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## A new prearranged tripodant ligand N,N',N''-trimethyl-N,N',N''-tris(3-pyridyl)-1,3,5-benzene tricarboxamide is easily obtained via the N-methyl amide effect

Mikkel Jørgensen\* and Frederik C. Krebs

The Danish Polymer Centre, Risø National Laboratory, PO Box 49, DK-4000 Roskilde, Denmark

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Abstract—The *N*-methyl amide *cis* generating effect has been utilised to create a new prearranged tripodant ligand in two synthetic steps from benzene-1,3,5-tricarboxylic acid. Crystals of the ligand itself and of complexes with metal salts such as silver(I) triflate, copper(I) and copper(II) chloride and ruthenium(II) chloride have been prepared and the crystal structures solved by analysis of X-ray diffraction data. © 2001 Elsevier Science Ltd. All rights reserved.

Yamaguchi et al. and others have shown in a number of papers that N-methylation of benzoylanilides changes the normal trans-amide configuration to a cis configuration with the aryl groups arranged in a Vshaped plane-to-plane geometry.<sup>1,2</sup> In the following we will call this interesting effect the 'methyl amide effect'. The Cambridge Structural Database (CSD) has been searched for NH and N-methyl biaryl-carboxamide occurrences<sup>2</sup> showing that the conformational change from trans to cis is strictly adhered to. While the effect has been substantiated through numerous crystal structures of model compounds, there have been few reports that take specific advantage of the N-methyl effect. In the present work, we describe how to use the effect in a very simple way to create a new pre-arranged tripodal ligand.

In the special case of 1,3,5-benzene tricarboxamide with three *N*-methyl-aniline groups, all three anilide substituents were found to be orientated to the same side of the central benzene triamide ring.<sup>1</sup> The question was whether this structural feature would be preserved if the three aniline moieties were functionalised. In the case of such a general structure generating element it would be possible to make prearranged ligands for metal ions. Careful inspection of the native 1,3,5-benzene tricarboxamide structure showed that the three carbon atoms *meta* to the amide groups are close to the central  $C_3$ -axis. Substitution with nitrogen atoms in these positions would clearly aid in the construction of a tripodant ligand molecule. The orientation of the ligand atoms could thus be rigidly fixed to accommodate tetrahedral or octahedral complexes of transition metal ions.

The new tripodant ligand N,N',N''-trimethyl-N,N',N''-tris(3-pyridyl)-1,3,5-benzene tricarboxamide (**2a**) with three pyridine moieties prearranged to bind metal ions has been prepared in a one-step reaction between 3-methylamino-pyridine and 1,3,5-benzene tricarboxylic acid chloride. Crystals of the ligand itself and of complexes with metal salts such as silver(I) triflate, copper(I) and copper(II) chloride have been prepared and the crystal structures solved by analysis of X-ray diffraction data.

We set out to test the generality of being able direct all three anilide substituents to the same side of the central benzene ring by synthesising various substituted molecules according to Scheme 1. 1,3,5-Benzene tricarboxylic acid chloride was treated with either 4-nitroaniline or 4-amino-benzoic acid ethyl ester to prepare the corresponding NH amides. *N*-Methylation was carried out with potassium *t*-butoxide/methyl iodide in THF.<sup>2</sup> Alternatively, the aniline part could be methylated first, followed by reaction with the benzene tricarboxylic acid chloride. This route was investigated using 3-aminopyridine, which was *N*-methylated according to the procedure of Clarke–Lewis and Thompson.<sup>3</sup>

Proton NMR spectra of the *N*-methylated amides 2a-c are very simple (and different from the corresponding

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<sup>\*</sup> Corresponding author. E-mail: mikkel.joergensen@risoe.dk

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Scheme 1. i. C<sub>6</sub>H<sub>3</sub>(COCl)<sub>3</sub>, Et<sub>2</sub>N; ii. KO-t-Bu, THF, CH<sub>3</sub>I; iii. (a) TsCl, py.; (b) (CH<sub>3</sub>O)<sub>2</sub>SO<sub>2</sub>; (c) H<sub>2</sub>SO<sub>4</sub>.

NH amides 1a-c) suggesting that they have  $C_3$  symmetry regardless of the preparation route and substituents. Dramatic shielding effects are observed in the <sup>1</sup>H NMR spectra when comparing the NH amides 1a-b to the *N*-methylated amides **2a**–**c**. For the NH amide triester 1a, signals due to the 12 aryl protons on the three aniline rings occur together at 8.01 ppm, while in the N-methyl amide 2a, two doublets are seen at 8.00 and 6.61 ppm. The signals from six of these protons have thus changed by 1.4 ppm upfield in accordance with the magnetic shielding expected for the protons orientated towards the plane of adjacent rings.<sup>4</sup> Similar effects are observed for the other triamides prepared. The structures in solution of the N-methyl amides are therefore in accordance with the crystal structure obtained by Yamaguchi for the native compound.

Crystals of sufficient quality for X-ray diffraction were grown from acetonitrile/ethanol. The crystal structures of these compounds (see Figs. 1–3) clearly show that the *N*-methyl amide effect is a general and powerful structure determinant. In all cases, the three aniline substituents bend to the same side of the central ring in a propeller like arrangement. The edge of each ring makes contact with the neighbouring ring plane, suggesting that the  $C_3$  symmetric conformer is especially stabilised by these Van der Waals interactions.

The molecular geometry as established from the X-ray structures for the neutral compounds **2a**, **2b** and **2c** is very similar to the previously reported parent tribenzenoid system.<sup>1</sup> In the case of **2a** we found a cubic space group in contrast to the original authors, and as suggested in a recent errata<sup>5</sup> for this parent compound. While **2a** is different (differing with three less hydrogen atoms) it is reasonable to expect that these compounds could be isostructural. The complexes with Ag(I) and Ru(II) have a near perfect octahedral coordination environment around the metal ion. It is noticeable that the ruthenium complex is more contracted due to the doubly charged cation. This is reflected in the plane-toplane distance between the benzene rings in the com-



Figure 1. A stereoview of the molecular geometry as determined from the X-ray structure of the ligand 2a. Compounds 2b and 2c have a very similar molecular geometry. The solvent molecule of 2a has been omitted for clarity.



Figure 2. A Stereoview of the molecular geometry of the transition metal complex of 2a with Ag(I). The counter ion and solvent molecule are omitted for clarity. The geometry of the Ru(II) complex is very similar.



Figure 3. Stereoviews of the molecular geometry of the transition metal complexes of 2a with Cu(I) (above) and Cu(II) (below). Counter ions, solvent molecules and the disordered chlorine atom for the Cu(II) salt are omitted for clarity.

plex 11.047(2) Å for the Ag(I) complex and 10.362(8) Å for the Ru(II) complex. The Cu(I) complex shows a near tetrahedral coordination of the metal ion, whereas the Cu(II) complex shows a near square pyramidal coordination of the metal ion involving two chloride ions and two pyridine nitrogen atoms in the square. The typical pyridine nitrogen to metal distances observed are 2.524(3), 2.137(12), 2.068(2) and 2.104(3) Å for the Ag(I), Ru(II), Cu(I) and Cu(II) complexes, respectively. The data shows that the ligand 2a can adapt to varying coordination numbers, as well as metal-to-ligand distances.

## **Experimental procedures**

**1a**: 1,3,5-Benzenetricarboxylic acid (2.10 g, 10 mmol) was refluxed together with thionyl chloride (25 mL) for 1 h. Excess thionyl chloride was distilled at reduced pressure leaving the benzenetricarboxylic acid chloride as an oil. This oil was dissolved in methylene chloride (20 mL) and added slowly to a mixture of 4-aminobenzoic acid ethyl ester (5 g, 30 mmol) and triethyl amine (3 mL) in methylene chloride (50 mL). The mixture was stirred at ambient temperature for an additional 30 min to complete the reaction, whereupon the solvents were

removed in vacuum. The residue was recrystallised from 96% ethanol to give N,N',N''-tris(4-ethoxycarbonylphenyl)-1,3,5-benzenetricarboxamide **1a** as a white crystalline powder (6.25 g, 95% yield). Mp 238– 9°C. Anal. found: C, 64.25; H, 5.37; N, 6.16. Calcd for C<sub>36</sub>H<sub>33</sub>N<sub>3</sub>O<sub>9</sub>·H<sub>2</sub>O: C, 64.57; H, 5.27; N, 6.27; <sup>1</sup>H NMR  $\delta_{\rm H}$  (250.1 MHz, CDCl<sub>3</sub>–DMSO- $d_6$ , 1:1): 10.62 (3H, s), 8.87 (3H, s), 8.01 (12H, s), 4.34 (6H, q, *J* 7 Hz), 1.40 (9H, t, *J* 7 Hz) ppm. <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>– DMSO- $d_6$ , 1:1)  $\delta$ : 14.4, 60.7, 119.8, 125.6, 130.4, 130.6, 135.5, 143.4, 165.1, 165.9.

**1b**: Obtained from 4-nitroaniline and benzene-1,3,5-tricarboxylic acid chloride, as described in Reference 6.

2a: 3-Methylaminopyridine (3.3 g, 30.5 mmol) and triethylamine (3.5 g, 35 mmol) were dissolved in chloroform (150 mL). 1,3,5-Benzene tricarboxylic acid chloride (2.65 g, 10 mmol) in chloroform (50 mL) was added dropwise. The reaction mixture was stirred at ambient temperature for a further hour and then the solvents were evaporated in vacuum. The residue was triturated with methanol (100 mL), filtered and washed with methanol and petrol. Finally, the product N,N', N''-trimethyl-N,N',N''-tris(3-pyridyl)-1,3,5-benzene tricarboxamide was crystallised from methylene chloride/acetonitrile (yield: 3.4 g, 71%.). Mp 199-200°C. Anal. found: C, 59.40; H, 4.74; N, 14.76. Calcd for C<sub>27</sub>H<sub>24</sub>N<sub>6</sub>O<sub>3</sub>·CH<sub>2</sub>Cl<sub>2</sub>: C, 59.47; H, 4.63; N, 14.86. <sup>1</sup>H NMR (250.1 MHz, CDCl<sub>3</sub>)  $\delta$ : 3.39 (9H, s), 7.04 (3H, d, J 7 Hz), 7.12 (3H, s), 7.26–7.32 (3H, m), 8.05 (3H, s), 8.48 (3H, d, J 7 Hz). <sup>13</sup>C NMR (62.9 MHz,  $CDCl_3$ )  $\delta$ : 38.6, 124.4, 130.8, 134.3, 135.8, 141.1, 148.19, 148.24, 168.7 ppm. Crystal data: C<sub>29</sub>H<sub>30</sub>N<sub>6</sub>O<sub>4</sub>, M = 526.59, cubic space group Pa-3, a, b, c =17.4437(13) Å,  $\alpha$ ,  $\beta$ ,  $\gamma = 90^{\circ}$ , V = 5307.8(7) Å<sup>3</sup>, Z = 8,  $D_{\rm c} = 1.318 \text{ g cm}^{-3}$ , T = 120(2) K,  $\mu = 0.090 \text{ cm}^{-1}$ ,  $wR_2 =$ 0.2658 (1702 unique reflections  $[I > 2\sigma(I)]$ ), R = 0.0774.

**2b**: Triamide **1a** (3.0 g, 4.7 mmol) was dissolved in THF (200 mL) together with methyl iodide (2 mL). Potassium *t*-butoxide (1.8 g) was added and the reaction mixture was stirred 48 h whereupon the solvent was removed. The remaining solid was partitioned between cold dilute hydrochloric acid (50 mL) and methylene chloride (100 mL). The slightly yellow organic phase was evaporated to dryness and crystallised from ethanol (20 mL) to give **2b** as colourless crystals of N,N',N'' - trimethyl - N,N',N'' - tris(4 - ethoxycarbonyl-phenyl)-1,3,5-benzene tricarboxamide (1.65 g, 51%). Mp 218–219°C. Anal. found: C, 66.99; H, 5.74; N, 6.15. Calcd for C<sub>39</sub>H<sub>39</sub>N<sub>3</sub>O<sub>9</sub>·0.5EtOH: C, 67.03; H, 5.91; N, 5.86; <sup>1</sup>H NMR (250.1 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.00 (6H, d, *J* 8 Hz), 7.08 (3H, s), 6.61 (6H, d, *J* 8 Hz), 4.39 (6H, q, *J* 

7 Hz), 3.39 (9H, s), 1.40 (9H, s) ppm. <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>)  $\delta$ : 14.7, 38.1, 61.8, 127.1, 129.0, 130.7, 131.0, 136.1, 148.7, 165.8, 169.0 ppm. *Crystal data*: C<sub>39</sub>H<sub>39</sub>N<sub>3</sub>O<sub>9</sub>, *M*=693.73, trigonal space group *R*-3*c*, *a*, *b*=14.2571(15) Å, *c*=61.462(9) Å,  $\alpha$ ,  $\beta$ =90°,  $\gamma$ =120°, *V*=10819(2) Å<sup>3</sup>, *Z*=12, *D*<sub>c</sub>=1.278 g cm<sup>-3</sup>, *T*=120(2) K,  $\mu$ =0.091 cm<sup>-1</sup>, *wR*<sub>2</sub>=0.1293 (1915 unique reflections [*I*>2 $\sigma$ (*I*)], *R*=0.0421.

**2c**: Prepared from **1b**, potassium *t*-butoxide and methyl iodide as above. Recrystalised from dilute ethanol to give N,N',N''-trimethyl-N,N',N''-tris(4-nitrophenyl)-1,3, 5-benzene tricarboxamide (yield: 67%). Mp 131–132°C. Anal. found: C, 56.86; H, 4.13; N, 13.06. Calcd for C<sub>30</sub>H<sub>24</sub>N<sub>6</sub>O<sub>9</sub>·H<sub>2</sub>O: C, 57.14; H, 4.16; N, 13.33; <sup>1</sup>H NMR (250.1 MHz, CDCl<sub>3</sub>–DMSO- $d_6$ , 1:1)  $\delta$ : 3.33 (9H, s), 7.16 (6H, d, J 9 Hz), 7.25 (3H, s), 8.14 (6H, d, J 9 Hz) ppm. <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>–DMSO- $d_6$ , 1:1)  $\delta$ : 38.2, 125.0, 127.9, 130.3, 136.5, 145.7, 150.3, 168.5 ppm. *Crystal data*: C<sub>32</sub>H<sub>30</sub>N<sub>6</sub>O<sub>10</sub>, *M*=658.62, trigonal space group *R*-3, *a*, *b*=12.1180(12) Å, *c*=37.310(5) Å,  $\alpha, \beta = 90^{\circ}, \gamma = 120^{\circ}, V = 4744.8(9) Å^3, Z = 6, D_c = 1.383$  g cm<sup>-3</sup>, *T*=120(2) K,  $\mu = 0.105$  cm<sup>-1</sup>, *wR*<sub>2</sub>=0.2863 (1479 unique reflections [*I*>2 $\sigma(I)$ ]), *R*=0.0968.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44-1223/ 336033; e-mail: deposit@ccdc.cam.ac.uk] on quoting the depository numbers CCDC-162962 (2a), CCDC-162963 (2b), CCDC-162964 (2c), CCDC-162965 (Ag(2a)<sub>2</sub>), CCDC-162966 (Cu(I)2a), CCDC-162967 (Cu(II)2a), CCDC-162968 (Ru(2a)<sub>2</sub>).

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