Cucurbit[8]uril directed solution phase photodimerization of \textit{trans}-1,2-bis\textit{n}-pyridyl)ethylenes

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1. Molecular structure of host CB[8]:

![Molecular structure of CB[8]](image)

C_{48}H_{48}N_{32}O_{16}

Molecular weight - 1328

2. Complexation of hydrochlorides of trans-1,2-bis(n-pyridyl)ethylenes and n-stilbazoles with CB[8]:

Cucurbit[8]uril (CB[8]) was prepared and purified according to reported procedure and used for host-guest chemistry. Trans-1,2-bis(4-pyridyl)ethylene (5 mg) was weighed and transferred into round bottomed flask. The compound was dissolved in 10 mL methanol and 0.5 mL of aqueous dil. HCl was added to the solution. The solvent was evaporated in vacuo and dried to remove the solvent completely to obtain trans-1,2-bis(4-pyridyl)ethylene dihydrochloride (4-BPE.2HCl (1)). The obtained salt (2mg) was dissolved in 20 mL of water to which 8 mg of CB[8] (slightly higher amount than half equivalents of the olefin) was added. The solution was heated and sonicated in a sonic bath for 30 min to disperse CB[8] and obtain a clear solution of the inclusion complex. The solution was filtered to remove any undissolved particles remaining and used for further experiments. Samples of trans-1,2-bis(3-pyridyl)ethylene dihydrochloride (3-BPE.2HCl (7)) trans-1,2-bis(2-pyridyl)ethylene, dihydrochloride (2-BPE.2HCl (12)), 4-stilbazole (4SA.HCl (17)) and 2-stilbazole (2SA.HCl (22)) were prepared in the same procedure as mentioned above.

3. Irradiation and extraction of guests included within CB[8] in water:

Solutions of the complexes were taken in pyrex test tubes and sealed with a rubber septum and purged with nitrogen for 10 min. The purged samples were irradiated with a 450 Watts medium pressure mercury lamp for 1 hr. In case of stilbazoles, irradiation was performed with a 375 nm cutoff filter. After irradiation, 10% aq. NaOH was added in drops to bring the pH down to 8 as tested with a pH paper – the solution would turn turbid at this point indicating neutralization of the guest and decomplexation from CB[8]. The turbid solution was extracted with 40 mL of dichloromethane in a separatory funnel to collect the reactants and products in the organic layer. The solution was dried over anhydrous MgSO₄ and filtered and concentrated invacuo. The sample was dried and analyzed by 400 MHz Bruker ¹H NMR.
4. $^1$H NMR data for syn and anti dimers from trans-1,2-bis($n$-pyridyl)ethylenes 1, 7, 12 and $n$-stilbazoles 17 and 22:

**Syn dimer of 4-BPE.2HCl (5):**
$^1$H NMR (400 MHz, CDCl$_3$, TMS) $d =$ 4.52 (d, 4H), 6.95 (d, 8H, J=8.4 Hz), 8.42 (d, 8H, J=8.4 Hz).

**Anti dimer of 4-BPE.2HCl (6):**
$^1$H NMR (400 MHz, CDCl$_3$, TMS) $d =$ 3.72 (s, 4H), 7.12 (d, 8H, J=8.4 Hz), 8.52 (d, 8H, J=8.4 Hz)

**Syn dimer of 3-BPE.2HCl (10):**
$^1$H NMR (400 MHz, CDCl$_3$, TMS) $d =$ 4.53 (s, 4H), 7.07 (m, 4H), 7.38 (d, 4H), 8.35 (d, 4H), 8.42 (s, 4H)

**Anti dimer of 3-BPE.2HCl (11):**
$^1$H NMR (400 MHz, CDCl$_3$, TMS) $d =$ 3.71 (s, 4H), 7.15 (m, 4H), 7.45 (d, 4H), 8.4 (m,8H)

**Syn dimer of 2-BPE.2HCl (15):**
$^1$H NMR (400 MHz, CDCl$_3$, TMS) $d =$ 5.18 (s, 4H), 6.90 (q, 4H), 7.07 (d, 4H), 7.39 (t, 4H), 8.6 (d, 4H)

**Anti dimer of 2-BPE.2HCl (16):**
$^1$H NMR (400 MHz, CDCl$_3$, TMS) $d =$ 4.39 (s, 4H), 7.1 (q, 4H), 7.25 (d, 4H), 7.55 (d, 4H), 8.65 (d, 4H)

**SynH-T dimer of 4-SA.HCl (20):**
$^1$H NMR (400 MHz, CDCl$_3$, TMS) $d =$ 4.48 (m, 4H), 7.08-7.4 (m, 14 H), 8.35 (d, 4H)

**Anti H-H dimer of 4SA.HCl (21):**
$^1$H NMR (400 MHz, CDCl$_3$, TMS) $d =$ 3.7 (m, 4H), 7.1-7.4 (m, 14 H), 8.55 (d, 4H)

**Syn H-T dimer of 2SA.HCl (25):**
$^1$H NMR (400 MHz, CDCl$_3$, TMS) $d =$ 4.9-5.0 (bs, 4H), 7.1-7.6 (m, 16 H), 8.42 (d, 2H)
5. Shifts in $^1$H NMR signals of guests in absence and presence of CB[8]:

2BPE.2HCl included within CB[8]

Figure 1. $^1$H NMR spectra of (a) 2-BPE.2HCl in D$_2$O; (b) 2-BPE.2HCl in presence of 0.5 equivalent of CB[8] in D$_2$O

3BPE.2HCl included within CB[8]

Figure 2. $^1$H NMR spectra of (a) 3-BPE.2HCl in D$_2$O; (b) 3-BPE.2HCl in presence of 0.5 equivalent of CB[8] in D$_2$O.
6. \textit{1H} NMR titration plot for the determination of complex stoichiometry in solution

   – Change in chemical shift vs. ratio of host to guest:

   \textit{1H} NMR titration was performed for the determination of stoichiometry of host-guest complex. Owing to the fact that the solubility of \textbf{CB[8]} (in the absence of cationic guest) in water is extremely low, concentration of the guest was maintained at a concentration at which the host dissolved so that host-guest ratio higher than the actual stoichiometry could be studied. Absence of two distinct peaks of complexed and uncomplexed forms throughout the titration imply that the equilibrium existing between the forms of the guest with \textbf{CB[8]} is faster than the NMR time scale.

   \begin{figure}
   \centering
   \includegraphics[width=0.6\textwidth]{figure3.png}
   \caption{Plot of shift in Hc \textit{1H} NMR signal vs. increasing molar ratio of \textbf{CB[8]-4BPE.2HCl}.}
   \end{figure}

   \textbf{CB[8]} (10 mg) was taken in 1 mL of D$_2$O and heated to facilitate solubilization. The saturated solution was filtered with a Whatmann filter paper of fine porosity to remove undissolved \textbf{CB[8]}. The filtrate (0.6 mL) was taken in a NMR tube and \textit{1H} NMR was recorded and peaks corresponding to \textbf{CB[8]} dissolved in D$_2$O were observed. To this solution 1 mL of \textbf{4-BPE.2HCl} in D$_2$O (20 mg/mL) was added. The solution was shaken well for a minute and \textit{1H} NMR spectrum recorded. The ratio of the signals of the
H_a proton in the guest and the host protons were used to calculate molar ratios in the solution (to begin with, the host guest molar ratio was found to be 1:1 based on peak integration). The procedure was repeated till the host guest ratio approached 0.26:1. The differences in chemical shifts of H_c protons in presence of CB[8] compared to the chemical shifts in the absence of the host were calculated (Δ ppm) and plotted against the corresponding host:guest ratio. From the NMR titration spectra presented, it could be noted that as the molar ratio of guest:host changes from 1:1 to 1:0.55 the H_c signal at 7.0 ppm shifts upfield till it reaches 6.8 ppm. Once the ratio goes further down the H_c signal starts shifting downfield from 6.8 ppm tending towards 7.9 ppm. The maximum is reached around 0.55 equivalents of CB[8] with respect to 4BPE.2HCl indicating the stoichiometry of the host guest complex to be 1:2.
7. **Double reciprocal plot for the 1:2 complex formation of 4BPE.2HCl with CB[8]**:

A double reciprocal plot of 1/shift vs. 1/conc. of CB[8] was plotted (Figure. 7) based on the $^1$H NMR titration spectra. The titration was performed at a fixed concentration of $3.8 \times 10^{-3}$ M for 4BPE.2HCl (1) and CB[8] (0.5 mg approximately each time) was added, sonicated and $^1$H NMR spectra recorded. Ratio of the host:guest was determined by $^1$H NMR signals integration based on which the concentration of CB[8] was deduced. Linear fit for the data yielded a $R^2$ value of 0.9932. A nonlinear fit for the data was obtained with a $R^2$ value of 0.9996 which implied that the complex is not of simple 1:1 stoichiometry. In the plot, $S_0$ is the chemical shift (in ppm) of Hc signal of 4BPE.2HCl in D$_2$O without any host and S is the chemical shift of Hc signal in the presence of a given amount of CB[8].

![Figure 4. Double reciprocal plot based on $^1$H NMR titration of complexation with varying ratios of host to guest.](image-url)
8. MALDI-TOF analysis of CB[8] inclusion complexes:

Figure 5. MALDI-TOF of 4BPE.2HCl included within CB[8]. m/z 1511, 1693 correspond to CB[8]+4BPE.2H^2+ (1512-1), CB[8]+(4BPE.2H^2+)$_2$ (1696-3) respectively.

Figure 6. MALDI-TOF of 3BPE.2HCl included within CB[8]. m/z 1351, 1511, 1693 correspond to CB[8]+Na^+, CB[8]+3BPE.2H^2+ (1512-1), CB[8]+(3BPE.2H^2+)$_2$ (1696-3) respectively.
**Figure 7.** MALDI-TOF of 2BPE.HCl included within CB[8]. m/z 1351, 1511, 1693 correspond to CB[8]+Na⁺, CB[8]+2BPE.2H⁺ (1512-1), CB[8]+(2BPE.2H⁺)₂ (1696-3) respectively.

**Figure 8.** MALDI-TOF of 4SA.HCl in CB[8]. m/z 1510 corresponds to CB[8]+4SA.H⁺ (1509+1) and m/z 1692 corresponds to CB[8]+(4SA.H⁺)₂.
**Figure 9.** MALDI-TOF of 2SA.HCl in CB[8]. m/z 1510 corresponds to CB[8]+2SA.H⁺ (1509+1) and m/z 1692 corresponds to CB[8]+ (2SA.H⁺)₂.
9. Crystal structure determination

The crystal of the inclusion complex was mounted in a Cryoloop™ with Paratone oil and placed in the cold nitrogen stream of the Kryoflex™ attachment of the Bruker APEX CCD diffractometer. A full sphere of data was collected using 606 scans in \( \theta \) (0.3° per scan) at \( \theta = 0, 120 \) and 240°. The raw data were reduced to \( F^2 \) values using the SAINT+ software¹ and a global refinement of unit cell parameters employing 3685 reflections chosen from the full data set was performed. Multiple measurements of equivalent reflections provided the basis for empirical absorption corrections as well as corrections for any crystal deterioration during the data collection (SADABS²). The structure was solved by direct methods (SHELXS-97³) and completed by successive cycles of full-matrix least-squares refinement followed by calculation of a difference map. The refinement was hampered by the presence of a considerable amount of electron density in channels between the host molecules which are presumably due to solvent water molecules but which appeared to be significantly disordered and consequently was difficult to adequately model. All calculations were performed with the SHELXTL⁴ program package.

References: