Chinese Journal of Chemistry, **2004**, *22*, 498—501 **Article**

Synthesis of (*p*-Formylphenyl)azo Calix[4]arenes

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Five novel azo calix[4]arenes were reported. The *p*-aminobenzaldehyde was diazotized with sodium nitrite in aqueous hydrochloride solution. Mono-, bis-, tris- and tetrakis(*p*-formylphenyl)azo calix[4]arenes (including *proximal* and *distal* isomers) were obtained respectively by diazo-coupling in different molar ratio to calix[4]arene (**1**) under pH＝7.5—8.5 at 0—5 ℃. All (*p*-formylphenyl)azo calix[4]arenes were characterized by ^{1}H NMR, ^{13}C NMR, IR, MS (ESIMS) spectroscopies and elemental analysis.

Keywords calix[4]arene, azo calix[4]arene, diazo-coupling, isomer, NMR

Introduction

Organic compounds with second-order nonlinear optical (NLO) properties have various potentialities in the development of materials for applications such as frequency doubling and optical switching.[1,2] Traditional organic NLO materials are organic molecules containing electron-donating and electron-accepting groups connected via a conjugated π system, *i.e.* so called D-π-A structure. Generally, the second-order nonlinear hyperpolarizability β of a molecule increases with increasing length of the conjugated π system and increasing strength of the donor and acceptor.[3]

Unfortunately, an increase in the β value is accompanied by a red shift in the absorption spectra due to a larger π-conjugated length and/or stronger donor and acceptor substituents, *i.e.*, there is a tradeoff between nonlinearity and transparency.[4] To resolve this problem, much efforts have been made in designing organic molecules with both high β value and good transparency.[4]

Calixarenes are cyclic oligomers having phenolic units linked by methylene groups. When the strong electron-withdrawing moieties are introduced to the upper rim of calix[4]arene with the cone conformation, the multi-D-π-A units in the same molecule are oriented at nearly the same direction. Therefore, they have higher β value than corresponding mono-D-π-A molecule, and no red shift of the charge transfer band has been observed.[5] We have also demonstrated that *p*-nitroaryl- azo calix[4]arene system is a promising organic molecule with both high β value and good transparency.[6] In order to increase β value in each D-π-A unit, novel substituted arylazo calix[4]arenes with NLO activities have been prepared by the diazo-coupling reaction of calix[4]arene with a diazotate salt solution from *p*-aminobenzaldehyde, followed by the condensation of the aldehyde group and the strong electron-withdrawing moieties such as malononitrile, isophorone. In the preparing process, (*p*-formylphenyl)azo calix[4]arenes are important intermediates. The synthetic method of azocalixarenes has been reported by several groups,[7-9] in which tetrakis(arylazo)-substituted calix[4]arenes were always obtained as a main product. Therefore, these methods are only suitable for the preparation of tetrakis-(arylazo)-substituted calix[4]arenes. Recently, our group developed a novel synthetic method[10,11] for arylazo calix[4]arenes, in which arylamines were diazotized with *iso*amyl nitrite in EtONa/EtOH, and the diazo-coupling reactions were carried out in the presence of carbon dioxide gas in non-aqueous solution at 0—5 ℃. This method is suitable for the preparation of mono-, bis-, tris- and tetrakis(*p*-substituted aryl)azo calix[4]-arenes. However, the diazotization of *p*-aminobenzaldehyde in EtONa/EtOH can not be achieved because of the activity of aldehyde group in strong base solution. In this paper, the synthetic method of mono-, bis-, tris- and tetrakis(*p*-formylphenyl)azo calix[4]arenas was reported, in which *p*-aminobenzaldehyde was diazotized with sodium nitrite in aqueous hydrochloride solution, followed by the diazo-coupling with calix[4]arene in the presence of sodium acetate (Scheme 1).

Results and discussion

The synthetic pathway is shown in Scheme 1. The diazotization reactions of the *p*-aminobenzaldehyde was carried out with sodium nitrite as a source of nitrous acid in aqueous hydrochloride solution at 0—5 ℃. When calix[4]arene **1** and different molar ratio of *p*-aminobenzaldehyde were used, and the diazo-coupling

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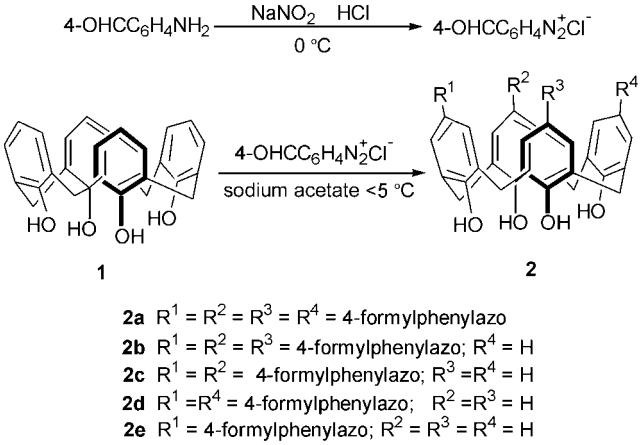
Scheme 1



2a $R^1 = R^2 = R^3 = R^4$ = 4-formylphenylazo
2b $R^1 = R^2 = R^3$ = 4-formylphenylazo; R^4 = H
2c $R^1 = R^2$ = 4-formylphenylazo; $R^3 = R^4$ = H
2d $R^1 = R^4$ = 4-formylphenylazo; $R^2 = R^3$ = H
2e R^1 = 4-formylphenylazo; $R^2 = R^3 = R^4$ = H

reaction solutions were adjusted to pH=7.5—8.5 by adding sodium acetate at 0—5 ℃, corresponding mono-, bis- tris- or tetrakis(*p*-formylphenyl)azo calix[4]arenes were produced with yields 38.7% (**2a**), 14.2% (**2b**), 31.9% (**2c**+**2d**) and 34.6% (**2e**), respectively. The products were purified by silica gel column chromatography eluenting with petroleum ether (60—90 ℃)/chloroform (4∶1, *V*∶*V*), followed with chloroform/methanol (5∶1, *V*∶*V*). The *proximal* (5,11-disubstituted) **2c** and *distal* (5,17-disubstituted) **2d** isomers were also separated. The yields are 18.4% and 13.5%, respectively, and this might be due to the higher statistical probability at the *proximal* positions than at the *distal* position in the diazo-coupling reactions.

In the ^{1}H NMR spectra of isomers **2c** and **2d**, the aromatic protons peaks (Figure 1, peaks a and b) of the 4-formylphenyl moieties in both **2c** and **2d** appear at about δ 8.0 (d, J=8.4 Hz). The peak (Figure 1, peak g) of *para* proton in the phenol moiety displays at about δ 6.80 and is spitted as three peaks with coupling constant 7.6 Hz. However, the obvious difference in δ 6.5—8.0 region can be clearly observed (Figure 1) because **2d** displays better symmetry than **2c**. The aromatic protons of the azo phenol moiety in compound **2d** display only one single peak (Figure 1 **2d**, peak c) at δ 7.77, whereas the aromatic protons of the azo phenol moiety in compound **2c** display two single peak at δ 7.78 and 7.85 (Figure 1 **2c**, peaks c and d). The aromatic *meta*-protons of the phenol moiety display in compound **2d** only one doublet peak (Figure 1 **2d**, peak e) at δ 7.24 (J=7.6 Hz), whereas those in compound **2c** display one pair of doublets (Figure 1 **2c**, peaks e and f) with coupling constant 7.6 Hz. In the ^{13}C NMR spectra, only one peak of the methylene carbons Ar**C**H$_2$Ar in calix[4]arene moiety of compound **2d** appears at δ 32.1, whereas in compound **2c** three peaks of the methylene carbons appear at δ 31.8, 32.1, 33.3. Therefore, **2c** and **2d** are 5,11-disubstituted (*proximal*) and 5,17-disubstituted (*distal*) isomers, respectively.

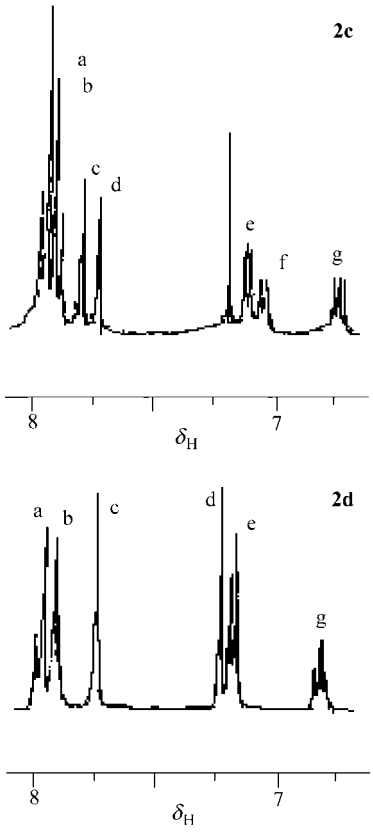


Figure 1 ^{1}H NMR partial spectra of isomers **2c** and **2d** (in δ_H 6.5—8.0 region).

Experimental

Melting points were determined on a Yanaco micro melting point apparatus. Samples for elemental analysis were dried *in vacuo* at 60 ℃. Elemental analyses were carried out using a Perkin Elmer 240C instrument. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker AM 300 (Germany). Mass spectra were recorded by a electrospray mass spectrometer (LCQ, Finnigan) in negative mode. IR spectra were recorded on a Bruker IFS 66v spectrometer (Germany). Preparative column chromatographic separations were performed on G60 silica gel, while precoated silica gel plates (GF_{254}) were used for analytical TLC. All solvents were purified by standard procedures. Compound **1** was synthesized according to the reported method.[12]

Preparation of (*p*-formylphenyl)azo calix[4]arenes derivatives

General procedure A solution of *p*-aminobenzaldehyde (2.4 g, 20 mmol) in 37% concentrated hydrochloride (10 mL) and water (40 mL) was slowly dropped to a solution of $NaNO_2$ (2.5 g, 36 mmol) in water (10 mL) under stirring at 0—5 ℃ to give a diazo salt solution. A solution of a given amount of calix[4]arene **1** in 30 mL of CH_3OH/DMF (5∶8, *V*∶*V*) was dropped to the diazo salt solution under stirring at 0—5 ℃ and sodium acetate was added in order to ad-

just the pH value of the solution to pH=7.5—8.5. The mixture was stirred for 1 h at 0—5 ℃ and additional 30 min at 60 ℃. After be cooled, the red precipitate was collected by filtration and wished with water (3×50 mL), methanol (3×50 mL), which was separated by column chromatography to give (*p*-formylphenyl)azo calix[4]arenes.

5,11,17,23-Tetrakis-[(4-formylphenyl)azo]-25,26,27,28-tetrahydroxycalix[4]arene (2a) Yield 38.7%, m.p.>300 ℃, R_f=0.32 ($CHCl_3$∶MeOH, 10∶1); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 10.30 (bs, 4H, OH), 10.08 (s, 4H, ArCHO), 8.01 (d, J=8.4 Hz, 8H, ArH in the 4-formylphenyl moiety), 7.88 (s, 8H, ArH in the azo phenol moiety), 7.75 (d, J=8.4 Hz, 8H, ArH in the 4-formylphenyl moiety), 5.06 (bs, 4H, $ArCH_2Ar$), 3.91 (bs, 4H, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$, 300 MHz) δ: 32.2 (Ar**C**H_2Ar), 122.4, 127.3, 131.5, 137.4, 147.4, 150.1, 154.0, 156.5 (aromatic C), 192.2 (Ar**C**HO); IR (KBr) *v*: 1594.5 (N=N), 1701.2 (ArCH=O) cm^{-1}; MS (ESIMS) *m/z*: 951.2 ($[M-H]^-$, calcd 951.3). Anal. calcd for $C_{56}H_{40}N_8O_8$: C 70.58, H 4.23, N 11.76; found C 70.06, H 4.65, N 11.91.

5,11,17-Tris-[(4-formylphenyl)azo]-25,26,27,28-tetra-hydroxycalix[4]arene (2b) Yield 14.2%, m.p. >300 ℃, R_f=0.51 ($CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 10.29 (bs, 4H, OH), 10.10 (s, 3H, ArCHO), 8.00 (d, J=8.4 Hz, 6H, ArH in the 4-formylphenyl moiety), 7.94 (d, J=8.4 Hz, 6H, ArH in the 4-formyl-phenyl moiety), 7.88 (s, 2H, ArH in the azo phenol moiety), 7.87 (s, 2H, ArH in the azo phenol moiety), 7.79 (s, 2H, ArH in the azo phenol moiety), 7.23 (d, J= 7.5 Hz, 2H, ArH in the phenol moiety), 6.74 (t, J=7.5 Hz, 1H, ArH in the phenol moiety), 4.40 (bs, 4H, $ArCH_2Ar$), 3.77—3.90 (bs, 4H, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$, 300 MHz) δ: 32.3, 32.7 (Ar**C**H_2Ar), 122.8, 122.9, 123.4, 125.0, 127.9, 128.4, 128.8, 129.3, 129.4, 129.6, 129.7, 131.1, 131.3, 137.4, 147.9, 149.0, 153.2, 156.7 (aromatic C), 192.3 (Ar**C**HO); IR (KBr) *v*: 1597.0 (N=N), 1698.8 (ArCH=O) cm^{-1}; MS (ESIMS) *m/z*: 819.1 ($[M-H]^-$, calcd 819.3). Anal. calcd for $C_{49}H_{36}N_6O_7$: C 71.70, H 4.42, N 10.24; found C 71.60, H 4.13, N 10.04.

5,11-Bis-[(4-formylphenyl)azo]-25,26,27,28-tetra-hydroxycalix[4]arene (2c) Yield 13.5%, m.p.> 300 ℃, R_f=0.66 ($CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 10.27 (bs, 4H, OH), 10.12 (s, 2H, ArCHO), 8.02 (d, J=8.4 Hz, 4H, ArH in the 4-formylphenyl moiety), 7.96 (d, J=8.4 Hz, 4H, ArH in the 4-formylphenyl moiety), 7.85 (s, 2H, ArH in the azo phenol moiety), 7.78 (s, 2H, ArH in the azo phenol moiety), 7.18 (d, J= 7.6 Hz, 2H, ArH in the phenol moiety), 7.12 (d, J=7.6 Hz, 2H, ArH in the phenol moiety), 6.80 (t, J=7.6 Hz, 2H, ArH in the phenol moiety), 4.35 (bs, 4H, $ArCH_2Ar$), 3.75 (bs, 4H, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$, 300 MHz) δ: 31.8, 32.1, 33.3 (Ar**C**H_2Ar), 123.0, 123.3, 123.5, 125.0, 127.9, 128.4, 128.8, 129.2, 129.4, 129.7, 129.9, 131.2, 132.3, 137.5, 148.5, 149.0, 153.2, 156.7 (aromatic C), 192.0 (Ar**C**HO); IR (KBr) *v*: 1595.2 (N=N), 1699.2 (ArCH=O) cm^{-1}; MS (ESIMS) *m/z*: 687.1 ($[M-H]^-$, calcd. 687.2). Anal. calcd for $C_{42}H_{32}N_4O_6$: C 73.24, H 4.68, N 8.13; found C 73.01, H 4.87, N 8.20.

5,17-Bis-[(4-formylphenyl)azo]-25,26,27,28-tetra-hydroxycalix[4]arene (2d) Yield 18.4%, m.p.> 300 ℃, R_f=0.76 ($CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 10.26 (bs, 4H, OH), 10.08 (s, 2H, ArCHO), 8.00 (d, J=8.4 Hz, 4H, ArH in the 4-formylphenyl moiety), 7.93 (d, J=8.4 Hz, 4H, ArH in the 4-formylphenyl moiety), 7.77 (s, 4H, ArH in the azo phenol moiety), 7.24 (d, J=7.6 Hz, 4H, ArH in the phenol moiety), 6.85 (t, J=7.6 Hz, 2H, ArH in the phenol moiety), 4.34 (bs, 4H, $ArCH_2Ar$), 3.75 (bs, 4H, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$, 300 MHz) δ: 32.1 (Ar**C**H_2Ar), 122.8, 123.4, 125.0, 127.9, 128.8, 129.3, 129.6, 129.7, 147.4, 148.6, 153.1, 156.8 (aromatic C), 192.2 (Ar**C**HO); IR(KBr) *v*: 1594.9 (N=N), 1696.4 (ArCH=O); MS(ESIMS) *m/z*: 687.2 ($[M-H]^-$, calcd 687.2). Anal. calcd for $C_{42}H_{32}N_4O_6$: C 73.24, H 4.68, N 8.13; found C 73.02, H 4.91, N 8.07.

5-Mono-[(4-formylphenyl)azo]-25,26,27,28-tetra-hydroxycalix[4]arene (2e) Yield 34.6%, m.p.> 300 ℃, R_f=0.56 ($CHCl_3$∶petroleum ether, 1∶1, *V*∶*V*); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 10.25 (bs, 4H, OH), 10.10 (s, 1H, ArCHO), 8.02 (d, J=8.4 Hz, 2H, ArH in the 4-formylphenyl moiety), 7.95 (d, J=8.4 Hz, 2H, ArH in the 4-formylphenyl moiety), 7.76 (s, 2H, ArH in the azo phenol moiety), 7.18 (d, J=7.6 Hz, 2H, ArH in the phenol moiety), 7.12 (d, J=7.60 Hz, 2H, ArH in the phenol moiety), 7.08 (d, J=7.6 Hz, 2H, ArH in the phenol moiety), 6.80 (t, J=7.6 Hz, 2H, ArH in the phenol moiety), 6.74 (t, J=7.6 Hz, 1H, ArH in the phenol moiety), 4.32 (bs, 4H, $ArCH_2Ar$), 3.60—3.73 (bs, 4H, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$, 300 MHz) δ: 32.0, 32.2 (Ar**C**H_2Ar), 122.8, 122.9, 123.4, 125.0, 127.9, 128.4, 128.8, 129.3, 129.4, 129.6, 129.7, 131.1, 131.3, 137.4, 147.9, 149.0, 153.2, 156.7 (aromatic C), 191.8 (Ar**C**HO); IR(KBr) *v*: 1597.0 (N=N), 1695.3 (ArCH=O) cm^{-1}; MS(ESIMS) *m/z*: 555.0 ($[M-H]^-$, calcd 555.2). Anal. calcd for $C_{35}H_{28}N_2O_5$: C 75.53, H 5.07, N 5.04; found C 75.20, H 5.45, N 4.95.

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