

The Need for Both Mo and Cu X-ray Radiation in the Elucidation of the Challenging Crystal Structures of Two Derivatised Resorcarenes

Application Note

X-ray Crystallography

Background

A research group at the Ruhr University in Bochum, are investigating a series of bowlshaped resorcarene molecules derivatised with pendant amino acid groups. When four amino acids or peptides are fixed around the rim of a resorcarene they adopt conformations and geometries uncommon in free peptides. The resulting derivatised resorcarene are able to recognize protein surfaces, as demonstrated by the cyclopeptide-calixarenes. Consequently, the peptide cavitands are expected to enclose organic guest molecules and small peptide sequences and to facilitate catalytic function.



Figure 2. The co-mounted Mo and Cu Enhance X-ray sources of the Gemini diffractometer.



Agilent Technologies

Authors

Dr. Neil R. Brooks Agilent Technologies UK

Christian M Hülsbusch Prof. Martin Feigel Organische Chemie I Ruhr-University Bochum D-44780 Germany

Priv. Doz. Dr. Iris M Müller Analytische Chemie Ruhr-University Bochum D-44780 Germany In Bochum the have synthesized a new resorcarene derivative having four pendant amino acid arms. This was achieved via the reaction of a bromo-derivatised resorcarene molecule with a functionalized methionine amino acid (Figure 1).

Herein are reported the challenging single crystal X-ray diffraction studies of both the bromo-derivatised resorcarene and the final reaction product of the functionalized methionine pendant resorcarene.



Figure 1. Reaction scheme.

Experimental

Crystals of the bromo-resorcarene and the functionalised methionine pendant resorcarene were re-crystallized from acetonitrile and a bromo-resorcarene crystal was mounted onto an Agilent Gemini R diffractometer (Figure 2). Data were then collected over 22 hours using Mo radiation at 100K.

Upon completion of the molybdenum data collection, the pendant resorcarene crystal was mounted onto the same Gemini R diffractometer and data were collected over a further 38 hours, this time using Cu radiation, at 100K. In this case the 6× increased X-ray intensity and up to 8× diffracting power afforded by Cu radiation proved important, due to the crystals being small and weakly diffracting. The use of Cu radiation was also essential in order to determine the correct stereochemistry at the molecule's 4 chiral centers.

Results

The crystal structure of the bromo-resorcarene was found to contain one independent molecule in the asymmetric unit and two acetonitrile solvent molecules (Figure 3). As expected with materials of this type the side chains of the resorcarene were disordered over more than one position. These were successfully modelled with the final R1 refining to 6.7%. One of the acetonitrile solvent molecules was found in the cavity of the resorcarene and one was located in between the pentyl groups.

In contrast the crystal structure of the functionalised methionine pendant resorcarene (Figure 4) contained two independent molecules in the asymmetric unit with eight solvent molecules. One of these acetonitrile solvent molecules was encapsulated within the resorcarene bowl. As in the structure of the bromo compound the pentyl groups were extremely disordered, as were the methionine arms and the bulk solvent molecules.

Since Cu radiation was used in data collection it was possible to unequivocally assign the stereochemistry of the four chiral centres in the structure as being the S configuration, the absolute structure factor (Flack) parameter refining to 0.08(5) and the overall final R1 of the structure refining to 11.2%.



Crystal structure of the bromo-resorcarene. Figure 3.

$$\label{eq:c56} \begin{split} & \mathsf{C}_{56}\mathsf{H}_{68}\mathsf{O}_8\mathsf{Br}_4{}^{\bullet}(\mathsf{CH}_3\mathsf{CN})_2{}^{\bullet}(\mathsf{H}_2\mathsf{O})_{0.5}, \, \mathsf{M} = 1280 \text{ g mol}^{-1}.\\ & \text{Triclinic, } \mathsf{PT} \text{ with } \mathsf{a} = 11.770(2), \, \mathsf{b} = 13.142(2), \, \mathsf{c} = 19.826(3) \, \mathring{\mathsf{A}}, \end{split}$$
 $\alpha = 77.314(14), \beta = 76.605(14), \gamma = 84.059(13)^{\circ}; V = 2906.0(8) Å^{3}.$ 6724 reflections observed out of 11084 unique reflections. Crystal size $0.35 \times 0.16 \times 0.08$ mm. Final R1 = 6.7%, wR2 = 19.0%. Resolution 50° = 0.84 Å.



Figure 4. Crystal structure of the functionalised methionine pendant-resorcarene.

$$\begin{split} & \mathsf{C}_{108}\mathsf{H}_{136}\mathsf{N}_8\mathsf{O}_{20}\mathsf{S}_4\text{+}(\mathsf{CH}_3\mathsf{CN}), \, \mathsf{M} = 2035.6 \text{ g mol}^{-1}.\\ & \mathsf{Monoclinic}, \, \mathsf{P2}_1 \text{ with } \mathsf{a} = 18.0146(8), \, \mathsf{b} = 18.2152(8), \, \mathsf{c} = 34.4405(13) \, \mathring{\mathsf{A}},\\ & \boldsymbol{\beta} = 99.237(4)^\circ, \, \mathsf{V} = 11154.7(8) \, \mathring{\mathsf{A}}. \end{split}$$
17246 reflections observed out of 22321 unique reflections.

Crystal size 0.30 × 0.20 × 0.08 mm. Final R1 = 11.2%, wR2 = 28.0%. Flack parameter: 0.08(5). Resolution 101.2° = 1.0 Å.

Conclusions

The unique design of the Gemini system provided for both Mo and Cu wavelengths. The relatively rigid structure of the bromo-resorcarene was obtained using the small molecule crystallography standard: Mo radiation. However, the weakly diffracting nature of the large "floppy" methionine pendant resorcarene prevented any useful data being collected with Mo radiation. This was ascertained by a series of diffraction images recorded using Mo, before the wavelength was changed to Cu with the crystal *in situ*. This wavelength changeover was achieved via a software switch and less than 3 min later Cu data collection had started. The increased flux and diffraction power afforded by the Cu radiation allowed the methionine pendant resorcarene structure to be solved and importantly the stereochemistry to be correctly determined.

The presence of the acetonitrile molecule within the resorcarene cavity of the functionalised pendant resorcarene proved that a small molecule can be encapsulated. Future work will investigate the encapsulation of larger more interesting molecules and the study of catalytic functionality within the cavity.

References

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