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Tetrahedron Letters
Tetrahedron Letters 46 (2005) 5277–5279

Synthesis of 1,2,9,10-tetrakis(*N*-phenylamino)[2.2]metacyclophane by SmI_2-mediated reductive coupling of diimine

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Received 30 April 2005; revised 7 June 2005; accepted 9 June 2005

Abstract—SmI_2/HMPA-mediated double reductive coupling of *N*,*N*′-(*m*-xylylidene)dianiline affords 1,2,9,10-tetrakis(*N*-phenylamino)[2.2]metacyclophane in good yield.

Reductive coupling reaction of imines (imino-pinacol coupling) is an important method to form a carbon–carbon bond with 1,2-diamino moieties.[1] The reaction is mediated by various metal reagents[2–5] such as zinc powder, low-valent titanium, and divalent samarium. An intramolecular version of the reaction affords the corresponding cyclic 1,2-diamines from bis-imines.[6] To the best of our knowledge, however, bimolecular cyclization by double reductive coupling of diimines has not been investigated. Recently, it was reported that highly strained all-equatorial-1,2,9,10-tetrahydroxy[2.2]metacyclophanes (MCPs) were produced in the intermolecular double pinacol coupling of benzene-1,3-dialdehydes in one step, by using aluminum as a mediator under strongly alkaline conditions.[7] Unfortunately, this procedure failed to give the corresponding [2.2]MCP-1,2,9,10-tetraamine derivatives when applied to a benzene-1,3-diimine. Under the same conditions, only polymeric products were formed. We now report our finding that 1,2,9,10-tetrakis(*N*-phenylamino)[2.2]MCP **2** was obtained successfully by the SmI_2-mediated double reductive coupling of *N*,*N*′-(*m*-xylylidene)dianiline **1**.

The SmI_2-mediated imino-pinacol coupling of **1** was carried out in THF and the desired 1,2,9,10-tetrakis(*N*-phenylamino)[2.2]MCP **2** was formed as a mixture of two stereoisomers, **2(I)** and **2(II)** in the yields shown in Table 1.[8] A mixture **4** of higher homologues was also obtained. The isomers of the [2.2]MCP **2** were separated through column chromatography. The structures were determined by spectral data and elemental analyses[9] and established by X-ray crystallographic analyses.[10] The [2.2]MCP skeleton of **2(I)** and **2(II)** has *anti*-conformation. Isomer **2(I)** has four *N*-phenylamino groups all in equatorial positions, whereas **2(II)** is a racemate that has three equatorial and one axial *N*-phenylamino groups (Figs. 1 and 2). The yields of **2** are dependent upon the additives (Table 1). HMPA[11] and DMPU[12] are known to promote SmI_2-mediated pinacol coupling of carbonyl compounds[13] and also are effective for the double imino-pinacol coupling of **1**. The addition of DMPU raised the yield of **2** up to 29% (entry 2) from 10% obtained in the reaction without additive (entry 1). A more remarkable increase (62%) was observed by the addition of four equivalents of HMPA (entry 3). The reductive cyclization proceeded less effectively at the lowered temperature, giving **2** in 50% yield. Diamine **3** was formed as a side product in 15% yield (entry 4). Isomer **2(II)** was obtained as a major product in the reactions mentioned above (entry 1–4), though **2(II)** seems sterically less favored than **2(I)** having *N*-phenylamino

Keywords: Diimine; Reductive coupling; Samarium diiodide; [2.2]-Metacyclophane.
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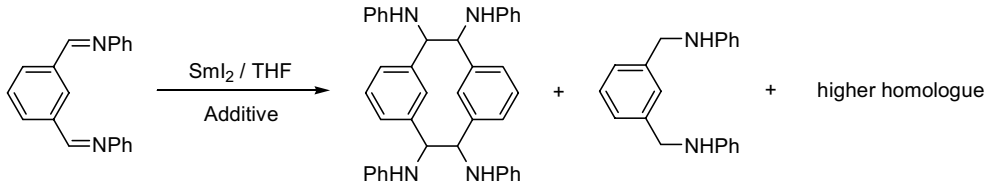
doi:10.1016/j.tetlet.2005.06.038

Table 1. Reaction of diimine **1** with SmI_2 under several conditions



1 **2** **3** **4**

Entry	Conditions			Isolated yield (%)			
	Additive	Temperature (°C)	Time (h)	**2**	(**I**/**II**)[b]	**3**	**4**[c]
1	—	65	24	10	(13/87)	nd[d]	90
2	DMPU[a]	65	24	29	(12/88)	nd[d]	71
3	HMPA[a]	65	0.5	62	(40/60)	nd[d]	38
4	HMPA[a]	20	0.5	50	(36/64)	15	35

[a] Additives were used four equivalent to Sm(II).
[b] Diastereomer ratio.
[c] Weight percent yield.
[d] Not detected.

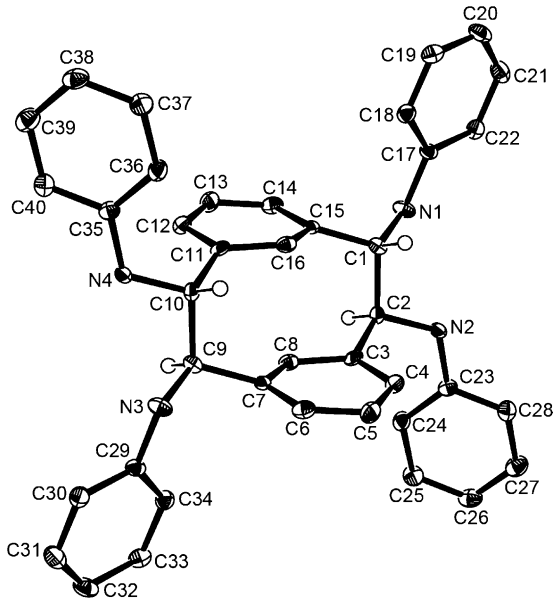


Figure 1. X-ray crystal structure of **2**(**I**). Solvent molecule (1,4-dioxane) and H atoms except those on C1, C2, C9, and C10 are omitted for clarity.[10]

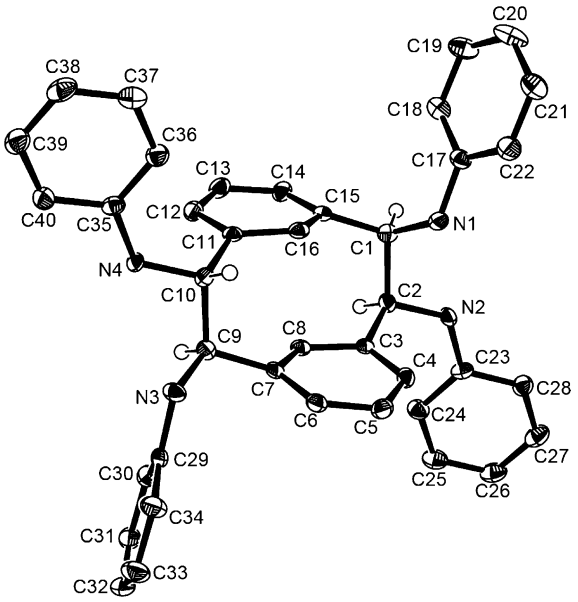


Figure 2. X-ray crystal structure of (1*R**,2*S**,9*R**,10*R**)-**2**(**II**). Solvent molecule (acetone) and H atoms except those on C1, C2, C9, and C10 are omitted for clarity.[10]

groups all on equatorial positions. In order to obtain the informations about the selectivity on the first-step intermolecular reductive coupling of **1**, *N*-benzylideneaniline (PhCH=NPh) was treated under the same conditions with those of entry 3 in Table 1. The corresponding 1,2-diamine was obtained in 97% yield with a low diastereoselectivity (*dl*/meso = 60/40). Suppose that the first-step intermolecular coupling of **1** proceeds in a non-selective manner, the observed diastereomeric ratio of **2** (**I**/**II** = 40/60) in entry 3 suggests that the second-step intramolecular reaction proceeds with a low diastereoselectivity. Tetraamine isomers having more than two axial *N*-phenylamino groups are unfavorable due to steric reasons.

In conclusion, we have achieved the first synthesis of a [2.2]MCP-1,2,9,10-tetraamine via double imino-pinacol coupling of a benzene-1,3-diimine. Further work is under way to elucidate the mechanism and scope of the reductive cyclization.

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8. Representative procedure (entry 3 in Table 1): 0.1 M SmI_2–THF solution was prepared from Sm (turnings, 3.0 mmol) and iodine (2.5 mmol) in dry THF (25 ml) under reflux over 6 h under argon. HMPA (10 mmol) was added to the resulting 0.1 M SmI_2–THF solution. To the solution under reflux, a solution of **1** (1.0 mmol) in THF (10 ml) was added at once.[14] The reaction mixture was stirred at 65 °C for 0.5 h under argon, then cooled to room temperature, and quenched with MeOH (0.5 ml). After additional stirring for 1 h, saturated Na_2SO_3 solution (20 ml) and brine (30 ml) were added to the reaction mixture, then the mixture was filtered through a Celite pad. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (15 ml × 3). The organic layer and the extract were combined, washed with water (10 ml × 5) and brine (20 ml × 2), dried over anhydrous Na_2SO_4, and concentrated in vacuo to give a pale yellow solid. The solid was column chromatographed on silica gel (Wako-gel, C-300). The first fraction eluted with benzene gave **2(I)** and the second one gave **2(II)**. Finally, **4** was eluted with ethyl acetate.
9. Compound **2(I)**: Colorless prisms (hexane/CH_2Cl_2); Mp 256–258 °C; IR (KBr) ν 3359, 3052, 1601, 1503, 1426, 1314, 1267, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.88 (s, 4H), 4.79 (s, 2H), 4.86 (s, 4H), 6.67 (d, J = 7.6 Hz, 8H), 6.74 (t, J = 7.6 Hz, 4H), 7.16 (t, J = 7.6 Hz, 8H), 7.30 (t, J = 7.3 Hz, 2H), 7.42 (d, J = 7.3 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 66.8, 114.4, 118.3, 124.5, 129.1, 129.3, 134.0, 137.5, 146.7; HRMS (FAB) calcd for $C_{40}H_{37}N_4$ ($M+H^+$): 573.3021, found: 573.3013. Anal. Calcd for $C_{40}H_{36}N_4$: C, 83.88; H, 6.34; N, 9.78. Found: C, 83.92; H, 6.36; N, 9.82. Compound **2(II)**: Colorless prisms (acetone/H_2O); Mp 202–205 °C; IR (KBr) ν 3400, 3050, 1601, 1501, 1428, 1314, 1262, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.79–3.91 (m, 3H), 4.16–4.19 (m, 1H), 4.63 (s, 1H), 4.80 (d, J = 5.5 Hz, 1H), 4.84 (d, J = 5.2 Hz, 1H), 4.88 (s, 1H), 4.99 (d, J = 5.8 Hz, 1H), 5.12 (dd, J = 9.6, 3.6 Hz, 1H), 6.58–7.41 (m, 26H); ^{13}C NMR ($CDCl_3$) δ 63.2, 65.0, 66.4, 66.6, 113.7, 114.2, 114.38, 114.41, 117.7, 118.3, 118.4, 118.5, 124.5, 124.6, 124.7, 127.3, 128.26, 128.33, 129.22, 129.28, 129.30, 129.37, 131.8, 133.6, 134.1, 137.4, 138.5, 138.7, 146.1, 146.4, 146.5, 146.7; HRMS (FAB) calcd for $C_{40}H_{37}N_4$ ($M+H^+$): 573.3021, found: 573.3018. Anal. Calcd for $C_{40}H_{36}N_4$: C, 83.88; H, 6.34; N, 9.78. Found: C, 83.91; H, 6.29; N, 9.83.
10. Crystal data for **2(I)**: $C_{40}H_{36}N_4{\cdot}(C_4H_8O_2)_4$, FW = 925.18, colorless prism, triclinic, space group: P-1, T = 123 K, a = 9.784(5) Å, b = 10.323(5) Å, c = 13.921(7) Å, α = 100.760(4)°, β = 105.151(5)°, γ = 109.287(5)°, V = 1222.1(11) $Å^3$, Z = 1, D_c = 1.257 g cm^{-3}, $F(000)$ = 496, μ(Mo Kα) = 0.84 cm^{-1}, Final R_1 = 0.052 (for 5321 reflections with $I > 2\sigma(I)$) and wR_2 = 0.109 for all data. ORTEP diagram is given in Figure 1. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre; deposition number CCDC 259438.
Crystal data for **2(II)**: $C_{40}H_{36}N_4{\cdot}(C_3H_6O)_2$, FW = 688.91, colorless prism, monoclinic, space group: $P2_1/n$, T = 123 K, a = 9.438(2) Å, b = 19.887(4) Å, c = 20.119(5) Å, β = 97.3043(11)°, V = 3745.5(15) $Å^3$, Z = 4, D_c = 1.222 g cm^{-3}, $F(000)$ = 1472, μ(Mo Kα) = 0.75 cm^{-1}, Final R_1 = 0.055 (for 8446 reflections with $I > 2\sigma(I)$) and wR_2 = 0.088 for all data. ORTEP diagram is given in Figure 2. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre; deposition number CCDC 259439.
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14. A slow dropwise addition (30 min) of diimine **1** in THF (0.1 M) did not improve the yield of **2**. Also the reaction at a dilute concentration (0.025 M) was ineffective to raise the yield.