Pergamon

Tetrahedron Letters 41 (2000) 8517–8521

TETRAHEDRON
LETTERS

Vanadium-catalyzed stereoselective cyclodimerization of arylidene malononitrile in the presence of chlorosilane and zinc

Longhu Zhou and Toshikazu Hirao*

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Yamada-oka, Suita, Osaka 565-0871, Japan

Received 26 July 2000; revised 6 September 2000; accepted 8 September 2000

Abstract

A catalytic cyclodimerization of arylidene malononitriles proceeded diastereoselectively with reversible redox between vanadium and zinc in the presence of chlorotrimethylsilane. The reductive coupling reaction strongly depended on the co-reductant, additive, solvent, and substrate. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: vanadium catalyst; diastereoselective cyclization; one-electron reduction; silylating reagent; co-reductant.

Catalytic reactions for the stoichiometric electron transfer process has attracted increasing attention due to the synthetic utility and efficiency of the process. This concept has been demonstrated in the pinacol coupling reaction catalyzed by cat. $Cp_2TiCl_2/RMgBr$[1] and electrochemical coupling using cat. $SmCl_3$.[2] Recently, a catalytic reductive coupling procedure has been developed independently by Fürstner's group[3] and our group[4] by using a combination of an early transition metal catalyst, a chlorosilane and a zerovalent metal as a co-reductant. Our system has been revealed to work in the diastereoselective pinacol coupling reactions of aldehydes and aldimines, giving the corresponding vicinal diols and diamines with excellent *dl*- and *meso*-selectivity, respectively. In order to extend the versatility of our catalytic system, we herein report that a combination of cat. $Cp_2VCl_2/Me_3SiCl/Zn$ effects the diastereoselective cyclodimerization of arylidene malononitriles.

Treatment of benzylidene malononitrile (**1a**) with a catalytic amount of Cp_2VCl_2, Me_3SiCl, and zinc powder led to the formation of the cyclodimerization compound **2a** via one-electron reductive coupling followed by cyclization (Eq. (1)). To construct an efficient reduction system, the effect of vanadium catalysts, metallic co-reductants, and silylating reagents was investigated as shown in Table 1.

---

* Corresponding author. Fax: +81 6 6879 7415; e-mail: hirao@ap.chem.eng.osaka-u.ac.jp

PII: S0040-4039(00)01540-9

(1)

1a **2a**

Table 1

Cyclodimerization of **1a** with cat. Cp_2VCl_2 in the presence of additive[a]

Entry	Cp_2VCl_2	Metal	$MeSi_3Cl$[b]	Isolated yield (%)	*trans*:*cis*[c]
1	+		−	0	
2	+		+	0	
3	+	Zn	−	38	88:12
4	−	Zn	+	25	74:26
5	−	Zn	−	0	
6	+	Zn	+	79	83:17
7	+	Al	+	81	71:29
8	+	Mn	+	62	77:23
9	+	In	+	66	54:46
10	+	Mg	+	Mixture	
11	+	Sm	+	Mixture	

[a] Reaction conditions: **1a** (1 mmol), Cp_2VCl_2 (5 mol%), metal (2 mmol), Me_3SiCl (2 mmol), DMF (5 mL), Ar, rt, 3 h.

[b] Distilled Me_3SiCl was used.

[c] Determined by ^1H NMR.

When **1a** was stirred in DMF with a catalytic or even stoichiometric amount of Cp_2VCl_2 at room temperature for 24 h, no reaction took place (entry 1). Although a combination of cat. Cp_2VCl_2 and Me_3SiCl did not effect the reduction of **1a** (entry 2), the use of cat. Cp_2VCl_2 and zinc powder gave the cyclization product **2a** in 38% yield (entry 3). The attempted reduction of **1a** using a Zn/Me_3SiCl system[5] only resulted in low yields and moderate stereoselectivity (entry 4). Since no reaction took place with zinc powder alone (entry 5), the active reductive species is likely to be a low-valent vanadium species formed in situ by the reduction of Cp_2VCl_2 with zinc. The fact that the addition of Me_3SiCl to the Cp_2VCl_2–Zn system successfully improved the yield of **2a** with good stereoselectivity (entry 6) clearly indicates that efficient cyclodimerization of **1a** requires a combination of cat. Cp_2VCl_2, Me_3SiCl, and Zn. Although the use of Al as a co-reductant raised the yield of **2a**, the diastereoselectivity decreased (entry 7). The employment of In and Mn gave only low yields and poor stereoselectivity (entries 8 and 9). Moreover, an attempted reaction of **1a** using Mg (entry 10) or Sm (entry 11) as a co-reductant only gave rise to a complex mixture.

Since the cat. Cp_2VCl_2/Me_3SiCl/Zn system was revealed to be the best combination for the cyclodimerization of **1a**, the influence of the silyl compound, solvent, and temperature was examined (Table 2). Surprisingly, the reaction of **1a** provided poor yields and no diastereoselectivity by switching the solvent from DMF to THF (entry 1). When DME was used in place of THF or DMF, the reductive cyclization reaction proceeded very slowly without any diastereoselection (entry 2). Use of toluene and dichloromethane gave only a trace amount of the desired

Table 2
The influence of silyl compound, solvent, and temperature on the cyclodimerization of **1a**[a]

Entry	Silyl compound	Solvent	Time (h)	Isolated yield (%)	*trans*:*cis*[b]
1	Me_3SiCl	THF	24	45	49:51
2	Me_3SiCl	DME	72	47	49:51
3	Me_3SiCl	Toluene	3	Trace	
4	Me_3SiCl	CH_2Cl_2	3	Trace	
5[c]	Me_3SiCl	DMF	3	77	87:13
6	$PhMe_2SiCl$	DMF	3	78	83:17
7	$Ph_2MeSiCl$	DMF	3	61	71:29

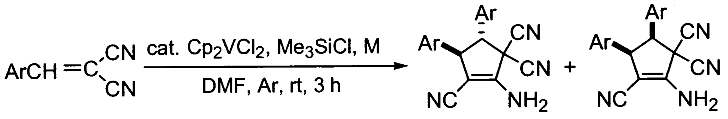
[a] Reaction conditions: **1a** (1 mmol), Cp_2VCl_2 (5 mol%), Zn (2 mmol), R_3SiCl (2 mmol), solvent (5 mL), Ar, rt, 3 h.

[b] Determined by ^1H NMR.

[c] Reaction temperature, −30°C.

product (entries 3 and 4). The cyclization reaction at −30°C improved the diastereoselectivity up to 87:13 with 77% yield (entry 5). When $PhMe_2SiCl$ was employed as a silylating reagent, good yields and diastereoselectivity could be attained (entry 6). The more sterically hindered $Ph_2MeSiCl$ may be expected to induce higher diastereoselectivity, which resulted in moderate yields with moderate stereoselectivity (entry 7).

Optimized reaction conditions were employed in the cyclodimerization of arylidene malononitriles (Eq. (2), Table 3). Cyclodimerization of **1** induced by the cat. $Cp_2VCl_2/Me_3SiCl/Zn$ system in DMF afforded the desired product **2** successfully. The cyclization product **2b** was obtained in good yields with moderate diasteroselectivity (entry 2). In particular, excellent *trans* selectivity was observed with **1c** and **1d** bearing a *p*-bromo or *p*-chloro group (entries 3 and 4). In the case of **1e** bearing an *o*-substituent, the diastereoselectivity considerably decreased (entry 5). Similar results were observed with the substrates **1f** and **1g** (entries 6 and 7). These findings indicate that



1 **2**

(2)

Table 3
Cat. $Cp_2VCl_2/Me_3SiCl/Zn$ induced cyclodimerization of **1**[a]

Entry	1	Ar	2	Isolated yield (%)	*trans*:*cis*[b]
1	**1a**	C_6H_5	**2a**	79	83:17
2	**1b**	*p*-$CH_3OC_6H_4$	**2b**	70	75:25
3	**1c**	*p*-BrC_6H_4	**2c**	74	89:11
4	**1d**	*p*-ClC_6H_4	**2d**	83	90:10
5	**1e**	*o*-ClC_6H_4	**2e**	78	63:37
6	**1f**	*m*-ClC_6H_4	**2f**	64	59:41
7	**1g**	*o*-BrC_6H_4	**2g**	72	57:43

[a] Reaction conditions: **1** (1 mmol), Cp_2VCl_2 (5 mol%), Zn (2 mmol), Me_3SiCl (2 mmol), DMF (5 mL), Ar, rt, 3 h.

[b] Determined by ^1H NMR.

the diastereoselectivity also strongly depends on the electronic and steric effects of the substituent on the benzene ring at the one-electron reduction or coupling step. The cyclodimerization of **1** has also been reported to be achieved by using a stoichiometric reductant such as $TiCl_3$, $TiCl_4$–Zn, SmI_2, and Sm/Me_3SiCl/H_2O.[6] Similar stereoselectivity is observed by using $TiCl_3$ as a reductant. For example, the reaction of **1a** with stoichiometric $TiCl_3$ at room temperature results in *trans*:*cis* = 87:13.[6a]

The structure and relative configuration of **2** were readily confirmed by the spectroscopic data and X-ray analysis. The X-ray diffraction study on a single crystal of the major isomer of **2c** supports the *trans*-isomer (Fig. 1).

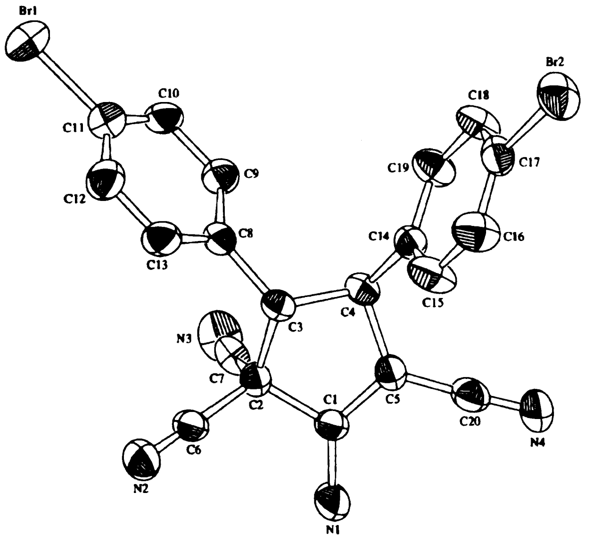
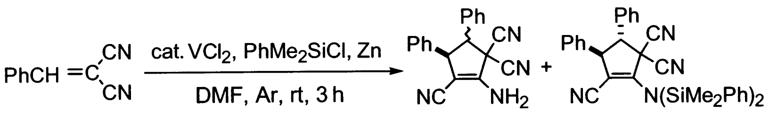


Figure 1. ORTEP diagram of the major isomer of **2c**

Treatment of **1a** with cat. VCl_2/$PhMe_2SiCl$/Zn under similar conditions afforded the silyl-substituted cyclization product **3a**[7] in 24% yield with excellent diastereoselectivity (98:2) along with the product **2a** (58%, 80:20, Eq. (3)). The compound **3a** was converted to **2a** on treatment with silica gel overnight. When the reaction time was prolonged to 18 h, only **2a** was formed, indicating that the silyl compound **3a** is involved as an initial product in the reductive cyclization.



(3)

1a **2a** **3a**

Acknowledgements

The use of the facilities of the Analytical Center, Faculty of Engineering, Osaka University is acknowledged. This work was partly supported by a Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Science and Culture. We thank the Japan Society for the Promotion of Science (JSPS) for postdoctoral fellowships to L.Z.

References

1. Zhang, Y.; Liu, T. *Synth. Commun.* **1988**, *18*, 2173.
2. Léonard, E.; Duñach, E.; Périchon, J. *J. Chem. Soc., Chem. Commun.* **1989**, 276.
3. Fürstner, A.; Hupperts, A. *J. Am. Chem. Soc.* **1995**, *117*, 4468.
4. Hirao, T.; Hasegawa, T.; Muguruma, Y.; Ikeda, I. *Abstracts for 6th International Conference on New Aspects of Organic Chemistry*, 1994; p. 175 and *J. Org. Chem.* **1996**, *61*, 366. Hirao, T.; Asahara, M.; Muguruma, Y.; Ogawa, A. *J. Org. Chem.* **1998**, *63*, 2812. Hatano, B.; Ogawa, A.; Hirao, T. *J. Org. Chem.* **1998**, *63*, 9421. Hirao, T.; Hatano, B.; Imamoto, Y.; Ogawa, A. *J. Org. Chem.* **1999**, *64*, 7665.
5. So, J. H.; Park, M. K.; Boudjouk, P. *J. Org. Chem.* **1988**, *53*, 587.
6. (a) Sera, A.; Tsuzuki, T.; Satoh, E.; Itoh, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3068; (b) Zhou, L.; Tu, S.; Shi, D.; Dai, G.; Chen, W. *Synthesis* **1998**, 851; (c) Zhou, L.; Zhang, Y. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2399; (d) Wang, L.; Zhang, Y. *Tetrahedron* **1998**, *54*, 11129.
7. **3a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.54 (s, $SiCH_3$), 0.68 (s, $SiCH_3$), 0.69 (s, $SiCH_3$), 0.71 (s, $SiCH_3$), 3.43 (d, $J=10.8$ Hz, CH), 4.49 (d, $J=10.8$ Hz, CH), 6.71 ~ 7.81 (m, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.39, 1.04, 2.48, 2.59, 49.61, 51.89, 62.87, 111.32, 113.21, 114.64, 116.72, 127.75, 127.89, 127.97, 128.05, 128.40, 128.62, 128.86, 128.91, 129.57, 130.18, 130.38, 134.54, 134.66, 135.19, 135.27, 135.77, 156.49; MS (70 eV) m/z (relative intensity) 578 (M^+, 15), 563 (17), 462 (13), 448 (36), 424 (24), 289 (17), 263 (41), 135 (100); exact mass M^+ 578.2328 (calcd for $C_{36}H_{34}N_4Si_2$ 578.2322) (1.0 ppm).