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Highly functionalised 3,4,5-trisubstituted 1,2,4-triazoles for future use as ligands in coordination polymers

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ABSTRACT

An optimised synthesis of 3,4,5-trisubstituted 1,2,4-triazoles, that can be used as linkers for metal organic frameworks (MOFs), is described. The substituents in 3- and 5-position of the triazole have a significant impact on the torsion angles between the aromatic rings and therefore influence on solubility and coordination behaviour of these ligands.

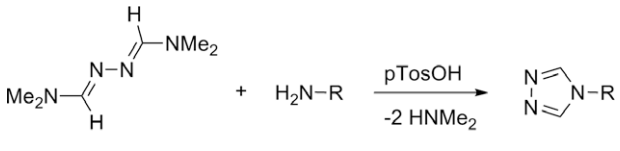
Microporous materials such as coordination polymers, so called MOFs, but also microporous organic polymers such as polymers of intrinsic microporosity (PIMs) have gained increasing interest in the last decade.[1,2] MOFs possess a narrow pore size distribution due to the underlying crystallinity of these materials. In addition, they can reach high surface areas making them interesting for adsorption applications as impressively demonstrated by $Cu_3(btc)_2$ (btc = 1,3,5-benzene tricarboxylate).[3,4]

Carboxylate ligands have been extensively studied as polyfunctional linkers.[5–7] Apart from this, MOFs containing linkers with a combination of both neutral donor groups such as pyridines or 1,2,4-triazoles and charged functional groups such as carboxylates are of interest.[8–13] A convenient way for the preparation of 3,5-unsubstituted 1,2,4-triazoles was reported by Bartlett and Humphrey in 1967 (Scheme 1).[14]

An optimised procedure was presented by Naik et al. in 2008.[15] This method involves the reaction of *N,N*-dimethyl formamide azine **1** with primary amines mediated by *p*-toluene sulfonic acid. The driving force of this reaction is the release of dimethyl amine as well as the stability of the aromatic heterocycle formed. **1** can be obtained through reaction of the Vilsmeier–Haack reagent with hydrazine hydrate. As we observed, simple adaptations of this method using different *N,N*-dimethyl-substituted amides in order to obtain the corresponding azines failed. Eventually *N,N*-dimethyl acetamide azine **2** was obtained in 25% yield by using anhydrous hydrazine and phosphorus oxychloride instead of hydrazine hydrate and thionyl chloride similarly to a procedure of Zelenin et al.[16] Because of the limited stability of these azines a further modification does not appear to be promising.

The synthesis of **3** was first reported by Guo et al. using a more complicated approach.[12] We obtained compounds **3**–**7** (Scheme 2) in good yields using Bartlett's method, **5** was obtained as the respective monodimethyl ammonium salt. Nevertheless, a more sophisticated approach to the synthesis of 3,5-disubstituted 1,2,4-triazoles is the reaction of 2,5-disubstituted 1,3,4-oxadiazoles with respective primary amines (Scheme 4). 1,3,4-Oxadiazoles can be easily obtained either through reaction of carboxylic acid hydrazides with triethyl orthoacetate or by reaction of 5-substituted tetrazoles with carboxylic anhydrides or acid chlorides (Scheme 3).[17,18] Following up a modified procedure of Brooker et al. involving a condensation reaction of thioamides and hydrazides we were not able to obtain the respective products.[19]

2,5-Dimethyl-1,3,4-oxadiazole as the simplest 1,3,4-oxadiazole was obtained on a molar scale in 85% optimised yield from acetyl hydrazine and triethyl orthoacetate following the known reaction procedure.[20,21] In a similar manner, we obtained the corresponding 3- and 4-pyridine-substituted oxadiazoles **12** and **13**. Although these oxadiazoles are known in the literature, our route combines



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Scheme 1. General procedure for synthesis of 3,5-unsubstituted 1,2,4-triazoles.[14,15]

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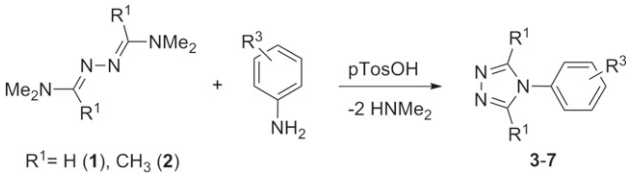
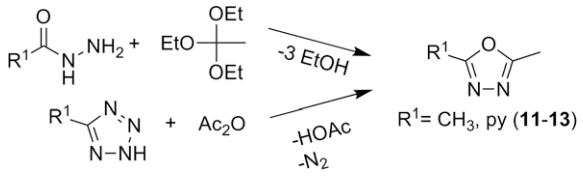
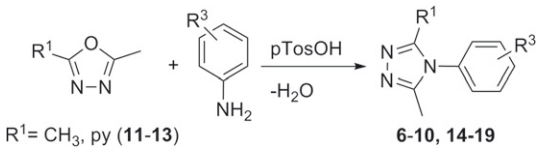


R^1	R^3	Product	compound	yield in %	Mp. in °C (decomp.)
H	p-CO_2H	**3**	H(trz-pba)	70	327
H	m-CO_2H	**4**	H(trz-mba)	65	264
H	m,m'-CO_2H	**5**	(H_2NMe_2)H(trz-ia)	45	238
CH_3	p-CO_2H	**6**	H(Me_2trz-pba)	77	322
CH_3	m-CO_2H	**7**	H(Me_2trz-mba)	81	257

Scheme 2. Synthesis of **3**–**7**.



Scheme 3. Synthesis of 2,5-disubstituted 1,3,4-oxadiazoles.



R^1	R^3	Product	compound	yield in %	Mp. in °C (decomp.)
CH_3	p-CO_2H	**6**	H(Me_2trz-pba)	58	322
CH_3	m-CO_2H	**7**	H(Me_2trz-mba)	62	257
CH_3	m,m'-CO_2H	**8**	H_2(Me_2trz-ia)	85	261
CH_3	m-CO_2H, m'-NH_2	**9**	H(3-Me_2trz-5-NH_2-ba)	72	287
CH_3	m-CO_2H, m'-Me_2trz	**10**	H(3,5-(Me_2trz)$_2$-ba)	54	326
*2*py	p-CO_2H	**14**	H(Me-2py-pba)	48	287
*2*py	m-CO_2H	**15**	H(Me-2py-mba)	52	234
*3*py	p-CO_2H	**16**	H(Me-3py-pba)	45	293
*3*py	m-CO_2H	**17**	H(Me-3py-mba)	41	211
*4*py	p-CO_2H	**18**	H(Me-4py-pba)	68	275
*4*py	m-CO_2H	**19**	H(Me-4py-mba)	34	253

Scheme 4. Synthesis of **6**–**10** and **14**–**19**.

both easier access and higher yields.[22–24] Nevertheless, applying this method, the respective 2-pyridine-substituted oxadiazole **11** is not accessible making it necessary to switch to a more general approach. Therefore the corresponding pyridyl-substituted tetrazoles were synthesised starting from the nitriles according to the literature methods.[25]

Eventually the synthesis of the 1,2,4-triazoles was performed applying a modified method of Meyer, who achieved the triazole synthesis by the condensation of 2,5-dialkyl- or 2-alkyl-5-aryl-substituted 1,3,4-oxadiazoles and highly reactive primary amines such as aniline and methyl amine.[26] In our case, the reactivity of the amines used is not sufficient to succeed in the formation of triazoles, hence we improved the reaction by the addition of *p*-toluene sulphonic acid to enable the reaction.

Performing the reaction in xylene under reflux the reaction time is about two days. The desired products were isolated by simple filtration. Scheme 4 summarises the syntheses of **6**–**10** and **14**–**19** with yields ranging from 34% to 85%. The products were characterised by standard proton and carbon NMR and IR spectroscopy as well as by mass spectrometry and elemental analysis.

1. Single crystal structure determinations

Suitable crystals for single crystal X-ray structure analysis were obtained in case of eight 1,2,4-triazolyl benzoic acids by hydrothermal recrystallisation. The X-ray diffraction data were collected on diffractometers IPDS-I and IPDS-2T (STOE) using Mo-K_α radiation (λ = 71.073 pm). The structures were solved by direct methods and refined using SHELX.[27] Non-hydrogen atoms were refined anisotropically. Hydrogen atoms of the water molecule in **5** were located and refined isotropically, whereas the coordinates of the remaining hydrogen atoms were calculated for idealised positions.

Despite the fact that the molecular structures of the ligands show no exceptional specialities, the crystal structures reveal interesting details due to the packing in solid state.

In general, the single molecules are hydrogen-bonded via the carboxylic functions and triazole rings, in case of **16** additionally

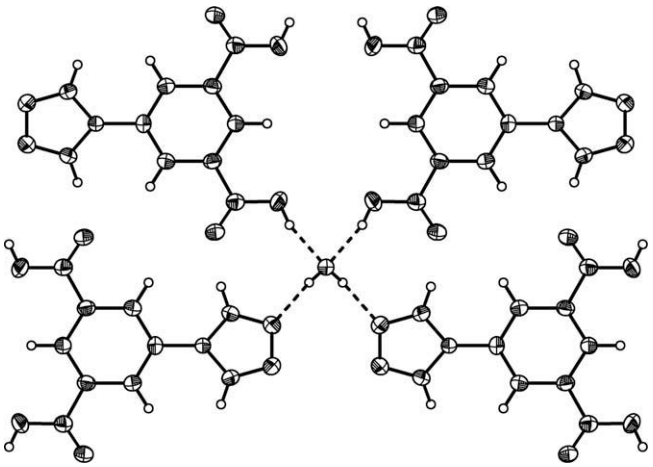


Figure 1. Hydrogen bonding of **5** in solid state.

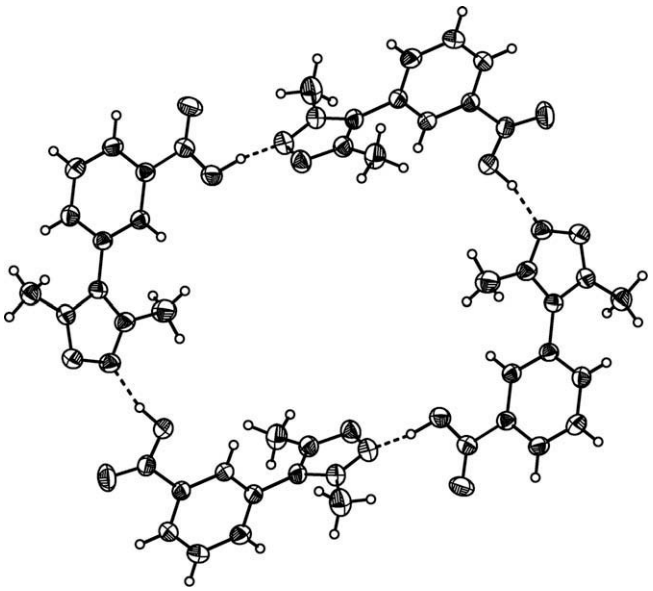


Figure 2. Four-membered macrocycles in **7** formed by hydrogen bonds.

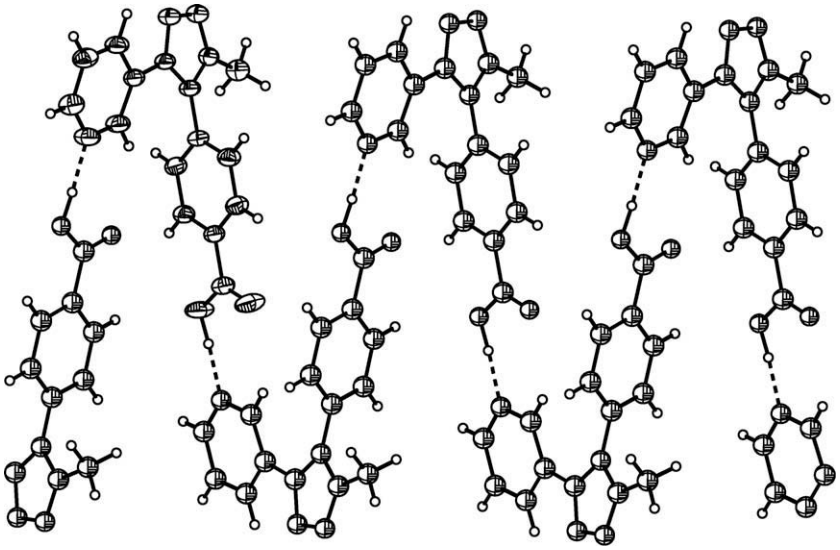


Figure 3. Molecular structure of **14**.

the pyridine ring is involved. Whereas carboxylic acids typically form hydrogen-bonded dimers, this behaviour is not observed in case of the present ligands. Nevertheless, the carboxylic acids behave as donors while the triazole and pyridine rings act as acceptors.

Although there are the same functional groups in very similar arrangements, a large variety of hydrogen-bonded networks is observed. In the solid state structure of **5** (Fig. 1) a three-dimensional network is formed by hydrogen bonding of both the carboxylic functions and the triazole groups with the water molecules present in the crystal structures. In contrast, **7** contains four-membered macrocycles (Fig. 2) formed by hydrogen bonds.

While **3**, **4**, **6**, **14** and **16** form simple chains, **8** builds up layers due to the second carboxyl group. Interestingly, the one-dimensional network of **16** is built up by the combination of carboxyl and pyridyl groups exclusively (Fig. 3), leaving out triazoles, whereas in the other cases only carboxyl and triazole groups interact.

Furthermore, different π–π stacking interactions, especially offset-face to face arrangements are observable in most of the structures.[28] The crystal structure of **13** displays short distances of 335 pm between the triazole rings (Fig. 4).

The crystal structures allow to draw conclusions on solubility and melting points taking into account the torsion angles between the aromatic rings (Table 1). Sterically more demanding substituents in 3- and 5-position of the triazole lead to higher torsion angles between the phenyl and the triazole ring. This results in weaker π–π stacking interactions of the aromatic rings in solid state leading to lower melting points and to an increase of solubility in common organic solvents.

Table 1
Selected torsion angles

	Torsion angle phenyl–triazole (°)	Torsion angle triazole–pyridine (°)
3[a]	33.80(7), 20.77(7)	—
4	30.2(1)	—
5	47.4(3)	—
6	59.40(5)	—
7[a]	70.25(5), 80.84(5)	—
8	59.86(6)	—
14	56.11(5)	25.59(6)
16	74.81(4)	16.11(7)

[a] Two different torsion angles are observed due to two crystallographic independent molecules in the asymmetric unit.

As an example, **3** shows a relatively small torsion angle of 20.77(7)° or 33.80(7)°, respectively, and has the highest melting point of 327 °C due to the unsubstituted ring. Molecules containing 3,5-dimethylated triazol rings with a higher sterical demand lead to torsion angles of 56–81°. The dimethylated derivative **5** shows a lower melting point associated with the observed torsion angles.

Furthermore, pyridyl substituents do not significantly influence the torsion angles between the triazole and the phenyl ring in comparison with the dimethylated compounds. The torsion angle between the triazole and the pyridine is about 16–26°. Therefore the presence of isolated π-systems on each aromatic ring can be concluded. As can be seen from the decomposition temperatures the pyridine substituted molecules **14** and **16** have the lowest thermal stability.

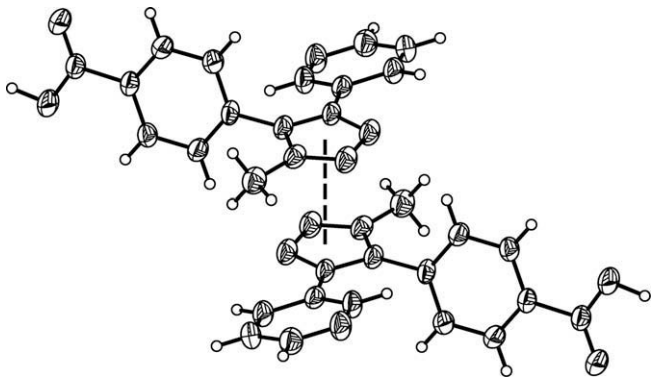


Figure 4. π–π stacking interactions between triazole rings of **16**.

2. Conclusions

We presented the syntheses of 3,5-disubstituted 1,2,4-triazolyl benzoic acids, that might be potentially useful ligands for the preparation of coordination polymers. We established a straightforward route for the synthesis of ligands combining the properties of both functional groups. Furthermore, we introduced pyridine substituents as additional nitrogen donor groups into the 1,2,4-triazole ring. Up to now, the combination of these substituents has been unknown in the literature to our knowledge. Currently, we

are investigating coordination polymers incorporating these ligands.

Acknowledgements

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Supplementary data

CCDC 751484–751491 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data (experimental and spectroscopic data) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.11.098.

References and notes

1. Carta, M.; Msayib, K. J.; Budd, P. M.; McKeown, N. B. *Org. Lett.* **2008**, *10*, 2641–2643.
2. McKeown, N. B.; Budd, P. M. *Chem. Soc. Rev.* **2006**, *35*, 675–683.
3. Chui, S. S.-Y.; Lo, S. M.-F.; Charmant, J. P. H.; Guy Orpen, A.; Williams, I. D. *Science* **1999**, *283*, 1148–1150.
4. Hartmann, M.; Kunz, S.; Himsl, D.; Tangermann, O.; Ernst, S.; Wagener, A. *Langmuir* **2008**, *24*, 8634–8642.
5. Li, H.; Eddaoudi, M.; O'Keeffe, M.; Yaghi, O. M. *Nature* **1999**, *402*, 276–279.
6. Férey, G.; Mellot-Draznieks, C.; Serre, C.; Millange, F.; Dutour, J.; Surblé, S.; Margiolaki, I. *Science* **2005**, *309*, 2040–2042.
7. Latroche, M.; Surblé, S.; Serre, C.; Mellot-Draznieks, C.; Llewellyn, P. L.; Lee, J.-H.; Chang, J.-S.; Jhung, S. H.; Férey, G. *Angew. Chem.* **2006**, *118*, 8407–8411.
8. Klingele, M. H.; Brooker, S. *Coord. Chem. Rev.* **2003**, *241*, 119–132.
9. Beckmann, U.; Brooker, S. *Coord. Chem. Rev.* **2003**, *245*, 17–29.
10. Haasnoot, G. *Coord. Chem. Rev.* **2000**, *200*, 131–185.
11. Lukashuk, L. V.; Lysenko, A. B.; Rusanov, E. B.; Chernega, A. N.; Domasevitch, K. V. *Acta Crystallogr., Sect. C* **2007**, *63*, m140–m143.
12. Zou, R.-Q.; Cai, L.-Z.; Guo, G.-C. *J. Mol. Struct.* **2005**, *737*, 125–129.
13. Bondar, O. A.; Lukashuk, L. V.; Lysenko, A. B.; Krautscheid, H.; Rusanov, E. B.; Chernega, A. N.; Domasevitch, K. V. *Cryst. Eng.* **2008**, *10*, 1216–1226.
14. Bartlett, R. K.; Humphrey, I. R. *J. Chem. Soc. C* **1967**, 1664–1667.
15. Naik, A. D.; Marchand-Brynaert, J.; Garcia, Y. *Synthesis* **2008**, *1*, 149–154.
16. Zelenin, K. V.; Khrustalev, V. A.; Sergutina, V. P. *Zh. Org. Khimii* **1980**, *16*, 276–281.
17. Jursic, B. S.; Zdravkovskif, Z. *Synth. Commun.* **1994**, *24*, 1575–1582.
18. Vereshchagin, L. I.; Petrov, A. V.; Kizhnyaev, V. N.; Pokatilov, F. A.; Smirnov, A. I. *Russ. J. Org. Chem.* **2006**, *42*, 1049–1055.
19. Klingele, M. H.; Brooker, S. *Eur. J. Org. Chem.* **2004**, 3422–3434.
20. Curtius, Th.; Schöfer, G.; Schwan, N. *J. Prakt. Chem.* **1892**, *51*, 180–196.
21. Ainsworth, C.; Hackler, R. E. *J. Org. Chem.* **1966**, *31*, 3442–3444.
22. Efimova, Y. A.; Artamonova, T. V.; Koldobskii, G. I. *Russ. J. Org. Chem.* **2008**, *44*, 1345–1347.
23. Rigo, B.; Fasseur, D.; Cauliez, P.; Couturier, D. *Synth. Commun.* **1989**, *19*, 2321–2335.
24. Navarrete-Vazquez, G.; Molina-Salinas, G. M.; Duarte-Fajardo, Z. V.; Vargas-Villarreal, J.; Estrada-Soto, S.; Gonzalez-Salazar, F.; Hernandez-Nunez, E.; Said-Fernandez, S. *Bioorg. Med. Chem.* **2007**, *15*, 5502–5508.
25. Finnegan, W. G.; Henry, R. A.; Lofquist, R. *J. Am. Chem. Soc.* **1958**, *80*, 3908–3911.
26. Meyer, R. DRP No. 574944, 1933.
27. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **2008**, *64*, 112–122.
28. Meyer, E. A.; Castellano, R. K.; Diederich, F. *Angew. Chem.* **2003**, *115*, 1244–1287.