Pergamon

Tetrahedron Letters 39 (1998) 8499–8502

TETRAHEDRON LETTERS

Palladium(0) Catalysed Rearrangements of Allylic Sulfoximines to Allyl Sulfinimidic Acid Esters and Optically Active *N*-Cbz Protected γ-Amino-Enones#

Stephen G. Pyne*, Dorothy M. David and Zemin Dong

Department of Chemistry, University of Wollongong, Wollongong, NSW, 2522, Australia.

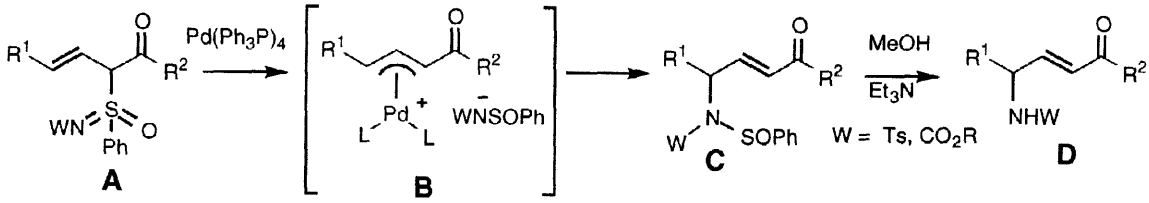
Received 22 July 1998; accepted 1 September 1998

Abstract

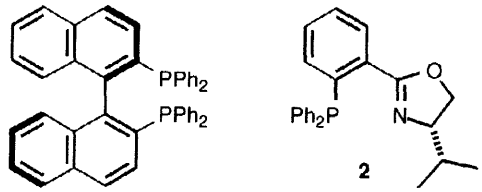
N-Tosyl allylic sulfoximines undergo rearrangement to allyl sulfinimidic acid esters in the presence of bidentate chiral ligands while *N*-Cbz allylic sulfoximines give optically active *N*-Cbz protected γ-amino-enones.

Keywords: asymmetric synthesis, palladium and compounds, sulfoximines, rearrangements

We recently reported a general method for the preparation of racemic γ-amino α,β-unsaturated ketones **D** *via* the palladium(0) catalysed rearrangement of racemic α-keto-allylic sulfoximines **A** to α-keto-allylic sulfinamides **C** [1,2].



In principle this methodology can be extended to the catalytic asymmetric synthesis of enantiomerically enriched γ-amino α,β-unsaturated ketones by the use of chiral ligands for palladium(0) [3]. We report here our studies on the reactions of α-keto-allylic sulfoximines with palladium(0) in the presence of the chiral ligands (*R*)-BINAP **1** and the chiral phosphino-oxazoline **2** [4].

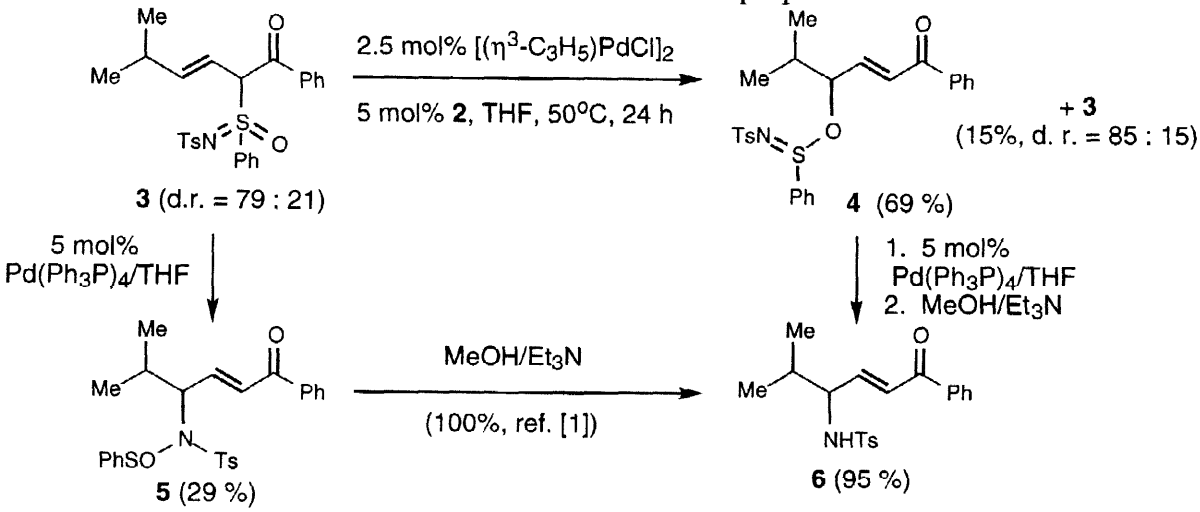


(*R*)-BINAP **1** **2**

This paper is dedicated to Prof. E. J. Corey on the occasion of his 70th birthday.

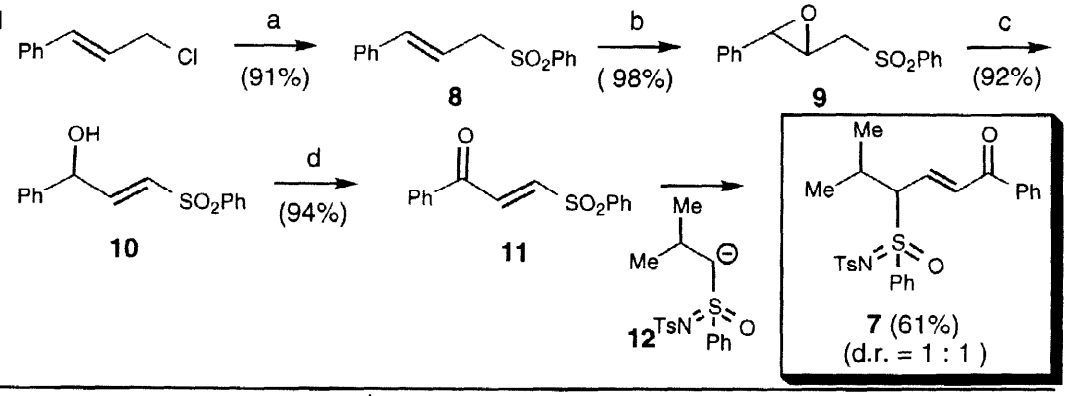
0040-4039/98/$ - see front matter
PII: S0040-4039(98)01847-4

In contrast to the chemistry described above using $Pd(Ph_3P)_4$ as catalyst, that normally takes 15-30 min at RT, the reactions of **3** with the catalysts formed *in situ* from either $Pd_2(dba)_3.HCCl_3$ and **1** or $[(\eta^3\text{-}C_3H_5)PdCl]_2$ and **2** required long reaction times (24 h) and/or heating at 50°C. Treatment of the racemic **3** (d. r. = 79 : 21) with the catalyst formed *in situ* from 2.5 mol% $[(\eta^3\text{-}C_3H_5)PdCl]_2$ and 5 mol% **2**, according to the method of Pfaltz [4], at 50°C in a sealed tube gave, surprisingly, not the expected rearrangement product **5** but the racemic (specific rotation was zero) benzenesulfinimidic acid ester **4** in 69% yield after chromatography. A small amount (15%) of the starting compound **3** was also isolated as a mixture of diastereomers (d.r. = 85 : 15). Such an allylic sulfoximine to allyl sulfinimidic acid ester rearrangement has not been reported before. Gais, however, has suggested an allyl sulfinimidic acid ester intermediate to explain the thermal rearrangement of an allylic sulfoximine to its isomeric allylic sulfinamide without a 1,3-allylic shift [5]. The structure of **4** was evident when a comparison was made between the NMR spectra of **4** and its isomeric sulfinamide **5** and sulfoximine **7**. The sulfoximine **7** was prepared as shown in Scheme 1.



Cinnamyl chloride was converted to the sulfone **8** which underwent epoxidation to the epoxy-sulfone **9** in 89% overall yield. Treatment of **9** with ^{t}BuOK/THF gave the γ-hydroxy-sulfone **10** that underwent oxidation with Jones reagent to the β-sulfonyl-enone **11** [6]. Addition of a THF solution of **11** to a THF solution of lithiated **12** at -78°C followed by warming to 0°C gave compound **7** as a 1:1 mixture of diastereomers. One diastereomer of **7** crystallised pure from EtOAc/hexane. The NMR data of this compound is given in Table 1.

Scheme 1



[a] $PhSO_2Na$ (1.2 equiv,) DMF, RT, 16h; [b] *m*-CPBA (1.1 equiv.)/CH_2Cl_2 0°C-RT, 48h; [c] ^{t}BuOK (0.1equiv)/THF, 0°C, 2h ; [d] Jones oxidation;

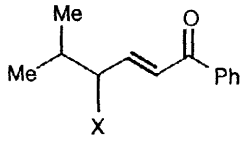
A comparison of the ^{1}H and ^{13}C NMR chemical shifts for H4 and C4, respectively, for compounds **4**, **5** and **7** are shown in Table 1. Clearly H4 and C4 in compound **4** come significantly further downfield from those respective resonances in the isomeric compounds the sulfinamide **5** and sulfoximine **7**. Such downfield chemical shifts are consistent with resonances from a proton or carbon atom having an oxygen substituent rather than a sulfur or nitrogen substituent. Further evidence for the structure **4** came from a comparison of the IR spectra (nujol) of **4** and **7**. The latter compound showed typical sulfoximine stretching bands at 1219 and 1150 cm^{-1} while the IR of **4**, in this particular region, showed only a band at 1149 cm^{-1}. Interestingly, treatment of **4** or **7** with 5 mol% of $Pd(Ph_3P)_4$, followed by treatment of crude reaction mixture with $MeOH/Et_3N$ gave the *N*-tosyl γ-amino enone **6** in 95% and 68% overall yields, respectively.

When the reactions of **3** and **7** with 5 mol% of $Pd(Ph_3P)_4$ were performed in d_8-THF and monitored by ^{1}H NMR only compounds **5** and **13** could be seen to be increasing in concentration with time and no **4** could be detected. This result suggested that if **4** was being formed in these reactions then it was only a transient intermediate and was rapidly being converted to **5**.

Table 1. NMR data of compounds **4**, **5** and **7**

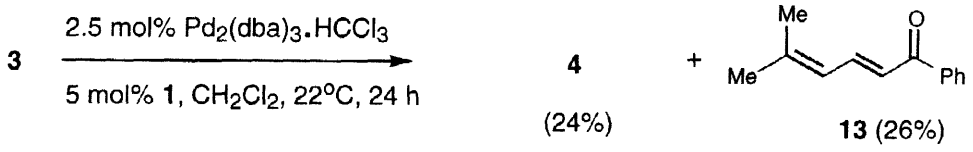
Compound	^{1}H NMR[a] (H4)	^{13}C NMR[a] (C4)
4	4.93	84.8
5	3.85	61.2
7	4.17	75.8

[a] chemical shifts in ppm from TMS in $CDCl_3$ solution.

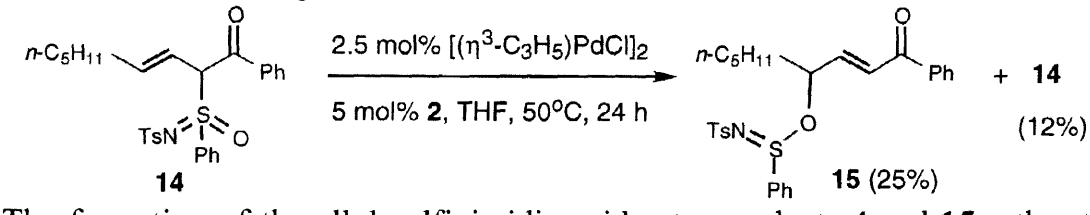


4; X = TsN=S(Ph)O-
5; X = Ts(PhSO)N-
7; X = Ph(NTs)S(O)-

When (*R*)-BINAP **1** was employed as the ligand the reaction proceeded at 22°C and compound **4** was again isolated, albeit in poorer yield (24%), along with the elimination product **13** (26 % yield).

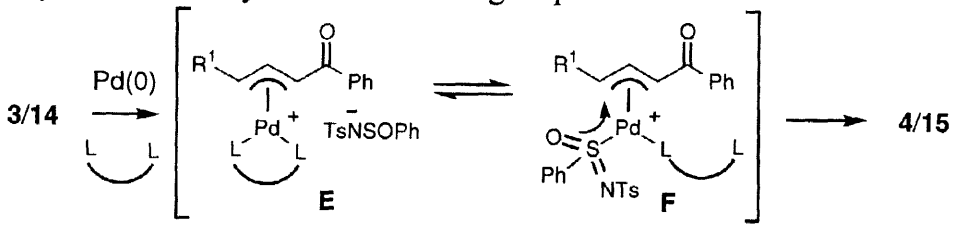


The racemic α-keto-allylic sulfoximine **14** underwent a similar rearrangement reaction as **3** using the chiral ligand **2** and gave the sulfinimidic acid ester **15** in 25% isolated yield along with recovered starting **14** (12%).

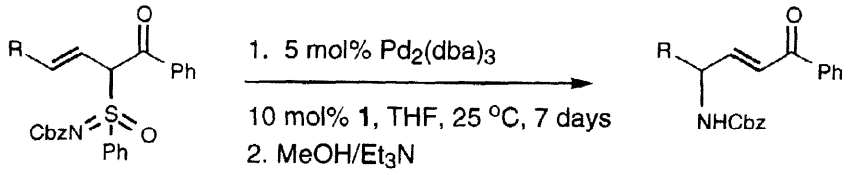


The formation of the allyl sulfinimidic acid ester products **4** and **15** rather than the expected products arising from the well established allylic sulfoximine to allylic sulfinamide rearrangement can be rationalized in the following scheme. It is possible that when a bidentate ligand like **1** or **2** is employed rather than triphenylphosphine then there is an equilibrium between the complexes **E** and **F**. In the latter complex the ambident sulfinamide

anion acts as a ligand to palladium through the softer sulfur atom rather than the harder oxygen or nitrogen atoms. Complex **F** would more likely be favoured when the ligand **2** is used since the *N*-donor group would be expect to dissociate more readily from the palladium than a *P*-donor group. Intramolecular delivery of the sulfinamide anion as an oxygen centred anion to the allyl cation moiety in **F** would then give products **4** and **15**.



In contrast to **3** and **14**, their *N*-Cbz analogues **16** and **17** were recovered unchanged when treated with 2.5 mol% $[(\eta^3\text{-}C_3H_5)PdCl]_2$ and 5 mol% **2** at 50°C in a sealed tube for 24 h. These compounds however could be converted to their desired *N*-Cbz protected γ-amino-enones **18** and **19** respectively, *via* their rearranged sulfinamides, using 10 mol% Pd(0)/(*R*)-BINAP over 7 days. The *N*-Cbz protected γ-amino-enone **18** was obtained in poor yield (28%) in 62% enantiomeric excess from chiral HPLC analysis (Chiracel OD or OD-H column, 4.5 mm I. D., 15% 2-propanol/hexane, 0.5 mL/min) while **19** was obtained in good yield (69%) but with a poor enantiomeric excess (20% ee).



16 (R = Me_2CH-)
17 (R = *n*-C_5H_{11}-)

18 (R = Me_2CH-) 28%, ee 62%
19 (R = *n*-C_5H_{11}-) 69%, ee 20%

In conclusion, we have found a novel palladium(0) catalysed allylic sulfoximine to allyl sulfinimidic acid ester rearrangement using bidentate ligands and demonstrated the potential of preparing optically active *N*-Cbz protected γ-amino-enones from racemic α-keto-allylic sulfoximines using palladium(0) catalysis in the presence of chiral ligands. We are currently searching other ligands to enhance the efficiency and enantioselectivities of these reactions.

Acknowledgment: We thank the Australian Research Council for financial support and for a DIST grant for SP to visit Prof. Pfaltz's laboratories at Muelheim and Andreas Pfaltz and his research group for their hospitality, especially Karin Radkowski for her technical assistance.

References

[1] David, D. M.; O'Meara, G. W.; Pyne, S. G. Tetrahedron Lett.; 1996; 37: 5417.
[2] Pyne, S. G.; O'Meara, G. W.; David, D. M. Tetrahedron Lett.; 1997; 38: 3623.
[3] For other procedures for preparing these compounds in optically active form see: Ikota, N. Heterocycles; 1995; 41: 983. Wei, Z. Y.; Knaus, E. E. Org. Prep. & Proc. Int; 1994; 26: 243. Maryanoff, B. E.; Greco, M. N.; Zhang, H.-G.; Andrade-Gordon, P.; Kauffman, J. A.; Nicolaou, K. C.; Liu, A.; Brungs, P. H. J. Am. Chem. Soc; 1995; 117: 1225. Reetz, M. T.; Rohrig, D. Angew. Chem., Int. Ed. Engl.;1989; 28: 1706. Enders, D.; Bettray, W. Pure Appl. Chem.; 1996; 68: 569.
[4] von Matt, P.; Pfaltz, A. Angew. Chem., Int. Ed.; 1993; 32: 566. Sprinz, J.; Helmchen, G. Tetrahedron Lett.; 1993; 34: 1769. Frost, C. G.; Williams, J. M. J. Tetrahedron Lett.; 1993; 34: 2015.
[5] Gais, H.-J. Scommoda, M., Lenz, D. Tetrahedron Lett.; 1994; 35: 7361.
[6] For related procedures see: Haynes, R. K.; Vonwiller, S. C.; Stokes, J. P.; Merlino, L. M. Aust. J. Chem.; 1988; 41: 881.