ORGANIC LETTERS

2002
Vol. 4, No. 7
1107−1109

Enantioselective Aziridination of Alkenes with *N*-Aminophthalimide in the Presence of Lead Tetraacetate-Mediated Chiral Ligand

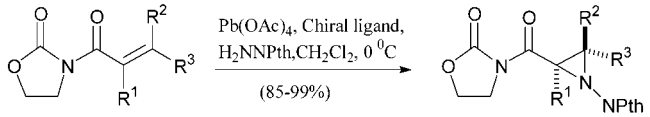
Kung-Shou Yang and Kwunmin Chen*

Department of Chemistry, National Taiwan Normal University, 88 Sec. 4, TingChow Road, Taipei, Taiwan 116, ROC

kchen@scc.ntnu.edu.tw

Received December 28, 2001

ABSTRACT



5a-f **6a-f** (67-95% ee)

Reaction of various *N*-enoyl oxazolidinones 5a–f with *N*-aminophthalimide and lead tetraacetate in the presence of camphor-derived chiral ligands provides the desired *N*-phthalimidoaziridines 6a–f in good to high enantiomeric excess (67–95% ee) at 0 °C within 15 min. The absolute stereochemistry of the corresponding aziridine derivatives was established by chemical correlations.

The synthesis of chiral nonracemic aziridines has received much attention in recent years. They are not only attractive intermediates for organic synthesis but also can serve as useful chiral auxiliaries, chiral reagents, and chiral ligands in asymmetric synthesis.[1] Among the various routes that have been developed so far, the use of copper-catalyzed addition from a range of alkenes and (*N*-(*p*-toluenesulfonyl)imino)-phenyliodinane (PhI═NTs) is of particular potential.[2] The disadvantage of this aziridination procedure is the necessity of using the expensive and inconvenient PhI═NTs as the nitrenoid source.[3] The reaction of chiral 3-acetoxyamino-quinazolinone derivatives with various alkenes in the presence of Lewis acid provides aziridines with excellent diastereoselectivities.[4] The stereospecific aziridination of alkenes with chiral nitridomanganese complexes provides the desired products with high enantioselectivity.[5] Vederas et al. have reported the oxidation of *N*-aminophthalimide with lead tetraacetate in the presence of *N*-enoylbornane[10,2]-sultams, resulting in stereospecific *syn* addition to afford the corresponding *N*-phthalimidoaziridines with 33−95% de.[6] We have applied the analogous process by reacting various chiral camphor *N*-enoyl pyrazolidinones with *N*-amino-phthalimide in the presence of lead tetraacetate.[7] The desired *N*-phthalimidoaziridines were obtained with high levels of diastereoselectivities (up to >90% de) with excellent material yields (86−95%) at 0 °C in 5 min. In continuation with our work in designing novel camphor-derived ligands for asymmetric synthesis, we were intrigued by the potential of using

(1) (a) Osborn, H. M. I.; Sweeney, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1693. (b) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599.

(2) (a) Brandt, P.; Sodergren, M. J.; Andersson, P. G.; Norrby, P.-O *J. Am. Chem. Soc.* **2000**, *122*, 8013. (b) Sodergren, M. J.; Alonso, D. A.; Bedekar, A. V.; Andersson, P. G. *Tetrahedron Lett.* **1997**, *38*, 6897. (c) Muller, P.; Baud, C.; Jacquier, Y. *Tetrahedron* **1996**, *52*, 1543. (d) Harm, A. M.; Knight, J. G.; Stemp, G. *Tetrahedron Lett.* **1996**, *37*, 6189. (e) Li, Z.; Quan, R. W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5889. (f) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742. (g) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. Anderson, B. A.; Barnes, D. M. *J. Am. Chem. Soc.* **1993**, *115*, 5328. (h) Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 5326. (i) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Org. Chem.* **1991**, *56*, 6744.

(3) Sodergren, M. J.; Alonso, D. A.; Andersson, P. G. *Tetrahedron: Asymmetry* **1997**, *8*, 3563.

(4) Atkinson, R. S.; Gattrell, W. T.; Ayscough, A. P.; Raynham, T. M. *Chem. Commun*. **1996**, 1935.

(5) Minakata, S.; Ando, T.; Nishimura, M.; Ryu, I.; Komatsu, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 3392.

(6) Kapron, J. T.; Santarsiero, B. D.; Vederas, J. C. *J. Chem. Soc., Chem. Commun.* **1993**, 1074.

(7) Yang, K.-S.; Chen, K. *J. Org. Chem.* **2001**, *66*, 1676.

10.1021/ol0173073 CCC: $22.00 © 2002 American Chemical Society
Published on Web 03/08/2002

a lead tetraacetate-mediated chiral ligand for the preparation of enantiomerically enriched aziridines. The novel camphor-derived carboxylic acid containing ligands **1**−**4** (Figure 1)

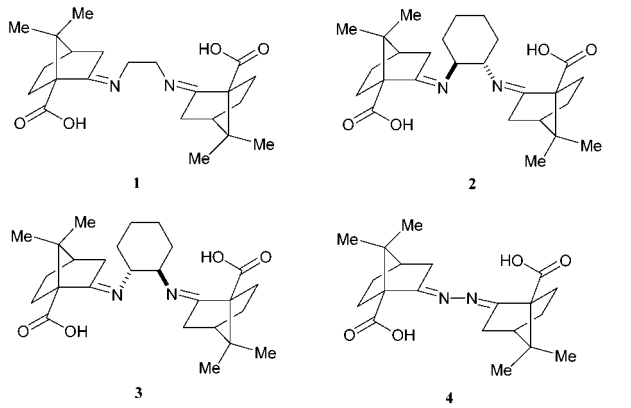


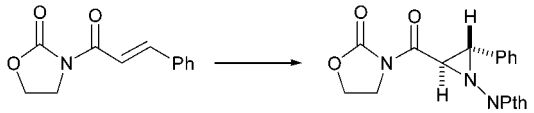
Figure 1. The structures of camphor-derived ligands **1**−**4**.

were prepared from this laboratory and were proven to be synthetically useful in catalytic synthesis.[8] In this regard, the use of lead tetraacetate complexed with enantiopure ligand might aziridinate alkene enantioselectively in the presence of *N*-aminophthalimide. The carboxylic acid moiety may serve as a good donor group by taking advantage of the oxophilic nature of lead tetraacetate. Since the aziridination takes place extremely fast (5 min at 0 °C) under these reaction conditions, the oxidative cleavage of the chiral ligand by lead tetraacetate may not interfere with the reaction.

The use of 1,3-oxazolidin-2-one as an excellent achiral template in a variety of enantioselective transformations has been documented.[9] The 3-((*E*)-3-phenyl-2-propenoyl)-1,3-oxazolidin-2-one **5a** was chosen as a probe substrate for this reaction to avoid the potential *N*-interconversion of the adduct.[7] Thus, treatment of **5a** with ligand **1** with lead tetraacetate in the presence of *N*-aminophthalimide provide the desired aziridines in excellent chemical yields (Table 1, entry 1). The relative configuration of the aziridine moiety was assigned by ^{1}H NMR spectral analysis ($^3J_{trans} = 5.2$ Hz)[10] which, however, reveals a mixture of two *N*-invertomers in a ratio of ca. 9:1. The structure of the major *N*-invertomer with the phthalimido group and the 2-carboxyl group *cis*-disposed in the aziridine ring system was confirmed by single-crystal X-ray analysis.

The stereoselectivity was determined to be 75% ee by HPLC analysis using a Daicel Chiralcel Chiralpak AD column. The use of chiral ligands **2** and **3** gave the desired

Table 1. Aziridination of 3-((*E*)-3-Phenyl-2-propenoyl)-1,3-oxazolidin-2-one **5a** with $Pb(OAc)_4$ and Chiral Ligands **1**−**4** in the Presence of *N*-Aminophthalimide[a]



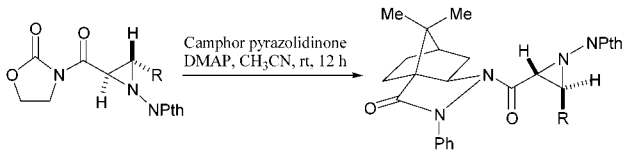
5a **6a**

entry	ligand	solvent	yield (%)[b]	% ee[c]	config
1	**1**	CH_2Cl_2	95	75	(2*R*,3*S*)
2	**2**	CH_2Cl_2	92	27	(2*R*,3*S*)
3	**3**	CH_2Cl_2	95	0	
4	**4**	CH_2Cl_2	83	95	(2*R*,3*S*)[d]
5	(+)-tartaric acid	CH_2Cl_2	80	42	(2*S*,3*R*)
6	**4**	$CHCl_3$	82	92	(2*R*,3*S*)
7	**4**	THF	85	10	(2*R*, *S*)

[a] All reactions are conducted using activated alkenes (0.46 mmol), $Pb(OAc)_4$ (0.72 mmol), chiral ligand (0.72 mmol), and *N*-aminophthalimide (0.68 mmol) in the solvent indicated at 0 °C for 5 min. [b] Isolated yield. [c] Determined by HPLC analysis using a Daicel Chiracel Chiralpak AD column. [d] Absolute stereochemistry is established by chemical correlation (see text).

aziridines in low to nil stereoselectivities with excellent material yields (entries 2 and 3). To our surprise the use of chiral ligand **4** provided **6a** in 95% ee under the same reaction conditions (entry 4). The newly generated stereogenic centers were determined to be in the (2*R*,3*S*) configuration by chemical correlations with the known aziridine.[7] Thus, treatment of aziridine **6a** with camphor pyrazolidinone (5.0 equiv; DMAP, CH_3CN, rt, 12 h; 80% yield) gave the known *N*-phthalimidoaziridine **7a** (Scheme 1). Spectroscopic

Scheme 1. Formation of Camphor Pyrazolidinone-Derived *N*-Phthalimidoaziridines **7a** and **7c**



6a R=Ph
6c R=Me

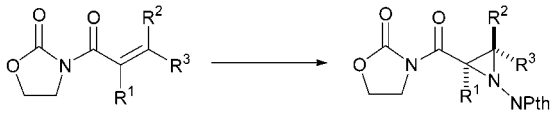
7a R=Ph (80%)
7c R=Me (75%)

data analyses (^{1}H, ^{13}C NMR) indicate that both compounds are identical, and optical rotation measurements confirm the absolute configurations ($[\alpha]_D = -86.1°$ ($c = 1$, $CHCl_3$), with a value comparable with that of a previously prepared compound: $[\alpha]_D = -88.0°$ ($c = 1$, $CHCl_3$). The use of (+)-tartaric acid gave **6a** in 42% ee, favoring the opposite stereochemistry (entry 5). Next we studied the solvent effect. The use of $CHCl_3$ provide the desired product in a comparable result while the stereoselectivity diminished significantly when THF was used (entries 6 and 7).

To further determine the feasibility of this system, various *N*-enoyl oxazolidinones **5b**−**f** were then studied under the optimum conditions, and the results are tabulated in Table

(8) Pan, J.-F.; Chen, K. *J. Mol. Catal. A: Chem.* **2001**, *176*, 19.
(9) (a) Ager, D. J.; East, M. B. *Asymmetric Synthetic Methodology*; CRC Press: Boca Raton, 1996. (b) Kobayashi, S.; Kawamura, M. *J. Am. Chem. Soc.* **1998**, *120*, 5840. (c) Gothelf, K. V.; Thomsen, I.; Jorgensen, K. A. *J. Am. Chem. Soc.* **1996**, *118*, 59. (d) Sibi, M. P.; Liu, M. *Org. Lett.* **2000**, *2*, 3393. (e) Kanemasa, S.; Kanai, T. *J. Am. Chem. Soc.* **2000**, *122*, 10710. (f) Kanemasa, S.; Oderaotoshi, Y.; Wada, E. *J. Am. Chem. Soc.* **1999**, *121*, 8675. (g) Ghosh, A. K.; Matsuda, H. *Org. Lett.* **1999**, *1*, 2157.
(10) Chilmonczyk, Z.; Egli, M.; Behringer, C.; Dreiding, A. S. *Helv. Chim. Acta* **1989**, *72*, 1095.

Table 2. Asymmetric Aziridination of Various Activated Alkenes with Chiral Ligand **4** and $Pb(OAc)_4$ in the Presence of *N*-Aminophthalimide



5b-f **6b-f**

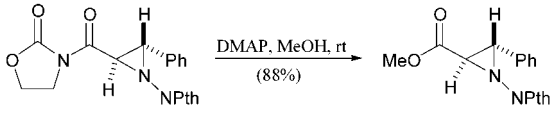
entry	substrate	*t* (min)	yield (%)[a]	% ee [b]
1	**5b**: R^1= R^2= R^3= H	5	99	80[c]
2	**5c**: R^1= R^2= H, R^3=Me	5	95	87[d]
3	**5d**: R^1= R^2= H, R^3= Pr	5	95	90
4	**5e**: R^1= Me, R^2= R^3= H	15	85	67[e]
5	**5f**: R^1= R^2= H, R^3= *p*-ClPh	10	95	83

[a] Isolated yield. [b] Determined by HPLC analysis using a Daicel Chiracel Chiralpak AD column. [c] Determined by HPLC analysis using a Daicel Chiracel OD column. [d] Based on optical measurements after converting to **7c** ($[\alpha]_D = -102.2°$ (*c* = 1, $CHCl_3$), compares with that of previously prepared sample (90% ee):[7] $[\alpha]_D = -105.4°$ (*c* = 1, $CHCl_3$) (Scheme 1). [e] The absolute stereochemistry was not determined.

2. Thus, the use of *N*-acryloylxazolidinone (**5b**) gave the desired product in 80% ee (entry 1). The β-alkyl substituent provide the desired products in high enantioselectivity (entries 2 and 3). The stereoselectivity drops when an α-substituent is present. Thus, the use of *N*-methacryloyl-oxazolidinone (**5e**) gave **6e** in 67% ee (entry 4).

The oxazolidinone moiety of the substrate plays an indispensable role in this reaction. The use of aryl acrylates and unfunctionalized olefins led either to low stereoselectivity or low chemical yield. For examples, the use of 3-phenyl-acrylic acid phenyl ester affords the desired product in 80% chemical yield (<10% ee) while the use of cyclohexene gave only a 24% yield. A detailed mechanistic speculation of this reaction is premature at this stage. The coordination of the ligand-mediated Lewis acid to the bidentate acyl oxazolidinone may account for these rersults.[9g] Work is currently underway to study this phenomenon in more detail. The achiral template can be easily cleaved under standard deacylation conditions.[11] Exposure of **6a** to MeOH and DMAP at rt provides the desired 2-carboxylaziridine **11** in 88% material yield (Scheme 2).

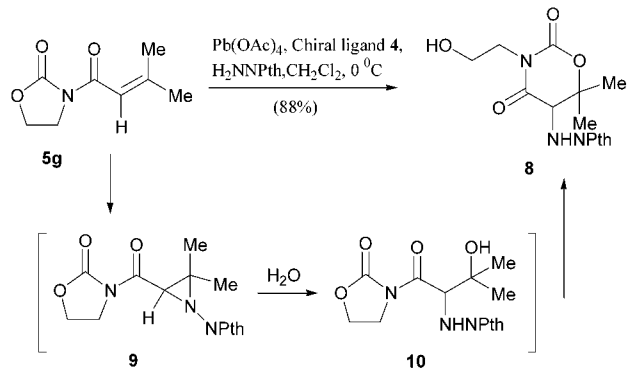
Scheme 2. Formation of 2-Carboxyaziridine **11**



6a **11**

An interesting 1,3-oxazinane-2,4-dione derivative, **8**, was isolated when a β,β-dimethyl substituent was used (**5g**: R^1 = H, R^2 = R^3 = Me). Toward this end, treatment of **5g** with chiral ligand **4**, *N*-aminophthalimide, and $Pb(OAc)_4$ in CH_2Cl_2 affords compound **8** in 88% yield. The strucutre was initially assigned by spectroscopic (^{1}H and ^{13}C NMR) and HRMS analyses and further confirmed by single crystal X-ray analysis. This was believed to proceed through the opening of the initially formed aziridine ring by a water molecule to give the corresponding amino alcohol **10**. This was, in the presence of Lewis acid, followed by attack of the tertiary alcohol on the oxazolidinone carbonyl group and subsequent oxazinanedione ring formation to provide compound **8** (Scheme 3).

Scheme 3. Formation of 1,3-Oxazinane-2,4-dione **8**



5g **8** **9** **10**

In conclusion, we have developed a simple and efficient method for the enantioselective synthesis of highly optically enriched *N*-phthalimidoaziridine adducts **6a**−**f**. The reaction takes place within 15 min at 0 °C with various *N*-enoyl oxazolidinones. Further investigations on the catalytic enantioselective version of alkenes aziridination are currently undergoing.

Acknowledgment. This work was supported by the National Science Council of the Republic of China and the National Taiwan Normal University (ORD 91-2). The X-ray crystal data were collected and processed by Taipei Instrumentation Center, College of Science (National Taiwan University), and Professor C. -H. Ueng (National Taiwan Normal University) is gratefully acknowledged.

Supporting Information Available: Experimental procedure and physical data for all new products **6a**−**f** and **8** and X-ray crystallographic data (tables of experimental details, bond lengths and angles, and ORTEP diagrams) for structures **6a**, **6c**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0173073

(11) Wang, Y.-C.; Su, D.-W.; Lin, S.-M.; Tseng, H.-L.; Li, C.-L.; Yan, T.-H. *J. Org. Chem.* **1999**, *64*, 6495.