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COMMUNICATIONS

Published on Web 01/11/2003

Catalytic Asymmetric Silane Alcoholysis: Practical Access to Chiral Silanes

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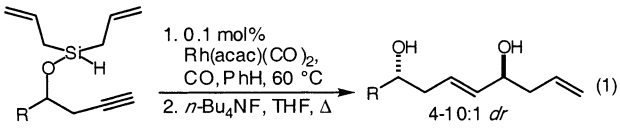
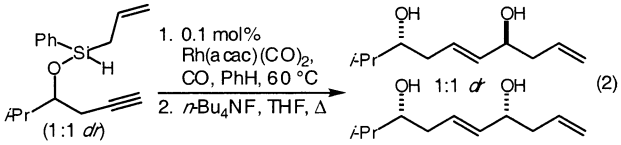
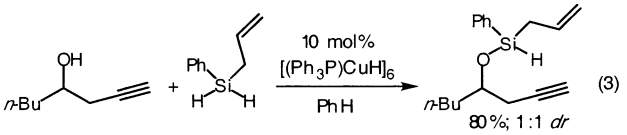
Tandem silylformylation-allylsilylation of alkynes allows for the efficient synthesis of 1,5-*anti*-diols (eq 1).[1] We have proposed that the diastereoselectivity is due to preferential transfer of one of the diastereotopic allyl groups, with the minor diastereomer arising from transfer of the other allyl group. This suggested that the diastereoselective synthesis of chiral silanes bearing only one allyl group would allow the synthesis of either the syn or the anti diol diastereomer, with the selectivity dependent only on the selectivity at silicon and independent of the structure of the homopropargylic alcohol. This hypothesis was strongly supported by the illustrated experiment with a chiral silane (eq 2),[1a] and we therefore set out to develop a selective chiral silane synthesis.



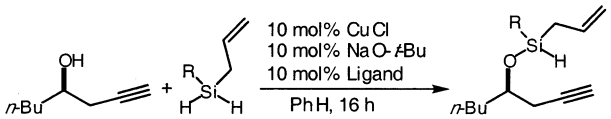


Only a limited number of reports have described asymmetric syntheses of chiral silanes.[2] One particularly appealing approach, pioneered by Corriu, involves the selective alcoholysis of a prochiral dihydrosilane catalyzed by a chiral phosphine-modified rhodium complex.[2h] While at the outset it was tempting to revisit the Corriu system armed with the modern plethora of chiral phosphine ligands, it was also anticipated that rhodium complexes might be expected to further catalyze alkyne hydrosilylation in the silyl ether products. We therefore noted with some interest the report of Lorenz and Schubert describing the use of $[(PPh_3)CuH]_6$ as a hydrosilane alcoholysis catalyst[3] and readily established that with a homopropargylic alcohol and allylphenylsilane a smooth alcoholysis occurred accompanied by no alkyne hydrosilylation (eq 3).



In preparing to assess chiral phosphine ligands, we decided to employ chiral enantiomerically enriched (>98% ee) alcohol substrates so that a simple ^{1}H NMR or GC assay for selectivity could be employed. The influence (or lack thereof) of this chirality on the selectivity could be measured simply by using both enantiomers of the ligand in separate experiments. In addition to allylphenylsilane, allyl-2,6-dimethylphenylsilane and allyl-*tert*-butylsilane were selected as the standard silanes to maximize the steric and electronic difference between the allyl group and the spectator group. Using the in situ catalyst preparation reported by Buchwald for the enantioselective conjugate reduction of enones,[4] we began the screening of chiral phosphines (Table 1). It quickly became apparent that allylphenylsilane provided only marginal reactivity and diastereoselectivity with many different phosphines (entries 1−3, BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl; JOSIPHOS = 1-[2-(diphenylphosphino)ferrocenyl]-ethyldicyclohexylphosphine; BDPP = 2,4-bis(diphenylphosphino)-pentane). Allyl-2,6-dimethylphenylsilane proved better (entries 4−6) and with (*R*)-BINAP gave 61:39 diastereoselectivity (entry 4). Allyl-*tert*-butylsilane proved better still, providing encouraging selectivity with two different phosphines and acceptable reactivity (entries 7 and 9). On the basis of this initial screen, allyl-*tert*-butylsilane and BDPP were selected for further study.

Table 1. Identification of Effective Chiral Phosphine Ligands



entry	R	ligand	conv. (%)[a]	dr[b]
1	Ph	(*R*)-BINAP	2	58:42
2	Ph	(*R*)-(*S*)-JOSIPHOS	2	54:46
3	Ph	(*R*,*R*)-BDPP	2	58:42
4	2,6-$Me_2C_6H_3$	(*R*)-BINAP	47	61:39
5	2,6-$Me_2C_6H_3$	(*R*)-(*S*)-JOSIPHOS	84	59:41
6	2,6-$Me_2C_6H_3$	(*R*,*R*)-BDPP	99	47:53
7	*t*-Bu	(*R*)-BINAP	58	80:20
8	*t*-Bu	(*R*)-(*S*)-JOSIPHOS	23	77:23
9	*t*-Bu	(*R*,*R*)-BDPP	75	80:20

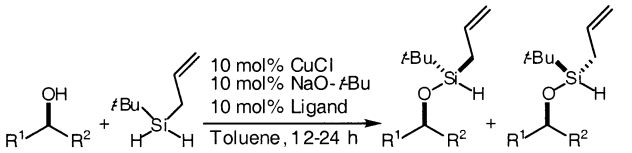
[a] Conversion of alcohol measured by GC versus an internal standard. [b] Diastereomeric ratio measured by ^{1}H NMR or GC analysis.

An investigation of substrate scope was undertaken, and in every case both enantiomers of the ligand were employed in separate experiments (Table 2). With a linear alkyl homopropargylic substituent, the chirality of the alcohol has no effect, and 4:1 selectivity may be achieved for either diastereomer (entries 1 and 2).[5] However, with a branched group (*i*-Pr, entries 3 and 4) significant matching/mismatching is observed, and moderate selectivity can be achieved only for one diastereomer. When benzylic alcohols were employed (entries 5−8), significantly higher selectivities may be achieved, albeit with some matching/mismatching. Especially encouraging are entries 5 and 6, where the diastereomeric silanes may be synthesized in good yield and diastereoselectivity.

It was of interest to explore structural variations on the BDPP ligand, and it quickly became apparent that substitution on the aryl groups could have a significant effect on the selectivity of the reaction (Table 3). Furthermore, a clear trend could be discerned, with electron-poor aryl groups providing the best results.[6] Thus, the 3,5-difluorophenyl analogue (entry 5) provided superior selectivity (97:3 dr), albeit with compromised reactivity relative to the parent ligand. While this line of enquiry will continue, this result clearly establishes that excellent selectivities may be achieved.

10.1021/ja0283201 CCC: $25.00 © 2003 American Chemical Society

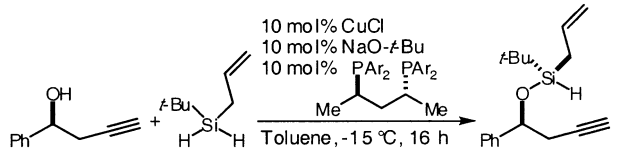
Table 2. Catalytic Asymmetric Silane Alcoholysis



entry	R^1	R^2	ligand	yield (%)[a]	dr[b]
1	*n*-Pr	CH_2CCH	(*R*,*R*)-BDPP	75	80:20
2	*n*-Pr	CH_2CCH	(*S*,*S*)-BDPP	89	20:80
3	CH_2CCH	*i*-Pr	(*R*,*R*)-BDPP	91	82:18
4	CH_2CCH	*i*-Pr	(*S*,*S*)-BDPP	93	36:64
5[c]	Ph	CH_2CCH	(*R*,*R*)-BDPP	83	90:10
6[c]	Ph	CH_2CCH	(*S*,*S*)-BDPP	82	12:88
7[c]	Et	Ph	(*R*,*R*)-BDPP	99	78:22
8[c]	Et	Ph	(*S*,*S*)-BDPP	99	12:88

[a] Isolated yield of the mixture of diastereomers. [b] Diastereomeric ratio measured by ^{1}H NMR or GC analysis. [c] Reaction run at −15 °C for 16 h.

Table 3. Electronic Tuning of the BDPP Ligand



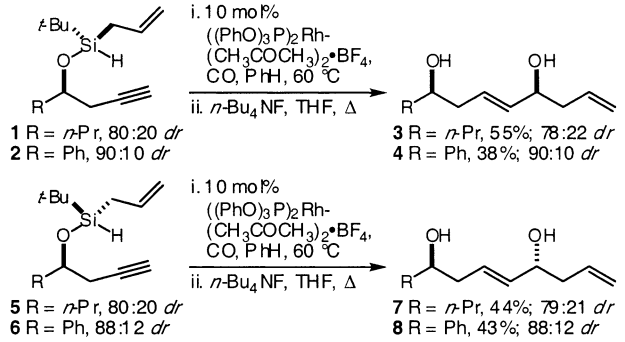
entry	Ar	conv. (%)[a]	dr[b]
1	*p*-OMe-C_6H_4	30	86:14
2	*p*-Me-C_6H_4	62	89:11
3	C_6H_5	88	90:10
4	*p*-F-C_6H_4	51	93:7
5	3,5-F_2-C_6H_3	54	97:3

[a] Conversion of alcohol measured by GC versus an internal standard. [b] Diastereomeric ratio measured by ^{1}H NMR or GC analysis.

With access to diastereomerically enriched silanes secured, the silylformylation-allylsilylation could be examined. Unfortunately, when the silanes were subjected to the standard reaction conditions (cat. Rh(acac)$(CO)_2$, 900 psi CO, PhH, 60 °C), it quickly became apparent that the presence of the *tert*-butyl group on the silane has a dramatically deleterious effect on the carbonylation chemistry. We therefore were forced to reoptimize the catalyst for this variant of the reaction, and it was eventually found that $((PhO)_3P)_2Rh$-$(CH_3COCH_3)_2 \cdot BF_4$ provided better results. Using this catalyst, we found that silanes **1** and **2** (prepared as described in Table 2) gave 1,5-*syn*-diols **3** and **4**, respectively, in moderate yields (Scheme 1). Conversely, silanes **5** and **6** (prepared as described in Table 2) gave 1,5-*anti*-diols **7** and **8**, respectively. In all cases, the diastereoselectivity was essentially identical to the dr of the starting silane. This serves as strong support for the stereochemical model for these reactions that we have developed. More importantly, the 1,5-*syn*-diol diastereomers are now available with moderate to good diastereoselectivity.

We have described a catalytic asymmetric silane alcoholysis that delivers useful synthons for the stereoselective synthesis of polyketide fragments. While we have demonstrated one application

Scheme 1



of this chiral silane synthesis, it is certainly possible to imagine many other reactions that might derive stereoselectivity from a temporary *chiral* silicon connection.[7] Efforts to optimize the generality and scope of the reaction and to explore its possible applications are in progress.

Acknowledgment. The National Institutes of Health (NIGMS − GM58133) is acknowledged for support of this work and for a postdoctoral fellowship to D.R.S. We thank Pharmacia for a graduate fellowship to S.J.O. J.L.L. is a recipient of a Pfizer Award for Creativity in Organic Chemistry.

Supporting Information Available: Experimental procedures, characterization data, and stereochemical proofs (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) For stereochemical assignments at silicon, see the Supporting Information.

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JA0283201