Catalytic Asymmetric Synthesis of Optically Active Alkynyl Alcohols by Enantioselective Alkynylation of Aldehydes and by Enantioselective Alkylation of Alkynyl Aldehydes

Seiji Niwa and Kenso Soai *
Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Shinjuku, Tokyo 162, Japan

Catalytic asymmetric synthesis of optically active secondary alkynyl alcohols (**1**) by enantioselective addition of organozinc reagents to aldehydes in the presence of a small amount of catalyst was examined. Enantioselective alkynylation of benzaldehyde by alkynylzinc reagents using (1*S*,2*R*)-(−)-*N*,*N*-dibutylnorephedrine (**2c**) as a chiral catalyst gave (**1**) in moderate enantiomeric excess (e.e.). On the other hand, enantioselective addition of dialkylzinc reagents to alkynyl aldehydes using (*S*)-(+)-(1-methylpyrrolidin-2-yl)diphenylmethanol (**3**) as a chiral catalyst afforded (**1**) in high e.e. The reaction of 3-trimethylsilylprop-2-ynal with diethylzinc in toluene at −20 °C using (*S*)-(+)-(**3**) (5 mol%) afforded (−)-1-trimethylsilylpent-1-yn-3-ol in 78% e.e. (*S*)-(−)-Oct-1-yn-3-ol (**6**) (precursor of the prostaglandin side chain) was also synthesized in 69% e.e. by employing dipentylzinc.

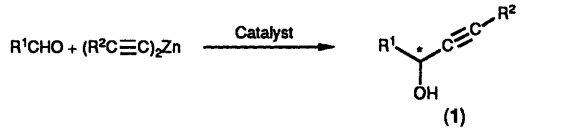
Increasing interest has been directed to catalytic asymmetric carbon–carbon bond-forming reactions.[1] Nucleophilic addition of dialkylzinc reagents to aldehydes is usually very slow.[2] In 1978, Mukaiyama and his co-workers reported[3a] that (2*S*,2′*S*)-2-hydroxymethyl-1-[(1-methylpyrrolidin-2-yl)methyl]pyrrolidine (chiral β-amino alcohol derived from the amino acid)[4] catalyses the addition of diethylzinc to benzaldehyde to afford 1-phenylpropan-1-ol. During our continuing study of the enantioselective addition of dialkylzinc reagents to aliphatic aldehydes (A), aromatic aldehydes (B), α,β-unsaturated aldehydes (C), and formyl esters (D), we have reported highly enantioselective reactions using chiral β-amino alcohol derivatives as catalysts, *i.e.*, chiral pyrrolidinylmethanols (for A, B, and C),[3b] *N*,*N*-dibutylnorephedrine (**2c**, DBNE) (for A, B, and D),[3c,d] polymer-bound *N*-alkylnorephedrines (for A and B),[3e] and an ephedrine derivative (for B).[3f,5] We also reported that the dilithium salt of a chiral piperazine was a highly enantioselective catalyst for B.[3g] In order to afford versatile optically active compounds, including natural products, the optically active secondary alcohols must have another functional group. In this context, we reported the catalytic asymmetric synthesis of alkyl substituted lactones[3d] and hydroxy ketones[6] using dialkylzinc reagents by the enantioselective and chemoselective alkylation of formyl esters and oxoaldehydes, respectively.

Optically active secondary-alkynyl alcohols (**1**) form an important class of compounds. They serve as intermediates for preparation of hydroxy carboxylic acids,[7] and natural products such as steroids,[8] avenaciolide,[9] vitamin E,[10] prostaglandins,[11] pheromones,[12] tetrahydrocerulenin,[13] and biologically active prostacyclin mimetics.[14] Conventional methods for the asymmetric synthesis of (**1**) require stoicheiometric amounts of chiral auxiliaries for the reduction of acetylenic ketones,[15] during the alkynylation of aldehydes,[16] and during the reductive cleavage of acetylenic acetals.[17]

We report here the catalytic asymmetric synthesis of alkynyl alcohols (**1**) by the enantioselective addition of alkynylzinc reagents to aldehydes and alkynyl aldehydes in the presence of a small amount of amino alcohols as catalysts.[18] Enantioselective alkynylation of benzaldehyde with alkynylzinc reagents using (1*S*,2*R*)-(−)-dibutylnorephedrine (**2c**, DBNE) as a chiral catalyst gave (**1**) in moderate enantiomeric excess (e.e.). On the other hand, enantioselective addition of dialkylzinc reagents to alkynyl aldehydes using (*S*)-(+)-(1-methylpyrrolidin-2-yl)diphenylmethanol (**3**, MPDPM) as a chiral catalyst afforded (**1**) in high e.e.

Results and Discussion

Enantioselective Addition of Alkynylzinc Reagents to Aldehydes.—We examined the enantioselective addition of dialkynylzinc reagents to aldehydes in the presence of a chiral amino alcohol as catalyst (Scheme 1). The dialkynylzinc reagents were



(**1**)

a; $R^1 = R^2 = Ph$
b; R^1 = Octyl, $R^2 = Ph$
c; R^1 = *trans*-PhCH=CH, $R^2 = Ph$
d; $R^1 = Ph$, R^2 = Hexyl
e; $R^1 = Ph$, R^2 = Bu
f; $R^1 = Ph$, $R^2 = Me_3Si$
g; R^1 = Octyl, $R^2 = Me_3Si$
h; $R^1 = Ph$, R^2 = cyclohexyl

Scheme 1.

prepared *in situ* by heating the corresponding alkynes with diethylzinc in an appropriate solvent according to the literature procedure.[19]

Treatment of bis(2-phenylethynyl)zinc with benzaldehyde at room temperature in the presence of 5 mol% of (1*S*,2*R*)-(−)-DBNE (**2c**) in hexane–tetrahydrofuran (THF) (2:3, v/v) afforded 1,3-diphenylprop-2-yn-1-ol (**1a**) in 99% yield and 34% e.e. (Table 1, entry 4). Hexane–tetrahydropyran as solvent was comparable with hexane–THF (entry 7). We have previously reported that hydrocarbons were more effective solvents than others during the enantioselective addition of dialkylzinc reagents to aldehydes.[3b] We then examined the reaction using hydrocarbon solvents. Interestingly, using hexane–toluene, the reaction was complete within 2 h and the enantioselectivity had decreased to 5% e.e. (entry 10). The dialkynylzinc precipitated in

Table 1. Effect of solvent in the 2-phenylethynylation of benzaldehyde.[a]

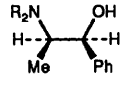
Entry	Solvent (v/v)	Time/h	(*R*)-(**1a**) % Yield	(*R*)-(**1a**) % E.e.[b,c]
1	Hexane–THF (4:1)	16	100	18
2	Hexane–THF (3:2)	17	99	30
3	Hexane–THF (1:1)	16	100	33
4	Hexane–THF (2:3)	14	99	34
5	Hexane–THF (1:4)	19	95	32
6	THF	39	94	29
7	Hexane–tetrahydropyran (2:3)	14	100	28
8	Hexane–1,2-dimethoxyethane (2:3)	17	100	20
9	Hexane–dipropyl ether (2:3)	2	98	6
10	Hexane–toluene (2:3)	2	96	5
11	Hexane–1,4-dioxane (2:3)	3	100	1

[a] The reactions were carried out at room temperature in the presence of (1*S*,2*R*)-(**2c**). Molar ratio, PhCHO:dialkynylzinc:(**2c**) = 1.0:2.0:0.05. [b] Based on HPLC analyses using a chiral column (Daicel Chiralcel OD, 250 mm; 254 nm UV detector); eluant 10% propan-2-ol in hexane; flow rate 1.0 ml/min; retention time (t_R/min), 13.3 for major peak, 24.0 for minor peak. [c] Configuration was determined by correlation with the HPLC peak; see footnote *c* of Table 5.

Table 2. Effect of temperature and molar ratio of dialkynylzinc in the 2-phenylethynylation of benzaldehyde.[a]

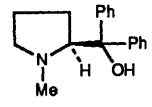
Entry	Temp./°C	Equiv. of reagent	Time/h	(*R*)-(**1a**) % Yield	(*R*)-(**1a**) % E.e.[b,c]
1	0	2.0	18	80	29
2	R.t.[d]	2.0	14	99	34
3	50	2.0	3	94	23
4	R.t.	1.2	14	98	22
5	R.t.	3.0	14	100	29

[a] The reactions were carried out in hexane–THF (2:3) in the presence of 5 mol% of (1*S*,2*R*)-(**2c**). [b] Based on HPLC analyses using a chiral column; see footnote *b* of Table 1. [c] Configuration was determined by correlation with the HPLC peak; see footnote *c* of Table 5. [d] R.t. = room temperature.

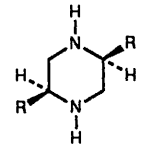


(1*S*,2*R*)-(**2**)

a; R = Et
b; R = Pr
c; R = Bu (DBNE)
d; R = Pentyl
e; R = Hexyl
f; RR = $-[CH_2]_4-$
g; R = Allyl



(*S*)-(**3**) (MPDPM)



(2*S*,5*S*)-(**4**)

a; R = $PhCH_2$
b; R = Pr^i

hexane–toluene, hexane–dioxane, and hexane–dipropyl ether (entries 9–11). The low selectivity in these solvents may then be attributed to the aggregation of the dialkynylzinc. In hexane–THF, the dialkynylzinc remained suspended to some extent. When only THF was used as the solvent, the solution was nearly clear and the reaction was slower (entry 6). It was better to carry out the reactions at room temperature than at 0 or 50 °C (Table 2, entries 1–3). At 0 °C, the dialkynylzinc precipitated. Best results were obtained with 2 mol equiv. of the zinc reagent (Table 2, entries 2, 4, and 5).

The effect of the structure of catalyst in the 2-phenylethynylation of benzaldehyde is shown in Table 3. *N*,*N*-Dialkylnorephedrines (**2a–f**) as catalysts gave (**1a**) in similar e.e. (entries 1–3 and 5–7). Furthermore, *N*,*N*-diallylnorephedrine (**2g**) showed comparable enantioselectivity (entry 8). When the catalyst (**2c**) was used after treatment with an equimolar amount of Et_2Zn at room temperature for 1 h [ethylzinc alkoxide of (**2c**) was formed], the e.e. of (**1a**) decreased to 23% (entry 4). Thus, for enantioselective alkynylation, the alkynylzinc alkoxide of the catalyst (formed *in situ* by the reaction of the dialkynylzinc and the catalyst) was more effective than the ethylzinc alkoxide. (*S*)-MPDPM (**3**)[3b] and chiral piperazines (**4**)[3g] were less effective for the enantioselective alkynylation of aldehydes (entries 9–11). Regardless of the catalyst, the dialkynylzinc reagents attacked aldehydes from the same side as the dialkylzinc reagents. Determination of the absolute configuration of (**1a**) will be described later.

The effect of the structure of the aldehyde and the dialkynylzinc on enantioselectivities was examined using 5 mol% of (1*S*,2*R*)-DBNE (**2c**). The results are shown in Table 4. In the 2-phenylethynylations, the aliphatic aldehyde nonanal reacted faster than the aromatic aldehydes. However, the e.e. of the corresponding alcohol (**1b**) was lower (entry 2). The reaction with an α,β-unsaturated aldehyde also showed low selectivity (entry 3). With regard to the alkynyl substituent of the zinc reagent, addition of the straight-chain dialkynylzinc, dioct-1-

ynylzinc, to benzaldehyde afforded 1-phenylnon-2-yn-1-ol (**1d**) in 81% yield and 22% e.e. (entry 4). For enantioselective alkylation, a zinc reagent with a primary alkyl substituent, *e.g.* diethylzinc, was effective. We then thought that the enantioselectivity might be increased using a zinc reagent with a shorter alkynyl group. However, enantioselectivity did not increase during the reaction of dihex-1-ynylzinc which has a shorter alkynyl group than dioct-1-ynylzinc (entry 5).

We then examined the addition of bis(2-trimethylsilylethynyl)-zinc, which reacted slowly with benzaldehyde in the presence of 5 mol% of catalyst at room temperature, affording 3-trimethylsilyl-1-phenylprop-2-yn-1-ol (**1f**) in only 36% yield even after 7 days (entry 6), possibly owing to the bulkiness of the trimethylsilyl group. Also the e.e. was not increased (21%). However, this reagent reacted smoothly with the aliphatic aldehyde nonanal and afforded (**1g**) in reasonable yield (entry 7), and with an e.e. which was comparable with that for (**1f**) obtained from the aromatic benzaldehyde. This contrasts with the results in entries 1 and 2, where the enantioselectivity for the aliphatic aldehyde was lower for 2-phenylethynylation. Bis(2-cyclohexylethynyl)zinc, which, like bis(2-phenylethynyl)zinc, has a six-membered ring, gave (**1h**) in low e.e. (entry 8). This result suggests that the alkynylzinc reagent with π-electrons in the alkynyl substituent was more effective than those without π-electrons. As previously described, the reaction of bis(2-phenylethynyl)zinc with benzaldehyde proceeded smoothly in the presence of (**2c**) and gave (**1a**) in high yield. Among the above-mentioned alkynylations, the best enantioselectivity was observed during 2-phenylethynylation.

Table 3. Effect of structure of catalyst in the 2-phenylethynylation of benzaldehyde.[a]

			(**1a**)	
Entry	Catalyst	Time/h	%Yield	% E.e.[b,c]
1	(1*S*,2*R*)-(**2a**)	15	100	29 (*R*)
2	(1*S*,2*R*)-(**2b**)	16	100	34 (*R*)
3	(1*S*,2*R*)-(**2c**)	14	99	34 (*R*)
4[d]	(1*S*,2*R*)-(**2c**)	14	98	23 (*R*)
5	(1*S*,2*R*)-(**2d**)	14	100	34 (*R*)
6	(1*S*,2*R*)-(**2e**)	16	96	33 (*R*)
7	(1*S*,2*R*)-(**2f**)	14	96	32 (*R*)
8	(1*S*,2*R*)-(**2g**)	14	100	35 (*R*)
9	(*S*)-(**3**)	14	92	4 (*R*)
10	(2*S*,5*S*)-(**4a**)	24	91	15 (*S*)
11	(2*S*,5*S*)-(**4b**)	28	92	6 (*S*)

[a] The reactions were carried out in hexane–THF (2:3) at room temperature. Molar ratio, PhCHO:bis(2-phenylethynyl)zinc:catalyst = 1.0 : 2.0 : 0.05. [b] Based on HPLC analyses using a chiral column; see footnote *b* of Table 1. [c] Configuration was determined by correlation with the HPLC peak; see footnote *c* of Table 5. [d] The catalyst was used after treatment with an equimolar amount of Et_2Zn.

The effect of the molar proportion of the catalyst is shown in Table 5. When 20 mol% of (1*S*,2*R*)-DBNE (**2c**) with respect to benzaldehyde was used as a catalyst, the highest e.e. of (**1a**) (43%) was observed (entry 4). The absolute configuration of (**1a**) was determined as (*R*) by correlation with (*S*)-(−)-1,3-diphenylpropan-1-ol {$[\alpha]_{365}^{25}$ −31.7° (*c* 2 in CH_2Cl_2); lit.,[20] $[\alpha]_{365}^{27}$ +81.2° (*c* 1 in CH_2Cl_2) for (*R*)-isomer} obtained by catalytic hydrogenation (10% Pd/C) of (**1a**) (43% e.e.).

The structure of the alkynylzinc reagent was then further examined using alkylalkynylzinc reagents during the 2-phenylethynylation of benzaldehyde (Scheme 2; Table 6). The

Scheme 2.

enantioselectivity increased when ethyl- or methyl-(2-phenylethynyl)zinc was used instead of the dialkynylzinc in the presence of 5 mol% of (**2c**) (entries 2 and 4). These alkylalkynylzinc reagents were prepared by heating Et_2Zn or Me_2Zn with an equimolar amount of phenylethyne. Also, products of ethylation or methylation were not formed and (**1a**) was obtained in high yield. Thus alkynylation was faster than alkylation. However, the use of 20 mol% of (**2c**) did not increase the enantioselectivity (entry 3).

Table 4. Effect of the structure of the aldehyde (R^1CHO) and the dialkynylzinc [$(R^2C{\equiv}C)_2Zn$] using (1*S*,2*R*)-(**2c**) as a catalyst.[a]

				(**1**)			
Entry	R^1	R^2	Time/h		$[\alpha]^{25}$ (*c*, $CHCl_3$)	% Yield	% E.e.
1	Ph	Ph	14	(**a**)	$[\alpha]_D$ +2.26° (6.63)	99	34[b] (*R*)[c]
2	$Me[CH_2]_7$	Ph	5	(**b**)	$[\alpha]_{365}$ −2.24° (6.43)	78	9[b]
3	*trans*-PhCH=CH	Ph	14	(**c**)	$[\alpha]_{577}$ +1.22° (4.11)	97	10[b]
4	Ph	$Me[CH_2]_5$	44	(**d**)	$[\alpha]_D$ +5.11° (3.52)	81	22[b]
5	Ph	Bu	52	(**e**)	$[\alpha]_D$ +5.44° (5.08)	93	20[b]
6	Ph	Me_3Si	168	(**f**)	$[\alpha]_D$ +10.3° (3.29)	36	21[b] (*R*)[d]
7	$Me[CH_2]_7$	Me_3Si	48	(**g**)	$[\alpha]_{365}$ −1.27° (4.85)	80	24[e] (*R*)[f]
8	Ph	cyclo-C_6H_{11}	48	(**h**)	$[\alpha]_{365}$ −6.32° (5.06)	88	7[b]

[a] The reactions were carried out at room temperature in hexane–THF (2:3) in the presence of (1*S*,2*R*)-(**2c**). Molar ratio, R^1CHO:dialkynylzinc:(**2c**) = 1.0:2.0:0.05. [b] Based on HPLC analyses using a chiral column. For (**1a**), see footnote *b* of Table 1. For (**1b**), eluant 7% propan-2-ol in hexane; flow rate 1.0 ml/min; t_R 6.1 min for major peak, 15.2 min for minor peak. For (**1c**), eluant 10% propan-2-ol in hexane; flow rate 1.0 ml/min; t_R 18.8 min for major peak, 55.3 min for minor peak. For (**1d**), eluant 4% propan-2-ol in hexane; flow rate 1.0 ml/min; t_R 8.0 min for minor peak, 12.8 min for major peak. For (**1e**), eluant 4% propan-2-ol in hexane; flow rate 0.5 ml/min; t_R 18.9 min for minor peak, 26.5 min for major peak. For (**1f**), eluant 4% propan-2-ol in hexane; flow rate 0.5 ml/min; t_R 12.5 min for minor peak, 18.2 min for major peak. For (**1h**), eluant 10% propan-2-ol in hexane; flow rate 0.5 ml/min; t_R 12.6 min for minor peak, 16.5 min for major peak. [c] Configuration was determined by the correlation with the HPLC peak; see footnote *c* of Table 5. [d] Based on (*S*)-(+)-1-phenylprop-2-yn-1-ol which was obtained from (**1f**) by hydrolysis (0.2M NaOH in MeOH) {$[\alpha]_D^{25}$ +7.51° (*c* 3.25 in $CHCl_3$); lit.,[24] $[\alpha]_D^{20}$ −26.8° (*c* 3.5 in $CHCl_3$) for (*R*)-isomer in 86% e.e.}. [e] The e.e. was determined by HPLC analysis using a chiral column of the corresponding (−)-α-methoxy-α-(trifluoromethyl)phenylacetate (MTPA) ester[22] after removal of the trimethylsilyl group of (**1g**). Eluant 0.25% propan-2-ol in hexane; flow rate 1.0 ml/min; t_R 7.4 min for major peak, 9.8 min for minor peak. [f] Based on (*R*)-(+)-undec-1-yn-3-ol which was obtained from (**1g**) by hydrolysis (0.2M NaOH in MeOH) {$[\alpha]_D^{25}$ +4.80° (*c* 3.03 in Et_2O); lit.,[25] $[\alpha]_D^{21}$ −16.5° (*c* 0.86 in Et_2O) for (*S*)-isomer in 96% e.e.}.

Table 5. Effect of molar ratio of catalyst (**2c**) in 2-phenylethynylation of benzaldehyde.[a]

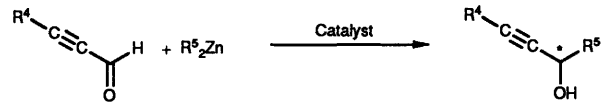
Entry	Mol% of (**2c**)	(*R*)-(**1a**) % Yield	(*R*)-(**1a**) % E.e.[b,c]
1	5	99	34
2	10	98	37
3	15	98	40
4	20	99	43
5	25	98	42
6	30	99	39
7	50	100	36

[a] The reactions were carried out at room temperature in hexane–THF (2:3) for 13–17 h. Molar ratio, PhCHO:dialkynylzinc = 1.0:2.0. [b] Based on HPLC analyses using a chiral column; see footnote *b* of Table 1. [c] Configuration of (**1a**) (entry 4) was determined as (*R*) by correlation with (*S*)-(−)-1,3-diphenylpropan-1-ol obtained from (**1a**) by hydrogenation (10% Pd/C) {$[\alpha]_{365}^{25}$ −31.7° (*c* 2.00 in CH_2Cl_2); lit.,[20] $[\alpha]_{365}^{27}$ +81.2° (*c* 1 in CH_2Cl_2) for (*R*)-isomer}. Configuration of the other (**1a**) samples (entries 1–3 and 5–7) was determined by the correlation with the HPLC peak.

Table 6. Effect of alkynylzinc reagent in alkynylation of benzaldehyde.[a]

Entry	Zinc reagent	(*R*)-(**1a**) % Yield	(*R*)-(**1a**) % E.e.[b,c]
1	Bis(2-phenylethynyl)zinc	99	34
2	Ethyl(2-phenylethynyl)zinc	95	40
3[d]	Ethyl(2-phenylethynyl)zinc	98	39
4	Methyl(2-phenylethynyl)zinc	96	39

[a] The reactions were carried out at room temperature in hexane–THF (2:3) for 12–15 h in the presence of (1*S*,2*R*)-(**2c**). Molar ratio, PhCHO:zinc reagent:(**2c**) = 1.0:2.0:0.05 except in entry 3. [b] Based on HPLC analyses using a chiral column; see footnote *b* of Table 1. [c] Configuration was determined by correlation with the HPLC peak; see footnote *c* of Table 5. [d] 20 mol% of catalyst was used.



(**5**) (**1**)

a; R^4 = Me_3Si
b; R^4 = Ph
c; R^4 = Bu

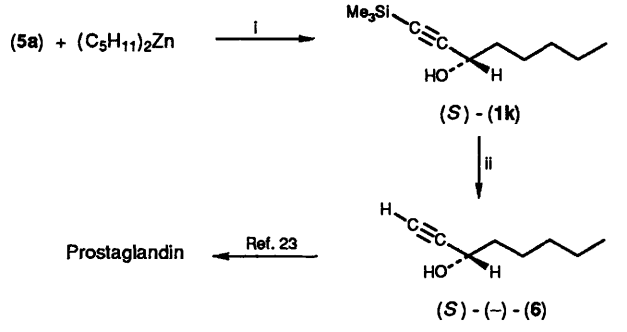
i; R^4 = Me_3Si, R^5 = Et
j; R^4 = Me_3Si, R^5 = Bu
k; R^4 = Me_3Si, R^5 = Pentyl
l; R^4 = Me_3Si, R^5 = Pr^i
m; R^4 = Ph, R^5 = Me
n; R^4 = Ph, R^5 = Et
o; R^4 = Ph, R^5 = Bu
p; R^4 = Bu, R^5 = Et

Scheme 3.

Thus, optically active alkynyl alcohols (**1**) were obtained by the enantioselective addition of alkynylzinc reagents to aldehydes in moderate e.e.

Enantioselective Addition of Dialkylzinc Reagents to Alkynyl Aldehydes.—We next examined the enantioselective addition of dialkylzinc reagents to alkynyl aldehydes (Scheme 3). We investigated different reaction conditions using 3-phenylprop-2-ynal (**5b**) as substrate. The results are summarized in Table 7. When (**5b**) was treated with diethylzinc in hexane at 0 °C using the lithium salt of (*S*)-MPDPM (**3**) (5 mol%) as catalyst, (−)-1-phenylpent-1-yn-3-ol (**1n**) was obtained in 60% e.e. (the e.e. was determined by HPLC analysis using a chiral column) (entry 1). The amount of catalyst did not have a significant effect on the e.e. of (**1n**) (entries 2 and 3). A similar enantioselectivity was observed when (*S*)-(**3**) was used without lithiation (entry 4). On the other hand, with (1*S*,2*R*)-DBNE (**2c**) as catalyst, the e.e. of (**1n**) was low (entry 5). As to the effect of solvent, the enantioselectivity obtained in cyclohexane was comparable with that in hexane (entry 6). In toluene, however, the e.e. of (**1n**) increased to 67% (entry 8). The reaction in toluene at −20 °C gave (**1n**) in 70% e.e. (entry 10).

Since various alkynyl aldehydes (**5**) can be easily prepared from ethyl formate and the corresponding alkynes,[21] the present method can be applied to the synthesis of a variety of alkynols (**1**). The results of the *catalytic* asymmetric addition of dialkylzinc reagents to various aldehydes (**5**) are summarized in Table 8. When 3-trimethylsilylprop-2-ynal (**5a**) was treated with diethylzinc in toluene at −20 °C using (*S*)-(**3**) (5 mol%), (−)-1-trimethylsilylpent-1-yn-3-ol (**1i**) was obtained in 67% yield with 78% e.e. [the optical purity was determined by analysis of the corresponding (−)-α-methoxy-α-(trifluoromethyl)phenylacetate[22] using a chiral HPLC column] (entry 1). The trimethylsilyl group of (**1i**) can be removed by treatment with methanolic NaOH,[9] and further functional modification of the acetylenic group is possible. The addition of diethylzinc to compounds (**5**) with aryl (**5b**) or aliphatic (**5c**) substituents afforded (**1n**) and (**1p**) in 70 and 64% e.e., respectively (entries 6 and 8). Though the addition of di-isopropylzinc (entry 4) and dimethylzinc (entry 5) afforded the corresponding (**1l**) and (**1m**) in moderate e.e., the reactions using dibutylzinc gave enantioselectivities which were comparable with those for diethylzinc (67–72% e.e., entries 2 and 7). Furthermore, the addition of dipentylzinc to (**5a**) afforded (*S*)-1-trimethylsilyloct-1-yn-3-ol (**1k**) in reasonable e.e. (69%, entry 3). Hydrolysis of (**1k**) with 0.2M NaOH in MeOH afforded (*S*)-oct-1-yn-3-ol (**6**) of 70% e.e. which is a building block for prostaglandin synthesis[23] (Scheme 4).



Scheme 4. *Reagents:* i, 5 mol% catalyst (*S*)-(**3**); ii, 0.2M NaOH in MeOH.

Conclusion

Optically active secondary alkynyl alcohols were obtained by the enantioselective addition of organozinc reagents to aldehydes in the presence of a small amount of catalyst. Enantioselective alkynylation of benzaldehyde with alkynylzinc reagent using (1*S*,2*R*)-(−)-DBNE (**2c**) as a chiral catalyst gave alkynyl alcohols in moderate enantiomeric excesses. On the other hand, enantioselective addition of dialkylzinc reagents to alkynyl aldehydes using (*S*)-(+)-MPDPM (**3**) as a chiral catalyst afforded alkynyl alcohols in high e.e. The present methods may be useful for the asymmetric synthesis of various

Table 7. Effects of catalyst, solvent, and temperature in enantioselective ethylation of the alkynyl aldehyde (**5b**).[a]

				(*S*)-(**1n**)		
Entry	Catalyst	Mol%	Solvent	Temp. (°C)	% Yield	% E.e.[b]
1	(*S*)-(**3**)–Li	5	Hexane	0	79	60
2	(*S*)-(**3**)–Li	2	Hexane	0	86	58
3	(*S*)-(**3**)–Li	10	Hexane	0	77	59
4	(*S*)-(**3**)	5	Hexane	0	81	60
5	(1*S*,2*R*)-(**2c**)	5	Hexane	0	81	21
6	(*S*)-(**3**)	5	Cyclohexane–hexane	0	89	60
7	(*S*)-(**3**)	5	Toluene–hexane	0	81	64
8	(*S*)-(**3**)	5	Toluene	0	76	67
9	(*S*)-(**3**)	5	Toluene	−10	77	69
10	(*S*)-(**3**)	5	Toluene	−20	70	70
11	(*S*)-(**3**)	5	Toluene	−30	71	67
12	(*S*)-(**3**)	5	Toluene	−50	22	60
13	(*S*)-(**3**)	5	Toluene	−78	17	38
14[c]	(*S*)-(**3**)	5	Toluene	−20	64	68
15[d]	(*S*)-(**3**)	5	Toluene	−20	77	69

[a] Molar ratio of (**5b**):diethylzinc was 1.0:2.0 unless otherwise noted. [b] Based on HPLC analyses using a chiral column. Eluant 7% propan-2-ol in hexane; flow rate 1.0 ml/min; t_R 7.6 min for minor peak, 17.0 min for major peak. [c] 1 Equiv. of Et_2Zn was used. [d] 3 Equiv. of Et_2Zn was used.

Table 8. Catalytic asymmetric synthesis of optically active alkynyl alcohols (**1i–p**) by enantioselective alkylation of alkynyl aldehydes (**5**).[a]

			(**1**)			
Entry	(**5**), R^4	R^5_2Zn, R^5		$[\alpha]^{25}$ (*c*, solvent)	% Yield	% E.e.
1	Me_3Si	Et	(**i**)	$[\alpha]_{365}$ −5.16° (2.13, $CHCl_3$)	67	78[b]
2	Me_3Si	Bu	(**j**)	$[\alpha]_{365}$ −4.71° (2.00, $CHCl_3$)	54	72[b] (*S*)[c]
3	Me_3Si	$Me[CH_2]_4$	(**k**)	$[\alpha]_{365}$ +6.57° (5.02, $CHCl_3$)	55	69[b] (*S*)[d]
4	Me_3Si	Pr^i	(**l**)	$[\alpha]_{365}$ +3.99° (3.71, $CHCl_3$)	52	43[b]
5	Ph	Me	(**m**)	$[\alpha]_D$ −8.39° (1.37, $CHCl_3$)	26	40[e] (*S*)[f]
6	Ph	Et	(**n**)	$[\alpha]_D$ −13.7° (2.00, Et_2O)	70	70[e] (*S*)[g]
7	Ph	Bu	(**o**)	$[\alpha]_D$ +6.24° (1.33, $CHCl_3$)	61	67[e]
8	Bu	Et	(**p**)	$[\alpha]_{365}$ −5.90° (3.05, Et_2O)	71	64[h] (*S*)[i]

[a] Reaction conditions: molar ratio of (**3**):(**5**):R^5_2Zn = 0.05:1.0:2.0; 12–14 h at −20 °C in toluene. [b] Based on HPLC analyses of the corresponding (−)-MTPA esters[22] using a chiral column. Eluant 0.01% propan-2-ol in hexane; flow rate 0.5 ml/min; (−)-MTPA ester of (**1i**), t_R 13.6 min for major peak, 17.7 min for minor peak. For (−)-MTPA ester of (**1j**), t_R 12.8 min for major peak, 16.0 min for minor peak. For (−)-MTPA ester of (**1k**), t_R 17.8 min for major peak, 23.2 min for minor peak. For (−)-MTPA ester of (**1l**), t_R 13.5 min for major peak, 16.1 min for minor peak. [c] Based on (*S*)-(−)-hept-1-yn-3-ol which was obtained from (**1j**) by hydrolysis (0.2M NaOH in MeOH) {$[\alpha]_D^{25}$ −13.7° (*c* 2.13 in Et_2O); lit.,[26] $[\alpha]_D$ −3.2° (Et_2O) for 14% e.e.}. [d] Based on (*S*)-(−)-oct-1-yn-3-ol which was obtained from (**1k**) by hydrolysis (0.2M NaOH in MeOH) {$[\alpha]_D^{22}$ −15.6° (*c* 2.16 in Et_2O); lit.,[15a] $[\alpha]_D^{21}$ − 18.8° (*c* 1.30 in Et_2O) for 84% e.e.}. [e] Based on HPLC analyses using a chiral column. For (**1m**), eluant 5% propan-2-ol in hexane; flow rate 1.0 ml/min; t_R 11.4 min for minor peak, 30.7 min for major peak. For (**1n**), see footnote *b* of Table 7. For (**1o**), eluant 5% propan-2-ol in hexane; flow rate 1.0 ml/min; t_R 9.3 min for minor peak, 30.2 min for major peak. [f] Based on the reported value of $[\alpha]_D^{24}$ +36.88° (*c* 2.47 in $CHCl_3$) for (*R*)-(**1m**) in 80% e.e.[17] [g] Based on (*S*)-(+)-1-phenylpentan-3-ol which was obtained from (**1n**) by hydrogenation (10% Pd/C) {$[\alpha]_D^{25}$ +19.6° (*c* 2.43 in EtOH); lit.,[27] $[\alpha]_D$ + 26.8° (*c* 5 in EtOH)}. [h] ^1H NMR (500 MHz) analysis of the MTPA ester. [i] Based on (*S*)-(+)-nonan-3-ol which was obtained from (**1p**) by hydrogenation (10% Pd/C) {$[\alpha]_D^{25}$ +5.54° (*c* 2.00 in $CHCl_3$); lit.,[28] $[\alpha]_D$ +9.6° (*c* 8.3 in $CHCl_3$)}.

alkynyl alcohols, a catalytic method which has not so far been reported.

Experimental

General.—IR spectra and optical rotations were recorded with a Hitachi 260-10 spectrophotometer and a JASCO DIP-181 polarimeter, respectively. ^1H NMR spectra were recorded with a JEOL JNM-PMX-60 spectrometer. HPLC analysis was carried out with a Shimadzu LC-8A instrument. Bulb-to-bulb distillation was carried out with a Shibata Glass Tube Oven GTO-250 apparatus. Hexane, tetrahydrofuran (THF), and toluene were distilled over lithium aluminium hydride. All the reactions were performed under an argon atmosphere. Diethylzinc in hexane was purchased from Kanto Chemical Co. Other dialkylzinc reagents were prepared according to the literature procedure.[29]

Typical Procedure for the Enantioselective Alkynylation of Aldehydes (*Table* 1, *entry* 4).—To a solution of ethynylbenzene (0.415 g, 4.06 mmol) in THF (2 ml), diethylzinc (2.0 mmol, 2.0 ml of 1M hexane solution) was added. The mixture was heated at 70 °C (bath temp.) for 5 h, then cooled to room temperature. (1*S*,2*R*)-(−)-*N*,*N*-dibutylnorephedrine (**2c**) (0.013 g, 0.05 mmol) in THF (1 ml) was added and the mixture stirred at room temperature for 20 min. Benzaldehyde (0.1 ml, 1.0 mmol) was added and the mixture stirred at room temperature for 14 h. Hydrochloric acid (1M; 5 ml) was then added, and extraction (CH_2Cl_2; 4 × 15 ml), drying (Na_2SO_4), evaporation, and purification by TLC on silica gel ($CHCl_3$ as eluant) afforded 1,3-diphenylprop-2-yn-1-ol (**1a**) (0.202 g, 99%).

1,3-Diphenylprop-2-yn-1-ol (**1a**) had ν_{max} 3 350, 3 060, 2 200, 1 600, and 1 500 cm^{-1}; $\delta(CDCl_3)$ 2.50 (1 H, s), 5.63 (1 H, s), and 7.13–7.73 (10 H, m) [Found: M^+ (EI), 208.0895. $C_{15}H_{12}O$ requires *M*, 208.0889].

1-Phenylundec-1-yn-3-ol (**1b**) had ν_{max} 3 340, 2 900, 2 840, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 0.70–2.06 (18 H, m), 4.30–4.57 (1 H, m), and 7.05–7.43 (5 H, m) [Found: M^+ (EI), 244.1819. $C_{17}H_{24}O$ requires M, 244.1828].

1,5-Diphenylpent-1-en-4-yn-3-ol (**1c**) had ν_{max} 3 400, 3 040, 2 255, and 1 500 cm^{-1}; $\delta(CDCl_3)$ 2.32 (1 H, s), 5.16–5.40 (1 H, m), 6.13–6.81 (2 H, m), and 6.95–7.80 (10 H, m) [Found: M^+ (EI), 234.1040. $C_{17}H_{14}O$ requires M, 234.1045].

1-Phenylnon-2-yn-1-ol (**1d**) had ν_{max} 3 350, 2 920, 2 850, and 2 200 cm^{-1}; $\delta(CDCl_3)$ 0.67–1.56 (11 H, m), 2.00–2.47 (2 H, m), 2.73 (1 H, s), 5.33 (1 H, s), and 7.07–7.60 (5 H, m) [Found: M^+ (EI), 216.1508. $C_{15}H_{20}O$ requires M, 216.1515].

1-Phenylhept-2-yn-1-ol (**1e**) had ν_{max} 3 380, 3 000, 2 900, and 2 210 cm^{-1}; $\delta(CDCl_3)$ 0.77–1.20 (3 H, m), 1.20–1.87 (4 H, m), 1.90–2.77 (3 H, m), 5.30–5.53 (1 H, m), and 7.17–7.70 (5 H, m) [Found: M^+ (EI), 188.1191. $C_{13}H_{16}O$ requires M, 188.1202].

1-Phenyl-3-trimethylsilylprop-2-yn-1-ol (**1f**) had ν_{max} 3 350, 2 970, 2 200, and 1 500 cm^{-1}; $\delta(CDCl_3)$ 0.21 (9 H, s), 2.23 (1 H, s), 5.53 (1 H, s), and 7.27–7.77 (5 H, m) [Found: M^+ (EI), 204.0961. $C_{12}H_{16}OSi$ requires M, 204.0971].

1-Trimethylsilylundec-1-yn-3-ol (**1g**) had ν_{max} 3 350, 2 920, 2 850, and 2 180 cm^{-1}; $\delta(CDCl_3)$ 0.17 (9 H, s), 0.63–1.03 (3 H, m), 1.05–1.90 (14 H, m), 2.35 (1 H, s), and 4.18–4.47 (1 H, m). Treatment of (**1g**) with 0.2M NaOH in MeOH afforded (*R*)-(+)-undec-1-yn-3-ol: ν_{max} 3 350, 2 920, 2 850, and 2 130 cm^{-1}; $\delta(CDCl_3)$ 0.63–1.01 (3 H, m), 1.04–2.03 (14 H, m), 2.35–2.45 (2 H, m), 2.57 (1 H, s), and 4.17–4.49 (1 H, m).

3-Cyclohexyl-1-phenylprop-2-yn-1-ol (**1h**) had ν_{max} 3 380, 2 960, 2 880, and 2 250 cm^{-1}; $\delta(CDCl_3)$ 1.07–1.99 (10 H, m), 2.17–2.63 (2 H, m), 5.36–5.50 (1 H, m), and 7.13–7.65 (5 H, m) [Found: M^+ (EI), 214.1344. $C_{15}H_{18}O$ requires M, 214.1358].

Typical Procedure for the Enantioselective Addition of Dialkylzinc Reagents to Alkynylaldehydes (*Table* 8, *entry* 1).—A mixture of (**5a**) (0.126 g, 1.00 mmol) and (*S*)-(+)-(**3**) (0.013 g, 0.05 mmol) in toluene (2 ml) was stirred at room temperature for 30 min, and then cooled to −20 °C. Diethylzinc (2.0 mmol; 2.0 ml of 1M toluene solution) was added during 10 min, and the reaction mixture was stirred at −20 °C for 12 h. The reaction was quenched with 1M hydrochloric acid (5 ml), the organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 × 10 ml). The combined organic layers were dried (Na_2SO_4) and then evaporated under reduced pressure. The residue was purified by TLC over silica gel [$CHCl_3$–hexane (4:1) as eluant] to afford (**1i**) (0.104 g, 0.67 mmol, 67%).

1-Trimethylsilylpent-1-yn-3-ol (**1i**) had ν_{max} 3 350, 2 960, and 2 180 cm^{-1}; $\delta(CDCl_3)$ 0.16 (9 H, s), 0.78–1.18 (3 H, m), 1.45–1.87 (2 H, m), 2.28–2.38 (1 H, m), and 4.13–4.45 (1 H, m).

1-Trimethylsilylhept-1-yn-3-ol (**1j**) had ν_{max} 3 350, 2 960, 2 860, and 2 180 cm^{-1}; $\delta(CDCl_3)$ 0.17 (9 H, s), 0.86–1.18 (3 H, m), 1.23–1.90 (6 H, m), 2.33 (1 H, s), and 4.36–4.60 (1 H, m). Treatment of (**1j**) with 0.2M NaOH in MeOH afforded (*S*)-(−)-hept-1-yn-3-ol: ν_{max} 3 300, 2 950, and 2 860 cm^{-1}; $\delta(CDCl_3)$ 0.63–1.95 (9 H, m), 2.40–2.53 (1 H, m), 2.70 (1 H, s), and 4.16–4.53 (1 H, m).

1-Trimethylsilyloct-1-yn-3-ol (**1k**) had ν_{max} 3 350, 2 980, 2 880, and 2 190 cm^{-1}; $\delta(CDCl_3)$ 0.17 (9 H, s), 0.67–1.07 (3 H, m), 1.10–1.93 (8 H, m), 2.20 (1 H, s), and 4.17–4.50 (1 H, m). Compound (**1k**) (85.6 mg, 0.43 mmol) was converted into (*S*)-(−)-oct-1-yn-3-ol (**6**) by treatment with NaOH (0.6 mmol; 3.0 ml of 0.2M MeOH solution) at room temperature for 3 h. Water (5 ml) was then added and the mixture extracted with dichloromethane (4 × 10 ml). The combined organic layers were dried (Na_2SO_4) and then evaporated under reduced pressure. The residue was purified by bulb-to-bulb distillation to give (*S*)-(−)-(**6**) (49 mg, 0.39 mmol, 90%) of 70% e.e. (based on optical rotation); b.p. 120 °C at 20 mmHg (lit.,[15a] 130 °C at 25 mmHg); $[\alpha]_D^{22}$ −15.6° (*c* 2.16 in Et_2O) {lit.,[15a] $[\alpha]_D^{21}$ −18.8° (*c* 1.30 in Et_2O) for 84% e.e.}; ν_{max} 3 300, 2 930, and 2 850 cm^{-1}; $\delta(CDCl_3)$ 0.63–1.97 (11 H, m), 2.23 (1 H, s), 2.42–2.47 (1 H, m), and 4.20–4.50 (1 H, m).

4-Methyl-1-trimethylsilylpent-1-yn-3-ol (**1l**) had ν_{max} 3 350, 2 960, 2 900, and 2 170 cm^{-1}; $\delta(CDCl_3)$ 0.15 (9 H, s), 0.83–1.13 (6 H, m), 1.50–2.07 (1 H, m), 2.27 (1 H, s), and 4.10–4.27 (1 H, m).

4-Phenylbut-3-yn-2-ol (**1m**) had ν_{max} 3 350, 2 970, 1 600, and 1 490 cm^{-1}; $\delta(CDCl_3)$ 1.40–1.60 (3 H, m), 2.58 (1 H, s), 4.43–4.90 (1 H, m), and 7.01–7.42 (5 H, m).

1-Phenylpent-1-yn-3-ol (**1n**) had ν_{max} 3 350, 3 000, 2 900, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 0.90–1.23 (3 H, m), 1.53–2.00 (2 H, m), 3.35 (1 H, m), 4.35–4.57 (1 H, m), and 7.02–7.45 (5 H, m) [Found: M^+ (EI), 160.0883. $C_{11}H_{12}O$ requires M, 160.0880].

1-Phenylhept-1-yn-3-ol (**1o**) had ν_{max} 3 350, 2 960, 2 850, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 0.69–2.01 (9 H, m), 3.13 (1 H, m), 4.34–4.70 (1 H, m), and 7.02–7.53 (5 H, m) [Found: M^+ (EI), 188.1195. $C_{13}H_{16}O$ requires M, 188.1202].

Non-4-yn-3-ol (**1p**) had ν_{max} 3 350, 2 980, 2 900, and 2 350 cm^{-1}; $\delta(CDCl_3)$ 0.67–1.97 (12 H, m), 1.98–2.43 (3 H, m), and 4.01–4.50 (1 H, m).

Acknowledgements

We thank Tri Chemical Inc. for a generous gift of dimethylzinc.

References

1 'Asymmetric Catalysis,' ed. B. Bosnich, Martinus Nijhoff, Dordrecht, 1986.
2 B. Marx, E. H.-Basch, and P. Freon, *C. R. Acad. Sci., Ser. C.*, 1967, **264**, 527.
3 (*a*) T. Sato, K. Soai, K. Suzuki, and T. Mukaiyama, *Chem. Lett.*, 1978, 601; T. Mukaiyama, K. Soai, T. Sato, H. Shimizu, and K. Suzuki, *J. Am. Chem. Soc.*, 1979, **101**, 1455; (*b*) K. Soai, A. Ookawa, K. Ogawa, and T. Kaba, *J. Chem. Soc., Chem. Commun.*, 1987, 467; K. Soai, A. Ookawa, T. Kaba, and K. Ogawa, *J. Am. Chem. Soc.*, 1987, **109**, 7111; (*c*) K. Soai, S. Yokoyama, K. Ebihara, and T. Hayasaka, *J. Chem. Soc., Chem. Commun.*, 1987, 1690; (*d*) K. Soai, S. Yokoyama, T. Hayasaka, and K. Ebihara, *Chem. Lett.*, 1988, 843; (*e*) K. Soai, S. Niwa, and M. Watanabe, *J. Org. Chem.*, 1988, **53**, 927; *J. Chem. Soc., Perkin Trans. 1*, 1989, 109; (*f*) K. Soai, M. Nishi, and Y. Ito, *Chem. Lett.*, 1987, 2405; (*g*) K. Soai, S. Niwa, Y. Yamada, and H. Inoue, *Tetrahedron Lett.*, 1987, **28**, 4841.
4 T. Mukaiyama, K. Soai, and S. Kobayashi, *Chem. Lett.*, 1978, 219.
5 For related reactions B, C, see M. Kitamura, S. Suga, K. Kawai, and R. Noyori, *J. Am. Chem. Soc.*, 1986, **108**, 6071; N. Oguni, Y. Matsuda, and T. Kaneko, *ibid.*, 1988, **110**, 7877; M. Kitamura, S. Okada, S. Suga, and R. Noyori, *ibid.*, 1989, **111**, 4028; P. A. Chaloner and S. A. R. Perera, *Tetrahedron Lett.*, 1987, **28**, 3013; E. J. Corey and F. Hannon, *ibid.*, 1987, **28**, 5233, 5237; W. Oppolzer and R. N. Radinov, *ibid.*, 1988, **29**, 5645; M. Yoshioka, T. Kawakita, and M. Ohno, *ibid.*, 1989, **30**, 1657.
6 K. Soai, M. Watanabe, and M. Koyano, *J. Chem. Soc., Chem. Commun.*, 1989, 534.
7 M. M. Midland and P. E. Lee, *J. Org. Chem.*, 1981, **46**, 3934.
8 W. S. Johnson, B. Frei, and A. S. Gopalan, *J. Org. Chem.*, 1981, **46**, 1512.
9 T. Mukaiyama and K. Suzuki, *Chem. Lett.*, 1980, 255.
10 K. K. Chan, N. C. Cohen, J. P. DeNoble, A. C. Specian, Jr., and G. Saucy, *J. Org. Chem.*, 1976, **41**, 3497.
11 J. J. Partridge, N. K. Chadha, and M. R. Uskokovic, *J. Am. Chem. Soc.*, 1973, **95**, 7171; J. Fried and J. C. Sih, *Tetrahedron Lett.*, 1973, 3899.
12 W. H. Pirkle and C. W. Boeder, *J. Org. Chem.*, 1978, **43**, 2091; K. Mori and H. Akao, *Tetrahedron Lett.*, 1978, 4127; K. Sato, T. Nakayama, and K. Mori, *Agric. Biol. Chem.*, 1979, **43**, 1571.
13 J. P. Vigneron and J. M. Blauchard, *Tetrahedron Lett.*, 1980, **21**, 1739.
14 A. F. Kluge, D. J. Kertesz, C. O-Yang, and H. Y. Wu, *J. Org. Chem.*, 1987, **52**, 2860.
15 (*a*) R. Noyori, I. Tomino, M. Yamada, and M. Nishizawa, *J. Am. Chem. Soc.*, 1984, **106**, 6717; (*b*) B. T. Cho and W. S. Park, *Bull. Korean Chem. Soc.*, 1987, **8**, 257, and references cited therein.

16 T. Mukaiyama, K. Suzuki, K. Soai, and T. Sato, *Chem. Lett.*, 1979, 447.
17 K. Ishihara, A. Mori, I. Arai, and H. Yamamoto, *Tetrahedron Lett.*, 1986, **26**, 983.
18 Preliminary communication, K. Soai and S. Niwa, *Chem. Lett.*, 1989, 481.
19 O. Y. Okhlobystin and L. I. Zakharkin, *J. Organomet. Chem.*, 1965, **3**, 257.
20 C. Belzecki and I. Panfil, *J. Org. Chem.*, 1979, **44**, 1212.
21 H. Hauptmann and M. Mader, *Synthesis*, 1978, 307.
22 J. A. Dale, D. L. Dull, and H. S. Mosher, *J. Org. Chem.*, 1969, **34**, 2543.
23 Y. Kitano, T. Matsumoto, S. Okamoto, T. Shimazaki, Y. Kobayashi, and F. Sato, *Chem. Lett.*, 1987, 1523; M. Suzuki, A. Yanagisawa, and R. Noyori, *J. Am. Chem. Soc.*, 1988, **110**, 4718; C. R. Johnson and T. D. Penning, *ibid.*, 1988, **110**, 4726; J. Fried, C. Lin, M. Mehra, W. Kao, and P. Dalven, *Ann. N.Y. Acad. Sci.*, 1971, **180**, 38.
24 B. I. Glanzer, K. Faber, and H. Griengl, *Tetrahedron*, 1987, **43**, 5791.
25 M. Nishizawa, M. Yamada, and R. Noyori, *Tetrahedron Lett.*, 1981, **22**, 247.
26 K. Mori and H. Akao, *Tetrahedron Lett.*, 1978, **43**, 4127.
27 P. A. Levene and P. G. Stevens, *J. Biol. Chem.*, 1930, **87**, 375; L. F. Hewitt and J. Kenyon, *J. Chem. Soc.*, 1925, **127**, 1094.
28 T. Mukaiyama and K. Hojo, *Chem. Lett.*, 1976, 893.
29 C. R. Noller, *Org. Synth.*, 1966, Coll. Vol. II, 184.

Paper 9/03800K
Received 6*th September* 1989
Accepted 25*th October* 1989