ASYMMETRIC ADDITION OF ACETYLIDE TO ALIPHATIC ALDEHYDES -----PREPARATION OF OPTICALLY ACTIVE 5-OCTYL-2(5H)-FURANONE------

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Various optically active acetylenic alcohols (40-80%e.e.) were obtained by enantioface-differentiating addition of lithium trimethylsilylacetylide to aliphatic aldehydes utilizing (2S, 2'S)-2hydroxymethyl-1-[(1-methylpyrrolidin-2-yl)methyl]pyrrolidine as a chiral ligand. Optically active (R)-1-trimethylsilyl-1-undecyn-3ol (80%e.e.) was transformed into optically active 5-octyl-2(5H)-furanone in good yield.

It is well known that 5-substituted-2(5H)-furanones are useful key intermediates in the total synthesis of some natural products, such as avenaciolide,^{1a)} isoavenaciolide,^{1b)} and protolichesterinic acid.^{1c)} However, the preparation of these compounds in optically active form is one of the important problems remained

R=n-C8H17-R=n-C13H27-Protolichesterinic acid unresolved.²⁾ In the previous communication, 3)we have reported

the highly enantioselective addition of acetylene derivatives to benzaldehyde by employing (2S, 2'S)-2-hydroxymethyl-1-[(1-methylpyrrolidin-2-yl)methyl]pyrrolidine (1) as a chiral ligand. Since optically active acetylenic alcohols are regarded as the suitable precursors of 5-alkyl-2(5H)-furanone derivatives,⁴⁾ we studied on i)the preparation of various chiral alkynyl alcohols 2 by enantioface-differentiating addition of lithium trimethylsilylacetylide to aliphatic aldehydes, and ii)the transformation of chiral 1-undecyn-3-ol into the optically active 5-octyl-2(5H)-furanone.

In the first place, the asymmetric addition of lithium trimethylsilylacetylide to various aliphatic aldehydes was investigated employing the chiral amino alcohol $\underline{1}$ as the chiral ligand. The results are summarized in Table I.



It should be noted that the present asymmetric reaction provides various chiral alkynyl alcohols by a simple procedure in high optical purity just starting from aliphatic aldehydes, while the conventional methods involve some

	Trimethylsilylacetylide to Aliphatic Aldehydes			
Run ^{a)}	R	<u>S.</u> Y. (%)	0.Y.(%) ^{b)}	Config.
1	$n - C_2 H_5 -$	77	68	R
2	$n - C_5 H_{11} -$	87	76	R
3	$n - C_8 H_{17} -$	83	80	R
4	$n - C_{11}H_{23}$	82	70	R
5	$n - C_{13}H_{27}$	76	73	R
6	(CH ₃) ₂ CHCH ₂ -	54	65	R
7	CH ₃ (CH ₂) ₂ CH=CH-	74	40	R

Table I Enantioselective Addition of Lithium

a) The reaction was carried out in a similar manner as described in the previous communication. b) The optical purity of the resulting alcohol was determined by NMR measurement of its MTPA derivative (Mosher's method)⁶) utilizing benzene-d⁶ as a solvent.

disadvantages, that is, the method of asymmetric reduction of acetylenic ketone consists of laborious multistep sequence, and chemical^{5b)} or microbial^{5c)} resolution method wastes half of the material.

Next, the optically active (R)-1-trimethylsilyl-1-undecyn-3-ol (2a) was transformed into 5-octy1-2(5H)-furanone in 61% overall yield according to Scheme I.



Hydrolysis of 2a with 0.1N NaOH-MeOH(room temperature, 3h) afforded (R)-1-undecyn-3-ol (2b)(89%; $[\alpha]_D^{24}$ +12°, (c 12, Et₂0)),^{5c)} which was treated with two equivalents of BuLi in THF at -50°C for 30 min, followed by carboxylation in a sealed tube to yield (R)-4-hydroxy-2-dodecynoic acid (3) (73%; $[\alpha]_D^{25}$ +0.6(c 11, CH_2Cl_2). This acetylenic acid was partially hydrogenated in MeOH using Pd-BaSO₄-quinoline to afford (R)-5-octyl-2(5H)-furanone (4)(94%; [α]_D²⁴-53°(c 2.6, EtOH)).

The obtained lactone had R-configuration, and therefore could lead to naturally occurring avenaciolide⁷⁾ according to the stereoselective sequence reported by Schlessinger et al.^{1a)}

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