Pergamon

Tetrahedron Letters, Vol. 37, No. 36, pp. 6573-6574, 1996
Copyright © 1996 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)01402-5

Diastereoselective 1,3-Dipolar Cycloaddition of Sm(III)-Azomethine Ylides to α,β-Unsaturated Esters

Carlos Alvarez-Ibarra*, Aurelio G. Csákÿ, M. Martínez and M. Luz Quiroga

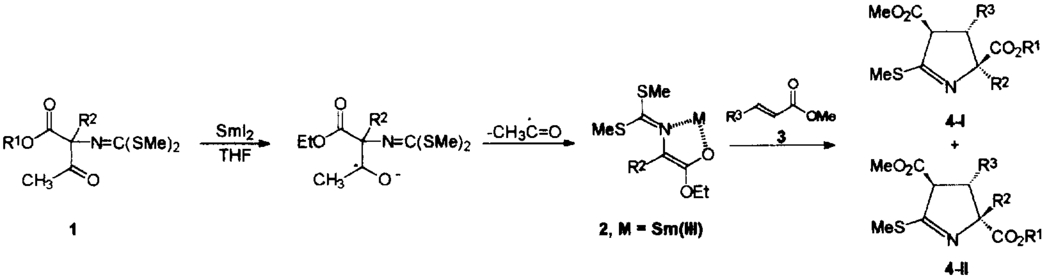
Departamento de Química Orgánica I, Facultad de Química, Universidad Complutense. 28040 - Madrid

Abstract: Sm(III)-Azomethine ylides were generated by fragmentation of the iminodithiocarbonates **1** with SmI_2 in THF. 1,3-Dipolar cycloaddition of these species with α,β-unsaturated esters **3** afforded the highly functionalized 2-methylthio-Δ^1-pyrrolines **4** with good yields and diastereoselectivities.

The 1,3-dipolar cycloaddition of metallo-azomethine ylides to electron deficient alkenes has found wide use in the asymmetric synthesis of functionalized five-membered nitrogen-containing heterocyclic rings.[1] However, no lanthanide reagents have been yet used to date in this arena[2] despite the favourable coordination abilities of these large cations.

2-Methylthio-Δ^1-pyrrolines are becoming important as key steps in the preparation of pharmaceutically relevant targets.[3] In connection with the implications of conformational constraints in the response of biologically active molecules,[4] we have been interested in the introduction of asymmetric quaternary centres[5] in these heterocycles.

We report herein the generation of the Sm(III)-azomethine ylides **2** and their 1,3-dipolar cycloadditions with α,β-unsaturated esters **3** to yield the highly functionalized 2-methylthio-Δ^1-pyrrolines[7] **4** (Scheme, Table). Initial single electron transfer from SmI_2 to the ketone group of iminodithiocarbonates[6] **1** should give rise to a radical anion. Unimolecular fragmentation of this species should be thermodynamically favoured as a consequence of aza-allylic resonance stabilisation of ylides **2**. This reaction constitutes a novel application of SmI_2 in organic synthesis.[2]



Scheme

Table. 1,3-Dipolar Cycloaddition of Azomethine Ylides **2** with Esters **3**

No.	R^1	R^2	R^3	**1**	**2, M = Sm (III)**	**3**	**4**	**4-I: 4-II**[a] (%)[b]
1	Et	CH_3	CH_3	**1a**	**2a**	**3a**	**4a**	90 : 10 (90)
2	Et	CH_3	^{t}Bu	**1a**	**2a**	**3b**	**4b**	90 : 10 (85)
3	Et	CH_3	$PhCH_2$	**1a**	**2a**	**3c**	**4c**	95 : 05 (70)
4	Et	$PhCH_2$	CH_3	**1b**	**2b**	**3a**	**4e**	90 : 10 (80)
5	Et	$PhCH_2$	^{t}Bu	**1b**	**2b**	**3b**	**4f**	95 : 05 (80)
6	CH_3	Ph	CH_3	**1c**	**2c**	**3a**	**4d**	60 : 40 (55)

(a) Determined by integration of the ^{1}H-NMR spectra ($CDCl_3$, 300 MHz) of the crude reaction products.
(b) Pure isolated yields.

Treatment of compounds **1** with 0.1 M SmI_2 in THF (1.0 eq) in the presence of the esters **3** (1.5 eq, rt, 2 h) gave rise to compounds **4** as a mixture of two diastereomers.[8] The *E* geometry of the starting esters was retained in the cycloaddition products **4** (3,4-*anti*). High diastereoselectivities in favour of isomers **4I** (R^2,R^3-*syn*) were observed in all cases except for R^1 = Me and R^2 = Ph (Table 1, entry 6). A slight drop in yield was noticed upon increasing the steric volume of either R^2 or R^3.

It is worth mentioning that the corresponding alkaline enolates of **2a** (M = Li, K), generated by enolization of ethyl N-[Bis(methylthio)methylene]alaninate with LDA or KO^{t}Bu (THF, -78°, 1 h), gave rise to complex mixtures of Michael addition products and pyrrolines **4** with poor diastereoselectivities[9] in their reaction with esters **3**.

Further research and synthetic development of these findings is under progress and will be published in due course.

Acknowledgements: The Dirección General de Investigación Científica y Técnica (Project PB93-0025) is gratefully acknowledged for finantial support.

References and Notes:

1. See for example: (a) Waldmann, H.; Bläser, E.; Jansen, M.; Letschert, H. P. *Chem. Eur. J.* **1995**, *1*, 150-154. (b) Barr, D. A.; Dorriti, M. J.; Grigg, R.; Hargreaves, S.; Malone, J. F.; Montgomery, J.; Redpath, J.; Stevenson, P., Thornton-Pett, M. *Tetrahedron* **1995**, *51*, 273-294. (c) Grigg, R. *Tetrahedron Asymm.* **1995**, *6*, 2475-2486. (d) Galley, G.; Liebscher, G.; Pätzel, M. *J. Org. Chem.* **1995**, *60*, 5005-5010 and therein cited references.
2. Molander, G. A., Harris, C. R. *Chem. Rev.* **1996**, *96*, 307-338.
3. (a) Grigg, R.; Basanagoudar, L. D.; Kennedy, D. A.; Malone, F. J. *Tetrahedron Lett.* **1982**, 2803 - 2806. (b) Sardina, F. J.; Howard, M. H.; Morningstar, M.; Rapoport, H. *J. Org. Chem.* **1990**, *55*, 5025-5033. (c) Hashimoto, M., Terashima, S. *Tetrahedron Lett.* **1994**, *35*, 9409-9412. (d) Bachi, M. D.; Melman, A. *J. Org. Chem.* **1995**, *55*, 6242-6244. (e) Bachi, M. D.; Melman, A. *Synlett* **1996**, 60-62.
4. Hunt, S., *Methods in Plant Biochemistry*; Rogers, L. J., Ed.; Academic Press: New York, 1991.
5. Fuji, K. *Chem. Rev.* **1993**, *93*, 2037-2066.
6. (a) Hoppe, D. *Angew Chem. Int. Ed.* **1975**, *14*, 424-426. (b) Hoppe, D.; Beckmann, L. *Lieb. Ann. Chem.* **1979**, 2066-2075.
7. All componds gave satisfactory analyses. The relative configurations have been determined by NOE measurements.
8. All compounds herein described are racemic pairs.
9. Alvarez-Ibarra, C.; Csákÿ, A. G.; Maroto, M.; Quiroga, M. L. *J. Org. Chem.* **1995**, *60*, 6700-6705.

(*Received in UK* 21 *May* 1996; *revised* 16 *July* 1996; *accepted* 19 *July* 1996)