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Enantioselective Synthesis of α-Alkyl, α-Vinyl Amino Acids via [2,3]-Sigmatropic Rearrangement of Selenimides

Alan Armstrong* and Daniel P. G. Emmerson

Department of Chemistry, Imperial College London, South Kensington, London, SW7 2AZ, U.K.

A.Armstrong@imperial.ac.uk

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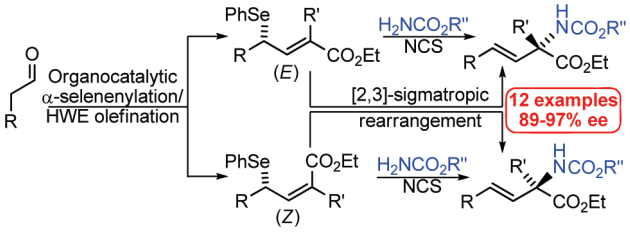
ABSTRACT



Chiral α-alkyl,α-vinyl amino acids (quaternary vinyl glycine derivatives) are prepared with high levels of enantiomeric purity by [2,3]-sigmatropic rearrangement of allylic selenimides. The required trisubstituted allylic selenides are prepared by an organocatalytic α-selenenylation of aldehydes followed by Horner−Wadsworth−Emmons (HWE) olefination. Both (*E*)-and (*Z*)-geometrical isomers are available giving access to both enantiomers of the desired products.

The asymmetric synthesis of quaternary amino acids has attracted the interest of organic chemists due to the biological importance of these structures. Although there is now a wide range of methodology for the synthesis of these compounds,[1] few of these methods are useful for the asymmetric synthesis of α-alkyl,α-vinyl amino acids.

α-Vinyl amino acids have shown potential as mechanism-based inhibitors of PLP (pyridoxal phosphate) enzymes.[2] Possible mechanisms of this irreversible inhibition include α-deprotonation, resulting in conjugation of the double bond giving a Michael acceptor, which reacts with nucleophilic residues at the enzyme active site, irreversibly inactivating it. α-Alkyl,α-vinyl amino acids lacking an α-proton are also interesting targets for PLP-dependent decarboxylase enzymes,[3] in which an analogous 'vinyl-trigger' mechanism can operate; here, an α-decarboxylation

(1) For reviews on the asymmetric synthesis of α,α-disubstituted α-amino acids, see: (a) Vogt, H.; Bräse, S. *Org. Biomol. Chem.* **2007**, *5*, 406–430. (b) Cativiela, C.; Diaz-de-Villegas, M. D. *Tetrahedron: Asymmetry* **1998**, *9*, 3517–3599. (c) Cativiela, C.; Diaz-de-Villegas, M. D. *Tetrahedron: Asymmetry* **2000**, *11*, 645–732. (d) Cativiela, C.; Diaz-de-Villegas, M. D. *Tetrahedron: Asymmetry* **2007**, *18*, 569–623. (e) Cativiela, C.; Diaz-de-Villegas, M. D. *Tetrahedron: Asymmetry* **2009**, *20*, 1–63. (f) Mosey, R. A.; Fisk, J. S.; Tepe, J. J. *Tetrahedron: Asymmetry* **2008**, *19*, 2755–2762. For selected, more recent examples, see:(g) Branca, M.; Pena, S.; Guillot, R.; Gori, D.; Alezra, V.; Kouklovsky, C. *J. Am. Chem. Soc.* **2009**, *131*, 10711–10718. (h) Green, J. E.; Bender, D. M.; Jackson, S.; O'Donnell, M. J.; McCarthy, J. R. *Org. Lett.* **2009**, *11*, 807–810. (i) Fu, P.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 5530–5541. (j) Mitani, M.; Tanaka, Y.; Sawada, A.; Misu, A.; Matsumoto, Y. *Eur. J. Org. Chem.* **2008**, 1383–1391. (k) Cabrera, S.; Reyes, E.; Alemán, J.; Milelli, A.; Kobbelgaard, S.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 12031–12037. (l) Huang, X. L.; He, L.; Shao, P. L.; Ye, S. *Angew. Chem., Int. Ed.* **2009**, *48*, 192–195. (m) Uraguchi, D.; Asai, Y.; Ooi, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 733–737. (n) Hayashi, Y.; Obi, K.; Ohta, Y.; Okamura, D.; Ishikawa, H. *Chem.—Asian J.* **2009**, *4*, 246–249. (o) Dickstein, J. S.; Fennie, M. W.; Norman, A. L.; Paulose, B. J.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 15794–15795. (p) Fesko, K.; Uhl, M.; Steinreiber, J.; Gruber, K.; Griengl, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 121–124. (q) Konishi, H.; Lam, T. Y.; Malerich, J. P.; Rawal, V. H. *Org. Lett.* **2010**, *12*, 2028–2031.

(2) For a review covering synthesis and biochemical aspects of α-vinyl amino acids, see: Berkowitz, D. B.; Charette, B. D.; Karukurichi, K. R.; McFadden, J. M. *Tetrahedron: Asymmetry* **2006**, *17*, 869–882.

(3) (a) Ribéreau-Gayon, G.; Danzin, C.; Palfreyman, M. G.; Aubry, M.; Wagner, J.; Metcalf, B. W.; Jung, M. J. *Biochem. Pharmacol.* **1979**, *28*, 1331–1335. (b) Berkowitz, D. B.; Jahng, W.-J.; Pedersen, M. L. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2151–2156. (c) Danzin, C.; Casara, P.; Claverie, N.; Metcalf, B. W. *J. Med. Chem.* **1981**, *24*, 16–20.

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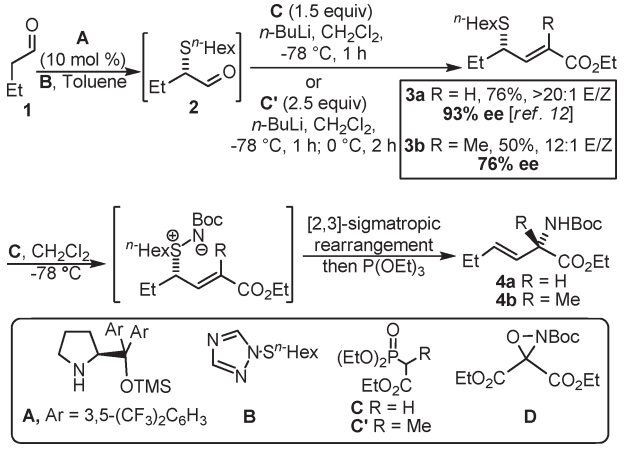
Scheme 1. Vinyl Glycine Synthesis *via* Organocatalytic Sulfenylation/HWE Olefination Followed by Amination/Rearrangement[12c]



rather than an α-deprotonation brings the double bond into conjugation.

The choice of currently available methods for the asymmetric synthesis of α-alkyl,α-vinyl amino acids is dominated by chiral auxiliary-directed methods. For instance, Marsden and co-workers[4] and Berkowitz and co-workers[5] have reported decongugative alkylation of dienolates derived from dehydro amino acids. Several other methods rely on chiral auxiliary-directed stereoselective formation of the carbon—vinyl bond through addition of organometallic vinyl synthons.[6] An alkylation of an oxazoline derived from L-vinyl glycine is notable in that no chiral auxiliary is required, chiral information being derived instead from the starting material.[5,7] Other methods typically rely on asymmetric alkylation using chiral auxiliaries in combination with multistep installation of a vinyl group.[8] Catalytic methods are much rarer,[9] the outstanding example being Shibasaki's bifunctional gadolinium-derived catalyst for the Strecker reaction of vinyl ketimines.[10]

It is interesting to note the scarcity of methods relying on the formation of the C−N bond as the key step.[11] Motivated by our longstanding interest in asymmetric carbon−heteroatom bond formation, we wished to develop an asymmetric synthesis of α-alkyl,α-vinyl amino acids.

As part of an ongoing research program on sulfur amination/[2,3]-sigmatropic rearrangement of allylic and propargylic sulfimides in our laboratatory,[12] we recently reported the synthesis of vinyl glycine derivatives, e.g. **4a** *via* amination/rearrangement of allylic sulfides (Scheme 1). This method relies on an asymmetric organocatalytic α-sulfenylation of aldehydes,[13] followed by *in situ* Horner−Wadsworth−Emmons (HWE) olefination giving disubstituted allylic sulfides, e.g. **3a**.[14] *S*-Amination is carried out by treating allylic sulfides **3** with oxaziridine **D**,[12a] whereupon [2,3]-sigmatropic rearrangement of the resulting sulfimide occurs spontaneously; *in situ* treatment with triethyl phosphite results in N−S bond cleavage giving α-vinyl amino acids, e.g. **4a**. However attempts to use this method for the synthesis of α-alkyl,α-vinyl amino acid **4b** met with difficulties: olefination to give the required trisubstituted allylic sulfide **3b** needed higher temperatures for full conversion such that partial racemization of the α-sulfenyl aldehyde **2** was unavoidable (Scheme 1).

Attracted by recent reports of an organocatalytic α-selenenylation of aldehydes,[15] we sought to use selenium in place of sulfur.[16] This has a number of potential advantages over the sulfur system: (a) the relative stability of α-selenenyl aldehydes with respect to racemization has been noted,[15a] and use of these aldehydes might prevent significant racemization under the conditions of the HWE reaction at the higher temperature required for full conversion; (b) the synthesis of α-selenenyl aldehydes can be conducted using a stable commercially available reagent *N*-(phenylseleno)phthalimide (NPSP), avoiding the use of triazole-derived sulfenylation reagent **B** which must be

(4) Jones, M. C.; Marsden, S. P.; Muños Subtil, D. M. *Org. Lett.* **2006**, *8*, 5509–5512.

(5) Berkowitz, D. B.; Chisowa, E.; McFadden, J. M. *Tetrahedron* **2001**, *57*, 6329–6343.

(6) (a) Crucianelli, M.; De Angelis, F.; Lazzaro, F.; Malpezzi, L.; Volonterio, A.; Zanda, M. *J. Fluorine Chem.* **2004**, *125*, 573–577. (b) Wipf, P.; Stephenson, C. R. J. *Org. Lett.* **2003**, *5*, 2449–2452. (c) Murga, J.; Portolés, R.; Falomir, E.; Carda, M.; Marco, J. A. *Tetrahedron: Asymmetry* **2005**, *16*, 1807–1816. (d) Portolés, R.; Murga, J.; Falomir, E.; Carda, M.; Uriel, S.; Marco, J. A. *Synlett* **2002**, 711–714.

(7) Berkowitz, D. B.; McFadden, J. M.; Chisowa, E.; Semerad, C. L. *J. Am. Chem. Soc.* **2000**, *122*, 11031–11032. Pedersen, M. L.; Berkowitz, D. B. *J. Org. Chem.* **1993**, *58*, 6965–6975.

(8) (a) Di Giacomo, M.; Vinci, V.; Serra, M.; Colombo, L. *Tetrahedron: Asymmetry* **2008**, *19*, 247–257. (b) Ma, D.; Zhu, W. *J. Org. Chem.* **2000**, *66*, 348–350. (c) Avenoza, A.; Cativiela, C.; Corzana, F.; Peregrina, J. M.; Zurbano, M. M. *J. Org. Chem.* **1999**, *64*, 8220–8225. (d) Colson, P.-J.; Hegedus, L. S. *J. Org. Chem.* **1993**, *58*, 5918–5924.

(9) For a general review on organocatalytic formation of quaternary stereocenters including α-amination of α-branched carbonyl compounds, see: Bella, M.; Gasperi, T. *Synthesis* **2009**, 1583–1614.

(10) Masumoto, S.; Usuda, H.; Suzuki, M.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 5634–5635.

(11) Palladium-catalyzed [3,3]-sigmatropic rearrangements of trifluoro- or trichloro-acetimidates give protected *β*-amino alcohols which may be converted to the corresponding vinyl amino acids by oxidation. For an example giving racemic quaternary vinyl amino acids, see: (a) Berkowitz, D. B.; Wu, B.; Li, H. *Org. Lett.* **2006**, *8*, 971–974. For an example giving enantiomerically enriched vinyl amino acids, see:(b) Mehmandoust, M; Petit, Y; Larchevêque, M. *Tetrahedron Lett.* **1992**, *33*, 4313–4316.

(12) (a) Armstrong, A.; Cooke, R. S. *Chem. Commun.* **2002**, 904–905. (b) Armstrong, A.; Challinor, L.; Cooke, R. S.; Moir, J. H.; Treweeke, N. R. *J. Org. Chem.* **2006**, *71*, 4028–4030. (c) Armstrong, A.; Challinor, L.; Moir, J. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 5369–5372. (d) Armstrong, A.; Emmerson, D. P. G. *Org. Lett.* **2009**, *11*, 1547–1550.

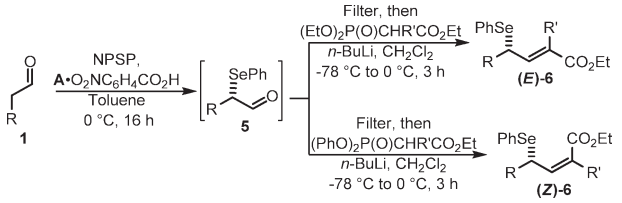
(13) Marigo, M.; Wabnitz, T. C.; Fielenbach, D.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 794–797.

(14) An alternative method of preparing disubstituted allylic sulfides in high ee has recently been reported: Sun, J.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 4568–4569.

(15) (a) Tiecco, M.; Carlone, A.; Sternativo, S.; Marini, F.; Bartoli, G.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 6882–6885. (b) Sundén, H.; Rios, R.; Córdova, A. *Tetrahedron Lett.* **2007**, *48*, 7865–7869.

(16) During the preparation of this manuscript two reports of a similar strategy to synthesize α-hydroxy and α-chloro-(*E*)-*β*,*γ*-unsaturated esters have appeared. These authors report an alternative method for the *in situ* olefination giving disubstituted allylic sulfides: (a) Hess, L. C.; Posner, G. H. *Org. Lett.* **2010**, *12*, 2120–2122. The α-chloro-(*E*)-*β*,*γ*-unsaturated esters may be converted into vinylogogous α-amino acids:(b) Genna, D. T.; Hencken, C. P.; Siegler, M. A.; Posner, G. H. *Org. Lett.* **2010**, *12*, 4694–4697.

Table 1. Organocatalytic α-Selenenation of Aldehydes/HWE Olefination[a]



entry		R	R′	*E*/*Z*[b]	yield/%[c]	ee/%[d]
1	(*E*)-**6a**[e]	Et	H	>20:1	75	96
2	(*E*)-**6b**	Et	Me	4.7:1	69	95
3	(*E*)-**6c**[f]	*t*-Bu	Me	12:1	38	91
4	(*E*)-**6d**[g]	$TBSOCH_2$	H	>20:1	54	88
5	(*E*)-**6e**	Allyl	Me	4.6:1	52	94
6	(*Z*)-**6e**	Allyl	Me	1:>20	63	95
7	(*Z*)-**6f**	*i*-Pr	Me	1:>20	41	nd[h]
8	(*Z*)-**6 g**	*i*-Pr	Et	1:>20	44	nd[h]
9	(*Z*)-**6 h**	Bn	Me	1:18	70	97
10	(*Z*)-**6i**	Bn	Bn	1:15	60	95
11	(*Z*)-**6j**	$TBSOCH_2$	Me	1:>20	50	88

[a] For full experimental details see Supporting Information. Aldehyde (0.4 mmol, 1.3 M), NPSP (0.48 mmol), **A** (5 mol %), $O_2NC_6H_4CO_2H$ (5 mol %), 0 °C, 16 h; then phosphonate (0.8 mmol), *n*-BuLi (0.76 mmol), CH_2Cl_2, −78 °C → 0 °C, 3 h. [b] By ^1H NMR analysis of crude reaction mixture. [c] Yield over two steps of the purified major geometric isomer after column chromatography. [d] Ee determined by chiral HPLC. [e] Methyl ester prepared. [f] 4 equiv of phosphonate anion added in 3 stages. [g] Sulfenylation at a concentration of 2 M for 40 h. [h] Separation of isomers by chiral hplc was not possible.

prepared immediately before use; (c) the amination/rearrangement can be carried out using commercially available reagents according to the method of Hopkins[17] (NCS and an amide or carbamate: RNH_2), potentially giving access to a choice of nitrogen protecting group; (d) this method requires no additional step to cleave the N−Se bond: this weak bond is broken under the reaction conditions.

For our purposes it was crucial that there was no unreacted aldehyde **1** remaining after the α-selenenylation reaction as we wished to perform the HWE reaction *in situ*.[18] Since the established method[15a] for organocatalytic α-selenenylation requires an excess of aldehyde, our first task was to find conditions for this reaction under which full consumption of aldehyde was possible, while maintaining high enantioselectivity. Fortunately, we were able to achieve this goal using 1.2 equiv of NPSP and a higher reaction concentration (see Supporting Information for further details).

Next, we needed to develop an *in situ* olefination which would not result in racemization. Our initial attempts met with very limited success: high conversion could not be achieved even when a 3-fold excess of phosphonate anion was used. Finally, we found that good yields of the allyl selenides could be isolated when the organocatalytic reaction was simply filtered prior to the HWE reaction, presumably removing phthalimide, the byproduct of the selenenylation. We were pleased to find generally moderate-to-good *E*/*Z* selectivities (Table 1, entries 1−5) even for trisubstituted alkenes (R′ = Me). Furthermore, the geometric isomers could easily be separated by column chromatography in all cases to give moderate-to-good yields (38−75%, over two steps) of **(*E*)-6**. A more sterically encumbered substrate proved the most challenging; longer reaction times and a greater excess of phosphonate anion were required in the synthesis of **(*E*)-6c**, which bears a *tert*-butyl side chain (entry 3). Keen to expand the scope of the asymmetric organocatalytic α-selenenylation to aldehydes bearing β-heteroatoms, previously unused in the α-selenenylation,[19] we were pleased to find that the aldehyde $TBSO(CH_2)_2CHO$ was a substrate for the reaction, albeit requiring further concentration and a prolonged reaction time (entry 4).

Our attempts to prepare trisubstituted alkenes substituted with alkyl groups other than methyl by this method were less successful, resulting in low *E*/*Z* selectivity and poor conversion.[20] Ando[21] reported (*Z*)-selective HWE olefinations of α-substituted ethyl (diphenylphosphono)-acetates, and we hoped that this type of reagent might allow access to a wider range of trisubstituted allylic selenides **(*Z*)-6**.[22] Furthermore, we have previously noted[12c] that (*Z*)-geometric isomers of allylic sulfides undergo amination/rearrangement to give the enantiomer of the vinyl glycine derivative produced from the (*E*)-isomer thus making either enantiomer of **7** readily available without recourse to the organocatalyst derived from the un-natural enantiomer of proline.

We therefore investigated the synthesis of the (*Z*)-alkenes using the Ando-modified phosphonates $(PhO)_2P(O)CHR'CO_2Et$. Pleasingly, this was successful, giving the allylic selenides **(*Z*)-6e−j** in acceptable yields and, crucially, high ee's and *Z*/*E* ratios (Table 1, entries 6−11). In contrast to the conventional HWE reagents,

(17) Shea, R. G.; Fitzner, J. N.; Fankhauser, J. E.; Spaltenstein, A.; Carpino, P. A.; Peevey, R. M.; Pratt, D. V.; Tenge, B. J.; Hopkins, P. B. *J. Org. Chem.* **1986**, *51*, 5243–5252. These authors include a single example of an α-vinyl,α-alkyl amino acid, but the enantiomeric purity was limited by the lack of methods to prepare allylic selenides in high ee at that time.

(18) α-Selenenyl aldehydes undergo partial racemization during purification by flash chromatography so a purification-free method is required.

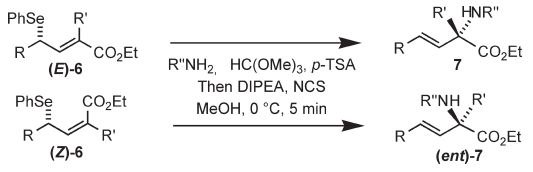
(19) For a nonselective organocatalytic α-selenenylation of an α,β-oxygen-substituted ketone, see: Wang, J.; Li, H.; Mei, Y. J.; Lou, B. S.; Xu, D. G.; Xie, D. Q.; Guo, H.; Wang, W. *J. Org. Chem.* **2005**, *70*, 5678–5687.

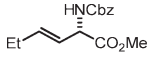
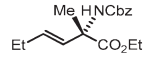
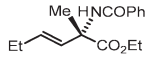
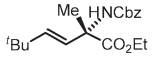
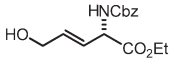
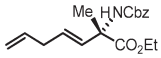
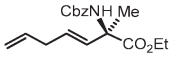
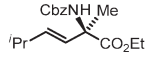
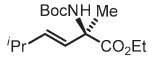
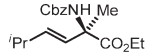
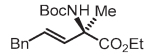
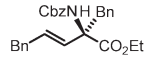
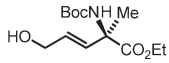
(20) For instance, in the HWE olefination to form **(*E*)-6** (R = Bn, R′ = Et) no conversion of **5** was observed under the conditions used in the other examples. When **5** (R = Bn) was isolated and subjected to the HWE conditions, 60% conversion and a 2.6:1 *E*/*Z* ratio were observed. For further details, see Supporting Information.

(21) Ando, K. *J. Org. Chem.* **1998**, *63*, 8411–8416.

(22) For an example of high (*Z*)-selectivity in Ando modified olefinations on α-heteroatom-substituted aldehydes to afford trisubstituted alkenes, see: (a) Wascholowski, V.; Giannis, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 827–830. For examples of improved (*Z*)-selectivity compared to Still−Gennari modified olefinations on such systems, see:(b) Dias, L. C.; Meira, P. R. R. *J. Org. Chem.* **2005**, *70*, 4762–4773. (c) Vicario, J. L.; Job, A.; Wolberg, M.; Muller, M.; Enders, D. *Org. Lett.* **2002**, *4*, 1023–1026. (d) Enders, D.; Vicario, J. L.; Job, A.; Wolberg, M.; Muller, M. *Chem.—Eur. J.* **2002**, *8*, 4272–4284. (e) Yoshimura, T.; Yakushiji, F.; Kondo, S.; Wu, X.; Shindo, M.; Shishido, K. *Org. Lett.* **2006**, *8*, 475–478.

Table 2. Amination/Rearrangement[a]



allylic selenide **6**			vinyl glycine derivative **7**			
entry		ee/%	structure		yield/%[b]	ee/%[c]
1	**(*E*)-6a**	96		**7a**	66	96
2	**(*E*)-6b**	95		**7b**	81	94
3	**(*E*)-6b**	93		**7c**	31	93 (96)[d]
4	**(*E*)-6c**	91		**7d**	67	91
5	**(*E*)-6d**	91		**7e**	57	90
6	**(*E*)-6e**	94		**7f**	59	93
7	**(*Z*)-6e**	95		**(*ent*)-7f**	63	95
8	**(*Z*)-6f**	nd[e]		**(*ent*)-7g**	80	90
9	**(*Z*)-6f**	nd[e]		**(*ent*)-7h**	61	90[f]
10	**(*Z*)-6g**	nd[e]		**(*ent*)-7i**	80	94
11	**(*Z*)-6h**	97		**(*ent*)-7j**	70	97
12	**(*Z*)-6i**	95		**(*ent*)-7k**	67	95
13	**(*Z*)-6j**	88		**(*ent*)-7l**	-[g]	

[a] For full experimental details see Supporting Information. [b] After column chromatography. [c] Ee determined by chiral hplc. [d] After recrystallization from Et_2O/hexane. [e] Separation of isomers by chiral HPLC was not possible. [f] Determined by chiral HPLC of Cbz protected product **(*ent*)-7f**, prepared by deprotection/Cbz protection of the protuct **(*ent*)-7 g**. [g] Complex mixture produced; none of the desired product isolated.

the α-ethyl- and α-benzyl-substituted Ando-modified phosphonates underwent highly selective olefination affording allylic selenides **(*Z*)-6 g,i** (*Z*/*E* ratios of > 20:1 and 15:1 respectively, entries 8 and 10) with little or no racemization of the selenides. The aldehyde $TBSO(CH_2)_2CHO$ was once again used as a substrate, giving the α-oxygen substituted selenide **(*Z*)-6j**.

We now investigated the NCS-mediated amination/rearrangement using conditions reported by Hopkins and co-workers in the 1980s.[17] The reaction has been shown to proceed *via* chlorination of selenium followed by displacement of chloride by the nitrogen reagent giving the allylic selenimide which undergoes [2,3]-sigmatropic rearrangement.[17]

We initially chose benzyl carbamate as the nitrogen source, since this would give versatile Cbz-protected amino acid derivatives. Pleasingly, this method afforded α-alkyl, α-vinyl amino acids **7** in moderate-to-good yields (Table 2). A key advantage of this method is that the nitrogen source in this reaction may be varied, giving a choice of protecting groups. For example, we have used *tert*-butyl carbamate, giving Boc-protected amino acids (Table 2, entries 9 and 11) and benzamide, giving a benzoyl-protected amino acid (entry 3). In the latter case a lower yield (31%) could be accounted for by observation of the unrearranged selenimide intermediate, which was isolated from the reaction as a single diastereomer. This supports a hypothesis in which one diastereomer of the selenimide undergoes rearrangement faster than the other due to a less sterically encumbered transition state, in line with a similar observation by us in a related reaction.[11c] In all cases, the ee of the products was at least 90% and was conserved during the rearrangement, consistent with a concerted mechanism (Table 2).

Particularly pleasing was the rearrangement of **(*E*)-6d**, which occurred with loss of the TBS group in 57% yield (Table 2, entry 5). Unfortunately, the rearrangement of **(*Z*)-6j**, the corresponding (*Z*)-trisubstituted allylic selenide, was unsuccessful (Table 2, entry 13).

In conclusion, we have developed a new, highly enantioselective synthesis of α-alkyl,α-vinyl amino acid derivatives *via* [2,3]-sigmatropic rearrangement of allylic selenimides. The required trisubstituted allylic selenides were prepared *via* an asymmetric, organocatalytic α-selenenylation of aldehydes followed by HWE olefination. This strategy is the first example of a general, asymmetric synthesis of α-alkyl,α-vinyl amino acid derivatives in which the C−N bond is formed in the key step. This versatile method facilitates the introduction of a range of protecting groups on nitrogen in the resulting quaternary amino acid derivatives. The use of selenium in this report shows several key advantages over the corresponding sulfur-based method.

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Supporting Information Available. Experimental details, copies of ^1H and ^{13}C NMR spectra and HPLC traces for **6a**−**j** and **7a**−**l**. This material is available free of charge via the Internet at http://pubs.acs.org.