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DETERMINATION OF ENANTIOMERIC PURITY OF AXIALLY CHIRAL BIARYLS[1]

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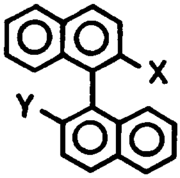
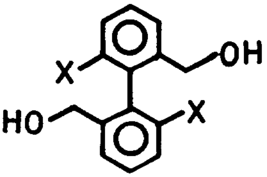
Summary: Enantiomeric purities of axially chiral biaryls with hydroxyl, amino, and carboxyl groups can be easily determined by pmr spectra using MTPA derivatives and shift reagent.

Recently, Behnam et al. have reported[2] that the methyl proton signals in racemic biaryls such as dimethyl 6,6'-dimethoxy-2,2'-diphenate were separated into two peaks in the presence of large amount of the chiral shift reagent, Pr(tfc)$_3$. The separation of the peaks, however, seems not to be sufficiently enough for the correct enantiomeric purity determination. This work prompted us to report our convenient and reliable method on determination of enantiomeric purity of biaryls with hydroxyl, amino, and carboxyl group.

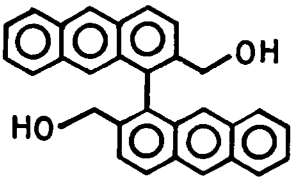
The compounds of three types shown in the figure were examined: (Type 1) binaphtyls with OH or NH$_2$ group attached directly to the aromatic rings, (Type 2) primary alcohols of biaryls, (Type 3) secondary alcohols of bridged biphenyls. These partially active biaryls were completely acylated[3] with excess acid chloride of (R)-(+)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA, Mosher's Reagent) in the presence of excess 4-dimethylaminopyridine to give the diastereomeric pairs of mono and di-(R)-MTPA derivatives (**1**, **3**, **8** and **2**, **4**, **5**, **6**, **7**, respectively).



1 X=OH, Y=H
2 X=Y=OH
3 X=NH$_2$, Y=H
4 X=Y=NH$_2$
Type 1



5 X=Me
6 X=NO$_2$



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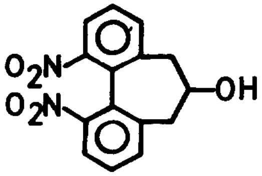
Type 2



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Type 3

The undoped spectra (90MHz) of these diastereomeric pairs showed the unresolved or partially resolved MeO signals, except for the cases of **2** and **4**[4] These signals were resolved into two peaks by the progressive addition of Eu(fod)$_3$.[5] The relative peak area of the well separated MeO signals at the shift reagent concentration indicated on the Table allowed determination of accurate enantiomeric purity of the original biaryls. Eu(dpm)$_3$ was used for the MTPA amide (3) in place of Eu(fod)$_3$ because of rapid signal broadening caused by latter. The results are summarized in the Table. The enantiomeric purities thus obtained showed good agreement (±3%) with optical purities calculated from the optical rotations.

Table. Enantiomeric Purities of Partially Active Biaryls Determined by (R)-MTPA Derivative/Shift Reagent Method

Biaryls				
	$[\alpha]_D$ (C, solvent, temp. °C)	$\Delta\delta$ (ppm)^a	Equiv. of Eu(fod)$_3$	% e.e.(optical purity)^b
1	-6.8°(1.61, THF, 20°)	0.18	0.1	52 (54)
2	+16.0°(2.48, THF, 25°)	0.18	0	50 (47)
3	-28.7°(1.0, THF, 25°)	0.81	0.3^{c,d}	44 ( )^e
4	+77.6°(1.64, benzene, 30°)	0.18	0^d	50 (51)
5	+18.1°(1.85, MeOH, 24°)	0.16	0.5	57 (58)
6	-51.6°(0.73, AcOEt, 20°)	0.20	0.8	76 (79)
7	+393° (1.25, acetone, 20°)	0.18	0.4	77 ( )^e
8	+151° (0.24, AcOEt, 27°)	0.70	0.1	22 (23)

[a] Spectra determined at 90MHz on CCl$_4$ solutions. [b] Based on the following absolute rotation values; 1, -12.6°, K. Kabuto, F. Yasuhara, and S. Yamaguchi, unpublished result; 2, +34.3°, D. J. Cram et al., J. Org. Chem., 42, 4173 (1977)· 4, -156°, K. Mislow, and P. A. Graseman, J. Org. Chem., 23, 2027 (1958); 5, +31°, M. Siegel, and K. Mislow, J. Amer. Chem. Soc., 80, 473 (1958); 6, -65°; 8, +696°, P. Newman, P. Rutkin and K. Mislow, ibid., 80, 465 (1958). [c] Shift reagent, Eu(dpm)$_3$. [d] Solvent, CDCl$_3$. [e] Absolute rotations have not been reported.

As is seen from the Table, the present method is applicable not only to the biaryls with functional groups directly connected with the aromatic rings (1~4), but also to the ones with the functional groups remote from the chiral axis(5~8). Since the primary alcohols(5~7) can be easily derived from the corresponding diacids without detectable racemization, the present technique is also applicable to determination of enantiomeric purities of biaryls with carboxyl group.

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