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Organosilanols as Catalysts in Asymmetric Aryl Transfer Reactions

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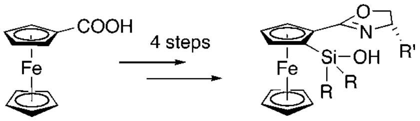
ABSTRACT



Various ferrocene-based organosilanols have been synthesized in four steps starting from achiral ferrocene carboxylic acid. Applying these novel planar-chiral ferrocenes as catalysts in asymmetric phenyl transfer reactions to substituted benzaldehydes afforded products with high enantiomeric excesses. The best result (91% ee) was achieved in the addition to *p*-chlorobenzaldehyde with organosilanol 2b, which has a *tert*-butyl substituent on the oxazoline ring and an isopropyl group on the silanol fragment.

Organosilanols have found important applications in various fields,[1] especially in the production of silicon-based polymeric materials.[2] In organic synthesis they have been used in palladium-catalyzed cross-coupling reactions[3] and as anchoring elements for *ortho*-metalation directors, for example.[4] Furthermore, several organosilanols showed bioactivity,[5] and some of them were applied as structural components in transition-state analogues of metalloprotease inhibitors.[6] To the best of our knowledge, however, they have never been utilized as chiral ligands in catalytic asymmetric reactions.[7]

On the other hand, it is well-established that 1,2-disubstituted ferrocenes are very useful as versatile chiral ligands in asymmetric metal catalysis.[8] Following Ugi's pioneering work in 1970,[9] they are commonly prepared starting from monosubstituted ferrocenes by *ortho*-lithiation[10] with directing groups such as amines and hydrazones,[11] sulfoxides,[12] acetals,[13] or oxazolines[14] and subsequent trapping of the resulting lithium reagent with an appropriate electrophile.

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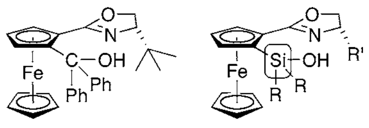


1 2

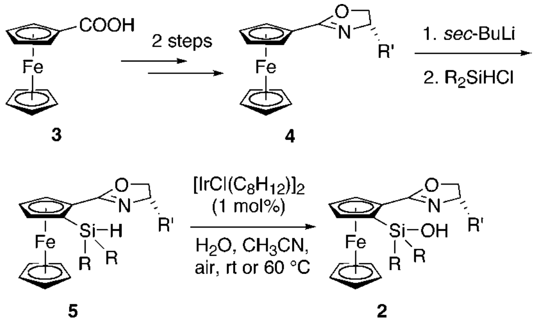
Figure 1.

Recently, we have demonstrated that *ortho*-substituted ferrocene **1** (Figure 1) with oxazolinyl- and diphenylhydroxy methyl groups is an effective catalyst for the asymmetric aryl transfer reaction to aldehydes leading to products with up to 99% ee.[15] Motivated by those results, we wondered about the applicability of structurally analogous organosilanols **2**. Those compounds have the same oxazolinyl-substituted ferrocene backbone but differ in the hydroxyl-bearing side chain.[16] The resulting steric and electronic modification was expected to have an impact on the examined catalyst system and alter its activity and selectivity.[17,18]

Organosilanols **2** were prepared in two steps, starting from chiral ferrocenyl oxazolines **4**, which were readily available from ferrocene carboxylic acid (**3**) following known literature protocols.[14] Subsequent diastereoselective *ortho*-lithiations of ferrocenyl oxazolines **2** with *s*-BuLi at −78 °C in THF,[14a] followed by electrophilic attack with various chlorosilanes, gave diastereomerically enriched 1,2-disubstituted ferrocenes **5** in good yields (60−91%).[19]

Using a method recently introduced by Chang and coworkers,[20] the silyl group of **5** was oxidized in air with $[IrCl(C_8H_{12})]_2$ as catalyst giving ferrocenyl organosilanols **2**. After column chromatography and isolation of the major diastereomer, stereochemically homogeneous samples of **2** were obtained in 43−91% yield (Table 1). Most of the ferrocenyl organosilanols **2** were solid, air-stable compounds, which could be stored for weeks without any indication of decomposition.

Table 1. Synthesis of Planar-Chiral Ferrocene-Based Organosilanols **2**



entry	R′	R	compd (yield, %)[a]	compound (yield, %)[b]
1	*t*-Bu	CH_3	**5a** (64)	**2a** (91)[c]
2	*t*-Bu	*i*-Pr	**5b** (64)	**2b** (75)[d]
3	*t*-Bu	Ph	**5c** (91)	**2c** (77)[d]
4	Ph	*i*-Pr	**5d** (70)	**2d** (57)[d]
5	Ph	Ph	**5e** (68)	**2e** (53)[d]
6	*i*-Pr	*i*-Pr	**5f** (81)	**2f** (65)[c]
7	*i*-Pr	Ph	**5g** (85)	**2g** (72)[c]
8	CH_2Ph	*i*-Pr	**5h** (82)	**2h** (45)[c]
9	CH_2Ph	Ph	**5i** (60)	**2i** (43)[c]

[a] See comment in ref 19. [b] Yields of diastereomerically pure products. [c] Reaction was performed at room temperature. [d] Reaction was performed at 60 °C.

The catalytic properties of organosilanols **2** were explored in asymmetric phenyl-transfer reactions from organozinc reagents to benzaldehydes **6** giving diarylmethanols **7**.[21] The results are summarized in Table 2.

Initially, mixtures of diphenyl- and diethylzinc were used as phenyl source and *p*-chlorobenzaldehyde (**6a**) as substrate. Most organosilanols showed good enantioselectivities (up to 91% ee) and afforded product **7a** in respectable yields (40−87%). The best result was obtained with organosilanol **2b**, which had a *tert*-butyl substituent on the oxazoline ring and isopropyl groups on the silanol fragment (Table 2, entry 2). Catalysts with methyl or phenyl substituents on the silicon

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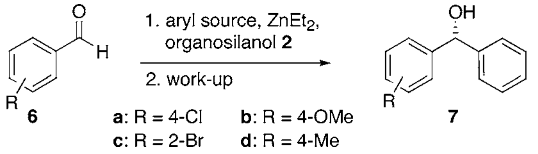
Table 2. Asymmetric Phenyl Transfer Reaction to Substituted Benzaldehydes (**6**) Using Organosilanol-Based Catalysts and Various Zinc Reagents[a]



entry	substrate	organosilanol	method[b] (product)	yield[c] (%)	ee[d] (%)
1	**6a**	**2a**	A (**7a**)	40	30
2	**6a**	**2b**	A (**7a**)	82	91
3	**6a**	**2c**	A (**7a**)	84	89
4	**6a**	**2d**	A (**7a**)	82	87
5	**6a**	**2e**	A (**7a**)	76	85
6	**6a**	**2f**	A (**7a**)	87	78
7	**6a**	**2g**	A (**7a**)	73	76
8	**6a**	**2h**	A (**7a**)	85	63
9	**6a**	**2i**	A (**7a**)	nd[e]	58
10	**6a**	**2c**	B (**7a**)	73	88
11	**6a**	**2c**	C (**7a**)	67	83
12	**6b**	**2c**	A (**7b**)	81	87
13	**6c**	**2c**	A (**7c**)	70	84
14	**6d**	**2c**	A (**7d**)	84	83

[a] All reactions were run on a 0.25 mmol scale using 10 mol % of **2**. [b] Method A: use of Ph_2Zn (0.65 equiv) and Et_2Zn (1.3 equiv) in toluene at 10 °C for 12 h. Method B: use of BPh_3 (1.0 equiv) and Et_2Zn (3.0 equiv) at 10 °C for 12 h. Method C: use of $PhB(OH)_2$, (2.4 equiv), Et_2Zn (7.2 equiv), and DiMPEG (10 mol %; MW = 2000 $g \cdot mol^{-1}$) in toluene (first at 60 °C for 12 h, then at 10 °C for 12 h). [c] After column chromatography. [d] Enantiomeric ratios were determind by HPLC analysis using a chiral column. The major product had *R* configuration. [e] Not determined.

atom (entries 1 and 3) led to products with lower ee values (**7a** with 30 and 89% ee for **2a** and **2c**, respectively). In light of our previous results,[14e,f,15,16,22] this observation is rather remarkable, since until now achieving high enantioselectivities in the aryl-transfer reactions always required the presents of the “magic” diphenylhydroxymethyl unit[23] in the 2 position of planar-chiral metallocenes.

When the *tert*-butyl group on the oxazoline was substituted by a phenyl, an isopropyl, or a benzyl substituent giving organosilanols **2d**,**e**, **2f**,**g**, and **2h**,**i**, respectively, the resulting catalysts were less enantioselective (Table 2, entries 4−9).[24]

Using triphenylborane (method B, Table 2, entry 10)[25] instead of diphenylzinc as aryl source (in combination with a catalyst derived from **2c**) had only a minor effect on the ee of the aryl-transfer reaction. With phenylboronic acid (method C, Table 2, entry 11)[15d,e,17c,26] both yield and ee were lower.

Other aryl aldehydes reacted well too as demonstrated in catalyses with organosilanol **2c** (Table 2, entries 12−14). For example, 4-methoxybenzaldehyde afforded the corresponding product (**7b**) with 87% ee in 81% yield. A remarkable enantioselectivity was also observed in the phenyl addition to *o*-bromobenzaldehyde, which gave **7c** with 84% ee in 70% yield.

In summary, we have described the synthesis of planar-chiral ferrocene-based organosilanols **2** and demonstrated their catalytic use in asymmetric phenyl-transfer reactions to substituted benzaldehydes. High enantioselectivities and yields of up to 91 and 87%, respectively, have been achieved using both zinc- and boron-based aryl sources. To the best of our knowledge, this is the first application of chiral organosilanols in asymmetric catalysis, and we are currently exploring the potential use of this new ligand class in other enantioselective reactions.

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Supporting Information Available: Experimental procedures and full characterization (^1H and ^{13}C NMR data and spectra, MS, IR, and CHN analyses) for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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