A Contribution to the Asymmetric Synthesis of 3-Amino β-Lactams: The Diastereoselective [2+2] Cycloaddition Reaction of Chiral Aminoketene Equivalents with Enolizable Aldehyde-Derived Imines

Claudio Palomo,* Jesus M. Aizpurua,* Marta Legido, Antonia Mielgo, and Regina Galarza

Abstract: *N*-[Bis(trimethylsilyl)methyl]imines **9** show unique chemical properties when compared with conventional imines. Their reaction with optically pure aminoketenes derived from dehydrochlorination of **14** and **15** affords the corresponding 3-amino-4-alkyl-β-lactams **16** and **17** in good yields and high diastereoselectivities. The mild deprotection of bis(trimethylsilyl)methyl- and phenyloxazolidinone moieties with, respectively, cerium(IV) ammonium nitrate and lithium/ammonia or hydrogen/$Pd(OH)_2$ allows the preparation of a variety of β-lactam antibiotic building blocks.

Keywords
asymmetric synthesis · cycloadditions · imines · lactams · silicon

Introduction

The β-lactam skeleton is the key structural element of the most widely employed class of antimicrobial agents, the β-lactam antibiotics.[1] Some of the well-known representatives, shown in Figure 1, are penicillins (**1**), cephalosporins (**2**), cephamycins (**3**), 1-oxacephalosporins (**4**), and monobactams like aztreonam (**5**) and carumonam (**6**), among many others.[1, 2] In fact, since the discovery and structural elucidation of penicillin G and the closely related cephalosporin C, much work has been carried out in this important field of research for two main reasons: first, because of the constant need for new drugs displaying broader antibacterial activity and/or different biological properties, and, second, because of the requirement for new β-lactam antibiotics to combat bacteria which have built up a resistance against most traditional compounds.[3] As a consequence of this interest, a large number of methods for the production of β-lactams have been developed and the topic has been amply documented and reviewed several times.[4] Among the existing methods, however, the hydroxamate methodology,[5] the metalloester enolate–imine condensation,[6] the chromium carbene–imine reaction,[7] and the [2+2] cycloaddition of ketenes with imines, also known as the Staudinger reaction,[8] have been most often employed for the construction of the azetidin-2-one ring. In particular, the last provides useful and economical access to 3-amino β-lactams,[9] mainly due to the ready availability of ketenes generated by dehydrohalogenation of their corresponding acid chlorides and a tertiary organic base. Consequently, it is not surprising that this reaction has acquired central importance for the asymmetric synthesis of β-lactams during recent years, from both academic and industrial standpoints.[10, 11] One example is the cycloaddition of Evans–Sjögren ketenes, generated from chiral oxazolidinylacetic acid chlorides and triethylamine, with imines, generally providing good yields and excellent diastereoselectivity, typically ≥96% *d.e.*[12] The exceptional quality of stereochemical control imparted by the oxazolidinone moiety has also been demonstrated in the reaction of 4-(*S*)-phenyloxazolidinyl ketene with imines derived from substituted benzaldehydes and either (*R*)- or (*S*)-α-amino esters.[13] This reaction has also been employed by us and others to synthesise homochiral 3-amino β-lactams as building

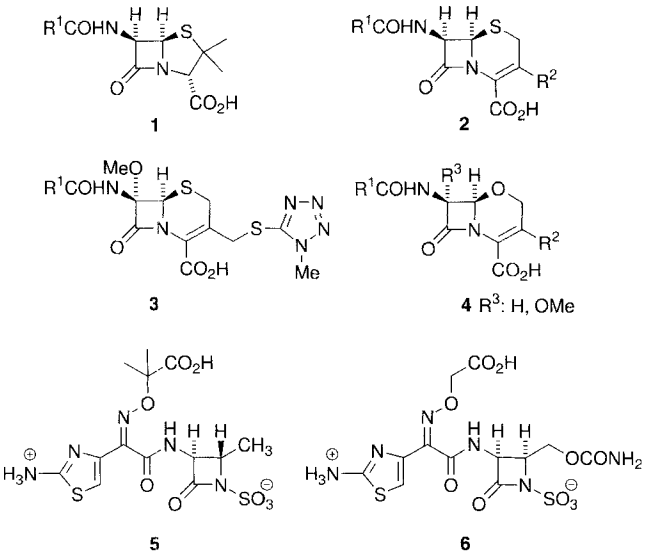


Figure 1. Representative families of β-lactam antibiotics characterized by the presence of the amino function at the Cα position of the β-lactam carbonyl.

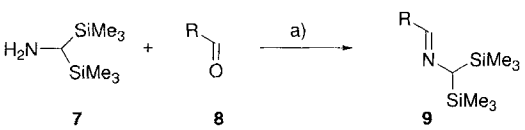
[*] Prof. Dr. C. Palomo, J. M. Aizpurua, M. Legido, A. Mielgo, R. Galarza
Departamento de Química Orgánica
Universidad del País Vasco, Facultad de Química
Apdo 1072, 20080 San Sebastián (Spain)
Fax: Int. code +(43)212-236
e-mail: qppaiipj@sc.ehu.es

0947-6539/97/0309-1432 $ 17.50+.50/0

blocks of diverse target molecules.[14] Nevertheless, despite the advances made in this area, virtually all of the investigations on this subject have dealt with the use of non-enolizable aldehyde-derived imines, and thus, successive chemical elaborations of the C_4 substituent are usually required to get the desired targets. Actually, ketene–enolizable aldimine cycloadditions, which would generate a wider range of substitution patterns at the C_4 position of the β-lactam ring, have not proved very viable, in part because of the instability of the starting imines and in part because of the presence of competitive deprotonations.[15] Ideally, the construction of β-lactams with any desired substituent at the C_4 position should be possible at low cost and with a large synthetic extent. Therefore, we have been concerned with the question of how β-lactams could be prepared in one step by [2+2] cycloadditions with imines derived from enolizable aldehydes. Recent research from this laboratory has addressed this issue and found that *N*-[bis(trimethylsilyl)methyl]imines fulfil these requirements, furnishing a route to a number of 3-amino β-lactams.[16] We thought that these imines might provide a solution to the above-mentioned problems for two reasons: firstly because of the ability of silyl groups to stabilize electron-deficient carbon centers in the β- and/or γ-position[17] and, secondly, because of the zwitterionic character of the reaction intermediate proposed for this kind of cycloaddition.[18] Herein we wish to disclose details of our investigation along with the development of a new chiral aminoketene equivalent.

Results and Discussion

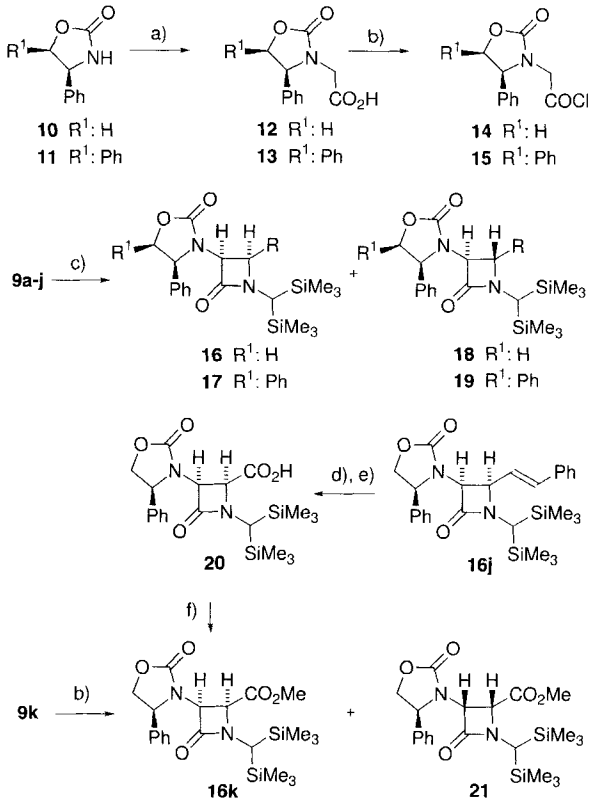
To evaluate the success of the above proposal, the behaviour of some representative imines **9**, derived from the *C,C*-bis(trimethylsilyl)methylamine (**7**)[19] and the enolizable aldehydes **8a–g** and **8l–n** (Scheme 1), towards aminoketene equivalents was examined. We initially investigated the reaction of the Evans–Sjögren acid chloride **14** (Scheme 2), prepared from the oxazolidinone **10** via the carboxylic acid **12**,[6] with imines **9**, and found that the expected cycloaddition proceeded in refluxing chloroform or benzene as solvents to give **16** (*cis*) and **18** (*trans*) with good to excellent diastereomeric selectivity ratios, typically 90:10 to 98:2, and, most notably, with complete asymmetric induction at the C_3 position (see below). On the basis of these results and in view of the existing precedents for asymmetric transformations with the oxazolidinone **11**,[20] we next examined the reaction of the aminoketene generated from the acid



7 **8** **9**

a R: CH_3 **h** R: c-C_6H_{11}
b R: CH_2CH_3 **i** R: C_6H_5
c R: $CH_2CH_2CH_3$ **j** R: CH=CHPh
d R: CH_2CH_2Ph **k** R: CO_2Me
e R: $CH_2CH(CH_3)_2$ **l** R: CH_2OCH_2Ph
f R: $CH(CH_3)_2$ **m** R: CH_2Ph
g R: $CH(CH_2CH_3)_2$ **n** R: $CH_2CH_2CO_2tBu$

Scheme 1. a) Molecular sieves (4 Å), CH_2Cl_2, 1 h, RT.



Scheme 2. a) NaH, THF, $BrCH_2CO_2Me$, 2 h, 0 °C, then NaOH, H_2O, 2h, RT; b) ClCOCOCl, CH_2Cl_2, DMF cat., 1 h, RT; c) **14** or **15**, NEt_3, molecular sieves (4 Å), $CHCl_3$, reflux, 20 h; d) O_3, CH_2Cl_2, −78 °C, 10 min, then Me_2S, −78 °C → RT; e) $NaIO_4$, $KMnO_4$, Me_2CO/H_2O, RT, 2 h; f) Cl_2SO, CH_2Cl_2, reflux, then MeOH.

chloride **15**, the latter prepared from the oxazolidinylacetic acid **13** that, in turn, was prepared from **11** according to the Evans procedure,[6] with imines **9**. The primary aim was to see whether an additional stereogenic center on the chiral inductor could improve the stereochemical outcome of the cycloaddition. In any case, the use of this aminoketene equivalent would permit easy access to 3-amino-β-lactams by simple hydrogenolytic cleavage of the oxazolidinone moiety. As Scheme 2 illustrates, treatment of **9** with a twofold excess of **15** and triethylamine in refluxing chloroform gave the corresponding **17** (*cis*) along with small amounts of the respective *trans* isomers **19** epimeric at the C_4 position. The relative *cis*/*trans* stereochemistry was determined on the basis of the coupling constants, $J_{3,4} \approx 5$ Hz for the *cis* isomers and $J_{3,4} \approx 2$ Hz for the *trans* isomers.

As expected, the reaction also worked well with non-enolizable imines. For example, the reaction of **9i** and **9j** with **15** afforded the respective adducts **17i** and **17j** as virtually single diastereomers. However, to our surprise, on treatment with both **14** and **15** and triethylamine the glyoxylate imine **9k** provided a nearly equimolar mixture of the corresponding diastereomeric *cis*-β-lactams **16k**/**21**.[21] In both cases, the assignment of the relative *cis* stereochemistry between the C_3 and the C_4 positions of the β-lactam ring was based on the coupling constant values, vide supra, and the stereochemical course of the reaction by conversion of **16j** into **16k** via the same 4-carboxy β-lactam **20** through simple chemical transformations as shown in Scheme 2. Taking into account the lack of stereoselection in

  0947-6539/97/0309-1433 $ 17.50+.50/0

the above cycloaddition reaction, we examined an alternative way to install functionality at the C_4 position of the β-lactam ring. Specifically, we evaluated the reaction of the imine **9l**, derived from the easily enolizable glycoaldehyde,[22] with both **14** and **15** which, in turn, would provide a suitable precursor of the antibiotic carumonam (**6**, Figure 1). In these instances, the reaction proceeded to give the respective adducts **16l** and **17l**, almost as single diastereomers. The results of this study are summarized in Table 1 to show the efficiency of this method for

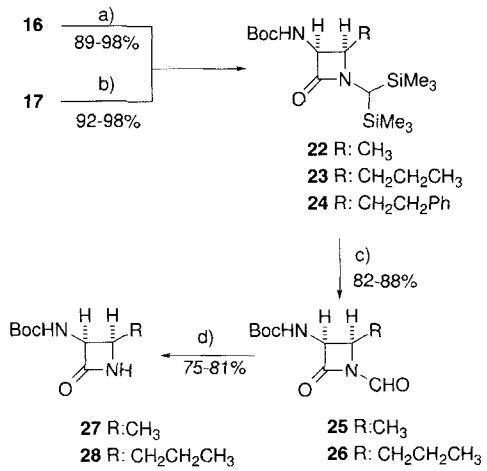
Table 1. Cycloaddition of **14** and **15** with imines **9**.

Compound	R	Yield [%] [a]	*cis*:*trans* [b]
16a	CH_3	70	81:19
17a	CH_3	65	85:15
16b	CH_2CH_3	75	>98:2
16c	$CH_2CH_2CH_3$	75	90:10
17c	$CH_2CH_2CH_3$	75	95:5
16d	CH_2CH_2Ph	72	92:8
17d	CH_2CH_2Ph	79	91:9
16e	$CH_2CH(CH_3)_2$	70	85:15
16f	$CH(CH_3)_2$	78	>98:2
17g	$CH(CH_2CH_3)_2$	70	85:15
17h	c-C_6H_{11}	72	>98:2
17i	C_6H_5	74	>98:2
16j	(*E*)-CH=CHPh	70	>98:2
17j	(*E*)-CH=CHPh	80	>98:2
16k	CO_2Me	66 [c]	
16l	CH_2OCH_2Ph	70	>98:2
17l	CH_2OCH_2Ph	70	>98:2
16m	CH_2Ph	55	>98:2
16n	$CH_2CH_2CO_2tBu$	65	>98:2

[a] Yield of the corresponding mixture of *cis*- and *trans*-β-lactams. [b] Determined by ^1H NMR analysis of the reaction crude by integration of the doublets at $\delta = 4.51$ and 4.40, which correspond to the *cis*- and *trans*-positioned protons at C3. [c] A diastereomeric mixture of the corresponding *cis* isomers was obtained in 53:47 ratio.

the direct construction of homochiral β-lactams with linear as well as branched chains at the C_4 position. Remarkably, even the imine **9m** derived from the easily enolizable phenylacetaldehyde also afforded the expected β-lactam **16m**, whereas the corresponding *N*-benzyl and *N*-(4-methoxy)phenyl imines gave only enamides and hydrolysis products. The same enolization trend was observed for *N*-(4-methoxy)phenyl imines derived from both acetaldehyde and propionaldehyde.[23] A further example that defines the potential scope of this approach is illustrated in the reaction of **14** with the enolizable aldehyde-derived imine **9n** to give in a single step the β-lactam **16n** as precursor of the antibiotic loracarbef.[24]

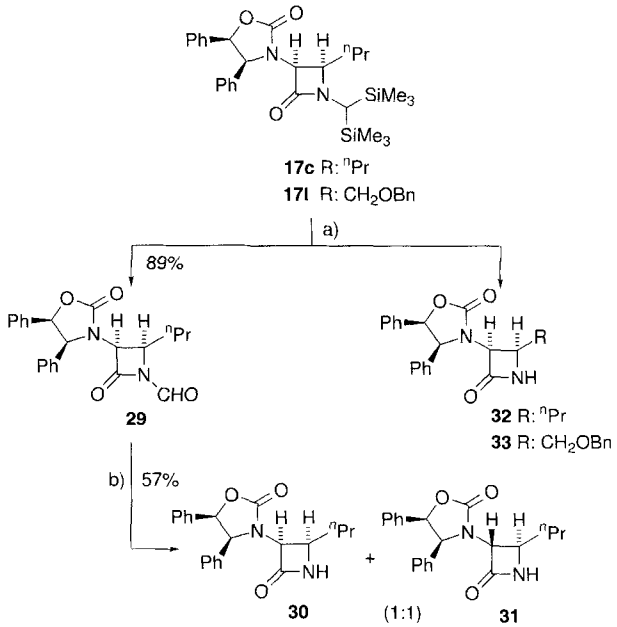
Conversion of these adducts into *N*-Boc-protected 3-amino β-lactams (Scheme 3) was first accomplished by removal of the oxazolidinone moiety according to the Evans procedure and subsequent introduction of the Boc group under the usual conditions, but, as pointed out, better yields were attained by removal of the oxazolidinone moiety in compounds **17** under hydrogenolytic conditions. For example, whilst **16a** led to **22** in 72% yield over the two steps, a solution of **17a** containing di-*tert*-butyldicarbonate exposed to hydrogen over Perlman's catalyst gave the same compound **22** in 95% isolated yield. Likewise, **17c** afforded **23** in 96% yield. Under these conditions, the hydrogenolytic cleavage of the oxazolidinone moiety in **17j** (R: CH=CHPh) proceeded with concomitant reduction of the double bond to give **24** (R: CH_2CH_2Ph) in 90% yield. The same compound **24** was also obtained in similar yield from **17d**. In



Scheme 3. a) Li (6 eq), NH_3, THF/*t*BuOH (5/0.5 v/v), −78 °C, 3 min, NH_4Cl (6 eq), then $(Boc)_2O$, CH_2Cl_2, RT, 3 h; b) H_2 (60 psi), $Pd(OH)_2$ (cat.), EtOH, RT, 20 h; c) CH_3CN/H_2O (6/2 v/v), CAN (3 eq), 0 °C, 3 h; d) $NaHCO_3$, Na_2CO_3, CH_3COCH_3, H_2O, RT, 24 h.

addition, these two last experiments served to corroborate the initially assigned stereochemistry for the adducts.

Since removal of the *N*-[bis(trimethylsilyl)methyl] moiety is an indispensable condition in order for these β-lactams to be of use in β-lactam chemistry, at this stage we addressed this issue and, after screening our previously reported method,[25] we found that cerium ammonium nitrate (CAN) was very effective in promoting C–Si bond cleavage. Thus, treatment of **22** with CAN in acetonitrile/water afforded the *N*-formyl derivative **25** in 92% yield after 6 h at room temperature. Subsequent *N*-deformylation under slightly basic conditions[25, 26] gave the known compound **27**[27] in 95% isolated yield. In a similar way, when **23** (obtained as above) was treated with CAN in acetonitrile/water, followed by *N*-deformylation of the resulting β-lactam **26**, the product **28** was formed in 88% yield. Alternatively, as Scheme 4 illustrates, upon exposure to CAN in

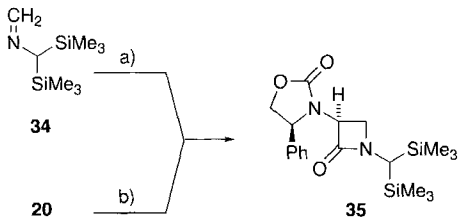


Scheme 4. a) CAN (5 eq), MeOH, RT, 4 h; b) CH_3COCH_3, $NaHCO_3$, Na_2CO_3, RT, 48 h.

0947-6539/97/0309-1434 $ 17.50+.50/0 *Chem. Eur. J.* **1997**, *3*, No. 9

CH_3CN/H_2O, **17c** furnished the *N*-formyl compound **29** in 89% yield, but attempted *N*-deformylation of **29** led to an equimolar mixture of epimeric β-lactams **30** and **31**.[28] Nevertheless, prolonged exposure of β-lactams **17c** and/or **17l** to CAN in methanol either at room temperature or under gentle reflux provided the corresponding *N*-unsubstituted β-lactams **32** and **33** in 75% and 80% yield respectively. Compound **32** was then transformed into the *N*-Boc derivative **26** under the established conditions, vide supra, in essentially quantitative yield. This novel method of deprotection of *N*-[bis(trimethylsilyl)methyl]amides expands their usefulness in synthesis considerably, representing a cationic (radical) umpolung complementary to the known fluoride-mediated reactivity of α-amido carbanions developed in our laboratory.[29]

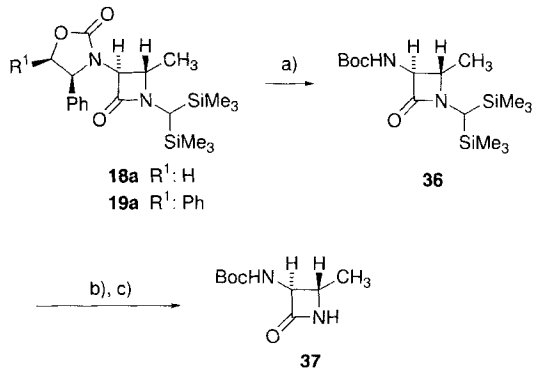
In conjunction with the studies discussed above, these results suggest that imines derived from enolizable aldehydes and *C,C*-bis(trimethylsilyl)methylamine exhibit pronounced thermal stability with regard to the behaviour of standard imines in [2+2] cycloadditions with ketenes.[30] This remarkable stability also became apparent in the reaction of **14** with the methanimine **34** (Scheme 5) leading to the β-lactam **35** in 75% yield.[31] This



Scheme 5. a) **14**, NEt_3, $CHCl_3$, molecular sieves (4 Å), reflux, 20 h; b) $(COCl)_2$, CH_2Cl_2, reflux, 30 min; then $(Me_2Si)_3SiH$, AIBN, toluene, 80 °C, 3 h.

result contrasts with the fact that the cycloaddition between the Evans–Sjögren acid chloride **14** and methanimine trimers (derived from benzylamine and trimethylsilylmethylamine) affords only traces of the expected β-lactams (<15%) together with major amounts of the carboxylic acid **12** under the reported conditions.[32] In addition, the total asymmetric induction observed during the single-step convergent formation of the β-lactam **35** was particularly noteworthy when compared with the limited diastereomeric excesses achieved in comparable approaches reported to date.[22, 27, 33] To further corroborate the stereochemical outcome of these cycloadditions, the β-lactam **20** was first transformed into its acid chloride and then chlorodecarbonylated according to the procedure of Chatgilialoglu.[34] The resulting product was identical in all respects to that obtained by the direct cycloaddition route.

Finally, to assess completely the stereochemical course of the cycloaddition reaction (Scheme 6), **18a** was transformed into **36**, which was identical to that obtained from **19a**. Next, **36** was converted into the known compound **37**[27] by removal of the bis(trimethylsilyl)methyl moiety and subsequent *N*-deformylation of the resulting *N*-formyl intermediate. The relative stereochemistry of the other *trans* diastereomers was established by analogy and by the assumption of a uniform reaction mechanism. This latter aspect as well as the synthesis of β-lactams with quaternary centers at the C_4 position will be described in separate communications.[14g]



Scheme 6. a) H_2 (60 psi), $Pd(OH)_2$, $(Boc)_2O$, EtOAc, RT, 20 h; b) CAN (5 eq), MeOH, RT, 4 h; c) CH_3COCH_3, $NaHCO_3$, Na_2CO_3, RT, 48 h.

Conclusions

The most significant finding of this work is the development of *N*-alkylidene *C,C*-bis(trimethylsilyl)methyl amines as a new class of stable and isolable imines to overcome the major limitations associated, up till now, with the Staudinger reaction involving ketenes generated from acid chlorides and a tertiary organic base. As a result, ketene-enolizable aldehyde–imine cycloadditions, which have hitherto been impracticable for a convergent synthesis of β-lactams, can now be efficiently employed for the construction of these important small rings with a greater range of substitution patterns at the C_4 position.

Experimental Section

General: All reactions involving *C,C*-bis(trimethylsilyl) methyl imines were carried out under an atmosphere of dry N_2 with oven-dried glassware and syringes. Hexane, acetone, and acetonitrile were dried and purified by distillation. THF was distilled over sodium and benzophenone ketyl under N_2 immediately prior to use. CH_2Cl_2 and $CHCl_3$ were dried with K_2CO_3 and distilled over P_2O_5 under N_2. Molecular sieves (4 Å) were used after drying under vacuum (0.01 mm Hg) at 200 °C overnight. Commercially available compounds were used without further purification. *C,C*-Bis(trimethylsilyl)methylamine (**7**),[19] [(4*S*)-2-oxo-4-phenyloxazolidin-3-yl]acetyl chloride (**14**),[12] and (4*S*,5*R*)-4,5-diphenyl-2-oxooxazolidine (**11**)[20c] were prepared according to literature procedures. Melting points were determined on a Büchi SMP-20 capillary apparatus and were uncorrected. Infrared spectra were obtained on a Shimadzu IR-435 spectrometer. Proton nuclear magnetic resonance (300 MHz) spectra and ^{13}C spectra (75 MHz) were recorded on a Varian VXR 300 spectrometer at room temperature in $CDCl_3$ solution, unless otherwise stated. All chemical shifts are reported as δ values relative to residual $CHCl_3$ ($\delta_H = 7.26$) and $CDCl_3$ ($\delta_C = 77.0$) as internal standards, respectively. Low-resolution electron impact mass spectra (EI-LRMS) were obtained on a Finnigan MAT GCQ spectrometer (70 eV) using GC-MS coupling (column: fused silica gel, 15 m, 0.25 mm, 0.25 mm phase SPB-5). Optical rotations were measured on a Perkin–Elmer 243 B polarimeter at 25 ± 0.2 °C in CH_2Cl_2 unless otherwise stated. HPLC separations were performed on a preparative column (25 cm, 3.0 cm, 7 mm phase Lichrosorb-Si60) with flow rates of 10 mL min^{-1} and a UV detector (254 nm). Flash chromatography was executed with Merck Kieselgel 60 (230–400 mesh); eluants were mixtures of EtOAc and hexane.

General Procedure for the Preparation of Imines 9 and 34: *C,C*-bis(trimethylsilyl)methylamine (1.75 g, 10 mmol) was added to a solution of the corresponding aldehyde (10 mmol) in dry dichloromethane (10 mL) containing 4 Å molecular sieves, and the mixture was stirred at 20 °C and monitored by GC-MS until completion (typically, 30 min). The molecular sieves were filtered off, the solvent was evaporated, and the corresponding imine was either purified by reduced pressure distillation or used directly in subsequent reactions.

  0947-6539/97/0309-1435 $ 17.50+.50/0

Data for 9a: Yield: 90%. Colorless oil. 94/6 Mixture of (*E*) and (*Z*) isomers. IR (NaCl, film): $\tilde{\nu}$ = 1645 cm^{-1}. Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.05 (s, 18H; $6CH_3$), 1.92 (d, ^3J(H,H) = 4.9 Hz, 1H; CH_3), 2.54 (s, 1H; CHSi), 7.43 (q, ^3J(H,H) = 4.9 Hz, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.3, 21.6, 58.7, 155.8; MS (70 eV, EI): *m*/*z* (%) = 186 (58) [M^+ − 15], 128 (30), 73 (100), 59 (45), 45 (37). Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.07 (s, 18H; $6CH_3$), 1.76 (d, ^3J(H,H) = 4.9 Hz, 1H; CH_3), 3.07 (s, 1H; CHSi), 7.75 (q, ^3J(H,H) = 4.9 Hz, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.2, 22.0, 61.2, 156.2; MS (70 eV, EI): *m*/*z* (%) = 186 (63) [M^+ − 15], 128 (45), 73 (100), 59 (62), 45 (38).

Data for 9b: Yield: 85%. Colorless oil. IR (NaCl, film): $\tilde{\nu}$ = 1645 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = −0.07 (s, 18H; $6CH_3$), 1.02 (t, ^3J(H,H) = 7.4 Hz, 1H; CH_2CH_3), 2.19 (m, 2H; CH_2CH_3), 2.49 (s, 1H, CHSi), 7.34 (t, ^3J(H,H) = 4.9 Hz, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.3, 11.2, 28.8, 58.3, 161.6; MS (70 eV, EI): *m*/*z* (%) = 215 (1) [M^+], 200 (9), 186 (10), 142 (56), 73 (100).

Data for 9c: Yield: 88%. Colorless oil. IR (NaCl, film): $\tilde{\nu}$ = 1644 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.02 (s, 18H; $6CH_3$), 0.94 (t, ^3J(H,H) = 7.2 Hz, 3H; CH_3), 1.51 (m, 2H; CH_2CH_3), 2.20 (m, 2H; CH_2CH=), 2.53 (s, 1H, CHSi), 7.38 (t, ^3J(H,H) = 5.1 Hz, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.2, 13.8, 20.2, 37.6, 58.6, 160.6; MS (70 eV, EI): *m*/*z* (%) = 229 (2) [M^+], 214 (13), 186 (12), 165 (75), 128 (7), 73 (100).

Data for 9d: Yield: 97%. Colorless oil. IR (NaCl, film): $\tilde{\nu}$ = 1645 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.31 (s, 18H; $6CH_3$), 2.56 (s, 1H, CHSi), 2.59 (td, ^3J(H,H) = 7.6, 4.8 Hz, 2H; CH_2CHN), 2.86 (t, ^3J(H,H) = 7.6 Hz, 2H; CH_2Ph), 7.19–7.28 (m, 5H; ArH), 7.44 (t, ^3J(H,H) = 4.8 Hz, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.3, 32.8, 36.9, 58.7, 125.8, 128.1, 128.4, 141.4, 159.2; MS (70 eV, EI): *m*/*z* (%) = 291 (3) [M^+], 73 (100).

Data for 9e: Yield: 95%. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 0.07 (s, 18H; $6CH_3$), 0.99 (d, ^3J(H,H) = 6.5 Hz, 6H; $2CH_3$), 1.91 (m, 1H, $HCCH_2$), 2.17 (m, 2H; $HCCH_2$), 2.59 (s, 1H; *H*CSi), 7.44 (t, ^3J(H,H) = 5.3 Hz, 1H; *H*C=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.8, 21.9, 26.2, 44.0, 58.2, 159.5; MS (70 eV, EI): *m*/*z* (%) = 292 (0.9) [M^+ − 14], 216 (13), 186 (11), 128 (19), 112 (11), 91 (50), 73 (100).

Data for 9f: Yield: 98%. Colorless oil. IR (NaCl, film): $\tilde{\nu}$ = 1644 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.04 (s, 18H; $6CH_3$), 1.06 (d, ^3J(H,H) = 6.8 Hz, 6H; $2CH_3$), 2.47 (m, 1H; $CHCH_3$), 2.51 (s, 1H, CHSi), 7.25 (d, ^3J(H,H) = 5.6 Hz, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.3, 20.0, 34.0, 57.9, 165.3; MS (70 eV, EI): *m*/*z* (%) = 229 (1) [M^+], 186 (7), 156 (64), 140 (9), 73 (100).

Data for 9g: Yield: 86%. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 0.04 (s, 18H; $6CH_3$), 0.89 (t, ^3J(H,H) = 7.5 Hz, 6H; $2CH_2CH_3$), 1.40–1.51 (m, 4H; $2CH_2CH_3$), 2.01–2.16 (m, 1H; *H*CSiMe$_3$), 7.18 (d, ^3J(H,H) = 6.6 Hz, 1H; *H*C=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −0.7, 12.1, 25.8, 48.4, 59.0, 165.1; MS (70 eV, EI): *m*/*z* (%) = 243 (8), 242 (34) [M^+ − 15], 228 (54), 186 (28), 184 (100), 154 (12), 73 (80), 59 (12).

Data for 9h: Yield: 90%. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 0.03 (s, 18H; $6CH_3$), 1.13–1.35 (m, 5H; *c*-C_6H_5), 1.58–1.78 (m, 5H; *c*-C_6H_5), 2.16–2.20 (m, 1H; *H*CCH), 2.48 (s, 1H; *H*CSi), 7.23 (d, ^3J(H,H) = 5.6 Hz, 1H; *H*C=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.4, 25.9, 30.2, 43.3, 58.1, 164.2; MS (70 eV, EI): *m*/*z* (%) = 269 (5) [M^+], 254 (10) [M^+ − 15], 196 (100), 186 (15), 73 (41).

Data for 9i: Yield: 97%. Colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.06 (s, 18H; $6CH_3$), 2.82 (s, 1H, CHSi), 7.33–7.69 (m, 5H; ArH), 8.03 (s, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.3, 59.5, 127.1, 128.2, 128.9, 137.4, 155.6; MS (70 eV, EI): *m*/*z* (%) = 262 (3) [M^+ − 2], 190 (7), 73 (100).

Data for 9j: Yield: 97%. Colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.08 (s, 18H; $6CH_3$), 2.75 (s, 1H, CHSi), 6.79 (d, ^3J(H,H) = 16.0 Hz, 1H; C*H*Ph), 7.00 (dd, ^3J(H,H) = 8.6, 16.0 Hz, 1H; C*H*=CHN); 7.26–7.50 (m, 5H, ArH), 7.83 (d, ^3J(H,H) = 8.6 Hz, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −0.6, 61.3, 127.4, 128.9, 129.2, 129.5, 138.9, 138.4, 159.6; MS (70 eV, EI): *m*/*z* (%) = 257 (4) [M^+ − 14], 216 (40), 73 (100).

Data for 9k: Yield: 91%. Yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.03 (s, 18H; $6CH_3$), 2.96 (s, 1H, CHSi), 3.79 (s, 3H; CH_3), 7.46 (s, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.4, 52.0, 62.3, 147.8, 163.6; MS (70 eV, EI): *m*/*z* (%) = 230 (3) [M^+ − 15], 73 (100), 59 (14), 45 (28).

Data for 9l: Yield: 98%. Colorless oil. IR (NaCl, film): $\tilde{\nu}$ = 1646 cm^{-1} ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.07 (s, 18H; $6CH_3$), 2.69 (s, 1H, CHSi), 4.16 (d, ^3J(H,H) = 4.4 Hz, 2H; OCH_2CH =), 4.57 (s, 2H; $PhCH_2O$), 7.39–7.32 (m, 5H; ArH), 7.55 (d, ^3J(H,H) = 4.3 Hz, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −0.9, 59.5, 72.2, 72.8, 128.2, 128.7, 130.0, 133.3, 157.8; MS (70 eV, EI): *m*/*z* (%) = 292 (1) [M^+ − 15], 216 (13), 186 (11), 128 (19), 112 (11), 91 (50), 73 (100).

Data for 9m: Yield: 87%. Colorless oil. IR (NaCl, film): $\tilde{\nu}$ = 1643 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.04 (s, 18H; $6CH_3$), 2.57 (s, 1H, CHSi), 3.58 (d, ^3J(H,H) = 5.2 Hz, 2H; CH_2Ph), 7.32–7.21 (m, 5H; ArH), 7.42 (t, ^3J(H,H) = 5.3 Hz, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.3, −0.8, 42.9, 59.0, 126.7, 128.9, 19.4, 137.9, 159.0; MS (70 eV, EI): *m*/*z* (%) = 292 (12) [M^+], 262 (7), 204 (44), 186 (5), 91 (7), 85 (9), 77 (3), 73 (100).

Data for 9n: Yield: 94%. Colorless oil. IR (NaCl, film): $\tilde{\nu}$ = 1643 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.07 (s, 18H; $6CH_3$), 1.43 (s, 9H, $C(CH_3)_2$), 2.50–2.30 (m, 4H; CH_2CH_2), 2.53 (s, 1H; *CH*Si), 7.43 (t, ^3J(H,H) = 1.0 Hz, 1H; C*H*=N); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.1, 24.6, 28.1, 31.5, 38.8, 58.4, 159.2, 170.2; MS (70 eV, EI): *m*/*z* (%) = 314 (2) [M^+], 257 (23), 186 (22), 128 (18), 73 (100).

Compound 34: Yield: 77%. Colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = −0.03 (s, 18H; $6CH_3$), 2.67 (s, 1H, CHSi), 7.02 (d, ^2J(H,H) = 17.1 Hz, 1H; CH_2), 7.02 (d, ^2J(H,H) = 17.1 Hz, 1H; CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = −1.6, 61.9, 148.2; MS (70 eV, EI): *m*/*z* (%) = 187 (1) [M^+], 186 (5), 172 (100), 128 (17), 115 (29), 114 (99), 86 (46), 73 (98).

[(4*S*,5*R*)-4,5-Diphenyloxazolidin-2-oxo-3-yl]acetyl chloride (15): Sodium hydride (40 mmol, 95%) was added to a solution of (4*S*,5*R*)-4,5-diphenyl-2-oxooxazolidine (**11**, 40 mmol) in THF (200 mL) under nitrogen atmosphere. Then methyl bromoacetate (40 mmol) was added dropwise at the same temperature and the resulting mixture was stirred for 2 h at 0 °C. A solution of NaOH (8 g) in H_2O/THF (80/100 mL) was then added and after being stirred for 2 h at room temperature the mixture was acidified with conc. HCl and extracted with Cl_2CH_2 (3100 mL). Elimination of the solvents under reduced pressure gave the acid **13**, which was used in the next step without further purification. Yield: 97%. White solid, m.p. 152–153 °C. $[\alpha]_D^{25}$ = +124.5 (*c* = 1.0 in CH_2Cl_2); IR (KBr): $\tilde{\nu}$ = 1734 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 3.45 (d, ^2J(H,H) = 18.2 Hz, 1H, HC*H*), 4.53 (d, ^2J(H,H) = 18.1 Hz, 1H, *H*CH), 5.35 (d, ^3J(H,H) = 8.6 Hz, 1H, *H*CPh), 5.94 (d, ^3J(H,H) = 8.3 Hz, 1H, *H*CPh), 6.80–7.11 (m, 11H, Ar*H*, COO*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = 43.6, 64.7, 80.0, 127.8, 128.0, 128.3, 128.5, 128.6, 133.0, 134.3, 158.8, 172.7. This compound was transformed, prior to use, into the acid chloride **15** by the following procedure: Oxalyl chloride (33 mmol) and DMF (cat.) were slowly added to a solution of the acid (22 mmol) in dry CH_2Cl_2 (55 mL) cooled at 0 °C. The mixture was stirred at room temperature for 1 h, the solvent was evaporated under reduced pressure and the acid chloride (yield: 98%) was used immediately for cycloaddition reactions.

General Procedure for the Preparation of β-Lactams: Triethylamine (5.6 mL, 40 mmol) and a solution of the acid chloride of choice (**14** or **15**, 20 mmol) in chloroform (10 mL) were added dropwise to a magnetically stirred suspension of the appropriate imine **9** or **34** (10 mmol) and molecular sieves (3 g) in freshly distilled dry chloroform (30 mL) at 0 °C. The resulting mixture was stirred overnight at reflux temperature and worked up by washing it successively with 1 M HCl (50 mL), $NaHCO_3$ (50 mL, saturated solution), and H_2O (50 mL). Drying and evaporation of solvents yielded the respective β-lactams, whose major isomers were separated by column chromatography (eluant: hexane/CH_2Cl_2 10/1).

0947-6539/97/0309-1436 $ 17.50+.50/0 *Chem. Eur. J.* **1997**, *3*, No. 9

Data for 16a: Yield: 70%, m.p. 142–144 °C. $[\alpha]_D^{25} = +91.9$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1734\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.04$ (s, 9H; $3CH_3$), 0.82 (s, 9H; $3CH_3$), 1.10 (d, $^3J(H,H) = 6.3$ Hz, 3H, CH_3), 2.12 (s, 1H; C*H*Si), 3.67 (m, 1H; C*H*CH_3), 4.23 (dd, $^3J(H,H) = 6.2$ Hz, $^2J(H,H) = 8.9$ Hz, 1H; CH_2O), 4.52 (d, $^3J(H,H) = 4.8$ Hz, 1H; C*H*CO), 4.73 (t, $^3J(H,H) = 8.9$ Hz, $^2J(H,H) = 9.1$ Hz, 1H; CH_2O), 5.08 (dd, $^3J(H,H) = 6.2$, 9.1 Hz, 1H; C*H*Ph), 7.43 (s, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = -0.2$, −0.1, 13.8, 38.0, 56.7, 59.4, 60.4, 71.2, 127.6, 128.9, 129.1, 138.5, 158.4, 162.3; MS (70 eV, EI): m/z (%) = 390 (3) [$M^+ - 14$], 204 (21), 104 (72), 73 (100); $C_{20}H_{32}N_2O_3Si_2$: C 59.40, H 7.92, N 6.93; found C 59.67, H 8.09, N 6.98.

Data for 16b: Yield: 75%, m.p. 152–154 °C; $[\alpha]_D^{25} = +74.1$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1748\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.00$ (s, 9H; $3CH_3$), 0.04 (s, 9H; $3CH_3$), 0.87 (t, $^3J(H,H) = 7.6$ Hz, 3H; CH_3), 1.24–1.07 (m, 1H; C*H*CH_3), 1.39–1.22 (m, 1H; C*H*CH_3), 2.04 (s, 1H; C*H*Si), 3.33 (m, $^3J(H,H) = 4.6$ Hz, 1H; C*H*CH_2), 4.20 (dd, $^3J(H,H) = 6.0$ Hz, $^2J(H,H) = 8.8$ Hz, 1H; CH_2O), 4.55 (d, $^3J(H,H) = 4.5$ Hz, 1H; C*H*CO), 4.66 (t, $^3J(H,H) = 8.9$ Hz, $^2J(H,H) = 9.2$ Hz, 1H; CH_2O), 5.05 (dd, $^3J(H,H) = 6.2$, 9.3 Hz, 1H; C*H*Ph), 7.47–7.38 (m, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = -0.1$, 0.2, 10.5, 21.9, 38.8, 59.6, 60.6, 63.1, 71.3, 126.7, 127.7, 129.3, 138.9, 161.7, 163.0; MS (70 eV, EI): m/z (%) = 404 (1) [$M^+ - 15$], 172 (4), 104 (84), 91 (12), 73 (100); $C_{21}H_{34}N_2O_3Si_2$: C 60.24, H 8.18, N 6.69; found C 60.53, H 8.09, N 6.81.

Data for 16c: Yield: 73%, m.p. 138–139 °C; $[\alpha]_D^{25} = +67.1$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1749$, 1753 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.03$ (s, 9H; $3CH_3$), 0.07 (s, 9H; $3CH_3$), 0.89 (t, $^3J(H,H) = 6.6$ Hz, 3H; CH_3), 1.20–1.35 (m, 4H; CH_2C$H_2$$CH_3$), 2.05 (s, 1H; C*H*Si), 3.45–3.40 (m, 1H; NC*H*CH_2), 4.20 (dd, $^3J(H,H) = 5.9$ Hz, $^2J(H,H) = 8.7$ Hz, 1H; CH_2O), 4.60 (d, $^3J(H,H) = 4.8$ Hz, 1H; C*H*CO), 4.69 (t, $^3J(H,H) = 8.8$ Hz, $^2J(H,H) = 8.8$ Hz, 1H; CH_2O), 5.07 (dd, $^3J(H,H) = 5.8$, 8.9 Hz, 1H; C*H*Ph), 7.26–7.34 (m, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.0$, 0.2, 14.2, 19.4, 31.1, 38.9, 59.4, 60.6, 61.5, 71.3, 127.7, 129.2, 129.3, 139.0, 159.2, 163.0; MS (70 eV, EI): m/z (%) = 202 (10), 172 (4), 104 (66), 91 (14), 73 (100), 59 (20), 45 (18); $C_{22}H_{36}N_2O_3Si_2$: C 61.07, H 8.38, N 6.47; found C 61.12, H 8.25, N 6.52.

Data for 16d: Yield: 72%, colorless oil purified by preparative HPLC. $[\alpha]_D^{25} = +30.2$ ($c = 1.0$ in CH_2Cl_2); IR (film): $\tilde{\nu} = 1743$, 1737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.04$ (s, 9H; $3CH_3$), 0.07 (s, 9H; $3CH_3$), 1.50–1.85 (m, 2H; CH_2CH_2Ph), 2.04 (s, 1H; C*H*Si), 2.64 (t, $^3J(H,H) = 7.8$ Hz, 2H; CH_2Ph), 3.50 (m, 1H; NC*H*CH_2), 4.18 (dd, $^3J(H,H) = 5.9$ Hz, $^2J(H,H) = 8.8$ Hz, 1H; CH_2O), 4.58 (d_b, 1H; C*H*CO), 4.65 (t, $^3J(H,H) = 8.8$ Hz, $^2J(H,H) = 8.8$ Hz, 1H; CH_2O), 4.94 (m, 1H; C*H*Ph), 7.14–7.38 (m, 10H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = -0.2$, −0.1, 29.8, 32.1, 38.6, 59.2, 60.5, 60.9, 71.1, 126.0, 127.5, 128.2, 128.4, 129.0, 129.2, 138.6, 140.7, 158.4, 162.7; MS (70 eV, EI): m/z (%) = 219 (36), 73 (100), 59 (35); $C_{27}H_{38}N_2O_3Si_2$: C 65.54, H 7.74, N 5.88; found C 65.83, H 7.80, N 5.68.

Data for 16e: Yield: 70%, m.p. 163–164 °C; $[\alpha]_D^{25} = +60.4$ ($c = 1.0$ in CH_2Cl_2); IR (film): $\tilde{\nu} = 1761\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.05$ (s, 9H; $3CH_3$), 0.08 (s, 9H; $3CH_3$), 0.89 (t, $^3J(H,H) = 6.4$ Hz, 6H; $2CH_3$), 1.17–1.25 (m, 2H; *H*CH, *H*C$(CH_3)_2$), 1.54–1.68 (m 1H; HC*H*), 2.04 (s, 1H; *H*CSi), 3.55 (m, 1H; *H*CCH_2), 4.23 (dd, $^3J(H,H) = 6.0$ Hz, $^2J(H,H) = 8.9$ Hz, 1H; CH_2O), 4.58 (d, $^3J(H,H) = 4.7$ Hz, 1H; *H*CN), 4.69 (t, $^3J(H,H) = 8.9$ Hz, CH_2O), 5.05 (dd, $^3J(H,H) = 6.0$ Hz, $^2J(H,H) = 9.2$ Hz, 1H; *H*CPh), 7.40–7.43 (m, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.06$, 0.23, 22.5, 23.0, 25.1, 37.6, 38.8, 59.5, 59.7, 60.7, 71.3, 127.8, 129.2, 129.3, 138.8, 158.6, 162.9; MS (70 eV, EI): m/z (%) = 431 (21) [$M^+ - 15$], 345 (11), 318 (25), 245 (34), 228 (16), 202 (100), 158 (10), 104 (18), 91 (21), 73 (40); $C_{23}H_{38}N_2O_3Si_2$: C 61.85, H 8.59, N 6.27; found C 61.96, H 8.72, N 6.35.

Data for 16f: Yield: 56%, m.p. 157–159 °C; $[\alpha]_D^{25} = +91.1$ ($c = 1.0$ in CH_2Cl_2); IR (film): $\tilde{\nu} = 1746\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.08$ (s, 9H; $3CH_3$), 0.14 (s, 9H; $3CH_3$), 0.82 (d, $^3J(H,H) = 6.5$ Hz, 3H; CH_3), 0.90 (d, $^3J(H,H) = 6.5$ Hz, 3H; CH_3), 1.30–1.55 (m, 1H; C*H*CH_3), 2.21 (s, 1H; C*H*Si), 3.16 (dd, $^3J(H,H) = 4.8$, 10.2 Hz, 1H; NC*H*-Ph), 4.22 (dd, $^3J(H,H) = 5.6$ Hz, $^2J(H,H) = 8.8$ Hz, 1H; CH_2O), 5.56 (s_b, 1H; C*H*CO), 4.68 (t, $^3J(H,H) = 8.8$ Hz, $^2J(H,H) = 8.8$ Hz, 1H; CH_2O), 5.05 (m, 1H; C*H*Ph), 7.40 (s, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.1$, 0.4, 19.6, 21.1, 29.4, 40.4, 59.7, 60.2, 68.2, 70.9, 127.3, 129.0, 129.2, 138.6, 158.2, 163.9; MS (70 eV, EI): m/z (%) = 417 (7) [$M^+ - 15$], 104 (53), 73 (100); $C_{22}H_{36}N_2O_3Si_2$: C 61.11, H 8.33, N 6.48; found C 61.34, H 8.55, N 6.57.

Data for 16j: Yield: 63%, m.p. 144–146 °C; $[\alpha]_D^{25} = +43.7$ ($c = 1.0$ in CH_2Cl_2); IR (film): $\tilde{\nu} = 1745\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.08$ (s, 9H; $3CH_3$), 0.11 (s, 9H; $3CH_3$), 2.25 (s, 1H; *H*CSi), 4.10 (dd, $^3J(H,H) = 7.0$ Hz, $^2J(H,H) = 9.0$ Hz, 1H; CH_2O), 4.18 (dd, 1H, $^3J(H,H) = 4.9$, 9.4 Hz, *H*CN), 4.55 (d, $^3J(H,H) = 4.9$ Hz, *H*CCO), 4.61 (t, $^3J(H,H) = 9.0$ Hz CH_2O), 4.91 (dd, $^3J(H,H) = 7.0$ Hz $^2J(H,H) = 9.0$ Hz, 1H; *H*CPh), 6.0 (dd, $^3J(H,H) = 15.9$, 9.4 Hz, 1H; *H*C=CH), 6.64 (d, $^3J(H,H) = 15.9$ Hz, HC=C*H*), 7.30–7.45 (m, 10H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.02$, 38.4, 59.8, 61.5, 64.5, 70.9, 124.2, 126.7, 127.5, 128.4, 128.6, 129.2, 129.4, 135.5, 137.0, 137.6, 157.9, 163.0; $C_{27}H_{36}N_2O_3Si_2$: C 65.81, 7.36, N 5.68; found C 65.78, H 7.38, N 5.64.

Compounds 16k + 21: A 47/53 (v/v) mixture of both compounds was obtained in 66% and separated by column chromatography (hexane/EtOAc: 5/1).

Data for 16k: Yield: 28%, m.p. 123–125 °C;. $[\alpha]_D^{25} = +97.9$ ($c = 1.0$ in CH_2Cl_2); IR (film): $\tilde{\nu} = 1765$, 1738 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.06$ (s, 9H; $3CH_3$), 0.22 (s, 9H; $3CH_3$), 2.61 (s, 1H; C*H*Si), 3.77 (s, 3H; COOMe), 4.03 (t, $^3J(H,H) = 8.7$ Hz, $^2J(H,H) = 8.7$ Hz, 1H; OCH_2), 4.16 (d, $^3J(H,H) = 5.5$ Hz, 1H; C*H*NCHSi), 4.28 (d, $^3J(H,H) = 5.5$ Hz, 1H; C*H*CO), 4.63 (t, $^3J(H,H) = 8.7$ Hz, $^2J(H,H) = 8.7$ Hz, 1H; OCH_2), 4.97 (t, $^3J(H,H) = 8.7$ Hz, 1H; NC*H*Ph), 7.41 (m, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.1$, 0.2, 39.2, 52.3, 59.5, 59.7, 60.7, 70.9, 127.1, 129.0, 129.5, 136.4, 157.2, 163.3, 168.7; MS (70 eV, EI): m/z (%) = 320 (19), 216 (27), 104 (31), 73 (100); $C_{21}H_{32}N_2O_5Si_2$: C 56.22, H 7.19, N 6.24; found C 56.37, H 7.15, N 6.15.

Data for 21: Yield: 25%, m.p. 134–136 °C; $[\alpha]_D^{25} = +79.7$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1762$, 1739 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.07$ (s, 9H; $3CH_3$), 0.18 (s, 9H; $3CH_3$), 2.53 (s, 1H; C*H*Si), 3.80 (s, 3H; COOMe), 4.10 (t, $^3J(H,H) = 8.7$ Hz, $^2J(H,H) = 8.7$ Hz, 1H; OCH_2), 4.22 (d, $^3J(H,H) = 5.5$ Hz, 1H; C*H*NCHSi), 4.58 (t, $^3J(H,H) = 8.7$ Hz, $^2J(H,H) = 8.7$ Hz, 1H; OCH_2), 4.80 (d, $^3J(H,H) = 5.5$ Hz, 1H; C*H*CO), 4.98 (t, $^3J(H,H) = 8.7$ Hz, 1H; NC*H*Ph), 7.41 (m, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.0$, 1.1, 39.1, 52.4, 60.1, 60.7, 61.1, 71.3, 126.7, 126.8, 129.1, 137.8, 157.3, 162.7, 169.1; MS (70 eV, EI): m/z (%) = 320 (19), 216 (25), 104 (31), 73 (100); $C_{21}H_{32}N_2O_5Si_2$: C 56.22, H 7.19, N 6.24; found C 56.18, H 7.15, N 6.23.

Data for 16l: Yield: 70%, colorless oil purified by preparative HPLC. $[\alpha]_D^{25} = +73.8$ ($c = 1.0$ in CH_2Cl_2); IR (film): $\tilde{\nu} = 1753\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.09$ (s, 18H; $6CH_3$), 2.31 (s, 1H; C*H*Si), 3.47 (dd, $^3J(H,H) = 6.3$, 9.1 Hz, 1H; C*H*NCHSi), 3.70 (m, 2H; CH_2OCH$_2$Ph), 4.35 (d, $^3J(H,H) = 4.8$ Hz, 1H; NCH_2CO), 4.42 (d, $^2J(H,H) = 11.8$ Hz, 1H; OCH_2Ph), 4.49 (d, $^2J(H,H) = 11.6$ Hz, 1H; OCH_2Ph), 4.53 (t, $^3J(H,H) = 8.9$ Hz, $^2J(H,H) = 8.9$ Hz, 1H; OCH_2CH_2-Ph), 4.91 (dd, $^3J(H,H) = 8.9$ Hz, $^2J(H,H) = 7.0$ Hz, 1H; NC*H*Ph), 7.27–7.46 (m, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = -0.1$, 0.0, 39.5, 59.1, 59.9, 69.3, 70.9, 73.6, 127.4, 127.8, 128.0, 128.5, 129.2, 129.4, 137.5, 137.8, 158.1, 163.0; MS (70 eV, EI): m/z (%) = 496 (9) [$M^+ - 15$], 405 (13), 332 (40), 73 (100); $C_{27}H_{38}N_2O_4Si_2$: C 63.49, H 7.50, N 5.48; found C 63.57, H 7.33, N 5.77.

Data for 16m: Yield: 55%, colorless oil purified by preparative HPLC. $[\alpha]_D^{25} = +80.0$ ($c = 1.0$ in CH_2Cl_2); IR (film): $\tilde{\nu} = 1720\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.04$ (s, 9H; $3CH_3$), 0.05 (s, 9H; $3CH_3$), 2.12 (s, 1H; C*H*Si), 3.04 (m, 2H; CH_2Ph), 3.70 (m, $^3J(H,H) = 5.3$ Hz, 1H; C*H*CH$_2$Ph), 3.97 (m, 2H; C*H*O, NC*H*CO), 4.07 (t, $^3J(H,H) = 4.7$ Hz, 1H; OC*H*), 4.32 (t, $^3J(H,H) = 8.8$ Hz, 1H; C*H*Ph), 7.10–7.46 (m, 10H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.1$, 34.4, 38.3, 59.9, 61.8, 70.4, 126.7, 126.9, 128.3, 128.7, 129.0, 129.3, 137.4, 157.5, 163.1; MS (70 eV, EI): m/z (%) = 105 (3), 104 (13), 91 (8), 73 (100), 59 (18); $C_{26}H_{36}N_2O_3Si_2$: C 64.96, H 7.55, N 5.83; found C 65.18, H 7.61, N 5.89.

Data for 16n: Yield: 55%, colorless oil purified by preparative HPLC. $[\alpha]_D^{25} = +44.9$ ($c = 1.0$ in CH_2Cl_2); IR (film): $\tilde{\nu} = 1763$, 1737, 1720 cm^{-1};

  0947-6539/97/0309-1437 $ 17.50+.50/0

^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = -0.06$ (s, 9H; $3CH_3$), 0.00 (s, 9H; $3CH_3$), 1.40 (s, 9H; $3CH_3$), 1.61–1.80 (m, 2H; $CH_2CH_2CO_2tBu$), 1.99 (s, 1H; C*H*Si), 2.22–2.10 (m, 2H; $CH_2CH_2CO_2tBu$), 3.36 (m, ^3J(H,H) = 9.7, 4.6 Hz, 1H; NC*H*CH_2CH_2), 4.17 (dd, ^3J(H,H) = 6.2 Hz, ^2J(H,H) = 8.8 Hz, 1H; OC*H*), 4.56 (d, ^3J(H,H) = 4.4 Hz, 1H; NC*H*CO), 4.65 (t, ^3J(H,H) = 8.8 Hz, ^2J(H,H) = 8.8 Hz, 1H; OC*H*), 5.05 (dd, ^3J(H,H) = 8.9 Hz, ^3J(H,H) = 6.0 Hz, 1H; C*H*Ph), 7.20–7.35 (m, 15H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = -0.1$, 23.9, 28.1, 31.5, 38.8, 59.4, 60.7, 71.4, 80.7, 127.8, 128.2, 129.4, 138.9, 158.8, 162.6, 171.8; MS (70 eV, EI): *m/z* (%) = 519 (1) [M^+], 447 (20), 417 (12), 390 (41), 334 (19), 299 (22), 261 (100), 236 (33), 215 (40), 193 (25), 172 (12), 104 (27), 73 (36); $C_{26}H_{42}N_2O_5Si_2$: C 60.18, H 8.17, N 5.40; found C 60.32, H 8.18, N 5.28.

Data for 17a: Yield: 65%, m.p. 136–138 °C; $[\alpha]_D^{25} = -0.7$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1757$, 1729 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.08$ (s, 9H; $3CH_3$), 0.09 (s, 9H; $3CH_3$), 1.18 (d, ^3J(H,H) = 6.3 Hz, 3H; CH_3), 2.15 (s, 1H; C*H*Si), 3.71 (m, 1H; C*H*CH_3), 4.48 (d, ^3J(H,H) = 4.9 Hz, 1H; C*H*CO), 5.21 (d, ^3J(H,H) = 8.4 Hz, 1H; C*H*Ph), 5.95 (d, ^3J(H,H) = 8.3 Hz, 1H; C*H*Ph), 6.94–7.11 (m, 10H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.0$, 13.8, 37.9, 57.1, 61.0, 64.8, 80.6, 125.9, 127.8, 128.2, 128.4, 134.3, 157.9, 162.7; MS (70 eV, EI): *m/z* (%) = 73 (17), 149 (100), 225 (23), 281 (69), 341 (13), 355 (16), 397 (36), 415 (25) [$M^+ - 51$]; $C_{26}H_{36}N_2O_3Si_2$: C 65.79, H 7.66, N 5.90; found C 66.01, H 7.61, N 5.88.

Data for 17c: Yield: 71%, syrup. $[\alpha]_D^{25} = -13.7$ ($c = 1.3$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1740$ cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.12$ (s, 9H; $3CH_3$), 0.19 (s, 9H; $3CH_3$), 0.85–1.02 (m, 5H, $CH_2CH_2CH_2CH_3$), 1.28–1.57 (m, 2H, $CH_2CH_2CH_3$), 2.18 (s, 1H; C*H*Si), 3.54 (m, 1H; C*H*N), 4.47 (d, ^3J(H,H) = 4.7 Hz, 1H; C*H*CO), 5.17 (d, ^3J(H,H) = 8.2 Hz, 1H; C*H*Ph), 5.93 (d, ^3J(H,H) = 8.2 Hz, 1H; C*H*Ph), 7.00–7.19 (m, 10H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = -0.1$, 0.0, 14.1, 19.7, 30.4, 38.2, 60.8, 61.4, 65.2, 80.4, 125.8, 127.7, 127.9, 128.0, 128.1, 128.2, 134.0, 134.1, 157.5, 162.8; MS (70 eV, EI): *m/z* (%) = 73 (47), 156 (22), 207 (90), 225 (37), 265 (27), 281 (100), 355 (39), 452 (26), 479 (30) [($M^+ - 28$]; $C_{28}H_{40}N_2O_3Si_2$: C 66.09, H 7.92, N 5.50; found C 66.15, H 7.82, N 5.47.

Data for 17d: Yield: 79%, m.p. 128–130 °C; $[\alpha]_D^{25} = -41.4$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1739$ cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.09$ (s, 9H; $3CH_3$), 0.18 (s, 9H; $3CH_3$), 1.90–2.12 (m, 2H, CH_2CH_2Ph), 2.14 (s, 1H; C*H*Si), 2.75 (t, ^3J(H,H) = 7.5 Hz, 2H; CH_2Ph), 3.56–3.65 (m, 1H; C*H*N), 4.42 (d, ^3J(H,H) = 4.7 Hz, 1H; C*H*CO), 4.82 (d, ^3J(H,H) = 8.2 Hz, 1H; C*H*Ph), 5.83 (d, ^3J(H,H) = 8.2 Hz, 1H; C*H*Ph), 6.93–7.41 (m, 15H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.0$, 0.1, 29.3, 32.9, 38.3, 61.0, 61.4, 65.1, 80.5, 125.9, 126.3, 127.7, 128.0, 128.3, 128.4, 128.7, 134.2, 140.9, 157.7, 162.9; MS (70 eV, EI): *m/z* (%) = 73 (26), 149 (140, 207 (64), 221 (43), 281 (100), 355 (82), 429 (70), 503 (29) [$M^+ - 68$]; $C_{33}H_{42}N_2O_3Si_2$: C 69.43, H 7.42, N 4.90; found C 69.21, H 7.63, N 4.81.

Data for 17g: Yield: 70%, colorless oil. $[\alpha]_D^{25} = -14.8$ ($c = 1.2$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1762$, 1753 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.10$ (s, 9H; $3CH_3$), 0.28 (s, 9H; $3CH_3$), 0.82–1.27 (m, 10H; $2CH_2CH_3$), 2.28 (s, 1H; C*H*Si), 3.54 (dd, ^3J(H,H) = 4.7, 10.3 Hz, 1H; C*H*N), 4.39 (d, ^3J(H,H) = 4.7 Hz, 1H, C*H*CO), 5.09 (d, ^3J(H,H) = 8.2 Hz, 1H; C*H*Ph), 5.88 (d, ^3J(H,H) = 8.2 Hz, 1H; C*H*Ph), 6.90–7.29 (m, 10H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.1$, 0.3, 20.0, 21.0, 29.1, 40.1, 60.5, 65.7, 67.9, 80.2, 125.8, 125.9, 127.6, 127.7, 127.9, 128.1, 128.9, 133.9, 157.4, 163.8; MS (70 eV, EI): *m/z* (%) = 73 (9), 180 (65), 290 (75), 334 (100) [$M^+ - 203$]; $C_{30}H_{44}N_2O_3Si_2$: C 61.61, H 7.58, N 4.79; found C 61.87, H 7.52, N 4.70.

Data for 17h: Yield: 72%, m.p. 102–104 °C; $[\alpha]_D^{25} = -32.1$ ($c = 1.1$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1743$ cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.05$ (s, 9H; $3CH_3$), 0.18 (s, 9H; $3CH_3$), 0.92–1.27 (m, 5H, *c*-C_6H_5), 1.53–1.82 (m, 5H; *c*-C_6H_5) 2.25 (s, 1H; C*H*Si), 3.24 (dd, ^3J(H,H) = 4.3, 10.1 Hz, 1H; C*H*N), 4.47 (d, ^3J(H,H) = 4.3 Hz, 1H; C*H*CO), 5.10 (d, ^3J(H,H) = 8.0 Hz, 1H; C*H*Ph), 5.85 (d, ^3J(H,H) = 8.0 Hz, 1H; C*H*Ph), 6.92–7.06 (m, 10H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.2$, 0.4, 24.9, 25.1, 25.9, 29.5, 29.7, 30.9, 38.5, 40.9, 60.8, 65.3, 66.6, 80.6, 125.9, 127.7, 128.2, 134.0, 134.4, 157.7, 164.0; MS (70 eV, EI): *m/z* (%) = 73 (33), 94 (11), 149 (100), 167 (99), 196 (93), 209 (17), 279 (34) [$M^+ - 270$], 355 (6); $C_{31}H_{44}N_2O_3Si_2$: C 67.83, H 8.08, N 5.10; found C 67.55, H 7.83, N 5.29.

Data for 17i: Yield: 74%, m.p. 124–126 °C; $[\alpha]_D^{25} = +18.4$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1749$ cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.15$ (s, 9H; $3CH_3$), 0.34 (s, 9H; $3CH_3$), 2.34 (s, 1H; C*H*Si), 4.48 (d, ^3J(H,H) = 4.8, 10.1 Hz, 1H; C*H*), 4.50 (d, ^3J(H,H) = 8.4 Hz, 1H, C*H*-Ph), 4.83 (d, ^3J(H,H) = 4.8 Hz, 1H; C*H*), 5.13 (d, ^3J(H,H) = 8.4 Hz, 1H; C*H*Ph), 6.77–7.11 (m, 10H; Ar*H*), 7.48–7.55 (m, 5H, Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.3$, 0.4, 38.1, 63.0, 64.5, 64.8, 79.4, 125.7, 127.4, 127.5, 127.7, 128.2, 128.7, 132.9, 133.1, 133.8, 156.4, 162.7; MS (70 eV, EI): *m/z* (%) = 73 (9), 91 (49), 173 (14), 208 (78), 236 (33), 252 (33), 281 (16), 343 (100) [$M^+ - 200$]; $C_{31}H_{38}N_2O_3Si_2$: C 68.59, H 7.05, N 5.16; found C 68.38, H 7.23, N 4.98.

Data for 17j: Yield: 80%, m.p. 132–134 °C; $[\alpha]_D^{25} = +14.1$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1747$ cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.12$ (s, 9H; $3CH_3$), 0.13 (s, 9H; $3CH_3$), 2.30 (s, 1H; C*H*Si), 4.26 (dd, ^3J(H,H) = 4.8, 9.8 Hz, 1H; C*H*N), 4.57 (d, ^3J(H,H) = 4.8 Hz, 1H; C*H*CO), 5.13 (d, ^3J(H,H) = 8.2 Hz, 1H; C*H*Ph), 5.83 (d, ^3J(H,H) = 8.2 Hz, 1H; C*H*Ph), 6.21 (dd, ^3J(H,H) = 9.8, 15.9 Hz, 1H; *H*C=CH), 6.71 (d, ^3J(H,H) = 15.9 Hz, 1H; HC=C*H*), 6.89–7.37 (m, 15H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 0.1$, 0.2, 38.3, 62.3, 64.9, 65.0, 80.4, 124.3, 126.0, 126.8, 127.7, 128.1, 128.7, 133.7, 134.2, 135.6, 137.3, 157.7, 163.2; MS (70 eV, EI): *m/z* (%) = 73 (24), 207 (100), 211 (22), 225 (11), 267 (25), 281 (99), 355 (23), 429 (13) [$M^+ - 140$]; $C_{33}H_{40}N_2O_3Si_2$: C 69.67, H 7.08, N 4.92; found C 69.55, H 6.92, N 5.03.

Data for 17l: Yield: 70%, m.p. 97–98 °C; $[\alpha]_D^{25} = +10.2$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1761$, 1750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.11$ (s, 9H; $3CH_3$), 0.17 (s, 9H; $3CH_3$), 2.35 (s, 1H; C*H*Si), 3.64 (m, 1H; *H*CH_2O), 3.80 (m, 2H; HCH_2O), 4.34 (d, ^3J(H,H) = 4.6 Hz, 1H; C*H*CO), 4.57 (d, ^2J(H,H) = 11.8 Hz, 1H; O*H*CH), 5.04 (d, ^3J(H,H) = 8.5 Hz, 1H; C*H*Ph), 5.63 (d, ^3J(H,H) = 8.5 Hz, 1H; C*H*Ph), 6.83–7.11 (m, 10H; Ar*H*), 7.36–7.43 (m, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = -0.03$, 0.06, 39.4, 59.9, 60.0, 65.1, 69.3, 73.7, 80.3, 126.0, 127.8, 127.9, 128.0, 128.4, 128.6, 128.9, 129.0, 129.1, 133.9, 134.3, 137.7, 157.6, 163.1; MS (70 eV, EI): *m/z* (%) = 73 (27), 207 (96), 225 (27), 281 (100), 355 (49), 429 (33), 503 (14) [$M^+ - 84$]; $C_{33}H_{42}N_2O_4Si_2$: C 67.54, H 7.21, N 4.77; found C 67.73, H 7.18, N 4.73.

Data for 35: Yield: 85%, m.p. 150–151 °C; $[\alpha]_D^{25} = +89.6$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1741$ cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.43$ (s, 9H; $3CH_3$), 0.53 (s, 9H; $3CH_3$), 2.63 (s, 1H, C*H*Si), 3.09 (dd, ^3J(H,H) = 2.6 Hz, ^2J(H,H) = 5.5 Hz, 1H; CH_2N), 3.32 (t, ^3J(H,H) = 5.5 Hz, ^2J(H,H) = 5.5 Hz, 1H; CH_2N), 4.05 (dd, ^3J(H,H) = 6.0 Hz, ^2J(H,H) = 8.8 Hz, 1H; CH_2O), 4.67 (t, ^3J(H,H) = 8.8 Hz, ^2J(H,H) = 8.8 Hz, 1H; CH_2O), 4.99 (dd, ^3J(H,H) = 8.8, 6.0 Hz, 1H; CH_2Ph), 5.06 (dd, ^3J(H,H) = 2.6, 5.5 Hz, 1H; C*H*CO), 7.43–7.27 (m, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = -0.51$, −0.33, 37.6, 48.8, 57.8, 58.9, 71.0, 126.6, 127.3, 129.2, 129.4, 138.7, 157.9, 164.3; MS (70 eV, EI): *m/z* (%) = 375 (2) [$M^+ - 15$], 262 (18), 104 (38), 73 (100), 54 (36); $C_{19}H_{30}N_2O_3Si_2$: C 58.46, H 7.69, N 7.18; found C 58.50, H 7.72, N 7.20.

Compound 20: Ozone was bubbled until saturation (slight blue color) through a stirred solution of the styryl β-lactam **16j** (2.46 g, 5 mmol) in CH_2Cl_2 (50 mL) cooled to −78 °C. Then N_2 was bubbled through the solution for 10 min to remove the excess ozone and a solution of dimethyl sulfide (2 mL) in CH_2Cl_2 (5 mL) was added dropwise at the same temperature. The mixture was allowed to warm to room temperature and washed successively with H_2O (4 × 20 mL) and NaCl (4 × 20 mL, sat. aq. soln.). The organic layer was separated, dried, and evaporated to give an oil (the intermediate 4-formyl β-lactam), which was immediately dissolved in acetone/H_2O (28 mL/26 mL). Sodium periodate (2.75 g, 12.9 mmol) and $KMnO_4$ (0.34 g, 2.15 mmol) were added at room temperature and the mixture was stirred for 2 h. Then H_2O (20 mL) was added, the mixture was cooled at 0 °C and $NaHSO_3$ (40% aq. solution) was added dropwise until decoloration. Acidification with conc. HCl until pH 1, extraction with EtOAc (2 × 60 mL) and evaporation yielded compound **20**, which was purified by crystallization from hexane. Yield: 72%; IR (film): $\tilde{\nu} = 2200$–3500, 1766, 1728 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.06$ (s, 9H; $3CH_3$), 0.23 (s, 9H; $3CH_3$), 2.73 (s, 1H; C*H*Si), 4.06 (t, ^3J(H,H) = 8.7 Hz, ^2J(H,H) = 8.7 Hz, 1H; OCH_2), 4.18 (d,

0947-6539/97/0309-1438 $ 17.50+.50/0 Chem. Eur. J. 1997, 3, No. 9

^3J(H,H) = 5.5 Hz, 1H; C*H*NCHSi), 4.24 (d, ^3J(H,H) = 5.5 Hz, 1H; C*H*CO), 4.71 (t, ^3J(H,H) = 8.7 Hz, ^2J(H,H) = 8.7 Hz, 1H; OCH_2), 5.05 (t, ^3J(H,H) = 8.7 Hz, 1H; NC*H*Ph), 7.38–7.47 (m, 5H; Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = 0.2, 0.4, 39.2, 59.4, 61.1, 71.52, 127.3, 129.4, 129.7, 136.2, 163.5, 170.4.

Radical Decarboxylation of β-Lactam 20: Oxalyl chloride (0.17 mL, 2 mmol) was slowly added at 0 °C to a solution of **20** (1 mmol) in CH_2Cl_2 (4 mL) and the mixture was stirred for 1 h. The solvent was evaporated and replaced by dry toluene (8.2 mL). Tris(trimethylsilyl)silane (0.5 g, 2.0 mmol) and a solution of AIBN (0.3 mL 1N in toluene) were added dropwise to the mixture, which was heated at 80 °C and stirred for 3 h. Evaporation of solvents under reduced pressure and flash column chromatography of the resulting crude product (silica gel 70–230 mesh; eluant: hexane, then CH_2Cl_2) afforded β-lactam **35**. Yield 69%.

General Procedure for Simultaneous Hydrogenolysis and N-Boc Protection of β-Lactams 17: Pearlman's catalyst (Acros, 200 mg) and di-*tert*-butyldicarbonate (0.16 g, 0.75 mmol) were added succesively to a solution of the corresponding 3-oxazolidinyl-β-lactam (**17**, 0.5 mmol) in EtOH (15 mL). The resulting mixture was stirred at room temperature under a hydrogen atmosphere (60 psi) for 20 h. Then the mixture was filtered through Celite and, after evaporation of the filtrate under reduced pressure, the resulting crude was purified by flash column chromatography to furnish the corresponding 3-*tert*-butoxycarbonylamino-β-lactam.

Data for 22: Yield: 72%, m.p. 98–100 °C; $[\alpha]_D^{25}$ = + 32.8 (*c* = 1.0 in CH_2Cl_2); IR (film): $\tilde{\nu}$ = 3240, 1727, 1705 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.12 (s, 9H; $3CH_3$), 0.15 (s, 9H; $3CH_3$), 1.14 (d, ^3J(H,H) = 6.2 Hz, 3H; CH_3), 1.14 (s, 9H; $3CH_3$), 2.21 (s, 1H; C*H*Si), 3.80 (m, 1H; C*H*CH_3), 4.91 (dd, ^3J(H,H) = 4.6, 7.5 Hz, 1H; NC*H*CO), 5.10 (d_b, ^3J(H,H) = 7.5 Hz, 1H; N*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = − 0.1, 0.0, 13.4, 28.2, 37.2, 56.8, 58.6, 80.1, 155.3, 165.2; MS (70 eV, EI): *m*/*z* (%) = 301 (100) [M^+ − 57], 101 (38), 73 (42), 57 (100); $C_{16}H_{34}N_2O_3Si_2$: C 53.63, H 9.50, N 7.82; found C 53.45, H 9.43, N 7.59.

Data for 23: Yield: 72%; colorless oil. $[\alpha]_D^{25}$ = + 8.3 (*c* = 0.9 in CH_2Cl_2); IR (KBr): $\tilde{\nu}$ = 3230, 1747, 1698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.07 (s, 9H; $3CH_3$), 0.10 (s, 9H; $3CH_3$), 0.89 (t, ^3J(H,H) = 7.0 Hz, 3H, CH_2CH_3), 1.23–1.35 (m, 4H, $CH_2CH_2CH_3$), 1.38 (s, 9H, $3CH_3$), (s, 1H; C*H*Si), 3.45–3.51 (m, 1H, C*H*N), 4.89 (dd, ^3J(H,H) = 4.7, 8.0 Hz, 1H, C*H*CO), 5.84 (d, ^3J(H,H) = 8.0 Hz, N*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = − 0.2, −0.1, 14.0, 18.9, 27.7, 28.1, 30.5, 37.5, 58.1, 61.1, 79.6, 155.2, 165.6; MS (70 eV, EI): *m*/*z* (%) = 330 (8) [M^+ − 57], 315 (68), 287 (36), 257 (22), 230 (32), 185 (31), 129 (100), 100 (46), 73 (69), 56 (33); $C_{18}H_{38}N_2O_3Si_2$: C 55.91, H 9.90, N 7.24; found C 56.22, H 9.78, N 7.30.

Data for 24: Yield: 80%, m.p. 97–98 °C; $[\alpha]_D^{25}$ = + 2.0 (*c* = 0.25 in CH_2Cl_2); IR (KBr): $\tilde{\nu}$ = 3270, 1746, 1725 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.10 (s, 9H; $3CH_3$), 0.13 (s, 9H; $3CH_3$), 1.47 (s, 9H, $3CH_3$), 1.87–2.15 (m, 2H, CH_2CH_2Ph), 2.17 (s, 1H; C*H*Si), 2.44–2.72 (m, 2H, CH_2Ph), 3.60 (m, 1H, C*H*N), 5.01 (dd, ^3J(H,H) = 4.3, 7.8 Hz, 1H, C*H*CO), 5.12 (d, ^3J(H,H) = 8.6 Hz, N*H*), 7.16–7.36 (m, 5H, Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = − 0.09, −0.02, 28.2, 30.3, 31.8, 37.6, 53.4, 58.4, 80.4, 126.1, 128.3, 141.0, 155.2, 165.3; MS (70 eV, EI): *m*/*z* (%) = 448 (2) [M^+], 429 (4), 359 (7), 348 (16), 333 (44), 316 (9), 292 (55), 276 (14), 242 (12), 218 (49), 186 (24), 172 (23), 147 (27), 91 (18), 73 (72), 56 (100); $C_{23}H_{40}N_2O_3Si_2$: C 61.57, H 9.00, N 6.24; found C 61.83, H 8.91, N 6.35.

Data for 36: Yield: 79%, colorless oil. $[\alpha]_D^{25}$ = + 1.5 (*c* = 1.0 in CH_2Cl_2); IR (KBr): $\tilde{\nu}$ = 3246, 1725, 1713 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.14 (s, 9H; $3CH_3$), 0.16 (s, 9H; $3CH_3$), 1.34 (d, ^3J(H,H) = 6.2 Hz, 3H; CH_3), 1.44 (s, 9H; $3CH_3$), 2.14 (s, 1H, C*H*Si), 3.37 (m, 1H; C*H*CH_3), 3.43 (d_b, 1H; C*H*CO), 5.29 (d, ^3J(H,H) = 7.5 Hz, 1H; N*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = − 0.1, 16.4, 28.2, 36.8, 60.5, 62.9, 80.1, 155.3, 165.5; MS (70 eV, EI): *m*/*z* (%) = 302 (1) [M^+ − 56], 101 (46), 73 (56), 57 (100); $C_{16}H_{34}N_2O_3Si_2$: C 53.63, H 9.50, N 7.82; found C 54.03, H 9.48, N 7.50.

General Procedure for the Oxidative Desilylation of *N*-Bis(trimethylsilyl)methyl β-Lactams: Cerium(IV) ammonium nitrate (10.96 g, 20 mmol) was added at 25 °C to a solution of the appropriate *N*-[bis(trimethylsilyl)methyl]-β-lactam **22**, **23**, **24**, or **36** (5 mmol) in dry methanol (40 mL), and the suspension was stirred at the same temperature and monitored by tlc. After 6 h, the reaction mixture was taken up over water (50 mL) and extracted with EtOAc (380 mL). The organic layer was washed successively with aqueous $NaHCO_3$ (100 mL, sat. soln.), aqueous $NaHSO_3$ (350 mL, 40%), aqueous $NaHCO_3$ (100 mL, sat. soln.), and aqueous NaCl (100 mL, sat. soln.). Evaporation of solvents yielded the corresponding *N*-formyl-β-lactams.

Data for 25: Yield: 92%, m.p. 156–157 °C; $[\alpha]_D^{25}$ = − 43.4 (*c* = 1.0 in CH_2Cl_2); IR (film): $\tilde{\nu}$ = 3343, 1801, 1689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 1.41 (d, ^3J(H,H) = 6.5 Hz, 3H; CH_3), 1.46 (s, 9H; $3CH_3$), 4.37 (m, 1H; C*H*CH_3), 5.12 (m, 2H; NC*H*CO, N*H*Boc), 8.85 (s, 1H; CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = 13.2, 28.1, 53.5, 60.1, 81.3, 154.8, 156.4, 166.0; MS (70 eV, EI): *m*/*z* (%) = 101 (11), 57 (100), 41 (29); $C_{10}H_{16}N_2O_4$: C 52.63, H 7.02, N 12.28; found C 52.54, H 7.25, N 12.24.

Data for 26: Yield: 88%, m.p. 120–122 °C; $[\alpha]_D^{25}$ = − 26.8 (*c* = 1.0 in CH_2Cl_2); IR (KBr): $\tilde{\nu}$ = 3330, 1799, 1689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.91–0.98 (m, 3H, CH_3), 1.43 (s_a, 13H, $3CH_3$, $CH_2CH_2CH_3$), 4.18–4.27 (m, 1H, C*H*N), 5.18 (dd_a, 1H, *H*CCO), 4.89 (dd, ^3J(H,H) = 4.7, 8.0 Hz, 1H, C*H*CO), 5.78 (d_a, N*H*), 8.82 (s, 1H, C*H*O); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = 13.9, 19.3, 28.0, 57.7, 59.9, 80.9, 155.3, 156.6, 159.8; MS (70 eV, EI): *m*/*z* (%) = 201 (3) [M^+ − 57], 183 (19), 155 (31), 129 (100), 100 (73), 85 (13), 56 (46); $C_{12}H_{20}N_2O_4$: C 56.24, H 7.86, N 10.93; found C 55.99, H 8.01, N 10.75.

Data for 29: Yield: 88%, m.p. 228–230 °C; $[\alpha]_D^{25}$ = − 32.1 (*c* = 1.0 in CH_2Cl_2); IR (KBr): $\tilde{\nu}$ = 1781, 1739, 1701 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 1.06 (t, ^3J(H,H) = 7.5 Hz, 3H, CH_3), 1.46–1.90 (m, 3H, HC*H*CH_2CH_3), 2.09–2.19 (m, 1H, *H*CHCH_2), 4.23–4.39 (m, 1H, *H*CN), 4.41 (d, ^3J(H,H) = 4.5 Hz, 1H, *H*CCO), 5.05 (d, ^3J(H,H) = 8.2 Hz, 1H, *H*CPh), 5.97 (d, ^3J(H,H) = 8.2 Hz, *H*CPh), 6.93–7.28 (m, 10H, Ar*H*), 8.90 (s, 1H, C*H*O); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = 14.1, 20.3, 30.5, 58.1, 62.1, 66.3, 80.7, 126.0, 127.8, 128.0, 128.4, 128.7, 129.0, 132.9, 133.5, 156.8, 157.5, 163.3; MS (70 eV, EI): *m*/*z* (%) = 295 (100) [(M^+ − 99], 252 (38), 208 (46), 191 (11), 162 (14), 118 (13), 91 (34); $C_{22}H_{22}N_2O_4$: C 69.82, H 5.86, N 7.40; found C 70.03, H 5.73, N 7.51.

General Procedure for the *N*-Deformylation of β-Lactams 25, 26: A mixture of the appropriate *N*-formyl-β-lactam (1 mmol), $NaHCO_3$ (1.66 mL, sat. aq. soln.) and Na_2CO_3 (0.028 g, 0.1 mmol) in acetone (1.66 mL) was stirred at room temperature for 2 h. The mixture was filtered through a pad of silica gel and washed with acetone. Drying and evaporation yielded the corresponding *NH*-β-lactam, which was purified by crystallization from EtOAc/hexane.

Data for 27: Yield: 99%, m.p. 182–183 °C; $[\alpha]_D^{25}$ = + 53.0 (*c* = 1.0 in MeOH); IR (film): $\tilde{\nu}$ = 3347, 3216, 1720, 1690 cm^{-1}; ^{1}H NMR (300 MHz, [D_6]DMSO, 90 °C): δ = 1.14 (d, ^3J(H,H) = 6.1 Hz, 3H; CH_3), 1.45 (s, 9H; $3CH_3$), 3.76 (q, ^3J(H,H) = 5.9 Hz, 1H; C*H*CH_3), 4.76 (s, 1H; C*H*CH_3); ^{13}C NMR (75.5 MHz, [D_6]DMSO, 90 °C): δ = 15.9, 28.2, 50.6, 60.3, 80.4, 155.1, 168.0; MS (70 eV, EI): *m*/*z* (%) = 157 (1) [M^+ − 43], 144 (1), 101 (16), 57 (100), 44 (57); $C_9H_{16}N_2O_3$: C 53.98, H 8.06, N 13.99; found C 54.22, H 8.23, N 14.26.

Data for 28: Yield: 81%, m.p. 122–124 °C; $[\alpha]_D^{25}$ = + 57.3 (*c* = 0.97 in $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 3320, 1751, 1693 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 0.94 (t, ^3J(H,H) = 7.0 Hz, 3H, CH_3), 1.21–1.38 (m, 4H, $CH_2CH_2CH_3$), 1.43 (s, 9H, $3CH_3$), 3.75 (m, 1H, *H*CN), 5.02 (t_a, 1H, *H*CCO), 5.51 (d_a, ^3J(H,H) = 6.6 Hz, N*H*), 6.70 (s_a, 1H, N*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): δ = 19.1, 28.2, 32.6, 55.0, 60.0, 80.2, 155.2, 168.6; MS (70 eV, EI): *m*/*z* (%) = 185 (3) [M^+ − *n*Pr], 155 (32), 129 (100), 100 (56), 85 (25), 72 (58), 56 (49); $C_{11}H_{20}N_2O_3$: C 57.87, H 8.83, N 12.27; found C 57.95, H 8.59, N 12.41.

Direct Formation of *NH*-β-Lactams from *N*-[Bis(trimethylsilyl)methyl]-β-lactams: Cerium(IV) ammonium nitrate (1.09 g, 2 mmol) was added to a solution of the appropriate *N*-[bis(trimethylsilyl)methyl]-β-lactam **17c**, **17l**, or **36** (0.5 mmol) in dry MeOH (3 mL) at 25 °C, and the suspension was stirred at the same temperature for 16 h (60 °C, 3 h for **17c**). The reaction mixture was worked up as for the general oxidative desilylation procedure to yield the corresponding *NH*-β-lactams.

  0947-6539/97/0309-1439 $ 17.50+.50/0

Data for 32: Yield: 70%, m.p. 226–228 °C; $[\alpha]_D^{25} = -7.3$ ($c = 0.3$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 3342, 1765, 1747\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.97$ (t, $^3J(H,H) = 7.6$ Hz, 3H, CH_3), 1.23–1.58 (m, 1H, HCN), 4.42 (d, $^3J(H,H) = 5.0$ Hz, 1H, HCCO), 5.11 (d, $^3J(H,H) = 8.2$ Hz, 1H, HCPh), 5.95 (d, $^3J(H,H) = 8.2$ Hz, HCPh), 6.12 (s, 1H, NH), 6.94–7.16 (m, 10H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 14.0, 19.8, 32.2, 55.4, 62.8, 65.8, 80.4, 126.0, 127.9, 128.0, 128.1, 128.5, 128.6, 133.7, 134.1, 156.9, 164.7$; MS (70 eV, EI): m/z (%) = 350 (4) [M^+], 307 (10) [$M^+ - n$Pr], 234 (6), 180 (100), 84 (18), 51 (20); $C_{21}H_{22}N_2O_3$: C 71.98, H 6.33, N 7.99; found C 72.18, H 6.25, N 7.68.

Data for 33: Yield: 75%, m.p. 198–200 °C; $[\alpha]_D^{25} = +21.3$ ($c = 0.3$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 3372, 1774, 1753\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 3.70–3.75$ (m, 1H, HCHO), 3.88 (m, 1H, HC), 3.92–4.02 (m, 1H, HCHO), 4.37 (d, $^3J(H,H) = 4.8$ Hz, HCCO), 4.51, (d, $^2J(H,H) = 11.5$ Hz, 1H, HCH), 4.59 (d, $^2J(H,H) = 11.5$ Hz, 1H, HCH), 5.03 (d, $^3J(H,H) = 8.4$ Hz, 1H, HCPh), 5.65 (d, 1H, $^3J(H,H) = 8.4$ Hz, 1H, HCPh), 6.09 (s, 1H, NH), 6.83–7.42 (m, 15H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 53.8, 62.1, 65.5, 69.8, 73.8, 80.2, 126.0, 127.9, 128.0, 128.1, 128.5, 128.6, 133.5, 134.1, 137.7, 157.6, 164.4$; MS (70 eV, EI): m/z (%) = 429 (14) [M^+], 384 (60), 294 (23), 276 (37), 240 (36), 206 (61), 180 (89), 91 (95); $C_{26}H_{24}N_2O_4$: C 72.87, H 5.60, N 6.53; found C 72.67, H 5.73, N 6.23.

Data for 37: Yield: 78%, m.p. 134–136 °C; $[\alpha]_D^{25} = -55.1$ ($c = 1.0$ in MeOH); IR (KBr): $\tilde{\nu} = 3278, 1749, 1689\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 1.43$ (d, $^3J(H,H) = 6.3$ Hz, 3H; CH_3), 1.45 (s, 9H; $3CH_3$), 4.27 (dq, $^3J(H,H) = 6.3, 1.9$ Hz, 1H; CHCH$_3$), 5.13 (d_b, 1H; NHBoc), 5.87 (s, 1H; NH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = 19.4, 28.2, 54.3, 64.8, 80.3, 155.0, 167.4$; MS (70 eV, EI): m/z (%) = 57 (100), 44 (38), 41 (36); $C_9H_{16}N_2O_3$: C 53.98, H 8.06, N 13.99; found C 53.82, H 8.27, N 13.74.

***N*-(Trimethylsilyl)methyl-*N*-vinyl-[(4*S*)-2-oxo-4-phenyloxazolidin-3-yl]acetamide (38)**:[30] Yield: 28%, syrup. $[\alpha]_D^{25} = +112.7$ ($c = 1.0$ in CH_2Cl_2); IR (KBr): $\tilde{\nu} = 1736, 1670\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 0.05$ (s, 9H; $3CH_3$), 3.17 (d, $^3J(H,H) = 1.5$ Hz, 2H; CH_2Si), 3.47 (d, $^2J(H,H) = 16.9$ Hz, 1H; CHCO), 4.14 (t, $^3J(H,H) = 8.6$ Hz, CH_2O), 4.32 (dd, $^2J(H,H) = 13.3$ Hz, $^3J(H,H) = 8.6$ Hz, 1H, $=CH_2$), 4.44 (dd, $^2J(H,H) = 13.3$ Hz, $^3J(H,H) = 1.3$ Hz, 1H, $=CH_2$), 4.53 (d, $^2J(H,H) = 17.0$ Hz, 1H; CHCO), 4.73 (t, $^3J(H,H) = 8.7$ Hz, 1H; CH_2O), 5.17 (t, $^3J(H,H) = 8.4$ Hz, 1H; CHPh), 6.59 (dd, $^2J(H,H) = 15.0$ Hz, $^3J(H,H) = 8.6$ Hz, 1H; $=CH$), 7.45–7.28 (m, 5H; ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 20 °C): $\delta = -1.4, -0.1, 33.5, 43.2, 60.0, 70.1, 95.5, 129.1, 129.2, 132.0, 139.0, 158.7, 165.0$; MS (70 eV, EI): m/z (%) = 73 (100), 260 (35), 333 (2) [M^+]; $C_{17}H_{25}N_2O_3Si$: C 61.23, H 7.56, N 8.40; found C 61.01, H 7.84, N 8.38.

Acknowledgements: This work was supported by the Spanish Ministerio de Educación y Ciencia (MEC) (Project SAF: 95/0749), the Basque Country University (Project UPV 170.215-EA 115/96) and in part by the Basque Government (Project PI 95/93).

Received: February 18, 1997 [F618]

[1] For some reviews on β-lactam antibiotics, see: a) W. Dürkheimer, J. Blumbach, R. Lattrell, K. H. Scheunemann, *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 180; b) *Chemistry and Biology of β-Lactam Antibiotics, Vol. 1–3* (Eds.: R. B. Morin, M. Gorman), Academic Press, New York, **1982**; c) R. Southgate, C. Branch, S. Coulton, E. Hunt, in *Recent Progress in the Chemical Synthesis of Antibiotics and Related Microbial Products, Vol. 2* (Ed.: G. Lukacs), Springer, Berlin, **1993**, p. 621; d) R. Southgate, *Contemp. Org. Synth.* **1994**, *1*, 417.

[2] R. Southgate, S. Elson, in *Progress in the Chemistry of Organic Natural Products, Vol. 47* (Eds.: W. Herz, H. Grisebach, G. W. Kirby, C. Tamm), Springer, Vienna, **1985**, p. 1.

[3] *The Chemistry of β-Lactams* (Ed.: M. I. Page), Chapman and Hall, London, **1992**.

[4] For comprehensive general reviews, see: a) G. A. Koppel, in *Small Ring Heterocycles, Vol. 42* (Ed.: A. Hassner), Wiley, New York, **1983**, p. 219; b) J. Backes, in *Houben–Weyl, Methoden der Organischen Chemie* (Eds.: E. Muller, O. Bayer), *Band E16B*, Thieme, Stuttgart, **1991**, p. 31; c) N. DeKimpe, in *Comprehensive Heterocyclic Chemistry II, Vol. 1B* (Ed.: A. Padwa), **1996**, p. 507.

[5] M. J. Miller, *Acc. Chem. Res.* **1995**, *28*, 299.

[6] a) D. J. Hart, D. C. Ha, *Chem. Rev.* **1989**, *89*, 1447; b) M. J. Brown, *Heterocycles* **1989**, *29*, 2225; c) G. I. Georg, in *Studies in Natural Product Chemistry, Vol. 4* (Ed.: A.-ur-Rahman), Elsevier, Amsterdam, **1989**, p. 431; d) T. Fujisawa, M. Shimizu, *Rev. Heteroatom. Chem.* **1996**, *15*, 203; e) G. Cainelli, M. Panunzio, P. Andreoli, G. Martelli, G. Spunta, D. Giacomini, E. Bandini, *Pure Appl. Chem.* **1990**, *62*, 605; f) G. Cainelli, M. Panunzio, D. Giacomini, G. Martelli, G. Spunta, E. Bandini, in *Chemical Synthesis, Gnosis to Prognosis* (Eds.: C. Chatgilialoglu, V. Snieckus), Kluwer Academic, Amsterdam, **1996**, p. 25.

[7] L. S. Hegedus, *Acc. Chem. Res.* **1995**, *28*, 299. For a review on organometallic reagents in β-lactam synthesis, see: A. G. M. Barrett, M. A. Sturgess, *Tetrahedron* **1988**, *44*, 5615.

[8] H. Staudinger, *Liebigs Ann. Chem.* **1907**, *356*, 51.

[9] For a review: F. H. van der Steen, G. van Koten, *Tetrahedron* **1991**, *47*, 7503.

[10] For recent reviews on asymmetric synthesis of β-lactams, see: a) R. C. Thomas, in *Recent Progress in the Chemical Synthesis of Antibiotics* (Eds.: G. Lukacs, M. Ohno), Springer, Berlin, **1990**, p. 533; b) R. J. Ternansky, J. M. Morin, Jr., in *The Organic Chemistry of β-Lactams* (Ed.: G. I. Georg), VCH, New York, **1993**, p. 257; c) L. Ghosez, J. Marchand-Brynaert in *Comprehensive Organic Synthesis, Vol. 5* (Eds.: B. Trost, I. Fleming), Pergamon, Oxford, **1991**, p. 85.

[11] For reviews on the asymmetric Staudinger reaction, see: a) R. D. G. Cooper, B. W. Daugherty, D. B. Boyd, *Pure Appl. Chem.* **1987**, *59*, 485; b) ref. [9]; c) G. I. Georg, V. T. Ravikumar, in *The Organic Chemistry of β-Lactams* (Ed.: G. I. Georg), VCH, New York, **1993**, p. 295.

[12] D. A. Evans, E. B. Sjögren, *Tetrahedron Lett.* **1985**, *27*, 3783, *ibid.* **1985**, *26*, 3787.

[13] a) I. Ojima, in *The Organic Chemistry of β-Lactams* (Ed.: G. I. Georg), VCH, New York, **1993**, p. 197; b) I. Ojima, *Acc. Chem. Res.* **1995**, *28*, 383.

[14] a) J. A. Eudalay, W. J. Hornback, R. J. Johnson, C. L. Jordan, J. E. Munroe, W. E. Wright, C. Y. E. Wu, in *Recent Advances in the Chemistry of β-Lactam Antibiotics* (Eds.: P. H. Bentley, R. Southgate), Royal Society of Chemistry, London, **1989**, p. 333; b) M. Muller, D. Bur, T. Tschamber, J. Streith, *Helv. Chim. Acta* **1991**, *74*, 767; c) D. L. Boger, J. B. Myers, Jr., *J. Org. Chem.* **1991**, *56*, 5385; d) C. Palomo, J. M. Aizpurua, J. I. Miranda, A. Mielgo, J. M. Odriozola, *Tetrahedron Lett.* **1993**, *34*, 6325; e) R. A. Holton, J. H. Liu, *Bioorg. Med. Chem. Lett.* **1993**, *3*, 2475; f) C. Palomo, J. M. Aizpurua, A. Mielgo, A. Linden, *J. Org. Chem.* **1996**, *61*, 9186; g) C. Palomo, J. M. Aizpurua, J. M. García, R. Galarza, M. Legido, R. Urchegui, P. Román, A. Luque, J. Server-Carrió, A. Linden, *J. Org. Chem.* **1997**, *62*, 2070; h) B. Alcaide, Y. Martin-Cantalejo, J. Perez-Castells, M. A. Sierra, *J. Org. Chem.* **1996**, *61*, 9516. For a new chiral aminoketene precursor, see: i) E. Bandini, G. Martelli, G. Spunta, M. Panunzio, *Synlett* **1996**, 1017; j) W. Duczek, K. Jähnisch, A. Kunath, G. Reck, G. Winter, B. Schulz, *Liebigs Ann. Chem.* **1992**, 781. From aminocarbene complexes, see: k) H. A. Schwindt, J. R. Miller, L. S. Hegedus, *J. Organomet. Chem.* **1991**, *413*, 143; l) B. Alcaide, L. Casarrubios, G. Dominguez, M. A. Sierra, A. Monge, *J. Am. Chem. Soc.* **1995**, *117*, 5604.

[15] For a recent physical and theoretical study on the factors determining the stability of imines, see: M. Dal Colle, G. Distefano, D. Jones, A. Guerrino, G. Seconi, A. Modelli, *J. Chem. Soc. Perkin Trans. 2*, **1994**, 789.

[16] C. Palomo, J. M. Aizpurua, M. Legido, R. Galarza, P. M. Deya, J. Dunogues, J. P. Picard, A. Ricci, G. Seconi, *Angew. Chem.* **1996**, *108*, 1317; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1239.

[17] a) L. A. Paquette, *Science* **1982**, *217*, 793; b) L. A. Paquette, *Science* **1982**, *217*, 793; c) J. B. Lambert, *Tetrahedron* **1990**, *46*, 2677; d) J. M. White, *Aust. J. Chem.* **1995**, *48*, 1227. Colvin suggested that a silicon-induced β-effect governs the regiochemistry of the cycloaddition between allylsilanes and chlorosulphonyl isocyanate to give racemic β-lactams, see: e) E. W. Colvin, M. A. Loreto, M. Monteith, I. Tommasini, in *Frontiers of Organosilicon Chemistry* (Eds.: A. R. Bassindale, P. P. Gaspar), Royal Society of Chemistry, **1991**, p. 356. For a review on organosilicon and organotin compounds in the synthesis of β-lactams, see: f) G. A. Veinberg, E. Lukevics, *Heterocycles* **1994**, *38*, 2309.

[18] a) L. S. Hegedus, J. Montgomery, Y. Narukawa, D. C. Snustad, *J. Am. Chem. Soc.* **1991**, *113*, 5784; b) J. A. Sordo, J. González, T. Sordo, *J. Am. Chem. Soc.* **1992**, *114*, 6249; c) F. P. Cossio, J. M. Ugalde, X. Lopez, B. Lecea, C. Palomo, *ibid.* **1993**, *115*, 995.

[19] *C,C*-bis(trimethylsilyl)methylamine can be prepared in gram quantities from commercially available *N,N*-dimethylcyanamide or cyanotrimethylsilane: a) J. P. Picard, S. Grelier, T. Constantieux, J. Dunoguès, J. M. Aizpurua, C. Palomo, M. Petraud, B. Barbe, L. Lunnazi, J. M. Leger, *Organometallics*, **1993**, *12*, 1378; b) S. Grelier, T. Constantieux, D. Deffieux, M. Bordeau, J. Dunoguès, J. P. Picard, C. Palomo, J. M. Aizpurua, *Organometallics* **1994**, *13*, 3711, and also from bis(trimethyl silyl)chloromethane, see: C. Palomo, J. M. Aizpurua, J. M. Garcia, M. Legido, *J. Chem. Soc. Chem. Commun.* **1991**, 524.

[20] For some representative examples, see: a) W. H. Pearson, A. C. Linbdeck, J. W. Kampf, *J. Am. Chem. Soc.* **1993**, *115*, 2622; b) P. A. Lander, L. S. Hegedus, *ibid.* **1994**, *116*, 8126; c) D. Badone, J. M. Bernassau, R. Cardamone, U. Guzzi, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 535. For a review on oxazolidinones, see: d) D. A. Ager, I. Prakash, D. R. Schaad, *Chem. Rev.* **1996**, *96*, 835.

[21] The same trend was observed in the reaction of **14** with *N*-*p*-methoxyphenyl and *N*-benzyl glyoxylate imines, thus indicating that this anomalous behaviour

0947-6539/97/0309-1440 $ 17.50+.50/0

of Evans Sjögren ketenes is inherent to these kind of imines. No reason for this has been found yet.

[22] For an ester enolate–imine approach to carumonam using glycoaldehyde imines, see: L. E. Overman, T. Osawa, *J. Am. Chem. Soc.* **1985**, *107*, 1698.

[23] For another paper documenting this aspect, see: D. Dugat, G. Just, S. Sahoo, *Can. J. Chem.* **1987**, *65*, 88.

[24] The synthesis of loracarbef usually involves the reaction of aminoketene equivalents with non-enolizable imines that invariably needs various steps to get the required C_4 side chain for further ring closure. For detailed information on this subject, see: R. D. G. Cooper in ref. [3], p. 272.

[25] J. Lasarte, C. Palomo, J. P. Picard, J. Dunoguès, J. M. Aizpurua, *J. Chem. Soc. Chem. Commun.* **1989**, 72.

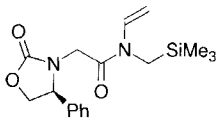
[26] a) V. Farina, S. I. Hauck, D. Walker, *Synlett* **1992**, 761; b) G. I. Georg, P. He, J. Kant, Z.-j. Wu, *J. Org. Chem.* **1993**, *58*, 5771.

[27] L. S. Hegedus, J. Montgomery, Y. Narukawa, D. C. Snustad, *J. Am. Chem. Soc.* **1991**, *113*, 5784.

[28] The mixture of **30**/**31** was not separated. The *cis*/*trans* ratio was determined on the basis of coupling constants and epimerization at the C3 position was assigned on the basis of previous observations made on related compounds; see: C. Palomo, J. M. Aizpurua, C. Cuevas, A. Mielgo, R. Galarza, *Tetrahedron Lett.* **1995**, *36*, 9027.

[29] a) C. Palomo, J. M. Aizpurua, J. M. García, I. Ganboa, F. P. Cossío, B. Lecea, M. C. López, *J. Org. Chem.* **1990**, *55*, 2498; b) C. Palomo, J. M. Aizpurua, J. M. García, J. P. Picard, J. Dunoguès, *Tetrahedron Lett.* **1990**, *31*, 1921; c) C. Palomo, J. M. Aizpurua, M. Legido, J. P. Picard, J. Dunoguès, T. Constanticux, *Tetrahedron Lett.* **1992**, *33*, 3903.

[30] Natural bonding orbital (NBO) computational studies are under way to determine the actual nature of the orbital interactions accounting for the formation of *N*-bis(trimethylsilyl)methyl-β-lactams from enolizable aldehyde-derived imines and the Evans–Sjögren ketene. As an experimental fact, the reaction of the (*E*)-ethylidenetrimethylsilylmethylamine ($MeCH{=}NCH_2SiMe_3$) and the ketene derived from **14** gave no trace of the expected *N*-trimethylsilylmethyl-β-lactam, showing that the presence of two α-silyl groups was necessary to promote the azetidin-2-one formation. Instead, the enamide **38** was the only isolable pure compound of such a reaction in 28% yield.



38

[31] C. Palomo, J. M. Aizpurua, M. Legido, R. Galarza, *J. Chem. Soc. Chem. Commun.* **1997**, 233.

[32] O. Nakaguchi, T. Oku, H. Takeno, M. Hashimoto, T. Kamiya, *Chem. Pharm. Bull.* **1987**, *35*, 3985.

[33] a) B. Alcaide, L. Casarrubios, G. Dominguez, M. A. Sierra, *J. Org. Chem.* **1994**, *59*, 7934; b) C. Palomo, A. Arrieta, B. Lecea, F. P. Cossio, *J. Org. Chem.* **1988**, *53*, 3784.

[34] M. Ballestri, C. Chatgilialoglu, N. Cardi, A. Sommazzi, *Tetrahedron Lett.* **1992**, *33*, 1787.

  0947-6539/97/0309-1441 $ 17.50+.50/0