Tetrahedron Letters,Vol.28,No.37,pp 4331-4334,1987
Printed in Great Britain

0040-4039/87 $3.00 + .00
Pergamon Journals Ltd.

DIASTEREOSELECTION IN TRIMETHYLSILYL TRIFLUOROMETHANESULPHONATE CATALYZED REACTION OF SILYL KETENE ACETALS WITH IMINES

Giuseppe Guanti,* Enrica Narisano, and Luca Banfi

Istituto di Chimica Organica dell'Università, Centro CNR di Studio sui Diariloidi,

Corso Europa 26, I-16132 Genova (Italy)

Summary: The trimethylsilyl trifluoromethanesulphonate catalyzed condensation of silyl ketene acetals with imines afforded β-amino esters with prevalent anti relative diastereoselectivity (up to 100%). Some anti β-amino esters have been then cyclized to trans β-lactams.

β-Lactams are compounds of primary importance as they are components of many naturally occurring antibiotics, such as penicillins, cephalosporins, monobactams, thienamycin, etc.. Consequently, many efforts have been done in these last years to develop new strategies in the construction of azetidinone ring.[1] An effective and straightforward route is based on the condensation between imines and carboxylic acid derivatives. Recently, we studied this type of approach in the synthesis of β-lactams, using both Bose's[2] and strongly basic conditions.[3] Our interest in acid catalyzed aldol condensation of silyl ketene acetals[4] has now prompted us to study the synthesis of β-lactams also under acidic conditions using trimethylsilyl trifluoromethanesulphonate (TMSTf) as catalyst. Some data on the acid catalyzed condensation of silyl ketene acetals with imines have been published, but they are quite scanty and mainly concern the use of $TiCl_4$[5 - 7] and ZnI_2[8] as catalyst. We were particularly interested in the use of TMSTf because, differently from $TiCl_4$ and ZnI_2, it can be used in true catalytic amount and moreover no information are known on the stereochemical outcome of its catalysis in this reaction.[9, 10].

SCHEME 1

1 2 *syn*-3 *anti*-3

a: R = R^1 = R^2 = Ph
b: R = Ph, R^1 = $Me_2Bu^tSiC{\equiv}C$, R^2 = p-$MeOC_6H_4$
c: R = Ph, R^1 = PhCH=CH, R^2 = p-$MeOC_6H_4$
d: R = Me, R^1 = R^2 = Ph
e: R = Me, R^1 = $Me_2Bu^tSiC{\equiv}C$, R^2 = p-$MeOC_6H_4$

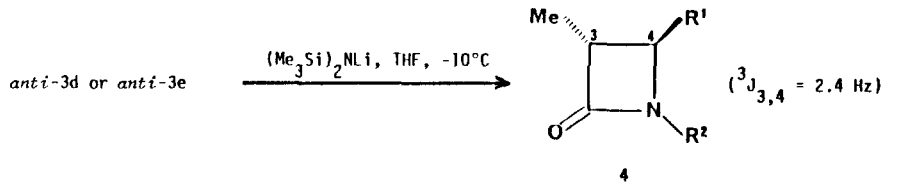
TABLE

Entry	R	*E* : *Z* ratio[a] in 1	R^1	R^2	Solvent (T/°C)	[1] : [2]	Yield[b]/%	*syn* : *anti* ratio[c] in 3
1	Ph	36 : 64	Ph	Ph	CH_2Cl_2 (-65)	1 : 1	85	14 : 86
2	Ph	36 : 64	$Me_2Bu^tSiC{\equiv}C$	p-$MeOC_6H_4$	CH_2Cl_2 (-65)	1 : 1	69	45 : 55
3	Ph	36 : 64	PhCH=CH	p-$MeOC_6H_4$	CH_2Cl_2 (-20)	1 : 1	~20	n.d.[d]
4	Ph	36 : 64	PhCH=CH	p-$MeOC_6H_4$	THF (-20)	1 : 1	~30	n.d.[d]
5[e]	Ph	36 : 64	PhCH=CH	p-$MeOC_6H_4$	THF (-65)	1 : 1	~20	n.d.[d]
6	Ph	36 : 64	PhCH=CH	p-$MeOC_6H_4$	THF (-65)	1.5 : 1	45	15 : 85
7	Ph	36 : 64	PhCH=CH	p-$MeOC_6H_4$	THF (-65)	2 : 1	78	15 : 85
8	Me	75 : 25	Ph	Ph	CH_2Cl_2 (-65)	1 : 1	85	0 :100
9	Me	75 : 25	$Me_2Bu^tSiC{\equiv}C$	p-$MeOC_6H_4$	CH_2Cl_2 (-65)	1 : 1	65	37 : 63

[a]Determined by ^{1}H n.m.r. spectroscopy; see R.E. Ireland, R.H. Mueller, A. K. Willard, *J. Am. Chem. Soc.*, 98, 2868 (1976). [b]Based on isolated chromatographically pure 3. [c]Determined by ^{1}H n.m.r. spectroscopy. [d]n.d. = not determined. [e]A stoichiometric amount of TMSTf was used.

Our report deals with the acid catalyzed condensation between two different silyl ketene acetals (with different geometry at C-C double bond) and some non-enolizable imines under different conditions (Scheme 1 and Table). The reaction afforded in acceptable to good chemical yield[11] the β-amino-esters, with sometimes quite high diastereoselection (entry 1, 7 - 8). The predominant isomer is always the anti one, unregarding the stereochemistry of starting silyl ketene acetal (cfr. entry 1 and 8), though the anti selectivity is slightly better when the silyl ketene acetal has predominant E configuration. The stereochemistry of products was established on the base of vicinal coupling constant $^3J_{2,3}$ ($J_{anti} > J_{syn}$),[6, 12] and confirmed by cyclizing some anti β-amino esters to trans β-lactams in 70-80% yield (Scheme 2).

SCHEME 2



4

A preferential anti induction has been reported to occur both in $TiCl_4$[6] and ZnI_2[8] reaction of silyl ketene acetals with imines, while the reversed selectivity takes place in TMSTf catalyzed condensation of enol silyl ethers with acetals[13] and disagreeing results have appeared on reactions with carbonyl compounds:[14] at this stage, it seems difficult to propose a single reaction model that can hold for quite different combinations of reactants and conditions. Further investigations aimed at elucidating the nature of the transition state and the applications of this reaction to the synthesis of biologically important β-lactams are actively in progress in our laboratory.[15]

Experimental: Imine was dissolved in the appropriate solvent and added with the silyl ketene acetal, cooled to -70°C, and TMSTf (0.1 mmol/mmol of imine) was added. After 15 h the reaction was quenched with water, 10% aqueous NH_4OH was added to basic pH, and reaction mixture extracted with MeCOOEt. The crude product (obtained after usual work-up) was subjected to silica gel chromatography (petroleum ether - Et_2O) to give the pure β-amino ester. β-Amino ester 3d (or 3e), as a pure anti diastereomer, was dissolved in dry THF and added to a 0.5 M THF solution of $(Me_3Si)_2NLi$ at -10°C under inhert athmosphere (N_2). After 30 min., quenching the reaction with saturated aqueous NH_4Cl, usual work-up (MeCOOEt, Na_2SO_4), and silica gel chromatography (petroleum ether - Et_2O) afforded trans β-lactam.[16] Under similar conditions, both syn β-amino ester 3e and anti β-amino esters 3a and 3b failed to undergo cyclization.

Aknowledgements: We wish to thank Mr. Andrea Grassi for his technical assistance.

REFERENCES AND NOTES

1) W. Durckheimer, J. Blumbach, R. Lattrell, K.H. Scheunemann, Angew. Chem. Int. Ed. Engl., 24, 180 (1985); M.J. Miller, Acc. Chem. Res., 19, 49 (1986).

2) G. Guanti, L. Banfi, E. Narisano, S. Thea, J. Chem. Soc., Chem. Commun., 1984, 861 and references therein.

3) G. Guanti, L. Banfi, E. Narisano, C. Scolastico, E. Bosone, Synthesis, 1985, 609 and references therein; E. Baldaro, L. Banfi, G. Guanti, E. Narisano, unpublished results, presented at "XVI Convegno Nazionale della Divisione di Chimica Organica dalla S.C.I.", Urbino (Italy), 7-12/9/1986.

4) G. Guanti, L. Banfi, E. Narisano, Tetrahedron Lett., 26, 3517 (1985).

5) I. Ojima, S. Inaba, K. Yoshida, Tetrahedron Lett., 21, 2077, 2081 (1980).

6) C. Gennari, I. Venturini, G. Gislon, G. Schimperna, Tetrahedron Lett., 28, 227 (1987).

7) J.-E. Dubois, G. Axiotis, Tetrahedron Lett., 25, 2143 (1984); G. Cainelli, M. Contento, A. Drusiani, M. Panunzio, L. Plessi, J. Chem. Soc., Chem. Commun., 1985, 240.

8) E.W. Colvin, D.G. McGarry, J. Chem. Soc., Chem. Commun., 1985, 539.

9) T. Morimoto, M. Sekiya, Chem. Lett., 1985, 1371.

10) Some related works dealing with synthetic equivalents of imines have appeared [K.Ikeda, K. Achiwa, M. Sekiya, Tetrahedron Lett., 24, 916, 4707 (1983); K. Okano, T. Morimoto, M. Sekiya, J. Chem. Soc., Chem. Commun., 1984, 883], but stereochemical aspects have not been studied.

11) In the case of 3c low yields were observed (entries 3,4), probably due to the low solubility of the corresponding imine both in CH_2Cl_2 and THF. A stoichiometric amount of TMSTf was useless (entry 5), while an increase in molecular ratio [1] : [2] (entries 6, 7) improved the chemical yield up to 78%, without affecting diastereoselectivity.

12) Coupling constant $^3J_{2,3}$ for **3a - e** are as follow: syn-**3a**: 8.0 Hz; anti-3a: 9.9 Hz; syn-**3b**: 7.7 Hz; anti-3b: 8.7 Hz; syn-3c: 7.4 Hz; anti-3c: 8.8 Hz; anti-3d: 7.3 Hz; syn-**3e**: 4.8 Hz; anti-**3e**: 7.6 Hz.

13) S. Murata, M. Suzuki, R. Noyori, J. Am. Chem. Soc., 102, 3248 (1980).

14) T.H. Chan, T. Aida, P.W.K. Lau, V. Gorys, D.N. Harpp, Tetrahedron Lett., 1979, 4029; J.-E. Dubois, G. Axiotis, E. Bertounesque, Tetrahedron Lett., 25, 4655 (1984); T. Hvidt, O.R. Martin, W.A. Szarek, Tetrahedron Lett., 27, 3807 (1986); C.H. Heathcock, S.K. Davidsen, K.T. Hug, L.A. Flippin, J. Org. Chem., 51, 3027 (1986) and references therein; see also ref. 4.

15) The synthesis of a thienamycin model is reported in the following paper.

16) Yields referred to isolated chromatographic pure componds and have not been optimized. Satisfactory analytical and spectral data were obtained on each isolated synthetic intermediate.

(Received in UK 9 June 1987)