

Supplementary Material

Combining topochemical [2+2] photoreactions and hydrothermal isomerisation for the regioselective and quantitative preparation of *rtct*-pyridylcyclobutanes

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1. Experimental Section

All reagents were obtained from commercial sources and used without further purification. The ^1H NMR spectra were recorded on a Bruker AVANCE-300 Spectrometer in CDCl_3 .

Synthesis of *rctt*-pyridylcyclobutanes (tpcb)

The cyclobutane derivatives were prepared from controlled [2+2] cycloaddition reactions in the solid state of *trans*-bis(2-pyridyl)ethylene (**2,2'-bpe**), *trans*-bis(4-pyridyl)ethylene (**4,4'-bpe**), *trans*-1-(2-pyridyl)-2-(4-pyridyl)ethylene (**2,4'-bpe**) and 4-Chorostilbazole (**4-Cl-Stb**), according to previously published procedures (see reference section). The different photoproducts obtained were characterised before the hydrothermal reaction by NMR spectroscopy: ***rctt*-2,2'-tpcb** (^1H NMR (300 MHz, CDCl_3), δ_{H} (ppm), J (Hz): 8.42(4H_a, ddd, $J_{\text{ab}}=4.9$, $J_{\text{ac}}=1.8$, $J_{\text{ad}}=0.9$), 7.33(4H_b, td, $J_{\text{bc}}=7.7$, $J_{\text{bd}}=1.8$), 6.9(4H_c, ddd, $J_{\text{cd}}=7.8$) 7.07(4H_d, dd), and 5.13(4H_e, s); ***rctt*-4,4'-tpcb** (300 MHz, CDCl_3), δ_{H} (ppm), J (Hz): 8.45(8H_a, dd, $J_{\text{ab}}=4.5$), 7.00(8H_b, dd), and 4.48(4H_c, s); ***rctt*-2,4'-tpcb-ht** (300 MHz, CDCl_3), δ_{H} (ppm), J (Hz): 8.43(2H_a, ddd, $J_{\text{ab}}=4.8$, $J_{\text{ac}}=1.7$, $J_{\text{ad}}=0.9$), 8.29(4H_e, ddd, $J_{\text{ef}}=6.0$), 7.42(2H_c, td, $J_{\text{bc}}=7.7$), 7-6.96(8H_{b,d,f}, m, $J_{\text{bd}}=1.8$, $J_{\text{dc}}=7.5$), 4.86(2H_g, td, $J_{\text{gh}}=8.7$) and 4.71(2H_h, td); ***rctt*-2,4'-tpcb-hh** (300 MHz, CDCl_3), δ_{H} (ppm), J (Hz): 8.44(2H_a, ddd, $J_{\text{ab}}=4.6$, $J_{\text{ac}}=1.7$), 8.34(4H_e, ddd, $J_{\text{ef}}=6.0$), 7.39(2H_b, td, $J_{\text{bc}}=7.7$), 7.04(4H_f, dd), 6.97-6.94(4H_{c,d} m), 4.94(2H_g, td, $J_{\text{gh}}=6.4$) and 4.60(2H_h, td); ***rctt*-4-Cl-dpcb-ht**: [*rctt*-1,3-bis(4-pyridyl)-2,4-bis(4-

chlorophenyl) cyclobutane head-to-tail] (300 MHz, DMSO), δ_{H} (ppm), J (Hz): 8.38(4H_a, d, $J_{\text{ab}}=4.7$), 8.02(2H, s, template (bta)), 7.27(4H_c, d, $J_{\text{cd}}=6.1$) 7.21(8H_{b,d}, s), and 4.57(4H_{e,d}, m).

General procedure for the isomerisation of *rcct*-pyridylcyclobutanes derivatives (tpcb) under reflux in presence of metal salts (MnCl₂·4H₂O and AlCl₃·6H₂O).

A round-bottom flask was charged with the different *rcct*-tpcb (60 mg) dissolved in methanol (10 mL), and combined with MnCl₂·4H₂O (55 mg) or AlCl₃·6H₂O (66 mg) in 1:2 molar ratio previously dissolved in water (20 mL), respectively. The mixture was refluxed (T=80-82°C) for 24 h and after slow cooling to room temperature. The products were extracted with CH₂Cl₂ and characterised by ¹H-NMR spectroscopy.

General procedure for the isomerisation of *rcct*-pyridylcyclobutanes derivatives (tpcb) under hydrothermal conditions

A mixture was prepared by adding of 1,2,4,5 benzenetetracarboxylic acid (bta, 46mg) or AlCl₃·6H₂O (66mg) and each pyridyl compounds (50mg), respectively in 1:2 molar ratio in 10 mL of H₂O. These mixtures were heated at 140°C for 24-48h. Slow evaporation of the resulting solutions at room temperature gave crystals of good quality for X-ray single crystal analysis of 1-3. The crude product were extracted with CH₂Cl₂ or after the dissolution of solid phases in a NaOH solution (pH~ 12) and after the extraction with CH₂Cl₂. All the products were characterised by ¹H-NMR. ***rtct-2,2'-tpcb***: ¹H NMR (300 MHz, CDCl₃), δ_{H} (ppm), J (Hz): 8.66(4H_a, ddd, $J_{\text{ab}}=5.8$, $J_{\text{ac}}=1.9$, $J_{\text{ad}}=0.9$), 7.54(4H_c, td), 7.19 (4H_b, td, $J_{\text{bc}}=7.1$, $J_{\text{bd}}=1.4$), 7.13(4H_d, d) and 4.37(4H_e, s). ***rtct-4,4'-tpcb***: ¹H NMR (300 MHz, CDCl₃), δ_{H} (ppm), J (Hz): 8.57(8H_a, dd, $J_{\text{ab}}=6.0$), 7.14(8H_b, dd) and 3.69(4H_c, s). ***rtct-2,4'-tpcb-ht***: ¹H NMR (300 MHz, CDCl₃), δ_{H} (ppm), J (Hz): 8.68(2H_a, ddd, $J_{\text{ab}}=4.5$, $J_{\text{ac}}=1.8$, $J_{\text{ad}}=0.9$), 8.46(4H_e, dd, $J_{\text{ef}}=4.7$), 7.63(2H_c, ddd, $J_{\text{bc}}=7.7$), 7.24(4H_f, m), 7.19(2H_b, ddd, $J_{\text{bd}}=1.2$), 7.13(2H_d, ddd) 4.32(2H_g, t, $J_{\text{gh}}=9.7$) and 3.72(2H_h, t). ***rtct-2,4'-tpcb-hh***: ¹H NMR (300 MHz, CDCl₃), δ_{H} (ppm), J (Hz): 8.66(2H_a, dd, $J_{\text{ab}}=4.5$, $J_{\text{ac}}=1.8$), 8.50(4H_e, dd, $J_{\text{ef}}=6.1$), 7.54(2H_c, td, $J_{\text{cd}}=7.7$, $J_{\text{bc}}=7.6$), 7.24(4H_f, dd, $J_{\text{ef}}=6.1$), 7.15(2H_b, m, $J_{\text{bd}}=1.0$), 7.02(2H_d, d), 4.13(2H_g, m) and 4.01(2H_h, m). ***rcct-4-Cl-dpcb-ht***: [*rcct*-1,3-bis(4-pyridyl)-2,4-bis(4-chlorophenyl) cyclobutane] (300 MHz, DMSO), δ_{H} (ppm), J (Hz): 8.30(4H_a, d, $J_{\text{ab}}=5.8$), 8.02(2H, s, template (bta)), 7.67(2H_e, d, $J_{\text{ef}}=8.4$), 7.40(2H_c, d, $J_{\text{cd}}=8.5$), 7.14(4H_b, d), 6.94(4H_{d,f}, s), 4.95(1H_h, t, $J_{\text{ac}}=1.7$, $J_{\text{hg}}=11.8$), 4.58(1H_i, t, $J_{\text{ig}}=9.0$), and 4.36(2H_g, t).

Crystal structure determination. Intensity data were recorded at room temperature on a Rigaku AFC-7S diffractometer equipped with a CCD bidimensional detector using monochromated Mo(K α) radiation ($\lambda = 0.71073 \text{ \AA}$). An empirical absorption correction (multi-scan) was applied using the package CrystalClear. The structures were solved by Direct Methods and refined by full-matrix least-squares on F^2 using the SHELXTL-PLUS package. Hydrogen atoms on C and N atoms were placed at fixed positions using the HFIX instruction, except for the structure **5**, which were found from the Difference Fourier map. All the H atoms were refined with isotropic displacement parameters set to $1.2 \times U_{eq}$ of the attached atom. In the crystal structure of **5** water molecules were found disordered. Attempts were made to model this disorder or split it into two positions, but were unsuccessful. PLATON/SQUEZZE routine was used to correct the data for the presence of disordered solvent. A potential solvent volume of 2132 \AA^3 was found. The stoichiometry of the solvent was calculated to be approximately 5 molecules of water per formula unit, which results in a total of 837 electrons per unit cell. In the crystal structure **6** and **7**, the water molecules found with partial population of 0.64 and 0.31 for **6** and **7**, respectively. The H atoms on the water molecules were not located in the density map in the structure of **7**.

Figure 1. Ball and stick representation of the pyridylcyclobutanes found in the structure of **5** (*rtct*-4,4'-tpcb (a)), **6** (*rtct*-2,4'-tpcb-ht (b)) and **7** (*rcct*-4-Cl-dpcb-ht)

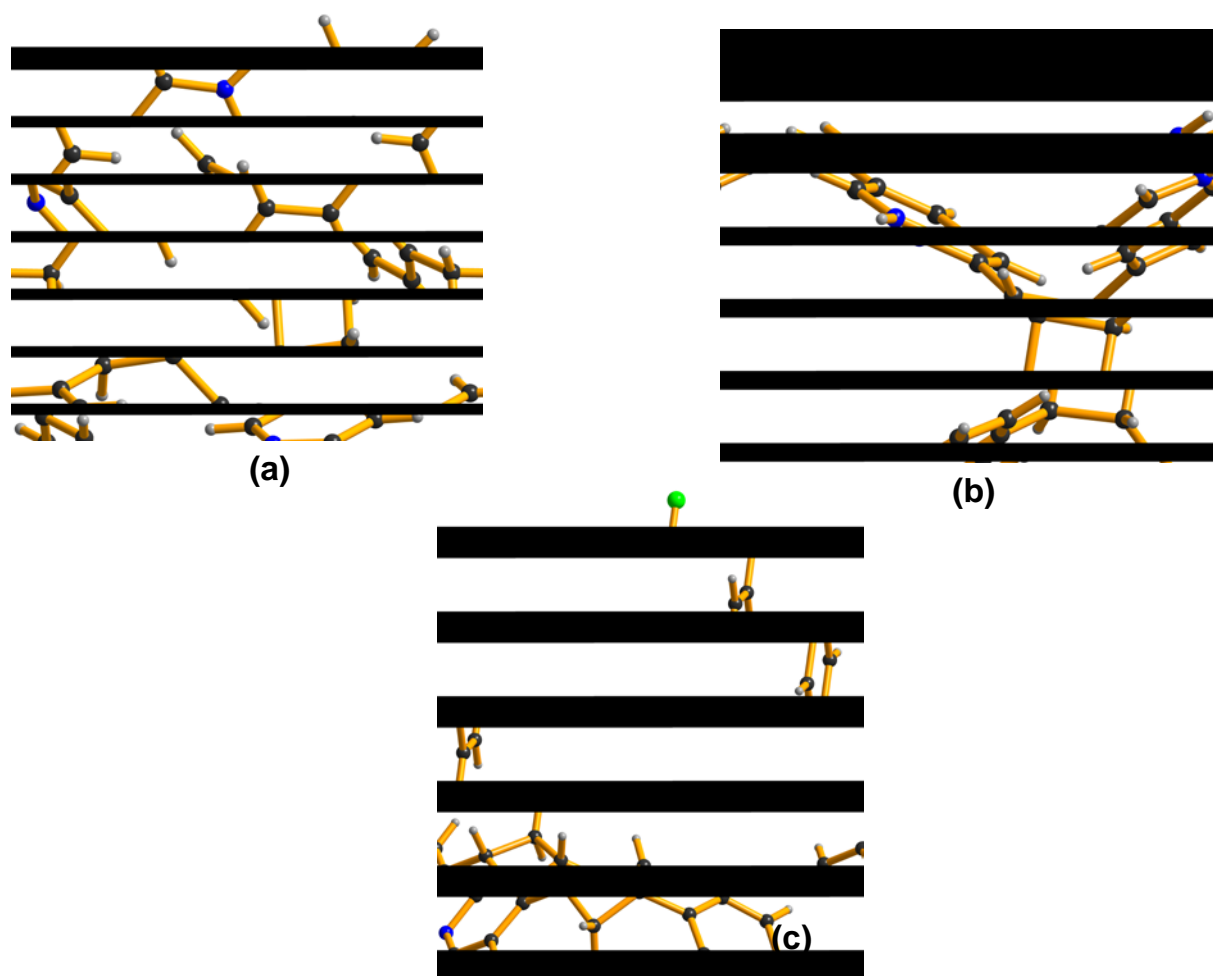
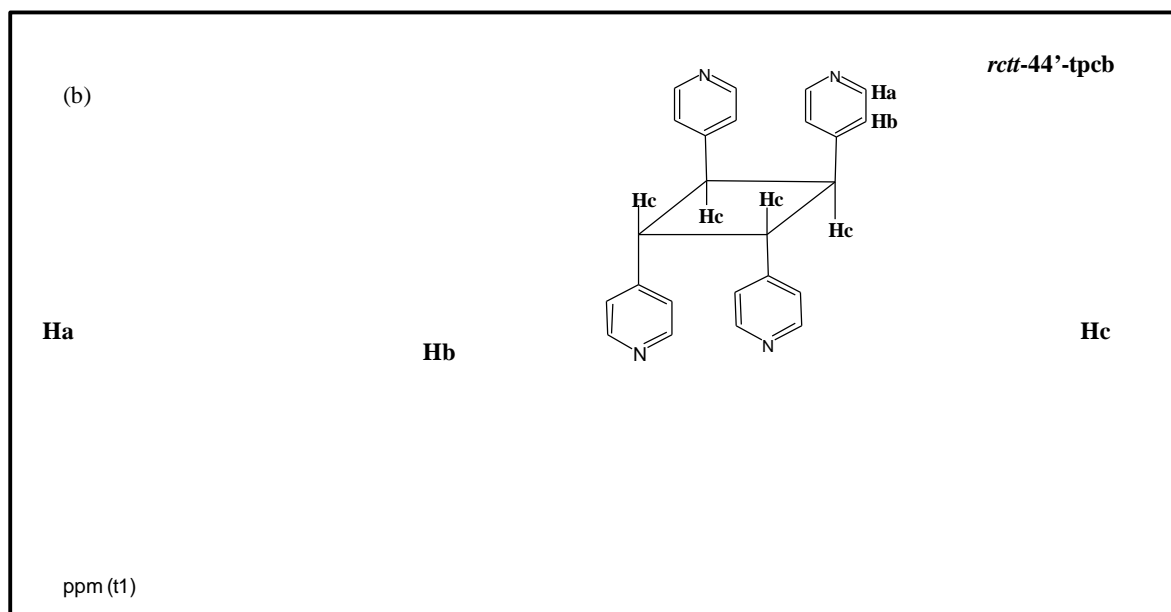
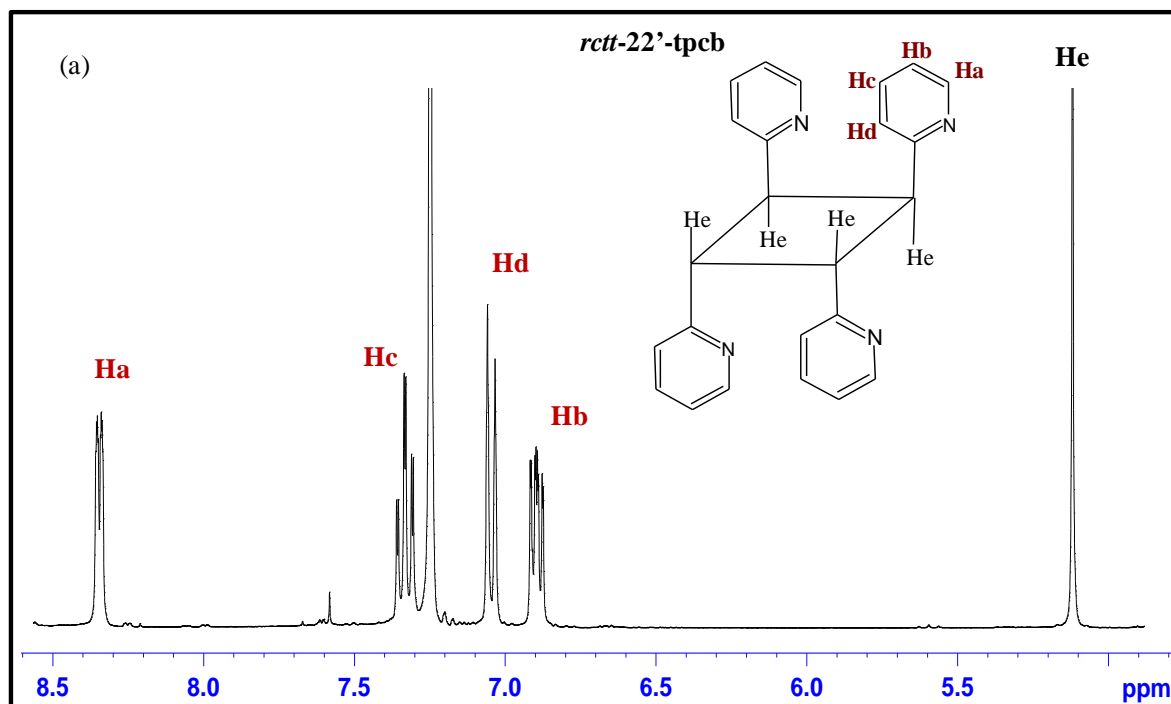


Figure 2. ^1H NMR spectrum of the starting *rctt*-pyridylcyclobutanes *rctt*-2,2'-tpcb (a), *rctt*-4,4'-tpcb (b), *rctt*-2,4'-tpcb-ht(c), *rctt*-2,4'-tpcb-hh (d).



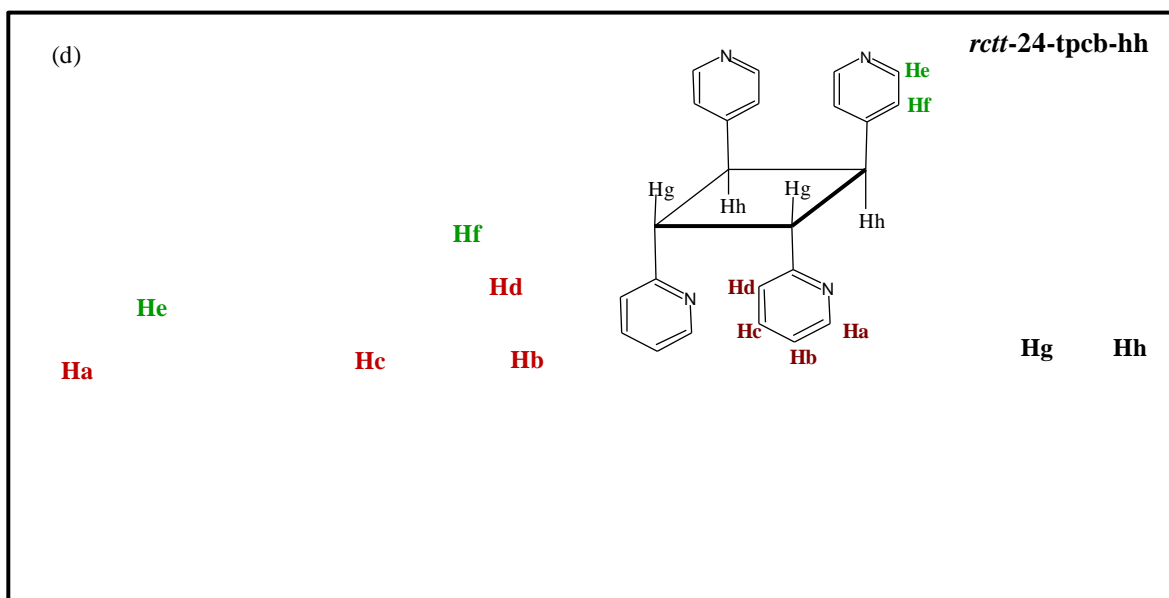
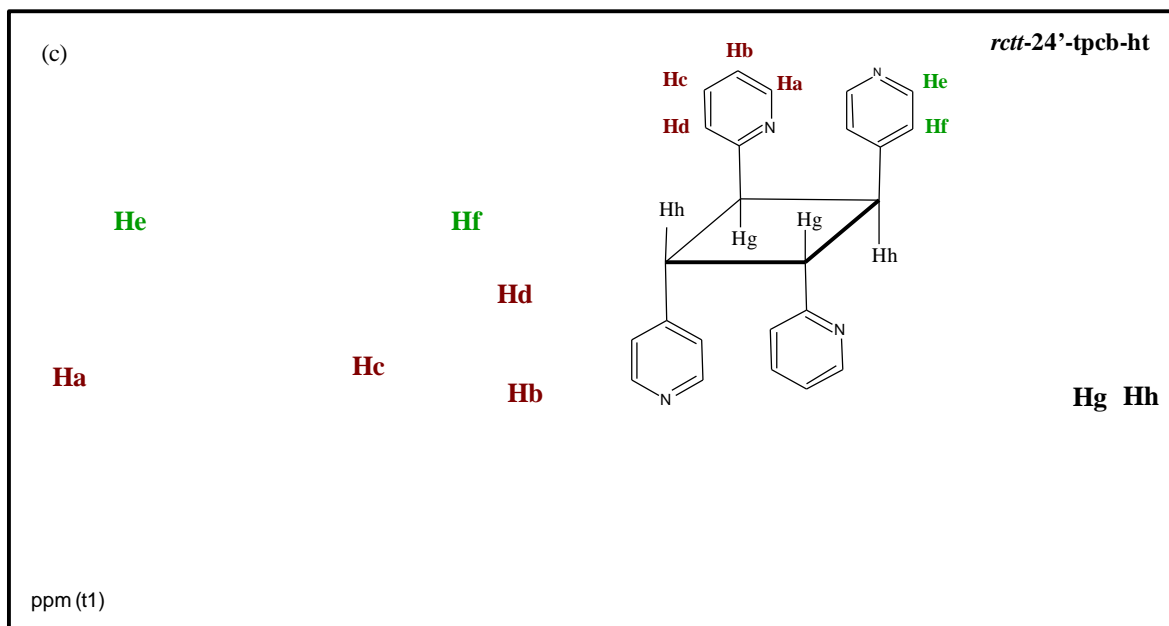


Figure S3. (a) $^1\text{H-NMR}$ spectrum of the mixture of products (*rctt*- and *rtct*- 2,2'-tpcb isomers) obtained from the reflux with $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$. (b) $^1\text{H-NMR}$ spectrum of the mixture of products (*rctt*- and *rtct*- 2,2'-tpcb isomers) obtained from the reflux with $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$.

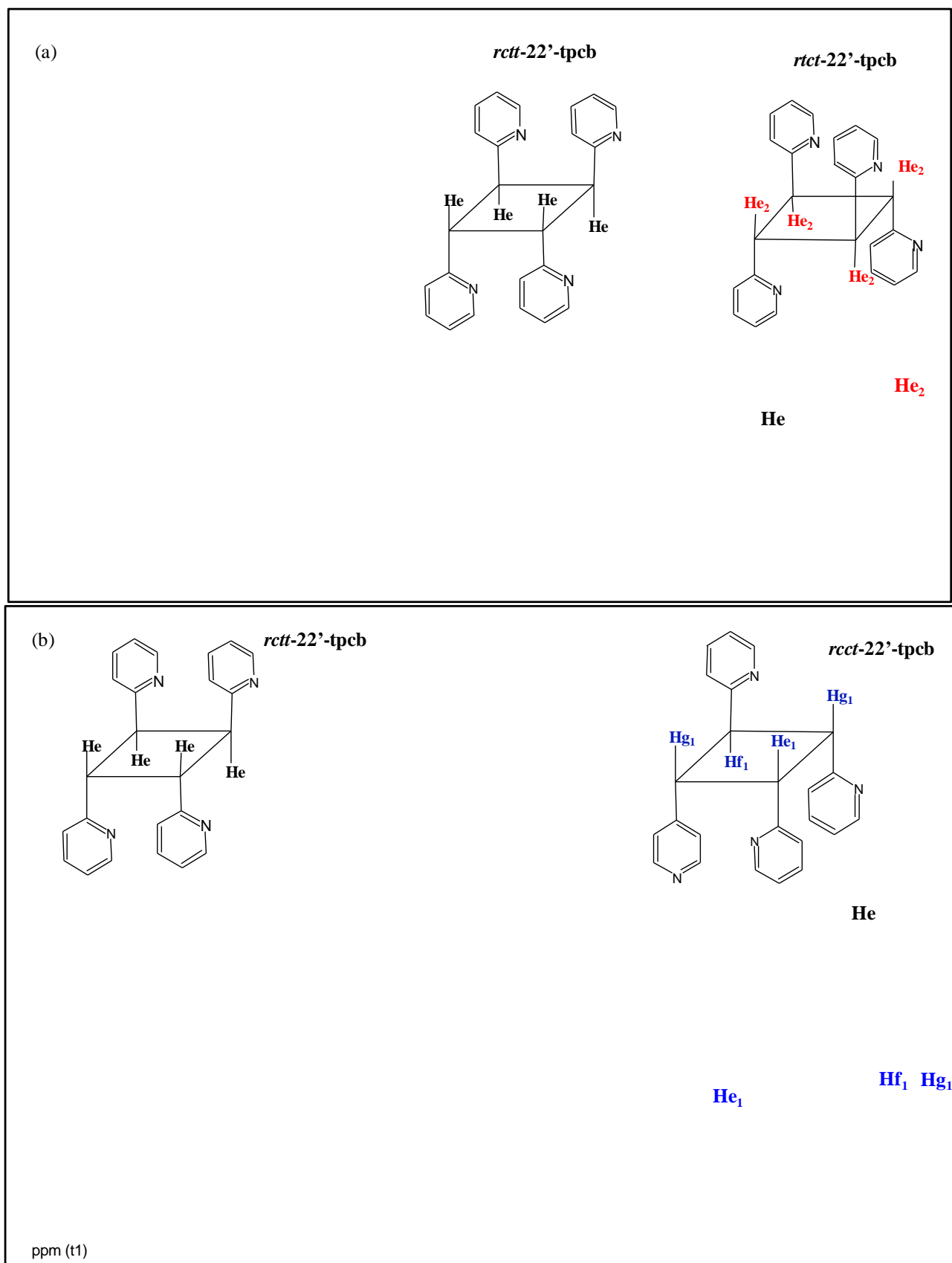


Figure S4. (a) $^1\text{H-NMR}$ spectrum of the isomer *rcctt*-4,4'-tpcb obtained from the reflux with $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$. (b) $^1\text{H-NMR}$ spectrum of the mixture of products (*rcctt*- and *rcct*-4,4'-tpcb isomers) obtained from the reflux with $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$.

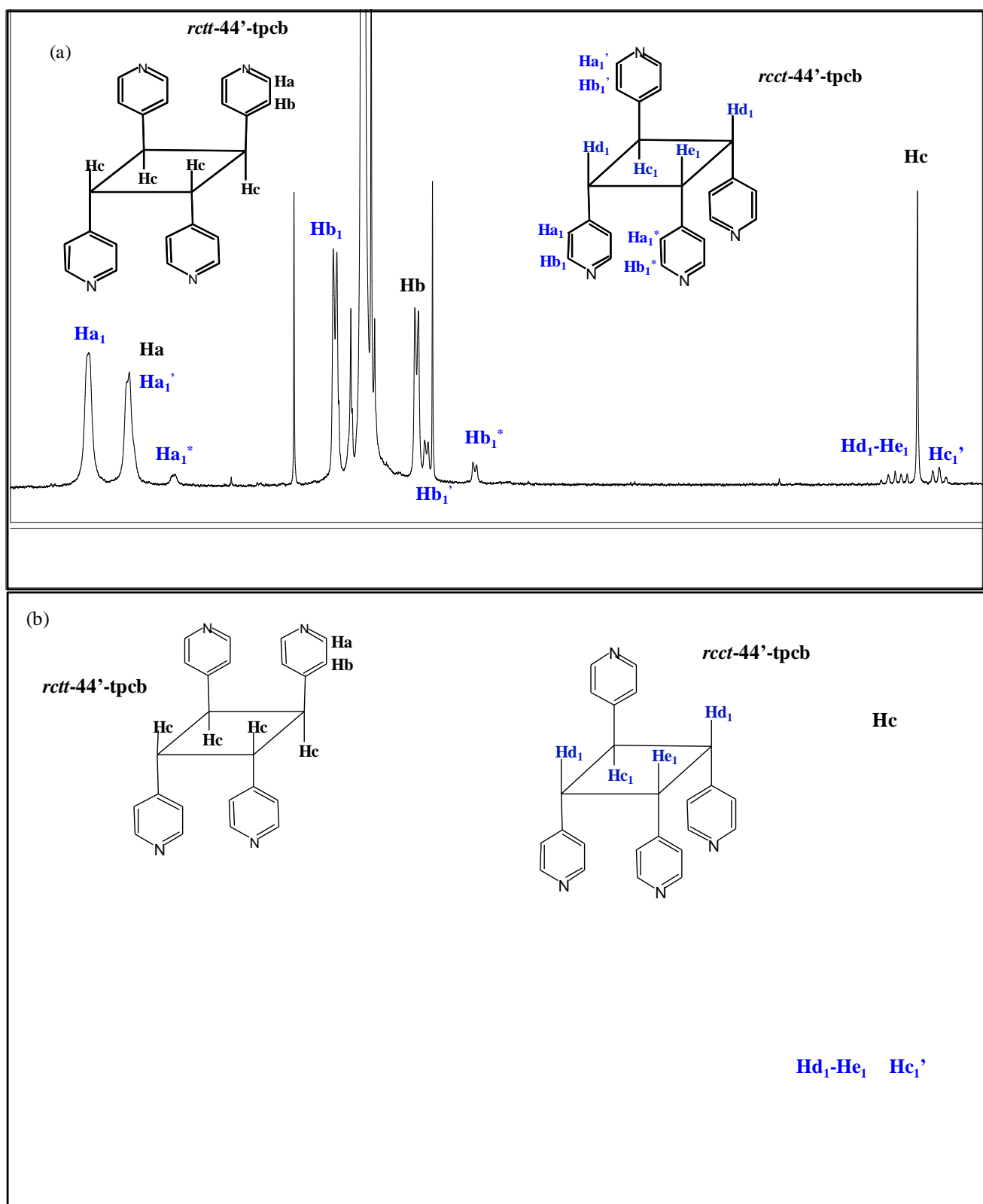


Figure S5. (a) $^1\text{H-NMR}$ spectrum of the mixture of products (*rcctt*- and *rcctt*- 2,4'-tpcb-ht isomers) obtained from the reflux with $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$. (b) $^1\text{H-NMR}$ spectrum of the mixture of products (*rcctt*-, *rttt* and *rcctt*- 2,4'-tpcb-ht isomers) obtained from the reflux with $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$.

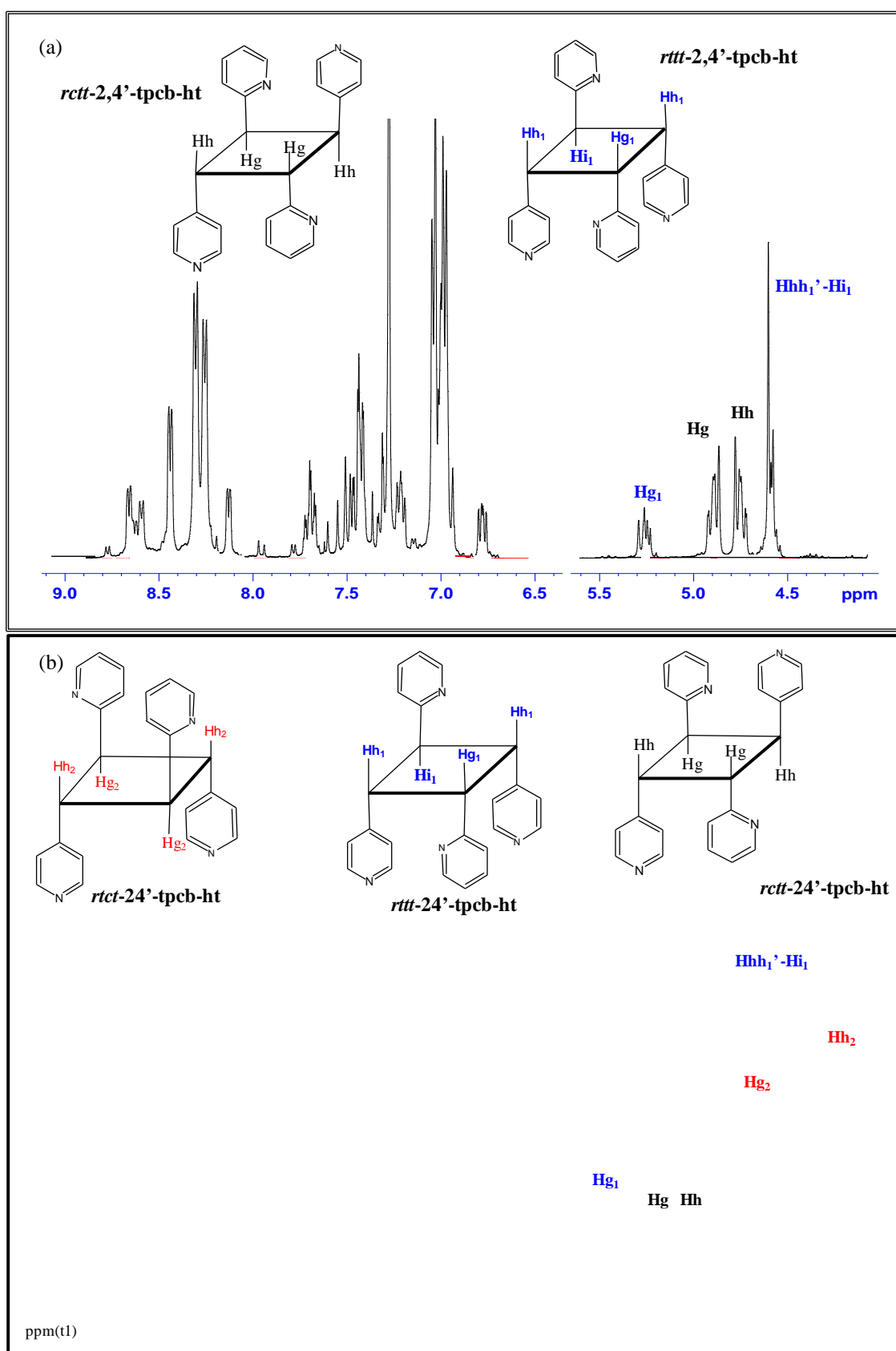


Figure S6. a) $^1\text{H-NMR}$ spectrum of the mixture of products (*rctt*- and *rcct*- 2,4'-tpcb-hh isomers) obtained from the reflux with $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$. (b) $^1\text{H-NMR}$ spectrum of the mixture of products (*rctt*-, and *rcct* 2,4'-tpcb-hh isomers) obtained from the reflux with $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$.

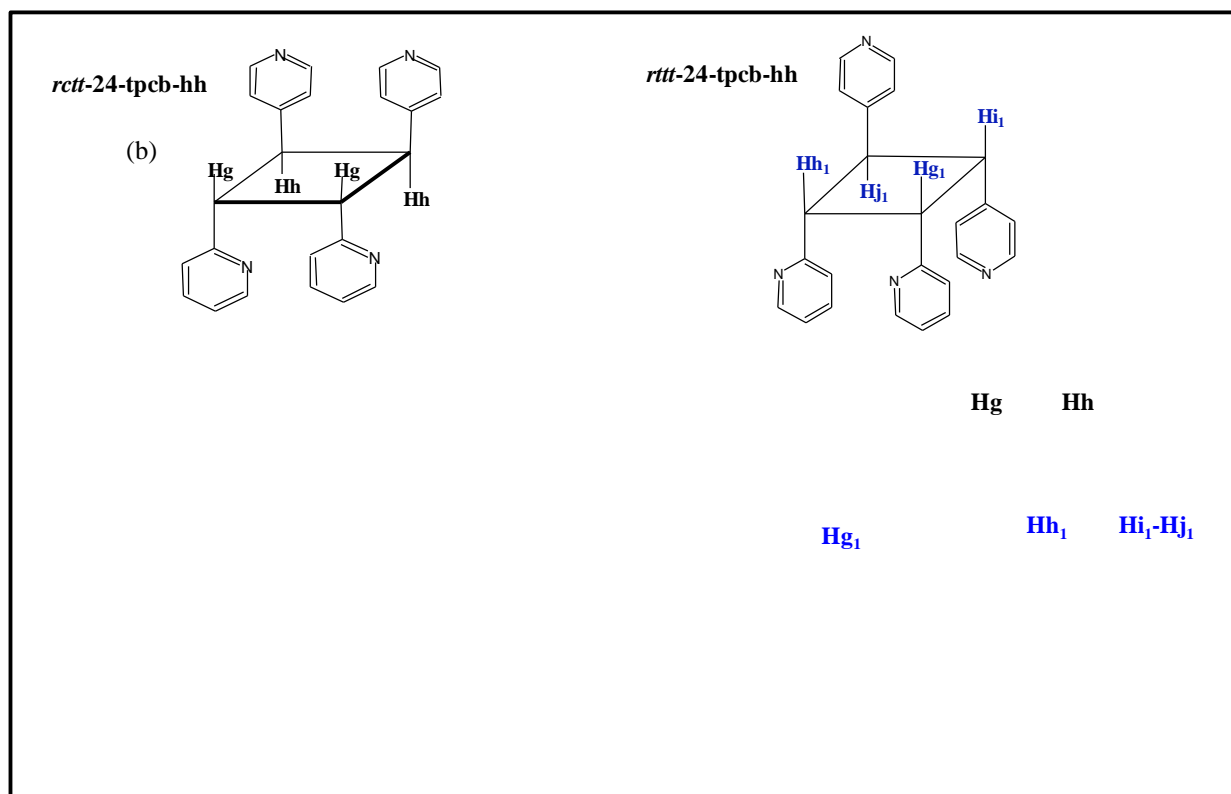
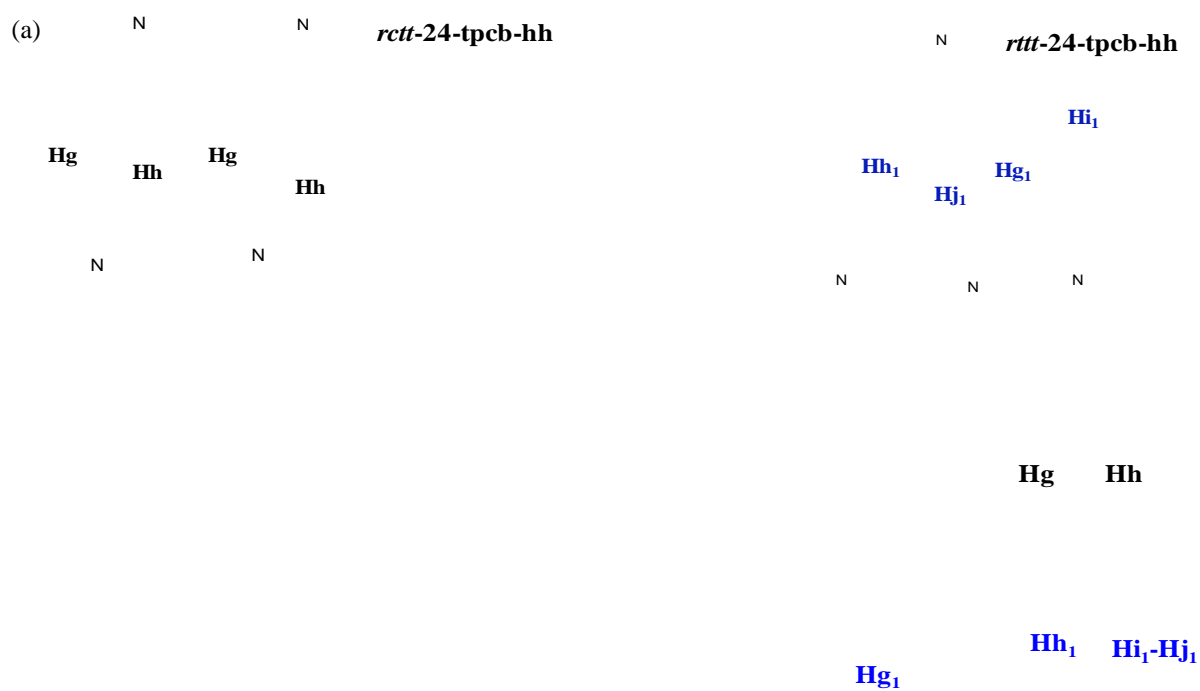


Figure S7. Comparative ^1H -NMR spectrum of the *rctt*-2,2'-tpcb isomer before (a) and after the heating upon hydrothermal conditions either with bta or $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$. Representative ^1H -NMR spectrum of the *rtct*-2,2'-tpcb isomer (b).

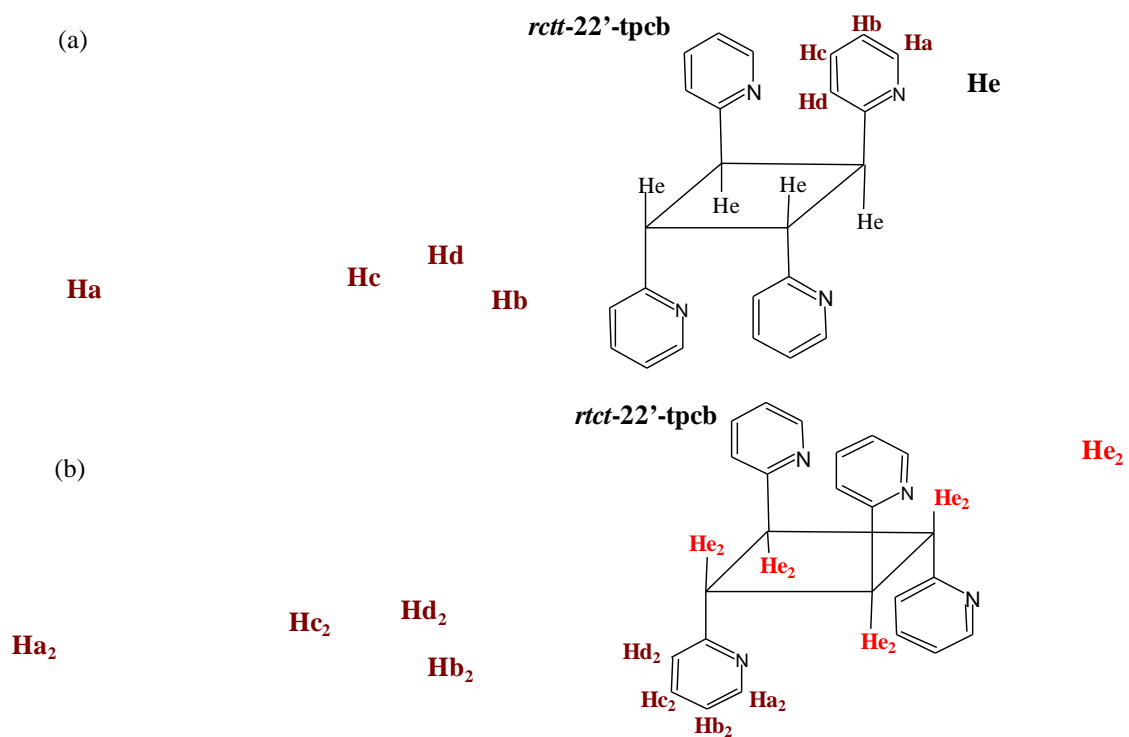


Figure S8. Comparative ^1H -NMR spectrum of the *rctt*-4,4'-tpcb isomer before (a) and after the heating upon hydrothermal conditions either with bta or $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$. Representative ^1H -NMR spectrum of the *rtct*-4,4'-tpcb isomer (b).

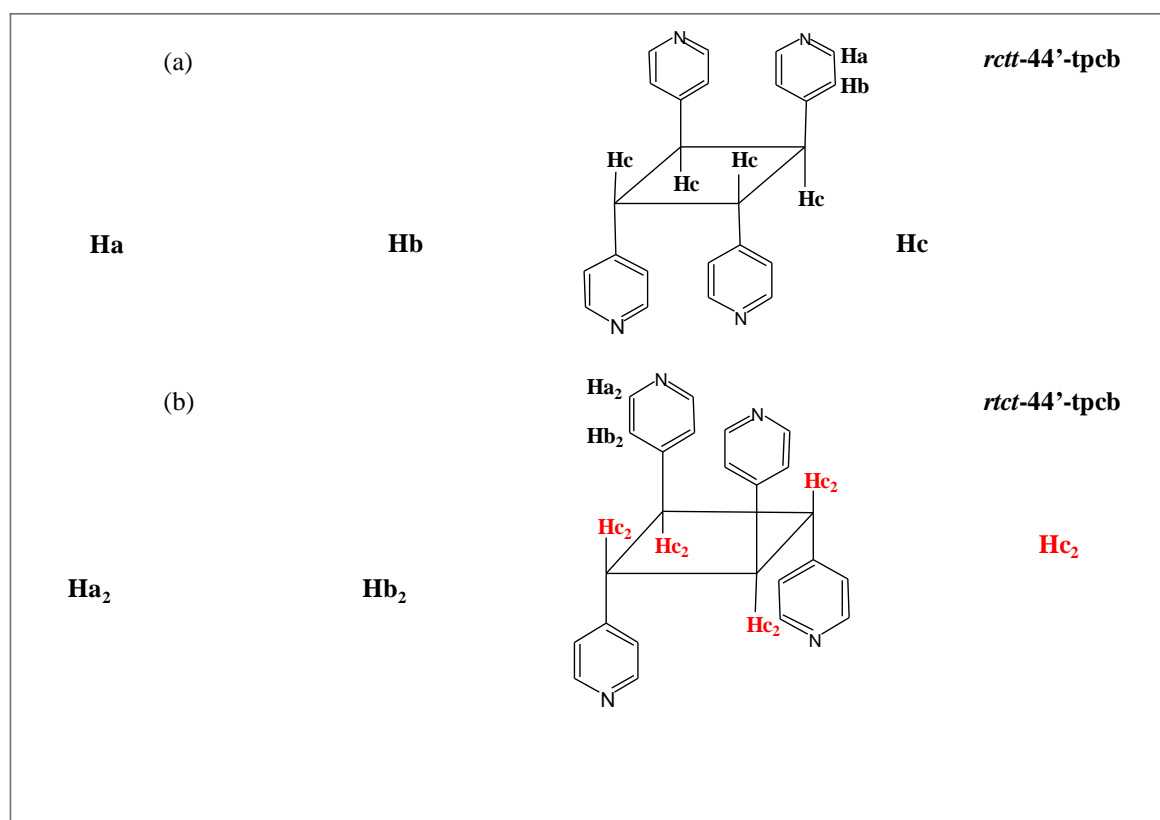


Figure S9. Comparative $^1\text{H-NMR}$ spectrum of the *rtct*-2,4'-tpcb-ht isomer before (a) and after the heating upon hydrothermal conditions either with bta or $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$. Representative $^1\text{H-NMR}$ spectrum of the *rtct*-2,4'-tpcb-ht isomer (b).

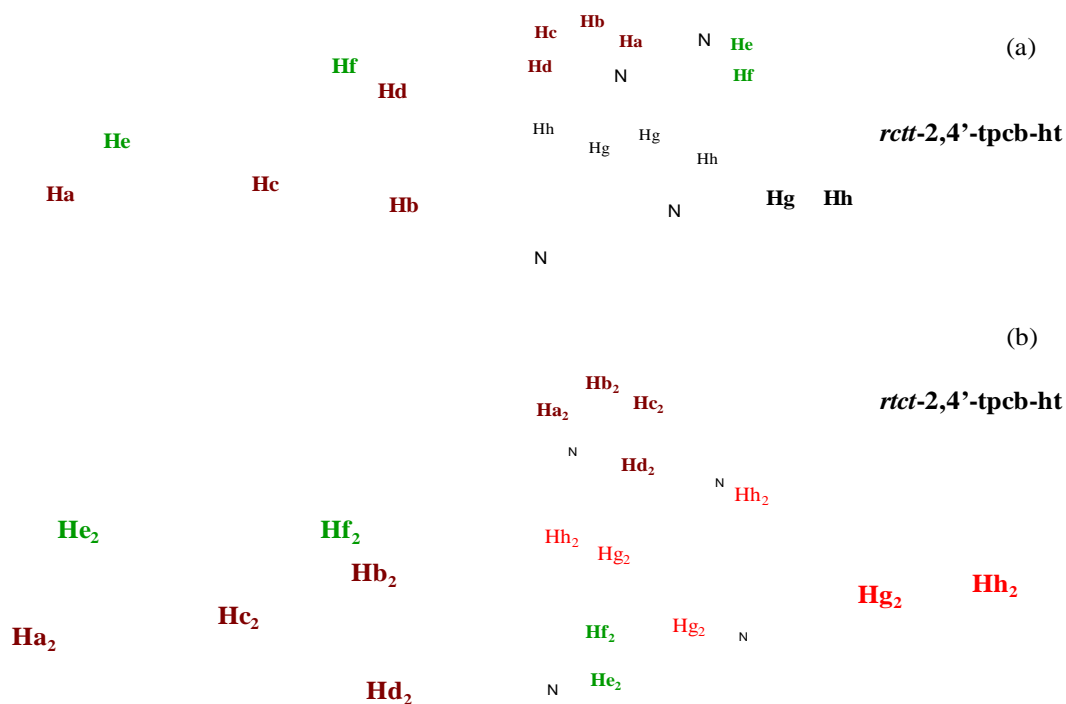


Figure S10. Comparative $^1\text{H-NMR}$ spectrum of the *rtct*-2,4'-tpcb-ht isomer before (a) and after the heating upon hydrothermal conditions either with bta or $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$. Representative $^1\text{H-NMR}$ spectrum of the *rtct*-2,4'-tpcb-hh isomer (b).

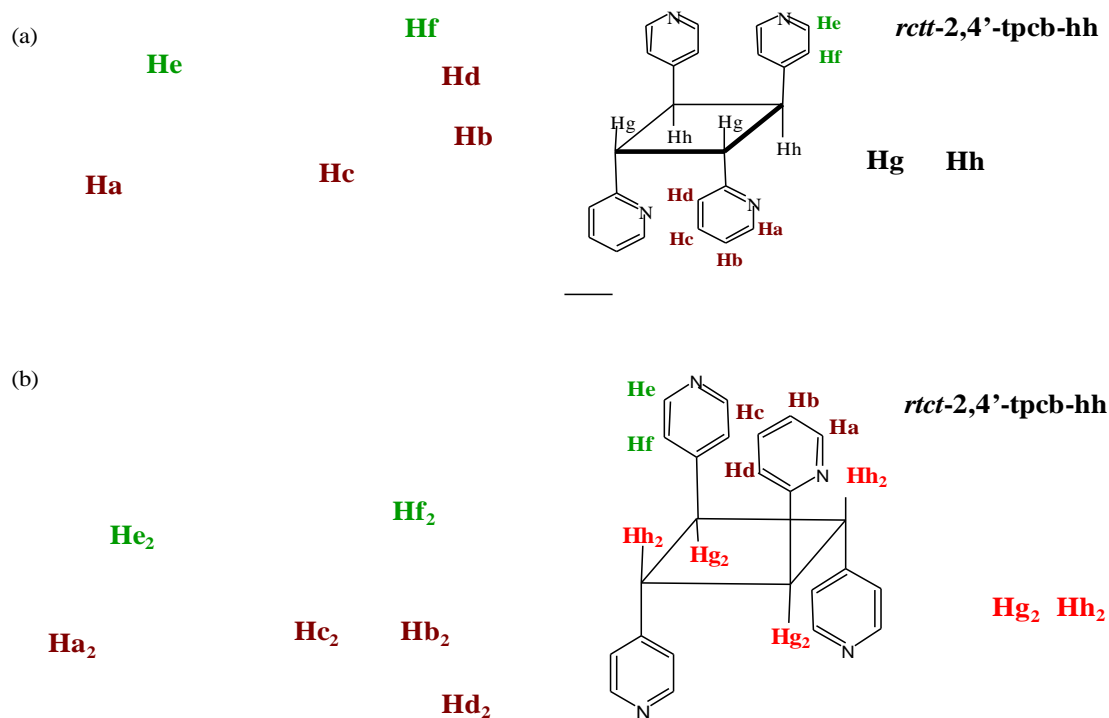


Figure S11. Comparative ^1H -NMR spectrum of the irradiated sample of $(\text{bta}^{2-})\cdot 2(4\text{-Cl-HStb}^+)$, containing *rctt*-1,3-bis(4-pyridyl)-2,4-bis(4-chlorophenyl)cyclobutane head-to-tail (*rctt*-4-Cl-dpcb-ht) before (a). ^1H -NMR spectrum of the mixture of products (*rctt*-, and *rcct*-4-Cl-dpcb-ht isomers) obtained after the heating upon hydrothermal conditions with bta (b). T = template (bta) ; * = *rctt*-isomer

