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The first example of asymmetric Michael reaction catalyzed by chiral alkali metal alkoxides

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Some chiral sodium alkoxides can be used as catalysts in the asymmetric Michael reaction as exemplified by the 1,4-addition of an achiral Ni^{II} complex of the Schiff base derived from glycine and *N*-(2-pyridylcarbonyl)-*o*-aminobenzophenone (**1**) to methyl methacrylate (**2**) or methyl acrylate (**14**). The products of the reaction of **1** with **2**, *viz.*, the corresponding diastereomeric complexes of 4-methylglutamic acid, are formed in dissimilar amounts (*de* 26—85%); the *ee* value for the major diastereomer (2*S*,4*R*)-**3a** is 28%. After recrystallization, the enantiomeric purity of complex **3a** increases to *ee* > 85%. Acid-catalyzed hydrolysis of the enantiomerically enriched complex **3a** affords (2*S*,4*R*)-4-methylglutamic acid (*ee* > 85%). The complex of glutamic acid **15** resulting from the reaction of **1** with **14** is formed with an *ee* of 45%. After recrystallization, the enantiomeric purities of complex **15** and glutamic acid increase to *ee* > 90%.

Key words: asymmetric Michael reaction, diastereoselectivity, enantioselectivity; chiral catalysts, chiral alkali metal alkoxides; (2*S*,4*R*)-4-methylglutamic acid, (*S*)-glutamic acid.

Chiral alkali metal alkoxides (AMA) are quite promising reagents for modern asymmetric synthesis, owing to their accessibility and because they can be used as chiral basic catalysts of many reactions in which C—C bonds are formed. Nevertheless, up to now, only few examples of the use of chiral AMA in asymmetric synthesis have been reported.[1,2] For example, recently it was shown for the first time that potassium alkoxides derived from chiral β-amino alcohols can act as efficient reagents and catalysts of enantioselective dehydrohalogenation.[2,3]

The purpose of the present work was to accomplish the asymmetric version of one of the most important reactions of C—C bond formation, *i.e.* Michael reaction, using chiral AMA as catalysts.

Examples of asymmetric Michael reaction catalyzed by chiral alkoxide complexes of some transition metals, in particular Cu^{II},[4] and by mixed bimetallic La—Na—BINOL[5] complex have been reported. However, almost nothing is known about the use of much more readily accessible AMA as the catalysts of asymmetric Michael addition.

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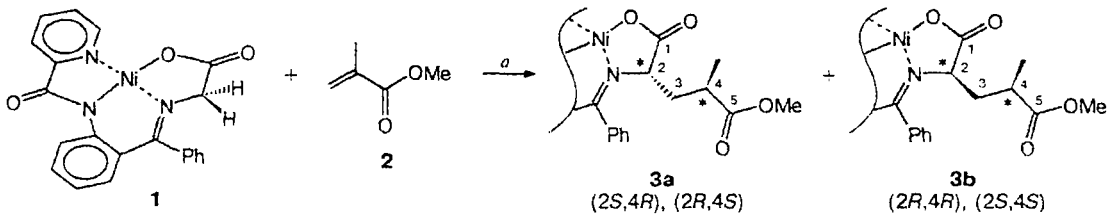
Scheme 1



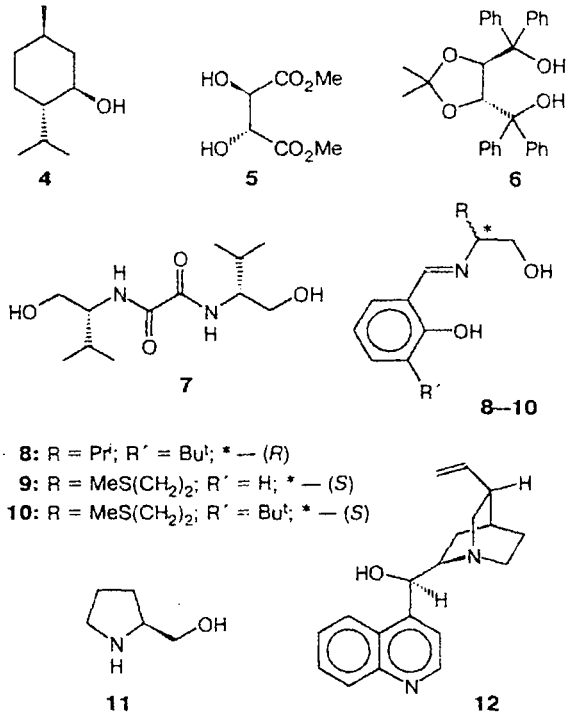
Reagents and conditions: *a*. 10—100 mol.% the catalyst (chiral alcohol **4**—**12** + 1 or 2 equiv. NaH), CH_2Cl_2, Ar, 20 °C.

Results and Discussion

As the CH acid, we used a synthetic equivalent of the glycine synthon, *viz.*, achiral square-planar complex of Ni^{II} with Schiff base derived from glycine and *N*-(2-pyridylcarbonyl)-*o*-aminobenzophenone (**1**); this compound can be easily prepared in a high yield by a two-step procedure starting from available reagents:[6,7] α-picolinic acid, *o*-aminobenzophenone, glycine, and an inorganic Ni^{II} salt. It has been found[8] that the amino-acid fragment in complexes of this type possesses high CH-acidity (pK_a ~19, DMSO). This permits the glycine fragment of the complex to be easily alkylated at the α-C atom in the presence of bases such as MOH or MOAlk (M = Na, K, *etc.*).[6]

The Michael addition of complex **1** to methyl methacrylate (**2**) studied in this work is shown in Scheme 1. This reaction yields diastereomeric complexes **3a,b**; for convenience, these compounds are shown in the Scheme as single enantiomers: (2*S*,4*R*) for **3a** and (2*R*,4*R*) for **3b**. The reaction was catalyzed by sodium alkoxides derived from chiral alcohols **4**—**12**. The catalysts were obtained *in situ* by the interaction of the corresponding alcohol with an equivalent amount of NaH.

The rate of the reaction and the yield of the diastereomers depend appreciably on the structure of the alkoxide used (Table 1). We found that sodium alkoxides derived from simple alcohols containing only one OH group (for example, MeOH, PrⁱOH, L-menthol (**4**)) are virtually unable to catalyze the Michael addition of substrate **1** to methyl methacrylate. Catalytic properties are manifested when the molecule of the starting alcohol contains one more OH group, as in the case of compounds **6**—**10**. When the two hydroxyl groups are vicinal (for example, in (*R*,*R*)-dimethyl tartrate (**5**)), the corresponding alkoxide is also inactive in this reaction. However, compounds containing an amide (**7**), imine (**8**—**10**), or amine (**11**, **12**) group in the β-position with respect to the OH group do exhibit catalytic activity. It should be noted that this reaction occurs absolutely smoothly and does not give any side products. In particular, no 1,2- and bis-addition products are formed; this is an advantage of CH acid **1** over those used traditionally in the Michael addition, for example, malonic acid or ethyl



8: R = Prⁱ; R′ = Buᵗ; * — (*R*)
9: R = $MeS(CH_2)_2$; R′ = H; * — (*S*)
10: R = $MeS(CH_2)_2$; R′ = Buᵗ; * — (*S*)

acetoacetate. Furthermore, both the initial complex **1** and addition products **3a,b** are brightly colored, which makes the TLC monitoring of the reaction easier. Owing to the high specific rotations of complexes like **3a** ($[\alpha]_D$ > 1000° ($CHCl_3$)), the enantioselectivity of the reaction carried out with small amounts of substances can be precisely determined based on the $[\alpha]_D$ values. After completion of the reaction, the two diastereomers can be easily separated and isolated in pure states by preparative TLC (SiO_2, $CHCl_3$—EtOAc, 1 : 1).

To establish the absolute configurations of diastereomers **3a** and **3b**, we carried out enantiomeric analysis of 4-methylglutamic acid resulting from acid hydrolysis of complex **3a** (Scheme 2).

First, we carried out enantiomeric enrichment of the complex **3a** ($[\alpha]_D^{20}$ +870° (*c* 0.02, $CHCl_3$)) formed in the reaction by crystallizing it from a MeOH—$CHCl_3$ mixture with diethyl ether added as a precipitating agent. As a result, the racemate precipitated from the solution,

Table 1. Dependence of the results of the asymmetric Michael addition of complex **1** to methyl methacrylate **2** catalyzed by chiral sodium alkoxides on the structure of the initial alcohol[a]

Entry	Catalyst	Solvent	*t* /min	The yield of **3a**+**3b** (%)	Complex **3a**			Complex **3b**, $[\alpha]_D$/deg [b] ($CHCl_3$)
					de (%)	$[\alpha]_D$/deg [b] ($CHCl_3$)	*ee* (%)[c]	
1	**4**	CH_2Cl_2	60	~0	—	—	—	—
2	**5**	CH_2Cl_2	60	~0	—	—	—	—
3	**6**	CH_2Cl_2	15	51	38	+870	28 (2*S*,4*R*)	−555 (2*R*,4*R*)
4	**6**	CH_2Cl_2	40	61	26	+780	25 (2*S*,4*R*)	−440 (2*R*,4*R*)
5	**6** [d]	CH_2Cl_2	90	12	80	+260	9 (2*S*,4*R*)	Was not isolated
6	**6** [e]	CH_2Cl_2	40	15	71	+375	12 (2*S*,4*R*)	−210 (2*R*,4*R*)
7	**6**	THF	60	20	64	−210	7 (2*R*,4*S*)	+535 (2*S*,4*S*)
8	**6**	MeCN	15	15	50	+390	13 (2*S*,4*R*)	+475 (2*S*,4*S*)
9	**6**	PhMe	40	38	31	+725	24 (2*S*,4*R*)	+470 (2*S*,4*S*)
10	**6** [f]	PhMe	40	25	61	+140	4 (2*S*,4*R*)	−405 (2*R*,4*R*)
11	**7**	CH_2Cl_2	720	30	58	−270	9 (2*R*,4*S*)	+125 (2*S*,4*S*)
12	**8**	CH_2Cl_2	15	56	64	+145	5 (2*S*,4*R*)	−155 (2*R*,4*R*)
13	**9**	CH_2Cl_2	15	47	40	+590	19 (2*S*,4*R*)	−50 (2*R*,4*R*)
14	**9** [e]	CH_2Cl_2	60	70	85	+660	21 (2*S*,4*R*)	Was not isolated
15	**10**	CH_2Cl_2	60	44	47	−310	10 (2*R*,4*S*)	−140 (2*R*,4*R*)
16	**11**	CH_2Cl_2	15	20	47	+90	3 (2*S*,4*R*)	+130 (2*S*,4*S*)
17	**12**	CH_2Cl_2	10	40	29	+20	1 (2*S*,4*R*)	−25 (2*R*,4*R*)
18	**6**[g]	CH_2Cl_2	40	56	56	+620	20 (2*S*,4*R*)	−215 (2*R*,4*R*)

[a] Ratio of the reactants: **1** : **2** : chiral alcohol **4**—**12** : NaH = 1 : 4 : 1 : 1 (for **4**, **11**, **12**) or 2 (for **5**—**10**). The reactions were carried out in an atmosphere of an inert gas (Ar) and at ~20 °C.

[b] Precise low concentrations (weighed portions) of substances were checked by UV spectroscopy (for λ_{max} and ε, see Experimental), in addition to weighing.

[c] The absolute configuration of the enantiomer is given in parentheses. For enantiomerically pure (2*S*,4*R*)-**3a**, an $[\alpha]_D$ value of +3075° (*c* 0.02, $CHCl_3$) was calculated after enantiomeric GLC analysis of the (2*S*,4*R*)-4-methylglutamic acid isolated from the (2*S*,4*R*)-**3a** sample.

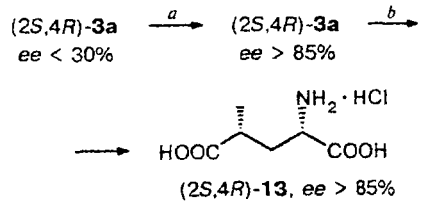
[d] At −20 °C.

[e] Ratio of the reactants: **1** : **2** : **6** : NaH = 1 : 4 : 1 : 1.

[f] At 0 °C.

[g] With 10 mol.% the catalyst, *i.e.*, at a **1** : **2** : **6** : NaH ratio of 1.0 : 4.0 : 0.1 : 0.2.

Scheme 2



Reagents and conditions: *a*. Crystallization (MeOH—$CHCl_3$); *b*. HCl(aq.).

and the mother liquor became enriched in the corresponding excessive enantiomer. The enantiomerically enriched complex **3a** ($[\alpha]_D^{20}$ +2630° (*c* 0.02, $CHCl_3$)) isolated from the mother liquor was decomposed by refluxing in concentrated HCl, and then 4-methylglutamic acid (**13**) and *N*-(2-pyridylcarbonyl)-*o*-aminobenzophenone (which can be used once again for the synthesis of the initial complex **1**) were isolated by a procedure described previously.[10] Enantiomeric GLC analysis (see Experimental) and a comparison with authentic samples of all the four stereoisomers of 4-methylglutamic acid, whose absolute configurations had been determined previously,[10] made it possible to identify the sample of 4-methylglutamic acid isolated from the complex as the (2*S*,4*R*)-enantiomer with a 85.5% enantiomeric purity. Based on the enantiomeric purity of this amino acid and on the specific rotation found for complex **3a**, we found the $[\alpha]_D^{20}$ value for enantiomerically pure (2*S*,4*R*)-**3a** as being equal to +3075° (*c* 0.02, $CHCl_3$). Thus, the magnitudes of optical rotation of the complexes were converted into optical purity values for enantiomer **3a**, which are listed in Table 1. It is known[10,11] that the character of the Cotton effect in the region of d—d transition of the metal atom in this type of complexes is mostly determined by the configuration of the α-C atom (C(2)) and scarcely depends on the configurations of distant asymmetric centers in the side chain of the amino-acid fragment. In this particular case, positive Cotton effect[10] corresponds to the *S*-configuration of the C(2) atom. Therefore, having determined the absolute configuration of complex **3a**, we were immediately able to determine the absolute configuration of **3b** knowing only the sign of the optical rotation angle: the "minus" sign corre-

sponds to the (*R*,*R*)-enantiomer, whereas the "plus" sign corresponds to the (*S*,*S*)-enantiomer of **3b** (see Table 1).

It can be seen from Table 1 that the best results were attained using disodium alkoxide derived from (4*R*,5*R*)-2,2-dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol (**6**, TADDOL[9]); in this case, the enantiomeric purity of the major product **3a** reached 28% (entry *3*). When the reaction duration was increased from 15 min (entry *3*) to 40 min (entry *4*), the yield of the addition products increased; however, the diastereoselectivity of the reaction somewhat decreased. A decrease in the temperature to −20 °C resulted in sharp deceleration of the reaction (yield 12% over a period of 90 min; see Table 1, entry *5*); however, diastereoselectivity markedly increased (from 38 to 85%). Special experiments with pure complexes **3a** and **3b** have demonstrated that diastereoselectivity of the reaction decreases with an increase in the reaction duration or the temperature. This is due to the fact that under the action of a strong base (alkoxide) taken in an equimolar or a catalytic amount, the addition products are able to undergo interconversion due to epimerization at the asymmetric C(2) center (Figs. 1 and 2, Tables 2 and 3). At room temperature in a CH_2Cl_2 solution containing 100 mol.% disodium alkoxide of alcohol **6** (as well as under the reaction conditions), an equilibrium between diastereomers **3a** and **3b** is established over a period of 24 h. The ratio **3a**/**3b** ≈ 1 indicates that thermodynamic stabilities of these diastereomers are approximately equal. When the experiment is carried out with racemic diastereomers under conditions of kinetic control (2—3 h, see Fig. 1), enantioselective recognition of substrates is observed. Thus at the early stage of epimerization, the initial racemic complex **3b** is enriched in the (2*S*,4*S*)-form (see Fig. 1), because the other (2*R*,4*R*)-enantiomer is preferentially converted into (2*S*,4*R*)-**3a** owing to the inversion at the α-C atom. It is even more significant that during epimerization of complex **3a**, the (2*S*,4*R*)-enantiomer is mostly converted into (2*R*,4*R*)-**3b**. Thus, the data listed in Table 1 reflect a superimposition of the enantioselective reaction of C—C bond formation and enantioselective epimerization of diastereomer **3a**, which is initially formed in excess. To make interpretation of the results easier, the experiments at room temperature (see Table 1) were carried out over the shortest possible periods, so that the complete conversion of the substrate was not reached. If only 1 mole of NaH per mole of diol **6** was taken to prepare the catalyst, the reaction occurred much more slowly (see Table 1, entry *6*), probably due to the sharp decrease in the concentration of dialkoxide, which actually catalyzes the process. The replacement of CH_2Cl_2 by another solvent (MeCN, THF, or toluene) decreased in the general case both the yield and the enantioselectivity of the reaction (entries *7*—*10*).

Among the rest of the chiral alcohols **7**—**12** that we studied in this Michael reaction (entries *11*—*17*), the Schiff base formed from (*S*)-methioninol and salicylaldehyde **9** is noteworthy; at 0 °C, the corresponding disodium alkoxide makes it possible to obtain complex (2*S*,4*R*)-**3a** with an enantiomeric purity of 21% in a good yield (65%) and with a high diastereoselectivity (85%) (entry *14*). The catalyst prepared from diamide **7** also deserves attention. In this case, addition product **3a** was

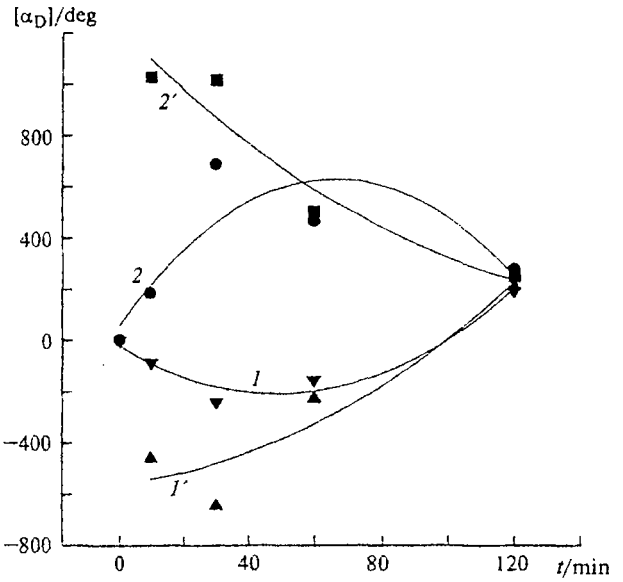


Fig. 1. Epimerization of diastereomers (±)-**3a** (*1*, *1′*) and (±)-**3b** (*2*, *2′*) induced by an equimolar amount of the chiral alkoxide, prepared from diol (4*R*,5*R*)-**6** and 2 equiv. of NaH, in CH_2Cl_2: initial **3a** (*1*); **3b** formed from it (*1′*); initial **3b** (*2*); **3a** formed from it (*2′*).

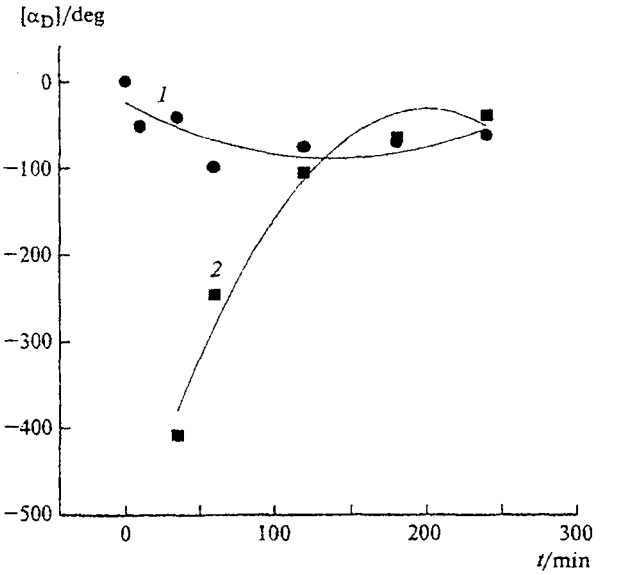


Fig. 2. Epimerization of diastereomer (±)-**3a** in the presence of catalytic quantities (10 mol.%) of the chiral alkoxide, prepared from diol (4*R*,5*R*)-**6** and 2 equiv. of NaH, in CH_2Cl_2: initial **3a** (*1*); resulting **3b** (*2*).

formed with high diastereomeric purity (58%), despite the fact that the reaction lasted for 12 h at room temperature. Since standard experiments were carried out with small amounts of substrate **1** (<0.25 mmol), in practice it was convenient to use equimolar amounts of the catalyst; however, it was found in a special experiment (see Table 1, entry *18*) that the outcome of the reaction (the yield and the enantioselectivity) remain the same if the reaction is conducted with 10 mol.% the alkoxide. Moreover, the diastereoselectivity even increases owing to a decrease in the rate of epimerization (see Fig. 2).

Unfortunately, asymmetric epimerization of complexes **3a** and **3b** induced by chiral catalysts **6**—**12** hampers identification of the steps responsible for the stereochemistry of the process. The question arises of whether asymmetric catalysts do recognize the prochiral sides of the carbanion at the step of formation of the C—C bond in the reaction with a Michael acceptor. To clarify this point, we carried out a similar Michael reaction using methyl acrylate (**14**) as the acceptor (Scheme 3). It may be expected that this sterically less hindered substrate would form the C—C bond faster than methyl methacrylate and this would make it possible to detect a kinetically controlled excess of one enantiomer of **15** over the other, because racemization of the enantiomerically enriched complex **15** under the action of the chiral catalyst would occur more slowly.

Table 2. Ratio of diastereomers **3a** and **3b** during their epimerization[a] induced by the disodium salt of **6**

t /min	**3a** : **3b** ratio[b]	
	initial **3a**	initial **3b**
0	100 : 0	0 : 100
10	96 : 4	12 : 88
30	77 : 23	39 : 61
60	51 : 49	46 : 54
120	44 : 56	51 : 49

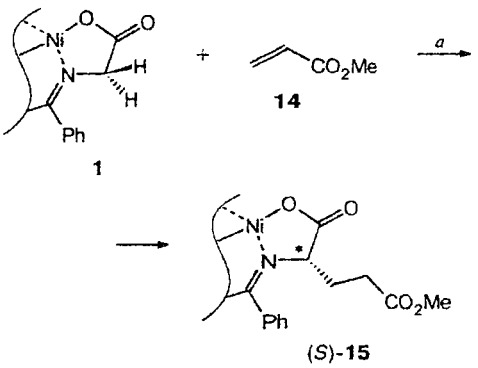
[a] Experimental conditions: 0.05 *M* solutions of pure diastereomers **3a** and **3b** in CH_2Cl_2 were treated at ~20 °C under Ar with 1 equiv. of disodium salt of **6** (see Experimental). At certain intervals, aliquot volumes of the reaction mixture were withdrawn.
[b] The ratio of the diastereomers after isolation was determined by spectrophotometry.

Table 3. Ratio of diastereomers **3a** and **3b** during epimerization[a] of complex **3a** induced by catalytic amounts (10 mol.%) of disodium salt of **6**

t /min	**3a** : **3b** ratio[b]	*t* /min	**3a** : **3b** ratio[b]
0	100 : 0	120	84 : 16
10	—	180	78 : 22
35	86 : 14	240	79 : 21
60	84 : 16		

[a] Experimental conditions: a 0.2 *M* solution of pure diastereomer **3a** in CH_2Cl_2 was treated at ~20 °C under Ar with 10 mol.% disodium salt of **6** (see Experimental). At certain intervals, aliquot volumes of the reaction mixture were withdrawn.
[b] The ratio of the diastereomers after isolation was determined by spectrophotometry.

Scheme 3



Reagents and conditions: *a*. 100 mol.% (**6** + 2 NaH), CH_2Cl_2, Ar.

The absolute configuration of complex **15** was determined in the same way as that of enantiomer **3a**; in this case, we analyzed the (*S*)-glutamic acid resulting from hydrolysis of compound **15**. The $[\alpha]_D^{20}$ value found for enantiomerically pure (*S*)-**15**, as for complex (2*S*,4*R*)-**3a**, was +3505° (*c* 0.02, $CHCl_3$). According to the results obtained (Table 4), the reaction yields mostly the *S*-enantiomer; this is consistent with the configuration of the C(2) atom in the major product **3a** formed in the reaction of compound **1** with methyl methacrylate.

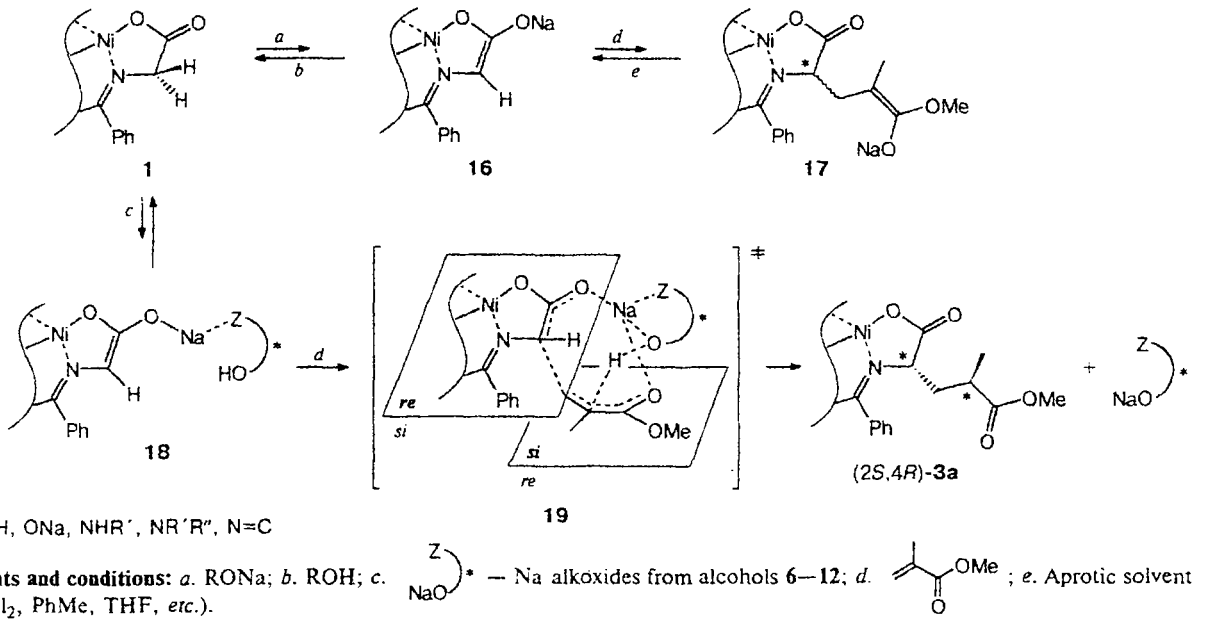
When the experiment is carried out at room temperature over a period of 5 min, the enantiomeric purity of product (*S*)-**15** formed in 76% yield amounts to 18%

Table 4. Results of asymmetric Michael addition[a] of complex **1** to methyl acrylate **14** catalyzed by disodium alkoxide derived from chiral alcohol **6**

Entry	*T* /°C	*t* /min	Yield (%)	$[\alpha]_D$/deg ($CHCl_3$)[b]	*ee* (*S*)[c] (%)
1	+25	5	76	+620	18
2	+25	15	95	+290	8
3	−20	30	48	+1595	45
4	−20	90	64	+1365	39

[a] **1** : **2** : **6** : NaH = 1 : 4 : 1 : 2.
[b] Precise low concentrations (weighed portions) of substances were checked by UV spectroscopy (for λ_{max} and ε, see Experimental), in addition to weighing.
[c] The $[\alpha]_D$ value of +3505° (*c* 0.02, $CHCl_3$) for enantiomerically pure (*S*)-**15** was calculated after enantiomeric GLC analysis of the (*S*)-glutamic acid isolated from the sample of (*S*)-**15**.

Scheme 4



(see Table 4, entry *1*). When the duration of the reaction increases to 15 min, *ee* markedly decreases as a result of racemization of the product occurring under reaction conditions (entry *2*). Therefore, it is obvious that the observed *ee* values are markedly lower that the true enantioselectivity of the reaction. This was confirmed by experiments carried out at a lower temperature (−20 °C) at which racemization occurs more slowly. In this case, the reaction products were produced in good yields over a period of 0.5—1.5 h, and the enantiomeric purity of product (*S*)-**15** reached 45% after 30 min (entries *3*, *4*) and was 39% after 90 min. Rough extrapolation of these values to the beginning of the reaction indicates that the kinetically controlled enantiomeric excess of the addition product is at least 50%.

The results obtained imply a high degree of asymmetric induction at the α-C atom of the glycine fragment in the addition of complex **1** to methyl methacrylate in the presence of chiral alkoxides. The fact that alkoxides derived from alcohol **4** (or the other aliphatic alcohols) and *vic*-diol **5** are unable to catalyze this reaction, whereas alkoxides formed from 1,4-diol **6** and alcohols containing an N^{III} atom in the β-position with respect to the OH group exhibit substantial catalytic activities, can be explained in the following way. The abstraction of the proton from CH acid **1** by the alkoxide yields sodium enolate **16** (Scheme 4). The addition of complex **16** to methyl methacrylate is thermodynamically unfavorable, because it affords a enolate derived from a much weaker CH acid (for initial complex **1**, pK_a ~19,[8] while for esters of type $R'CH_2CO_2R'$, pK_a ~25 [12]).

Therefore, to obtain the final product of 1,4-addition, the formation of enolate **17** needs to be accompanied by its simultaneous protonation. When the reaction is carried out in aprotic solvents, rapid protonation can be accomplished only by alcohol ROH, whose concentration is low. This accounts for the low observed rate of the addition of CH acid **1** to methyl methacrylate in the presence of alkoxides of the RONa type. In the case of alkoxides formed from amino alcohols or diols, the situation is different. Scheme 4 also shows the mechanism of catalysis and asymmetric induction that we propose for the Michael addition of complex **1** to methyl methacrylate in the presence of chiral sodium alkoxides prepared from alcohols **6**—**12**. Since these alkoxides contain groups capable of forming complexes with a metal ion (group Z in Scheme 4), deprotonation of complex **1** may give enolate **18** containing a molecule of the corresponding chiral alcohol coordinated to metal. Thus, a high "local" concentration of the protonating agent with respect to the deprotonated substrate **1** is attained. Therefore, the subsequent addition of complex **18** to methyl methacrylate is facilitated by the possibility of simultaneous protonation of the arising "Michael adduct" as shown in transition state **19**. This is in good agreement with the high degree of asymmetric induction at the α-C atom, which is explained by the fact that the chiral alcoholic group in enolate **18** screens predominantly one of the sides of the plane in which the molecule lies and thus facilitates the attack by the methyl methacrylate molecule on the other side. In addition, the high diastereoselectivity observed in this reaction also implies substantial stereoselectivity of the protonation of the carbanionic center arising in the methyl methacrylate molecule.

However, in terms of this scheme, it is difficult to explain why a 1,2-diol, (*R*,*R*)-dimethyl tartrate, does not exhibit catalytic activity. In our opinion, this re-

quires additional experimental data including study of other 1,2-diols and, perhaps, 1,3-diols.

We hope that subsequent studies of the catalytic effects of chiral alkoxides carried out with other substrates would permit the enantioselectivity of the process to be increased. This is important, among other reasons, because it is the (2*S*,4*R*)-enantiomer of 4-methylglutamic acid **13** that exhibits an extreme selectivity with respect to the cahincic acid receptors.[13]

Experimental

The solvents were purified by a known procedure.[14] The reactions were monitored by TLC on Silufol plates; in the case of preparative TLC, SiO_2 (Merck, 60 F254) was used. ^1H NMR spectra were recorded on a Bruker 200 spectrometer using C_6D_6 as the external standard. Optical rotation was measured on a Perkin—Elmer 241 polarimeter. Electronic absorption spectra were recorded on a Specord M-40 instrument. Enantiomeric GLC analysis was carried out on a 3700-00 chromatograph ("Khromatograf", Moscow).

(*S*)-Prolinol (**11**), (*R*)-valinol, and (*S*)-methioninol were prepared by standard procedures[15] from the corresponding (*S*)-amino acids.

(4*R*,5*R*)-2,2-Dimethyl-α,α,α',α'-tetraphenyl-1,3-dioxolane-4,5-dimethanol (6) was synthesized from (*R*,*R*)-tartaric acid by a procedure described previously.[9] M.p. 196—198 °C, $[\alpha]_D^{20}$ −61.5° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$), δ: 1.05 (s, 6 H, Me); 4.01 (s, 2 H, CH); 7.3—7.5 (m, 20 H, ArH). Lit. data:[9] m.p. 193—195 °C, $[\alpha]_D^{20}$ −66.7° (*c* 1, $CHCl_3$).

(2*R*,7*R*)-1,8-Dihydroxy-2,7-bis(1-methylethyl)-3,6-diazaoctane-4,5-dione (diamide of oxalic acid and (*R*)-valinol) (7) was synthesized by analogy with the previously described procedure[16] from dimethyl oxalate and (*R*)-valinol in MeOH. Yield 77%, m.p. 205 °C, $[\alpha]_D^{20}$ +35.0° (*c* 1, MeOH). Found (%): C, 55.13; H, 9.13; N, 10.55. $C_{12}H_{24}N_2O_4$. Calculated (%): C, 55.02; H, 9.18; N, 10.56. ^1H NMR ($CDCl_3$), δ: 0.96 (m, 12 H, 4 Me); 1.10 (m, 2 H, 2 Me_2CH); 3.79 (m, 6 H, CH—CH_2). Lit. data[17] for the (*S*,*S*)-diastereomer: m.p. 205—206 °C.

The Schiff base derived from (*R*)-valinol and *o*-(*tert*-butyl)salicylaldehyde (compound 8) was prepared by a procedure described for its (*S*)-enantiomer.[18] Yield 70%, m.p. 58—60 °C, $[\alpha]_D^{20}$ +35° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$), δ: 0.93, 0.97 (d, 3 H, Me, *J* = 7 Hz); 1.40 (s, 9 H, Bu^t); 1.60 (m, 1 H, CH); 2.0 (m, 1 H, CH); 3.80 (m, 2 H, CH_2); 6.8—7.5 (m, 3 H, Ar); 8.4 (s, 1 H, CH=N); 13.5 (s, 1 H, OH). Lit. data[18] for (*S*)-enantiomer: m.p. 57—58 °C, $[\alpha]_D^{20}$ −39.8° (*c* 1, $CHCl_3$).

The Schiff base derived from (*S*)-methioninol and salicylaldehyde (compound 9) was prepared by a known procedure.[19] Yield 80%, m.p. 43 °C, $[\alpha]_D^{20}$ −120° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$), δ: 1.80 (m, 2 H, CH_2); 2.05 (s, 3 H, SMe); 2.20 (m, 2 H, CH_2); 3.30 (m, 1 H, CH); 3.60 (m, 2 H, CH_2); 6.8—7.3 (m, 4 H, Ar); 8.30 (s, 1 H, CH=N); 13.5 (*c*, 1 H, OH). Lit. data:[19] m.p. 43—45 °C, $[\alpha]_D^{20}$ −133° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$), δ: 2.08 (s, 3 H, SMe), 8.40 (s, 1 H, CH=N).

The Schiff base derived from (*S*)-methioninol and *o*-(*tert*-butyl)salicylaldehyde (compound 10) was prepared similarly[19] to Shiff base **9**. Yield 77%, $[\alpha]_D^{20}$ −95.7° (*c* 1, $CHCl_3$). Found (%): C, 65.44; H, 8.14. $C_{16}H_{25}NO_2S$. Calculated (%): C, 65.05; H, 8.53. ^1H NMR ($CDCl_3$), δ: 1.40 (s, 9 H, Bu^t); 1.80 (m, 2 H, 2 CH); 2.05 (s, 3 H, SMe); 2.2 (m, 2 H, CH_2); 3.3 (m, 1 H, CH); 3.6 (m, 2 H, CH_2); 6.8—7.3 (m, 3 H, Ar); 8.30 (s, 1 H, CH=N); 13.5 (s, 1 H, OH).

Ni^{II} complex of the Schiff base of glycine and *N*-(2-pyridylcarbonyl)-*o*-aminobenzophenone (1) was synthesized by a procedure described previously[6] and dried first in air and then *in vacuo* at 110 °C for ~24 h until no traces of water or the alcohol remained (^1H NMR monitoring). Yield 95%, decomp.p. >280 °C (without melting). Found (%): C, 60.89; H, 3.62; N, 10.02; Ni, 13.78. $C_{21}H_{15}N_3NiO_5$. Calculated (%): C, 60.62; H, 3.63; N, 10.10; Ni, 14.11. ^1H NMR ($CDCl_3$), δ: 3.82 (s, CH_2); 6.8—8.9 (m, 13 H). Lit. data:[6] decomp.p. 280 °C.

Reaction of complex 1 with CH acids 2 or 14 in the presence of equimolar amounts of chiral alkoxides (general procedure). The reactants were thoroughly dried in order to prevent hydrolysis of the reaction products. The reaction flask was twice evacuated, and heated in an open flame of a burner being simultaneously filled with Ar; then it was slowly cooled to ~20 °C. Chiral alcohol **4**—**12** (0.1 mmol) in 2 mL of an anhydrous solvent was placed into the flask, and NaH (0.1 or 0.2 mmol) was added to it with stirring. Five minutes later, complex **1** (0.1 mmol) and compound **2** or **14** (0.02 mL, 0.30 mmol) were added in an Ar flow. The course of the reaction was monitored by TLC ($CHCl_3$—EtOAc, 1 : 1). The mixture was quenched by adding 0.5 mL of glacial AcOH in 5 mL of H_2O. The aqueous layer was separated, while the organic layer was extracted with $CHCl_3$ (3×5 mL). The chloroform extracts were combined and concentrated. The initial and final complexes were separated by preparative TLC on SiO_2 using a $CHCl_3$—Me_2CO (6 : 1) or a $CHCl_3$—EtOAc (1 : 1) mixture as the eluent. **Complex (±)-3a:** decomp.p. ≥250 °C (without melting). Found (%): C, 60.82; H, 4.73; N, 8.34; Ni, 11.14. $C_{26}H_{23}N_3NiO_5$. Calculated (%): C, 60.50; H, 4.49; N, 8.14; Ni, 11.37. ^1H NMR ($CDCl_3$), δ: 0.86 (d, 3 H, Me); 1.56 (m, 1 H, CH_2); 2.56 (m, 1 H, CH_2); 3.25 (m, 1 H, MeCH); 3.50 (s, 3 H, OMe); 3.99 (m, 1 H, CH); 6.76—8.89 (m, 13 H, Ar). UV ($CHCl_3$), λ_{max}/nm (log ε): 306 (3.98), 459 (3.65). **Complex (±)-3b:** decomp.p. ≥278 °C (without melting). Found (%): C, 59.70; H, 4.53; N, 8.28; Ni, 11.99. $C_{26}H_{23}N_3NiO_5$. Calculated (%): C, 60.50; H, 4.49; N, 8.14; Ni, 11.37. ^1H NMR ($CDCl_3$), δ: 1.12 (d, 3 H, Me); 2.04 (m, 1 H, CH_2); 2.38 (m, 1 H, CH_2); 2.91 (m, 1 H, MeCH); 3.33 (s, 3 H, OMe); 4.00 (m, 1 H, CH); 6.70—8.83 (m, 13 H, ArH). UV ($CHCl_3$), λ_{max}/nm (log ε): 305 (3.98), 458 (3.65). **Complex (±)-15:** m.p. 258—260 °C. Found (%): C, 59.70; H, 4.16; N, 8.16. $C_{25}H_{21}N_3NiO_5$. Calculated (%): C, 59.80; H, 4.22; N, 8.37. ^1H NMR ($CDCl_3$), δ: 1.88 (m, 1 H, β-CH_2); 2.39 (m, 1 H, β-CH_2); 2.55 (m, 1 H, γ-CH_2); 3.20 (m, 1 H, γ-CH_2); 3.56 (s, 3 H, OMe); 4.04 (m, 1 H, α-CH); 6.76—8.89 (m, 13 H, ArH). UV ($CHCl_3$), λ_{max}/nm (log ε): 306 (3.99), 459 (3.65).

The reaction conditions and yields and *ee* of the products are listed in Tables 1 and 4.

Reaction of complexes 1 and 2 catalyzed by chiral alkoxides (general procedure). The reaction flask was twice evacuated and heated in an open flame of a burner being simultaneously filled with Ar; then it was slowly cooled to ~20 °C, and compound (4*R*,5*R*)-**6** (0.225 g, 0.48 mmol)) in 2 mL of anhydrous CH_2Cl_2 was added. Sodium hydride (0.0385 g, 0.96 mmol) was added with stirring (as a 60% suspension in vaseline oil). Five minutes later, complex **1** (2.00 g, 4.8 mmol) and then complex **2** (2 mL, 19 mmol) were added, and the mixture was stirred for 1 h. Quenching of the mixture, its analysis, and separation of the complexes were carried out by a procedure similar to that described above to give 1.2 g of diastereomer **3a**, yield 45%, $[\alpha]_D^{20}$ +597° (*c* 0.02, $CHCl_3$) (*ee*

19.4%). The product was recrystallized from a MeOH—$CHCl_3$ mixture, the complex was precipitated with ether. Enantiomerically enriched **3a** with $[\alpha]_D^{20}$ +2628° (*ee* 85.5%), yield 12.5%, was isolated from the mother liquor. Crystallization gave virtually racemic **3a** with $[\alpha]_D^{20}$ +62° (*ee* 0.2%), yield 32.5%. For pure diastereomer **3a**, $[\alpha]_D^{20}$ +3075° (*c* 0.02, $CHCl_3$).

The conditions of the other reactions and the yields and the *ee* values for the reaction products are listed in Table 1.

Isolation of (2*S*,4*R*)-γ-methylglutamic acid from complex 3a and (*S*)-glutamic acid from complex 15. The procedures for decomposition of the enantiomerically enriched complexes and for the isolation of the amino acid were described previously.[10] Enantiomeric GLC analysis (a Chirasil-Val phase, a 40000×0.23 mm quartz capillary column, T = 165 °C, He as the carrier gas (1.75 bar); comparison with authentic samples; retention times: (*R*,*R*)-enantiomer, 473 s; (*R*,*S*)-enantiomer, 491 s; (*S*,*S*)-enantiomer, 504 s; (*S*,*R*)-enantiomer, 536 s) showed that the optical purity of the amino acid was 85.5%. ^{1}H NMR ($CDCl_3$), δ: 1.75 (d, 3 H, Me, J = 7 Hz); 2.85, 3.50 (m, 2 H, CH_2); 4.20 (m, 1 H, CH); 4.60 (m, 1 H, CH).

Similarly, (*S*)-glutamic acid was isolated from complex (*S*)-**15**. Enantiomeric GLC analysis (a Chirasil-Val phase, a 32000×0.24 mm quartz capillary column, T = 155 °C, He (1.8 bar) as a carrier gas; comparison with authentic samples; retention times: *R*-enantiomer, 274.0 s; *S*-enantiomer, 283.3 s) showed that the optical purity of the amino acid was >90%.

Epimerization of diastereomeric complexes 3 induced by an equimolar amount of sodium alkoxide derived from diol (4*R*,5*R*)-6. Epimerization was carried out for diastereomerically pure racemic complexes **3a** and **3b**. A solution of diol (4*R*,5*R*)-**6** (41.1 mg, 0.088 mmol) in 1.5 mL of CH_2Cl_2 and NaH (7.1 mg, 0.176 mmol) were placed in a reaction flask. Then diastereomer **3a** (45.5 mg, 0.088 mmol) was added, and the mixture was stirred for 2 h. After 10, 30, 60, and 120 min, samples 0.2 mL each were withdrawn from the reaction mixture and resolved by preparative TLC on SiO_2 using $CHCl_3$—Me_2CO (6 : 1) and $CHCl_3$—EtOAc (1 : 1) mixtures as eluents, as described above. The results of the experiment are presented in Fig. 1 and in Table 2. The ratio of diastereomers (**3a**/**3b**) after isolation was determined by spectrophotometry; after 120 min, it amounted to 0.78 : 1.00.

Epimerization of diastereomer **3b** was carried out in a similar way, and the products were analyzed as described above. The result of the experiment is presented in Fig. 1 and in Table 2. After 120 min, the **3a** : **3b** ratio was 1 : 1.

Epimerization of diastereomer **3a** in the presence of catalytic quantities of complex (4*R*,5*R*)-**6** was carried out in a similar way (see Fig. 2 and Table 3).

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