En Route to Molecular Bracelets: The Synthesis of Linear Pentacyclic Bis(benzodiazocino)benzenes

Ying Cheng,[a*] Qing–Xiang Liu,[a] Otto Meth–Cohn[b*]

[a]Department of Chemistry, Beijing Normal University, Beijing 100875, China

[b]Department of Chemistry, University of Sunderland, Sunderland SR1 3SD, UK

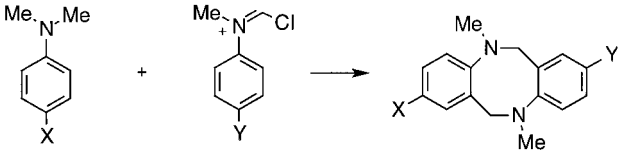
Fax: +44(191)5152587; E-mail: otto.meth-cohn@sunderland.ac.uk

Received 5 January 2000

Abstract: The title compounds, namely dibenzo[b,b′]benzo[1,2-f:4,5-f′]bis[1,5]diazocines, have been synthesised in a single step in two alternative ways by application of the 'tertiary amino effect': (i) the action of bis-Vilsmeier reagents derived from *N*,*N*′-dimethyl-*N*,*N*′-diformyl-*p*-phenylenediamine upon 4-substituted *N*,*N*-dimethylanilines, and (ii) the action of Vilsmeier reagents derived form 4-substituted *N*-methylformanilides on bis(dimethylamino)benzenes.

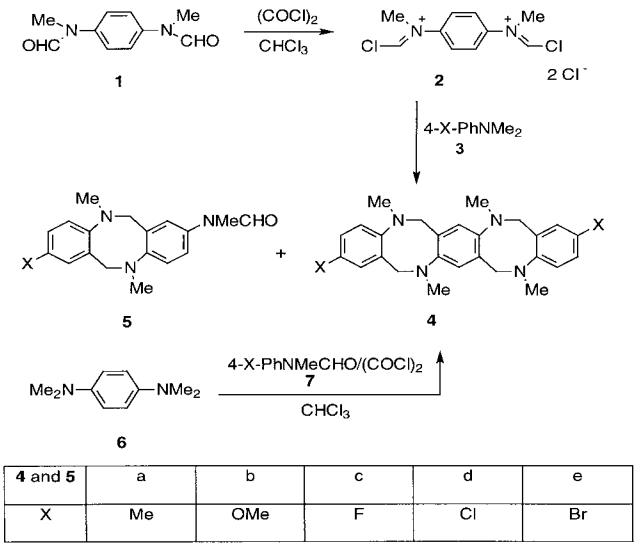
Key words: Vilsmeier, bisdiazocines, bracelets

In earlier work, we established a simple one-pot reaction for the synthesis of 5,6,11,12-tetrahydrodibenzo[b,f][1,5]diazocines[1] by the treatment of 4-substituted *N*,*N*-dimethylanilines with *N*-methylformanilides in $POCl_3$ (Scheme 1). These systems are known[2] to prefer a boat conformation and consequently we envisaged that larger assemblies of linear fused analogues could be of interest in the synthesis of novel macrocycles such as 'molecular bracelets'. To this end, we have now extended this methodology to the synthesis of 5,6,8,9,14,15,17,18-octahydrodibenzo[b,b′]benzo[1,2-f:4,5-f′]bis[1,5]diazocines **4**, a novel linear pentacyclic heterocycle.



Scheme 1

When treated with oxalyl chloride in chloroform, *N*,*N*′-dimethyl-*N*,*N*′-diformyl-*p*-phenylenediamine **1** formed a solid Vilsmeier reagent **2**, which reacted with 4-substituted *N*,*N*′-dimethylanilines **3** on heating to reflux in chloroform for 10–11 hours. After basic work-up dibenzo[b,b′]benzo[1,2-f;4,5-f′]bis[1,5]diazocines **4** were obtained in 22–56% yield (Scheme 2, Table 1–2). In some cases, a half-cyclized product **5** was also obtained in 13–36% yield. The formation of the half-cyclized product **5** was probably due to the incomplete conversion of the formanilide **1** into the bis-Vilsmeier reagent.



4 and 5	a	b	c	d	e
X	Me	OMe	F	Cl	Br

Scheme 2

The same product **4** could also be obtained by treatment of 1,4-bis(dimethylamino)benzene **6** with the Vilsmeier's reagents **7** derived from a 4-substituted *N*-methylformanilide and oxalyl chloride, though yields were lower (~15%) (Scheme 2).

Table 1 Preparation and Properties of Compounds **4** and **5**

Starting Materials	Product	Reaction Method	Yield (%)	Mp (°C)	Molecular Formula
1 and **3**	**4a**	A	40	227–229	$C_{28}H_{34}N_4$
1 and **3**	**4b**	A	56	238–240	$C_{28}H_{34}N_4O_2$
1 and **3**	**4c**	A	22	239–241	$C_{26}H_{28}N_4F_2$
1 and **3**	**5c**	A	36	166–168	$C_{18}H_{20}N_3FO$
1 and **3**	**4d**	A	52	> 300	$C_{26}H_{28}N_4Cl_2$
1 and **3**	**5d**	A	13	210–212	$C_{18}H_{20}N_3ClO$
1 and **3**	**4e**	A	23	282–283	$C_{26}H_{28}N_4Br_2$
1 and **3**	**5e**	A	30	212–214	$C_{18}H_{20}N_3BrO$
6 and **7**	**4d**	B	13		
6 and **7**	**4e**	B	15		

Table 2 Spectroscopic Data for Compounds **4** and **5**

Compound[a]	IR (KBr) ν (cm^{-1})	^1H NMR ($CDCl_3$) δ (ppm), *J* (Hz)	^{13}C NMR ($CDCl_3$) δ (ppm)	MS *m/z* (%)
4a	1620 (w), 1520 (s)	7.00 (d, 2 H, *J* = 8.0), 6.95 (s, 1 H), 6.85 (br s, 1 H), 4.14−4.35 (br, 4 H, NCH_2), 2.87 (br s, 6 H, NCH_3), 2.27 (br s, 3 H, ArMe)	148.9, 143.7, 132.1, 128.4, 128.0, 127.4, 120.4, 115.7, 59.1, 58.8, 40.0, 39.5, 20.3	426 (M^+, 100)
4b	1600 (w), 1500 (s), 1040 (m)	7.21 (br s, 1 H), 6.77 (d, 2 H, *J* = 8.7), 6.72 (s, 1 H), 4.16−4.39 (br, 4 H, $2NCH_2$), 3.77 (s, 3 H, OCH_3), 2.87 (br s, 6 H, $2NCH_3$)	125.7, 145.7, 144.1, 130.3, 128.9, 120.3, 117.4, 112.8, 59.3, 59.2, 55.8, 40.0, 39.9	458 (M^+, 100)
4c	1620 (w), 1520 (s)	6.89−6.90 (m, 4 H), 4.10−4.70 (br, 4 H, NCH_2), 2.87 (br s, 6 H, NCH_3)		434 (M^+, 100)
4d	1590 (w), 1500 (s)	7.25 (s, 1 H), 7.23 (d, 1 H, *J* = 6.7), 6.92−7.00 (m, 2 H), 4.35−4.41 (br, 4 H, NCH_2), 2.97 (br s, 6 H, NCH_3)		466 (100) / 468 (68) / 470 (13) (M^+)
4e	1610, 1520	7.34 (d, 1 H, *J* = 8.7), 7.31 (s, 1 H), 7.05 (s, 1 H), 6.91 (d, 1 H, *J* = 8.5), 4.47 (s, 2 H, NCH_2), 4.38 (s, 2 H, NCH_2), 3.06 (s, 3 H, NCH_3), 2.93 (s, 3 H, NCH_3)		554 (51)/556 (100)/558 (50) (M^+)
5c	1660 (s) (C=O), 1520 (s), 1500 (s)	8.35 (s, 1 H, CHO), 7.04 (s, 2 H), 6.92−6.99 (m, 2 H), 6.87 (dd, 2 H, *J* = 8.6, 2.8), 4.47 (s, 2 H, NCH_2), 4.41 (s, 2 H, NCH_2), 3.24 (s, 3 H, NCH_3), 3.02 (s, 6 H, NCH_3)	162.4, 157.8, 154.2, 149.5, 146.9, 133.0, 128.6/128.5/128.2 (t), 126.6, 123.3, 117.7/117.4/117.1/117.0 (q), 116.3, 114.5/114.2 (d), 58.5, 58.1, 39.5, 39.2, 32.7	313 (M^+, 100)
5d	1660 (s) (C=O), 1520 (s), 1500 (s)	8.36 (s, 1 H, CHO), 6.85−7.17 (m, 6 H,), 4.31 (s, 2 H, NCH_2), 4.29 (s, 2 H, NCH_2), 3.27 (s, 3 H, NCH_3), 2.88 (s, 3 H, NCH_3), 2.85 (s, 3 H, NCH_3)	162.4, 149.3, 149.0, 132.8, 131.0, 127.9, 127.5, 126.7, 123.4, 122.8, 116.6, 116.5, 116.1, 58.2, 57.9, 39.1, 32.7, 30.7	329 (100) / 331 (33) (M^+)
5e	1670 (s) (C=O), 1520 (s), 1500 (s)	8.26 (s, 1 H, CHO), 6.79−7.31 (m, 6 H), 4.30 (s, 4 H, $2NCH_2$), 3.27 (s, 3 H, NCH_3), 2.91 (s, 3 H, NCH_3), 2.84 (s, 3 H, NCH_3)	161.0, 148.3, 147.8, 132.5, 131.4, 129.5, 127.3, 126.1, 125.4, 122.0, 115.8, 114.8, 108.3, 56.7, 56.5, 37.9, 31.4, 28.3	373 (100)/375 (98) (M^+), 189 (48), 177 (51), 117 (59)

[a] All compounds gave satisfactory elemental analysis; C, ± 0.49; H, ± 0.21; N, ± 0.40

The bis-(benzodiazocino)benzenes **4** are insoluble both in water and in most organic solvents such as DMSO, methanol, acetone, acetonitrile and ethyl acetate. They are slightly soluble in $CHCl_3$ forming a yellow solution. It is interesting that the yellow chloroform solution turns to blue on exposure to light. The blue solution changes back to yellow when it is kept in the dark for a few minutes. We believe the bis-diazocinobenzenes **4** will prove to be effective building blocks in the construction of supramolecular systems and this work is ongoing.

Mps are uncorrected. ^1H and ^{13}C NMR spectra in $CDCl_3$ were obtained on a Varian Unity 200 MHz and 300 MHz spectrometers. IR spectra were recorded with a HITACHI-260-50 spectrometer. Mass spectra were recorded with a KYKY-ZHT-5 instrument. Elemental analyses were performed on a Perkin–Elmer 240C instrument.

***N, N′*-Dimethyl-*N, N′*- diformyl-*p*-phenylenediamine (1)**

Formic acid (>98%, 23 g, 0.5 mol) and acetic anhydride (51 g, 0.5 mol) were mixed and warmed for 2 h at 60 °C. *p*-Phenylenediamine (10.8 g, 0.1 mol) was added with cooling in an ice-water bath. The mixture was stirred at 80–90 °C for 2 h, H_2O was added and the precipitate filtered, washed with H_2O and dried. Recrystallization from MeOH gave *N,N′*-diformylphenylenediamine in 60% yield, mp 204–206 °C [Lit.[3] 204–205 °C]. IR: $\nu_{c=o}$= 1680 cm^{-1}.

To *N,N′*-diformylphenylenediamine (8.2 g, 0.05 mol) in dry DMF (50 mL) was added NaH (2.4 g, 0.06 mol, 60% in paraffin) under N_2 atm with ice-bath cooling. After gas evolution ceased, MeI (8.46 g, 0.06 mol) in dry DMF (20 mL) was added dropwise and the mixture stirred at 80 °C for 2 h, and then at r.t. for 24 h. After removal of the DMF under vacuum, H_2O was added (150 mL) and the product **1** filtered, washed with H_2O and dried, and further purified by recrystallization from EtOH (71%). Mp 199–201 °C. [Lit.[3] 201–202 °C]. IR: $\nu_{c=o}$ = 1680 cm^{-1}.

^1H NMR: δ (ppm) = 8.51 (s, 2H, CHO); 7.41 (s, 4H, PhH); 3.21 (s, 6H, NCH_3).

5,6,8,9,14,15,17,18-Octahydro-5,8,14,17-tetramethyl-2,11-disubstituted dibenzo [b,b′]benzo[1,2-f:4,5- f′]bis[1,5]diazocines 4, and 5,6,11,12-tetrahydro-5,11-dimethyl-8-halogen-2-(*N*-me-

thyl-*N*-formylamino)dibenzo[b,f][1,5]diazocines 5; General Procedure

Method A: To *N*,*N*′-dimethyl-*N*,*N*′-diformylphenylenediamine (**1**) (1.92 g, 0.01 mol) was added oxalyl chloride (2 mL) under N_2. The mixture was stirred for 30 min at r.t., dry $CHCl_3$ (30 mL) was then added, and stirring continued for 1 h at 40–50 °C. The mixture was cooled in an ice-bath while a solution of 4-substituted *N*,*N*-dimethylaniline **3** (0.02 mol) in dry $CHCl_3$ (30 mL) was added dropwise. The resulting red brown solution was then refluxed for 11 h. After removal of the solvent, the residue was basified with aq NaOH (10%) to pH 9–10. In the case of the halo derivatives, addition of $CHCl_3$ (100 mL) caused precipitation of the bis-benzodiazocines **4**, while the products **5** dissolved in the solvent. The bis-benzodiazocines **4** were filtered and recrystallised from $CHCl_3$/CH_3OH. The products **5** were obtained by drying ($MgSO_4$), evaporating the $CHCl_3$ solution, and purified by chromatography. The products **4** (X = Me, OMe) were isolated by chromatography and purified further by recrystallization from EtOAc. The products and their properties are recorded in Tables 1 and 2.

*Method B***:** The 4-substituted *N*-methylformanilide 7 (0.02 mol) was mixed with oxalyl chloride (2 mL) under N_2 with cooling in an ice-bath to form a red solution. *N*,*N*,*N*′*N*′-Tetramethyl-*p*-phenylenediamine (6) in dry $CHCl_3$ (50 mL) was then added dropwise. The mixture was refluxed for 11 h and after removal of the solvent, the residue was basified with aq NaOH (10%) to pH 9–10. The work-up was as for method A, and the products and their properties are recorded in Tables 1 and 2.

Acknowledgement

This work was supported by the National Natural Science Foundation of China to whom we are most grateful (Grant No. 29772003).

References

(1) Meth–Cohn, O.; Taylor, D. L. *J. Chem. Soc., Chem. Commum.* **1995**, 1463.
Cheng, Y; Meth–Cohn, O.; Taylor; D. L. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1257.
(2) Crossley, R.; Downing, A. P.; Nogradi, M.; Braga de Oliviera, A.; Ollis, W. D.; Sutherland, I. O. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1257.
(3) Sekiya, M.; Takayama, S.; Ito, K.; Suzuki, J.; Suzuki, K.; Terao, Y. *Chem. Pharm. Bull.* **1972**, *20*, 2661.

Article Identifier:
1437-210X,E;2000,0,05,0640,0642,ftx,en;P00400SS.pdf