Diastereoselective Condensation Reactions with an Easily Accessible Intramolecularly Coordinated Zinc-Enamine. Molecular Structure of a Self-Assembled Polymer of Diethylzinc and Zinc-Aldolates

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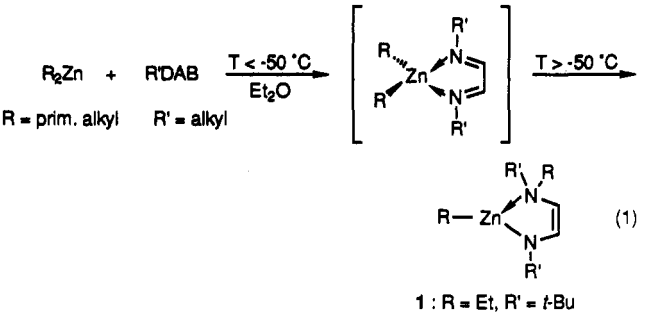
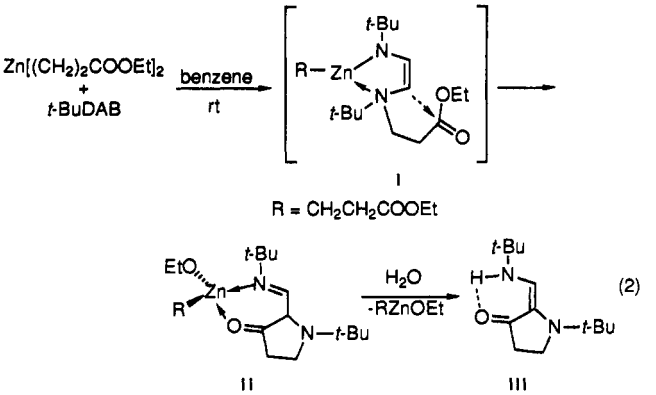
The zinc-enamine EtZn(*t*-BuNCH=CHN(Et)-*t*-Bu) 1 is easily accessible via the reaction of Et_2Zn with the α-diimine *t*-BuN=CHCH=N-*t*-Bu (*t*-BuDAB) and is reactive in C-C coupling reactions with aldehydes to form dimeric zinc-aldolates. The reactions of 1 with aryl aldehydes, like benzaldehyde and 2-, 3-, and 4-pyridinecarboxaldehyde, afford exclusively the *anti* zinc-aldolates, whereas the reactions with alkyl aldehydes like propionaldehyde and 2-methylpropionaldehyde afford a mixture of *syn* and *anti* zinc-aldolates. Quenching of either the *anti* zinc-aldolate or the mixture of *syn* and *anti* zinc-aldolates with trimethylsilyl chloride affords the *anti* diastereoisomers, which can be isolated in high yields. The condensation reaction of 1 with pyridine-2-carboxaldehyde results in the formation of a thermally unstable zinc-aldolate that subsequently rearranges to a 2,3-diaminoindolizine. With the enones, benzylideneacetone, and chalcone, the corresponding Michael addition products are obtained in good yield. The dimeric zinc-aldolate that results from the C-C coupling reaction of 1 with pyridine-4-carboxaldehyde forms a coordination polymer upon addition of 0.5 equiv of Et_2Zn. The X-ray structure of the polymer, wherein the 4-pyridine nitrogens act as complexating agents to bridging Et_2Zn entities, shows the monomeric zinc-aldolate units to have a distorted boat conformation resulting from the steric hindrance of the N(Et)-*t*-Bu substituents. The polymeric structure is a nice example of self-assembly of different molecules, (*R*)- and (*S*)-zinc-aldolates, and Et_2Zn units, with the right match of stereochemical and electronic information.

Introduction

Since its discovery by Wittig[1] the imine anion in metallo-enamines was recognized as a successful alternative for the enolate anion in several C-C couplings reactions.[2] The enhanced nucleophilicity of the enamine anion, with respect to the enolate anion, often justifies the additional steps required for the conversion of a carbonyl function of the starting material into the corresponding imine. Metallo-enamines are readily prepared by regioselective deprotonation of the imine with suitable, non-nucleophilic bases like lithium dialkylamides and Grignard reagents. Recently, we developed a novel route for the synthesis of metallo-enamines from 1,4-diaza-1,3-butadienes.[3] In the reaction of R_2Zn (R = primary alkyl group) with R'N=CH—CH=NR' (= R'DAB) a 1:1 coordination complex is first formed, and upon heating this undergoes a quantitative and regioselective transfer of an alkyl group from zinc to a nitrogen atom of the chelate-bonded R'DAB ligand. This results in the formation of the intramolecularly coordinated zinc-enamines, RZn[R'NCH=CHNRR']; see eq 1.



The nucleophilicity of these N-alkylated organozinc complexes has already been observed in the reaction of the primary dialkylzinc compound $Zn[(CH_2)_2COOEt]_2$ with *t*-BuDAB which yielded a 3-pyrrolidinone derivative **III**; see eq 2.[4] In this reaction the N-alkylated zinc-



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† Debye Research Institute.
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(1) Wittig, G.; Schmidt, H.-J.; Renner, H. *Chem. Ber.* **1962**, *95*, 2377.
(2) (a) Whitesell, J. K.; Whitesell, M. A. *Synthesis* **1983**, 517. (b) Martin, S. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Flemming, I., Eds.; Pergamon: New York, 1991; Vol. 2, pp 475-502.
(3) (a) Klerks, J. M.; Jastrzebski, J. T. B. H.; van Koten, G.; Vrieze, K. *J. Organomet. Chem.* **1982**, *224*, 107. (b) van Koten, G. In *Organometallics in Organic Synthesis*; de Meijere, A., tom Dieck, H., Eds.; Springer-Verlag: New York, 1987; p 277. (c) Kaupp, M.; Stoll, H.; Preuss, H.; Kaim, W.; Stahl, T.; van Koten, G.; Wissing, E.; Smeets, W. J. J.; Spek, A. L. *J. Am. Chem. Soc.* **1991**, *113*, 5606.

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Table I. Aldol Condensation Reactions of the Zinc–Enamine (1) with Aldehydes and α,β-Unsaturated Ketones

R″CHO, R″ =	zinc–aldolate, yield (%)	*syn:anti* ratio[a] (2)	TMS–aldolate, yield (%)	*syn:anti* ratio (3)
Et (a)	**2a**, 99	40:60	**3a**, 86	<1:>99
Pr (b)	**2b**, 94	n.o.[b]	**3b**, 84	<1:>99
Bu (c)	**2c** (n.o.)[c]	n.o.[c]	**3c**, 87	<1:>99
Ph (d)	**2d**, 98	<1:>99	**3d**, 81	<1:>99
2-pyridyl (e)	**2e**, 97[d]	<1:>99	**3e**, 70	<1:>99
3-pyridyl (f)	**2f**, 98	<1:>99	**3f**, 54[e]	<1:>99
4-pyridyl (g)	**2g**, 98	<1:>98	not isolated	
2-furyl (h)	**2h**, 98	<1:>99	**3h**, 81	<1:>99
$C(CH_3)=CH_2$ (i)	**2i**, 98	<1:>99	**3i**, 86	<1:>99
CH=CHPh (j)	**2j**, 98	<1:>99	**3j**, 79	<1:>99

[a] *Syn/anti* ratio determined by ^1H NMR spectroscopy at rt. [b] Not observed because of broad lines in ^1H and ^{13}C NMR spectra. [c] Compound **2c** was not observed with NMR spectroscopy. [d] Compound **2e** is only stable for a few minutes and than eliminates EtZnOH. [e] Isolated as a 1:1 adduct with EtOZnCl.

enamine species **I** was considered to be an intermediate that rearranged *via* a Dieckmann-like condensation reaction to the heterocyclic organozinc coordination complex **II**, which upon aqueous workup afforded **III**.

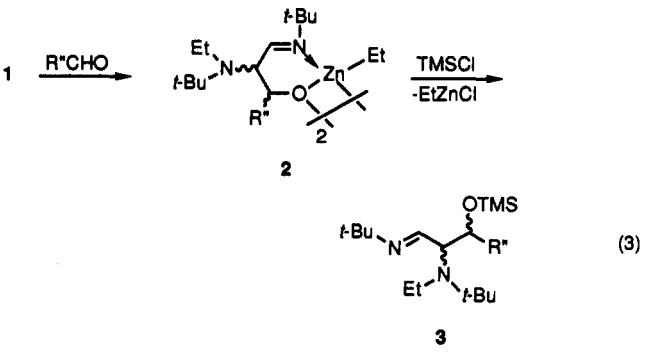
Since the synthesis of the zinc–enamine **1** is applicable for all primary dialkylzinc compounds (with the exception of Me_2Zn)[3c,5] with a large variety of R′DAB systems (R′ = alkyl, aryl[6]), we have selected **1** as representative model compound for a study of the reactivity of the zinc–enamines RZn(R′NCH=CHNEtR′) in C–C coupling reactions with aldehydes and α,β-unsaturated ketones.

Results

The zinc–enamine **1**, EtZn[*t*-BuNCH=CHN(Et)-*t*-Bu], was prepared by the 1:1 reaction of Et_2Zn with *t*-BuDAB at 0 °C in a nonprotic solvent, *e.g.*, hexane, diethyl ether, benzene, or tetrahydrofuran, and was successfully prepared on a scale of 1–150 mmol. Compound **1** was isolated as an air- and moisture-sensitive oil which is stable for months when stored under a nitrogen atmosphere. In **1** both nitrogen atoms are coordinated to zinc; *i.e.*, the enamine ligand has the same configuration as the *t*-BuDAB ligand in the starting 1:1 coordination complex Et_2Zn-*t*-BuDAB. The *Z*-configuration of the enamine anion is imposed by the intramolecular coordination of the N(Et)-*t*-Bu group. The diastereotopicity of the methylene protons of the ethylamino group in the ^1H NMR spectrum of **1** indicate that there is intramolecular coordination of the amine nitrogen to the zinc atom.[3a]

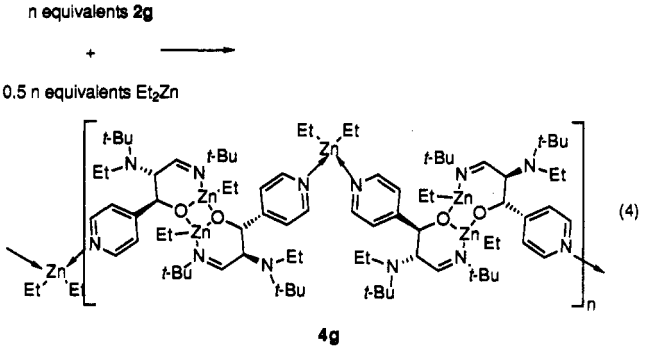
The zinc–enamine **1** is reactive toward aldehydes,[7] and in fast, exothermic 1:1 condensation reactions with most aryl and alkyl aldehydes it forms quantitatively the zinc–aldolates **2a–j** (see Table I). These aldolates are isolated as white solids (except for **2c**) and can be crystallized from hexane or diethyl ether. The C–C coupling reaction occurs with high diastereoselectivity. The reaction with aryl aldehydes, leading to the zinc–aldolates **2d–h**, results in the exclusive formation of the *anti* diastereoisomer (no *syn* diastereoisomer observed with ^1H NMR spectroscopy), whereas in the reaction with alkyl aldehydes, *e.g.*, propionaldehyde, a *syn/anti* ratio of 40/60 was found, corresponding to a de of 20%. The *anti*-configuration of the zinc–aldolates formed in condensation reactions with aryl aldehydes was confirmed by an X-ray structure determination of a coordination polymer of **2g** with diethylzinc (*vide infra*).

The degrees of association of the zinc–aldolates **2a**, **2c**, **2g**, and **2h** were determined by cryoscopy in benzene, and these compounds were found to be concentration-independent dimers (range 0.018–0.052 M). The zinc–aldolates in which a functional group introduced *via* the condensation reaction (see eq 3) is present are of particular



(3)

interest; examples include the dimers **2e–g** that have two pyridyl groups and **2h** that has two furyl groups. The complexation ability of pyridines to dialkylzinc compounds has been known since 1965 when Thiele *et al.*[8] prepared the first $R_2Zn(pyridine)_2$ (R = Me, Et) complexes. It is therefore not surprising that **2g**, which has two free 4-pyridine nitrogen atoms, should undergo a reaction with Et_2Zn as shown in eq 4. Addition of 0.5 equiv of Et_2Zn



(4)

to a solution of **2g** in diethyl ether leads to the formation of an interesting polymeric coordination complex (**4g**), in which two 4-pyridyl groups from different dinuclear zinc–aldolate units coordinate to a single Et_2Zn molecules.

The polymeric structure of **4g** was unambiguously confirmed by an X-ray structure determination and is shown in Figure 1. The dinuclear zinc–aldolate moieties in the polymer chain contain a central four-membered Zn_2O_2 ring with bridging oxygen atoms. Coordination of the imine nitrogen atoms to zinc results in a six-membered ZnOCCCN chelate ring that completes the tetragonal coordination of the zinc atoms. This chelate ring has a distorted boat conformation and an *anti*-configuration with respect to the newly formed C–C bond. The Zn–O

(4) Wissing, E.; Klein, H.; Boersma, J.; van Koten, G. *Recl. Trav. Chim. Pays-Bas*, submitted for publication.

(5) Me_2Zn reacts with R′DAB systems to afford stable 1:1 coordination complexes that upon heating react further to a mixture of N- and C-alkylated products and a C–C-coupled dimeric species.[3]

(6) R′DAB substrates containing phenyl groups with large ortho substituents (e.g., like 2,6-diisopropylphenyl) bonded to the imine N-atoms undergo selective C-alkylation instead of N-alkylation, most probably as a result of steric hinderance at the N-atoms.

(7) Wissing, E.; Havenith, R. W. A.; Boersma, J.; van Koten, G. *Tetrahedron Lett.* **1992**, *33*, 7933.

(8) Thiele, K. H.; Schroeder, S. *Z. Anorg. Allgem. Chem.* **1965**, *337*, 14.

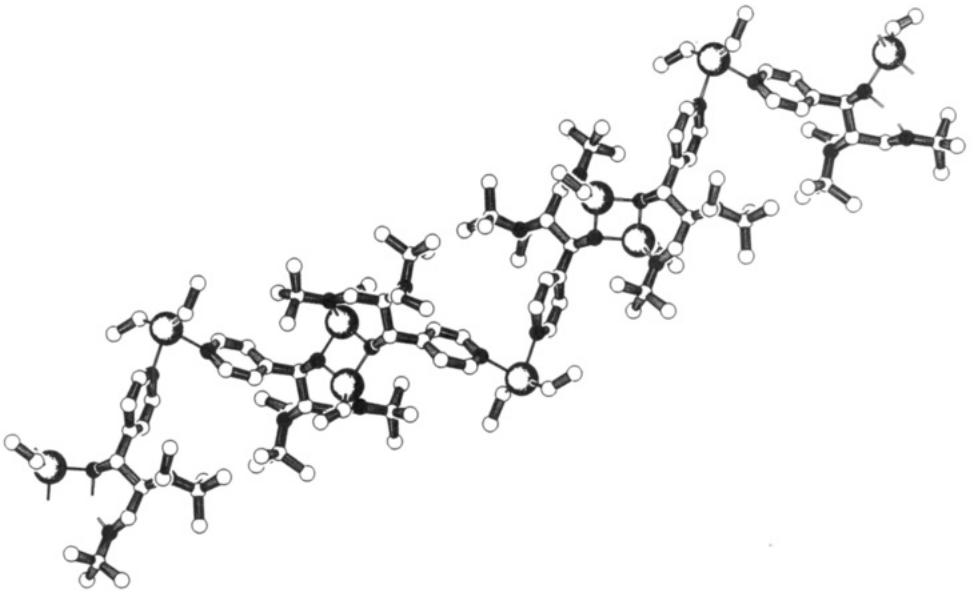


Figure 1. Molecular structure of the polymer **4g**.

bond lengths in the Zn_2O_2 ring have values (1.991(7) and 2.028(7) Å) that are comparable with Zn–O bond lengths found in the Zn_2O_2 units of methylzinc (–)-3-*exo*-(dimethylamino)isoborneolate (1.98(1) and 2.06(1) Å).[9] It is of interest to see that the intramolecular dative Zn–O bond lengths (1.991(7) Å) in **4g** are shorter than the intramolecular Zn–O bonds (2.028(7) Å) within the six-membered chelate ring. We have observed this feature earlier in the tetrameric organozinc ester–enolate [EtZnO(MeO)C=C-(H)N(*t*-Bu)Me]$_4$.[10]

The zinc atoms in the bridging Et_2Zn molecules have a distorted tetrahedral surrounding with C–Zn–C and N–Zn–N angles of 145.7(6)° and 89.4(4)°, respectively. So far no dialkylzinc(pyridine)$_2$ structures are known, and with regard to this part of the polymer complex **4g** is best compared with bis(1,4-dihydropyridin-1-yl)bis(pyridine)-zinc,[11] bis(1,3,5-trimethyl-1,3,5-triazinane)dimethylzinc[12] and the intramolecularly coordinated, "butterfly" complex $Zn[(CH_2)_3NMe_2]_2$,[13] which have N–Zn–N angles of 98°, 106°, and 109.7°, respectively. The large variation in the N–Zn–N angles indicate that only small electronic and/or steric effects in these complexes can cause a large distortion in their geometries.[14]

The crystallographic repeating unit consists of two six-membered ZnOCCCN units linked by a bridging Et_2Zn. The mirror-imaged alternating sequence of these units, each consisting of a pair of two opposite zinc-aldolate enantiomers, results in a zig–zag polymeric structure. This alternating sequence is the reason for the relatively flat stereochemistry of the polymeric chain. We believe that the polymer will have a helix-like structure when the dinuclear zinc–aldolate is enantiomerically pure. The polymeric structure of **4g** is a good example of the self-assembly of different molecules with the right match of stereochemical and electronic information into a polymeric structure.

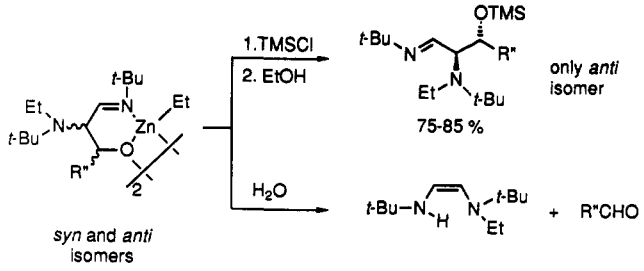
The ^{1}H NMR spectra of **2g** and the polymer **4g** do not differ as far as the dinuclear zinc–aldolate unit is concerned. This implies that the *anti*-configuration of the formed C–C bond as well as the boat conformation as found for each chelate ring in the dinuclear units of the polymer in the solid state are also present in the solution structure of the dimeric **2g** and may occur in the other zinc–aldolates in solution as well.

The zinc–aldolates **2d–h** (except for **2e**, R″ = 2-pyridyl, see Scheme II), resulting from condensation reactions of **1** with aryl aldehydes, show a high thermal stability, whereas the zinc–aldolates **2a–c**, resulting from the condensation reactions of **1** with alkyl aldehydes, have only limited thermal stability. Variable-temperature ^{1}H NMR spectroscopy of the zinc–aldolate **2a** showed that upon raising the temperature from room temperature to 50 °C the initial *syn*/*anti* ratio of 40/60 changes to 50/50. At temperatures above 60 °C **2a** decomposes into the starting zinc–enamine **1** and propionaldehyde. This decomposition is reversible and when the temperature is lowered to room temperature the zinc–aldolate **2a** reforms again. This reformation process initially gives **2a** in a *syn*/*anti* ratio of 50/50, but this then slowly changes into the original ratio of 40/60. These observations indicate that there is an equilibrium between the zinc–aldolate **2a** and the starting materials **1** and propionaldehyde. The same phenomenon was observed in the case of zinc–aldolate **2b**, though it was observed only at temperatures below –10 °C. The zinc–aldolate **2c** was not even observed at –50 °C, implying that in this case with trimethylacetaldehyde the equilibrium lies far to the side of the zinc–enamine **1**.

On controlled hydrolysis of the zinc–aldolates **2a–j** with water or ethanol complete retroaldolization occurs and the aldehyde and the protonated enamine, *i.e.*, *t*-Bu(H)-NCH=CHN(Et)-*t*-Bu (**1a**), were recovered. However, quenching the zinc–aldolate solutions with trimethylsilyl chloride produced stable, isolable trimethylsilyl ether

(9) Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028.
(10) van der Steen, F. H.; Boersma, J.; Spek, A. L.; van Koten, G. *Organometallics* **1991**, *10*, 2467.
(11) de Koning, A. J.; Boersma, J.; van der Kerk, G. J. M. *J. Organomet. Chem.* **1980**, *186*, 159.
(12) (a) Hursthouse, M. B.; Motevalli, M.; O'Brien, P.; Walsh, J. R. *Organometallics* **1991**, *10*, 3196. (b) Spek, A. L. *Cryst. Struct. Commun.* **1982**, *11*, 1621.
(13) Dekker, J.; Boersma, J.; Fernholt, L.; Haaland, A.; Spek, A. L. *Organometallics* **1987**, *6*, 1202.
(14) Dekker, J. Ph.D. Dissertation, University of Utrecht, The Netherlands, 1986; pp 82–85.

Scheme I



adducts of the aldolates in good yield.[15] The latter trimethylsilyl aldolates **3d–j** have the same high diastereoselectivity as the initially formed zinc–aldolates **2d–j**. The organic aldolates **3a** and **3b**, formed from quenching of the *syn/anti* mixtures of **2a** and **2b** with trimethylsilyl chloride, were obtained only in the *anti* diastereoisomeric form.

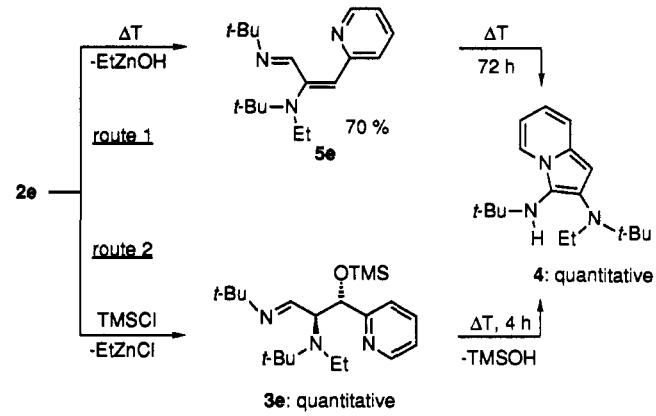
The aldolate **3f** (R″ = 3-pyridyl) was isolated as a coordination complex with EtOZnCl. Apparently, its amine, imine and pyridine nitrogens are so positioned that it can act as good terdentate ligand.

Although the zinc–aldolate **2c** was not observed with ^{1}H NMR spectroscopy at −50 °C, the treatment of a 1:1 mixture of **1** and *t*-BuCHO with trimethylsilyl chloride does give the aldolate **3c** as its trimethylsilyl ether and then exclusively in the *anti* diastereoisomeric form.

Attempts to achieve an enantioselective condensation reaction with the chiral alkyl aldehyde (1*R*)-2,3-*O*-isopropylideneglyceraldehyde (**k**) failed. Although, as stated above, the *syn/anti* mixtures **2a–c** eventually resulted in only the *anti* organic aldolates **3a–c**, in the case of **3k** the *syn* isomer was formed as well. A different approach to such an enantioselective reaction, involving the use of an enantiomerically pure R′DAB (R′ = (*R*)-1-ethylaminophenyl), was not successful. The 1:1 reaction of Et_2Zn with ((*R*)-PhC(Me)H)DAB resulted in the formation of two diastereoisomeric zinc–enamines without measurable enantiomeric excess.

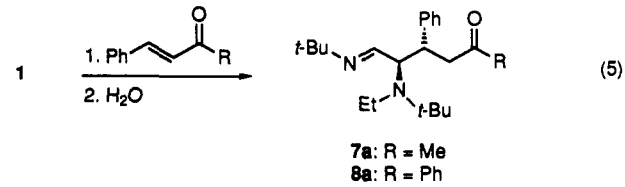
Except for **2e** (R″ = 2-pyridyl) the zinc–aldolates obtained in the reaction of **1** with aryl aldehydes show a high thermal stability.[7] Complex **2e** is only stable in solution for a few minutes at room temperature and gradually eliminates EtZnOH to afford enamine-H (**1a**) (30%) and for 70% to an unsaturated compound **5e** whose ^{1}H and ^{13}C NMR spectra are in accordance with the structure (**5e**) shown in route 1 in Scheme II. This elimination reaction is complete within 1 day at room temperature, but the reaction time is reduced to 1 h by heating the reaction mixture at 50 °C in benzene. Upon heating **5e** at 80 °C for 3 days in benzene solution in the presence of the eliminated zinc salts complete rearrangement to the isomeric 2,3-diaminoindolizine **4** occurs. The ^{1}H NMR spectrum of **4** shows a broad N*H* signal at 2.90 ppm and five aromatic protons with a characteristic singlet for the proton at position 1 (see Scheme II). The indolizine **4** was also obtained by heating the TMS aldolate **3e** at 80 °C for 4 h (route 2 in Scheme II). In this reaction sequence **5e** was not observed as intermediate. Apparently the eliminated trimethylsilanol catalyzes the formation of the

Scheme II



indolizine, as was confirmed by the fact that pure **5e** rearranges 40 times faster upon addition of separately prepared trimethylsilanol[16] than without.

Despite the high reactivity of **1** toward aldehydes, its reaction with ketones bearing α-hydrogens only resulted in deprotonation of the ketone and the formation of the protonated enamine-H (**1a**) and zinc–enolates. With ketones having no α-hydrogens, like benzophenone, no reaction was observed at all. As expected, a conjugated ketone function (as found in benzylidene acetone (**7**) and chalcone (**8**) gives rise to competition between the 1,4 addition reaction and deprotonation of the ketone. In the case of benzylideneacetone 55% 1,4-addition (**7a**) and 45% deprotonation occur, whereas in the case of chalcone only the Michael addition product **8a** is formed (see eq 5).



(5)

Discussion

The synthesis of the zinc–enamine **1** from *t*-BuDAB, simply by the reaction with the primary dialkylzinc compound Et_2Zn, is unprecedented. Comparable results of metallo–enamine or –enolate formation have so far only been obtained in the reaction of primary dialkylzinc compounds with DAB-related systems like α-imino ketones (*t*-BuN=CHCMe=O) and imino-esters (*t*-BuN=CHCOOEt) that also afforded N-alkylated products, RZn[OCMe=CHN(R)-*t*-Bu][17] and RZn[OC(OEt)=CHN(R)-*t*-Bu],[18a] respectively. The latter zinc–ester enolates are extremely reactive in the enolate–imine condensation reaction and were found to be useful precursors for the diastereo- and sometimes also enantioselective synthesis of compounds with the 2-azetidinone ring that is a building block of many β-lactams.[18]

In a recent publication the use of the lithium–enamine of the DAB system (R′N=CMeCMe=NR′) as nucleophilic

(15) After quenching of **2a–j** with trimethylsilyl chloride an additional equivalent of EtOH was necessary for converting soluble EtZnCl into slightly soluble EtOZnCl. Interestingly, after a quench of the zinc–aldolates with trimethylsilyl chloride, additional quenching with water instead of ethanol resulted in a mixture of aldolates with an imine or a deprotected aldehyde functionality.

(16) Trimethylsilanol was prepared by hydrolysis of trimethylsilyl chloride with 1 equiv of H_2O in diethyl ether. It is known that trimethylsilanol decomposes to hexamethyldisiloxane and H_2O. Pure, commercially available hexamethyldisiloxane or H_2O alone did not increase the rate of rearrangement from **5e** to **4**. However, hexamethyldisiloxane in combination with a drop of H_2O added to **5e** resulted, again, in an increase of the reaction rate.

(17) van Vliet, M. R. P.; van Koten, G.; Buysingh, P.; Jastrzebski, J. T. B. H.; Spek, A. L. *Organometallics* **1987**, *6*, 537.

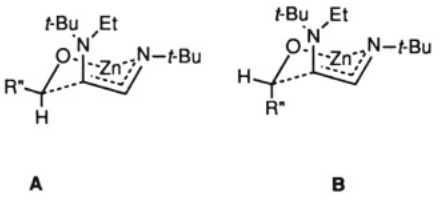


Figure 2. Proposed transition states in the condensation reaction of the zinc–enamine 1 with aldehydes.

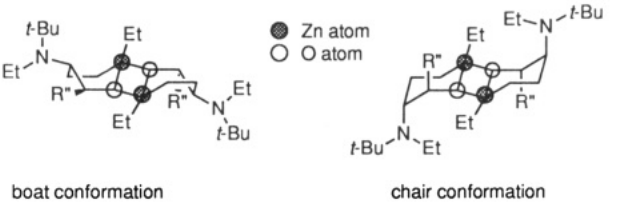
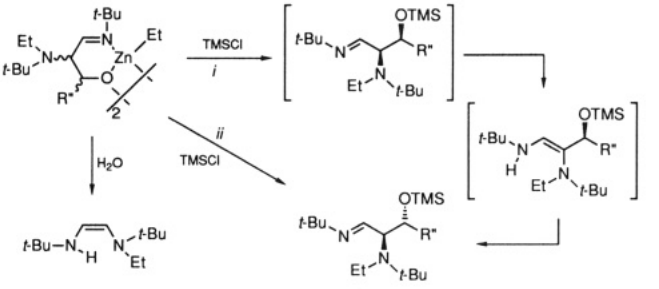


Figure 3. Boat and chair conformations of the zinc–aldolates **2a–j**.

Scheme III[a]



[a] Key: (i) via *syn* zinc–aldolate; (ii) via *anti* zinc–aldolate.

reagent in alkylation reactions was described. However, this lithium–enamine, prepared by deprotonation of the methyl group bound to the 1,4 diaza-1,3-butadiene system by LDA, has an exocyclic structure.[19]

The electronic structures of N-alkylated compounds, like 1, have been calculated by means of localized and canonical MOs as well as by Mulliken charges, and these calculations show that the most likely configuration for the ZnNCCN chelate ring in the zinc–enamines is an almost planar chelate ring with three-center delocalization within the *t*-BuNCHCH part.[3c,20] These features and charge distributions are indicative for a formulation of such compounds as enamine anions coordinated to RZn^+ cations. Former studies have shown that 1 is monomeric, probably because the stability of the planar conformation of the enamine hampers association.[3a]

We have limited our study of the reactivity of 1 to condensation reactions with aldehydes and α,β-unsaturated compounds. The diastereoselectivity in these reactions is extremely high and can be explained by considering the transition states in these C–C coupling reactions. Several transition states for aldol-type reactions have been proposed,[21] the most common of which is the "closed" transition state first proposed by Zimmerman and Taxler.[21d] We believe that our reactions proceed along similar lines as the closed transition state pathway. A decisive role in the transition state and product formation will be played by the *Z*-configuration of 1, which is imposed by the intramolecular coordination of the β-amino group. This leads to two possible transition states (**A** and **B**) for the aldol condensation reaction, which result in the formation of *syn* and *anti* aldols, respectively (see Figure 2).

In transition state **A** steric interference between the N(Et)-*t*-Bu group and the R″ group of aldehydes (R″CHO) is present, and this, in the case of large R″ groups, makes **A** less favorable. Accordingly, the exclusive formation of the *anti* isomer in the case of bulky aldehydes (R″CHO) is explained by assuming the involvement of transition state **B**, where the steric hindrance between these groups is minimized. When aldehydes with small R″ groups like propionaldehyde are used, the steric interference in **A** is decreased, and transition state **A** will become somewhat more favored, and this is reflected in the partial formation of the *syn*-aldolate in those cases.

The zinc–aldolates thus formed dimerize, and as shown by the dinuclear units in the crystal structure of **2g**, they have a distorted boat conformation. This is clearly the favored conformation since the chair conformation would place both the R″ group and the N(Et)-*t*-Bu group in axial positions, so inducing severe steric interactions between these groups and the Et groups bound to the zinc atoms (see Figure 3).

There is good evidence, especially in the case of the aldolates formed in the condensation reaction of 1 with alkyl aldehydes **2a–c**, that an equilibrium exists between the zinc–aldolate and the starting materials. Firstly, the TMS aldolate **3c** could be isolated after quenching the reaction mixture of 1 and pivaldehyde with trimethylsilyl chloride, whereas the zinc–aldolate **2c** was not even observable by ^1H NMR spectroscopy. Apparently, the equilibrium in this latter case lies almost completely to the side of the starting materials. Secondly, in the case of **2a** the *syn*/*anti* ratio of 40/60 found at room temperature changes reversibly to a 50/50 ratio at 50 °C. Finally, quenching of the zinc–aldolates with water or EtOH did not afford the organic aldolates but afforded the hydrolyzed enamine instead. This result can be explained when there is an equilibrium between the starting materials and the zinc–aldolate and when one uses the fact that the Zn–N bond in 1 is much more sensitive to hydrolysis than the Zn–O bond in the zinc–aldolates, and therefore, the former is quenched more rapidly.

In all cases, the TMS aldolates, **3a–j**, have the *anti*-configuration. Even **2a**, with a *syn*/*anti* ratio of 40/60, when quenched with trimethylsilyl chloride resulted in the formation of the *anti* diastereoisomer **3a**. We believe that the *syn* isomer of **3a** rearranges *via* a fast imine–enamine tautomerization (see Scheme III) to the *anti* isomer **3a**, which probably has the thermodynamically more stable configuration. Such a tautomerization reac-

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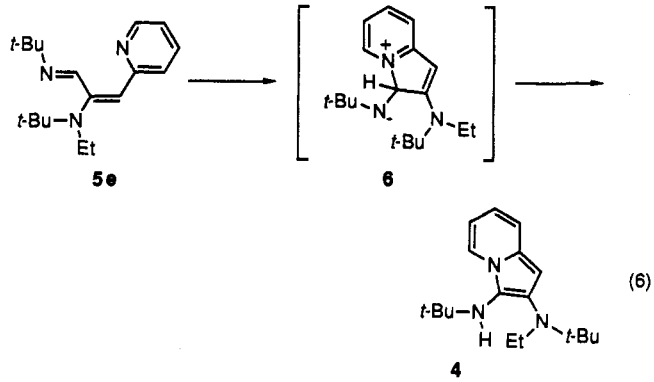
tion was found earlier for the products obtained in alkylation reactions of ketone dimethylhydrazones; here, the alkylated products that were first obtained in a *Z* imine configuration slowly isomerize to the *E* isomer.[22]

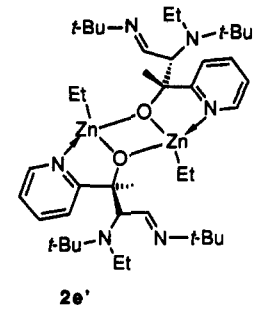
Conversion of 2e to Indolizine. The thermal instability of **2e** that stands in contrast to the good stability of other zinc–aldolates is most probably due to intramolecular coordination of the pyridine nitrogen to zinc. Earlier studies in our group on stable dimeric zinc–enolates with an intramolecularly coordinating amine has shown that the Zn–N bond is easily broken upon addition of Lewis bases like pyridine.[10] In the case of **2e** this would result in the formation of **2e'** (see Figure 4), which is a dimeric zinc–alkoxide with two five-membered chelate rings. Complexes like **2e'** have been investigated intensively in our laboratory and were found to be stable dimeric or tetrameric compounds,[23,24] and there is *a priori* no reason why **2e'** should be unstable. Nevertheless, the pyridine nitrogen can only coordinate to zinc when the boat conformation of the zinc–aldolate **2e** twists to the sterically highly unfavorable chair conformation (see Figure 3 chair/boat). It is possibly this conformation that leads to **2e'**, which because of its steric crowding eliminates EtZnOH so resulting in the α,β-unsaturated system **5e** (70%) and enamine-H (30%) that arises from a protonation reaction of **2e** by the eliminated EtZnOH. Efforts to prepare corresponding α,β-unsaturated systems from comparable zinc-aldolates like **2d**, **2f** and **2g** upon addition of pyridine failed, probably because of the inability of these systems to form compounds like **2e'**.

The unsaturated species **5e** is unstable as well and rearranges fully to the isomeric indolizine **4** within 72 h at 80 °C in benzene. The mechanism we propose for the formation of **4** involves the elimination of EtZnOH from the *anti* zinc–aldolate **2e** by an E_2 reaction, leading to the formation of the unsaturated species **5e** in an *E* configuration, followed by an intramolecular nucleophilic attack of the pyridine lone pair at the imine carbon, leading to the zwitterionic intermediate **6** (see eq 6). The metal salts



(6)

present, zinc salts in route 1 and hexamethylsiloxane[16] in route 2 (see Scheme II), may stabilize intermediate **6** by coordinating to the negatively charged nitrogen atom. Intermediate **6** may then subsequently rearrange *via* a 1,2



2e'

Figure 4. Structure of **2e'**, a dimeric zinc–alkoxide with intramolecular coordination *via* the pyridyl nitrogens.

H-shift from the formal imine carbon to the nitrogen atom. The same mechanism probably accounts for the reaction starting with the TMS ether aldolate **3e** (see route 2), although the unsaturated species **5e** was not observed in this case.

The accelerating effect of the Lewis acids in the cyclization reaction to the indolizine was shown by a 40-fold increase in the rearrangement rate of **3** to **4** upon the addition of trimethylsilyl hydroxide. Overall, the driving force for the rearrangement of **5e** to the indolizine **4** is the formation of an aromatic species with a delocalized 10π-electron system.[25] The intermediates **5e** and **6** were also suggested by Flitsch *et al.*[26] in their synthesis of 3-aminoindolizines from 2-cyanovinylpyridine.

Concluding Remarks

The easily accessible zinc–enamine **1** shows an interesting reactivity toward aldehydes that in a diastereoselective condensation reaction affords almost exclusively *anti* aldolates. The high diastereoselectivity is partly caused by the intramolecular coordination of the N(Et)-*t*-Bu group to the zinc atom, which ensures a *Z*-configuration of the zinc–enamine. This in combination with the bulk of the N(Et)-*t*-Bu group produces, especially in the reaction with aryl aldehydes, only the *anti* condensation product. Of special interest is the unique structure of the coordination polymer **4g**, which is the result of self-assembly of a zinc-aldolate and Et_2Zn. The reactivity of the polymer with aldehydes is of interest in the synthesis of secondary alcohols.[27] Therefore, we are now extending our research in this field to the synthesis of enantiomerically pure coordination polymers, which could act as chiral precursors in the enantioselective addition reaction of Et_2Zn to aldehydes.

Experimental Section

General Data. All experiments were carried out under a dry and oxygen-free nitrogen atmosphere, using standard Schlenk techniques. Solvents were carefully dried and distilled from sodium/benzophenone prior to use. All standard chemicals were purchased from Aldrich Chemical Co. or Janssen Chimica. The starting material *N,N'*-di-*tert*-butyl-1,4-diaza-1,3-butadiene (*t*-BuDAB)[28] was prepared according to literature procedures. 2,3-*O*-Isopropylidene-D-glyceraldehyde was prepared from D-man-

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nitol according to literature procedures.[29] ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200 or Bruker AC-300 spectrometer in C_6D_6, using TMS as an external standard (0.0 ppm). Boiling and melting points are uncorrected. Elemental analyses were performed by Dornis and Kolbe, Germany.

General Procedure for the Synthesis of Trimethylsilyl Ether Aldolates. To a stirred solution containing 1.68 g (10 mmol) of *t*-BuDAB in 25 mL of hexane at 0 °C was added 10 mmol of Et_2Zn (10 mL of a 1.0 M solution in hexane). The resulting solution was stirred for 1 min and then 10 mmol of an appropriate aldehyde was added. (Most zinc–aldolates could easily be obtained as white solid compounds in quantitative yield by crystallization from hexane at −20 °C.) The reaction mixture was allowed to warm to rt and quenched with trimethylsilyl chloride (1.27 mL, 10 mmol). After the mixture was stirred for 15 min 1 equiv of EtOH (10 mmol, 0.58 mL) was added carefully.[16] To accomplish complete hydrolysis of the organozinc intermediate the mixture was stirred for an additional 30 min after which the solid material was separated by centrifugation and the clear solution collected by decantation. The solid was then extracted with hexane (2 × 10 mL). The combined organic extracts were concentrated *in vacuo* to afford the organic product.

Zinc–aldolate of propionaldehyde (2a): white solid, yield 3.46 g (99%); ^1H NMR spectroscopy revealed the product to be a mixture of two diastereomers in a 62:38 ratio; ^1H NMR (main diastereomer) δ 7.89 (d, *J* = 3.5 Hz, 1H, N=C*H*), 4.05 (m, 1H, CHCO*H*Et), 3.43 (dd, *J* = 8.9, 3.5 Hz, 1H, NC*H*CO), 2.67, 2.43 (m, 2 × 1H, NC*HH'*CH_3), 2.1 (m, 2H, CHOC$H_2$$CH_3$), 1.65 (t, 3H, ZnC$H_2CH_3$), 1.32 (s, 9H, *t*-Bu), 1.31 (t, 3H, CHOCH_2CH_3), 1.04 (t, 3H, NCH_2CH_3), 1.00 (s, 9H, *t*-Bu), 0.50 (q, 2H, ZnC$H_2$$CH_3$); ^{13}C NMR: δ 172.8 (N=*C*H), 75.4 (*C*HO), 65.5 (N*C*H), 59.1, 55.5 (*C*(CH_3)$_3$), 41.0 (N*C*$H_2$$CH_3$), 29.9, 29.1 (C(*C*$H_3$)$_3$), 28.0 (CHO*C*$H_2$-$CH_3$), 19.9 (NC$H_2$*C*$H_3$), 14.3 (CHOC$H_2$*C*$H_3$), 8.9 (ZnC$H_2$*C*$H_3$), −0.48 (Zn*C*$H_2$$CH_3$); ^1H NMR (minor diastereomer) δ 7.91 (d, *J* = 2.4 Hz, 1H, N=C*H*), 4.00 (m, 1H, CHCO*H*Et), 3.53 (dd, *J* = 8.8, 2.4 Hz, 1H, NC*H*CO), 2.67, 2.43 (m, 2 × 1H, NC$H_2$$CH_3$), 2.1 (m, 2H, CHOC*HH'*$CH_3$), 1.65 (t, 3H, ZnC$H_2CH_3$), 1.32 (s, 9H, *t*-Bu), 1.26 (t, 3H, CHOCH_2CH_3), 1.04 (s, 9H, *t*-Bu), 0.99 (t, 3H, NCH_2CH_3), 0.50 (q, 2H, Zn*C*$H_2$$CH_3$); ^{13}C NMR δ 173.6 (N=*C*H), 76.3 (*C*HO), 65.7 (N*C*H), 59.1, 55.3 (*C*(CH_3)$_3$), 40.9 (N*C*$H_2$$CH_3$), 29.9, 29.1 (C(*C*$H_3$)$_3$), 28.57 (CHO*C*$H_2$$CH_3$), 20.1 (NC$H_2$*C*$H_3$), 14.3 (CHOC$H_2$*C*$H_3$), 10.1 (ZnC$H_2$*C*$H_3$), 1.3 (Zn*C*$H_2$$CH_3$). Anal. Calcd for $C_{17}H_{36}N_2OZn$: C, 58.36; H, 10.37; N, 8.01. Found: C, 58.18; H, 10.35; N, 7.86.

Trimethylsilyl ether of propionaldehyde aldolate (3a): colorless oil; yield 2.82 g (86%); bp 78 °C (0.1 mmHg); ^1H NMR δ 7.83 (d, *J* = 6.3 Hz, 1H, N=C*H*), 4.01 (m, 1H, CHCO*H*Et), 3.71 (dd, *J* = 6.3, 7.9 Hz, 1H, NC*H*CO), 2.94, 2.70 (2 × m, 2 × 1H, NC*HH'*CH_3), 1.90, 1.76 (m, 2 × 1H, COHC*HH'*CH_3), 1.20, 1.10 (s, 2 × 9H, *t*-Bu), 1.03 (t, 3H, COHCH_2CH_3), 1.00 (t, 3H, NCH_2CH_3), 0.18 (s, 9H, Si(CH_3)$_3$); ^{13}C NMR δ 159.3 (N=*C*H), 76.2 (*C*HO), 64.0 (N*C*H), 57.0, 55.9 (*C*(CH_3)$_3$), 38.8 (N*C*$H_2$$CH_3$), 29.7, 29.4 (C(*C*$H_3$)$_3$), 27.3 (CHO*C*$H_2$$CH_3$), 20.3 (NC$H_2$*C*$H_3$), 9.5 (CHOC$H_2$*C*$H_3$), 0.9 (Si(*C*$H_3$)$_3$).

Desilylation Products 4a and 5a. Compound **3a** was heated in hexane at 68 °C for 24 h after which the solvent was removed *in vacuo* leaving a pale yellow oil. ^1H NMR spectroscopy revealed the product to be a mixture of two isomers: *t*-BuN=CHC(N-*t*-Bu(Et))=CHEt (**4a**) (72%) and *trans*-*t*-BuN(H)CH=C(N-*t*-Bu(Et))CH=CHCH$_3$ (**5a**) (28%): ^1H NMR **4a** (70 °C) δ 7.65 (s, 1H, N=C*H*), 5.92 (t, *J* = 7.2 Hz, 1H, C=C*H*CH$_2$), 3.09 (brq, 2H, NCH_2CH$_3$), 2.29 (brdq, 2H, C=CHCH_2CH$_3$), 1.23, 1.15 (s, 2 × 9H, *t*-Bu), 0.93 (t, 3H, NCH$_2$CH_3), 0.92 (t, 3H, C=CHCH$_2$CH_3); ^1H NMR **5a** (25 °C): δ 6.25 (d, *J* = 12.6 Hz, 1H, NHC*H*), 6.00 (dq, *J* = 15.3, ^4J = 1.41 Hz, 1H, C*H*=CHCH$_3$), 5.49 (dq, *J* = 15.3, 6.46 Hz, 1H, CH=C*H*CH$_3$), 4.39 (d, *J* = 12.6 Hz, 1H, N*H*), 2.85 (q, 2H, NCH_2CH$_3$), 1.75 (dd, *J* = 6.5 Hz, ^4J = 1.4 Hz, 3H, CH=CHCH_3), 1.20, 1.03 (s, 2 × 9H, *t*-Bu), 1.01 (t, 3H, NCH$_2$CH_3).

Zinc Aldolate of Isobutyraldehyde (2b). Compound **2b** was obtained as a white solid, yield 3.41 g (94%). No reliable NMR data were obtained because of broad signals. Anal. Calcd for $C_{18}H_{38}N_2OZn$: C, 59.41; H, 10.53; N, 7.70. Found: C, 58.67; H, 10.31; N, 7.80.

Trimethylsilyl ether of isobutyraldehyde aldolate (3b): colorless oil; yield 2.87 g (84%); bp 81 °C (0.1 mmHg); ^1H NMR: δ 7.83 (d, *J* = 6.2 Hz, 1H, N=C*H*), 3.92 (dd, *J* = 1.8 Hz, *J* = 8.6 Hz, 1H, CHCO*H*-*i*-Pr), 3.82 (dd, *J* = 6.2, 8.6 Hz, 1H, NC*H*CO), 2.96, 2.70 (m, 2 × 1H, NC*HH'*CH$_3$), 2.47 (dsep, *J* = 1.8 Hz, *J* = 7.1 Hz, 1H, COHC*H*((CH_3)$_2$), 1.22, 1.12 (s, 2 × 9H, *t*-Bu), 1.06 (d, *J* = 7.1 Hz, 3H, CH(C*H*$_3$)CH'$_3$), 1.04 (t, 3H, NCH$_2$C*H*$_3$), 1.00 (d, *J* = 7.1 Hz, 3H, CH(CH$_3$)C*H'*$_3$), 0.18 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR: δ 159.2 (N=*C*H), 79.6 (*C*HO), 63.5 (N*C*H), 57.2, 55.9 (*C*(CH_3)$_3$), 38.9 (NCH$_2$CH$_3$), 29.6, 29.5 (C(*C*H$_3$)$_3$), 29.4 (CHO*C*H-(CH$_3$)$_2$), 21.1 (20.5 (CH(*C*H$_3$)$_2$), 15.9 (NCH$_2$*C*H$_3$), 1.3 (Si(*C*H$_3$)$_3$).

Trimethylsilyl ether of pivaldehyde aldolate (3c): white solid; yield 3.09 (87%); mp 43 °C; ^1H NMR δ 7.73 (d, *J* = 6.9 Hz, 1H, N=C*H*), 4.09 (dd, *J* = 2.8, 6.9 Hz, 1H, NC*H*CO), 3.80 (d, *J* = 2.8 Hz, CHCO*H*-*t*-Bu), 3.04, 2.87 (m, 2 × 1H, NC*HH'*CH$_3$), 1.22, 1.12, 1.04 (s, 3 × 9H, *t*-Bu), 1.17 (t, 3H, NCH$_2$C*H*$_3$), 0.20 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR: δ 159.6 (N=*C*H), 85.7 (*C*HO), 64.4 (N*C*H), 56.7, 56.3 (*C*(CH_3)$_3$), 39.5 (C(OSiMe$_3$)*C*(CH$_3$)$_3$), 37.4 (NCH$_2$CH$_3$), 29.5, 29.3, 26.7 (C(*C*H$_3$)$_3$), 21.8 (NCH$_2$CH$_3$), 1.3 (Si-(*C*H$_3$)$_3$). Anal. Calcd for $C_{20}H_{44}N_2OSi$: C, 67.35; H, 12.43; N, 7.85. Found: C, 67.87; H, 12.43; N, 7.79.

Zinc–aldolate of benzaldehyde (2d): white solid; yield 3.89 g (98%); ^1H NMR δ 7.91 (d, *J* = 3.9 Hz, 1H, N=C*H*), 7.62–7.16 (m, 5H, aryl), 4.88 (d, *J* = 8.9 Hz, 1H, CHCO*H*Ph), 3.88 (dd, *J* = 8.9, 3.9 Hz, 1H, NC*H*CO), 2.57 (m, 2H, NC*HH'*CH$_3$), 1.81 (t, 3H, ZnCH$_2$C*H*$_3$), 0.96 (s, 9H, *t*-Bu), 0.91 (t, 3H, NCH$_2$C*H*$_3$), 0.80 (s, 9H, *t*-Bu), 0.69 (q, 2H, ZnC*H*$_2$CH$_3$); ^{13}C NMR δ 172.0 (N=*C*H), 147.4, 129.4, 127.5, 126.6 (aryl), 79.1 (*C*HO), 68.1 (N*C*H), 58.7, 55.3 (*C*(CH_3)$_3$), 41.0 (N*C*H$_2$CH$_3$), 29.4, 28.8 (C(*C*H$_3$)$_3$), 19.7 (NCH$_2$*C*H$_3$), 14.7 (ZnCH$_2$*C*H$_3$), −1.3 (Zn*C*H$_2$CH$_3$). Anal. Calcd for $C_{42}H_{72}N_4O_2Zn_2$: C, 63.39; H, 9.12; N, 7.04. Found: C, 62.80; H, 9.22; N, 7.08.

Trimethylsilyl ether of benzaldehyde aldolate (3d): colorless oil; yield 3.05 g (81%); ^1H NMR δ 7.93 (d, *J* = 6.3 Hz, 1H, N=C*H*), 7.38–7.05 (m, 5H, aryl), 4.91 (d, *J* = 8.1 Hz, 1H, CHCO*H*Ph), 3.88 (dd, *J* = 8.1, 6.2 Hz, 1H, NC*H*CO), 2.99, 2.83 (m, 2 × 1H, NC*HH'*CH$_3$), 1.21 (s, 9H, *t*-Bu), 1.11 (t, 3H, NCH$_2$C*H*$_3$), 0.88 (s, 9H, *t*-Bu), 0.02 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR δ 159.1 (N=*C*H), 144.4, 128.1, 127.6, 127.3 (aryl), 77.2 (*C*HO), 67.6 (N*C*H), 57.0, 55.7 (*C*(CH_3)$_3$), 39.1 (N*C*H$_2$CH$_3$), 29.6, 29.0 (C(*C*H$_3$)$_3$), 19.9 (NCH$_2$*C*H$_3$), 0.4 (Si(*C*H$_3$)$_3$). Anal. Calcd for $C_{22}H_{40}N_2OSi$: C, 70.15; H, 10.70; N, 7.44. Found: C, 70.08; H, 10.65; N, 7.51.

Zinc–aldolate of 2-pyridinecarboxaldehyde (picolinealdehyde) (2e): white solid; only stable for a few hours as a solid and for a few minutes in solution; ^1H NMR (broad signals at 25 °C) δ 8.19 (s, 1H, pyridine), 8.01 (d, *J* = 5.8 Hz, 1H, N=C*H*), 7.33 (d, *J* = 7.3 Hz, 1H, pyridine), 6.98 (t, *J* = 7.5 Hz, 1H, pyridine), 6.55 (t, 1H, pyridine), 5.62 (br s, 1H, CHCO*H*), 3.69 (dd, *J* = 5.8 Hz, 1H, NC*H*), 3.31, 2.91 (m, 2 × 1H, NC*HH'*CH$_3$), 1.63 (t, 3H, ZnCH$_2$C*H*$_3$), 1.31 (t, 3H, NCH$_2$C*H*$_3$), 1.08, 0.96 (s, 2 × 9H, *t*-Bu), 0.66 (q, 2H, Zn*C*H$_2$CH$_3$).

Trimethyl Ether of Picolinealdehyde Aldolate (3e). Compound **3e** could only be isolated in a 70:30 mixture with enamine-H. Mixture is a pale yellow oil. During attempted purification by distillation **3e** rearranged quantitatively to 2-(*tert*-butylethylamino)-3-(*tert*-butylamino)indolizine (**5e**): ^1H NMR **3e** δ 8.41 (m, 1H, pyridine), 7.98 (d, *J* = 6.3 Hz, 1H, N=C*H*), 7.32 (d, *J* = 7.9 Hz, 1H, pyridine), 7.12 (m, 1H, pyridine), 6.63 (m, 1H, pyridine), 5.29 (d, *J* = 7.6 Hz, 1H, CHCO*H*), 4.25 (dd, *J* = 7.6, 6.3, 1H, NC*H*), 3.08, 2.92 (m, 2 × 1H, NC*HH'*CH$_3$), 1.63 (t, 3H, ZnCH$_2$C*H*$_3$), 1.19 (s, 9H, *t*-Bu), 1.18 (t, 3H, NCH$_2$C*H*$_3$), 1.02 (s, 9H, *t*-Bu), 0.06 Si(C*H*$_3$)$_3$; ^{13}C NMR δ 163.9 (pyridine), 158.6 (N=*C*H), 148.3, 135.3, 132.0, 122.0, 121.9 (pyridine), 79.3 (*C*HO), 66.7 (N*C*H), 57.0, 55.9 (*C*(CH_3)$_3$), 39.4 (N*C*H$_2$CH$_3$), 29.6, 29.3 (C(*C*H$_3$)$_3$), 19.6 (NCH$_2$*C*H$_3$), 0.3 (Si(*C*H$_3$)$_3$).

Dehydration Product of 2-Pyridinecarboxaldehyde Zinc–Aldolate (4e) and 2-(*tert*-Butylethylamino)-3-(*tert*-butylamino)indolizine (5e). Dissolution of **2e** in C_6H_6 (15 mL) and heating at 70 °C for 30 min leads to the formation of **4e** (80%) and the hydrolyzed starting zinc–enamine, enamine-H (**1a**) (20%). After removal of the solvent *in vacuo* hexane (15 mL) was added. The solid material was separated by centrifugation and the clear solution collected by decantation. The solid was extracted with hexanes (2 × 10 mL). The combined organic extracts were concentrated *in vacuo*, affording the organic

(29) (a) Kuszmann, J.; Tomori, E.; Meerwald, I. *Carbohydr. Res.* **1984**, *128*, 87. (b) Hubschwerlen, C. *Synthesis* **1986**, 962.

product mixture. The enamine-H was removed by careful distillation of the mixture under reduced pressure (0.1 mmHg) leaving a thick yellow oil. The ^{1}H NMR spectrum of the yellow oil showed the partial conversion of **4e** to the indolizine **5e**. Dissolution of the yellow oil in benzene and subsequent heating at 80 °C for 72 h led to the quantitative formation of the indolizine **5e**. The reaction time could be decreased to 6 h by addition of TMSOH:[10] ^{1}H NMR **4e** (60 °C) δ 8.92 (dt, 1H, pyridine), 8.58 (m, 1H, pyridine), 7.80 (s, 1H, N=C*H*), 7.42 (s, 1H, C=C*H*(C_5H_4N)), 7.19 (m, 1H, pyridine), 6.63 (m, 1H, pyridine), 3.31 (q, 2H, NCH_2CH$_3$), 1.27 (s, 9H, *t*-Bu), 1.15 (t, 3H, NCH$_2$CH_3), 1.11 (s, 2 × 9H, *t*-Bu); ^{13}C NMR δ 157.4 (N=CH), 156.9, 149.8 (pyridine), 147.7 (*C*=CH), 140.8 (C=*C*H), 134.8, 124.7, 122.0 (pyridine), 57.2, 55.9 (*C*(CH_3)$_3$), 39.8 (NCH_2CH$_3$), 29.5, 29.2 (C(*C*H$_3$)$_3$), 15.7 (NCH$_2$*C*H$_3$); ^{1}H NMR of **5e** δ 8.19 (d, 1H, pyridine), 7.12 (d, 1H, pyridine), 6.43 (dt, 1H, pyridine), 6.29 (s, 1H, C=C*H*C_5H_4N), 6.24 (dt, 1H, pyridine), 3.03 (q, 2H, NCH_2CH$_3$), 2.90 (bs, 1H, N*H*), 1.21, 1.06 (s, 9H, C(CH_3)$_3$), 1.00 (t, 3H, NCH$_2$CH_3); ^{13}C NMR of **te** δ 132.1 C(3), 127.7 C(2), 125.3 C(9), 122.5 C(5), 118.5 C(8), 115.7 C(7), 108.7 C(6), 95.70 C(1), 57.0, 55.0 (*C*(CH_3)$_3$), 44.1 (NCH_2CH$_3$), 31.2, 27.8 (C(*C*H$_3$)$_3$), 15.7 (NCH$_2$*C*H$_3$). Anal. Calcd for $C_{18}H_{29}N_3$: C, 75.21; H, 10.17; N, 14.62. Found: C, 75.17; H, 10.20; N, 14.69.

Zinc–aldolate of 3-pyridinecarboxaldehyde (nicotinealdehyde) (2f): white solid; yield 3.90 g (98%); ^{1}H NMR δ 9.01 (d, 1H, aryl), 8.58 (m, 1H, aryl), 7.84 (d, *J* = 3.8 Hz, 1H, N=C*H*), 7.73 (m, 1H, aryl), 6.95 (m, 1H, aryl), 4.85 (d, *J* = 9.0 Hz, 1H, CHCO*H*), 3.80 (dd, *J* = 9.0, 3.8 Hz, 1H, NC*H*), 2.54, 2.39 (m, 2 × 1H, NC*HH'*CH$_3$), 1.70 (t, 3H, ZnCH$_2$CH_3), 0.90 (s, 9H, *t*-Bu), 0.82 (t, 3H, NCH$_2$CH_3), 0.73 (s, 9H, *t*-Bu), 0.59 (q, 2H, ZnCH_2CH$_3$); ^{13}C NMR δ 171.7 (N=*C*H), 151.3, 148.5, 142.1, 135.6, 122.6 (aryl), 76.9 (*C*HO), 67.8 (*N*CH), 59.0, 55.4 (*C*(CH_3)$_3$), 41.0 (NCH_2CH$_3$), 29.3, 28.6 (C(*C*H$_3$)$_3$), 19.5 (NCH$_2$*C*H$_3$), 14.5 (ZnCH$_2$*C*H$_3$), −1.4 (Zn*C*H$_2$CH$_3$). Anal. Calcd for $C_{40}H_{70}N_6O_2Zn_2$: C, 60.22; H, 8.84; N, 10.53. Found: C, 60.28; H, 8.81; N, 10.36.

Trimethylsilyl Ether of Nicotinealdehyde Aldolate (3f). Compound **3f** formed a stable 1:1 complexation adduct with ClZnOEt, which was crystallized from Et_2O at −20 °C: white solid; yield 2.82 (54%); ^{1}H NMR (70 °C) δ 9.19 (s, 1H, pyridine), 8.76 (d, *J* = 4.6 Hz, 1H, pyridine), 7.84 (d, *J* = 5.8 Hz, 1H, N=C*H*), 7.72 (m, 1H, pyridine), 6.98 (m, 1H, pyridine), 5.09 (d, *J* = 8.7 Hz, 1H, CHCO*H*), 4.14 (br q, 2H, ClZnOCH_2CH$_3$), 3.72 (dd, *J* = 8.7, 5.82 Hz, 1H, NC*H*), 2.99, 2.84 (m, 2 × 1H, NC*HH'*CH$_3$), 1.31 (brt, 3H, ClZnOCH$_2$CH_3), 1.18 (s, 9H, *t*-Bu), 1.12 (s, 3H, NCH$_2$CH_3), 0.80 (s, 9H, *t*-Bu), 0.01 (s, 9H, Si(CH_3)$_3$); ^{13}C NMR δ 158.4 (N=*C*H), 149.2, 147.6, 142.5, 138.3, 124.4 (pyridine), 72.7 (*C*HO), 67.6 (*N*CH), 63.1 (ClZnOCH$_2$CH$_3$), 57.2, 55.7 (*C*(CH_3)$_3$), 39.5 (NCH_2CH$_3$), 29.5, 29.0 (C(*C*H$_3$)$_3$), 21.0 (NCH$_2$*C*H$_3$), 19.6 (ClZnOCH$_2$*C*H$_3$), 0.3 (Si(*C*H$_3$)$_3$). No satisfactory elemental analysis was obtained. Most probably the product consists partly of TMS aldolate **3f** without EtZnOEt complexed to it.

Zinc–aldolate of 4-pyridinecarboxaldehyde (2g): white solid; yield 3.91 g (98%); ^{1}H NMR δ 8.69 (d, *J* = 5.8 Hz, 2H, aryl), 7.81 (d, *J* = 3.7 Hz, 1H, N=C*H*), 7.36 (d, *J* = 5.8 Hz, 2H, aryl), 4.74 (d, *J* = 9.0 Hz, 1H, CHCO*H*), 3.75 (dd, *J* = 9.0, 3.7 Hz, 1H, NC*H*), 2.54, 2.38 (m, 2 × 1H, NC*HH'*CH$_3$), 1.72 (t, 3H, ZnCH$_2$CH_3), 0.88 (t, 3H, NCH$_2$CH_3), 0.85, 0.71 (s, 2 × 9H, *t*-Bu), 0.60 (q, 2H, ZnCH_2CH$_3$); ^{13}C NMR δ 171.7 (N=*C*H), 155.2, 149.7, 124.3 (aryl), 78.3 (*C*HO), 67.4 (*N*CH), 59.0, 55.4 (*C*(CH_3)$_3$), 41.2 (NCH_2CH$_3$), 29.3, 28.5 (C(*C*H$_3$)$_3$), 19.6 (NCH$_2$*C*H$_3$), 14.5 (ZnCH$_2$*C*H$_3$), −1.4 (Zn*C*H$_2$CH$_3$). Anal. Calcd for $C_{20}H_{35}N_3OZn$: C, 60.22; H, 8.84; N, 10.53. Found: C, 58.85; H, 8.71; N, 10.45.

Polymer of Zinc–Aldolate of 4-Pyridinecarboxaldehyde (4g). The zinc–aldolate **2g** (3.98 g, 10 mmol) was dissolved in Et_2O (100 mL), and 0.5 equiv of Et_2Zn (5 mL of a 1 M solution in hexane) was added. The solvent was removed *in vacuo*, affording the polymeric compound **4g** as a yellow solid in quantitative yield. Suitable crystals for an X-ray determination of **4g** were obtained from a warm hexane solution:[30] ^{1}H NMR δ 8.54 (d, *J* = 5.8 Hz, 4H, aryl), 7.84 (d, *J* = 3.7 Hz, 2H, N=C*H*), 7.35 (d, *J* = 5.8 Hz, 4H, aryl), 4.74 (d, *J* = 9.0 Hz, 2H, CHCO*H*), 3.74 (dd, *J* = 9.0 Hz, *J* = 3.7 Hz, 2H, NC*H*), 2.59, 2.41 (m, 2 × 2H, NC*HH'*CH$_3$), 1.65 (t, 6H, ZnCH$_2$CH_3), 1.48 (t, 3H, Zn(CH$_2$CH_3)$_2$), 0.88 (t, 3H, NCH$_2$CH_3), 0.86, 0.71 (s, 2 × 9H, *t*-Bu), 0.53 (m, 6H, ZnCH_2CH$_3$); ^{13}C NMR δ 171.8 (N=*C*H), 155.2, 149.1, 124.5 (aryl), 78.2 (*C*HO), 67.4 (*N*CH), 59.1, 55.4 (*C*(CH_3)$_3$), 41.1 (NCH$_2$CH$_3$), 29.4, 28.6 (C(*C*H$_3$)$_3$), 19.5 (NCH$_2$*C*H$_3$), 14.3 (ZnCH$_2$*C*H$_3$), 12.0 (Zn(CH$_2$*C*H$_3$)$_2$), 4.4 (Zn(*C*H$_2$CH$_3$)$_2$), −1.4 (Zn*C*H$_2$CH$_3$). Anal. Calcd for $C_{44}H_{90}N_6O_2Zn_3$: C, 57.36; H, 8.75; N, 9.12. Found: C, 56.41; H, 8.64; N, 8.92.

Zinc–aldolate of 2-furaldehyde (2h): white solid; yield 3.79 (98%); ^{1}H NMR δ 7.87 (d, *J* = 3.9 Hz, 1H, N=C*H*), 7.19 (s, 1H, furan), 6.19 (m, 2H, furan), 4.97 (d, *J* = 9.3 Hz, 1H, CHCO*H*), 4.04 (dd, *J* = 9.3, 3.9 Hz, 1H, NC*H*), 2.65, 2.47 (m, 2 × 1H, NC*HH'*CH$_3$), 1.76 (t, 3H, ZnCH$_2$CH_3), 1.10 (s, 9H, *t*-Bu), 1.00 (t, 3H, NCH$_2$CH_3), 0.89 (s, 9H, *t*-Bu), 0.64 (q, 2H, ZnCH_2CH$_3$); ^{13}C NMR δ 171.1 (N=*C*H), 159.9, 139.9, 109.8, 107.0 (furan), 71.9 (*C*HO), 66.5 (*N*CH), 59.1, 55.2 (*C*(CH_3)$_3$), 41.1 (NCH_2CH$_3$), 29.3, 28.8 (C(*C*H$_3$)$_3$), 20.1 (NCH$_2$*C*H$_3$), 14.4 (ZnCH$_2$*C*H$_3$), −1.8 (Zn*C*H$_2$CH$_3$). Anal. Calcd for $C_{19}H_{34}N_2O_2Zn$: C, 58.84; H, 8.84; N, 7.22. Found: C, 58.98; H, 8.99; N, 7.12.

Trimethylsilyl ether of furaldehyde aldolate (3h); pale yellow oil; yield 2.96 g (81%); ^{1}H NMR δ 7.86 (d, *J* = 5.7 Hz, 1H, N=C*H*), 7.10 (d, *J* = 0.2 Hz, 1H, furan), 6.11 (m, 2H, furan), 5.06 (d, *J* = 8.9 Hz, 1H, CHCO*H*), 4.22 (dd, *J* = 8.9, 5.7 Hz, 1H, NC*H*), 2.94, 2.68 (m, 2 × 1H, NC*HH'*CH$_3$), 1.20 (s, 9H, *t*-Bu), 1.04 (t, 3H, NCH$_2$CH_3), 0.99 (s, 9H, *t*-Bu), 0.04 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR δ 158.2 (N=*C*H), 156.6, 140.9, 110.2, 108.1 (furan), 70.4 (*C*HO), 64.9 (*N*CH), 57.0, 55.7 (*C*(CH_3)$_3$), 38.6 (NCH_2CH$_3$), 29.6, 29.2 (C(*C*H$_3$)$_3$), 20.0 (NCH$_2$*C*H$_3$), 0.1 (Si(*C*H$_3$)$_3$).

Zinc–aldolate of methacrolein (2i): white solid; yield 3.54 g (98%); ^{1}H NMR δ 7.89 (d, *J* = 4.4 Hz, 1H, N=C*H*), 5.17, 5.00 (d, ^2J = 1.7 Hz, 2 × 1H, C*HH'*=C), 4.38 (d, *J* = 8.7 Hz, 1H, CHCO*H*), 3.57 (dd, *J* = 8.7, 4.4 Hz, 1H, NC*H*), 2.66, 2.49 (m, 2 × 1H, NC*HH'*CH$_3$), 2.07 (s, 3H, CH$_2$=C(CH_3), 1.69 (t, 3H, ZnCH$_2$CH_3), 1.29 (s, 9H, *t*-Bu), 1.04 (t, 3H, NCH$_2$CH_3), 0.99 (s, 9H, *t*-Bu), 0.54 (q, 2H, ZnCH_2CH$_3$); ^{13}C NMR δ 171.7 (N=*C*H), 149.4 (CH$_2$=*C*H$_3$), 113.7 (*C*H$_2$=CCH$_3$), 80.3 (*C*HO), 66.7 (*N*CH), 58.7, 55.8 (*C*(CH_3)$_3$), 40.9 (NCH$_2$CH$_3$), 29.7, 29.1 (C(*C*H$_3$)$_3$), 20.1 (NCH$_2$*C*H$_3$), 17.3 (CH$_2$=*C*H$_3$), 14.6 (ZnCH$_2$*C*H$_3$), −1.5 (Zn*C*H$_2$CH$_3$). Anal. Calcd for $C_{18}H_{36}N_2OZn$: C, 59.74; H, 10.03; N, 7.74. Found: C, 59.86; H, 9.96; N, 7.77.

Trimethylsilyl ether of methacrolein aldolate (3i): colorless oil; yield 2.92 g (86%); ^{1}H NMR δ 7.82 (d, *J* = 6.5 Hz, 1H, N=C*H*), 5.99, 4.84 (m, 2 × 1H, C*HH'*=C), 4.36 (d, *J* = 6.9 Hz, 1H, CHCO*H*), 3.77 (dd, *J* = 6.9, 6.5 Hz, 1H, NC*H*), 2.98, 2.83 (m, 2 × 1H, NC*HH'*CH$_3$), 1.74 (s, 3H, CH$_2$=C(CH_3), 1.18, 1.10 (s, 2 × 9H, *t*-Bu), 1.08 (t, 3H, NCH$_2$CH_3), 0.12 (s, 9H, Si(CH_3)$_3$); ^{13}C NMR δ 158.9 (N=*C*H), 146.8 (CH$_2$=*C*CH$_3$), 113.1 (*C*H$_2$=CCH$_3$), 79.8 (*C*HO), 64.2 (*N*CH), 56.9, 55.9 (*C*(CH_3)$_3$), 39.2 (NCH_2CH$_3$), 29.5, 29.4 (C(*C*H$_3$)$_3$), 20.0 (NCH$_2$*C*H$_3$), 18.3 (CH$_2$=*C*CH$_3$), 0.3 (Si(*C*H$_3$)$_3$).

Zinc–aldolate of cinnamaldehyde (2j): white crystals; yield 4.15 g (98%); ^{1}H NMR δ 7.87 (d, *J* = 3.9 Hz, 1H, N=C*H*), 7.50–7.06 (m, 5H, aryl), 6.74 (d, *J* = 15.8 Hz, 1H, PhC*H*=CH), 6.57 (dd, *J* = 15.8, 7.6 Hz, 1H, PhCH=C*H*), 4.57 (dd, *J* = 8.8, 7.6 Hz, 1H, CHCO*H*), 3.58 (dd, *J* = 8.8, 3.9 Hz, 1H, NC*H*), 2.68, 2.53 (m, 2 × 1H, NC*HH'*CH$_3$), 1.75 (t, 3H, ZnCH$_2$CH_3), 1.22 (s, 9H, C(CH_3)$_3$), 1.06 (t, 3H, NCH$_2$CH_3), 0.93 (s, 9H, C(CH_3)$_3$), 0.62 (q, 2H, ZnCH_2CH$_3$); ^{13}C NMR δ 171.0 (N=*C*H), 138.8 (aryl), 138.0, 130.1 (*C*=C), 128.9, 127.1, 126.6 (aryl), 77.0 (*C*HO), 68.5 (*N*CH), 59.5, 55.2 (*C*(CH_3)$_3$), 41.1 (NCH_2CH$_3$), 29.5, 28.9 (C(*C*H$_3$)$_3$), 19.6 (NCH$_2$*C*H$_3$), 14.7 (ZnCH$_2$*C*H$_3$), −1.4 (Zn*C*H$_2$CH$_3$).

Trimethylsilyl ether of cinnamaldehyde aldolate (3j): colorless oil; yield 3.17 g (79%); ^{1}H NMR δ 7.89 (d, *J* = 5.7 Hz, 1H, N=C*H*), 7.40–6.90 (m, 5H, aryl), 6.66 (d, *J* = 16.0 Hz, 1H, PhC*H*=CH), 6.58 (dd, *J* = 16.0 Hz, *J* = 7.2 Hz, 1H, PhCH=C*H*), 4.77 (dd, *J* = 7.5, 7.2 Hz, 1H, CHCO*H*), 3.89 (dd, *J* = 7.5, 5.65 Hz, 1H, NC*H*), 3.00, 2.78 (m, 1 × H, NC*HH''*CH$_3$), 1.24 (s, 9H, C(CH_3)$_3$), 1.13 (t, 3H, NCH$_2$CH_3), 1.09 (s, 9H, C(CH_3)$_3$), 0.20 (s, 9H, SiCH_3)$_3$); ^{13}C NMR δ 158.8 (N=*C*H), 137.8 (aryl), 133.3, 130.2 (*C*=C), 128.9, 127.5, 126.6 (aryl), 75.7 (*C*HO), 66.6 (*N*CH), 57.0, 55.8 (*C*(CH_3)$_3$), 39.0 (NCH_2CH$_3$), 29.7, 29.4 (C(*C*H$_3$)$_3$), 19.9 (NCH$_2$*C*H$_3$), 0.8 (Si(*C*H$_3$)$_3$). Anal. Calcd for $C_{24}H_{42}N_2OSi$: C, 71.58; H, 10.51; N, 6.96. Found: C, 71.62; H, 10.57; N, 7.06.

General Procedure for Michael Addition Reactions. To a stirred solution of 1 (10 mmol, 2.91 g) in THF (25 mL) was

(30) The authors have deposited atomic coordinates for **4g** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

added a solution of 10 mmol of an α,β-unsaturated ketone (benzylidene acetone 7, chalcone 8) in THF (5 mL). The reaction mixture was stirred for 30 min and then quenched with H_2O (20 mmol, 0.26 mL) (leading to **7a** and **8a**). After evaporation of the solvent hexane (25 mL) was added for quantitative separation of the zinc salt. The solid material was separated by centrifugation and the clear solution collected by decantation. The solid was extracted with hexane (2 × 10 mL). The combined organic extracts were concentrated *in vacuo*, affording the organic products.

Michael Addition Product 7a. ^{1}H NMR spectroscopy revealed the product to be a mixture of the Michael addition product **7a**, enamine-H, and 7 in a ratio of 1.8:1:1. The volatile enamine-H and 7 were carefully separated by distillation at reduced pressure (0.1 mmHg) leaving **7a** as a yellow oil, yield 2.23 g (65%): ^{1}H NMR δ 7.76 (d, J = 6.5 Hz, 1H, N=C*H*), 7.3–6.9 (m, 5H, aryl), 3.86 (dd, J = 10.6, 6.5 Hz, 1H, NC*H*), 3.69 (m, 1H, CPh*H*), 3.11 (m, 1H, NC*H*HCH$_3$), 2.80 (dd, J = 7.2, 18.0 Hz, 1H, C*H*HCO), 2.73 (m, 1H, NCH*H*CH$_3$), 2.36 (dd, J = 5.0, 18.0 Hz, 1H, CH*H*CO), 1.57 (s, 3H, COC*H*$_3$), 1.16 (s, 9H, C(C*H*$_3$)$_3$), 1.05 (t, 3H, NCH$_2$C*H*$_3$), 0.88 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR δ 205.7 (*C*=O), 160.7 (N=*C*), 145.2, 129.2, 128.0, 126.2 (aryl), 67.3 (N*C*H), 56.8, 55.3 (*C*(CH$_3$)$_3$), 48.5 (*C*H$_2$CO), 42.3 (*C*PhH), 38.5 (N*C*H$_2$CH$_3$), 30.1 (CO*C*H$_3$), 29.3, 29.3 (C(*C*H$_3$)$_3$), 20.3 (NCH$_2$*C*H$_3$).

Michael addition product 8a: colorless oil; yield 3.69% (91%); ^{1}H NMR δ 7.86 (d, J = 6.2 Hz, 1H, N=C*H*), 7.75–6.9 (m, 10H, aryl), 4.03 (m, 1H, NC*H*), 4.03 (m, 1H, CPh*H*), 3.60 (dd, J = 7.8, 18.4 Hz, 1H, C*H*H'CO), 3.36 (m, 1H, NC*H*H'CH$_3$), 2.96 (dd, J = 3.1, 18.4 Hz, 1H, CH*H*'CO), 2.82 (m, 1H, NCH*H*'CH$_3$), 1.16 (t, 3H, NCH$_2$C*H*$_3$), 1.01, 0.92 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR δ 197.9 (*C*=O), 160.6 (N=*C*H), 145.8, 137.5, 132.7, 129.3, 128.5, 128.3, 127.5, 126.2 (aryl), 67.9 (N*C*H), 56.7, 55.4 (*C*(CH$_3$)$_3$), 43.9 (*C*H$_2$CO), 42.3 (*C*PhH), 38.7 (N*C*H$_2$CH$_3$), 29.3, 29.1 (C(*C*H$_3$)$_3$), 20.5 (NCH$_2$*C*H$_3$). Anal. Calcd for $C_{27}H_{38}N_2O$: C, 79.76; H, 9.42; N, 6.89. Found: C, 79.68; H, 9.59; N, 6.46.

Crystal Structure Determination of 4g. X-ray data were collected on a Enraf Nonius CAD4 diffractometer for a crystal mounted inside a Lindemann glass capillary. $C_{44}H_{80}N_6O_2Zn_3$, M_w = 921.33, $P\bar{1}$, a = 11.1443(5) Å, b = 14.8506(7) Å, c = 17.3929 (7) Å, α = 114.50(1)°, β = 94.12(1)°, γ = 99.20(1)°, Z = 2, d_x = 1.198 g cm^{-3}, V = 2554.9(3) Å^3. A total of 7339 reflections were scanned and reduced into a unique set of 2543 reflections with $I > 2.5\sigma(I)$. Corrections were applied for a linear decay of 4.5%, Lp, and absorption (DIFABS). The structure was solved with DIRDIF92 and refined with SHELX 76. Convergence was reached at R = 0.054. Hydrogens atoms were introduced at calculated positions. Full details may be obtained from one of the authors (A.L.S.).

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Supplementary Material Available: NMR spectra (^{1}H and ^{13}C) of all new compounds (44 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.