An Easy Entry to 4-Substituted 1-Aza-1,3-dienes from Simple Allylic Amines

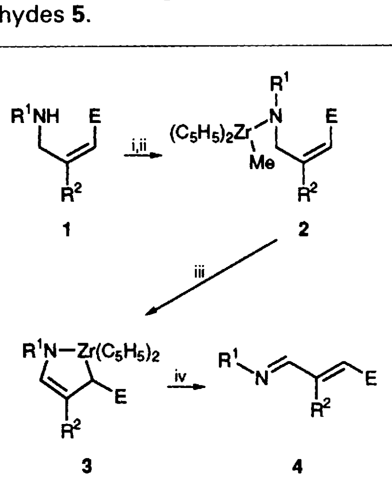
José Barluenga,* Roberto Sanz, Rosario González and Francisco J. Fañanás

Instituto Universitario de Química Organometálica Enrique Moles, Julián Clavería s/n, Universidad de Oviedo, 33071-Oviedo, Spain

Simple allylic amines are easily converted into 4-substituted 1-aza-1,3-dienes **4** *via* organozirconium complexes; the hydrolysis of the azadienes leads to β-substituted α,β-unsaturated aldehydes **5**.

Buchwald[1] and Whitby[2] have recently shown that η^2-imine complexes of zirconium can be generated from amines *via* loss of methane from methylzirconocene amides. The application of this reaction to allylic amines leads to 1-aza-1,3-diene zirconocene complexes by rearrangement of the first formed η^2-imine complexes.[3] Moreover, the most direct route to the 1-aza-1,3-diene zirconocene complexes results from the complexation of 1-azadienes to zirconocene,[2,4] prepared from zirconocene dichloride.[5] On the other hand, we have reported[6] the regio- and stereo-selective lithiation of secondary allylic amines and the reaction of the resulting dianions with different electrophiles (E). In the present communication we describe the preparation of 4-substituted 1-aza-1,3-dienes from allylic amines *via* organozirconium complexes.

Deprotonation with butyllithium of allylic amines **1**, obtained by regio- and stereo-selective lithiation of simple allylic amines and reaction of the resulting dianions with several electrophilic reagents (chlorotrimethylsilane, tributyltin chloride, and dimethyl disulfide),[6] followed by reaction with zirconocene methyl chloride at −78 °C afforded the corresponding methylzirconocene amides **2**, which lose methane rapidly at 20 °C to produce the azazirconacyclopentene derivatives **3**,† by rearrangement of the previously formed η^2-imine complexes.[3] It is important to note that in the case of **2f,g** the thermolysis to **3f,g** was carried out at 110 °C (toluene). This large difference observed for methane loss for **2a–e** compared to **2f,g** is presumably owing to reduced availability of the lone pairs on nitrogen in these latter complexes.[7] Further treatment of zirconocycles **3** with dry oxygen (or dry air)[8] at 20 °C yielded the 4-substituted 1-aza-1,3-dienes **4**. It is worth noting that only the products with the s-*trans* conformation and with the *E*-configuration at the C=N bond and at the C=C bond were observed throughout, except in the case of **4e**, which was obtained as a *E*/*Z* mixture at the C=C bond (Scheme 1 and Table 1).



	R^1	R^2	E
a	Ph	H	$SiMe_3$
b	Ph	H	$SnBu_3$
c	Ph	H	SMe
d	$4\text{-}MeOC_6H_4$	H	$SiMe_3$
e	Ph	Me	$SiMe_3$
f	$c\text{-}C_6H_{11}$	H	$SiMe_3$
g	$c\text{-}C_6H_{11}$	H	$SnBu_3$

Scheme 1 *Reagents and conditions*: i, BuLi, −50 °C; ii, $Cl(Me)Zr(C_5H_5)_2$, −78 °C; iii, 20 °C (R^1 = Ph, $4\text{-}MeOC_6H_4$), 110 °C (R^1=$c\text{-}C_6H_{11}$); iv, O_2 (or air), 20 °C

Table 1 Preparation of 4-substituted 1-aza-1,3-dienes **4** and β-substituted α,β-unsaturated aldehydes **5** from allylic amines **1**

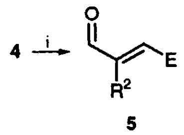
Amine	R^1	R^2	E	Product[a]	Yield (%)[b]	R_F[c]
1a	Ph	H	$SiMe_3$	**4a**	82	0.21(25:1)
1b	Ph	H	$SnBu_3$	**4b**	76	0.26(25:1)
1c	Ph	H	SMe	**4c**	71	0.23(15:1)
1d	$4\text{-}MeOC_6H_4$	H	$SiMe_3$	**4d**	81	0.39(10:1)
1e	Ph	Me	$SiMe_3$	**4e**	69	0.23(25:1)[d]
1f	$c\text{-}C_6H_{11}$	H	$SiMe_3$	**4f**	62	0.34(20:1)[d]
1g	$c\text{-}C_6H_{11}$	H	$SnBu_3$	**4g**	60	0.25(50:1)
4a	Ph	H	$SiMe_3$	**5a**	96[e]	0.29(20:1)
4b	Ph	H	$SnBu_3$	**5b**	95[e]	0.34(50:1)

[a] All products were fully characterized by spectroscopic methods (IR, ^1H and ^{13}C NMR, and mass spectrometry). [b] Isolated yield based on the amine **1**. [c] Deactivated silica gel with hexane–ethyl acetate (ratio in parentheses) as eluent. [d] Basic alumina with hexane–ethyl acetate (ratio in parentheses) as eluent. [e] From the azadiene **4**.

Alternatively, the transformation of the zirconocycles **3** into the azadienes **4** can be carried out with chelating ligands such as 2,2′-bipyridyl (bpy) or 1,2-bis(diphenylphosphino)ethane (dppe) instead of oxygen but the reaction is slower. Furthermore, we have observed that the zirconocycles **3** also decompose very slowly to the azadienes **4** in the absence of oxygen or ligands.

The hydrolysis of the azadienes **4** led to the corresponding β-substituted α,β-unsaturated aldehydes **5**, which are available with difficulty, by other synthetic methods[9] (Scheme 2 and Table 1).

A typical reaction was performed as follows. A solution of butyllithium (3 mmol) in hexane was added to a solution of the amine **1** (3 mmol) in THF (15 ml) at −50 °C under argon and stirred for 20 min. The resulting solution was added to a solution of zirconocene methyl chloride (3 mmol) in THF (15 ml) at −78 °C under argon. The reaction mixture was allowed to warm to 20 °C then stirred at this temperature for a further 3 h.‡ Dry oxygen (or dry air) was bubbled over a 3 h period at 20 °C through the resulting mixture. Solvent was removed under reduced pressure, the residue taken up in hexane (30 ml), and filtered through celite. Hexane was removed under reduced pressure, and the residue was purified by flash column chromatography (see Table 1).



5

Scheme 2 *Reagent and conditions*: i, HCl (3 mol dm^{-3}), 20 °C

In conclusion, we have developed a convenient method for the formation of 4-substituted 1-aza-1,3-dienes from a simple secondary allylic amine, an electrophile and oxygen or air. We believe that the experimental simplicity, and the mildness of the reaction conditions should allow the application of this methodology for the preparation of useful 4-substituted 1-aza-1,3-dienes, and therefore the corresponding β-substituted α,β-unsaturated carbonyl compounds.

This work was supported by the DGICYT (PB 89-0538). R. S. and R. G. thank the Ministerio de Educación y Ciencia for a fellowship.

Received, 4th January 1994; Com. 4/00010B

Footnotes

† All the zirconocycles were characterized by ^1H and ^{13}C NMR spectroscopy.

‡ When an aliphatic amine was used as starting material the mixture was heated in toluene at reflux for 3 h.

References

1 S. L. Buchwald, M. W. Wannamaker and B. T. Watson, *J. Am. Chem. Soc.*, 1989, **111**, 776; S. L. Buchwald, B. T. Watson, M. W. Wannamaker and J. C. Dewan, *J. Am. Chem. Soc.*, 1989, **111**, 4486.

2 N. Coles, R. J. Whitby and J. Blagg, *Synlett*, 1990, 271.

3 J. M. Davis, R. J. Whitby and A. Jaxa-Chamiec, *J. Chem. Soc., Chem. Commun.*, 1991, 1743.

4 J. Scholz, M. Nolte and C. Krüger, *Chem. Ber.*, 1993, **126**, 803.

5 E. Negishi, S. J. Holmes, J. M. Tour, J. A. Miller, F. E. Cederbaum, D. R. Swanson and T. Takahashi, *J. Am. Chem. Soc.*, 1989, **111**, 3336.

6 J. Barluenga, F. J. Fañanás, F. Foubelo and M. Yus, *J. Chem. Soc., Chem. Commun.*, 1988, 1135; J. Barluenga, F. Foubelo, F. J. Fañanás and M. Yus, *J. Chem. Res. (S)*, 1989, 200; (*M*), 1524; J. Barluenga, R. González and F. J. Fañanás, *Tetrahedron Lett.*, 1992, **33**, 831.

7 D. C. Bradley and M. H. Chisholm, *Acc. Chem. Res.*, 1976, **9**, 273.

8 H. Yasuda, Y. Kajihara, K. Mashima, K. Nagasuna, K. Lee and A. Nakamura, *Organometallics*, 1982, **1**, 388.

9 C. R. Johnson and J. F. Kadow, *J. Org. Chem.*, 1987, **52**, 1493.