N-Alkyloxycarbonyl-3-aryloxaziridines: Their Preparation, Structure, and Utilization as Electrophilic Amination Reagents

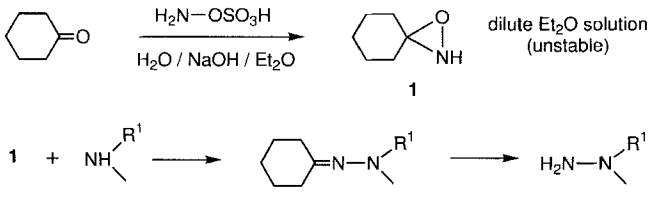
Joëlle Vidal,* Stéphanie Damestoy, Laure Guy, Jean-Christophe Hannachi, André Aubry, and André Collet*

Abstract: This paper reports the synthesis of a series of *N*-protected oxaziridines (*N*-Moc, Boc, Z or Fmoc) and discusses their ability to deliver their *N*-alkoxycarbonyl fragment to amines, enolates, sulfur, and phosphorus nucleophiles (electrophilic amination). These oxaziridines are prepared by oxidation of the corresponding imines with oxone or anhydrous MCPBA lithium salt as the source of oxygen. They transfer their *N*-protected fragment to primary and secondary amines to give protected hydrazines in fair to excellent yield. The nitrogen transfer to free amino acids (in form of their R_4N^+ salts) is particularly fast, even at low temperature, providing L (or D) *N*-protected α-hydrazino acids. Enolates are *C*-aminated to give *N*-protected α-amino ketones, esters, or amides in modest yield, due to a side aldol reaction of the unreacted enolate with the released benzaldehyde. With tertiary amines (Et_3N), sulfides (PhSMe), and phosphines (Ph_3P), amination and oxidation proceed in a parallel way; the amount of amination product increases when the temperature is lowered (kinetic control). Some of the factors that can orient the oxaziridine reactivity towards amination or oxidation of nucleophiles are considered.

Keywords
aminations · electrophilic substitutions · hydrazines · oxaziridines · pseudopeptides

Introduction

The amination of nucleophiles by oxaziridines such as **1** derived from dialkylketones (Scheme 1) was first reported by Schmitz and coworkers in 1964.[1] This elegant electrophilic amination methodology,[2] which is actually involved in the industrial production of hydrazine from ammonia,[3] has been used in the commercial production of carbidopa (the α-hydrazino acid corresponding to α-methyldopa).[4] Owing to their instability, Schmitz oxaziridines are prepared in situ, and this circumstance somewhat restricts their utilization in organic synthesis. The primary purpose of the present work was to make this process more practical and to extend the scope of its application. To this end, we focused on the design of oxaziridines stable enough to be isolated, and which would deliver an *N*-protected group, rather than a free amino group, to the nucleophilic substrate. This last requirement is particularly desirable in the context of α-hydrazino acid synthesis and hydrazinopeptide chemistry, an area which is the object of current research interest.[5] In preliminary reports we have shown[6–8] that these objectives could be met by means of the 3-aryl-*N*-alkyloxycarbonyl oxaziridines **2a** and **4a**. These reagents are crystalline solids, which transfer their *N*-methoxycarbonyl (*N*-Moc) and *N*-*tert*-butoxycarbonyl (*N*-Boc) fragments, respectively, to nucleophiles such as primary and secondary amines, amino acids, and carbanions under mild conditions. Several applications of **2a** and **4a**, and of their *N*-benzyloxycarbonyl (*N*-Z) analogue **5**, to the synthesis of carbazates,[9] α-hydrazino acids,[10, 11] and hydrazinopeptides[12] have since been reported; reagent **4a** has recently become commercially available.



Scheme 1. Schmitz electrophilic amination methodology.

In order to explore further the scope of application and the structure–reactivity pattern of these reagents, we have extended these investigations to a number of new 3-aryl-*N*-protected oxaziridines. We report here in details our results concerning the preparation, structure and reactivity of the *N*-Moc derivatives **2a–h** and **3**, and of their *N*-Boc, *N*-Z, and *N*-Fmoc analogues **4a–d**, **5** and **6**, respectively (Scheme 2). We have studied the reactivity of these compounds towards a variety of nucleophiles

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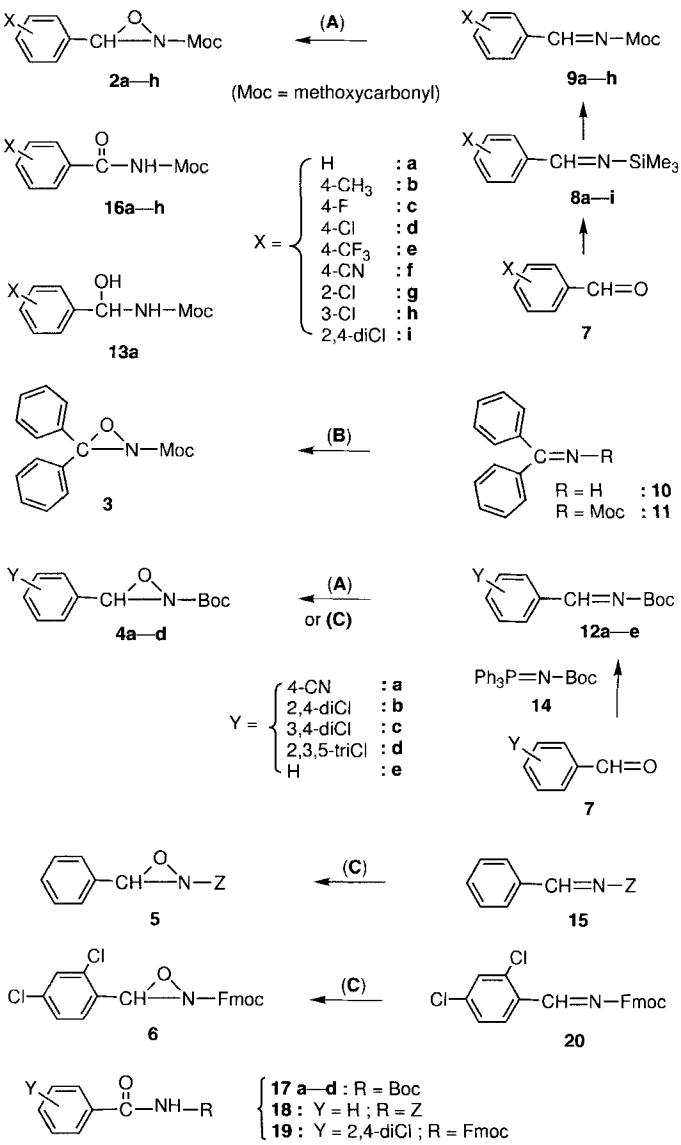
including amines, aminoacids, enol ethers and enolates, alkenes, sulfides, and phosphines, and we confirm that these *N*-alkyloxycarbonyl oxaziridines generally transfer their amino group, rather than their oxygen, to these substrates. This behavior is unlike that of *N*-sulfonyl,[13] *N*-phosphinoyl,[14] or *N*-fluoroalkyl oxaziridines,[15] which are used in organic synthesis to deliver their oxygen to a variety of nucleophilic substrates. We show that this difference in reactivity is the result of subtle effects, where the size of the substituent borne by the oxaziridine nitrogen, combined with the oxaziridine LUMO energy, and the nature of the incoming nucleophile all play a role in determining the initial course of the reaction as well as its subsequent development to the products.

Results and Discussion

Preparation of *N*-alkyloxycarbonyl oxaziridines: Although the oxaziridine ring can be prepared in a number of ways,[16] the insertion of oxygen into a -C = N- bond by means of conventional oxidizing reagents is certainly the most widely employed process for this purpose. When applied to an *N*-alkyloxycarbonyl phenylimine (**9**, **12**, **15**, and **20** in Scheme 2), this reaction proved somewhat difficult to achieve, because in addition to the desired oxaziridine it also afforded the isomeric amide (**16**–**19**), which in some cases was the major product. The differently substituted oxaziridines considered here were eventually synthesized according to three different oxygen insertion methods (**A**, **B**, and **C** in Scheme 2) depending on their substitution pattern. These methods utilize either basic buffered peroxymonosulfate (oxone), *m*-chloroperoxybenzoic acid (MCPBA), or the anhydrous MCPBA lithium salt, respectively, as the source of oxygen.

Abstract in French: *Nous présentons la synthèse d'une série d'oxaziridines substituées sur l'azote par les groupes protecteurs Moc, Boc, Z ou Fmoc et décrivons leur capacité à transférer leur groupe N-protégé à des nucléophiles comme les amines, les énolates, les sulfures ou les phosphines (amination électrophile). Ces oxaziridines sont préparées par oxydation des imines correspondantes au moyen de l'oxone ou du sel de lithium anhydre de l'acide m-chloroperbenzoïque. Elles transfèrent leur groupe N-alkoxycarbonyle aux amines primaires et secondaires pour donner des hydrazines protégées, avec des rendements moyens à excellents. La réaction est particulièrement rapide même à basse température sur les aminoacides L (ou D), sous forme de leurs sels d'ammonium quaternaires, et constitue une très bonne méthode d'accès aux α-hydrazinoacides N-protégés L (ou D). Le groupe N-alkoxycarbonyle est aussi transférable aux énolates, pour donner les α-amino cétones, esters ou amides N-protégés avec des rendements moyens, en raison de la condensation parasite entre l'énolate et l'aldéhyde libéré par l'oxaziridine. Dans le cas des amines tertiaires (Et_3N), des sulfures (PhSMe) et des phosphines (Ph_3P) on observe non seulement le transfert du groupe N-alkoxycarbonyle (amination) mais aussi le transfert de l'oxygène (oxydation). Certains des facteurs pouvant orienter la réactivité des oxaziridines vers l'amination ou l'oxydation de nucléophiles sont mis en évidence.*



Scheme 2. Method **A**: biphasic conditions; oxone and K_2CO_3 in H_2O/*N*-alkyloxycarbonyl imine in $CHCl_3$; 0–4 °C. Method **B**: biphasic conditions; MCPBA in $CHCl_3$/K_2CO_3 in H_2O; 20 °C. Method **C**: BuLi in hexane added to MCPBA in CH_2Cl_2, −78 °C.

Method **A** allowed us to synthesize the *N*-Moc oxaziridines **2a**–**h** from the corresponding *N*-Moc imines **9a**–**h**, these *N*-Moc imines being themselves prepared by acylation of the corresponding *N*-silylimines **8a**–**h** in the presence of methyl chloroformate (Table 1).[17] In method **A**, the *N*-Moc imine dissolved in chloroform is allowed to react under biphasic conditions with a *basic* aqueous solution of oxone and K_2CO_3 at 0–4 °C (the temperature is critical). We investigated in detail the conversion of the parent compound **9a** to the oxaziridine **2a**; in this case the above conditions furnished the desired oxaziridine in 68% yield, the main byproduct being the *N*-Moc benzamide **16a** (23%). The photochemical, thermal, or catalyzed rearrangment of oxaziridines to amides is a well-documented reaction.[18] However, we did not observe evidence of isomerization of isolated **2a** to **16a** under the different conditions used for the oxidation of **9a**. When the oxone oxidation of **9a** was carried out at room temperature, the major product was the hemiaminal **13a** resulting from the addition of water to imine **9a**.[19] The same hemiami-

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Table 1. Synthesis of *N*-Moc oxaziridines **2a–g** by method **A**.

Entry	X substituent in **7**	Silylimine **8a–h** (%)	Moc-imine **9a–h** (%)	Oxaziridine **2a–h** (%)	Amide **16a–h** (%)	**9**:**2** ratio [a]
1	**a**: H	84	80	68	23	<1:99
2	**b**: 4-CH_3	42	77	25 [b]	24	40:60
3	**c**: 4-F	71	77	61	25	6:94
4	**d**: 4-Cl	90	70	70	19	52:48
5	**e**: 4-CF_3	55	56	52	39	26:74
6	**f**: 4-CN	84	50	45	41	5:95
7	**g**: 2-Cl	73	79	78	0	30:70
8	**h**: 3-Cl	63	50	53	25	20:80

[a] The imine vs. oxaziridine ratio after 1 h reaction was determined by ^{1}H NMR of the crude mixture. [b] Aldehyde **7b** (30% isolated) was formed from the oxaziridine, which decomposed during the chromatographic workup.

nal was quantitatively obtained under homogeneous conditions by reaction of **9a** with water in acetone; on reaction with basic buffered oxone, **13a** was not converted to the benzamide **16a**, which must therefore be formed by a different mechanism (see below). When *neutral* (instead of basic) buffered oxone was employed in the oxidation of **9a**, the amide **16a** was the sole product, even at 0 °C. Oxidation of **9a** by MCPBA under various conditions (CH_2Cl_2/K_2CO_3, −50 °C; $CH_2Cl_2/H_2O/K_2CO_3$, 0 °C, method **B**) also gave **16a**, although these oxidants have commonly been used for the conversion of *N*-alkyl, *N*-sulfonyl, or *N*-phosphinoyl imines to oxaziridines.

The *N*-Moc imines **9b–h** were similarly converted by method **A** to the corresponding oxaziridines **2b–h** in fair to good yield (Table 1). The conversion of **9b–h** to **2b–h** was slower than that of **9a**, as seen by the value of the **9**:**2** ratio after one hour of reaction. We suspected that this effect was due to an increased lipophilicity of the substituted aromatic ring decreasing the concentration of imine **9** at the water/$CHCl_3$ interface where oxidation is thought to take place, rather than to steric or electronic effects of the X substituent. However, the use of a phase-transfer catalyst (Bu_4NBr) did not improve this, the addition of water to imine **9** becoming the major reaction under these conditions.

The retardation of the desired reaction occurring with substituted imines raised an additional problem, due to the relatively fast decomposition of oxone in basic aqueous solutions[20] (we estimated the half-life of the reagent at 15 min under the required operating conditions). This problem was circumvented by discarding the aqueous phase every hour and replacing it by a fresh K_2CO_3–oxone solution until the conversion of imine **9** was complete. In this way, the *N*-Moc oxaziridines **2c–h** were obtained in 25–78% yield (Table 1). The lowest yield (25%, entry 2) was in fact a result of partial decomposition of the *p*-methyl derivative **2b** to anisaldehyde during the isolation workup involving flash chromatography over silica gel. The isomeric *N*-Moc benzamides **16b–h** were isolated in ca. 20–25% yields, except when strongly electron-withdrawing substituents were present on the benzene ring (entries 5 and 6, ca. 40%), and in the case of the 2-chloro derivative (entry 7) where no benzamide **16g** was detected.

The *N*-Moc imine **11**, prepared by acylation of benzophenone imine **10** by methyl chloroformate, did not react in the presence of basic buffered oxone or basic tetrabutylammonium peroxomonosulfate.[21] The use of MCPBA in chloroform at room temperature led to unidentified products. We eventually obtained oxaziridine **3** in 60% yield by using MCPBA under biphasic conditions (chloroform/water) with a basic (K_2CO_3) aqueous solution (method **B**).

We now turn to the synthesis of the *N*-Boc oxaziridines **4a–d**, which bear a more synthetically useful protecting group[22] than the Moc.[23] As the conversion of silylimine **8a** to the desired *N*-Boc imine **12e** (using Boc_2O or even Boc-F) proved difficult to achieve,[24] we focused on the aza-Wittig reaction between benzaldehydes **7** and the *N*-Boc iminophosphorane **14**. The reaction of **14** with moderately electrophilic aldehydes such as benzaldehyde itself was very slow (only 75% conversion to **12e** after 111 h reaction in refluxing toluene), probably due to the electron-withdrawing character of the Boc group. We were able to improve on this significantly by using more electrophilic benzaldehydes (**7**, Y = 4-CN, 2,4- or 3,4-di-Cl, 2,3,5-tri-Cl); the reaction was then essentially complete after the reasonable times indicated in Table 2, the shortest being observed for the 4-CN

Table 2. Synthesis of *N*-Boc-oxaziridines **4a–d**, *N*-Z-oxaziridine **5**, and *N*-Fmoc-oxaziridine **6**.

Entry	Y or X in **7**	Protecting group	Imine	Imine synthesis	Oxidation method	Oxaziridine, %
1	4-CN	Boc	**12a**	aza-Wittig (17 h) [a]	**A**	**4a** 50
2	"	"	**12a**	"	**B**	**4a** 0 [b]
3	"	"	**12a**	"	**C**	**4a** 65 [c]
4	2,4-diCl	"	**12b**	aza-Wittig (86 h) [a]	**A**	**4b** 0 [d]
5	"	"	**12b**	"	**B**	**4b** 25 [e]
6	"	"	**12b**	"	**C**	**4b** 79
7	3,4-diCl	"	**12c**	aza-Wittig (30 h) [a]	**C**	**4c** 70
8	2,3,5-diCl	"	**12d**	aza-Wittig (86 h) [a]	**C**	**4d** 59
9	H	Z	**15**	silylimine **8a**	**C**	**5** 35
10	2,4-diCl	Fmoc	**20**	silylimine **8i**	**C**	**6** 59

[a] The aza-Wittig reaction of benzaldehyde **7** and iminophosphorane **14** in refluxing toluene was complete after the time indicated in parentheses. [b] Amide **17a** was isolated in 63% yield. [c] The overall yield from 4-cyanobenzaldehyde was 60%. [d] Imine **12b** was recovered unreacted. [e] Amide **17b** was isolated in 56% yield.

(17 h) and 3,4-di-Cl (30 h) derivatives. This reaction suffers from a significant retardation (probably due to steric hindrance) when the benzaldehyde bears a substituent on the *ortho* position.

The reaction of the *N*-Boc imine **12a** with basic buffered oxone according to method **A** was slower than that of the corresponding *N*-Moc imine **9f**, the observed oxaziridine/imine ratio being only 1:9 after one hour (Table 2). After six to ten cycles with fresh oxone solution, the conversion was complete and the *N*-Boc oxaziridine **4a** was isolated in 50% yield (similar to that obtained in ca. 1 h with the analogous **9f**, Table 1). The slowing down is possibly due to the steric hindrance of the Boc group, and to its increased lipophilicity with respect to the Moc group. This reaction also afforded the *N*-Boc benzamide **17a** (25%), which was easily separated from **4a** by chromatographic filtration on silica gel. In large-scale preparations, we did not find it necessary to isolate the intermediate *N*-Boc imine **12a**, and starting from 46 g of 4-cyanobenzaldehyde we could consistently obtain 34–36 g of pure **4a** per batch (41–44% yield from the aldehyde).

Method **A** did not work with the dichlorinated imine **12b**, which proved unreactive when treated with basic buffered ox-

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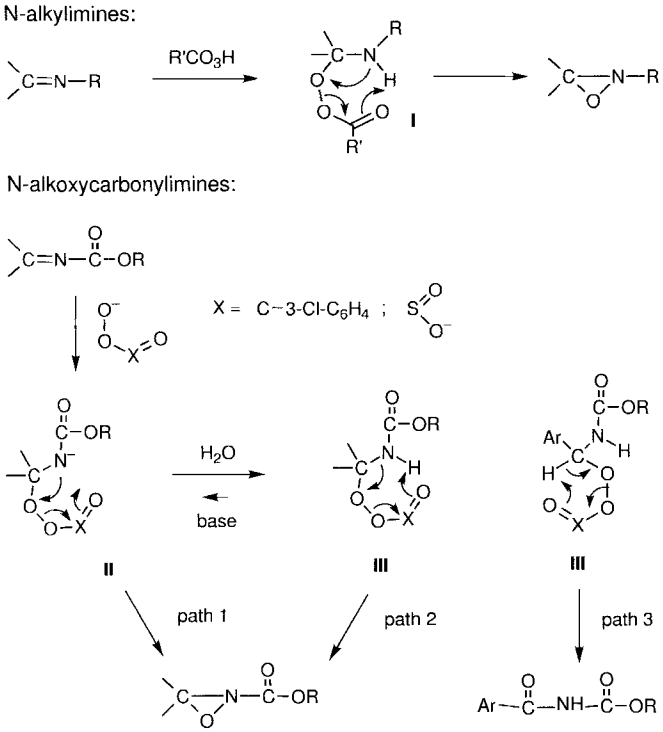
one. With MCPBA under basic biphasic conditions (method **B**), a small amount (25%) of oxaziridine **4b** was obtained, together with the benzamide **17b** (60%); under the same conditions, only benzamide **17a** was formed from **12a** (Table 2).

At this stage, we found it necessary to look more closely at this reaction in order to identify some of the factors that direct its course towards oxaziridine or amide formation. It has been proposed that the formation of oxaziridines from an *N*-alkylimine and a peracid involves the addition of the latter to the C=N double bond to give intermediate **I** (Scheme 3), followed



Scheme 3. Oxidation of imines to oxaziridines and amides.

by an intramolecular attack of the nucleophilic nitrogen to the peroxo bridge.[25] We postulate that a similar mechanism holds for the oxidation of *N*-alkyloxycarbonyl imines. In the basic aqueous medium required for the reaction, we assume that intermediate **II** (bearing a nucleophilic N^- center) is first formed; in the presence of water, this strongly basic intermediate undergoes protonation to **III**, in which the acylated nitrogen is no longer nucleophilic. For this reason, we consider that the oxaziridine is formed from **II** (path 1) rather than **III** (path 2), even though the equilibrium between **II** and **III** is shifted towards the latter. This explains why the presence of the base (K_2CO_3) is required, to keep a sufficient level of **II** at the chloroform/water interface (as reported above, no oxaziridine is formed under neutral conditions). When the C=N carbon is monosubstituted (as in **9**, **12**, **15**, **20**), intermediate **III** can also fragment differently, leading to the amide (path 3). This path is favored when a peracid rather than a peroxosulfate reagent (oxone) is employed, because a carboxylate ion is a poorer leaving group than a sulfate ion. It is also favored when the presence of strong electron-withdrawing substituents on the benzene ring makes the C(H)–N hydrogen more acidic (Table 1, entries 5 and 6). It is disfavored in the presence of a sterically demanding substituent on the *ortho* position of the benzene ring (Table 1, entry 7; Table 2, entries 2 and 5). If our views are correct, a way to suppress the amide formation by path 3 is to form intermediate **II** under conditions where it cannot equilibrate to **III**. This was achieved by the use of an organic peracid salt in aprotic medium (method **C**).

We prepared the lithium salt of MCPBA by adding at $-78\,^{\circ}C$ one equivalent of butyllithium to an anhydrous CH_2Cl_2 solution of the pure peracid, and the resulting suspension was allowed to react in situ with the *N*-Boc imines **12a–d** (Table 2). In this way, the oxaziridines **4a–d** were isolated in 59–79% yields, and the amount of isomeric benzamide **17a–d** was small (0–15%). We could successfully apply this method (method **C**) to the preparation of the *N*-Z oxaziridine **5** (Table 2, entry 9, 35% yield from **7a**). This oxaziridine had previously been prepared by the Schmitz method in only 12% yield from **7a**.[11] Most interestingly, method **C** allowed the oxidation of the base-sensitive *N*-Fmoc imine **20**, prepared (98%) from silylimine **8i** and Fmoc-Cl; the resulting *N*-Fmoc oxaziridine **6** was isolated in 59% yield, and no benzamide **19** was detected.

Characterization and physical properties of *N*-alkyloxycarbonyl oxaziridines: *N*-alkyloxycarbonyl oxaziridines **2–6** are colorless crystalline solids melting in the range 40–60 °C, except **2f** and **6** which have higher m.p.s (118 and 100 °C respectively) (Table 3). Their stability was probed by differential scanning microcalorimetry (DSC). The onset of their decomposition exotherm at a heating rate of 5 K min^{-1} was observed to occur in the range 75–120 °C (Table 3), depending on the substitution pattern of the aromatic ring. The most stable oxaziridines are those bearing strong electron-withdrawing substituents, such as **2f**, **4d**, and **4a**. All these oxaziridines (except **2b**) have been stored for several years below 4 °C without decomposition.

Table 3. Physical properties, thermal stabilities, and *cis* *trans* equilibria of *N*-alkyloxycarbonyl oxaziridines.

Entry	Protecting group	Oxaziridine	M.p. (°C) [a]	Decomp. (°C) [b]	*cis*/*trans* ($CDCl_3$, 27 °C)	$\Delta G^{\ddagger}_{trans \rightarrow cis}$ (kcal mol^{-1})
1	Moc	**2a**	41	75	9:91	17.4
2	"	**2b**	48	54	9:91	
3	"	**2c**	29	75	7:93	
4	"	**2d**	39	75	7:93	
5	"	**2e**	40	110	8:92	
6	"	**2f**	118	121	7:93	
7	"	**2g**	45	100	10:90	
8	"	**2h**	31	95	7:93	
9	"	**3**	61	80		
10	Boc	**4a**	61	115	12:88	18.3
11	"	**4b**	47	112	19:81	
12	"	**4c**	51	91	8:92	18.1
13	"	**4d**	39	120	20:80	18.6
14	Z	**5**	56	80	12:88	
15	Fmoc	**6**	100	103	10:90	

[a] Recorded by differential scanning calorimetry (DSC). [b] Onset of the decomposition exotherm observed by DSC at a heating rate of 5 K min^{-1}.

They were characterized by ^1H and ^{13}C NMR spectroscopy, and by elemental analysis or mass spectrometry (see Experimental section). An X-ray structure[26] of a crystal of **2a** grown from Et_2O/pentane at 0 °C (Figure 1) showed that the nitrogen

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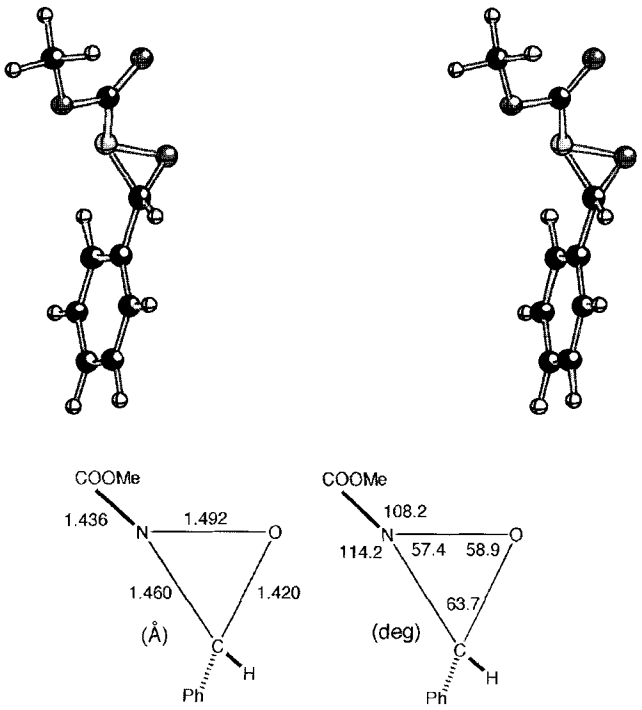
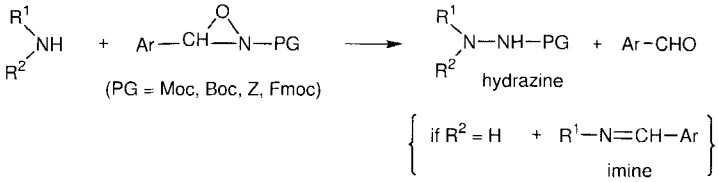


Figure 1. Stereoview of **2a** in the crystal state and dimensions of the oxaziridine ring.

atom is pyramidal (sum of angles at N: 279.8°) with the length of the N–O bond being 1.49 Å. These values are similar to those found for an *N*-methyl oxaziridine (279.4° and 1.51 Å),[27] several *N*-sulfonyl oxaziridines (278–283° and 1.49 Å),[28] or an *N*-phosphinoyl oxaziridine (279.9° and 1.51 Å).[29] The phenyl group and the Moc group are in a *trans* conformation, and the plane of the phenyl ring bisects the O-C-N angle of the oxaziridine ring. The N–CO bond in **2a** (1.44 Å) is longer than in a planar carbamate (1.33 Å),[30] and approaches the length of an N–C bond in amines (1.47 Å), indicating that the conjugation between the nitrogen lone pair and the carbonyl group is weak. The carbamate C=O bond is particularly short (1.17 Å); this seems to be in line with the unusually high IR frequency of the C=O stretching (see below).

In solution, oxaziridines **2**, **4**, **5**, and **6** exist as a mixture of *trans* (80–93%) and *cis* (7–20%) conformers (Table 3); these conformers give separate ^{1}H NMR resonances at room temperature due to the slow inversion of the pyramidal nitrogen on the 200 MHz spectrometer time scale.[31] In oxaziridines **2a** and **4a–d**, the coalescence of the two ^{1}H NMR signals of the heterocyclic hydrogen ($\delta = \approx 5-6$) occurs in the range 70–80 °C (in $(CDCl_2)_2$). The nitrogen inversion barrier $\Delta G^{\neq}$ from *trans* to *cis* was estimated from lineshape analysis[32] at 17.4–18.6 kcal mol^{-1} at 27 °C (Table 3). These barriers are lower than those reported[31] for *N*-alkyl oxaziridines (22–34 kcal mol^{-1}), and higher than those of *N*-acyloxaziridines (11–12 kcal mol^{-1}). This finding can be rationalized by assuming that conjugation of the planar nitrogen with the CO(OR) group lowers the transition state with respect to *N*-alkyl oxaziridines, but not as much as in *N*-acyl oxaziridines. The half-life of a conformer is of the order of 3 s at 20 °C, and 35 min at −30 °C; isolation of the pure *trans* and *cis* stereoisomers of *N*-alkyloxycarbonyl oxaziridines is therefore impossible in solution at room temperature. In all these oxaziridines the strong IR C=O stretching band observed in solution is split into two sharp bands (e.g., at 1777 and 1753 cm^{-1} for **2a**, intensity ratio ca. 4:3); these bands probably originate from rotational conformers of the N–CO_2R group rather than from the above discussed *cis* and *trans* isomers (this splitting is also observed in **3**, which has no such *cis–trans* isomerism).

Amination of amines: In earlier reports[6–8] we have shown that oxaziridines **2a** and **4a** transfer their *N*-alkyloxycarbonyl group to amines to give the corresponding N_{β}-protected hydrazines (Scheme 4). All new oxaziridines described herein were found to



Scheme 4. Amination products and by-products in the reaction of oxaziridines with amines.

behave similarly, the only significant differences between them being the rate of transfer of the N–CO_2R fragment, and to a minor extent the amount of by-products such as the imine (Schiff base) formed from the released benzaldehyde when the nucleophilic substrate is a primary amine.

The reaction of these oxaziridines with secondary amines such as morpholine, ephedrine and pseudoephedrine, proline methyl ester, prolinamide, the dipeptide H–Pro–Val–OMe, and (*S*)-2-methoxymethylpyrrolidine, proceeded rapidly at room temperature and afforded the N_{β}-protected hydrazines **21–27** in 58–92% (isolated) yields (Table 4, entries 1–11, and Scheme 5). We took advantage of the fact that the reaction with morpholine was particularly smooth and clean at room temperature to perform competitive amination experiments using ox-

Table 4. Amination of secondary, primary, and aromatic amines by oxaziridines.

Entry	Protecting group	Oxaziridine	Amination product (%)		Reaction conditions	Hydrazine: imine
1	Moc	**2a**	**21a**	91	RT; 0.5 h	–
2	Boc	**4a**	**21b**	92	RT; 0.5 h	
3	Z	**5**	**21c**	89	RT; 0.5 h	
4	Fmoc	**6**	**21d**	89	RT; 0.5 h	–
5	Moc	**2a**	**22a**	77	RT; 5 h	–
6	Boc	**4a**	**22b**	70	RT; 5 h	
7	Moc	**2a**	**23**	76	RT; 5 h	
8	Moc	**2a**	**24**	60	RT; 1.5 h	
9	Moc	**2a**	**25**	58	RT; 3 h	–
10	Moc	**2a**	**26**	79	RT; 2 h	
11	Boc	**4a**	**27**	78	RT; 1 h	–
12	Moc	**2a**	**28**	80	RT; 0.7 h	85:15
13	Moc	**2a**	**29**	75	RT; 1 h	90:10
14	Moc	**2a**	**30a**	57	60 °C; 3 h	70:30
15	Moc	**2d**	**30a**		RT; 24 h	75:25
16	Moc	**2g**	**30a**		RT; 24 h	80:20
17	Moc	**2h**	**30a**	80	RT; 24 h	90:10
18	Boc	**4a**	**30b**	44	RT; 48 h	55:45
19	Boc	**4c**	**30b**		RT; 48 h	59:41
20	Boc	**4d**	**30b**		RT; 24h	58:42
21	Moc	**2a**	**31**	25	RT; 4 h	50:50
22	Boc	**4a**	**32**	67	RT; 4 h	70:30
23	Moc	**2a**	**33**	76	RT; 24 h	–

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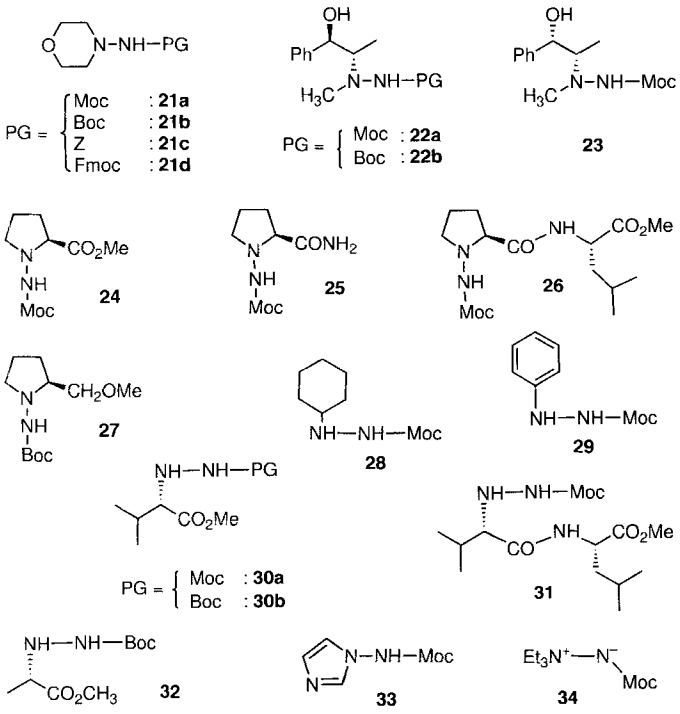

Scheme 5. Amination of amines.

aziridine **2a** as the reference. The ratio of the benzaldehydes resulting from the reaction with morpholine with an excess of 1:1 mixture of **2a** and another oxaziridine provided the relative amination transfer rates listed in Table 5. In the Moc series **2a**–**f**, the rate of the amination reaction followed a linear Hammett correlation ($r^2 = 0.997$) with a positive slope ($\rho = 0.83$); we will return to this result below. The presence of electron-withdrawing substituents on the phenyl ring speeds up the amination reaction significantly. This is particularly true for the 4-cyano derivative **2f**, which delivers its nitrogen group four times faster than **2a**. Probably because of the steric requirement of the *tert*-butyl group, the *N*-Boc oxaziridine **4a** is less reactive than its Moc analogue **2f**, but is still slightly more reactive than **2a**. In the Boc series, the fastest amination is obtained with the 2,3,5-trichlorophenyl derivative **4f**, which is 2.4 times more reactive than **2a**. Interestingly, the 2,4-dichlorophenyl-*N*-Fmoc oxaziridine **6** proved to be very reactive, delivering its *N*-Fmoc fragment to morpholine 5.5 times faster than does **2a**. In contrast, no reaction occurred at room temperature between morpholine and the *C*-diphenyl substituted oxaziridine **3**; heating resulted in decomposition of **3** to unidentified products.

The amination of primary amines (Table 4, entries 12–22) was complicated by a side reaction whereby the released benzaldehyde and the starting amine formed the corresponding imine; the hydrazine vs. imine ratio in the final reaction mixture was in the range 9:1 to 1:1, depending on the nature of the substrate and of the oxaziridine. The trend is that the amount of imine increases when the transfer of the *N*-protected group is slow. With **2a**, cyclohexylamine and aniline afforded the corresponding *N*-Moc hydrazines **28** and **29** in excellent yield; the amination was fast at room temperature, and less than 15% of imine was formed. In the case of methyl valinate (Table 4, entries 14–17), the transfer of the *N*-Moc group to give **30a** was much slower (24 h at room temperature), even when the more reactive oxaziridines **2d**, **2g**, or **2h** were employed. The best result (80% yield) was obtained with the 3-chlorophenyl oxaziridine **2h**. The transfer of an *N*-Boc group to the same substrate with **4a** was slower still and, because the released 4-cyanobenzaldehyde is a strong electrophile, the hydrazine/imine ratio was not good (55:45); the use of **4c** and **4d** only led to a minor improvement of this ratio (Table 4, entries 18–20). In contrast, the less hindered amino ester Ala–OMe afforded N_β-Boc hydrazinoalanine methyl ester **32** in 67% yield after only 4 h reaction with **4a**. Although the amination of the dipeptide H–Val–Leu–OMe was relatively fast, the hydrazinopeptide **31** was isolated in only 25% yield together with the same quantity of imine (entry 21). The low yield is mostly due to the circumstance that a large part of the starting dipeptide is converted into the corresponding diketopiperazine during the course of the reaction.

The reaction of oxaziridine **2a** with imidazole was slow but clean, and furnished the corresponding hydrazine **33** in 76% yield. Pyrrole and pyridine reacted very slowly with **2a** to give several unidentified products. With tertiary amines such as triethylamine, the reaction of **2a** took a different course. At room temperature, 95% of a 1:1 mixture of triethylamine oxide and *N*-Moc phenylimine **9a** was formed within a few minutes, together with 5% of a 1:1 mixture of aminimide **34**[33] and benzaldehyde. The amount of amination product **34** significantly increased when the reaction temperature was lowered. At −78 °C, the *N*-oxide/aminimide ratio became 70:30, and after 10 h reaction triethylamine oxide and aminimide **34** were isolated in 69% and 30% yield, respectively. The behavior of **2a** towards tertiary amines thus resembles somewhat that of *N*-sulfonyloxaziridines, although, contrary to **2a**, these reagents also oxidize primary and secondary amines.[34] We shall return to this question below.

Amination of free amino acids: We now consider the amination of free amino acids **35** to give the corresponding N_β-protected hydrazino acids **37** (Scheme 6). These compounds are currently employed for the synthesis of hydrazinopeptides[5, 10, 35] by

Table 5. Relative rate constants for amination of morpholine by oxaziridines **2**, **4**, **5**, and **6** [a].

	H	4-CH_3	4-F	4-Cl	4-CF_3	4-CN	2-Cl	3-Cl	2,4-diCl	3,4-diCl	2,3,5-triCl
Moc	**2a**: 1	**2b**: 0.81	**2c**: 1.42	**2d**: 1.81	**2e**: 2.90	**2f**: 4.0	**2g**: 2.9	**2h**: 2.5			
Boc						**4a**: 1.2			**4b**: 1.4	**4c**: 1.2	**4d**: 2.4
Z or Fmoc	**5**: 0.8 [b]								**6**: 5.5		

[a] A 1:1 mixture of **2a** and another oxaziridine was allowed to react in $CDCl_3$ (20 °C) with a small amount of morpholine, and the ratio of the released benzaldehydes was measured by ^{1}H NMR, providing the relative rate constants of the amination reaction (see Experimental section). [b] In this case the competition was effected between **5** and **4a** (relative amination rate 0.74).

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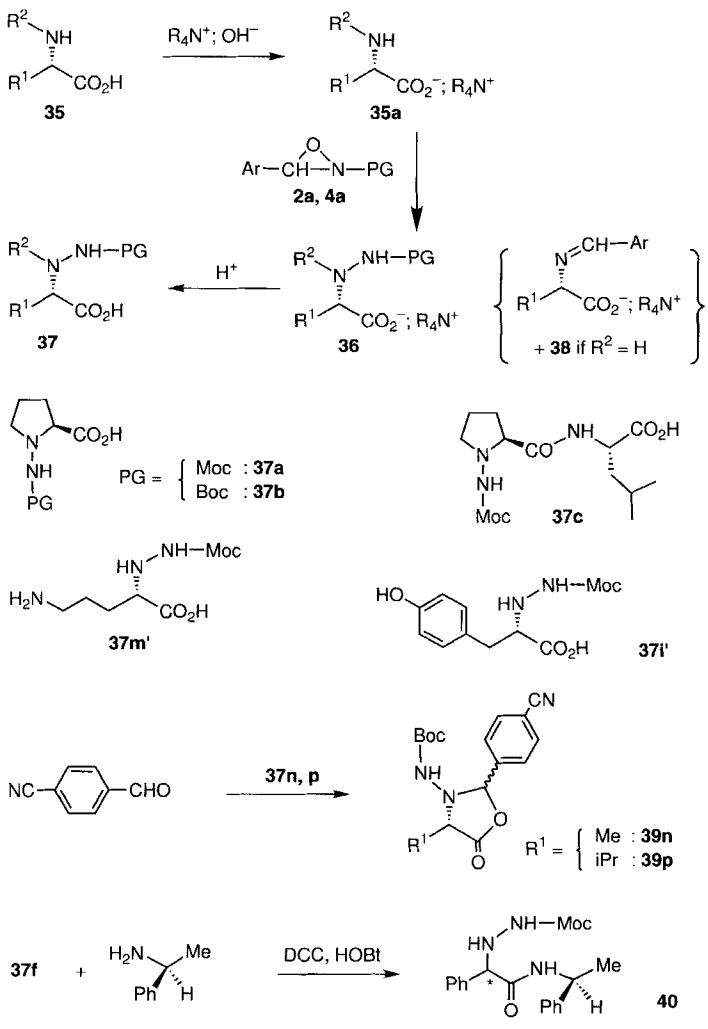

Scheme 6. Amination of amino acids.

conventional peptide synthesis methods involving carbamate protection of the amino function. These amino acid surrogates can be used without protection of the N_α group, or (preferably) in the form of their N_α-benzyl–N_β-Boc (or Fmoc) derivatives (R^2 = benzyl in **37**) which can be prepared[36] from the corresponding *N*-benzyl amino acids by the oxaziridine methodology reported here.

For solubility reasons, it was necessary to convert in situ the starting amino acids **35** into their benzyltrimethyl or tetrabutylammonium salts **35a**; these salts are soluble in CH_2Cl_2 and $CHCl_3$. Their reaction with oxaziridines **2a** or **4a** turned out to be very fast and in all cases was complete within less than one hour at −30 to −15 °C (Table 6). This acceleration of the reaction with respect to that of simple amines is certainly due to the ionization of the carboxylic acid group, which enhances the basicity and nucleophilic character of the amino group, as evidenced by the pK_a increase on going from Val–OMe (7.6) to Val–O^- (9.7).[37] *N*-Moc and *N*-Boc hydrazinoproline (**37a** and **b**) were thus obtained in 85 and 95% yield, respectively, while *N*-Moc hydrazino acids **37d–m** deriving from primary amino acids were obtained in 48–75% yield, with in all cases less than 15% of imine **38**. Lowering the temperature has a favorable effect on the hydrazine (**36**) *vs.* imine (**38**) ratio; with valine, imine formation was almost suppressed at −15 °C (entries 4 and 5 of Table 6). The workup was particularly simple. In the case of the water-soluble N_β-Moc derivatives **37a** and **37d–m** the resulting ammonium salt **36** was extracted into water, the ammonium cation was eliminated by means of a strongly acidic ion-exchange resin and the released acid was lyophilized. The acid-sensitive N_β-Boc derivatives **37b** and **37n–r**, and the lipophilic hydrazinodipeptide **37c** were precipitated from the aqueous phase at pH 3 or were extracted.

N_β-Moc hydrazino acids **37e–m** bearing functional groups on the side chains were prepared in good yields by this method (Table 6, entries 5–14). We used the conventional Bzl and Z protections of the basic side chains of tyrosine (phenate) or lysine (primary amine). In **37i** and **37m** these protecting groups could subsequently be removed by catalytic hydrogenation without noticeable cleavage of the N–N bond, to yield **37i'** (97%) and **37m'** (85%), respectively. The imidazole and indole side chains in histidine and tryptophan did not require protection, only the primary amino group being sufficiently reactive to be aminated by oxaziridine **2a** under these conditions.

Table 6. Amination of aminoacids by oxaziridines **2a** and **4a**.

Entry	Amino acid	R^1	R^2	Protecting group	Product (**37**)	*T* (°C)	Yield (%)	$[\alpha]_D^{25}$	Solvent
1	L-Pro	$(CH_2)_4$		Moc	**a**	−15	85	−61.8	95% EtOH
2	L-Pro	$(CH_2)_4$		Boc	**b**	−15	95	−41.2	95% EtOH
3	L-Pro–L-Leu	(see Scheme 6)		Moc	**c**	−15	72	−53.0	95% EtOH
4	L-Val	*i*Pr	H	Moc	**d**	0	57 [a]		
5	L-Val	*i*Pr	H	Moc	**d**	−15	70 [b]	−36.5	95% EtOH
6	Gly	H	H	Moc	**e**	−15	65 [c]		
7	D-Phg	Ph	H	Moc	**f**	−15	72 [c]	−60.8	$CHCl_3$
8	DL-Phg	Ph	H	Moc	**g**	−15	75 [c]		
9	L-Phe	Bzl	H	Moc	**h**	−15	60	−5.6	MeOH
10	L-Tyr(OBzl)	4-Bzl–$OC_6H_4CH_2$	H	Moc	**i**	−15	67	+16.1	DMSO
11	L-Ser	CH_2OH	H	Moc	**j**	−15	48 [c]	−21.2	MeOH
12	L-His	4-methyleneimidazole	H	Moc	**k**	−15	67	+7.5	H_2O
13	L-Trp	3-methyleneindole	H	Moc	**l**	−15	55	−16.4	95% EtOH
14	L-Lys(εZ)	$(CH_2)_4CO_2Bzl$	H	Moc	**m**	−15	65	−5.5	MeOH
15	L-Ala	Me	H	Boc	**n**	−30	50 [d]	−20.4	MeOH
16	L-Phe	Bzl	H	Boc	**o**	−30	36	+20.0	DMF
17	L-Val	*i*Pr	H	Boc	**p**	−30	21 [e]	−12.6	CH_2Cl_2
18	L-Ala	Me	Bzl	Boc	**q**	0	88	+22.8	methanol
19	L-Val	*i*Pr	Bzl	Boc	**r**	0	68	+25.6	methanol

[a] The hydrazine/imine (**36**/**38**) ratio was 85:15 (^{1}H NMR of the crude reaction mixture). [b] Hydrazine/imine ratio 97:3. [c] Dicyclohexylammonium salt. [d] Hydrazine/imine ratio 85:15 at −30 °C. [e] Hydrazine/imine ratio 55:45 at 0 °C and 75:25 at −30 °C.

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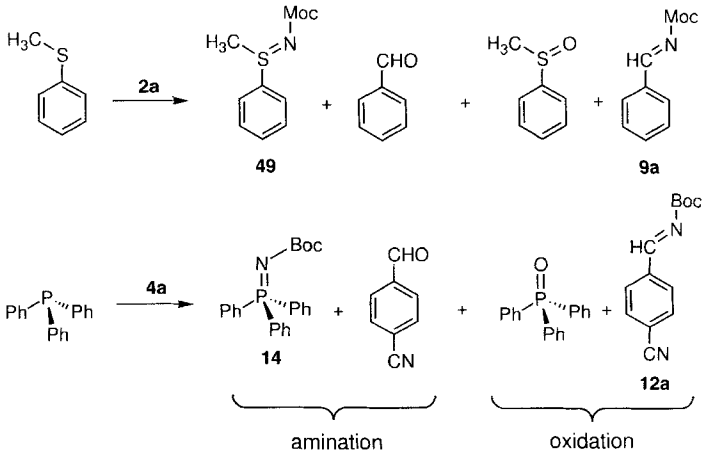
The reaction of **4a** with primary amino acids such as alanine, phenylalanine, and valine to give the corresponding *N*-Boc hydrazino acids **37n–p** proved somewhat less efficient than that of **2a**, essentially because relatively larger amounts of imine **38** were formed, even at −30 °C (Table 6, entries 15–17). A further complication arose in the case of alanine and valine where oxazolidinones **39n** and **p** (Scheme 6) were isolated besides the desired N_β-Boc hydrazino acids. These oxazolidinones, which were not present in the final reaction mixture, were in fact formed during the workup, by reaction of **37n** or **37p** with the 4-cyanobenzaldehyde resulting from acidic hydrolysis of the corresponding imines **38**. We were unable to suppress this side reaction. Separate experiments confirmed that **37n** and 4-cyanobenzaldehyde reacted rapidly in chloroform to give **39n**. In spite of these circumstances, this straightforward one-pot synthesis of **37n–p** turns out to be at least as efficient as the previously reported multistep synthesis of the same compounds.[38] Alternatively, the use of *N*-benzyl amino acids as starting materials furnishes the orthogonally protected N_β-Boc–N_α-Bzl hydrazino acids in excellent yield (e.g., **37q–r**, entries 18–19 in Table 6).

Racemization is not normally a critical problem here because the asymmetric center is not involved in the amination reaction. However, there is a risk that some racemization occurs during the preliminary step where the amino acid is converted to its R_4N^+ salt **35a**. We examined this question in the case of phenylglycine, which is easily racemizable. To this end, the *N*-Moc derivative **37f** resulting from the reaction of (*R*)-phenylglycine with **2a** was coupled with (*S*)-(−)-α-methylbenzylamine (DCC/HOBt) to give **40**. The ^{1}H NMR spectrum of **40** showed that only a trace amount of the (*SS*) diastereomer was present, and this result means that the enantiomeric excess of **37f** was certainly greater than 95%. The same conclusion was drawn for **37d**, which on reaction with iodotrimethylsilane[39] afforded (*S*)-(+)-hydrazinovaline (73%) showing the same rotation as that of a reference sample.[38]

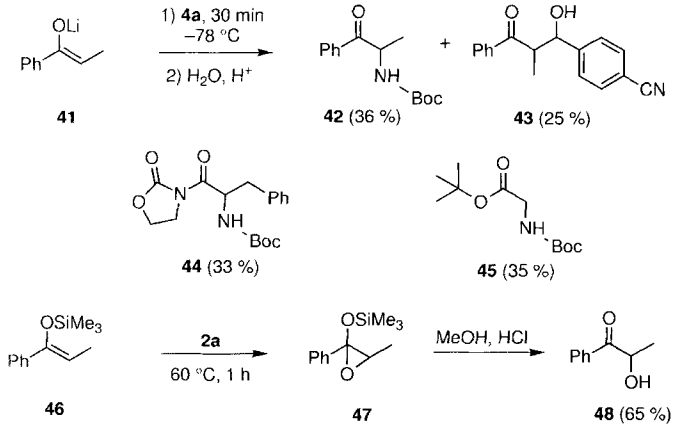
Reaction of *N*-alkyloxycarbonyl oxaziridines with carbon nucleophiles: The reaction of these oxaziridines with various enolates proved to be fast and afforded the electrophilic amination product in modest yield, owing to the occurrence of a parallel aldol condensation between the released aldehyde and the enolate (Scheme 7). Propiophenone lithium enolate thus reacted with **4a** in less than 30 min at −78 °C to give racemic *N*-Boc cathinone **42** (36%) together with aldol **43** (25%). The amine/aldol ratio was not significantly dependent on the reaction conditions. Direct or inverse trapping of the enolate, exchange of lithium for sodium or potassium, or change of the temperature at which the reaction was conducted gave identical results. The reaction of **4a** with amide and ester enolates similarly afforded the α-*N*-Boc amino compounds **44** (33%) and **45** (35%) together with the corresponding aldols. It is noteworthy that the α-hydroxyketone **48** was not detected in the crude reaction mixture of lithium enolate **41** and **4a**, whereas it is produced in good yield from the corresponding potassium enolate and *N*-sulfonyl oxaziridines.[40]

Propiophenone silyl enol ether **46** was not aminated in the presence of oxaziridine **2a**, but instead the double bond was epoxidized (60 °C, 1 h) to give the unstable epoxide **47**, which in turn afforded **48** in 65% overall yield. In contrast, a simple alkene such as cyclohexene did not react with **2a**, even after several hours at 60 °C, although the same substrate can be aminated by oxaziridine **1**[1] and epoxidized by *N*-sulfonyl oxaziridines.[13]

Reactivity of *N*-alkyloxycarbonyl oxaziridines with phosphorus and sulfur nucleophiles: We also examined the reactivity of *N*-alkyloxycarbonyl oxaziridines **2a** or **4a** towards representative sulfide and phosphine nucleophiles (Scheme 8 and Table 7). The



Scheme 8. Amination vs. oxidation of S and P nucleophiles.



Scheme 7. Amination or oxidation of carbon nucleophiles.

results are qualitatively similar to those reported above for the reaction of **2a** with triethylamine. Thioanisole reacted rapidly with oxaziridine **2a** (less than 15 min, RT, $CDCl_3$; entry 1) to give a four-component mixture consisting of 34% of a 1:1 mixture of sulfilimine[41] **49** and benzaldehyde (resulting from amination of thioanisole) and 66% of a 1:1 mixture of methylphenylsulfoxide and imine **9a** (resulting from oxidation of thioanisole). The composition of this mixture did not change on standing for 24 h at room temperature, indicating that there is no cross-reaction between **49** and benzaldehyde to give methylphenylsulfoxide and **9a**. We conclude that amination and oxidation of thioanisole in the presence of **2a** proceed in parallel. Amination is favored at low temperature (Table 7, entries 1–4), suggesting that this reaction is under kinetic control, and

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Table 7. Amination vs. oxidation in the reaction of thioanisole and triphenylphosphine with oxaziridines **2a** and **4a**.

Entry	Nucleophile	Oxaziridine	Concentration (mol L^{-1})	Solvent	T (°C)	Amination/oxidation
1	PhSMe	**2a**	0.5	$CDCl_3$	19	34:66
2	"	"	0.1	$CDCl_3$	19	34:66
3	"	"	0.5	$CDCl_3$	0	45:55
4	"	"	0.5	$CDCl_3$	−34	52:48
5	"	"	0.4	Et_2O	0	15:85
6	"	"	0.5	CH_3CN	19	48:52
7	"	"	0.5	CH_3CN	0	58:42
8	"	"	0.5	CH_3CN	−35	67:33 [a]
9	Ph_3P	**4a**	0.1	$CDCl_3$	19	45:55
10	"	"	0.1	$CDCl_3$	0	51:49
11	"	"	0.1	Et_2O	19	40:60
12	"	"	0.1	CH_3CN	19	65:35
13	"	**2a**	0.1	$CDCl_3$	19	65:35

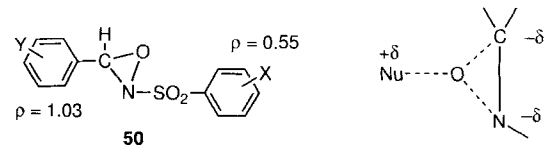
[a] Methyl phenyl sulfilimine **49** and methyl phenyl sulfoxide were isolated in 50% and 26% yield, respectively.

in polar solvents, probably because of the highly dipolar character of sulfilimine **49**.

A similar product distribution was observed when triphenylphosphine was allowed to react with oxaziridine **4a** to give phosphinimine **14** and 4-cyanobenzaldehyde (amination), together with triphenylphosphine oxide and imine **9a** (oxidation; Table 7, entries 9–13). The reaction was fast even at −94 °C (35% conversion in less than 30 min in CD_2Cl_2)[42] where the amination/oxidation ratio reached 95:5. No further species (such as oxazaphosphetane or betaine intermediates)[43] were detected by ^{31}P NMR spectroscopy of the reaction mixture in the range $\delta = -150$ to $+50$ at −94 °C. At room temperature, the aza-Wittig reaction between the amination products **14** and 4-cyanobenzaldehyde to give the oxidation products **12a** and triphenylphosphine oxide is kinetically blocked.[44] In this case also, amination and oxidation are parallel reactions, and it seems that amination is under kinetic control while oxidation is under thermodynamic control, reflecting the affinity of phosphorus for oxygen. Oxidation is slightly preferred in the case of **4a**, which is bulkier than **2a** (entries 9 and 13).

Nitrogen vs. oxygen transfer: As already stated, some oxaziridines deliver their nitrogen atom whereas others deliver their oxygen, and the dual behavior is rarely observed. These reactions have in common their speed (generally) and high exothermicity, and are considered to involve the attack of a nucleophilic species to an electrophilic site of the oxaziridine, which may be either the oxygen or the nitrogen atom. Several mechanisms can be postulated to account for the course of these reactions, but thus far the reaction profile, the existence of intermediate species, and the factors that orient towards amination or oxidation are still a matter of discussion.

N-sulfonyl,[13] *N*-phosphinoyl,[14] and *N*-perfluoroalkyl oxaziridines[15] deliver their oxygen atoms to a variety of nucleophiles (sulfides, enolates, and alkenes) with no example of the inverse behavior. Chiral camphorsulfonyl oxaziridines[13] perform enantioselective *C*-hydroxylation of enolates (40–96% *ee*), which indicates that the reaction is attended with some steric or stereoelectronic control. For *N*-sulfonyl oxaziridines, Davis and coworkers postulated a symmetrical transition state with a negative charge developing both on the oxaziridine carbon and nitrogen atoms (Scheme 9).[45] These views were later refined by ab initio calculations of the reaction of the parent oxaziridine ring with ethylene,[46] and more recently with a sulfide or a sulfoxide[47] and a lithium enolate.[48] Although these calculations give consistency to the electrophilic character of the oxaziridine oxygen, their chemical relevance is questionable because, as can be anticipated from the results of Schmitz, this type of oxaziridine is expected to transfer its nitrogen, not its oxygen, to nucleophiles.



Scheme 9. Hammett correlations and postulated transition state for O transfer from Davis *N*-sulfonyl oxaziridines to nucleophiles (ref. [45]).

N-R-substituted oxaziridines with R = H and acyl,[1] alkyl,[49] or chlorine[50] generally tranfer their nitrogen and occasionally transfer their oxygen. Hata and Watanabe[49] have studied the reaction of oxaziridines bearing various *N*-alkyl groups with amines, phosphines, arsines, sulfides, thiols, and selenides. With small alkyl groups, only the ylide Nu^+-N^--R is formed. When the size of the group increases some oxide Nu^+-O^- is also observed. Our group has shown that the reaction of **2a** with chiral amines (proline and ephedrine derivatives) is attended by a moderate kinetic resolution of the oxaziridine;[51] this means that, as in the case of oxygen transfer, the nitrogen transfer is under steric or stereoclectronic control.

In order to reveal features that would account for the opposite reactivities of these two classes of compounds, we performed semiempirical MO calculations on **2a** and on its *N*-methylsulfonyl congener **50** (a model of Davis oxaziridines). These calculations were done on a qualitative basis with the AM1 method (MOPAC). The starting geometry of **2a** was the X-ray structure, which was relaxed in the MMX force field.[52] The structure of **50** was derived from that of **2a** by replacing the CO_2Me by a SO_2Me group; only the $N-SO_2-Me$ fragment was relaxed, in order to keep the phenyloxaziridine moiety identical in the two structures. The MO calculations were then performed without further geometry optimization. The Gasteiger charges and the LUMOs are shown in Figure 2. It is apparent that the LUMOs of **2a** and **50** do not differ significantly from one another and essentially consist of antibonding σ* NO fragments. These MOs are in fact quite similar to the LUMO of the parent oxaziridine ring,[47] and account well for the electrophilic nature of both nitrogen and oxygen. In **2a** the orbital coefficient is slightly larger on the nitrogen than on the oxygen, whereas in **50** the coefficient is the same on these two sites. Even if this difference reflects the good trend, it does not seem to be large enough to explain the opposite reactivities of these two compounds. The most salient difference is the fact that the LUMO of **50** is substantially lower in energy[53] (by ≈2.3 eV) than the LUMO of **2a**. Considering the charges, the oxaziridine nitrogen is almost neutral in both systems, while the oxygen bears an excess of ca. 0.25 e$^-$, which makes this site strongly negative. If these cal-

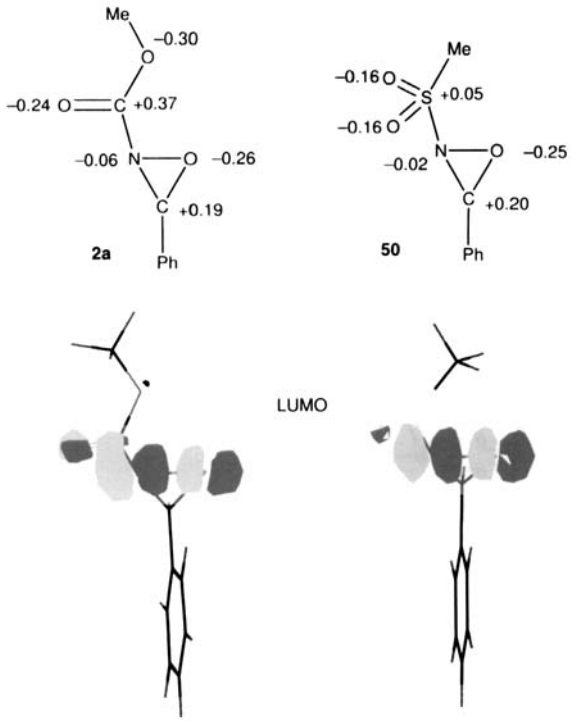
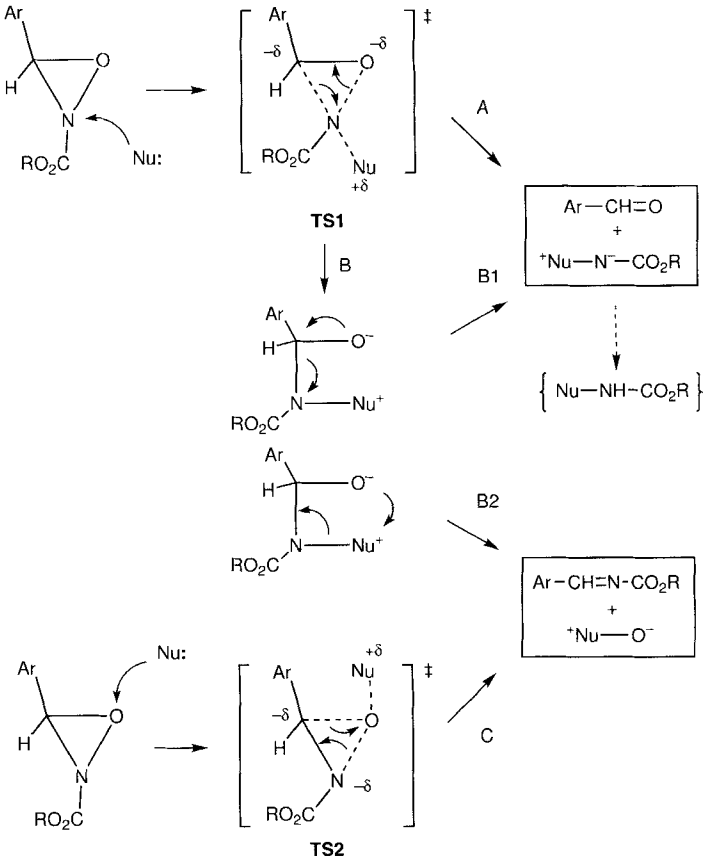


Figure 2. Gasteiger charges and sketch of the LUMO for oxaziridines **2a** and **50** (AM1 method).

culations are correct, then O transfer from Davis oxaziridines should be the consequence of a high degree of orbital control due to the low energy of the LUMO, favoring the attack of soft nucleophiles, combined with steric repulsion making the nucleophile approach to the nitrogen side difficult. N transfer from **2a** seems to result from a lack of steric and electrostatic repulsion at the nitrogen site (whereas the oxygen is negatively charged), with the orbital frontier control favoring harder nucleophiles in view of the higher energy of the LUMO. We wish to stress, however, that the concept of hardness or softness does not help very much in predicting which heteroatom will be transfered to the nucleophile, because whatever the oxaziridine class the LUMO coefficients at oxygen and nitrogen are equivalent. The degree of steric hindrance in the first sphere around the nitrogen atom seems to be a more reliable parameter from which to predict the orientation of the reaction, as judged from the data assembled in Table 8, where the substituent size (expressed as the *A* value) is apparently correlated with the O or N transfer properties: large groups favor oxidation, whereas small groups favor amination.

We have implicitly assumed that O transfer proceeds by attack of the nucleophile at the oxaziridine oxygen (and at the nitrogen for N transfer). However, alternative mechanisms in which O (or N) transfer would result from the opposite attack to N (or O) can also be advanced. This question is relevant for N-transferring oxaziridines that occasionally perform O transfer, as observed in the reactions of Et_3N, PhSMe, and Ph_3P with **2a**. In Scheme 10, we have sketched the two situations in which



Scheme 10. Possible mechanisms for amination and oxidation of nucleophiles by **2a**.

Nu···N and Nu···O attacks lead to transition states TS1 and TS2, respectively, for N-transferring oxaziridines reacting with a nucleophile Nu. These transition states are essentially similar to those postulated by Davis (Scheme 9), the increase of negative charge spread over the oxaziridine ring being justified by the Hammett correlations discussed above. If in the case of Davis oxaziridines a direct fragmentation of TS2 to Nu^+-O^- (path C, supported by ab initio calculations) seems likely, we suspect that this mechanism does not hold in the case of N transferring oxaziridines where both amination and oxidation probably result from Nu···N attack leading to TS1. This transition state can fragment either in a concerted way (path A) to yield $Nu^+-N^--CO_2R$ (followed by fast prototropy to Nu–NH–CO_2R in the case of non-tertiary amines or in general of protic nucleophiles), or via a betaine intermediate (path B). This betaine can then fragment to the amination product (path B1) or the oxidation product (path B2). The existence of betaine intermediates in such reactions has been postulated by Schmitz.[1] Although there is no experimental evidence for their existence, we have several arguments to support this hypothesis in the case of the reaction of **2a** with nitrogen, sulfur, and

Table 8. Nitrogen vs. oxygen transfer to nucleophiles as a function of the *A* value of the oxaziridine nitrogen substituent.

N substituent	*t*Bu	SO_2Me	Ph_2PO	CF_3	Me	CO_2Me	Cl	H
A value [a]	4.8	2.5	2.5	2.5	1.8	1.2	0.6	0
RSMe	O	O	O	O	N[b]	O/N		
RNH_2,RR'NH	– [c]	O			N	N	N	N

[a] In kcal mol^{-1}. [b] Amination has been postulated to occur in the initial stage of the reaction; for details see ref. [49]. [c] No reaction.

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phosphorus nucleophiles. Firstly, hindered secondary amines are aminated slowly, but in spite of this, are not oxidized. This suggests that a direct oxidation of Et_3N by Nu···O attack is unlikely. Secondly, the fact that the amination of Ph_3P, PhSMe, or Et_3N is favored at low temperature again supports the occurrence of a Nu···N attack producing TS1; then, at least a fraction of the reaction would follow path B where oxidation proceeds via path B2. These concepts possibly do not apply to carbon nucleophiles; we cannot yet provide any entirely consistent model for their reactivity with **2a** and other oxaziridines.

Experimental Section

General: ^1H, ^{13}C, and ^{31}P NMR spectra were recorded on Bruker AC200 or Varian Unity$^+$ 500 spectrometers. Melting points were measured by means of a Perkin-Elmer DSC7 microcalorimeter, with simultaneous check of purity. Specific rotations $[\alpha]$ (in $10^{-1}\,°\,cm^2\,g^{-1}$) were measured on a Perkin-Elmer 241 micropolarimeter in a 1 dm quartz cell at constant temperature (25 °C). Infrared spectra were recorded on a Perkin-Elmer FTIR 1600 spectrometer. Microanalysis and mass spectra were performed by the Service central d'analyses du Centre National de la Recherche Scientifique (Vernaison, France). Chromatographic separations were performed over silica gel 60 (Merck; 0.040–0.063 mm). Glassware was dried at 120 °C for several hours and cooled under argon prior to utilization. Hexamethyldisilazane (HMDS) was distilled over CaH_2 under argon. Tetrahydrofuran (THF) was dried over Na/benzophenone. Chlorotrimethylsilane (TMSCl) was distilled over quinoline under argon immediately before use. Hexane was dried by distillation over P_4O_{10} or by filtration through basic alumina (activity I), and was kept over 4 Å molecular sieves. Dry chloroform (for the preparation of acylimines) was obtained by distillation over P_4O_{10} followed by filtration through basic alumina (activity I) immediately before use.

***N*-Trimethylsilylbenzaldimine (8a)**: Following the method of Hart et al.[54] benzaldehyde (28 mL, 0.276 mol) afforded **8a** (39.75 g, 84%); yellow oil, b.p. 50–55 °C/0.04 Torr (refs. [55] b.p. 60–61 °C/0.1 Torr and [54] 45 °C/0.15 Torr). ^1H NMR ($CDCl_3$): $\delta = 0.27$ (s, 9H, $Si(CH_3)_3$), 7.41–7.44 (m, 3H, arom. H's), 7.78–7.82 (m, 2H, arom. H's), 8.98 (s, 1H, CH=N).

General procedure for the preparation of silylimines 8b–i: HMDS (7.4 mL, 35 mmol) was placed under argon in a septum-stoppered and magnetically stirred 50 mL three-necked flask; the flask was cooled to 0 °C and a solution of BuLi in hexane (1.6 M, 20 mL, 32 mmol) was slowly added from a syringe. After 10 min stirring at 0 °C, a solution of freshly distilled X-substituted benzaldehyde **7** (32 mmol) in 5 mL of THF was slowly added with a syringe. The reaction mixture was stirred for 1 h at room temperature, concentrated in vacuo, then treated with chlorotrimethylsilane (4.1 mL, 32 mmol). After 1 h, dry hexane (10 mL) was added, resulting in the precipitation of LiCl, which was filtered under argon through a sintered glass funnel covered with dry Na_2SO_4, and washed with a small quantity of dry hexane. The filtrate was concentrated and distilled in vacuo to give silylimines **8b–i** as extremely moisture-sensitive yellow liquids, which were immediately converted to the corresponding acylimines **9**, **15**, or **20** as described below.

***N*-Trimethylsilyl-4-methylbenzaldimine (8b)**: From *p*-tolualdehyde (3.84 g), imine **8b** (2.57 g, 42%) was obtained. Yellow liquid, b.p. 50–53 °C/0.08 mbar (ref. [55] 50–51 °C/0.02 Torr); ^1H NMR ($CDCl_3$): $\delta = 0.24$ (s, 9H, $Si(CH_3)_3$), 2.38 (s, 3H, CH_3), 7.24 (m, 2H, arom. H's), 7.68 (m, 2H, arom. H's), 8.93 (s, 1H, CH=N).

***N*-Trimethylsilyl-4-fluorobenzaldimine (8c)**: From 4-fluorobenzaldehyde (3.97 g), imine **8c** (4.43 g, 71%) was obtained. Yellow liquid, b.p. 37–40 °C/0.1 mbar; ^1H NMR ($CDCl_3$): $\delta = 0.23$ (s, 9H, $Si(CH_3)_3$), 7.04–7.13 (m, 2H, arom. H's), 7.74–7.81 (m, 2H, arom. H's), 8.91 (s, 1H, CH=N).

***N*-Trimethylsilyl-4-chlorobenzaldimine (8d)**: From 4-chlorobenzaldehyde (4.50 g), imine **8d** (6.09 g, 90%) was obtained. Yellow liquid, b.p. 58–65 °C/0.03 mbar; ^1H NMR ($CDCl_3$): $\delta = 0.25$ (s, 9H, $Si(CH_3)_3$), 7.36–7.40 (m, 2H, arom. H's), 7.69–7.73 (m, 2H, arom. H's), 8.90 (s, 1H, CH=N).

***N*-Trimethylsilyl-4-trifluoromethylbenzaldimine (8e)**: From 4-trifluoromethylbenzaldehyde (5.57 g), imine **8e** (4.37 g, 55%) was obtained. Yellow liquid, b.p. 47–57 °C/0.1 mbar; ^1H NMR ($CDCl_3$): $\delta = 0.26$ (s, 9H, $Si(CH_3)_3$), 7.65–7.69 (m, 2H, arom. H's), 7.87–7.91 (m, 2H, arom. H's), 8.99 (s, 1H, CH=N).

***N*-Trimethylsilyl-4-cyanobenzaldimine (8f)**: From 4-cyanobenzaldehyde (4.20 g), imine **8f** (5.43 g, 84%) was obtained. Yellow solid at room temperature, b.p. 95–100 °C/0.5 mbar; ^1H NMR ($CDCl_3$): $\delta = 0.24$ (s, 9H, $Si(CH_3)_3$), 7.67–7.71 (m, 2H, arom. H's), 7.84–7.88 (m, 2H, arom. H's), 8.95 (s, 1H, CH=N).

***N*-Trimethylsilyl-2-chlorobenzaldimine (8g)**: From 2-chlorobenzaldehyde (4.50 g) imine **8g** (4.95 g, 73%) was obtained. Yellow liquid, b.p. 102–108 °C/0.08 mbar; ^1H NMR ($CDCl_3$): $\delta = 0.25$ (s, 9H, $Si(CH_3)_3$), 7.26–7.36 (m, 3H, arom. H's), 7.98–8.03 (m, 1H, arom. H's), 9.35 (s, 1H, CH=N); ^{13}C NMR ($CDCl_3$): $\delta = -1.2$, 126.8, 127.9, 129.7, 131.9, 135.0, 136.3, 165.1.

***N*-Trimethylsilyl-3-chlorobenzaldimine (8h)**: From 3-chlorobenzaldehyde (4.50 g), imine **8h** (4.27 g, 63%) was obtained. Yellow liquid, b.p. 80–85 °C/0.1 mbar; ^1H NMR ($CDCl_3$): $\delta = 0.24$ (s, 9H, $Si(CH_3)_3$), 7.29–7.42 (m, 2H, arom. H's), 7.59–7.64 (m, 1H, arom. H), 7.79 (m, 1H, arom. H), 8.89 (s, 1H, CH=N); ^{13}C NMR ($CDCl_3$): $\delta = -1.2$, 128.9, 127.9, 129.8, 131.1, 134.9, 140.5, 166.6.

***N*-Trimethylsilyl-2,4-dichlorobenzaldimine (8i)**: From 2,4-dichlorobenzaldehyde **7i** (4.37 g), imine **8i** (4.73 g, 77%) was obtained. Yellow solid, b.p. 95–100 °C/0.2 mbar, m.p. 48 °C; ^1H NMR ($CDCl_3$): $\delta = 0.24$ (s, 9H, $Si(CH_3)_3$), 7.26 (d, $J = 8.2$ Hz, 1H, arom. H's), 7.37 (s, 1H, arom. H's), 7.96 (d, $J = 8.2$ Hz, 1H), 9.25 (s, 1H, CH=N); ^{13}C NMR ($CDCl_3$): $\delta = -1.2$, 127.5, 129.1, 129.6, 133.6, 136.8, 163.8.

General procedure for the preparation of *N*-methoxycarbonylimines 9a–h, *N*-benzyloxycarbonylimine (15) or *N*-fluorenylmethoxycarbonylimine (20): The following procedure is essentially that of Kupfer et al.[171] A solution of the appropriate chloroformate (10 mmol) in dry $CHCl_3$ (15 mL) was added dropwise to a solution of silylimine **8a–h** (10 mmol) in the same solvent (15 mL) under argon. The reaction mixture was kept at room temperature, or refluxed, until the yellow color of the silylimine had disappeared. After evaporation of the solvent (rotatory evaporator), the crude product was either distilled (**9a**, **9d**) or recrystallized from a dry solvent to give the desired alkyloxycarbonylimine.

***N*-Methoxycarbonylbenzaldimine (9a)**: According to the above procedure, silylimine **8a** (39.75 g) afforded **9a** (29.21 g, 80%) after 1 h reflux and distillation. B.p. 75–80 °C/0.06 mbar (ref. [17] 64 °C/0.03 Torr); ^1H NMR ($CDCl_3$): $\delta = 3.88$ (s, 3H, OCH_3), 7.40–7.49 (m, 3H, arom. H's), 7.87–7.91 (m, 2H, arom H's), 8.92 (s, 1H, CH=N).

***N*-Methoxycarbonyl-4-methylbenzaldimine (9b)**: Silylimine **8b** (2.57 g) afforded **9b** (1.83 g, 77%) after 1.5 h at room temperature and recrystallization from hexane. Colorless crystals, m.p. 78 °C; ^1H NMR ($CDCl_3$): $\delta = 2.41$ (s, 3H, CH_3), 3.89 (s, 3H, OCH_3), 7.27 and 7.81 (2 d, 2×2H, $J = 8.1$ Hz, arom. H's), 8.93 (s, 1H, CH=N); ^{13}C NMR ($CDCl_3$): $\delta = 21.9$, 53.9, 129.8, 130.5, 131.3, 145.1, 164.5, 171.5; anal. calcd for $C_{10}H_{11}NO_2$ (%): C 67.78, H 6.26, N 7.90; found: C 67.50, H 6.31, N 8.00.

***N*-Methoxycarbonyl-4-fluorobenzaldimine (9c)**: Silylimine **8c** (4.43 g) afforded **9c** (3.17 g, 77%) after 2 h at RT and recrystallization from THF/hexane. Colorless crystals, m.p. 60 °C; ^1H NMR ($CDCl_3$): $\delta = 3.88$ (s, 3H, OCH_3), 7.14 and 7.92 (2m, 2×2H, arom. H's), 8.89 (s, 1H, CH=N); ^{13}C NMR ($CDCl_3$): $\delta = 53.97$, 116.3 (d, $^2J_{C-F} = 22$ Hz), 130.2 (d, $^4J_{C-F} = 3$ Hz), 132.7 (d, $^3J_{C-F} = 9$ Hz), 164.1 (CH=N), 166.2 (d, $^1J_{C-F} = 256$ Hz), 169.8; anal. calcd for $C_9H_8FNO_2$ (%): C 59.67, H 4.45, N 7.73; found: C 58.54, H 4.44, N 7.55.

***N*-Methoxycarbonyl-4-chlorobenzaldimine (9d)**: Silylimine **8d** (6.09 g) afforded **9d** (3.98 g, 70%) after 1 night at room temperature and recrystallization from hexane. Colorless crystals, m.p. 84.5 °C; ^1H NMR ($CDCl_3$): $\delta = 3.88$ (s, 3H, OCH_3), 7.41–7.44 (m, 2H, arom. H's), 7.80–7.85 (m, 2H, arom. H's), 8.87 (s, 1H, CH=N); ^{13}C NMR ($CDCl_3$): $\delta = 54.0$, 129.3, 131.35, 132.2, 140.15, 163.95 (NCO_2), 169.7 (CH=N); anal. calcd for $C_9H_8ClNO_2$ (%): C 54.70, H 4.08, N 7.09; found: C 54.86, H 4.14, N 7.13.

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***N*-Methoxycarbonyl-4-trifluoromethylbenzaldimine (9e)**: Silylimine **8e** (4.37 g) afforded **9e** (2.30 g, 56%) after 3 h reflux and recrystallization from hexane. Colorless crystals, m.p. 79 °C; ^{1}H NMR ($CDCl_3$): δ = 3.92 (s, 3H, OCH_3), 7.73 and 8.02 (2d, 2×2H, J = 8 Hz, arom. H's), 8.94 (s, 1H, CH=N); ^{13}C NMR ($CDCl_3$): δ = 54.2, 123.5 (q, $^1J_{C-F}$ = 272 Hz, CF_3), 125.9 (q, $^3J_{C-F}$ = 3.8 Hz), 130.3, 134.9 (q, $^2J_{C-F}$ = 33 Hz), 136.8, 163.8 (NCO_2), 169.1 (CH=N); anal. calcd for $C_{10}H_8F_3NO_2$ (%): C 51.96, H 3.49, N 6.06; found: C 51.73, H 3.40, N 6.08.

***N*-Methoxycarbonyl-4-cyanobenzaldimine (9f)**: Silylimine **8f** (5.43 g) afforded **9f** (2.53 g, 50%) after 3 h reflux and recrystallization from THF; colorless crystals, m.p. 177 °C. ^{1}H NMR ($CDCl_3$): δ = 3.92 (s, 3H, OCH_3), 7.76 and 8.00 (2d, 2×2H, J = 8.2 Hz, arom. H's), 8.89 (s, 1H, CH=N); ^{13}C NMR ($CDCl_3$): δ = 54.3, 116.8, 117.8, 130.3, 132.7, 137.5, 163.6 (NCO_2), 168.4 (CH=N); anal. calcd for $C_{10}H_8N_2O_2$ (%): C 63.83, H 4.28:N, 14.89; found: C 63.80, H 4.29, N 14.58.

***N*-Methoxycarbonyl-2-chlorobenzaldimine (9g)**: Silylimine **8g** (4.95 g) afforded **9g** (3.65 g, 79%) after 1 night at room temperature and distillation. B.p. 100–105 °C/0.08 mbar, m.p. ≈ 10 °C; ^{1}H NMR ($CDCl_3$): δ = 3.90 (s, 3H, OCH_3), 7.28–7.51 (m, 3H, arom. H's), 8.16 (dd, 1H, J = 1.5 and 7.5 Hz, arom.), 9.32 (s, 1H, CH=N); ^{13}C NMR ($CDCl_3$): δ = 54.0, 127.2, 129.1, 130.2, 131.0, 134.5, 138.0, 164.0 (NCO_2), 167.2 (CH=N); anal. calcd for $C_9H_8ClNO_2$ (%): C 54.70, H 4.08, N 7.09; found: C 54.85, H 4.10, N 7.18.

***N*-Methoxycarbonyl-3-chlorobenzaldimine (9h)**: Silylimine **8h** (4.27 g) afforded **9h** (1.99 g, 50%) after 3 h reflux and recrystallization from hexane; m.p. 65 °C. ^{1}H NMR ($CDCl_3$): δ = 3.91 (s, 3H, OCH_3), 7.37–7.56 (m, 2H, arom. H's), 7.33–7.77 (m, 1H, arom.), 7.92 (m, 1H, arom.), 8.86 (s, 1H, CH=N); ^{13}C NMR ($CDCl_3$): δ = 54.1, 128.7, 129.6, 130.2, 133.7, 135.3, 135.6, 163.9 (NCO_2), 169.6 CH=N); anal. calcd for $C_9H_8ClNO_2$ (%): C 54.70, H 4.08, N 7.09; found: C 54.70, H 4.20, N 7.01.

***N*-Benzyloxycarbonylbenzaldimine (15)**: Silylimine **8a** (2.26 g), after 2 h at 55 °C, afforded **15** as an unstable white solid, which was immediately used without further purification. ^{1}H NMR ($CDCl_3$): δ = 5.30 (s, 2H, CH_2), 7.33–7.49 (m, 8H, arom. H's), 7.88–7.92 (m, 2H, arom.), 8.92 (s, 1H, CH=N).

***N*-Fluorenylmethoxycarbonyl-2,4-dichlorobenzaldimine (20)**: Silylimine **8i** (4.73 g) afforded **20** (7.47 g, 98%) after 20 h at 60 °C and recrystallization from THF/hexane (1:4); m.p. 126 °C. ^{1}H NMR ($CDCl_3$): δ = 4.34 (t, J = 7.1 Hz, 1H), 4.58 (d, J = 7.1 Hz, 2H), 7.27–7.49 (m, 6H), 7.64 (d, J = 7.4 Hz, 2H), 7.77 (d, J = 6.9 Hz, 2H), 8.19 (d, J = 8.5 Hz, 1H), 9.20 (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 46.8, 69.1, 120.1, 125.1, 127.2, 127.9, 129.8, 130.1, 138.6, 140.5, 141.3, 143.4, 163.3, 166.0; anal. calcd for $C_{22}H_{15}Cl_2NO_2$ (%): C 66.68, H 3.82, N 3.53; found: C 66.14, H 3.89, N 3.66.

***N*-Methoxycarbonylbenzophenone imine (11)**: Prepared according to Kupfer[17] from benzophenone imine and methyl chloroformate. Recrystallization from pentane, m.p. 69 °C (ref. [17] m.p. 65–66 °C).

***tert*-Butyl triphenylphosphoranylidenecarbamate (14)**: A solution of *tert*-butyl azidoformate[56] prepared from *tert*-butylcarbazate (13.27 g, 100 mmol) [**Caution**: to avoid the risk of explosion in large-scale preparations, it is not advised to concentrate the ether solution of *tert*-butyl azidoformate] in Et_2O (125 mL) was added dropwise to a suspension of triphenylphosphine (20.6 g, 78.5 mmol) in Et_2O (60 mL) until nitrogen evolution ceased. The white precipitate was filtered and then recrystallized from ethyl acetate to give **14** (23.16 g, 78%), followed by a second crop (4.10 g, 14%). M.p. 148 °C; ^{1}H NMR ($CDCl_3$): δ = 1.30 (s, 9H), 7.34–7.49 (m, 9H), 7.62–7.72 (m, 6H); ^{13}C NMR ($CDCl_3$) identical with that reported earlier.[57]

General procedure for *N*-*tert*-butoxycarbonylimines 12a–d: A mixture of the appropriate benzaldehyde (25 mmol) and iminophosphorane **14** (9.42 g, 25 mmol) was refluxed in dry toluene (17 mL) under argon for the time indicated in Table 2. After cooling, triphenylphosphine oxide was precipitated by addition of dry hexane (17 mL). After filtration and washing twice with a 1:1 mixture of dry toluene and hexane, the filtrate was concentrated in vacuo to give the desired *N*-*tert*-butoxycarbonylimine **12**, which was oxidized without further purification. In the case of **12a**, the crude imine obtained from 4-cyanobenzaldehyde (13.28 g) could be purified by rapid percolation (less than 15 min) through silica gel (350 g, Et_2O/hexane 2:1 as the eluant) to yield **12a** (17.5 g, 75%) as a colorless solid, m.p. 87 °C (from hexane). ^{1}H NMR ($CDCl_3$): δ = 1.57 (s, 9H), 7.74 (d, 2H)) and 7.99 (d, 2H, J = 8.2 Hz), 8.80 (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 27.9, 83.1, 116.4, 117.9, 130.1, 132.5, 137.8, 161.7, 166.7; anal. calcd for $C_{13}H_{14}N_2O_2$ (%): C 67.81, H 6.13, N 12.16; found: C 68.42, H 6.20, N 12.21.

***N*-Methoxycarbonyl-3-phenyloxaziridine 2a (method A, large scale)**: Cold solutions of imine **9a** (21.37 g, 0.131 mol) in amylene-stabilized chloroform (0.35 L) and of K_2CO_3 (128 g) in water (0.8 L) were placed in a three-necked flask (3 L) equipped with an efficient pneumatic stirrer and immersed in an ice-water bath. To this vigorously stirred two-phase mixture was added a chilled solution of oxone (165 g) in water (1.44 L) over 15 min, the internal temperature being kept at 0–4 °C. Stirring was continued for 45 min at this temperature. The water layer was separated and extracted with CH_2Cl_2. The organic layers were combined, washed successively with 5% aqueous $KHSO_4$, 5% aqueous $NaHCO_3$, and water, and dried over $MgSO_4$. The solvent was removed in vacuo (bath temp. < 30 °C) and the crude product was chromatographed over silica gel (220 g, Et_2O/CH_2Cl_2/pentane 1:1:3) to give **2a** (16.05 g, 68%), m.p. 41 °C. ^{1}H NMR ($CDCl_3$), equilibrium mixture of the *trans* and *cis* isomers of **2a** in 91:9 ratio at 300 K: δ = 3.54 (s, 3H, *cis*) and 3.89 (s, 3H, *trans*), 5.09 (s, 1H, *trans*) and 5.34 (s, 1H, *cis*), 7.43 (m, 5H, arom. H's of *cis* and *trans*); ^{13}C NMR ($CDCl_3$), *trans* isomer: δ = 54.9, 78.15, 127.9, 128.6, 131.1, 131.8, 162.6; IR (CCl_4) 1777, 1753 cm^{-1}; anal. calcd for $C_9H_9NO_3$ (%): C 60.33, H 5.06, N 7.82; found: C 60.51, H 4.70, N 7.77.

The corresponding ***N*-methoxycarbonyl benzamide 15a** was isolated on further elution with Et_2O/CH_2Cl_2 1:1, m.p. 118 °C (EtOH). ^{1}H NMR ($CDCl_3$): δ = 3.84 (s, 3H), 7.42–7.58 (m, 3H), 7.77–7.82 (m, 2H), 8.06 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 53.0, 127.7, 128.7, 132.8, 132.9, 151.9, 165.1; anal. calcd for $C_9H_9NO_3$ (%): C 60.33, H 5.06, N 7.82; found: C 59.96, H 5.14, N 7.86.

General procedure for the preparation of oxaziridines 2b–h (method A): A solution of acylimine **9b–h** (2.5 mmol) in amylene-stabilized $CHCl_3$ (12.5 mL) was placed in a 200 mL three-necked flask equipped with a pneumatic stirrer, followed by a chilled solution of K_2CO_3 (2.89 g, 21 mmol) in water (22.5 mL), and the flask was immersed in an ice-water bath. After 10 min a chilled solution of oxone (3.66 g, 6.0 mmol) in water (37 mL) was added to this vigorously stirred two-phase mixture . The mixture was stirred for 1.5 h at 0 °C. If the starting imine was not totally consumed, the aqueous phase was discarded and replaced by fresh solutions of K_2CO_3 and oxone, and the mixture was stirred for a further hour at 0 °C (several such cycles may be required). Then the aqueous phase was separated and extracted with 15 mL of CH_2Cl_2. The combined organic layers were washed three times with water and dried over $MgSO_4$, and the solvent was removed in vacuo (bath temp. < 30 °C). The crude product was flash-chromatographed over silica gel (15 g) with Et_2O/pentane 15:85 as the eluent, to give the desired oxaziridine **2b–h**; next, elution with CH_2Cl_2/Et_2O 1:1 provided the corresponding amide **16b–h**.

***N*-Methoxycarbonyl-3-(4-methylphenyl)oxaziridine (2b)**: In the above procedure, imine **9b** (443 mg) afforded oxaziridine **2b** (119 mg, 25%) and amide **16b** (116 mg, 24%). Oxaziridine **2b**, m.p. 48 °C (decomp.) proved to be very unstable and no elemental analysis could be done. ^{1}H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 91:9 ratio at 300 K: δ = 2.27 (s, 3H, *cis*) and 2.36 (s, 3H, *trans*), 3.57 (s, 3H, *cis*) and 3.88 (s, 3H, *trans*), 5.05 (s, 1H, *trans*) and 5.30 (s, 1H, *cis*), 7.18–7.22 and 7.32–7.36 (2m, 2×2H, arom. H's of *cis* and *trans*); IR (CCl_4): $\tilde{\nu}$ = 1778, 1753 cm^{-1}; ^{13}C NMR ($CDCl_3$): *trans* isomer: δ = 21.4, 54.9, 78.4, 127.0, 127.9, 129.4, 141.5, 162.8.

***N*-methoxycarbonyl-4-methylbenzamide (16b)**: m.p. 137 °C; ^{1}H NMR ($CDCl_3$): δ = 2.40 (s, 3H), 3.84 (s, 3H), 7.26 (m, 2H), 7.69 (m, 2H), 8.03 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 21.6, 53.2, 127.6, 129.6, 130.1, 143.9, 151.7, 164.5; anal. calcd for $C_{10}H_{11}NO_3$ (%): C 62.17, H 5.74, N 7.25; found: C 62.28, H 5.79, N 7.09.

***N*-Methoxycarbonyl-3-(4-fluorophenyl)oxaziridine (2c)**: Similarly, imine **9c** (453 mg) afforded oxaziridine **2c** (300 mg, 61%) and amide **16c** (122 mg, 25%). Oxaziridine **2c** had m.p. 29 °C. ^{1}H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 93:7 ratio at 300 K: δ = 3.56 (s, 3H, *cis*) and 3.89 (s, 3H, *trans*), 5.07 (s, 1H, *trans*) and 5.32 (s, 1H, *cis*), 7.05–7.14 and 7.42–7.49 (2m, 2×2H, arom. H's of *cis* and *trans*); ^{13}C NMR ($CDCl_3$),

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trans isomer: δ = 55.0, 77.5, 115.9 (d, $^2J_{C-F}$ = 22 Hz), 127.8 (d, $^4J_{C-F}$ = 3 Hz), 130.0 (d, $^3J_{C-F}$ = 9 Hz), 162.5, 164.5 (d, $^1J_{C-F}$ = 251 Hz); IR (CCl_4): $\tilde{\nu}$ = 1776, 1753 cm^{-1}; anal. calcd for $C_9H_8FNO_3$ (%): C 54.83, H 4.09, N 7.10; found: C 54.83, H 3.91, N 7.14.

***N*-methoxycarbonyl-4-fluorobenzamide (16c)**: m.p. 111 °C; ^1H NMR ($CDCl_3$): δ = 3.75 (s, 3H), 7.08 (m, 2H), 7.89 (m, 2H), 8.73 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 53.0, 115.8 (d, $^2J_{C-F}$ = 22 Hz), 128.9 (d, $^4J_{C-F}$ = 3 Hz), 130.4 (d, $^3J_{C-F}$ = 9 Hz), 152.0, 164.2, 165.5 (d, $^1J_{C-F}$ = 254 Hz); anal. calcd for $C_9H_8FNO_3$ (%): C 54.83, H 4.09, N 7.10; F 9.63; found: C 54.77, H 4.04, N 7.09; F, 9.41.

***N*-Methoxycarbonyl-3-(4-chlorophenyl)oxaziridine (2d)**: Imine **9d** (494 mg) afforded oxaziridine **2d** (374 mg, 70%), and amide **16d** (100 mg, 19%) after chromatographic workup. Oxaziridine **2d** had m.p. 39 °C. ^1H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 93:7 ratio at 300 K: δ = 3.54 (s, 3H, *cis*) and 3.86 (s, 3H, *trans*), 5.06 (s, 1H, *trans*) and 5.29 (s, 1H, *cis*), 7.36 (brs, 4H, arom. H's of *cis* and *trans*); ^{13}C NMR ($CDCl_3$), *trans* isomer: δ = 54.96, 77.3, 128.9, 129.2, 130.35, 137.2, 162.3; IR (CCl_4): $\tilde{\nu}$ = 1775, 1753 cm^{-1}; anal. calcd for $C_9H_8ClNO_3$ (%): C 50.60, H 3.77, N 6.56; found: C 50.44, H 3.73, N 6.60.

***N*-methoxycarbonyl-4-chlorobenzamide (16d)**: m.p. 155 °C; ^1H NMR ($CDCl_3$): δ = 3.75 (s, 3H), 7.41 and 7.78 (2d, 2 × 2H, J = 8.3 Hz), 8.51 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 53.1, 129.0, 129.2, 131.1, 139.4, 151.8, 164.1; anal. calcd for $C_9H_8ClNO_3$ (%): C 50.60, H 3.77, N 6.56, Cl 16.60; found: C 50.87, H 4.00, N 6.63, Cl 16.86.

***N*-Methoxycarbonyl-3-(4-trifluoromethylphenyl)oxaziridine (2e)**: Similarly, imine **9e** (578 mg) afforded oxaziridine **2e** (321 mg, 52%) and amide **16e** (239 mg, 39%) after chromatographic workup. Oxaziridine **2e** had m.p. 40 °C (by DSC). ^1H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 92:8 ratio at 300 K: δ = 3.56 (s, 3H, *cis*) and 3.91 (s, 3H, *trans*), 5.14 (s, 1H, *trans*) and 5.39 (s, 1H, *cis*), 7.59 and 7.68 (2d, 2 × 2H, J = 8.3 Hz, arom. H's of *cis* and *trans*); ^{13}C NMR (CD_3COCD_3), *trans* isomer: δ = 55.3, 77.3, 124.9 (q, $^1J_{C-F}$ = 270 Hz), 126.5 (q, $^3J_{C-F}$ = 4 Hz), 129.6, 133.1 (q, $^2J_{C-F}$ = 32 Hz), 138.0, 162.7; IR (CCl_4): $\tilde{\nu}$ = 1778, 1756 cm^{-1}; anal. calcd for $C_{10}H_8F_3NO_3$ (%): C 48.59, H 3.26, N 5.67; found: C 46.90, H 3.17, N 5.50.

***N*-Methoxycarbonyl-4-trifluoromethylbenzamide (16e)**: m.p. 153 °C; ^1H NMR ($CDCl_3$): δ = 3.85, 7.73 and 7.91 (2d, 2 × 2H, J = 8.3 Hz, arom. H's), 8.16 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 53.4, 123.4 (q, $^1J_{C-F}$ = 271 Hz), 125.9 (q, $^3J_{C-F}$ = 3.7 Hz), 128.2, 134.5 (q, $^2J_{C-F}$ = 33 Hz), 136.2, 151.6, 164.1; anal. calcd for $C_{10}H_8F_3NO_3$ (%): C 48.59, H 3.26, N 5.67, F 23.06; found: C 48.44, H 3.22, N 5.70, F 23.24.

***N*-Methoxycarbonyl-3-(4-cyanophenyl)oxaziridine (2f)**: Imine **9f** (470 mg) afforded oxaziridine **2f** (229 mg, 45%) and amide **16f** (209 mg, 41%) after chromatographic workup. Oxaziridine **2f** had m.p. 118 °C. ^1H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 93:7 ratio at 300 K: δ = 3.56 (s, 3H, *cis*) and 3.91 (s, 3H, *trans*), 5.14 (s, 1H, *trans*) and 5.37 (s, 1H, *cis*), 7.58 and 7.71 (2d, 2 × 2H, J = 8.2 Hz, arom. H's of *cis* and *trans*); ^{13}C NMR ($CDCl_3$), *trans* isomer: δ = 55.2, 76.7, 115.0, 117.9, 128.7, 132.4, 136.8, 161.9; IR (CCl_4):$\tilde{\nu}$ = 1762 cm^{-1}; anal. calcd for $C_{10}H_8N_2O_3$ (%): C 58.82, H 3.95, N 13.72; found: C 58.54, H 3.90, N 13.62.

***N*-methoxycarbonyl-4-cyanobenzamide (16f)**: m.p. 164 °C; ^1H NMR ($CDCl_3$): δ = 3.84 (s, 3H), 7.76 and 7.88 (2m, 2 × 2H), 8.10 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 53.5, 116.4, 117.6, 128.4, 132.6, 136.7, 151.4, 163.9; anal. calcd for $C_{10}H_8N_2O_3$ (%): C 58.82, H 3.95, N 13.72; found: C 58.56, H 3.80, N 13.46.

***N*-Methoxycarbonyl-3-(2-chlorophenyl)oxaziridine (2g)**: Imine **9g** (494 mg) afforded oxaziridine **2g** (416 mg, 78%), which was isolated by crystallization at 0 °C from a mixture of CH_2Cl_2 and pentane; the amide **16g** was not formed in this case. Oxaziridine **2g** had m.p. 45 °C. ^1H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 90:10 ratio at 300 K: δ = 3.50 (s, 3H, *cis*) and 3.91 (s, 3H, *trans*), 5.59 (s, 1H, *trans*) and 5.64 (s, 1H, *cis*), 7.29–7.34 (m, 4H, arom. H's of *cis* and *trans*); ^{13}C NMR ($CDCl_3$), *trans* isomer: δ = 55.1, 75.2, 127.3, 128.3, 129.5, 129.8, 131.7, 134.9, 162.3; IR (CCl_4): $\tilde{\nu}$ = 1781, 1757 cm^{-1}; anal. calcd for $C_9H_8ClNO_3$ (%): C 50.60, H 3.77, N 6.56; found: C 50.92, H 3.79, N 6.61.

***N*-Methoxycarbonyl-3-(3-chlorophenyl)oxaziridine (2h)**: Imine **9h** (494 mg) afforded oxaziridine **2h** (282 mg, 53%), and amide **16h** (132 mg, 25%) after chromatographic workup. M.p. 31 °C; ^1H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 93:7 ratio at 300 K: δ = 3.58 (s, 3H, *cis*) and 3.89 (s, 3H, *trans*), 5.06 (s, 1H, *trans*) and 5.29 (s, 1H, *cis*), 7.29–7.44 (m, 4H, arom. H's of *cis* and *trans*); ^{13}C NMR ($CDCl_3$), *trans* isomer: δ = 55.1, 77.3, 126.2, 127.9, 130.0, 131.3, 133.9, 134.9, 162.3; IR (CCl_4): $\tilde{\nu}$ = 1781, 1756 cm^{-1}; anal. calcd for $C_9H_8ClNO_3$ (%): C 50.60, H 3.77, N 6.56; found: C 50.85, H 3.47, N 6.72.

***N*-methoxycarbonyl-3-chlorobenzamide (16h)**: M.p. 141 °C; ^1H NMR ($CDCl_3$): δ = 3.84 (s, 3H), 7.40 (m, 1H), 7.53 (m, 1H), 7.67 (m, 1H), 7.80 (m, 1H), 8.24 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 53.3, 125.7, 128.0, 130.1, 133.0, 134.6, 135.0, 151.8, 163.7; anal. calcd for $C_9H_8ClNO_3$ (%): C 50.60, H 3.77, N 6.56; found: C 50.61, H 3.81, N 6.43.

***N*-*tert*-Butoxycarbonyl-3-(4-cyanophenyl)oxaziridine (4a, method A, large scale)**: A solution of crude imine **12a** prepared from 4-cyanobenzaldehyde (0.333 mol, 46 g) in amylene-stabilized $CHCl_3$ (1.1 L) and a chilled solution of K_2CO_3 (160 g, 1.15 mol) in water (1.2 L) were successively placed into a three-necked flask (6 L) equipped with an efficient pneumatic stirrer and immersed in an ice-water bath. After 15 min a chilled solution of oxone (200 g, 0.32 mol) in water (2 L) was added to this vigorously stirred two-phase mixture. After the mixture had been stirred for a further 50 min, the water phase was discarded and replaced by fresh solutions of K_2CO_3 and oxone. A total of 10 such cycles were effected. The organic phase was washed three times with water, dried over $MgSO_4$, and concentrated in vacuo (bath temp. < 30 °C). The crude product was divided in two equal parts, which were flash chromatographed over silica gel (650 g, CH_2Cl_2) to give **2a** (33.9 g, 41% from 4-cyanobenzaldehyde); m.p. 61 °C. ^1H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 88:12 ratio at 300 K: δ = 1.14 (s, 9H, *cis*) and 1.53 (s, 9H, *trans*), 5.04 (s, 1H, *trans*) and 5.33 (s, 1H, *cis*), 7.56 and 7.70 (m, 4H, arom. H's of *cis* and *trans*); ^{13}C NMR (CD_3OD) *trans* isomer: δ = 27.9, 77.3, 86.6, 115.6, 119.1, 129.9, 132.5, 139.3, 161.5; IR (CCl_4): $\tilde{\nu}$ = 1774, 1749 cm^{-1}; anal. calcd for $C_{13}H_{14}N_2O_3$ (%): C 63.40, H 5.73, N 11.38; found: C 63.59, H 5.69, N 11.39.

***N*-Methoxycarbonyl-3,3-diphenyloxaziridine (3, method B)**: A biphasic mixture of imine **11** (0.344 g, 1.44 mmol) in CH_2Cl_2 (10 mL) and a saturated aqueous solution of K_2CO_3 (10 mL) was allowed to react with a solution of technical (50–60%) *m*-chloroperbenzoic acid (1.4 g) in CH_2Cl_2 (10 mL) for 17 h at 0 °C under vigorous stirring. After dilution with water (60 mL) and extraction of the aqueous phase by CH_2Cl_2, the combined organic phases were washed by 5% aqueous K_2CO_3, water, dried on $MgSO_4$, and concentrated in vacuo (bath temp. < 30 °C). Flash chromatography over silica gel (10 g; Et_2O/CH_2Cl_2/pentane 4:6:90) afforded oxaziridine **3** (221 mg, 60%) as a colorless solid, m.p. 61 °C. ^1H NMR ($CDCl_3$): δ = 3.47 (s, 3H), 7.40–7.50 (m, 10 H); ^{13}C NMR ($CDCl_3$): δ = 54.0, 86.2, 128.0, 128.2, 128.6, 130.0, 132.0, 135.4, 160.6; IR (CCl_4): $\tilde{\nu}$ = 1778, 1752 cm^{-1}; MS (70 eV, EI): *m/z* (%) = 255 (28), 254 (33), 210 (25), 196 (25), 194 (21), 182 (31), 181 (25), 180 (76), 166 (31), 165 (75), 105 (72), 92 (22), 77 (100), 59 (31); HRMS: calcd for $C_{15}H_{13}NO_3$: 255.0895, found: 255.0885.

General procedure for the preparation of oxaziridines 4a–d, 5, 6 (method C): Technical MCPBA (70–75%, 2.5 g) purified[58] by washing first with phosphate buffer (pH = 7.5), then with water, was dissolved in CH_2Cl_2 (15 mL). The resulting solution was dried over $MgSO_4$, then over 4 Å molecular sieves immediately before use, and was titrated ($KI/Na_2S_2O_3$). To this anhydrous and *m*-chlorobenzoic-acid-free solution of MCPBA in CH_2Cl_2 (0.51 mol L^{-1}, 9.8 mL, 5 mmol) at −78 °C and under argon was added BuLi (1.6 M solution in hexane, 5 mmol). After 30 min, a solution of crude imine **12a** prepared from 4-cyanobenzaldehyde (0.707 g, 5.40 mmol) in anhydrous CH_2Cl_2 (6 mL) was added dropwise under mechanical stirring. The reaction proceeded over 2 h at −78 °C. Water (5 mL) was added and after 15 min the mixture was allowed to warm up to room temperature. The organic phase was washed three times with 5% aqueous $NaHCO_3$, dried over $MgSO_4$, concentrated in vacuo (bath temp. < 30 °C), and then flash-chromatographed over 26 g silica gel (CH_2Cl_2). The solid was washed with a 1:1 mixture of pentane and iPr_2O to yield oxaziridine **4a** (0.797 g, 65%, 60% from 4-cyanobenzaldehyde).

***N*-*tert*-Butoxycarbonyl-3-(2,4-dichlorophenyl)oxaziridine (4b)**: Crude imine **12b** prepared from 2,4-dichlorobenzaldehyde (203 mg, 1.16 mmol) afforded

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oxaziridine **4b** (420 mg, 79%) as a colorless solid after reaction with LiMCPBA (1.16 mmol) and flash chromatography over silica (4 g, eluant CH_2Cl_2/pentane 1:1). M.p. 47 °C; ^{1}H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 81:19 ratio at 300 K: δ = 1.13 (s, 9H, *cis*) and 1.53 (s, 9H, *trans*), 5.43 (s, 1H, *trans*) and 5.50 (s, 1H, *cis*), 7.18–7.50 (m, 3H); ^{13}C NMR ($CDCl_3$), *trans* isomer: δ = 27.7, 74.4, 85.7, 127.8, 129.0, 129.2, 129.4, 135.5, 137.1, 161.0; HRMS (FAB$^+$), calcd for $C_{12}H_{13}Cl_2NO_3$ + H: 290.0350, found: 290.0358.

***N*-*tert*-Butoxycarbonyl-3-(3,4-dichlorophenyl)oxaziridine (4c)**: Crude imine **12c** prepared from 3,4-dichlorobenzaldehyde (831 mg, 4.75 mmol) afforded oxaziridine **4c** (935 mg, 70%) as a colorless solid after reaction with LiMCPBA (4.75 mmol) and flash chromatography over silica (35 g, eluant CH_2Cl_2/pentane 1:1). M.p. 51 °C; ^{1}H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 92:8 ratio at 300 K: δ = 1.20 (s, 9H, *cis*) and 1.52 (s, 9H, *trans*), 4.96 (s, 1H, *trans*) and 5.24 (s, 1H, *cis*), 7.30 (dd, J = 8.3 and 2.0 Hz, 1H), 7.48 (d, J = 8.3 Hz, 1H), 7.55 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$), *trans* isomer: δ = 27.5, 76.1, 85.9, 127.1, 129.6, 130.6, 132.3, 132.9, 135.2, 159.6; IR (CCl_4): $\tilde{\nu}$ = 1774, 1750 cm^{-1}; anal. calcd for $C_{12}H_{13}Cl_2NO_3$ (%): C 49.68, H 4.52, N 4.83; found: C 49.97, H 4.60, N 4.88.

***N*-*tert*-Butoxycarbonyl-3-(2,3,5-trichlorophenyl)oxaziridine (4d)**: Crude imine **12d** prepared from 2,3,5-trichlorobenzaldehyde (1.86 g, 8.90 mmol) afforded oxaziridine **4d** (1.70 g, 59%) as a colorless solid after reaction with LiMCPBA (8.90 mmol) and flash chromatography over silica (60 g, eluant CH_2Cl_2/pentane 1:1). M.p. 39 °C. ^{1}H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 80:20 ratio at 300 K: δ = 1.17 (s, 9H, *cis*) and 1.54 (s, 9H, *trans*), 5.45 (s, 1H, *trans*) and 5.52 (s, 1H, *cis*), 7.38 (d, J = 2.4 Hz, 1H), 7.52 (d, J = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$), *trans* isomer: δ = 30.8, 77.3, 89.4, 129.7, 132.8, 135.1, 136.7, 136.8, 137.2, 162.6; IR (CCl_4) 1776, 1752 cm^{-1}; anal. calcd for $C_{12}H_{12}Cl_3NO_3$ (%): C 44.40, H 3.73, N 4.32; found: C 44.65, H 4.01, N 4.05.

***N*-Benzyloxycarbonyl-3-phenyloxaziridine (5)**: Crude imine **15**, prepared from **8a** (2.26 g, 12.7 mmol), afforded oxaziridine **5** (1.13 g, 35%) and amide **18** (1.00 g, 31%) as colorless solids after reaction with LiMCPBA (12.7 mmol) and flash chromatography over silica (96 g, eluant CH_2Cl_2/pentane 1:1). Oxaziridine **5** had m.p. 56 °C (ref. [11] oil). ^{1}H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 88:12 ratio at 300 K: δ = 4.94 (s, 2H, *cis*) and 5.34 (s, 1H, *cis*), 5.08 (s, 1H, *trans*) and 5.27 (d, J = 12 Hz, 1H, *trans*) and 5.28 (d, J = 12 Hz, 1H, *trans*), 6.98 (m, 1H, *cis*), 7.26–7.46 (m, 10H *trans* and 9H *cis*).

***N*-benzyloxycarbonyl benzamide (18)**: M.p. 117 °C. ^{1}H NMR ($CDCl_3$): δ = 5.25 (s, 2H), 7.28–7.80 (m, 10H), 8.07 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 67.86, 127.58, 128.0, 128.6, 128.7, 132.8, 132.9, 134.9, 150.8, 164.8; anal. calcd for $C_{15}H_{13}NO_3$ (%): C 70.58, H 5.13, N 5.49; found: C 70.85, H 5.22, N 5.31.

***N*-Fluorenylmethoxycarbonyl-3-(2,4-dichlorophenyl)oxaziridine (6)**: Imine **20** (12.24 g) dissolved in CH_2Cl_2 (46 mL) afforded oxaziridine **6** (6.90 g, 59%) as a colorless solid after chromatography over silica gel (130 g, eluant CH_2Cl_2/pentane 1:2.5). M.p. 100 °C; ^{1}H NMR ($CDCl_3$), equilibrium mixture of *trans* and *cis* isomers in 90:10 ratio at 300 K: δ = 4.21 (t, J = 7 Hz, 1H, *cis*) and 4.29 (t, J = 7 Hz, 1H, *trans*), 4.60 (d, J = 7 Hz, 2H), 5.43 (s, 1H, *trans*) and 5.63 (s, 1H, *cis*), 7.27–7.45 (m, 7H, *cis* and *trans*), 7.61 (m, 2H, *cis* and *trans*), 7.76 (m, 2H, *cis* and *trans*); ^{13}C NMR ($CDCl_3$): δ = 46.6, 70.0, 74.8, 120.2, 125.0, 127.3, 127.8, 128.1, 128.6,129.3, 129.4, 135.5, 137.4, 141.3, 141.4, 142.6, 142.8, 161.5; anal. calcd for $C_{22}H_{15}Cl_2NO_3$ (%): C 64.09, H 3.67, N 3.40; found: C 64.20, H 3.62, N 3.38.

***N*-*tert*-Butoxycarbonyl-4-cyanobenzamide (17a)**: Oxidation of imine **12a** (460 mg, 2 mmol) by method **B** afforded **17a** (310 mg, 63%) as a white solid, m.p. 143 °C, after recrystallization from EtOH. ^{1}H NMR ($CDCl_3$): δ = 1.50 (s, 9H), 7.74 (m, 2H), 7.87 (m, 2H), 7.95 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 27.8, 83.2, 115.9, 117.6, 128.4, 132.3, 137.2, 149.7, 164.4; anal. calcd for $C_{13}H_{14}N_2O_3$ (%): C 63.40, H 5.73, N 11.38; found: C 63.53, H 576, N 11.22.

***N*-*tert*-Butoxycarbonyl-2,4-dichlorobenzamide (17b)**: Oxidation of imine **12b** (2.74 g, 10 mmol) by method **B** afforded **4b** (0.725 g, 25%) as well as **17b** (4.06 g, 56%) as a white solid, m.p. 132 °C, after chromatography over silica gel (80 g; Et_2O/hexane 5:95 then 20:80). ^{1}H NMR ($CDCl_3$): δ = 1.42 (s, 9H), 7.29 (dd, J = 8.2 and 2.0 Hz, 1H), 7.40 (d, J = 2.0 Hz, 1H), 7.43 (d, J = 8.2 Hz, 1H), 7.91 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 27.7, 83.3, 127.3, 129.6, 130.1, 131.4, 133.1, 137.0, 149.2, 165.8; anal. calcd for $C_{12}H_{13}Cl_2NO_3$ (%): C 49.68, H 4.52, N 4.83; found: C 49.83, H 4.61, N 4.71.

Methyl 1-hydroxy-1-phenylmethylcarbamate (13a): A solution of *N*-Moc benzaldimine **9a** (326 mg, 2 mmol) in acetone (2 mL) was treated with water (2 mL). The resulting mixture was concentrated to 1.5 mL in vacuo and extracted three times into $CHCl_3$ (2 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo to afford **13a** (320 mg, 88%) as a white solid which decomposed rapidly in boiling CH_2Cl_2. ^{1}H NMR ($CDCl_3$): δ = 3.67 (s, 3H), 3.78 (brs, 1H), 5.51 (brs, 1H), 6.19 (dd, J = 8.2, 3.6 Hz, 1H), 7.30–7.50 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 52.4, 76.5, 125.7, 128.5, 139.1, 156.6; IR (CCl_4): 3298, 1697 cm^{-1}; HRMS (FAB$^+$), calcd for $C_9H_{11}NO_3$ + Li: 188.0899, found: 188.0895.

General procedure for the amination of amines by *N*-Moc oxaziridine (2a) or *N*-Boc oxaziridine (4a): A solution of the required amine (2 mmol) in Et_2O or $CHCl_3$ (2 mL) was treated at 0 °C by a solution of **2a** (376 mg, 2.1 mmol) or **4a** (516 mg, 2.1 mmol) in the same solvent (2 mL). At the end of the addition the cooling bath was removed. The reaction was monitored by TLC (secondary amines) or by NMR (primary amines). The reaction product was either recrystallized or chromatographed over silica gel to give the corresponding N_β-alkyloxycarbonylhydrazine **21**–**33**.

***N*-(Methoxycarbonylamino)morpholine (21a)**: Morpholine (0.166 mL) and **2a** were allowed to react for 30 min according to the procedure above. The solvent was evaporated and the residue was washed with pentane (2 × 2 mL) to give **21a** (277 mg, 91%); colorless crystals, m.p. 152 °C. ^{1}H NMR ($CDCl_3$): δ = 2.79 (t, J = 4.6 Hz, 4H), 3.69(s, 3H), 3.76 (t, J = 4.6 Hz, 4H), 5.55 (brs, 1H); anal. calcd for $C_6H_{12}N_2O_3$ (%): C 44.99, H 7.55, N 17.49; found: C 45.20, H 7.85, N 17.57.

***N*-(*tert*-Butoxycarbonylamino)morpholine (21b)**: Morpholine (0.166 mL) and **4a** were allowed to react for 30 min according to the procedure above. Chromatography over silica gel (21 g, Et_2O/CH_2Cl_2/hexane 1:1:1) gave **21b** (376 mg, 92%). Colorless crystals, m.p. 128 °C; ^{1}H NMR ($CDCl_3$): δ = 1.43 (s, 9H), 2.77 (t, J = 4.5 Hz, 4H), 3.75 (t, J = 4.5 Hz, 4H), 5.42 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 28.2, 56.1, 66.5, 80.2, 154.3; anal. calcd for $C_9H_{18}N_2O_3$ (%): C 53.45, H 8.97, N 13.85; found: C 53.22, H 9.04, N 13.61.

***N*-(Benzyloxycarbonylamino)morpholine (21c)**: Morpholine (0.59 mL) and **5** were allowed to react for 30 min according to the procedure above. The precipitate of **21c** was filtered off and washed with Et_2O (65 mg, 41%). Chromatography of the filtrate over silica gel (5 g, Et_2O/CH_2Cl_2 2.5:1) gave **21c** (77 mg, 48%, total yield 89%). Colorless crystals, m.p. 130 °C. ^{1}H NMR ($CDCl_3$): δ = 2.80 (t, J = 4.6 Hz, 4H), 3.77 (t, J = 4.6 Hz, 4H), 5.12 (s, 2H), 5.64 (brs, 1H), 7.33 (m, 5H); anal. calcd for $C_{12}H_{16}N_2O_3 \cdot 0.25H_2O$ (%): C 59.86, H 6.91, N 11.63; found: C 59.87, H 6.85, N 11.75.

***N*-(Fluorenylmethoxycarbonylamino)morpholine 21d**. Morpholine (0.87 mL) and **6** were allowed to react for 30 min according to the procedure above. The solvent was evaporated and the residue was washed with Et_2O (3 × 1.5 mL) to give **21d** (287 mg, 89%); colorless crystals, m.p. 175 °C. ^{1}H NMR ($CDCl_3$): δ = 2.76 (t, J = 4.6 Hz, 4H), 3.76 (s, 3H), 3.76 (t, J = 4.6 Hz, 4H), 4.21 (t, J = 6.7 Hz, 1H), 4.45 (t, J = 6.7 Hz, 2H), 5.62 (brs, 1H), 7.25–7.42 (m, 4H), 7.59 (m, 2H), 7.75 (m, 2H); anal. calcd for $C_{19}H_{20}N_2O_3$ (%): C 70.36, H 6.21, N 8.64; found: C 70.08, H 6.12, N 8.67.

***N*-(Methoxycarbonylamino)ephedrine (22a)**: Reaction of (1*R*,2*S*)-ephedrine (330 mg) and **2a** in Et_2O for 5 h gave a precipitate of **22a**, which was filtered off and washed with Et_2O (224 mg, 47%). The filtrate was chromatographed over silica gel (10 g, Et_2O/CH_2Cl_2/pentane 1.5:1:2.5) to give a further crop of **22a** (157 mg, 30%, total yield 77%). Colorless crystals, m.p. 127 °C. ^{1}H NMR ($CDCl_3$): δ = 0.85 (d, J = 6.7 Hz, 3H), 2.70 (s, 3H), 2.82 (qd, J = 6.7, 2.6 Hz, 1H), 3.50 (brs, 1H), 3.73 (s, 3H), 5.06 (d, J = 2.6 Hz, 1H), 5.90 (brs, 1H), 7.18–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 10.0, 43.6, 52.4, 66.7, 72.1, 125.6, 126.8, 127.9, 141.3, 157.3; $[\alpha]_D^{20}$ = −16.5 (c = 0.89, CH_2Cl_2); anal. calcd for $C_{12}H_{18}N_2O_3$ (%): C 60.49, H 7.61, N 11.76; found: C 60.37, H 7.68, N 11.83.

***N*-(*tert*-Butoxycarbonylamino)ephedrine (22b)**: Reaction of (1*R*,2*S*)-ephedrine (330 mg) and **4a** in Et_2O for 5 h gave a precipitate of **22b**, which was filtered off and washed with Et_2O (231 mg, 41%). The filtrate was

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chromatographed over silica gel (15 g, CH_2Cl_2/pentane 1:1) to give a further crop of **22b** (162 mg, 29%, total yield 70%). Colorless crystals, m.p. 144 °C; ^{1}H NMR ($CDCl_3$): δ = 0.81 (d, J = 6.6 Hz, 3H), 1.45 (s, 9H), 2.66 (s, 3H), 2.75 (qd, J = 6.6, 2.3 Hz, 1H), 3.91 (brs, 1H), 5.00 (d, J = 2.3 Hz, 1H), 5.63 (brs, 1H), 7.16–7.32 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 10.0, 28.2, 43.8, 67.4, 72.1, 80.8, 125.7, 126.7, 127.9, 141.3, 156.1; $[\alpha]_D^{25} = -14.2$ (c = 1.3, CH_2Cl_2); anal. calcd for $C_{15}H_{24}N_2O_3$ (%): C 64.26, H 8.63, N 9.99; found: C 64.31, H 8.61, N 10.08.

***N*-(Methoxycarbonylamino)pseudoephedrine (23)**: In the same way, reaction of (1*S*,2*S*)-pseudoephedrine (248 mg) and **2a** afforded **23** (271 mg, 76%) after chromatography over silica gel (15 g, Et_2O/CH_2Cl_2/pentane 2:2:1). Colorless crystals, m.p. 117 °C. ^{1}H NMR ($CDCl_3$): δ = 0.66 (d, J = 6.4 Hz, 3H), 2.11 (s, 1H), 2.62 (s, 3H), 2.71–2.79 (m, 1H), 3.73 (s, 3H), 4.13 (t, J = 9.4 Hz, 1H), 5.55 (brs, 1H), 7.20–7.27 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 7.2, 43.7, 52.8, 67.1, 75.6, 127.3, 127.8, 128.2, 140.8, 157.3; $[\alpha]_D^{25} = +42.5$ (c = 0.7, CCl_4); anal. calcd for $C_{12}H_{18}N_2O_3$ (%): C 60.49, H 7.61, N 11.76; found: C 60.63, H 7.58, N 11.86.

Methyl L-*N*-(Methoxycarbonylamino)prolinate (24): Methyl L-prolinate (266 mg; obtained by Et_2O extraction of a chilled solution of Pro–OMe, HCl in 1 M K_2CO_3) was treated with **2a** for 90 min in Et_2Oaccording to the procedure above. Chromatography over silica gel (17 g, Et_2O/hexane 1:1 then Et_2O) gave **24** (252 mg, 60%) as a colorless low melting solid, m.p. 34 °C; ^{1}H NMR ($CDCl_3$): δ = 1.81–2.00 (m, 3H), 2.22–2.30 (m, 1H), 3.14–3.21 (m, 2H), 3.67 (s, 3H), 3.70 (s, 3H), 3.94 (brs, 1H), 6.40 (brs, 1H); $[\alpha]_D^{25} = -78.2$ (c = 0.7, 95% EtOH); anal. calcd for $C_8H_{14}N_2O_4$ (%): C 47.52, H 6.98, N 13.85; found: C 47.85, H 5.12, N 13.58.

L-*N*-(Methoxycarbonylamino)prolinamide (25): Reaction of L-prolinamide (228 mg) with **2a** in $CHCl_3$ for 3 h according to the procedure above, followed by chromatography (17 g silica gel; Et_2O/CH_2Cl_2 90:10) afforded **25** (222 mg, 58%). Colorless solid, m.p. 187 °C; ^{1}H NMR ($CDCl_3$): δ = 1.73–2.02 (m, 3H), 2.16–2.31 (m, 1H), 2.59 (q, J = 8.6 Hz, 1H), 3.27–3.41 (m, 2H), 3.66 (s, 3H), 5.34 (brs, 1H), 5.83 (brs, 1H), 7.96 (brs, 1H); $[\alpha]_D^{25} = -58.7$ (c = 0.7, $CHCl_3$); anal. calcd for $C_7H_{13}N_3O_3$, 0.25 H_2O (%): C 43.86, H 7.00, N 21.93; found: C 44.08, H 6.83, N 21.88.

Methyl L-*N*-(methoxycarbonylamino)prolyl-L-leucinate (26): Reaction of methyl L-prolyl-L-leucinate (484 mg, obtained by Et_2O extraction of a chilled solution of HCl, Pro–Leu–OMe in 1 M K_2CO_3) with **2a** in Et_2O for 2 h min according to the procedure above gave a precipitate of **26**, which was filtered off and washed with Et_2O (498 mg, 79%). Colorless crystals, m.p. 145 °C. ^{1}H NMR ($CDCl_3$): δ = 0.91 (d, J = 6.0 Hz, 3H), 0.94 (d, J = 6.0 Hz, 3H), 1.62–1.72 (m, 3H), 1.76–1.89 (m, 3H), 2.22–2.35 (m, 1H), 2.67–2.80 (m, 1H), 3.36–3.43 (m, 2H), 3.66 (s, 3H), 3.69 (s, 3H), 4.46–4.52 (m, 1H), 5.94 (brs, 1H), 8.13 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 21.6, 22.2, 22.8, 24.9, 28.8, 40.3, 50.5, 51.9, 52.3, 55.9, 68.5, 157.1, 173.0, 173.3; $[\alpha]_D^{25} = -67.2$ (c = 1, CH_2Cl_2); anal. calcd for $C_{14}H_{25}N_3O_5$ (%): C 53.32, H 7.99, N 13.32; found: C 53.50, H 7.91, N 13.12.

***N*-*tert*-Butoxycarbonylamino-(*S*)-2-methoxymethylpyrrolidine (27)**: Reaction of (*S*)-2-methoxymethylpyrrolidine (230 mg) and **4a** in Et_2O for 1 h according to the procedure above, followed by chromatography (22 g silica gel; CH_2Cl_2) afforded **27** (359 mg, 78%). Colorless solid, m.p. 40 °C; ^{1}H NMR ($CDCl_3$): δ = 1.43 (s, 9H), 1.58–2.10 (m, 5H), 2.78 (m, 1H), 2.97 (m, 1H), 3.21 (m, 1H), 3.32 (s, 3H), 3.45 (*dd*, J = 9.4, 5.0 Hz, 1H), 5.54 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 21.1, 26.6, 28.2, 55.0, 59.0, 63.8, 75.1, 79.6, 155.0; $[\alpha]_D^{25} = -45.2$ (c = 1, acetone); anal. calcd for $C_{11}H_{22}N_2O_3$ (%): C 57.37, H 9.63, N 12.16; found: C 57.24, H 9.78, N 12.30.

***N*-(Methoxycarbonylamino)cyclohexylamine (28)**: The reaction of cyclohexylamine (0.230 mL) with **2a** in $CHCl_3$ for 40 min according to the procedure above gave a 85:15 mixture of **28** and *N*-(benzylidene)cyclohexylamine (δ(CHN) = 3.14). Chromatography (16 g silica gel; Et_2O/hexane 20:80) afforded **28** (275 mg, 80%). Colorless crystals, m.p. 63 °C (DSC; ref. [59]: 63.5–64.5 °C); ^{1}H NMR ($CDCl_3$): δ = 1.03–1.33 (m, 5H), 1.58–1.83 (m, 5H), 2.79 (m, 1H), 3.50 (brs, 1H), 3.70 (s, 3H), 6.16 (brs, 1H).

***N*-(Methoxycarbonylamino)aniline (29)**: The reaction of aniline (0.182 mL) with **2a** in $CHCl_3$ for 1 h according to the procedure above gave a 90:10 mixture of **29** and *N*-benzylideneaniline. Recrystallization of this mixture from EtOH afforded **29** (249 mg, 75%). Colorless crystals, m.p. 116 °C (DSC; ref. [60] 115–117 °C); ^{1}H NMR ($CDCl_3$): δ = 3.74 (s, 3H), 5.71 (s, 1H), 6.45 (brs, 1H), 6.79–6.92 (m, 3H), 7.19–7.27 (m, 2H).

Methyl L-*N*-(methoxycarbonylamino)valinate (30a): Reaction of methyl L-valinate (262 mg; obtained by Et_2O extraction of a chilled solution of L-Val–OMe, HCl in 1 M K_2CO_3) with **2a** in refluxing $CHCl_3$ for 3 h according to the procedure above gave a 70:30 mixture of **30a** and methyl L-*N*-(benzylidene)valinate (δ(CHα) = 3.64, δ(CHMe$_2$) = 2.36). This mixture was stirred with 1 M H_2SO_4 (5 mL) for 15 min. The organic phase was washed with water, dried over $MgSO_4$ and concentrated in vacuo. Chromatography (18 g silica gel; Et_2O/hexane 30:70) afforded **30a** (232 mg, 57%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 0.94 (d, J = 2.6 Hz, 3H), 0.98 (d, J = 2.6 Hz, 3H), 2.01 (m, 1H), 3.42 (t, J = 5.6 Hz, 1H), 3.67 (s, 3H), 3.72 (s, 3H), 4.16 (brs, 1H), 6.38 (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 18.4, 18.9, 29.8, 51.7, 52.4, 69.2, 157.4, 173.4; $[\alpha]_D^{23} = -40.8$ (c = 1, 95% EtOH); anal. calcd for $C_8H_{16}N_2O_4$ (%): C 47.05, H 7.90, N 13.72; found: C 47.34, H 7.86, N 13.50.

Methyl L-*N*-(*tert*-butoxycarbonylamino)valinate (30b): Following the procedure above, reaction of methyl L-valinate (262 mg) with **4a** in Et_2O for 48 h gave a 55:45 mixture of **30b** and methyl L-*N*-(4-cyanobenzylidene)valinate. Chromatography (twice; 22 g silica gel; CH_2Cl_2) afforded **30b** (218 mg, 44%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 0.95 (d, J = 4.3 Hz, 3H), 0.99 (d, J = 4.3 Hz, 3H), 1.42 (s, 9H), 2.00 (m, 1H), 3.42 (d, J = 5.3 Hz, 1H), 3.73 (s, 3H), 4.16 (brs, 1H), 6.10 (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 18.5, 19.0, 28.3, 30.0, 51.7, 69.4, 80.6, 156.2, 173.6; $[\alpha]_D^{23} = -37.3$ (c = 1, 95% EtOH); anal. calcd for $C_{11}H_{22}N_2O_4$ (%): C 53.64, H 9.00, N 11.37; found: C 53.98, H 9.18, N 11.40.

Methyl L-*N*-(Methoxycarbonylamino)valyl-L-leucinate (31): Following the above procedure, reaction of methyl L-valyl-L-leucinate (446 mg; obtained by Et_2O extraction of a chilled solution of Val–Leu–OMe, HCl in 1 M K_2CO_3) with **2a** in $CHCl_3$ for 4 h gave a 50:50 mixture of **31** and methyl L-*N*-(benzylidene)valylleucinate (δ(CHMe$_2$) = 2.33). This mixture was stirred with 1 M H_2SO_4 (5 mL) for 15 min. The organic phase was washed with water, dried over $MgSO_4$, and concentrated in vacuo. Chromatography (10 g silica gel; CH_2Cl_2/hexane 30/70) afforded **31** (145 mg, 25%). Colorless crystals, m.p. 94 °C; ^{1}H NMR ($CDCl_3$): δ = 0.93 (d, J = 5.8 Hz, 6H), 1.01 (d, J = 6.8 Hz, 6H), 1.54–1.76 (m,3H), 1.94 (m, 1H), 3.31 (d, J = 5.5 Hz, 1H), 3.68 (s, 3H), 3.72 (s, 3H), 4.26 (d, J = 5.2 Hz, 1H), 4.61–4.73 (m, 1H), 6.78 (brs, 1H), 7.11 (d, J = 9.1 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 18.7, 19.0, 21.3, 22.9, 25.0, 29.8, 40.8, 50.0, 52.4, 52.5, 71.2, 157.5, 172.1, 174.3; $[\alpha]_D^{20} = -110$ (c = 0.6, CH_2Cl_2); anal. calcd for $C_{14}H_{27}N_3O_5 \cdot 0.5H_2O$ (%): C 51.52, H 8.65, N 12.87; found: C 51.37, H 8.31, N 12.68.

Methyl L-*N*-(*tert*-Butoxycarbonylamino)alaninate (32): Following the above procedure, reaction of methyl L-alaninate (121 mg; obtained by Et_2O extraction of a chilled solution of Ala–OMe, HCl in 1 M K_2CO_3) with **4a** (300 mg) in $CHCl_3$ for 4 h afforded a 70:30 mixture of **32** and L-*N*-(benzylidene)alanine methyl ester (δ(CH=N) = 8.22). Chromatography (18 g silica gel; Et_2O/hexane 10:90) gave **32** (171 mg, 67%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.28 (d, J = 7.1 Hz, 1H), 1.41 (s, 9H), 3.68 (m, 1H), 3.70 (s, 3H), 4.12 (brs, 1H), 6.26 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 15.8, 28.1, 51.8, 58.2, 80.3, 156.3, 174.0; $[\alpha]_D^{25} = -44.7$ (c = 1, $CHCl_3$; ref. [61] +53.4 for the D isomer).

***N*-(Methoxycarbonylamino)imidazole (33)**: According to the above procedure, reaction of imidazole (136 mg) with **2a** in CH_2Cl_2 for 24 h gave a precipitate which was filtered and washed with CH_2Cl_2 to afford **33** (215 mg, 76%). Colorless crystals, m.p. 149 °C; ^{1}H NMR ($CDCl_3$): δ = 3.78 (s, 3H), 6.95 (m, 2H), 7.44 (s, 1H), 9.00 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 53.3, 121.7, 127.6, 136.6, 156.7; anal. calcd for $C_5H_7N_3O_2$ (%): C 42.55, H 5.00, N 29.77; found: C 42.85, H 5.13, N 29.48.

General procedure for the amination of aminoacids by *N*-Moc oxaziridine (2a): A solution containing 2 mmol of benzyltrimethylammonium hydroxide ($BnMe_3N^+OH^-$) or tetrabutylammonium hydroxide ($Bu_4N^+OH^-$) in MeOH was added to a suspension of amino acid **35** (2 mmol) in MeOH (1 mL), and the resulting mixture was stirred for 30 min. The solvent was evaporated in vacuo and replaced by $CHCl_3$ (2 mL). To the resulting solution of salt **35a** cooled to −15 °C was slowly added a solution of **2a** (2.1 mmol) in $CHCl_3$ (2 mL). After the mixture had been stirred for 1 h at −15 °C, it was extracted by water (4 × 5 mL). The aqueous phase containing salt **36** was

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allowed to percolate through a column of Dowex 50WX2-H^+ (10 mequiv). Unless otherwise stated, the resin was eluted with pure water, and the eluate was freeze-dried to afford the N_β-Moc hydrazino acid **37** in essentially pure form. When the resin was eluted with a mixture of water and an organic solvent, the eluate was evaporated to dryness to give the desired **37**.

L-*N*-(Methoxycarbonylamino)proline (37a): Following the above procedure, L-proline (230 mg, 2 mmol) was treated with a solution of $BnMe_3N^+OH^-$ (2.15 M in MeOH, 0.93 mL), then with **2a**, to give **37a** (320 mg, 85%). Colorless solid, m.p. 76 °C; ^{1}H NMR ($CDCl_3$): δ = 1.80 - 1.93 (m, 2H), 2.14 - 2.32 (m, 2H), 2.28 (q, J = 8.7 Hz, 1H), 3.44 (ddd, J = 9.0, 6.3, 2.6 Hz, 1H), 3.59 (dd, J = 10.1, 4.2 Hz, 1H), 3.74 (s, 3H), 6.16 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 23. 2, 29.1, 53.1, 56.3, 67.8, 157.8, 174.4; $[\alpha]_D^{21}$ = − 61.8 (c = 0.5, 95% EtOH); anal. calcd for $C_7H_{12}N_2O_4$ (%): C 44.68, H 6.43, N 14.89; found: C 44.86, H 6.46, N 14.57.

L-*N*-(Methoxycarbonylamino)prolyl-L-leucine (37c): L-Prolyl-L-leucine (457 mg, 2 mmol) was treated with a solution of $BnMe_3N^+OH^-$ (2.15 M in MeOH, 0.93 mL), then with **2a** as described above. After percolation through a Dowex-H^+ resin the aqueous eluate was acidified to pH 2 by solid $KHSO_4$. The precipitate was filtered and washed with water to afford **37c** (434 mg, 72%), which was recrystallized from EtOH (361 mg, 60%). Colorless solid, m.p. 209 °C; ^{1}H NMR ($CDCl_3$): δ = 0.91 (d, J = 5.2 Hz, 3H), 0.97 (d, J = 5.2 Hz, 3H), 1.73 - 1.84 (m, 6H), 2.26 - 2.33 (m, 1H), 2.67 - 2.79 (m, 1H), 3.37 - 3.46 (m, 2H), 3.68 (s, 3H), 4.42 (m, 1H), 6.12 (brs, 1H), 8.48 (brs, 1H); ^{13}C NMR (CD_3OD): δ = 21.7, 23.3, 23.4, 26.3, 29.9, 41.2, 52.0, 52.9, 56.6, 69.4, 159.8, 167.8, 175.5, 176.3; $[\alpha]_D^{25}$ = − 53 (c = 1, 95% EtOH); anal. calcd for $C_{13}H_{23}N_3O_5$ (%): C 51.82, H 7.69, N 13.94; found: C 51.75, H 7.82, N 13.90.

L-*N*-(Methoxycarbonylamino)valine (37d): In the same way, L-valine (234 mg, 2 mmol) was treated with a solution of $BnMe_3N^+OH^-$ (2.15 M in MeOH 0.93 mL), then with **2a**, to give **37d** (267 mg, 70%). Colorless solid, m.p. 89 °C; ^{1}H NMR ($CDCl_3$): δ = 1.00 (d, J = 5 Hz, 3H), 1.03 (d, J = 5 Hz, 3H), 2.09 (m, 1H), 3.44 (m, 1H), 3.72 (s, 3H), 7.60 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 18.4, 18.8, 29.6, 52.8, 69.3, 158.2, 176.4; $[\alpha]_D^{20}$ = − 36.5 (c = 1, 95% EtOH); anal. calcd. for $C_7H_{14}N_2O_4$ (%): C 44.20, H 7.42, N 14.73; found: C 44.35, H 7.43, N 14.43.

***N*-(Methoxycarbonylamino)glycine (37e)**: By the above procedure, glycine (158 mg, 2.1 mmol) was treated with a solution of $Bu_4N^+OH^-$ (0.8 M in MeOH, 2.6 mL), then with **2a** to give **37e** (246 mg, 70%) as a colorless hygroscopic solid. ^{1}H NMR ($CDCl_3$): δ = 3.68 (s, 2H), 3.72 (s, 3H), 6.38 (brs, 3H). A solution of **37e** (246 mg) in EtOH (1 mL) was treated with dicyclohexylamine (DCH, 320 μl, 1.61 mmol) and filtered to afford 430 mg (80%) of **37e**, DCH salt. Colorless solid, decomp. 156 °C; ^{1}H NMR ($CDCl_3$): δ = 1.19 - 2.01 (m, 20H), 2.95 (m, 2H), 3.37 (s, 2H), 3.68 (s, 3H), 7.15 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ = 24.7, 25.0, 29.3, 52.8, 55.8, 157.4, 175.9; anal. calcd for $C_{16}H_{31}N_3O_4 \cdot 0.25H_2O$ (%): C 57.55, H 9.51, N 12.58; found: C 57.52, H 9.52, N 12.69.

D-*N*-(Methoxycarbonylamino)phenylglycine (37f): By the above procedure, treatment of D-phenylglycine (302 mg, 2 mmol) with a solution of $Bu_4N^+OH^-$ (0.8 M in MeOH, 2.5 mL) then with **2a** afforded **37f** (381 mg, 85%) as a colorless hygroscopic solid after elution of the resin with water/*EtOH (1:3)*. ^{1}H NMR ($CDCl_3$): δ = 3.68 (s, 3H), 4.79 (s, 1H), 7.00 (brs, 1H), 7.33 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 52.8, 66.9, 128.2, 128.9, 129.0, 134.3, 157.9, 174.5. A solution of **37f** in EtOH (1 mL) was treated by dicyclohexylamine (340 µL, 1.71 mmol), affording **37f**, DCH salt (608 mg, 88%). Colorless solid, decomp. 142 °C; ^{1}H NMR ($CDCl_3$): δ = 1.06 - 1.27 (m, 10H), 1.58 - 1.85 (m, 10H), 2.73 (m, 2H), 3.64 (s, 3H), 4.39 (s, 1H), 6.56 (brs, 1H), 7.17 - 7.39 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 24.5, 24.6, 24.8, 28.7, 28.8, 52.0, 52.3, 69.8, 127.2, 127.9, 128.2, 138.9, 157.3, 174.9; $[\alpha]_D^{25}$ = − 60.8 (c = 1, $CHCl_3$); anal. calcd for $C_{22}H_{35}N_3O_4$ (%): C 65.16, H 8.70, N 10.36; found: C 65.01, H 8.65, N 10.06.

DL-*N*-(Methoxycarbonylamino)phenylglycine (37g): Similarly, DL-phenylglycine (302 mg, 2 mmol) afforded **37g**, DCH salt (634 mg, 75%). Colorless solid, decomp. 133 °C; NMR identical to that of **37f**, DCH salt; anal. calcd for $C_{22}H_{35}N_3O_4$ (%): C 65.16, H 8.70, N 10.36; found: C 65.33, H 8.64, N 10.38.

L-*N*-(Methoxycarbonylamino)phenylalanine (37h): By the above procedure, treatment of L-phenylalanine (330 mg, 2 mmol) with a solution of $BnMe_3N^+OH^-$ (2.15 M in MeOH, 0.93 mL), then with **2a**, and elution of the resin with water/MeOH (1:4), afforded **37h** (372 mg, 78%) as a colorless solid, which was recrystallized from THF (60%); m.p. 146 °C. ^{1}H NMR ($CDCl_3$): δ = 2.87 (dd, J = 14.1, 8.9 Hz, 1H), 3.18 (dd, J = 14.1, 4.3 Hz, 1H), 3.63 (s, 3H), 3.85 (dd, J = 8.9, 4.3 Hz, 1H), 6.68 (brs, 1H), 7.20 (m, 5H); ^{13}C NMR (CD_3OD): δ = 37.7, 52.8, 65.6, 127.7, 129.4, 130.3, 138.3, 159.9, 175.9; $[\alpha]_D^{25}$ = − 5.6 (c = 1, MeOH); anal. calcd for $C_{11}H_{14}N_2O_4 \cdot 0.25H_2O$ (%): C 54.43, H 6.02, N 11.54; found: C 54.54, H 6.00, N 11.56.

L-*O*-Benzyl-*N*-(methoxycarbonylamino)tyrosine (37i): L-*O*-benzyltyrosine (542 mg, 2 mmol) was treated with a solution of $Bu_4N^+OH^-$ (0.8 M in MeOH, 2.5 mL), then with **2a** as described above. The reaction mixture was concentrated, then diluted with water (100 mL). The aqueous phase was extracted with Et_2O (10 mL) and then left to percolate through Dowex-H^+ resin with $EtOH/CH_2Cl_2$ (1:2) as the eluant. After concentration the resulting solid was washed with Et_2O (2 × 2 mL) to give **37i** (462 mg, 67%). Colorless solid, decomp. 150 °C; ^{1}H NMR ([D$_6$]DMSO): δ = 2.77 (d, J = 5.7 Hz, 2H), 3.53 (s, 3H), 3.63 (t, J = 5.7 Hz, 1H), 5.04 (s, 2H), 6.88 (d, J = 8.2 Hz, 2H), 7.14 (d, J = 8.2 Hz, 2H), 7.37 (m, 5H); ^{13}C NMR ([D$_6$]DMSO): δ = 35.1, 51.5, 63.9, 69.1, 114.3, 127.6, 127.7, 128.4, 129.6, 130.3, 137.2, 156.9, 157.4, 173.3; $[\alpha]_D^{25}$ = + 16.1 (c = 1, DMSO); anal. calcd for $C_{18}H_{20}N_2O_5$ (%): C 62.78, H 5.85, N 8.13; found: C 62.84, H 5.82, N 8.11.

L-*N*-(Methoxycarbonylamino)serine (37j): As above, L-serine (210 mg, 2 mmol) was treated with a solution of $Bu_4N^+OH^-$ (0.8 M in MeOH, 2.5 mL) to give **37j** (353 mg, 99%) as a colorless hygroscopic solid. ^{1}H NMR (D_2O): δ = 3.57 (s, 3H), 3.63 (m, 1H), 3.75 (m, 2H); ^{13}C NMR (D_2O): δ = 52.7, 59.6, 64.1, 158.9, 173.7. A solution of **37j** (353 mg) in EtOH (3 mL) was treated with dicyclohexylamine (0.4 mL, 2 mmol), to give **37j**, DCH salt (345 mg, 48%), as a colorless solid, decomp. 160 °C. ^{1}H NMR (D_2O): δ = 1.17 (m, 10H), 1.51 - 1.91 (m, 10H), 3.11 (m, 2H), 3.30 (t, J = 5.0 Hz, 1H), 3.56 (s, 3H), 3.60 - 3.72 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 24.6, 25.0, 29.3, 52.3, 52.8, 61.2, 65.6, 158.1, 175.9; $[\alpha]_D^{25}$ = − 21.2 (c = 1, MeOH); anal. calcd for $C_{17}H_{33}N_3O_5$ (%): C 56.80, H 9.25, N 11.69; found: C 56.61, H 9.37, N 11.53.

L-*N*-(Methoxycarbonylamino)histidine (37k): Following the above procedure, treatment of L-histidine (310 mg, 2 mmol) with a solution of $BnMe_3N^+OH^-$ (2.15 M in MeOH, 0.93 mL), then with **2a**, afforded **37k** (305 mg, 67%) after elution of the resin with aqueous NH_3 (1 M), freeze-drying and washing of the yellow solid by a 1:10 mixture of DMSO and acetone; colorless solid, decomp. 210 °C. ^{1}H NMR (D_2O): δ = 2.91 (d, J = 5.8 Hz, 2H), 3.51 (t, J = 5.8 Hz, 1H), 3.56 (s, 3H), 7.12 (s, 1H), 8.43 (s, 1H); ^{13}C NMR (D_2O): δ = 24.9, 52.5, 63.9, 116.2, 130.0, 132.5, 159.6, 177.4; $[\alpha]_D^{25}$ = + 7.5 (c = 1, water); HRMS (FAB$^+$), calcd for $C_8H_{12}N_4O_4$ + H: 229.0936, found: 229.0920.

L-*N*-(Methoxycarbonylamino)tryptophan (37l): As above, L-tryptophan (408 mg, 2 mmol) was treated with a solution of $Bu_4N^+OH^-$ (0.8 M in MeOH, 2.5 mL), then with **2a**. After percolation through a Dowex-H^+ resin and freeze-drying, the yellow solid was washed twice with $CHCl_3$ to give **37l** (305 mg, 55%) as a colorless solid, m.p. 157 °C. ^{1}H NMR (DMSO): δ = 2.97 (d, J = 6.3 Hz, 2H), 3.53 (s, 3H), 3.78 (t, J = 6.3 Hz, 1H), 7.01 (m, 2H), 7.21 (d, J = 2.0 Hz, 1H), 7.32 (d, J = 7.7 Hz, 1H), 7.51 (d, J = 7.7 Hz, 1H), 8.55 (brs, 1H), 10.81 (brs, 1H); ^{13}C NMR (CD_3OD): δ = 27.6, 52.7, 64.8, 110.6, 112.2, 119.3, 119.7, 122.3, 124.6, 128.7, 138.0, 159.7, 176.4; $[\alpha]_D^{25}$ = − 16.4 (c = 1, 95% EtOH); anal. calcd for $C_{13}H_{15}N_3O_4$ (%): C 56.31, H 5.45, N 15.15; found: C 56.34, H 5.58, N 15.16.

L-*N*-ε-Benzyloxycarbonyl-*N*-α-(methoxycarbonylamino)lysine (37m): L-*N*-ε-benzyloxycarbonyl lysine (560 mg, 2 mmol) was treated with a solution of $Bu_4N^+OH^-$ (0.8 M in MeOH, 2.5 mL), then with **2a** as described above. The reaction mixture was concentrated, then diluted with water (60 mL). The aqueous phase was extracted with Et_2O (5 mL) and allowed to percolate through a Dowex-H^+ resin with EtOH/water 5:1 as the eluant. The eluate was evaporated and the resulting solid was washed with Et_2O (2 × 5 mL) to give **37m** (460 mg, 65%). Colorless solid, m.p. 93 °C; ^{1}H NMR ([D$_6$]DMSO) (350 K): δ = 1.35 - 1.61 (m, 6H), 3.01 (m, 2H), 3.39 (t, J = 6.0 Hz, 1H), 3.57 (s, 3H), 5.02 (s, 2H), 6.81 (brs, 1H), 7.33 (m, 5H), 8.15 (brs, 2H); ^{13}C NMR ([D$_6$]DMSO): δ = 22.3, 29.4, 29.9, 40.2, 51.5, 62.3, 65.2, 127.8, 128.4,

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137.3, 156.1, 157.5, 174.3; $[\alpha]_D^{25} = -5.5$ ($c = 1$, MeOH); anal. calcd for $C_{16}H_{23}N_3O_6$ (%): C 54.38, H 6.56, N 11.89; found: C 54.65, H 6.64, N 11.87.

L-*N*-(Methoxycarbonylamino)tyrosine (37i'): A suspension of **37i** (203 mg, 0.59 mmol) and 5% Pd/C (50 mg) in a 1:2 mixture of EtOH/CH_2Cl_2 was hydrogenated at atmospheric pressure for 3 h. After filtration (Celite) and evaporation in vacuo, **37i'** (145 mg, 97%) was obtained as a colorless solid which slowly darkened in air, m.p. 170 °C. ^{1}H NMR (CD_3OD): $\delta = 2.88$ (m, 2H), 3.63 (s, 3H), 3.75 (t, $J = 6.8$ Hz, 1H), 6.69 (d, $J = 8.5$ Hz, 2H), 7.07 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (CD_3OD): $\delta = 36.9$, 52.7, 65.8, 116.2, 128.8, 131.3, 157.3, 159.9, 176.0; $[\alpha]_D^{25} = -8.1$ ($c = 1$, MeOH); anal. calcd for $C_{11}H_{14}N_2O_5$ (%): C 51.97, H 5.55, N 11.02; found: C 52.24, H 5.25, N 10.94.

L-*N*-(Methoxycarbonylamino)lysine (37m'): A suspension of **37m** (199 mg, 0.56 mmol) and 5% Pd/C (50 mg) in a 1/2 mixture of EtOH/CH_2Cl_2 was hydrogenated at atmospheric pressure for 3 h, to give **37m'** (106 mg, 85%). Colorless solid, m.p. 210 °C; ^{1}H NMR (D_2O): $\delta = 1.31$–1.60 (m, 6H), 2.88 (t, $J = 7.1$ Hz, 2H), 3.21 (t, $J = 6.1$ Hz, 1H), 3.56 (s, 3H); ^{13}C NMR (CD_3OD): $\delta = 23.5$, 28.1, 31.0, 40.3, 52.7, 66.5, 159.8, 180.4; $[\alpha]_D^{25} = -37.5$ ($c = 1$, MeOH); anal. calcd for $C_8H_{17}N_3O_4 \cdot 0.25H_2O$ (%): C 42.85, H 7.88, N 18.78; found: C 42.98, H 7.71, N 18.44.

General procedure for the amination of aminoacids by *N*-Boc-3-(4-cyanophenyl)oxaziridine (4a): A suspension of the required amino acid (2 mmol) in MeOH (1 mL) was treated with a solution of $BnMe_3N^+OH^-$ or $Bu_4N^+OH^-$ in MeOH (2 mmol) for 30 min. MeOH was evaporated in vacuo and replaced by $CHCl_3$ (2 mL). To the resulting solution, cooled to −30 °C, was slowly added oxaziridine **4a** (2.1 mmol) in $CHCl_3$ (2 mL). The reaction mixture was stirred for 1 h at −30 °C and was then evaporated in vacuo. Water (8 mL) was added, and the precipitate of 4-cyanobenzaldehyde was filtered off. The basic aqueous phase was extracted with Et_2O (4 mL) and then acidified to pH 3 with solid $KHSO_4$. The desired *N*-Boc hydrazino acid **37** was isolated by filtration and/or by extraction of the aqueous phase with ethyl acetate or CH_2Cl_2 (3 × 5 mL).

L-*N*-(*tert*-Butoxycarbonylamino)proline (37b): As described above, L-proline (575 mg, 5 mmol) was treated with a solution of $BnMe_3N^+OH^-$ (2.15 M in MeOH, 2.32 mL), then with **4a**, to give **37b** (1.09 g, 95%). Colorless solid, m.p. 128 °C (ref. [62] 124–126 °C); ^{1}H NMR ($CDCl_3$): $\delta = 1.41$ (s, 9H), 1.84–1.72 (m, 2H), 2.32–2.03 (m, 2H), 2.88–2.75 (m, 1H), 3.56 (dd, $J = 4.1$, 10.1 Hz, 1H), 6.36 (brs, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 23.3$, 28.1, 29.0, 56.1, 67.9, 81.9, 156.9, 175.1; $[\alpha]_D^{25} = -41.2$ ($c = 1$, 95% EtOH).

L-*N*-(*tert*-Butoxycarbonylamino)phenylalanine (37o): Similarly, L-phenylalanine (330 mg, 2 mmol) treated with a solution of $BnMe_3N^+OH^-$ (2.15 M in MeOH, 0.93 mL), then with **4a**, afforded **37o** (200 mg, 36%) after recrystallization from EtOH. Colorless solid, m.p. 185 °C (ref. [63] 185–186 °C); ^{1}H NMR (DMSO): $\delta = 1.36$ (s, 9H), 2.83 (d, $J = 6.1$ Hz, 2H), 3.32 (m, 2H), 3.67 (t, $J = 6.1$ Hz, 1H), 7.23 (m, 5H); ^{13}C NMR (DMSO): $\delta = 28.1$, 36.0, 63.6, 78.6, 126.2, 128.0, 129.3, 137.7, 156.9, 171.5; $[\alpha]_D^{25} = +20$ ($c = 1$, DMF) (ref. [63] $[\alpha]_D^{25} = +21$ ($c = 1$, DMF).

L-*N*-(*tert*-Butoxycarbonylamino)alanine (37n): L-Alanine (445 mg, 5 mmol) was treated with a solution of $BnMe_3N^+OH^-$ (2.15 M in MeOH, 2.32 mL), then with **4a**. After evaporation of the solvent and addition of water, the aqueous phase was acidified by stirring for 2 h in the presence of a weakly acidic ion exchange resin (Duolite C 470, 20 mequiv); then it was allowed to percolate through a column filled with the same resin (11 mequiv). After elution with water and freeze-drying, pure **37n** (510 mg, 50%) was obtained. A further washing of the resin by MeOH afforded a 50:50 mixture of oxazolidinone **39n** and **37n** (227 mg). Compound **37n** is a colorless solid, m.p. 105 °C. ^{1}H NMR ($CDCl_3$): $\delta = 1.35$ (d, $J = 7$ Hz, 3H), 1.43 (s, 9H), 3.73 (q, $J = 6.7$ Hz, 1H), 6.86 (brs, 1H), 8.0 (brs, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 15.6$, 28.2, 58.3, 81.7, 156.9, 176.8; $[\alpha]_D^{25} = -20.4$ ($c = 1$, MeOH); anal. calcd for $C_8H_{16}N_2O_4$ (%): C 47.05, H 7.90, N 13.72; found: C 47.19, H 7.80, N 13.67.

A sample of **3-(tert-Butoxycarbonylamino)-2-(4-cyanophenyl)-4-methyl-1,3-oxazolidin-5-one (39n)** was obtained by recrystallization of the above **37n**/**39n** mixture from iPr_2O. Colorless solid, decomp. 142° C; mixture of two diastereomers. ^{1}H NMR (DMSO): $\delta = 2.29$ (m, 12H), 3.97 (m, 1H), 5.96 (m, 1H), 7.76 (d, $J = 7.9$ Hz, 2H), 7.92 (d, $J = 7.9$ Hz, 2H), 8.71 (brs, 1H); ^{13}C NMR (DMSO): δ = major diastereomer 14.4, 27.8, 57.4, 79.5, 91.5, 112.7, 118.4, 129.1, 132.4, 140.1, 154.6, 172.1; minor diastereomer 16.0, 28.1, 57.4, 78.6, 91.5, 116.2, 117.8, 129.8, 133.1, 138.6, 156.3, 174.5; IR: 2230, 1820, 1720 cm^{-1}; $[\alpha]_D^{25} = -89.3$ ($c = 1$, CH_2Cl_2); anal. calcd for $C_{16}H_{19}N_3O_4$ (%): C 60.56, H 6.03, N 13.24; found: C 60.43, H 6.18, N 13.26.

L-*N*-(*tert*-Butoxycarbonylamino)valine (37p): L-Valine (140 mg, 1.2 mmol) was treated with a solution of $BnMe_3N^+OH^-$ (2.15 M in MeOH, 0.50 mL), then with **4a** as described above. The resulting solution was treated by a sodium ion exchange resin (Dowex 50X2-Na^+, 5 mequiv). After filtration and water washing of the resin, the organic phase was extracted with water (2 × 3 mL). The combined aqueous phases were acidified to pH 3 with solid $KHSO_4$ and extracted by AcOEt to afford a mixture of **37p** and oxazolidinone **39p** (183 mg). Recrystallization from iPr_2O yielded pure **37p** (54 mg, 21%). Colorless solid, m.p. 90 °C; ^{1}H NMR ($CDCl_3$): $\delta = 0.99$ (d, $J = 9.1$ Hz, 3H), 1.03 (d, $J = 9.1$ Hz, 3H), 2.09 (m, 1H), 3.42 (m, 1H), 6.49 (brs, 1H), 7.01 (brs, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 18.3$, 19.0, 28.3, 30.9, 69.4, 81.4, 156.9, 176.3; $[\alpha]_D^{25} = -12.6$ ($c = 0.7$, CH_2Cl_2); anal. calcd for $C_{10}H_{20}N_2O_4$ (%): C 51.71, H 8.68, N 12.06; found: C 51.72, H 8.64, N 11.86.

L-*N*-Benzyl-*N*-(*tert*-butoxycarbonylamino)alanine (37q): A suspension of L-*N*-benzylalanine[64] (1.43 g, 8 mmol) in MeOH (3 mL) was treated with a solution of $Et_4N^+OH^-$ in MeOH (8 mmol) for 30 min. MeOH was evaporated in vacuo and replaced by CH_2Cl_2 (25 mL). Oxaziridine **4a** (8.4 mmol) in CH_2Cl_2 (8 mL) was slowly added to the resulting solution cooled to 0 °C. The reaction mixture was stirred for 18 h at 4 °C and was then evaporated in vacuo. Water (100 mL) was added, and the precipitate of 4-cyanobenzaldehyde was filtered off. The basic aqueous phase was extracted with Et_2O (4 × 8 mL) and then acidified to pH 3 with solid $KHSO_4$. After extraction by Et_2O (3 × 30 mL), drying over Na_2SO_4 and evaporation, **37q** (2.09 g, 88%) was obtained. Hygroscopic colorless solid, m.p. 117 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.32$ (s, 9H), 1.38 (d, $J = 7$ Hz, 3H), 3.64 (q, $J = 7$ Hz, 1H), 3.95 (s, 2H), 7.24–7.37 (m, 5H), 10.21 (brs, 1H). A solution of **37q** (0.261 mg) in Et_2O (2 mL) was treated with dicyclohexylamine (220 μL, 1.0 mmol), affording 365 mg (88%) of **37q**, DCH salt. Colorless solid, decomp. 170 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.22$–1.67 (m, 24H), 1.79 (m, 4H), 2.02 (m, 4H), 2.93 (m, 2H), 3.38 (q, $J = 7$ Hz, 1H), 4.01 (s, 2H), 7.23–7.39 (m, 5H); $[\alpha]_D^{25} = +43.7$ ($c = 1.3$, MeOH); anal. calcd for $C_{27}H_{45}N_3O_4 \cdot 0.25H_2O$ (%): C 67.54, H 9.55, N 8.75; found: C 67.30, H9.52, N 8.67.

L-*N*-Benzyl-*N*-(*tert*-butoxycarbonylamino)valine (37r): Similarly L-*N*-benzylvaline (207 mg, 1 mmol) afforded **37r** (220 mg, 68%). Colorless solid, decomp. 117 °C; ^{1}H NMR ($CDCl_3$): $\delta = 0.96$ (d, $J = 7$ Hz, 3H), 1.08 (d, $J = 7$ Hz, 3H), 1.36 (s, 9H), 2.09 (m, 1H), 3.11 (brs, 1H), 3.91 (m, 2H), 7.24–7.37 (m, 5H), 10.21 (brs, 1H); $[\alpha]_D^{25} = +25.6$ ($c = 1.2$, MeOH); anal. calcd for $C_{17}H_{26}N_2O_4$ (%): C 63.33, H 8.13, N 8.69; found: C 63.23, H 8.10, N 8.70.

Determination of the enantiomeric excess of D-*N*-(methoxycarbonylamino)-phenylglycine (37f): A solution of crude **37f** or **37g** (252 mg, 1.12 mmol) in dry DMF (2 mL) was treated at 0 °C with the salt of *N*-hydroxysuccinimide and (*S*)-(−)-α-methylbenzylamine (266 mg) and with dicyclohexylcarbodiimide (234 mg). After 1 h at 0 °C and 18 h at room temperature, the white precipitate was filtered off and washed in ethyl acetate. The filtrate was concentrated in vacuo, diluted by ethyl acetate, washed successively with aqueous citric acid and water, dried over $MgSO_4$, and concentrated in vacuo to afford **40** (348 mg) as a colorless viscous oil, which was analyzed by ^{1}H NMR ($CDCl_3$). (*S*)-1-phenylethyl-(*R*)-phenylglycinamide: $\delta = 1.46$ (d, $J = 6.9$ Hz, 3H), 3.70 (s, 3H), 4.26 (brs, 1H), 4.55 (s, 1H), 5.13 (m, 1H), 6.34 (brs, 1H), 7.23–7.34 (m, 11H); (*S*)-1-phenylethyl-(*S*)-phenylglycinamide: $\delta = 1.49$ (d, $J = 6$ Hz, 3H), 3.62 (s, 3H), 4.26 (brs, 1H), 4.55 (s, 1H), 5.13 (m, 1H), 6.26 (brs, 1H), 7.23–7.34 (m, 11H).

General procedure for the amination of carbanions by *N*-Boc-3-(4-cyanophenyl)oxaziridine (4a): A solution of the carbonyl compound (2 mmol) in THF (3 mL) was added dropwise at −78 °C to a solution of LiHMDS (2 mmol) in THF (1.5 mL). The mixture was stirred at −78 °C for 30 min and then treated with **4a** (495 mg, 2 mmol) in THF (2 mL) for a further 30 min, then quenched by saturated aqueous ammonium sulfate (5 mL). The aqueous phase was extracted with Et_2O (3 × 5 mL). The Et_2O phase was washed with brine, dried over Na_2SO_3, concentrated and flash-chromatogaphed over silica gel to give the amination product (**42**, **44**, **45**).

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***tert*-Butyl 1-methyl-2-oxo-2-phenylethylcarbamate (42)**: By the above procedure, after flash chromatography over silica gel (40 g; Et_2O/hexane 10:90 then Et_2O/hexane 50:50), propiophenone (248 mg, 2 mmol) afforded **42** (183 mg, 36%) and **43** as a mixture of diastereomers identical to an authentic sample prepared[65] from 4-cyanobenzaldehyde and propiophenone (132 mg, 25%). Compound **42** is a colorless solid, m.p. 81 °C. ^{1}H NMR ($CDCl_3$): $\delta = 1.38$ (d, $J = 7.0$ Hz, 3H), 1.44 (s, 9H), 5.27 (m, 1H), 5.51 (brs, 1H), 7.43–7.62 (m, 3H), 7.93–7.97 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 19.9$, 28.3, 51.1, 79.7, 128.6, 128.8, 133.7, 134.2, 155.1, 199.4; anal. calcd for $C_{14}H_{19}NO_3 \cdot 0.25\,H_2O$ (%): C 66.25, H 7.74, N 5.52; found: C 66.57, H 7.57, N 5.68.

***tert*-Butyl *N*-*tert*-butoxycarbonylglycinate (45)**: By the above procedure, *tert*-butyl acetate (232 mg, 2 mmol) and LiHMDS (2 mmol) afforded **45** (156 mg, 35%) after flash chromatography over silica gel (28 g; Et_2O/hexane 10:90). Colorless solid, m.p. 48 °C (ref. [66] 64 °C); ^{1}H NMR ($CDCl_3$): $\delta = 1.42$ (s, 9H), 1.44 (s, 9H), 3.77 (d, $J = 5.2$ Hz, 2H), 4.94 (brs, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 25.0$, 28.3, 43.1, 79.7, 81.9, 155.7, 169.7.

3-(2-*tert*-Butoxycarbonylamino-1-oxo-3-phenylpropyl)-1,3-oxazolidin-2-one (44): By the above procedure 3-(1-oxo-3-phenylpropyl)-1,3-oxazolidin-2-one (438 mg, 2 mmol) in THF (20 mL) gave **44** (221 mg, 33%) after flash chromatography over silica gel (37 g; Et_2O/hexane 30:70). Colorless solid, m.p. 139 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.33$ (s, 9H), 2.76 (dd, $J = 13.5$, 5 Hz, 1H), 3.17 (dd, $J = 13.5$, 4.3 Hz, 1H), 3.85–4.11 (m, 2H), 4.30–4.45 (m, 2H), 5.03 (d, $J = 5$ Hz, 1H), 5.67 (ddd, $J = 8.7$, 5.0, 4.3 Hz, 1H), 7.17–7.32 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 28.2$, 36.5, 42.5, 53.8, 79.9, 126.9, 128.5, 129.4, 135.9, 152.8, 155.1, 172.7; anal. calcd for $C_{11}H_{22}N_2O_5 \cdot 0.25\,H_2O$ (%): C 60.25, H 6.69, N 8.27; found: C 60.29, H 6.54, N 8.39.

Reaction of triethylamine with 2a: triethylammoniomethoxycarbonylamidate (34): A solution of **2a** (941 mg, 5.26 mmol) in CH_2Cl_2 (8 mL) under argon was treated at −78 °C with 0.732 mL (5.26 mmol) of triethylamine. After the mixture had been stirred at −78 °C for 12 h it was concentrated in vacuo and chromatographed over silica gel (30 g, MeOH/CH_2Cl_2 2:98) to give **34** (280 mg, 30%) and triethylaminoxyde (identical to an authentic sample[67]) (373 mg, 69%). Compound **34** is an oil; ^{1}H NMR ($CDCl_3$): $\delta = 1.16$ (t, $J = 7.2$ Hz, 9H), 3.47 (s, 3H), 3.48 (q, $J = 7.2$ Hz, 6H); ^{13}C NMR ($CDCl_3$): $\delta = 8.0$, 50.85, 53.9, 162.3; IR (CCl_4): 1634 cm^{-1}; HRMS (FAB$^+$), calcd for $C_8H_{18}N_2O_2 + H$: 175.1446, found: 175.1437.

Reaction of thioanisole with 2a: *S*-methyl-*N*-methoxycarbonyl-*S*-phenylsulfilimine (49): A solution of **2a** (537 mg, 3 mmol) in acetonitrile (6 mL) under argon was treated at −40 °C by thioanisole (0.352 mL, 3 mmol). After the mixture was stirred at −40 °C for 1 h it was concentrated in vacuo and chromatographed over silica gel (40 g, MeOH/CH_2Cl_2 2:98) to give methylphenylsulfoxide (109 mg, 26%) and **49** (296 mg, 50%) (oil); ^{1}H NMR ($CDCl_3$): $\delta = 2.79$ (s, 3H), 3.65 (s, 3H), 7.49–7.54 (m, 3H), 7.73–7.78 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 36.2$, 53.0, 126.2, 129.9, 132.3, 136.6, 165.2; IR (CCl_4): 1644 cm^{-1}; MS (70 eV, EI): m/z (%) = 197 (30), 182 (8), 166 (54), 151 (67), 140 (13), 138 (16), 124 (100), 123 (19), 121 (14), 105 (19), 104 (11), 91 (13), 78 (17), 77 (40), 65 (15), 51 (31), 50 (10), 45 (11); HRMS, calcd for $C_9H_{11}NO_2S$: 197.0511, found: 197.0510.

Relative amination rate of *N*-alkyloxycarbonyl-3-aryloxaziridines 7b–h, 4a–d, 5 and 6 against morpholine: The oxaziridines were carefully washed by pentane or a pentane/iPr_2O mixture before the experiment. A solution of **2a** (9.03 mg, 0.0504 mmol) kept at constant temperature (20 °C) and oxaziridine **2b–h**, **4a–d**, or **6** (0.0504 mmol) in $CDCl_3$ (0.25 mL) was stirred while a morpholine solution (0.0745 M in $CDCl_3$, 0.20 mL, 0.0149 mmol) was added. The ratio of the two benzaldehydes produced, 7(X = H)/7(X = H), was measured 30 min later by ^{1}H NMR (integration of the CHO groups).

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[1] S. Andreae, E. Schmitz, *Synthesis* **1991**, 327–341, and references cited therein.
[2] Recent reviews on electrophilic amination: J. Mulzer, H.-J. Altenbach, M. Braun, K. Krohn, H.-U. Reissig, *Organic Synthesis Highlights*, VCH, Weinheim, **1991**, pp. 45–53; E. Erdik, M. Ay, *Chem. Rev.* **1989**, *89*, 1947–1980. See also: C. Greck, L. Bischoff, F. Ferreira, J.-P. Genêt, *J. Org. Chem.* **1995**, *60*, 7010–7012; A. Alberti, F. Canè, P. Dembech, D. Lazzari, A. Ricci, G. Seconi, *J. Org. Chem.* **1996**, *61*, 1677–1681.
[3] W. Büchner, R. Schliebs, G. Winter, K. H. Büchel, *Industrial Inorganic Chemistry*, VCH, Weinheim, **1989**, pp. 45.
[4] E. Schmitz, S. Andreae, S. Schramm, F. M. Albert, D. Lohmann, DDR Patent 240818, **1986**; *Chem. Abstr.* **1987**, *107*, 198926g.
[5] J. Viret, J. Gabard, A. Collet, *Tetrahedron* **1987**, *43*, 891–894; J. Viret, A. Collet, A. Lecoq, M. Marraud, A. Aubry, *New J. Chem.* **1989**, *13*, 849–852; A. Aubry, J.-P. Mangeot, D. Bayeul, J. Vidal, S. Stérin, A. Collet, A. Lecoq, M. Marraud, *Biopolymers* **1991**, *31*, 793–801; M. Marraud, V. Dupont, V. Grand, S. Zercout, A. Lecoq, G. Boussard, J. Vidal, A. Collet, A. Aubry, *ibid.* **1993**, *33*, 1135–1148; A. Amour, A. Collet, C. Dubar, M. Reboud, *Int. J. Pept. Protein Res.* **1994**, *43*, 297–304; S. Zercout, A. Aubry, J. Vidal, A. Vicherat, V. Dupont, A. Collet, M. Marraud, *ibid.* **1994**, *44*, 378–387; S. Chen, R. A. Chrusciel, H. Nakanishi, A. Raktabutr, M. E. Johnson, A. Sato, D. Weiner, J. Hoxie, H. U. Saragovi, M. J. Greene, M. Kahn, *Proc. Natl. Acad. Sci. USA*, **1992**, *89*, 5872–5876.
[6] J. Vidal, J. Drouin, A. Collet, *J. Chem. Soc. Chem. Commun.* **1991**, 435–437.
[7] J. Vidal, L. Guy, S. Stérin, A. Collet, *J. Org. Chem.* **1993**, *58*, 4791–4793.
[8] J. Vidal, S. Damestoy, A. Collet, *Tetrahedron Lett.* **1995**, *36*, 1439–1442.
[9] R. Charnas, K. Gubernator, I. Heinze, C. Hubschwerlen (Hoffmann–La Roche), EP 508234, **1992**; *Chem. Abstr.* **1993**, *119*, 117025d.
[10] A. Aubry, J.-P. Mangeot, J. Vidal, A. Collet, S. Zerkout, M. Marraud, *Int. J. Peptide Protein Res.* **1994**, 43, 305–311.
[11] D. A. Niederer, J. T. Kapron, J. C. Vederas, *Tetrahedron Lett.* **1993**, *34*, 6859–6862.
[12] C. Klinguer, O. Melnyk, E. Loing, H. Gras-Masse, *Tetrahedron Lett.* **1996**, *40*, 7259–7262.
[13] F. A. Davis, A. C. Scheppard, *Tetrahedron* **1989**, *45*, 5703–5742; F. A. Davis, B. C. Chen, *Chem. Rev.* **1992**, *92*, 919–934.
[14] W. B. Jennings, S. P. Watson, D. R. Boyd, *Tetrahedron Lett.* **1989**, *30*, 235–238.
[15] V. A. Petrov, G. Resnati, *Chem. Rev.* **1996**, *96*, 1809–1823.
[16] M. J. Haddadin, J. P. Freeman, in *The Chemistry of Heterocyclic Compounds* (Eds.: A. Weissberger, E. C. Taylor), *Vol. 42, Small Ring Heterocycles, Part 3* (Ed.: A. Hassner), Wiley, **1985**, p. 283–350.
[17] R. Kupfer, S., Meier, E. U. Würthwein, *Synthesis* **1984**, 688.
[18] Y. Usuki, Y. Wang, J. Aubé, *J. Org. Chem.* **1995**, 60, 8028–8035 and references cited therein.
[19] *N*-acylimines are very sensitive to nucleophilic addition; for instance, see H. Ulrich, B. Tucker, A. A. R. Sayigh, *J. Org. Chem.* **1968**, *33*, 2887–2889.
[20] D. L. Ball, J. O. Edwards, *J. Am. Chem. Soc.* **1956**, *78*, 1125–1129.
[21] B. M. Trost, R. Braslau, *J. Org. Chem.* **1988**, *53*, 532–537.
[22] P. Kocienski, *Protecting groups*, Thieme, Stuttgart, **1994**. See also R. Geiger, W. König, in *The Peptides: Analysis, Synthesis, Biology, Vol 3, Protection of Functional Groups in Peptide Synthesis* (Eds.: E. Gross, J. Meienhofer), Academic Press, **1981**, pp. 3–88.
[23] The Moc group can be cleaved by reaction with BBr_3 or Me_3SiI.
[24] For another preparation of **12e** see A. M. Kanazawa, J.-N. Denis, A. E. Greene, *J. Org. Chem.* **1994**, *59*, 1238–1240.
[25] Y. Ogata, Y. Sawaki, *J. Am. Chem. Soc.* **1973**, *95*, 4687–4692.
[26] The structure of **2a** is monoclinic, $P2_1/c$ with $a = 6.285(1)$, $b = 7.050(2)$, $c = 20.226(3)$ Å, $\beta = 91.52(2)°$, $Z = 4$. A total of 933 reflections were observed ($\theta \leq 50°$); data collection was stopped after 48% decrease of the reflection intensity due to crystal damage; 631 reflections were used in the refinement with $I \geq 3\sigma(I)$; shift/esd's < 0.40; $R = 0.048$, $R_w = 0.051$; g.o.f = 1.16; $w = 1.19/(\sigma^2(F) + 0.0022F^2)$. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100235. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK (Fax: Int. code +(1223)336-033; e-mail: deposit@chemcrys.cam.ac.uk).
[27] D. Jerslev, *Acta Crystallogr.* **1967**, *23*, 645–649.
[28] W. H. Chen, W. H. Watson, F. A. Davis, J. F. Lamendola, U. K. Nadir, *Acta Crystallogr. B* **1978**, *34*, 2861–2863.
[29] S. D. Cook, T. A. Hamor, W. A. Jennings, A. A. Tebbutt, S. P. Watson, D. R. Boyd, *J. Chem. Soc. Perkin Trans. 2* **1991**, 1281–1285.
[30] A. G. Orpen, L. Brammer, F. H. Allen, O. Kennard, D. G. Watson, R. Taylor, in *Structure correlation, Vol. 2* (Eds.: H.-B. Bürgi, J. D. Dunitz), VCH, Weinheim, **1994**, see Appendix A.
[31] W. B. Jennings, D. R. Boyd, in *Cyclic Organonitrogen Stereodynamics* (Eds.: J. B. Lambert, Y. Takeushi), VCH, Weinheim, **1992**, pp. 105–158.
[32] Y. Takeushi In *Cyclic Organonitrogen Stereodynamics* (Eds.: J. B. Lambert, Y. Takeushi), VCH, Weinheim, **1992**, pp. 9–30.
[33] Review on aminimides: W. J. McKillip, E. A. Sedor, B. M. Cullbertson, S. Wawzonek, *Chem. Rev.* **1973**, *73*, 255–281.
[34] W. W. Zajac, Jr, T. R. Walters, M. G. Darcy, *J. Org. Chem.* **1988**, *53*, 5856–5860.
[35] L. Guy, Thèse de Doctorat, École Normale Supérieure de Lyon, **1995**.
[36] A. Collet, J. Vidal, J.-C. Hannachi, L. Guy (CNRS), *Brevet français* 95/10685, **1995**; PCT WO 97/09303, **1997**.
[37] R. W. Hay, L. J. Porter, *J. Chem. Soc. B.* **1967**, 1261–1264.

0947-6539/97/0310-1708 $ 17.50+.50/0

[38] J. Viret, A. Collet, *New. J. Chem.* **1988**, *12*, 253–256; see also H. Niedrich, G. Köller, *J. Prakt. Chem.* **1974**, 316, 729–740.
[39] M. E. Jung, M. A. Lyster, *J. Chem. Soc. Chem. Commun.* **1978**, 315–316.
[40] F. A. Davis, A. C. Sheppard, *J. Org. Chem.* **1987**, *52*, 955–957.
[41] Review on sulfilimines: T. L. Gilchrist, C. Moody, *Chem. Rev.* **1977**, *77*, 409–435.
[42] A solution of triphenylphosphine (17.66 mg in 0.25 mL CD_2Cl_2) in a NMR tube was frozen in liquid nitrogen and treated by **4a** (16.89 mg in 0.07 mL CD_2Cl_2). The mixture was then studied by NMR at −94 °C. ^{31}P NMR (CD_2Cl_2) (179 K): $\delta = -7.74$ (Ph_3P), 29.3 (Ph_3PO) and 19.92 (**14**).
[43] Oxazaphosphetanes are generally unstable except in a few instances where they have been observed by ^{31}P NMR (δ in the range −30 to −50) and characterized by X-ray crystallography: W. S. Sheldrick, D. Schomburg, A. Schmidpeter, T. von Criegern, *Chem. Ber.* **1980**, *113*, 55–69; T. Sasaki, S. Eguchi, T. Okano, *J. Am. Chem. Soc.* **1983**, *105*, 5912–5913.
[44] No change was observed in the composition of the reaction mixture left at room temperature for 6 h. The aza-Wittig reaction between **14** and **7** (Y = CN) only takes place at higher temperature: for instance 43% conversion is observed after 22 h in refluxing benzene ($c = 0.3$ mol L^{-1}), and 95% after 17 h in refluxing toluene ($c = 1.5$ mol L^{-1}).
[45] F. A. Davis, J. M. Billmers, D. J. Gosciniak, J. C. Towson, *J. Org. Chem.* **1986**, *51*, 4240–4245.
[46] R. D. Bach, G. J. Wolber, *J. Am. Chem. Soc.* **1984**, *106*, 1410–1415.
[47] R. D. Bach, B. A. Coddens, J. J. W. McDouall, H. B. Schlegel, *J. Org. Chem.* **1990**, *55*, 3325–3330.
[48] R. D. Bach, J. L. Andrés, F. A. Davis, *J. Org. Chem.* **1992**, *57*, 613–618.
[49] Y. Hata, M. Watanabe, *J. Am. Chem. Soc.* **1979**, *101*, 6671–6676; Y. Hata, M. Watanabe, *J. Org. Chem.* **1981**, *46*, 610–614.
[50] S. V. Varlamov, G. V. Shustov, A. Yu. Shibaev, Yu. P. Puzanov, I. I. Chervin, R. G. Kostyanovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1989**, 882–890.
[51] J. Vidal, C. Claessens, A. Collet, unpublished results; see ref. [6].
[52] PCmodel 5.0 from Serena Software. We found that the use of a NO bond slightly longer than that of the X-ray structure (≈ 1.6 Å instead of 1.493 Å) gave results easier to interpret in terms of MO assignments. Ab initio geometry optimization of the parent ring affords a NO distance of 1.53 Å; see ref. [47].
[53] The HOMO is in both cases a π orbital localized on the aromatic ring. The HOMO and LUMO energies (in eV) respectively are calculated as −10.01/−0.52 for **2a** and −10.43/−2.29 for **50**.
[54] D. J. Hart, K. I. Kanai, D. G. Thomas, T. K. Yang, *J. Org. Chem.* **1983**, *48*, 289–294.
[55] C. Betschart, B. Schmidt, D. Seebach, *Helv. Chim. Acta* **1988**, *71*, 1999–2021.
[56] M. Bodanszky, A. Bodanszky, *The Practice of Peptide Synthesis*, Springer, New York, **1984**, p. 242.
[57] H. Fritz, C. D. Weis, *J. Org. Chem.* **1978**, *43*, 4900–4901.
[58] L. F. Fieser, M. Fieser, *Reagents for Organic Synthesis, Vol. 1*, Wiley, New York, **1967**, p. 135.
[59] T. Tsuji, E. M. Kosower, *J. Am. Chem. Soc.* **1971**, *93*, 1992–1999.
[60] E. Schmitz, R. Ohme, S. Schramm, *Chem. Ber.* **1967**, *100*, 2600–2603.
[61] R. V. Hoffman, H. V. Kim, *Tetrahedron Lett.* **1990**, *31*, 2953–2956.
[62] E. Decorte, V. Caplar, A. Sega, V. Sunjic, *Acta Pharm. Jugoslav.* **1980**, *30*, 183–187.
[63] H. Niedrich, *Chem. Ber* **1967**, *100*, 3283–3288.
[64] P. Quitt, J. Hellerbach, K. Vogler, *Helv. Chim. Acta* **1963**, *46*, 327–332.
[65] C. H. Heathcock, C. T. Buse, W. A. Kleschick, M. C. Pirrung, J. E. Sohn, J. Lampe, *J. Org. Chem.* **1980**, *45*, 1066–1081.
[66] P. Münster, W. Steglich, *Synthesis* **1987**, 223–225.
[67] M. N. Sheng, J. G. Zajacek, *J. Org. Chem.* **1968**, *33*, 588–590.

  0947-6539/97/0310-1709 $ 17.50+.50/0