

A NEW OPTICAL RESOLUTION METHOD OF TERTIARY ACETYLENIC ALCOHOL
UTILIZING COMPLEXATION WITH BRUCINE

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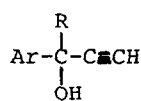
Summary: Some tertiary acetylenic alcohols were resolved efficiently utilizing complexation with brucine. The crystal structure of 1:1 brucine complex of 1-(o-bromophenyl)-1-phenyl-2-propynol ($[\alpha]_D^{25}$) was reported.

Optically active acetylenic alcohol is useful starting material to prepare various chiral compounds, because it has two functional groups. It is not easy, however, to obtain optically active acetylenic alcohol. Optical resolution of acetylenic alcohol by diastereomeric method for the phthalic acid half-ester of ¹ acetylenic alcohol is complicated and successful only in a few cases. Very recently, stereoselective reduction of α, β -acetylenic ketone to optically active ² acetylenic alcohol with using chiral reagent was reported. Synthesis of optically active acetylenic alcohol by stereoselective addition of lithium acetylide ³ to aldehyde in the presence of chiral ligand was also reported. These methods, however, are not applicable to prepare optically active tertiary acetylenic alcohol.

We have found that some tertiary acetylenic alcohols form stable 1:1 molecular complex with brucine and that the acetylenic alcohols can be resolved into enantiomers efficiently utilizing the complexation. For instance, when a solution of 4,4-dimethyl-3-phenyl-1-pentyn-3-ol ($[\alpha]_D^{25}$) (8.12 g, 43.4 mmole) and brucine dihydrate (17.1 g, 43.4 mmole) in acetone (260 ml) was kept overnight, 1:1 complex of

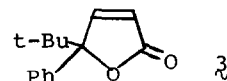
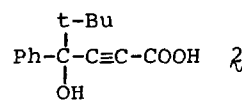
Table 1. Optical Resolution of λb - λe by Complexation with Brucine.

Compound	(+)-enantiomer			(-)-enantiomer		
	Yield (%)	$[\alpha]_D$ ($^{\circ}$)	%ee	Yield (%)	$[\alpha]_D$ ($^{\circ}$)	%ee
λb	42	+10.5	100	58	-7.3	70
λc	42	+21.1	94	57	-15.7	68
λd	35	+108	95	65	-52.1	46
λe	52	+31.3	53	45	-35.4	60



a: Ar=Ph; R=t-Bu

b: Ar=Ph; R=t-Am

c: Ar=Ph; R=o-Me-C₆H₄-d: Ar=Ph; R=o-Br-C₆H₄-e: Ar=Ph; R=o-F-C₆H₄-f: Ar=Ph; R=o-Cl-C₆H₄-g: Ar=p-Me-C₆H₄-;R=o-Cl-C₆H₄-

(*R*)-(+)- λa and brucine was formed as colorless prisms (12.2 g, 48%, mp 190-192 $^{\circ}$ C). Decomposition of the complex with dil HCl gave (*R*)-(+)- λa as colorless oil (3.92 g, 48%, $[\alpha]_D$ +8.8 $^{\circ}$, 100%ee). From the acetone solution, (*S*)-(-)- λa was obtained as colorless oil (4.05 g, 50%, $[\alpha]_D$ -8.2 $^{\circ}$, 93%ee). By the same procedure, λb - λe were also resolved (Table 1). In the case of R=alkyl (λa - λb), 1:1 brucine complex of the (+)-enantiomer crystallized out. In the case of R=aryl (λc - λe), however, 1:1 brucine complex of (-)-enantiomer crystallized out. Since an equimolar amount of brucine is necessary for the resolution, brucine complex may also be formed in the filtrate. Melting points of the 1:1 brucine complex of (+)- λb , (-)- λc , (-)- λd , and (-)- λe are 184-186, 177-179, 199-201, and 157-159 $^{\circ}$ C, respectively. All the complexes show ν_{OH} bands at lower frequencies, 3000-2300 cm^{-1} , suggesting the presence of strong hydrogen bond. Since none of PhHC(OH)C \equiv CH, PhMeC(OH)C \equiv CH, t-BuMeC(OH)C \equiv CH, and EtMeC(OH)C \equiv CH can form brucine complex, it might be essential for the complexation and then optical resolution that acetylenic alcohol is substituted with two aryl groups or with one aryl and one sterically-bulky alkyl groups.

In some cases, complete resolution was not achieved by one complexation (Table 1). Nevertheless, 100% optically pure compounds were obtained quite easily by repeating the complexation. For example, repeat of the complexation two times

furthermore for the partially resolved (-)- λ d (3.00 g) and (-)- λ e (3.51 g) which were obtained by one complexation (Table 1) gave 100% optically pure (-)- λ d (1.60 g, $[\alpha]_D -114^\circ$) and (-)- λ e (0.95 g, $[\alpha]_D -59.6^\circ$). By the similar procedure, 100% optically pure samples of (-)- λ f ($[\alpha]_D -129^\circ$) and (-)- λ g ($[\alpha]_D -126^\circ$) were easily obtained. Repetition of recrystallization of the brucine complex can also be used to obtain 100% optically pure sample. However, the repeat of the complexation is much more effective for the optical resolution.

Absolute configuration of (+)- λ a and (-)- λ a were determined to be (*R*) and (*S*), respectively, by the following method. Bubbling of CO_2 into the Grignard reagent prepared from (-)- λ a ($[\alpha]_D -8.8^\circ$, 100% ee) and EtMgBr gave (+)- λ as colorless needles (82%, mp $131-132^\circ\text{C}$, $[\alpha]_D +55$ (*c* 0.095 benzene)). Catalytic hydrogenation of the (+)- λ over 5% Pd-BaSO_4 in MeOH gave (*R*)-(-)- λ as colorless needles (94%, mp $178-179^\circ\text{C}$, $[\alpha]_D -165^\circ$ (*c* 0.024 benzene)). This $[\alpha]_D$ value is comparable to that of the authentic sample of (*R*)-(-)- λ (mp $175.6-175.8^\circ\text{C}$, $[\alpha]_D -164^\circ$) (

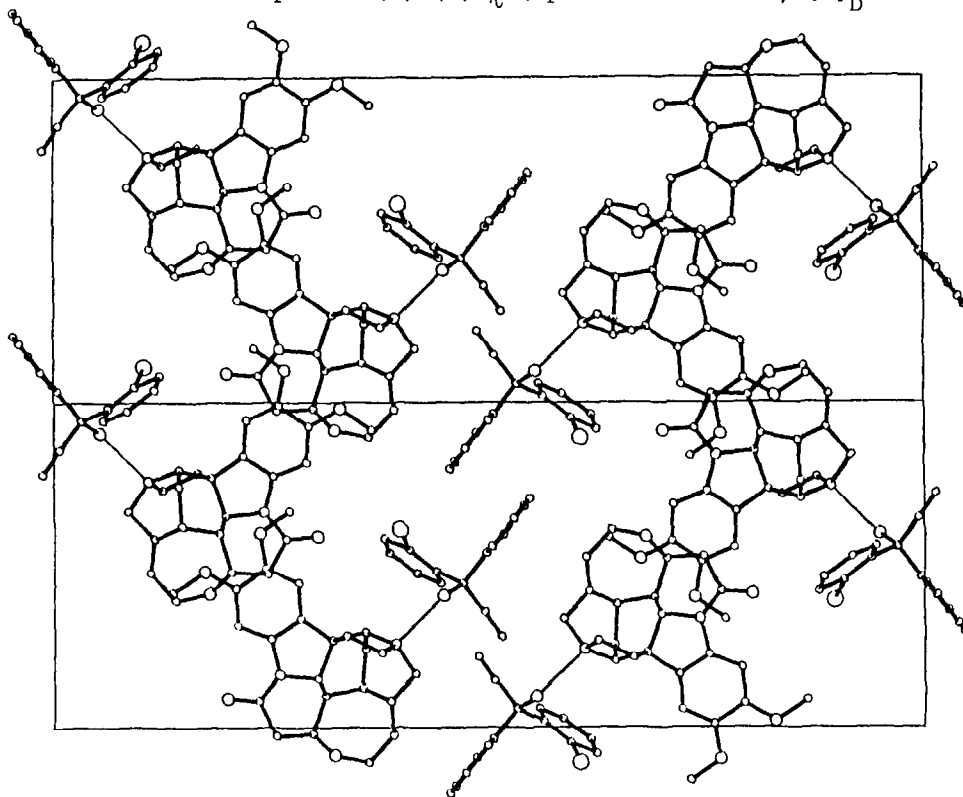


Figure 1. Packing Diagram in the Crystal of 1:1 Brucine Complex of (-)- λ d

benzene)). The same treatment of (+)- 1a ($[\alpha]_{\text{D}} +8.8^{\circ}$, 100%ee) gave (-)- 2 (82%, $[\alpha]_{\text{D}} -55^{\circ}$ (*c* 0.095 benzene)) and then (*S*)-(+)- 3 (94%, $[\alpha]_{\text{D}} +165^{\circ}$ (*c* 0.024, benzene)). Absolute configurations of (+)- 1b and (-)- 1b are probably (*S*) and (*R*), respectively. However, absolute configurations of 1c-g are not clear.

In order to know how brucine molecule can recognize so efficiently the chirality of tertiary acetylenic alcohol in the complex, we studied the crystal structure of the 1:1 brucine complex of 1d .⁶ The packing diagram (Figure 1) shows that hydrogen bond between OH of 1d and N of brucine plays an important role and that ethynyl, phenyl, and *o*-bromophenyl groups are arranged parallel with each other, respectively. Linearity of the acetylenyl group may also be important to form the complex. These results suggest that not only the acetylenic alcohol but also the compounds of the general structure of $\text{PhRC(OH)-}\overline{\text{X}}=\text{Y}$, PhRC(OH)-X=Y=Z such as allyl alcohol, cyanohydrin, allenic alcohol can also be resolved by the complexation with brucine. Optical resolution of these are under progress.

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3. T. Mukaiyama and S. Suzuki, *Chem. Lett.*, **1980**, 255.
4. All the $[\alpha]_{\text{D}}$ values were measured in MeOH (*c* 0.2) with a 1-dm cell at 25 °C, unless otherwise stated. Enantiomeric excess (ee) of 1 was determined by NMR analysis of its acetate in CDCl_3 with using the chiral shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium(III), Eu(hfc)_3 (Aldrich, 99+%).
5. K. Shingu, H. Kuritani, and S. Imajo, Abstract of the 31st Symposium on Organic Reaction Mechanisms (Nagoya, October, 1980), p. 131.
6. Orthorhombic, $\text{P2}_1\text{2}_1\text{2}_1$ (*Z*=4); $a=12.446(4)$, $b=33.446(5)$, $c=7.728(1)$ Å. Bond distances between O and N, and H and N of the hydrogen bond (O-H---N) are 2.703(7) and 1.79(8) Å, respectively. Bond angle of O-H---N is $164(8)^{\circ}$.

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