Insertion of Isocyanates, CO_2, and Ethylene Carbonate into the Zr-C and Zr-N Bonds of Imine Complexes. Construction of Chiral Centers Like Those in α-Amino Acids

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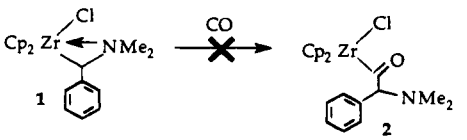
Abstract: In some cases zirconocene-imine complexes insert CO_2; more generally they insert isocyanates and cyclic carbonates. Isocyanates can insert into either the Zr-C or the Zr-N bond; protonolysis of the zirconacycle resulting from Zr-C insertion gives an amide, whereas protonolysis of the zirconacycle resulting from Zr-N insertion gives a urea. Steric hindrance on the imine nitrogen or the isocyanate discourages insertion into the Zr-N bond and gives clean Zr-C insertion. The molecular structure of an *N*-phenyl imine complex (**5a**) has been determined by single-crystal X-ray diffraction. A coordinated THF in **5a** exchanges with free THF by a dissociative mechanism. Coordination of isocyanates to the Zr of **5a** has not been observed before their insertion. The isocyanate insertion reactions of imine complexes such as **5** are irreversible. A chelating *o*-methoxy substituent on the *N*-phenyl of an imine complex (**18**) also prevents insertion into the Zr-N bond and gives clean Zr-C insertion. The treatment of **18** with ethylene carbonate gives a spirocyclic complex (**23**); methanolysis of **23** in benzene gives the methyl ester of phenylglycine. A crossover experiment suggests that the free β-hydroxyethyl ester is an intermediate in the benzene methanolysis of **23**.

Introduction

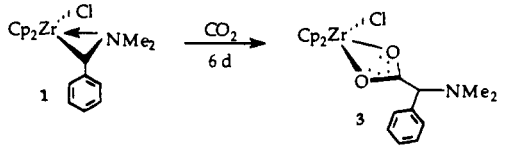
Although a multitude of methods exist for the racemic and asymmetric synthesis of α-amino acids,[1] the use of the group 4 metals for this purpose has not been reported. One reason to believe they would be useful is the availability of their chiral C_2-symmetric metallocene derivatives,[2] which have already been used in the stoichiometric asymmetric synthesis of allylic amines[3] and homoallylic alcohols,[4] and the catalytic asymmetric hydrogenation of imines[5a] and enamines.[5b]

One possible approach to α-amino acids would involve the formation of their C-CO_2H bonds via insertion into α-nitrogen-substituted Zr-C bonds. However, we have found that complex **1** is unaffected by CO after several hours at room temperature (eq 1).[6,7] (We have attributed the unreactive Zr-C bond in **1** to the Zr ← N interaction energy, about 8 kcal/mol.[6])



1 2 (1)

The insertion of CO_2 into Zr(Ti)-R bonds (R = alkyl, aryl) is common.[8] However, we are aware of no published reports of CO_2 insertion into α-nitrogen-substituted M-C bonds (M = Ti, Zr); CO_2 insertion has been reported into α-phosphorus-substituted M-C bonds[9a] and α-nitrogen-substituted M-Si bonds.[9b] Prolonged treatment of **1** with CO_2 does give the adduct **3** in low yield (eq 2).[10] (Again, as in eq 1, the Zr ← N interaction impedes insertion.)



1 3 (2)

We have therefore investigated the reactivity of the zirconocene-imine complexes **5**, developed by Buchwald and coworkers,[11] toward CO and CO_2. Treatment of **5b** with CO gives products unidentifiable from their ^{1}H NMR spectrum. Treat-

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[⊗] Abstract published in *Advance ACS Abstracts*, December 15, 1994.

(1) For reviews, see: (a) Williams, R. M.; Hendrix, J. A. *Chem. Rev.* **1992**, *92*, 889. (b) Williams, R. M. *Synthesis of Optically Active α-Amino Acids*; Pergamon: Oxford, 1989; Vol. 7. (c) *α-Amino Acid Synthesis*; O'Donnell, M. J., Ed. *Tetrahedron* **1988**, *44*, 5253-5614. (d) Wagner, I.; Musso, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 816.

(2) (a) Wild, F. R. W. P.; Wasiucionek, M.; Huttner, G.; Brintzinger, H. H. *J. Organomet. Chem.* **1985**, *288*, 63. For reviews of chiral cyclopentadienyl complexes: (b) Halterman, R. L. *Chem. Rev.* **1992**, *92*, 965. (c) Duthaler, R. O.; Hafner, A. *Chem. Rev* **1992**, *92*, 807.

(3) (a) Grossman, R. B.; Davis, W. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 2321. (b) Grossman, R. B. Ph.D. Thesis, Massachusetts Institute of Technology, Cambridge, MA, 1991.

(4) Collins, S.; Kuntz, B. A.; Hong, Y. *J. Org. Chem.* **1989**, *54*, 4154.

(5) (a) Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 7562. (b) Lee, N. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 5985.

(6) Complex **1** and its analogs show low reactivity toward electrophiles, nucleophiles, and electron donors: Plössl, K. P.; Norton, J. R.; Davidson, J. G.; Barefield, E. K. *Organometallics* **1992**, *11*, 534.

(7) *t*-BuNC inserts cleanly but slowly into the Zr-C bond of **1**. A complete account of the insertion reactions of **1** and its derivatives will be published separately.

(8) For a recent example: (a) Rosenthal, U.; Ohff, A.; Michalik, M., Görls, H.; Burlakov, V. V.; Shur, V. B. *Organometallics* **1993**, *12*, 5016. For reviews: (b) Kolominikov, I. S.; Lysyak, T. V. *Russ. Chem. Rev. (Engl. Transl.)* **1990**, *59*, 344. (c) Braunstein, P.; Matt, D.; Nobel, D. *Chem. Rev.*, **1988**, *88*, 747. (d) Behr, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 661. (e) Walther, D. *Coord. Chem. Rev.* **1987**, *79*, 135.

(9) (a) Etienne, M.; Choukroun, G. *J. Chem. Soc., Dalton Trans.* **1984**, 915. (b) Procopio, L. J.; Carroll, P. J.; Berry, D. H. *Organometallics* **1993**, *12*, 3087.

(10) Identification of **3** was based on known Zr-carboxylato complexes: Suzuki, H.; Takiguchi, T.; Kawasaki, Y. *Bull. Chem. Soc. Jap.* **1978**, *51*, 1764.

(11) Buchwald, S. L.; Watson, B. T.; Wannamaker, M. W.; Dewan, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 4486.

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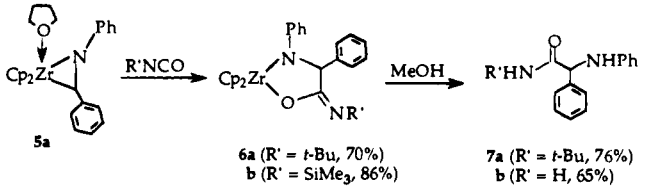
Table 1. Product Ratios and Yields of **7** and **8** from the Reaction of R'NCO with **5a**[a]

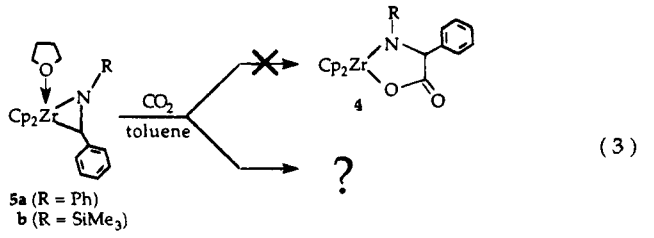
entry	R'	yield of amide PhNHCH(Ph)CONHR' (**7**)	yield of urea PhCH(D)N(Ph)CONHR' (**8**)	ratio **7/8**	total yield
a	*t*-Bu	76	0	100/0	76
b	Me_3Si	65	0	100/0	65
c	*i*-Pr	69	8	90/10	77
d	Et	31	52	37/63	83
e	Me	23	45	34/66	68
f	*o*-$MeOC_6H_4$	24	31	44/56	55
g	*p*-$MeOC_6H_4$	28	48	37/63	76
h	$PhCH_2$	29	48	37/63	77
i	Ph[b]	20	49	29/71	69
j	*p*-FC_6H_4	20	53	27/73	73

[a] **5a** was prepared in situ from Cp_2ZrMe_2. R'NCO was added to **5a** at room temperature in THF. [b] The **7i/8i** product ratio was 30/70 in benzene.

Scheme 1



ment of **5** with CO_2 gives a voluminous precipitate, sparingly soluble in CD_2Cl_2, with several broad unresolvable signals in the ^1H NMR (eq 3).[12]



(3)

Because isocyanates, isoelectronic analogs of CO_2, also insert into Zr−C bonds,[13] we have investigated their reaction with **5**. We will also report a novel zirconocene−imine complex that controls the regiochemistry of these insertion reactions, and the use of ethylene carbonate as a CO_2 synthon.

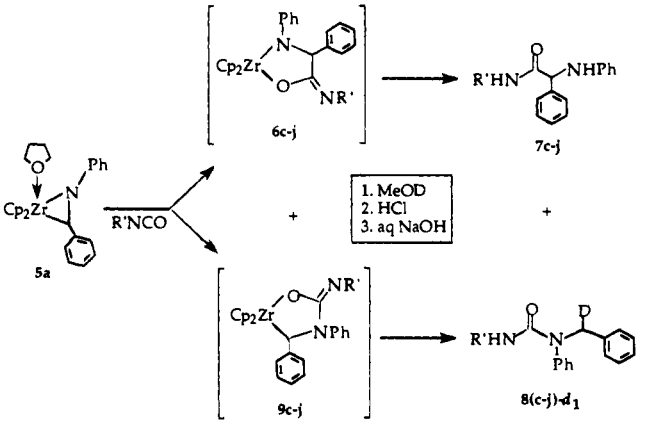
Results and Discussion

Reaction of *t*-BuNCO and Me_3SiNCO with Imine Complex 5a. When neat *t*-BuNCO was added to **5a**, an intense purple solution resulted that contained **6a** (70% isolated yield from **5a**) (Scheme 1); methanolysis or hydrolysis of the purple solution afforded the amide **7a**. Similarly, addition of Me_3SiNCO to **5a** gave the adduct **6b**, and methanolysis or hydrolysis gave the amide **7b** (Scheme 1).

Reaction of Other Isocyanates with Imine Complex 5a. However, lower yields of amides were obtained from other isocyanates. Only 20−31% of **7d−j** (Scheme 2, Table 1) was obtained after methanolysis of the mixture resulting from addition of R'NCO (R' = Et, Me, $PhCH_2$, or Ar) to **5a**. To our surprise, the principal products were the ureas **8d−j**. In the case of R' = *i*-Pr the major product was still the amide **7c**, but some of the urea **8c** was also observed. Reexamination of the *t*-BuNCO and Me_3SiNCO reactions (**a** and **b** in Table 1) offered no evidence for **8a** or **8b** (^1H NMR).

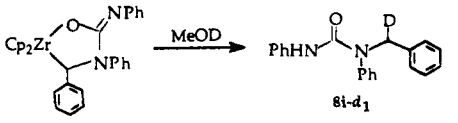
It seemed likely that the ureas were arising from **9**, the product of R'NCO insertion into the Zr−N bond.[14,15] Indeed, the

Scheme 2



insertion product **9i** was isolated (13%) and characterized from the reaction of **5a** with PhNCO.

The fact that Zr was attached to the benzyl carbon in **9** was confirmed by the use of MeOD in the methanolysis of **9i**; ^1H and ^{13}C NMR showed that the product (**8i-d_1**) was deuterated in the appropriate position (eq 4). The same result was obtained when MeOD was used to quench all the reactions in Table 1. The amides **7c−j** were separated as the hydrochloride salt from the ureas **8(c−j)-d_1**; the free amines were isolated after treatment with aqueous NaOH.



(4)

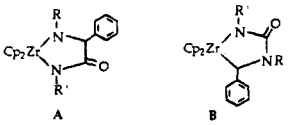
A number of trends are apparent in Table 1. (i) Insertion into the Zr−C bond, and eventual amide formation, is favored with isocyanates having a large R' (entries **a−c**). (ii) Insertion into the Zr−N bond, and eventual urea formation, is favored with isocyanates having a small R' (entries **d−j**). (iii) The **7/8**

(12) A similar result was obtained by Buchwald and co-workers (Buchwald, S. L., personal communication).

(13) Braunstein, P.; Nobel, D. *Chem. Rev.* **1989**, *89*, 1927.

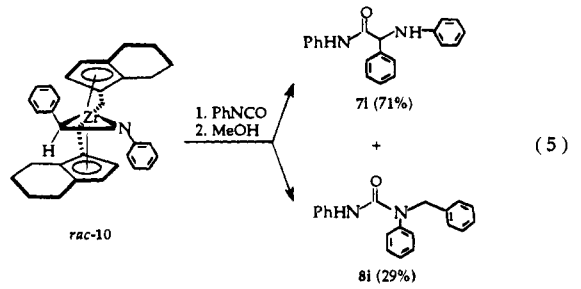
(14) No insertion reactions have previously been reported for the Zr−N bonds of zirconocene−imine complexes. Isocyanate insertions have been reported for the Zr−N bonds of homoleptic complexes $Zr(NR_2)_4$: Chandra, G.; Jenkins, A. D.; Lappert, M. F.; Srivastava, R. C. *J. Chem. Soc. A* **1970**, 2550.

(15) Because of the oxophilicity of zirconium, we have drawn ZrOC=NR' structures for **6**, **9**, **11**, and **14**; however, we cannot rule out ZrN(R')C=O structures like those in **A** and **B** below. Methanolysis of either a ZrN(R')C=O structure or a ZrOC=NR' structure would give the same product.



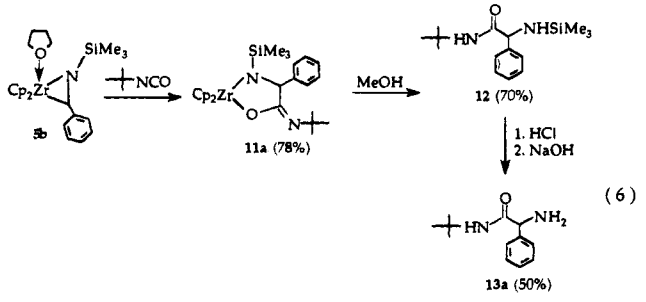
ratio varies substantially between the electronically similar substituents **f** (R′ = *o*-OMe) and **g** (R′ = *p*-OMe). (iv) The **7/8** ratio is unaffected by electron-withdrawing or -donating substituents (compare entries **f** and **g**–i). (v) In at least one case (i, R = Ph), the **7/8** ratio is unaffected by the presence or absence of a donor solvent: the same ratio is obtained in THF or in benzene.

The analog of **5a** (*rac*-**10**)[3] was prepared in order to see if the bulk of the indenyl ligand would direct insertion to the Zr–C bond. (Exchanging Cp ligands for indenyl ones increases the steric bulk around the Zr metal center of *rac*-**10**.[3a]) Indeed, methanolysis of the mixture arising from the reaction of PhNCO with *rac*-**10** gave a **7i/8i** product ratio of 71/29 (eq 5)—much greater than that found with Cp ligands (entry i, Table 1).



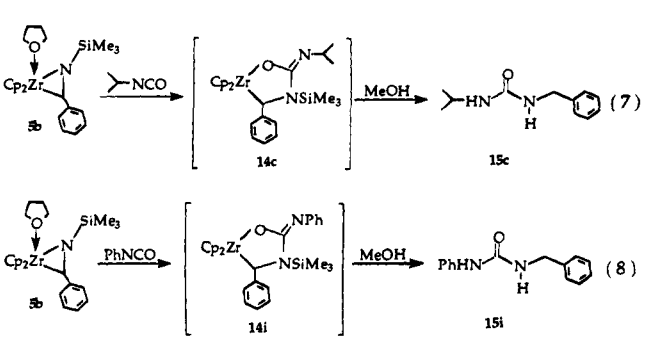
(5)

Reaction of Isocyanates with Imine Complex 5b. We then examined the reactions of **5b** with isocyanates in order to see whether the trimethylsilyl substituent in **5b** would affect the amide/urea ratios. The results are presented in Table 2. Only the *N*-silylated amide **12** (eq 6) was isolated upon methanolysis or hydrolysis of the deep red solution obtained by adding neat *t*-BuNCO to **5b**. Treatment of **12** with 6.0 M HCl, followed by aqueous NaOH, gave **13a**.



(6)

However, the result of adding *i*-PrNCO to **5b** was the urea **15c** in 56% overall yield; a similar result was obtained (Table 2) when PhNCO was added to **5b** (eqs 7 and 8). No evidence of the amides **13c** and **13i** was found. The selectivity for Zr–N over Zr–C bond insertion was therefore greater for the N–$SiMe_3$ derivative **5b** than for the N–Ph **5a**.



(7)
(8)

Table 2. Product Ratios and Yields of **13** and **15** from the Reaction of R′NCO with **5b**[a]

entry	R′	yield of amide $H_2NCH(Ph)CONHR'$ (**13**)	yield of urea $PhCH_2NHCONHR'$ (**15**)	ratio[a] **13/15**	total yield
a	*t*-Bu	50	0	100/0	50
c	*i*-Pr	0	56	0/100	56
i	Ph	0	56	0/100	56

[a] At room temperature in THF. **13/15** product ratios were determined in the ^1H NMR prior to workup.

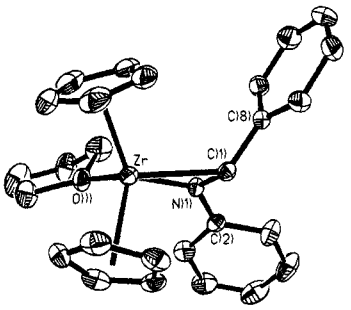


Figure 1. Molecular structure of **5a**. Thermal ellipsoids have been drawn at the 35% probability level. Selected bond lengths (Å) and angles (deg): Zr–N(1), 2.113(4); Zr–C(1), 2.299(5); N(1)–C(2), 1.375(7); Zr–O(1), 2.340(4); N(1)–C(1), 1.431(7); C(1)–C(8), 1.465(8); Zr–N(1)–C(2), 142.2(4); C(1)–N(1)–Zr, 78.3(3); N(1)–Zr–O(1), 80.7(2); N(1)–Zr–C(1), 37.6(2); C(1)–Zr–O(1), 117.2(2); Zr–C(1)–N(1), 64.1(3); Zr–C(1)–C(8), 126.1(4); C(2)–N(1)–C(1), 121.1(4); N(1)–C(1)–C(8), 119.6(5).

Molecular Structure of 5a vs That of 5b. In an effort to understand the difference in regioselectivity between **5a** and **5b**, we prepared crystals of **5a** suitable for X-ray analysis and compared its structure with the known one of **5b**.[14] The significant bond lengths and angles in **5a** are listed in Figure 1.

There is no appreciable difference between the geometries of the coordinated THF in **5a** and in **5b**. The Zr–N1 bond length in **5a** (2.113(4) Å) is equivalent to the Zr–N bond length (2.11(1) Å) reported[14] for **5b**. Similarly, the Zr–C1 bond length in **5a** (2.299(5) Å) is nearly equivalent to the Zr–C bond length in **5b** (2.26(1) Å). However, the N1–C2 bond distance in **5a** is 0.32 Å shorter than the N–Si bond length (1.69(1) Å) in **5b**, and the Si–N–Zr bond angle (148.1(6)°) in **5b** is 6° greater than the Zr–N1–C2 bond angle (142.2(4)°) in **5a**.

Regiochemistry Is the Result of Steric Control. The **7/8** ratios in Table 1 appear to arise entirely from steric effects. R′NCO with larger R′ prefer to insert into the Zr–C bond of **5a**, forming **6** and eventually the amide **7**. R′NCO with small R′ prefer to insert into the Zr–N bond of **5a**, forming **9** and eventually the urea **8**.

The greater Zr–N/Zr–C preference of the N–$SiMe_3$ **5b** relative to the N–Ph **5a** may also be the result of steric effects. Standard tables show a greater "*A* value" for Ph than for Me_3Si.[16,17]

Mechanism of Isocyanate Insertions into 5a and 5b. Braunstein has suggested that "precoordination of heterocumulenes [is] necessary (i) to bring in a close geometrical proximity the group onto which the alkyl can transfer and (ii) to enhance the polarity of the inserting molecule".[13] If coordination of

(16) March, J. *Advanced Organic Chemistry*; Wiley-Interscience: New York, 1985; p 126.

(17) The effective size of the phenyl substituent on nitrogen may be increased in **5a** by the fact that it is kept parallel to the Zr–N1–C1 plane by the two Cp rings. The effect is the reverse of that found for phenyls with geminal methyl groups: (a) Bailey, W. F.; Connon, H.; Eliel, E. L.; Wiberg, K. B. *J. Am. Chem. Soc.* **1978**, *100*, 2202. (b) Allinger, N. L.; Tribble, M. T. *Tetrahedron Lett.* **1971**, 3259.

Scheme 3

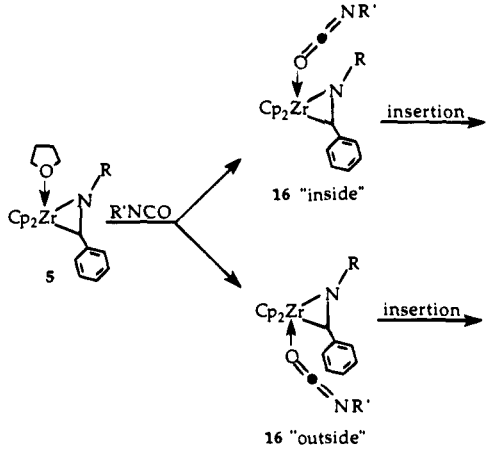
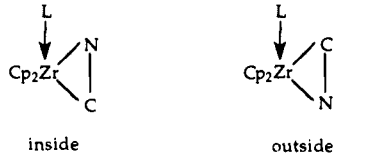


Table 3. Relative ^{1}H NMR Yields from the Sequential Addition of Two Isocyanates to **5a**[a]

entry	PhNCO and *then* *t*-BuNCO (equiv)	*t*-BuNCO and *then* PhNCO (equiv)	% NMR yields **7i/8i/7a**
1		1.0/3.0	37/56/7
2	3.0/1.0		31/57/12
3	1.0/1.5		28/51/21
4		1.5/1.0	28/50/22

[a] The first isocyanate was added to a cold (−80 °C) solution of **5a** (1.68 mmol) in THF; the second isocyanate was added 1 h later. The mixture was kept at −80 °C for an additional hour before gradually warming to room temperature.

R'NCO precedes its insertion into the Zr−N or Zr−C bond of **5**, we would expect the regiochemistry of insertion to be determined by the site of coordination. On electronic grounds we might expect a neutral ligand L to prefer the "N" region over the "C" region below. Heteroatoms such as nitrogen usually show an electronic preference for "inside" coordination, although bulky substituents on carbon can reverse this pattern.[18,19]



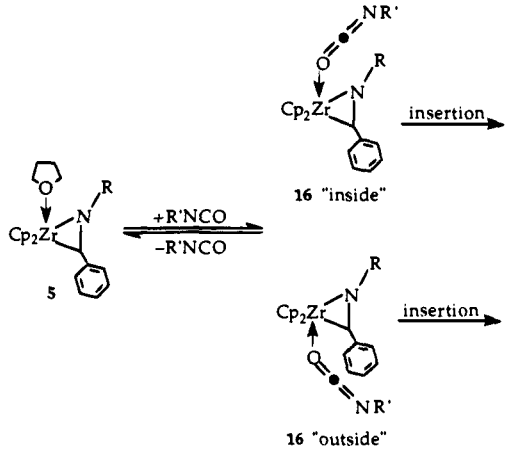
Competition Experiments. Experiments in which two isocyanates were added consecutively at low temperatures offered no evidence for *irreversible* coordination of R'NCO to **5** (Scheme 3). (Irreversible incorporation of the first isocyanate into an intermediate **16** would preclude coordination of the second isocyanate.) When **5** was treated with a mixture of *t*-BuNCO and PhNCO at −80 °C, the results were the same *regardless of the order of addition* (compare entries 1 and 2 in Table 3, or entries 3 and 4).

Direct Evidence for Coordination of R'NCO to 5? Direct observation of mixtures of **5a** and R'NCO at low temperatures offered no evidence for the presence of **16**. When *t*-BuNCO was added to **5a** in THF-d_8 (or toluene-d_8) at −80 °C, the orange color of **5a** remained, and its ^{1}H NMR resonances (Cp's at δ 5.89 and 5.67 and methine at δ 3.32) did not shift. There was no evidence for the coordinated isocyanate−imine complex **16**. As the sample was warmed, the ^{1}H NMR resonances of the Zr−C insertion product **6a** (Cp's at δ 6.52 and 6.43 and methine at δ 5.42) gradually appeared. Similar results were found when PhNCO or MeNCO was added to **5a** at low temperature.

(18) Extended Hückel calculations rationalize a preference for "inside" over "outside" coordination on the part of the oxygens in group 4 acyl complexes: Tatsumi, K.; Kakamura, A.; Hofmann, P.; Stauffert, P.; Hoffmann, R. *J. Am. Chem. Soc.* **1985**, *107*, 4440.

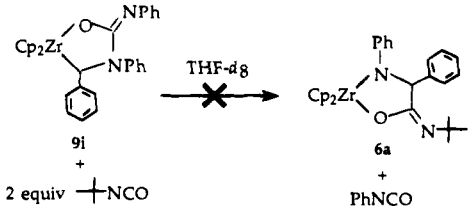
(19) Lubben, T. V.; Plössl, K. P.; Norton, J. R.; Miller, M. M.; Anderson, O. P. *Organometallics* **1992**, *11*, 122 and references therein.

Scheme 4

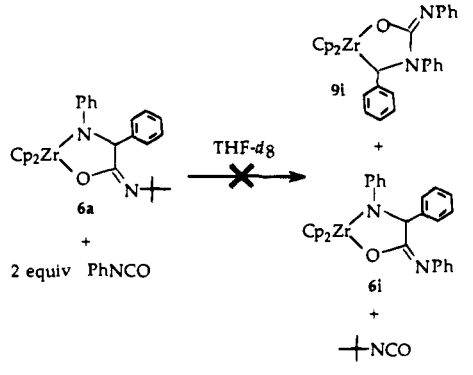


This experiment precludes the formation of significant amounts of **16** from **5** and R'NCO by either the irreversible mechanism in Scheme 3 or the reversible one in Scheme 4. The possibility of precoordination remains, but the amount of **16** formed must be small: either insertion occurs much faster than coordination in Scheme 3, or the equilibrium is unfavorable in Scheme 4.

Reversibility of the Insertion Reactions of 5? As a whole the insertion reactions of **5a** are irreversible. After several days at room temperature, *t*-BuNCO did not displace PhNCO from **9i** (eq 9) and PhNCO did not displace *t*-BuNCO from **6a** (eq 10).



(9)



(10)

Variable Temperature NMR of 5a. The temperature-dependent ^{1}H NMR spectra of **5a** in toluene-d_8 are shown in Figure 2. At −32 °C, two α-methylene signals at δ 3.32 (broad singlet, 2 H) and δ 2.71 (broad quartet, 2 H), and a β-methylene signal at δ 1.09 (broad multiplet, 4 H), were seen for coordinated THF; separate signals were seen for a small amount of free THF. At +10 °C, the α-methylenes broadened considerably, and the

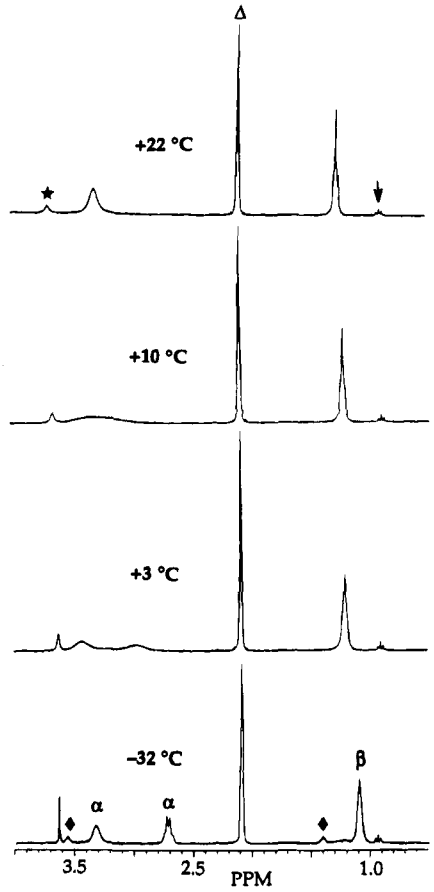


Figure 2. Temperature dependence of α- and β-THF resonances of **5a** in toluene-d_8: (★) methine signal of **5a**, (△) a residual toluene-d_8 proton resonance, (arrow) an impurity, (♦) free THF.

β-methylenes sharpened; both moved downfield as they began to average with the free THF resonances. At +22 °C, the α-methylenes showed a broad singlet (δ 3.30) and the β-methylenes a sharp multiplet (δ 1.25), at positions implying extensive dissociation. The Cp singlets remained sharp from −32 to +31 °C.

Rate of Exchange of Free and Coordinated THF in 5a. When ca. 1.4 equiv of protio THF was added to **5a** in toluene-d_8, the ^{1}H NMR showed free THF (δ 3.58 and 1.39) and coordinated THF (same resonances as above) at −35 °C (Figure 3).

Rate constants for the exchange of free and coordinated THF are shown in Table 4. As the $[THF]_{free}$ varies from 1.02 to 136.2 mM, k_{obs}, the observed first-order rate constant for $THF_{coord} \rightarrow THF_{free}$, does not change (at −12 or 0 °C). Coordinated THF thus exchanges with free THF by a dissociative mechanism.

It is thus reasonable to propose that THF dissociates from **5** before isocyanate insertion occurs. The fact that the **7/8** product ratio is unaffected by excess THF (entry i in Table 1) implies that R'NCO reacts with **5**(−**THF**) (path 1, Scheme 5) rather than with **5** itself; it is difficult to see how path 2 could give the Zr−N insertion product **8**! Under conditions of a dissociative pathway, the Zr−N and Zr−C sides are open to attack by isocyanate; this is consistent with the observation in entry i. A precoordination mechanism remains possible.

Synthesis of a Solvent-Free Imine Complex (18). It seemed likely that an oxygen ligand permanently attached in the N region of **5** would preclude R'NCO coordination in that region and thus prevent insertion into the Zr−N bond. We therefore prepared an analog of **5** with an *o*-methoxy substituent on the

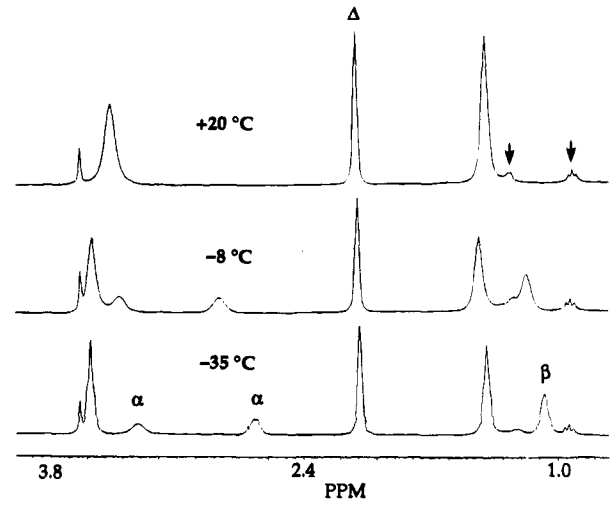


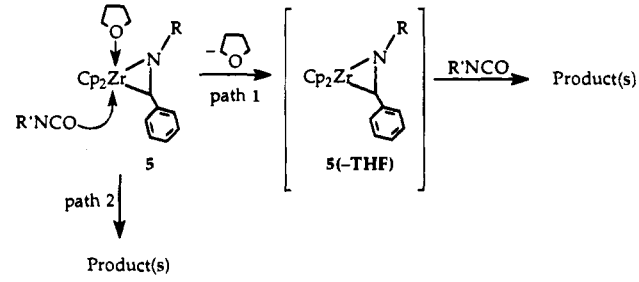
Figure 3. Temperature-dependent ^{1}H NMR spectra (toluene-d_8) of **5a** with added THF: (△) a residual toluene-d_8 proton resonance, (arrows) an impurity.

Table 4. Rate Constants for the Exchange of Coordinated THF in **5a**[a]

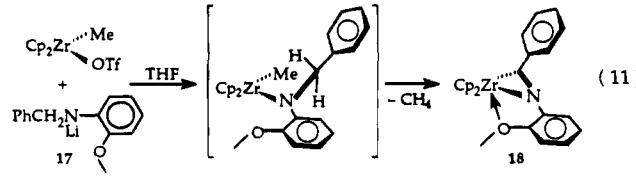
T (°C)	$[THF]_{free}$[a] (mM)	k_{obs}[b] (s^{-1})	T (°C)	$[THF]_{free}$[a] (mM)	k_{obs}[b] (s^{-1})
−12	1.02	53.7	0	1.02	134.9
	61.11	53.8		21.49	145.4
	136.19	54.3		136.19	147.0

[a] [**5a**] = 31.72 mM. $[THF]_{free}$ was determined by ^{1}H NMR relative to [**5a**]. [b] Obtained from the line widths of the δ 2.65 α-methylene ^{1}H NMR resonance.

Scheme 5

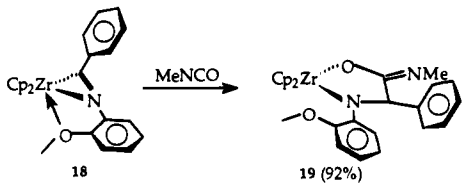


aromatic ring. When $Cp_2ZrMe(OTf)$ was treated with the *o*-anisidine lithium amide **17** in THF, the imine complex **18** was isolated in 93% overall yield; **18** was free of THF in the ^{1}H NMR (eq 11). The absence of coordinated THF in **18** suggests that the *o*-methoxy substituent is chelated to the Zr.

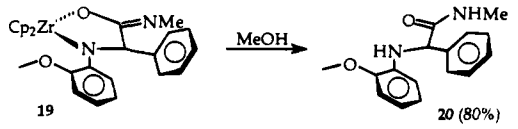


Regiospecific Addition of MeNCO and CO_2 to 18. When MeNCO was added to **18**, only a single product (**19**) was formed (eq 12). The regiochemistry of **18** was confirmed by the formation of **20** after methanolysis (eq 13); no evidence was found for insertion of MeNCO into the Zr−N bond of **18**.

Even CO_2 inserted into the Zr−C bond of **18**, giving a single product in quantitative yield (eq 14). However, we have not yet succeeded in removing the resulting α-aminocarboxylate ligand from **21**; acids tried include MeOH, HCl/Et_2O, HCl/H_2O,

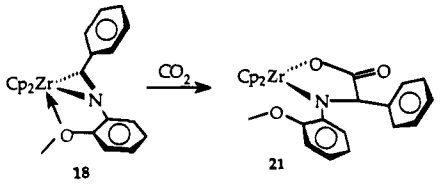


(12)

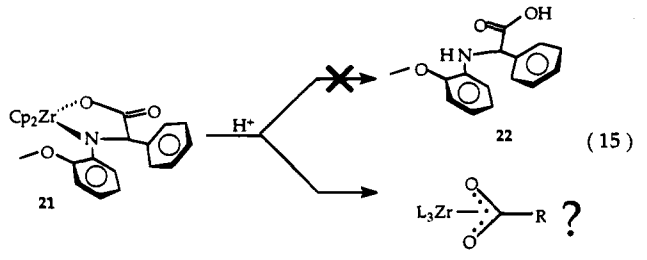


(13)

catechol,[20] H_2O_2/H_2O, trifluoroacetic acid, triflic acid, Me_3SiOTf/H_2O, and *o*-anisic acid. Presumably, the carboxylate fragment in **21** remains bound to the Zr (eq 15).



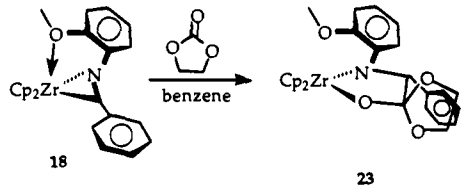
(14)



(15)

The fact that the insertion reaction involves the Zr−C bond in eq 14 as well as eq 12 is supported by the chemical shift of the methine proton of **21**. In the ^1H NMR spectrum that shift (δ 5.16) is within the range (δ 5.05−5.53) found in similar insertion products (**6a**, **6b**, and **19**) and well away from that (δ 4.50) in the Zr−N insertion product **9i**.

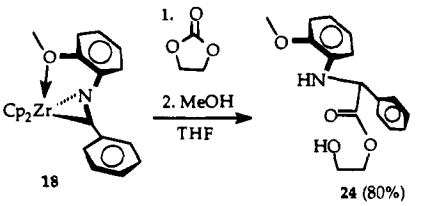
Addition of Ethylene Carbonate to 18 and 5. Because a carbonate is a CO_2 synthon, we have investigated its reaction with **18** and **5**. With **18** we obtained the spirocyclic complex **23** in quantitative yield (eq 16).[21] Its four inequivalent ethylene resonances in the ^1H NMR, and two inequivalent ethylene resonances in the ^{13}C NMR, are consistent with the structure shown.



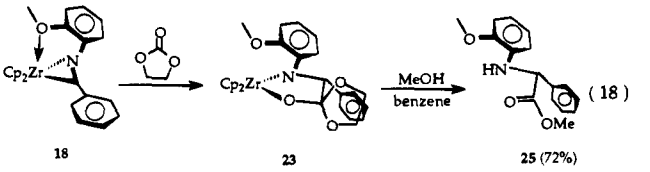
(16)

The β-hydroxyethyl ester **24** was isolated after methanolysis of **23** (generated in situ from **18**) in THF (eq 17).

However, to our surprise, addition of MeOH to the reaction mixture containing **23** in *benzene* gave the methyl ester **25** (eq 18)!

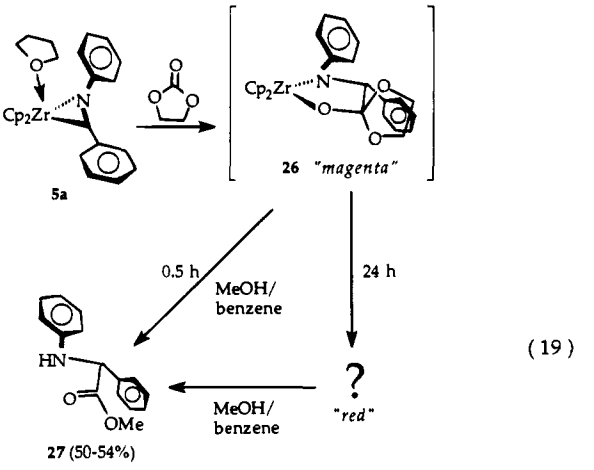


(17)



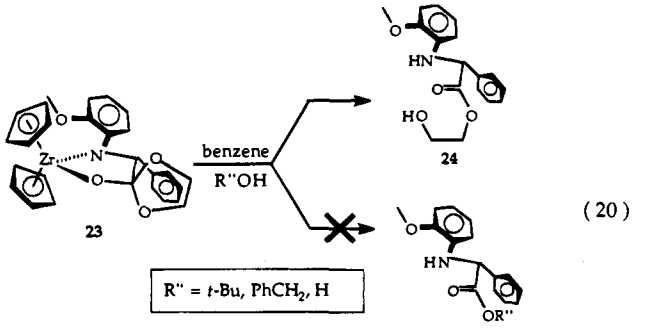
(18)

The imine complex **5a** also reacted with ethylene carbonate. ^1H NMR (C_6D_6) showed that the initial magenta solution contained a single initial product, the peaks of which gave way to several unresolvable signals as the color changed to red. However, methanolysis of either the magenta or red solutions gave the methyl ester **27** in similar yields. Because of the formation of **27**, we have assigned **26** the structure shown in eq 19; we have found no evidence for insertion of ethylene carbonate into the Zr−N bond of **5a**.



(19)

Mechanism of Reaction 18. We have briefly investigated the mechanism of eq 18, a remarkable methanolysis reaction which gives a methyl ester (e.g., **25**) from an ethylene carbonate insertion product (e.g., **23**). Other alcohols (*t*-BuOH, $PhCH_2OH$) and water do not give analogous products: the β-hydroxyethyl ester **24** was obtained after their addition to **23** (prepared in situ from **18** and ethylene carbonate) (eq 20).



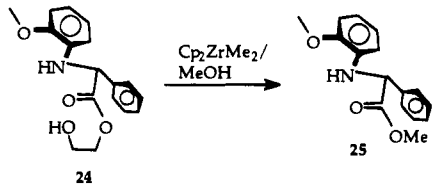
(20)

Ester interchange, presumably promoted by the powerfully oxophilic Zr(IV), occurs easily under these conditions. For example, when **24** was treated overnight with a benzene solution

(20) A similar method was used to remove H_2 from Cp_2ZrH_2 with catechol: Mannig, D.; Nöth, H. *J. Organomet. Chem.* **1984**, *275*, 161.

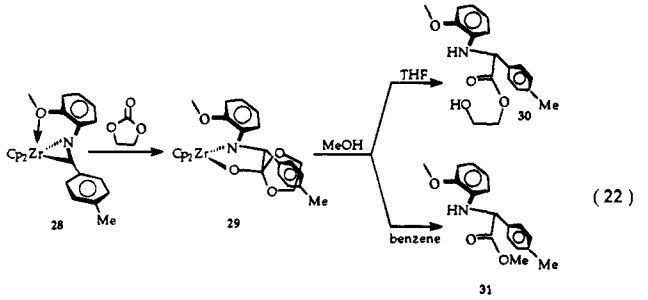
(21) Apparently the rigid framework of ethylene carbonate encourages insertion. When dimethyl carbonate was added to **18** and heated to 110 °C for several hours in toluene-d_8, ^1H NMR showed no reaction.

of Cp_2ZrMe_2 and excess MeOH, the only product (**25**) was the result of ester interchange (eq 21).



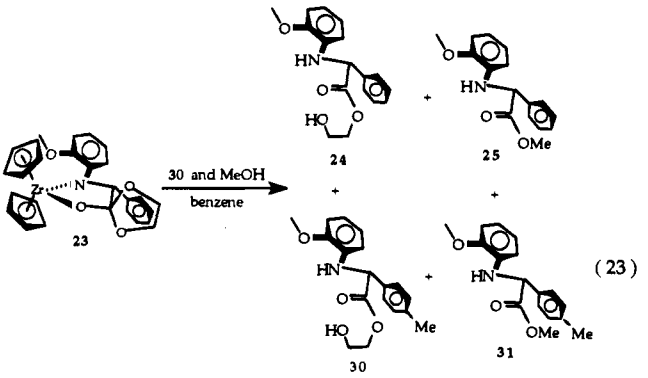
24 25 (21)

A crossover experiment showed that ester interchange occurred *during the methanolysis in eq 18*. Compound **29** was prepared from addition of ethylene carbonate to **28**; the β-hydroxyethyl ester **30** was prepared from **29** and MeOH in THF; the methyl ester **31** was prepared from the same reagents in benzene (eq 22).



(22)

When the spirocyclic insertion product **23** was treated with a solution containing **30** and an excess of MeOH, the result was equal amounts of **24**, **25**, **30**, and **31** (eq 23). The fact that the free β-hydroxyethyl ester **30** was converted into the methyl ester **31** during the conversion **23** → **25** suggested that the free β-hydroxyethyl ester **24** was an intermediate in eq 18 and related reactions; **30** should have been unchanged if **23** → **25** had not involved **24**.



23 24 25 30 31 (23)

Experimental Section

Materials. All air-sensitive compounds were prepared and handled under a nitrogen atmosphere, using standard Schlenk and inert-atmosphere-box techniques.[22] Most of the solvents used were distilled under N_2 from sodium benzophenone ketyl; hexanes were stirred over H_2SO_4 and distilled from sodium benzophenone ketyl in the presence of tetraglyme. Dichloromethane-d_2 was dried over P_2O_5 for 24 h, degassed by three freeze/pump/thaw cycles at −196 °C, and finally transferred into a flame-dried vacuum bulb. Trifluoromethanesulfonic acid (TfOH) was degassed and transferred into a flame-dried vacuum bulb. Isocyanates were stirred over P_2O_5 for 24 h and transferred by high vacuum into a flame-dried vacuum bulb. All other reagents employed were used without further purification. Cp_2ZrMe_2,[23] *rac*-[EBTHI]$ZrMe_2$,[24] and **5b**[11] were prepared by standard procedures. Cp_2ZrCl_2 was generously supplied by Boulder Scientific.

^{1}H NMR data were collected on a Bruker WNX 300-MHz FT spectrometer; residual solvent proton shifts were used as internal standards. Electron impact (EI) mass spectra were collected on a Fisons VG Quattro-SQ mass spectrometer. Elemental analyses of air- and moisture-sensitive compounds were performed by Analytische Laboratorien, Gummersbach, Germany; those of all other compounds were performed by Midwest Laboratories, Indianapolis, IN.

The product ratios in Table 1 were measured prior to workup. In all cases the ratios computed from ^{1}H NMR data agreed with those computed from the isolated yields of **7** and **8** within ±5%.

Preparation of 5a. The following procedure is modified from the one used by Grossman for the preparation of compound *rac*-**10**.[3] A solution containing Cp_2ZrMe_2 (2.01 g, 8.00 mmol) and THF (90 mL) was cooled to −78 °C and treated with TfOH (711 μL, 8.00 mmol). The pale yellow solution was warmed to room temperature, stirred for 1 h, and again cooled to −78 °C. In a separate flask BuLi (1.6 M, 5.0 mL, 8.00 mmol) was added to a cold (0 °C) THF (45 mL) solution containing $PhCH_2NHPh$ (1.47 g, 8.00 mmol) and stirred for 5 min. The $PhCH_2N(Li)Ph$ was transferred by cannula to the $Cp_2ZrMe(OTf)$, stirred for 0.5 h at −78 °C, warmed to room temperature, and stirred overnight. The solvent was evaporated, and the orange-yellow solid was treated with benzene (100 mL), filtered by cannula, and washed with benzene (2 × 30 mL). The filtrate was reduced to ca. 20 mL, and hexanes (150 mL) were added to give an orange precipitate. The solid was filtered by cannula, washed with hexanes (2 × 20 mL), and dried overnight under vacuum. Yield: 3.08 g (81%). ^{1}H NMR (THF-d_8): δ 7.09−6.71 (m, 7 H), 6.55−6.35 (m, 3 H), 5.86 (s, 5 H), 5.64 (s, 5 H), 3.62 (m, 4 H, protio THF displaced by solvent), 3.38 (s, 1 H), 1.78 (m, 4 H, protio THF displaced by solvent). ^{1}H NMR (toluene-d_8): δ 7.58−7.03 (m, 7 H), 6.87−6.67 (m, 3 H), 5.59 (s, 5 H), 5.38 (s, 5 H), 3.63 (s, 1 H), 3.56 (m, 4 H, coordinated THF), 1.47 (m, 4 H, coordinated THF).

X-ray Analysis of 5a. X-ray quality crystals of **5a** were obtained by recrystallization in ether/toluene/hexanes (1/10/20). The compound crystallized with 0.5 equiv of toluene solvent per Zr atom. Single crystal X-ray data were collected at 23 °C using a light yellow crystal of dimensions 0.50 × 0.50 × 0.40 mm on a Siemens R3m/V diffractometer equipped with a molybdenum tube [$\lambda(K\alpha_1)$ = 0.709 26 Å; $\lambda(K\alpha_2)$ = 0.713 54 Å] and a graphite monochromator. The compound crystallized in the centrosymmetric monoclinic space group $P2_1/c$ with four molecules in a cell of dimensions a = 13.370(3) Å, b = 10.362(2) Å, c = 18.758(4) Å, β = 97.00(3)°, and V = 2579.2(9) Å^3. A total of 4535 independent reflections were gathered (R_{int} = 0.029), the octants collected being $+h,+k,\pm l$, using the Wyckoff scan method. Three standard reflections were measured after every 100 reflections collected.

The structure was solved by direct methods and refined by full-matrix least-squares techniques using structure solution programs from the SHELXTL system.[25] The carbon atoms in the toluene molecule were refined isotropically, and the ring carbons were fitted to a regular hexagon (C−C = 1.39 Å). All other nonhydrogen atoms were refined anisotropically, while the hydrogen atoms were placed in fixed calculated positions (C−H = 0.96 Å) and refined isotropically. C15 in the THF ligand was disordered between two positions labeled C15a and C15b with percent occupancies of 47.0% and 53.0%, respectively. The structure has been refined to conventional R factor values of R = 0.0486 and R_w = 0.0577 on the basis of 2576 observed reflections with $I > 3\sigma(I)$ in the 2θ range 4−50°, giving a data to parameter ratio of 8.7/1. The maximum and minimum residual densities remaining were 0.86 and −0.52 e Å^{-3}, respectively. The data were corrected for absorption using semiempirical techniques.

(22) Shriver, D. F. *The Manipulation of Air Sensitive Compounds*; McGraw-Hill: New York, 1969.

(23) Samuel, E.; Rausch, M. D. *J. Am. Chem. Soc.* **1973**, *95*, 6263. Cp_2ZrMe_2 was prepared by treating Cp_2ZrCl_2 with excess MeLi·LiBr followed by Me_3SiCl (Buchwald, S. L., personal communication). This method eliminates the need for the sublimation step employed by Samuel and Rausch. We found MeLi·LiBr to give better results than MeLi itself.

(24) Waymouth, R. M.; Bangerter, F.; Pino, P. *Inorg. Chem.* **1988**, *27*, 758.

(25) Sheldrick, G. M. *SHELXTL Crystallographic System*, Version 4.2/Iris; Siemens Analytical X-ray Instruments. Inc.: Madison, WI. 1991.

Preparation of 6a. A 100 mL Schlenk flask was charged with **5a** (4.75 g, 10.0 mmol) and THF (50 mL). The orange solution changed to deep purple after adding *t*-BuNCO (1.26 mL, 11.0 mmol). The solvent was removed; the purple solid was treated with benzene (25 mL), followed by hexanes (100 mL), filtered by cannula, and dried overnight under vacuum. Yield: 3.53 g (70%). ^{1}H NMR (CD_2Cl_2): δ 7.37−7.15 (m, 7 H), 6.82 (t, 1 H), 6.55 (s, 5 H), 6.48 (d, 2 H), 6.33 (s, 5 H), 5.35 (s, 1 H), 1.38 (s, 9 H). ^{1}H NMR (THF-d_8): δ 7.48−7.21 (m, 4 H), 7.25−7.12 (m, 3 H), 6.80 (t, 1 H), 6.61 (d, 2 H), 6.45 (s, 5 H), 6.38 (s, 5 H), 5.47 (s, 1 H), 1.44 (s, 9 H). ^{13}C NMR (CD_2Cl_2): δ 174.4, 154.5, 141.7, 128.2, 127.9, 127.5, 127.4, 126.1, 119.6, 114.7, 114.6, 74.3, 56.4, 29.0.

Preparation of 6b was carried out as described for **6a**, except that Me_3SiNCO (1.49 mL, 11.0 mmol) replaced *t*-BuNCO. Yield: 4.45 g (86%). ^{1}H NMR (CD_2Cl_2): δ 7.40 (d, 2 H), 7.27 (t, 2 H), 7.12 (m, 3 H), 6.74 (t, 1 H), 6.60 (s, 5 H), 6.33 (s, 5 H), 6.22 (d, 2 H), 5.53 (s, 1 H), 0.26 (s, 9 H). ^{13}C NMR (CD_2Cl_2): δ 179.7, 153.1, 141.9, 129.2, 128.4, 128.2, 127.1, 119.6, 117.7, 116.1, 115.5, 76.8, 1.9.

Preparation of 11a. A 100 mL Schlenk flask was charged with **5b** (1.2 g, 2.55 mmol) and toluene (30 mL). The deep red solution changed to light red after adding *t*-BuNCO (320 μL, 2.8 mmol). The solvent was removed to yield a yellow solid (95% pure by ^{1}H NMR) which was treated with ether/hexanes (15 mL/60 mL), filtered by cannula, washed with hexanes (50 mL), and dried overnight under vacuum. Yield: 990 mg (78%). ^{1}H NMR (C_6D_6): δ 7.38 (m, 2 H), 7.26 (t, 2 H), 6.89 (t, 1 H), 5.66 (br s, 5 H), 5.35 (br s, 5 H), 3.77 (s, 1 H), 1.28 (s, 9 H), 0.28 (s, 9 H). ^{13}C NMR (C_6D_6): δ 149.8, 144.2, 128.2, 122.4, 122.1, 107.3, 106.3, 80.5, 53.2, 30.8, 0.6. Anal. Calcd for $C_{25}H_{34}N_2OSiZr$: C, 60.23; H, 6.78; N, 5.58; Si, 5.78. Found: C, 60.31; H, 6.88; N, 5.63; Si, 5.64.

$H_2NCH(Ph)CONH$-*t*-Bu (13a).[26] A 100 mL Schlenk flask was charged with **5b** (471 mg, 1.0 mmol) and THF (25 mL). After addition of the *t*-BuNCO (120 μL, 1.05 mmol), the golden yellow solution turned orange. It was stirred for 0.5 h and then treated with MeOH (1 mL) and stirred for 1 h. The solvent was evaporated, treated with CH_2Cl_2 (75 mL), and poured into saturated NaCl (50 mL). The solution was allowed to settle in a separatory funnel where three layers formed. The middle emulsion and lower organic layers were separated. The top aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL) and combined with the middle and lower layers, dried over $MgSO_4$, and evaporated to give crude (TMS)NHCH(Ph)CONH-*t*-Bu (**12**) as a white powder. Yield: 192 mg (70%), >98% pure by ^{1}H NMR. ^{1}H NMR (CD_2Cl_2): δ 7.32−7.02 (m, 5 H), 4.28 (d, 1 H), 4.21 (br s, 1 H), 3.98 (d, 1 H), 1.12 (s, 9 H), 0.01 (s, 9 H). The crude silyl amide was treated with 6 N HCl (4 mL) in CH_2Cl_2 (25 mL) and stirred for 3 h. The solution was treated with 6 N NaOH (20 mL), stirred for 0.5 h, and introduced into a separatory funnel. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined extracts were evaporated to a white solid. The solid was spotted on a Chromatotron plate and eluted with hexanes/ethyl acetate (1/1). The amide **13a** was isolated as a white solid. Yield: 104 mg (50%). ^{1}H NMR ($CDCl_3$, differing slightly from that reported[25]): δ 7.28−7.12 (m, 5 H), 5.15 (v br s, 1 H), 4.79 (br s, 1 H), 4.20 (br d, J = 5.04 Hz, 2 H), 1.25 (s, 9 H). ^{13}C NMR ($CDCl_3$): δ 157.9, 139.7, 128.5, 127.4, 127.0, 50.2, 44.1, 29.5. Anal. Calcd for $C_{12}H_{18}N_2O$: C, 69.87; H, 8.79; N, 13.58. Found: C, 69.62; H, 8.71; N, 13.48.

Preparation of $PhCH_2NHCONHPh$ (15c) was carried out as described for **13a**, except that PhNCO (100 μL, 0.92 mmol) replaced *t*-BuNCO. The residue that resulted from methanolysis was spotted on a Chromatotron plate and eluted with ethyl acetate/hexanes (4/1). The urea was isolated as a tan solid. Yield: 127 mg (56%). ^{1}H NMR ($(CD_3)_2CO$): δ 8.02 (br s, 1 H), 7.50 (d, 2 H), 7.34−7.20 (m, 7 H), 6.93 (t, 1 H), 6.24 (br s, 1 H), 4.41 (d, J = 5.82 Hz, 2 H). ^{13}C NMR ($(CD_3)_2CO$): δ 156.2, 141.6, 141.4, 129.4, 129.1, 128.1, 127.6, 122.3, 119.0, 44.1. Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 73.94; H, 6.14; N, 12.13.

Preparation of PhCH(D)NHCONHPh (15c-d_1) was carried out as described for **15c**, with MeOD replacing MeOH and a different amount of PhNCO (100 μL, 1.05 mmol) used. Yield: 107 mg (55%). ^{1}H NMR ($(CD_3)_2CO$): δ 4.38 (br s, 1 H). ^{13}C NMR ($(CD_3)_2CO$): δ 43.8 (t, J_{CD} = 21 Hz). LRMS: calcd for $C_{14}H_{13}DN_2O$ 227.29, found 227.07.

Preparation of $PhCH_2NHCONH$-*i*-Pr (15b) was carried out as described for the preparation of **15c**, except that *i*-PrNCO (103 μL, 1.05 mmol) replaced PhNCO. Yield: 109 mg (57%). ^{1}H NMR ($CDCl_3$): δ 7.23−7.19 (m, 5 H), 5.46 (br s, 1 H), 4.99 (br s, 1 H), 4.20 (d, J = 5.50 Hz, 2 H), 3.74 (m, 1 H), 1.01 (d, J = 6.43 Hz, 6 H). ^{13}C NMR ($CDCl_3$): δ 158.6, 139.9, 128.8, 127.6, 127.4, 44.5, 42.3, 23.7. Anal. Calcd for $C_{11}H_{16}N_2O$: C, 68.72; H, 8.39; N, 14.57. Found: C, 68.69; H, 8.36; N, 14.50.

$PhNHCH(Ph)CONH$-*t*-Bu (7a). A solution containing Cp_2ZrMe_2 (1.24 g, 4.93 mmol) and THF (40 mL) was cooled to −78 °C and treated with TfOH (435 μL, 4.92 mmol). The pale yellow solution was warmed to room temperature, stirred for 1 h, and again cooled to −78 °C. In a separate flask BuLi (2.5 M, 1.97 mL, 4.93 mmol) was added to a cold (0 °C) THF (25 mL) solution containing $PhCH_2NHPh$ (903 mg, 4.93 mmol), and the mixture stirred for 5 min. The $PhCH_2N(Li)Ph$ was transferred by cannula to the $Cp_2ZrMe(OTf)$ and stirred for 0.5 h at −78 °C, then warmed to room temperature, and stirred overnight. Addition of the *t*-BuNCO (600 μL, 5.25 mmol) resulted in an intense purple solution that was stirred for 0.5 h. Addition of MeOD (4 mL) resulted in a white suspension after 1 h. The solvent was removed, treated with ether (50 mL), and poured into saturated NaCl (100 mL). The ether layer resulted in an emulsion. The aqueous layer was extracted with ether (3 × 50 mL) and combined with the emulsion layer, dried over $MgSO_4$, and evaporated to a yellow residue. The residue was spotted on a Chromatotron plate and eluted with hexanes/ethyl acetate (7/1). $PhCH_2NHPh$ (typically, 5−10% was removed) (R_f 0.45) and **7a** (R_f 0.24) were separated. Compound **7a** was washed with hexanes and dried. Yield: 915 mg. An additional 145 mg was recovered from the filtrate to give 1.06 g of **7a** (76%). ^{1}H NMR ($CDCl_3$): δ 7.42−7.32 (m, 5 H), 7.17 (t, 2 H), 6.79 (t, 1 H), 6.61 (d, 2 H), 6.50 (br s, 1 H), 4.59 (br d, J = 1.94 Hz, 1 H), 4.49 (br s, 1 H), 1.31 (s, 9 H). ^{13}C NMR ($CDCl_3$): δ 170.5, 147.1, 139.6, 129.6, 129.5, 128.7, 127.6, 119.4, 114.2, 65.2, 51.5, 28.9. Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.48; H, 7.88; N, 10.00.

Preparation of $PhNHCH(Ph)CONH_2$ (7b) was carried out as described for the preparation of **7a**, except that (TMS)NCO (704 μL, 5.25 mmol) replaced *t*-BuNCO. Yield: 730 mg (65%). ^{1}H NMR (CD_2Cl_2): δ 7.49−7.36 (m, 5 H), 7.17 (t, 2 H), 6.76 (t, 1 H), 6.63 (d, 2 H), 6.41 (br s, 1 H), 6.02 (br s, 1 H), 4.84 (br s, 1 H), 4.78 (s, 1 H). ^{13}C NMR (CD_2Cl_2): δ 174.0, 147.0, 139.4, 129.6, 129.5, 128.9, 127.7, 118.9, 114.0, 63.5. Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.07; H, 6.12; N, 12.23.

Preparation of PhNHCH(Ph)CONHPh (7i) was carried out as described from the preparation of **7a** with the following modifications. The PhNCO (570 μL, 5.25 mmol) replaced *t*-BuNCO. The residue that resulted from MeOD quench was spotted on a Chromatotron plate; elution gave $PhCH_2NHPh$ (R_f 0.49), **7i**, and **8i-d_1** (R_f 0.31). The mixture of **7i** and **8i-d_1** was dissolved in ether (20 mL) and treated with 1.0 M HCl in ether (5 mL), and the white precipitate was filtered and washed with hexanes (50 mL; the filtrate was saved). The white solid was treated with 1 M NaOH (50 mL) in ether (50 mL) for 30 min. The mixture was introduced into a separatory funnel, the organic layer was separated, the aqueous layer was extracted with ether (2 × 25 mL), and the combined extracts were dried over $MgSO_4$, evaporated to dryness, and washed with hexanes. Yield: 296 mg (20%). ^{1}H NMR ($CDCl_3$): δ 8.72 (br s, 1 H), 7.53−7.19 (m, 11 H), 7.10 (t, 1 H), 6.85 (t, 1 H), 6.71 (d, 2 H), 4.82 (br d, J = 1.85 Hz, 1 H), 4.49 (br s, 1 H). ^{13}C NMR ($CDCl_3$): δ 169.6, 146.4, 138.4, 137.2, 129.4, 129.2, 128.9, 128.7, 127.4, 124.6, 120.0, 119.6, 114.0, 65.1. Anal. Calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.33; H, 6.02; N, 9.23.

Preparation of 9i was carried out as described above for the preparation of **7a** with the following modifications. The solvent was evaporated from **5a** and treated with benzene (100 mL). The golden yellow solution was filtered by cannula, and the color changed to deep red. The solid was washed with benzene (2 × 25 mL); the filtrate was treated with PhNCO (570 μL, 5.25 mmol) and stirred for 1 h. The volume of the solution was reduced to ca. 25 mL where a red solid precipitated. The red solid was filtered and washed with benzene (2

(26) Compound **13a** has been prepared by a different method: Katritzky, A. R.; Fan, W.-Q.; Akutagawa, K. *Synthesis* **1987**, 417.

× 5 mL) and dried overnight under vacuum. Yield: 344 mg (13%). ^{1}H NMR (CD_2Cl_2): δ 7.42−7.00 (m, 13 H), 6.70 (d, 2 H), 6.45 (s, 5 H), 5.67 (s, 5 H), 4.50 (s, 1 H). ^{1}H NMR (THF-d_8): δ 7.40−6.82 (m, 13 H), 6.68 (d, 2 H), 6.48 (s, 5 H), 5.68 (s, 5 H), 4.49 (s, 1 H). ^{13}C NMR (CD_2Cl_2): δ 162.4, 152.4, 147.1, 145.3, 128.1, 127.9, 125.1, 123.7, 123.0, 122.8, 122.6, 114.4, 111.8, 75.3. Anal. Calcd for $C_{30}H_{26}N_2OZr$: C, 69.06; H, 5.02; N, 5.37. Found: C, 68.83; H, 5.16; N, 5.26.

Preparation of $PhCH_2N(Ph)CONHPh$ (8i) from 5a was carried out as described for the preparation of **7i**, with MeOH replacing MeOD. The filtrate that was saved gave a tan solid. Recrystallization from hexanes/ether (10/1) gave transparent needles. Yield: 688 mg (46%). ^{1}H NMR ($CDCl_3$): δ 7.42−7.15 (m, 14 H), 6.97 (t, 1 H), 6.21 (br s, 1 H), 4.94 (s, 2 H). ^{13}C NMR ($CDCl_3$): δ 154.2, 141.1, 138.7, 138.1, 130.1, 128.7, 128.6, 128.4, 128.3, 128.1, 127.2, 122.8, 119.2, 53.0. Anal. Calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.27; H, 5.92; N, 9.11.

PhCH(D)N(Ph)CONHPh (8i-d_1). The filtrate saved from the preparation of **7i** gave a tan solid. Yield: 728 mg (49%), >98% pure by ^{1}H NMR. ^{1}H NMR ($CDCl_3$): δ 4.91 (br s, 1 H). ^{13}C NMR ($CDCl_3$): δ 52.8 (t, J_{CD} = 21 Hz). LRMS: calcd for $C_{20}H_{17}DN_2O$ 303.38, found 303.20.

Independent Synthesis of $PhCH_2N(Ph)CONHPh$ (8i). A two-neck round-bottom flask was charged with $PhCH_2NHPh$ (903.4 mg, 4.93 mmol), THF (85 mL), and PhNCO (570 μL, 5.25 mmol); the contents were refluxed for 48 h. The solvent was evaporated, the residue was treated with ether/brine (100 mL/100 mL), the aqueous layer was extracted with ether (3 × 50 mL), and the combined ether extracts were dried over $MgSO_4$ and evaporated to a tan oil. The oil was dissolved in ether (2 mL), treated with hexanes (75 mL), and washed with hexanes (50 mL). Yield: 1.03 g (69%).

Preparation of PhNHCH(Ph)CONH-*i*-Pr (7c) was carried out as described for the preparation of **7i**, except that *i*-PrNCO (551 μL, 5.25 mmol) replaced PhNCO. Yield: 916 mg (69%). ^{1}H NMR (C_6D_6): δ 7.29 (d, 2 H), 7.10−7.00 (m, 5 H), 6.71 (t, 1 H), 6.49 (d, 2 H), 5.92 (br d, 1 H), 4.74 (s, 1 H), 4.65 (d, J = 3.18 Hz, 1 H), 4.06 (m, 1 H), 0.79 (d, J = 6.58 Hz, 3 H), 0.71 (d, J = 6.56 Hz, 3 H). ^{13}C NMR (C_6D_6): δ 169.7, 147.2, 140.1, 129.5, 129.1, 128.3 (DEPT), 127.6 (DEPT), 118.9, 114.1, 63.9, 41.5, 22.3, 22.1. Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 75.88; H, 7.50; N, 10.40.

Isolation of PhCH(D)N(Ph)CONH-*i*-Pr (8c-d_1). The filtrate saved from the preparation of **7c** gave a purple oil. Yield: 123 mg, 8%, 95% pure by ^{1}H NMR. ^{1}H NMR ($CDCl_3$): δ 7.33−7.14 (m, 8 H), 7.05 (m, 2 H), 4.82 (br s, 1 H), 4.02−3.92 (m, 2 H), 1.02 (d, J = 6.27 Hz, 6 H). ^{13}C NMR ($CDCl_3$): δ 156.4, 141.8, 138.7, 129.7, 128.4, 128.2, 128.1, 127.3, 127.0, 52.6 (t, J_{CD} = 22 Hz), 42.5, 23.2. LRMS: calcd for $C_{17}H_{19}DN_2O$ 269.17, found 269.20.

Preparation of PhNHCH(Ph)CONHEt (7d) was carried out as described for the preparation of **7i**, except that EtNCO (415 μL, 5.25 mmol) replaced PhNCO. Yield: 375 mg (30%). ^{1}H NMR (C_6D_6): δ 7.28 (d, 2 H), 7.10−6.99 (m, 5 H), 6.70 (t, 1 H), 6.48 (d, 2 H), 6.00 (t, 1 H), 4.77 (br s, 1 H), 4.65 (d, J = 3.35 Hz, 1 H), 3.05−3.82 (m, 2 H), 0.66 (t, 3 H). ^{13}C NMR (C_6D_6): δ 170.4, 147.2, 140.1, 129.5, 129.1, 128.3 (DEPT), 127.6 (DEPT), 118.8, 114.1, 63.8, 34.5, 14.7. Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.75; H, 7.11; N, 11.05.

PhCH(D)N(Ph)CONHEt (8d-d_1). The filtrate saved from the preparation of **8d** gave a tan solid. Yield: 471 mg (38%), >98% pure by ^{1}H NMR. ^{1}H NMR ($CDCl_3$): δ 7.40−7.12 (m, 8 H); 7.05 (d, 2 H); 4.82 (br s, 1 H); 4.21 (br t, 1 H); 3.24−3.18 (m, 2 H); 1.01 (t, 3 H). ^{13}C NMR ($CDCl_3$): δ 157.0, 141.7, 138.6, 129.7, 128.5, 128.2, 128.1, 127.4, 126.9, 52.6 (t, J_{CD} = 21 Hz), 35.5, 15.4. LRMS: calcd for $C_{16}H_{17}DN_2O$ 255.15, found 255.19.

In situ generation of PhNHCH(Ph)CONHMe (7e) was carried out as described for the preparation of **7i**, except that MeNCO (310 μL, 5.25 mmol) replaced PhNCO. Yield: 273 mg (23%). ^{1}H NMR ($CDCl_3$): δ 7.43−7.24 (m, 5 H), 7.18 (t, 2 H), 6.79 (t, 1 H), 6.74 (br s, 1 H), 6.61 (d, 2 H), 4.73 (d, J = 2.22 Hz, 1 H), 4.58 (br s, 1 H), 2.80 (d, J = 4.90 Hz, 3 H). ^{13}C NMR ($CDCl_3$): δ 171.8, 146.6, 138.7, 129.3, 129.1, 128.5, 127.3, 119.0, 113.7, 64.0, 26.3. Anal. Calcd for $C_{15}H_{16}N_2O$: C, 74.99; H, 6.71; N, 11.66. Found: C, 74.75; H, 6.66; N, 11.40.

PhCH(D)N(Ph)CONHMe (7e-d_1). The filtrate saved from the preparation of **7e** gave a tan oil. Yield: 534 mg (45%), >98% pure by ^{1}H NMR. ^{1}H NMR ($CDCl_3$): δ 7.33−7.22 (m, 8 H), 7.05 (d, 2 H), 4.83 (br s, 1 H), 4.17 (br s, 1 H), 2.73 (d, J = 4.63 Hz, 3 H). ^{13}C NMR ($CDCl_3$): δ 158.1, 142.1, 139.0, 130.2, 129.0, 128.7, 128.6, 128.0, 127.4, 53.2 (t, J_{CD} = 21 Hz), 27.9. LRMS: calcd for $C_{15}H_{15}DN_2O$ 241.31, found 241.17.

PhNHCH(Ph)CONHC$_6$H$_4$-*o*-OMe (7f) was carried out as described for the preparation of **7i**, except that *o*-$MeOC_6H_4NCO$ (700 μL, 5.25 mmol) replaced PhNCO. Yield: 395 mg (24%). ^{1}H NMR (C_6D_6): δ 9.07−8.99 (s, NH, overlapped with the aromatic d, total 2 H), 7.30 (d, 1 H), 7.01 (m, 5 H), 6.98−6.76 (m, 3 H), 6.69 (t, 1 H), 6.51 (d, 2 H), 6.34 (d, 1 H), 4.77 (d, 1 H, J = 2.46 Hz), 4.62 (s, 1 H), 3.00 (s, 3 H). ^{13}C NMR (C_6D_6): δ 168.8, 148.4, 147.1, 139.7, 129.5, 129.3, 128.5 (DEPT), 127.8 (DEPT), 123.9, 121.6, 120.1, 119.3, 114.4, 110.5, 65.2, 55.3. Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.85; H, 6.03; N, 8.45.

PhCH(D)N(Ph)CONHC$_6$H$_4$-*o*-OMe (8f-d_1). The filtrate saved from the preparation of **8f** gave a yellow residue. The residue was dissolved in ether (2 mL) and overlayered with hexanes (60 mL). The homogeneous solution was cooled to −78 °C that gave a white precipitate. The solid was collected by cold filtration (−78 °C). Yield: 502 mg (31%), >98% pure by ^{1}H NMR. ^{1}H NMR ($CDCl_3$): δ 8.26 (d, 1 H), 7.39−7.16 (m, 9 H), 7.00−6.90 (m, 3 H), 6.71 (d, 1 H), 4.94 (br s, 1 H), 3.55 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 154.8, 148.1, 141.9, 138.7, 130.2, 129.4, 128.9, 128.7, 128.6, 128.2, 127.6, 122.4, 121.4, 118.9, 110.3, 55.9, 53.0 (t, J_{CD} = 21 Hz). LRMS: calcd for $C_{21}H_{19}DN_2O_2$ 333.38, found 333.21.

In situ generation of PhNHCH(Ph)CONHC$_6$H$_4$-*p*-OMe (7g) was carried out as described for the preparation **7i**, except that *p*-$MeOC_6H_4$-NCO (680 μL, 5.25 mmol) replaced PhNCO. Yield: 452 mg, 28%. ^{1}H NMR (C_6D_6): δ 8.09 (s, 1 H), 7.35 (d, 2 H), 7.24 (m, 2 H), 7.04 (m, 5 H), 6.72 (t, 1 H), 6.63 (d, 2 H), 6.49 (d, 2 H), 4.72 (br s, 1 H), 4.33 (s, 1 H), 3.21 (s, 3 H). ^{13}C NMR (CD_3CN): δ 170.6, 157.4, 147.9, 140.0, 132.2, 130.1, 129.8, 129.2, 128.5, 122.7, 119.0, 114.9, 114.6, 63.9, 56.0. Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.92; H, 6.16; N, 8.36.

PhCH(D)N(Ph)CONHC$_6$H$_4$-*p*-OMe (8g-d_1). The filtrate saved from the preparation of **7g** gave a brown oil. Yield: 789 mg (48 %), >98% pure by ^{1}H NMR. ^{1}H NMR ($CDCl_3$): δ 7.41−7.14 (m, 12 H), 6.78 (d, 2 H), 6.04 (br s, 1 H), 4.90 (br s, 1 H), 3.74 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 155.6, 154.7, 141.2, 138.2, 131.8, 130.1, 128.6, 128.4, 128.3, 128.0, 127.1, 121.5, 113.9, 55.4, 52.8 (t, J_{CD} = 22 Hz). LRMS: calcd for $C_{21}H_{19}DN_2O_2$ 333.16, found 333.24.

In situ generation of PhNHCH(Ph)CONHCH$_2$Ph (7h) was carried out as described for the preparation of **7i**, except that $PhCH_2NCO$ (648 μL, 5.25 mmol) replaced PhNCO. Yield: 458 mg (29%). ^{1}H NMR (CD_2Cl_2): δ 7.49−7.10 (m, 12 H), 7.08 (br t, 1 H), 6.78 (t, 1 H), 6.64 (d, 2 H), 4.83 (d, J = 3.27 Hz, 1 H), 4.77 (br s, 1 H), 4.41 (d, J = 6.04 Hz, 2 H). ^{13}C NMR (CD_2Cl_2): δ 171.3, 147.0, 139.5, 138.7, 129.6, 129.5, 128.9, 127.73, 127.71, 127.6, 119.1, 114.1, 64.1, 43.6. Anal. Calcd for $C_{21}H_{20}N_2O$: C, 79.72; H, 6.37; N, 8.85. Found: C, 79.84; H, 6.38; N, 8.85.

PhCH(D)N(Ph)CONHCH$_2$Ph (8h-d_1). The filtrate saved from the preparation of **7h** gave a pale pink oil. Yield: 756 mg (48%), >98% pure by ^{1}H NMR. ^{1}H NMR ($CDCl_3$): δ 7.42−7.11 (m, 13 H), 7.09 (d, 2 H), 4.90 (br s, 1 H), 4.64 (br s, 1 H), 4.43 (br d, 2 H). ^{13}C NMR ($CDCl_3$): δ 156.8, 141.2, 139.3, 138.3, 129.6, 128.3, 128.2, 128.1, 128.0, 127.4, 126.9, 126.8, 126.7, 52.7 (t, J_{CD} = 21 Hz), 44.4. LRMS: calcd for $C_{21}H_{19}DN_2O$ 317.17, found 317.25.

Preparation of PhNHCH(Ph)CONHC$_6$H$_4$-*p*-F (7j) was carried out as described for the preparation of **7i**, except that *p*-FC_6H_4NCO (597 μL, 5.25 mmol) replaced PhNCO. Yield: 316 mg (20%). ^{1}H NMR ($CDCl_3$): δ 8.79 (br s, 1 H), 7.45−7.37 (m, 7 H), 7.22 (t, 2 H), 6.96 (t, 2 H), 6.86 (t, 1 H), 6.70 (d, 2 H), 4.82 (s, 1 H), 4.49 (br s, 1 H). ^{13}C NMR ($CDCl_3$): δ 169.4, 158.0, 146.6, 138.2, 133.1, 129.5, 129.3, 128.8, 127.3, 121.8, 121.7, 119.8, 115.7, 115.0, 114.1, 65.4. Anal. Calcd for $C_{20}H_{17}FN_2O$: C, 74.98; H, 5.35; N, 8.74; F, 5.93. Found: C, 74.85; H, 5.31; N, 8.69; F, 6.06.

PhCH(D)N(Ph)CONHC$_6$H$_4$*p*-F (8j-*d*$_1$). The filtrate saved from the preparation of **7j** gave a tan oil. Yield: 838 mg (53%), >98% pure by ^{1}H NMR. ^{1}H NMR ($CDCl_3$): δ 7.39−7.15 (m, 12 H), 6.92 (t, 2 H), 6.19 (br s, 1 H), 4.91 (br s, 1 H). ^{13}C NMR ($CDCl_3$): δ 160.2, 156.9, 154.2, 140.9, 137.8, 134.6, 128.5, 128.3, 128.2, 128.1, 127.1, 121.2, 121.1, 115.3, 115.0, 52.9 (t, J_{CD} = 22 Hz). LRMS: calcd for $C_{20}H_{16}DFN_2O$ 321.14, found 321.22.

Measurement of the 7i/8i Product Ratio from PhNCO Addition to *rac*-10.[3b] Cp_2ZrMe_2 was replaced by *rac*-[EBTHI]$ZrMe_2$ (620 mg, 1.60 mmol) in 20 mL of THF in the procedure described for the preparation of **5a**. The pale orange solution turned red after adding PhNCO (183 μL, 1.68 mmol). After solvent removal the residue was spotted on a Chromatotron plate and eluted with hexanes/ethyl acetate (7/1). $PhCH_2NHPh$ (typically, 5−10% was recovered; R_f 0.50) was separated from the band that contained both $PhCH_2N(Ph)CONHPh$ (**8i**) and PhNHCH(Ph)CONHPh (**7i**) (R_f 0.29). ^{1}H NMR revealed 71% **7i** and **29%** **8i** (±5%). The presence of **7i** and **8i** was confirmed by the addition of authentic samples to the product mixture.

Competition Experiments. Four separate solutions of Cp_2ZrMe_2 (403 mg, 1.60 mmol) and THF (20 mL) were cooled to −78 °C and treated with TfOH (142 μL, 4.92 mmol). The mixtures were warmed to room temperature, stirred for 1 h, and again cooled to −78 °C. In four separate flasks, BuLi (1.6 M, 1.00 mL, 1.60 mmol) was added to cold (0 °C) THF (15 mL) solutions containing $PhCH_2NHPh$ (293 mg, 1.60 mmol) and stirred for 5 min. The $PhCH_2N(Li)Ph$ was transferred by cannula to the $Cp_2ZrMe(OTf)$, and the resulting mixtures were stirred for 0.5 h at −78 °C, warmed to room temperature, and stirred overnight.

With gentle stirring the solutions were recooled to −78 °C, and the first isocyanate was added; the second isocyanate was added 1 h later. *Amounts of the first isocyanate*: *t*-BuNCO (1.68 mmol); PhNCO (5.04 mmol); PhNCO (1.68 mmol); *t*-BuNCO (2.54 mmol). *Amounts of the second isocyanate*: PhNCO (5.04 mmol); *t*-BuNCO (1.68 mmol); *t*-BuNCO (2.54 mmol); PhNCO (1.68 mmol). The deep red mixtures were kept at −80 °C for an additional hour, then removed from the cooling baths, and stirred for 1 h. Each was treated with MeOH (2 mL) and stirred for an additional hour. After solvent evaporation, the residues were treated with CH_2Cl_2 (5 mL), hexanes (50 mL) were added, the solution was filtered, and the solvents were again removed. The residues were spotted on a Chromatotron plate and eluted with hexanes/ethyl acetate (7/1). $PhCH_2NHPh$ (typically, 5−10% was recovered; R_f 0.50) was separated from the band that contained $PhCH_2N(Ph)$-CONHPh (**8i**), PhNHCH(Ph)CONHPh (**7i**), and PhNHCH(Ph)CONH-*t*-Bu (**7a**) (R_f 0.29). The percent NMR yields of **7i**, **8i**, and **7a** were determined by ^{1}H NMR (±5%) to obtain the results in Table 3.

Variable Temperature ^{1}H NMR Spectra of 5a. The ^{1}H NMR spectra of **5a** were recorded in toluene-d_8 from −36 to +31 °C. Probe temperatures, estimated to be accurate to ±1.0 °C, were measured with a copper−constantan thermocouple. Care was taken to minimize the common sources of error in NMR line-broadening studies (temperature equilibration, constant spin rate, maximum point density, etc.) as discussed by Gutowsky.[27]

In variable temperature experiments with **5a**, the true probe temperature was determined from the peak separation of ethylene glycol.[28] The width ($\Delta\nu_{1/2}$) at half-height of the α-methylene group (δ 2.65) proved to be temperature dependent. The rate constant k_{obs} was obtained from $k_{obs} = \pi(\Delta\Delta\nu)$, where $\Delta\Delta\nu$ was the difference between the observed line widths at −12 °C ($\Delta\nu_{1/2}$ = 20.74 Hz at $[THF]_{free}$ = 1.02 mM, 20.77 Hz at $[THF]_{free}$ = 61.1 mM, and 20.90 Hz at $[THF]_{free}$ = 136.2 mM) or 0 °C ($\Delta\nu_{1/2}$ = 46.56 Hz at $[THF]_{free}$ = 1.02 mM, 49.90 Hz at $[THF]_{free}$ = 21.5 mM, and 50.43 Hz at $[THF]_{free}$ = 136.2 mM) and $\Delta\nu_{1/2}$ in the absence of exchange (taken as $\Delta\nu$ for the Cp resonance at the same temperature, 3.63 Hz).

Preparation of 18 was carried out as described for the preparation of **5a** with the following modifications. Cp_2ZrMe_2 (1.3 g, 5.15 mmol) in THF (40 mL) was treated with TfOH (456 μL, 5.15 mmol). BuLi (2.0 M, 2.57 mL, 5.15 mmol) was added to a cold (0 °C) THF (20 mL) solution containing $PhCH_2NH(o\text{-}OMeC_6H_4)$[29] (1.1 g, 5.15 mmol). The $PhCH_2N(Li)o\text{-}OMeC_6H_4$ was transferred by cannula to the Cp_2-ZrMe(OTf), stirred for 0.5 h at −78 °C, warmed to room temperature, and stirred overnight. The filtrate was reduced to dryness, and hexanes (150 mL) were added, a bright orange precipitate resulting after vigorous stirring. The solid was filtered by cannula, washed with hexanes (2 × 20 mL), and dried overnight under vacuum. Yield: 2.07 g (93%). ^{1}H NMR (C_6D_6): δ 7.36−7.27 (m, 4 H), 7.01 (t, 1 H), 6.89 (t, 1 H), 6.52 (d, 1 H), 6.44 (t, 1 H), 6.23 (d, 1 H), 5.47 (s, 10 H), 3.82 (s, 1 H), 2.97 (s, 3 H). ^{13}C NMR (C_6D_6): δ 153.6, 153.2, 147.6, 128.2, 124.6, 123.3, 122.0, 114.2, 113.2, 109.5, 108.2, 107.2, 62.4, 59.4. Anal. Calcd for $C_{24}H_{23}NOZr$: C, 66.62; H, 5.36; N, 3.24. Found: C, 66.27; H, 5.44; N, 2.99.

Preparation of 19. A 100 mL Schlenk flask was charged with **18** (558 mg, 1.29 mmol) and benzene (25 mL). The orange solution precipitated a yellow solid after the addition of MeNCO (80 μL, 1.36 mmol). Half of the solvent was evacuated and the rest of the solution treated with hexanes (50 mL), filtered by cannula, and dried overnight under vacuum. Yield: 579 mg (92%). ^{1}H NMR (CD_2Cl_2): δ 7.47 (d, 2 H), 7.36−7.18 (m, 3 H), 6.89 (d, 2 H), 6.69 (t, 1 H), 6.48 (t, 1 H), 6.35 (s, 5 H), 6.17 (s, 5 H), 6.03 (d, 2 H), 5.05 (s, 1 H), 4.22 (s, 3 H), 2.64 (s, 3 H). ^{13}C NMR (CD_2Cl_2): δ 178.7, 148.2, 144.1, 142.2, 128.6, 128.4, 127.6, 127.1, 124.2, 114.5, 114.2, 113.3, 109.3, 72.2, 60.3, 37.2.

Preparation of 21. A 300 mL thick-walled vacuum bulb contained a degassed solution of **18** (560 mg, 1.29 mmol) and benzene (20 mL). Dry ice (ca. 2−3 equiv) was transferred from a −78 °C bath to the vacuum bulb at −196 °C. Upon warming to room temperature, a yellow solid precipitated and the solution was allowed to stir for 1 h. The solution was treated with hexanes (75 mL) and filtered by cannula; the precipitate was washed with hexanes (75 mL) and dried overnight under vacuum. Yield: 464 mg (73%) of off-white powder. (The yield of **21** is quantitative if benzene is removed before addition of hexanes; however, the resulting pale yellow solid is contaminated with 5−15% benzene.) ^{1}H NMR (CD_2Cl_2): δ 7.47 (d, 2 H), 7.33−7.20 (m, 3 H), 6.91 (d, 1 H), 6.69 (t, 1 H), 6.46 (t, 1 H), 6.37 (s, 5 H), 6.24 (s, 5 H), 5.95 (d, 1 H), 5.16 (s, 1 H), 4.20 (s, 3 H), 2.25 (br s, 2H, H_2O). ^{13}C NMR (CD_2Cl_2): δ 178.0, 148.5, 143.5, 140.5, 128.6, 127.3, 127.2, 124.5, 115.1, 114.6, 114.3, 113.8, 109.4, 73.0, 60.1. Anal. Calcd for $C_{25}H_{23}NO_3Zr{\cdot}H_2O$: C, 60.70; H, 5.09; N, 2.83. Found: C, 60.73; H, 4.83; N, 2.67. The presence of 1 equiv of H_2O of crystallization was confirmed by ^{1}H NMR.

Attempted Hydrolysis of 21 to the α-Amino Acid 22. A suspension of **21** (200 mg, 0.42 mmol) in THF (10 mL) was treated with MeOH (1 mL) and stirred overnight. The solvent was removed and the resulting solid taken up in CH_2Cl_2 (20 mL). A saturated $NaHCO_3$ wash (60 mL) was extracted with CH_2Cl_2 (3 × 20 mL), and the combined CH_2Cl_2 extracts were dried over $NaHCO_3$ and evaporated to a tan solid (125 mg). ^{1}H NMR in $CDCl_3$ showed several broad unresolvable signals. Similar results were obtained when **21** was treated with HCl/Et_2O, HCl/H_2O, catechol,[25] H_2O_2/H_2O, H_2O_2/NaOH, trifluoroacetic acid, triflic acid, Me_3SiOTf/H_2O, and *o*-anisic acid.

Preparation of (*o*-OMeC$_6$H$_4$)NHCH(Ph)CONHMe (20) was carried out as described for the preparation of **19**. The yellow solution of **19** was treated with MeOH (1 mL). After chromatography (hexane/ethyl acetate, 10/1), 213 mg (79%) was isolated. ^{1}H NMR ($CDCl_3$): δ 7.45−7.24 (m, 5 H), 6.90−6.75 (m, 3 H), 6.53 (d, 1 H), 4.95 (br s, 1 H), 4.70 (s, 1 H), 3.82 (s, 3 H), 2.81 (d, 3 H). ^{13}C NMR ($CDCl_3$): δ 171.9, 146.9, 138.7, 136.5, 128.9, 128.3, 127.3, 121.1, 118.4, 111.1, 109.3, 64.2, 55.2, 26.1. Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.93; H, 6.69; N, 10.39.

Preparation of 23 was carried out as described for the preparation of **19** with the following modifications. Compound **18** (1.73 g, 2.11 mmol) in benzene (30 mL) was treated with ethylene carbonate (357 mg, 4.05 mmol). The solvent was removed and treated with hexanes (50 mL). Yield: 1.82 g (87%) of pale yellow solid. ^{1}H NMR (CD_2Cl_2): δ 7.38−7.12 (m, 5 H), 6.81 (d, 1 H), 6.62 (t, 1 H), 6.36 (s, Cp, overlapped with aromatic m, 6 H), 6.17 (s, 5 H), 5.86 (d, 1 H), 5.02 (s, 1 H), 4.09 (s, 3 H), 3.99−3.79 (m, 3 H), 3.28−3.24 (m, 1 H). ^{13}C NMR (CD_2Cl_2): δ 162.8, 148.8, 145.1, 142.5, 128.0, 127.8, 127.6,

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126.4, 123.9, 114.2, 113.3, 113.1, 108.7, 78.8, 64.7, 63.9, 58.8. Anal. Calcd for $C_{27}H_{27}NO_4Zr$: C, 62.28; H, 5.22; N, 2.69. Found: C, 62.02; H, 5.13; N, 2.53.

(*o*-OMeC$_6$H$_4$)NHCH(Ph)COOCH$_2$CH$_2$OH (24). A 100 mL Schlenk flask was charged with **18** (2.0 g, 4.62 mmol), THF (35 mL), and ethylene carbonate (441 mg, 5.0 mmol). After 0.5 h, the solution was treated with MeOH (4 mL) and allowed to stir overnight. The solvent was removed, the residue was treated with ether (60 mL) and filtered, and the filtrate was evaporated to dryness. The residue was spotted on a Chromatotron plate and eluted with ethyl acetate/hexanes (2/1) (R_f 0.43). Yield: 960 mg (70%). ^{1}H NMR ($CDCl_3$): δ 7.52 (d, 2 H), 7.39−7.31 (m, 3 H), 6.81−6.68 (m, 3 H), 6.40 (d, 1 H), 5.44 (br s, 1 H), 5.15 (s, 1 H), 4.23 (t, 2 H), 3.87 (s, 3 H), 3.68 (br q, 2 H), 1.92 (br s, 1 H). ^{13}C NMR ($CDCl_3$): δ 172.2, 147.0, 137.7, 135.9, 128.7, 128.2, 127.2, 121.0, 117.3, 110.6, 109.5, 60.7, 55.4, 52.6. LRMS: calcd for $C_{17}H_{19}NO_4$ 301.1, found 301.2.

Attempted Hydrolysis of (*o*-OMeC$_6$H$_4$)NHCH(Ph)COOCH$_2$CH$_2$-OH (24) to 22. According to a procedure described in the literature,[29] a suspension of **24** (860 mg, 2.62 mmol), K_2CO_3 (845 mg, 3.05 mmol), and water (3.6 mL) in benzene (40 mL) was refluxed for 72 h. Compound **24** was recovered in 90% yield.

Preparation of (*o*-OMeC$_6$H$_4$)NHCH(Ph)COOMe (25) was carried out as described for the preparation of **24**, except that benzene replaced THF before methanolysis. The residue was spotted on a Chromatotron plate and eluted with hexanes. Yield: 903 mg (72%). ^{1}H NMR ($CDCl_3$): δ 7.53 (d, 2 H), 7.41−7.30 (m, 3 H), 6.82−6.66 (m, 3 H), 6.39 (d, 1 H), 5.52 (br s, 1 H), 5.11 (d, 1 H), 3.89 (s, 3 H), 3.74 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 172.0, 146.9, 137.4, 135.8, 128.8, 128.3, 127.0, 120.9, 117.5, 110.6, 109.5, 66.8, 60.8, 60.7, 55.3. Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.96; H, 6.33; N, 5.23.

^{1}H and ^{13}C NMR of 26. A 5 mm NMR tube was charged with **5a** (32 mg, 0.067 mmol), C_6D_6 (0.6 mL), and ethylene carbonate (6.5 mg, 0.074 mmol). The sample was sealed, and the magenta solution was examined by NMR. ^{1}H NMR (C_6D_6): δ 7.64 (d, 2 H), d 7.20−6.98 (m, 5 H), 6.60 (t, 1 H), 6.43 (s, 5 H), 6.11 (d, 2 H), 5.94 (s, 5 H), 3.68 (m, 1 H), 3.55 (m, free THF overlapped with m from one ethylenic proton, 5 H total), 3.41 (m, 1 H), 2.70 (m, 1 H), 1.42 (m, free THF, 4 H). ^{13}C NMR (C_6D_6): δ 155.1, 153.5, 142.2, 129.5, 129.1, 127.7, 126.7, 117.1, 115.9, 115.1, 82.0, 65.1, 63.9, 63.7.

Preparation of (Ph)NHCH(Ph)COOMe (27) was carried out as described for the preparation of **25**, except that **5a** (800 mg, 1.68 mmol) replaced **18**. After 15 min, the magenta solution (in benzene) was treated with MeOH (2 mL) and allowed to stir overnight. The residue (slightly soluble in hexanes) was spotted on a Chromatotron plate and eluted with hexanes/ethyl acetate (15/1). Yield: 203 mg (50%). ^{1}H NMR ($CDCl_3$): δ 7.49 (d, 2 H), 7.45−7.29 (m, 3 H), 7.12 (t, 2 H), 6.70 (t, 1 H), 6.56 (d, 2 H), 5.08 (d, 1 H), 4.96 (br d, 1 H), 3.72 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 172.3, 145.9, 137.6, 129.2, 128.8, 128.3, 127.2, 118.1, 113.6, 60.7, 52.7. Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.40; H, 6.25; N, 5.84. The experiment was repeated and the magenta solution stirred for 24 h as the solution turned red. Yield: 230 mg (54%).

Preparation of 28 was carried out as described for the preparation of **5a** with the following modifications. Cp_2ZrMe_2 (2.26 g, 8.97 mmol) in THF (40 mL) was treated with TfOH (795 μL, 8.97 mmol). BuLi (2.0 M, 4.49 mL, 8.97 mmol) was added to a cold (0 °C) THF (20 mL) solution containing (*p*-MeC$_6$H$_4$)CH$_2$NH(*o*-OMeC$_6$H$_4$)[29] (2.04 g, 8.97 mmol). Yield: 3.07 g (77%). ^{1}H NMR (C_6D_6): δ 7.24 (d, 2 H), 7.15 (d overlapped with residual C_6D_6 proton shift, 2 H), 6.88 (t, 1 H), 6.56 (d, 1 H), 6.45 (t, 1 H), 6.26 (d, 1 H), 5.51 (s, 5 H), 5.50 (s, 5 H), 3.84 (s, 1 H), 3.00 (s, 3 H), 2.33 (s, 3 H). ^{13}C NMR (C_6D_6): δ 153.3, 150.5, 147.5, 130.7, 128.9, 124.6, 123.4, 114.1, 113.1, 109.5, 108.2, 107.1, 62.4, 59.4, 21.2.

Preparation of 29 was carried out as described for the preparation of **23** with the following modifications. Compound **28** (2.0 g, 4.49 mmol) in benzene (30 mL) was treated with ethylene carbonate (476 mg, 4.76 mmol). The solvent was removed and treated with hexanes (50 mL); the filtrate was saved. Yield: 1.32 g (55%) of pale yellow solid. ^{1}H NMR (C_6D_6): δ 7.54 (d, 2 H), 7.08 (d overlapped with residual C_6D_6 proton shift, 2 H), 6.71 (t, 1 H), 6.40−6.15 (m (aromatic), overlapped with s (Cp), total 8 H), 5.94 (s, 5 H), 5.47 (s, 1 H), 3.85 (t, 1 H), 3.65 (m, 2 H), 3.12−2.97 (m, ethylenic, overlapped with s, MeO, total 4 H), 2.13 (s, 3 H).

Preparation of (*o*-OMeC$_6$H$_4$)NHCH(*p*-MeC$_6$H$_4$)COOCH$_2$CH$_2$OH (30) was carried out as described for the preparation of **24**, except that **28** (1.0 g, 1.87 mmol) replaced **18**. Yield: 250 mg (42%). ^{1}H NMR ($CDCl_3$): δ 7.38 (d, 2 H), 7.15 (d, 2 H), 6.78−6.66 (m, 3 H), 6.38 (d, 1 H), 5.36 (br d, 1 H), 5.09 (d, 1 H), 4.24 (m, 2 H), 3.86 (s, 3 H), 3.70 (br m, 2 H), 2.32 (s, 3 H), 1.62 (br m, 1 H). ^{13}C NMR ($CDCl_3$): δ 172.3, 147.0, 138.2, 136.0, 134.6, 129.6, 127.1, 121.1, 117.5, 110.7, 109.7, 67.0, 61.0, 60.6, 55.5, 21.1.

(*o*-OMeC$_6$H$_4$)NHCH(*p*-MeC$_6$H$_4$)COOMe (31). The filtrate that was saved in the preparation of **29** (ca. 1 g, 1.9 mmol) was evacuated to dryness, and benzene was added; the product was purified by the procedure described for the preparation of **25**. Yield: 274 mg (51%). ^{1}H NMR ($CDCl_3$): δ 7.38 (d, 2 H), 7.15 (d, 2 H), 6.78−6.62 (m, 3 H), 6.35 (d, 1 H), 5.42 (br d, 1 H), 5.04 (d, 1 H), 3.87 (s, 3 H), 3.71 (s, 3 H), 2.32 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 172.4, 147.0, 138.0, 136.0, 129.5, 127.1, 121.0, 117.3, 110.6, 109.5, 60.4, 55.3, 52.6, 21.1.

Attempted Conversion of 23 to (*o*-OMeC$_6$H$_4$)NHCH(Ph)COOR″ with R″OH (R″ = *t*-Bu, PhCH$_2$, H) was carried out as described for the preparation of **25** with *t*-BuOH replacing MeOH. The ^{1}H NMR showed **24** and no evidence of (*o*-OMeC$_6$H$_4$)NHCH(Ph)COO-*t*-Bu. Similar results were obtained with $PhCH_2OH$ and H_2O.

Crossover Experiment. A 100 mL Schlenk flask was charged with **23** (269 mg, 0.517 mmol) and benzene (35 mL); a 50 mL Schlenk flask was charged with **24** (163 mg, 0.517 mmol), benzene (20 mL), and MeOH (500 μL). The contents of the second Schlenk flask, and a benzene wash (5 mL), were transferred by cannula to the first; the mixture was stirred overnight. The solvent was removed, and the off-white solid was taken up in ether (60 mL) and filtered; the solid was washed with ether (5 × 20 mL), and the filtrate was evaporated to dryness. The residue from the filtrate was spotted on a Chromatotron plate and eluted with hexanes/ethyl acetate (7/1). The first (R_f 0.55, a mixture of the methyl esters **25** and **31**) and second (R_f 0.17, a mixture of the β-hydroxyethyl esters **24** and **30**) bands were collected and examined by ^{1}H NMR; there were equal amounts of all four products. The presence of **24**, **30**, **25**, and **31** was confirmed by the addition of authentic samples to the product mixtures.

Zr-Promoted Transesterification of 24 to 25. A 50 mL Schlenk flask was charged with Cp_2ZrMe_2 (277 mg, 1.10 mmol) and benzene (15 mL). The solution was treated with MeOH (500 μL), stirred for 1 h, and treated with **24** (330 mg, 1.09 mmol) in benzene (15 mL). The remaining procedure is like that described above in the preparation of **25**. Yield: 196 mg (74%). The presence of **25** was confirmed by the addition of authentic sample to the product mixture.

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Supplementary Material Available: Tables of X-ray crystal and structural data for **5a**—atomic coordinates, isotropic and anisotropic displacement coefficients, bond lengths and angles, and hydrogen atom coordinates (7 pages). This material is contained in many 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.

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