Pergamon

Tetrahedron: *Asymmetry* 13 (2002) 563–567

TETRAHEDRON: *ASYMMETRY*

Use of α-amino esters as chiral auxiliaries in the enantioselective Michael alkylation of chiral imines

I. Jabin,[a,*] G. Revial,[b] M. Pfau[b] and P. Netchitaïlo[a]

[a]*URCOM, Université du Havre, Faculté des Sciences et Techniques, 25 rue Philippe Lebon, BP 540, 76058 Le Havre Cédex, France*

[b]*ESPCI, Laboratoire de Chimie Organique associé au CNRS (UMR 7084), 10 rue Vauquelin, 75231 Paris Cédex 05, France*

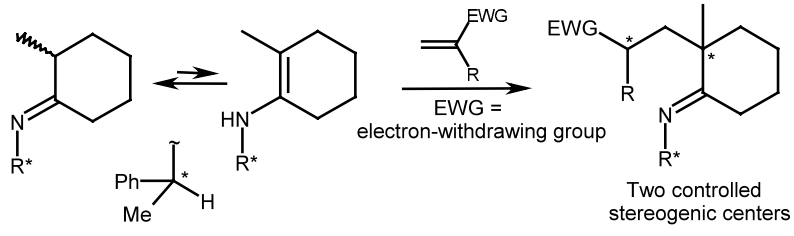
Received 28 March 2002; accepted 10 April 2002

Abstract—A study concerning the regio- and stereoselectivities of the Michael reaction between chiral imines and electrophilic olefins has been performed with α-amino esters as chiral auxiliaries. In all cases, optically active 1-phenylethylamine, which is usually employed to induce the stereoselectivity in this process, led to higher regio- and stereoselectivities. © 2002 Published by Elsevier Science Ltd.

The enantioselective Michael alkylation of chiral imines (derived from racemic 2-substituted cycloalkanones and optically active 1-phenylethylamine) with electrophilic olefins has been widely used for synthetic purposes.[1] Recently, the reaction has been extended with success to α- or β-substituted electrophilic olefins.[2] The use of such substituted electron-deficient alkenes is particularly interesting since a controlled tertiary stereogenic center is created in addition to the usual quaternary one (Scheme 1, example given with an α-substituted electrophilic olefin).

However, it has been shown that regioisomers resulting from α-alkylation at the less substituted position of the imine, are formed in significant proportions thus limiting the synthetic usefulness of these substituted alkenes. Moreover, a recent study from our laboratory concerning their use with chiral imines derived from non-α-substituted cycloalkanones has led to Michael adducts with poor stereoselectivities at the tertiary center of the diastereomeric adducts.[3]

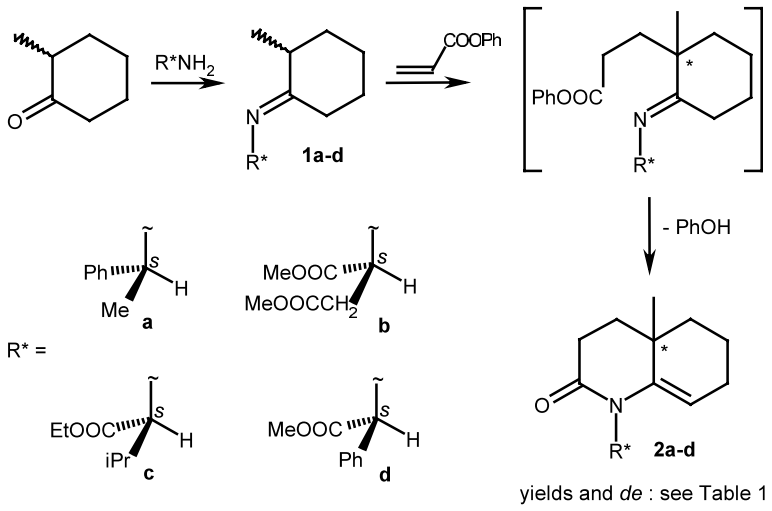
These limitations led us to investigate the influence of other chiral auxiliaries on the regioselectivity and the stereoselectivity of the Michael reaction. A study concerning the effect of the variation of the chiral amine on asymmetric induction with unsubstituted electrophilic olefins has already been undertaken but only non-functionalized primary amines, i.e. α-isopropylbenzylamine, 1-cyclohexylethylamine and isobornylamine, have been tested. The results had shown that in all examples the observed stereoselectivities were inferior to those obtained with 1-phenylethylamine.[4] It was therefore interesting to see if chiral imines derived from optically active functionalized primary amines such as α-amino esters could lead to better results. Indeed, such cheap chiral auxiliaries (i.e. esters of phenylglycine or valine) have been used successfully in similar Michael reac-



Scheme 1.

* Corresponding author. Tel.: +332 32 74 43 94; fax: +332 32 74 43 91; e-mail: ivan.jabin@univ-lehavre.fr

0957-4166/02/$ - see front matter © 2002 Published by Elsevier Science Ltd.
PII: S0957-4166(02)00171-4



Scheme 2.

tions. Thus, stereoselective aza-annulation of β-enaminoamides using the methyl ester of valine as chiral auxiliary, with acrylate derivatives, have led to conformationally restricted peptide mimetics with diastereoselectivities up to 98:2.[5] However the same chiral auxiliary used with β-enamino esters gave low asymmetric inductions.[6] This communication describes the use of various optically active α-amino esters in the stereoselective Michael reaction of imines with unsubstituted, as well as α- or β-substituted electrophilic olefins, in order to see if they can lead to high stereo- and regioselectivities and constitute a good alternative to the use of 1-phenylethylamine.

Three optically active α-amino esters[7] (i.e. (*S*)-aspartic acid dimethyl ester, (*S*)-valine ethyl ester, (*S*)-2-phenylglycine methyl ester) and (*S*)-phenylethylamine were first used to test the stereoselective efficiencies in the Michael reaction. For this purpose, imines **1a–d** derived from 2-methylcyclohexanone and optically active amines were prepared.[8] Phenyl acrylate[9] was chosen as the electrophilic olefin since its Michael reaction with imines is usually followed by an aza-cyclization leading in good yields to lactams which incorporate the chiral auxiliary. The stereoselectivity of the alkylation is then easily determined by GC–MS measurement of the diastereomeric excess (de) of the final lactam.[10] Thus, reaction[11] of imines **1a–d** with phenyl acrylate led to intermediate Michael adducts which cyclized under the reaction conditions giving lactams **2a–d**[12] (Scheme 2).

The diastereoselectivity of the Michael reaction was determined by GC–MS analysis of the crude cyclic enamides **2a–d** and the results are displayed in Table 1. They clearly show that (*S*)-1-phenylethylamine offers the best stereoselectivity (only one diastereomer was obtained) and also the best yield (entry 1). With α-amino esters as chiral auxiliaries, the stereoselectivities are low (entries 3 and 4) to moderate (entry 2). The poor stereoselectivity obtained with imine **1d** is quite surprising if we consider that (*S*)-2-phenylglycine methyl ester and (*S*)-1-phenylethylamine should lead to similar steric hindrance effects. Moreover, among the α-amino esters tested, the best diastereoselectivity was observed with (*S*)-aspartic acid dimethyl ester, the only chiral auxiliary which does not possess a bulky α-substituent (entry 2). These experimental observations suggest that steric hindrance of the different substituents borne by the chiral auxiliary is not the principal factor which governs the stereoselectivity of the Michael reaction and consequently prediction of the stereoselectivity based on the nature of the chiral auxiliary is tricky.

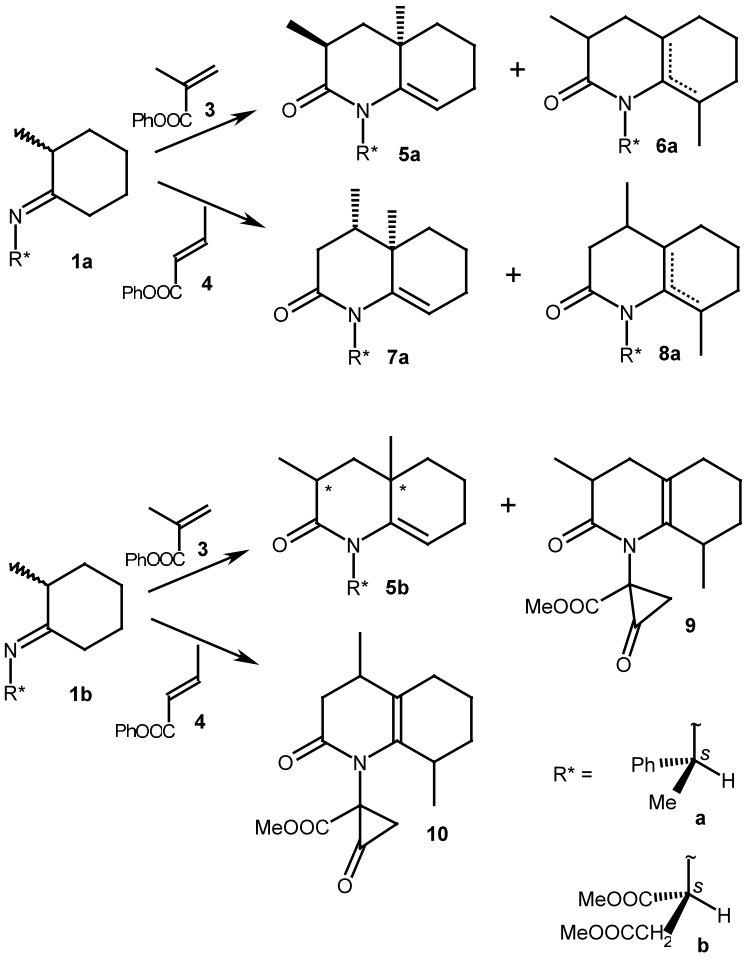
The two diastereomers of the lactams **2c–d** were separated by flash chromatography (FC) on silica gel and fully characterized. In the case of lactam **2b**, we were not able to separate the two diastereomers, so in this case only the mixture (ca. 4:1) was characterized. No chemical correlation was undertaken to determine the absolute configuration of the quaternary center of the major diastereomer of lactams **2a–d**. For compound **2a** the *R* configuration can be given with a high level of confidence by analogy with earlier results on similar compounds (see below for compounds **5a** and **7a**). This assignment is also in accordance with that which can be anticipated from the general heuristic rule elaborated previously[1c] and with all past examples of the use of chiral imines in Michael reactions.[1]

We then studied the regioselectivity of these reactions, using substituted electrophilic olefins. Due to the higher

Table 1. Stereoselectivity of the Michael reactions depicted in Scheme 2

Entry	Chiral imine	de (%)	Overall yield (%)[a]
1	**1a**	>99	61
2	**1b**	58	60
3	**1c**	12	45
4	**1d**	22	53

[a] Yield of the diastereomeric mixture after flash chromatography, calculated from 2-methylcyclhohexanone.



Scheme 3.

stereoselectivity observed with (*S*)-aspartic acid dimethyl ester in comparison with the other α-amino esters, this study was only conducted with this chiral auxiliary and the results were compared with the ones obtained with (*S*)-1-phenylethylamine which we have already reported.[1f] Thus, imines **1a**–**b** were reacted[13] with an α- and a β-substituted olefin, i.e. phenylmethacrylate **3** and phenylcrotonate **4**,[14] respectively (Scheme 3). As expected, the minor regioisomers **6a**, **8a**[15] and **9** (two diastereomers)[16] were obtained beside the major adducts **5a**, **7a** and **5b** (two diastereomers),[16] respectively. Reaction of **1b** and **4** did not afford any quaternary compound and only regioisomer **10**[16] was isolated by FC from its diastereomer. Moreover, in both reactions of **1b**, an unexpected intramolecular cyclization proceeded only with the regioisomeric adducts, leading to lactams **9** and **10** bearing a cyclopropanone moiety. This result can be tentatively rationalized if we consider that the cyclopropanation minimizes the important steric repulsion of the chiral auxiliary with the nearby methyl group.

The results concerning the regio- and stereoselectivity of the Michael reaction are displayed in Table 2.

In each case, the best results concerning selectivities and yields were obtained with (*S*)-1-phenylethylamine as chiral auxiliary (entries 1 and 2 versus entries 3 and 4). As already mentioned, with (*S*)-aspartic acid dimethyl ester and phenyl crotonate, the adduct resulting from the alkylation at the less substituted position of the imine has even been obtained exclusively (entry 4). The reaction of imine **1b** with phenylmethacrylate **3** has yielded the expected lactam **5b** with an acceptable stereoselectivity (entry 3) and with a relative percentage of regioisomeric adducts not far from that obtained with imine **1a** (entry 3 versus entry 1).

Table 2. Regio- and stereoselectivities of the reactions (Scheme 3)

Entry	Reactants	Regioselectivity[a]	Diastereoselectivity[a]	Yield (%)
1[b]	**1a**+**3**	**5a**:**6a** 73:27	**5a**: >99:1	74[c]
2[b]	**1a**+**4**	**7a**:**8a** 64:36	**7a**: 92:8	84[c]
3	**1b**+**3**	**5b**:**9** 65:35	**5b**: 87:13	
			9: 77:23	35[d]
4	**1b**+**4**	**10** >99	**10**: 60:40	28[d]

[a] Relative % by GC–MS determination.
[b] Ref. 1f.
[c] Total yield of the isomeric mixture after FC, calculated from 2-methylcyclohexanone.
[d] Yield of the diastereomeric mixture after FC, calculated from 2-methylcyclohexanone.

In conclusion, this study has shown that (*S*)-1-phenylethylamine is a better chiral auxiliary than optically active α-amino esters for the Michael reaction of imines with the electrophilic olefins used in this study since it leads to better regio- and stereoselectivities as well as higher yields.

Acknowledgements

We thank the students of the MST CIC RSA1 2002 class for the preliminary study made during their practical work.

References

1. (a) Pfau, M.; Revial, G.; Guingant, A.; D'Angelo, J. *J. Am. Chem. Soc.* **1985**, *107*, 273–274; (b) Pfau, M.; Revial, G. (KIREX) **1985**, PCT WO 85 04873. **Mechanisms**: (c) Sevin, A.; Tortajada, J.; Pfau, M. *J. Org. Chem.* **1986**, *51*, 2671–2675; (d) Sevin, A.; Masure, D.; Giessner-Prettre, C.; Pfau, M. *Helv. Chim. Acta* **1990**, *73*, 552–573; (e) Pfau, M.; Tomas, A.; Lim, S.; Revial, G. *J. Org. Chem.* **1995**, *60*, 1143–1147; (f) Jabin, I.; Revial, G.; Tomas, A.; Lemoine, P.; Pfau, M. *Tetrahedron: Asymmetry* **1995**, *6*, 1795–1812; (g) Lucero, M. J.; Houk, K. N. *J. Am. Chem. Soc.* **1997**, *119*, 826–827. **Reviews**: (h) Revial, G.; Pfau, M. *Org. Synth.* **1991**, *70*, 35–46; (i) Oare, D. A.; Heathcock, C. H. *Top. Stereochem.* **1991**, *20*, 87–170 (see pp. 114–115); (j) D'Angelo, J.; Desmaële, D.; Dumas, F.; Guingant, A. *Tetrahedron: Asymmetry* **1992**, *3*, 459–505 (k) D'Angelo, J.; Cavé, C.; Desmaële, D.; Dumas, F. *Trend. Org. Chem.* **1993**, *4*, 555–616; (l) Guingant, A. In *Advances in Asymmetric Synthesis*; JAI Press Inc., **1997**; Vol. 2, pp. 119–188 (see pp. 159–170). **Recent developments and applications**: (m) Keller, L.; Camara, C.; Pinheiro, A.; Dumas, F.; d'Angelo, J. *Tetrahedron Lett.* **2001**, *42*, 381–383; (n) Keller, L.; Dumas, F.; d'Angelo, J. *Tetrahedron Lett.* **2001**, *42*, 1911–1913; (o) Nour, M.; Tan, K.; Jankowski, R.; Cavé, C. *Tetrahedron: Asymmetry* **2001**, *12*, 765–769; (p) Tan, K.; Alvarez, R.; Nour, M.; Cavé, C.; Chiaroni, A.; Riche, C.; d'Angelo, J. *Tetrahedron Lett.* **2001**, *42*, 5021–5023; (q) Schenato, R. A.; dos Santos, E. M.; Tenius, B. S. M.; Costa, P. R. R.; Caracelli, I.; Zukerman-Schpector, J. *Tetrahedron: Asymmetry* **2001**, *12*, 579–584; (r) Jabin, I.; Revial, G.; Monnier-Benoit, N.; Netchitaïlo, P. *J. Org. Chem.* **2001**, *66*, 256–261; (s) Jabin, I.; Netchitaïlo, P. *Tetrahedron Lett.* **2001**, *42*, 7823–7827; (t) Revial, G.; Jabin, I.; Redolfi, M.; Pfau, M. *Tetrahedron: Asymmetry* **2001**, *12*, 1683–1688 and Ref. 1 included; (u) Revial, G.; Jabin, I.; Lim, S.; Pfau, M. *J. Org. Chem.* **2002**, *67*, 2252–2256.
2. Refs. 1f,r,s,t: (a) Jabin, I.; Revial, G.; Pfau, M.; Decroix B.; Netchitaïlo, P. *Org. Lett.* **1999**, *1*, 1901–1904; (b) Revial, G.; Jabin, I.; Pfau, M. *Tetrahedron: Asymmetry* **2000**, *11*, 4975–4983.
3. Monnier-Benoit, N. (URCOM, Université du Havre), unpublished thesis results.
4. d'Angelo, J.; Revial, G.; Guingant, A.; Riche, C.; Chiaroni, A. *Tetrahedron Lett.* **1989**, *30*, 2645–2648.
5. Benovsky, P.; Stephenson, G. A.; Stille, J. R. *J. Am. Chem. Soc.* **1998**, *120*, 2493–2500.
6. Barta, N. S.; Brode, A.; Stille, J. R. *J. Am. Chem. Soc.* **1994**, *116*, 6201–6206.
7. α-Amino esters were obtained by treatment of their corresponding commercial hydrochloride salt with aqueous NaOH solution (1 M) and subsequent extraction with dichloromethane.
8. Chiral imines **1a**–**d** were obtained from the corresponding amines and 2-methylcyclohexanone (1 equiv.) in refluxing toluene in a Dean–Stark water separator for 24 h.
9. Phenyl acrylate was prepared according to the literature: Ahlbretch, A.; Codding, D. W. *J. Am. Chem. Soc.* **1953**, *75*, 984.
10. Such a method for determination of the diastereoselectivity has already been used in similar cases: see Ref. 2.
11. Crude chiral imines **1a**–**d** were reacted under an argon atmosphere with phenyl acrylate (1.1 equiv.) at rt for 3 h and the reaction mixture was then heated at 100°C for 4 days. The reaction medium was then analyzed by GC–MS affording the de values displayed in Table 1. After dissolution in ether and basic aqueous washing (NaOH 1 M) the residue was purified by flash chromatography (EtOAc/cyclohexane) on silica gel.
12. Compound **2a**: white solid, mp 92–94°C (EtOAc/cyclohexane). $[\alpha]_D^{20}$ +73 (*c* 1.57, EtOH). *EIMS m/z* (rel. int.) 269 (M^+, 36%), 165 (base), 150 (70), 137 (36), 105 (87), 77 (47). IR ($CHCl_3$) 1664, 1632 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 1.10 (s, 3H), 1.30 to 2.00 (m, 8H), 1.58 (d, $J=7.0$ Hz, 3H), 2.60 (dd, $J_1=5.5$ Hz, $J_2=8.6$ Hz, 2H), 4.81 (dd, $J_1=3.1$ Hz, $J_2=5.5$ Hz, 1H), 6.22 (q, $J=7.0$ Hz, 1H), 7.13 to 7.34 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.43, 18.12, 23.24, 24.87, 29.61, 33.26, 34.28, 38.36, 50.55, 110.6, 125.8 (2C), 126.3, 128.3 (2C), 139.4, 142.5, 169.7. Anal. calcd for $C_{18}H_{23}NO$: C, 80.26; H, 8.61; N, 5.20. Found: C, 80.21; H, 8.40; N, 5.28%. Compound **2b** (ca. 4:1 mixture of the diastereomers): colorless oil. IR ($CHCl_3$) 1737, 1642 cm^{-1}. Major diastereomer: *EIMS m/z* (rel. int.) 309 (M^+, 66%), 223 (92), 218 (97), 194 (43), 164 (base), 137 (87), 55 (72). ^1H NMR (200 MHz, $CDCl_3$) δ 1.13 (s, 3H), 1.25 to 2.58 (m, 12H), 3.46 (dd, $J_1=9.4$ Hz, $J_2=17.2$ Hz, 1H), 3.64 (s, 3H), 3.68 (s, 3H), 4.78 (dd, $J_1=3.9$ Hz, $J_2=8.6$ Hz, 1H), 5.08 (dd, $J_1=3.1$ Hz, $J_2=4.7$ Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.93, 22.43, 24.93, 28.94, 33.06, 34.34, 34.53, 38.13, 52.09, 52.54, 56.01, 106.2, 143.0, 169.0, 170.3, 171.8. Minor diastereomer: *EIMS m/z* (rel. int.) 309 (M^+, 72%), 222 (96), 218 (79), 194 (47), 164 (99), 137 (base), 55 (75). ^1H NMR (200 MHz, $CDCl_3$) δ 1.02 (s, 3H), 1.25 to 2.58 (m, 12H), 3.35 (dd, $J_1=7.8$ Hz, $J_2=16.4$ Hz, 1H), 3.64 (s, 3H), 3.67 (s, 3H), 4.94 (dd, $J_1=5.5$ Hz, $J_2=7.8$ Hz, 1H), 5.23 (dd, $J_1\approx J_2\approx 4$ Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.03, 22.84, 24.96, 29.10, 33.17, 34.36, 34.64, 38.21, 52.02, 52.63, 55.82, 107.2, 142.9, 169.1, 170.6, 171.8. Compound **2c**: major diastereomer: colorless oil. *EIMS m/z* (rel. int.) 293 (M^+, 19%), 166 (base), 137 (77). IR ($CHCl_3$) 1738, 1663, 1636 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 0.76 (d, $J=7.0$ Hz, 3H), 0.80 to 1.28 (m, 8H), 1.14 (s, 3H), 2.01 to 2.21 (m, 2H), 2.48 to 2.71 (m, 2H), 3.94 to 4.23 (m, 3H), 4.95 (dd, $J_1=3.3$ Hz, $J_2=4.7$ Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.25, 17.89, 19.03, 22.21, 22.58, 25.03, 26.61, 29.02, 33.20, 34.32, 38.38, 60.83, 105.9, 143.4, 168.8, 170.9. Minor diastereomer:

colorless oil. *EIMS* m/z (rel. int.) 293 (M^+, 19%), 166 (base), 137 (83). IR ($CHCl_3$) 1738, 1666, 1633 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 0.76 (d, $J=7.0$ Hz, 3H), 0.80 to 1.70 (m, 6H), 1.06 (s, 3H), 1.08 (d, $J=7.0$ Hz, 3H), 1.14 (t, $J=7.0$ Hz, 3H), 1.90 to 2.10 (m, 2H), 2.30 to 2.60 (m, 3H), 3.95 to 4.16 (m, 2H), 4.99 (dd, $J_1 \approx J_2 \approx 5$ Hz, 1H), 5.22 (d, $J=10.2$ Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.18, 17.86, 18.08, 22.53, 22.63, 24.59, 29.06, 29.43, 32.95, 34.41, 38.20, 60.84, 61.41, 105.4, 141.9, 169.2, 171.0. Compound **2d**: major diastereomer: colorless oil. *EIMS* m/z (rel. int.) 313 (M^+, base), 281, (55), 254 (53), 226 (77), 198 (43), 121 (47), 91 (62). IR ($CHCl_3$) 1745, 1641 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 1.18 (s, 3H), 1.20 to 1.76 (m, 6H), 1.90 to 2.04 (m, 2H), 2.60 to 2.70 (m, 2H), 3.70 (s, 3H), 4.90 (dd, $J_1=3.1$ Hz, $J_2=4.7$ Hz, 1H), 5.24 (s, 1H), 7.12 to 7.41 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.00, 22.60, 24.86, 29.26, 33.34, 34.63, 38.05, 52.61, 64.56, 107.9, 127.9, 128.3 (2C), 128.4 (2C), 129.5, 135.2, 169.4, 169.6. Minor diastereomer: colorless oil. *EIMS* m/z (rel. int.) 313 (M^+, base), 281, (53), 254 (55), 226 (91), 198 (53), 121 (64), 91 (85). IR ($CHCl_3$) 1743, 1636 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 1.09 (s, 3H), 1.36 to 1.81 (m, 6H), 1.92 to 2.06 (m, 2H), 2.60 to 2.71 (m, 2H), 3.69 (s, 3H), 4.97 (dd, $J_1 \approx J_2 \approx 4$ Hz, 1H), 6.45 (s, 1H), 7.17 to 7.35 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.91, 22.45, 24.58, 29.20, 33.19, 34.37, 38.09, 52.37, 60.41, 108.3, 127.6, 128.0 (2C), 128.1 (2C), 134.5, 141.7, 168.9, 170.2.

13. The same procedure as described for phenyl acrylate (Ref. 11) was used with imine **1b**.
14. These two olefins were prepared according to Ref. 1f.
15. Lactams **6a** and **8a** were obtained as an isomeric mixture of compounds differing in their double bond position (Ref. 1f) while **9** could be separated in the present instance.
16. Compound **5b** (ca. 4:1 mixture of diastereomers): colorless oil. IR ($CHCl_3$) 1738, 1662, 1641 cm^{-1}. Major diastereomer: *EIMS* m/z (rel. int.) 323 (M^+, 38), 236, (53), 232 (74), 178 (42), 137 (base). ^1H NMR (200 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.19 (d, $J=6.3$ Hz, 3H), 1.21 to 1.80 (m, 6H), 2.00 to 2.25 (m, 2H), 2.46 (dd, $J_1=3.9$ Hz, $J_2=16.4$ Hz, 1H), 2.53 to 2.72 (m, 1H), 3.47 (dd, $J_1=8.6$ Hz, $J_2=16.4$ Hz, 1H), 3.65 (s, 3H), 3.69 (s, 3H), 4.71 (dd, $J_1=3.9$ Hz, $J_2=9.4$ Hz, 1H), 5.04 (dd, $J_1=3.1$ Hz, $J_2=5.5$ Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.88, 17.98, 22.90, 24.94, 33.45, 33.59, 34.75, 38.03, 43.68, 52.11, 52.54, 56.32, 105.5, 143.5, 170.2, 172.0, 172.3. **9**: major diastereomer: colorless oil. *EIMS* m/z (rel. int.) 291 (M^+, 23), 218, (base). IR (film) 1738, 1694, 1614 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 1.17 (d, $J=7.0$ Hz, 3H), 1.26 (d, $J=7.0$ Hz, 3H), 1.37 to 1.66 (m, 4H), 1.80 to 1.96 (m, 1H), 2.06 to 2.18 (m, 2H), 2.44 (dd, $J_1=7.0$ Hz, $J_2=12.5$ Hz, 1H), 2.74 (d, $J=14.1$ Hz, 1H), 2.87 (d, $J=13.3$ Hz, 1H), 3.03 (ddt, $J_1=J_2 \approx 7$ Hz, $J_3 \approx 13$ Hz, 1H), 3.18 to 3.33 (m, 1H), 3.59 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.61, 19.18, 19.24, 19.29, 30.29, 30.30, 36.23, 40.51, 41.56, 52.03, 68.41, 120.4, 169.0, 172.2, 175.6, 202.4. **10**: major diastereomer: colorless oil. *EIMS* m/z (rel. int.) 291 (M^+, 19), 218, (base). IR (film) 1738, 1694, 1614 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 1.19 (d, $J=6.2$ Hz, 3H), 1.25 (d, $J=7.0$ Hz, 3H), 1.40 to 2.18 (m, 5H), 2.33 to 2.53 (m, 1H), 2.58 (d, $J=5.5$ Hz, 1H), 2.81 (d, $J=1.6$ Hz, 2H), 3.15 to 3.32 (m, 1H), 3.56 (s, 3H), 3.61 to 3.74 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.03, 18.93, 19.27, 19.53, 30.08, 30.25, 36.24, 36.92, 43.31, 51.97, 71.83, 120.1, 163.3, 172.0, 202.1. Minor diastereomer: colorless oil. *EIMS* m/z (rel. int.) 291 (M^+, 34), 218, (base).^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (d, $J=7.0$ Hz, 3H), 1.27 (d, $J=7.0$ Hz, 3H), 1.40 to 2.25 (m, 6H), 2.54 (dt, $J_1 \approx J_2 \approx 7$ Hz, 1H), 2.76 (d, $J=14.1$ Hz, 1H), 2.92 (d, $J=14.1$ Hz, 1H), 3.15 (dd, $J_1=7.0$ Hz, $J_2=17.2$ Hz, 1H), 3.25 to 3.40 (m, 1H), 3.59 (s, 3H), 3.62 to 3.73 (m, 1H).