

# New Synthesis of (Z,E)-2,7-bis(4-cyanobenzylidene)cycloheptan-1-one under Stereospecific Constraints Induced by Host-Guest Interactions

Arnaud Grandeury<sup>a</sup>, Samuel Petit<sup>b</sup>, Servane Coste<sup>b</sup>, Gérard Coquerel<sup>b</sup>, Cécile Perrio<sup>c</sup>  
and Géraldine Gouhier\*<sup>d</sup>

<sup>a</sup>Max-Planck-Institut für Dynamic komplexer technischer Systeme, Sandorstraße 1, D-39106 Magdeburg, Germany

<sup>b</sup>UPRES EA 3233, SMS, IRCOF, Université de Rouen, 1 Rue Tesnière, F-76821 Mont Saint Aignan cedex, France

<sup>c</sup>UMR CEA, Centre Cycéron, Bd H. Becquerel, BP 5229, F-14074 Caen Cedex, France

<sup>d</sup>UMR CNRS 6014, LFAOC, IRCOF, Université de Rouen, 1 Rue Tesnière F-76821 Mont Saint Aignan cedex, France. Fax: (+33) 2-3552-2971; Tel: (+33) 2-3552-2467; E-mail: [geraldine.gouhier@univ-rouen.fr](mailto:geraldine.gouhier@univ-rouen.fr)

## Contents

General experimental section

General procedure to form crystalline complexes with Cds

Crystal growth and X-ray structure determination from single crystals

Synthesis and physical data for compounds **1a**, **1c**, **10a-b** and **11**

XRPD patterns of complexes **7a-b**, **8a-b**, **9a-b**

<sup>1</sup>H NMR spectrometries of **10a-b** and **11**

### General experimental section

Unless otherwise stated,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR spectra were recorded in deuterium solvent on a spectrometer Bruker AC 300, operating at 300 and 100 MHz respectively. Chemical shifts are expressed in parts per million (ppm). IR Spectra were recorded on a Perkin-Elmer 16 PC FT-IR and expressed in  $\text{cm}^{-1}$ . Chemicals were used without further purification. The XRPD patterns were recorded on a Siemens D5005 diffractometer (Cu-K $\alpha$ ).

### General procedure to form crystalline complexes with Cds

After the dissolution of the host in water (60°C for **4a**, **5a**, **6a** / 25°C for **4b**, **5b**, **6b**), addition of **3** (1:1 ratio) induces the appearance of an emulsion which disappears after about 2 hours under stirring. Crystallization is induced by cooling (0°C for Cds) due to normal solubility or by heating (40°C for PM-Cds) due to retrograde solubility. Crystals are filtrated at the same temperature to avoid partial dissolution.

### Crystal growth and X-ray structure determination from single crystals

Single crystals were grown within few days by slow isothermal (T=40°C) evaporation of an aqueous saturated solution. Data collection was performed with a Bruker Smart Apex automatic diffractometer equipped with a CCD detector, a graphite monochromator and Mo K $\alpha$  radiation (0.71073Å). Measured intensities were corrected for Lorentz-polarization effects, and an empirical absorption correction was applied. The SHELX-97 (G. M. Sheldrick, SHELX-97, University of Gottingen, Germany, 1997) program has been used for resolution and refinements. Initial atomic coordinates were obtained by applying direct methods and were subsequently refined by using the full-matrix least-square techniques. All non-hydrogen atoms were refined anisotropically whereas hydrogen atom positions were calculated without further refinement. In order to avoid divergences during the last refinement steps, geometric restraints were applied to the cyclic moieties of the guest (14 distances, 5 angles). Furthermore, the geometry of 7 out of the 24 methoxy groups of the host was improved by using 9 distances restraints and 2 angle restraints. Structural descriptions were performed with the modelling software Sybyl (v. 6.9, Tripos Ass. Inc., 2004) implemented on O2 Silicon Graphics workstations.

### Synthesis of **1a**, **1c**, **10a-b**

**3** or **9b** (first carefully ground for 30 minutes in a mortar until amorphization controlled by XRPD), **2** (1 or 2 equivalents) and PTSA (0.25 equivalent for **3** or 0.4 equivalent for **9b**) are introduced in an open tube suitable for MW irradiation with a magnetic stirrer. Samples are exposed to a focused MW (CEM Discover System™ Magnetron Frequency 2455 MHz) without considering any

temperature restriction: 35W / 7 minutes for **3**; to 100W / 20 minutes for **9b** (a maximum temperature of 110°C is detected in absence of supramolecular complexes; close to the melting point of **2**), whereas lower temperatures (50-60°C) were recorded from the starting material **9b**. Such important differences can be due to the presence of local hot spots in the supramolecular matrix. The crude product is washed and filtrated successively with diethyl ether and ethanol, to afford **1a**: 72%. **6b**, **1c**, **10a-b** are recovered by flash chromatography on silica and eluted with cyclohexane / ethyl acetate (85:15).

### Physical data for compounds **1a**, **1c**, **10a-b**, and **11**

**(E,Z)-2,7-bis(4-cyanobenzylidene)cycloheptan-1-one (1a)**; yellow powder; m.p. 192-194°C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 25°C): δ=7.59-7.14 (br, 9 H), 6.49 (s, 1 H), 2.70-2.55 (br, 2 H), 2.45-2.35 (br, 2 H), 2.00-1.80 (br, 4 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 25°C): δ=199.1, 147.9, 140.8, 140.3, 140.0, 135.5, 134.1, 132.3, 132.2, 130.1, 129.9, 129.8, 128.9, 118.7, 118.5, 112.1, 111.0, 35.9, 31.9, 29.8, 28.0; IR (CH<sub>2</sub>Cl<sub>2</sub>): ν=3055 (CN), 1679 (CO), 1265.

**(E,E)-2,7-bis(4-cyanobenzylidene)cycloheptan-1-one (1c)**; yellow pale powder; m.p. 225-227°C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 25°C): δ=7.68 (d, <sup>3</sup>J(H, H)=8.4 Hz, 4 H), 7.51 (d, <sup>3</sup>J(H, H)=8.4 Hz, 4 H), 7.36 (s, 2 H), 2.70-2.50 (br, 4 H); 2.00-1.80 (br, 4 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 25°C): δ=198.0, 143.8, 140.2, 134.0, 132.2, 129.7, 118.5, 111.6, 28.7, 27.9; IR (CH<sub>2</sub>Cl<sub>2</sub>): ν=3055 (CN), 1679 (CO), 1265.

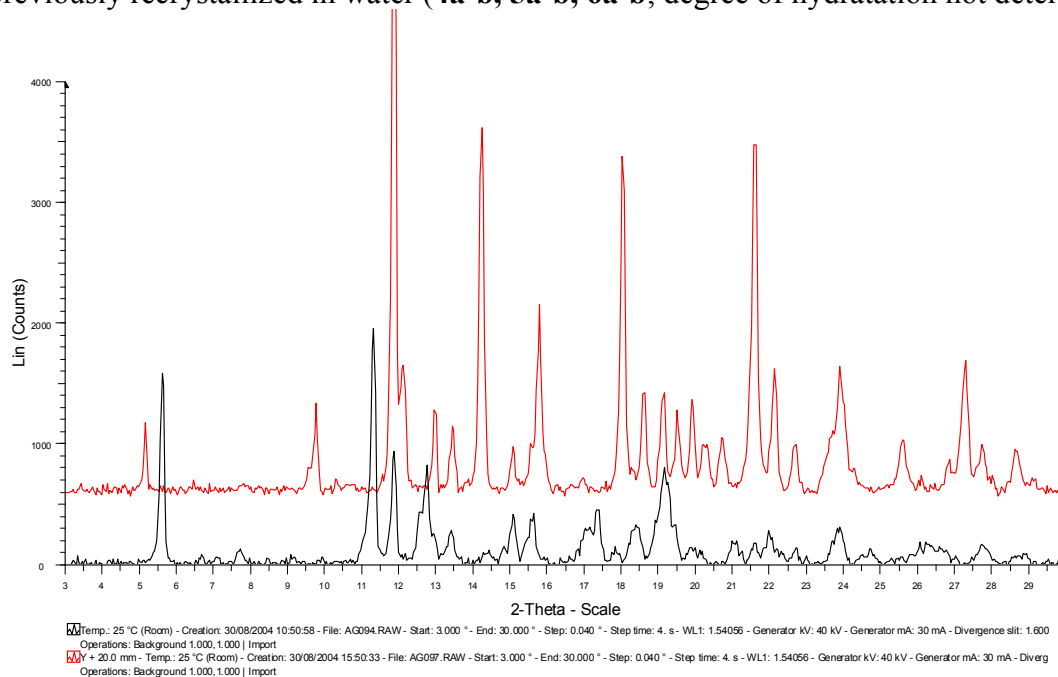
**(Z)-2-(4-cyanobenzylidene)cycloheptan-1-one (10a)**; yellow powder; m.p. 102-104°C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 25°C): δ=7.54 (d, <sup>3</sup>J(H, H)=8.6 Hz, 2 H), 7.31 (d, <sup>3</sup>J(H, H)=8.6 Hz, 2 H), 6.47 (s, 1 H), 2.65-2.28 (br, 4 H), 2.17-1.70 (br, 6 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 25°C): δ=209.1, 147.5, 140.7, 131.9, 129.6, 128.8, 118.8, 110.8, 43.2, 35.3, 30.7, 29.8, 24.3; IR (CH<sub>2</sub>Cl<sub>2</sub>): ν=3053(CN), 1684 (C=O), 1265.

**(E)-2-(4-cyanobenzylidene)cycloheptan-1-one (10b)**; pale powder; m.p. 108-110°C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 25°C): δ=7.66 (d, <sup>3</sup>J(H, H)=8.3 Hz, 2 H), 7.44 (s, 1 H), 7.40 (d, <sup>3</sup>J(H, H)=8.3 Hz, 2 H), 2.80-2.60 (br, 4 H), 1.80-1.60 (br, 6 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 25°C): δ=203.8, 143.0, 140.5, 132.9, 131.9, 129.6, 118.4, 111.1, 43.0, 30.8, 29.6, 27.4, 25.1; IR (CH<sub>2</sub>Cl<sub>2</sub>): ν=3053 (CN), 1684 (C=O), 1265.

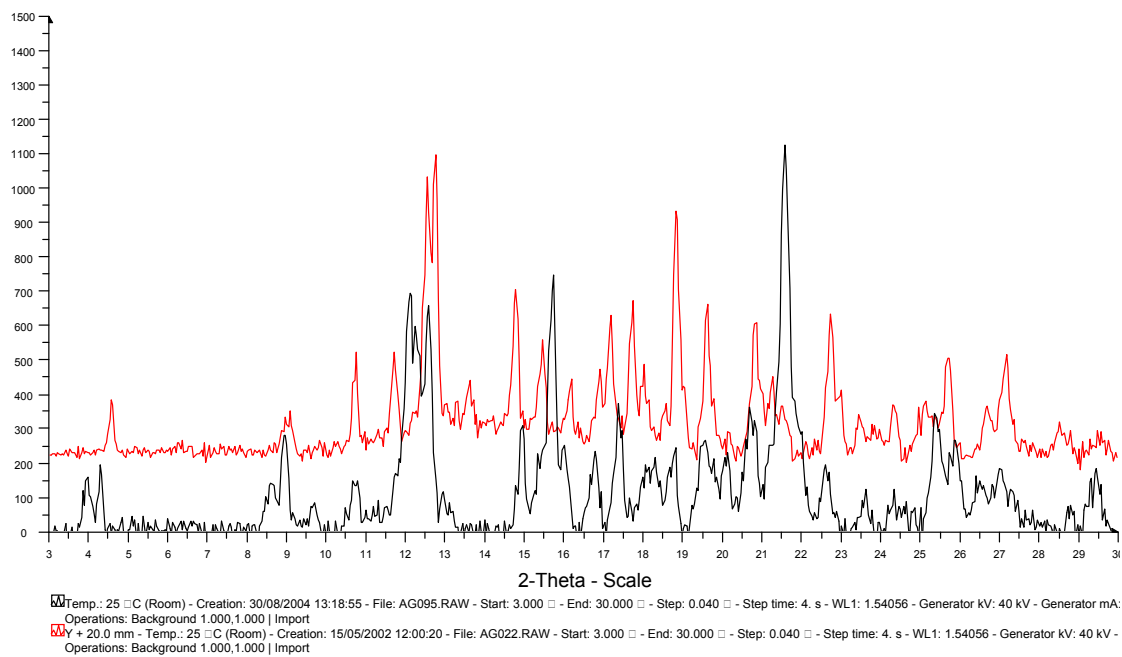
**Complex (γPM-CD / (Z)-CBCH) 11**; <sup>1</sup>H NMR (300 MHz, D<sub>2</sub>O, 25°C): δ=7.65 (d, <sup>3</sup>J(H, H)=8.3 Hz, 2 H), 7.31 (d, <sup>3</sup>J(H, H)=8.3 Hz, 2 H), 6.72 (s, 1 H), 5.35 (d, <sup>3</sup>J(H, H)=3.3 Hz, 8 H), 3.90-3.35 (br, H), 2.75-2.60 (br, 2 H), 2.50-2.30 (br, 2 H), 1.80-1.60 (br, 8 H).

## XRPD patterns of complexes 7a-b, 8a-b, 9a-b

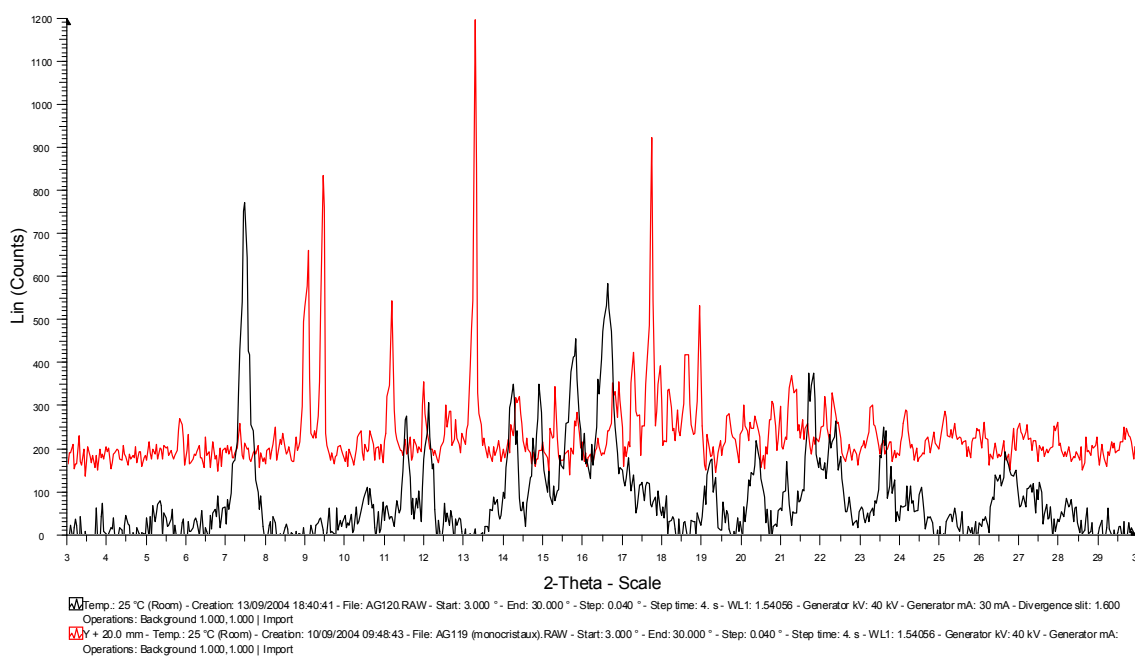
Superimposition of XRPD patterns of the complexes **7a-b**, **8a-b**, **9a-b** with the hosts alone, previously recrystallized in water (**4a-b**, **5a-b**, **6a-b**; degree of hydration not determined).



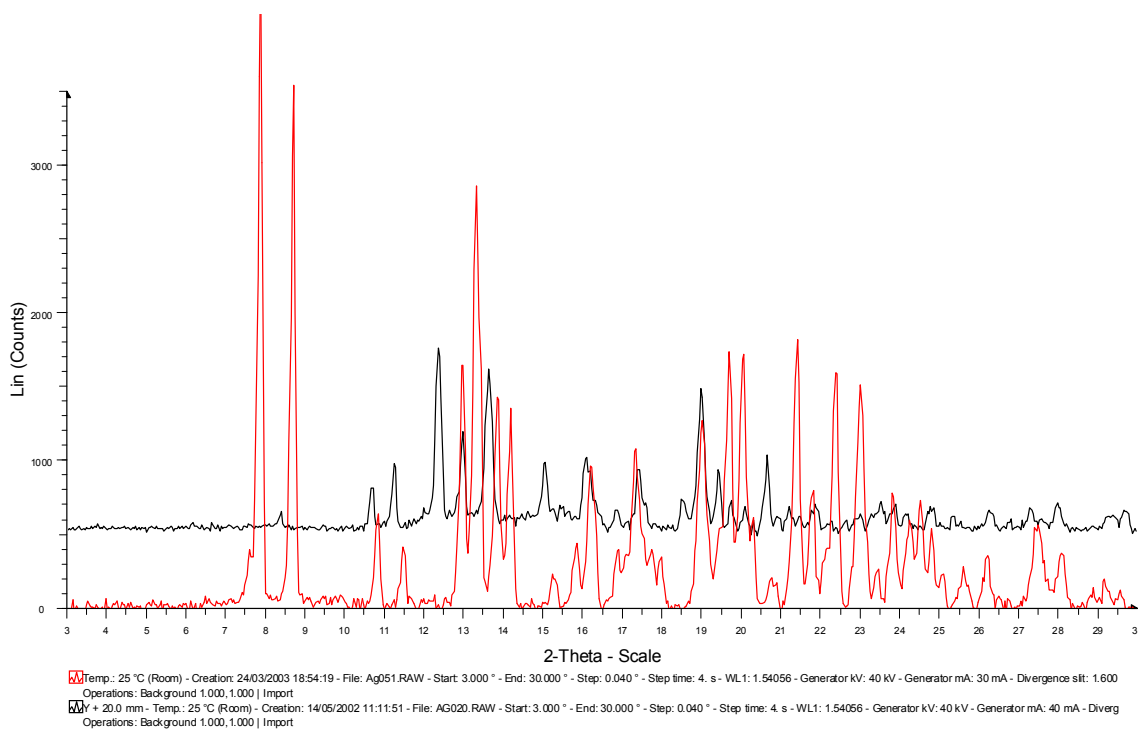
## AG097 (red) **4a**; AG094 (black) **7a**



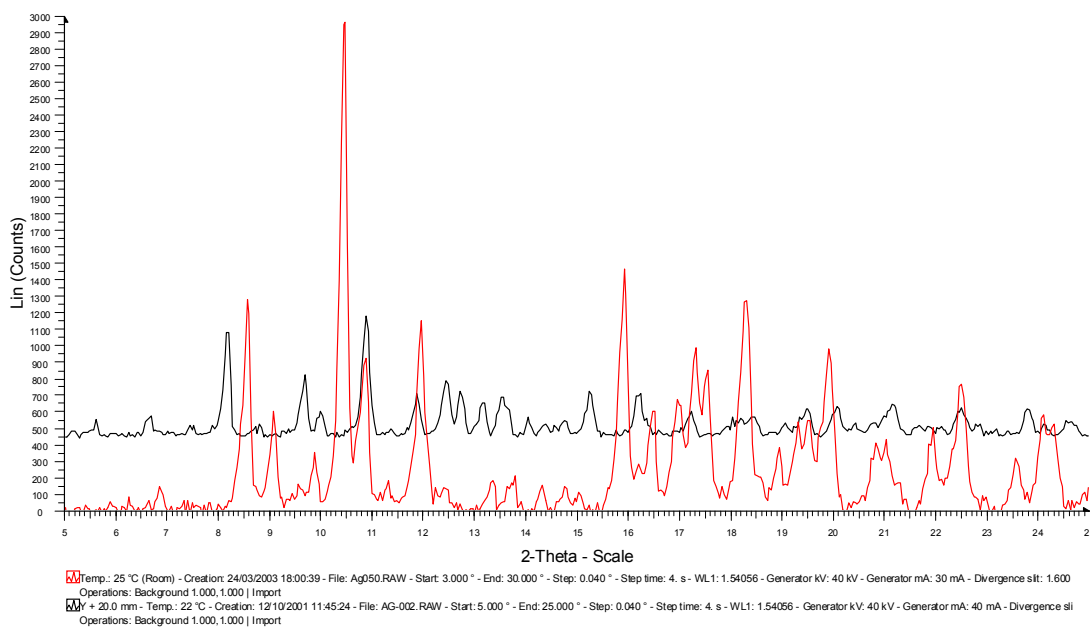
## AG022 (red) **5a**; AG095 (black) **8a**



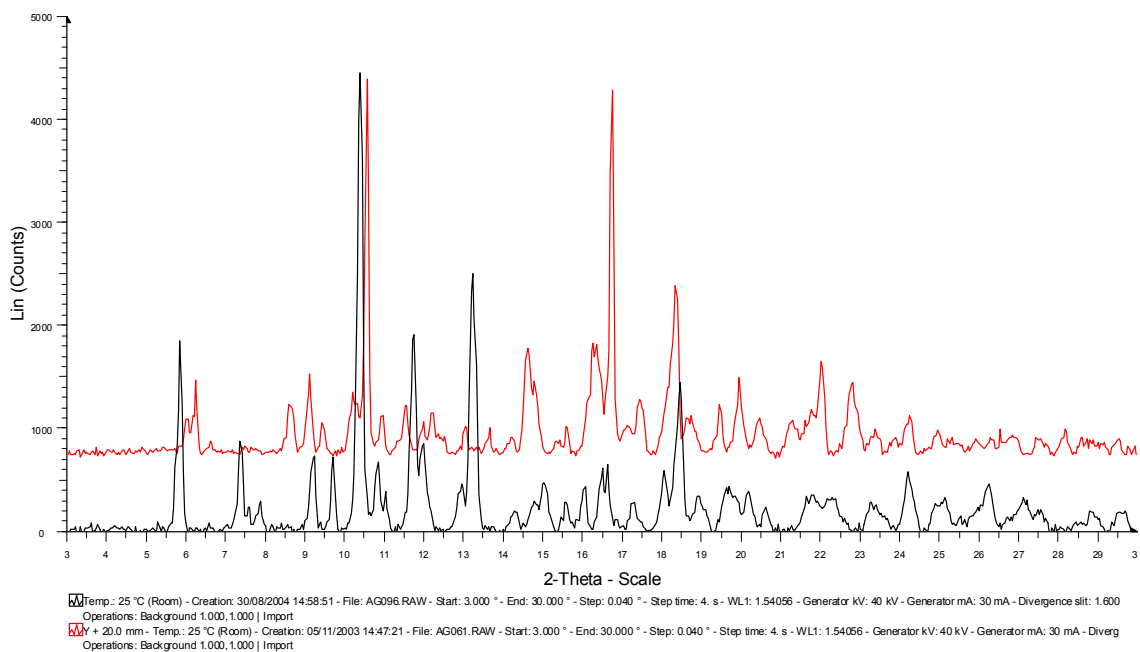
AG119 (red) **6a**; AG120 (black) **9a**



AG020 (black) **4b**; Ag051 (red) **7b**



AG002 (black) **5b**; Ag050 (red) **8b**



AG061 (red) **6b** ; AG096 (black) **9b**

### <sup>1</sup>H NMR spectrometries of **10a-b** and **11**

a) of (*Z*) and (*E*)-CBCH **10a-b** (95:5) in CDCl<sub>3</sub>; b) of (γPM-Cd **6b** / (*Z*)-CBCH **10a**) complex **11** in D<sub>2</sub>O.

