771.
2) F. Ishibashi and E. Taniguchi, Bull. Chem. Soc. Jpn., 61, 4361, (1988).
3) E. Taniguchi and Y. Oshima, Agric. Biol. Chem., 36, 1013 (1972).
4) E. Taniguchi and Y. Oshima, Agric. Biol. Chem., 36, 1489 (1972).
5) E. Taniguchi, K. Imamura, F. Ishibashi, T. Matsui, and A. Nishio, Agric. Biol. Chem., in preparation.
6) Mp 156-157 °C. 400 MHz ^{1}H NMR (CDCl$_3$) δ=2.14 (AcO, s), 2.90 (5α, m), 3.75 (MeO, s), 3.77 (MeO, s), 3.82 (8β, d, J=11), 4.05 (4β, dd, J=9 and 2), 4.38 (4α, dd, J=9 and 7), 4.62 (8α, d, J=11), 4.86 (6β, d, J=7), 5.68 (2β, s), 5.87 (1H of Md, d, J=1.5), 5.88 (1H of Md, d, J=1.5), 5.930 (1H of Md, d, J=1.5), 5.935 (1H of Md, d, J=1.5), 6.53 (2H of ArH, s), 6.84 (ArH, s), and 7.12 (ArH, s).
7) Resinous. 400 MHz ^{1}H NMR (CDCl$_3$) δ=2.08 (AcO, s), 3.06 (5α, m), 3.77 (MeO, s), 3.81 (MeO, s), 4.15 (8β, d, J=11), 4.23-4.31 (4α and 4β, m), 4.96 (8α, d, J=11), 5.15 (6β, dd, J=7.1 and 0.5), 5.66 (2α, s), 5.89 (1H of Md, d, J=1.5), 5.90 (1H of Md, d, J=1.5), 5.92 (Md, s), 6.52 (ArH, s), 6.58 (ArH, s), 6.76 (ArH, s), and 7.05 (ArH, d, J=0.5). Found: C, 59.14; H, 5.05. Calcd for $C_{22}H_{22}O_{10}$: C, 59.19; H, 4.97%.
8) Amorphous. 100 MHz ^{1}H NMR (CDCl$_3$) δ=2.80-3.10 (5α, m), 3.77 (MeO, s), 4.15 (8β, d, J=12), 4.20 (4β, dd, J=10 and 6), 4.41 (4α, dd, J=9 and 2), 4.54 (8α, d, J=12), 4.92 (6β, d, J=9), 5.93 (Md, s), 6.23 (2 , s), 6.51 (ArH, s), and 6.95 (ArH, s). MS (70 eV) m/z (rel intensity) 338 (M$^+$, 100), 277 (18), 191 (27), 181 (62), 161 (56), 152 (16), 133 (73), 118 (16), 89 (20), 81 (41), 65 (22), and 52 (40).
9) T. Mukaiyama and M. Murakami, Chem. Lett., 1983, 1733.

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