Enantioselective Vinylation of Aldehydes with Chiral β-Silylphosphorus Ylides

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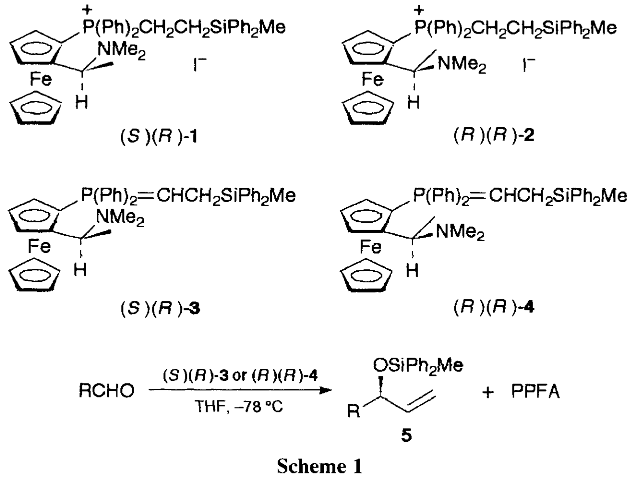
Both enantiomers of diastereoisomeric [1-(*N,N*-dimethylaminoethyl)ferrocenyl]diphenyl-(2-diphenylmethylsilylethylidene)phosphorane **3** and **4** are prepared; their reaction with benzaldehyde and aliphatic aldehydes is found to give vinylation products with variable enantiomeric excess (up to 92%).

The development of synthetic methods for obtaining enantiomerically pure compounds from carbonyl compounds is an important theme in current organic chemistry, in which various sophisticated methodologies have been introduced.[1] In connection with our work on the diastereoselective synthesis of allyl alcohol using β-silylphosphorus ylide,[2] we have explored the ylide reagents effecting asymmetric induction, which is the subject of this paper.

Our previous studies indicated that electron donating aryl substituents on the phosphorus atom of the ylide is expedient for the selective formation of allyl alcohol over the Wittig alkenation reaction.[3] We investigated the (dimethylamino)-ethylferrocenyl group as a chiral substituent because of its through space electronically donating character and its sterically congesting nature.[4]

Enantiomerically pure ferrocenylphosphonium salts **1** and **2** {(*S*)(*R*)-**1**, m.p. 207 °C (decomp.), $[\alpha]_D^{21}$ +44.9° (*c* 1.18, $CHCl_3$); (*R*)(*R*)-**2**, m.p. 135 °C (decomp.), $[\alpha]_D^{21}$ +6.6° (*c* 1.44, $CHCl_3$)} and their enantiomers are synthesised in two steps from the corresponding optically pure diastereoisomeric *N,N*-dimethyl-1-[2-(diphenylphosphino)ferrocenyl]ethylamines (PPFA)[5] in 54 and 49% yields [*i*, MeI–Et_2O, 0 °C to room temp.; *ii*, butyllithium–tetrahydrofuran (THF), 0 °C then $ICH_2SiMePh_2$, 0 °C to room temp.]. The chiral ylides **3** and **4** were generated *in situ* from **1** and **2**, respectively by butyllithium in THF and the reactions with aldehydes were carried out in THF at −78 °C. The allylic silyl ether **5** was obtained exclusively without formation of the Wittig alkena-



Scheme 1

Table 1 Reaction of chiral ylides with aldehydes

Entry	Aldehyde	Ylide	Lewis acid	E.e. (%)[a]	Config.	Yield (%)
1	PhCHO	(*R*)(*S*)-**3**	—	77	*R*	68
2		(*R*)(*S*)-**3**	Et_2AlOEt	70	*R*	83
3		(*S*)(*R*)-**3**	Et_2AlOEt	70	*S*	80
4		(*S*)(*S*)-**4**	—	47	*R*	24
5		(*S*)(*S*)-**4**	Et_2AlOEt	57	*R*	62
6	$PhCH_2CH_2CHO$	(*R*)(*S*)-**3**	—	9	*S*	34
7		(*S*)(*R*)-**3**	Et_2AlOEt[b]	25	*R*	95
8		(*R*)(*R*)-**4**	—	85	*R*	46
9		(*S*)(*S*)-**4**	—	80	*S*	44
10		(*S*)(*S*)-**4**	Et_2AlOEt	70	*S*	51
11	c-$C_6H_{11}CHO$	(*S*)(*R*)-**3**	—	13	*R*	27
12		(*S*)(*R*)-**3**	Et_2AlOEt	27	*R*	94
13		(*R*)(*R*)-**4**	—	92	*R*	43

[a] E.e. was determined by ^{1}H NMR (400 MHz) spectrum of the corresponding [methoxy(trifluoromethyl)phenylacetyl] (MTPA) ester derived in two steps (*i*, Bu_4NF–THF; *ii*, (+)- or (−)-MTPACl–C_5H_5N–CH_2Cl_2). [b] Lewis acids other than Et_2AlOEt gave similar results ($AlEt_3$, 27% e.e., 95% yield; $AlBu^i_3$, 23% e.e., 92% yield; $Ti(OPr^i)_4$, 27% e.e., 75% yield; BF_3–Et_2O, 22% e.e., 62% yield.

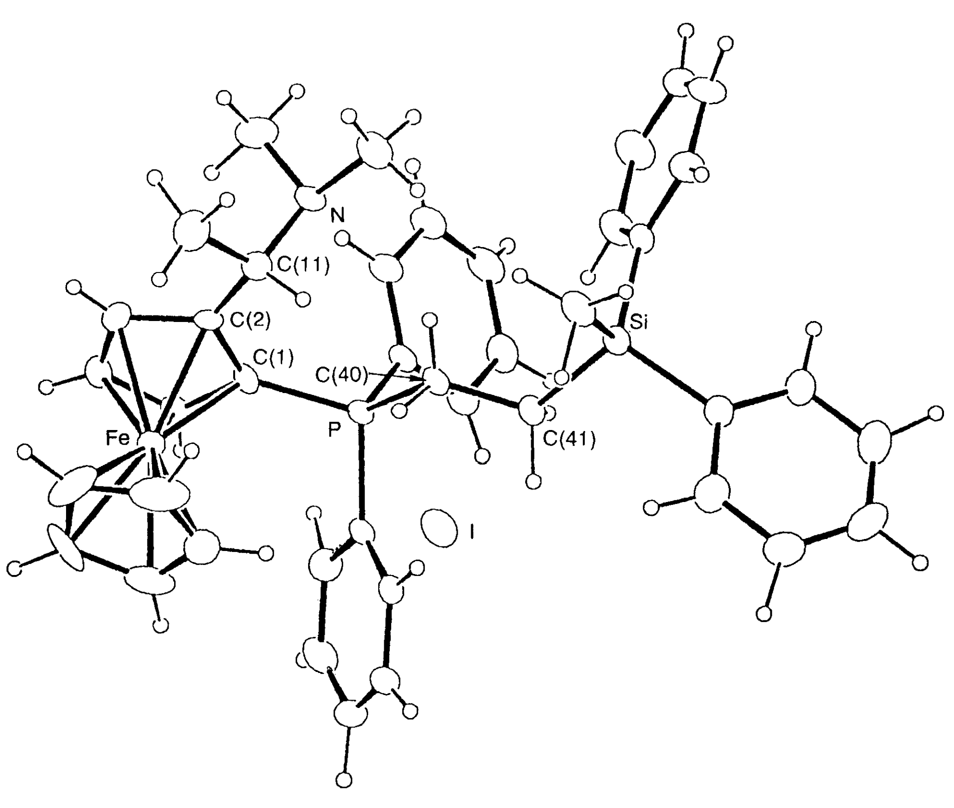


Fig. 1 X-Ray structure of (*S*)(*R*)-**1**

tion product and the recovered chiral phosphines PPFA could be recycled for the preparation of **1** and **2** (Scheme 1). The results of the reaction are shown in Table 1.

The ylide **3** gave **5** with 77% enantiomeric excess (e.e.) in the reaction with benzaldehyde. Although **3** yielded **5** with low e.e. in the reaction with the aliphatic aldehyde, high asymmetric induction up to 92% e.e. was attained in the reaction with ylide **4** and cyclohexylcarbaldehyde. The addition of diethylaluminium ethoxide did not affect the enantiometric excess but increased the yield of **5**. Both (*R*)(*S*)-**3** and (*S*)(*S*)-**4** gave the *R* enantiomer in the reaction with benzaldehyde, which means the chirality of **5** is mainly induced by the planar chirality of the ferrocenyl group rather than by the central chirality of the aminoethyl group.[6]

For reference purposes an X-ray single crystallographic analysis of (*S*)(*R*)-**1** was carried out and the resulting structure is reproduced in Fig. 1.† If the ylide (*S*)(*R*)-**3** has a configuration similar to (*S*)(*R*)-**1** in which C(40)–C(41) is

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† *Crystal data* for (*S*)(*R*)-**1**: $C_{41}H_{45}NSiPFeI$, $M = 793.59$, tetragonal, space group $P4_1$, $a = b = 9.755(4)$, $c = 39.96(1)$ Å, $U = 3803(3)$ Å^3, $Z = 4$, $D_c = 1.387$ g cm^{-3}, $\mu = 12.99$ cm^{-1}. 3414 reflections with $2\theta \leq 50.0°$ were recorded on a four-circle diffractometer using graphite-monochromated Mo-Kα radiation. Of these 2823 [with $I > 3\sigma(I)$] were judged observed. The structure was solved using Patterson methods. All hydrogen atoms could be located on a difference Fourier synthesis. Full matrix least-squares refinement with anisotropic temperature factors for non-hydrogen atoms and isotropic hydrogens converged to $R = 0.035$ and $R_w = 0.052$. The maximum and minimum residual electron densities in the final difference Fourier map were 0.82 and −1.25 e Å^{-3}. Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

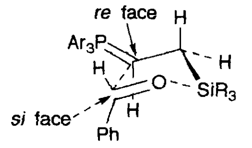

Fig. 2 Transition state for reaction of ylide (*S*)(*R*)-**3** with benzaldehyde

oriented antiperiplanar to the ferrocenyl group and the silyl group is tilted towards the *re* face of the planar sp^2 carbon C(40) [dihedral angles of C(1)–P–C(40)–C(41) and P–C(40)–C(41)–Si are 179.2 and 154.4° in (*S*)(*R*)-**1**, respectively],[7] then the *Si* face of benzaldehyde would approach the *Re* face of the ylide (*S*)(*R*)-**3** C(40) to avoid the non-bonding interaction between the phenyl group of the former and the substituent on the phosphorus atom in the latter.[8] The oxygen atom of benzaldehyde would interact with the tilted silicon atom to form a five-membered pentacoordinate silicate (see Fig. 2), which gives the product with *S* configuration. To the best of our knowledge, this is the first example of central chirality induction using a chiral phosphorus ylide.

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