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Convenient Enantioselective Hydrosilylation of Ketones Catalyzed by Zinc-Macrocyclic Oligoamine Complexes

Jadwiga Gajewy,[a] Marcin Kwit,[a,*] and Jacek Gawroński[a,*]

[a] Department of Chemistry, A. Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland
Fax: (+48)-61-829-1505; e-mail: Marcin.Kwit@amu.edu.pl or gawronsk@amu.edu.pl

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Dedicated to Professor Armin de Meijere on the occasion of his 70th birthday

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Abstract: Chiral macrocyclic tetra- and hexamine macrocycles derived from *trans*-1,2-diaminocyclohexane (DACH) in complexes with diethylzinc efficiently catalyze the asymmetric hydrosilylation of aryl alkyl ketones with enantiomeric excess of the product up to 89%. The cyclic structure of the trianglamine ligand increases the enantioselectivity of the reaction, in comparison to the catalysis with the acyclic *N,N′*-dibenzyl-DACH ligand. Density functional theory (DFT) computations on the structures of ligand-zinc complexes and on the structures of these complexes with a coordinated acetophenone molecule allow us to rationalize the direction of the asymmetric induction of the hydrosilylation reaction as well as the superiority of the cyclic ligand compared to the acyclic one. This is the first example of asymmetric catalysis for the hydrosilylation reaction of ketones with the use of a readily available, inexpensive, and reusable macrocyclic trianglamine ligand.

Keywords: asymmetric catalysis; density functional theory; hydrosilylation; oligoamine macrocycles; zinc complexes

Introduction

Asymmetric hydrosilylation (AHS) is one of the most useful catalytic methods for the synthesis of enantiomerically enriched secondary alcohols from prochiral ketones. Two other well-established methods rely either on asymmetric catalytic hydrogenation of ketones with the use of chiral rhodium complexes as catalysts or on asymmetric reduction of ketones with diborane, catalyzed by chiral oxazaborolidines. However, the asymmetric hydrosilylation presents the advantages of simplicity of the procedure combined with the use of inexpensive silanes as reducing agents. One of the main targets of current studies on AHS is the development of catalytic systems that would comply with the criteria of high efficiency (catalyst tunover, yield, enantioselectivity), low cost and feasibility of recovery of the catalyst as well as with possible environmental regulations. A number of experimental catalytic procedures for asymmetric hydrosilylation of ketones has been developed in recent years, see reviews.[1–8] These procedures usually make the use of inexpensive, easily handled, non-toxic and stable to air and moisture polymethylhydrosiloxane (PMHS)[9] or monomeric silanes as the reducing agents, in combination with metal complexes of Ru, Rh, Cu, Ti, Fe and Zn, among other. PMHS is the best hydride donor among other silanes and it is more selective toward functional groups compared to, for example, borane complexes. The chemoselectivity of reduction can be tuned by the choice of the catalyst and, in this context, Zn complexes appear to be highly promising in applications to cost-effective enantioselective hydrosilylation of ketones, as can be seen in the following discussion.

Chiral rhodium catalysts often use bidendate P,P, P,N or N,N ligands, such as PYTHIA,[10] PYBOX[11] or HETPHOX.[12] High enantioselectivities (over 90% *ee*) for the standard AHS of acetophenone were achieved with chiral diphosphine[13] or pyridine-phosphine[14] ligands having a ferrocene structural unit, as well as with a chiral P,S ligand reported by Evans.[15] Recently chiral C(carbene),N ligands for rhodium[16] and N-heterocyclic carbene ligands for ruthenium[17] were introduced. However, the catalytic systems

based on rhodium or ruthenium generally suffer from their high cost and require elaborate preparation.

Copper(I) hydride complexes, despite their known preference for conjugate addition to carbonyl compounds, are useful also in highly enantioselective hydrosilylation of (hetero)aryl alkyl ketones. However, these reductions require expensive chiral diphosphine ligands, such as 3,5-*xyl*-MeO-BIPHEP,[18] BINAP[19,20] or DTBM-SEG-PHOS,[21] although in several cases the catalyst could be used at a very low load (S/C > 1000:1).

Recently, an iron-catalyzed enantioselective hydrosilylation of aryl alkyl ketones has been disclosed by Beller et al.[22] The reaction in several cases was found highly enantioselective (up to 99% *ee*), with the use of a diphosphine ligand Me-DUPHOS.

Titanium catalysts for hydrosilylation are usually based on the titanocene chiral framework, titanium(IV) derivatives with other chiral ligands being less effective.[5] Notably, Buchwald et al. reported the use of *ansa*-titanocene EBTHI with tetrahydroindenyl substituents as ligands for titanium, giving the products of hydrosilylation of ketones with up to 99% *ee*.[23]

Zinc complexes of chiral secondary amines were introduced by Mimoun as chiral catalysts for the enantioselective hydrosilylation of ketones, with enantioselectivities up to 88% *ee*.[24] Most frequently used chiral secondary amines include derivatives of *trans*-1,2-diaminocyclohexane (DACH), *trans*-1,2-diaminocyclopentane, 1,2-diphenyl-1,2-diaminoethane and 1-phenylethylamine. Introduction of two different chiral centers into the ligand gave rise to synergistic effects, leading to an increase of the enantioselectivity of hydrosilylation reaction.[25,26] Chiral N,S chelating ligands appear to be less effective in the zinc-catalyzed hydrosilylation of ketones;[27] however, recent results with the use of bis-*tert*-thiophenylmethyl derivative of DACH were promising (enantioselectivities up to 83% *ee*).[28] Finally, it has been found that *ortho*-multisubstituted benzophenones can be enantioselectivelly reduced (up to 96% *ee* of the product) with chiral diamine-Zn-diol complexes (chirality residing in the diamine part of the complex).[29]

We reasoned that the ease of formation of chiral diamine-zinc complexes and their relatively high efficiency as chiral catalysts should lead to the development of more affordable and practical procedures for the enantioselective hydrosilylation of prochiral ketones. Improvements could be made by a judicious choice of chiral ligands. Among the synthetic chiral diamines, DACH appears to be the primary source of virtually unlimited diamine structures. Simple *N,N′*-dialkyl derivatives of DACH were earlier tested by Mimoun et al. in the asymmetric hydrosilylation of acetophenone; however, they provided the product of reduction with moderate 52–70% *ee*[24]

Results and Discussion

Asymmetric Hydrosilylation

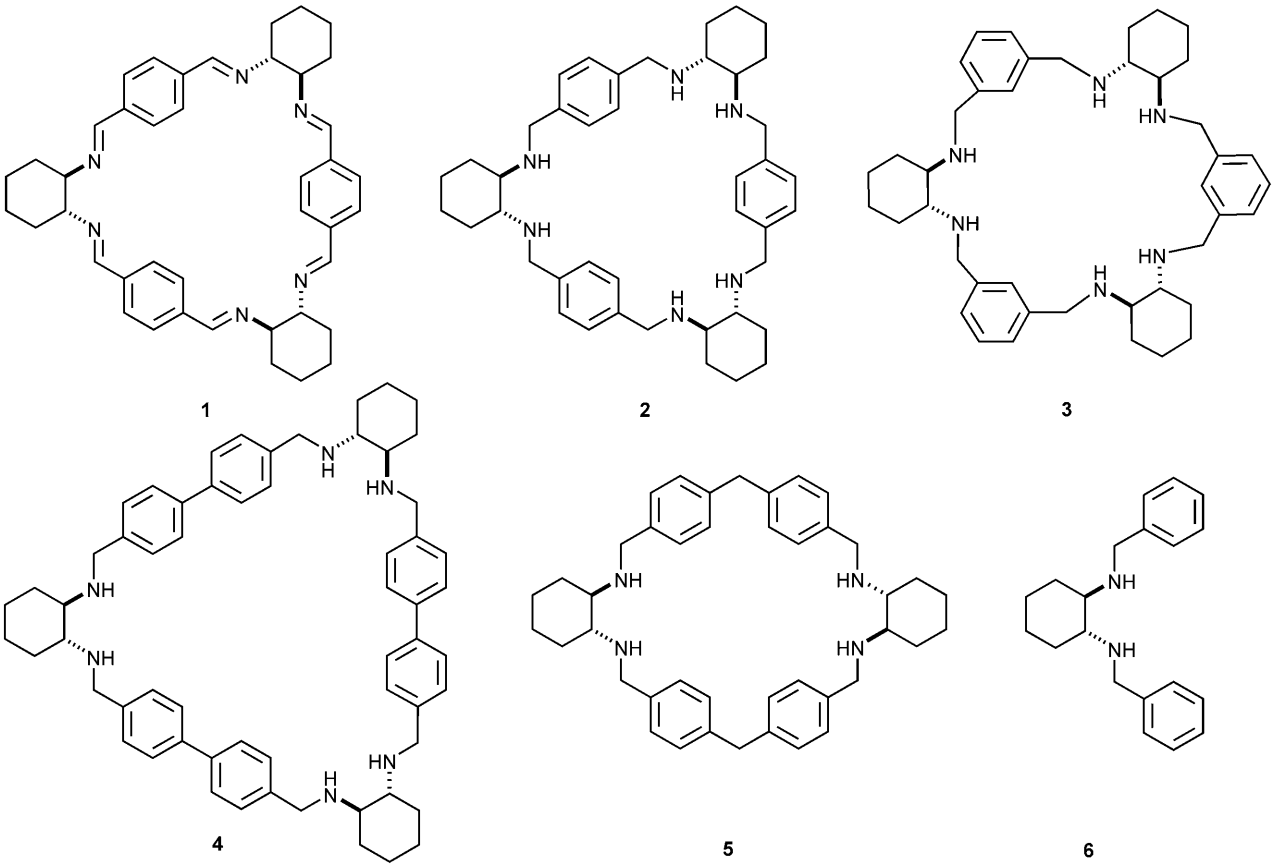
We have previously shown that DACH can be used for the ready, thermodynamically driven construction of various imine and amine macrocycles, by its condensation with dialdehydes, followed by reduction of the imine bonds. For the present study we have selected trianglimine **1**[30] trianglamines **2**, **3**,[30,31] **4**,[32,33] and rhombamine **5**,[34] as well as *N,N′*-dibenzyl-DACH (**6**) as a reference ligand.

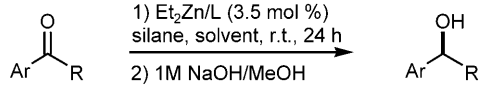
Trianglamine **2** can be obtained in a one-pot procedure from DACH and terephthaldehyde with a yield of over 95%.[31] Trianglamine **2** has already been used as a chiral shift reagent for NMR spectra,[35] as a chiral probe for anion recognition in ion-trap ESI-MS[36] and as a chiral ligand for copper-catalyzed enantioselective Henry reaction.[37]

Ligands **2–6** feature the same secondary 1,2-diamine structure embedded in the cyclohexane ring. We anticipated that the macrocyclic structures of the ligands would result in a higher degree of asymmetric induction of the hydrosilylation reaction of aryl alkyl ketones.

Standard conditions involved generation of the zinc complex by the addition of equimolar amount of diethylzinc in hexane to a solution the ligand in toluene (or any other solvent). After 0.5 h the ketone and the silane were added and the reaction was run at room temperature for 24 h and then quenched with methanolic NaOH solution (Scheme 1). The screening of ligands was conducted along with a screening of the type of silane and reaction conditions used for the hydrosilylation of acetophenone (Table 1). With a catalyst loading of 3.5 mol% we observed moderate to good enantioselectivity of the hydrosilylation of acetophenone in the case of ligands **2–6.** No reaction was observed with trianglimine ligand **1**, regardless the silane used (entries 1–4). This is in contrast to the results of Mimoun et al. who used successfully simple diimine derivatives of DACH for the hydrosilylation of acetophenone.[24]

A more detailed inspection of the data of Table 1 shows that the highest enantioselectivity (*ee* 88%) of the hydrosilylation of acetophenone was achieved with trianglamine ligand **2** in toluene solution using diphenylsilane as a reductor (entry 5). Lowering the temperature of reaction to −25 °C (entry 6) did not lead to any improvement of the enantioselectivity. Changing the solvent to dichloromethane or THF (entries 7 and 8) did improve the conversion of acetophenone from 85% to 95% at the expense of the enantioselectivity (drop to 77% or 81% *ee* of the product). Substituting diphenylsilane with PMHS (entries 9–11) resulted in a 5% drop in conversion and enantioselectivity of the hydrosilylation in toluene so-





Scheme 1. Hydrosilylation conditions.

lution and a further drop in enantioselectivity (to 65% *ee*) in dichloromethane and THF solutions. A product of lower *ee* (58–60%) was obtained in the hydrosilylation of acetophenone with phenylsilane and triethylsilane (entries 12 and 13).

Hexamine ligand **3** has a vase-like structure (according to molecular modelling), quite different from a planar triangular structure of **2**. Nevertheless, it also catalyzed the asymmetric hydrosilylation of acetophenone, although with slightly lower enantioselectivity (82%) compared to **2** (entries 14 and 15). The use of phenylsilane gave inferior results (entry 16) whereas triethylsilane did not give any significant amount of the reduction product (entry 17, see also entry 22).

Hydrosilylation of acetophenone with the large trianglamine ligand **4** gave inferior results (entries 18 and 19) in terms of enantioselectivity compared to the results with the smaller trianglamine ligand **2** (entries 5 and 9). The same applies to the comparison of the efficiency of rhombamine ligand **5** (entries 20 and 21) against the efficiency of ligand **2** (entries 5 and 9).

Table 1. Asymmetric hydrosilylation of acetophenone catalyzed by zinc-L complexes.

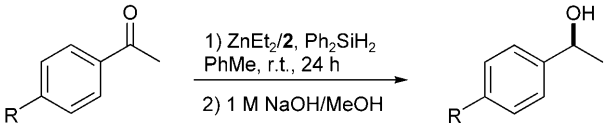
Entry	L	Silane	Solvent	Conv.[a] [%]	*ee*[a] [%]
1	**1**	Ph_2SiH_2	toluene	0	–
2	**1**	$PhSiH_3$	toluene	0	–
3	**1**	Et_3SiH	toluene	0	–
4	**1**	PMHS	toluene	0	–
5	**2**	Ph_2SiH_2	toluene	85	88 (*S*)
6	**2**[b]	Ph_2SiH_2	toluene	99	84 (*S*)
7	**2**	Ph_2SiH_2	DCM	95	77 (*S*)
8	**2**	Ph_2SiH_2	THF	95	81 (*S*)
9	**2**	PMHS	toluene	80	83 (*S*)
10	**2**	PMHS	DCM	88	65 (*S*)
11	**2**	PMHS	THF	trace	65 (*S*)
12	**2**	$PhSiH_3$	toluene	99	58 (*S*)
13	**2**	Et_3SiH	THF	trace	60 (*S*)
14	**3**	Ph_2SiH_2	toluene	99	82 (*S*)
15	**3**	PMHS	toluene	99	77 (*S*)
16	**3**	$PhSiH_3$	toluene	79	77 (*S*)
17	**3**	Et_3SiH	toluene	trace	–
18	**4**	Ph_2SiH_2	toluene	95	78 (*S*)
19	**4**	PMHS	toluene	99	71 (*S*)
20	**5**	Ph_2SiH_2	toluene	96	61 (*S*)
21	**5**	$PhSiH_3$	toluene	trace	–
22	**5**	Et_3SiH	toluene	0	–
23	**6**	PMHS	toluene	99	78 (*S*)
24	**6**	Ph_2SiH_2	toluene	0	–

[a] Conversions and enantiomeric excesses were determined by HPLC with a CHIRALPAK IA column.
[b] Reaction was carried out at −25 °C.

Table 2. Zinc-L catalyzed asymmetric hydrosilylation of various aryl alkyl ketones according to Scheme 1.

Entry	Ar	R	System[a]	Yield [%]	*ee*[b] [%]
1	Ph	Et	B	70	86 (*S*)
2	Ph	Cy	C	60	89 (*S*)
3	4-Me-C_6H_4	Me	A	63	82 (*S*)
4	4-Me-C_6H_4	Me	B	47	81 (*S*)
5	4-Me-C_6H_4	Me	C	59	78 (*S*)
6	4-MeO-C_6H_4	Me	A	60	43 (*S*)
7	4-MeO-C_6H_4	Me	C	98	54 (*S*)
8	4-CN-C_6H_4	Me	A	82	72 (*S*)
9	4-CN-C_6H_4	Me	C	78	64 (*S*)
10	4-F-C_6H_4	Me	A	63	81 (*S*)
11	Ph	CF_3	B	50	11 (*R*)
12	4-F-C_6H_4	CF_3	B	34	9[c]
13	2,4,6-$Me_3C_6H_2$	CF_3	B	52	19 (*R*)
14	1-indanone		C	65	76 (*S*)
15	α-tetralone		A	97	71 (*S*)
16	β-tetralone		A	62	12 (*S*)

[a] A = **2**, Ph_2SiH_2; B = **2**, PMHS; C = **3**, Ph_2SiH_2, catalyst 3.5 mol%, all reactions in toluene solution.
[b] See Table 1.
[c] Configuration not determined.



Scheme 2. Hydrosilylation conditions.

Table 3. Effect of amount and stoichiometry of catalyst **2**·$ZnEt_2$ on enantioselectivity of hydrosilylation of acetophenone and 4-methylacetophenone with Ph_2SiH_2.

Entry	R	**2**·$ZnEt_2$ [mol%]	Conv.[a] [%]	*ee*[a] [%]
1	H	3.5	85	88
2	H	3.5[b]	93	73
3	H	3.5[b]	98	12
4	H	3.5[b,d]	85	82
5	H	3.5[c,d]	99	63
6	Me	3.5	>99	82
7	Me	2.5	>99	74
8	Me	2.0	>99	74
9	Me	1.5	>99	74
10	Me	1.0	>99	75
11	Me	0.5	98	27
12	Me	0.1	96	26

[a] See Table 1.
[b] 2 equiv. of $ZnEt_2$ were used for 1 equiv. of **2**.
[c] 3 equiv. of $ZnEt_2$ were used for 1 equiv. of **2**.
[d] Reaction was carried out at −25 °C.

Acyclic *N*,*N*′-dibenzyl-DACH **6** is used in this study as a reference ligand. With the use of ligand **6** we obtained the product of the hydrosilylation of acetophenone with 78% *ee* (entry 23), lower than with the use of macrocyclic ligand **2** (88% *ee*). Surprisingly, no hydrosilylation product was obtained when diphenylsilane was used in the reaction (entry 24).

Efficiency of zinc catalysts with ligands **2** and **3** was investigated with various aryl alkyl ketones (Table 2).

Products of reduction with *ee*s over 75% were obtained with ketones bearing no other heteroatom (entries 1–5, 14). 4-Methoxyacetophenone and 4-cyanoacetophenone gave the products of hydrosilylation in lower *ee* (43–72%, entries 3–9), although 4-fluoroacetophenone reacted normally (*ee* 81%, entry 10). Pharmaceutically important aryl trifluoromethyl ketones were hydrosilylated with low enantioselectivity (entries 11–13), a result not surprising in view of the previously reported lack of success in similar cases. β-Tetralone having two methylene groups flanking the carbonyl group was hydrosilylated with low enantioselectivity (entry 16, *ee* 12%), in contrast to the result with a genuinely aryl alkyl ketone – α-tetralone (entry 15, *ee* 71%). The yields of isolated products reported in Table 2 vary significantly, depending on the substrate and the reduction system used.

A survey of the effect of the amount and stoichiometry of the zinc-ligand system on enantioselectivity of hydrosilylation of acetophenone and 4-methylacetophenone (Scheme 2) is summarized in Table 3.

Our initial studies were carried out with 3.5 mol% of the catalyst having a Zn/L ratio of 1:1 (entries 1, 6). Lower enantioselectivity was observed with a Zn/L ratio of 2:1 (entry 2) and even more pronouncedly with a Zn/L ratio of 3:1 (entry 3) which was expected to lead to a full saturation of ligand **2**. However, lowering the reaction temperature to −25 °C provided the hydrosilylation product in higher *ee* (entry 4, *ee* 82%, entry 5, *ee* 63%). Lowering the amount of the catalyst (Zn/L ratio of 1:1) from 3.5 mol% (entry 6) to 1.0 mol% (entries 7–10) caused a small drop in enantioselectivity which remained constant in the range 2.5 to 1.0 mol%. A further decrease of catalyst amount to 0.5 or 0.1 mol% led to a significant loss of enantioselectivity (entries 11, 12, *ee* 26–27%).

Stereochemical Considerations

In order to clarify the enantioselectivity of the hydrosilylation reaction using trianglamine ligands we performed DFT studies,[38] starting from the structures of the trianglimine **2**-dimethylzinc as well as *N*,*N*′-dibenzyl-DACH (**6**)-dimethylzinc complexes (dimethylzinc was used instead of diethylzinc in order to simplify the calculations). These structures were optimized with the use of the PM3 Hamiltonian and then single-point energies were calculated at the B3LYP/6-31G(D) level and fully optimized at this level for

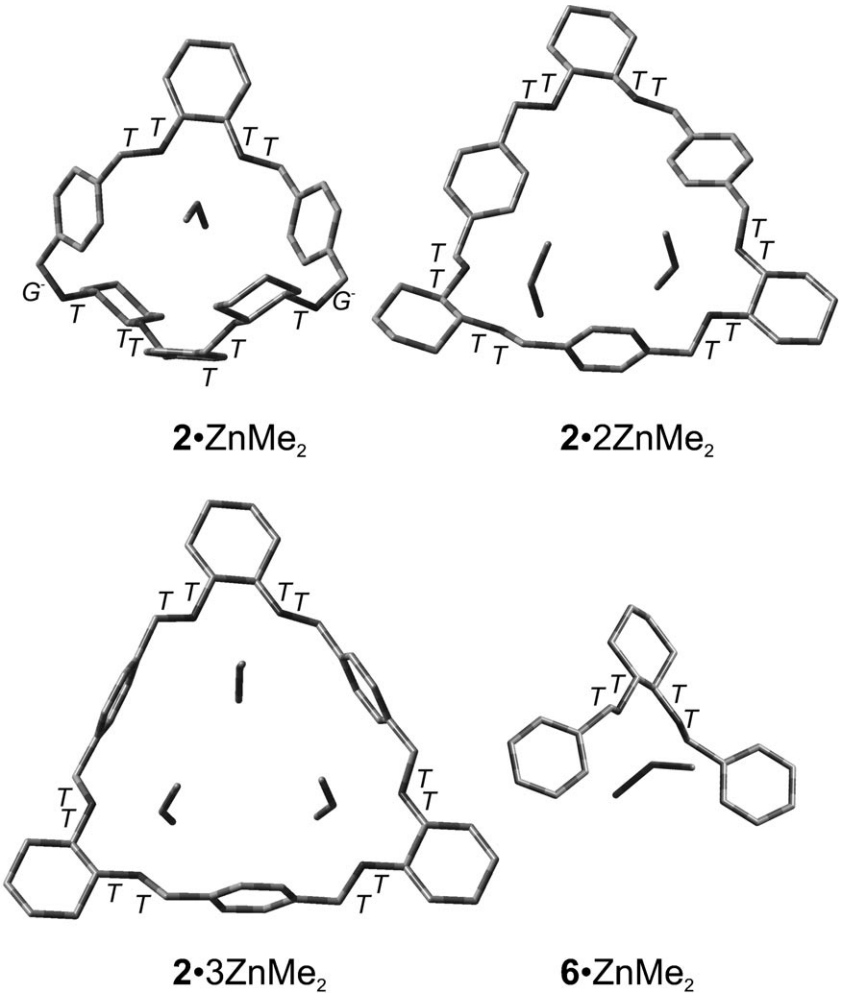


Figure 1. Calculated at the B3LYP/6-31G(D) level lowest energy structures of trianglamine **2**·$ZnMe_2$ complexes and the lowest-energy conformer of **6**·$ZnMe_2$ complex. Hydrogen atoms are omitted for clarity.

2·$ZnMe_2$ and **6**·$ZnMe_2$ complexes only (see Supporting Information for computational details).

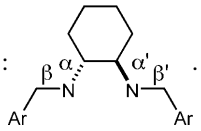
Both free trianglamine **2** and *N*,*N*′-dibenzyl-DACH (**6**) molecules show a remarkable ability to change their conformation as a consequence of rotation about the C–N bonds or by configuration inversion at nitrogen atoms. Our previous study has shown that free ligand **2** possesses a large number of conformers belonging to families of similar structures.[31] These structures are defined by the signs and values of torsion angles [α = C(N)–C(N)–N–C(H_2); β = C(N)–N–C(H_2)–C(Ar)] obtained from rotation of the carbon-nitrogen bonds forming the macrocycle. These torsion angles are normally restricted to either *gauche* (G^-) or *trans* (T) combinations. Whereas the number of T bond arrangements in the macrocycle is not limited, the number of G^- bond arrangements is, as each G^- angle produces additional ring folding. In the X-ray determined structures there are no more than three G^- bond arrangements in the entire ring (out of twelve α and β angles present in the macrocycle). This number is increased to four for the lowest-energy trianglamine conformer obtained by the MM3-AM1 protocol. Additionally, the macrocycle structures in which both β and β' correspond to G^- are not available. As a result of these restrictions, there are only a few sequences of torsion angles available for macrocyclic trianglamine **2**. It should be noted that *all-T* conformations of α and β angles, giving the expanded ring structure of the highest D_3 symmetry, is not of the lowest energy structure of **2**.

Starting from the *all-T* conformation of **2** we calculated the structures of trianglamine complexes with 1, 2 or 3 molecules of dimethylzinc (Figure 1). Following the X-ray data available, we assumed that amine hydrogen atoms are not displaced by dimethylzinc and that the zinc atom is bonded to vicinal nitrogen atoms through the electron lone pairs, as earlier proposed by Mimoun.[24] The *all-T* low energy structure is preserved in trianglamine-dimethylzinc complex **2**·2$ZnMe_2$ and **2**·3$ZnMe_2$, the latter having the highest symmetry D_3. In the most interesting case of

Table 4. Symmetries and sequences of torsion angles calculated for the structures of trianglamine **2**-dimethylzinc complexes and for **6**-dimethylzinc complex.

Complex	Sequence of torsion angles[c]				Symmetry
	β	α	α′	β′	
2·$ZnMe_2$[a]	161.7	166.2	166.2	161.7	C_2
	−74.1	157.3	169.1	−177.2	
	−177.2	169.1	157.3	−74.1	
2·2 $ZnMe_2$[b]	−176.0	171.0	171.0	−176.0	C_2
	162.0	162.4	172.1	−165.5	
	−165.5	172.1	162.4	162.0	
2·3 $ZnMe_2$[b]	−177.8	168.4	168.4	−177.8	D_3
	−177.8	168.4	168.4	−177.8	
	−177.8	168.4	168.4	−177.8	
6·$ZnMe_2$[a]	157.5	164.3	164.3	157.5	C_2

[a] Fully optimized structure at B3LYP/6-31G(D) level.
[b] Single-point energy at B3LYP/6-31G(D) level for PM3 optimized structures.
[c] Torsion angles assignment:



2·$ZnMe_2$ only one low energy conformer was found, characterized by two β angles in a G^- conformation. Note, however, that the conformation of the ligand around the Zn atom is *all-T* for the four consecutive β,α,α′,β′ angles. The structure of this conformer is close to the lowest-energy conformer of the free trianglamine ligand **2**. For structural details see Table 4.

A general feature of complexation of $ZnMe_2$ with trianglamine **2** is the formation of a fully expanded (*all-T*) structure of the ligand with the addition of two or three equivalents of $ZnMe_2$. Similarly, the *all-T* conformer of **2** is preferentially formed upon protonation or upon formation of methylene bridges between the vicinal NH groups in a reaction with formaldehyde.[34a]

Our data on the effect of the stoichiometry of Zn-trianglamine **2** complexes on the efficiency of hydrosilylation (Table 3) suggest that the 1:1 complex represents the structure of the most important species involved initially in the hydrosilylation reaction. Coordination of the ketone substrate to the Zn-trianglamine **2**·$ZnMe_2$ complex results in the release of a methane molecule with the formation of Zn–O coordinated species **A** (Figure 2), in which one of the nitrogen atoms forms a bond to the carbon atom of the carbonyl group.[39] Complexation of acetophenone molecule with C–N bond formation (structures **A1**, **A4**–**A6**) results in significant changes of the conformation of ligand **2** around the coordination site (e.g., $G^+G^-TG^+$ in **A1**, Figure 2, see also Figure A and Table A in Supporting Information). In the absence of the C–N bond (structures **A2**, **A3**) the conformation of the ring around the coordination site remains *TTTT*, as in the complex **2**·$ZnMe_2$. Note that structures **A1**/**A4**, **A2**/**A3** and **A5**/**A6** represent pairwise diastereomeric orientations of the acetophenone molecule, eventually leading to hydrosilylation products of opposite absolute configuration. Due to the energy differences of diastereoisomeric structures, the **A1**/**A4** pair favors the *S* configuration of the product whereas the *R* configuration is preferred in the case of the much less populated structures **A5**/**A6**.

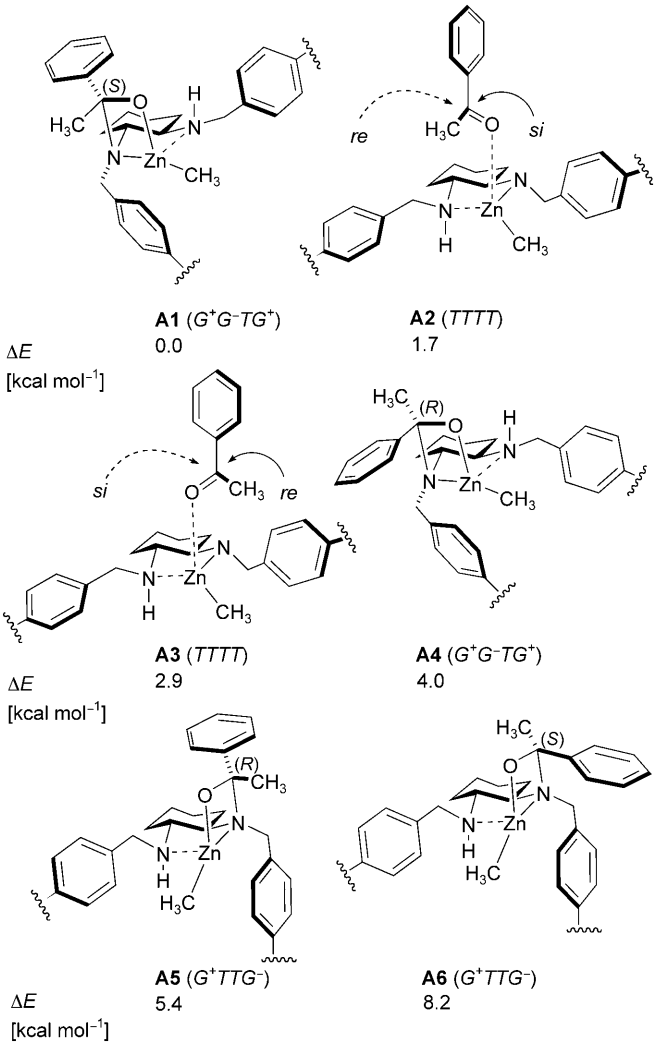


Figure 2. Calculated at the B3LYP/6-31G(D) level structures of trianglamine **2**-$ZnMe_2$-acetophenone complexes (only a fragment of the trianglamine ring is shown for clarity).

Out of six structures calculated, the lowest energy one (**A1**) appears to represent the transition structure leading to the product of preferred configuration. Since the absolute configuration of the newly formed chiral carbon atom in **A1** is *S* and since the substitution of the C–N bond by the C–H bond in the subsequent reaction with silane is believed to proceed with retention of configuration,[24] the preferred enantiomer of the aryl methyl carbinol product should have the *S* configuration. This is exactly as found experi-

mentally in all cases reported in Table 1 and Table 2 (note that there is a formal reversal of the absolute configuration of trifluoromethyl carbinols, entries 13–15 in Table 2).

Other calculated structures (**A2**/**A6**) are of higher energy and should participate in the reaction to a much lower extent. In the two diastereoisomeric structures **A2** and **A3** the addition of the hydride is more probable from the sterically less encumbered face (broken arrow), *re* in **A2** (leading to the product of *S* configuration) and *si* in **A3** (leading to *R* configuration of carbinol). Overall, the diversity of the calculated transition structures shows that full success in achieving control of enantioselectivity of hydrosilylation reaction with the present catalytic system has yet to be achieved.

According to calculations, there are two equal energy structures **B1** and **B2** of the Zn-diamine **6** complex with a coordinated acetophenone molecule (Figure 3). These two structures are diastereoisomeric with the respect to the orientation of acetophenone molecule, with the sequence of torsion angles G^+TTG^+, different from the sequence of torsion angles (*TTTT*) in the parent **6**·$ZnMe_2$ complex. There is no evidence of C(C=O)–N bond formation in these two structures.

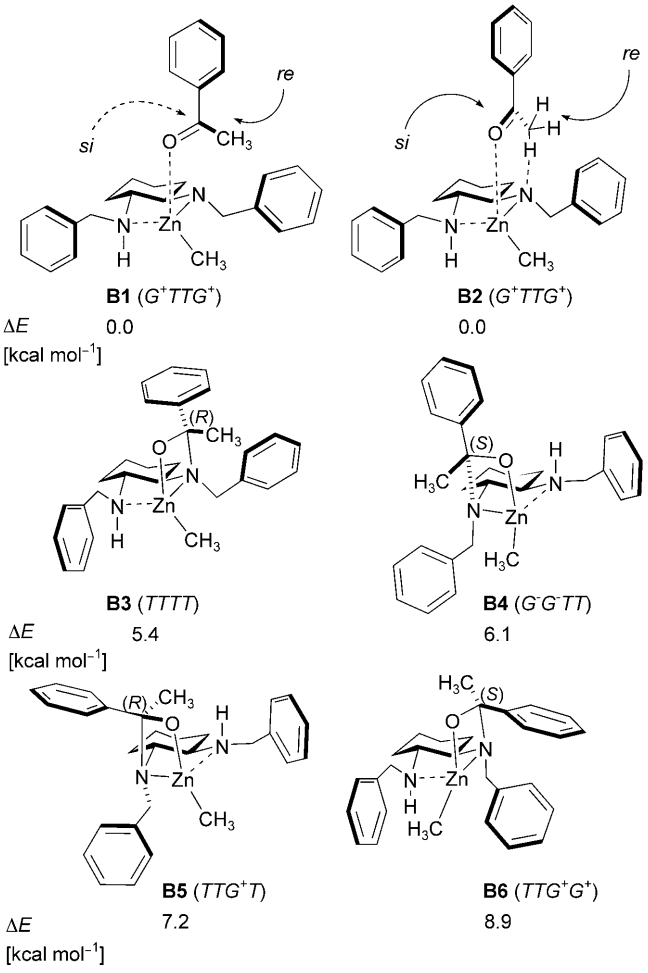


Figure 3. Calculated at the B3LYP/6-31G(D) level structures of diamine **6**-$ZnMe_2$-acetophenone complexes.

Addition of the hydride to the prochiral carbon atom of the carbonyl group in structure **B1** is preferred from the *re* face, leading to the product of *S* configuration. In the case of structure **B2** which is stabilized by interaction of one of the hydrogen atoms of the methyl group with a tertiary nitrogen atom, no preference for hydride attack towards *re* or *si* face is evident. Other calculated structures (**B3**–**B6**) are of much higher energy (>5 kcal mol^{-1}) and do not appear to play a significant role in determining the absolute configuration of the product. These structures are characterized by the presence of the $C_{(C=O)}$–N bond but, unlike the cases **A1**/**A6** discussed earlier, they are not pairwise similar, with the respect to the conformation of ligand **6**. This is evidently due to the flexible nature of acyclic ligand in complexes **B1**–**B6**. Only one of the structures (**B3**) retains the *all-T* conformation.

In summary, the contribution of two low energy structures **B1** and **B2** to the formation of the product provides a reasonable rationalization of the experimentally observed lower enantioselectivity of hydrosilylation with the use of flexible acyclic ligand **6**, compared to the more rigid macrocycle **2**.

Conclusions

We report here a convenient method for the enantioselective hydrosilylation of aryl alkyl ketones, based on the catalysis with zinc-polyamine macrocycles, readily available from DACH. The trianglamine **2**-$ZnEt_2$ (1:1) complex catalyzes the hydrosilylation of acetophenone in toluene solution, using diphenylsilane, with 88% *ee* of the product. This enantioselectivity is higher than that with the use of acyclic ligand **6** (*ee* 78%). Since trianglamine **2** can be conveniently prepared by a one-pot procedure from inexpensive tartrate salt of DACH and terephthalaldehyde,[31] the Zn complex of **2** is a good alternative to previously reported chiral catalysts.

In this paper we present, related to the previous mechanistic study of Mimoun,[24] a plausible rationalization of the observed enantioselectivity of hydrosilylation, by ligands derived from (*R*,*R*)-DACH which provide preferentially carbinols of *S* configuration. It is based on the DFT calculated low-energy structures of the ligand-$ZnMe_2$ (1:1) complexes, as well as the structures of the complexes with coordinated acetophenone molecules. The most stable structures found for cyclic (**2**) and acyclic (**6**) ligands, although structurally different, lead to the hydrosilylation products of the same absolute configuration.

Work is underway to develop a practical, safe and cost effective method for a large-scale enantioselective hydrosilylation of ketones, using PMHS as a hydride source.

Experimental Section

General Procedure for the Hydrosilylation of Ketones

In a 5-mL round-bottom flask $ZnEt_2$ (12.5 μL, 1 M in hexane; 0.0125 mmol) and the appropriate chiral ligand (0.0125 mmol) were dissolved in 1.5 mL of freshly distilled toluene and stirred under an argon atmosphere for 30 min. Then 0.344 mmol of the corresponding ketone or its solution in toluene (1 mL) and 0.413 mmol of silane were added to the mixture. The resulting solution was stirred at room temperature for 24 h. Then 1 mL NaOH (1 M in MeOH) was added with vigorous stirring The reaction mixture was stirred for an additional hour at room temperature and then solvents were evaporated. The precipitate was dissolved in a mixture of H_2O (10 mL) and 1 mL 10% HCl and extracted with diethyl ether (3×10 mL). The combined organic extracts were washed with saturated aqueous solution of $NaHCO_3$, H_2O and brine, dried over anhydrous $MgSO_4$ and concentrated under vacuum. The product was purified by column chromatography on silica gel with hexane-EtOAc (10:1) as eluent.

For data on the HPLC separation of enantiomers see Table B, for products literature references see Table C, Supporting Information.

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