13. Catalytic Asymmetric Synthesis of *Secondary* (*E*)-Allyl Alcohols from Acetylenes and Aldehydes *via* (1-Alkenyl)zinc Intermediates

Preliminary Communication

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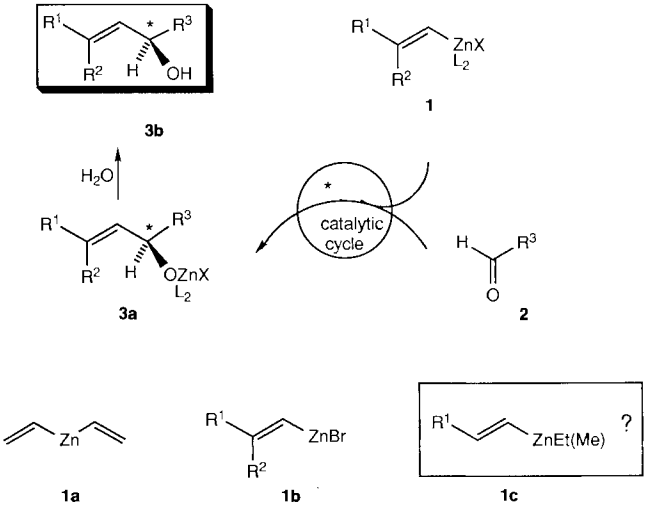
(10.XII.91)

Hydroboration of aliphatic 1-alkynes with freshly prepared dicyclohexylborane (1 mol-equiv., hexane), treatment of the resulting [(*E*)-1-alkenyl]boranes **5** with Et_2Zn or Me_2Zn (1.05 mol-equiv.) followed by addition of (−)-3-*exo*-(dimethylamino)isoborneol (DAIB, **8**; 0.01 mol-equiv.), subsequent addition of a solution of an aromatic or aliphatic aldehyde (1 mol-equiv., hexane), and quenching with aq. NH_4Cl provided (*E*)-allyl alcohols **6** usually in 70–95% yield with 79–98% enantiomeric excess (*Scheme 3* and *Table*).

Optically pure *secondary* allyl alcohols **3b** (as well as their antipodes) are key intermediates in organic synthesis. Recently, we have presented a new enantioselective approach to compounds of the type **3b** based on 'asymmetrically catalyzed' additions of (1-alkenyl)zinc reagents **1a** [1] and **1b** [2] to aromatic and aliphatic aldehydes (*Scheme 1*)[1]).

We now envisaged an analogous ligand-controlled 1-alkenyl transfer from mixed (1-alkenyl)(alkyl)zinc reagents such as **1c** focussing our attention on the following points: *1*) good accessibility, *2*) chemical and stereochemical stability[2]), *3*) exclusive transfer of

Scheme 1



[1]) Review on asymmetric additions of organozinc reagents to aldehydes: [3].

[2]) For the equilibrium between 'symmetrical' and mixed dialkylzinc species, see [4].

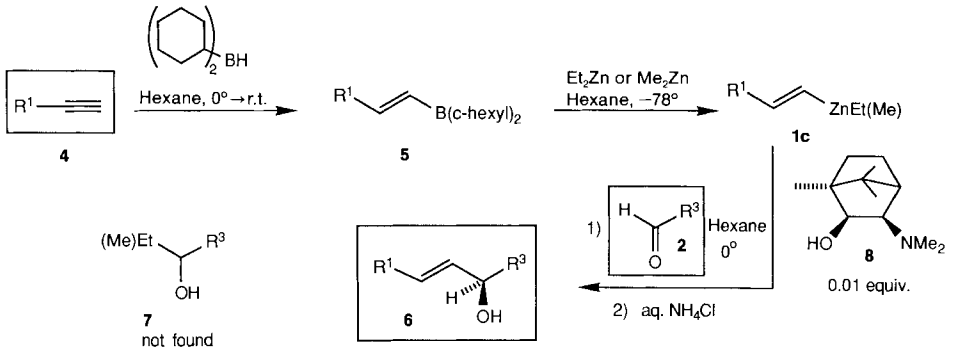
the 1-alkenyl ligand to aldehydes, and *4*) enantioselective catalysis of this addition reaction.

Transmetalation of readily available (1-alkenyl)boranes with Et_2Zn or Me_2Zn seemed a viable approach to Zn reagents **1c**, particularly in view of the recently reported metal exchange reaction of tris[(*Z*)-1,2-dialkyl-1-alkenyl]boranes with Et_2Zn [5][3]).

Hydroboration of 1-alkynes **4** with freshly prepared dicyclohexylborane gave [(*E*)-1-alkenyl]boranes **5** [7] which were directly treated with 1 mol-equiv. of Et_2Zn or Me_2Zn[4]).

Various aldehydes **2** were then added to the thus prepared Zn reagents **1c** at 0° in the presence of a catalytic amount of a chiral amino-alcohol. Good results, summarized in *Scheme 3* and in the *Table*, were achieved with (−)-3-*exo*-(dimethylamino)isoborneol (DAIB) [3] [8].

Scheme 3



Thus, DAIB (**8**; 0.01 mol-equiv.) was added to a mixture **5**/Et_2Zn or **5**/Me_2Zn (1:1.05) in hexane at −78°. Subsequent slow addition of an aldehyde in hexane at 0°,

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[3]) *N*-Methylpiperidine-catalyzed additions of the *in situ* obtained bis(1,2-dialkyl-1-alkenyl)zinc reagents to aldehydes (hexane, 0°, 12 h) afforded racemic allyl alcohols [5]. For the preparation of diallylzinc by transmetalation of triallylboranes with Me_2Zn, see [6].

[4]) The transmetalation reaction of [(*E*)-3,3-dimethylbut-1-enyl]dicyclohexylborane (**5**; $R^1 = t$-Bu) with Me_2Zn was monitored by ^{1}H-NMR measurements (in (D_8)toluene) and, thus, found to be complete at −65° within a few min to give two equilibrating alkenylzinc species (monomer/dimer?, ratio 2:1 at −40°). This temperature-dependent equilibrium is completely shifted towards the major species after warming to 0° (within 10 min). At 0°, slow decomposition became visible. Three-fold co-evaporation of the solution with (D_8)toluene at 0° produced no major changes in the spectrum (−40°) excluding an equilibrium between mixed and 'symmetrical' zinc species **1c**/**1d** (*Scheme 2*)[2]).

Scheme 2

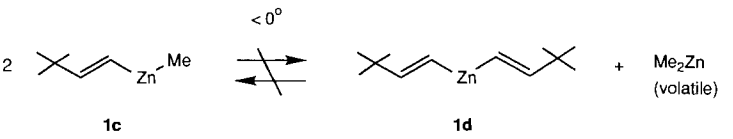


Table. *Asymmetric Synthesis of (E)-Allyl Alcohols from 1-Alkynes by Successive Addition of Dicyclohexylborane, Dialkylzinc, DAIB* (**8**), *and an Aldehyde at 0°*[a])

Entry	Series	Alkyne R^1	Dialkyl-zinc	**8** mol-equiv.	Aldehyde R^3	Allyl-Alcohol Product		
						Yield [%]	e.e.[b]) [%]	$[\alpha]_D$[c]) (*c*)
1	**a**	Bu	Me_2Zn	0.01	Ph	87	96	+ 38.0 (2.0)
2	**b**	C_6H_{13}	Et_2Zn	0.01	Ph	77	92	+ 33.1 (2.0)
3	**b**	C_6H_{13}	Me_2Zn	0.01	Ph	85	94	+ 34.4 (2.0)
4	**c**	C_6H_{13}	Et_2Zn	0.01	Et	91	84	+ 2.0 (1.7)
5	**c**	C_6H_{13}	Et_2Zn	0.05	Et	86	86	+ 2.0 (1.2)
6	**d**	C_6H_{13}	Et_2Zn	0.01	Bu	86	85	+ 5.0 (3.8)
7	**d**	C_6H_{13}	Me_2Zn	0.01	Bu	85	80	+ 4.7 (1.1)
8	**e**	C_6H_{13}	Et_2Zn	0.01	i-Bu	78	85	+ 6.4 (1.3)
9	**f**	C_6H_{13}	Et_2Zn	0.01	cyclohexyl	70	91	– 11.2 (1.6)
10	**g**	C_6H_{13}	Et_2Zn	0.01	*t*-Bu	28	73	– 10.0 (1.1)
11	**h**	cyclohexyl	Me_2Zn	0.01	Ph	83	95	+ 36.7 (1.6)
12	**i**	cyclohexyl	Et_2Zn	0.01	cyclohexyl	67	80	– 15.9 (1.5)
13	**j**	*t*-Bu	Me_2Zn	0.01	Ph	90	98	+ 49.3 (1.7)
14	**k**	*t*-Bu	Et_2Zn	0.01	Bu	94	79	+ 3.6 (1.7)
15	**k**	*t*-Bu	Me_2Zn	0.01	Bu	95	74	+ 3.0 (1.8)

a) All reactions were carried out in hexane, but Me_2Zn was added as a 2M solution in toluene (*Aldrich*). All isolated new compounds were characterized by IR, ^{1}H- and ^{13}C-NMR, and MS.

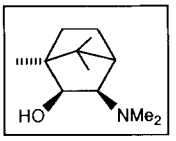
b) Enantiomeric excess (e.e.) determined by HPLC (*Chiracel OB: Entries 1, 2,* and *3*; *Chiracel OD, Entries 11* and *13*), or by ^{1}H-NMR (*Entries 8, 9,* and *12*) and GC analyses (*Entries 4, 5, 6, 7, 10, 14,* and *15*) of (1*S*)-camphanic-acid esters.

c) $[\alpha]_D$ measurements: *Entry 12* in EtOH at 23°; *Entry 9* in MeCN at 20°; other entries in $CHCl_3$ at 20°.

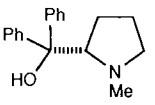
stirring at 0° for 1 h, and quenching of the mixture with aq. NH_4Cl afforded allyl alcohols **6** in good yields (except *Entry 10*)[5]).

Examination of the *Table* reveals the following trends. The use of either, Et_2Zn or Me_2Zn as the transmetalating agent is similarly effective (*cf. Entries 2/3, 6/7,* and *14/15*). No saturated products **7** could be found, consistent with an exclusive 1-alkenyl transfer from **1c** to the aldehydes. No (*Z*)-allyl alcohols were formed which reveals stereochemical retention in the transmetalation and addition steps **5**→**1c**→**6**. Increasing the amount of DAIB (**8**) did not change the extent of asymmetric induction (*Entries 4/5*). With benzaldehyde, very high enantioselectivities (92–98%, *Entries 1, 2, 3, 11,* and *13*) were achieved. Aliphatic straight-chain, β- and α-branched aldehydes furnished allyl alcohols **6** with up to 91% enantiomeric excess (e.e.). However, pivaldehyde gave alcohol **6c** in low yield and modest optical purity (73% e.e.; *Entry 10*). The (*R*)-configuration of major product **6i** (*Entry 12*) was determined *via* comparison of its optical rotation with the published value $[\alpha]_D = -19.8$ ($c = 1.46$, EtOH, $T = 23°$) [9]. It seems reasonable to assume an analogous

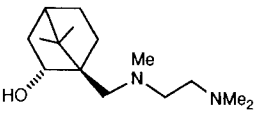
5) The following procedure is representative: cyclohexene (205 µl, 2 mmol) was added under Ar at 0° to a stirred 1M soln. of borane–(methyl sulfide) complex (100 µl, 1 mmol) in hexane (1 ml). After 3 h at 0°, oct-1-yne (150 µl, 1 mmol) was added, and the mixture was stirred at r.t. for 1 h. Then, the soln. was cooled to –78°. Addition (over 10 min) of a 1M soln. of Et_2Zn in hexane (1.05 ml, 1.05 mmol) followed by addition of DAIB (**8**; 2 mg, 0.01 mmol), immersion of the mixture into an ice-bath (0°), addition (over 20 min) of propionaldehyde (72 µl, 1 mmol) in hexane (4 ml), stirring the mixture at 0° for 1 h, addition of sat. aq. NH_4Cl soln., extraction (Et_2O), washing, drying, and evaporation of the extracts, and chromatography of the residue (SiO_2; hexane/Et_2O) yielded allyl alcohol **6c** (155 mg, 91%; e.e. 84%).



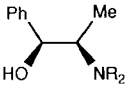
8 [8]



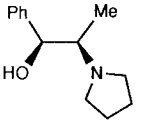
9 [10]



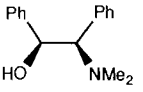
10 [1]



11 R = Me [2] [11]
12 R = Bu [11]



13 [11]



14 [2] [12]

sense of π-face discrimination for the other examples (*Table*) which also parallels the bias of DAIB (**8**) on the addition of Et_2Zn to aldehydes [3] [8].

Using the transformation **1c** ($R^1 = C_6H_{13}$)→**6c** (*Entries 4* and *5*) as a reference reaction, the inductive influence of further chiral amino-alcohols **9**–**14** (0.05 mol-equiv.) was tested.

Proline-derived ligand **9** scored at a level (80% e.e.) comparable to that of DAIB (**8**) but **10** to **14** performed less effectively (63–75% e.e.).

The nature of the reactive (1-alkenyl)zinc species as well as extensions and applications of this convenient approach to chiral allyl alcohols are subject of further studies in our laboratories.

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