filtered, and the filtrate was concentrated. Purification of the residue by column chromatography on neutral alumina [$CHCl_3$–ether (1:1)] gave yellow crystals of **18** in 22% yield. Mp: 130 °C dec. Anal. Calcd for $C_{23}H_{23}NO_8SFe$: C, 52.17; H, 4.35; N, 2.65. Found: C, 52.09; H, 4.48; N, 2.69. CI-MS (*m/e*): 530 $(M + 1)^+$, 474 $(M + 1 - 2CO)^+$, 446 $(M + 1 - 3CO)^+$, 390 (Ligand + 1)$^+$. IR ($CHCl_3$): ν(CO) 2065 (s), 1998 (br, s), 1695 (m, br) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.15 (t, 3 H, ^3J = 7.0 Hz, CH_2CH_3), 1.28 (t, 3 H, ^3J = 7.0 Hz, CH_2CH_3), 3.29 (s, 1 H, *CH*), 3.42 (s, 3 H, CO_2CH_3), 3.50 (m, 2 H, CH_2CH_3), 3.63 (s, 1 H, *CH*), 3.68 (m, 2 H, CH_2CH_3), 3.87 (s, 3 H, CO_2CH_3), 7.22–7.42 (m, 5 H, Ph) ppm.

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Supplementary Material Available: Tables of anisotropic temperature factors and torsion angles for **1**, **2**, and **14** (7 pages); listings of structure factors for **1**, **2**, and **14** (39 pages). Ordering information is given on any current masthead page.

Synthesis and Properties of Novel Organozinc Enolates of N,N-Disubstituted Glycine Esters. Molecular Structure of $[EtZnOC(OMe)=C(H)N(t\text{-}Bu)Me]_4$

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This report describes the first detailed characterization of synthetically useful organozinc ester enolates both in the solid state and in solution. Reactions of *N*-(ethylzincio)diisopropylamine with *N*,*N*-dialkylglycine esters afford pure ethylzinc ester enolates $EtZnO(RO)C{=}C(H)NR^1R^2$ (**4**) in almost quantitative yields. The ester enolate anions are chelate-bonded to the metal center through covalent Zn–O and dative Zn–N bonds. The strength of the Zn–N bond, and consequently the thermostability of the zinc enolates **4**, is influenced by the electronic properties of the amino-nitrogen substituents. A crystal structure determination of the ethylzinc enolate (**4b**) of *N*-methyl-*N*-*tert*-butyl-glycine methyl ester shows a tetrameric associate of four crystallographically independent ZnOCCN units (average Zn–O = 2.065 (4) Å) that are linked via Zn–O–Zn bridges (average Zn–O = 2.032 (2) Å). The title compound crystallizes as colorless crystals in the monoclinic space group $P2_1/n$ with a = 20.063 (1) Å, b = 12.875 (1) Å, c = 20.414 (1) Å, β = 101.72 (1)°, V = 5163.2 (6) Å^3, Z = 4, and T = 295 K. Blocked full-matrix least-squares refinement converged at R = 0.061 and R_w = 0.055. Chlorozinc enolates **3** were prepared by transmetalation of α-amino lithium ester enolates $LiO(RO)C{=}C(H)NR^1R^2$ (**2**) with $ZnCl_2$. Characterization of these enolates shows the presence of several aggregates, including mixed aggregates that contain both lithium and zinc cations. The structures and degree of association of zinc enolates **3** and **4** in solution are influenced by the presence of Lewis acids (Et_2Zn, EtZnCl) as well as Lewis bases (THF, pyridine). In solution, the title compound is present as a mixture of dimeric and tetrameric associates that are in an equilibrium which is slow on the NMR time scale. Furthermore, it is shown that in solution α-amino zinc ester enolates are present as *Z*-isomers containing an intramolecular Zn–N coordination bond. An exception to this generalization is zinc enolate **3e**, in which Zn–N coordination is absent (the amino nitrogen has a planar geometry and therefore is a poor Lewis base), and consequently this enolate is predominantly present as the *E*-isomer. Our findings reveal some of the factors that control the chemo- and stereoselectivity of the reactions of zinc ester enolates with imines that afford 2-azetidinones.

Introduction

In recent years metal enolates have become the most widely used reagents for carbon–carbon bond formation in organic synthesis. Especially alkylation[1] and aldol-type reactions[2,3] have been extensively developed. In view of controlling the stereochemistry of these reactions, the need for specific generation and characterization of the intermediate metal enolates has become a major challenge for synthetic chemists. Particularly the synthesis and characterization of alkali-metal enolates has received much attention, and nowadays the chemistry of these alkali-metal enolates is well-known.[4,5]

In contrast, still very little is known about the structure and nature of the enolates derived from less electropositive main-group metals, e.g. magnesium, aluminum, zinc, and tin.[6] This is illustrated by the fact that, whereas the

† Debye Research Institute, Department of Metal-Mediated Synthesis.

‡ Bijvoet Research Institute, Laboratory of Crystal and Structural Chemistry.

(1) See for example: Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 3, pp 1–110 and references cited therein.

(2) Heathcock, C. H. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 3, pp 111–212 and references cited therein.

(3) Evans, D. A.; Nelson, J. V.; Taber, T. R. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Wilen, S. H., Eds.; Wiley-Interscience: New York, 1982; Vol. 13, p 1.

(4) Jackman, L. M.; Lange, B. C. *Tetrahedron* **1977**, *33*, 2737.

(5) Seebach, D. *Angew. Chem.* **1988**, *100*, 1715.

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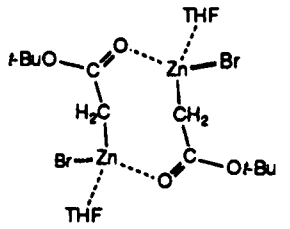
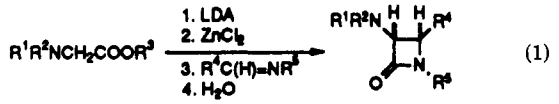


Figure 1. Schematic representation of the solid-state structure of a Reformatsky reagent, $[BrZnCH_2COO(t\text{-}Bu)THF]_2$.

Reformatsky reaction,[7] with zinc enolates as the active intermediates, has been known since 1887 and its versatile chemistry has been well-developed,[8] it was not until 1984 that the first structural data of a Reformatsky reagent were reported.[9] The X-ray structure determination showed that the Reformatsky reagent is dimeric in the solid state and that, surprisingly, the organic anion is bonded to the zinc atom through Zn–C as well as Zn–O bonds (Figure 1).

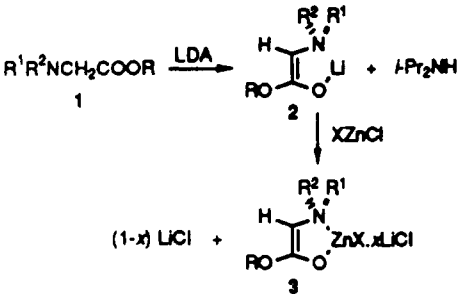
During the last decade, the condensation of metal ester enolates with imines has become one of the major synthetic routes to mono- and bicyclic β-lactam systems, which are potentially antibiotics.[10] We have developed a zinc-mediated, highly stereoselective route to *trans*-3-amino-2-azetidinones, the principal building blocks of Aztreonam and related monobactam antibiotics.[11] This route is characterized by the in situ preparation of α-amino zinc ester enolates that react with imines to afford *trans*-3-amino-2-azetidinones in high yields (eq 1). Moreover an excellent enantioselectivity is observed when an α-methylbenzyl group (R^5) is used as a chiral auxiliary.[11d,12]



(1)

In our opinion, the high trans stereoselectivity of these reactions is the result of the formation of a highly ordered transition-state complex of a *Z*-enolate with an *E*-imine.[12] We assume that the enolate anion is bonded to the zinc atom through N,O-chelation; i.e., that the reactions with imines are chelation-controlled. In order to find support for this hypothesis and to gain better insight into the bonding of α-heteroatom-substituted ester enolates, we have studied the structures and chemistry of the intermediate zinc ester enolates. Part of this work has been published in a short communication;[13] the full details of our work are present in this paper.

Scheme I



3a: R = Et	R^1 = Et	R^2 = Et	X = Et	x = 1.0
3b: R = Et	R^1 = Et	R^2 = Et	X = Cl	x = 0.5
3c: R = Me	R^1 = Me	R^2 = *t*-Bu	X = Cl	x = 0.25

Results

Synthesis of Organozinc Enolates of N,N-Disubstituted Glycine Esters. Zinc ester enolates are generally prepared by reaction of activated zinc with an α-bromoester (the Reformatsky reaction)[8] or by transmetalation of a preformed alkali-metal ester enolate with a suitable zinc salt, e.g. a zinc halide or a zinc alkoxide.[14] As the zinc enolates that we used in our synthesis of 3-amino-2-azetidinones were prepared by the latter method,[11] we started our investigations by isolating the intermediate zinc enolates (**3**) prepared from the preformed alkali-metal enolates (**2**). The latter enolates were prepared in nearly quantitative yields by deprotonation of the various N,N-disubstituted glycine esters (**1**) with an amide base, e.g. LDA (LDA = lithium diisopropylamine), LiTMP (TMP = 2,2,6,6-tetramethylpiperidine), LiHMDS (HMDS = hexamethyldisilazane), or NaHMDS. Transmetalation of these alkali-metal enolates with either ethylzinc chloride or zinc dichloride afforded the ethylzinc enolate **3a** and the chlorozinc enolates **3b** and **3c**, respectively (Scheme I).

Elemental analysis of **3a–c** showed the presence of tightly bonded lithium chloride that could not be separated from the zinc enolate species. Most likely mixed aggregates are formed, which hamper the isolation and characterization of well-defined samples of these zinc enolates. Attempts to grow single crystals suitable for an X-ray diffraction study failed.

The ^1H NMR spectra of **3a–c** are very complex and show broad resonances that do not sharpen upon heating (to 353 K) or cooling (to 193 K), and also the ^{13}C NMR spectra indicate the presence of several aggregates in solution. However, the ^1H and ^{13}C chemical shifts of zinc enolates **3a–c** are characteristic for oxygen-metalated species; the olefinic proton is found between 3.7 and 4.0 ppm, and the olefinic carbon is found between 83 and 86 ppm. Reformatsky reagents, which can be regarded as zinc enolates that are simultaneously both carbon- and oxygen-metalated (see Figure 1),[9,14] show characteristic ^1H signals that lie between 1.8 and 2.0 ppm and ^{13}C signals between 20 and 23 ppm,[15] more indicative for a carbon-metalated species.

As the formation of mixed zinc–sodium aggregates is less likely,[16] we tried to synthesize the chlorozinc enolate **3d**

(6) Of interest in this context is the recent work of Bergman and Heathcock, who have reported the isolation and characterization of some transition-metal enolates (M = W, Mo, Pd, Ni, Re, Rh, Ru). See for example (and references cited therein): (a) Hartwig, J. F.; Andersen, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1990**, *112*, 5670. (b) Burkhardt, E. R.; Bergman, R. G.; Heathcock, C. H. *Organometallics* **1990**, *9*, 30. (c) Stack, J. G.; Doney, J. J.; Bergman, R. G.; Heathcock, C. H. *Ibid* **1990**, *9*, 453. (d) Burkhardt, E. R.; Doney, J. J.; Bergman, R. G.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 2022.

(7) Reformatsky, S. N. *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 1210.

(8) Gaudemar, M. *Organomet. Rev A* **1972**, *8*, 184.

(9) Dekker, J.; Budzelaar, P. H. M.; Boersma, J.; van der Kerk, G. J. M.; Spek, A. L. *Organometallics* **1984**, *3*, 1403.

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(11) (a) Jastrzebski, J. T. B. H.; van der Steen, F. H.; van Koten, G. *Recl. Trav. Chim. Pays-Bas* **1987**, *106*, 516. (b) van der Steen, F. H.; Jastrzebski, J. T. B. H.; van Koten, G. *Tetrahedron Lett.* **1988**, *29*, 2467. (c) van der Steen, F. H.; Kleijn, H.; Jastrzebski J. B. T. H.; van Koten, G. *Ibid.* **1989**, *30*, 765. (d) van der Steen, F. H.; Kleijn, H.; Spek, A. L.; van Koten, G. *J. Chem. Soc., Chem. Commun.* **1990**, 503.

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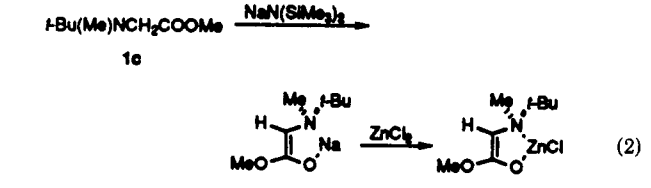
(13) van der Steen, F. H.; Boersma, J.; Spek, A. L.; van Koten, G. *J. Organomet. Chem.* **1990**, *390*, C21.

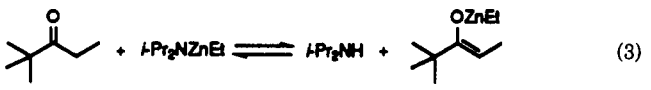
(14) Dekker, J.; Schouten, A.; Budzelaar, P. H. M.; Boersma, J.; van der Kerk, G. J. M.; Spek, A. L.; Duisenberg, A. J. M. *J. Organomet. Chem.* **1987**, *320*, 1.

(15) Orsini, F.; Pelizzoni, F.; Ricca, G. *Tetrahedron Lett.* **1982**, *23*, 3945.

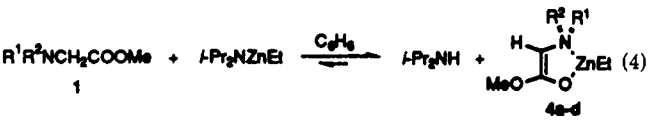
by transmetalation of the sodium enolate **2d** (eq 2).



(2)



(3)



(4)

a: $R^1 = R^2 = Me$; b: $R^1 = Me$, $R^2 = t$-Bu; c: $R^1 = R^2 = Et$; d: $R^1 = Me$, $R^2 = Ph$

(5)

Two fractions were obtained, one soluble in diethyl ether/benzene (ca. 40% yield) and one soluble in THF (ca. 60% yield). ^{1}H NMR spectra of both fractions showed the presence of the chlorozinc enolate **3d** but apparently again in the form of different aggregates.

During this work Hansen et al. reported the synthesis of metal-salt free *N*-(ethylzincio)diisopropylamine and showed that the basicity of this zinc amide is sufficient to deprotonate 2,2,-dimethyl-3-pentanone to form a zinc enolate and diisopropylamine (eq 3), although the equilibrium constant for this reaction is close to unity.[17]

We anticipated that the intramolecular coordination in our zinc enolates might drive the equilibrium in the reactions of zinc amides with N,N-disubstituted glycine esters **1** completely to the side of the product zinc enolates (**4**). This was indeed observed when esters **1a–d** were deprotonated with *N*-(ethylzincio)diisopropylamine, which reaction afforded the ethylzinc enolates **4a–d** in nearly quantitative yields (eq 4).

These pure ethylzinc enolates are very soluble in alkanes and aromatic solvents. Characterization of **4a–d** was difficult: the NMR spectra showed sharp resonances only for **4b**, whereas the resonances of **4a,c,d** were broad in the whole temperature range from 193 to 353 K.

The complex ^{1}H NMR spectrum of **4b** shows two distinct resonance patterns, with a both temperature- and concentration-dependent intensity ratio, that do not coalesce or broaden between 203 and 353 K. These observations point to the presence of two species in solution, which are involved in an equilibrium that is slow on the NMR time scale. Cryoscopic molecular weight determinations of **4b** in benzene are indicative for the existence of an equilibrium between a dimeric and a tetrameric species. The degrees of association calculated from concentration-dependent cryoscopy correlate well with those obtained by ^{1}H NMR spectroscopy (Table I), and this allows the assignment of the individual resonance patterns of each aggregate.

The data given in Table I and those obtained by temperature-dependent NMR spectroscopy show that the energy difference between the dimeric and tetrameric

(16) Sodium chloride has much less coordinating abilities than lithium chloride.

(17) Hansen, M. H.; Bartlett, P. A.; Heathcock, C. H. *Organometallics* 1988, *6*, 2069.

Table I. Degree of Association (n) in Benzene of [EtZnO(MeO)C=C(H)N(t-Bu)Me]$_n$ (4b), Determined by Means of Concentration-Dependent Cryoscopy and ^{1}H NMR Spectroscopy

cryoscopy		^{1}H NMR[a]	
c, mol L^{-1}	n	c, mol L^{-1}	n
0.025	2.2	0.015	2.4
0.042	2.4	0.037	2.5
0.053	2.6	0.074	2.9
0.096	2.7	0.120	3.0
0.191	2.8	0.240	3.1
0.210	3.0		

[a] The dimer to tetramer ratio was determined by integration of the HC=C signal at 281 K.

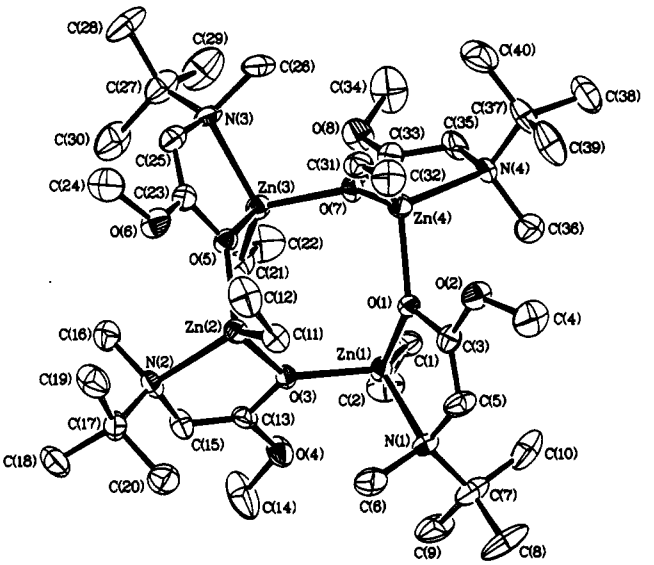


Figure 2. ORTEP drawing (30% probability level) of the molecular structure of [EtZnOC(OMe)=C(H)N(t-Bu)Me]$_4$ (**4b**), together with the adopted numbering scheme.

associate is very small at room temperature (ΔH = 72 kJ mol^{-1}; ΔS = 220 J mol^{-1} K^{-1}; ΔG(298 K) = 6.4 kJ mol^{-1}), the tetramer being the more stable species. Recrystallization of **4b** from hexane at −30 °C afforded the pure ethylzinc enolate as colorless crystals, suitable for an X-ray crystal structure determination (vide infra).

Attempts to synthesize the chlorozinc enolates of N,N-disubstituted glycine esters by deprotonation of glycine esters **1** with *N*-(chlorozincio)diisopropylamine was not possible, because the latter compound is not accessible via the reaction of LDA with zinc dichloride. Most probably, a Schlenk-type equilibrium between the zinc monoamide and zinc bisamide (eq 5) lies to far to the side of the symmetric species to allow isolation of the pure *N*-(chlorozincio)diisopropylamine.

Molecular Structure of [EtZnOC(OMe)=C(H)N(t-Bu)Me]$_4$ (4b). The crystal structure of **4b** is monoclinic. The unit cell contains four tetrameric units, each of which contains four crystallographically independent enolate units. Figure 2 presents a view of the tetrameric unit. Atomic coordinates and thermal parameters are listed in Table II. Selected bond distances and angles are listed in Table III.

Although each tetrameric unit has approximate S_4 axial symmetry, this symmetry element does not coincide with a crystallographic symmetry axis. The monomeric zinc enolate units of the tetramer are linked via zinc–oxygen–zinc bridges (average Zn–O–Zn angle of 131.8 (3)°), which form a central, eight-membered Zn_4O_4 ring (puckering

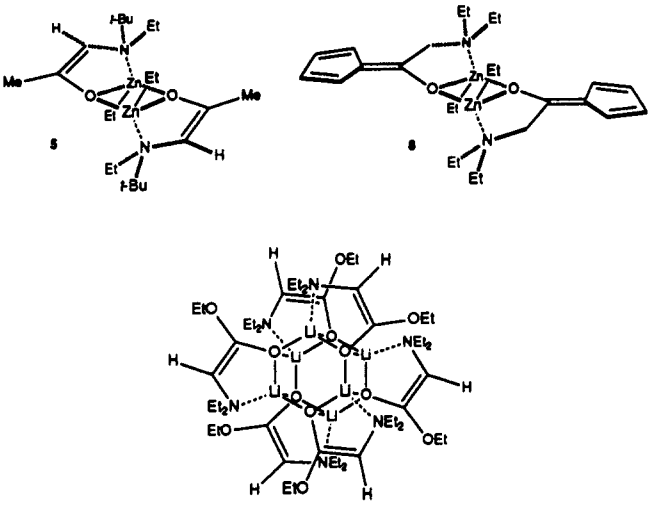


Figure 3. Schematic representations of the solid-state structures of some relevant enolates containing an intramolecular metal–nitrogen coordination.

amplitude Q = 2.561 (3) Å[18]).

The Zn–O bond lengths have normal values (2.028 (5)–2.076 (6) Å) but show a smaller spread than normally found in Zn_2O_2 rings (e.g. in the dimeric ethylzinc enolate of *N*-ethyl-*N*-*tert*-butyl-3-amino-2-propanone, [EtZnOC(Me)=C(H)N(*t*-Bu)Et]$_2$ (**5**) (see Figure 3) these bond lengths are 2.02 (1) and 2.12 (1) Å,[19a] and in dimeric methylzinc (–)-3-*exo*-(dimethylamino)isoborneolate (**6**) they are 1.98 (1) and 2.06 (1) Å).[20] Whereas the larger bond lengths in dimeric **5** and **6** correspond to dative Zn–O bonds,[21] in **4b** the longer Zn–O bonds correspond to the Zn–O bonds within each five-membered chelate ring and the smaller bond lengths to the Zn–O bonds that keep the tetramer together.[22] This suggests that the strength of the latter is responsible for the formation and relatively high stability of the tetrameric zinc enolate structure.

A comparison of the structures of **4b**, **5**, **6**, and the Reformatsky reagent **7** (see Figure 1) reveals an interesting trend (see Table IV): The placement of the negative charge changes from being localized on the alcoholato oxygen in β-amino alcoholate **6**, localized for the greater part on the enolato oxygen in α-amino enolate **5**, or delocalized in α-amino ester enolate **4b** to being primarily localized on the α-carbon in ester enolate **7**. Furthermore, the hybridization of the oxygen changes from sp^3 in **5** and **6** to sp^2 in **4b** and **7**. Consequently, the Lewis basicity of the oxygen decreases in the order **6** ≈ **5** > **4b** > **7**.

These changes have great consequences for both the coordination behavior and the reactivity of these compounds. Whereas in **5** and **6** a strong and a weak Zn–O bond are present, in **4b** the Zn–O bonds are of almost equal strength, and in **7** only one Zn–O bond is present (i.e. with the anion). Enolate **5** is unreactive toward aldehydes and imines,[19c] but both ester enolates **4b** and **7**, containing more electron density on the α-carbon (i.e. a higher nucleophilicity), react smoothly with these substrates.[7,8,11,12,23]

Remarkable in this context is the geometry of the dimeric ethylzinc enolate [EtZnOC(CH$_2$NEt$_2$)=Cp]$_2$ (**8**),[24]

Table II. Fractional Atomic Coordinates and Equivalent Isotropic Thermal Parameters (Å^2) with Esd's in Parentheses for the Non-Hydrogen Atoms of [EtZnO(MeO)C=C(H)N(*t*-Bu)Me]$_4$ (4b)

atom	*x*	*y*	*z*	U_{eq}
Zn(1)	0.47716 (5)	0.22861 (9)	0.15998 (5)	0.0403 (4)
Zn(2)	0.51604 (5)	0.23522 (9)	0.34712 (5)	0.0399 (4)
Zn(3)	0.59460 (5)	0.45626 (9)	0.26947 (5)	0.0389 (4)
Zn(4)	0.40485 (5)	0.46411 (9)	0.22674 (5)	0.0397 (4)
O(1)	0.4037 (3)	0.3160 (5)	0.1918 (3)	0.040 (2)
O(2)	0.2941 (3)	0.3297 (5)	0.1896 93)	0.060 (3)
O(3)	0.5283 (3)	0.1904 (5)	0.2536 (3)	0.042 (2)
O(4)	0.5784 (3)	0.0768 (6)	0.1989 (3)	0.063 (3)
O(5)	0.5549 (3)	0.3798 (4)	0.3425 (3)	0.037 (2)
O(6)	0.5539 (3)	0.3775 (5)	0.4497 (3)	0.057 (3)
O(7)	0.5024 (3)	0.4979 (5)	0.2147 (3)	0.038 (2)
O(8)	0.5636 (3)	0.5864 (5)	0.1573 (3)	0.061 (3)
N(1)	0.3956 (4)	0.1108 (6)	0.1447 (4)	0.047 (3)
N(2)	0.6118 (3)	0.1441 (6)	0.3786 (4)	0.043 (3)
N(3)	0.6068 (4)	0.5824 (6)	0.3445 (4)	0.048 (3)
N(4)	0.3781 (4)	0.5478 (6)	0.1314 (3)	0.046 (3)
C(1)	0.5226 (5)	0.2961 (8)	0.0941 (5)	0.061 (4)
C(2)	0.5764 (6)	0.2364 (9)	0.0667 (6)	0.108 (7)
C(3)	0.3444 (5)	0.2675 (9)	0.1776 (4)	0.045 (4)
C(4)	0.2269 (5)	0.2917 (8)	0.1726 (6)	0.084 (5)
C(5)	0.3369 (5)	0.1715 (8)	0.1541 (5)	0.052 (4)
C(6)	0.4102 (5)	0.0330 (7)	0.1998 (5)	0.060 (4)
C(7)	0.3840 (6)	0.0604 (10)	0.0760 (6)	0.069 (5)
C(8)	0.3254 (6)	–0.0171 (9)	0.0664 (5)	0.091 (6)
C(9)	0.4496 (6)	0.0052 (10)	0.0697 (6)	0.105 (6)
C(10)	0.3688 (6)	0.1457 (9)	0.0248 (5)	0.095 (6)
C(11)	0.4247 (4)	0.2073 (8)	0.3661 (5)	0.053 (4)
C(12)	0.4098 (5)	0.2430 (8)	0.4334 (5)	0.075 (5)
C(13)	0.5754 (5)	0.1199 (8)	0.2589 (5)	0.048 (4)
C(14)	0.6194 (6)	–0.0119 (10)	0.1965 (5)	0.101 (6)
C(15)	0.6179 (5)	0.0932 (7)	0.3163 (5)	0.054 (4)
C(16)	0.6701 (5)	0.2179 (8)	0.3982 (5)	0.069 (5)
C(17)	0.6075 (6)	0.0653 (10)	0.4323 (6)	0.074 (5)
C(18)	0.6756 (6)	0.0071 (9)	0.4553 (5)	0.089 (6)
C(19)	0.5935 (6)	0.1225 (9)	0.4934 (5)	0.096 (6)
C(20)	0.5502 (6)	–0.0106 (9)	0.4069 (6)	0.089 (6)
C(21)	0.6658 (5)	0.3824 (7)	0.2330 (5)	0.050 (4)
C(22)	0.6947 (5)	0.4327 (8)	0.1758 (5)	0.072 (5)
C(23)	0.5701 (5)	0.4337 (8)	0.3980 (5)	0.044 (4)
C(24)	0.5774 (6)	0.4136 (8)	0.5165 (4)	0.084 (5)
C(25)	0.5941 (5)	0.5302 (8)	0.4044 (5)	0.059 (4)
C(26)	0.5507 (5)	0.6612 (7)	0.3233 (7)	0.070 (5)
C(27)	0.6758 (6)	0.6317 (9)	0.3579 (6)	0.071 (5)
C(28)	0.6859 (6)	0.7161 (9)	0.4110 (6)	0.116 (7)
C(29)	0.6891 (6)	0.6772 (8)	0.2920 (8)	0.083 (5)
C(30)	0.7276 (6)	0.5482 (10)	0.3815 (6)	0.092 (6)
C(31)	0.3831 (4)	0.4954 (8)	0.3147 (4)	0.049 (4)
C(32)	0.3146 (5)	0.4580 (9)	0.3284 (5)	0.079 (5)
C(33)	0.4983 (5)	0.5581 (7)	0.1616 (5)	0.043 (4)
C(34)	0.5705 (5)	0.6466 (10)	0.1001 (6)	0.116 (7)
C(35)	0.4421 (5)	0.5857 (8)	0.1203 (5)	0.051 (4)
C(36)	0.3511 (5)	0.4730 (8)	0.0766 (4)	0.061 (4)
C(37)	0.3269 (5)	0.6354 (9)	0.1345 (5)	0.055 (4)
C(38)	0.3061 (5)	0.6922 (8)	0.0676 (5)	0.071 (5)
C(39)	0.2643 (5)	0.5907 (8)	0.1552 (5)	0.076 (5)
C(40)	0.3616 (5)	0.7136 (8)	0.1874 (5)	0.070 (5)

(18) Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354.

(19) (a) van Vliet, M. R. P.; van Koten, G.; Buysingh, P.; Jastrzebski, J. T. B. H.; Spek, A. L. *Organometallics* **1987**, *6*, 537. (b) The ^{1}H and ^{13}C NMR spectra were collected over the whole temperature range (193–353 K) by the authors for comparison to those of the enolate **4b**. (c) When solutions of **5** in toluene are heated (ca. 100 °C) in the presence of benzaldehyde or *N*-benzylidenemethylamine, no reactions, other than decomposition, are observed.

(20) Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028.

(21) (a) We use the term dative bond according to the definition of Haaland:[21b] the bond in a neutral, diamagnetic molecule is dative when the bond cleavage with the lowest increase of energy (in the gas phase or in an inert solvent) is the heterolytic cleavage of the molecule in two neutral, diamagnetic species. (b) Haaland, A. *Angew. Chem.* **1989**, *101*, 1017.

(22) It must be noted that the Zn–O bond lengths are also influenced by steric factors.

(23) Gilman and Speeter were the first to report the reaction of Reformatsky-type reagents with imines affording 2-azetidinones,[23a] and recently a renewed interest in this type of reaction has emerged.[23b] (a) Gilman, H.; Speeter, M. *J. Am. Chem. Soc.* **1943**, *65*, 2255. (b) Palomo, C.; Cossío, F. P.; Arrieta, A.; Odriozola, J. M.; Oiarbide, M.; Ontoria, J. M. *J. Org. Chem.* **1989**, *54*, 5736.

Table III. Selected Bond Lengths (Å) and Angles (deg) with Esd's in Parentheses for 4b

Zn(1)–O(1)	2.061 (6)	Zn(1)–O(3)	2.037 (6)	Zn(1)–N(1)	2.206 (8)
Zn(1)–C(1)	1.973 (1)	Zn(2)–O(3)	2.056 (6)	Zn(2)–O(5)	2.028 (5)
Zn(2)–N(2)	2.231 (7)	Zn(2)–C(11)	1.981 (9)	Zn(3)–O(5)	2.076 (6)
Zn(3)–O(7)	2.030 (6)	Zn(3)–N(3)	2.212 (8)	Zn(3)–C(21)	1.983 (10)
Zn(4)–O(1)	2.034 (7)	Zn(4)–O(7)	2.068 (6)	Zn(4)–N(4)	2.194 (7)
Zn(4)–C(31)	1.974 (8)	O(1)–C(3)	1.325 (12)	O(2)–C(3)	1.348 (12)
O(3)–C(13)	1.299 (12)	O(4)–C(13)	1.357 (12)	O(5)–C(23)	1.311 (12)
O(6)–C(23)	1.372 (12)	O(7)–C(33)	1.321 (11)	O(8)–C(33)	1.380 (12)
N(1)–C(5)	1.458 (13)	N(2)–C(15)	1.458 (13)	N(3)–C(25)	1.462 (13)
N(4)–C(35)	1.434 (13)	C(1)–C(2)	1.521 (16)	C(3)–C(5)	1.322 (15)
C(11)–C(12)	1.535 (14)	C(13)–C(15)	1.346 (14)	C(21)–C(22)	1.547 (14)
C(23)–C(25)	1.329 (15)	C(31)–C(32)	1.533 (13)	C(33)–C(35)	1.312 (14)

O(1)–Zn(1)–O(3)	95.3 (2)	O(1)–Zn(1)–N(1)	82.1 (3)	Zn(3)–O(7)–C(33)	120.3 (6)	Zn(4)–O(7)–C(33)	108.6 (6)
O(1)–Zn(1)–C(1)	115.7 (3)	O(3)–Zn(1)–N(1)	100.6 (3)	Zn(1)–N(1)–C(5)	102.0 (6)	Zn(1)–N(1)–C(6)	109.2 (6)
O(3)–Zn(1)–C(1)	122.1 (3)	N(1)–Zn(1)–C(1)	129.7 (4)	Zn(1)–N(1)–C(7)	113.2 (6)	Zn(2)–N(2)–C(15)	101.8 (6)
O(3)–Zn(2)–O(5)	95.4 (2)	O(3)–Zn(2)–N(2)	82.0 (3)	Zn(2)–N(2)–C(16)	108.9 (6)	Zn(2)–N(2)–C(17)	112.9 (6)
O(3)–Zn(2)–C(11)	114.9 (3)	O(5)–Zn(2)–N(2)	100.3 (3)	Zn(3)–N(3)–C(25)	103.2 (6)	Zn(3)–N(3)–C(26)	108.9 (6)
O(5)–Zn(2)–C(11)	123.7 (3)	N(2)–Zn(2)–C(11)	128.7 (4)	Zn(3)–N(3)–C(27)	114.0 (6)	Zn(4)–N(4)–C(35)	104.0 (6)
O(5)–Zn(3)–O(7)	94.7 (2)	O(5)–Zn(3)–N(3)	81.7 (3)	Zn(4)–N(4)–C(36)	109.5 (5)	Zn(4)–N(4)–C(37)	111.7 (5)
O(5)–Zn(3)–C(21)	116.9 (3)	O(7)–Zn(3)–N(3)	98.5 (3)	Zn(1)–C(1)–C(2)	119.3 (7)	O(1)–C(3)–O(2)	110.6 (9)
O(7)–Zn(3)–C(21)	124.4 (3)	N(3)–Zn(3)–C(21)	128.7 (4)	O(1)–C(3)–C(5)	123.4 (10)	O(2)–C(3)–C(5)	126.1 (9)
O(1)–Zn(4)–O(7)	95.7 (3)	O(1)–Zn(4)–N(4)	99.6 (3)	N(1)–C(5)–C(3)	120.9 (9)	Zn(2)–C(11)–C(12)	118.5 (7)
O(1)–Zn(4)–C(31)	121.4 (3)	O(7)–Zn(4)–N(4)	81.8 (3)	O(3)–C(13)–O(4)	112.1 (8)	O(3)–C(13)–C(15)	124.9 (9)
O(7)–Zn(4)–C(31)	117.1 (3)	N(4)–Zn(4)–C(31)	130.3 (3)	O(4)–C(13)–C(15)	123.0 (9)	N(2)–C(15)–C(13)	119.6 (9)
Zn(1)–O(1)–Zn(4)	131.6 (3)	Zn(1)–O(1)–C(3)	110.0 (6)	Zn(3)–C(21)–C(22)	119.5 (7)	O(5)–C(23)–O(6)	109.6 (8)
Zn(4)–O(1)–C(3)	117.7 (6)	Zn(1)–O(3)–Zn(2)	132.1 (3)	O(5)–C(23)–C(25)	126.6 (9)	O(6)–C(23)–C(25)	123.7 (9)
Zn(1)–O(3)–C(13)	117.8 (6)	Zn(2)–O(3)–C(13)	109.9 (6)	N(3)–C(25)–C(23)	117.9 (9)	Zn(4)–C(31)–C(32)	118.3 (6)
Zn(2)–O(5)–Zn(3)	132.5 (3)	Zn(2)–O(5)–C(23)	118.0 (6)	O(7)–C(33)–O(8)	107.8 (8)	O(7)–C(33)–C(35)	126.0 (9)
Zn(3)–O(5)–C(23)	108.3 (6)	Zn(3)–O(7)–Zn(4)	131.1 (3)	O(8)–C(33)–C(35)	126.2 (9)	N(4)–C(35)–C(33)	119.1 (9)

Table IV. Relevant Bond Lengths (Å) for Compounds Containing a ZnOC(R)CH(R′) Moiety

compd	O–C	C–C	Zn–O, character[a]	Zn–N
6	1.41 (3)[b]	1.58 (3)[b]	1.98 (1),[b] normal 2.055 (5),[b] dative	2.22 (3)[b]
5	1.40 (2)	1.27 (3)	2.02 (1), normal 2.12 (1), dative	2.21 (2)
4b	1.314 (6)[c]	1.327 (7)[b]	2.065 (4),[b] normal 2.032 (2),[b] normal	2.211 (8)
7	1.31 (2)	1.41 (2)	2.02 (1),[c] dative	

[a] For the definition of normal and dative bonds, see Haaland.[21] [b] The average of comparable bonds within one molecule. [c] Because of the higher Lewis acidity of Zn in **7**, i.e. Br–Zn vs alkyl–Zn, the dative bonds are expected to be shorter than in **4b**, **5**, and **6**.[21]

wherein the carbon–carbon double bond is exo with respect to ZnOCCN chelate ring (Figure 3).

The characteristic features observed for **4b** are also present in **8**, i.e. a short enolato C–O bond of 1.322 (3) Å and an intramolecular Zn–O bond that is longer (2.075 (2) Å) than its intermolecular counterpart (2.041 (2) Å). However, the bridging oxygen atoms in **8** are obviously sp^3 hybridized (the angles subtended at oxygen are 98.99 (7), 113.0 (2), and 125.3 (2)°, respectively). Most likely, the electron-withdrawing effect of the fulvene substituent in **8** is responsible for the short enolato carbon–oxygen bond, similar to the methoxy substituent in **4b**.

A comparison of the solid-state structure of the hexameric lithium enolate of *N,N*-diethylglycine ethyl ester (see Figure 3) with that of **4b** reveals some interesting aspects.[25] The geometries of the enolate anions are virtually the same, but the structure of the lithium enolate is based on a central Li_6O_6 hexagonal prism (consisting of ionic Li–O bonds), with sp^3-hybridized bridging oxygen atoms. Since during the synthesis only part of the lithium enolate is formed as a hexameric associate, the formation of the LiOCCN chelate ring apparently lowers the energy of the enolate only to a small extent; i.e., the formation of the intramolecular Li–N bond has a minor stabilizing effect.

The zinc atoms in **4b** have a distorted tetrahedral coordination geometry, with three small (≈82, 95, and 100°) and three large angles (≈116, 123, and 129°), similar to that found in **5** and **6**. The zinc–carbon distances (average 1.978 (3) Å) are in good agreement with those reported for **5**, **6**, and **8** (1.99 (2), 1.97 (2), and 1.957 (3) Å, respectively). The intramolecular Zn–N coordination in **4b** results in the formation of essentially planar five-membered ZnOCCN chelate rings, which are oriented at angles ranging from 60.9 (4) to 77.9 (4)° with respect to each other to form an overall propeller-like structure. The values of the zinc–nitrogen dative bond lengths (average 2.211 (8) Å) differ little from those found for other zinc compounds containing an intramolecularly coordinated amino group, e.g. 2.21 (2) Å for **5**, 2.19 (2) and 2.25 (2) Å for **6**, and 2.121 (2) Å for **8**. As a result of the intramolecular Zn–N coordination, the configuration of the enolate **4b** in the solid state is, as we had anticipated, *Z*.

Configuration of Lithium and Zinc Enolates of N,N-Disubstituted Glycine Esters in Solution. The configuration of enolates can be determined by quenching them with a trialkylsilyl chloride to form monomeric silyl enol ethers; the configurations of these can be easily assigned by NMR spectroscopy.[26] The reaction of ethylzinc enolate **4b** with trimethylsilyl chloride at both room temperature and 70 °C afforded the same (*Z*)-trimethylsilyl enol ether **9c** (for R, R^1, and R^2, see Table V) as a single isomer. Apparently no *E*/*Z* isomerization takes place in solution, and the dimeric associate of **4b**, which is almost exclusively present at 70 °C in solution, also has the *Z*-configuration.

Quenching of the in situ prepared chlorozinc enolates **3** with trimethylsilyl chloride was used to get an indication

(24) Jastrzebski, J. T. B. H.; Boersma, J.; van Koten, G.; Smeets, W. J. J.; Spek, A. L. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 263.

(25) Jastrzebski, J. T. B. H.; van Koten, G.; van de Mieroop, W. F. *Inorg. Chim. Acta* **1988**, *142*, 169.

(26) (a) House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1971**, *36*, 2361. (b) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, *25*, 495.

(27) Dr. R. O. Duthaler of Ciba-Geigy AG, Basel, Switzerland, is kindly acknowledged for sharing his results with us. The NOE difference ^1H NMR spectra he has obtained confirmed that we have correctly assigned the *E*-configuration of trimethylsilyl enol ether **9e**.

Table V. *E/Z* Ratios for Several in Situ Prepared Lithium and Zinc Enolates of N,N-Disubstituted Glycine Esters

				Li		Zn	
product	R^1	R^2	R	yield, %[a]	*E/Z*[b]	yield, %[a]	*E/Z*[b]
9a	Me	Me	Et	80	30/70	60	4/96
9b	Et	Et	Et	88	35/65	60	8/92
9c	*t*-Bu	Me	Me	84	52/48	80	<2/>98[c,d]
9d	Ph	Me	Me	80	92/8	82	2/98
9e[e]	Me_2Si	$SiMe_2$	Et	95	>98/<2[c,f]	60–95[g]	90/10[g]

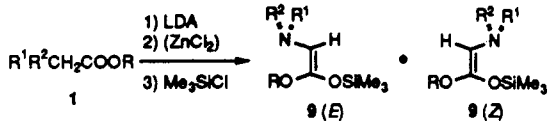
[a] Isolated yield. [b] Determined by ^1H NMR integration of the characteristic proton signals. [c] Only one isomer observed by ^1H NMR spectroscopy. [d] Irradiation of the enolate proton resulted in NOE enhancement of the OCH_3 (3.4%), NCH_3 (1.2%), and $NC(CH_3)_3$ (3.6%) signals only, confirming the *Z*-configuration of this product. [e] Reaction carried out at −50 °C because of the instability of the enolates **2e** and **3e** above this temperature (see Discussion). [f] Irradiation of the enolate proton resulted in NOE enhancement of $Si(CH_3)_3$ and $Si(CH_3)_2$ (3.9%) only, confirming the *E*-configuration of this product.[27] [g] Solvent dependent.

Table VI. Base and Solvent Effects on the Product Distribution (%) of the Quenching Reaction of $ClZnO(EtO)C{=}C(H)N(Me_2)SiCH_2CH_2SiMe_2$ (3e) with Me_3SiCl

entry	base	solvent	1g	*E*-9e	*Z*-9e[a]
1	LiTMP	Et_2O	30	35	35
2	LDA	Et_2O	35	55	10
3	LiHMDS	Et_2O	90	10	<2[b]
4	LDA	THF	<2[b]	93	7

[a] Determined by integration of the ^1H NMR signals of characteristic protons. [b] Not observed by ^1H NMR spectroscopy.

about the configuration of these enolates in solution (eq 6). Except for **9e**, all reactions were carried out at room temperature in benzene as well as in THF.



(6)

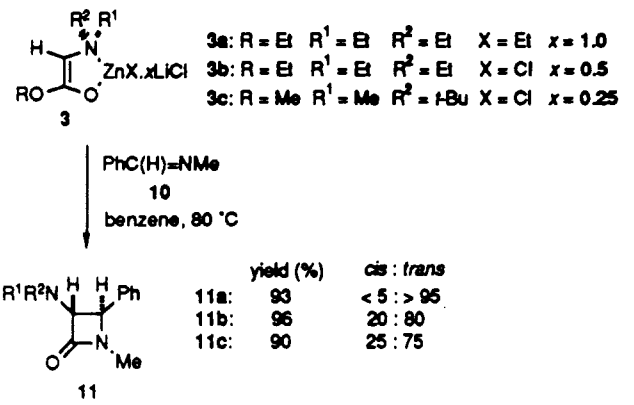
With the exception of the zinc enolate of 2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane-1-acetic acid ethyl ester (**1g**) (see Discussion), all the zinc enolates **3** are, within experimental error, present as *Z*-isomers in solution, irrespective of whether they are dissolved in an apolar (benzene) or in a (weakly) polar solvent (THF). The product distribution for the reaction of zinc enolate **3e** with trimethylsilyl chloride, however, depends on both the lithium base used for deprotonation and the solvent (Table VI).

Surprisingly, despite rigorously nonhydrolytic workup, considerable amounts of starting ester **1g** are isolated The amount of ester **1g** appears to increase with decreasing base strength (LiTMP → LiHMDS), and furthermore the *E/Z* ratio changes from 1/1 to ca. 10/1. The strong solvent effect is striking; whereas in the more polar solvent, THF, the silyl enol ether **9e** is isolated exclusively (entry 4), in the less polar diethyl ether a considerable amount of ester **1g** is isolated (entry 2). Besides that, a small effect on the *E/Z* ratio is observed: in THF more of the zinc enolate **3e** is present in the *E*-configuration than in diethyl ether.

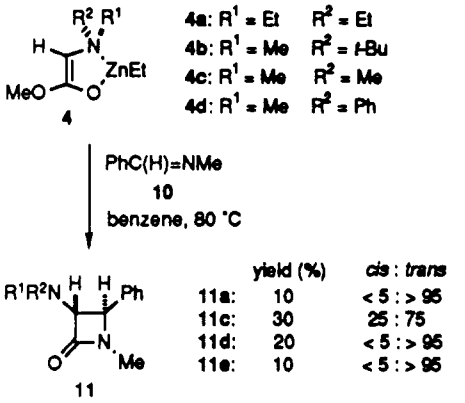
To enable a comparison between the properties of the chlorozinc enolates **3** and those of the parent lithium enolates of N,N-disubstituted glycine esters, in situ prepared lithium enolates (**2**) were also quenched with trimethylsilyl chloride (eq 6).

The lithium enolates **2** are present as a mixture of *E*- and *Z*-isomers (see Table V). This implies that the Li–N coordination is much weaker than the Zn–N coordination, because the presence of the MOCCN chelate ring is the driving force for the formation of *Z*-enolates (see Discussion). Furthermore, the amount of *E*-isomer present in solution is somewhat solvent dependent, e.g. for **2a** in benzene *E/Z* = 30/70 but in THF this ratio is 60/40.

Scheme II



Scheme III

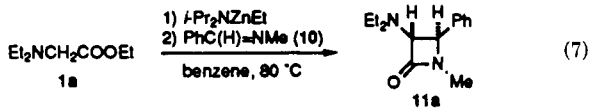


Reactions of Pure α-Amino Organozinc Ester Enolates with Imines. Reactions of the isolated chlorozinc enolates **3a–c** with *N*-benzylidenemethylamine (**10**) afford, like those of the in situ prepared chlorozinc enolates (see eq 1), 3-amino-2-azetidinones (**11**) in excellent yields. The trans stereoselectivity is similar for the reactions of both the isolated and the in situ prepared zinc enolates (Scheme II), indicating that in both cases the reactive species have a similar structure.

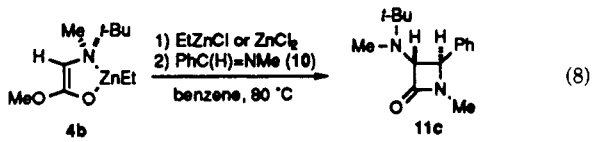
In contrast, reactions of the isolated ethylzinc enolates **4a–d** with imine **10** resulted only in low conversions (Scheme III). These low conversions are a consequence of the poor stability of the ethylzinc enolates at elevated temperatures; e.g., for **4b** $t_{1/2}$ is 8 min at 60 °C in benzene, whereas the rate constant for the reaction of **4b** with imine **10** is of a similar order.[28]

(28) Monitoring the reaction of zinc enolate **4b** with imine **10** by ^1H NMR spectroscopy revealed that the rate of decomposition of **4b** and the reaction rate of **4b** to afford 2-azetidinone **11c** are of the same magnitude. $t_{1/2}$ for **4b** was estimated to be ca. 8 min, deduced from ^1H NMR data obtained on samples of pure **4b** in benzene-d_6 at 60 and 70 °C.

However, high yields of 2-azetidinones 11 are obtained when the ethylzinc enolates 4 are not isolated but reacted in situ with an appropriate imine. For example, 1-methyl-3-(diethylamino)-4-phenyl-2-azetidinone (11a) was isolated in 80% yield with an excellent diastereoselectivity (cis/trans = 4/96) after addition of imine 10 to a benzene solution containing ethylzinc enolate 4c (eq 7).



(7)



(8)

Alternatively, the ethylzinc enolates 4 can be stabilized by addition of a suitable Lewis acid, e.g. EtZnCl or $ZnCl_2$ (but not Et_2Zn or LiCl; see Discussion). Consequently, 1/1 mixtures of EtZnCl or $ZnCl_2$ and ethylzinc enolate **4b** give a clean reaction with imine 10, affording 1-methyl-3-(*tert*-butylmethylamino)-4-phenyl-2-azetidinone (11c) in good yields (eq 8).

Discussion

General Considerations. The presence of a potentially coordinating tertiary amine group in the organozinc enolates of N,N-disubstituted glycine esters has far-reaching consequences for all aspects of the chemistry of these enolates. The high strength of Zn–N coordination bonds,[29] together with the chelating position of the amino nitrogen, is responsible for the stability of these enolates, which enables their structural characterization, and for the high stereoselectivity observed in their reaction with imines.[11,12]

The Zn–N bond strength is influenced by the electronic properties of the amino-N substituents. Electron-donating groups will increase the electron density, and therefore the Lewis basicity of the nitrogen atom, and hence a stronger Zn–N coordination will result. Electron-withdrawing groups have an opposite effect and will result in a weaker Zn–N coordination. Accordingly, the Zn–N coordination is expected to decrease in the order NMe_2 (**a**) ~ NEt_2 (**b**) ~ N(*t*-Bu)Me (**c**) > N(Ph)Me (**d**) ≫ $N(Me_2)$-$SiCH_2CH_2SiMe_2$ (**e**).

In the remaining part of this discussion the influence of the presence and the strength of the Zn–N coordination on various aspects of enolate chemistry and reactivity will be discussed.

Formation Reactions of Organozinc Enolates. Reactions of *N*-(ethylzincio)diisopropylamine with N,N-disubstituted glycine esters **1a–d** are relatively slow (24–48 h) compared to the reactions of LDA with the same esters, which are completed within a few minutes. Because of the covalent character of the zinc–nitrogen bond, the ethylzinc amide is less basic than the lithium amide, the basicity of the zinc amide most probably being of the same magnitude as that of the zinc enolate.[17] The fact that the reactions of α-amino esters **1a–d** with the ethylzinc amide nevertheless do go to completion (i.e. for esters **1a–c**; vide infra) is ascribed to intramolecular Zn–N coordination in the zinc enolate products **4a–d**.

Attempts to isolate pure chlorozinc enolates 3 of N,N-disubstituted glycine esters via transmetalation of lithium enolates 2 with zinc dichloride were not completely successful, because the isolated products contained inorganic impurities that could not be separated from the desired chlorozinc enolates. This may well be due to the nature of the enolates themselves (vide infra), since Seebach has shown that lithium enolates form stable dinuclear species with bridging halogen or alkoxy groups upon addition of lithium halides or alkoxides.[5]

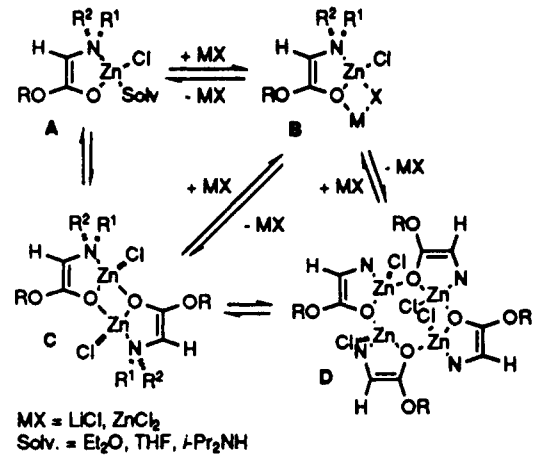


Figure 4. Schematic representations of the structures of chlorozinc ester enolate species, and equilibria between these species, that may be present in solutions.

Enolate Species That Are Present in Solution. Chlorozinc Enolates 3. Several species may be formed during the transmetalation of lithium (or sodium) enolates with zinc dichloride. Figure 4 shows a schematic representation of some enolate species (A–D) that may be present in solutions (or even in the solid state) of chlorozinc enolates 3.

A is a monomeric chlorozinc enolate, solvated to complete the coordination sphere around zinc, B is a heterodinuclear species, C is a dimeric chlorozinc enolate, and D is a tetrameric associate. Also, more highly associated species may be present. Furthermore, all these species may be interrelated by various equilibria as indicated in the figure. Monomeric species A have until now not been identified in metal enolate chemistry and seem unlikely because of the tendency of Lewis acidic metals to form higher associates through bridging oxygen or halogen atoms.[5,30] Dinuclear species of type B are not unprecedented and have been shown to exist in the case of lithium enolates.[5,31] Recently, we have characterized a dialkylaluminum ester enolate with a B-type structure as well as an dialkylaluminum ester enolate of type C.[32] Dimeric and tetrameric species of types C and D are common for organozinc coordination compounds and main-group metal enolates. As shown above for ethylzinc enolate **4b**, both dimeric and tetrameric species may be present in solution.

The elemental analysis of the isolated products **3a–d** all seem to indicate that at least part of the product is present as mixed aggregates of type B, MX being either zinc dichloride or lithium chloride. In the latter case the species might actually be present as zincates, $[Li]^+[RZnX_2]^-$. Triorganozincates $[Li]^+[R_3Zn]^-$ or $[MgX]^+[R_3Zn]^-$ have

(29) (a) According to the hard–soft acid–base (HSAB) principle,[29b] the "hard" zinc ions prefer "hard" ligands (N, O) and form strong coordination bonds with these ligands. (b) Pearson, R. G. *J. Am. Chem. Soc.* **1963**, *85*, 3533.

(30) For reviews, see for example: (a) Boersma, J. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: New York, 1982; Chapter 16, pp 824–851. (b) Setzer, W. N.; Schleyer, P. v. R. *Adv. Organomet. Chem.* **1986**, *24*, 354–450. (c) Oliver, J. P. *Ibid.* **1977**, *15*, 235–268.

(31) Bertrand, J.; Gorrichon, L.; Maroni, P.; Meyer, R.; Viteva, L. *Tetrahedron Lett.* **1982**, *23*, 1901.

(32) van der Steen, F. H.; van Mier, G. P. M., Spek, A. L.; Kroon, J.; van Koten, G. *J. Am. Chem. Soc.*, in press.

been proposed as active species in the 1,4-addition to α,β-unsaturated ketones.[33a] Recently, organomagnesiates $[M]^+[R_2MgOR]^-$ (M = Na, K) have been shown to exist in solution.[33b] The remaining part of products **3a–d** is most likely present in the form of dimeric (C) and/or tetrameric associates (D).

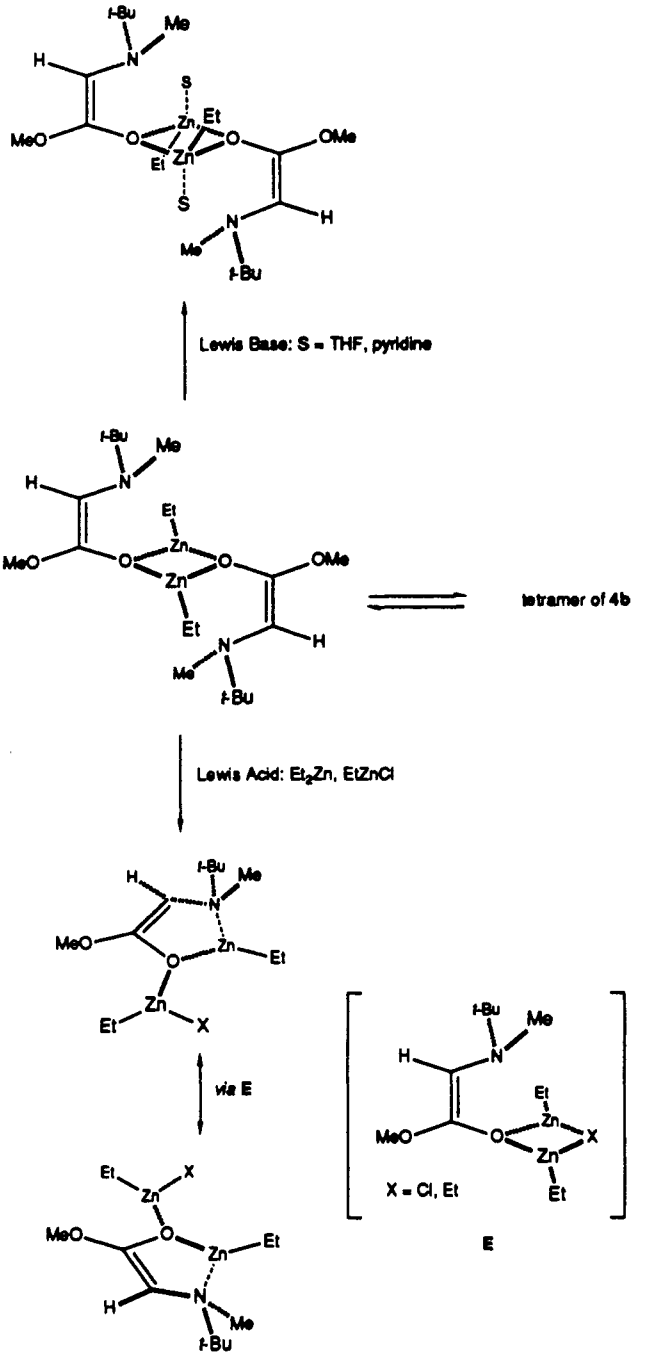
Ethylzinc Enolates 4. As discussed above for the chlorozinc enolates **3**, the ethylzinc enolates **4** also seem to be present as mixtures of several aggregates, e.g. dimers, tetramers, and hexamers, since the ^1H and ^{13}C NMR spectra of these ethylzinc enolates showed multiple and mostly broad signals. Fortunately, the NMR spectra of the ethylzinc enolate **4b** of *N*-methyl-*N*-*tert*-butylglycine methyl ester showed only two sets of sharp resonance patterns that could be identified as belonging to a dimeric and a tetrameric associate by correlation with cryoscopic data. The methylene protons of the ethylzinc fragment in the tetramer of **4b** are diastereotopic and appear as an $AB(X)_3$ pattern with a remarkable large chemical shift difference of 0.47 ppm. This diastereotopicity indicates that the zinc atom has become a stable chiral center by coordination of the amino nitrogen to zinc. In the dimer of **4b** the methylene protons of the ethylzinc fragment are not diastereotopic and appear as a single quartet. Therefore, the Zn–N nitrogen coordination in this dimer is either weak, giving rise to a rapid on–off movement of the nitrogen, or is totally absent. Since in the complete absence of Zn–N coordination the dimeric enolate would probably decompose at room temperature (vide infra), we assume the occurrence of a dynamic process, involving a rapid coordination/decoordination of the amino nitrogen to zinc.

The behavior of dimeric **4b** in solution is in striking contrast to that of the ethylzinc enolate of 3-(ethyl-*tert*-butylamino)-2-propanone (**5**), which is also a dimeric associate with intramolecular Zn–N coordination.[19a] The methylene protons of the ethylzinc fragment in **5** remain diastereotopic ($\Delta\delta$ = 0.03 ppm) between 203 and 343 K,[19b] and this indicates that the Zn–N coordination in **5** is stronger than in dimeric **4b**. As the Lewis basicity of the nitrogen atoms in **5** and dimeric **4b** are almost identical, the different Zn–N bond strengths must be caused by a different Lewis acidity of the zinc atoms; i.e., the zinc center in **4b** has the weaker Lewis acidity.

Effect of Lewis Acids and Bases on the Structure in Solution of Ethylzinc Enolate 4b. Although the addition of a weak Lewis base like THF to a solution of **4b** in benzene or toluene has only a small effect on the dimer/tetramer ratio, in the presence of a stronger Lewis base, like pyridine, only one set of resonances is observed by NMR spectroscopy (see Table VII). This most likely belongs to a dimeric species in which the intramolecular Zn–N coordination is replaced by intermolecular Zn–pyridine coordination and suggests that the original tetramer/dimer equilibrium is shifted to the side of the dimer (Scheme IV).

The addition of Lewis acids has some remarkable consequences. Addition of diethylzinc to a solution of **4b** in toluene did not affect the dimer/tetramer ratio, irrespective of the amount of added diethylzinc, and we may therefore conclude that tetrameric **4b** remains the most stable species present in solution. While the NMR spectra of these mixtures show that the ethyl groups of tetrameric **4b** remain unchanged, the resonances of the ethyl groups bonded to zinc in dimeric **4b** and those of diethylzinc

Scheme IV



become equivalent on the NMR time scale. These observations indicate that a rapid exchange of ethyl groups between two (or more) zinc centers occurs, probably involving the intermediate species E (Scheme IV). Noyori et al. have proposed a similar structure for the active intermediate in the enantioselective alkylations of aldehydes with dialkylzinc reagents that are catalyzed by chiral β-amino alcohols.[20]

The fact that the ethyl group bonded to zinc in tetrameric **4b** does not exchange with those of added diethylzinc implies that the Lewis acidity of diethylzinc is not sufficient to break down the tetrameric unit. However, when ethylzinc chloride, which is a stronger Lewis acid than diethylzinc, is added to a solution of **4b** in benzene, only one set of enolate anion and ethylzinc signals is observed by NMR spectroscopy, most likely belonging to an enolate species to which ethylzinc chloride is coordinated. The resonances are slightly broadened at room temperature but

(33) (a) Tückmantal, W.; Oshima, K.; Nozaki, H. *Chem. Ber.* **1986**, *119*, 1581. (b) Hanawalt, E. M.; Richey, G., Jr. *J. Am. Chem. Soc.* **1990**, *112*, 4983.

Table VII. ^1H and ^{13}C Chemical Shifts[a] (ppm) for EtZnO(MeO)C=C(H)N(*t*-Bu)Me (4b) and EtZnO(Me)C=C(H)N(*t*-Bu)Et (5) in the Presence of Lewis Acids and Bases

Compound (Additive)	$HC=C$	OCH_3 (CH_3)	NCH_3 (NCH_2)	$NC(CH_3)_3$	(NCH_2CH_3)	$ZnCH_2CH_3$	$ZnCH_2CH_3$
^1H NMR							
4b tetramer	3.83	3.31	2.34	1.20		1.74	0.62[b]
dimer	4.02	3.27	2.40	1.12		1.63	0.65
(THF)	3.82	3.30	2.32	1.17		1.66	0.57[b]
	4.02	3.29	2.32	1.10		1.57	0.58
(pyridine)	4.28	3.75	2.01	1.16		1.60	0.71
(Et_2Zn)	3.84	3.32	2.34	1.21		1.74	0.62[b]
	4.03	3.28	2.39	1.12		1.20	0.20
(EtZnCl; 296 K)	3.70	3.22[c]	2.25	0.82[c]		1.44[c]	0.67[c]
(EtZnCl; 333 K)	3.77	3.22	2.31	0.89		1.37	0.60
5 dimer	4.15	1.92	2.36[b]	1.13	1.09	1.60	0.52[b]
(Et_2Zn; 296 K)	4.15	1.92	2.36[b]	1.13	1.09	1.60[c]; 1.14	0.52[c]; 0.13
(Et_2Zn; 343 K)	4.20	1.88	2.50[b,c]	1.11	1.04	1.22[c]	0.25[c]
^{13}C NMR							
Compound (Additive)	$HC=C$	$HC=C$	OCH_3 (CH_3)	NCH_3 (NCH_2)	$NC(CH_3)_3$ (NCH_2CH_3)	$ZnCH_2CH_3$	$ZnCH_2CH_3$
4b tetramer	163.86	82.17	53.76	41.00	58.20; 26.01	13.67	2.99
dimer	165.17	84.96	53.11	42.20	58.70; 26.01	13.41	0.42
(Et_2Zn)	163.86	82.15	53.69	40.89	58.19; 26.01	13.64	2.99
	165.00	85.10	53.02	42.15	58.66; 26.01	10.95[c]	5.53[c]
(EtZnCl)	163.00	84.95	54.62	41.83[c]	60.83; 25.38[c]	11.79[c]	4.71[c]
5 dimer	160.0	104.6	20.8	45.0	58.6 ; 26.5 12.4	13.3	1.8
(EtZnCl)	159.08	104.66	20.92	45.07	58.65; 26.59 12.55	13.48; 10.49[c]	1.97; 6.7[c]

[a] Spectra recorded in benzene-d_6 at 296 K, unless stated otherwise. [b] Diastereostopic signals. [c] Broad signals.

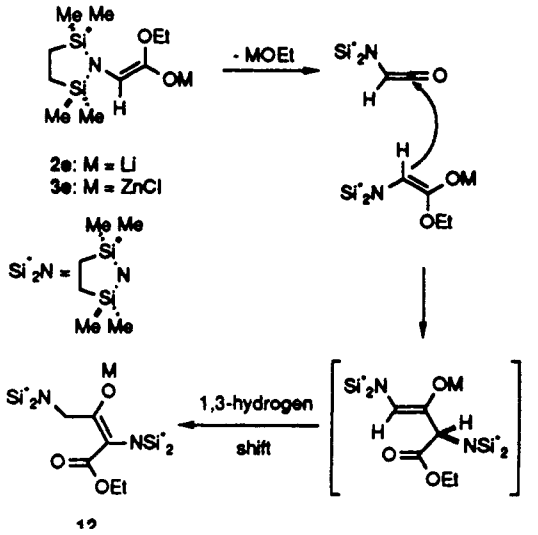
become sharp upon heating at 333 K. This indicates that at room temperature the process of Zn–N coordination/decoordination is not yet in the fast-exchange limit.

The fact that no exchange of ethyl groups between added diethylzinc and ethylzinc enolate **5** (with a strong Zn–N coordination) is observed at room temperature indicates that the exchange of ethyl groups between the zinc centers is possible in dimeric **4b** only, because of the weak Zn–N coordination in this associate (vide supra).

The presence of strong Zn–N coordination in **5** is supported by the fact that, in the presence of ethylzinc chloride, diastereotopicity of the methylene protons of the diethylamino group is observed in the ^1H NMR spectrum at room temperature and that, moreover, two sets of resonances of ethylzinc groups are present (Table VII). At 313 K the ethylzinc resonances start to broaden, and they coalesce at 343 K. The resonances of the diastereotopic methylene protons of the diethylamino group start to broaden at 328 K but do not completely coalesce at 343 K. Our interpretation is that upon heating the process of coordination/decoordination of the amino nitrogen to zinc is accelerated and a slower exchange process of ethyl groups between the different zinc atoms starts to take place.

Stability of the α-Amino Organozinc Ester Enolates. Although ethylzinc enolates **4a–c** are stable at room temperature, upon heating of solutions of **4a–c** to 60 °C the formation of self-condensation products is observed (vide infra).[28] In solution, ethylzinc enolate **4d** decomposes slowly already at room temperature. In contrast, solutions of chlorozinc enolates **3a–d** can be heated to 80 °C without any observable decomposition. Note, however, that **3e** decomposes rapidly at room temperature and even when stored at −30 °C in solution, both **3e** and the lithium

Scheme V



enolate **2e** are completely converted to self-condensation products within several days. The less stable zinc enolate **3e** decomposes into several self-condensation products, while decomposition of **2e** affords a single product (**12**) only, in almost quantitative yield. A possible route for the formation of **12** is shown in Scheme V and most likely starts by elimination of metal alkoxide from the ester enolate to form a ketene,[34] which then reacts via an aldol-type condensation with a second equivalent of enolate to form aldolates that in principle may undergo further aldol condensations.

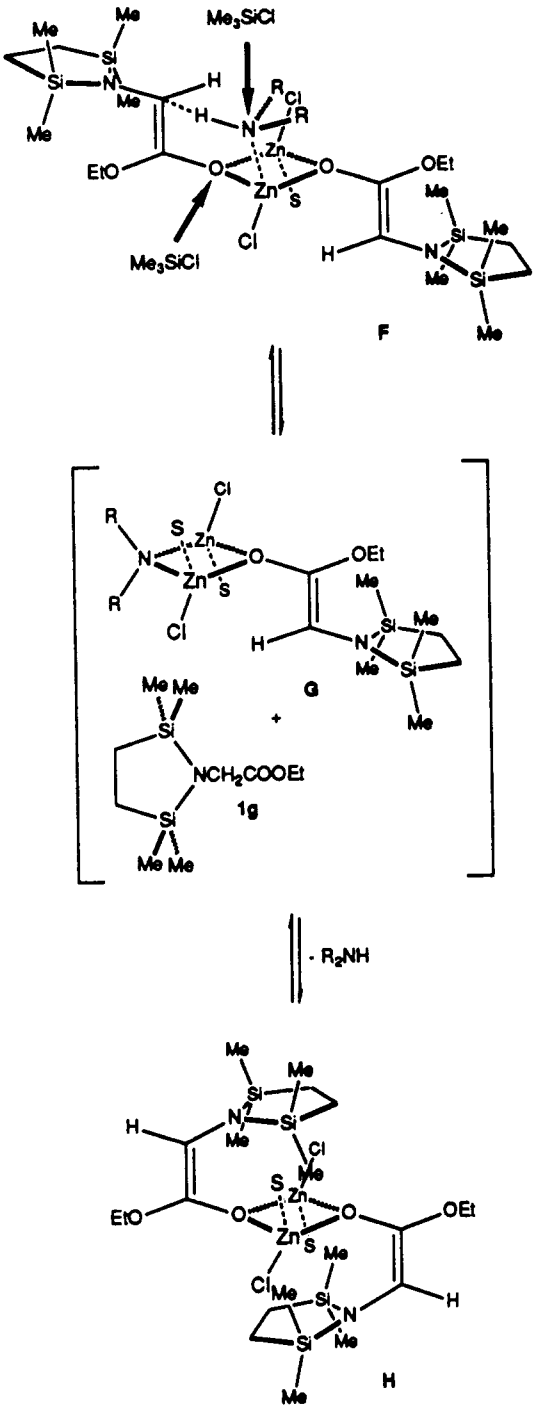
The low stability of **3e** is most probably associated with the absence of intramolecular Zn–N coordination, due to the poor Lewis basicity of the amino-nitrogen atom. This is supported by a crystal structure determination of an organic compound containing the 2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane ring (of **3e**) that reveals that the nitrogen has a planar configuration, i.e., is sp^2-hybridized.[11d] This configuration is stabilized as a result of delocalization of the electron density through interaction of the filled p_z orbital on the nitrogen atom with empty d orbitals on the silyl atoms. Consequently this nitrogen atom will be a very poor Lewis base.

Aspects of the Stereoselectivity of the Reactions of Zinc Ester Enolates with Imines. The present results are in accord with our previous assumption that reactions of zinc enolates **3a–e** with imines occur with an excellent trans stereoselectivity because (in solution) zinc enolates **3** (and **4**) have a *Z*-configuration, imposed by the presence of intramolecular Zn–N coordination.[11c,12] However, in the present study we have also found that zinc enolate **3e** is an exception to this generalization, since in this enolate Zn–N coordination is absent and (in solution) the bulk of enolate **3e** has the *E*-configuration. Nevertheless, reactions of **3e** with imines still proceed with a high trans stereoselectivity,[11b] which indicates that the *Z*-isomer of **3e** must be the reactive species. An possible explanation for our observations is given in Scheme VI and is supported by the results of the quenching reactions (see Table VI).

Both the *E*-isomer (complex F) as well as the *Z*-isomer (complex H) of the zinc enolate **3e** may contain coordinated solvent molecules (S = THF, Et_2O, $(i\text{-}Pr)_2NH$, TMP, HMDS, etc.). Since the *E*-enolate has more space to ac-

(34) (a) Vaughan, W. R.; Bernstein, S. C.; Lorber, M. E. *J. Org. Chem.* **1965**, *30*, 1790. (b) Vaughan, W. R.; Knoes, H. P. *Ibid.* **1970**, *35*, 2394. (c) Sullivan, D. F.; Woodbury, R. P.; Rathke, M. W. *Ibid.* **1977**, *42*, 2038.

Scheme VI



commodate solvent molecules than the *Z*-enolate, sterically demanding secondary amines are likely to be coordinated to the *E*-enolate (as represented in complex F) rather than to the *Z*-enolate.

Lithium enolates containing coordinated secondary amines have been isolated and structurally characterized.[35] Furthermore, it was shown that upon hydrolysis of lithium enolates containing coordinated diisopropylamine, the transferred proton originates from the complexed secondary amine rather than from the hydrolyzing agent.[35] In the same paper it was also shown that addition of other electrophiles, e.g. methyl iodide or benzyl bromide, to lithium enolates containing complexed diisopropylamine afforded mixtures of alkylated enolates and tertiary amines.

Hence, upon addition of trimethylsilyl chloride to zinc enolate **3e** two reaction paths are possible, as indicated by the arrows in complex F. One is an attack on the enolato oxygen to give the expected trimethylsilyl enol ether **9e**; the other is attack on the coordinated secondary amine to give the starting ester **1g** (through proton transfer of the amine to the α-carbon atom of the enolate) and a tertiary amine. Indeed, when LiTMP was used as base, careful analysis of the isolated products revealed the presence of small amounts of the tertiary amine 1-trimethylsilyl-2,2,6,6-tetramethylpiperidine. In a strongly coordinating solvent, like THF, the amine is replaced by a solvent molecule and the quenching reaction yields trimethylsilyl enol ether **9e** as a single product (entry 4 in Table VI).

The amount of complexed secondary amine is determined by the Lewis basicity as well as the bulkiness of these amines. Hexamethyldisilazane, being the weakest Lewis base and bulkiest amine, has the least coordinating abilities and hence should only form small amounts of complexes like F. However, in the presence of this amine the amount of starting ester **1g** that is isolated from the quenching reaction with trimethylsilyl chloride is exceptionally high. An additional factor that has to be taken into account is the Brønsted base strength of the amides.[36] In the presence of the most acidic amine, hexamethylsiliazane, the equilibria as shown in Scheme VI will be shifted more to the side of the free ester **1g** than in the presence of the less acidic diisopropylamine and 2,2,6,6-tetramethylpiperidine.

In the case of zinc enolates, the existence of these equilibria is not unprecedented: when secondary amines are added to a solution of the ethylzinc enolate of 2,2-dimethyl-3-pentanone in benzene, a considerable amount of enolate is protonated to form free 2,2-dimethyl-3-pentanone and an ethylzinc amide.[17] An intermediate in (or product of) this process may well be a mixed zinc amide-/zinc enolate species G (Scheme VI). Recently, such an mixed lithium aggregate has been isolated and structurally characterized.[37]

A further implication of the existence of the equilibria presented in Scheme VI is the fact that in the presence of secondary amines the *E*- and *Z*-isomers of zinc enolate **3e** can easily isomerize. The significance of this fact with regard to the reactions of zinc ester enolate **3e** with imines will be discussed in a forthcoming paper.[12]

Concluding Remarks

Pure α-amino ethylzinc ester enolates **4** can be obtained by deprotonation of N,N-disubstituted glycine esters **1** with *N*-(ethylzincio)diisopropylamine.

The synthesis of α-amino chlorozinc ester enolates **3** by transmetalation of the alkali-metal enolate precursors **2** with zinc dichloride does not give pure chlorozinc enolates, because of formation of mixed aggregates.

The stability and reactivity of zinc ester enolates can be tuned by influencing the Lewis acidity of the zinc atoms and/or the Lewis basicity of the α-amino-nitrogen atoms. A strong Zn–N coordination results in a good thermostability of the zinc enolates but a poor reactivity because of a high energy of activation for reaction with imines. This activation energy is mainly determined by the energy required to break the Zn–N coordination bond, resulting in

(35) Laube, T.; Dunitz, J. D.; Seebach, D. *Helv. Chim. Acta* **1985**, *68*, 1373.

(36) (a) The pK_a of hexamethyldisilazane (29.5) is several units higher than that of diisopropylamine (35.7) and 2,2,6,6-tetramethylpiperidine (37.3).[36b] (b) Fraser, R. R.; Mansour, T. S. *J. Org. Chem.* **1984**, *49*, 3442.

(37) Williard, P. G.; Hintze, M. J. *J. Am. Chem. Soc.* **1987**, *109*, 5539.

a free coordination site required to accommodate the nitrogen of the imine, which is then sufficiently activated.[12] The Lewis acidity of the zinc atoms also influences the rate of reaction with imines, which coordinate more readily to a strong Lewis acid (e.g. a ClZn center) than a weak one (e.g. a EtZn center).

For enolate **3e**, in which the Zn–N coordination bond is absent, the present of a rapid equilibrium between the *E*- and *Z*-isomers is likely, whereas for the other zinc ester enolates reported in this paper, containing a (strong) Zn–N coordination bond, the configuration is exclusively *Z*.

We have shown that the *Z*-enolates are the reactive species,[38] being most likely dimeric enolates (type C in Figure 4) or dinuclear monomeric species (type B in Figure 4), in their reactions with imines and that these reactions are chelation controlled. On the basis of the structural aspects of the zinc enolates described in this paper, we have proposed two highly ordered transition states that allow an explanation of the stereoselectivities of the reactions of α-amino zinc ester enolates with imines that we have observed thus far.[11a-c,12]

Furthermore, a comparison of the solid-state structures of ethylzinc ester enolate **4b**, ethylzinc enolate **5**, and Reformatsky reagent **7** has shown that the reactivity of enolates in aldol-type reactions is governed by delocalization of the charge density; i.e., compound **5**, where the negative charge is mainly localized on the enolato oxygen, is unreactive toward aldehydes and imines, whereas **4b** and **7**, where the negative charge is distributed along the skeleton of the whole anion (**4b**) or mainly located on the α-carbon (**7**), are highly reactive toward aldehydes and imines.

The insights obtained through our structural studies enabled us to develop a highly enantioselective synthesis of 3-amino-azetidinones.[11d,12]

Experimental Section

General Data. All manipulations were carried out under a dry, oxygen-free, nitrogen atmosphere by using standard Schlenk techniques. Solvents were dried and distilled from sodium/benzophenone prior to use. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200 or Varian EM-360 NMR spectrometer at 295 K, unless stated otherwise. Chemical shifts are in ppm, relative to Me_4Si as an external standard. Coupling constants are in Hz. Cryoscopy was performed in equipment that is based on a design by Bauer and Seebach.[39] Elemental analyses were performed by the Institute of Applied Chemistry (TNO), Zeist, The Netherlands.[40]

N-(ethylzincio)diisopropylamine,[17] sodium bis(trimethylsilyl)amide,[41] and 2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane-1-acetic acid ethyl ester (**1g**)[42] were synthesized according to published methods.

Synthesis of the N,N-Disubstituted Glycine Esters (1). The N,N-disubstituted glycine esters **1a–f** were prepared by condensation of equimolar amounts of ethyl bromoacetate or methyl bromoacetate and an appropriate secondary amine in diethyl ether or benzene. The liberated hydrogen bromide was removed by addition of a second equivalent of the secondary amine or addition of a tertiary amine, e.g. Et_3N or $Et(i\text{-}Pr)_2N$. After completion of the reaction, the precipitated ammonium salts were removed by washing with a small amount of water. After drying of the organic layer with Na_2SO_4, the solvents were removed in vacuo to yield the crude esters **1a–f**. These were then purified by distillation at reduced pressure and stored under a nitrogen atmosphere at −30 °C. Physical data are as follows.

Et_2NCH_2COOEt (1a): Colorless liquid, isolated yield 88%, bp 65 °C/12 mmHg. ^1H NMR (C_6D_6): δ 3.98 (q, 2 H, OCH_2CH_3), 3.21 (s, 2 H, NCH_2COO), 2.60 (q, 4 H, $N(CH_2CH_3)_2$), 1.10 (t, 3 H, OCH_2CH_3), 1.00 (t, 6 H, $N(CH_2CH_3)_2$).

Me(*t*-Bu)NCH_2COOMe (1b): Colorless liquid, isolated yield 75%, bp 65 °C/12 mmHg. ^1H NMR (C_6D_6): δ 3.36 (s, 3 H, OCH_3), 3.09 (s, 2 H, NCH_2COO), 2.23 (s, 3 H, NCH_3), 0.90 (s, 9 H, $C(CH_3)_3$).

Me_2NCH_2COOMe (1c): Colorless liquid, isolated yield 84%, bp 31 °C/12 mmHg. ^1H NMR (C_6D_6): δ 3.37 (s, 3 H, OCH_3), 2.96 (s, 2 H, NCH_2COO), 2.18 (s, 6 H, $N(CH_3)_2$).

Me(Ph)NCH_2COOMe (1d): Yellow oil, isolated yield 80%, bp 90 °C/0.4 mmHg. ^1H NMR ($CDCl_3$): 7.20–6.35 (m, 5 H, Ar *H*), 3.58 (s, 3 H, OCH_3), 2.90 (s, 2 H, NCH_2COO), 2.98 (s, 3 H, NCH_3).

Me_2NCH_2COOEt (1e): Colorless liquid, isolated yield 87%, bp 43 °C/12 mmHg. ^1H NMR (C_6D_6): δ 3.94 (q, 2 H, OCH_2CH_3), 3.13 (s, 2 H, NCH_2COO), 2.17 (s, 6 H, $N(CH_3)_2$), 1.08 (t, 3 H, OCH_2CH_3).

Et_2NCH_2COOMe (1f): Colorless liquid, isolated yield 88%, bp 53 °C/12 mmHg. ^1H NMR ($CDCl_3$): δ 3.56 (s, 3 H, OCH_3), 3.31 (s, 2 H, NCH_2COO), 2.53 (q, 4 H, $N(CH_2CH_3)_2$, 0.97 (t, 6 H, $N(CH_2CH_3)_2$).

Synthesis of Lithium and Sodium Enolates 2a–d. General Procedure. To a stirred solution containing LDA or NaHMDS in benzene at 0 °C was slowly added a solution of the appropriate ester **1a–d** in benzene. The resulting pale yellow solution was stirred for 30 min at 0 °C and then for another 30 min at room temperature. Removal of all volatile material in vacuo at 50 °C afforded **2a–d** as off-white or pale yellow solids. The crude enolates are of sufficient purity for synthetic purposes but may be purified by washing with small portions of cold pentane (−30 °C) to afford the pure enolates as colorless solids. It is important to carry out these reactions in benzene and to dry in vacuo at 50 °C in order to avoid the undesired incorporation of free diisopropylamine in the enolate products.

$LiO(EtO)C{=}C(H)NEt_2$ (2a): Off-white solid, isolated yield 96%. Characterization of this compound by NMR spectroscopy is very difficult because of the presence of different aggregates in solution (see text). ^1H NMR spectra of a hydrolized sample of the solid showed the presence of starting ester **1a** only. Recrystallization from *n*-pentane at −80 °C affords hexameric **2a** as colorless crystals, mp >135 °C dec. Even the ^1H NMR spectrum of a solution of hexameric **2a** is very complicated, e.g. it shows four multiplet resonances for the anisochronous NCH_2CH_3 protons at 1.95, 2.51, 3.05, and 3.20 ppm, respectively.[25]

LiO(MeO)C=C(H)N(*t*-Bu)Me (2b): Pale yellow solid, isolated yield 92%. ^1H NMR (C_6D_6): δ 3.67 (br s, 1 H, *HC*=C), 3.34 (br s, 3 H, OCH_3), 2.39 (s, 3 H, NCH_3), 1.20 (s, 9 H, $C(CH_3)_3$. ^{13}C NMR (C_6D_6): δ 166.45 (C(H)=*C*OO), 79.03 (*C*(H)=COO), 55.81 (OCH_3), 52.61 ($C(CH_3)_3$), 39.90 (NCH_3), 26.06 ($C(CH_3)_3$).

$LiO(MeO)C{=}C(H)NMe_2$ (2c): White solid, isolated yield 97%, mp >130 °C dec. ^1H NMR (C_6D_6): δ 3.86 (br s, 1 H, *HC*=C), 3.28 (br s, 3 H, OCH_3), 2.48 (br s, 6 H, $N(CH_3)_2$). ^{13}C NMR (C_6D_6): δ 165.13 (C(H)=*C*OO), 89.39 (*C*(H)=COO), 52.94 (OCH_3), 48.66 ($N(CH_3)_2$). Anal. Calcd for $C_5H_{10}NO_2Li$: C, 48.80; H, 8.19; N, 11.38. Found: C, 45.81; H, 7.73; N, 10.45.[40]

NaO(MeO)C=C(H)N(*t*-Bu)Me (2d): Pale yellow solid, isolated yield 94%. ^1H NMR (C_6D_6): δ 3.67 (br s, 1 H, *HC*=C), 3.34 (br s, 3 H, OCH_3) 2.39 (s, 3 H, NCH_3), 1.20 (s, 9 H, $C(CH_3)_3$. ^{13}C NMR (C_6D_6): δ 166.45 (C(H)=*C*OO), 79.03 (*C*(H)=COO), 55.81 (OCH_3), 52.61 ($C(CH_3)_3$), 39.90 (NCH_3), 26.06 ($C(CH_3)_3$).

Synthesis of $EtZnO(EtO)C{=}C(H)NEt_2{\cdot}LiCl$ (3a). To a stirred solution containing 2.02 g (20 mmol) of diisopropylamine in 30 mL of diethyl ether was added 20 mmol of *n*-BuLi (13.33 mL of a 1.5 M solution in hexanes). The resulting solution was stirred for 10 min, and then 3.18 g (20 mmol) of *N,N*-diethylglycine ethyl ester (**1a**) was added at room temperature to form a white suspension of the lithium enolate **2a**. This suspension was stirred for 30 min and then cooled to −35 °C. At this temperature, a solution containing 2.60 g (20 mmol) of EtZnCl in 15 mL of diethyl

(38) Examination of the ^{13}C chemical shifts of the trimethylsilyl enol ethers **9** reveals that the electron density and hence the nucleophilicity of the α-carbon atoms of the *Z*-isomers is higher (shifted more upfield) than of the *E*-isomers. This indicates that in principle the *Z*-isomers should be more reactive than the *E*-isomers.

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(40) Elemental analyses of air-sensitive compounds containing volatile organic fragments always show low values for the C, H, and N analyses because of partial hydrolysis during sampling.

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ether was added with stirring, resulting in the formation of a heavy precipitate in a colorless solution. This suspension was stirred for 30 min at −35 °C and then allowed to warm up to room temperature and stirred for another 30 min. The clear solution was then decanted from the precipitate, which was washed three times with 15-mL portions of *n*-pentane. The remaining solid was dried in vacuo at ambient temperature, yielding 4.50 g (76%) of air-sensitive, white, ethylzinc enolate **3a**, mp >95 °C dec. ^{1}H NMR (C_6D_6): δ 3.70 (br s, 1 H, *HC*=C), 3.60 (br m, 2 H, OCH_2CH_3), 2.65 (br m, 4 H, $N(CH_2CH_3)_2$), 1.55 (t, 3 H, $ZnCH_2CH_3$), 1.15 (m, 9 H, $N(CH_2CH_3)_2$ and OCH_2CH_3), 0.50 (br m, 2 H, $ZnCH_2CH_3$). Anal. Calcd for $C_{10}H_{21}NO_2ZnLiCl$: C, 40.70; H, 7.17; N, 4.74; Zn, 22.16. Found: C, 40.56; H, 7.58; N, 4.65; Zn, 22.09.

Synthesis of ClZnO(EtO)C=C(H)NEt$_2$·$^1/_2$LiCl (3b). To a stirred suspension of 1.65 g (10 mmol) lithium enolate **2a** in 25 mL of diethyl ether was added 10 mmol (10.0 mL of a 1.0 M solution in diethyl ether) of $ZnCl_2$ at room temperature. A slightly exothermic reaction occurred. The reaction mixture was stirred for 1 h at room temperature, resulting in a pale yellow solution containing some white precipitated material (LiCl). The solid was removed by filtration and extracted with two 20-mL portions of diethyl ether. The combined ethereal extracts were concentrated in vacuo, affording a pale yellow foamy solid. This was washed with two 30-mL portions of *n*-pentane. Finally the product was dried in vacuo, yielding 2.25 g (75%) of the chlorozinc enolate **3b** as an air-sensitive pale yellow solid. The ^{1}H NMR spectrum unfortunately showed only broad signals (from 193 to 353 K) and indicated the presence of complexed diethyl ether. Hydrolysis of the compound afforded only the starting glycine ester **1a**, which indicated that no side products were formed. The ^{13}C NMR spectrum showed broad and multiple resonances, but the presence of the enolate structure was obvious. ^{13}C NMR (C_6D_6): δ 162.99 (C(H)=*C*OO), 85.21 (*C*(H)=COO), 63.19 (OCH_2CH_3), 52.17 (NCH_2CH_3), 14.68 (OCH_2CH_3), 10.50 ($N(CH_2CH_3)_2$). Anal. Calcd for $C_8H_{16}NO_2ZnCl$·$^1/_2LiCl$·$^1/_4Et_2O$: C, 36.17; H, 6.24; N, 4.69; Cl, 17.80; Li, 1.16; Zn, 21.88. Found: C, 35.19; H, 6.28; N, 4.49; Cl, 17.72; Li, 1.20; Zn, 21.47.[43]

Synthesis of ClZnO(MeO)C=C(H)N(*t*-Bu)Me (3c). To a stirred solution of 1.54 g (9.3 mmol) of lithium enolate **2b** in 50 mL of benzene was added 9.3 mmol (9.3 mL of a 1.0 M solution in diethyl ether) of $ZnCl_2$ at room temperature. Immediately a white solid (LiCl) started to precipitate. The yellow suspension was stirred for 4 h at room temperature. The solid was removed by centrifugation and extracted twice with 30-mL portions of diethyl ether/benzene (1/1 v/v). The combined extracts were concentrated in vacuo to afford 2.12 g (88%) of an off-white solid that did not dissolve in benzene, mp >115 °C dec. NMR spectra showed that the product contained diethyl ether. This diethyl ether could not be removed by heating to 50 °C at 0.05 mmHg, implying that it was strongly coordinated to the product. ^{1}H NMR (tol-d_8/THF-d_8): δ 3.93 (br s, 1 H, *HC*=C), 3.29 (br s, 3 H, OCH_3), 3.22 (q, 4 H, $(CH_3CH_2)_2O$), 2.53 (br s, 3 H, NCH_3), 1.10 (br s, 9 H, $C(CH_3)_3$), 1.04 (t, 6 H, $(CH_3CH_2)_2O$). ^{13}C NMR (tol-d_8/THF-d_8): δ 164.64 (C(H)=*C*OO), 83.27 (*C*(H)=COO), 67.19 ($(CH_3CH_2)_2O$), 60.06 ($C(CH_3)_3$), 53.95 (OCH_3), 43.17 (NCH_3), 25.80 ($C(CH_3)_3$), 15.53 ($(CH_3CH_2)_2O$). Elemental analysis showed that the product contained lithium chloride as well as $ZnCl_2$. Anal. Calcd for $C_8H_{16}NO_2ZnCl$·$^1/_4LiCl$·$^3/_4ZnCl_2$·$^3/_4Et_2O$: C, 30.91; H, 5.54; N, 3.28; Zn, 26.77; Cl, 22.81. Found: C, 27.74; H, 4.69; N, 3.10; Zn, 25.42; Cl, 22.09.[43]

Synthesis of ClZnO(MeO)C=C(H)N(*t*-Bu)Me (3d). To a stirred solution of 1.37 g (7.6 mmol) sodium enolate **2d** in 50 mL of benzene was added 7.6 mmol (7.6 mL of a 1.0 M solution in diethyl ether) of $ZnCl_2$ at room temperature. Immediately, a white solid (NaCl) started to precipitate. The pale yellow suspension was stirred for 4 h at room temperature. The solid was removed by centrifugation and extracted twice with 30-mL portions of diethyl ether/benzene (1/1 v/v). The combined extracts were concentrated in vacuo to afford 1.00 g of a white solid that did not dissolve in benzene. The residue was extracted with two 30-mL portions of THF to yield a second fraction. The combined THF extracts were concentrated in vacuo to afford 1.84 g of a white solid, mp >125 °C dec. The NMR spectra showed that the products contained several impurities, and both the ^{1}H and ^{13}C NMR spectra showed broad resonances. The ^{1}H NMR spectra of both fractions are slightly different, but the ^{13}C spectra are virtually the same. ^{1}H NMR (tol-d_8/THF-d_8): Et_2O/benzene extract, δ 3.97 (br s, 1 H, *HC*=C), 3.40 (br s, 3 H, OCH_3), 2.53 (br s, 3 H, NCH_3), 1.19 (br s, 9 H, $C(CH_3)_3$); THF extract, δ 3.86 (br s, 1 H, *HC*=C), 3.33 (br s, 3 H, OCH_3), 2.52 (br s, 3 H NCH_3), 1.12 (br s, 9 H, $C(CH_3)_3$). ^{13}C NMR (tol-d_8/THF-d_8): δ 162.60 (C(H)=COO), 84.54 (*C*(H)=COO), 60.57 ($C(CH_3)_3$), 54.77 (OCH_3), 42.88 (NCH_3), 25.74 ($C(CH_3)_3$). Elemental analysis of the THF fraction showed that the product contained tightly bound THF as well as $ZnCl_2$. Anal. Calcd for $C_8H_{16}NO_2ZnCl$·$^1/_4ZnCl_2$·$^1/_4C_4H_8O$: C, 34.74; H, 5.83; N, 4.50; Zn, 26.27; Cl, 17.09. Found: C, 34.26; H, 5.40; N, 4.36; Zn, 25.76; Cl, 16.62.[43]

Synthesis of EtZnOC(OMe)=C(H)NMe$_2$ (4a). To a stirred solution containing 3.40 g (17.5 mmol) of *N*-(ethylzincio)diisopropylamine in 40 mL of benzene was added 2.10 g (17.5 mmol) of Me_2NCH_2COOMe (**1c**). After 24 h at room temperature the presence of unreacted **1c** could not be detected with ^{1}H NMR spectroscopy. The volatile components were removed in vacuo to yield 3.40 g (93%) of **4a** as an off-white semisolid. The ^{1}H NMR spectrum at 295 K showed at least four different (broad) quartets for the methylene protons of the ethylzinc moiety. ^{1}H NMR (tol-d_8): δ 3.95–3.32 (br m, 4 H, *HC*=C and OCH_3), 2.90–1.83 (br m, 6 H, $N(CH_3)_2$), 1.70–1.32 (m, 3 H, $ZnCH_2CH_3$), 0.68–0.05 (br m, 2 H, $ZnCH_2CH_3$).

Synthesis of EtZnOC(OMe)=C(H)N(Me)*t*-Bu (4b). To a stirred solution containing 3.38 g (17.4 mmol) of *N*-(ethylzincio)diisopropylamine in 40 mL of benzene was added 2.75 g (17.5 mmol) of Me(*t*-Bu)NCH_2COOMe (**1b**). After 24 h at room temperature the presence of unreacted **1b** could not be detected with ^{1}H NMR spectroscopy. All volatile material was removed in vacuo, yielding 4.40 g (100%) of **4b** as a pale yellow solid. The crude product was washed with two 10-mL portions of cold pentane (−50 °C) to afford 4.27 g (97%) of **4b** as a white solid. The product was recrystallized from hexane at −30 °C, which yielded analytically pure **4b** as colorless crystals, mp 124 °C dec. ^{1}H NMR (tol-d_8): dimer, δ 4.02 (s, 1 H, *HC*=C), 3.29 (s, 3 H, OCH_3), 2.36 (s, 3 H, NCH_3), 1.56 (t, 3 H, J = 8.0, CH_2CH_3), 1.11 (s, 9 H, $C(CH_3)_3$), 0.55 (q, 2 H, J = 8.0, CH_2CH_3); tetramer, δ 3.83 (s, 1 H, *HC*=C), 3.33 (s, 3 H, OCH_3), 2.37 (s, 3 H, NCH_3), 1.64 (t, 3 H, J = 8.1, CH_2CH_3), 1.20 (br s, 9 H, $C(CH_3)_3$), 0.76 (dq, 1 H, J = 8.1 and 13.1, $CH_aH_bCH_3$), 0.29 (dq, J = 8.1 and 13.1 $CH_aH_bCH_3$). ^{13}C NMR (tol-d_8): dimer, δ 165.17 (C(H)=*C*OO), 84.96 (*C*(H)=COO), 58.70 ($C(CH_3)_3$), 53.11 (OCH_3), 42.20 (NCH_3), 26.01 ($C(CH_3)_3$), 13.41 ($ZnCH_2CH_3$), 0.42 ($ZnCH_2CH_3$); tetramer, δ 163.86 (C(H)=*C*OO), 82.17 (*C*(H)=COO), 58.20 ($C(CH_3)_3$), 53.76 (OCH_3), 41.00 (NCH_3), 26.01 ($C(CH_3)_3$), 13.67 ($ZnCH_2CH_3$), 2.99 ($ZnCH_2CH_3$). Anal. Calcd for $C_{10}H_{21}NO_2Zn$: C, 47.07; H, 8.38; N, 5.51; Zn, 26.50. Found: C, 47.54; H, 8.41; N, 5.54; Zn, 25.88.

Synthesis of EtZnOC(OMe)=C(H)NEt$_2$ (4c). To a stirred solution containing 2.76 g (13.8 mmol) of *N*-(ethylzincio)diisopropylamine in 40 mL of benzene was added 2.03 g (14.0 mmol) of Et_2NCH_2COOMe (**1f**). After 24 h at room temperature the presence of unreacted **1f** could not be detected with ^{1}H NMR spectroscopy. All volatile material was removed in vacuo, yielding 3.25 g (97%) of **4c** as a pale yellow oil. Attempts to crystallize **4c** from *n*-pentane at −70 °C were unsuccessful. The ^{1}H NMR spectra (from 193 to 353 K) of the product are very complex and show the presence of several different aggregates (see text). ^{1}H NMR (C_6D_6): δ 3.83–3.61 (m, 1 H, *HC*=C), 3.53 and 3.42 (s, 3 H, OCH_3), 3.13–2.22 (br m, 4 H, $N(CH_2CH_3)_2$), 1.64–1.30 (br m, 3 H, $ZnCH_2CH_3$), 1.30–0.66 (br m, 6 H, $N(CH_2CH_3)_2$), 0.66–0.12 (br m, 2 H, $ZnCH_2CH_3$).

Synthesis of EtZnOC(OMe)=C(H)N(Ph)Me (4d). To a stirred solution containing 3.03 g (15.6 mmol) of *N*-(ethylzincio)diisopropylamine in 40 mL of benzene was added 2.8 g (15.6 mmol) of Me(Ph)NCH_2COOMe (**1d**). After 48 h at room tem-

(43) Since these compounds are mixtures of different aggregates with unknown composition (see Discussion), it is difficult to give the correct calculate values for elemental analyses. Therefore, significant deviations may arise; however, the elemental analyses do show the presence of complexed solvents (confirmed by NMR) and metal salts.

Table VIII. Summary of X-ray Diffraction Data for [EtZnOC(OMe)=C(H)N(t-Bu)Me]$_4$ (4b)

(a) Crystal Data	
formula	$C_{40}H_{84}N_4O_8Zn_4$
mol wt	1010.64 (tetramer)
space group	$P2_1/n$
a, Å	20.063 (1)
b, Å	12.875 (1)
c, Å	20.414 (1)
β, deg	101.72 (1)
V, Å^3	5163.2 (6)
Z	4
D_{calc}, g cm^{-3}	1.300
F(000), electrons	2144
μ(Mo Kα), cm^{-1}	19.3
crystal dimens, mm	0.35 × 0.25 × 0.15
(b) Data Collection	
temp, K	295
radiatn, Å	0.710 73 (Zr filtered)
2θ limits, deg	2.04–56.98
$\omega/2\theta$ scan, deg	0.62 + 0.35 tan θ
ref reflcns	024, 404, 420
no. of data collcd	13 923
no. of unique data	13 018
no. of obsd data ($I > 2.5\sigma(I)$)	4114
tot. X-ray exp time, h	89
decay, %	3.5
(c) Refinement	
R	0.061
R_w	0.055
w^{-1}	$\sigma^2(F)$
no. of refined params	507
$(\Delta/\sigma)_{max}$	0.065
S	1.97
max final resid dens, e Å^{-3}	0.54

perature the ^{1}H NMR spectra of a sample showed the presence of unreacted **1d** and *N*-(ethylzincio)diisopropylamine (ca. 20%). Stirring was continued for another 4 h at 50 °C, but the composition of the reaction mixture did not change. All volatile material was removed in vacuo, yielding 4.85 g of a yellow oil. This oil was washed twice with 40 mL of cold pentane (−30 °C). The residue was dried in vacuo to afford 4.50 g of a pale yellow solid. The ^{1}H NMR spectra (from 193 to 353 K) of the product were very complex and showed the presence of starting ester **1d** and *N*-(ethylzincio)diisopropylamine. Furthermore, the integral values indicated that the product was most likely not the expected zinc enolate **4d** but rather a self-condensation product of **4d** (see text). ^{1}H NMR (tol-d_8/py-d_5): δ 7.31–6.64 (m, 10 H, Ar *H*), 4.19 and 4.12 (br s, 2 H, *HC*=C), 3.37 and 3.22 (br s, 3 H, OCH_3), 2.97 and 2.93 (br s, 6 H, NCH_3), 1.74 and 1.63 (t, 3 H, ZnCH$_2$CH_3), 0.97–0.68 (br m, 2 H, ZnCH_2CH$_3$).

The self-condensation product Me(Ph)NCH$_2$C(O)C(H)(N-(Ph)Me)C(O)OEt (**13**) of the ethylzinc enolate **4d** was identified by ^{1}H NMR spectroscopy and comparison with an authentic sample obtained via self-condensation of the dimethylaluminum enolate of ester **1d**.[32] ^{1}H NMR ($CDCl_3$): δ 7.72–7.50 (m, 2 H, Ar *H*), 7.42–7.20 (m, 2 H, Ar *H*), 6.96–6.60 (m, 6 H, Ar *H*), 4.33 (d, 1 H, J = 16.7, NCH_aH$_b$C(O)), 4.16 (d, 1 H, J = 16.7, NCH$_a$CH_bC(O)), 3.73 (s, 3 H, OCH_3), 3.17 and 3.05 (s, 3 H, NCH_3).

X-ray Data Collection, Structure Determination, and Refinement of [EtZnOC(OMe)=C(H)N(t-Bu)Me]$_4$ (4b). A colorless crystal, obtained by crystallization from hexane, was sealed under nitrogen in a Lindemann glass capillary and mounted for data collection on an Enraf-Nonius CAD4F diffractometer. Numerical data on the structure determination have been collected in Table VIII. Unit cell dimensions were calculated from the setting angles of 21 carefully centered reflections. The data of one quadrant of the reflection sphere ($\pm h,+k,+l$) were collected in the $\omega/2\theta$ scan mode, by using Zr-filtered Mo Kα radiation, and corrected for Lorentz, polarization, and absorption effects (DIFABS).[44] The structure was solved by standard Patterson and Fourier methods and refined on F by blocked full-matrix least-squares techniques. Hydrogen atoms were introduced on calculated positions (C–H = 0.98 Å) and refined by riding on their carrier atoms with two common isotropic thermal parameters: one for the CH_3 groups and one for the CH_2 and CH groups, their final values amounting to 0.103 (7) and 0.061 (13) Å^2, respectively. The refinement converged at R = 0.061. Scattering factors were taken from Cromer and Mann and corrected for anomalous dispersion.[45] The structure determination and refinement were carried out on an in-house micro-Vax cluster, with a locally adapted implementation of SHELX-76 and SHELXS-86.[46] All derived geometry calculations were performed with the programs of the EUCLID package.[47]

Quenching Reactions of in Situ Prepared Lithium and Zinc Enolates of N,N-Disubstituted Glycine Esters with Trimethylsilyl Chloride. Method A. To a stirred solution containing 10 mmol of LDA in 30 mL of dry benzene was added 10 mmol of a glycine ester **1** at room temperature, resulting in an almost clear yellow solution. This solution was stirred for 15 min at room temperature, and then 12 mmol (1.30 g) of trimethylsilyl chloride was added, resulting in a pale yellow suspension. This suspension was stirred for 4 h, and then all volatile material was removed in vacuo at 0 °C. The residue was extracted with two 40-mL portions of pentane, and the LiCl was removed by centrifugation. The combined extracts were concentrated in vacuo at 0 °C, and the crude products **9** were purified by distillation at reduced pressure.

Method B. To a stirred solution of 10 mmol of LDA in 30 mL of dry benzene was added 10 mmol of glycine ester **1** at room temperature, resulting in an almost clear yellow solution. This solution was stirred for 15 min at room temperature, and then 10 mL of a 1.0 M solution of dry $ZnCl_2$ in diethyl ether was added. The reaction mixture was stirred for 1 h, during which some white material (LiCl) precipitated. Then 12 mmol (1.30 g) of trimethylsilyl chloride was added, and the yellow suspension was stirred for 4 h, after which all volatile material was removed in vacuo at 0 °C. The residue was extracted with two 40-mL portions of pentane, and the solid was removed by centrifugation. The combined extracts were concentrated in vacuo at 0 °C, and the crude products **9** were purified by distillation at reduced pressure.

Me$_3$SiO(EtO)C=C(H)NMe$_2$ (9a). Method A: Isolated yield 1.69 g (80%) of a 3/7 mixture of the *E*- and *Z*-isomers of **9a** as a colorless liquid, bp 40 °C/0.4 mmHg.

Method B: Isolated yield 1.27 g (60%) of a 1/24 mixture of *E*- and *Z*-**9a**. ^{1}H NMR (C_6D_6): *E*, δ 4.55 (s, 1 H, *HC*=C), 3.97 (q, 2 H, J = 7.1, OCH_2CH$_3$), 2.34 (s, 6 H, N(CH_3)$_2$), 1.12 (t, 3 H, J = 7.1, OCH$_2$CH_3), 0.16 (s, 9 H, Si(CH_3)$_3$); *Z*, δ 4.27 (s, 1 H, *HC*=C), 3.48 (q, 2 H, J = 7.1, OCH_2CH$_3$), 2.28 (s, 6 H, N(CH_3)$_2$), 1.02 (t, 3 H, J = 7.1, OCH$_2$CH_3), 0.22 (s, 9 H, Si(CH_3)$_3$). ^{13}C NMR (C_6D_6): *E*, δ 149.73 (HC=C), 106.22 (*HC*=C), 64.43 (OCH_2CH$_3$), 46.05 (N(CH$_3$)$_2$), 15.28 (OCH$_2$CH$_3$), −0.03 (Si(CH$_3$)$_3$); *Z*, δ 152.24 (HC=*C*), 101.24 (*HC*=C), 63.16 (OCH_2CH$_3$), 46.29 (N(CH_3)$_2$), 14.67 (OCH$_2$CH_3), 0.44 (Si(CH_3)$_3$). Anal. Calcd for $C_9H_{21}NO_2Si$: C, 53.16; H, 10.41; N, 6.89; Si, 13.81. Found: C, 54.06; H, 10.63; N, 6.61; Si, 12.95.[40]

Me$_3$SiO(EtO)C=C(H)NEt$_2$ (9b). Method A: Isolated yield 2.04 g (88%) of a 1/2 mixture of the *E*- and *Z*-isomers of **9b** as a colorless liquid, bp 60 °C/0.4 mmHg.

Method B: Isolated yield 1.45 g (60%) of a 2/23 mixture of *E*- and *Z*-**9b**. ^{1}H NMR (C_6D_6): *E*, δ 4.29 (s, 1 H, *HC*=C), 4.03 (q, 2 H, J = 7.1, OCH_2CH$_3$), 2.53 (q, 4 H, J = 7.1, N(CH_2CH$_3$)$_2$), 1.13 (t, 3 H, J = 7.1, OCH$_2$CH_3), 1.04 (t, 6 H, J = 7.1, N-(CH$_2$CH_3)$_2$), 0.18 (s, 9 H, Si(CH_3)$_3$); *Z*, δ 4.09 (s, 1 H, *HC*=C), 3.49 (q, 2 H, J = 7.1, OCH_2CH$_3$), 2.60 (q, 4 H, J = 7.1, N-(CH_2CH$_3$)$_2$), 1.08 (t, 6 H, J = 7.1, N(CH$_2$CH_3)$_2$), 1.03 (t, 3 H, J = 7.1, OCH$_2$CH_3), 0.25 (s, 9 H, Si(CH_3)$_3$). ^{13}C NMR (C_6D_6): *E*, δ 153.13 (HC=C), 101.62 (*HC*=C), 64.39 (OCH_2CH$_3$), 50.76 (N-

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($CH_2CH_3)_2$), 15.36 (OCH_2CH_3), 13.39 ($N(CH_2CH_3)_2$), 0.08 ($Si(CH_3)_3$); *Z*, δ 154.13 (HC=C), 96.98 (HC=C), 63.38 (OCH_2CH_3), 50.36 ($N(CH_2CH_3)_2$), 14.69 (OCH_2CH_3), 13.27 ($N(CH_2CH_3)_2$), 0.61 ($Si(CH_3)_3$). Anal. Calcd for $C_{11}H_{25}NO_2Si$: C, 57.09; H, 10.89; N, 6.05; Si, 12.14. Found: C, 57.21; H, 10.85; N, 6.13; Si, 12.01.

$Me_3SiO(MeO)C=C(H)N(t\text{-}Bu)Me$ (9c). Method A: Isolated yield 1.94 g (84%) of a 1/1 mixture of the *E*- and *Z*-isomers of **9c** as a colorless liquid, bp 75 °C/0.4 mmHg.

Method B: Isolated yield 1.84 g (80%) of pure *Z*-**9c**. ^1H NMR (C_6D_6): *E*, δ 4.66 (s, 1 H, HC=C), 3.59 (s, 3 H, OCH_3), 2.38 (s, 3 H, NCH_3), 1.05 (s, 9 H, $C(CH_3)_3$), 0.17 (s, 9 H, $Si(CH_3)_3$); *Z*, δ 4.38 (s, 1 H, HC=C), 3.19 (s, 3 H, OCH_3), 2.37 (s, 3 H, NCH_3), 1.07 (s, 9 H, $C(CH_3)_3$), 0.24 (s, 9 H, $Si(CH_3)_3$). ^{13}C NMR (C_6D_6): *E*, δ 154.06 (HC=C), 99.66 (HC=C), 55.98 (OCH_3), 54.81 ($C(CH_3)_3$), 37.84 (NCH_3), 26.19 ($C(CH_3)_3$), 0.08 ($Si(CH_3)_3$); *Z*, δ 155.40 (HC=C), 94.88 (HC=C), 54.78 (OCH_3), 54.77 ($C(CH_3)_3$), 37.68 (NCH_3), 26.27 ($C(CH_3)_3$), 0.56 ($Si(CH_3)_3$). Anal. Calcd for $C_{11}H_{25}NO_2Si$: C, 57.09; H, 10.89; N, 6.05; Si, 12.14. Found: C, 56.92; H, 10.84; N, 6.30; Si, 11.72.

$Me_3SiO(MeO)C=C(H)N(Ph)Me$ (9d). Method A: Isolated yield 2.01 g (80%) of a 10/1 mixture of the *E*- and *Z*-isomers of **9d** as a yellow oil, bp 100 °C/0.4 mmHg.

Method B: Isolated yield 2.07 g (82%) of a 1/47 mixture of *E*- and *Z*-**9d**. ^1H NMR (C_6D_6): *E*, δ 7.15–7.29 (m, 2 H, Ar *H*), 6.74–6.85 (m, 3 H, Ar *H*), 4.97 (s, 1 H, HC=C), 3.30 (s, 3 H, OCH_3), 2.90 (s, 3 H, NCH_3), 0.14 (s, 9 H, $Si(CH_3)_3$); *Z*, δ 7.15–7.27 (m, 2 H, Ar *H*), 6.72–6.84 (m, 3 H, Ar *H*), 4.70 (s, 1 H, HC=C), 3.14 (s, 3 H, OCH_3), 2.92 (s, 3 H, NCH_3), 0.09 (s, 9 H, $Si(CH_3)_3$). ^{13}C NMR (C_6D_6): *E*, δ 155.17 (HC=C), 149.72, 129.28, 117.12, 112.86 (Ar *C*), 96.75 (HC=C), 55.28 (OCH_3), 38.97 (NCH_3), −0.07 ($Si(CH_3)_3$); *Z*, δ 156.87 (HC=C), 149.72, 129.28, 116.86, 112.76 (Ar *C*), 92.01 (HC=C), 54.84 (OCH_3), 38.70 (NCH_3), 0.23 ($Si(CH_3)_3$). Anal. Calcd for $C_{13}H_{21}NO_2Si$: C, 62.11; H, 8.42; N, 5.57; Si, 11.17. Found: C, 61.75; H, 8.52; N, 5.69; Si, 10.87.

$Me_3SiO(EtO)C=C(H)\overline{NSi(Me_2)CH_2CH_2SiMe_2}$ (9e). All reactions given in Table VI were carried out according to the procedure given here for the reaction in THF. To a stirred solution containing 5 mmol of LDA in 30 mL of dry THF was added 1.22 g (5 mmol) of ester **1g** at −78 °C. The clear pale yellow solution was stirred for 15 min at −78 °C, and then 5 mL of a 1.0 M solution of dry $ZnCl_2$ in diethyl ether was added. The clear solution was stirred for 1 h at −78 °C, during which period some white material (LiCl) precipitated. Then 5.5 mmol of trimethylsilyl chloride was added, and the solution was stirred for 1 h at −78 °C. The clear pale yellow solution was then gradually warmed up, and at −45 °C a white precipitate was formed. The reaction mixture was stirred for 1 h at 0 °C, and then all volatiles were removed in vacuo at 0 °C. The sticky residue was extracted with two 30-mL portions of pentane, and the solid was removed by centrifugation. The combined extracts were concentrated in vacuo at 0 °C, affording 1.60 g (100%) of crude **9e** as a pale yellow oil. The product was purified by distillation at reduced pressure. The isolated yield was 1.57 g (99%) of a 13/1 mixture of the *E*- and *Z*-isomers of **9e** as a colorless liquid, bp 50 °C/0.08 mmHg. ^1H NMR (C_6D_6): *E*, δ 4.79 (s, 1 H, HC=C), 3.74 (q, 2 H, OCH_2CH_3), 1.10 (t, 3 H, OCH_2CH_3), 0.80 (s, 4 H, $SiCH_2CH_2Si$), 0.19 (s, 15 H, $Si(CH_3)_3$ and $Si(CH_3)_2$), 0.16 (s, 6 H, $Si(CH_3)_2$); *Z*, δ 4.42 (s, 1 H, HC=C), 3.39 (q, 2 H, OCH_2CH_3), 1.11 (t, 3 H, OCH_2CH_3), 0.80 (s, 4 H, $SiCH_2CH_2Si$), 0.21 (s, 15 H, $Si(CH_3)_3$ and $Si(CH_3)_2$), 0.18 (s, 6 H, $Si(CH_3)_2$). ^{13}C NMR (C_6D_6): *E*, δ 149.55 (HC=C), 94.33 (HC=C), 62.67 (OCH_2CH_3), 14.95 (OCH_2CH_3), 8.87 ($SiCH_2CH_2Si$), −0.18 and −0.29 ($Si(CH_3)_3$ and $Si(CH_3)_2$); *Z*, δ 85.00 (HC=C), 63.96 (OCH_2CH_3), 14.63 (OCH_2CH_3), 8.49 ($SiCH_2CH_2Si$), 0.87 and −0.56 ($Si(CH_3)_3$ and $Si(CH_3)_2$).

Self-Condensation Reaction of Lithium Enolate 2e. To a solution containing 20 mmol LDA in 50 mL of hexane at −78 °C was added 20 mmol of 2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane-1-acetic acid ethyl ester (**1g**), resulting in a pale yellow solution. After the solution was stirred for 1 h at −78 °C, the Schlenk tube was stored under nitrogen at −30 °C. After 2 days some colorless crystals had been precipitated. Crystallization was complete after 2 weeks at −30 °C. The solution was decanted from the crystals, which were washed with two 20-mL portions of cold (−30 °C) pentane. Drying in vacuo afforded 3.63 g (81%) of colorless crystals, mp >185 °C dec. NMR spectra of these crystals revealed that, instead of the expected lithium enolate **2e**, self-condensation product **12** was isolated. ^1H NMR (C_6D_6/THF-d_8): δ 4.02 (s, 2 H, NCH_2COLi), 4.02 (q, 2 H, OCH_2CH_3), 1.17 (t, 3 H, OCH_2CH_3), 0.91 (m, 4 H, $SiCH_2CH_2Si$), 0.90 (s, 4 H, $SiCH_2CH_2Si$), 0.25 (s, 12 H, $Si(CH_3)_2$), 0.20 and 0.13 (s, 6 H, $Si(CH_3)_2$). ^{13}C NMR (C_6D_6/THF-d_8): δ 187.01 (EtOC=O), 170.23 (NC=COLi), 95.81 (NC=COLi), 57.75 (OCH_2CH_3), 47.66 (NCH_2COLi), 14.49 (OCH_2CH_3), 9.35, 8.74 ($SiCH_2CH_2Si$), 1.31, 0.41, −0.67 ($Si(CH_3)_2$). Anal. Calcd for $C_{18}H_{39}N_2O_3Si_4Li$: C, 47.96; H, 8.72; N, 6.21; Si, 24.92; Li, 1.54. Found: C, 46.46; H, 8.58; N, 6.11; Si, 21.6; Li, 1.59.[40]

Reactions of Isolated α-Amino Organozinc Ester Enolates 3 and 4 with *N*-Benzylidenemethylamine (10). These reactions were all carried out according to a standard procedure that is given below for the reaction of ethylzinc enolate **3a**. The crude isolated materials were analyzed by using ^1H NMR spectroscopy, and the yields of the *trans*-2-azetidinones **11** were determined from the ^1H NMR spectra. The *trans*-2-azetidinones were identified by comparison with the ^1H NMR spectra of authentic samples.[11]

To a solution containing 2.95 g (10 mmol) of ethylzinc enolate **3a** in 40 mL of dry benzene was added 1.19 g (10 mmol) of PhC(H)=NMe (**10**) at room temperature. This solution was stirred for 2 h at 80 °C and after cooling to room temperature diluted with 30 mL of diethyl ether and then quenched with 30 mL of a saturated aqueous NH_4Cl solution. The water layer was extracted with three 30-mL portions of diethyl ether. The combined extracts were dried over Na_2SO_4 and concentrated in vacuo, yielding 2.16 g (93%) of *trans*-1-methyl-3-(diethylamino)-4-phenyl-2-azetidinone (**11a**) as an off-white solid with the same properties as an authentic sample.[11]

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Supplementary Material Available: Tables of bond distances, bond angles, anisotropic thermal parameters, hydrogen atomic and thermal parameters, and torsion angles (12 pages); tables of structure factors (78 pages). Ordering information is given on any current masthead page.