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Synthesis of chiral homoallylic alcohols from aldehydes and diallyltin dibromide in the presence of monosodium-(+)-diethyl tartrate

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Abstract

The reaction of diallyltin dibromide, readily prepared from allyl bromide and tin powder, with aldehydes in the presence of monosodium-(+)-diethyl tartrate affords the corresponding homoallylic alcohols in good yields with enantiomeric excesses in the range 42 to 71%.

The reactions of chiral allyl- and/or crotyl-metal compounds with aldehydes are of considerable interest in the context of acyclic stereoselection [1], since the enantiomerically or diastereomerically pure homoallylic alcohols obtained are immediate precursors of the β-hydroxy carbonyl framework present in many naturally occurring and pharmacologically useful compounds [2].

The objective our research in this area is the development of methods and reagents suitable for synthesis of chiral homoallylic alcohols. Recently we reported the synthesis of optically active secondary homoallylic alcohols by reaction of aldehydes with allylic tin(IV) complexes containing (+)-diethyl tartrate (DET) as chiral auxiliary ligand [3]. The allylic tin(IV) complexes were obtained by oxidative addition of a tin(II) diethyl tartrate species to an allylic bromide [4].

This interesting finding prompted us to investigate this reaction further, and we now describe a one-pot enantioselective synthesis of homoallylic alcohols involving in situ formation of a chiral tin(IV) complex from diallyltin dibromide and diethyl tartrate monosodium salt (Na^+DET^-) as the chiral auxiliary followed by treatment of the complex with an aldehyde.

The procedure is very simple. Thus, diallyltin dibromide [5], directly prepared from allyl bromide and tin powder, undergoes ligand exchange upon treatment with the monosodium salt of (+)-diethyl tartrate (prepared from DET and NaH), followed by the addition of an aldehyde (Scheme 1).

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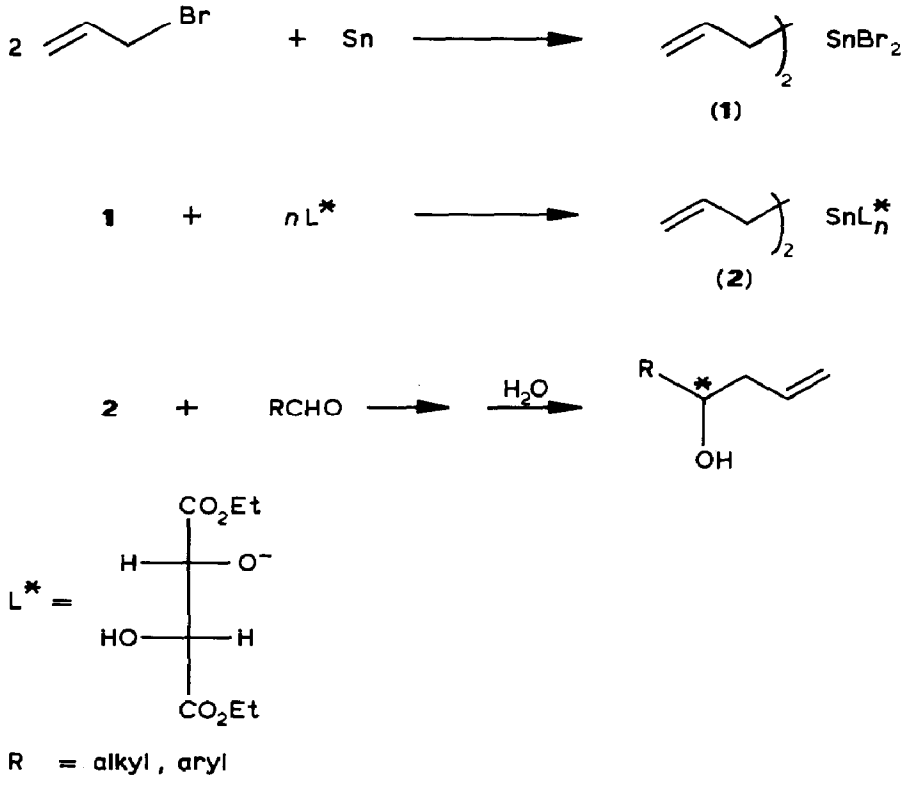

Scheme 1

Addition takes place cleanly and the corresponding homoallylic alcohols are obtained in good to excellent yields.

In Table 1 are shown the results of a study of the effects of the reaction conditions on the outcome of the reaction with benzaldehyde and nonanal. When the number of the chiral alkoxides bound to tin is increased, there is an increase in the facial preference of the allyl stannane as a consequence of the cooperative effect of the ligands; on the other hand the steric hindrance to the approaching aldehydes increases too, resulting in a lower degree of conversion. The best results are obtained by using a 3/1/2 Na^+DET^-/diallyltindibromide/RCHO molar ratio, and carrying out the whole process in THF at $-55°C$ (run 7). Tetrahydrofuran is preferred as the reaction solvent; use of dichloromethane appears to reduce the enantioselectivity (Table 1).

As shown in Table 2, the procedure seems to be of wide applicability and is satisfactory for alkyl, aryl and α,β-unsaturated aldehydes. The e.e. of the homoallylic alcohols ranges between 42 and 71%. It is noteworthy that with both nonanal and cyclohexanecarboxaldehyde no self condensation products are obtained. The absolute configurations of the homoallylic alcohols, as determined by comparison of their optical activities with those reported in the literature [6–8], show that reaction takes place preferentially on the *si* face of the aldehyde when (+)-diethyl tartrate is present as chiral ligand in **2**.

We have no direct knowledge of the structure of the actual chiral reagent. More than two molecules of chiral auxiliary may coordinate to tin in the chiral tin

Table 1

Effect of the variation of the molar ratio of the reagents on the enantiomeric excess [a]

Run	Aldehyde	Molar ratio [b]	Reaction temperature (°C)	Reaction time (h)	Product (yield) [c]	$[\alpha]_D^{23}$, deg (*c*)	% E.e. (config.)	Ref.
1	C_6H_5CHO	1/1/2	25	24	$C_6H_5CHCH_2CH{=}CH_2$ [d] (90) OH	−7.5(7.38) [e]	16 (*S*)	6
2	C_6H_5CHO	2/1/2	25	24	$C_6H_5CHCH_2CH{=}CH_2$ (80) OH	−14.0(7.38) [e]	30 (*S*)	6
3	C_6H_5CHO	3/1/2	25	24	$C_6H_5CHCH_2CH{=}CH_2$ (75) OH	−17.8(7.38) [e]	38 (*S*)	6
4	C_6H_5CHO	4/1/2	25	24	$C_6H_5CHCH_2CH{=}CH_2$ (60) OH	−30.4(7.38) [e]	65 (*S*)	6
5	n-$C_8H_{17}CHO$	3/1/2	25	24	n-$C_8H_{17}CHCH_2CH{=}CH_2$ (85) OH	+3.4(2.50) [f]	32 (*R*)	7
6	n-$C_8H_{17}CHO$	4/1/2	25	24	n-$C_8H_{17}CHCH_2CH{=}CH_2$ (65) OH	+4.7(2.50) [f]	44 (*R*)	7
7	n-$C_8H_{17}CHO$	3/1/2	−55	36	n-$C_8H_{17}CHCH_2CH{=}CH_2$ (65) OH	+4.9(2.50) [f]	46 (*R*)	7
8	n-$C_8H_{17}CHO$	4/1/2	−55	36	n-$C_8H_{17}CHCH_2CH{=}CH_2$ (60) OH	+6.1(2.50) [f]	57 (*R*)	7

[a] All the reactions were carried out in anhydrous THF. [b] Diethyl tartrate monosodium salt/diallyltin dibromide/aldehyde. [c] Isolated yields. [d] The e.e. was 10% when the reaction was carried out in CH_2Cl_2 at room temperature. [e] $[\alpha]_D^{23}$ determined in benzene. [f] $[\alpha]_D^{23}$ determined in CCl_4.

Table 2

Enantioselective syntheses of chiral homoallylic alcohols from diallyltin dibromide [a]

Run	Aldehyde	Reaction temperature (°C)	Product yield [b]	$[\alpha]_D^{23}$, deg (*c*)	% E.e. (config.)	Ref.
1	C_6H_5CHO	−55	$C_6H_5CHCH_2CH{=}CH_2$ (65) OH	−33.2(7.38) [c]	71 (*S*)	6
2	n-$C_8H_{17}CHO$	−55	n-$C_8H_{17}CHCH_2CH{=}CH_2$ (65) OH	+4.9(2.50) [d]	46 (*R*)	7
3	cyclo-$C_6H_{11}CHO$	−55	cyclo-$C_6H_{11}CHCH_2CH{=}CH_2$ (71) OH	−0.3(4.3) [d]	42 (*R*)	7
4	$C_6H_5CH{=}CHCHO$	−55	$C_6H_5CH{=}CHCHCH_2CH{=}CH_2$ (70) OH	+7.0(10.08) [e]	47 (*S*)	8

[a] The reactions were carried out for 36 h with a 3/1/2 molar ratio of diethyl tartrate-monosodium salts, diallyltin dibromides, and aldehyde in anhydrous THF. [b] Isolated yields. [c] $[\alpha]_D^{23}$ determined in benzene. [d] $[\alpha]_D^{23}$ determined in CCl_4. [e] $[\alpha]_D^{23}$ determined in diethyl ether.

complex to give species containing penta-, hexa-, or even hepta-coordinate tin atoms [9].

The simplicity of the procedure we describe, coupled with the facts that it uses the cheap tartaric ester and is widely applicable, makes it a very convenient route to chiral homoallylic alcohols. We are examining the extension of our approach to other metals bearing (+)-diethyl tartrate as chiral auxiliary, and to the development of new efficient chiral ligands.

Experimental

General

^{1}H NMR spectra were measured in $CDCl_3$ at 90 MHz on Varian EM 390 instrument; chemical shifts are reported in δ units using Me_4Si as internal standard. Infrared (IR) spectra were measured on a Perkin–Elmer PE 682 spectrophotometer and frequencies are reported in wavenumbers (cm^{-1}). Optical rotations are measured on a Perkin–Elmer PE 241 polarimeter. Capillary GLC was performed on a Carlo Erba HR 5300 Mega Series apparatus using a 0V1 (0.1-μm film thickness, 15m, 2 ml/min flow rate of helium, 45/1 split ratio) and a Carbowax 20M (0.4-μm film thickness, 20m, 2 ml/min flow rate of hydrogen, 50/1 split ratio) columns. Products were purified by flash-chromatography (cyclohexane/ether 9/1 as eluent) on 70/230 mesh silica gel (Merck). TLC analyses were carried out on Merck plastic sheets coated with silica gel 60 F_{254} (layer thickness, 0.2 mm). All reactions were conducted in flame-dried glassware under argon. Tetrahydrofuran (THF) was distilled over $LiAlH_4$. Aldehydes were distilled prior to use; all the other reagents involved were obtained from Fluka or Aldrich, and used as received.

Synthesis of diallyltin dibromide (***1***)

A three-necked round-bottomed flask equipped with mechanical stirrer, reflux condenser dropping funnel and with an argon inlet, so that an argon atmosphere was maintained throughout, was charged with 8.9 g (0.075 mol) of tin powder and 75 ml of toluene. To this suspension was added 0.25 g (0.001 mol) of mercuric chloride, and the resulting mixture was boiled under reflux for 30 min with stirring, then cooled, and 0.1 g (0.001 mol) of triethylamine was added. The mixture was again heated at the reflux temperature and 6.51 ml (0.075 mol) of allyl bromide were added dropwise with efficient stirring. After the initial fall, the boiling point of the mixture rose to 111°C. After 2 h the mixture was cooled to room temperature, the unchanged tin was filtered off, and the filtrate was evaporated under reduced pressure. The residual oil (13.5 g) was distilled in vacuo to give 11.5 g (84.3%) of diallyltin dibromide, b.p. 77–79°C/2 mmHg; IR (neat; cm^{-1}): 3090, 2920, 1810, 1635, 1427, 1395, 1305, 1182, 1100, 1030, 985, 905, 760, 740; ^{1}H NMR (δ (ppm)): 2.75(d, 2H), 5.15(t, 2H), 5.50–6.25(m, 1H).

Synthesis of 1-phenylbut-3-en-1-ol (Table 2, run 1)

General procedure

A 50% dispersion of NaH in mineral oil (0.36 g, 7.5 mmol) was placed in a three-necked round-bottom flask equipped with mechanical stirrer and argon inlet, and washed with anhydrous pentane (3 × 5 ml), covered with THF (10 ml), the

suspension was cooled to 0 °C, and a solution of (+)-diethyl tartrate (1.55 g, 7.5 mmol) in THF (3 ml) was added dropwise at 0 °C with vigorous stirring during 30 min. The mixture become coagulated. After 30 min stirring at 0 °C, a solution of diallyltin dibromide (0.9 g, 2.5 mmol) in THF (5 ml) was added during 5 min at 0 °C, and rapid dissolution took place. After 30 min the mixture was cooled to −55 °C and freshly distilled benzaldehyde (0.51 ml, 5 mmol) in THF (10 ml) was added dropwise. The progress of the reaction was monitored by capillary GLC. After 35 h there had been a 65% aldehyde conversion. The amount of by-products was usually less than 5%. Quenching was carried out by adding a solution of NAOH 0.05 *N* (10 ml) at −55 °C and allowing the mixture to warm to room temperature. The organic layer was separated, and the aqueous layer extracted with diethyl ether. The combined solutions were washed with brine, dried over anhydrous sodium sulfate, and concentrated under vacuum. 1-Phenylbut-3-en-1-ol (0.48 g, 65%) was isolated by flash chromatography; $[\alpha]_D^{23}$ −33.2° (*c*, 7.38, benzene), corresponding to the *S* isomer in 71% e.e. a sample of the (*S*)-alcohol with 96% e.e. is reported [6] to have $[\alpha]_D^{23}$ −44.92° (*c* 7.4, benzene); IR (neat; cm^{-1}); 3420, 3035, 3010, 1640, 910, 755, 695; ^1H NMR (δ (ppm)): 1.9 (s, 1H, OH), 2.3–2.6 (m, 2H), 4.6–5.0 (m, 1H), 5.0–5.5 (m, 2H), 5.5–6.4 (m, 1H), 75 (s, 5H).

The following alcohols were made in the same way:

1-Dodecen-4-ol: IR (neat; cm^{-1}) 3360, 3080, 2920, 2860, 1640, 1470, 1135, 1000, 915, 740; ^1H-NMR (δ (ppm)): 0.7–1.1 (m, 3H), 1.1–1.7 (m, 14H), 1.9 (s, OH), 2.0–2.4 (m, 2H), 3.5–3.9 (m, 1H), 5.0–5.3 (m, 2H), 5.6–6.2 (m, 1H).

1-Cyclohexylbut-3-en-1-ol: IR (neat; cm^{-1}) 3380, 2930, 2860, 1450, 1040, 990, 910; ^1H NMR 0.8–2.5 (m, 14H), 3.1–3.5 (m, 1H), 4.8–5.3 (m, 2H), 5.4–6.1 (m, 1H).

1-Phenyl-1,5-hexadien-3-ol: IR (neat; cm^{-1}) 3380, 3080, 3030, 1640, 1030, 970, 920, 750, 700; ^1H NMR (δ (ppm)): 2.1–2.5 (m, 2H), 3.0 (s, OH), 4.0–4.5 (m, 1H), 4.9–5.4 (m, 2H), 5.5–6.8 (m, 3H), 7.3 (s, 5H).

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References

1 (a) R.W. Hoffmann, Angew. Chem. Int. Ed. Engl., 21 (1982) 555; (b) Y. Yamamoto, T. Komatsu and K. Maruyama, J. Chem. Soc., Chem. Commun., (1983) 191; (c) M. Reetz, Angew. Chem. Int. Ed. Engl., 23 (1984) 556; (d) J. Otera, Y. Yoshinaga, T. Yamaji, T. Yoshioka and Y. Kawasaki, Organometallics, 4 (1985) 1213; (e) M. Braun, Angew. Chem. Int. Ed. Engl., 26 (1987) 24; (f) N. Minowa and T. Mukaiyama, Bull. Chem. Soc. Jap., 60 (1987) 3697; (g) Y. Yamamoto, Acc. Chem. Res., 20 (1987) 243; (h) Y. Yamamoto, Aldrichim. Acta, 20 (1987) 45; (i) R.W. Hoffmann, Angew. Chem. Int. Ed. Engl., 26 (1987) 489.

2 (a) W.R. Roush and A.D. Palkowitz, J. Am. Chem. Soc., 109 (1987) 953; (b) W.R. Roush, M.R. Michaelides, D.F. Tai and W.K.M. Chong, ibid., 109 (1987) 7575; (c) J. Mulzer, L. Autenrieth-Ansorge, H. Kirstein, T. Matsuoka and W. Münch, J. Org. Chem., 52 (1987) 3784.

3 (a) G.P. Boldrini, E. Tagliavini, C. Trombini and A. Umani-Ronchi, J. Chem. Soc., Chem. Commun., (1986) 685; (b) G.P. Boldrini, L. Lodi, E. Tagliavini, C. Tarasco, C. Trombini and A. Umani-Ronchi, J. Org. Chem., 52 (1987) 5447.

4 Concerning preparations of allylic tin(IV) complexes via oxidative addition of tin(II) species to allylic halides, see, for example: (a) S. Shoda, T. Mukaiyama, Chem. Lett., (1981) 723; (b) T. Harada, T. Mukaiyama, Chem. Lett., (1981) 1109; (c) T. Mukaiyama, M. Yamaguchi and J. Kato, Chem. Lett., (1981) 1505; (d) J. Nokami, T. Tamaoka, H. Ogawa and S. Wakabayashi, Chem. Lett., (1986) 541.
5 K. Sisido and Y. Takeda, J. Org. Chem., 26 (1961) 2301.
6 H.C. Brown and P.K. Jadhav, J. Am. Chem. Soc., 105 (1983) 2092.
7 P.A. Bartlett, W.S. Johnson and J.D. Elliot, J. Am. Chem. Soc., 105 (1983) 2088.
8 R.W. Hoffmann and T. Herold, Chem. Ber., 114 (1981) 375.
9 (a) W.F. Howard, Jr., R.W. Crecely and W.H. Nelson, Inorg. Chem., 24 (1985), 2204; (b) T.P. Lockhart and F. Davidson, Organometallics, 6 (1987) 2471; (c) T.P. Lockhart, J.C. Calabrese and F. Davidson, ibid., 6 (1987) 2479.