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A NEW PREPARATIVE METHOD FOR OPTICALLY ACTIVE DIARYLCARBINOLS

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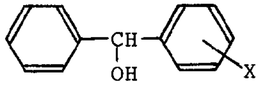
Abstract: Some diarylcarbinols were resolved efficiently by complexation with brucine.

The preparation of optically active diarylcarbinols (**1**) is not easy, and only one successful synthetic method for producing optically active 1 by enantioselective addition of titanium reagents derived from chiral 2,2'-dihydroxy-1,1'-binaphthyl to aromatic aldehydes has been reported so far.[1] This method is a little complicated and the reaction needs to be carried out at -78 °C. We now report a very simple and very efficient preparative method for preparing optically active **1** by complexation of rac-**1** with brucine (**2**).

For example, when a solution of rac-**1c** (1.0 g, 4.57 mmol) and **2** (1.8 g, 4.56 mmol) in MeOH-hexane (9:1, 2 ml) was kept at room temperature for 2 h, a 1:1 complex of (+)-**1c** and **2** was obtained (1.21 g). Two recrystallizations of the crude crystals from MeOH-hexane (9:1) gave pure crystals (0.80 g, mp 136-137 °C), which upon chromatography on silica gel (AcOEt) gave (+)-**1c** of 99.2% ee in 56% yield. The optical purity was determined by HPLC on the optically active solid phase, Chiralcel OB.[2] Evaporation of the solvent from the filtrate left after separation of the crude inclusion crystals of (+)-**1c** and **2**, followed by chromatography on silica gel and distillation, gave (-)-**1c** of 72.4% ee in 98% yield.

The $[\alpha]_D$ value, optical purity, and yield of optically active **1a-b** and **1d-i** obtained by the same resolution method applied to **1c** are summarized in Table 1. However, ortho isomers of **1a-i** were not resolved, although these also formed complexes with **2**. In the case of the para isomer of **1g**, its racemate formed complex with **2** and no resolution occurred. In all cases, other enantiomers which do not form complex with **2** were isolated from filtrates in fairly high optical yields (Table 1).



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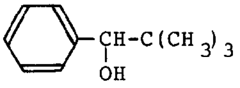

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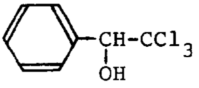

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Table 1. The $[\alpha]_D$ value, optical purity, and yield of the enantiomer obtained by complexation with **2**[a]

1		enantiomer[b,c]			
	X	$[\alpha]_D$	(c in MeOH)	% ee[d]	yield (%)
a	*m*-Me	-2.5	(0.32)	92.1	61.3
b	*p*-Me	-10.1	(0.13)	92.6	2.6
c	*m*-Cl	+36.9	(0.52)	99.2	56.0
d	*p*-Cl	+13.5	(0.53)	97.0	30.4
e	*m*-Br	+34.2	(0.69)	98.0	44.0
f	*p*-Br	+13.5	(0.67)	100.0	20.0
g	*m*-OMe	+20.9	(0.44)	93.0	32.0
h	*m*-NO_2	+54.9	(0.63)	99.6	47.8
i	*p*-NO_2	+50.0	(0.62)	85.5	72.0

[a] All the complexations were carried out in MeOH-hexane (9:1).

[b] Enantiomers were isolated by chromatography on silica gel followed by distillation in vacuo from the purified complex by two recrystallizations of the initially formed one.

[c] From the filtrate left after separation of the complex crystal, (+)-**1a** of 51.6% ee (120%), (+)-**1b** of 7.3% ee (158%), (-)-**1c** of 72.4% ee (98%), (-)-**1d** of 26% ee (80%), (-)-**1e** of 70.8% ee (84%), (-)-**1f** of 29.4% ee (141%), (-)-**1g** of 60.8% ee (115%), (-)-**1h** of 46.8% ee (108%), and (-)-**1i** of 53.5% ee (102%) were obtained in the yield shown in parentheses.

[d] Optical purity was determined by HPLC on the optically active solid phase, Chiralcel OB.[2]

Not only **1** but also the secondary alcohols which are substituted with one aryl group and one sterically bulky alkyl group, such as **3** and **4**, were also resolved efficiently by the complexation with **2**. For example, when a solution of **3** (12.3 g, 75.4 mmol) and **2** (29.7 g, 75.4 mmol) in MeOH (20 ml) was kept at room temperature for 12 h, a 1:1 complex of (-)-**3** and **2** was obtained, after three recrystallization from MeOH, as colorless prisms (mp 112-115 °C, 4.20 g), which upon heating in vacuo gave (-)-**3** of 100% ee by distillation, $[\alpha]_D$ -32.2 (c 1.0 in MeOH), 1.22 g (19.8% yield). Similarly, **4** was dissolved to give finally (-)-**4** of 100% ee, $[\alpha]_D$ -36.9 (c 1.0 in MeOH) in 38% yield.

The present resolution of **1**, **3**, and **4** is much more efficient than the previously reported resolution of propargyl alcohols with **2**.[3]

References

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