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Reaction of vinyl triflates of α-keto esters and imides with secondary amines: synthesis of α,β-diamino carboxylic acid derivatives through aziridinium ions

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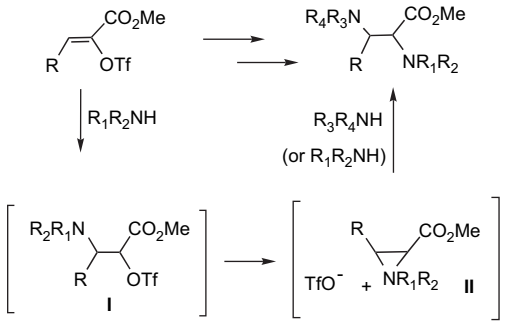
Abstract—Reaction between secondary amines and vinyl triflates of α-keto esters and imides under solvent-free condition provides a ready access to α,β-diamino carboxylates.

1. Introduction

Tandem (also described as domino or cascade) reactions, which permit complex molecules to be constructed in a one-pot assembly, are an important topic in organic synthesis.[1] Vinyl triflates of α-keto acid derivatives, which contain three contiguous electrophilic centres, are therefore very promising substrates in this field. However, it is rather surprising to note that this readily available class of compounds remains unexplored.[2] We have recently started investigating their potential in a series of tandem reactions and showed their effectiveness in this area.[3,4] We notably demonstrated that such molecules are highly reactive with primary amines to provide a reliable access to aziridine carboxylates[4,5] through an overall aza-MIRC (Michael intramolecular ring closure) process.[6] The logical progression in terms of substitution pattern now called for the addition of secondary amines which, through sequential conjugate addition–intramolecular nucleophilic substitution, should provide an unprecedented route towards aziridinium ions (type **II**, Scheme 1).[7] The latter, which are recognized as very reactive transient electrophilic intermediates,[8] are expected to be ring opened during their formation by a second equivalent of amine to provide α,β-diamino carboxylic acid derivatives (Scheme 1).[9]



Scheme 1.

Herein are reported preliminary results establishing that this path can be accomplished offering a new route to α,β-diamino carboxylic esters through an unusual aziridinium ion formation mode.

2. Results and discussion

2.1. Reaction of the vinyl triflates with 2 equiv of a single secondary amine

In a first series of experiments, the cinnamate derivative **1** (R=Ph in Scheme 1) was reacted with various secondary amines in neat conditions. These solvent-free conditions were selected to overcome the intrinsic low reactivity of cinnamate acceptors towards aza-nucleophiles.[4] Amines were used in excess to ensure homogeneous reaction conditions with this crystalline substrate (Table 1). Once formed, the intermediate **I** (Scheme 1) was expected to evolve spontaneously into an aziridinium ion **II** owing to the very high electrophilic character of the Cα atom bearing the triflate and ester functionalities. Accordingly, the reactions were carried out at room temperature unless otherwise indicated. Since α,β-primary diamino carboxylic acids would be particularly useful final products, both diallylamine and dibenzylamine were examined as synthetic ammonia equivalents.

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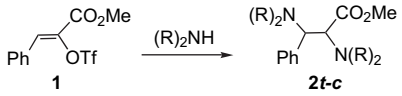
Table 1. Reaction of vinyl triflate **1** with secondary amines



1 **2t-c**

Runs[a]	Amine	Time	Products *t–c* (yields %)[b]		Yields (%)[b]
1	$(Me)_2NH$[10]	24 h	**2a*t*** (38)[c]	**2a*c*** (51)	
2	$(Me)_2NH$[d]	30 min	**2a*t*** (39)[c]	**2a*t*** (50)	
3[e]	$(Et)_2NH$	4 d	**2b*t*** (33)	**2b*c*** (20)[c]	53[c]
4[f]	$(Allyl)_2NH$	7 d	**2c*t*/2c*c*** 2:1	59(73)[g,h]	
5[f]	$(Bn)_2NH$	7 d	No reaction		
6	Morpholine	1 h	**2e*t*** (61)	**2e*c*** (23)[i]	84
7	Pyrrolidine	1 h	**2f*t*** (51)	**2f*c*** (18)[c]	
8	Piperidine	1 h	**2g*t*** (70)	**2g*c*** (30)[i]	100

[a] Unless otherwise indicated, the reactions were conducted at room temperature.
[b] Isolated yields.
[c] The stereochemistry of **2a*t***, **2b*t*** and **2f*t*** was determined by spectroscopic correlation (see Section 2.3).
[d] An aqueous solution (50%) was used.
[e] Enamine **3b** was isolated in 11% yield.
[f] The reaction was stirred at 40 °C for 7 days.
[g] Yield in brackets based on recovered starting triflate.
[h] Enamine **3c** was isolated in 14% yield.
[i] The stereochemistry of **2e*t*** and **2g*t*** was determined by chemical correlation using the Sharpless method[8c,d] (see Section 2.3).

Of the acyclic amines tested (runs 1–5), only dimethylamine, rapidly and cleanly provided the expected diamino adducts **2a*t*–*c*** in a 1:1.3 ratio (run 1).[10] More interestingly, even aqueous $(Me)_2NH$ could be used, affording a prompt reaction with an identical stereochemical profile (run 2).[11]

The lack of stereoselectivity obtained in this reaction was similar to that previously observed in cases of aziridine syntheses, and suggests a non stereoselective protonation of the enolate formed after the conjugate addition of the amine.[4] The reaction of diethylamine (run 3) was slow and provided the expected diamino esters **2b*t*–*c*** (1.4:1 ratio) in moderate yield, contaminated by side-products (TLC monitoring) among them the enamine **3b** (stereochemistry not determined) (Fig. 1). Type **3** enamines are common impurities in this type of chemistry.[12] An even slower but more selective reaction took place with diallylamine, affording, after 1 week the stereomeric mixture of inseparable diamino esters **2c*t*–*c*** (2.3:1 ratio) in correct yield along with the enamine **3c** as a unique impurity (run 4).

On the other hand, no trace of addition product of dibenzylamine could be detected even after prolonged heating. This first set of experiments clearly shows that the reaction strongly depends on steric effects.

As expected, the less sterically demanding and more nucleophilic cyclic amines reacted equally well as dimethylamine, giving a stereomeric mixture of all separable diamines **2e*t*–g*t*** of *anti* stereochemistry[11] and **2e*c*–g*c*** of *syn* stereochemistry[11] (runs 6–8) with a *anti*/*syn* ratio ranging from 2.3:1 to 2.8:1. The successful set of results depicted in runs 1, 2 and 6–8 compares favourably with similar reactions carried out on methyl cinnamate itself, and is testament of the powerful role served by the triflate group to accelerate the ordinarily slow uncatalyzed 1,4-additions of the weak Michael donor secondary amines.

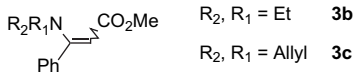
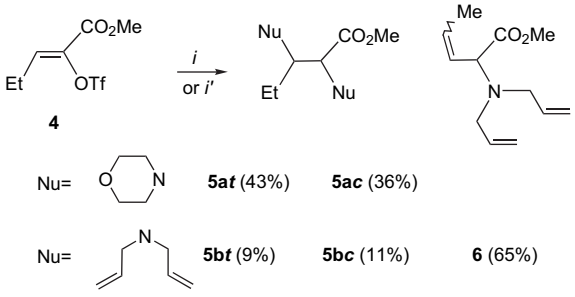


Figure 1. Structure of the enamines **3b** and **c** obtained as side-products through this work.

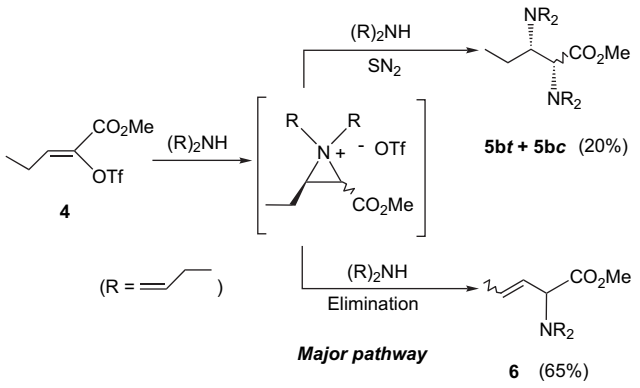
Overall, the low reactivity of the acyclic hindered amines towards the cinnamate derivative **1** provides a severe limit for the reaction. In terms of reactivity, conjugate acceptors substituted by an alkyl group at the β-position ordinarily outperform their β-aryl analogues in the 1,4-addition reactions of amines. Therefore, we next evaluated the β-ethyl vinyl triflate **4** as a prototypic more electrophilic candidate for this aza-MIRC process (Scheme 2).



Scheme 2. (*i*) Morpholine (3.5 equiv), rt, 5 min; (*i'*) Diallylamine (3.5 equiv), rt, 8 h (not optimized).

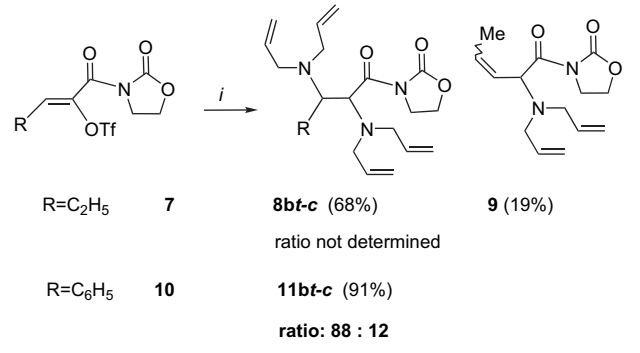
Since compound **4** is an oil, a minimum amount of the amines (3.5 equiv) was used. Substrate **4** actually turned out to be exceedingly responsive towards both cyclic and acyclic amines, as proven first by its reaction with morpholine, which readily gave the separable desired dimorpholino esters **5a*t*–*c*** in 80% yield and almost no diastereoselectivity. The vinyl triflate **4** also disappeared rapidly upon reaction with diallylamine, to afford separable adducts **5b*t*** and **5b*c*** in only 20% yield (Scheme 2). In this case, the major product was the allylic α-amino ester **6**, obtained as a sole geometrical isomer *Z* or *E*, the stereochemistry of which could not be determined due to interference in the ^1H NMR spectrum between the vinylic protons at C3 and C4 and the vinylic hydrogen atoms of the diallylamine moiety. Carrying out the reaction at 60 °C did not change the reaction profile, with similar yields of **5b*t*–*c*** and **6** being obtained. This disappointing result markedly contrasts with a set of examples recently published by Zhu and co-workers[13] describing the highly α-selective and generally efficient-opening of an *N*,*N*-dibenzyl aziridinium salt derived from serine methyl ester by a range of nucleophiles, including the sterically demanding and poorly nucleophilic *N*,*N*-dibenzyl amine.[14] In line with Zhu's results, it should be postulated that the diamines **5a*t*–*c*** and **5b*t*–*c*** obtained herein originate from an α-regioselective aziridinium opening, which is the inverse to the β-selectivity expected for the reactions involving the cinnamate derivative **1**.[15] Overall, this result supports the occurrence of an aziridinium pathway (Scheme 1), the opening of which, either in the cis or trans form, is retarded at the expense of a less sterically demanding elimination process leading to compound **6** (Scheme 3).

The result of the reaction between **4** and diallylamine clearly reveals that a more generally acceptable solution must be



Scheme 3.

found for an efficient aza-MIRC reaction of acyclic secondary amines towards vinyl triflates derived from α-keto acids. This prompted us to examine the use of unsaturated imides as more electrophilic substrates.[16] Hence, imides **7** and **10** were prepared in three steps (a. LiOH, b. $(COCl)_2$/cat DMF then c. *N*-lithium salt of oxazolidin-2-one) from the methyl esters **1** and **4** and their reaction with diallylamine was evaluated (Scheme 4). Conjugate addition to imide **7** was immediately rewarded by yield enhancement (68% yield for **8b*t*–*c*** as an inseparable mixture vs 20% yield for **5b*t*–*c***). Hence, the formation of the allylic α-amino acid derivative **9** (one geometrical isomer, analogous to the product **6**) was reduced from 65% (Scheme 2) to 19%. Reaction of the cinnamoyl derivative **10** with diallylamine provided additional insight into the beneficial impact of an imide acceptor. In this case, the reaction rate was enhanced by at least a seven-fold factor (in comparison with the reaction of **1**), affording an inseparable mixture of diamino imides **11b*t*–*c*** in high yield and with an increased diastereomeric ratio of 88:12 (see for comparison Table 1, run 3).



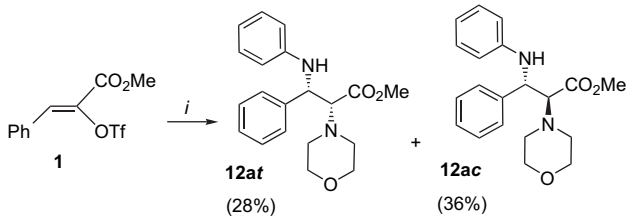
Scheme 4. (*i*) Diallylamine (3.5 equiv), rt, 1 h for **7**, 24 h (unoptimized) for **10**.

The diamino compounds so obtained could, in principle, have been obtained by direct intermolecular S_N2 substitution of the triflate group in the β-amino α-triflyloxy carbonyl intermediate **I** (Scheme 1) without the need to invoke an aziridinium ion. Owing to the above-mentioned very high electrophilic character expected for the α-carbon in type **I** intermediate, in conjunction with the comments relative to Scheme 3 and with several recent publications in the area of diamine synthesis from vicinal *N*,*N*-dialkylamino alcohols, wherein the contribution of aziridinium forms was clearly demonstrated,[13,17] it is likely that aziridiniums are the active intermediates in the chemistry exposed herein. Moreover, the replacement of the methoxy carbonyl group in the cinnamate derivative **1** by the more activating imide function in compound **10** questions about the influence of such an imide group on the regioselectivity of the aziridinium opening process (α- vs β-), which is known to be highly β-selective in the ester series.[15]

2.2. Reaction of the vinyl triflates 1 and 10 with two amines of different nucleophilicities

In order to expand the scope of the present methodology, we sought to develop conditions by which the aziridinium **II** (Scheme 1) could be continuously trapped by a second nucleophile (Nu_2) weaker than the first reactive amine (Nu_1).

A model reaction was investigated by which morpholine (3 equiv) was added to a solution of substrate **1** in aniline (30 equiv). A very slow reaction took place at room temperature[18] to afford the easily separable diastereomers **12a*t*** (less polar, *syn*)[11] and **12a*c*** (more polar, *anti*)[11] in 64% yield, along with the dianilino adduct (not shown) in 8% yield (Scheme 5). Although the formation of this dianilino adduct is, in the present case, anecdotic, it reveals that the aniline derivatives behave as secondary amines rather than as primary ones, an interesting feature that could potentially be exploited to expand the scope of the chemistry practiced herein.

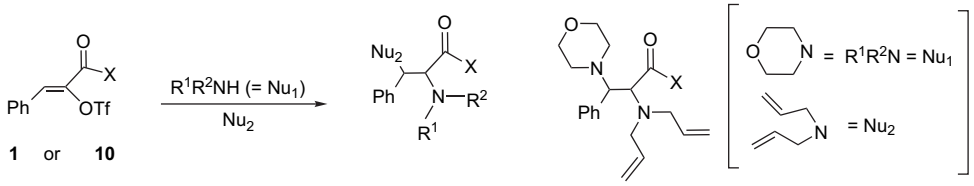


Scheme 5. (*i*) Aniline (30 equiv), morpholine (3 equiv), rt, 168 h.

The structure of **12a*t*–*c*** could be tentatively assigned by means of ^1H and ^{13}C NMR spectroscopies, which shows that one molecule each of morpholine and aniline has been incorporated in both cases. Regiochemistry was confirmed by GC/MS analysis as the fragment ion $[C_6H_5CHNHC_6H_5]^+$ was clearly observed for both diastereomers. *These results strongly support an aziridinium mechanism* since direct intermolecular displacement of the triflate group by aniline in type **I** intermediate (Scheme 1) should have led to the formation of the opposite regioisomer. Moreover, this result corroborates with recent literature precedents, which have revealed high levels of regiocontrol in openings of unsymmetrical benzyl aziridinium ions.[15]

These solvent-free conditions were effective across a series of combination of good and weak amine donors (R_1R_2NH and Nu_2, respectively) to give the crossed diamines in the 31–65% range of yields (Table 2). Combined with aniline, piperidine and pyrrolidine displayed quite higher reactivity than morpholine (2 h vs 7 days), and the outcome of their reactions was improved at 40 °C (runs 2 and 3). Generally, a virtually perfect regiocontrol did occur, favouring products of types **12** and **14** resulting from an opening of the aziridinium at the benzylic position (runs 1–4 and 6).[15] Use of diallylamine as the weak nucleophile in combination with

Table 2. Reactions of vinyl triflates **1** and **10** with two amines of different nucleophilicities



12a*t*c-12e*t*c (X = OMe) **13b** (X = OMe, 6%)

14a*t*c-14b*t*c (X = Oxazolidinone) **15b** (X = Oxazolidinone, 11%)[g]

Runs	X	R^1R^2NH (equiv)	Nu_2 (equiv)	Conditions	Products (yields %)[a]		*anti*/*syn*
1[b]	OMe	Morpholine (3)	Aniline (30)	168 h, 20 °C	**12a*t*** (28)	**12a*c*** (36)	56/44[h]
2[c]	OMe	Piperidine (2)	Aniline (30)	2 h, 40 °C	**12b*t*** (27)[d]	**12b*c*** (32)	54/46[h]
3[c]	OMe	Pyrrolidine (2)	Aniline (30)	2 h, 40 °C	**12c*t*** (46)	**12c*c*** (19)	30/70[i]
4[c]	OMe	Morpholine (1.5)	^{t}BuNH$_2$ (30)	30 min, 20 °C	**12d*t*/12d*c*** 1:2 (31)[e]		66/33[h]
5[c]	OMe	Morpholine (1.5)	Diallylamine (30)	24 h, 40 °C	**12e*t*/12e*c*** 1:1 (41)[f]		[j]
6[c]	Oxazolidinone	Morpholine (2)	Aniline (10)	1 h, 20 °C	**14a*t*** (43)	**14a*c*** (8)	16/84[k]
7[c]	Oxazolidinone	Morpholine (2)	Diallylamine (10)	1 h, 20 °C	**14b*t*** (28)	**14b*c*** (10)[g]	[j]

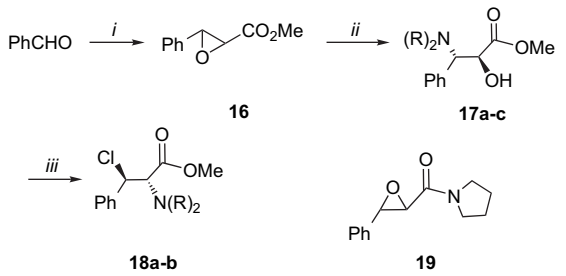
[a] Isolated yields.
[b] When the reaction was carried out at 40 °C, no acceleration was observed and **12a*t*** and **12a*c*** were isolated in 12 and 22% yields, respectively.
[c] Time not optimized.
[d] A pure sample of the less polar adduct **12b*t*** could not be secured due to contamination by the *anti* dipiperidino ester **2g*t***. A similar reaction profile was observed carrying out the reaction at rt.
[e] The adducts were not separable. Moreover, stereomeric aziridine carboxylates and dimorpholino esters **2e*t*–*c*** were also isolated in 25 and 28% yields, respectively.
[f] The regioisomer **13b** (one stereomer, stereochemistry not determined) was isolated in 6% yield.
[g] The regioisomers **15b*t*** and **15b*c*** (stereochemistry not determined) were isolated in 8 and 3% yields, respectively.
[h] Stereochemistry determined by chemical correlation using the Sharpless method[8c,d] (see Table 3 and comments thereof).
[i] Stereochemistry determined by spectroscopic correlation (see Table 3 and comments thereof).
[j] Stereochemistry not determined.
[k] Stereochemistry determined by chemical correlation using the Sharpless method[8c,d] after methanolysis (see Scheme 8 and comments thereof).

morpholine made exception to this rule, with the expected adducts **12e*t*–*c*** and **14b*t*–*c*** being accompanied by low amounts of regioisomers **13** and **15** (runs 5 and 7). This observation compares with the previous Chuang–Sharpless reports and supports the evidence that the nature of the nucleophile is a key parameter in the regiochemical outcome of type **II** aziridinium (Scheme 1) opening.[8c,d] When the imide **10** (X=oxazolidinone) was processed, yields similar to those exhibited in the ester series were observed whereas stereoselectivity was improved (as also previously observed in the case of using only one amine: Scheme 4) and, perhaps more interestingly, its sense reversed (runs 6 and 7 vs runs 1 and 2). The presence of intense peaks for the fragments ions $[C_6H_5CHNHC_6H_5]^+$ and $[C_6H_5CHN(C_3H_5)_2]^+$ in the GC/MS spectra of the major isomers **14a*t*–*c*** and **14b*t*–*c*** accounts for a usual β-selective aziridinium opening pathway, and furthermore proves that the functional group interconversions at the carbonyl moiety is less influential than the amine structure with respect to the regiochemical outcome of aziridinium opening.

Even if closer inspection of the reaction conditions is further needed to maximize the yield of the desired products in these crossed reactions, we have shown for the first time that addition of two different amines to the double bond of activated vinyl triflates is possible through an original pathway including aziridinium ion formation followed by in situ opening by a second amine.

2.3. Stereochemical determination

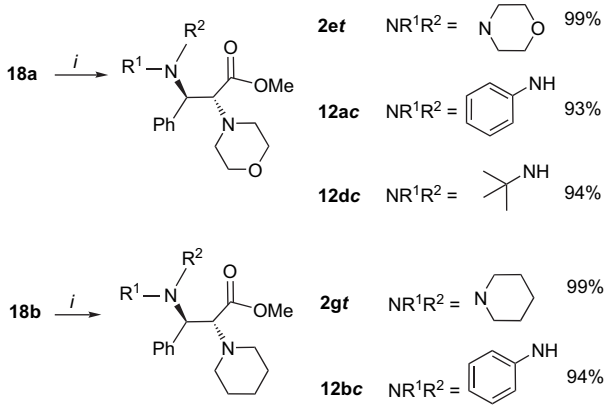
The last part of this work was aimed at determining the stereochemistry of the diamino carboxylic acid derivatives obtained in a stereochemically pure form throughout this study. Several attempts to obtain crystals suitable for X-ray crystallography from diamines **2e*t*–*g*t**, **12a*t*–*c*t** failed. Therefore, we elected to use a sequence recently implemented by Sharpless and Chuang to synthesize *anti* 2,3-diamino ethyl esters from ethyl glycidate.[8c,d] Methyl glycidic ester **16** was synthesized in 48% yield (not optimized) by a Darzens' reaction between α-chloro methyl acetate and benzaldehyde promoted by NaH (Scheme 6). In agreement with the Chuang and Sharpless results, compound **16** was efficiently transformed in two steps into the aziridinium reservoirs **18a** ($N(R)_2$=morpholine) and **18b** ($N(R)_2$=piperidine) as depicted in Scheme 6. The use of pyrrolidine as the amine component was less satisfactory, affording in the oxirane ring opening step the desired amino alcohol **17c** in a disappointing 26% yield after flash-chromatography on silica



Scheme 6. (*i*) α-Chloro methyl acetate (1 equiv), NaH (1 equiv), THF, 0 °C, 1 h, 48% yield; (*ii*) $(R)_2NH$ (1 equiv), MeOH, reflux, 12 h, $(R)_2=(CH_2CH_2)_2O$ **17a** (74%), $(R)_2=(CH_2)_5$ **17b** (78%), $(R)_2=(CH_2)_4$ **17c** (26%); (*iii*) MsCl (1.05 equiv), NEt_3 (1.05 equiv), CH_2Cl_2, 0 °C to rt, 3 h, $(R)_2=(CH_2CH_2)_2O$ **18a** (94%), $(R)_2=(CH_2)_5$ **18b** (96%), $(R)_2=N(CH_2)_4$ **19** (90%).

gel. An even worse result was obtained during the mesylation protocol aimed at producing the required 3-chloro-2-pyrrolidino methyl ester **18c**. The latter was indeed not formed and the oxiranyl *N*-pyrrolidino carboxamide **19** was isolated instead in 90% yield.

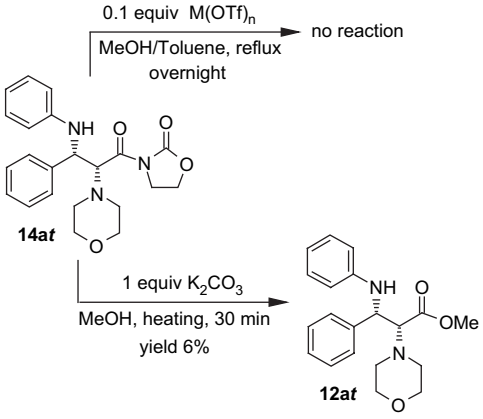
With the stereochemically pure (*anti*) aziridinium ion reservoirs **18a** and **18b** in hand, the stage was now set for the stereochemical establishments. In line with the Chuang–Sharpless results, subjection of **18a** and **18b** to the appropriate amines under optimal conditions (1 equiv each of the amine and K_2CO_3 in refluxing acetonitrile) gave in all cases examined a single product in nearly quantitative yields (Scheme 7). The comparison of the physical and analytical data of the diamino esters so obtained (R_f, mp, ^{1}H NMR spectra) with those obtained through our aza-MIRC approach (Table 3, lines 1 and 2 and 6–8) led to the following conclusions.



Scheme 7. (*i*) K_2CO_3 (1 equiv), R^1R^2NH (1.1 equiv), CH_3CN, reflux, 3 h.

When the cinnamate triflate **1** is processed by 2 equiv of the same amine, the diamino ester with the *anti* stereochemistry is produced as the less polar isomer and, correspondingly, the diamino ester with the *syn* stereochemistry is formed as the more polar isomer. In stark contrast, in the cases of using two different amines, the diamine with the *anti* stereochemistry is formed as the more polar isomer. Key data ascertaining these stereochemical establishments, including R_f values, melting points and chemical shifts in ^{1}H NMR spectroscopy for the MeO group in the case of adducts bearing two identical amino groups (lines 1–5),[19] are provided in Table 3.

To complete this study on the stereochemical outcome of the crossed reactions, we verified whether the rationale applied to the methyl ester series would be also effective in the imide series. To this end, attempts to transform **14a*t*–*c*** into their methyl ester analogues using a recent $Cu(OTf)_2$-catalyzed methanolysis procedure[20] left the substrates untouched (Scheme 8). Processing other metal triflate catalysts (Yb, Sn, Sc) also failed to give the expected esters **12a**. After a considerable number of trials, we found that, when treated with K_2CO_3 (1 equiv) in refluxing dry methanol the less polar (major) oxazolidinone adduct **14a*t*** was totally consumed within 30 min to give several products among them the less polar methyl ester **12a*t*** was isolated in a disappointingly low 6% yield (Scheme 8) and proved to be identical in all respects (R_f, mp, ^{1}H and ^{13}C NMR) with the *syn* adduct **12a*t*** previously characterized. No trace of the diastereoisomer **12a*c*** could be detected. Provided that no epimerization has taken place at the enolizable position, this experiment demonstrates that the stereochemistry of the crossed imide adducts correlates well with that of the corresponding methyl esters, that is, the less polar adduct **14a*t*** is the *syn* isomer and the more polar one **14a*c*** is the *anti* isomer.



Scheme 8.

3. Conclusion

To summarize, we have shown that vinyl triflates of α-keto esters and imides react with secondary amines in solvent-free conditions to provide α,β-diamino carboxylates in good yields, yet modest stereoselectivity through the probable occurrence of an aziridinium ion. This reaction involves an unprecedented aza-MIRC process leading to an aziridinium ion, which is opened in situ by a second equivalent of amine. We have also demonstrated that introduction of two amines of markedly different nucleophilicities may be possible.

4. Experimental

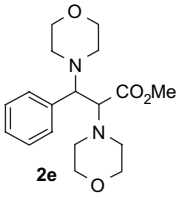
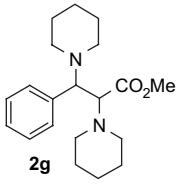
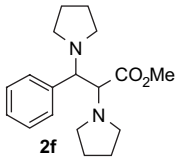
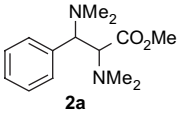
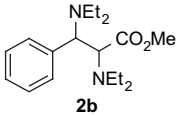
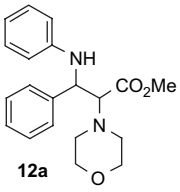
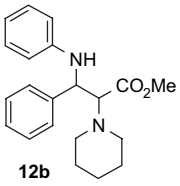
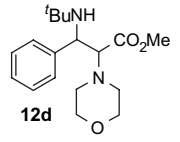
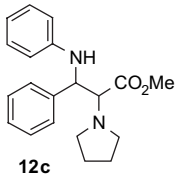
4.1. General

^{1}H and ^{13}C NMR spectra were recorded, respectively, at 200 and 50 MHz. The infrared spectra were recorded on a Perkin–Elmer FT-IR paragon 1000 spectrometer. Thin-layer chromatographies (TLC) were performed with aluminium plates (0.20 mm) precoated with fluorescent silica gel, using EtOAc/hexanes as eluent. Reaction components were then visualized under UV light and dipped in a Dragendorff solution. Silica gel (230–400 mesh) was used for flash-chromatography separations. Gas chromatography/mass spectrometry (GC/MS) was performed with a GC apparatus equipped with a 12 m capillary column, at 90 °C for 2 min, then 10 °C min^{-1} up to 290 °C. The elemental analyses were carried out by the microanalysis laboratory of INSA, F-76130 Mt St Aignan, France.

4.2. Formation of the vinyl triflates 1, 4, 7 and 10

The preparation and analytical data of the methoxy carbonyls vinyl triflates **1** and **4** were reported recently.[4]

Table 3. Stereochemical establishments for the diamines originating from the methyl cinnamate-derived vinyl triflate **1**

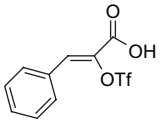
Structure	Stereochemistry	R_f	Mp (°C)	δ MeO[a]
 **2e**	Chuang–Sharpless	0.60[b]	162	3.76
	Aza-MIRC *t anti*	*0.60*	*160–165*	*3.76*
	Aza-MIRC *c*	0.41	100	3.38
 **2g**	Chuang–Sharpless	0.55[c]	102	3.84
	Aza-MIRC *t anti*	*0.55*	*101–103*	*3.84*
	Aza-MIRC *c*	0.38	123–125	3.36
 **2f**	Aza-MIRC *t anti*	*0.68*[d]		*3.69*
	Aza-MIRC *c*	0.37		3.29
 **2a**	Aza-MIRC *t anti*	*0.44*[e]		*3.75*
	Aza-MIRC *c*	0.12		3.38
 **2b**	Aza-MIRC *t anti*	*0.65*[c]		*3.65*
	Aza-MIRC *c*	0.34		3.43
 **12a**	Chuang–Sharpless	0.22[c]	117	3.41
	Aza-MIRC *t*	0.33	135–136	3.52
	Aza-MIRC *c anti*	*0.22*	*116–118*	*3.41*
 **12b**	Chuang–Sharpless	0.43[c]	183	3.40
	Aza-MIRC *t*	0.58	[f]	3.49
	Aza-MIRC *c anti*	*0.43*	*183–184*	*3.40*
 **12d**	Chuang–Sharpless	0.30[c]		3.70
	Aza-MIRC *t*[g]	0.32		3.63
	Aza-MIRC *c anti*	*0.30*		*3.70*
 **12c**	Aza-MIRC *t*	0.60[c]		
	Aza-MIRC *c anti*	*0.42*		

[a] Values in parts per million corresponding to the chemical shift in ^{1}H NMR spectroscopy.
[b] Eluent: cyclohexane/EtOAc 4:6.
[c] Eluent: cyclohexane/EtOAc 8:2.
[d] Eluent: cyclohexane/EtOAc 6:4.
[e] Eluent: cyclohexane/EtOAc 5:5.
[f] No melting point is given due to contamination of the less polar stereomer **12b*t*** by the dipiperidino adduct **2g*t***.
[g] The two stereomers **12d*t*–*c*** were not separated. However, their ratio could be evaluated by ^{1}H NMR spectroscopy (**12dc**/**12d*t***=2:1).

4.2.1. General procedures for the preparation of the imides triflates 7 and 10.

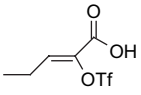
4.2.1.1. Saponification. A solution of anhydrous LiOH (3 equiv) in water (15 ml) was added dropwise over 30 min at 0 °C to a solution of the methyl ester **1** or **4** (1 g) in THF (15 ml). At the end of the addition, the reaction was stirred for an additional period of 15 min at 0 °C. The cryogenic bath was removed and the stirring was pursued for 10 min. An aqueous solution of sodium hydrogen carbonate (10%) was added, the two phases were decanted and the aqueous layer was extracted rapidly three times with ether. The aqueous phase was carefully acidified using 6 M hydrochloric acid, saturated with sodium chloride and extracted three times with dichloromethane. After two washings with brine, drying over magnesium sulfate and evaporation of the solvent, the crystals were dried under high vacuum and used directly without purification.

4.2.1.1.1. (Z)-3-Phenyl-2-trifluoromethylsulfonyloxy propenoic acid.



Yield 60–70%. Pale green solid, mp 104 °C (decomposition); IR (ν, cm^{-1}, $CHCl_3$) 1712; ^1H NMR (200 MHz, $CDCl_3$) δ 7.45–7.55 (m, 3H), 7.65–7.75 (m, 3H), 12 (COOH, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 108.7 (CF_3), 115.1 (CF_3), 121.5 (CF_3), 127.9 (CF_3), 129, 129.4, 130.9, 131.8, 133.7, 133.8, 134.2, 138.2, 166.5.

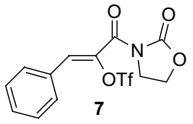
4.2.1.1.2. (Z)-2-Trifluoromethylsulfonyloxy pentenoic acid.



Yield 81%. White solid; ^1H NMR (200 MHz, $CDCl_3$) δ 1.15 (t, J=7.8 Hz, 3H), 2.41 (quint, J=7.8 Hz, 2H), 6.91 (t, J=7.8 Hz, 1H).

4.2.1.2. Imide formation. To a solution of the above carboxylic acids (1 equiv) in dry dichloromethane (2 ml $mmol^{-1}$) were added dropwise under an argon atmosphere oxalyl chloride (2 equiv) and DMF (one drop). After stirring for 1 h, the volatiles were carefully evaporated and dry tetrahydrofuran (5 mP) was added under argon to the acid chloride. This solution was kept at −80 °C. In the same time, to a solution of 2-oxazolidinone (1.05 equiv) in dry THF (2 ml $mmol^{-1}$) was added under an argon atmosphere at −80 °C a commercially available solution of *n*-butyllithium 1.6 M in hexane (1.05 equiv per substrate equiv). After stirring for 30 min, this solution was added dropwise at −80 °C to the solution of the acid chloride. After stirring for 1 h, water and ethyl ether (5 ml $mmol^{-1}$) and solid NaCl were added until saturation of the aqueous phase. After decantation, the aqueous layer was extracted three times with ethyl ether (5 ml $mmol^{-1}$). The organic layer was dried over magnesium sulfate and concentrated to afford a crude product, which was purified by flash-chromatography.

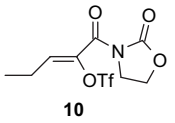
*4.2.1.2.1. (Z)-3-Phenyl-2-trifluoromethanesulfonyloxy propenoic N-oxazolidin-2-one carboxamide (**7**).*



7

Yield 50%. White solid, mp 112 °C; IR (ν, cm^{-1}, $CHCl_3$) 1794.2, 1587.3; ^1H NMR (200 MHz, $CDCl_3$) δ 4.09 (t, J=7.8 Hz, 2H), 4.52 (t, J=7.8 Hz, 2H), 7.09 (s, 1H), 7.4–7.48 (m, 3H), 7.6–7.7 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 43.3, 62.9, 108.7 (CF_3), 115.1 (CF_3), 121.5 (CF_3), 127.9 (CF_3), 128.9, 129.6, 130.7, 131.2, 136.4, 152.1, 162.3; LRMS *m/z* 365 (M^+, 5), 232 (45), 204 (64), 105 (45), 89 (Base). Anal. Calcd for $C_{13}H_{10}NO_6F_3S$ (365.28): C, 42.74; H, 2.76; N, 3.83. Found: C, 42.57; H, 2.98; N, 3.70.

*4.2.1.2.2. (Z)-2-Trifluoromethylsulfonyloxy pentenoic N-oxazolidin-2-one carboxamide (**10**).*



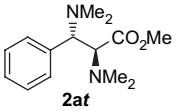
10

Yield 45%. White solid, mp 43 °C; IR (ν, cm^{-1}, $CHCl_3$) 1797.0, 1698.2; ^1H NMR (200 MHz, $CDCl_3$) δ 1.11 (t, J=7.8 Hz, 3H), 2.39 (quint, J=7.8 Hz, 2H), 4.03 (t, J=7.8 Hz, 2H), 4.46 (t, J=7.8 Hz, 2H), 6.39 (t, J=7.8 Hz, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 12.2, 19.9, 43.3, 62.7, 112.1 (CF_3), 116.3 (CF_3), 120.6 (CF_3), 124.8 (CF_3), 137.2, 137.6, 149.0, 161.6; LRMS *m/z* 231 (M^+−96, 2), 184 (32), 114 (29), 88 (67), 69 (Base). Anal. Calcd for $C_9H_{10}NO_6F_3S$ (317.24): C, 34.07; H, 3.17; N, 4.41. Found: C, 34.27; H, 3.09; N, 4.26.

4.3. General procedure for the reaction of amines with the alkoxymethyl vinyl triflates 1 and 4

To 100 mg of the triflate was added in one portion 1 ml of the amine. The mixture was magnetically stirred for 1 h, the excess of solvent was removed under vacuum and the residue was purified by flash-column chromatography, eluting with cyclohexane/EtOAc.

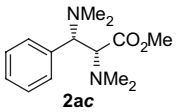
4.3.1. Methyl 2,3-bis-dimethylamino-3-phenyl propanoate (2a). The reaction gave two diastereomers but only the less polar diamino adduct **2a*t*** could be recovered. Eluent used for the flash-column chromatography: cyclohexane/EtOAc 60:40 to EtOAc.



2a*t*

Less polar isomer **2a*t***, R_f=0.44 (cyclohexane/EtOAc 50:50). White solid; yield 31 mg, 38%; mp 101–103 °C; IR (ν, cm^{-1}, $CHCl_3$) 1725.7; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.05 (s, 6H), 2.20 (s, 6H), 3.75 (s, 3H), 3.85 (d, J=11.7 Hz, 1H), 3.99 (d, J=11.7 Hz, 1H), 7.06–7.19 (m, 2H), 7.21–7.41 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 41.2, 41.3, 50.8, 67.5, 67.7, 127.3, 127.6, 129.5,

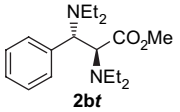
171.5; LRMS *m/z* 205 (M^+-45, <1), 191 (9), 134 (Base). Anal. Calcd for $C_{14}H_{22}O_2N_2$ (250.34): C, 67.17; H, 8.86; N, 11.19. Found: C, 67.27; H, 8.93; N, 11.06.



2ac

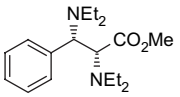
More polar isomer **2ac**, R_f=0.12 (cyclohexane/EtOAc 50:50). White solid; yield 41 mg, 51%; mp 57 °C; IR (*ν*, cm^{-1}, $CHCl_3$) 1725.7; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) *δ* 2.19 (s, 6H), 2.46 (s, 6H), 3.38 (s, 3H), 3.92 (d, *J*=11.7 Hz, 1H), 4.03 (d, *J*=11.7 Hz, 1H), 7.12–7.18 (m, 2H), 7.25–7.39 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) *δ* 40.7, 41.4, 50.5, 66.0, 67.3, 127.6, 127.7, 129.5, 132.7, 169.6; LRMS *m/z* 206 (M^+-44, 1), 191 (6), 134 (Base). Anal. Calcd for $C_{14}H_{22}O_2N_2$ (250.34): C, 67.17; H, 8.86; N, 11.19. Found: C, 67.09; H, 8.95; N, 11.13.

4.3.2. Methyl 2,3-bis-diethylamino-3-phenyl propanoate (2b). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 80:20.



2bt

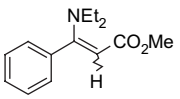
Less polar diastereomer **2bt**, R_f=0.65. Colourless oil; yield 33 mg, 33%; IR (*ν*, cm^{-1}, $CHCl_3$) 1725.7; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) *δ* 0.75 (t, *J*=7.0 Hz, 6H), 0.96 (t, *J*=7.0 Hz, 6H), 1.90–2.12 (m, 2H), 2.20–2.40 (m, 2H), 2.49–2.79 (m, 4H), 3.69 (s, 3H), 4.02 (d, *J*=11.7 Hz, 1H), 4.24 (d, *J*=11.7 Hz, 1H), 7.08–7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) *δ* 13.6, 14.0, 44.1, 44.2, 50.5, 63.1, 64.2, 126.7, 127.3, 129.7, 135.5, 173.2; LRMS *m/z* 247 (M^+-59, 2), 175 (2), 162 (80), 91 (Base). Anal. Calcd for $C_{18}H_{30}O_2N_2$ (306.45): C, 70.54; H, 9.86; N, 9.14. Found: C, 70.30; H, 9.99; N, 9.26.



2bc

More polar diastereomer **2bc**, R_f=0.34. Colourless oil; yield 20 mg, 20%; IR (*ν*, cm^{-1}, $CHCl_3$) 1725.7; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) *δ* 1.03 or 1.09 (t, *J*=7.0 Hz, 12H), 2.03–2.19 (m, 2H), 2.29–2.46 (m, 2H), 2.58–2.76 (m, 2H), 2.80–2.99 (m, 2H), 3.43 (s, 3H), 4.02 (d, *J*=10.9 Hz, 1H), 4.25 (d, *J*=10.9 Hz, 1H), 7.12–7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) *δ* 13.9, 13.9, 43.2, 44.0, 50.5, 61.5, 64.0, 127.1, 127.8, 128.3, 129.1, 137.2, 172.0; LRMS *m/z* 247 (M^+-59, 2), 175 (2), 162 (80), 91 (Base). Anal. Calcd for $C_{18}H_{30}O_2N_2$ (306.45): C, 70.54; H, 9.86; N, 9.14. Found: C, 70.71; H, 9.97; N, 9.41.

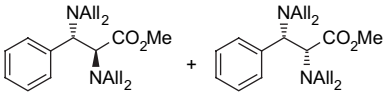
4.3.3. Methyl 3-diethylamino-3-phenyl propenoate (3b).



3b

R_f=0.36. Yellow oil (contaminated by **2bc**); yield 12 mg, 11% (estimated by ^1H NMR spectroscopy); ^1H NMR (200 MHz, $CDCl_3$) *δ* 1.03 or 1.09 (t, *J*=7.0 Hz, 6H), 3.05–3.20 (m, 2H), 3.34 (s, 3H), 4.80 (s, 1H), 7.10–7.20 (m, 3H), 7.35–7.45 (m, 2H).

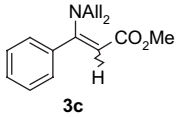
4.3.4. Methyl 2,3-bis-diallylamino-3-phenyl propanoate (2c). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 80:20. Stereomeric adducts **2ct** and **2cc** were obtained as an inseparable mixture in an approximative 2.3:1 ratio. R_f=0.57.



2ct **2cc**

Colourless oil; yield 69 mg, 59%; IR (*ν*, cm^{-1}, $CHCl_3$) 1728.4; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) *δ* 2.40–2.56 (2dd, *J*=8.6 Hz, 14.1 Hz, 2H, *diast.* 1+*diast.* 2), 2.75–2.95 (2dd, *J*=8.6 Hz, 14.1 Hz, 2H, *diast.* 1+*diast.* 2), 3.2–3.4 (m, 6H, *diast.* 1+*diast.* 2), 3.35 (s, 3H, *diast.* 1), 3.49–3.59 (m, 6H, *diast.* 1+*diast.* 2), 3.73 (s, 3H, *diast.* 2), 4.10 (d, *J*=11.7 Hz, 1H, *diast.* 1), 4.14 (d, *J*=11.7 Hz, 1H, *diast.* 2), 4.28 (d, *J*=11.7 Hz, 1H, *diast.* 1), 4.33 (d, *J*=11.7 Hz, 1H, *diast.* 2), 4.9–5.3 (m, 8H, *diast.* 1+*diast.* 2), 5.2–5.5 (m, 1H, *diast.* 1+*diast.* 2), 5.6–6.0 (m, 3H, *diast.* 1+*diast.* 2), 7.05–7.19 (m, 2H, *diast.* 1+*diast.* 2), 7.22–7.36 (m, 3H, *diast.* 1+*diast.* 2); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) *δ* 50.6, 52.5, 53, 53.3, 53.3, 60.6, 61.8, 62.4, 62.8, 116.8, 116.9, 117, 117.3, 127, 127.4, 127.5, 127.9, 129.3, 129.8, 134.1, 135.4, 136.2, 136.8, 137.3, 137.4, 171.4, 172.6.

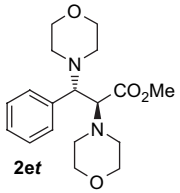
4.3.5. Methyl 3-diallylamino-3-phenyl propenoate (3c).



3c

R_f=0.26. Yellow oil; yield 10 mg, 14%; IR (*ν*, cm^{-1}, $CHCl_3$) 1725.4; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) *δ* 3.43 (s, 3H), 3.7–3.8 (m, 4H), 4.89 (s, 1H), 5.10–5.30 (m, 4H), 5.60–5.85 (m, 2H), 7.15–7.25 (m, 2H), 7.35–7.45 (m, 3H); LRMS *m/z* 258 (M^++1, 3), 257 (M^+, 27), 226 (22), 216 (33), 186 (Base).

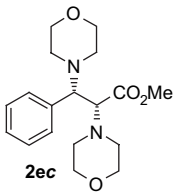
4.3.6. Methyl 2,3-dimorpholino-3-phenyl propanoate (2e). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 40:60.



2et

Less polar diastereomer **2et**, R_f=0.60. White solid; yield 33 mg, 61%; mp 160–63 °C; IR (*ν*, cm^{-1}, $CHCl_3$) 1728.4; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) *δ* 2.10–2.26 (m, 2H), 2.39–2.65 (m, 6H), 3.19–3.36 (m, 2H), 3.36–3.48 (m, 2H), 3.51–3.59 (m, 4H), 3.76 (s, 3H), 3.85 (d, *J*=11.7 Hz, 1H),

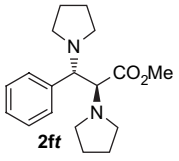
4.02 (d, J=11.7 Hz, 1H), 7.05–7.12 (m, 2H), 7.25–7.36 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 49.6, 49.9, 50.9, 67.1, 67.4, 67.7, 67.8, 127.4, 127.6, 129.2, 133.1, 171.5; LRMS m/z 275 (M^+-59, 5), 176 (Base). Anal. Calcd for $C_{18}H_{26}O_4N_2$ (334.42): C, 64.65; H, 8.08; N, 8.37. Found: C, 64.89; H, 8.29; N, 8.26.



2ec

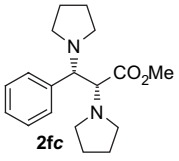
More polar diastereomer **2ec**, R_f=0.41. Yellow solid; yield 12 mg, 23%; mp 100 °C; IR (ν, cm^{-1}, $CHCl_3$) 1731.1 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.34–2.60 (m, 4H), 2.68–2.90 (m, 4H), 3.38 (s, 3H), 3.60–3.75 (m, 8H), 3.87 (d, J=11.7 Hz, 1H), 4.05 (d, J=11.7 Hz, 1H), 7.07–7.17 (m, 2H), 7.23–7.35 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 49.2, 49.7, 51.0, 66.0, 67.2, 67.5, 67.7, 127.9, 128.0, 129.1, 134.2, 170.0; LRMS m/z 275 (M^+-59, 5), 176 (Base). Anal. Calcd for $C_{18}H_{26}O_4N_2$ (334.42): C, 64.65; H, 8.08; N, 8.37. Found: C, 64.71; H, 8.16; N, 8.31.

4.3.7. Methyl 2,3-dipyrrolidino-3-phenyl propanoate (2f). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 60:40.



2ft

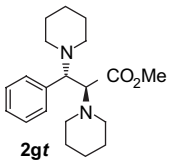
Less polar diastereomer **2ft**, R_f=0.68. Yellow solid; yield 25 mg, 51%; mp 99–102 °C; IR (ν, cm^{-1}, $CHCl_3$) 1725.7; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.35–1.62 (m, 8H), 2.19–2.56 (m, 6H), 2.57–2.74 (m, 2H), 3.69 (s, 3H), 4.06 (d, J=11.7 Hz, 1H), 4.24 (d, J=11.7 Hz, 1H), 7.09–7.20 (m, 2H), 7.21–7.36 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 22.7, 23.4, 47.9, 49.1, 50.9, 65.1, 66.5, 127.0, 127.4, 129.6, 134.2, 172.8; 243 (M^+-59, 3), 160 (Base). Anal. Calcd for $C_{18}H_{26}O_2N_2$ (302.42): C, 71.49; H, 8.66; N, 9.26. Found: C, 71.62; H, 8.81; N, 9.13.



2fc

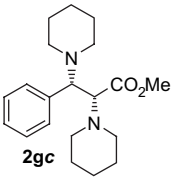
More polar diastereomer **2fc**, R_f=0.37. White solid; yield 9 mg, 18%; mp 78–81 °C; IR (ν, cm^{-1}, $CHCl_3$) 1725.4; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.52–1.80 (m, 8H), 2.33–245 (m, 2H), 2.55–2.92 (m, 6H), 3.29 (s, 3H), 3.88 (d, J=9.4 Hz, 1H), 3.98 (d, J=9.4 Hz, 1H), 7.10–7.32 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 22.9, 23.5, 49.7, 50.6, 51.1, 67.4, 68.4, 127.4, 127.7, 129.2, 170.6; LRMS m/z 243 (M^+-59, 3), 160 (Base). Anal. Calcd for $C_{18}H_{26}O_2N_2$ (302.42): C, 71.49; H, 8.66; N, 9.26. Found: C, 71.73; H, 8.52; N, 9.11.

4.3.8. Methyl 2,3-dipiperidino-3-phenyl propanoate (2g). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 80:20.



2gt

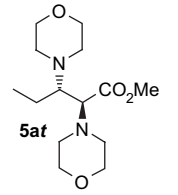
Less polar diastereomer **2gt**, R_f=0.55. White solid; yield 40 mg, 70%; mp 101–103 °C; IR (ν, cm^{-1}, $CHCl_3$) 1726.9; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 0.97–1.54 (m, 12H, piperidine), 1.97–2.18 (m, 2H), 2.31–2.58 (m, 6H), 3.72 (s, 3H), 3.84 (d, J=11.7 Hz, 1H), 4.02 (d, J=11.7 Hz, 1H), 7.02–7.17 (m, 2H), 7.18–7.35 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 24.5, 26.3, 26.8, 50.5, 50.6, 51.0, 68.4, 68.6, 126.7, 127.2, 129.4, 134.4, 172.3; LRMS m/z 243 (M^+-31, 4), 174 (Base). Anal. Calcd for $C_{20}H_{30}O_2N_2$ (330.47): C, 72.69; H, 8.15; N, 8.47. Found: C, 72.53; H, 8.06; N, 8.44.



2gc

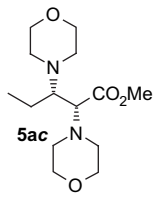
More polar diastereomer **2gc**, R_f=0.38. White solid; yield 18 mg, 30%; mp 123–125 °C; IR (ν, cm^{-1}, $CHCl_3$) 1731.9; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.20–1.62 (m, 12H), 2.20–2.52 (m, 4H), 2.60–2.80 (m, 4H), 3.36 (s, 3H), 3.84 (d, J=11.7 Hz, 1H), 4.03 (d, J=11.7 Hz, 1H), 7.08–7.15 (m, 2H), 7.19–7.31 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 24.7, 24.9, 26.7, 26.9, 50.1, 50.5, 50.6, 66.7, 67.9, 127.2, 127.7, 129.1, 135.5, 171.0; LRMS m/z 243 (M^+-31, 4), 174 (Base). Anal. Calcd for $C_{20}H_{30}O_2N_2$ (330.47): C, 72.69; H, 8.15; N, 8.47. Found: C, 72.93; H, 8.38; N, 8.57.

4.3.9. Methyl 2,3-dimorpholino pentanoate (5a). Only the less polar diastereoisomer could be isolated in pure form. Eluent used for the flash-column chromatography: cyclohexane/EtOAc 60:40.



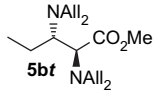
5at

Less polar diastereomer **5at**, R_f=0.40. White solid; yield 44 mg, 43%; mp 109 °C; IR (ν, cm^{-1}, $CHCl_3$) 1691.1; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.0 (t, J=7.8 Hz, 3H), 1.30–1.80 (m, 2H), 2.42–2.60 (m, 6H), 2.64–2.89 (m, 3H), 3.09 (d, J=10.9 Hz, 1H), 3.42–3.70 (m, 8H), 3.67 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 13.2, 20.6, 49.8, 50.2, 50.6, 63.8, 67.4, 67.9, 71.2, 171.5; LRMS m/z 227 (M^+-59, 20), 128 (Base). Anal. Calcd for $C_{14}H_{26}O_4N_2$ (286.37): C, 58.72; H, 9.15; N, 9.78. Found: C, 58.83; H, 9.07; N, 9.54.

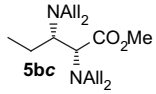


More polar diastereomer **5ac**, R_f=0.34 (contaminated by the first diastereomer). Orange solid; yield 21 mg, 36%; mp 69–70 °C; IR (ν, cm^{-1}, $CHCl_3$) 1725.7; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 0.91 (t, J=7.8 Hz, 3H), 1.30–1.80 (m, 2H), 2.47–2.60 (m, 6H), 2.7–2.96 (m, 3H), 3.18 (d, J=9.4 Hz, 1H), 3.42–3.70 (m, 8H), 3.67 (s, 3H).

4.3.10. Methyl 2,3-bis-diallylamino pentanoate (5b). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 95:05.

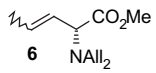


Less polar diastereomer **5b*t***, R_f=0.40. Yellow oil; yield 10 mg, 9%; IR (ν, cm^{-1}, $CHCl_3$) 1725.7; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 0.95 (t, J=7.04 Hz, 3H), 1.32–1.76 (m, 2H), 2.70–3.50 (m, 10H), 3.64 (s, 3H), 4.98–5.22 (m, 8H), 5.53–5.83 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 13.1, 21.1, 50.4, 53.6, 54.0, 59.6, 66.2, 116.0, 117.0, 136.4, 137.8, 172.5; LRMS *m/z* 247 (M−59, 6), 138 (Base). Anal. Calcd for $C_{18}H_{30}O_2N_2$ (306.45): C, 70.54; H, 9.86; N, 8.47. Found: C, 70.83; H, 10.13; N, 8.24.



More polar diastereomer **5b*c***, R_f=0.28. Yellow oil; yield 12 mg, 11%; IR (ν, cm^{-1}, $CHCl_3$) 1722.9; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 0.88 (t, J=7.04 Hz, 3H), 0.92–1.80 (m, 2H), 2.70–3.55 (m, 10H), 3.64 (s, 3H), 4.94–5.30 (m, 8H), 5.54–5.91 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 12.1, 23.0, 50.7, 52.9, 53.8, 58.0, 64.8, 115.7, 117.5, 136.4, 138.5, 172.0; LRMS *m/z* 247 (M−59, 6), 138 (Base). Anal. Calcd for $C_{18}H_{30}O_2N_2$ (306.45): C, 70.54; H, 9.86; N, 8.47. Found: C, 70.64; H, 10.00; N, 8.39.

4.3.11. Methyl 2-diallylamino pent-3-enoate (6).

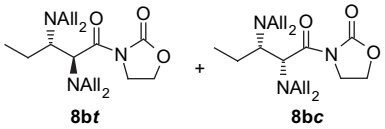


R_f=0.14. Yellow oil; yield 46 mg, 65%; IR (ν, cm^{-1}, $CHCl_3$) 1731.1; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.71 (d, J=6.3 Hz, 3H), 3.08–3.3 (d, J=6.3 Hz, 4H), 3.68 (s, 3H), 3.91 (d, J=7.8 Hz, 1H), 5.05–5.22 (m, 4H), 5.42–5.90 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 18.0, 51.6, 53.5, 65.7, 117.7, 125.6, 131.2, 135.6, 172.9; LRMS *m/z* 209 (M^+, 1), 182 (6), 150 (Base). Anal. Calcd for $C_{12}H_{19}O_2N$ (209.29): C, 68.86; H, 9.15; N, 6.69. Found: C, 68.77; H, 9.19; N, 6.81.

4.4. General procedure for the reaction of diallylamine with the oxazolidinone vinyl triflates 7 and 10

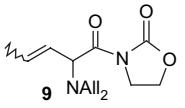
To 100 mg of the triflate was added in one portion 4 equiv of diallylamine (0.15 ml for the reaction with triflate **7**, 0.13 ml for the reaction with triflate **10**). The mixture was magnetically stirred for 5 h (case of triflate **7**) or for 20 h (case of triflate **10**) and directly purified by flash-column chromatography, eluting with cyclohexane/EtOAc 60:40.

4.4.1. 2,3-Bis-diallylamino pentanoic *N*-oxazolidin-2-one carboxamide (8b). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 60:40. Stereomeric adducts **8b*t*** and **8b*c*** were obtained as an inseparable mixture in a nearly 1.5:1 ratio. R_f=0.53.



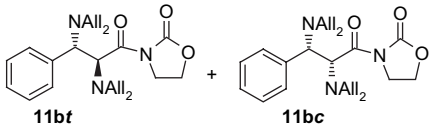
Colourless oil; yield 63 mg, 68%; IR (ν, cm^{-1}, $CHCl_3$) 1690.0, 1775.0 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 0.87 (t, J=7.04 Hz, 3H, *diast.* 1), 0.99 (t, J=7.04 Hz, 3H, *diast.* 2), 0.9–1.1 (m, 1H, *diast.* 2), 1.35–1.50 (m, 1H, *diast.* 2), 1.50–1.75 (m, 2H, *diast.* 1), 2.89–3.57 (m, 10H, *diast.* 1+*diast.* 2), 3.97 (t, J=8.6 Hz, 2H, *diast.* 1+*diast.* 2), 4.32 (t, J=8.6 Hz, 2H, *diast.* 1), 4.34 (t, J=8.6 Hz, 2H, *diast.* 2), 4.95–5.3 (m, 8H, *diast.* 1+*diast.* 2), 5.51–5.96 (m, 4H, *diast.* 1+*diast.* 2); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 12.1, 13.4, 20.9, 22.2, 42.3 (2), 52.9, 53.2, 53.5, 53.9, 58.6, 60.3, 61.5, 61.7, 61.8, 62.6, 115.6 (2), 116.4, 116.9, 136.1, 136.2, 137.2, 138.5, 153.3, 153.5, 173.2, 173.8.

4.4.2. (*Z* or *E*)-2-Diallylamino pent-3-enoic *N*-oxazolidin-2-one carboxamide (9).



R_f=0.34. Yellow oil; yield 13 mg, 23%; IR (ν, cm^{-1}, $CHCl_3$) 1698.2, 1780.5; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.72 (d, J=6.3 Hz, 3H), 2.89–3.40 (m, 4H), 3.98 (t, J=7.8 Hz, 2H), 4.37 (t, J=7.8 Hz, 2H), 5.05–5.25 (m, 4H), 5.31 (d, J=7.8 Hz, 1H), 5.46–5.95 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 18.2, 42.6, 53.9, 62.0, 62.8, 117.5, 124.8, 135.7, 152.7, 174.9; LRMS *m/z* 264 (M^+, <1), 223 (6), 150 (Base). Anal. Calcd for $C_{14}H_{20}O_3N_2$ (264.32): C, 63.61; H, 7.62; N, 10.60. Found: C, 63.68; H, 7.70; N, 10.43.

4.4.3. 2,3-Bis-diallylamino-3-phenyl propanoic *N*-oxazolidin-2-one carboxamide (11b). Stereomeric adducts **11b*t*** and **11b*c*** were obtained as an inseparable mixture in a nearly 7:1 ratio. Eluent used for the flash-column chromatography: cyclohexane/EtOAc 70:30. R_f=0.5.

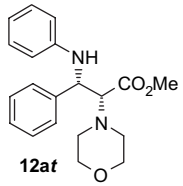


Colourless oil; yield 91 mg, 91%; IR (ν, cm^{-1}, $CHCl_3$) 1692.7, 1775.0; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.4 (dd, J=7.8 Hz, 14.8 Hz, 2H, *diast.* 2), 2.62 (dd, J=8.6 Hz, 14.1 Hz, 2H, *diast.* 1), 3.30–3.8 (m, 8H, *diast.* 1+*diast.* 2), 3.91–4.25 (m, 1H, *diast.* 1+*diast.* 2), 4.3–4.5 (m, 1H, *diast.* 1+*diast.* 2), 4.4 (d, J=10.9 Hz, 1H, *diast.* 1+*diast.* 2), 5.05–5.25 (m, 8H, *diast.* 1+*diast.* 2), 5.7 (d, J=10.9 Hz, 1H, *diast.* 1+*diast.* 2), 5.8–6 (m, 4H, *diast.* 1+*diast.* 2); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 42.3, 52.9, 53.2, 59.7, 61.5, 62.0, 116.1, 116.2 (*diast. min.*), 116.3 (*diast. min.*), 117.0, 127.4, 127.5 (*diast. min.*), 127.8, 129.6, 130.0 (*diast. min.*), 135.1, 136.0 (*diast. min.*), 136.9 (*diast. min.*), 137.2, 152.8, 172.8.

4.5. Crossed reactions of two different amines with vinyl triflate 1

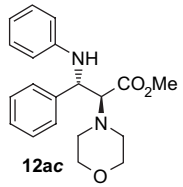
4.5.1. General procedure. To 100 mg of the triflate **1** were successively added in one portion 30 equiv of the less nucleophilic amine (0.88 ml aniline or 1 ml *tert*-butylamine or 1.19 ml diallylamine) and the more nucleophilic amine: morpholine (3 equiv, 89 µl), piperidine (2 equiv, 73 µl), pyrrolidine (2 equiv, 53 µl) (cases of aniline and *tert*-butylamine), or morpholine (1.5 equiv, 44 µl) (case of diallylamine). The mixture was stirred at the temperature indicated in Table 2 until total disappearance of the starting material (TLC monitoring). The excess of the less nucleophilic amine was removed under vacuum and the crude mixture was directly purified by flash-column chromatography, eluting with cyclohexane/EtOAc.

4.5.1.1. Methyl 3-anilino-2-morpholino-3-phenyl propanoate (12a). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 80:20.



12a*t*

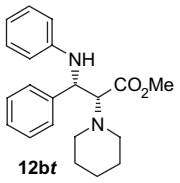
Less polar diastereomer **12a*t***, R_f=0.33. Yellow solid; yield 28 mg, 28%; mp 135–136 °C; IR (ν, cm^{-1}, $CHCl_3$) 1731.3; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.50–2.75 (m, 4H), 3.32 (d, J=10.9 Hz, 1H), 3.52 (s, 3H), 3.59–3.82 (m, 4H), 4.49 (d, J=10.9 Hz, 1H), 5.34 (s, 1H, NH), 6.51 (d, J=8.6 Hz, 2H), 6.66 (t, J=7.04 Hz, 1H), 7.05 (t, J=8.6 Hz, 2H), 7.20–7.35 (m, 3H), 7.40–7.48 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 49.5, 51.1, 56.0, 67.4, 73.6, 113.9, 118.0, 127.4, 127.8, 128.7, 129.1, 140.7, 147.8, 169.0; LRMS m/z 340 (M^+, 10), 281 (35), 180 (Base). Anal. Calcd for $C_{20}H_{24}O_3N_2$ (340.42): C, 70.56; H, 7.10; N, 8.23. Found: C, 70.64; H, 7.25; N, 8.15.



12ac

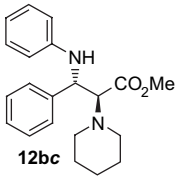
More polar diastereomer **12a*c***, R_f=0.22. White solid; yield 35 mg, 35%; mp 116–118 °C; IR (ν, cm^{-1}, $CHCl_3$) 1736.9; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.42–2.68 (m, 4H), 3.31 (d, J=6.3 Hz, 1H), 3.41 (s, 3H), 3.61–3.72 (t, J=4.7 Hz, 4H), 4.72 (d, J=6.3 Hz, 1H), 6.51 (d, J=8.6 Hz, 2H), 6.63 (t, J=7.0 Hz, 1H), 7.07 (dd, J=7.0 Hz, 8.6 Hz, 2H), 7.20–7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 51.1, 51.4, 56.4, 66.8, 74.0, 113.3, 117.5, 126.6, 127.6, 128.5, 129.1, 139.5, 146.9, 170.8; LRMS m/z 340 (M^+, 10), 281 (35); 180 (Base). Anal. Calcd for $C_{20}H_{24}O_3N_2$ (340.42): C, 70.56; H, 7.10; N, 8.23. Found: C, 70.71; H, 7.28; N, 8.11.

4.5.1.2. Methyl 3-anilino-2-piperidino-3-phenyl propanoate (12b). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 80:20.



12b*t*

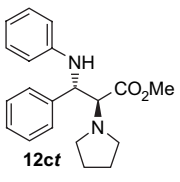
Less polar diastereomer **12b*t*** (contaminated by the dipiperidino compound **2g*t***; **12b*t*/2g*t***=1:0.66 deduced from the ^1H NMR spectrum), R_f=0.58. Yellow solid; yield 48 mg (29 mg **12b*t***, 19 mg **2g*t***), 27%; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.35–1.78 (m, 6H), 2.38–2.57 (m, 4H), 3.26 (d, J=10.2 Hz, 1H), 3.49 (s, 3H), 4.45 (d, J=10.2 Hz, 1H), 5.5 (s, 1H, NH), 6.49 (d, J=7.8 Hz, 2H), 6.62 (t, J=7.0 Hz, 1H), 7.0–7.15 (m, 2H), 7.20–7.35 (m, 3H), 7.41 (d, J=7.0 Hz, 2H).



12b*c*

More polar diastereomer **12b*c***, R_f=0.43. White solid; yield 35 mg, 32%; mp 183–184 °C; IR (ν, cm^{-1}, $CHCl_3$) 1731.1; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.35–1.78 (m, 6H), 2.38–2.57 (m, 4H), 3.26 (d, J=6.2 Hz, 1H), 3.40 (s, 3H), 4.70 (d, J=6.2 Hz, 1H), 5.2 (s, 1H, NH), 6.51 (d, J=7.0 Hz, 2H), 6.66 (t, J=7.0 Hz, 1H), 7.05 (t, J=7.0 Hz, 2H), 7.20–7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 24.3, 25.9, 51.2, 51.9, 56.6, 74.6, 113.4, 117.3, 126.8, 127.4, 128.4, 129.0, 140.0, 146.2, 171.4; LRMS m/z 194 (M^+-156, 1); 182 (Base). Anal. Calcd for $C_{21}H_{26}O_2N_2$ (338.46): C, 74.52; H, 7.74; N, 8.27. Found: C, 74.41; H, 7.88; N, 8.11.

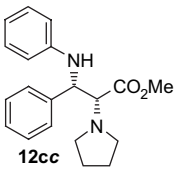
4.5.1.3. Methyl 3-anilino-2-pyrrolidino-3-phenyl propanoate (12c). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 80:20.



12c*t*

Less polar diastereomer **12c*t***, R_f=0.60. White solid; yield 48 mg, 46%; mp 134–135 °C; IR (ν, cm^{-1}, $CHCl_3$) 1725.7; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.72–1.85 (m, 4H), 2.60–2.75 (m, 2H), 2.80–2.97 (m, 2H), 3.48 (s, 3H), 3.65

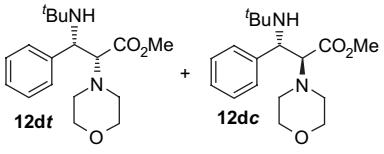
(d, J=10.2 Hz, 1H), 4.49 (d, J=10.2 Hz, 1H), 5.0 (s, 1H, NH), 6.54 (d, J=8.6 Hz, 2H), 6.66 (t, J=7.0 Hz, 1H), 7.06 (dd, J=7.0 Hz, 8.6 Hz, 2H), 7.18–7.38 (m, 3H), 7.46 (d, J=7.0 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 23.5, 48.2, 50.9, 58.1, 69.5, 114.0, 117.7, 127.3, 127.6, 128.5, 128.9, 141.1, 148.1, 170.1; LRMS m/z 194 (M^+-130, 1), 182 (Base). Anal. Calcd for $C_{20}H_{24}O_2N_2$ (324.42): C, 74.04; H, 7.45; N, 8.63. Found: C, 73.94; H, 7.52; N, 8.55.



12cc

More polar diastereomer **12cc**, R_f=0.42. Pale yellow oil; yield 18 mg, 17%; IR (ν, cm^{-1}, $CHCl_3$) 1736.9; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.75–1.90 (m, 4H), 2.55–2.72 (m, 4H), 3.28 (d, J=4.7 Hz, 1H), 3.42 (s, 3H), 4.65 (d, J=4.7 Hz, 1H), 5.45 (br, 1H, NH), 6.53 (d, J=7.8 Hz, 2H), 6.65 (t, J=7.8 Hz, 1H), 7.08 (t, J=7.0 Hz, 2H), 7.23–7.40 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 23.2, 51.4, 51.8, 58.8, 73.6, 113.2, 117.1, 126.5, 127.5, 128.5, 129.0, 139.8, 147.4, 171.4; LRMS m/z 194 (M^+-130, 1), 182 (Base). Anal. Calcd for $C_{20}H_{24}O_2N_2$ (324.42): C, 74.04; H, 7.45; N, 8.63. Found: C, 74.09; H, 7.48; N, 8.39.

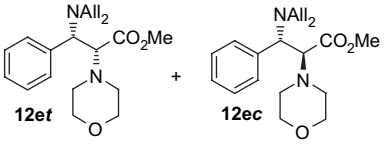
4.5.1.4. Methyl 3-*tert*-butylamino-2-morpholino-3-phenyl propanoate (12d). The stereomeric adducts **12d*t*** and **12d*c*** were obtained as an inseparable mixture in an approximative 1:2 ratio. Eluent used for the flash-column chromatography: cyclohexane/EtOAc 80:20.



12dt **12dc**

R_f=0.32. White solid; yield 33 mg, 31%; IR (ν, cm^{-1}, $CHCl_3$) 1728.4; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 0.81 (s, 9H, *diast. min.*), 0.85 (s, 9H, *diast. maj.*), 2.05–2.5 (m, 4H, *diast. min.*+*diast. maj.*), 3.11 (d, J=10.9 Hz, 1H, *diast. min.*), 3.25–3.35 (m, 4H, *diast. min.*), 3.40–3.50 (m, 4H, *diast. maj.*), 3.55 (d, J=10.9 Hz, 1H, *diast. maj.*), 3.63 (s, 3H, *diast. min.*), 3.70 (s, 3H, *diast. maj.*), 3.98 (d, J=10.9 Hz, 1H, *diast. maj.*), 4.04 (d, J=10.9 Hz, 1H, *diast. min.*), 7.20–7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 29.1 and 30.3, 49.9 and 50.3, 50.8 and 51.7, 55.9 and 57.3, 67.4 and 67.5, 73.0 and 75.3, 126.7, 127.1, 127.7, 127.9, 128.0, 128.6, 129.4, 133.0, 171.0 and 177.0; LRMS m/z 248 (M^+-72, 1), 106 (Base).

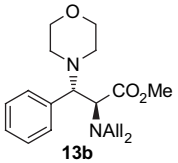
4.5.1.5. Methyl 3-diallylamino-2-morpholino-3-phenyl propanoate (12e). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 80:20. Stereomeric adducts **12e*t*** and **12e*c*** were obtained as an inseparable mixture of diastereomers in a nearly 1:1 ratio.



12et **12ec**

R_f=0.40. White solid; yield 44 mg, 41%; mp 108 °C; IR (ν, cm^{-1}, $CHCl_3$) 1728.4; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.40–2.92 (m, 6H, *diast.* 1+*diast.* 2), 3.22–3.5 (m, 4H, *diast.* 1+*diast.* 2), 3.42 (s, 3H, *diast.* 1), 3.71–3.78 (m, 2H, *diast.* 1+*diast.* 2), 3.78 (s, 3H, *diast.* 2), 3.89 (d, J=11.7 Hz, 1H, *diast.* 1), 3.93 (d, J=11.7 Hz, 1H, *diast.* 2), 4.31 (d, J=11.7 Hz, 1H, *diast.* 1), 4.36 (d, J=11.7 Hz, 1H, *diast.* 2), 5.10–5.25 (m, 4H), 5.62–5.95 (m, 2H), 7.15–7.25 (m, 2H), 7.30–7.42 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 49.7 (CH_2), 50.8 (CH_3), 52.7 (CH_2), 53.4 (CH_2), 60.3 (CH), 60.6 (CH), 67.2 (CH_2), 67.6 (CH_2), 116.9 (CH_2), 127.1 (CH), 127.5 (CH), 127.6 (CH), 128.0 (CH), 129.2 (CH), 129.4 (CH), 137.1 (CH), 137.4 (CH), 170.0 (C=O), 171.3 (C=O); LRMS m/z 285 (M^+-59, 8), 186 (92). Anal. Calcd for $C_{20}H_{28}O_3N_2$ (344.46): C, 69.74; H, 8.19; N, 8.13. Found: C, 69.69; H, 8.25; N, 8.21.

4.5.1.6. Methyl 2-diallylamino-3-morpholino-3-phenyl propanoate (13b). This product was obtained as a single stereomer.



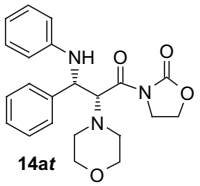
13b

R_f=0.45. Colourless oil; yield 6 mg, 6%; IR (ν, cm^{-1}, $CHCl_3$) 1695.5, 1777.8; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.28–2.52 (m, 4H), 2.93 (dd, J=7.05 Hz, 14.1 Hz, 2H), 3.37 (s, 3H), 3.45–3.75 (m, 6H), 4.01 (d, J=11.7 Hz, 1H), 4.10 (d, J=11.7 Hz, 1H), 5.05–5.3 (m, 4H), 5.75–5.95 (m, 2H), 7.08–7.19 (m, 2H), 7.23–7.38 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 49.4, 50.8, 53.3, 62.0, 67.2, 67.4, 117.1, 127.7, 127.9, 129.2, 136.8, 171.3; LRMS m/z 285 (10, M^+-59, 2), 176 (Base). Anal. Calcd for $C_{20}H_{28}O_3N_2$ (344.46): C, 69.74; H, 8.19; N, 8.13. Found: C, 69.86; H, 8.33; N, 7.96.

4.6. Crossed reactions of two different amines with vinyl triflate 10

4.6.1. General procedure. To a mixture of 10 equiv of the less nucleophilic amine (0.25 ml aniline or 0.33 ml diallylamine) and 2 equiv of the more nucleophilic amine (48 µl morpholine) was added 100 mg of the triflate in one portion. The mixture was stirred for 3 h, the residual less nucleophilic amine was removed under vacuum and the crude mixture directly purified by flash-column chromatography, eluting with cyclohexane/EtOAc.

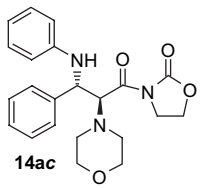
4.6.1.1. 3-Anilino-2-morpholino-3-phenyl pentanoic *N*-oxazolidin-2-one carboxamide (14a). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 40:60.



14at

Less polar diastereomer **14a*t***, R_f=0.36. White solid; yield 46 mg, 43%; mp 170–173 °C; IR (ν, cm^{-1}, $CHCl_3$)

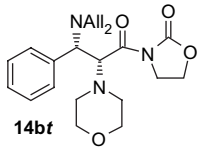
1783.3; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.57–2.88 (m, 4H), 3.43–4.27 (m, 6H), 4.38–4.59 (d+t, J_d=10.2 Hz, J_t=7.4 Hz, 3H), 5.22 (d, J=10.2 Hz, 1H), 5.22 (s, 1H, NH), 6.52 (d, J=8.6 Hz, 2H), 6.60–6.8 (m, 1H), 7.05 (t, J=8.6 Hz, 2H), 7.20–7.35 (m, 3H), 7.40–7.48 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 42.2, 47.8, 49.3, 57.0, 61.7, 62.8, 67.5, 67.6, 113.1, 113.9, 118.0, 118.1, 127.8, 127.9, 128.5, 129.0, 129.3, 140.0, 147.9, 152.7, 170.3; LRMS *m*/*z* 213 (M^+−182, 3), 182 (Base). Anal. Calcd for $C_{22}H_{25}O_4N_3$ (395.46): C, 66.82; H, 6.37; N, 10.62. Found: C, 66.89; H, 6.43; N, 10.38.



14a*c*

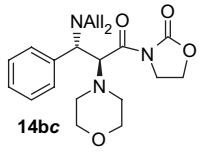
More polar diastereomer **14a*c***, R_f=0.31.Yellow solid; yield 8 mg, 8%; mp 170 °C; IR (ν, cm^{-1}, $CHCl_3$) 1777.8; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.51–2.78 (m, 4H), 3.37–3.74 (m, 5H), 3.74–4.0 (m, 2H), 4.12–4.33 (m, 1H), 4.83 (d, J=7.8 Hz, 1H), 5.16 (d, J=7.8 Hz, 1H), 6.54 (d, J=7.8 Hz, 2H), 6.64 (t, J=7.8 Hz, 1H), 7.07 (t, J=7.8 Hz, 2H), 7.16–7.42 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 42.5, 50.6, 57.0, 61.9, 67.0, 67.8, 113.8, 117.8, 126.9, 127.6, 128.5, 129.1, 139.7, 146.7, 173.3, 181.5; LRMS *m*/*z* 213 (M^+−182, 3), 182 (Base).

4.6.1.2. 3-Diallylamino-2-morpholino-3-phenyl pentanoic *N*-oxazolidin-2-one carboxamide (14b). Eluent used for the flash-column chromatography: cyclohexane/EtOAc 50:50.



14b*t*

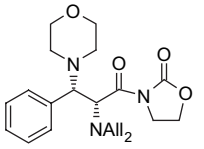
Less polar diastereomer **14b*t***, R_f=0.30. Colourless oil; yield 30 mg, 28%; IR (ν, cm^{-1}, $CHCl_3$) 1775.0, 1695.5; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.65 (dd, J=8.6 Hz, 13.3 Hz, 2H), 2.85–3.0 (m, 3.5H), 3.4–3.65 (m, 3.5H), 3.65–3.80 (m, 3.5H), 3.80–3.95 (m, 1H), 4.02–4.35 (m, 2.5H), 4.44 (d, J=11.7 Hz, 1H), 5.1–5.3 (m, 4H), 5.69 (d, J=11.7 Hz, 1H), 5.80–6.05 (m, 2H), 7.15–7.45 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 42.1, 49.5, 52.9, 60.6, 61.6, 61.9, 67.8, 117.2, 127.4, 128, 129.3, 129.7, 135.0, 137.0, 153.3, 170.1; LRMS *m*/*z* 287 (M^++2−114, 2), 186 (Base). Anal. Calcd for $C_{22}H_{29}O_4N_3$ (399.49): C, 66.14; H, 7.31; N, 10.52. Found: C, 66.28; H, 7.49; N, 10.28.



14b*c*

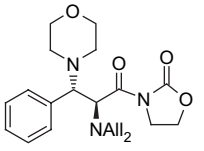
More polar diastereomer **14b*c***, R_f=0.14. Yellow oil; yield 11 mg, 10%; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.6 (dd, J=8.6 Hz, 14.1 Hz, 2H), 2.85–2.95 (m, 3H), 3.4–3.9 (m, 7H), 4.03–4.15 (m, 1H), 4.19–4.32 (m, 1H), 4.4 (d, J=11.7 Hz, 1H), 5.05–5.3 (m, 4H), 5.65 (d, J=11.7 Hz, 1H), 5.7–5.95 (m, 2H), 7.15–7.45 (m, 5H); LRMS *m*/*z* 287 (M^++2−114, 2), 186 (Base).

4.6.1.3. 2-Diallylamino-3-morpholino-3-phenyl pentanoic *N*-oxazolidin-2-one carboxamide (15).



15b*t*

Less polar diastereomer **15b*t***, R_f=0.51. Colourless oil; yield 8 mg, 8%; IR (ν, cm^{-1}, $CHCl_3$) 1725.7; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.28–2.42 (m, 2H), 2.5–2.65 (m, 2H), 3.30–3.80 (m, 10H), 3.9–4.4 (m, 2H), 4.2 (d, J=11.7 Hz, 1H), 5.1–5.3 (m, 4H), 5.67 (d, J=11.7 Hz, 1H), 5.75–5.98 (m, 2H), 7.1–7.3 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 42.4, 49.7, 53.6, 61.7, 67.2, 68.0, 77.2, 116.3, 127.8, 128.0, 128.6, 129.3, 137.2, 153.0, 170.2; LRMS *m*/*z* 223 (M^+−176, 1), 176 (Base).



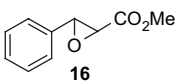
15b*c*

More polar diastereomer **15b*c***, R_f=0.34. Colourless oil; yield 3 mg, 3%; IR (ν, cm^{-1}, $CHCl_3$) 1775.04, 1695.48; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.35–2.52 (m, 4H), 2.55–2.7 (m, 2H), 3.12–3.35 (m, 6H), 4.0–4.1 (m, 2H), 4.3–4.42 (m, 2H), 4.35 (d, J=12.5 Hz, 1H), 5.0–5.15 (m, 4H), 5.5–5.7 (m, 2H), 5.67 (d, J=12.5 Hz, 1H), 7.12–7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C) δ 42.4, 49.5, 53.4, 61.3, 61.8, 62.2, 67.3, 116.3, 127.2, 127.6, 129.7, 134.0, 136.8, 153.0, 171.7; LRMS *m*/*z* 223 (M^+−176, 10), 176 (Base).

4.7. Stereochemical determinations

4.7.1. Stereochemical determination of diamine carboxylates.

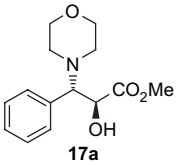
4.7.1.1. Methyl 3-phenyl glycidate (16). To a solution of benzaldehyde (10.6 g, 100 mmol) and methyl chloro acetate (10.86 g, 100 mmol) in dry tetrahydrofuran (200 ml) was added NaH (4 g, 100 mmol, 60% in suspension in oil) by small portions at 0 °C. After stirring for 1 h, the solution was quenched with an aqueous solution of 0.5 M HCl (100 ml). Ether (100 ml) was added, the aqueous layer was extracted three times with ether (30 ml) and the combined organic layers were dried over $MgSO_4$. After concentration under vacuum, the crude mixture was purified by flash-column chromatography, eluting with cyclohexane/EtOAc 80:20 (R_f=0.18), to afford the title compound as a colourless oil (8.1 g, 48% yield).



16

^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 3.51 (d, J=1.6 Hz, 1H), 3.82 (s, 3H), 4.08 (d, J=1.6 Hz, 1H), 7.20–7.40 (m, 5H).

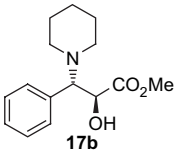
4.7.1.2. Methyl 2-hydroxy-3-morpholino-3-phenylpropanoate (17a). The title compound was synthesized using the Sharpless protocol[8c,d] (epoxy ester **16** 4.6 g, 25.84 mmol, morpholine 2.26 ml, 25.84 mmol, methanol 25 ml). Recrystallization of the crude product from ether gave the pure regioisomer **17a** (5 g, 74%) as a colourless crystalline solid.



17a

Mp 96 °C; R_f=0.18 (cyclohexane/EtOAc 6:4); IR (ν, cm^{-1}, $CHCl_3$) 1739.4; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.38–2.65 (m, 4H+OH), 3.57 (d, J=3.9 Hz, 1H), 3.62 (s, 3H), 3.73 (t, J=4.7 Hz, 4H), 4.79 (d, J=3.9 Hz, 1H), 7.30–7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 51.5, 52.2, 67.0, 70.1, 72.3, 128.2, 128.3, 129.0, 135.5, 173.1; LRMS m/z 206 (M^+-59, 2), 176 (Base). Anal. Calcd for $C_{14}H_{19}O_4N$ (265.31): C, 63.38; H, 7.21; N, 5.28. Found: C, 63.33; H, 7.34; N, 5.24.

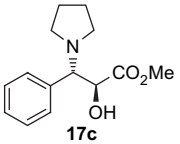
4.7.1.3. Methyl 2-hydroxy-3-piperidino-3-phenylpropanoate (17b). The title compound was synthesized using the Sharpless protocol[8c,d] (epoxy ester **16** 3 g, 16.85 mmol, piperidine 1.75 ml, 17.69 mmol, methanol 19 ml). Purification of the crude product by flash-column chromatography, eluting with cyclohexane/EtOAc 5:5 gave the pure regioisomer **17b** as the major compound (3.5 g, 78%) as a colourless crystalline solid (the other regioisomer was also isolated (188 mg, 4%).



17b

Mp 88 °C; R_f=0.32 (cyclohexane/EtOAc 5:5); IR (ν, cm^{-1}, $CHCl_3$) 1739.4; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.32–1.70 (m, 6H), 1.6 (br s, 1H), 2.35–2.5 (m, 4H), 3.58 (s, 3H), 3.59 (d, J=5.5 Hz, 1H), 4.81 (d, J=5.5 Hz, 1H), 7.29–7.34 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.3, 26.1, 51.9, 52.0, 70.7, 72.5, 127.9, 128.1, 129.0, 136.1, 173.3; LRMS m/z 204 (M^+-59, 5), 174 (Base). Anal. Calcd for $C_{15}H_{21}O_3N$ (263.34): C, 68.41; H, 8.03; N, 5.32. Found: C, 68.48; H, 7.99; N, 5.35.

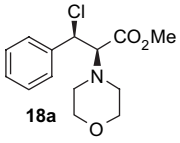
4.7.1.4. Methyl 2-hydroxy-3-pyrrolidino-3-phenylpropanoate (17c). The title compound was synthesized using the Sharpless protocol[8c,d] (epoxy ester **16** 3.5 g, 19.74 mmol, pyrrolidine 1.73 ml, 20.73 mmol, methanol 20 ml). Purification of the crude product by flash-column chromatography, eluting with cyclohexane/EtOAc 3:7 to 0:10 gave the epoxide amide **19** (600 mg, 13%) and the desired pure regioisomer **17c** (1.3 g, 26%) as colourless crystalline solids.



17c

Mp 84 °C; R_f=0.16 (cyclohexane/EtOAc 2:8); IR (ν, cm^{-1}, $CHCl_3$) 1646.1; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.75–1.85 (br s, 1H+m, 4H), 2.45–2.6 (m, 2H), 2.62–2.76 (m, 2H), 3.56 (d, J=3.1 Hz, 1H), 3.58 (s, 3H), 4.72 (d, J=3.1 Hz, 1H), 7.24–7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.4, 52.1, 52.8, 72.3, 72.4, 128.0, 128.1, 128.6, 137.4, 172.5; LRMS m/z 218 (M^+-31, 2), 82 (Base). Anal. Calcd for $C_{14}H_{19}O_3N$ (249.31): C, 67.44; H, 7.68; N, 5.62. Found: C, 67.72; H, 7.79; N, 5.57.

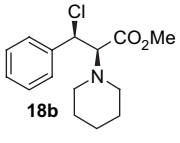
4.7.1.5. Methyl 3-chloro-2-morpholino-3-phenylpropanoate (18a). The title compound was synthesized using the Sharpless protocol[8c,d] (amino alcohol **17a** 4.24 g, 16 mmol, triethylamine 2.45 ml, 17.6 mmol, methanesulfonyl chloride 1.36 ml, 17.6 mmol, dichloromethane 16 ml). After stirring for 3 h, the ammonium mesylate was removed by treating the solution on a plug of silica gel, eluting with ether. Concentration under vacuum afforded **18a** (4.41 g, 97%, colourless crystalline solid) as a regioisomeric 3:1 mixture.



18a

Mp 112–113 °C; R_f=0.57 (cyclohexane/EtOAc 6:4); IR (ν, cm^{-1}, $CHCl_3$) 1733.9; ^1H NMR (200 MHz, $CDCl_3$, 25 °C) δ 2.25–2.72 (m, 4H, two regioisomers), 3.28–3.45 (m, 4H, major regioisomer), 3.28–3.45 (m, 4H, major regioisomer), 3.55–3.62 (m, 4H, minor regioisomer), 3.74 (d, J=10.9 Hz, 1H, major regioisomer), 3.84 (s, 3H, two regioisomers), 4.08 (d, J=10.9 Hz, 1H, minor regioisomer), 4.78 (d, J=10.9 Hz, 1H, minor regioisomer), 5.16 (d, J=10.9 Hz, 1H, major regioisomer), 7.30–7.45 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 50.1, 51.6, 52.7 (minor), 55.3 (minor), 59.1, 61.9 (minor), 67.0, 67.2 (minor), 72.2 (minor), 73.6, 127.8, 128.2 (minor), 128.3 (minor), 128.4, 128.6, 128.9 (minor), 138.4, 169.2; LRMS m/z 224 (M^+-59, 16), 158 (Base). Anal. Calcd for $C_{14}H_{18}O_3NCl$ (283.75): C, 59.26; H, 6.39; N, 4.94. Found: C, 59.33; H, 6.41; N, 5.01.

4.7.1.6. Methyl 3-chloro-2-piperidino-3-phenylpropanoate (18b). The title compound was synthesized using the Sharpless protocol[8c,d] (amino alcohol **17b** 2.48 g, 9.43 mmol, triethylamine 1.44 ml, 10.37 mmol, methanesulfonyl chloride 802 µl, 10.37 mmol, dichloromethane 10 ml). After stirring for 3 h, the ammonium mesylate was removed by treating the solution on a plug of silica gel, eluting with ether. Concentration under vacuum afforded the pure regioisomer **18b** (2.53 g, 96%) as a colourless crystalline solid. In contrast to its morpholino analogue **18a**, compound **18b** decomposes on standing at room temperature and therefore must be stored in the freezer at −20 °C. At this temperature, **18b** is indefinitely quite stable.

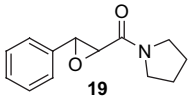


18b

Mp 88 °C; R_f=0.69 (cyclohexane/EtOAc 8:2); IR (ν, cm^{-1}, $CHCl_3$) 1731.1; ^1H NMR (200 MHz, $CDCl_3$, 25 °C)

δ 1.1–1.3 (br s, 1H+m, 6H), 2.20–2.35 (m, 2H), 2.50–2.65 (m, 2H), 3.71 (d, J=11 Hz, 1H), 3.83 (s, 3H), 5.17 (d, J=11 Hz, 1H), 7.30–7.40 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.2, 26.2, 51.1, 51.3, 59.6, 74.2, 127.9, 128.2, 128.3, 138.9, 169.7; LRMS m/z 246 (M^+−35, 2), 156 (Base). Anal. Calcd for $C_{15}H_{20}O_2NCl$ (281.78): C, 63.94; H, 7.15; N, 4.97. Found: C, 63.90; H, 7.21; N, 4.91.

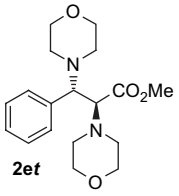
4.7.1.7. *trans*-2,3-Epoxy-3-phenyl-propenoic *N*,*N*-pyrrolidinylcarboxamide (19). The title compound was obtained instead of the expected chloro amine **18c** using the Sharpless protocol[8c,d] (amino alcohol **17c** 1.3 g, 5.22 mmol, triethylamine 800 µl, 5.74 mmol, methanesulfonyl chloride 444 µl, 5.74 mmol, dichloromethane 5 ml). After stirring for 3 h, the ammonium mesylate was removed by filtering the solution on a plug of silica gel, eluting with ether. Concentration under vacuum afforded the pure compound **19** (1.02 g, 90%) as a colourless crystalline solid.



19

Mp 56 °C; R_f=0.25 (cyclohexane/EtOAc 3:7); IR (ν, cm^{-1}, $CHCl_3$) 1739.4; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 1.85–2.15 (m, 4H), 2.52–3.75 (m, 4H), 3.57 (d, J=1.6 Hz, 1H), 4.15 (d, J=1.6 Hz, 1H), 7.32–7.42 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.3, 51.9, 52.6, 72.2, 125.6, 127.5, 127.9, 135.7, 172.4; LRMS m/z 217 (M^+, 7), 82 (Base). Anal. Calcd for $C_{13}H_{15}O_2N$ (217.76): C, 71.86; H, 6.96; N, 6.44. Found: C, 72.0; H, 6.91; N, 6.31.

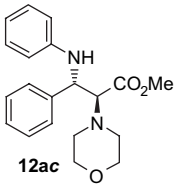
4.7.1.8. Methyl 2,3-dimorpholino-3-phenyl propanoate (2e*t*).



2e*t*

The title compound was synthesized using the Sharpless protocol[8c,d] (amino chloride **18a** 284 mg, 1 mmol, K_2CO_3 138 mg, 1 mmol, morpholine 96 µl, 1.1 mmol, acetonitrile 2 ml). The pure compound **2e** so obtained (331 mg, 99%) gave analytical data identical in all respects with those described for the less polar product **2e*t*** obtained by our aza-MIRC methodology.

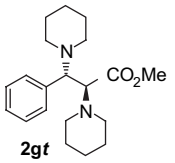
4.7.1.9. Methyl 3-anilino-2-morpholino-3-phenyl propanoate (12a*c*).



12ac

The title compound was synthesized using the Sharpless protocol[8c,d] (amino chloride **18a** 284 mg, 1 mmol, K_2CO_3 138 mg, 1 mmol, aniline 100 µl, 1.1 mmol, acetonitrile 2 ml). The pure compound **12a** so obtained (316 mg, 93%) gave analytical data identical in all respects with those described for the more polar product **12a*c*** obtained by our aza-MIRC methodology.

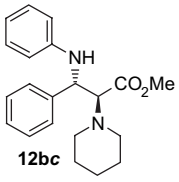
4.7.1.10. Methyl 2,3-dipiperidino-3-phenyl propanoate (2g*t*).



2g*t*

The title compound was synthesized using the Sharpless protocol[8c,d] (amino chloride **18b** 282 mg, 1 mmol, K_2CO_3 138 mg, 1 mmol, morpholine 109 µl, 1.1 mmol, acetonitrile 2 ml). The pure compound **2g** so obtained (327 mg, 99%) gave analytical data identical in all respects with those described for the less polar product **2g*t*** obtained by our aza-MIRC methodology.

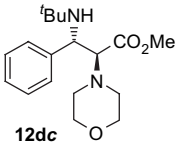
4.7.1.11. Methyl 3-anilino-2-piperidino-3-phenyl propanoate (12b*c*).



12bc

The title compound was synthesized using the Sharpless protocol[8c,d] (amino chloride **18b** 282 mg, 1 mmol, K_2CO_3 138 mg, 1 mmol, aniline 100 µl, 1.1 mmol, acetonitrile 2 ml). The pure compound **12b** so obtained (317 mg, 94%) gave analytical data identical in all respects with those described for the more polar product **12b*c*** obtained by our aza-MIRC methodology.

4.7.1.12. Methyl 3-*tert*-butylamino-2-morpholino-3-phenyl propanoate (12d*c*).



12dc

The title compound was synthesized using the Sharpless protocol[8c,d] (amino chloride **18a** 284 mg, 1 mmol, K_2CO_3 138 mg, 1 mmol, *tert*-butylamine 114 µl, 1.1 mmol, acetonitrile 2 ml). The ^{1}H NMR spectrum of the pure compound **12d** so obtained (300 mg, 94%, mp 90 °C) exhibited signals identical to those of the major stereomer in the adduct **12d*t*–*c*** obtained by our aza-MIRC methodology. ^{13}C NMR (50 MHz, $CDCl_3$) δ 30.4, 50.3, 50.8, 51.3, 55.9, 67.2, 75.4, 126.7, 127.1, 128.0, 133.0, 171.0. Anal. Calcd for $C_{18}H_{28}O_3N_2$ (320.43): C, 67.47; H, 8.82; N, 8.74. Found: C, 67.64; H, 8.95; N, 8.85.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.07.085.

References and notes

1. For recent reviews on tandem reactions, see: (a) Bunce, R. A. *Tetrahedron* **1995**, *51*, 13103; (b) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115; (c) Simon, C.; Constantieux, T.; Rodriguez, J. *Eur. J. Org. Chem.* **2004**, 4957; (d) Ramon, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1602; (e) Guo, H.; Ma, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 354; (f) Pellissier, H. *Tetrahedron* **2006**, *62*, 1619; (g) Pellissier, H. *Tetrahedron* **2006**, *62*, 2143.
2. To the best of our knowledge, only a few examples of use of this class of compounds, each dealing with Pd-catalyzed coupling reactions, have been reported. See: (a) Beccalli, E. M.; Gelmi, M. L.; Marchesini, A. *Tetrahedron* **1998**, *54*, 6909; (b) Beccalli, E. M.; Clerici, F. L.; Marchesini, A. *Tetrahedron* **2000**, *56*, 2699; (c) Ceccarelli, S.; Piarulli, U.; Gennari, C. *J. Org. Chem.* **2000**, *65*, 3105; (d) Siegel, K.; Brückner, R. *Chem.—Eur. J.* **1998**, *4*, 1116; (e) Kalwinsh, I.; Metten, K.; Brückner, R. *Heterocycles* **1995**, *40*, 939.
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4. Tranchant, M. J.; Dalla, V.; Jabin, I.; Decroix, B. *Tetrahedron* **2002**, *58*, 8425.
5. See also: (a) de Saint-Fuscien, C.; Tarrade, A.; Dauban, P.; Dodd, R. H. *Tetrahedron Lett.* **2000**, *41*, 6393; (b) Tarrade, A.; Dauban, P.; Dodd, R. H. *J. Org. Chem.* **2003**, *68*, 9521.
6. For some recent developments in the aza-MIRC chemistry: (a) For the use of α,β-unsaturated carbonyl derivatives α-substituted by a leaving group. See Ref. 5 and references therein; (b) For the use of *N*-alkoxy amines, see: Cardillo, G.; Gentilucci, L.; De Matteis, V. *J. Org. Chem.* **2002**, *67*, 5957 and Ref. 8 cited therein; (c) For the use of nosyloxycarbamates, see: Fioravanti, S.; Pellacani, L.; Stabile, S.; Tardella, P. A. *Tetrahedron* **1998**, *54*, 6169; Fioravanti, S.; Pellacani, L.; Morreale, S.; Tardella, P. A. *Synthesis* **2001**, 1975; Fioravanti, S.; Pellacani, L.; Morreale, S.; Tardella, P. A. *J. Org. Chem.* **2002**, *67*, 4972.
7. Recently, a comparable but inverse approach for accessing transient aziridinium ions, based on sequential alkylation followed by aza-Michael addition of N–H aziridine to electron-deficient 6-iodo alkynes, has been published. Zhu, W.; Cai, G.; Ma, D. *Org. Lett.* **2005**, *7*, 5545.
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9. For the utility of α,β-diamino acids and esters, see the following reviews: (a) Lucet, D.; Le Gall, T. L.; Mioskowski, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 2580; (b) Viso, A.; Fernandez de le Pradilla, R.; Garcia, A.; Flores, A. *Chem. Rev.* **2005**, *105*, 3167.
10. In the course of related work aimed at developing these reactions in solution, we discovered that dissolving compound **1** in freshly distilled DMF which had been refluxed overnight on potassium hydroxide produced a smooth reaction leading to the α,β-diamino adducts **2a*t*–*c***. Applying this procedure to an *m*-nitro aryl analogue of **1** as the vinyl triflate component even gave a spontaneous and exothermic reaction furnishing the stereomeric diamino adducts within few minutes. This technique may be considered as a valuable water-free source of dimethylamine.
11. Letters *t* and *c* referred to the less and more polar diastereomers, respectively. The stereochemical attribution of these adducts has been made by chemical correlation using the Sharpless methodology[8c,d] (details are included in Section 2.3 at the end of the manuscript).
12. The formation of type **3** enamines was a major problem encountered during the development of similar reactions in solution. After screening various solvents, it was found that reaction could be conducted efficiently in DME, enamine formation being reduced to a great extent. Dalla, V.; Tranchant, M. J., unpublished results.
13. Couturier, C.; Blanchet, J.; Schlama, T.; Zhu, J. *Org. Lett.* **2006**, *8*, 2183.
14. Diallylamine is expected to be a higher nucleophile than dibenzylamine. This seems to be confirmed by the results in Table 1, runs 4 and 5.
15. For previous studies documenting the highly regioselective opening of benzylic aziridinium salts, see: (a) Refs. 8a–d and 8h of the present article; (b) Dieter, K. R.; Deo, N.; Lagu, B.; Dieter, L. W. *J. Org. Chem.* **1992**, *57*, 1663; (c) Freedman, J.; Vaal, M. J.; Huber, E. W. *J. Org. Chem.* **1991**, *56*, 670; (d) Okuda, M.; Tomioka, K. *Tetrahedron Lett.* **1994**, *35*, 4585; (e) Rossiter, B. E.; Miao, G. *J. Org. Chem.* **1995**, *60*, 8424; (f) Saravanan, P.; Bisai, A.; Baktharanan, S.; Chandrasekhar, M.; Singh, V. K. *Tetrahedron* **2002**, *58*, 4693; (g) Andrews, D. R.; Dahanukar, V. H.; Eckert, J. M.; Gala, D.; Lucas, B. S.; Schumacher, D. P.; Zavialov, I. A. *Tetrahedron Lett.* **2002**, *43*, 6121.
16. See Ref. 6b.
17. For representative example, see Refs. 8a–d (especially Ref. 8b) of the present manuscript and references cited therein.
18. No substantial enhancement of the reaction rate was observed at 40 °C, these conditions actually compromising the reaction profile, with notable formation of increased quantities of dimorpholino adducts **2e*t*–*c***.
19. Unfortunately, no NMR correlations were found for the crossed diamino esters and therefore no conclusive evidence could be drawn for the overall series (Table 3, case of **12c**, last line). Also, the NMR correlation did not match the diamines **5a–b*t*–*c*** derived from the β-ethyl vinyl triflate **4** (see Scheme 2), the stereochemistry of which, therefore, could not be determined.
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