1,5-Dimethyl-4-phenylimidazolidin-2-one-Derived Iminic Glycinimides: Useful New Reagents for Practical Asymmetric Synthesis of α-Amino Acids

Gabriela Guillena and Carmen Nájera*

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, Apartado 99, 03080 Alicante, Spain

cnajera@ua.es

Received March 6, 2000

New 1,5-dimethyl-4-phenylimidazolidin-2-one-derived acyclic chiral iminic glycine reagents have been prepared and diastereoselectively alkylated with activated alkyl halides and electrophilic olefins in the presence of lithium chloride under (a) strong bases (LHMDS, KOBu^t) and low temperature (−78 °C) conditions, (b) solid−liquid phase-transfer catalysis reaction (LiOH, TBAB, −20 °C) conditions, and (c) in the presence of organic bases (DBU, BEMP, TMG, −20 °C). In the case of dielectrophiles *C*- and *N*-alkylation takes place to afford heterocyclic derivatives. Hydrolysis of alkylated products has been carried out (a) in two-step procedures with LiOOH or LiOH followed by acidic hydrolysis or Dowex purification, (b) in one single-step under refluxing water to give the corresponding α-amino acid, (c) in the presence of DBU in methanol to provide *N*-protected α-amino acids methyl esters, or (d) by a protection−hydrolysis procedure to afford *N*-Boc-protected α-amino acids. The chiral imidazolidinone has generally been recovered in good yield. This methodology has been shown to be useful for the synthesis of acyclic and heterocyclic (*S*)- and (*R*)-α-amino acids.

Introduction

The synthesis of defined nonproteinogenic α-amino acids is an important goal in the field of asymmetric synthesis due to the wide range of biomedicinal and chemical applications as free amino acids and as components of peptides and other biomolecules.[1] One of the most important strategies developed in the last 20 years is the diastereoselective alkylation of chiral glycine and alanine enolates.[2] Several types of reagents with cyclic and acyclic structures have been employed as equivalents of these enolates. However, very strong bases (BuLi, LDA, LiHMDS, NaHMDS, etc.), very low temperatures, and strict anhydrous conditions have to be used for the generation of these enolates. These extreme reaction conditions are not compatible with economical large-scale syntheses.

Imines derived from glycine are very useful reagents because they can be readily prepared and are easily enolizable under mild reaction conditions (phase-transfer catalysis, organic bases, palladium catalysis). Moreover, the desired amino acid and the chiral auxiliary can be easily recovered after alkylation also under mild hydrolysis conditions.[3] In addition, recent advances in the asymmetric alkylation of achiral iminic glycinates using chiral phase-transfer catalysts have been described.[3,4] The chiral auxiliary in the case of acyclic iminic glycine templates can be present at the iminic moiety or at the carboxylic function. In the first type of reagents, chiral carbonyl compounds such as hydroxyketones for **1**[5] and **2**,[6] camphor in the case of **3**[7] and **4**,[8] (*S*)-*O*-[*N*-(*N*-benzylpropyl)amino]benzophenone and benzaldehyde **5**,[9,10] aldehydes **6**,[11] **7**,[12] and **8**,[13] and pyridoxal imines **9**[14] have been used as chiral auxiliaries. Chiral esters derived from menthol or 8-phenylmenthol, such as **10**,[15] binaphthol **11**,[16] and carbohydrates **12**,[17] are reagents belonging to the second strategy as well as amides **13**[18] and **14**[19] and imides **15**[20] and **16**.[21] Phase-transfer catalysis (PTC) has been used with good de in the case of Belokon's reagent

* To whom the correspondence should be addressed. URL: www.ua.es/dept.quimorg.

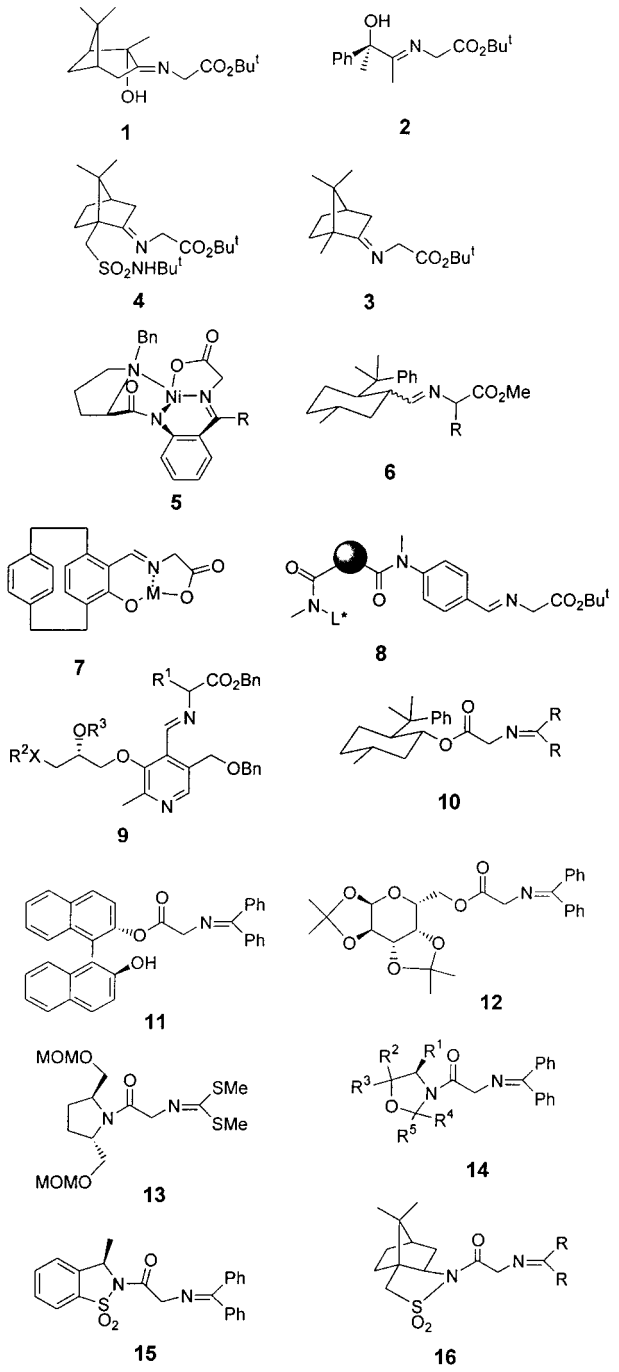
(1) (a) Williams, R. M. *Synthesis of Optically Active Amino Acids*; Pergamon Press: Oxford, 1989. (b) Heimgartner, H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 238−264. (c) Cintas, P. *Tetrahedron* **1991**, *47*, 6079−6111. (d) Duthaler, R. O. *Tetrahedron* **1994**, *50*, 1540−1650. (e) Bailey, P. D.; Clayson, J.; Boa, A. N. *Contemp. Org. Synth.* **1995**, 173−187. (f) North, M. *Contemp. Org. Synth.* **1996**, 323−343. (g) Studer, A. *Synthesis* **1996**, 793−815. (h) Seebach, D.; Sting, A. R.; Hoffmann, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2709−2748. (i) Highlights of the chemistry of AMAAs: Wirth, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 225−227. (j) Cativiela, C.; Díaz-de-Villegas, M. D. *Tetrahedron: Asymmetry* **1998**, *9*, 3517−3599. (k) *Amino Acids, Peptides and Proteins*; Specialist Periodical Reports, Royal Chemistry Society: London, 1968−1995; Vol. 1−28.

(2) For recent applications of Schöllkopf's reagent, see: (a) Phelan, J. C.; Skelton, N. J.; Braisted, A. C.; McDowell, R. S. *J. Am. Chem. Soc.* **1997**, *119*, 455−460. (b) Ojea, V.; Conde, S.; Ruíz, M.; Fernández, M. C.; Quintela, J. M. *Tetrahedron Lett.* **1997**, *38*, 4311−4314. (c) Kremminger, P.; Undheim, K. *Tetrahedron: Asymmetry* **1998**, *9*, 1183−1189. (d) Bull, S. D.; Chernegu, A. N.; Davies, S. G.; Moss, W. O.; Parkin, R. M. *Tetrahedron* **1998**, *54*, 10379−10388. (e) Kobayashi, S.; Furuta, T. *Tetrahedron* **1998**, *54*, 10275−10294. (f) Hammer, K.; Romming, C.; Undheim, K. *Tetrahedron* **1998**, *54*, 10837−10850. (g) Löhr, B.; Orlich, S.; Kunz, H. *Synlett* **1999**, 1139−1141. (h) Ohba, M.; Nishimura, Y.; Kato, M.; Fujii, T. *Tetrahedron* **1999**, *55*, 4999−5016. (i) Mazón, A.; Pedregal, C.; Prowse, W. *Tetrahedron* **1999**, *55*, 7057−7064. (j) Sano, S.; Ishii, T.; Migua, T.; Nagao, Y. *Tetrahedron Lett.* **1999**, *40*, 3013−3016. (k) Ruíz, M.; Ojea, V.; Quintela, J. M. *Synlett* **1999**, 204−206. (l) Ruíz, M.; Ruanova, T. M.; Ojea, V.; Quintela, J. M. *Tetrahedron Lett.* **1999**, *40*, 2021−2024. (m) Bailey, P. D.; Boa, A. N.; Baker, S. R.; Clayson, J.; Murray, E. J.; Rosair, G. M. *Tetrahedron Lett.* **1999**, *40*, 7557−7560. (n) Adamczyk, M.; Akireddy, S. R.; Reddy, R. E. *Tetrahedron: Asymmetry* **1999**, *10*, 3107−3110. (o) Li, Y.-Q.; Sugase, K.; Ishiguro, M. *Tetrahedron Lett.* **1999**, *40*, 9097−9100. For recent applications of Williams's reagent, see: (p) Bender, D. M.; Williams, R. M. *J. Org. Chem.* **1997**, *62*, 6690−6691. (q) Aoyagi, Y.; Williams, R. M. *Synlett* **1998**, 1099−1101. For recent applications of Seebach's reagent see ref 1h.

(3) For a review about iminic reagents see: Abellán, T.; Chinchilla, R.; Galindo, N.; Guillena, G.; Nájera, C.; Sansano, J. M. *Eur. J. Org. Chem.* **2000**, 2689−2697.

10.1021/jo000321t CCC: $19.00
Published on Web 09/22/2000

5[9,10] and Oppolzer's sultam derivatives **16**[21] in alkylation with alkyl halides and electrophilic olefins. In the case of camphor glycinate **3**,[7b,c] 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or triethylamine in the presence of LiBr has been employed as a base for the Michael addition to α,β-unsaturated esters.



Recent studies in this laboratory have focused on the development of new chiral glycine and alanine reagents for the asymmetric synthesis of α-amino acids under mild and simple reaction conditions amenable to easily scalable processes,[3] resulting in alanine templates with structure of oxazinone **17**[22] and pyrazinone **18**[23] (R = Me). These cyclic iminic systems with a stereogenic center at the 6-position can be alkylated at room temperature under (a) PTC conditions with activated alkyl halides and

(4) (a) O'Donnell, M. J.; Esikova, I. A.; Mi, A.; Shullenberger, D. F.; Wu, S. In *Phase-Transfer Catalysis*; ACS Symposium Series 659, Halpern, M. E., Ed; ACS: Washington D. C., 1997; Chapter 10. (b) O'Donnell, M. J.; Delgado, F.; Hostettler, C.; Schwesinger, R. *Tetrahedron Lett*. **1998**, *39*, 8775−8778. (c) O'Donnell, M. J.; Delgado, F.; Pottorf, R. S. *Tetrahedron* **1999**, *55*, 6347−6362. (d) Lygo, B.; Wainwright, P. G. *Tetrahedron Lett*. **1997**, *38*, 8595−8598. (e) Lygo, B.; Crosby, J.; Peterson, J. A. *Tetrahedron Lett*. **1999**, *40*, 1385−1388. (f) Lygo, B. *Tetrahedron Lett*. **1999**, *40*, 1389−1392. (g) Lygo, B.; Crosby, J.; Peterson, J. A. *Tetrahedron Lett*. **1999**, *40*, 8671−8674. (h) Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc*. **1997**, *119*, 12414−12415. (i) E. J. Corey, M. C. Noe, F. Xu, *Tetrahedron Lett*. **1998**, *39*, 5347−5350. (j) Belokon', Y. N.; Kotchetkov, K. A.; Churkina, T. D.; Ikonnikov, N. S.; Chesnokov, A. A.; Larionov, O. V.; Parmár, V. S.; Kumar, R.; Kagan, H. B. *Tetrahedron*: *Asymmetry* **1998**, *9*, 851−857. (k) Belokon', Y. N.; Kotchetkov, K. A.; Churkina, T. D.; Ikonnikov, N. S.; Vyskocil, S.; Kagan, H. B. *Tetrahedron*: *Asymmetry* **1999**, *10*, 1723−1728. (l) Belokon', Y. N.; North, M.; Kublitski, V. S.; Ikonnikov, N. S.; Krasik, P. E.; Maleev, V. I. *Tetrahedron Lett*. **1999**, *40*, 6105−6108. (m) Dehmlow, E. V.; Wagner, S.; Müller, A. *Tetrahedron* **1999**, *55*, 6335−6346. (n) Ooi, T.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc*. **1999**, *121*, 6519−6520.

(5) Yamada, S.; Oguri, T.; Shioiri, T. *J. Chem. Soc., Chem. Commun*. **1976**, 136−137.

(6) Nakatsuka, T.; Miwa, T.; Mukaiyama, T. *Chem. Lett*. **1981**, 279−282.

(7) (a) McIntosh, J. M.; Leavitt, R. K.; Mishra, P.; Cassidy, K. C.; Drake, J. E.; Chadha, R. *J. Org. Chem*. **1988**, *53*, 1947−1952. (b) Kanemasa, S.; Uchida, O.; Wada, E. *J. Org. Chem*. **1990**, *55*, 4411−4417. (c) Kanemasa, S.; Uchida, O.; Wada, E. *J. Org. Chem*. **1990**, *56*, 2875−2883.

(8) Yeh, T.-L.; Liao, C.-C.; Uang, B.-J. *Tetrahedron* **1997**, *53*, 11141−11152.

(9) (a) Belokon', Y. N. *Pure Appl. Chem*. **1992**, *64*, 1917−1924. (b) Belokon', Y. N. *Janssen Chim. Acta* **1992**, *2*, 4−12. (c) Belokon', Y. N.; Tararov, V. I.; Maleev, V. I.; Savel'eva, T. F.; Ryzhov, M. G. *Tetrahedron*: *Asymmetry* **1998**, *9*, 4249−4252.

(10) For recent applications, see: (a) Fishwick, C. W. G.; Sanderson, J. M.; Findlay, J. B. C. *Tetrahedron Lett*. **1994**, *35*, 4611−4614. (b) Tararov, V. I.; Savel'eva, T. F.; Kuznetsov, N. Y.; Ikonnikov, N. S.; Orlova, S. A.; Belokon', Y. N.; North, M. *Tetrahedron*: *Asymmetry* **1997**, *8*, 79−83. (c) Soloshonok, V. A.; Cai, C.; Hruby, V. J.; Meervelt, L. V.; Mischenko, N. *Tetrahedron* **1999**, *55*, 12031−12044. (d) Soloshonok, V. A.; Cai, C.; Hruby, V. J.; Meervelt, L. V. *Tetrahedron* **1999**, *55*, 12045−12058.

(11) Meyer, L.; Poirier, J. M.; Duhamel, P.; Duhamel, L. *J. Org. Chem*. **1998**, *63*, 8094−8059.

(12) Rozenberg, V.; Kharitonov, V.; Antonov, D.; Sergeeva, E.; Aleskin, A.; Ikonnikov, N.; Orlova, S.; Belokon', Y. N. *Angew. Chem., Int. Ed. Engl*. **1994**, *33*, 91−92.

(13) Calmes, M.; Daunis, J.; Ismaili, H.; Jacquier, R.; Kondou, J.; Knusi, G.; Zonanate, A. *Tetrahedron* **1990**, *46*, 6021−6032.

(14) (a) Miyashita, K.; Miyabe, H.; Tai, K.; Kurozumi, C.; Imanishi, T. *Chem. Commun*. **1996**, 1073−1074. (b) Miyashita, K.; Miyabe, H.; Tai, K.; Kurozumi, C.; Iwaki, H.; Imanishi, T. *Tetrahedron* **1999**, *55*, 12109−12124.

(15) (a) Fasth, K.-J.; Antoni, G.; Langström, B. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3081−3084. (b) Alvarez-Ibarra, C.; Csàkỳ, A. G.; Maroto, R.; Quiroga, M. L. *J. Org. Chem*. **1995**, *60*, 7934−7940.

(16) Tanaka, K.; Ahn, M.; Watanabe, Y.; Fuji, K. *Tetrahedron*: *Asymmetry* **1996**, *7*, 1771−1782.

(17) Solladié, G.; Saint Clair, J.-F.; Philippe, M.; Semeria, D.; Maignan, J. *Tetrahedron*: *Asymmetry* **1996**, *7*, 2359−2364.

(18) (a) Ikemani, S.; Hayama, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett*. **1986**, *27*, 3403−3406. (b) Ikemani, S.; Uchiyama,. S.; Hayama, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron* **1988**, *44*, 5333−5342.

(19) Kanemasa, S.; Mori,; Tatsukama, A. *Tetrahedron Lett*. **1993**, *34*, 8293−8296.

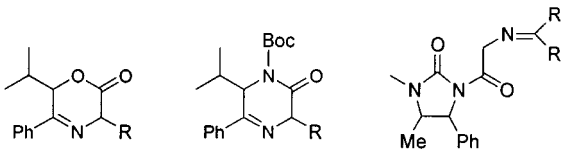
(20) Oppolzer, W.; Rodríguez, I.; Starkemann, C.; Walther, E. *Tetrahedron Lett*. **1990**, *31*, 5019−5022.

(21) (a) Oppolzer, W.; Moretti, R.; Thomi, S. *Tetrahedron Lett*. **1989**, *30*, 6009−6010. (b) Josien, H.; Martin, A.; Chassaing, G. *Tetrahedron Lett*. **1991**, *32*, 6547−6550. (c) Oppolzer, W.; Moretti, R.; Zhou, C. *Helv. Chim. Acta* **1994**, *77*, 2363−2380. (d) Ayoub, M.; Chassain, G.; Loffet, A.; Lavielle, S. *Tetrahedron Lett*. **1995**, *36*, 4069−4072. (e) López, A.; Pleixats, R. *Tetrahedron*: *Asymmetry* **1998**, *9*, 1967−1977. (f) Liu, W.-Q.; Roques, B. P.; Garbay, C. *Tetrahedron Lett*. **1997**, *38*, 1389−1392. (g) Beenett, F. A.; Barlow, D. J.; Dodoo, A. N. O.; Hider, R. C.; Lansley, A. B.; Lawrence, M. J.; Marriott, C.; Bansai, S. S. *Tetrahedron Lett*. **1997**, *38*, 7449−7452.

(22) Chinchilla, R.; Falvello, L. R.; Galindo, N.; Nájera, C. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 995−997. (b) Chinchilla, R.; Galindo, N.; Nájera, C. *Tetrahedron*: *Asymmetry* **1998**, *9*, 2769−2772. (c) Chinchilla, R.; Galindo, N.; Nájera, C. *Synthesis* **1999**, 704−717.

(23) Abellán, T.; Nájera, C.; Sansano, J. M. *Tetrahedron*: *Asymmetry* **1998**, *9*, 2211−2214.

electrophilic olefins, (b) organic base conditions for unactivated alkyl halides and electrophilic olefins, and (c) palladium(0) catalysis under neutral conditions with allylic carbonates with very high diastereoselective bias. This methodology has been used for the synthesis of acyclic and heterocyclic α-methyl α-amino acids.[1i] However, glycine templates **17** and **18** (R = H) suffered dialkylation at the 3-position under the above-mentioned conditions probably due to steric reasons. In this paper, we report the preparation of new chiral iminic glycine imides **19** derived from ephedrine imidazolidinones[24] and their diastereoselective monoalkylation under mild reaction conditions such as PTC and organic bases.[25]



Results and Discussion

Preparation of Imidazolidinone-Derived Glycinimide Reagents. (−)-(4*R*,5*S*)-1,5-Dimethyl-4-phenylimidazolidin-2-one [(−)-**20**] is commercially available but can be economically prepared by heating (−)-ephedrinium chloride and urea.[26] The glycine moiety was introduced stepwise by acylation of deprotonated imidazolidinone (−)-**20** with α-chloroacetyl chloride at −78 °C to afford product (−)-**21** in 77% yield.[24a] To achieve a better procedure for multigram scale synthesis of compound **21**, the recent conditions described by Clark and Bender[27] for acylation of this imidazolidinone were applied. By heating the chiral auxiliary (−)-**20** with α-chloroacetyl chloride in acetonitrile at 80 °C for 4 h product (−)-**21** was obtained in 95% yield. The reaction of chloroacetylimidazolidinone (−)-**21** with NaN_3[28] in refluxing acetonitrile for 3 d followed by palladium on carbon catalyzed hydrogenation[29] in methanol in the presence of concentrated hydrochloric acid (1.5 equiv) gave imidazolidinone-derived glycine hydrochloride (−)-**22** in 86% overall yield.

The formation of the *N*-[bis(methylthio)methylene]-glycinimide (−)-**23** was carried out by treatment with carbon disulfide and methyl iodide and subsequent alkylation with methyl iodide in the presence of K_2CO_3 in acetone in 50% yield.[30] Benzophenone derivative (−)-**24** was prepared in 68% yield by reaction of hydrochloride (−)-**22** with benzophenone imine in dichloromethane for 1 d at room temperature.[31] The corresponding enantiomer (+)-**24** was obtained in 55% overall yield based on imidazolidinone (+)-(4*S*,5*R*)-**20** following the same four steps procedure (Scheme 1 and Table 1). Reagents (−)-**23** and **24** were obtained as crystalline compounds and their physical data are summarized in Table 1. All compounds were stable at room temperature for several months; however, compounds **24** were sensitive to acidic

Scheme 1

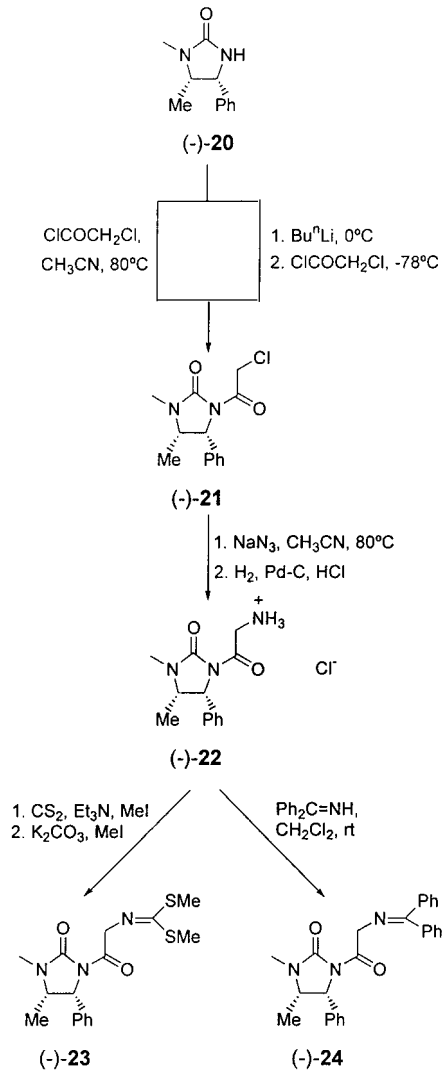


Table 1. Synthesis of Imidazolidinone-Derived Glycinimides

imidazolidinone	no.	yield[a] (%)	mp[b] (°C)	$[\alpha]^{25}_{D}$ [c]
(−)-**20**	(−)-**23**	41[d]	98−101[e]	−93.0
(−)-**20**	(−)-**24**	55	121−123	−94.5
(+)-**20**	(+)-**24**	54	120−123	+95.7

[a] Yield of isolated after crystallization based on **20**. [b] From hexane/EtOAc/ether. [c] In $CHCl_3$, $c = 1$. [d] After column chromatography (silica gel) hexane/EtOAc: 1/1. [e] From hexane/EtOAc.

(24) For recent uses of this auxiliary in asymmetric synthesis, see for instance: (a) Orena, M.; Porzi, G.; Sandri, S. *Tetrahedron Lett.* **1992**, *33*, 3797−3800. (b) Jenssen, K. N.; Roos, G. H. P. *Tetrahedron*: *Asymmetry* **1992**, *3*, 1553−1554.(c) Melnyk, O.; Stephan, E.; Pourcelot, G.; Cresson, P. *Tetrahedron* **1992**, *48*, 841−850. (d) Drewes, S. E.; Malissar, D. G. S.; Roos, G. H. P. *Chem. Ber.* **1993**, *126*, 2663−2673. (e) Anand, R. C.; Singh, V. *Tetrahedron* **1993**, *49*, 6515−6520. (f) Cardillo, G.; De Simone, A.; Gentilucci, L.; Sabatino, P.; Tomasini, C. *Tetrahedron Lett.* **1994**, *35*, 5051−5054. (g) Van Heerden, P. S.; Bezuidenhoudt, B. C. B.; Ferreira, D. *Tetrahedron Lett.* **1997**, *38*, 1821−1824. (h) Bongini, A.; Cardillo, G.; Gentilucci, L.; Tomasini, C. *J. Org. Chem.* **1997**, *62*, 9148−9153. (i) Trost, B. M.; Ceschi, M. A.; König, B. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1486-1489. (j) Caddick, S.; Jenkins, K.; Treweeke, N.; Candeias, S. X.; Afonso, C. A. M. *Tetrahedron Lett.* **1998**, *39*, 2203−2206. (k) Roos, G. H. P.; Balasubramaniam, S. *Synth. Commun.* **1998**, *28*, 3877−3884. (l) Versttg, M.; Bezmidenhoudt, B. C. B.; Ferreira, D. *Tetrahedron* **1999**, *55*, 3365−3376. (m) Cardillo, G.; Gentilucci, L.; Tolomelli, A. *Tetrahedron Lett.* **1999**, *40*, 8261−8264.

(25) For preliminary communications, see: (a) Guillena, G.; Nájera, C. *Tetrahedron*: *Asymmetry* **1998**, *9*, 1125−1129. (b) Guillena, G.; Nájera, C. *Tetrahedron*: *Asymmetry* **1998**, *9*, 3935−3938.

(26) Roder, H,; Helmchen, G.; Peters, E. M.; von Schnering, H. G. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 898−899.

(27) Clark, W. M.; Bender, C. *J. Org. Chem.* **1998**, *63*, 6732−6734.

(28) Caddick, S.; Jenkins, R. *Tetrahedron Lett.* **1996**, *37*, 1301−1304.

(29) Evans, D. A.; Weber, A. E. *J. Am. Chem. Soc.* **1986**, *108*, 6757−6761.

(30) Hoppe, D.; Beckmann, L. *Liebigs Ann. Chem.* **1979**, 2066−2075.

(31) O'Donnell, M. J.; Polt, R. L. *J. Org. Chem.* **1982**, *47*, 2663−2666.

Table 2. Aprotic Alkylation of Imidazolidinone-Derived Glycinimide (−)-23

entry	base (equiv)	additive[a]	RHal	temp[b] (°C)	product	yield[c] (%)	de[d] (%)
1	Bu^{n}Li (1)	DMPU	CH_2CHCH_2I	−78 → 0	(−)-**25a**	43	72
2	LDA (1)	DMPU	CH_2CHCH_2I	−78 → −20	(−)-**25a**	53	54
3	LiHMDS (1)		CH_2CHCH_2I	−78 → 0	(−)-**25a**	55	58
4	KOBu^t (1.5)		CH_2CHCH_2I	−78 → −50	(−)-**25a**	45	70
5	KOBu^t (3)	LiCl	CH_2CHCH_2I	−78 → −20	(−)-**25a**	77	86
6	LiHMDS (1)	LiCl	CH_2CHCH_2I	−78 → 0	(−)-**25a**	86	96
7	LiHMDS (1)	LiBr	CH_2CHCH_2I	−78 → 0	(−)-**25a**	89	84
8	LiHMDS (1)	LiCl	$C_6H_5CH_2I$	−78 → 0	(−)-**25b**	68	90
9	LiHMDS (1)	LiCl[e]	$C_6H_5CH_2Br$	−78 → 0	(−)-**25b**	66	92
10	KOBu^t (3)	LiCl[e]	$C_6H_5CH_2Br$	−78 → −20	(−)-**25b**	54	82
11	LiHMDS (1)	LiCl[e]	$HCCCH_2Br$	−78 → −20	(−)-**25c**	58	92
12	LiHMDS (1)	LiCl	$Bu^tO_2CH_2I$	−78 → −20	(−)-**25d**	63	74
13	LiHMDS (1)	LiCl	EtO_2CCH_2I	−78 → 0	(−)-**25e**	73	40
14	KOBu^t (3)	LiCl	EtO_2CCH_2I	−20[f]	(−)-**25e**	76	46
15	KOBu^t (3)	LiCl	CH_3I	−20[g]	(−)-**25f**	37	64
16	KOBu^t (3)	LiCl	CH_3OTf	−20[h]	(−)-**25f**	50	60
17	KOBu^t (3)	LiCl	$NCCH_2I$	−78 → −20	(−)-**25g**	55	60
18	LiHMDS (1)	LiCl[e]	$EtO_2CCHCHCH_2Br$[i]	−78 → 0	(−)-**25h**	70	86
19	KOBu^t (3)	LiCl[e]	$EtO_2CC(CH_2)CH_2Br$	−20[f]	(−)-**25i**	62	70

[a] In the case of DMPU, a mixture of THF/DMPU 4/1 was used and 6 equiv of LiCl or LiBr. [b] All reactions were carried out allowing the temperature to rise in ca. 2.5 h (otherwise stated). [c] Yield of isolated product after column chromatography, based on compound (−)-**23**. [d] Determined by ^{1}H NMR (300 MHz). [e] LiI (3 equiv) was added. [f] Reaction time 4 h. [g] Reaction time 15 h. [h] Reaction time 5 h. [i] *E*-Configuration.

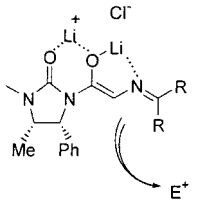


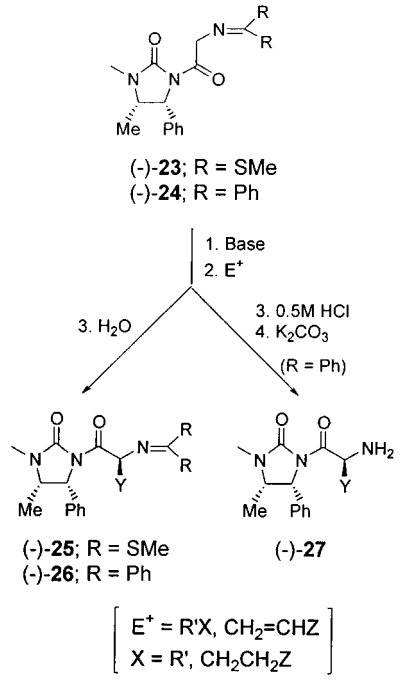
Figure 1. Proposed reactive conformation of enolate.

conditions as well as to silica gel. Attempts to prepare these reagents by direct trimethylaluminum-mediated acylation[21c] of imidazolidinones **20** with methyl *N*-[bis-(methylthio)methylene] or *N*-(diphenylmethylene) glycinates failed.

Alkylation of (−)-Imidazolidinone-Derived Glycinimide Reagents. Initial alkylation studies were carried out with reagent (−)-**23** in the presence of strong bases and allyl iodide as electrophile in THF as solvent at low temperatures (Table 2). LiHMDS and KOBu^t were the best bases working at temperatures ranging between −78 to 0 °C and −78 to −20 °C, respectively. As additives, *N*,*N*′-dimethylpropyleneurea (DMPU), LiBr, and LiCl were examined, the presence of the latter being imperative for good chemical yields and diastereoselectivities. These reaction conditions were used with other activated alkyl halides to provide alkylated products (−)-**25** in 58−86% yields and 76−96% de (Scheme 2 and Table 2). The stereochemical outcome of this alkylation process was determined after hydrolysis to the corresponding (*S*)-α-amino acids (see below). These results can be explained by participation of a chelated *Z*-enolate in which lithium chloride acts as Lewis acid to change the degree of aggregation and the conformation of the complex from anti to syn.[32] Moreover, lithium chloride can activate electrophiles by a general salt effect, which changes the effective polarity of the solvent (Figure 1).[33]

When K_2CO_3 or KOH were used as bases and tetrabutylammonium bromide (TBAB) as catalyst for the

Scheme 2



alkylation of reagents (−)-**23** and (−)-**24** at room temperature in acetonitrile, mainly cleavage of the *N*-acyl group was observed. However, when LiOH was used as base under the same solid−liquid PTC conditions at −20 °C and in the presence of LiCl (6 equiv), the alkylation took place in 57−90% yield and 84−94% de (Scheme 2 and Table 3). Both reagents behave in a similar fashion with activated electrophiles but in the case of products (−)-**26**, partial deprotection of the imine moiety was observed during purification by column chromatography. For this reason, after alkylation, crude products were transformed into amines (−)-**27** by extractive workup with 0.5 M HCl and saturated aqueous K_2CO_3. Reagent (−)-**24** was preferred in order to avoid the use of the unpleasant carbon disulfide, because it is slightly superior to (−)-**23** in the alkylation reaction and since the hydrolysis conditions are simpler (see below). When the reaction was carried out in the absence of LiCl and with

(32) Kanai, M.; Muraoka, A.; Tanaka, T.; Sawada, M.; Ikota, N.; Tomioka, K. *Tetrahedron* **1995**, *51*, 9349−9352.

(33) Seebach, D.; Beck, A. K.; Studer, A. In *Modern Synthetic Methods 1995*; VCH: Basel, 1995; pp 1−178.

Table 3. PTC Alkylation of Imidazolidinone-Derived Glycinimides (−)-23 and (−)-24[a]

entry	reagent	electrophile	time, h	product	yield[b] (%)	de[c] (%)
1	(−)-**23**	CH_2CHCH_2I	1	(−)-**25a**	90[d]	84
2	(−)-**24**	CH_2CHCH_2I	3.5	(−)-**27a**	80	86
3	(−)-**24**	CH_2CHCH_2I[e]	6	(−)-**27a**	40	0
4	(−)-**24**	$C_6H_5CH_2Br$[f]	15	(−)-**27b**	57	86
5	(−)-**24**	$EtO_2CCHCHCH_2Br$[f,g]	3.5	(−)-**27h**	76	94
6	(−)-**24**	$CH_2CHCO_2Bu^t$	72	(−)-**27r**	25	94

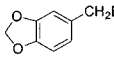
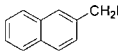
[a] All reactions were carried out at −20 °C in dry CH_3CN with LiOH (3 equiv) as base and in the presence of LiCl (6 equiv). [b] Yield of isolated crude product based on starting reagent. [c] Determined by ^1H NMR (300 MHz). [d] After column chromatography. [e] CsOH (3 equiv) were used in the absence of LiCl. [f] LiI (3 equiv) was added. [g] *E*-Configuration.

CsOH as base, lower yield and no diastereoselection was obtained (Table 3, entry 3). Poor yield was obtained in the Michael addition to *tert*-butyl acrylate (Table 3, entry 6).

The organic bases DBU, tetramethylguanidine (TMG), and Schwesinger's 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP)[34] were used in the presence of LiCl in acetonitrile. In general DBU gave better results with both reagents (−)-**23** and (−)-**24**, the alkylation taking place in shorter reaction times and better de than under PTC conditions (Table 4). The use of LiCl is crucial for the diastereoselection (Table 4, entry 5), and the temperature should be kept at −20 °C to avoid hydrolysis of the imide function. Activated alkyl halides and electrophilic olefins were extensively studied with substrate (−)-**24**. In the case of bromides, the reaction also was carried out in the presence of LiI to increase the reactivity of the electrophile by bromine−iodide interchange (compare entries 7 and 8 in Table 4). When allyl bromide in the presence of LiI was used as electrophile, similar yields but lower de and longer reaction time were observed (Table 4, entries 2 and 8). The Michael addition to *tert*-butyl acrylate was carried out using substoichiometric amounts of DBU (Table 4, entries 21 and 22). In the case of ethyl propiolate isomerization of the double bond took place using a stoichiometric amount of DBU to afford diastereoselectively compound (−)-**28**. Its *Z*-configuration was deduced from the $^{1,3}J = 3.7$ Hz in proton-coupled ^{13}C NMR spectrum for the carbonyl group of glycine and the olefinic proton[35] and also from the chemical shift of this proton as previously reported for related products.[36] However, when 0.1 mol % of DBU was used as base, a 9:1 mixture of compound (−)-**26t**, with *Z*-configuration, and (−)-**28** was obtained (Table 4, entry 25). These products were isolated after column chromatography on deactivated silica gel in 32 and 17% yield, respectively. The addition to Eschenmoser's salt gave product (−)-**29** in 74% de in the presence of DBU as base (Table 4, entry 27) whereas product (−)-**29** was obtained quantitatively as a single diastereomer under LHMDS conditions (from 300 MHz ^1H NMR).

An extension of this alkylation methodology for the preparation of heterocyclic α-amino acids was achieved by using dielectrophiles. For example, in situ dialkylation of benzophenone derivative (−)-**24** with α,α′-dibromo-*o*-xylene and (*Z*)-1,4-dichloro-2-butene gave directly C- and N-dialkylated products (−)-**30** and (−)-**31**, respectively (Table 4, entries 28 and 29). In the case of methyl vinyl ketone, Michael addition followed by condensation of the

Table 4. Organic Bases-Mediated Alkylation of Imidazolidinone-Derived Glycinimides (−)-23 and (−)-24[a]

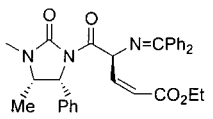
entry	Reagent	base	electrophile	time (h)	product	yield[b] (%)	de[c] (%)
1	(-)-**23**	DBU	CH_2CHCH_2I	1	(-)-**25a**	95	84
2	(-)-**24**	DBU	CH_2CHCH_2I	1	(-)-**27a**	86	98
3	(-)-**23**	BEMP	CH_2CHCH_2I	4	(-)-**25a**	87	86
4	(-)-**24**	BEMP	CH_2CHCH_2I	3.5	(-)-**27a**	60	98
5	(-)-**24**	BEMP[d]	CH_2CHCH_2I	4	(-)-**27a**	10	0
6	(-)-**24**	TMG	CH_2CHCH_2I	2	(-)-**27a**	60	98
7	(-)-**24**	DBU	CH_2CHCH_2Br	5	(-)-**27a**	70	90
8	(-)-**24**	DBU	CH_2CHCH_2Br[e]	3	(-)-**27a**	83	90
9	(-)-**24**	DBU	$C_6H_5CH_2Br$	3	(-)-**27b**	73	96
10	(-)-**24**	DBU	$HCCCH_2Br$	5	(-)-**27c**	69	98
11	(-)-**24**	DBU	EtO_2CCH_2I	3	(-)-**27e**	86	96
12	(-)-**24**	DBU	$EtO_2CCHCHCH_2Br$[f]	2	(-)-**27h**	78	96
13	(-)-**24**	DBU	CH_2CBrCH_2Br[e]	8	(-)-**27j**	21	96
14	(-)-**24**	DBU	$CH_2C(CH_3)CH_2Br$[e]	7	(-)-**27k**	64	98
15	(-)-**24**	DBU	$(CH_3)_2CCHCH_2Br$[e]	12	(-)-**27l**	57	98
16	(-)-**24**	DBU	$PhCHCHCH_2Br$[e,f]	1	(-)-**27m**	40	98
17	(-)-**24**	DBU		2	(-)-**27n**	38	84
18	(-)-**24**	DBU		1	(-)-**27o**	35	98
19	(-)-**24**	DBU	$C_6H_5COCH_2Br$[e]	5	(-)-**27p**	49	92
20	(-)-**24**	DBU	CH_2CHCO_2Me	8	(-)-**27q**	61	80
21	(-)-**24**	DBU	$CH_2CHCO_2Bu^t$	18	(-)-**27r**	32	94
22	(-)-**24**	DBU[g]	$CH_2CHCO_2Bu^t$	12	(-)-**27r**	54	92
23	(-)-**24**	DBU	CH_2CHCN	24	(-)-**26s**	26	96
24	(-)-**24**	DBU	$HCCCO_2Et$	4	(-)-**28**	18[h]	
25	(-)-**24**	DBU[g]	$HCCCO_2Et$	4	(-)-**26t**[i]	32[j]	90
26	(-)-**24**	DBU	$CH_2C(CH_3)CO_2Me$	24	(-)-**26u**[k]	44[l]	70
27	(-)-**24**	DBU	$[CH_2N(CH_3)_2]^+ I^-$	5	(-)-**29**	40	74[m]
28	(-)-**24**	DBU		3	(-)-**30**	36	88
29	(-)-**19**	DBU	$ClCH_2CHCHCH_2Cl$[e,n]	12	(-)-**31**	50	94
30	(-)-**19**	DBU	$CH_2CHCOCH_3$	4	(-)-**32**	60	-[o]

[a] All reactions were carried out at −20 °C in dry CH_3CN with 1.5 equiv of base and in the presence of LiCl (6 equiv). [b] Yield of isolated crude product based on starting reagent. [c] Determined by ^1H NMR (300 MHz). [d] Without LiCl. [e] LiI (3 equiv) were added. [f] *E*-Configuration. [g] 0.1 equiv of base was used. [h] After column chromatography, partial decomposition was observed. [i] A 9/1 mixture of compounds (−)-**26t** and (−)-**28** was obtained. [j] Compound (−)-**28** (18%) was also obtained. [k] 1/1 mixture of diastereomers. [l] 40% of the other diasteromer also was obtained after column chromatography. [m] When LHMDS conditions were used, product (−)-**29** was quantitatively obtained as a single diastereomer. [n] *Z*-Configuration. [o] Not determined.

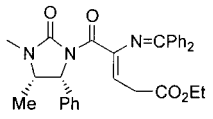
(34) Schwesinger, R.; Willaredt, J.; Schlemper, H.; Keller, M.; Schmitt, D.; Fritz, H. *Chem. Ber.* **1994**, *127*, 2435−2454.

(35) Cativiela, C.; Diaz-de-Villegas, M. D.; Gálvez, J. A. *Tetrahedron: Asymmetry* **1992**, *3*, 567−572.

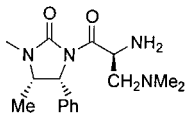
(36) (a) O'Donnell, M. J.; Arasappan, A.; Hornback, W.; Huffman, J. C. *Tetrahedron Lett.* **1990**, *31*, 157−160. (b) Alvarez-Ibarra, C.; Csàkÿ, A. G.; Martin, M. E.; Quiroga, M. L. *Tetrahedron* **1999**, *55*, 7319−7330.



(-)-**26t**

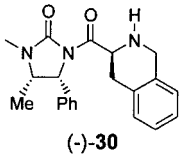


(-)-**28**

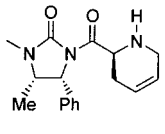


(-)-**29**

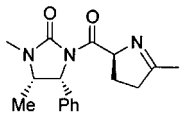
amino group with the carbonyl group afforded pyrroline (−)-**32**, with a de that could not be determined. The same behavior has been reported with the Oppolzer reagent.[21e]



(-)-**30**



(-)-**31**



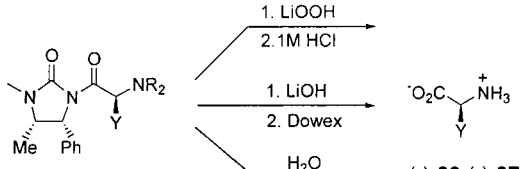
(-)-**32**

The alkylation of compound (−)-**24** was also carried out using palladium(0) catalysis under neutral conditions. Thus, using allyl methyl carbonate, $Pd(PPh_3)_4$, bis-(diphenylphosphinoethane) (dppe) and substrate (−)-**24** in THF at room temperature afforded product (−)-**26a** in 42% yield and 52% de, whereas the allylation reaction failed in the presence of LiCl.

Hydrolysis of Alkylated (−)-Imidazolidinone-Derived Glycinimide Reagents. Several hydrolysis conditions were assayed with compounds (−)-**25** and (−)-**26**−**32** (Scheme 3 and Table 5). Reaction conditions for compounds (−)-**25a**,**b** and (−)-**26a** (method A) involved treatment with lithium hydroperoxide in THF/H_2O: 3/1 to cleave the chiral auxiliary, which was recovered in greater than 90% yield by simple extractive workup. Then the imine was hydrolyzed with aqueous 1 M HCl in THF at room temperature for 1 d, and the resulting hydrochloride salt was treated with propylene oxide in EtOH for 2 h at room temperature[37] to give (*S*)-allylglycine (**33a**) and (*S*)-phenylalanine (**33b**) as free α-amino acids in 56 and 36% yield based on reagent (−)-**23** and (−)-**24** (Table 5, entries 1−3).

Products (−)-**27**-(−)**32** were hydrolyzed (method B) with LiOH in THF/H_2O: 2/1 at room temperature, the imidazolidinone (−)-**20** being recovered also by extractive workup. After purification by ion-exchange chromatography (Dowex), the corresponding (*S*)-α-amino acids (−)-**33a**,**b** and baikiain (−)-**34** were obtained (Table 5, entries 4−6). Compound (−)-**32**, derived from methyl vinyl ketone, was transformed into compound (−)-**35** (ee 89%) by hydrolysis with 1 M HCl followed by *N*-protection with di-*tert*-butyl dicarbonate in EtOH in the presence of $NaHCO_3$ (Table 5, entry 7).[21e]

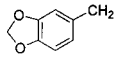
Scheme 3



(-)-**25**; R-R =C(SMe)$_2$
(-)-**27**; R = H
(-)-**30**-**32**

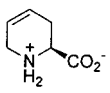
(-)-**33**-(-)-**37**

Table 5. Hydrolysis of Alkylated Imidazolidinone-Derived Glycinimides. Synthesis of L-α-Amino Acids

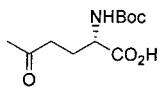
entry	starting compound (de, %)	method[a]	Y	product	yield[b,c] (%)	ee[d] (%)
1	(-)-**25a** (88)	A	CH_2CHCH_2	(-)-**33a**	56 (90)	88
2	(-)-**25b** (90)	A	$C_6H_5CH_2$	(-)-**33b**	36 (90)	90
3	(-)-**26a** (98)	A	CH_2CHCH_2	(-)-**33a**	51 (87)	90
4	(-)-**27a** (96)	B	CH_2CHCH_2	(-)-**33a**	50 (83)	94
5	(-)-**27b** (96)	B	$C_6H_5CH_2$	(-)-**33b**	69 (73)	87
6	(-)-**31** (94)	B		(-)-**34**	48 (68)	81[e]
7	(-)-**32**	B		(-)-**35**	62 (92)	89[f]
8	(-)-**27a** (90)	C	CH_2CHCH_2	(-)-**33a**	87 (98)	82[e]
9	(-)-**27l** (98)	C	$(CH_3)_2CCHCH_2$	(-)-**33l**	87 (99)	90[e]
10	(-)-**27n** (84)	C		(-)-**33n**	69 (99)	-[g]
11	(-)-**27r** (92)	C		(-)-**36**	45 (99)	96[e]
12	(-)-**30** (76)	C		(-)-**37**	65 (95)	66[e]

[a] Method A: (i) LiOOH, 12 h, (ii) 1 M HCl, 1 d, (iii) propylene oxide, EtOH; method B: (i) LiOH, (ii) Dowex; method C: H_2O, reflux 12 h. [b] Based on starting compound after purification. [c] In parentheses yield of recovered imidazolidinone (−)-**20**. [d] By HPLC crownpack CR (+). [e] From [α] values. [f] Determined from the [α] value of the *N*-Boc-protected amino acid. [g] $[\alpha]^{25}_D = -27.36$ (*c* 0.9, 1 M HCl).

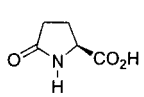
The simplest procedure for the hydrolysis of *N*-unprotected derivatives (−)-**27** is refluxing in water (method C) according to the method used by Myers for pseudoephedrine glycinamide reagents.[38] Following this protocol (*S*)-α-amino acids (−)-**33a**,**l**,**n**, L-pyroglutamic acid (**36**) and the tetrahydroisoquinoline derivative (−)-**37**



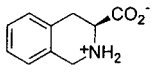
(-)-**34**



(-)-**35**



(-)-**36**



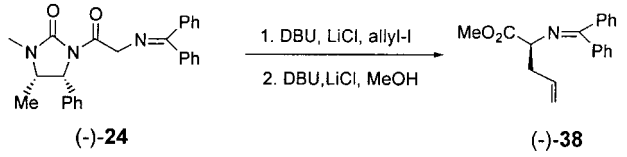
(-)-**37**

were quantitatively obtained after simple extractive workup of the imidazolidinone (−)-**20** (Table 5, entries 8−12). Method C gave, in general, less epimerization

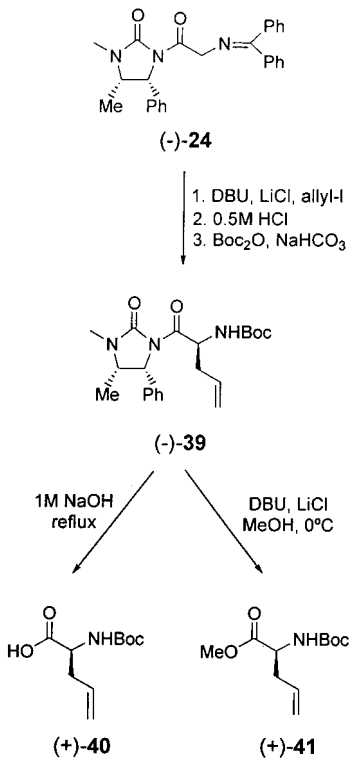
(37) Oppolzer, W.; Lienard, P. *Helv. Chim. Acta* **1992**, *75*, 2572−2582.

(38) Myers, A. G.; Gleason, J. L.; Yoon, T.; Kung, D. W. *J. Am. Chem. Soc.* **1997**, *119*, 656−673.

Scheme 4



Scheme 5



than method B for compounds (−)-**27**, and the chiral auxiliary was recovered in nearly quantitative yield.

Other hydrolyses to afford protected α-amino acids were studied with alkylated product (−)-**26a**. For instance, compound (−)-**24** was allylated under DBU conditions with allyl iodide to give crude product (−)-**26a** (98% de), which was treated with DBU and LiCl in MeOH for 1 d at 0 °C to afford imino ester (−)-**38** and imidazolidinone (−)-**20** in 43 and 85% yield, respectively. Compound (−)-**38** was obtained partially epimerized in 87% ee deduced from [α] values[39] (Scheme 4).

N-Boc-protected α-amino acids were obtained by a protection−hydrolysis procedure. Thus, crude compound (−)-**27a** hydrochloride (94% ee), obtained by DBU alkylation of (−)-**24** and hydrolysis with 0.5 M HCl, was transformed into product (−)-**39** by treatment with di-*tert*-butyl dicarbonate in EtOH in the presence of $NaHCO_3$ for 1 h at room temperature (Scheme 5). Starting from this compound, two different hydrolytic procedures were applied. Treatment with 0.5 M NaOH reflux for 3 h afforded (*S*)-*N*-Boc-allylglycine (**40**) in 39% yield and 81% ee deduced from [α] values.[40] Alternatively, treatment of product (−)-**39** with DBU−LiCl in MeOH at 0 °C[41] for 1 h allowed isolation of (*S*)-*N*-Boc-allylglycine methyl ester (**41**) in 27% overall yield and 96% ee.[42] The chiral imidazolidinone was recovered in 73% yield after column chromatography (Scheme 5).

For *N*-Fmoc protection of α-amino acids the tetrahydroisoquinoline derivative (−)-**30** was hydrolyzed with water to provide compound (−)-**37** (see Table 5, entry 12), which was treated in situ with *N*-(9-fluorenylmethoxycarbonyloxy)succinimide (FmocONSu, 1 equiv) in the presence of Et_3N (1 equiv) and acetonitrile as cosolvents (1:1 mixture) for 6 h at room temperature to give *N*-Fmoc-(−)-**37** in 46% overall yield.

Synthesis of D-α-Amino Acids. We have extended this methodology to the synthesis of (*R*)-α-amino acids starting from (+)-ephedrine derived (+)-(4*S*,5*R*)-1,5-dimethyl-4-phenylimidazolidin-2-one (+)-**20**. The benzophenone-derived reagent (+)-**24** was isolated in 54% overall yield (Table 1) and alkylated under DBU−LiCl conditions with representative alkyl halides and *tert*-butyl acrylate to lead to compounds (+)-**27** and (+)-**30** after acidic−basic extractive workup (Scheme 6 and Table 6). In this case hydrolysis of the alkylated products was carried out by using refluxing water (method C) to furnish (*R*)-α-amino acids allylglycine (**33a**), 3,4-dimethyl-D-Dopa (**33v**), D-pyroglutamic acid (**36**), and tetrahydroisoquinoline D-derivative (+)-**37**.

Scheme 6

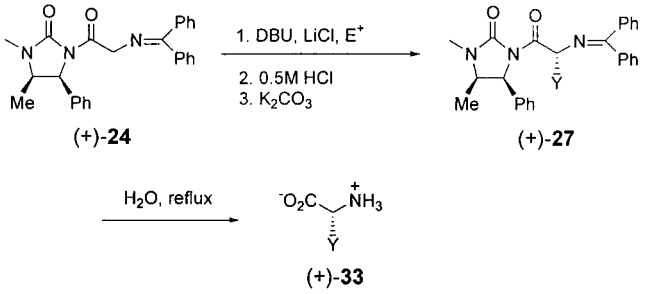
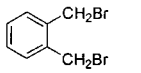
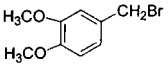


Table 6. DBU−LiCl-Mediated Alkylation of (+)-24. Synthesis of D-α-Amino Acids

	Alkylated product				D-α-Amino Acid[a]		
time (h)	electrophile	product	yield[b] (%)	de[c] (%)	product	yield[d,e] (%)	ee[f] (%)
1	CH_2CHCH_2I	(+)-**27a**	79	98	(+)-**33a**	90 (84)	90
12	$CH_2CHCO_2Bu^t$ [g]	(+)-**27r**	46	94	(+)-**36**	82[h] (80)	91
3		(+)-**30**	33	68	(+)-**37**	81 (90)	64
4		(+)-**27v**	74	94	(+)-**33v**	59 (95)	94

[a] Method C was used. [b] Yield of isolated crude product, based on starting compound (+)-**24**. [c] From ^1H NMR. [d] Based on alkylated product. [e] In parentheses yield of recovered imidazolidinone (+)-**20**. [f] From [α] values. [g] A 10 mol % of DBU was used. [h] A mixture of dioxane/H_2O 1/1 was used for hydrolysis.

Conclusions

We conclude that iminic ephedrine-imidazolidinone glycinimides **23** and **24** are practical reagents for the asymmetric synthesis of L- and D-α-amino acids by alkylation−hydrolysis reactions under very mild reaction

(39) Genêt, J. P.; Juge, S.; Ruiz-Montes, J.; Gaudin, J. M. *J. Chem. Soc., Chem. Commun.* **1988**, 718−719.
(40) Myers, A. G.; Gleason, J. L. *Org. Synth.* **1998**, *76*, 57−76.
(41) Seebach, D.; Thaler, A.; Blaser, D.; Ko, S. Y. *Helv. Chim. Acta* **1991**, *74*, 1102−1118.
(42) Ohfune, Y.; Nishio, H. *Tetrahedron Lett.* **1984**, *25*, 4133−4136.

conditions. The benzophenone derivative **24** is specially useful for the diastereoselective alkylation with activated alkyl halides and electrophilic olefins under PTC conditions and with DBU−LiBr as base. The basis for the observed diastereoselectivity is the chelation by LiCl of both carbonyl groups, which hinders the conformotional mobility of the molecule. This model allows the prediction of the stereochemical course of the reaction. An important feature of this methodology is the easy hydrolysis of the alkylated products using only water in a single step to give the free α-amino acid with recovery of the chiral auxiliary.

Experimental Section

General. Melting points were obtained with a hot plate apparatus. FT-IR spectra were obtained as films as neat liquids unless otherwise stated. NMR spectra were recorded at 300 MHz for ^{1}H and 75 MHz for ^{13}C using $CDCl_3$ (otherwise stated) as solvent and TMS as internal standard. ^{13}C NMR assignments were made on the basis of DEPT experiments. Mass spectra (EI and DIP) were obtained at 70 eV. High-resolution mass and elemental analyses were performed in the Mass Spectrometry and Microanalyses Services at the University of Alicante. Enantiomeric excesses were determined by HPLC (Crownpack CR(+) column, pH 1.5 $HClO_4$ mobile phase, 200 nm) or by comparation with α-values measured referring to sodium lamp. Chromatographic analyses (GLC) were determined with a 25 m WCOT capillary column (0.22 mm diameters, 0.2 μm film thickness OV-101 stationary phase) using nitrogen (2 mL/min) as the carrier gas, $T_{injector}$ = 270 °C, T_{column} = 60 °C, and 60−270 (15 °C/min). Thin-layer chromatography (TLC) was carried out on plates coated with a 0.2 mm layer of silica gel with UV, iodine, or nihydrine visualization. Column chromatography was performed using silica or pretreated silica gel 60 (washed with hexane/triethylamine 20/1 until pH = 7) of 70−230 mesh and hexane/EtOAc as eluant. All starting materials were commercially available of the best grade and were used without further purification. THF was dried with sodium benzophenone ketyl under an argon atmosphere and distilled before use. LiCl was dried by heating at 140 °C under reduced preassure (0.1 Torr). CH_3CN was stored under nitrogen atmosphere and dried over molecular sieves (4 Å).

(4*S*,5*R*)-(−)-1-(2′-Chloroacetyl)-3,4-dimethyl-5-phenyl-2-imidazolidinone[(−)-21].[27] To a solution of (−)-**20** (4.75 g, 25 mmol) in dry THF (80 mL) at 0 °C was added *n*-BuLi (1.6M in hexane, 18.75 mL, 30 mmol) under argon atmosphere, and the resulting mixture was stirred for 1 h at 0 °C. Then, the resulting solution was transferred (via cannula) to a solution of α-chloroacetyl chloride (4.33 mL, 50 mmol) in dry THF (50 mL) at −78 °C. The mixture was stirred overnight allowing the temperature rise to room temperature. Then, a saturated solution of NH_4Cl (100 mL) was added, and the resulting mixture was extracted with EtOAc (3 × 75 mL), dried (Na_2SO_4), and evaporated (15 Torr), yielding a crude compound (−)-**21** that was purified by column chromatography to afford 5.5 g (77%) of pure product.

Multigram Scale Synthesis of (−)-21. To a solution of (−)-**20** (5 g, 26.3 mmol) in CH_3CN (50 mL) under argon atmosphere was added α-chloroacetyl chloride (2.62 mL, 32.9 mmol) in one portion at 25 °C. The mixture was heated 4 h at 80 °C and cooled at room temperature. The solvent was removed by evaporation, the residue was partitioned between CH_2Cl_2 and H_2O, and the organic layer was washed with saturated Na_2CO_3 and brine, dried (Na_2SO_4), and evaporated (15 Torr), yielding compound (−)-**20** that was purified by recrystallization from hexane/EtOAc to afford 6.8 g (95%) of pure product. R_f 0.47 (hexane/EtOAc 1/2); mp 87−89 °C (hexane/EtOAc); $[\alpha]^{27}_D$ −87.1° (*c* 1.0, $CHCl_3$); {lit.[27] mp 89.0−90.5 (EtOH/H_2O), $[\alpha]^{25}_D$ −88.4° (*c* 1.0, $CHCl_3$)}.

(4*S*,5*R*)-(−)-1-(2′-Amidoacetyl)-3,4-dimethyl-5-phenyl-2-imidazolidinone Chloride [(−)-22]. To a solution of (−)-**20** (4.00 g, 15 mmol) in CH_3CN (50 mL) was added sodium azide (2.9 g, 45 mmol), and the resulting mixture was refluxed for 3 d. Then, solvent was removed in a vacuum (15 Torr), and water (75 mL) was added. The corresponding azide was extracted with EtOAc (3 × 50 mL), dried (Na_2SO_4), and evaporated (15 Torr), yielding 3.5 g of the corresponding azide (87%): R_f 0.63 (hexane/EtOAc 1/2); mp 81−83 °C (hexane/EtOAc); $[\alpha]^{25}_D$ −138.66° (*c* 1.1, $CHCl_3$); t_R 15.46 and 12.62 min; IR (KBr) 2192, 2107, 1731, 1703; ^{1}H NMR δ 0.82 (d, J = 6.7, 3H), 2.82 (s, 3H), 3.98 (dq, J = 6.7, 8.6, 1H), 4.49, 4.61 (2d, J = 18.0, 2H), 5.31 (d, J = 8.6, 1H), 7.14, 7.32 (2m, 5H); ^{13}C NMR δ 14.6, 27.9, 52.5, 57.4, 57.9, 126.7, 128.1, 128.3, 128.4, 135.4, 155.2, 167.0; MS *m/e* 245 (M^+ − 28, 2), 58 (100); HRMS calcd for $C_{13}H_{15}N_3O_2$: 245.1164. Found 245.1195. To a solution of (4*S*,5*R*)-(−)-1-(2′-azidoacetyl)-3,4-dimethyl-5-phenyl-2-imidazolidinone (1.36 g, 5 mmol) in MeOH (15 mL) were added palladium on charcoal (0.136 g, 10% weight) and concentrated HCl (0.63 mL, 7.5 mmol). The mixture was stirred under hydrogen atmosphere overnight and filtered through a pad of Celite. The solvent was evaporated (15 Torr), yielding 1.42 g of compound (−)-**22** (100%): mp 129−131 °C (MeOH); IR (KBr) 3600−3000, 1728, 1693; ^{1}H NMR δ (CD_3OD) 0.43 (d, J = 6.7, 3H), 2.45 (s, 3H), 3.79 (dq, J = 6.7, 8.6, 1H), 4.08 (s, 2H), 5.05 (d, J = 8.6, 1H), 7.05 (m, 5H), 7.67 (br s, 1H); ^{13}C NMR δ (CD_3OD) 14.9, 28.3, 43.8, 55.8, 60.2, 128.1, 129.0, 129.4, 137.4, 156.8, 166.6; MS *m/e* (DIP) 283 (M^+, 1), 58 (100); HRMS calcd for $C_{13}H_{18}N_3O_2Cl$: 283.1088. Found 283.1191.

(4*S*,5*R*)-(−)-1-[2′-[Bis(methylsulfanyl)methylene]aminoacetyl]-3,4-dimethyl-5-phenyl-2-imidazolidinone [(−)-23]. To a solution of compound (−)-**22** (1.15 g, 4 mmol) and CS_2 (0.25 mL, 4.15 mmol) in $CHCl_3$ (15 mL) was slowly added Et_3N (1.15 mL, 8.3 mmol). The mixture was stirred for 1 h at room temperature, and then MeI (0.66 mL, 4.6 mmol) was added. The resulting mixture was refluxed for 1 h protected from light. After cooling, the solution was washed with water (2 × 10 mL) and evaporated (15 Torr) to dryness. The residue was dissolved in Et_2O (20 mL), and the resulting solution was washed with water (2 × 10 mL), dried (Na_2SO_4), and evaporated (15 Torr). The residue was dissolved in acetone (8 mL), and to the resulting solution were added MeI (1.15 mL, 4.6 mmol) and anhydrous potassium carbonate (0.66 g, 5.4 mmol). The resulting mixture was refluxed for 2 h protected from light. After cooling, the mixture was filtered and evaporated in a vacuum. The residue was dissolved in Et_2O (20 mL), and the resulting solution was washed with water (2 × 10 mL), dried (Na_2SO_4), and evaporated (15 Torr), yielding a crude product that was purified by column chromatography to afford 0.7 g (50%) of pure product (−)-**23**: R_f 0.56 (hexane/EtOAc 1/1); mp 98−101 °C (hexane/EtOAc); $[\alpha]^{25}_D$ −92.99° (*c* 1.0, $CHCl_3$); IR (KBr) 1717, 1704, 1577; ^{1}H MNR δ 0.82 (d, J = 6.7, 3H), 2.40, 2.52 (2s, 6H), 2.84 (s, 3H), 3.94 (dq, J = 6.7, 8.5, 1H), 4.93 (s, 2H), 5.32 (d, J = 8.5, 1H), 7.16, 7.27 (2m, 5H); ^{13}C NMR δ 14.5, 14.9, 14.95, 28.1, 54.3, 56.4, 59.2, 127.0, 128.0, 128.4, 128.5, 136.3, 155.7, 162.5, 168.7; MS *m/e* 353 (M^+ + 2, 2), 352 (M^+ + 1, 4), 351 (M^+, 18), 56 (100); Anal. calcd for $C_{16}H_{21}N_3O_2S_2$ C, 54.68; H, 6.03; N, 11.96. Found: C, 54.61; H, 6.08; N, 12.25.

(4*S*,5*R*)-(−)-1-[2′-(Diphenylmethyleneamino)acetyl]-3,4-dimethyl-5-phenyl-2-imidazolidinone [(−)-24]. To a solution of compound (−)-**22** (2.1 g, 7.4 mmol) in dry CH_2Cl_2 (30 mL) was added benzophenone imine (1.35 g, 7.4 mmol). The mixture was stirred for 24 h at room temperature, filtered to remove NH_4Cl, and evaporated (15 Torr). The residue was taken up in Et_2O (30 mL), filtered, washed with water (10 mL), dried ($MgSO_4$), and evaporated (15 Torr), yielding a crude that was purified by column chromatography (pretreated silica gel) or recrystallization in a mixture Et_2O/EtOAc/hexane seeded with a crystal of pure product, to afford 2.05 g (68%) of pure product (−)-**24**: R_f 0.33 (hexane/EtOAc 1/2); mp 121−123 °C (hexane/Et_2O/EtOAc); $[\alpha]^{25}_D$ −94.5° (*c* 1.0, $CHCl_3$); IR (melt) 1731, 1694, 1578; ^{1}H NMR δ 0.65 (d, J = 6.5, 3H), 2.64 (s, 3H), 3.77 (dq, J = 6.4, 8.6, 1H), 4.74, 4.88 (2d, J = 18.0, 2H), 5.20 (d, J = 8.6, 1H), 7.01, 7.13 7.51, 7.69 (4m, 15H); ^{13}C NMR δ 14.8, 28.0, 54.1, 57.4, 59.1, 127.0, 127.6, 127.8, 127.9, 128.2, 128.3, 128.5, 128.6, 128.7, 129.9, 132.2, 136.1, 136.4, 137.5, 155.6, 169.2, 171.0; MS *m/e* (DIP) 412 (M^+ + 1, <1), 411 (M^+,

1), 91 (100). Anal. Calcd for $C_{16}H_{21}N_3O_2S_2$: C, 75.89; H, 6.12; N, 10.21. Found: C, 75.27; H, 6.16; N, 9.11.

(4*R*,5*S*)-(−)-1-[2′-(Diphenylmethyleneamino)acetyl]-3,4-dimethyl-5-phenyl-2-imidazolidinone [(+)-24]. The same procedure as explained above for the obtention of compound (−)-**24** was applied in this case, starting from compound (+)-**20**. Compound (+)-**24** was obtained in 54% overall yield calculated from (+)-**20**, spectral data was identical to those from (−)-**24**. Physical data follow: mp 120−123 °C (hexane/Et_2O/EtOAc); $[\alpha]^{25}_D$ +95.7° (*c* 1.0, $CHCl_3$).

Aprotic Alkylation of Imidazolidinone-Derived Glycinimide (−)-23. Synthesis of Compounds (−)-25a−i. General Procedure. A solution of compound (−)-**23** (0.105 g, 0.3 mmol) in dry THF (3 mL) and LiCl (0.065 g, 1.8 mmol) under argon atmosphere was stirred for 20−30 min at the corresponding temperature (see Table 2). Then the corresponding base (1 or 1.5 equiv, see Table 2) was added. After 30 min stirring, if the reaction was carried out at −78 °C, or 10 min if is carried out at −20 °C, the corresponding electrophile was added (0.6 mmol for alkyl halides). The mixture was allowed to rise to −20 or 0 °C if the reaction was carried out at −78 °C or stirred for a few hours at −20 °C (see Table 2). Then, water was added (10 mL), and the mixture was extracted with EtOAc (3 × 10 mL), dried (Na_2SO_4), and evaporated (15 Torr). The residue was purified by column chromatography, giving the corresponding pure products (−)-**25**. Yields are included in Table 2; spectral and analytical data follow (asterisk denotes minor diastereomer).

(2*S*,4′*S*,5′*R*)-1-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-2-[bis(methylsulfanyl)methyleneamino]-4-penten-1-one [(−)-25a, de 96%]: R_f 0.41 (hexane/EtOAc 1/1); mp 71−74 °C (hexane/EtOAc); IR (melt) 1731, 1704, 1651, 1568; ^{1}H NMR δ 0.82 (d, J = 6.7, 3H), 2.37*, 2.39, 2.52*, 2.54 (4s, 6H), 2.83*, 2.85 (2s, 3H), 2.50, 2.72 (2m, 2H), 3.92 (dq, J = 6.7, 8.6, 1H), 5.00 (m, 2H), 5.20*, 5.30 (d, J = 9.1, 1H), 5.77 (m, 2H), 7.15, 7.28 (2m, 5H); ^{13}C NMR δ 14.2*, 14.7*, 14.8, 14.9*, 15.05, 15.10, 28.1*, 28.3, 36.2*, 38.3, 53.85, 53.9*, 58.1*, 59.3, 63.0, 63.1*, 117.0*, 117.3, 127.1*, 127.2, 127.5*, 127.8*, 128.0, 128.3, 128.4*, 134.3, 134.8*, 136.5, 155.3, 159.9, 170.9*, 171.1; MS *m/e* (DIP) 392 (M^+ + 1, 4), 391 (M^+, 4), 343 (100); HRMS calcd for $C_{19}H_{25}N_3O_2S_2$: 391.1388. Found 391.1393.

(2*S*,4′*S*,5′*R*)-1-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-2-[bis(methylsulfanyl)methyleneamino]-3-phenylpropan-1-one [(−)-25b, de 92%]: R_f 0.55 (hexane/EtOAc 1/1); IR 1728, 1693, 1574; ^{1}H NMR δ 0.71*, 0.78 (2d, J = 6.7, 3H), 2.34, 2.38*, 2.40, 2.45* (4s, 6H), 2.71*, 2.86 (2s, 3H), 2.91, 3.33 (2dd, 2H, J = 8.7, 12.6, 4.7, 12.6); 3.90 (dq, J = 6.7, 8.6, 1H), 5.10*, 5.35 (d, 1H, J = 8.2), 5.97 (dd, J = 4.7, 8.7, 1H), 7.07, 7.17, 7.22 (3m, 10H); ^{13}C NMR δ 14.7*, 14.75, 14.9*, 15.0, 15.15, 15.20*, 28.0*, 28.2, 39.6*, 39.7, 53.8*, 53.9, 59.2, 64.9*, 65.0, 125.9, 126.9*, 127.8*, 127.9, 128.1*, 128.2*, 128.3, 129.1*, 129.75, 129.8, 129.85, 136.4*, 138.0, 138.05, 138.1*, 155.1*, 155.15, 161.0, 161.6*, 171.0*, 171.05; MS *m/e* (DIP) 443 (M^+ + 2, 1), 442 (M^+ + 1, 2), 441 (M^+, 4), 393 (100); HRMS calcd for $C_{23}H_{27}N_3O_2S_2$: 441.1545. Found 441.1552.

(2*S*,4′*S*,5′*R*)-1-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-2-[bis(methylsulfanyl)methyleneamino]-4-pentyn-1-one [(−)-25c, de 92%]: R_f 0.65 (hexane/EtOAc 1/1); IR 1726, 1690, 1571; ^{1}H MNR δ 0.76*, 0.79 (2d, J = 6.7, 3H), 1.84 (s, 1H) 2.30*, 2.37, 2.52*, 2.55 (4s, 6H), 2.72*, 2.81 (2m, 2H), 2.81*, 2.83 (2s, 3H), 3.97 (dq, J = 6.7, 8.9, 1H), 5.32 (d, J = 8.9, 1H), 5.89 (t, J = 6.7, 1H), 7.17, 7.25 (2m, 5H); ^{13}C MNR d 14.9, 15.1, 15.3, 23.4, 28.3, 54.0, 59.5, 62.2, 70.2, 80.7, 127.2, 128.0, 128.4, 128.6, 136.3, 155.1, 162.6, 171.4; MS *m/e* (DIP) 391 (M^+ + 2, 1), 390 (M^+ + 1, 2), 389 (M^+, 5), 342 (100); HRMS calcd for $C_{19}H_{23}N_3O_2S_2$: 389.1232. Found 389.1230.

***tert*-Butyl (3*S*,4′*S*,5′*R*)-4-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-3-[bis(methylsulfanyl)methyleneamino]-4-oxobutanoate [(−)-25d, de 74%]:** R_f 0.78 (hexane/EtOAc 1/1); IR 1736, 1724, 1688, 1571; ^{1}H NMR δ 0.77*, 0.79 (2d, J = 6.4, 3H), 1.41, 1.42* (2s, 9H), 2.29*, 2.30, 2.55 (3s, 6H), 2.62, 2.93 (2dd, J = 7.6, 15.3, 5.2, 15.3, 2H), 2.80*, 2.85 (2s, 3H), 3.95 (m, 1H), 5.30 (d, J = 8.9, 1H), 5.96 (t, J = 6.4, 1H), 7.15, 7.28 (2m, 5H); ^{13}C MNR d 14.5*, 14.6, 14.9, 15.0*, 27.8, 27.9*, 28.1, 28.2*, 36.55*, 36.6, 53.75*, 53.8, 59.0*, 59.3, 60.5, 80.2, 80.3, 126.95, 127.75*, 127.8, 128.0*, 128.3, 136.3, 154.9, 161.8*, 162.3, 169.6, 170.3, 178.5*; MS *m/e* (DIP) 465 (M^+, 2), 361 (100); HRMS calcd for $C_{22}H_{31}N_3O_4S_2$: 465.1756. Found 465.1735.

Ethyl (3*S*,4′*S*,5′*R*)-4-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-3-[bis(methylsulfanyl)methyleneamino]-4-oxobutanoate [(−)-25e, de 46%]: R_f 0.61 (hexane/EtOAc 1/1); IR 1749, 1731, 1694, 1619, 1574; ^{1}H NMR δ 0.79 (d, J = 6.7, 3H), 1.25 (m, 3H), 2.30*, 2.32, 2.56, 2.57* (4s, 6H), 2.70, 3.03 (2m, 2H), 2.81*, 2.84 (2s, 3H), 4.16 (m, 3H), 5.34, 5.35* (2d, 1H, J = 8.8), 5.97*, 5.98 (2t, J = 6.7, 1H), 7.16, 7.28 (2m, 5H); ^{13}C NMR δ 13.6*, 13.9, 13.95*, 14.0*, 14.5, 14.6, 14.8*, 14.85, 14.9, 28.0, 28.2*, 34.65*, 37.3, 53.7*, 53.75, 59.3, 59.4*, 60.2, 60.25*, 125.8, 126.7*, 127.7*, 127.8, 128.0, 128.2, 128.3*, 129.1*, 136.1, 136.2*, 154.8*, 154.85, 162.4, 162.8*, 170.2*, 170.3, 170.5, 171.1*; MS *m/e* (DIP) 437 (M^+, 2), 389 (100); HRMS calcd for $C_{20}H_{27}N_3O_4S_2$: 437.1443. Found 437.1442.

(2*S*,4′*S*,5′*R*)-1-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-2-[bis(methylsulfanyl)methyleneamino]-propan-1-one [(−)-25f, de 64%]: R_f 0.64 (hexane/EtOAc 1/1); IR 1728, 1692, 1571; ^{1}H NMR δ 0.78*, 0.81 (2d, J = 6.7, 3H), 1.37*, 1.41 (2d, 3H, J = 6.7), 2.34*, 2.39, 2.53*, 2.55 (4s, 6H), 2.82*, 2.84 (2s, 3H), 3.92 (dq, J = 6.7, 8.9, 1H), 5.33*, 5.34 (2d, J = 8.9, 1H), 5.67*, 5.75 (2q, J = 6.7, 1H), 7.15, 7.28 (2m, 5H); ^{13}C NMR δ 14.2*, 14.65*, 14.7, 15.0, 15.05, 15.1*, 17.2*, 18.9, 28.2, 28.3*, 54.0, 54.05*, 58.9, 59.25*, 59.3, 127.0, 127.95*, 128.0, 128.2*, 128.5, 136.4*, 136.6, 155.3, 160.0, 160.6*, 172.6; MS *m/e* (DIP) 367 (M^+ + 2, 1), 366 (M^+ + 1, 2), 365 (M^+, 8), 318 (100); HRMS calcd for $C_{17}H_{23}N_3O_2S_2$: 365.1231. Found 365.1224.

(3*S*,4′*S*,5′*R*)-4-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-3-[bis(methylsulfanyl)methyleneamino]-4-oxobutanonitrile [(−)-25g, de 60%]: R_f 0.24*, 0.29 (hexane/EtOAc 1/1); IR 2223, 1731, 1693, 1568; ^{1}H NMR δ 0.81*, 0.82 (2d, J = 6.7, 3H), 2.35*, 2.40, 2.51*, 2.59 (4s, 6H), 2.79, 2.95 (2m, 2H), 2.82*, 2.86 (2s, 3H), 3.95 (dq, J = 6.7, 8.6, 1H,), 5.31, 5.34* (2d, J = 8.5, 1H), 5.86 (2t, J = 5.7, 6.9, 1H), 7.14, 7.26 (2m, 5H); ^{13}C NMR δ 14.9, 15.0, 15.05*, 15.1*, 15.35, 15.4*, 22.1, 28.2*, 28.4, 54.2, 54.4*, 56.5, 59.2, 59.8*, 117.5, 127.2*, 128.1*, 128.2, 128.35, 128.4*, 128.5, 135.4, 155.2, 165.9, 168.9; MS *m/e* (DIP) 392 (M^+ + 2, 2), 391 (M^+ + 1, 1), 390 (M^+, 14), 270 (100); HRMS calcd for $C_{18}H_{22}N_4O_2S_2$: 390.1175. Found 390.1184.

(2*E*,5*S*,4′*S*,5′*R*)-Methyl 6-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-5-[bis(methylsulfanyl)methyleneamino]-6-oxo-2-hexenoate [(−)-25h, de 86%]: R_f 0.55 (hexane/EtOAc 1/1); IR 1728, 1717, 1693, 1569; ^{1}H NMR δ 0.78*, 0.81 (2d, J = 6.7, 3H), 2.35*, 2.37, 2.52*, 2.54 (4s, 6H), 2.68 (m, 2H), 2.82*, 2.85 (2s, 3H), 3.68, 3.70* (2s, 3H), 3.99 (dq, J = 6.4, 8.5, 1H), 5.32 (d, J = 8.9, 1H), 5.79 (m, 2H), 6.91 (m, 1H), 7.13, 7.28 (2m, 5H); ^{13}C NMR δ 14.6*, 14.7, 14.9, 14.95, 15.0*, 28.05, 28.1*, 35.0*, 36.5, 51.1, 51.2*, 53.8, 53.9*, 59.2, 61.5*, 62.1, 122.9*, 123.0, 126.9, 127.85*, 127.9, 128.1*, 128.3, 136.3, 145.1, 145.4*, 155.0, 161.9, 166.5, 166.6*, 170.9; MS *m/e* (DIP) 449 (M^+, (1), 402 (100); HRMS calcd for $C_{21}H_{27}N_3O_4S_2$: 449.1443. Found 449.1435.

(2*S*,4′*S*,5′*R*)-Ethyl 2{-3-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-2-[bis(methylsulfanyl)methyleneamino]-3-oxopropyl}acrylate [(−)-25i, de 70%]: R_f 0.30 (hexane/EtOAc 1/1); IR 1731, 1693, 1571; ^{1}H NMR δ 0.77*, 0.80 (2d, J = 6.7, 3H), 1.27*, 1.30 (2t, J = 7.0, 3H), 2.30*, 2.33 2.47*, 2.52 (4s, 6H), 2.73, 2.94 (2dd, J = 7.6, 13.6, 5.8, 13.6, 2H), 2.81*, 2.83 (2s, 3H), 3.91 (dq, J = 6.7, 8.6, 1H), 4.12 (q, J = 7.0, 2H), 5.26*, 5.32 (2d, J = 8.6, 1H), 5.37, 6.07 (2d, J = 1.5, 2H), 5.96*, 6.00 (2dd, J = 5.8, 7.6, 1H), 7.15, 7.29 (2m, 5H); ^{13}C NMR δ 14.1, 14.6, 14.9, 15.0, 28.1, 28.2*, 34.5*, 35.3, 53.8, 53.9*, 59.3*, 59.4, 60.3*, 60.5, 62.0*, 62.1, 127.5, 127.0*, 127.2, 127.4, 127.8*, 127.9, 128.1*, 128.3, 128.4, 136.3, 136.5*, 136.6, 155.0, 161.3, 166.85, 166.9*, 170.7*, 171.0; MS *m/e* (DIP) 464 (M^+ + 1, <1), 416 (100); HRMS calcd for $C_{22}H_{29}N_3O_4S_2$: 463.1600. Found 463.1638.

PTC-Alkylation of Imidazolidinone-Derived Glycinimides (−)-23 and (−)-24. Synthesis of Compounds (−)-25a and (−)-27. General Procedure. A solution of compound [(−)-**23** or (−)-**24**] (0.070 or 0.105 g, 0.2 or 0.26 mmol) in CH_3-

CN (3 mL) and LiCl (0.053 or 0.085 g, 6 equiv) under argon atmosphere was stirred for 20−30 min at −20 °C and then LiOH (0.025 or 0.033 g, 3 equiv) was added. After 5 min stirring, the corresponding electrophile was added (0.6 mmol for alkyl halides, 1.1 mmol for Michael acceptors). The mixture was stirred for a few hours at −20 °C (see Table 3). Then, water was added (10 mL), and the mixture was extracted with EtOAc (3 × 10 mL) if compound (−)-**25a** was obtained, dried (Na_2SO_4), and evaporated (15 Torr), yielding a crude compound that is purified by column chromatography on silica gel for pure (−)-**25a**. To obtain compounds (−)-**27**, the reaction was quenched with HCl 0.5 N (15 mL) and extracted with EtOAc (3 × 10 mL). The organic layer was washed once with HCl 0.5 N (20 mL). To the aqueous phase was added solid K_2CO_3 until pH = 8−9 and extracted with CH_2Cl_2 (3 × 10 mL), dried (Na_2SO_4), and evaporated (15 Torr) to give pure products (−)-**27**. Yields are included in Table 3; spectral and analytical data follow (astersik denotes minor diastereomer peaks).

Organic Bases-Mediated Alkylation of Imidazolidinone-Derived Glycinimides (−)-23 and (−)-24. Synthesis of Compounds (−)-25a, (−)-26s, (−)-26t, (−)-26u, (−)-27-(−)-32. General Procedure. A solution of compound (−)-**23** or (−)-**24** (0.105 g, 0.3 or 0.26 mmol) in CH_3CN (3 mL) and LiCl (0.065 to 0.085 g, 6 equiv) under argon atmosphere was stirred for 20−30 min −20 °C, and then the corresponding base (1.5 equiv or 0.1 equiv, see Table 4) and electrophile (0.6 mmol for alkyl halides, 1.1 mmol for Michael acceptors) was added. The mixture was stirred for a few hours at −20 °C (see Table 4). Then, water was added (10 mL), and the mixture was extracted with EtOAc (3 × 10 mL) if compounds (−)-**25a**, (−)-**26**, or (−)-**28** were obtained, dried ($MgSO_4$), and evaporated (15 Torr), yielding a crude compound that was purified by column chromatography on silica gel for compound (−)-**25a** or silica gel pretreated with a mixture of hexane/Et_3N 20/1 until pH = 7 for compounds (−)-**26** and (−)-**28**, giving the corresponding pure products. To obtain compounds (−)-**27** and (−)-**29**−(−)-**32** the reaction was quenched with HCl 0.5 N (15 mL) and extracted with EtOAc (3 × 10 mL). The organic layer was washed once with HCl 0.5 N (20 mL). To the aqueous phase was added solid K_2CO_3 until pH = 8−9 and extracted with CH_2Cl_2 (3 × 10 mL), dried (Na_2SO_4), and evaporated (15 Torr) to give pure products. Yields are included in Table 4; spectral and analytical data follow (asterisk denotes minor diastereomer peaks).

(3*S*,4′*S*,5′*R*)-4-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-3-(diphenylmethyleneamino)-4-oxopentanenitrile [(−)-26s, de 96%]: R_f 0.41 (hexane/EtOAc: 1/1); $[\alpha]^{25}_D$ −99.61° (*c* 1.0, $CHCl_3$); IR 2246, 1727, 1685, 1574; ^{1}H NMR δ 0.74 (d, *J* = 6.7, 3H), 2.25, 2.60 (2m, 4H), 2.69 (s, 3H), 3.60 (dq, *J* = 6.7, 8.5, 1H), 4.97 (d, *J* = 8.6, 1H), 5.55 (dd, *J* = 4.3, 8.5, 1H), 7.04, 7.17, 7.36, 7.63 (4m, 15H); ^{13}C NMR δ 13.7, 14.9, 28.1, 30.0, 53.8, 59.0, 61.0, 126.8, 127.7, 128.0, 128.25, 128.3, 128.35, 128.6, 128.65, 130.1, 130.6, 132.4, 136.3, 137.5, 139.0, 154.5, 171.2, 171.8; MS *m*/*e*(DIP) 424 (M^+ − 40, 8), 185 (100); HRMS calcd for $C_{29}H_{28}N_4O_2$: 464.2212. Found 464.2211.

(3*Z*,4*S*,4′*S*,5′*R*)-Ethyl 5-(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl) -4-(diphenylmethyleneamino)-5-oxo-3-pentenoate [(−)-26t, de 98%]: R_f 0.40 (hexane/EtOAc: 1/1); mp 115−118 °C (hexane/EtOAc); $[\alpha]^{25}_D$ −112.56° (*c* 1.0, $CHCl_3$); t_R 17.59; IR (melt) 1737, 1693, 1667, 1574; ^{1}H NMR δ 0.76 (d, *J* = 6.7, 3H) 1.14 (t, *J* = 7.3, 3H), 2.77 (2s, 3H), 3.38, 3.88 (dq, *J* = 6.7, 8.5, 1H), 3.93 (q, *J* = 7.3, 2H), 5.32 (d, *J* = 8.5, 1H), 5.59 (dd, *J* = 1.2, 11.6, 1H), 6.12 (dd, *J* = 8.5, 11.6, 1H), 7.03 (dd, *J* = 1.2, 8.5, 1H), 7.27, 7.63 (2m, 15H); ^{13}C NMR δ 14.1, 15.0, 28.2, 53.8, 59.6, 59.9, 62.3, 120.6, 127.8, 127.9, 128.3, 128.4, 128.8, 129.5, 129.6, 130.2, 136.5, 136.6, 139.9, 144.1, 154.6, 164.9, 171.4; *m*/*z* (DIP) 509 (M^+, 100); HRMS calcd for $C_{31}H_{31}N_3O_4$: 509.2315. Found 509.2274.

(4*S*,4′*S*,5′*R*)-Methyl 5-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-4-(diphenylmethyleneamino)-2-methyl-5-oxopentanoate (1st diasteromer, [(−)-26u, de 70%]: R_f 0.23 (hexane/EtOAc: 1/1); mp 129−131 °C (hexane/EtOAc); IR (melt) 1726, 1703, 1681, 1575; ^{1}H NMR δ 0.72*, 0.74 (2d, *J* = 6.7, 3H), 1.03, 1.08* (2d, *J* = 7.3, 3H) 1.89, 1.94*, 2.27*, 2.31 (4m, 2H), 2.58, 2.61* (2m, 1H), 2.66*, 2.72 (2s, 3H), 3.54, 3.57* (2s, 3H), 3.59*, 3.81 (2dq, *J* = 6.7, 8.5, 1H), 5.05*, 5.24 (2d, *J* = 8.5, 1H), 5.34, 5.50 (2dd, *J* = 4.9, 8.5, 1H), 7.09, 7.31*, 7.36, 7.57, 7.62* (5m, 15H); ^{13}C NMR δ 14.9, 14.95*, 17.2, 17.9*, 28.1, 28.3*, 36.2*, 36.4, 37.9, 38.0*, 51.4, 51.45*, 53.8*, 54.0, 59.1*, 59.5, 60.9*, 62.2, 127.0*, 127.3, 127.8, 127.85, 127.9*, 128.0*, 128.05, 128.1*, 128.2, 128.25, 128.3, 128.4*, 128.5, 128.7*, 128.8, 130.0, 130.1*, 136.55, 136.6*, 136.7, 136.9*, 154.55*, 154.8, 171.1, 172.4, 174.2, 176.4*; MS *m*/*e* (DIP) 480 (M^+ − 31, 8), 165 (100); HRMS calcd for $C_{39}H_{33}N_3O_4$: 511.2471. Found 511.2454.

(2*S*,4′*S*,5′*R*)-2-Amino-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-4-penten-1-one [(−)-27a, de 98%]: R_f 0.36 (MeOH); $[\alpha]^{25}_D$ −29.73° (*c* 1.5, $CHCl_3$); t_R = 14.23*, 14.39; IR 3865−3110, 1728, 1682; ^{1}H NMR δ 0.78 (d, *J* = 6.7, 3H), 1.78 (br s, 2H, NH_2), 2.21, 2.57 (2m, 2H), 2.81 (s, 3H), 3.98 (dq, *J* = 6.7, 8.5, 1H), 4.80 (br s, 2H), 5.03 (m, 2H), 5.32 (d, *J* = 8.5, 1H), 5.62 (m, 2H), 7.12, 7.28 (2m, 5H); ^{13}C NMR δ 15.05, 28.2, 39.5, 52.7, 54.1, 59.2, 118.5, 127.0, 128.2, 128.5, 133.7, 136.5, 155.4, 174.8; MS *m*/*e* 287 (M^+, <1), 70 (100); HRMS calcd for $C_{16}H_{21}N_3O_2$; 287.1634. Found 287.1632.

(2*S*,4′*S*,5′*R*)-2-Amino-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-3-phenylpropan-1-one [(−)-27b, de 96%]: R_f 0.35 (MeOH); mp 131−134 °C (CH_2Cl_2/EtOAc); $[\alpha]^{25}_D$ −27.97° (*c* 1.7, $CHCl_3$); t_R 16.88*, 17.17; IR (KBr) 3698−3135, 1726, 1681; ^{1}H NMR δ 0.82 (d, *J* = 6.7, 3H), 1.75 (br s, 2H, NH_2), 2.41, 3.28 (2dd, 2H, *J* = 9.2, 13.4, 4.3, 13.4); 2.86 (s, 3H); 3.94 (dq, *J* = 6.7, 8.6, 1H), 5.00 (dd, *J* = 4.3, 9.2, 1H), 5.34 (d, *J* = 8.6, 1H), 7.23 (m, 5H); ^{13}C NMR δ 15.0, 28.3, 41.8, 54.1, 55.0, 59.3, 126.4, 127.0, 128.2, 128.4, 128.6, 129.6, 136.5, 138.0, 155.5, 174.9; MS *m*/*e* 337 (M^+, <1), 58 (100); HRMS calcd for $C_{20}H_{23}N_3O_2$: 337.1790. Found 337.1791.

(2*S*,4′*S*,5′*R*)-2-Amino-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-4-pentyn-1-one [(−)-27c, de 98%]: R_f 0.51 (MeOH); $[\alpha]^{25}_D$ −97.46° (*c* 1.5, $CHCl_3$); t_R 14.38*, 14.54; IR 3718−3110, 1721, 1678; ^{1}H NMR δ 0.78 (d, *J* = 6.7, 3H), 1.79 (br s, 2H, NH_2), 1.88 (t, *J* = 2.4, 1H), 2.52, 2.68 (2ddd, *J* = 2.4, 6.7, 17.0, 2.4, 4.9, 17.0, 2H), 2.81 (s, 3H), 3.90 (dq, *J* = 6.7, 8.6, 1H), 4.80 (dd, *J* = 4.9, 6.7, 1H), 5.30 (d, *J* = 8.6, 1H), 7.11, 7.25 (2m, 5H); ^{13}C NMR δ 15.1, 25.3, 28.2, 52.4, 54.2, 59.3, 70.9, 80.0, 126.9, 128.1, 128.5, 136.2, 155.2, 173.5; MS *m*/*e* 285 (M^+, <1), 58 (100); HRMS calcd for $C_{16}H_{19}N_3O_2$: 285.1477. Found 285.1476.

(3*S*,4′*S*,5′*R*)-Ethyl 3-amino-4-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-4-oxobutanoate [(−)-27e, de 96%]: R_f 0.54 (MeOH); $[\alpha]^{25}_D$ −43.79° (*c* 1.0, $CHCl_3$); t_R 15.76*, 15.86; IR 3716−3139, 1716, 1681, 1651; ^{1}H NMR δ 0.80 (d, *J* = 6.7, 3H), 1.17 (t, *J* = 7.1, 3H0), 1.75 (br s, 2H, NH_2), 2.41, 2.82 (2dd, *J* = 8.2, 15.9, 4.9, 15.9, 2H), 2.84 (s, 3H), 3.93 (dq, *J* = 6.7, 8.6, 1H), 4.06 (q, *J* = 7.1, 2H), 5.01 (dd, *J* = 4.9, 8.2), 5.31 (d, *J* = 8.6, 1H), 7.14, 7.30 (2m, 5H); ^{13}C NMR δ 14.1, 15.0, 28.2, 39.4, 50.9, 54.2, 59.4, 60.6, 126.9, 128.2, 128.5, 136.3, 155.3, 171.1, 173.7; MS *m*/*e* 333 (M^+, 1), 58 (100); HRMS calcd for $C_{17}H_{23}N_3O_4$: 333.1689. Found 333.1700.

(*E*,5*S*,4′*S*,5′*R*)-Methyl 5-amino-6-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-6-oxo-2-hexenoate [(−)-27h, de 96%]: R_f 0.46 (MeOH); $[\alpha]^{25}_D$ −48.22° (*c* 2.0, $CHCl_3$); IR 3710−3133, 1728, 1682, 1659; ^{1}H NMR δ 0.78 (d, *J* = 6.7, 3H), 1.78 (br s, 2H, NH_2), 2.69 (m, 2H), 2.81 (s, 3H), 3.66 (s, 3H), 3.93 (dq, *J* = 6.7, 8.6, 1H), 5.30 (d, *J* = 8.9, 1H), 5.82 (d, *J* = 15.3, 1H), 6.86 (dt, *J* = 7.3, 15.9, 1H), 7.10 (d, *J* = 7.3, 1H), 7.28 (m, 5H); ^{13}C NMR δ 15.0, 28.2, 37.7, 51.3, 52.5, 54.1, 59.3, 123.9, 126.9, 128.2, 128.6, 136.3, 144.6, 155.3, 166.4, 174.1; MS *m*/*e* 345 (M^+, (1), 58 (100); HRMS calcd for $C_{18}H_{23}N_3O_4$: 345.1689. Found 345.1697.

(2*S*,4′*S*,5′*R*)-2-Amino-4-bromo-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-4-penten-1-one [(−)-27j, de 96%]: R_f 0.63 (MeOH); $[\alpha]^{25}_D$ −50.22° (*c* 1.0, $CHCl_3$); IR 3676−3112, 1731, 1687; ^{1}H NMR δ 0.82 (d, *J* = 6.7, 3H), 1.76 (br s, 2H, NH_2), 2.22, 2.99 (2dd, *J* = 4.6, 8.6, 14.0, 2H), 2.95 (s, 3H), 3.93 (dq, *J* = 6.7, 8.5), 5.14 (m, 1H), 5.30 (d, *J* = 8.5, 1H), 5.50, 5.59 (2s, 2H), 7.11, 7.29 (2m, 5H); ^{13}C NMR δ 14.6, 27.8, 45.8, 51.5, 53.7, 58.9, 119.6, 126.5, 127.8, 128.2, 129.4, 135.9, 154.8, 173.5; MS *m*/*e* 367 (M^+ + 2, 6), 365 (M^+, 6), 58 (100); HRMS calcd for $C_{16}H_{20}N_3O_2Br$: 365.0721. Found 365.0748.

(2*S*,4′*S*,5′*R*)-2-Amino-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-4-methyl-4-penten-1-one [(−)-27k, de 98%]: R_f 0.43 (MeOH); $[\alpha]^{25}_D$ −73.09° (*c* 4.6, $CHCl_3$); IR 3688−3179, 1736, 1678; ^{1}H NMR δ 0.79 (d, J = 6.7, 3H), 1.80 (s, 3H), 1.72 (br s, 2H, NH_2), 1.87, 2.62 (2dd, 2H, J = 3.0, 10.0, 12.8), 2.82 (s, 3H), 3.91 (dq, J = 6.7, 8.6, 1H), 4.70, 4.83 (2s, 2H), 4.87 (dd, J = 3.7, 9.8, 1H), 5.22*, 5.31 (d, J = 8.6, 1H), 7.12, 7.29 (m, 5H); ^{13}C NMR δ 14.9*, 15.0, 21.7, 22.1*, 28.1*, 28.2, 43.3*, 43.9, 51.3, 51.5*, 54.0*, 54.1, 59.3, 59.5*, 113.3*, 113.9, 126.9, 128.0*, 128.2, 128.25*, 128.3*, 128.5, 132.4*, 136.5, 142.0, 155.3, 175.2*, 175.3; MS *m/e* 301 (M^+, 7), 84 (100); HRMS calcd for $C_{17}H_{23}N_3O_2$: 301.1815. Found 301.1790.

(2*S*,4′*S*,5′*R*)-2-Amino-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-5-methyl-4-hexen-1-one [(−)-27l, de 98%]: R_f 0.42 (MeOH); $[\alpha]^{25}_D$ −50.09° (*c* 3.3, $CHCl_3$); IR 3703−3112, 1735, 1686; ^{1}H NMR δ 0.78 (d, J = 6.7, 3H), 1.54, 1.63 (2s, 6H), 1.74 (br s, 2H, NH_2), 2.14, 2.46 (2m, 2H), 2.80 (s, 3H), 3.89 (dq, J = 6.7, 8.6, 1H), 4.71 (m, 1H), 5.00 (t, J = 7.3, 1H), 5.27 (d, J = 8.6, 1H), 7.12, 7.31 (m, 5H); ^{13}C NMR δ 15.1, 17.9, 26.9, 28.2, 53.5, 54.1, 59.2, 119.7, 127.0, 128.1, 128.5, 134.9, 136.5, 155.4, 175.6; MS *m/e* 315 (M^+,<1), 246 (100); HRMS calcd for $C_{18}H_{25}N_3O_2$: 315.1976. Found 315.1947.

(2*S*,4*E*,4′*S*,5′*R*)-2-Amino-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-5-phenyl-4-penten-1-one [(−)-27m, de 98%]: R_f 0.35 (MeOH); $[\alpha]^{25}_D$ −43.28° (*c* 3.2, $CHCl_3$); IR 3672−3156, 1732, 1682; ^{1}H NMR δ 0.80 (d, J = 6.7, 3H), 1.79 (br s, 2H, NH_2), 2.39, 2.74 (2m, 2H), 2.83 (s, 3H), 3.92 (dq, J = 6.7, 8.5, 1H), 4.89 (m, 1H), 5.34 (d, J = 8.5, 1H), 6.05 (dt, J = 7.3, 15.9, 1H), 6.36 (d, J = 15.9, 1H), 7.26 (m, 10H); ^{13}C NMR δ 15.1, 28.3, 39.1, 53.1, 54.1, 59.3, 125.5, 126.2, 127.1, 128.1, 128.4, 128.5, 130.1, 133.2, 136.5, 137.2, 155.4, 175.1; MS *m/e* (DIP) 348 (M^+ − 17, 1), 246 (100); HRMS calcd for $C_{22}H_{25}N_3O_2$: 363.1947. Found 363.1948.

(2*S*,4′*S*,5′*R*)-2-Amino-3-(1,3-benzodioxol-5-yl)-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)propan-1-one [(−)-27n, de 84%]: R_f 0.34 (MeOH); IR 3673−3181, 1727, 1681; ^{1}H NMR δ 0.74*, 0.80 (d, J = 6.7, 3H), 1.75 (br s, 2H, NH_2), 2.30, 2.46*, 2.99*, 3.17 (2dd, J = 3.7, 9.1, 13.4, 2H), 2.82*, 2.84 (s, 3H), 3.93 (dq, J = 6.7, 8.6, 1H), 4.87 (m, 1H), 5.26*, 5.32 (d, J = 8.6, 1H), 5.90 (s, 2H), 6.64, 6.67, 7.12, 7.29 (4m, 8H); ^{13}C NMR δ 15.0, 28.1*, 28.2, 41.4, 54.1, 55.1, 59.2, 100.8, 108.8, 109.9, 122.6, 127.0, 128.2, 128.6, 131.7, 136.5, 146.2, 147.6, 155.4, 174.8; MS *m/e* (DIP) 381 (M^+, 5), 369 (M^+ − 12, 10), 44 (100); HRMS calcd for $C_{20}H_{25}N_3O_4$: 369.1689. Found 369.1658.

(2*S*,4′*S*,5′*R*)-2-Amino-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-3-(2-naphthyl)propan-1-one [(−)-27o, de 98%]: R_f 0.34 (MeOH); $[\alpha]^{25}_D$ −27.01° (*c* 1.6, $CHCl_3$); IR 3716−3131, 1720, 1678; ^{1}H NMR δ 0.70*, 0.78 (d, J = 6.7, 3H), 1.73 (br s, 2H, NH_2), 2.61, 3.42 (2m, 2H), 2.84, 2.91* (s, 3H), 3.95 (dq, J = 6.7, 8.6, 1H), 5.16 (m, 1H), 5.36 (d, J = 8.6, 1H), 7.23, 7.42, 7.57, 7.68, 7.76 (5m, 12H); ^{13}C NMR δ 14.8*, 14.9, 28.0*, 28.3, 29.7, 53.9*, 54.2, 57.7*, 58.1, 59.0*, 59.2, 125.2*, 125.6, 125.7*, 125.8, 126.8*, 127.1*, 127.2, 127.5, 127.6*, 127.8, 127.9, 128.0*, 128.1, 128.15*, 128.3, 128.4*, 128.5, 130.1, 132.4, 133.1*, 133.4, 133.7*, 134.1, 135.5*, 136.3, 155.1*, 155.3, 171.2; MS *m/e* (DIP) 388 (M^+ + 1, 3), 387 (M^+, 11), 248 (100); HRMS calcd for $C_{24}H_{25}N_3O_2$: 387.1947. Found 387.1934.

(2*S*,4′*S*,5′*R*)-2-Amino-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-4-phenylbutane-1,4-dione [(−)-27p, de 92%]: R_f 0.19 (MeOH); IR 3722−3144, 1736, 1678; ^{1}H NMR δ 0.77*, 0.80 (2d, J = 6.7, 3H), 1.80 (br s, 2H, NH_2), 2.81*, 2.83 (s, 3H), 3.08, 3.40*, 3.54, 3.73* (4dd, J = 4.9, 7.3, 17.1, 2H), 3.98 (dq, J = 6.7, 8.6, 1H), 5.18*, 5.32 (2d, J = 8.6, 1H), 5.24, 5.41* (dd, J = 5.5, 7.3, 1H), 7.37, 7.90 (m, 10H); ^{13}C NMR δ 15.1, 15.2*, 28.1*, 28.3, 41.5*, 43.4, 50.4, 54.1*, 54.2, 59.4, 127.0, 127.9*, 128.1, 128.3*, 128.4*, 128.5, 128.55, 128.7*, 132.6*, 133.0, 136.2, 136.8, 137.0*, 155.4, 174.3, 197.5; MS *m/e* (DIP) 385 (M^+, <2), 77 (100); HRMS calcd for $C_{21}H_{23}N_3O_3$: 365.1739. Found 365.1771.

(4*S*,4′*S*,5′*R*)-Methyl 4-amino-5-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-5-oxopentanoate [(−)-27q, de 80%]: R_f 0.56 (MeOH); t_R 16.95*, 17.50; IR 3746−3100, 1726, 1692, 1677; ^{1}H NMR δ 0.77 (d, J = 6.7, 3H), 1.65 (m, 4H), 1.78 (br s, 2H, NH_2), 2.79, 2.81* (2s, 3H), 3.62, 3.63* (2s, 3H), 3.92 (dq, J = 6.7, 8.6, 1H), 4.56*, 5.63 (2dd, J = 4.3, 8.5, 1H), 5.25*, 5.29 (2d, J = 8.5, 1H), 7.11, 7.31 (2m, 5H); ^{13}C NMR δ 15.1, 28.1*, 28.2, 29.2*, 29.6*, 30.2, 30.7, 51.5, 52.8*, 53.0, 54.1, 59.2, 126.9, 128.2, 128.4*, 128.6, 128.7*, 132.4*, 136.4, 155.3, 168.9, 175.6; MS *m/e* 333 (M^+, (<1), 58 (100); HRMS calcd for $C_{17}H_{23}N_3O_4$: 333.1689. Found 333.1664.

***tert*-Butyl (4*S*,4′*S*,5′*R*)-4-amino-5-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-5-oxopentanoate [(−)-27r, de 94%]:** R_f 0.78 (MeOH); $[\alpha]^{25}_D$ −25.81° (*c* 2.4, $CHCl_3$); IR 3749−3110, 1724, 1678, 1642; ^{1}H NMR δ 0.79 (d, J = 6.7, 3H), 1.38*, 1.41 (2s, 9H), 1.80 (br s, 2H, NH_2), 1.68, 2.03 (2m, 4H), 2.27 (m, 2H), 2.76*, 2.85 (2s, 3H), 3.91 (dq, J = 6.7, 8.6, 1H), 4.66 (dd, J = 4.0, 8.5, 1H), 5.19*, 5.31 (2d, J = 8.7, 1H), 7.14, 7.30 (2m, 5H); ^{13}C NMR δ 15.1, 28.2, 29.1, 30.3, 32.0, 53.0, 54.1, 59.2, 80.5, 126.9, 128.2, 128.6, 136.5, 155.3, 172.7, 175.6; MS *m/e* (DIP) 375 (M^+, <1), 102 (100); HRMS calcd for $C_{20}H_{29}N_3O_4$: 375.2158. Found 375.2110.

Ethyl (3*Z*,4′*S*,5′*R*)-5-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-4-diphenylmethyleneamino-5-oxo-3-pentenoate [(−)-28]: R_f 0.39 (hexane/EtOAc: 1/1); IR 1737, 1693, 1667, 1574; ^{1}H NMR δ 0.68 (d, J = 6.3, 3H) 1.23 (t, J = 7.0, 3H), 1.73 (br s, 2H, NH_2), 2.78 (2s, 3H), 3.38, 3.49 (2dd, J = 7.3, 17.1, 6.7, 17.1, 2H), 3.53 (dq, J = 6.7, 8.5, 1H), 4.11 (q, J = 7.1, 2H), 4.74 (d, J = 8.5, 1H), 5.07 (t, J = 16.7, 1H), 7.00, 7.32, 7.69 (3m, 15H); ^{13}C NMR δ 14.2, 15.1, 28.3, 32.9, 53.7, 59.4, 60.7, 70.0, 121.5, 126.9, 127.7, 127.9, 128.0, 128.4, 129.0, 129.5, 129.6, 130.6, 136.1, 137.3, 139.5, 154.0, 168.1, 171.1, 171.2; MS *m/e* (DIP) 511 (M^+ + 2, 1), 510 (M^+ + 1, 4), 509 (M^+, 9), 165 (100); HRMS calcd for $C_{30}H_{29}N_3O_4$: 509.2315. Found 509.2367.

(2*S*,4′*S*,5′*R*)-2-Amino-3-(dimethylamino)-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl]propan-1-one [(−)-29, de 74%]: R_f 0.46 (MeOH); IR 3710−3100, 1726, 1650; ^{1}H NMR δ 0.73*, 0.76 (d, J = 6.7, 3H), 1.78 (br s, 2H, NH_2), 2.26, 2.28* (s, 6H), 2.52 (dd, J = 4.0, 14.6, 1H), 2.76 (m with 2s at 2.74 and 2.81, 4H), 3.92 (dq, J = 6.7, 8.5, 1H), 4.87 (dd, J = 4.0, 9.8, 1H), 5.25*, 5.31 (d, J = 8.6, 1H), 7.13, 7.28 (m, 5H); ^{13}C NMR δ 14.9*, 15.0, 28.1*, 28.2, 45.6, 45.8*, 51.5*, 51.8, 54.0*, 54.1, 59.2, 59.6*, 63.0*, 63.6, 128.1*, 128.3, 128.5, 128.55*, 128.6 130.0, 136.4, 155.3, 174.2; MS *m/e* (DIP) 304 (M^+, <1%), 58 (100); HRMS calcd for $C_{16}H_{24}N_4O_2$: 304.1899. Found 304.1854.

(3′*S*,4*R*,5*S*)-1,5-Dimethyl-4-phenyl-3-(1′,2′,3′,4′-tetrahydro-3′-isoquinolinylcarbonyl]-2-imidazolidinone [(−)-30, de 88%]: R_f 0.55 (MeOH); $[\alpha]^{25}_D$ −58.24° (*c* 1.05, $CHCl_3$); t_R 17.98*, 18.24; IR 3723−3103, 1726, 1681; ^{1}H NMR δ 0.78*, 0.81 (2d, J = 6.7, 3H), 1.81 (br s, 1H, NH), 2.64, 3.15 (2dd, J = 10.4, 16.5, 4.3, 16.5, 2H), 2.79*, 2.83 (2s, 3H), 3.93 (dq, J = 6.7, 8.6, 1H), 4.00, 4.01* (2s, 2H), 5.00 (dd, J = 4.3, 10.4, 1H), 5.30*, 5.36 (2d, J = 8.6, 1H), 7.09, 7.31 (2m, 9H); ^{13}C NMR δ 15.0, 28.2, 31.4, 32.1*, 46.6*, 47.1, 54.0*, 54.1, 55.2, 57.6*, 59.2, 125.6, 126.0, 126.1, 126.9, 127.0*,127.2*, 128.0*, 128.2, 128.3*, 128.5*, 128.6, 129.2, 133.8, 135.5, 136.5, 155.3, 172.8; MS *m/e* (DIP) 349 (M^+, <1), 132 (100); HRMS calcd for $C_{21}H_{23}N_3O_2$: 349.1790. Found 349.1765.

(2*S*,4′*S*,5′*R*)-[(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)(1,3,4,6-tetrahydro-2-pyridinyl)]methanone [(−)-31, de 94%]: R_f 0.33 (MeOH); IR 3697−3127, 3054, 3032, 1727, 1686;^{1}H NMR δ 0.77 (d, J = 6.7, 3H), 1.82 (br s, 1H, NH), 1.93, 2.47 (2m, 2H), 2.80 (s and m, 5H, CH_3N), 3.93 (dq, J = 6.7, 8.6, 1H), 4.83 (dd, J = 4.3, 9.8, 1H), 5.34 (d, J = 8.6, 1H), 5.68, 5.78 (2m, 2H), 7.11, 7.27 (2m, 5H); ^{13}C NMR δ 15.3, 28.1, 28.4, 44.1, 54.4, 54.5, 59.3, 124.6, 127.0, 127.1, 128.4, 128.8, 136.8, 155.5, 172.9; MS *m/e* 300 (M^+ + 1, 1), 299 (M^+, 4), 82 (100); HRMS calcd for $C_{17}H_{21}N_3O_2$: 299.1638. Found 299.1639.

(2*S*,4′*S*,5′*R*)-[(3′,4′-Dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)−(5-methyl-3,4-dihydro-2*H*-2-pyrrolyl)]methanone [(−)-32]: R_f 0.51 (MeOH); t_R 15.50; IR 1726, 1688, 1677; ^{1}H NMR δ 0.75 (d, J = 6.7, 3H), 1.93, 2.50 (2m, 4H), 2.09 (s, 3H), 2.79 (s, 3H), 3.91 (dq, J = 6.7, 8.6, 1H), 5.25 (d, J = 8.6, 1H), 5.97 (t, J = 7.3, 1H), 7.12, 7.25 (2m, 5H); ^{13}C NMR δ 14.8, 19.4, 26.4, 28.1, 32.5, 54.0, 59.3, 72.3, 126.9, 128.1, 128.5, 136.5, 155.4, 170.9, 180.9; MS *m/e* 301 (M^+ + 2, (1), 300 (M^+ + 1, 2), 299 (M^+, 12), 41 (100); HRMS calcd for $C_{17}H_{21}N_3O_2$: 299.1638. Found 299.1639.

Hydrolysis of Alkylated Imidazolidinone-Derived Glycinimide Compounds.

Obtention of Free α-Amino Acids (−)-33-(−)-37. General Procedure. Method A. To a solution of compound (−)-**25** or (−)-**26a** (0.31 mmol) in a mixture THF (5 mL) and H_2O (1.6 mL) were added LiOH (0.052 g, 0.72 mmol) and H_2O_2 (0.19 mL, 1.86 mmol) at 0 °C. The temperature was allowed to rise to room temperature, and the mixture was stirred for 12 h. Then, a 1 M solution of Na_2SO_3 (0.7 mL) was added at 0 °C. The pH of the mixture must be basic; if not, a saturated solution of $NaHCO_3$ was added. The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were dried (Na_2SO_4) and evaporated (15 Torr), recovering the chiral imidazolidinone (−)-**20** (see Table 5). The aqueous layer was acidified with 1 N HCl until pH = 2−3 and extracted with EtOAc (3 × 10 mL), dried (Na_2SO_4), and evaporated (15 Torr) to yield the corresponding imino acid, which was dissolved in THF (7 mL) and HCl 1 M (0.25 mL). The corresponding solution was stirred for 24 h at room temperature. The solvent was removed. Water (10 mL) was added and washed with CH_2Cl_2 (10 mL). Water was removed (15 Torr), the residue was dissolved in EtOH (2 mL), propylene oxide was added (1 mL), and the mixture was stirred for 2 h at room temperature. The solvent was removed, and the corresponding free amino acids were obtained with yields an ee's indicated in Table 5.

Method B. To a solution of compound (−)-**27** or (−)-**31**-(−)-**32** (0.26 mmol) in a mixture THF (6 mL) and H_2O (3 mL) was added at room temperature LiOH (0.043 g, 1 mmol). The mixture was stirred for a few hours (TLC monitored), and water (10 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were dried (Na_2SO_4) and evaporated (15 Torr), recovering the chiral imidazolidinone (−)-**20** (see Table 5). The aqueous layer was evaporated and suspended in 1 mL of water and purified by Dowex obtaining the pure free amino acid with yields a ee's indicated in Table 5.

Method C. A suspension of compound (−)-**27** or (−)-**30** (0.26 mmol) in H_2O (3 mL) was heated at reflux for 12 h. The reaction mixture was cooled at 25 °C and water (10 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were washed with water (10 mL) and were dried (Na_2SO_4) and evaporated (15 Torr), recovering the chiral imidazolidinone (−)-**20** (see Table 5). The aqueous layer was concentrated to afford a solid residue. The solid was triturated with ethanol (10 mL) and dried in vacuo to afford the pure free amino acid with yields and ee's indicated in Table 5.

(*S*)-Allylglycine (33a): $[\alpha]^{25}_D$ −30.5° (*c* 4, H_2O) {lit.[43] $[\alpha]^{25}_D$ −37.1° (*c* 4, H_2O)}.

(*S*)-Phenylalanine (33b): $[\alpha]^{25}_D$ −31.5° (*c* 1, H_2O) {lit.[43] $[\alpha]^{25}_D$ −34.5° (*c* 1, H_2O)}.

(*S*)-Baikiain [(*S*)-4,5-Didehydropipecolic Acid] (34): $[\alpha]^{25}_D$ −162.7 (*c* 1, H_2O) {lit.[44] $[\alpha]^{25}_D$ −201.6° (*c* 1, H_2O)}.

(*S*)-2-(*tert*-Butoxycarbonylamino)-5-oxohexanoic acid (35). $[\alpha]^{25}_D$ −12.5° (*c* 0.78, $CHCl_3$) {lit.[21e] $[\alpha]^{25}_D$ −14.0° (*c* 1.15, $CHCl_3$)}.

(*S*)-Prenylglycine (33l): $[\alpha]^{25}_D$ −3.72° (*c* 1, HCl 1 M) {lit.[45] $[\alpha]^{25}_D$ −4.0° (*c* 1, HCl 1 M)}.

(*S*)-3,4-(Methylenedioxy)phenylalanine (33n, Hydrochloride): mp 282−284 decomp (ether/ethanol) [lit.[46] 284 decomp (ether/ethanol)].

(*S*)-Pyroglutamic acid (36): $[\alpha]^{25}_D$ −9.8° (*c* 5, H_2O) {lit.[43] $[\alpha]^{25}_D$ −10.1° (*c* 5, H_2O)}.

(*S*)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid (37): $[\alpha]^{25}_D$ −110.2° (*c* 2, NaOH 1 M) {lit.[43] $[\alpha]^{25}_D$ −167° (*c* 2, NaOH 1 M)}.

Alkylation and Hydrolysis in Situ of Compound (−)-24. Obtention of Methyl (2S)-2-(Diphenylmethyleneamino)-4-pentenoate [(−)-38].[39] A solution of compound (−)-**24** (0.300 g, 0.73 mmol) in the CH_3CN (6 mL) and LiCl (0.191 g, 4.4 mmol) under argon atmosphere was stirred for 20−30 min at −20 °C. Then DBU (0.15 mL, 1.1 mmol) was added, the corresponding electrophile was added (0.15 mL, 1.5 mmol), and the reaction was stirred for a 1.30 h at −20 °C. Then, DBU (0.2 mL, 1.5 mmol) and dry MeOH (6 mL) was added, and the reaction was heated until 0 °C and stirred for 24 h at that temperature. The reaction was quenched with NH_4Cl (20 mL) and extracted with EtOAc (3 × 25 mL). The organics layers were dried over Na_2SO_4 and evaporated (15 Torr). The residue was purified by column chromatography on silica gel to afford 0.118 g of (−)-**20** and 0.092 g (43%) of (−)-**38** (87% ee): $[\alpha]^{25}_D$ −102.94 (*c* 1, $CHCl_3$); R_f 0.45 (hexane/EtOAc: 4/1); IR 1741, 1598; ^{1}H NMR δ 2.66 (m, 2H), 3.72 (s, 3H), 4.17 (dd, J = 5.5, 7.9, 1H), 5.05 (m, 2H), 5.66 (m, 1H), 7.16, 7.45, 7.81 (3m, 10H); ^{13}C NMR δ 38.2, 52.1, 65.3, 117.7, 127.9, 128.0, 128.5, 128.7, 128.9, 130.4, 134.3, 136.4, 170.7, 172.6; MS *m/e* 295 (M^+ + 2, <1), 294 (M^+ + 1, 2), 293 (M^+, 10), 77 (100).

Preparation (2*S*,4′*S*,5′*R*)-2-(*N*-*tert*-Butoxycarbonylamino)-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl]-4-penten-1-one [(−)-39]. Di-*tert*-butyl dicarbonate (0.100 g, 0.41 mmol) was added to a biphasic mixture of (−)-**27a** hydrochloride (0.100 g, 0.38 mmol) in dioxane (1.5 mL) and $NaHCO_3$ (0.061 g, 0.72 mmol) in H_2O (1 mL). After stirring the mixture vigorously for 1 h at 25 °C, water (10 mL) and ether (25 mL) were added, and the layers were separated. The aqueous layer was extrated with a second portion of ether (10 mL), and the combined organic layers were dried over Na_2SO_4 and evaporated (15 Torr). The residue was purified by column cromatography on silica gel to afford of (−)-**39**, 0.135 g (92%): $[\alpha]^{25}_D$ −41.9 (*c* 1.7, $CHCl_3$); R_f 0.44 (hexane/EtOAc: 1/1); IR 3436, 3368, 1808, 1731, 1681, 1643; ^{1}H NMR δ 0.77 (d, J = 6.7, 3H), 1.37 [s,9H, $(CH_3)_3$], 2.33, 2.58 (2m, 2H), 2.79 (s, 3H), 3.90 (dq, J = 6.7, 8.5, 1H), 5.00 (m, 2H), 5.28 (d, J = 8.5, 1H), 5.48 (m, 2H), 7.09, 7.26 (2m, 5H); ^{13}C NMR δ 15.0, 27.4, 28.2, 36.8, 52.2, 54.1, 59.1, 79.4, 118.7, 127.0, 128.2, 128.5, 132.5, 136.5, 146.7, 155.40 171.6; MS *m/e* 387 (M^+, 9), 386 (M^+ − 1, 8), 58 (100); HRMS calcd for $C_{16}H_{20}N_3O_2$: 286.1556. Found 286.1535.

Hydrolysis of Compound (−)-39. Synthesys of *N*-Boc-L-Allylglycine [(+)-40].[40] A solution of (−)-**39** (0.073 g, 0.19 mmol) and 1 M aqueous sodium hydroxide (0.48 mL, 0.48 mmol) in methanol (4 mL) was heated at reflux. After 3 h refluxing, the solution was cooled and methanol was removed by concentration in a vacuum. The resulting aqueous product mixture was cooled in a ice bath and acidified to pH 1 by the slow addition of 1 M HCl. The acidified aqueous solution was extracted with EtOAc (2 × 25 mL). The organics layers were dried over Na_2SO_4 and evaporated (15 Torr). The residue was purified by column cromatography on silica gel to afford 0.031 g (85%) of (−)-**20** and 0.016 mg (39%) of (+)-**40**[40] (81% ee): $[\alpha]^{25}_D$ +9.65° (*c* 1.4, MeOH) {lit.[40] $[\alpha]^{25}_D$ +11.9° (*c* 1.4, MeOH)}.

Hydrolysis of Compound (−)-39. Obtention of *N*-Boc-L-Allylglycine Methyl Ester [(+)-41].[42] To a solution of (−)-**39** (0.072 g, 0.18 mmol) in methanol (2 mL) were added LiBr (0.078 g, 0.9 mmol) and DBU (0.05 mL, 0.36 mmol, 2 equiv) at 0 °C. The resulting mixture was stirred for 1 h at 0 °C. Then a saturated solution of NH_4Cl (10 mL) was added and extracted with EtOAc (2 × 25 mL). The organics layers were dried over Na_2SO_4 and evaporated (15 Torr). The residue was purified by column cromatography on silica gel to afford 0.025 g (73%) of (−)-**20** and 0.010 g (27%) of *N*-Boc-L-allylglycine methyl ester (+)-**41**[42] (96% ee): $[\alpha]^{25}_D$ +18.59° (*c* 1.4, $CHCl_3$) {lit.[43] $[\alpha]^{25}_D$ +19.3° (*c* 13, $CHCl_3$)}.

DBU-Mediated Alkylation of Imidazolidinone-Derived Glycinimide (+)-24. Synthesis of Compounds (+)-27a, (+)-27r, (+)-27v, and (+)-30. General Procedure. The prodecure was identical as above-described for the alkylation of (−)-**24**. Yields are included in Table 6; spectral and analytical data for compounds (+)-**27a**, (+)-**27r**, and (+)-**30** were identical to the corresponding enantiomers (see above). Spec-

(43) *Dictionary of Organic Compounds*, 6th ed.; Chapman and Hall; London, 1996.

(44) Mazón, A.; Nájera, C. *Tetrahedron*: *Asymmetry* **1997**, *8*, 1855−1859.

(45) Smith III, A. B.; Benowitz, A. B.; Favor, D. A.; Sprengeler, P. A.; Hirschmann, R. *Tetrahedron Lett*. **1997**, *38*, 3809−3812.

(46) Barry, R. H.; Mattocks, A. M.; Hartung, W. H. *J. Am. Chem. Soc*. **1948**, *25*, 4133−4134.

tral and analytical data for compound (+)-**27v** and optical rotation for (+)-**27a**, (+)-**27r**, and (+)-**30** follow.

(2*R*,4′*R*,5′*S*)-2-Amino-1-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-4-penten-1-one [(+)-27a]: $[\alpha]^{25}_D$ +29.27° (*c* 1.5, $CHCl_3$).

***tert*-Butyl (4*R*,4′*R*,5′*S*)-4-amino-5-(3′,4′-dimethyl-2′-oxo-5′-phenyl-1′-imidazolydinyl)-5-oxopentanoate [(+)-(22r)].** $[\alpha]^{25}_D$ +23.65 (*c* 2.1, $CHCl_3$).

(2*R*,4′*R*,5′*S*)-2-Amino-3-(3,4-dimethoxyphenyl)-1-(3′,5′-dimethyl-2′-oxo-4′-phenyl-1′-imidazolydinyl)propan-1-one [(+)-27v)]: R_f 0.30 (MeOH); $[\alpha]^{25}_D$ +10.92° (*c* 1.3, $CHCl_3$); IR 3756−3050, 1721, 1649; ^{1}H NMR δ 0.75 (d, J = 6.1, 3H), 1.78 (br s, 2H NH_2), 2.43 (dd, J = 13.4, 8.5, 1H), 2.78*, 2.81 (2s, 3H), 3.15 (dd, J = 13.4, 4.9, 1H), 3.71, 3.81 (2s, 6H), 3.86 (dq, J = 8.5, 6.1, 1H), 4.98 (dd, J = 8.6, 4.9, 1H), 5.30 (d, J = 8.5, 1H), 6.70, 6.73, 7.04, 7.25 (4m, 8H); ^{13}C NMR δ 15.0, 28.2, 41.3, 54.1, 54.7, 55.7, 55.8, 59.2, 111.1, 112.7, 121.7, 126.9, 128.1, 128.5, 128.7, 130.4, 136.5, 147.6, 155.4, 176.0; *m*/*z* (DIP) 399 (M^+ + 2, <1), 398 (M^+ + 1, 1), 397 (M^+, 4), 246 (100); HRMS calcd for $C_{22}H_{27}N_3O_4$: 397.2001. Found 397.2008.

(3′*R*,4*S*,5*R*)-1,5-Dimethyl-4-phenyl-3-(1′,2′,3′,4′-tetrahydro-3′-isoquinolinylcarbonyl]-2-imidazolidinone [(+)-30]: $[\alpha]^{25}_D$ +46.00° (*c* 0.8, $CHCl_3$).

Hydrolysis of Alkylated Imidazolidinone-Derived Glycinimide Compounds (+)-27a, (+)-27r, (+)-27v, and (+)-30. Obtention of Free α-Amino Acids (+)-33a, (+)-33v, (+)-36, and (+)-37. General Procedure. Method C was used for all compound as described above. In the case of hydrolysis of compound (+)-**27r** a mixture of dioxane/H_2O 1/1 was used. Yields and ee's are indicated in Table 6.

(*R*)-Allylglycine (33a): $[\alpha]^{25}_D$ +33.4° (*c* 4, H_2O) {lit.[43] $[\alpha]^{25}_D$ +37.1° (*c* 4, H_2O)}.

(*R*)-Dimethyl-DOPA (33v): $[\alpha]^{25}_D$ +4.7° (*c* 4, HCl 1 M) {lit.[43] $[\alpha]^{25}_D$ +5.0° (*c* 4, HCl 1 M)}.

(*S*)-Pyroglutamic Acid (36): $[\alpha]^{25}_D$ +9.1° (*c* 5, H_2O) {lit.[43] $[\alpha]^{25}_D$ +10.1° (*c* 5, H_2O)}.

(*S*)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic Acid (37). $[\alpha]^{25}_D$ +108.2° (*c* 1, NaOH 1 M) {lit.[43] $[\alpha]^{25}_D$ −167° (*c* 2, NaOH 1 M)}.

Acknowledgment. We thank the Spanish Ministerio de Educación y Cultura (MEC, Project PB97-0123) for financial support.

JO000321T