

Preparation and characterization through electronic properties of 1,2,4,5-tetrazine-ligands and its Ru- thenium-complexes*

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Inorganic Chemistry at the University of
Stuttgart)

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1. Introduction

In recent years the chemistry of substituted 1,2,4,5-tetrazine-ligands and its Ruthenium- and Copper-complexes has proved to be very interesting.

This interest is fed by the fact, that those ligand systems, due to their very low-lying π^* -levels, yield Ruthenium(II)-complexes with rather positive reduction potentials and low-energy charge-transfer absorptions.[1]

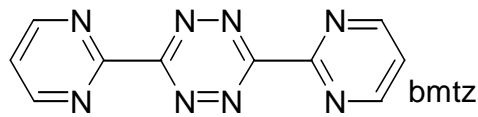
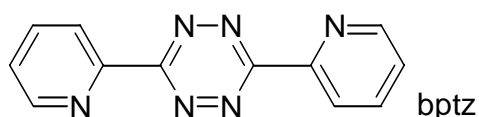
Indeed Hückel MO perturbation calculations reveal the presence of two close-lying unoccupied MOs. One localized in the tetrazine-ring (LUMO), the other one more delocalized over the whole ligand (SLUMO).[2]

Other reasons for the growing interest in those ligands are that they have free basic (chelate) sites for protons or other electrophiles, and that its complexes show huge differences of more than 600mV between the first and second reduction waves.[3]

Therefore such Ruthenium-complexes have applications as photosensitizers in water photolysis systems[4] used for solar energy-technology. They are, like the copper-complexes of the same ligands, also used in supramolecular chemistry[5,6], for molecular bridged arrangements[2] (promoted metal-metal interaction) or pH-control of physical properties involving charge-transfer excited states[2].

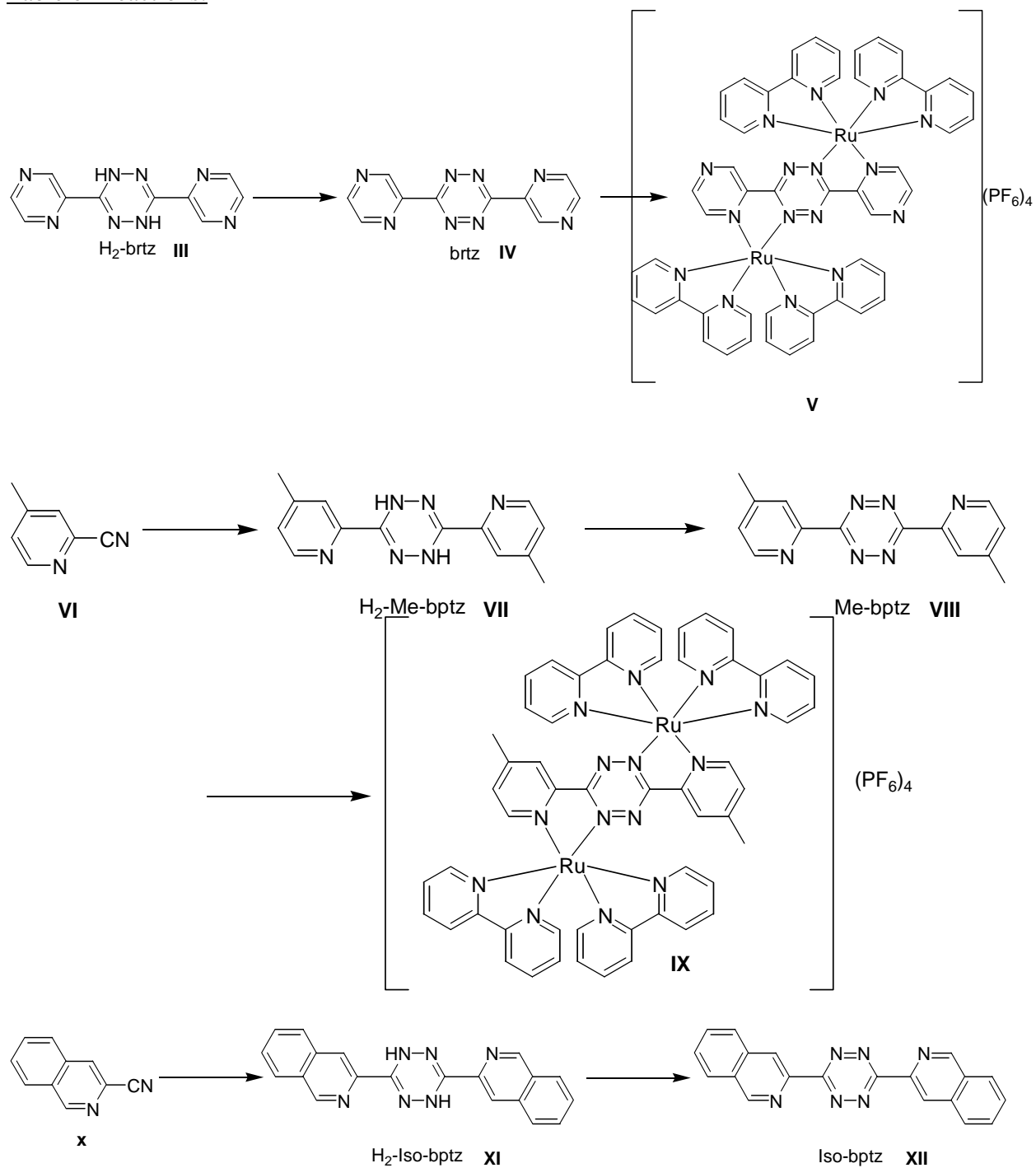
2. Target

The target of the research practical course was the preparation and characterization of substituted tetrazine-ligands in order to check the possibility of preparing dinuclear Ruthenium(II)-complexes with those ligands. The electronic properties of those ligands and complexes should have been also examined, to check if they fit the properties of the already known compounds (like **I** and **II** and its corresponding Ruthenium- and Copper-complexes) and therefore can be used in similar applications with slightly different properties.

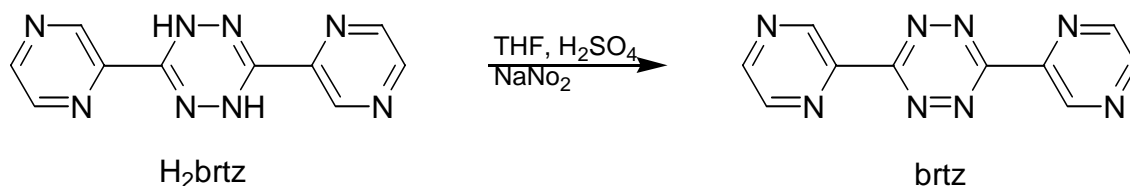


3. Own Results

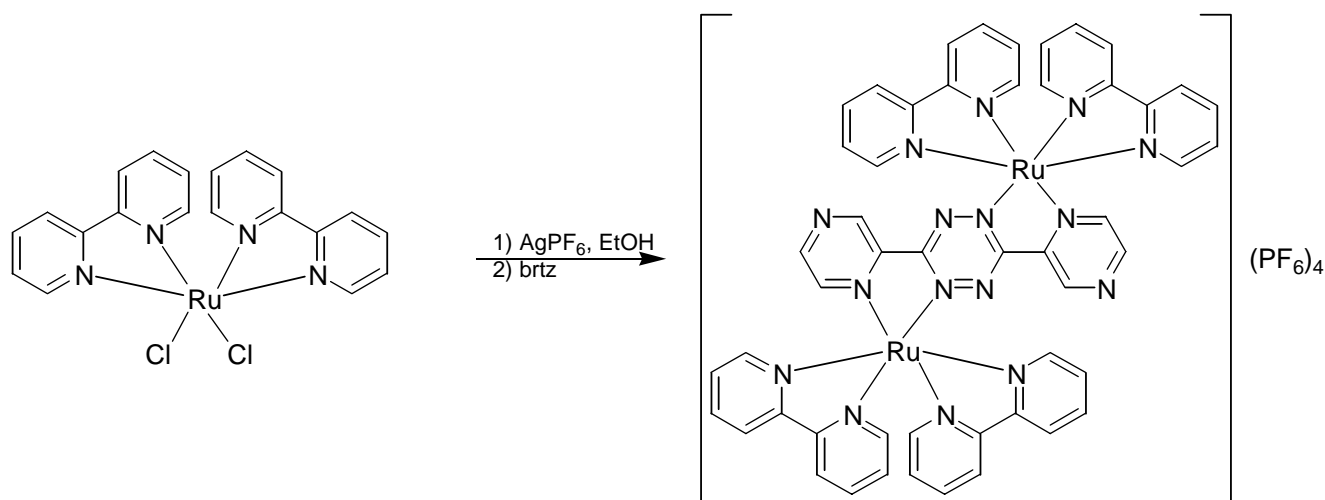
Table of Reactions:



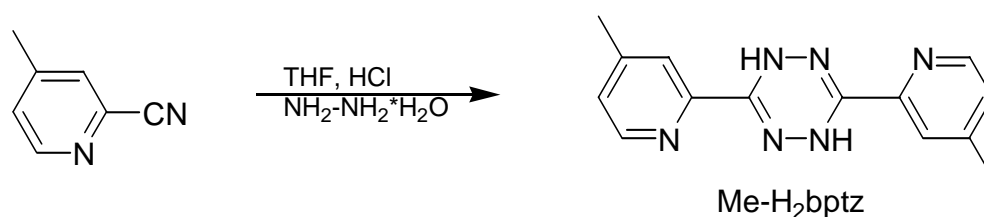
Reactions:



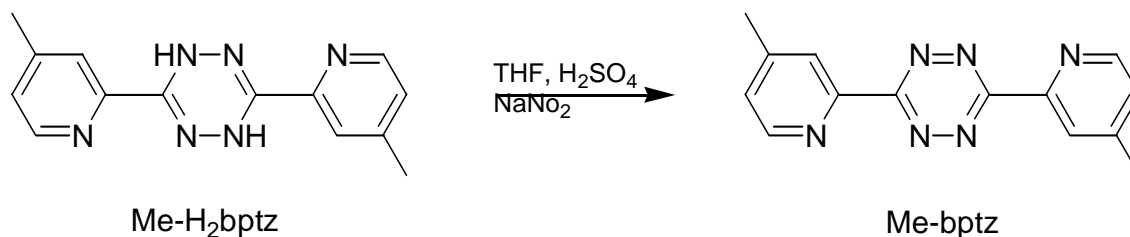
The deprotonation of H₂brtz showed poor yields, due to the bad solubility of H₂brtz in THF. The amounts of sulphuric acid and sodium nitrite used were therefore varied. The amounts stated in the experimental section represent the concentrations, volumes and masses with which the best results were yielded.



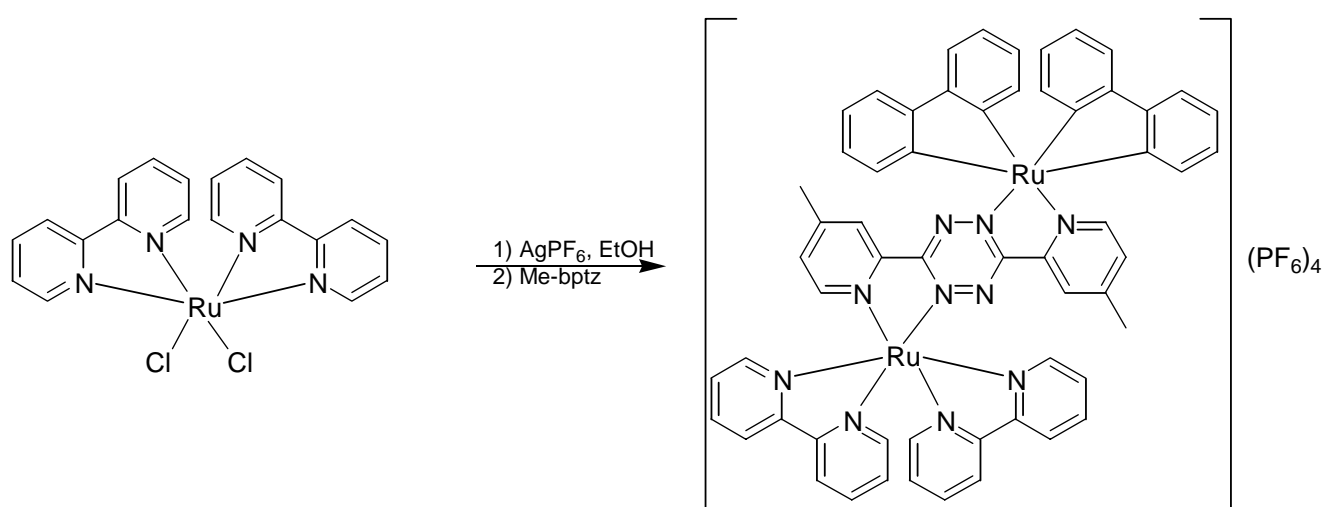
Two Ruthenium-complexes were coupled by the prepared ligand, to yield a dinuclear Ruthenium(II)-complex.



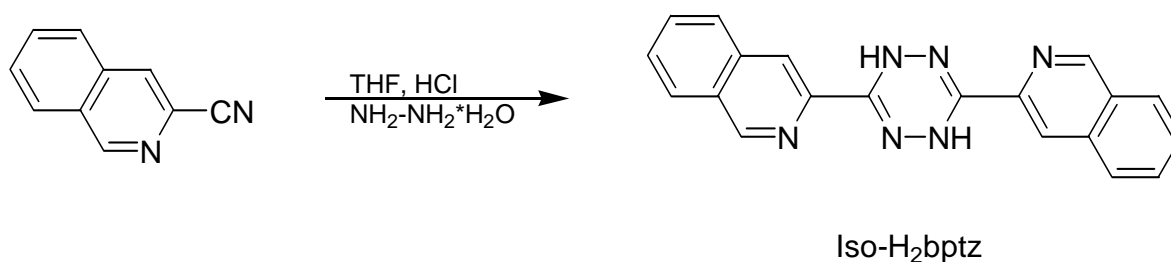
At first the reaction was allowed to stir for just two hours and equimolar amounts of Hydrazine were used for the preparation of the protonated ligand. In some tries the reaction didn't take place, in others the yield was very low, so the reaction time was increased, whereupon a reaction over night showed the best results. Also Hydrazine was used in large excesses, which proved helpful.



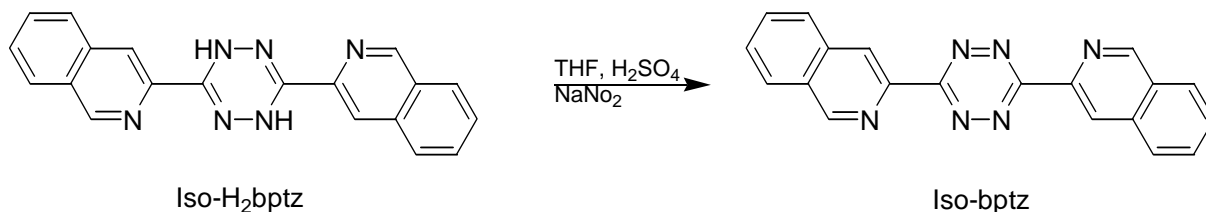
Deprotonation of Me-H₂bptz was done equivalent to Deprotonation of H₂bptz. The difference was the far better solubility of Me-H₂bptz in THF. Therefore the solvent is evaporated after the reaction took place and before the product is extracted in Dichloromethane. The yield was much higher than in the oxidation-step of H₂bptz, although the reaction-time was reduced to 30 minutes.



The same procedure was used to prepare a dinuclear Ruthenium(II)-complex with Me-bptz as coupling ligand, as it was used with bptz.



As the preparation of substituted, protonated tetrazine-ligands with Hydrazine was already optimized with the preparation of Me-H₂bptz, the same procedure was used for preparation of Iso-H₂bptz. The yield was a little bit worse than for Me-H₂bptz, although the reaction has been run a little longer.



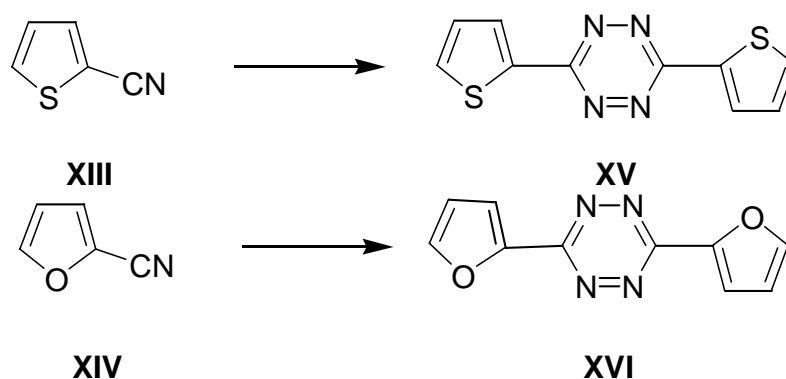
Iso-H₂bptz was well soluble in THF, so that the same procedure was used for its deprotonation than it was used for the deprotonation of Me-H₂bptz.

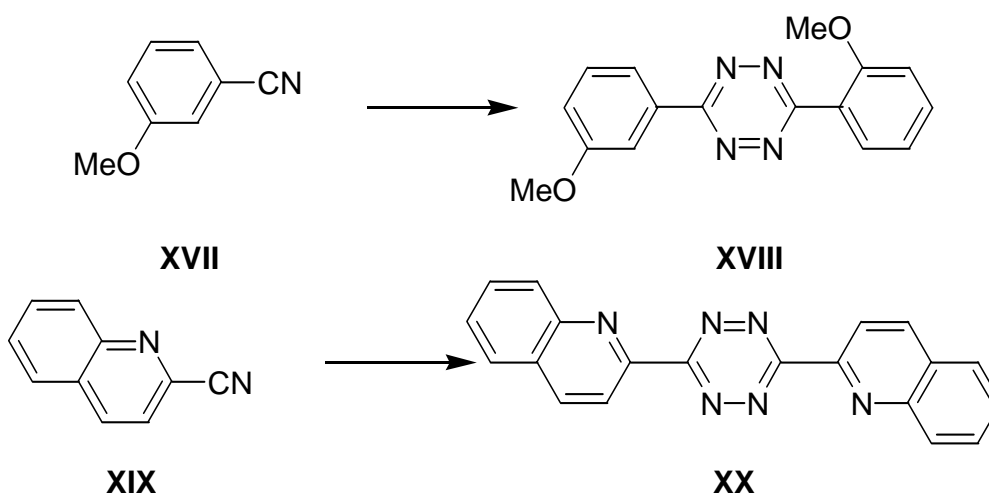
4. Discussion and Outlook

The research practical course proved, that it is possible to prepare different kinds of substituted tetrazine-ligands by the simple method, stated in the experimental section. These ligands could have been also used to generate dinuclear Ruthenium(II)-complexes. This creates new possibilities of preparing other ligands and complexes, as shown below. The properties of the newly created ligands and complexes match the properties of the already known species quite well, so that they can be used for similar applications, to have a broader range of applicable molecules.

Further works on these topics will contain:

- the preparation of a dinuclear Ruthenium(II)-complex with ligand Iso-bptz, which could not be done during the practical-course, due to matters of time
- the preparation of new tetrazine-ligands with the same method by variation of the heteroatom (**XV**, **XVI**), variation of substituents (**XVIII**) and variation of the position of the nitrogen-atom (**XX**).





- the preparation of complexes with the above and already known tetrazine-ligands with another metal-center. Osmium- or copper-complexes might suit for this purpose.

5. Experimental section

Commercially received chemicals:

Ethanol, Tetrahydrofuran, Dichloromethane, Acetonitrile, Sodium nitrite, Sulphuric acid, Hydrazine-Monohydrate, Dimethylsulphoxide, 3-Cyano-isoquinoline, 2-Cyano-4-methyl-pyridin, Ruthenium-bis-bipyridine-dichloride, Silver(I)- hexafluorophosphate

Devices:

- 1) ¹H-NMR-Spectra: Bruker AC 250 F (250 MHz)
- 2) ESR-Spectra: Bruker ESR 300 (9.5GHz)

Preparations:

Bis-pyrazine-1,2,4,5-tetrazine (IV) (brtz)

Compound	Molar Mass [g/mol]	Volume Mass	Density [g/ml]	Amount [mmol]
Bis-pyrazine-1,4-dihydro-1,2,4,5-tetrazine	240.23	101mg	-	0.420
Tetrahydrofuran	72.11	15ml	0.88	183.05
Sulphuric acid	98.08	15ml (0.001M) +45ml (0.01M)	-	-
Sodiumnitrite	69.00	600mg	-	8.696

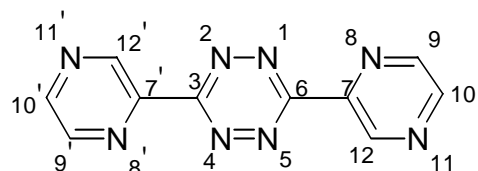
Execution:

0.01 M sulphuric acid is made by adding 0.3ml concentrated sulphuric acid in 500ml water.

101mg of Bis-pyrazine-1,4 dihydro-2,5-tetrazine (H₂-brtz) is dissolved in 15ml THF. After 15ml of 0.01 M sulphuric acid is added, the ligand falls off again. The mixture is cooled down to 0°C and 150mg of Sodium nitrite in water is added. After that the sulphuric acid is concentrated to 0.1 M, by adding 3ml of 98% (concentrated) acid. 15 ml of this acid is added to the reaction mixture, followed by again 150mg of Sodium nitrite, 15ml of 0.1 M sulphuric acid, 300mg of Sodium nitrite and finally 15ml of 0.1 M sulphuric acid. In the meantime the colour of the reaction mixture changes from orange to a deep-red and becomes almost violet/pink after allowing it to stir for at least 2 hours at 0°C. The remaining mixture is now extracted three times with Dichloromethane. After drying it over Sodium sulphate, the volume is reduced so that the product starts to precipitate. Finally the flask is put into the refrigerator over night and the product is filtered off and washed with absolute Ethanol.

Due to the bad solubility of Bis-pyrazine-1,4 dihydro-2,5-tetrazine in THF, the yield is quite poor.

Yield: 21mg = 21.0%



¹H-NMR (250.13MHz, CDCl₃): δ(ppm)= 8.90 (s, 2H, on C-atoms 10,10'); 8.95 (s, 2H, on C-atoms 9,9'); 9.95 (s, 2H, on C-atoms 12,12')

ESR (anion-radical, room temperature): nonett, expected: nonett (2nI + 1; I_(N₂)=1; n=4)
g=2.0041 compared to g=2.0023 for a free electron in vacuo

-> electronic coupling to all 4 nitrogen-atoms in the tetrazine-ring
(3,6-Bis-4'-methyl-pyridine)-1,4-dihydro-1,2,4,5-tetrazine(VII)

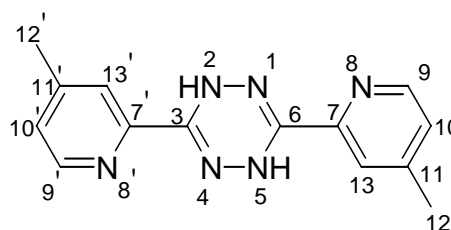
(Me-H₂-bptz)

Compound	Molar Mass [g/mol]	Volume Mass	Density [g/ml]	Amount [mmol]
2-Cyano-4-methyl-pyridine	118.14	500mg	-	4.232
Tetrahydrofuran	72.11	10ml	0.88	122.04
Hydrochloric acid	36.46	0.8ml	0.91	19.97
Hydrazine-Monohydrate	50.06	4.5ml	1.02	91.69

Execution:

0.5g of 4-Methyl-2-Cyano-pyridine is dissolved in 10-15ml THF and 0.8ml HCl(conc.) is added. A pale to colourless precipitate is formed and the mixture is stirred for 20 minutes. 4.5ml of Hydrazine-Monohydrate is added very slowly via a dropping-funnel. After that, the mixture is heated under reflux for at least 5 hours. Refluxing over night should be preferred. After cooling the THF is evaporated and about 50ml of water is added to the residue. At last the product can be filtered and recrystallized from Ethanol. If one allows the filtrate to stand overnight, even more product is precipitated.

Yield: 316mg = 28.1%



¹H-NMR (250.13MHz, CDCl₃): δ(ppm)= 2.40 (s, 6H, on C-atoms 12,12'); 7.15 (m, 2H, on C-atoms 10,10' or 13,13'); 7.85 (d, 2H, on C-atoms 9,9'); 8.40 (m, 2H, on C-atoms 10,10' or 13,13'); 8.55 (s,broad, 2H, on N-atoms 2+5)

After D₂O-wash:

¹H-NMR (250.13MHz, CDCl₃): δ(ppm)= 2.40 (s, 6H, on C-atoms 12,12'); 7.15 (m, 2H, on C-atoms 10,10' or 13,13'); 7.85 (d, 2H, on C-atoms 9,9'); 8.40 (m, 2H, on C-atoms 10,10' or 13,13'); peak at 8.55 ppm disappeared.

(3,6-Bis-4'-methyl-pyridine)-1,2,4,5-tetrazine(VIII) (Me-bptz)

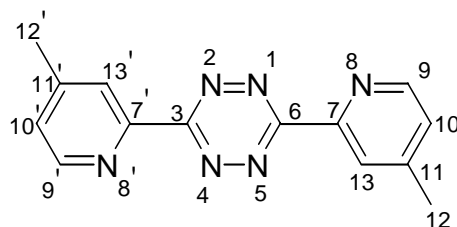
Compound	Molar Mass [g/mol]	Volume Mass	Density [g/ml]	Amount [mmol]
Bis-4-methyl-pyridine-1,4-dihydro-1,2,4,5-tetrazine	266.31	70mg	-	0.263
Tetrahydrofuran	72.11	5ml	0.88	61.02
Sulphuric acid	98.08	10ml (0.001M) +40ml (0.01M)	-	-
Sodium nitrite	69.00	400mg	-	5.797

Execution:

0.01 M sulphuric acid is made by adding 0.3ml concentrated sulphuric acid in 500ml water.

70mg of Bis-4-methyl-pyridine-1,4-dihydro-1,2,4,5-tetrazine (Me-H₂-bptz) is dissolved in 5ml THF. After 10ml of 0.01 M sulphuric acid is added, the ligand falls off again. The mixture is cooled down to 0°C and 100mg of Sodium nitrite in water is added. After that the sulphuric acid is concentrated to 0.1 M, by adding 3ml of 98% (concentrated) acid. 10 ml of this acid is added to the reaction mixture, followed by again 100mg of Sodium nitrite, 10ml of 0.1 M sulphuric acid, 200mg of Sodium nitrite and finally 20ml of 0.1 M sulphuric acid. In the meantime the colour of the reaction mixture changes from orange to a deep-red and becomes almost violet/pink after allowing it to stir for at least 30 minutes at 0°C. The THF is evaporated after this and the remaining mixture extracted three times with Dichloromethane. After drying it over Sodium sulphate, the volume is reduced, so that, the product starts to precipitate. Finally the flask is put into the refrigerator over night and the product is filtered off and washed with absolute Ethanol.

Yield: 44mg = 63.3%



¹H-NMR (250.13MHz, CDCl₃): δ(ppm)= 2.55 (s, 6H, on C-atoms 12,12'); 7.40 (m, 2H, on C-atoms 10,10' or 13,13'); 8.55 (d, 2H, on C-atoms 9,9'); 8.80 (m, 2H, on C-atoms 10,10' or 13,13')

ESR (anion-radical, room temperature): nonett, expected: nonett (2nI + 1; I_(N₂)=1; n=4)
g=2.0039

(3,6-Bis-3'-isoquinoline)-1,4-dihydro-1,2,4,5-tetrazine(XI)

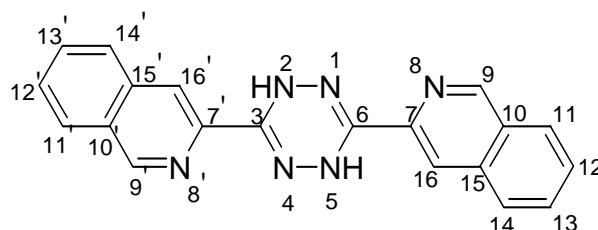
(Iso-H₂-bptz)

Compound	Molar Mass [g/mol]	Volume Mass	Density [g/ml]	Amount [mmol]
3-Cyano-isoquinoline	154.17	500mg	-	3.243
Tetrahydrofuran	72.11	5ml	0.88	61.02
Hydrochloric acid	36.46	0.6ml	0.91	14.98
Hydrazine-Monohydrate	50.06	5ml	1.02	101.86

Execution:

0.5g of 3-Cyano-isoquinoline is dissolved in 5-10ml THF and 0.6ml HCl(conc.) is added. A pale to colourless precipitate is formed and the mixture is stirred for 20 minutes. 5ml of Hydrazine-Monohydrate is added very slowly via a dropping-funnel. After that, the mixture is heated under reflux for at least 6 hours. Refluxing over night should be preferred. After cooling the THF is evaporated and about 50ml of water is added to the residue. At last the product can be filtered and recrystallized from Ethanol. If one allows the filtrate to stand overnight, even more product is precipitated.

Yield: 385mg = 35.1%



¹H-NMR (250.13MHz, CDCl₃): δ(ppm)= 7.6-8.0 (m, 8H, on C-atoms 11,11',12,12',13,13',14,14'); 8.50 (s, 2H, on C-atoms 9,9' or 16, 16'); 8.75 (s, broad, 2H, on N-atoms 2+5); 9.25 (s, 2H, on C-atoms 9,9' or 16,16')

After D₂O-wash:

¹H-NMR (250.13MHz, CDCl₃): δ(ppm)= 7.6-8.0 (m, 8H, on C-atoms 11,11',12,12',13,13',14,14'); 8.50 (s, 2H, on C-atoms 9,9' or 16, 16'); 9.25 (s, 2H, on C-atoms 9,9' or 16,16'); peak at 8.75ppm disappeared.

(3,6-Bis-3'-isoquinoline)-1,2,4,5-tetrazine(XII)

(Iso-bptz)

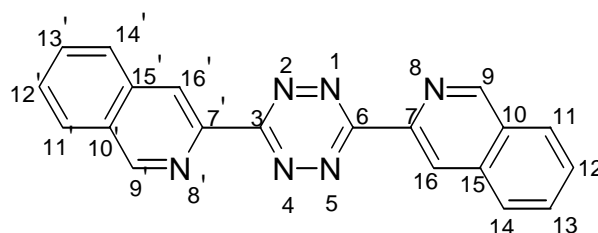
Compound	Molar Mass [g/mol]	Volume Mass	Density [g/ml]	Amount [mmol]
Bis-3-isoquinoline-1,4-dihydro-1,2,4,5-tetrazine	338.37	32mg	-	0.095
Tetrahydrofuran	72.11	1.5ml	0.88	18.31
Sulphuric acid	98.08	3ml (0.001M) + 12ml (0.01M)	-	-
Sodium nitrite	69.00	165mg	-	2.391

Execution:

0.01 M sulphuric acid is made by adding 0.3ml concentrated sulphuric acid in 500ml water.

32mg of Bis-3-isoquinoline-1,4-dihydro-1,2,4,5-tetrazine (Iso-H₂-bptz) is dissolved in 1.5ml THF. After 3ml of 0.01 M sulphuric acid is added, the ligand falls off again. The mixture is cooled down to 0°C and 55mg of Sodium nitrite in water is added. After that the sulphuric acid is concentrated to 0.1 M, by adding 3ml of 98% (concentrated) acid. 3 ml of this acid is added to the reaction mixture, followed by again 55mg of Sodium nitrite, 3ml of 0.1 M sulphuric acid, 55mg of Sodium nitrite and finally 12ml of 0.1 M sulphuric acid. In the meantime the colour of the reaction mixture changes from orange to a deep-red and becomes almost violet/pink after allowing it to stir for at least 30 minutes at 0°C. The THF is evaporated after this and the remaining mixture extracted three times with Dichloromethane. After drying it over Sodium sulphate, the volume is reduced, so that, the product starts to precipitate. Finally the flask is put into the refrigerator over night and the product is filtered off and washed with absolute Ethanol.

Yield: 15mg = 46.9%



¹H-NMR (250.13MHz, CDCl₃): δ(ppm)= 7.85-8.00 (m, 4H, on C-atoms 11,11',14,14' or 12,12',13,13'); 8.35 (m, 4H, on C-atoms 11,11',14,14' or 12,12',13,13'); 9.25 (s, 2H, on C-atoms 9,9' or 16,16'); 9.65 (s, 2H, on C-atoms 9,9' or 16,16')

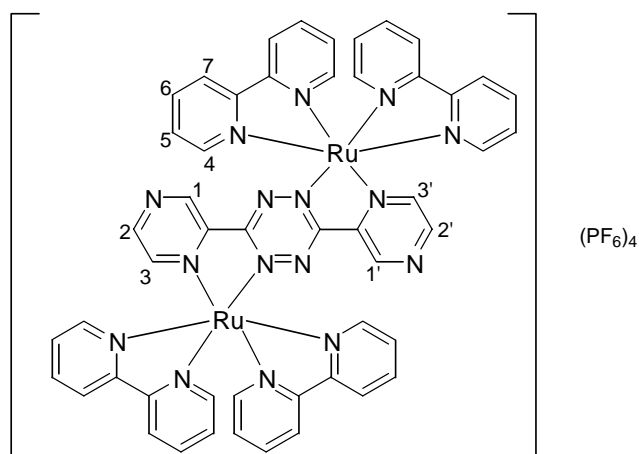
Bis-(Ruthenium-bis-bipyridine)-pyrazine-1,2,4,5-tetrazine(V) $\{[\text{Ru}(\text{bpy})_2]_2\text{-brtz}\}(\text{PF}_6)_4$

Compound	Molar Mass [g/mol]	Volume Mass	Density [g/ml]	Amount [mmol]
Ruthenium-bis-bipyridine-dichloride	328.16	97mg	-	0.300
Silver(I)- hexafluorophosphate	252.83	101mg	-	0.400
Ethanol	46.07	15ml	0.78	253.96
Bis-pyrazine-1,2,4,5-tetrazine	238.21	24mg	-	0.100

Execution:

A mixture of 97mg of Ruthenium-bis-bipyridine-dichloride and 101mg of Silver(I)-hexafluorophosphate is heated to reflux for 1 hour in 15ml of dry Ethanol. After cooling and filtration of the precipitated silverchloride, the filtrate is collected, 24mg of Bis-pyrazine-1,2,4,5-tetrazine (brtz) is added to the filtrate and refluxed overnight. A dark blue solid falls off. The solid is collected by filtration, washed with cold Ethanol and recrystallized from Dichloromethane/Heptane (1:5)

Yield: not determined



ESR (reduction, room temperature): more than nine peaks, because nitrogen-atoms in tetrazine-ring are no longer equivalent (two attached to Ruthenium-centers, two have a free site)-> more couplings. $g=2.0044$

ESR (reduction, 4K): doublet; almost every coupling disappeared, due to the low temperature; $g= 2.0169; 1.993; 1.9833; 1.975$

Bis-(Ruthenium-bis-bipyridine)-4-methyl-pyridine-1,2,4,5-tetrazine(IX)
 {[Ru(bpy)₂]₂-Me-bptz}(PF₆)₄

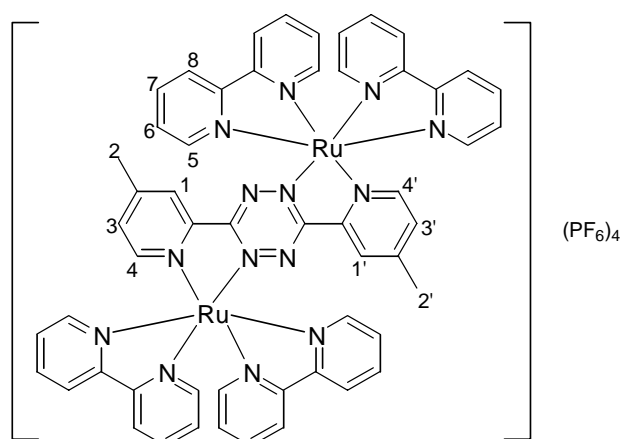
Compound	Molar Mass [g/mol]	Volume Mass	Density [g/ml]	Amount [mmol]
Ruthenium-bis-bipyridine-dichloride	122.12	50g	-	409.4
Silver(I)- hexafluorophosphate	197.07	110g	-	558.2
Ethanol	138.20	36g	-	260.5
Bis-4-methyl-pyridine - 1,2,4,5-tetrazine	73.10	500ml	0.94	6430

Execution:

A mixture of 97mg of Ruthenium-bis-bipyridine-dichloride and 101mg of Silver(I)-hexafluorophosphate is heated to reflux for 1 hour in 15ml of dry Ethanol. After cooling and filtration of the precipitated silverchloride, the filtrate is collected, 27 mg of Bis-4-methyl-pyridine-1,2,4,5-tetrazine (Me-bptz) is added to the filtrate and refluxed overnight. A dark blue solid falls off. The solid is collected by filtration, washed with cold Ethanol and recrystallized from Dichloromethane/Heptane (1:5)

Bis-4-methyl-pyridine-1,2,4,5-tetrazine (Me-bptz)

Yield: not determined



ESR (reduction, room temperature): more than nine peaks, because nitrogen-atoms in tetrazine-ring are no longer equivalent (two attached to Ruthenium-centers, two have a free site)-> more couplings. g=2.0042

ESR (reduction, 110K): pentett; most couplings disappeared, due to the low temperature;

g=2.01733; 1.97502

6. Appendix

¹H-NMR-Data of:

brtz
Me-H₂bptz
Me-H₂bptz after D₂O-wash
Me-bptz
Iso-H₂bptz
Iso-H₂bptz after D₂O-wash
Iso-bptz

ESR-Data of:

brtz
Me-bptz
[Ru(bpy)₂]₂brtz (2x)
[Ru(bpy)₂]₂-Me-bptz (2x)

7. Literature

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