Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 3031–3034

TETRAHEDRON LETTERS

Reagent-controlled diastereoselective aminations with a new chiral nosyloxycarbamate

Stefania Fioravanti,* Alberto Morreale, Lucio Pellacani* and Paolo A. Tardella*

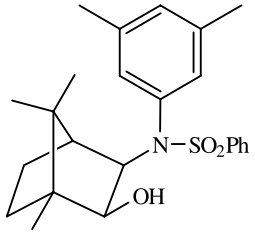
Dipartimento di Chimica dell'Università degli Studi di Roma 'La Sapienza', P. le Aldo Moro 2, I-00185 Roma, Italy

Received 14 February 2003; accepted 27 February 2003

Abstract—The synthesis of a new chiral nosyloxycarbamate derived from Helmchen's auxiliary is described. Reactions performed with this aminating reagent successfully give the formation of diastereomeric allylic carbamates or diastereomeric aziridines starting from different kinds of olefins.

Arylsulfonyloxycarbamates ($ArSO_3NHCO_2R$) are useful reagents for direct amination reactions. They are stable compounds that can be decomposed in basic media. Ethyl nosyloxycarbamate ($NsONHCO_2Et$)[1] and other similar carbamates,[2] were used either in direct electrophilic or nucleophilic aziridinations[3] of different kind of olefins.

Asymmetric C–N bond formation is an important topic in organic syntheses. Methods for reagent-controlled stereoselective amination reactions are few in number.

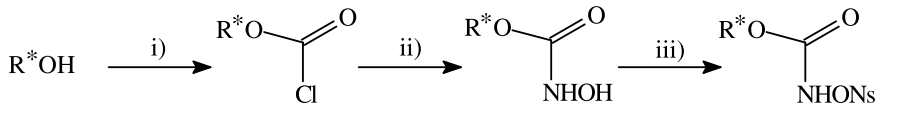


1

Figure 1.

In particular the stoichiometric aziridination of olefins has received relatively little attention.[4] Atkinson and co-workers achieved moderate to high diastereoselectivities with *N*-aminoquinazolinone derivatives.[5] Attempts to obtain chiral aziridination of styrene by (–)-bornyl nosyloxycarbamate failed under the various conditions employed.[6] Poor diastereoselectivity was recently observed in the addition reaction of chiral *N*-arylhydroxamates to prochiral olefins.[7] In the past we reported the synthesis of azidoformates derived from chiral enol ethers that gave high diastereoselective intramolecular cycloaddition[8] and also the synthesis of the optically active carbamoyl azide derived from Oppolzer's sultam affording amination reactions with satisfactory diastereoselective induction.[9]

We report here the preparation and the use of a new chiral aminating agent, obtained from the chiral Helmchen's alcohol **1** (Fig. 1). A simple synthetic sequence provides the preparation of **2**, without the need of purification at any step (Scheme 1). The chiral carbamate **2** was obtained in 81% overall yield by reaction of nosyl chloride with the hydroxycarbamate, prepared



1

2 (81% overall)

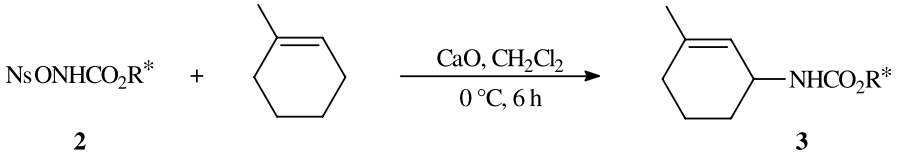
Scheme 1. *Reagents and conditions*: (i) triphosgene, pyridine, toluene, 0°C; (ii) $NH_2OH{\cdot}HCl$, K_2CO_3, Et_2O, rt; (iii) NsCl, Et_3N, Et_2O, 0°C.

* Corresponding author. Fax: +39-06-490631; e-mail: lucio.pellacani@uniroma1.it

0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00558-6

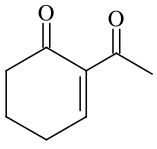
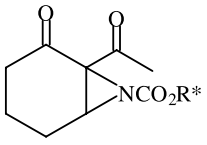
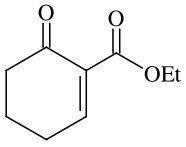
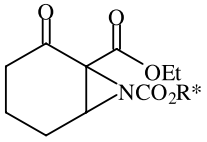
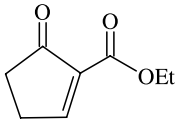
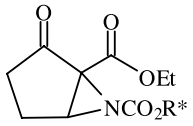
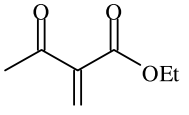
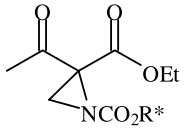
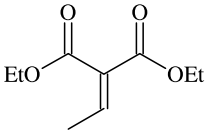
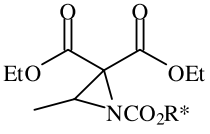
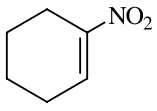
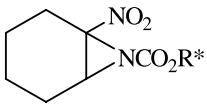
from hydroxylamine and the chloroformate of the alcohol **1**.[10]

First of all, we tested the reactivity of **2** toward electron-rich species, such as ethyl 2-methylacetoacetate[11] or 1-methylcyclohexene in the presence of calcium oxide. While the former did not give any products, and the starting material was collected in almost quantitative amounts, the expected chiral nitrene (NCO_2R^*) was trapped by 1-methylcyclohexene leading to the formation of diastereomeric allylic[12] carbamates **3** (Scheme 2) as the only products (45%) with a 30% diastereomeric excess, as showed by NMR and HPLC analyses performed on the crude reaction mixture.

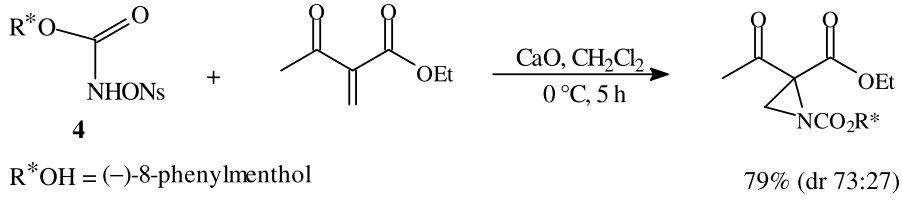


Scheme 2. Allylic amination of 1-methylcyclohexene.

Table 1. Aziridination of prochiral electron-poor olefins with **2** in CH_2Cl_2 at 0°C

Entry	Substrate	Product[a]	Substrate:CaO:**2** (molar ratio)	Yield (%)	Diastereomeric ratio (%)[b]
1			1:2.5:1.2	82	72:28
2			1:2.5:1.2	88	87:13
3			1:2.5:1.2	86	85:15
4			1:2.5:1.2	83	85:15
5			1:3:1.5	76	73:27
6			1:2:1	64	76:24

[a] All spectral data are in agreement with assigned structures.
[b] By NMR spectra and/or HPLC analyses on crude mixtures.



Scheme 3. Aziridination of ethyl 2-acetylcrotonate.

Steric hindrance probably prevents the formation of the aziridines, the main expected products,[1] and since **3** cannot derive from the aziridines themselves, it follows that the insertion reaction does indeed take place at this allylic position.

On the contrary, we observed that **2** very efficiently reacted with different prochiral electron-poor olefins, giving the expected aziridines likely by the aza-Michael pathway proposed by us.[3] The results are listed in Table 1.

With a small excess of **2**, the functionalized aziridines[13] were obtained mostly in satisfactory yields and with good diastereoselective induction, as shown by analyses of ^{1}H and ^{13}C NMR spectra of the crude reaction mixtures. Best results both for chemical yields and diastereomeric inductions were obtained on β-oxo enoates (entries 2–4).

Another chiral nosyloxycarbamate **4** obtained in 78% overall yield from (−)-8-phenylmenthol[14] through the procedure depicted above for **2**, successfully aziridinates ethyl 2-acetylcrotonate (Scheme 3).

At the best of our knowledge, these are the first examples reporting the successful use of chiral carbamates giving asymmetric amination reactions. Owing to the biological and synthetic importance of optical active aziridines,[15] examples of stereoselective reagent-controlled amination here reported are interesting and very promising for direct formation of chiral C–N bonds.

Acknowledgements

This research was carried out within the framework of the National Project 'Stereoselezione in Sintesi Organica. Metodologie ed Applicazioni', supported by the Italian Ministero dell'Istruzione dell'Università e della Ricerca (MIUR) and by the Università degli Studi di Roma 'La Sapienza'.

References

1. Lwowski, W.; Maricich, T. J. *J. Am. Chem. Soc.* **1965**, *87*, 3630–3637.
2. Greck, C.; Bischoff, L.; Girard, A.; Hajicek, J.; Genêt, J. P. *Bull. Soc. Chim. Fr.* **1994**, *131*, 429–433.
3. Fioravanti, S.; Pellacani, L.; Stabile, S.; Tardella, P. A.; Ballini, R. *Tetrahedron* **1998**, *54*, 6169–6176.
4. For a recent review, see: Faul, M. M.; Evans, D. A. In *Asymmetric Oxidation Reactions*; Katsuki, T., Ed.; Oxford University Press: Oxford, 2001; pp. 115–128.
5. Atkinson, R. S. *Tetrahedron* **1999**, *55*, 1519–1559.
6. Banks, M. R.; Blake, A. J.; Cadogan, J. I. G.; Dawson, I. M.; Gosney, I.; Grant, K. J.; Gaur, S.; Hodgson, P. K. G.; Knight, K. S.; Smith, G. W.; Stevenson, D. E. *Tetrahedron* **1992**, *48*, 7979–8006.
7. Aires-de-Sousa, J.; Prabhakar, S.; Lobo, A. M.; Rosa, A. M.; Gomes, M. J. S.; Corvo, M. C.; Williams, D. J.; White, A. J. P. *Tetrahedron: Asymmetry* **2001**, *12*, 3349–3365.
8. de Santis, M.; Fioravanti, S.; Pellacani, L.; Tardella, P. A. *Eur. J. Org. Chem.* **1999**, 2709–2711.
9. Del Signore, G.; Fioravanti, S.; Pellacani, L.; Tardella, P. A. *Tetrahedron* **2001**, *57*, 4623–4627.
10. *General synthetic procedure*. To a solution of triphosgene (6.0 mmol; **CAUTION**: toxic if inhalated or swallowed) in 40 mL of anhydrous toluene, commercially available alcohol **1** (4.0 mmol) and freshly distilled pyridine (6.0 mmol) were added in 1 h at 0°C. The solution was stirred for 24 h. After filtration, toluene was removed under reduced pressure and the chloroformate was obtained as a white solid in quantitative yield after crystallization from pentane. This product (4.0 mmol) was stirred for 24 h in diethyl ether in the presence of hydroxylamine hydrochloride (4.0 mmol), K_2CO_3 (4.0 mmol) and 80 μl of H_2O. After dilution with additional 100 mL of diethyl ether, the solution was filtered and dried over Na_2SO_4. Solvent removal gave the corresponding hydroxycarbamate (97% yield, white solid) that was reacted with equimolar amounts of nosyl chloride and freshly distilled triethylamine in anhydrous diethyl ether at 0°C. The chiral nosyloxy carbamate **2** was obtained in 83% yield as a pale yellow solid and stored at −20°C under argon. Mp: 118–119°C (from pentane); $[\alpha]_D = +7.69$ (*c* 3.9, $CHCl_3$); IR ($CHCl_3$): 3496, 1771, 1537 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.62 (s, 3H), 0.79 (s, 3H), 0.85 (s, 3H), 1.13–1.38 (m, 2H), 1.40–1.55 (m, 1H), 1.55–1.72 (m, 1H), 1.80 (d, $J = 4.5$ Hz, 1H), 1.96 (s, 3H), 2.29 (s, 3H), 3.76 (d, $J = 6.9$ Hz, 1H), 4.88 (d, $J = 6.9$ Hz, 1H), 5.63 (s, 1H), 6.80 (s, 1H), 7.02 (s, 1H), 7.23–7.34 (m, 4H), 7.41–7.58 (m, 1H), 8.19–8.34 (m, 4H), 8.89 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.8, 20.6, 21.1, 21.3, 27.4, 31.8, 47.3, 48.3, 50.2, 67.1, 84.5, 123.9, 128.1, 128.4, 129.4, 131.2, 131.6, 132.6, 136.5, 138.1, 139.0, 150.9, 155.1. ESI MS *m*/*z* 658 (M^++1).
11. This compound easily reacted with $NsONHCO_2Et$. See: Fioravanti, S.; Morreale, A.; Pellacani, L.; Tardella, P. A. *Tetrahedron Lett.* **2001**, *42*, 1171–1173.
12. For a recent review of allylic amination, see: Johannsen, M.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689–1708.

13. *General aziridination procedure*. To a stirred solution of the substrate (2.0 mmol) in CH_2Cl_2, CaO and **2** were added batchwise at 0°C in the ratio reported in Table 1. Upon completion (3–6 h) the crude mixture was diluted with 10 mL of CH_2Cl_2 and filtered. After solvent evaporation under reduced pressure, the residue was purified by flash chromatography on silica gel (70:30, hexane/ethyl acetate). The aziridines reported in entry 1 were obtained as pure distereomers by HPLC separation (80:20, hexane/ethyl acetate). Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.54 (s, 3H), 0.65 (s, 3H), 0.95 (s, 3H), 1.05–1.71 (m, 7H), 1.74 (d, $J=3.9$ Hz, 1H), 1.81–2.46 (m, 2H), 1.98 (s, 3H), 2.39 (s, 3H), 2.51 (s, 3H), 2.72–2.90 (m, 1H), 3.42 (s, 1H), 3.84 (d, $J=6.9$ Hz, 1H), 5.05 (d, $J=6.9$ Hz, 1H), 5.54 (s, 1H), 6.82 (s, 1H), 7.10 (s, 1H), 7.20–7.51 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5, 17.7, 20.8, 21.5, 23.5, 28.0, 30.5, 32.2, 38.3, 47.3, 47.9, 48.3, 50.1, 51.8, 67.4, 85.1, 127.8, 128.0, 129.1, 132.1, 137.1, 137.8, 157.8, 199.4, 200.9; ESI MS m/z 594 (M^++1).
14. Recently we reported that both (–)-8-phenylmenthol and Helmchen's alcohol are valuable chiral auxiliaries. See: Fioravanti, S.; Morreale, A.; Pellacani, L.; Tardella, P. A. *J. Org. Chem.* **2002**, *67*, 4972–4974.
15. For recent reviews, see: (a) Dodd, R. H. *Molecules* **2000**, *5*, 293–298; (b) McCoull, W.; Davis, F. A. *Synthesis* **2000**, 1347–1365.