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# Atropisomerism of Biflavones. Confirmation of the Enantiomeric Purity of WB1 by Using a Chiral Nuclear Magnetic Resonance Shift Reagent

Wasiur Rahman,[a] Mohd. Ilyas,[a] Masayoshi Okigawa,[b] and Nobusuke Kawano*,[b]

*Department of Chemistry, Aligarh Muslim University,[a] Aligarh, U.P.,*
*India and Faculty of Pharmaceutical Sciences, Nagasaki*
*University,[b] 1-14 Bunkyo-machi, Nagasaki 852, Japan*

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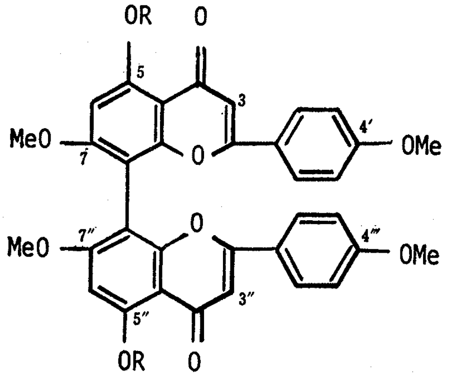
The optical purity of WB1, (−)-4′,4‴,7,7″-tetra-*O*-methylcupressuflavone (1) was estimated from proton nuclear magnetic resonance ($^1$H-NMR) studies of its dimethyl ether (2) by using a chiral NMR-shift reagent and found to be satisfactory.

**Keywords**——atropisomerism; optically active biflavone; (−)-4′,4‴,7,7″-tetra-*O*-methylcupressuflavone; enantiomeric purity; chiral NMR-shift reagent

Although optically active biflavones belonging to the cupressuflavone,1) agathisflavone,2) or amentoflavone3) series have been isolated from natural sources, they were thought to be optically labile and easily racemizable compounds because of Adams' theory4) that hydroxy or methoxy groups at the *ortho* positions of biphenyl compounds do not interfere sufficiently to allow optical resolution. However, the optical stability of active biflavones should be reconsidered since the role of *ortho*-substituted methoxy groups was recently found to be very important5) for atropisomerism, contrary to Adams' theory.



1 : R = H

2 : R = Me

WB1, (−)-4′,4‴,7,7″-tetra-*O*-methylcupressuflavone (1) has been isolated as the first optically active biflavone from *Araucaria cunninghamii* and *A. cookii*.1) The melting point(mp) of WB1 was reported as 151°C, while that of the racemic compound (1)6) has been reported as 259—261°C. The mp of hexa-*O*-methylcupressuflavone (2) has been reported2b) as 299°C. However, the mp of the hexamethyl ether derived from the active WB1 by methylation was 161°C,1) suggesting that the hexamethyl ether is also optically active.

In order to confirm the enantiomeric purity7) of WB1 and its dimethyl ether a chiral NMR-shift reagent (CSR), tris [3-(trifluoromethylhydroxymethylene)-*d*-camphorato] europium (III)8) was used in $^1$H-NMR studies of the hexamethyl ether (2). As shown in Table I, the active ether (2) showed only one set of signals with no splitting even in the presence of one molar ratio ($\Delta$Eu)9) of the CSR whereas the signals due to MeO-5,5″,7, and 7″, and 7, and H-6 and 6″, of the racemic ether showed signal splitting in the presence of a half molar ratio of the CSR. This observation indicates that the enantiomeric purity of the active hexamethyl ether (2) is satisfactory.

Accordingly, WB1 should be optically pure and also stable against methylation in boiling acetone solution with dimethyl sulfate and potassium carbonate. The active hexamethyl ether showed $[\alpha]_D^{12}$ −25°, $[\alpha]_{500}^{12}$ −21°, $[\alpha]_{460}^{12}$ 0°, $[\alpha]_{450}^{12}$ +9°, $[\alpha]_{400}^{12}$ +300°, and $[\alpha]_{375}^{12}$ +880° (0.50% chloroform solution). WB1 and its dimethyl ether may be optically very stable, like 2,2′,6,6′-tetramethoxy-3,3′-dicarboxybiphenyl.5)

Table 1. $^1$H-NMR Data ($\delta$) for the Hexamethyl Ether 2

| Protons | Molar ratio of CSR[a] | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Inactive 2[b] with CSR | | | | | Active 2[c] with CSR | | | | |
| | 0 | 0.170 | 0.573 | 0.769 | ⊿Eu | 0.060 | 0.124 | 0.325 | 0.863 | ⊿Eu |
| MeO-4′,4‴ | 3.73 | 3.72 | 3.71 | 3.70 | −0.04 | 3.73 | 3.72 | 3.71 | 3.70 | −0.03 |
| -7,7″ | 3.82 | 3.90 | 4.10<br>4.15 | 4.25<br>4.30 | 0.61<br>0.74 | 3.86 | 3.88 | 4.04 | 4.44 | 0.70 |
| -5,5″ | 4.08 | 4.80<br>4.92 | 6.8[d]<br>7.4[d] | 8.0[d]<br>8.7[d] | 5.2[d]<br>6.1[d] | 4.28 | 4.64 | 6.00 | 9.52 | 6.55 |
| H-3,3″ | 6.55 | 6.62 | 6.80 | 6.92 | 0.42 | 6.60 | 6.64 | 6.76 | 6.98 | 0.52 |
| -6,6″ | 6.55 | 6.95<br>7.04 | 8.08<br>8.32 | 8.7[d]<br>9.0[d] | 3.1[d]<br>3.6[d] | 6.69 | 6.89 | 7.64 | 9.52 | 3.44 |
| -3′,5′,3‴,5‴ | 6.74 | 6.75 | 6.82 | 6.92 | 0.22 | 6.78 | 6.80 | 6.84 | 6.94 | 0.23 |
| -2′,6′,2‴,6‴ | 7.26 | 7.34 | 7.50 | 7.62 | 0.44 | 7.32 | 7.37 | 7.48 | 7.73 | 0.51 |

*a*) NMR chiral shift reagent;[8] see the text. *b*) A solution of 13.5 mg of racemic 2 in 0.5 ml of $CDCl_3$ was used. *c*) A solution of 16.3 mg of active 2 in 0.5 ml of $CDCl_3$ was used. *d*) It was difficult to read exact values due to signal broadenings.

## References and Notes

1) M. Ilyas, J.N. Usmani, S.P. Bhatnagar, M. Ilyas, W. Rahman, and A. Pelter, *Tetrahedron Lett.*, **1968**, 5515.
2) *a*) A. Pelter, R. Warren, J.N. Usmani, R.H. Rizvi, M. Ilyas, and W. Rahman, *Experientia*, **25**, 351 (1969); *b*) N.U. Khan, M. Ilyas, W. Rahman, T. Mashima, M. Okigawa, and N. Kawano, *Tetrahedron*, **28**, 5689 (1972).
3) *a*) A. Pelter, R. Warren, M. Ilyas, J.N. Usmani, S.P. Bhatnagar, R.H. Rizvi, M. Ilyas, and W. Rahman, *Experientia*, **25**, 350 (1969); *b*) K.K. Chexal, B.K. Handa, W. Rahman, and N. Kawano, *Chem. and Ind.* (London), **1970**, 28.
4) *a*) R. Adams, *Rec. Chem. Prog.*, 91 (1949); *b*) E.L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, 1962, p. 156.
5) N. Kawano, M. Okigawa, N. Hasaka, I. Kouno, Y. Kawahara, and Y. Fujita, *J. Org. Chem.*, **46**, 389 (1981).
6) V.V.S. Murti, P.V. Raman, and T.R. Seshadri, *Tetrahedron*, **23**, 397 (1967).
7) M.D. McCreary, D.W. Lewis, D.L. Wernick, and G.M. Whitesides, *J. Amer. Chem. Soc.*, **96**, 1038 (1974).
8) R.R. Fraser, M.A. Petit, and J.K. Sanders, *J. Chem. Soc., D*, **1971**, 1450.
9) M. Okigawa, N.U. Khan, N. Kawano, and W. Rahman, *J. Chem. Soc. Perk* 1, **1975**, 1563.