Tetrahedron: Asymmetry Vol. 4, No. 7, pp. 1501-1504, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00
Pergamon Press Ltd

Circular Dichroic Method for the Determination of Absolute Configuration of α-Furfuryl Amines

Wei-Shan Zhou, [a] **Xue-You Zhu** [b] **and Jie-Fei Cheng** [a]

[a] State key laboratory of bioorganic and natural products chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China
[b] Department of Biological Engineering, Sichuan University, Chengdu, Sichuan, China

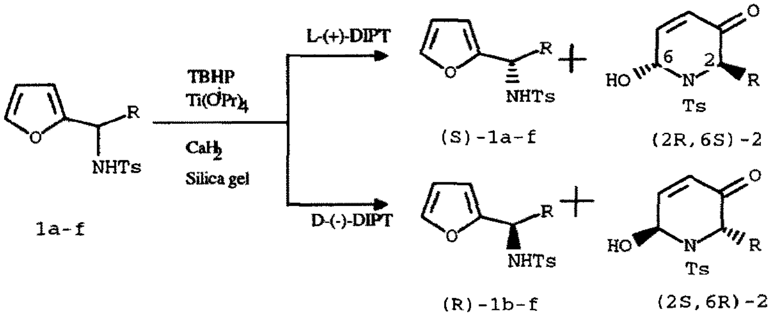
(*Received in Japan* 23 *February* 1993; *accepted* 22 *March* 1993)

Abstract: An unambiguous assignment of absolute configuration of α-furfuryl amines by using the circular dichroic method is described.

Kinetic resolution of secondary allylic alcohols by Sharpless asymmetric epoxidation using tert-butyl hydroperoxide(TBHP) in the presence of a chiral titanium-tartrate catalyst,[1] has been widely used in the synthesis of chiral natural products. We have recently reported for the first time the kinetic resolution of racemic a-furfuryl amides 1a-f with the modified Sharpless reagent,[1b] providing chiral **1** and **2** both in high chemical and optical yields (Scheme 1).[2] Moreover, upon using L-(+)-DIPT, the fast-reacting enantiomers are R whereas S-enantiomers are the fast-reacting ones when D-(-)-DIPT is used in these kinetic resolution processes.[2] This result is just the opposite to that expected by the empirical rule reported by Sharpless and co-workers.[1a] In this paper we wish to report a direct and facile circular dichroic method for determining the absolute configuration in α-furfuryl amines.

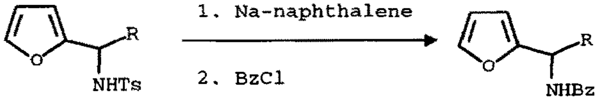
The α-furfuryl amines only show weak Cotton effects(CE's) which are not suitable for assignment of the absolute configurations. The corresponding benzamides which could be readily obtained by cleavage of the tosyl protecting group in **1** followed by benzoylation of the resulting α-furfuryl amines, however, display two bisignate CE's in the region of 215-230nm (Scheme 2, Table 1). Thus compound **3** exhibits a positive Cotton effect at λext 228 (Δε +3.02)nm and a negative one at λext 220(-1.75) nm. On the other hand, its enantiomer **4** shows a negative first CE at λext 231(-2.48) nm and a positive second CE at λext 216(4.39) nm. Similar results were observed for compound **6** and its enantiomer **7**. Since they are observed within the π–π* bands of the benzamide (225 nm)[5] and 2-alkylfuran chromophore (215-220nm), these bisignate Cotton effects should originate from the exciton coupling of the electric transition moments of the two allowed transitions. According to the exciton chirality method,[5] the sign of the Cotton effect is diagnostic of the absolute configuration of α-furfuryl carbon.

Scheme 1



1a-f: R=Me, Et, Pr, n-Bu, i-Bu, n-Hex

Scheme 2



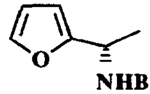
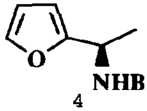
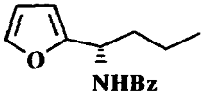
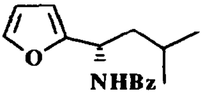
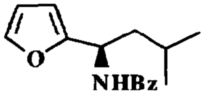
R= Me, n-Pr, iBu

Although defining the major conformer of these benzamides in solution using the spectral data in hand is of difficulty, it has been reported[4] that in the major conformer of 2-furylcarbinol benzoates system, the alkyl and benzoxyl substituents are located on both sides of the furan ring plane. Thus by analogy with 2-furylcarbinol benzoates, it could be concluded that the α-furfuryl amine benzamide with negative chirality i.e., showing a negative first Cotton effect around 228nm and a positive second Cotton effect around 215nm possesses a R configuration at the α-carbon.

The crucial evidence supporting the above conclusion arises from the chemical correlation. Thus oxidation[2] of compound **1a** (R=Me) with RuO_4 afforded the corresponding N-tosyl α-aminopropanic acid which shows identical spectroscopic data to authentic (S)-N-tosyl alanine.[3]

In summary, a facile exciton chirality method for determination of absolute configuration in α-furfuryl amines has been developed.

Table 1. Chiroptical data for benzamides of a-furfuryl amines in CH_3CN

Benzamides	Config.	CD $\Delta\varepsilon$(nm)	UV ε(nm)
 3	S	-1.8(220) +3.0(228)	11200(228)
 4	R	+4.4(216) -2.5(231)	12000(228)
 5	S	-1.5(215) +1.4(228)	12800(228)
 6	S	-4.2(216) +4.3(228)	12500(228)
 7	R	+4.3(216) -3.6(230)	13000(228)

Experimental

All mps were determined on a Buchi 535 instrument and are uncorrected. IR spectra were recorded on a Shimadzu 440 spectrometer. ^1H NMR spectra were obtained on a Varian EM-360(60MHz) spectrometer, using $CDCl_3$ as solvent and TMS as an internal standard. Mass spectra were obtained on a Finnigan 4021 spectrometer(70eV for EI). Elemental analyses were performed by the Analytical Department of this Institute. Optical rotations were measured with a Perkin Elmer 241C polarimeter in EtOH at 20°C. CD and UV spectra were recorded in spectrograde acetonitrile on a JASCO J500C dichrograph and on a 8451A spectrophotometer respectively. Preparative chromatography was performed on pre-prepared TLC with silica gel H (10-40μ).

General procedure for preparation of benzamides:

A solution of the α-furfuryl amine (0.5mmol),[2] benzoyl chloride(0.75mmol), pyridine(0.4ml) in CH_2Cl_2(5ml) was stirred overnight at room temperature. The mixture was transferred to a separatory funnel and washed with brine. Dried over Na_2SO_4 followed by concentration of the organic solvent gave a residue which was purified by preparative TLC with CH_2Cl_2-petroleum ether as eluant to afford the corresponding benzamide.

Compound 3: mp 107-108°C; $[\alpha]_D^{20}$ -85.2(c 0.5, EtOH); ^1H NMR δ 1.0-1.4(q, 3H), 5.4-5.5(d, 1H), 6.4(d, 1H), 7.1-7.7(m, 6H), 8.0-8.1(m, 2H); MS m/z 214(M^+-1); IR ν_{max} 1680 cm^{-1}.

Compound 4: mp 105.5-106°C; $[\alpha]_D^{20}$ +72.4(c 0.4, EtOH); ^1H NMR δ 1.3(q, 3H), 5.45(d, 1H), 6.4(d, 1H), 7.15-7.71(m, 6H), 8.05-8.1(m, 2H); MS m/z 215(M^+); IR ν_{max} 1680 cm^{-1}.

Compound 5: mp 75.9-76.2°C; $[\alpha]_D^{20}$ -82.2(c 0.4, EtOH); ^1H NMR δ 0.8 (t, 3H), 1.15-2.05(m, 4H), 5.35(q, 1H), 6.1-6.3(m, 2H), 6.6(d, 1H), 7.2-8.0(m, 6H); MS m/z 243(M^+); IR ν_{max} 1660 cm^{-1}; Anal. Calcd. for $C_{15}H_{17}NO_2$: C 74.07, H 7.00, N 5.76; Found: C 73.69, H 6.79, N 5.66.

Compound 6: mp 68.3-68.7°C; $[\alpha]_D^{20}$ -78.2 (c 0.5, EtOH); ^1H NMR δ 0.95-1.05 (m, 6H), 1.55-1.7(m, 1H), 1.8-1.88(m, 2H), 5.4-5.5(m, 1H), 6.25-6.35(m, 3H), 7.30-7.52(m, 4H), 7.8(d, 2H); MS m/z 258(M^++1); IR ν_{max} 1690 cm^{-1}; Anal. Calcd. for $C_{16}H_{19}NO_2$: C 74.71, H 7.39, N 5.45; Found C 74.27, H 7.11, N 5.23.

Compound 7: mp 69-69.4°C; $[\alpha]_D^{20}$ +65.2 (c 0.5, EtOH); ^1H NMR δ 0.9-1.05(m, 6H), 1.5-1.7(m, 1H), 1.8-1.88(m, 2H), 5.4-5.5(m, 1H), 6.2-6.3(m, 3H), 7.35-7.50(m, 4H), 7.8(d, 2H); MS m/z 257(M^+); IR ν_{max} 1690 cm^{-1}; Anal. Calcd. for $C_{16}H_{19}NO_2$: C 74.71, H 7.39, N 5.45; Found C 74.20, H 7.25, N 5.30.

References:

1. a. Martin V. S.; Woodard, S.S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B.; *J. Am. Chem. Soc.*, **1981**, 103, 6237.
   b. Wang Z. M.; Zhou W. S.; Lin, G. Q., Tetrahedron Lett., 1985, 26, 6721;
   Wang, Z. M.; Zhou, W. S., *Tetrahedron*, **1987**, 43, 2953.
2. Zhou, W. S.; Lu, Z. H.; Wang Z. M., *Tetrahedron Lett.*, **1991**, 32, 1467; *Tetrahedron*, in press.
3. Theodoropoulos, O.; Craig. L. C.; *J. Org. Chem.*, **1956**, 21, 1367.
4. Gawronski, J.; Radocki, D.; Jurczak, J.; Pakulski, Z.;Raczko, J.; Ramza, J.; Zamojski, A., *J. Org. Chem.*, **1990**, 55, 1118.
5. Harada, N.; Nakanishi, K., *Circular Dichroic Spectroscopy, Exciton Coupling in Organic Stereochemistry*; University Science Books: Mill Valley, 1983.