# Designing hexaphyrins for high-potential NLO switches: The synergy of core-modifications and meso-substitutions

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## **CINDES** workflow

CINDES is a python package that contains two modules: *evaluation* and *algorithm*. The first module is responsible for the HPC automation of job submission and processing the output files. The second module contains all the algorithms to perform the combinatorial optimizations, in our case the BFS algorithm. Below a workflow in bullet points is found together with an overview figure as a summary (Figure 1).

- 1. Selection of M sites to be functionalized
- 2. Construction of functionalization library of size  $N_i$  per site i

Automatization process:

- 3. Generation of starting molecular switch: selection of random functionalizations for each of the sites
- 4. Generation of random site order

For every site i (following site order determined in 4):

- 5. Z-matrix construction of **28R** and **30R** structures with on site *i* one of the functionalizations of that site's library  $\rightarrow$  generation of  $N_i$  switches
- 6. Geometry optimization and vibrational frequency calculation of all  $N_i$  switches using the selected level of theory
- 7. If no imaginary frequencies: reorientation of the optimized structures into the right plane and subsequent NLO calculation
- 8. Extraction of the first hyperpolarizability tensor components
- 9. Calculation of  $\beta_{HRS}$  of **28R** and **30R** structures and the contrast values
- 10. Selection of functionalization on site i yielding the highest contrast value

#### End iteration over sites

- 11. Final switch improved over initial switch?
  - (a) Yes: Go back to 4
  - (b) No: Termination of program



Figure 1: (A) Overview of the CINDES workflow. (B) Example of the best-first search algorithm applied on the hexaphyrin-based redox switch  $(30R \rightarrow 28R)$  with five modifiable sites, considered pairwise, three *meso*-substituents and two core-modifications.

### Comparison of the three NLO metrics

In our previous study (Ref. 31), we noted a serious drawback of the ratio-based contrast to assess the performance of the hexaphyrins switch when a centrosymmetric OFF-state is encountered upon optimization. In this case, the OFF state's  $\beta_{HRS}$  value is 0 and the ratio-based contrast becomes infinite. In Ref. 31, this disadvantage of the ratio metric was mitigated by implementing the following condition within the BFS procedure: if the  $\beta_{HRS}$ value of the OFF state became lower than 10 a.u., the denominator was set to a value of 0.001 a.u. Nevertheless, using an arbitrary nonzero value for the centrosymmetric OFF state's  $\beta_{HRS}$  naturally has a large impact on the final contrast value. As illustrated in Figure 2, only the switches with a low  $\beta_{HRS}$  value for the OFF state will be selected when the ratiobased contrast is employed. However, switches such as the encircled orange dots in Figure 2, where the OFF state's response is still quite low compared to that of the ON state, will never be selected, despite their potential.



Figure 2: Scatterplot of NLO ratio (in units of 1.0 x 10<sup>7</sup>) versus the  $\beta_{HRS}$  for the **30R** structures. Structures missed when applying the NLO ratio metric are encircled.

The difference-based definition overcomes the issue of the contrast going towards infinity

for centrosymmetric OFF states. However, structures can be selected with an OFF state's response significantly higher than centrosymmetric OFF states (e.g., by 2000-3000 a.u.) One example is the encircled green dot in Figure 3 that would be preferred over the previous encircled orange dots.



Figure 3: Scatterplot of NLO difference versus the  $\beta_{HRS}$  for the **30R** structures. The structures, where the NLO ratio difference fails are encircled.

Therefore, we opted for a new metric that overcomes both issues. With our new contrast definition, the more desirable switches with low  $\beta_{HRS}$  OFF states and high  $\beta_{HRS}$  ON states are preferred over switches with higher  $\beta_{HRS}$  OFF states (Figure 4).



Figure 4: Scatterplot of NLO contrast versus the NLO difference for the **30R** structures.

## Equations related to the $\beta_{HRS}$

When positioning the laser's propagation plane perpendicular to the incoherent scattered light, the HRS intensity equation can be written as Eq. 1:

$$\beta_{HRS}(-2\omega;\omega,\omega) = \sqrt{\langle \beta_{ZZZ}^2 \rangle + \langle \beta_{ZXX}^2 \rangle}$$
(1)

Where  $\langle \beta_{ZZZ}^2 \rangle$  and  $\langle \beta_{ZXX}^2 \rangle$  represent the orientational averages of  $\beta$  and describe the isotropic distribution of molecular orientations.

The full descriptions of these tensor components are written in Eq. 2 and 3.

$$\langle \beta_{ZZZ}^2 \rangle = \frac{1}{7} \sum_{i}^{x,y,z} \beta_{iii}^2 + \frac{4}{35} \sum_{i \neq j}^{x,y,z} \beta_{iij}^2 + \frac{2}{35} \sum_{i \neq j}^{x,y,z} \beta_{iii} \beta_{ijj} + \frac{4}{35} \sum_{i \neq j}^{x,y,z} \beta_{jii} \beta_{iij} + \frac{4}{35} \sum_{i \neq j}^{x,y,z} \beta_{jii} \beta_{jii} + \frac{1}{35} \sum_{i}^{x,y,z} \beta_{jii}^2 + \frac{4}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{iij} \beta_{jkk} + \frac{1}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{jii} \beta_{jkk} + \frac{4}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{iij} \beta_{kkj} + \frac{2}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{ijk}^2 + \frac{4}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{ijk} \beta_{jik}$$

$$+ \frac{4}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{iij} \beta_{kkj} + \frac{2}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{ijk}^2 + \frac{4}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{ijk} \beta_{jik}$$

$$(2)$$

$$\langle \beta_{ZXX}^2 \rangle = \frac{1}{35} \sum_{i}^{x,y,z} \beta_{iii}^2 + \frac{4}{105} \sum_{i \neq j}^{x,y,z} \beta_{iii} \beta_{ijj} - \frac{2}{35} \sum_{i \neq j}^{x,y,z} \beta_{iii} \beta_{jji} + \frac{8}{105} \sum_{i \neq j}^{x,y,z} \beta_{iij}^2 + \frac{3}{35} \sum_{i \neq j}^{x,y,z} \beta_{ijj}^2 - \frac{2}{35} \sum_{i}^{x,y,z} \beta_{ijj} \beta_{jii} + \frac{1}{35} \sum_{i \neq j \neq k}^{x,y,z} \beta_{ijj} \beta_{jkk} - \frac{2}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{iik} \beta_{jjk} - \frac{2}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{iij} \beta_{jkk} + \frac{2}{35} \sum_{i \neq j \neq k}^{x,y,z} \beta_{ijk}^2 - \frac{2}{105} \sum_{i \neq j \neq k}^{x,y,z} \beta_{ijk} \beta_{jik}$$
(3)

## BFS procedure A: starting point NH\_NH\_H\_H\_H



Figure 5: Chronological site order of the BFS for maximization of the contrast for the  $28R \rightarrow 30R$  switch starting from the NH\_NH\_H\_H The black lines separate the global iterations. The site order varies in every global iteration.

Table 1: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the  $28R \approx 30R$  switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 1	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30{ m R})$	NLO contrast
	NH_NH_H_H_H	$5.04  imes 10^{-3}$	$2.18 \times 10^3$	$2.18 \times 10^3$
	NH_NH_H_H_F	$3.24 \times 10^0$	$2.62 \times 10^3$	$2.61 \times 10^3$
	NH_NH_H_H_CN	$4.05  imes 10^{-1}$	$4.83  imes 10^3$	$4.83 \times 10^3$
Substitution $R_{3,6}$	$NH_NH_H_NO_2$	$4.23 \times 10^0$	$6.41  imes 10^3$	$6.40  imes 10^3$
	$\rm NH\_NH\_H\_H\_CH_3$	$1.32 \times 10^0$	$2.53 \times 10^3$	$2.53 \times 10^3$
	NH_NH_H_H_OH	$9.93  imes 10^{-1}$	$2.96 \times 10^3$	$2.96 \times 10^3$
	$\rm NH\_NH\_H\_H\_NH_2$	$1.04  imes 10^{-1}$	$3.49 \times 10^3$	$3.49 \times 10^3$
	$NH_NH_H_H_NO_2$	$4.23 \times 10^0$	$6.41 \times 10^3$	$6.40 \times 10^3$
	$\rm NH_O_H_H_NO_2$	$1.01 \times 10^0$	$9.30 \times 10^3$	$9.30 \times 10^3$
Y	$NH_S_H_NO_2$	$1.09 \times 10^0$	$5.51 \times 10^3$	$5.50  imes 10^3$
	$\rm NH\_Se\_H\_H\_NO_2$	$2.00 \times 10^0$	$4.66 \times 10^3$	$4.66 \times 10^3$
	$\rm NH_O_H_H_NO_2$	$1.01 \times 10^0$	$9.30 \times 10^3$	$9.30 \times 10^3$
	$NH_O_H_F_NO_2$	$5.88  imes 10^2$	$8.41 \times 10^3$	$6.80 \times 10^3$
	$NH_O_H_CN_NO_2$	$0.00  imes 10^0$	$1.25  imes 10^4$	$1.25  imes 10^4$
Substitution $R_{2,5}$	$\rm NH_O_H_NO_2_NO_2$	$1.29 \times 10^{3}$	$5.02 \times 10^3$	$2.21 \times 10^3$
	$\rm NH_O_H_CH_3_NO_2$	$1.03 \times 10^{3}$	$8.00 \times 10^{3}$	$5.38 \times 10^3$
	$\rm NH_O_H_OH_NO_2$	$8.51  imes 10^{-1}$	$7.70 \times 10^{3}$	$7.70 \times 10^{3}$
	$\rm NH_O_H_NH_2_NO_2$	$1.12 \times 10^3$	$9.02 \times 10^3$	$6.16 \times 10^{3}$
	$\rm NH_O_H_CN_NO_2$	$0.00  imes 10^0$	$1.25\times 10^4$	$1.25\times 10^4$
	$O_O_H_CN_NO_2$	$0.00 \times 10^0$	$6.13  imes 10^3$	$6.13 \times 10^3$
$\mathbf{X}$	$S_O_H_CN_NO_2$	$5.88 \times 10^2$	$7.34 \times 10^3$	$5.75 \times 10^3$
	$Se_O_H_CN_NO_2$	$7.12 \times 10^2$	$6.33 \times 10^3$	$4.48 \times 10^{3}$
	$\rm NH\_O\_H\_CN\_NO_2$	$0.00 \times 10^0$	$1.25\times 10^4$	$1.25 \times 10^4$
	$NH_O_F_CN_NO_2$	$0.00 \times 10^0$	$1.35 \times 10^4$	$1.35 \times 10^4$
	$\rm NH_O_CN_NO_2$	$0.00 \times 10^0$	$4.29 \times 10^3$	$4.29 \times 10^3$
Substitution $R_{1,4}$	$\rm NH_O_NO_2\_CN_NO_2$	$5.88  imes 10^2$	$3.49 \times 10^3$	$2.06 \times 10^3$
	$\rm NH_O_CH_3_CN_NO_2$	$8.08  imes 10^2$	$7.47 \times 10^3$	$5.36 \times 10^3$
	$\rm NH_O_OH_CN_NO_2$	$2.74 \times 10^{0}$	$1.74 \times 10^{4}$	$1.74 \times 10^{4}$
	NH_O_NH2_CN_NO2	$3.96 \times 10^3$	$1.24 \times 10^4$	$4.34 \times 10^{3}$

Table 1: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the  $28R \approx 30R$  switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 2	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30{ m R})$	NLO contrast
Substitution R <sub>3,6</sub>	NH_O_OH_CN_H NH_O_OH_CN_F NH_O_OH_CN_CN NH_O_OH_CN_NO <sub>2</sub> NH_O_OH_CN_CH <sub>3</sub> NH_O_OH_CN_OH NH_O_OH_CN_OH NH_O_OH_CN_NH <sub>2</sub>	$2.62 \times 10^{0}$ $1.85 \times 10^{1}$ $2.67 \times 10^{0}$ $2.74 \times 10^{0}$ $1.12 \times 10^{0}$ $1.58 \times 10^{0}$ $1.07 \times 10^{0}$	$7.47 \times 10^{3}$ $6.71 \times 10^{3}$ $1.42 \times 10^{4}$ $1.74 \times 10^{4}$ $7.24 \times 10^{3}$ $7.50 \times 10^{3}$ $7.22 \times 10^{3}$	$7.46 \times 10^{3}$ $6.66 \times 10^{3}$ $1.42 \times 10^{4}$ $1.74 \times 10^{4}$ $7.24 \times 10^{3}$ $7.50 \times 10^{3}$ $7.22 \times 10^{3}$
Y	$\begin{array}{c} \mathrm{NH\_NH\_OH\_CN\_NO_2}\\ \mathrm{NH\_O\_OH\_CN\_NO_2}\\ \mathrm{NH\_S\_OH\_CN\_NO_2}\\ \mathrm{NH\_Se\_OH\_CN\_NO_2}\\ \end{array}$	$\begin{array}{c} 0.00 \times 10^{0} \\ 2.74 \times 10^{0} \\ 3.01 \times 10^{0} \\ 7.66 \times 10^{-1} \end{array}$	$\begin{array}{c} 7.06 \times 10^{3} \\ 1.74 \times 10^{4} \\ 1.14 \times 10^{4} \\ 9.49 \times 10^{3} \end{array}$	$\begin{array}{c} 7.06 \times 10^{3} \\ 1.74 \times 10^{4} \\ 1.14 \times 10^{4} \\ 9.49 \times 10^{3} \end{array}$
Substitution $R_{1,4}$	NH_O_H_CN_NO <sub>2</sub> NH_O_F_CN_NO <sub>2</sub> NH_O_CN_CN_NO <sub>2</sub> NH_O_NO <sub>2</sub> _CN_NO <sub>2</sub> NH_O_CH <sub>3</sub> _CN_NO <sub>2</sub> NH_O_OH_CN_NO <sub>2</sub> NH_O_NH <sub>2</sub> _CN_NO <sub>2</sub>	$\begin{array}{c} 0.00 \times 10^{0} \\ 0.00 \times 10^{0} \\ 0.00 \times 10^{0} \\ 5.88 \times 10^{2} \\ 8.08 \times 10^{2} \\ 2.74 \times 10^{0} \\ 3.96 \times 10^{3} \end{array}$	$\begin{array}{c} 1.25\times 10^4\\ 1.35\times 10^4\\ 4.29\times 10^3\\ 3.49\times 10^3\\ 7.47\times 10^3\\ 1.74\times 10^4\\ 1.24\times 10^4 \end{array}$	$\begin{array}{c} 1.25\times 10^{4}\\ 1.35\times 10^{4}\\ 4.29\times 10^{3}\\ 2.06\times 10^{3}\\ 5.36\times 10^{3}\\ 1.74\times 10^{4}\\ 4.34\times 10^{3} \end{array}$
Substitution $R_{2,5}$	NH_O_OH_H_NO <sub>2</sub> NH_O_OH_F_NO <sub>2</sub> NH_O_OH_CN_NO <sub>2</sub> NH_O_OH_NO <sub>2</sub> _NO <sub>2</sub> NH_O_OH_CH <sub>3</sub> _NO <sub>2</sub> NH_O_OH_OH_NO <sub>2</sub> NH_O_OH_OH_NO <sub>2</sub> NH_O_OH_NH <sub>2</sub> _NO <sub>2</sub>	$\begin{array}{c} 2.05\times10^{0}\\ 9.01\times10^{-1}\\ 2.74\times10^{0}\\ 1.37\times10^{-1}\\ 2.23\times10^{3}\\ 2.08\times10^{0}\\ 0.00\times10^{0} \end{array}$	$\begin{array}{c} 1.35\times 10^4\\ 1.25\times 10^4\\ 1.74\times 10^4\\ 5.86\times 10^3\\ 1.12\times 10^4\\ 1.11\times 10^4\\ 1.39\times 10^4 \end{array}$	$\begin{array}{c} 1.35 \times 10^{4} \\ 1.25 \times 10^{4} \\ 1.74 \times 10^{4} \\ 5.85 \times 10^{3} \\ 5.97 \times 10^{3} \\ 1.11 \times 10^{4} \\ 1.39 \times 10^{4} \end{array}$
X	NH_O_OH_CN_NO2           O_O_OH_CN_NO2           S_O_OH_CN_NO2           Se_O_OH_CN_NO2	$\begin{array}{c} 2.74 \times 10^{0} \\ 0.00 \times 10^{0} \\ 1.57 \times 10^{3} \\ 1.67 \times 10^{3} \end{array}$	$\begin{array}{c} 1.74 \times 10^{4} \\ 1.46 \times 10^{4} \\ 6.94 \times 10^{3} \\ 6.44 \times 10^{3} \end{array}$	$\begin{array}{c} 1.74 \times 10^{4} \\ 1.46 \times 10^{4} \\ 3.38 \times 10^{3} \\ 2.80 \times 10^{3} \end{array}$



BFS procedure B: starting point  $S_O_NH_2_F_OH$ 

Figure 6: Chronological site order of the BFS for maximization of the contrast for the  $28R \rightarrow 30R$  switch starting from the  $S_O_NH_2_F_OH$  The black lines separate the global iterations. The site order varies in every global iteration

Table 2: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the  $28R \approx 30R$  switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 2 continued	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
	$\rm NH\_Se\_NH_2\_CN\_H$	$2.85\times10^{-2}$	$5.81 \times 10^3$	$5.81 \times 10^3$
	$\rm NH_Se_NH_2_CN_F$	$8.36 \times 10^0$	$5.68 \times 10^3$	$5.65 \times 10^3$
	$\rm NH\_Se\_NH_2\_CN\_CN$	$1.43 \times 10^0$	$1.14 \times 10^4$	$1.14 \times 10^4$
Substitution $R_{3,6}$	$\rm NH\_Se\_NH_2\_CN\_NO_2$	$2.63 \times 10^0$	$1.20 \times 10^4$	$1.20  imes 10^4$
	$\rm NH_Se_NH_2_CN_CH_3$	$1.64  imes 10^{-1}$	$5.67  imes 10^3$	$5.67 \times 10^3$
	$\rm NH_Se_NH_2_CN_OH$	$5.19  imes 10^2$	$6.07 \times 10^3$	$4.67 \times 10^3$
	$\rm NH\_Se\_NH_2\_CN\_NH_2$	$1.65 \times 10^0$	$7.11 \times 10^3$	$7.11 \times 10^3$
	NH_Se_NH <sub>2</sub> _CN_NO <sub>2</sub>	$2.63 \times 10^0$	$1.20 \times 10^4$	$1.20 \times 10^4$
	$O\_Se\_NH_2\_CN\_NO_2$	$1.06 \times 10^0$	$1.12 \times 10^4$	$1.12 \times 10^4$
Core-modifications X	$S_Se_NH_2_CN_NO_2$	$6.85 \times 10^2$	$6.76 \times 10^3$	$4.96 \times 10^3$
	$Se\_Se\_NH_2\_CN\_NO_2$	$2.00 \times 10^3$	$5.76  imes 10^3$	$1.82 \times 10^3$
	NH_NH_NH2_CN_NO2	$2.31 \times 10^0$	$8.92 \times 10^3$	$8.91 \times 10^3$
	$\rm NH_O_NH_2_CN_NO_2$	$3.96 \times 10^3$	$1.24 \times 10^4$	$4.34 \times 10^3$
Core-modifications Y	NH_S_NH <sub>2</sub> _CN_NO <sub>2</sub>	$6.73  imes 10^{-1}$	$1.35 \times 10^4$	$1.35  imes 10^4$
	$\rm NH\_Se\_NH_2\_CN\_NO_2$	$2.63 \times 10^0$	$1.20 \times 10^4$	$1.20 \times 10^4$
Global iteration 3	$X_Y_R_{1,4}R_{2,5}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
	NH_S_NH2_H_NO2	$1.48\times 10^{-1}$	$1.00 \times 10^4$	$1.00 \times 10^4$
	NH_S_NH2_F_NO2	$2.25 \times 10^0$	$9.70 \times 10^3$	$9.69 \times 10^3$
	$NH_S_NH_2_CN_NO_2$	$6.73  imes 10^{-1}$	$1.35  imes 10^4$	$1.35  imes 10^4$
Substitution $R_{2.5}$	NH_S_NH <sub>2</sub> _NO <sub>2</sub> _NO <sub>2</sub>	$0.00 \times 10^0$	$6.40 \times 10^3$	$6.40 \times 10^3$
	NH_S_NH <sub>2</sub> _CH <sub>3</sub> _NO <sub>2</sub>	$1.02  imes 10^{-1}$	$1.06 \times 10^4$	$1.06 \times 10^4$
	NH_S_NH2_OH_NO2	$8.31 \times 10^2$	$1.17 \times 10^4$	$9.40 \times 10^3$
	$\rm NH\_S\_NH_2\_NH_2\_NO_2$	$4.58 \times 10^{0}$	$1.11 \times 10^4$	$1.11 \times 10^4$
	NH_S_NH <sub>2</sub> _CN_H	$4.31\times 10^{-2}$	$6.52 \times 10^3$	$6.52 \times 10^3$
	$NH_S_NH_2_CN_F$	$1.03 \times 10^1$	$6.27 \times 10^3$	$6.24 \times 10^3$
	$NH_S_NH_2_CN_CN$	$1.42 \times 10^0$	$1.35  imes 10^4$	$1.35  imes 10^4$
Substitution $R_{3,6}$	$NH_S_NH_2_CN_NO_2$	$6.73  imes 10^{-1}$	$1.35 \times 10^4$	$1.35  imes 10^4$
	NH_S_NH <sub>2</sub> _CN_CH <sub>3</sub>	$8.02 \times 10^0$	$6.37 \times 10^3$	$6.34 \times 10^3$
	NH_S_NH <sub>2</sub> _CN_OH	$0.00 \times 10^0$	$6.50 \times 10^3$	$6.50 \times 10^3$
	$\rm NH\_S\_NH_2\_CN\_NH_2$	$2.66 \times 10^0$	$7.80 \times 10^3$	$7.79 \times 10^3$
	NH_S_H_CN_CN	$7.42\times10^{-2}$	$6.77 \times 10^3$	$6.77 \times 10^3$
	NH_S_F_CN_CN	$1.66 \times 10^0$	$8.89 \times 10^3$	$8.89 \times 10^3$
	NH_S_CN_CN_CN	$6.06  imes 10^{-1}$	$3.31 \times 10^3$	$3.31 \times 10^3$
Substitution $R_{3,6}$	$NH_S_NO_2_CN_CN$	$1.08 \times 10^3$	$4.15 \times 10^3$	$1.79 \times 10^3$
	NH_S_CH <sub>3</sub> _CN_CN	$2.15  imes 10^{-1}$	$8.22 \times 10^3$	$8.22 \times 10^3$
	NH_S_OH_CN_CN	$0.00 \times 10^0$	$1.20 \times 10^4$	$1.20 \times 10^4$
	NH_S_NH <sub>2</sub> _CN_CN	$1.42 \times 10^{0}$	$1.35 \times 10^4$	$1.35 \times 10^{4}$
	$\rm NH\_S\_NH_2\_CN\_CN$	$1.42 \times 10^0$	$1.35 \times 10^4$	$1.35 \times 10^4$
	$O_S_NH_2_CN_CN$	$3.36 \times 10^{0}$	$1.72 \times 10^{4}$	$1.72 \times 10^{4}$
X	S_S_NH <sub>2</sub> _CN_CN	$1.18 \times 10^{3}$	$1.20 \times 10^{4}$	$8.87 \times 10^{3}$
	$Se_S_NH_2_CN_CN$	$1.54 \times 10^3$	$1.10 \times 10^{4}$	$7.13 \times 10^{3}$
	O_NH_NH2_CN_CN	$2.09 \times 10^0$	$1.57 \times 10^4$	$1.57 \times 10^4$
	O_O_NH <sub>2</sub> _CN_CN	$6.18 \times 10^{-1}$	$2.08 \times 10^{4}$	$2.08 \times 10^{4}$
Y	O_S_NH <sub>2</sub> _CN_CN	$3.36 \times 10^{0}$	$1.72 \times 10^{4}$	$1.72 \times 10^{4}$
	$O\_Se\_NH_2\_CN\_CN$	$8.47 \times 10^{-1}$	$1.34 \times 10^4$	$1.34 \times 10^4$

Table 2: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the  $28R \approx 30R$  switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 1	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30{ m R})$	NLO contrast
	$S_O_NH_2_F_H$	$1.35 \times 10^3$	$3.46 \times 10^3$	$9.22 \times 10^2$
Substitution $R_{3,6}$	$S_O_NH_2_F_F$	$1.24 \times 10^3$	$2.98  imes 10^3$	$7.16  imes 10^2$
	$S_O_NH_2_F_CN$	$1.99 \times 10^3$	$7.56 \times 10^3$	$3.25 \times 10^3$
	$S_O_NH_2_F_NO_2$	$3.27 \times 10^3$	$1.06 \times 10^4$	$3.88 \times 10^3$
	$S_O_NH_2_F_CH_3$	$1.55 \times 10^3$	$3.14 \times 10^3$	$5.38  imes 10^2$
	S_O_NH <sub>2</sub> _F_OH	$1.47 \times 10^3$	$2.47 \times 10^3$	$2.53 \times 10^2$
	$S\_O\_NH_2\_F\_NH_2$	$1.57 \times 10^3$	$2.65 \times 10^3$	$2.76 \times 10^2$
	S_O_H_F_NO <sub>2</sub>	$1.23 \times 10^3$	$5.06 \times 10^3$	$2.33 \times 10^3$
	$S_O_F_F_NO_2$	$1.63 \times 10^3$	$5.79 \times 10^3$	$2.33 \times 10^3$
	$S_O_CN_F_NO_2$	$1.42 \times 10^3$	$3.68 \times 10^3$	$1.00 \times 10^{3}$
Substitution $R_{1,4}$	$S_O_NO_2_F_NO_2$	$1.36 \times 10^{3}$	$2.86 \times 10^3$	$5.31 \times 10^2$
	$S_O_CH_3_F_NO_2$	$1.67  imes 10^3$	$5.39  imes 10^3$	$1.97 \times 10^3$
	$S_O_OH_F_NO_2$	$2.47 \times 10^3$	$6.98 \times 10^3$	$2.15 \times 10^3$
	$S_O_NH_2_F_NO_2$	$3.27 \times 10^{3}$	$1.06 \times 10^{4}$	$3.88 \times 10^{3}$
	$S\_NH\_NH_2\_F\_NO_2$	$2.89\times10^3$	$2.91 \times 10^3$	$7.20\times10^{-2}$
	$S_O_NH_2_F_NO_2$	$3.27 \times 10^3$	$1.06 \times 10^4$	$3.88 \times 10^3$
Core-modifications Y	$S_S_NH_2_F_NO_2$	$2.44 \times 10^3$	$4.66 \times 10^3$	$6.94 \times 10^2$
	$S_Se_NH_2_F_NO_2$	$7.95  imes 10^{-1}$	$4.08 \times 10^3$	$4.08 \times 10^{3}$
	$\rm NH\_Se\_NH_2\_F\_NO_2$	$2.27 \times 10^{0}$	$8.64 \times 10^{3}$	$8.63 \times 10^{3}$
	$O\_Se\_NH_2\_F\_NO_2$	$3.39 \times 10^{0}$	$6.55 \times 10^{3}$	$6.54 \times 10^{3}$
Core-modifications X	$S_Se_NH_2_F_NO_2$	$7.95 \times 10^{-1}$	$4.08 \times 10^{3}$	$4.08 \times 10^{3}$
	Se_Se_NH <sub>2</sub> _F_NO <sub>2</sub>	$0.00 \times 10^{0}$	$3.77 \times 10^{3}$	$3.77 \times 10^3$
	$\rm NH\_Se\_NH_2\_H\_NO_2$	$6.77\times10^{-1}$	$8.95\times10^3$	$8.94 \times 10^3$
	$NH_Se_NH_2_F_NO_2$	$2.27 \times 10^0$	$8.64 \times 10^{3}$	$8.63 \times 10^{3}$
	$\rm NH\_Se\_NH_2\_CN\_NO_2$	$2.63 \times 10^0$	$1.20 \times 10^4$	$1.20  imes 10^4$
Substitution $R_{2,5}$	$NH_Se_NH_2_NO_2_NO_2$	$1.86 \times 10^2$	$6.20 \times 10^3$	$5.67 \times 10^{3}$
	$\rm NH_Se_NH_2\_CH_3\_NO_2$	$2.88  imes 10^{-1}$	$9.58 \times 10^3$	$9.58 \times 10^3$
	$\rm NH_Se_NH_2_OH_NO_2$	$0.00 \times 10^{0}$	$1.04 \times 10^4$	$1.04 \times 10^4$
	$\rm NH\_Se\_NH_2\_NH_2\_NO_2$	$4.36 \times 10^{0}$	$1.04 \times 10^4$	$1.03 \times 10^4$
Global iteration 2	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
	$NH_Se_NH_2_H_NO_2$	$6.77 \times 10^{-1}$	$8.95 \times 10^{3}$	$8.94 \times 10^{3}$
	$NH_Se_NH_2_F_NO_2$	$2.27 \times 10^0$	$8.64 \times 10^3$	$8.63 \times 10^3$
	$\rm NH_Se_NH_2_CN_NO_2$	$2.63 \times 10^{0}$	$1.20  imes 10^4$	$1.20  imes 10^4$
Substitution $R_{2.5}$	NH_Se_NH <sub>2</sub> _NO <sub>2</sub> _NO <sub>2</sub>	$1.86 \times 10^2$	$6.20 \times 10^3$	$5.67 \times 10^3$
_,_	NH_Se_NH <sub>2</sub> _CH <sub>3</sub> _NO <sub>2</sub>	$2.88\times10^{-1}$	$9.58 \times 10^3$	$9.58 \times 10^3$
	$\rm NH_Se_NH_2_OH_NO_2$	$0.00 \times 10^0$	$1.04 \times 10^4$	$1.04 \times 10^4$
	$\rm NH\_Se\_NH_2\_NH_2\_NO_2$	$4.36 \times 10^0$	$1.04 \times 10^4$	$1.03 \times 10^4$
	NH_Se_H_CN_NO <sub>2</sub>	$3.27\times 10^{-1}$	$6.20 \times 10^{3}$	$6.20 \times 10^{3}$
	$\rm NH\_Se\_F\_CN\_NO_2$	$7.92 \times 10^0$	$7.42 \times 10^3$	$7.39  imes 10^3$
	$\rm NH\_Se\_CN\_CN\_NO_2$	$8.32  imes 10^{-1}$	$4.30 \times 10^3$	$4.30 \times 10^3$
Substitution $R_{1,4}$	$\rm NH\_Se\_NO_2\_CN\_NO_2$	$6.32 \times 10^2$	$4.38 \times 10^3$	$2.80 \times 10^3$
,	$NH_Se_CH_3_CN_NO_2$	$5.50  imes 10^{-1}$	$7.20 \times 10^3$	$7.20 \times 10^3$
	$\rm NH\_Se\_OH\_CN\_NO_2$	$7.66\times10^{-1}$	$9.49 \times 10^3$	$9.49 \times 10^3$
	$\rm NH\_Se\_NH_2\_CN\_NO_2$	$2.63 \times 10^0$	$1.20 \times 10^4$	$1.20 \times 10^4$

Table 2: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the  $28R \approx 30R$  switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 4	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
	O_O_NH2_H_CN	$2.20\times 10^{-2}$	$1.06 \times 10^4$	$1.06 \times 10^4$
	$O_O_NH_2_F_CN$	$1.19 \times 10^0$	$1.00 \times 10^4$	$1.00 \times 10^4$
	O_O_NH2_CN_CN	$6.18  imes 10^{-1}$	$2.08 \times 10^4$	$2.08  imes 10^4$
Substitution $R_{2,5}$	$O_O_NH_2_NO_2_CN$	$1.98  imes 10^2$	$1.72 \times 10^4$	$1.66  imes 10^4$
	$O_O_NH_2_CH_3_CN$	$1.18 \times 10^0$	$9.86 \times 10^3$	$9.86 \times 10^3$
	$O_O_NH_2_OH_CN$	$2.31 \times 10^{-1}$	$7.49 \times 10^3$	$7.49 \times 10^3$
	$O_O_NH_2_NH_2_CN$	$3.20 \times 10^2$	$7.89 \times 10^3$	$6.98 \times 10^{3}$
	NH_O_NH2_CN_CN	$6.66\times 10^{-1}$	$1.70 \times 10^4$	$1.70 \times 10^4$
	$O_O_NH_2_CN_CN$	$6.18 imes10^{-1}$	$2.08 \times 10^4$	$2.08 \times 10^4$
$\mathbf{X}$	$S_O_NH_2_CN_CN$	$2.13 \times 10^3$	$1.71 \times 10^4$	$1.17 \times 10^4$
	$Se_O_NH_2_CN_CN$	$2.17 \times 10^3$	$1.39 \times 10^4$	$8.55 \times 10^3$
	$O_O_NH_2_CN_H$	$1.29\times 10^{-1}$	$1.07 \times 10^4$	$1.07 \times 10^4$
	$O_O_NH_2_CN_F$	$1.31 \times 10^0$	$8.94 \times 10^3$	$8.94 \times 10^3$
	$O_O_NH_2_CN_CN$	$6.18 imes10^{-1}$	$2.08 \times 10^4$	$2.08  imes 10^4$
Substitution $R_{3,6}$	$O_O_NH_2_CN_NO_2$	$0.00 \times 10^0$	$1.71 \times 10^4$	$1.71 \times 10^4$
	$O_O_NH_2_CN_CH_3$	$2.63  imes 10^{-1}$	$8.84 \times 10^3$	$8.84 \times 10^3$
	$O_O_NH_2_CN_OH$	$2.79  imes 10^2$	$6.43 \times 10^3$	$5.64  imes 10^3$
	$O_O_NH_2_CN_NH_2$	$3.99 \times 10^2$	$7.47 \times 10^3$	$6.36 \times 10^3$
	O_NH_NH2_CN_CN	$2.09 \times 10^0$	$1.57 \times 10^4$	$1.57 \times 10^4$
	$O_O_NH_2_CN_CN$	$6.18 imes10^{-1}$	$2.08 \times 10^4$	$2.08  imes 10^4$
Y	$O_S_NH_2_CN_CN$	$3.36 \times 10^0$	$1.72 \times 10^4$	$1.72 \times 10^4$
	$O\_Se\_NH_2\_CN\_CN$	$8.47\times10^{-1}$	$1.34 \times 10^4$	$1.34 \times 10^4$
	O_O_H_CN_CN	$8.95\times10^{-2}$	$7.16  imes 10^3$	$7.16 \times 10^3$
	O_O_F_CN_CN	$8.06  imes 10^{-1}$	$9.04 \times 10^3$	$9.04 \times 10^3$
	O_O_CN_CN_CN	$1.00 \times 10^0$	$3.07 \times 10^3$	$3.07 \times 10^3$
Substitution R <sub>1,4</sub>	$O_O_NO_2_CN_CN$	$3.38 \times 10^2$	$3.18 \times 10^3$	$2.30 \times 10^3$
	$O_O_CH_3_CN_CN$	$1.78  imes 10^{-1}$	$8.08 \times 10^3$	$8.07 \times 10^3$
	O_O_OH_CN_CN	$1.19 \times 10^0$	$1.61 \times 10^4$	$1.61 \times 10^4$
	$O_O_NH_2_CN_CN$	$6.18  imes 10^{-1}$	$2.08 \times 10^4$	$2.08  imes 10^4$



BFS procedure C: starting point  $O_NH_CN_NO_2F$ 

Figure 7: Chronological site order of the BFS for maximization of the contrast for the **28R**  $\rightarrow$  **30R** switch starting from the **O\_NH\_CN\_NO\_2\_F** The black lines separate the global iterations. The site order varies in every global iteration

Table 3: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the  $28R \approx 30R$  switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 1	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30{ m R})$	NLO contrast
	NH_NH_CN_NO <sub>2</sub> _F	$2.57\times 10^2$	$5.98 \times 10^3$	$5.26 \times 10^3$
	O_NH_CN_NO2_F	$2.29 \times 10^2$	$5.20 \times 10^3$	$4.56  imes 10^3$
X	$S_NH_CN_NO_2_F$	$1.32 \times 10^3$	$4.74 \times 10^3$	$1.93 \times 10^3$
	$Se\_NH\_CN\_NO_2\_F$	$1.60 \times 10^3$	$4.92 \times 10^3$	$1.70 \times 10^3$
	NH_NH_CN_NO <sub>2</sub> _F	$2.57\times 10^2$	$5.98 \times 10^3$	$5.26 \times 10^3$
	NH_O_CN_NO <sub>2</sub> _F	$5.56  imes 10^2$	$8.09  imes 10^3$	$6.56  imes 10^3$
Y	NH_S_CN_NO <sub>2</sub> _F	$1.54  imes 10^2$	$8.44  imes 10^3$	$7.99 imes10^3$
	$\rm NH\_Se\_CN\_NO_2\_F$	$1.78 \times 10^2$	$7.47 \times 10^3$	$6.96 \times 10^3$
	$NH_S_H_NO_2_F$	$2.65\times 10^2$	$3.74 \times 10^3$	$3.01 \times 10^3$
	$NH_S_F_NO_2_F$	$2.78 \times 10^2$	$4.14 \times 10^3$	$3.37 \times 10^3$
	NH_S_CN_NO <sub>2</sub> _F	$1.54  imes 10^2$	$8.44  imes 10^3$	$7.99  imes 10^3$
Substitution R <sub>1,4</sub>	NH_S_NO <sub>2</sub> _NO <sub>2</sub> _F	$7.94  imes 10^2$	$9.17  imes 10^3$	$7.04  imes 10^3$
,	$\rm NH_S_CH_3_NO_2_F$	$1.66 \times 10^2$	$4.40 \times 10^3$	$3.93 \times 10^3$
	$NH_S_OH_NO_2_F$	$1.56  imes 10^3$	$4.97 \times 10^3$	$1.77 \times 10^3$
	$\rm NH\_S\_NH_2\_NO_2\_F$	$1.46 \times 10^2$	$5.61 \times 10^3$	$5.19 \times 10^{3}$
	NH_S_CN_H_F	$1.10\times 10^{-2}$	$6.59 \times 10^3$	$6.59 \times 10^3$
	NH_S_CN_F_F	$2.17 \times 10^0$	$5.95 \times 10^3$	$5.95 \times 10^3$
	NH_S_CN_CN_F	$1.17 \times 10^{0}$	$8.80  imes 10^3$	$8.80  imes 10^3$
Substitution $R_{2,5}$	$NH_S_CN_NO_2_F$	$1.54 \times 10^2$	$8.44 \times 10^3$	$7.99  imes 10^3$
	$NH_S_CN_CH_3_F$	$6.03 imes10^{-1}$	$6.36  imes 10^3$	$6.36  imes 10^3$
	NH_S_CN_OH_F	$7.18  imes 10^2$	$6.41 \times 10^3$	$4.54 \times 10^3$
	NH_S_CN_NH <sub>2</sub> _F	$1.00 \times 10^{0}$	$6.53 \times 10^3$	$6.53 \times 10^{3}$
	NH_S_CN_CN_H	$2.83\times 10^{-2}$	$6.82 \times 10^3$	$6.82 \times 10^3$
	NH_S_CN_CN_F	$1.17 \times 10^0$	$8.80  imes 10^3$	$8.80  imes 10^3$
	NH_S_CN_CN_CN	$6.06 imes10^{-1}$	$3.31 \times 10^3$	$3.31 \times 10^3$
Substitution $R_{3,6}$	$NH_S_CN_CN_NO_2$	$8.96 imes10^{-1}$	$4.33 \times 10^{3}$	$4.33 \times 10^{3}$
	$\rm NH_S_CN_CN_CH_3$	$6.49 \times 10^{-1}$	$7.80 \times 10^{3}$	$7.79 \times 10^{3}$
	NH_S_CN_CN_OH	$8.76 \times 10^{2}$	$1.05 \times 10^{4}$	$8.14 \times 10^{3}$
	NH_S_CN_CN_NH <sub>2</sub>	$2.77 \times 10^{0}$	$1.36 \times 10^4$	$1.36 \times 10^{4}$

Table 3: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the  $28R \approx 30R$  switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 2	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30{ m R})$	NLO contrast
	$NH_NH_CN_CN_NH_2$	$7.75\times10^{-1}$	$1.25 \times 10^4$	$1.25 \times 10^4$
	$\rm NH_O_CN_CN_NH_2$	$6.57 imes10^{-1}$	$1.20 \times 10^4$	$1.20 \times 10^4$
Y	$\rm NH_S_CN_CN_NH_2$	$2.77 \times 10^{0}$	$1.36  imes 10^4$	$1.36  imes 10^4$
	$\rm NH\_Se\_CN\_CN\_NH_2$	$1.38 \times 10^0$	$1.29\times 10^4$	$1.29\times 10^4$
	NH_S_CN_CN_H	$2.83\times10^{-2}$	$6.82 \times 10^3$	$6.82 \times 10^3$
	NH_S_CN_CN_F	$1.17 \times 10^0$	$8.80 \times 10^3$	$8.80 \times 10^3$
	NH_S_CN_CN_CN	$6.06 imes10^{-1}$	$3.31 \times 10^3$	$3.31 \times 10^3$
Substitution R <sub>3,6</sub>	$NH_S_CN_CN_NO_2$	$8.96 imes10^{-1}$	$4.33  imes 10^3$	$4.33  imes 10^3$
	$\rm NH_S_CN_CM_3$	$6.49 imes10^{-1}$	$7.80  imes 10^3$	$7.79  imes 10^3$
	NH_S_CN_CN_OH	$8.76  imes 10^2$	$1.05 \times 10^4$	$8.14  imes 10^3$
	$\rm NH\_S\_CN\_CN\_NH_2$	$2.77 \times 10^{0}$	$1.36  imes 10^4$	$1.36  imes 10^4$
	$NH_S_H_CN_NH_2$	$2.53\times10^{-2}$	$6.95  imes 10^3$	$6.95 \times 10^3$
	$NH_S_F_CN_NH_2$	$2.56 \times 10^0$	$6.57  imes 10^3$	$6.56  imes 10^3$
	$\rm NH_S_CN_CN_NH_2$	$2.77 \times 10^0$	$1.36  imes 10^4$	$1.36  imes 10^4$
Substitution R <sub>1,4</sub>	$\rm NH_S_NO_2_CN_NH_2$	$0.00  imes 10^0$	$1.67 \times 10^4$	$1.67  imes 10^4$
	$\rm NH_S_CH_3_CN_NH_2$	$1.02 \times 10^0$	$6.77 \times 10^3$	$6.76 \times 10^3$
	$\rm NH_S_OH_CN_NH_2$	$6.42 \times 10^2$	$7.32 \times 10^3$	$5.61 \times 10^3$
	$\rm NH\_S\_NH_2\_CN\_NH_2$	$2.66 \times 10^0$	$7.80 \times 10^3$	$7.79 \times 10^3$
	$\rm NH\_S\_NO_2\_H\_NH_2$	$3.44\times 10^{-1}$	$1.45 \times 10^4$	$1.45 \times 10^4$
	$NH_S_NO_2_F_NH_2$	$2.27 \times 10^0$	$1.34 \times 10^4$	$1.34  imes 10^4$
	$\rm NH_S_NO_2\_CN\_NH_2$	$0.00 \times 10^0$	$1.67  imes 10^4$	$1.67  imes 10^4$
Substitution $R_{2,5}$	$\rm NH_S_NO_2_NO_2_NH_2$	$1.14 \times 10^3$	$1.44 \times 10^4$	$1.13  imes 10^4$
	$\rm NH_S_NO_2\_CH_3\_NH_2$	$1.18 \times 10^0$	$1.34 \times 10^4$	$1.34  imes 10^4$
	$\rm NH_S_NO_2_OH_NH_2$	$5.41 \times 10^2$	$1.46 \times 10^4$	$1.31  imes 10^4$
	$\rm NH_S\_NO_2\_NH_2\_NH_2$	$0.00 \times 10^0$	$1.44 \times 10^4$	$1.44 \times 10^4$
	NH_S_NO <sub>2</sub> _CN_NH <sub>2</sub>	$0.00 \times 10^{0}$	$1.67 \times 10^4$	$1.67 \times 10^{4}$
	$O\_S\_NO_2\_CN\_NH_2$	$2.96  imes 10^2$	$1.38  imes 10^4$	$1.29 \times 10^4$
$\mathbf{X}$	$S\_S\_NO_2\_CN\_NH_2$	$2.84 \times 10^3$	$1.00 \times 10^4$	$4.01 \times 10^3$
	$Se\_S\_NO_2\_CN\_NH_2$	$3.03 \times 10^3$	$9.04 \times 10^3$	$2.99\times 10^3$

Table 3: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the  $28R \approx 30R$  switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 3	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30{ m R})$	NLO contrast
Substitution $R_{2,5}$	NH_S_NO <sub>2</sub> _H_NH <sub>2</sub> NH_S_NO <sub>2</sub> _F_NH <sub>2</sub> NH_S_NO <sub>2</sub> _CN_NH <sub>2</sub> NH_S_NO <sub>2</sub> _NO <sub>2</sub> _NH <sub>2</sub> NH_S_NO <sub>2</sub> _CH <sub>3</sub> _NH <sub>2</sub> NH_S_NO <sub>2</sub> _OH_NH <sub>2</sub> NH_S_NO <sub>2</sub> _NH <sub>2</sub> _NH <sub>2</sub>	$\begin{array}{l} 3.44 \times 10^{-1} \\ 2.27 \times 10^{0} \\ 0.00 \times 10^{0} \\ 1.14 \times 10^{3} \\ 1.18 \times 10^{0} \\ 5.41 \times 10^{2} \\ 0.00 \times 10^{0} \end{array}$	$\begin{array}{l} 1.45 \times 10^{4} \\ 1.34 \times 10^{4} \\ 1.67 \times 10^{4} \\ 1.44 \times 10^{4} \\ 1.34 \times 10^{4} \\ 1.46 \times 10^{4} \\ 1.44 \times 10^{4} \end{array}$	$\begin{array}{c} 1.45 \times 10^{4} \\ 1.34 \times 10^{4} \\ 1.67 \times 10^{4} \\ 1.13 \times 10^{4} \\ 1.34 \times 10^{4} \\ 1.31 \times 10^{4} \\ 1.44 \times 10^{4} \end{array}$
Y	NH_NH_NO <sub>2</sub> _CN_NH <sub>2</sub> NH_O_NO <sub>2</sub> _CN_NH <sub>2</sub> NH_S_NO <sub>2</sub> _CN_NH <sub>2</sub> NH_Se_NO <sub>2</sub> _CN_NH <sub>2</sub>	$\begin{array}{l} 2.92 \times 10^{3} \\ 2.80 \times 10^{3} \\ 0.00 \times 10^{0} \\ 1.46 \times 10^{0} \end{array}$	$\begin{array}{l} 9.86 \times 10^{3} \\ 1.17 \times 10^{4} \\ 1.67 \times 10^{4} \\ 1.61 \times 10^{4} \end{array}$	$3.77 \times 10^{3}$ $5.48 \times 10^{3}$ $1.67 \times 10^{4}$ $1.61 \times 10^{4}$
Substitution $R_{3,6}$	NH_S_NO <sub>2</sub> _CN_H NH_S_NO <sub>2</sub> _CN_F NH_S_NO <sub>2</sub> _CN_CN NH_S_NO <sub>2</sub> _CN_NO <sub>2</sub> NH_S_NO <sub>2</sub> _CN_CH <sub>3</sub> NH_S_NO <sub>2</sub> _CN_OH NH_S_NO <sub>2</sub> _CN_OH	$\begin{array}{c} 6.50 \times 10^2 \\ 6.73 \times 10^2 \\ 1.08 \times 10^3 \\ 6.26 \times 10^2 \\ 1.72 \times 10^3 \\ 0.00 \times 10^0 \\ 0.00 \times 10^0 \end{array}$	$\begin{array}{c} 8.94\times 10^{3}\\ 1.07\times 10^{4}\\ 4.15\times 10^{3}\\ 4.38\times 10^{3}\\ 8.99\times 10^{3}\\ 1.28\times 10^{4}\\ 1.67\times 10^{4} \end{array}$	$\begin{array}{c} 7.17\times10^{3}\\ 8.83\times10^{3}\\ 1.79\times10^{3}\\ 2.81\times10^{3}\\ 4.94\times10^{3}\\ 1.28\times10^{4}\\ 1.67\times10^{4} \end{array}$
Substitution $R_{1,4}$	NH_S_H_CN_NH <sub>2</sub> NH_S_F_CN_NH <sub>2</sub> NH_S_CN_CN_NH <sub>2</sub> NH_S_NO <sub>2</sub> _CN_NH <sub>2</sub> NH_S_CH <sub>3</sub> _CN_NH <sub>2</sub> NH_S_OH_CN_NH <sub>2</sub> NH_S_OH_CN_NH <sub>2</sub> NH_S_NH <sub>2</sub> _CN_NH <sub>2</sub>	$\begin{array}{c} 2.53 \times 10^{-2} \\ 2.56 \times 10^{0} \\ 2.77 \times 10^{0} \\ 0.00 \times 10^{0} \\ 1.02 \times 10^{0} \\ 6.42 \times 10^{2} \\ 2.66 \times 10^{0} \end{array}$	$\begin{array}{c} 6.95\times10^{3}\\ 6.57\times10^{3}\\ 1.36\times10^{4}\\ 1.67\times10^{4}\\ 6.77\times10^{3}\\ 7.32\times10^{3}\\ 7.80\times10^{3} \end{array}$	$\begin{array}{c} 6.95\times 10^{3}\\ 6.56\times 10^{3}\\ 1.36\times 10^{4}\\ 1.67\times 10^{4}\\ 6.76\times 10^{3}\\ 5.61\times 10^{3}\\ 7.79\times 10^{3} \end{array}$
X	NH_S_NO <sub>2</sub> _CN_NH <sub>2</sub> O_S_NO <sub>2</sub> _CN_NH <sub>2</sub> S_S_NO <sub>2</sub> _CN_NH <sub>2</sub> Se_S_NO <sub>2</sub> _CN_NH <sub>2</sub>	$\begin{array}{c} 0.00 \times 10^{0} \\ 2.96 \times 10^{2} \\ 2.84 \times 10^{3} \\ 3.03 \times 10^{3} \end{array}$	$\begin{array}{c} 1.67 \times 10^4 \\ 1.38 \times 10^4 \\ 1.00 \times 10^4 \\ 9.04 \times 10^3 \end{array}$	$\begin{array}{c} 1.67 \times 10^{4} \\ 1.29 \times 10^{4} \\ 4.01 \times 10^{3} \\ 2.99 \times 10^{3} \end{array}$



BFS procedure D: starting point

Figure 8: Chronological site order of the BFS for maximization of the contrast for the **28R**  $\rightarrow$  **30R** switch starting from the **O\_O\_NH**<sub>2</sub>-**CN\_NH**<sub>2</sub> The black lines separate the global iterations. The site order varies in every global iteration

Table 4: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the  $28R \approx 30R$  switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 1	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30{ m R})$	NLO contrast
Y	NH_O_NH2_OH_NH2 O_O_NH2_OH_NH2 S_O_NH2_OH_NH2 Se_O_NH2_OH_NH2	$\begin{array}{l} 9.16\times 10^{-1}\\ 2.55\times 10^{3}\\ 2.60\times 10^{3}\\ 2.85\times 10^{3} \end{array}$	$\begin{array}{l} 2.00 \times 10^{3} \\ 2.21 \times 10^{3} \\ 1.71 \times 10^{3} \\ 2.35 \times 10^{3} \end{array}$	$\begin{array}{l} 2.00\times 10^{3}\\ 2.40\times 10^{1}\\ 1.84\times 10^{2}\\ 4.65\times 10^{1} \end{array}$
X	NH_NH_NH <sub>2</sub> _OH_NH <sub>2</sub> NH_O_NH <sub>2</sub> _OH_NH <sub>2</sub> NH_S_NH <sub>2</sub> _OH_NH <sub>2</sub> NH_Se_NH <sub>2</sub> _OH_NH <sub>2</sub>	$\begin{array}{l} 1.12\times 10^{3}\\ 9.16\times 10^{-1}\\ 7.67\times 10^{2}\\ 8.24\times 10^{2} \end{array}$	$\begin{array}{c} 2.60 \times 10^{3} \\ 2.00 \times 10^{3} \\ 3.27 \times 10^{3} \\ 3.67 \times 10^{3} \end{array}$	$5.94 \times 10^{2}$ $2.00 \times 10^{3}$ $1.55 \times 10^{3}$ $1.81 \times 10^{3}$
Substitution $R_{1,4}$	NH_O_H_OH_NH <sub>2</sub> NH_O_F_OH_NH <sub>2</sub> NH_O_CN_OH_NH <sub>2</sub> NH_O_NO <sub>2</sub> _OH_NH <sub>2</sub> NH_O_CH <sub>3</sub> _OH_NH <sub>2</sub> NH_O_OH_OH_NH <sub>2</sub> NH_O_OH_OH_NH <sub>2</sub>	$\begin{array}{c} 9.88 \times 10^{-1} \\ 2.75 \times 10^{0} \\ 6.11 \times 10^{2} \\ 1.11 \times 10^{3} \\ 8.50 \times 10^{-1} \\ 7.64 \times 10^{2} \\ 9.16 \times 10^{-1} \end{array}$	$\begin{array}{c} 2.48 \times 10^{3} \\ 2.01 \times 10^{3} \\ 8.67 \times 10^{3} \\ 9.37 \times 10^{3} \\ 2.20 \times 10^{3} \\ 2.33 \times 10^{3} \\ 2.00 \times 10^{3} \end{array}$	$\begin{array}{c} 2.48 \times 10^{3} \\ 2.00 \times 10^{3} \\ 7.00 \times 10^{3} \\ 6.51 \times 10^{3} \\ 2.19 \times 10^{3} \\ 7.94 \times 10^{2} \\ 2.00 \times 10^{3} \end{array}$
Substitution $R_{2,5}$	NH_O_CN_H_NH2         NH_O_CN_F_NH2         NH_O_CN_CN_NH2         NH_O_CN_NO2_NH2         NH_O_CN_CH3_NH2         NH_O_CN_OH_NH2         NH_O_CN_OH_NH2         NH_O_CN_NH2_NH2	$\begin{array}{c} 1.60 \times 10^{0} \\ 1.96 \times 10^{0} \\ 6.57 \times 10^{-1} \\ 1.31 \times 10^{3} \\ 5.49 \times 10^{1} \\ 6.11 \times 10^{2} \\ 1.14 \times 10^{3} \end{array}$	$\begin{array}{c} 8.15\times 10^{3}\\ 7.69\times 10^{3}\\ 1.20\times 10^{4}\\ 4.70\times 10^{3}\\ 7.85\times 10^{3}\\ 8.67\times 10^{3}\\ 8.38\times 10^{3} \end{array}$	$\begin{array}{c} 8.15\times10^{3}\\ 7.68\times10^{3}\\ 1.20\times10^{4}\\ 1.91\times10^{3}\\ 7.68\times10^{3}\\ 7.00\times10^{3}\\ 5.49\times10^{3} \end{array}$
Substitution R <sub>3,6</sub>	NH_O_CN_CN_H NH_O_CN_CN_F NH_O_CN_CN_CN NH_O_CN_CN_NO <sub>2</sub> NH_O_CN_CN_CH <sub>3</sub> NH_O_CN_CN_OH NH_O_CN_CN_NH <sub>2</sub>	$\begin{array}{c} 7.81\times10^{-1}\\ 8.95\times10^{-1}\\ 5.66\times10^{-1}\\ 0.00\times10^{0}\\ 3.61\times10^{-1}\\ 0.00\times10^{0}\\ 6.57\times10^{-1} \end{array}$	$\begin{array}{c} 6.92\times 10^{3}\\ 8.36\times 10^{3}\\ 3.55\times 10^{3}\\ 4.29\times 10^{3}\\ 7.44\times 10^{3}\\ 9.71\times 10^{3}\\ 1.20\times 10^{4} \end{array}$	$\begin{array}{c} 6.92 \times 10^{3} \\ 8.36 \times 10^{3} \\ 3.55 \times 10^{3} \\ 4.29 \times 10^{3} \\ 7.44 \times 10^{3} \\ 9.71 \times 10^{3} \\ 1.20 \times 10^{4} \end{array}$

Table 4: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the 28R  $\approx$  30R switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 2	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30{ m R})$	NLO contrast
Substitution $R_{2,5}$	NH_O_CN_H_NH <sub>2</sub> NH_O_CN_F_NH <sub>2</sub> NH_O_CN_CN_NH <sub>2</sub> NH_O_CN_NO <sub>2</sub> _NH <sub>2</sub> NH_O_CN_CH <sub>3</sub> _NH <sub>2</sub> NH_O_CN_OH_NH <sub>2</sub> NH_O_CN_OH_NH <sub>2</sub> NH_O_CN_NH <sub>2</sub> _NH <sub>2</sub>	$\begin{array}{c} 1.60 \times 10^{0} \\ 1.96 \times 10^{0} \\ 6.57 \times 10^{-1} \\ 1.31 \times 10^{3} \\ 5.49 \times 10^{1} \\ 6.11 \times 10^{2} \\ 1.14 \times 10^{3} \end{array}$	$\begin{array}{c} 8.15\times 10^{3}\\ 7.69\times 10^{3}\\ 1.20\times 10^{4}\\ 4.70\times 10^{3}\\ 7.85\times 10^{3}\\ 8.67\times 10^{3}\\ 8.38\times 10^{3} \end{array}$	$\begin{array}{c} 8.15 \times 10^{3} \\ 7.68 \times 10^{3} \\ 1.20 \times 10^{4} \\ 1.91 \times 10^{3} \\ 7.68 \times 10^{3} \\ 7.00 \times 10^{3} \\ 5.49 \times 10^{3} \end{array}$
Substitution $R_{1,4}$	NH_O_H_CN_NH <sub>2</sub> NH_O_F_CN_NH <sub>2</sub> NH_O_CN_CN_NH <sub>2</sub> NH_O_NO <sub>2</sub> _CN_NH <sub>2</sub> NH_O_CH <sub>3</sub> _CN_NH <sub>2</sub> NH_O_OH_CN_NH <sub>2</sub> NH_O_OH_CN_NH <sub>2</sub>	$\begin{array}{c} 1.58\times 10^{0}\\ 1.33\times 10^{0}\\ 6.57\times 10^{-1}\\ 2.80\times 10^{3}\\ 9.78\times 10^{-1}\\ 1.07\times 10^{0}\\ 1.12\times 10^{0} \end{array}$	$\begin{array}{c} 6.18 \times 10^{3} \\ 6.25 \times 10^{3} \\ 1.20 \times 10^{4} \\ 1.17 \times 10^{4} \\ 6.10 \times 10^{3} \\ 7.22 \times 10^{3} \\ 7.94 \times 10^{3} \end{array}$	$\begin{array}{c} 6.17 \times 10^{3} \\ 6.24 \times 10^{3} \\ 1.20 \times 10^{4} \\ 5.48 \times 10^{3} \\ 6.10 \times 10^{3} \\ 7.22 \times 10^{3} \\ 7.93 \times 10^{3} \end{array}$
X	$\begin{array}{c} \mathrm{NH\_O\_CN\_CN\_NH_2}\\ \mathrm{O\_O\_CN\_CN\_NH_2}\\ \mathrm{S\_O\_CN\_CN\_NH_2}\\ \mathrm{Se\_O\_CN\_CN\_NH_2} \end{array}$	$\begin{array}{c} 6.57\times 10^{-1} \\ 1.73\times 10^{0} \\ 2.17\times 10^{3} \\ 2.36\times 10^{3} \end{array}$	$\begin{array}{c} 1.20\times 10^{4}\\ 1.40\times 10^{4}\\ 8.94\times 10^{3}\\ 8.96\times 10^{3} \end{array}$	$\begin{array}{c} 1.20 \times 10^{4} \\ 1.40 \times 10^{4} \\ 4.12 \times 10^{3} \\ 3.85 \times 10^{3} \end{array}$
Y	$\begin{array}{c} O\_NH\_CN\_CN\_NH_2\\ O\_O\_CN\_CN\_NH_2\\ O\_S\_CN\_CN\_NH_2\\ O\_Se\_CN\_CN\_NH_2 \end{array}$	$\begin{array}{c} 1.57 \times 10^{0} \\ 1.73 \times 10^{0} \\ 0.00 \times 10^{0} \\ 1.65 \times 10^{0} \end{array}$	$\begin{array}{c} 1.58 \times 10^{4} \\ 1.40 \times 10^{4} \\ 1.52 \times 10^{4} \\ 1.31 \times 10^{4} \end{array}$	$\begin{array}{c} 1.58 \times 10^{4} \\ 1.40 \times 10^{4} \\ 1.52 \times 10^{4} \\ 1.31 \times 10^{4} \end{array}$
Substitution $R_{3,6}$	O_NH_CN_CN_H O_NH_CN_CN_F O_NH_CN_CN_CN O_NH_CN_CN_NO <sub>2</sub> O_NH_CN_CN_CH <sub>3</sub> O_NH_CN_CN_OH O_NH_CN_CN_NH <sub>2</sub>	$\begin{array}{l} 8.95\times10^{-1}\\ 7.11\times10^{-1}\\ 5.68\times10^{-1}\\ 2.43\times10^{0}\\ 5.12\times10^{-1}\\ 1.78\times10^{0}\\ 1.57\times10^{0} \end{array}$	$\begin{array}{l} 5.11 \times 10^3 \\ 6.80 \times 10^3 \\ 3.13 \times 10^3 \\ 3.38 \times 10^3 \\ 6.36 \times 10^3 \\ 1.22 \times 10^4 \\ 1.58 \times 10^4 \end{array}$	$\begin{array}{c} 5.11 \times 10^{3} \\ 6.80 \times 10^{3} \\ 3.13 \times 10^{3} \\ 3.37 \times 10^{3} \\ 6.36 \times 10^{3} \\ 1.22 \times 10^{4} \\ 1.58 \times 10^{4} \end{array}$

Table 4: Global iteration structures of the BFS procedure on the maximization of the NLO contrast of the  $28R \approx 30R$  switch with the X\_Y\_R<sub>1,4</sub>\_R<sub>2,5</sub>\_R<sub>3,6</sub> pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

Global iteration 3	$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30{ m R})$	NLO contrast
	O_NH_CN_CN_NH <sub>2</sub>	$1.57 \times 10^{0}$	$1.58 \times 10^4$	$1.58 \times 10^4$
	$O_O_CN_CN_NH_2$	$1.73 \times 10^{\circ}$	$1.40 \times 10^{4}$	$1.40 \times 10^{4}$
Y	$O_S_CN_CN_NH_2$	$0.00 \times 10^{0}$	$1.52 \times 10^4$	$1.52 \times 10^4$
	$O\_Se\_CN\_CN\_NH_2$	$1.65 \times 10^0$	$1.31 \times 10^4$	$1.31 \times 10^{4}$
	O_NH_CN_CN_H	$8.95\times10^{-1}$	$5.11 \times 10^3$	$5.11 \times 10^3$
	O_NH_CN_CN_F	$7.11  imes 10^{-1}$	$6.80 \times 10^3$	$6.80 \times 10^3$
	O_NH_CN_CN_CN	$5.68 imes10^{-1}$	$3.13 \times 10^3$	$3.13 \times 10^3$
Substitution R <sub>3.6</sub>	$O_NH_CN_CN_NO_2$	$2.43 \times 10^0$	$3.38 \times 10^3$	$3.37 \times 10^3$
,	O_NH_CN_CN_CH <sub>3</sub>	$5.12  imes 10^{-1}$	$6.36 \times 10^3$	$6.36 \times 10^3$
	O_NH_CN_CN_OH	$1.78 \times 10^{0}$	$1.22 \times 10^4$	$1.22 \times 10^4$
	$O\_NH\_CN\_CN\_NH_2$	$1.57 \times 10^0$	$1.58  imes 10^4$	$1.58 \times 10^4$
	O_NH_CN_H_NH <sub>2</sub>	$0.00 \times 10^0$	$9.00 \times 10^3$	$9.00 \times 10^{3}$
	$O_NH_CN_F_NH_2$	$1.12 \times 10^3$	$8.43 \times 10^3$	$5.59  imes 10^3$
	$O_NH_CN_CN_NH_2$	$1.57  imes 10^0$	$1.58  imes 10^4$	$1.58  imes 10^4$
Substitution $R_{2,5}$	$O_NH_CN_NO_2_NH_2$	$1.94 \times 10^2$	$7.57 \times 10^3$	$7.01 \times 10^3$
,	$O_NH_CN_CH_3_NH_2$	$1.44 \times 10^3$	$8.65 \times 10^3$	$5.15 \times 10^3$
	O_NH_CN_OH_NH <sub>2</sub>	$1.15 \times 10^3$	$8.46 \times 10^{3}$	$5.57 \times 10^3$
	$O_NH_CN_NH_2_NH_2$	$1.16\times 10^3$	$8.03 \times 10^3$	$5.14 \times 10^3$
	NH_NH_CN_CN_NH <sub>2</sub>	$7.75\times10^{-1}$	$1.25 \times 10^4$	$1.25 \times 10^4$
	$O_NH_CN_CN_NH_2$	$1.57  imes 10^0$	$1.58  imes 10^4$	$1.58 imes10^4$
$\mathbf{X}$	$S_NH_CN_CN_NH_2$	$3.47 \times 10^3$	$9.30 \times 10^3$	$2.66 \times 10^3$
	$Se\_NH\_CN\_CN\_NH_2$	$3.23 \times 10^3$	$7.92 \times 10^3$	$1.97 \times 10^3$
	$O_NH_H_CN_NH_2$	$4.15 \times 10^0$	$8.55 \times 10^3$	$8.54 \times 10^3$
	$O_NH_F_CN_NH_2$	$2.83 \times 10^0$	$6.95 \times 10^3$	$6.95 \times 10^3$
	$O_NH_CN_CN_NH_2$	$1.57  imes 10^0$	$1.58  imes 10^4$	$1.58 imes10^4$
Substitution R <sub>1,4</sub>	$O_NH_NO_2_CN_NH_2$	$6.01 \times 10^2$	$1.02 \times 10^4$	$8.50  imes 10^3$
,	$O_NH_CH_3_CN_NH_2$	$1.07 \times 10^0$	$7.03  imes 10^3$	$7.02 \times 10^3$
	O_NH_OH_CN_NH <sub>2</sub>	$2.02 \times 10^2$	$5.53  imes 10^3$	$4.95 \times 10^3$
	$O_NH_NH_2_CN_NH_2$	$2.18 \times 10^0$	$6.58  imes 10^3$	$6.57 \times 10^3$

## **BFS** Database

Table 5: Collection of the dataset generated during the BFS and prestudy containing the individual first hyperpolarizabilities of the OFF- and ON-state, NLO contrast of the  $28R \Rightarrow 30R$  switch pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
O_O_NH2_CN_CN	$6.18  imes 10^{-1}$	$2.08 \times 10^4$	$2.08 \times 10^{4}$
NH_O_OH_CN_NO <sub>2</sub>	$2.74 \times 10^0$	$1.74 \times 10^4$	$1.74 \times 10^4$
$O_S_NH_2_CN_CN$	$3.36 \times 10^0$	$1.72 \times 10^4$	$1.72 \times 10^4$
$O_O_NH_2_CN_NO_2$	$0.00 \times 10^0$	$1.71 \times 10^4$	$1.71 \times 10^4$
$\rm NH_O_NH_2_CN_CN$	$6.66 imes10^{-1}$	$1.70  imes 10^4$	$1.70 \times 10^4$
$\rm NH_S_NO_2_CN_NH_2$	$0.00 \times 10^0$	$1.67  imes 10^4$	$1.67  imes 10^4$
$O_O_NH_2_NO_2_CN$	$1.98 \times 10^2$	$1.72 \times 10^4$	$1.66 \times 10^4$
$\rm NH\_Se\_NO_2\_CN\_NH_2$	$1.46 \times 10^0$	$1.61 \times 10^4$	$1.61 \times 10^4$
O_O_OH_CN_CN	$1.19 \times 10^0$	$1.61 \times 10^4$	$1.61 \times 10^4$
$O_NH_CN_CN_NH_2$	$1.57 \times 10^0$	$1.58 \times 10^4$	$1.58 \times 10^4$
$O_NH_NH_2_CN_CN$	$2.09 \times 10^0$	$1.57 \times 10^4$	$1.57 \times 10^4$
$O_S_CN_NH_2$	$0.00 \times 10^0$	$1.52 \times 10^4$	$1.52 \times 10^4$
$O_O_OH_CN_NO_2$	$0.00 \times 10^0$	$1.46 \times 10^4$	$1.46 \times 10^4$
$\rm NH_S_NO_2_H_NH_2$	$3.44  imes 10^{-1}$	$1.45 \times 10^4$	$1.45 \times 10^4$
$\rm NH_S_NO_2_NH_2_NH_2$	$0.00 \times 10^0$	$1.44 \times 10^4$	$1.44 \times 10^4$
NH_O_OH_CN_CN	$2.67 \times 10^0$	$1.42 \times 10^4$	$1.42 \times 10^4$
$O_O_CN_CN_NH_2$	$1.73 \times 10^0$	$1.40 \times 10^4$	$1.40 \times 10^4$
$\rm NH_O_OH_NH_2_NO_2$	$0.00 \times 10^0$	$1.39 \times 10^4$	$1.39 \times 10^4$
$\rm NH_S_CN_CN_NH_2$	$2.77 \times 10^{0}$	$1.36 \times 10^4$	$1.36 \times 10^4$
$\rm NH_S_NH_2_CN_CN$	$1.42 \times 10^0$	$1.35 \times 10^4$	$1.35 \times 10^4$
$\rm NH_O_F_CN_NO_2$	$0.00 \times 10^0$	$1.35 \times 10^4$	$1.35 \times 10^4$
$\rm NH_S_NH_2_CN_NO_2$	$6.73  imes 10^{-1}$	$1.35 \times 10^4$	$1.35 \times 10^4$
$\rm NH_O_OH_H_NO_2$	$2.05 \times 10^0$	$1.35 \times 10^4$	$1.35 \times 10^4$
$NH_Se_NO_2_CH_3_NH_2$	$1.85 \times 10^0$	$1.34 \times 10^4$	$1.34 \times 10^4$
$O_Se_NH_2_CN_CN$	$8.47  imes 10^{-1}$	$1.34 \times 10^4$	$1.34 \times 10^4$
$\rm NH_S_NO_2_F_NH_2$	$2.27 \times 10^{0}$	$1.34 \times 10^4$	$1.34 \times 10^4$
$\rm NH_S_NO_2\_CH_3\_NH_2$	$1.18 \times 10^0$	$1.34 \times 10^4$	$1.34 \times 10^4$
$\rm NH\_Se\_NO_2\_OH\_NH_2$	$5.43  imes 10^2$	$1.48 \times 10^4$	$1.32 \times 10^4$
$\rm NH\_S\_NO_2\_OH\_NH_2$	$5.41 \times 10^2$	$1.46 \times 10^4$	$1.31 \times 10^4$
$O\_Se\_CN\_CN\_NH_2$	$1.65 \times 10^0$	$1.31 \times 10^4$	$1.31 \times 10^4$

Table 5: Collection of the dataset generated during the BFS and prestudy containing the individual first hyperpolarizabilities of the OFF- and ON-state, NLO contrast of the  $28R \Rightarrow 30R$  switch pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

$X_Y_R_{1,4}R_{2,5}R_{3,6}$	$eta_{HRS}( ext{28R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
$O_S_NO_2_CN_NH_2$	$2.96 \times 10^2$	$1.38 \times 10^4$	$1.29 \times 10^4$
$\rm NH\_Se\_CN\_CN\_NH_2$	$1.38 \times 10^0$	$1.29 \times 10^4$	$1.29 \times 10^4$
NH_S_NO <sub>2</sub> _CN_OH	$0.00 \times 10^0$	$1.28 \times 10^4$	$1.28 \times 10^4$
$\rm NH\_Se\_NO_2\_NO_2\_NH_2$	$2.13 \times 10^2$	$1.32 \times 10^4$	$1.26 \times 10^4$
$\rm NH_NH_CN_CN_NH_2$	$7.75  imes 10^{-1}$	$1.25 \times 10^4$	$1.25 \times 10^4$
$\rm NH_O_H_CN_NO_2$	$0.00 \times 10^0$	$1.25 \times 10^4$	$1.25 \times 10^4$
$\rm NH_O_OH_F_NO_2$	$9.01  imes 10^{-1}$	$1.25 \times 10^4$	$1.25 \times 10^4$
$O_Se_NO_2_CN_NH_2$	$0.00 \times 10^0$	$1.23 \times 10^4$	$1.23 \times 10^4$
O_NH_CN_CN_OH	$1.78 \times 10^{0}$	$1.22 \times 10^4$	$1.22 \times 10^4$
NH_S_OH_CN_CN	$0.00 \times 10^0$	$1.20 \times 10^4$	$1.20 \times 10^4$
$\rm NH\_Se\_NO_2\_H\_NH_2$	$1.50  imes 10^{-1}$	$1.20 \times 10^4$	$1.20 \times 10^4$
$\rm NH_O_CN_CN_NH_2$	$6.57 imes10^{-1}$	$1.20 \times 10^4$	$1.20 \times 10^4$
$\rm NH\_Se\_NH_2\_CN\_NO_2$	$2.63 \times 10^0$	$1.20 \times 10^4$	$1.20 \times 10^4$
$\rm NH\_Se\_NO_2\_CN\_OH$	$0.00 \times 10^0$	$1.18 \times 10^4$	$1.18 \times 10^4$
$S_O_NH_2_CN_CN$	$2.13 \times 10^3$	$1.71 \times 10^4$	$1.17 \times 10^4$
$\rm NH_NH_NH_2-CN_CN$	$1.87  imes 10^{-2}$	$1.15 \times 10^4$	$1.15 \times 10^4$
$\rm NH\_Se\_NH_2\_CN\_CN$	$1.43 \times 10^0$	$1.14 \times 10^4$	$1.14 \times 10^4$
$\rm NH\_S\_OH\_CN\_NO_2$	$3.01 \times 10^0$	$1.14 \times 10^4$	$1.14 \times 10^4$
$NH_Se_NO_2_NH_2_NH_2$	$0.00 \times 10^{0}$	$1.13 \times 10^4$	$1.13 \times 10^4$
$\rm NH_S_NO_2_NO_2_NH_2$	$1.14 \times 10^3$	$1.44 \times 10^4$	$1.13 \times 10^4$
$O\_Se\_NH_2\_CN\_NO_2$	$1.06 \times 10^{0}$	$1.12 \times 10^4$	$1.12 \times 10^4$
$\rm NH_O_OH_OH_NO_2$	$2.08 \times 10^0$	$1.11 \times 10^{4}$	$1.11 \times 10^{4}$
$NH_S_NH_2_NH_2_NO_2$	$4.58 \times 10^{0}$	$1.11 \times 10^{4}$	$1.11 \times 10^{4}$
$NH_Se_NO_2_F_NH_2$	$3.28 \times 10^{0}$	$1.09 \times 10^4$	$1.09 \times 10^{4}$
$O_O_NH_2_CN_H$	$1.29 \times 10^{-1}$	$1.07 \times 10^4$	$1.07 \times 10^4$
$O_O_NH_2_H_CN$	$2.20\times10^{-2}$	$1.06 \times 10^{4}$	$1.06 \times 10^{4}$
$\rm NH_S_NH_2_CH_3_NO_2$	$1.02 \times 10^{-1}$	$1.06 \times 10^{4}$	$1.06 \times 10^{4}$
$\rm NH\_Se\_NH_2\_OH\_NO_2$	$0.00 \times 10^{0}$	$1.04 \times 10^{4}$	$1.04 \times 10^{4}$
$NH_Se_NH_2_NH_2_NO_2$	$4.36 \times 10^{0}$	$1.04 \times 10^4$	$1.03 \times 10^4$
$\rm NH_S_NH_2_H_NO_2$	$1.48 \times 10^{-1}$	$1.00 \times 10^4$	$1.00 \times 10^4$
$O_O_NH_2_F_CN$	$1.19 \times 10^0$	$1.00 \times 10^4$	$1.00 \times 10^4$
$O_O_NH_2_CH_3_CN$	$1.18 \times 10^0$	$9.86 \times 10^3$	$9.86 \times 10^3$
NH_O_CN_CN_OH	$0.00 \times 10^0$	$9.71 \times 10^3$	$9.71 \times 10^3$

Table 5: Collection of the dataset generated during the BFS and prestudy containing the individual first hyperpolarizabilities of the OFF- and ON-state, NLO contrast of the  $28R \Rightarrow 30R$  switch pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

$X_Y_R_{1,4}R_{2,5}R_{3,6}$	$eta_{HRS}( ext{28R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
NH_S_NH2_F_NO2	$2.25 \times 10^0$	$9.70 \times 10^{3}$	$9.69 \times 10^{3}$
NH_Se_NH <sub>2</sub> _CH <sub>3</sub> _NO <sub>2</sub>	$2.88  imes 10^{-1}$	$9.58 \times 10^3$	$9.58  imes 10^3$
$\rm NH\_Se\_NO_2\_CN\_F$	$1.34 \times 10^0$	$9.56 \times 10^3$	$9.56  imes 10^3$
O_NH_NH2_H_CN	$1.67  imes 10^{-2}$	$9.51 \times 10^3$	$9.51 \times 10^3$
$\rm NH\_Se\_OH\_CN\_NO_2$	$7.66 imes10^{-1}$	$9.49 \times 10^3$	$9.49 \times 10^3$
$\rm NH_S_NH_2_OH_NO_2$	$8.31 \times 10^2$	$1.17 \times 10^4$	$9.40 \times 10^3$
NH_O_H_H_NO <sub>2</sub>	$1.01 \times 10^0$	$9.30 \times 10^3$	$9.30 \times 10^3$
$\rm NH_O_NH_2_H_CN$	$1.54  imes 10^{-2}$	$9.07 \times 10^3$	$9.07 \times 10^3$
O_O_F_CN_CN	$8.06 imes10^{-1}$	$9.04 \times 10^3$	$9.04 \times 10^3$
$O_NH_CN_H_NH_2$	$0.00 \times 10^0$	$9.00 \times 10^3$	$9.00 \times 10^3$
$\rm NH\_Se\_NH_2\_H\_NO_2$	$6.77  imes 10^{-1}$	$8.95 \times 10^3$	$8.94 \times 10^3$
$O_O_NH_2_CN_F$	$1.31 \times 10^{0}$	$8.94 \times 10^3$	$8.94 \times 10^3$
NH_NH_NH2_CN_NO2	$2.31 \times 10^0$	$8.92 \times 10^3$	$8.91 \times 10^3$
NH_S_F_CN_CN	$1.66 \times 10^{0}$	$8.89 \times 10^3$	$8.89 \times 10^3$
$S_S_NH_2_CN_CN$	$1.18 \times 10^3$	$1.20 \times 10^4$	$8.87 \times 10^3$
$O_O_NH_2_CN_CH_3$	$2.63\times 10^{-1}$	$8.84 \times 10^3$	$8.84 \times 10^3$
$\rm NH_S_NO_2_CN_F$	$6.73 \times 10^2$	$1.07 \times 10^4$	$8.83 \times 10^3$
NH_S_CN_CN_F	$1.17 \times 10^0$	$8.80 \times 10^3$	$8.80  imes 10^3$
$\rm NH\_Se\_NH_2\_F\_NO_2$	$2.27 \times 10^0$	$8.64  imes 10^3$	$8.63 \times 10^3$
$Se_O_NH_2_CN_CN$	$2.17 \times 10^3$	$1.39 \times 10^4$	$8.55  imes 10^3$
$O_NH_H_CN_NH_2$	$4.15 \times 10^0$	$8.55  imes 10^3$	$8.54  imes 10^3$
$O_NH_NO_2_CN_NH_2$	$6.01 \times 10^2$	$1.02 \times 10^4$	$8.50 \times 10^3$
NH_O_CN_CN_F	$8.95  imes 10^{-1}$	$8.36 \times 10^3$	$8.36 \times 10^3$
$\rm NH\_Se\_NO_2\_CN\_CH_3$	$0.00 \times 10^0$	$8.22 \times 10^3$	$8.22 \times 10^3$
$\rm NH_S_CH_3_CN_CN$	$2.15  imes 10^{-1}$	$8.22 \times 10^3$	$8.22 \times 10^3$
$\rm NH_O_CN_H_NH_2$	$1.60 \times 10^0$	$8.15  imes 10^3$	$8.15  imes 10^3$
NH_S_CN_CN_OH	$8.76 \times 10^2$	$1.05 \times 10^4$	$8.14 \times 10^3$
$O_O_CH_3_CN_CN$	$1.78  imes 10^{-1}$	$8.08 \times 10^3$	$8.07 \times 10^3$
$\rm NH_S_CN_NO_2_F$	$1.54 \times 10^2$	$8.44 \times 10^3$	$7.99  imes 10^3$
$\rm NH_O_NH_2_CN_NH_2$	$1.12 \times 10^0$	$7.94  imes 10^3$	$7.93  imes 10^3$
$\rm NH_S_CN_CN_CH_3$	$6.49  imes 10^{-1}$	$7.80  imes 10^3$	$7.79 \times 10^3$
$\rm NH\_S\_NH_2\_CN\_NH_2$	$2.66 \times 10^0$	$7.80  imes 10^3$	$7.79 \times 10^3$
$\rm NH\_Se\_NO_2\_CN\_H$	$2.53\times 10^{-2}$	$7.78  imes 10^3$	$7.78  imes 10^3$

Table 5: Collection of the dataset generated during the BFS and prestudy containing the individual first hyperpolarizabilities of the OFF- and ON-state, NLO contrast of the  $28R \Rightarrow 30R$  switch pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}( ext{28R})$	$eta_{HRS}(30{ m R})$	NLO contrast
NH_O_H_OH_NO <sub>2</sub>	$8.51  imes 10^{-1}$	$7.70 \times 10^3$	$7.70 \times 10^3$
$\rm NH_O_CN_F_NH_2$	$1.96 \times 10^{0}$	$7.69 \times 10^3$	$7.68  imes 10^3$
$\rm NH_O_CN_CH_3_NH_2$	$5.49  imes 10^1$	$7.85  imes 10^3$	$7.68  imes 10^3$
NH_O_OH_CN_OH	$1.58 \times 10^0$	$7.50  imes 10^3$	$7.50  imes 10^3$
$O_O_NH_2_OH_CN$	$2.31  imes 10^{-1}$	$7.49  imes 10^3$	$7.49  imes 10^3$
NH_O_OH_CN_H	$2.62 \times 10^0$	$7.47 \times 10^3$	$7.46  imes 10^3$
NH_NH_NH2_H_CN	$2.34\times10^{-2}$	$7.45 \times 10^3$	$7.45 \times 10^3$
NH_O_CN_CN_CH <sub>3</sub>	$3.61  imes 10^{-1}$	$7.44  imes 10^3$	$7.44 \times 10^3$
$NH_Se_F_CN_NO_2$	$7.92 \times 10^0$	$7.42 \times 10^3$	$7.39 \times 10^3$
NH_O_OH_CN_CH <sub>3</sub>	$1.12 \times 10^0$	$7.24 \times 10^3$	$7.24 \times 10^3$
$\rm NH_O_OH_CN_NH_2$	$1.07 \times 10^0$	$7.22 \times 10^3$	$7.22 \times 10^3$
$NH_Se_CH_3_CN_NO_2$	$5.50  imes 10^{-1}$	$7.20  imes 10^3$	$7.20  imes 10^3$
$\rm NH_S_NO_2_CN_H$	$6.50  imes 10^2$	$8.94 \times 10^3$	$7.17 \times 10^3$
O_O_H_CN_CN	$8.95  imes 10^{-2}$	$7.16  imes 10^3$	$7.16  imes 10^3$
$Se_S_NH_2_CN_CN$	$1.54 \times 10^3$	$1.10 \times 10^4$	$7.13  imes 10^3$
$NH_Se_NH_2_CN_NH_2$	$1.65 \times 10^{0}$	$7.11 \times 10^3$	$7.11 \times 10^3$
$\rm NH\_NH\_OH\_CN\_NO_2$	$0.00 \times 10^{0}$	$7.06 \times 10^3$	$7.06 \times 10^3$
$NH_S_NO_2_NO_2_F$	$7.94 \times 10^2$	$9.17 \times 10^3$	$7.04 \times 10^3$
$O_NH_CH_3_CN_NH_2$	$1.07 \times 10^0$	$7.03 \times 10^3$	$7.02 \times 10^3$
$O_NH_CN_NO_2_NH_2$	$1.94 \times 10^2$	$7.57 \times 10^3$	$7.01 \times 10^3$
$\rm NH_O_CN_OH_NH_2$	$6.11 \times 10^2$	$8.67 \times 10^3$	$7.00 \times 10^3$
$O_O_NH_2_NH_2_CN$	$3.20 \times 10^2$	$7.89 \times 10^3$	$6.98 \times 10^3$
$NH_Se_CN_NO_2_F$	$1.78 \times 10^2$	$7.47 \times 10^3$	$6.96 \times 10^3$
$O_NH_F_CN_NH_2$	$2.83 \times 10^0$	$6.95 \times 10^3$	$6.95  imes 10^3$
$\rm NH_S_H_CN_NH_2$	$2.53\times10^{-2}$	$6.95 \times 10^3$	$6.95 \times 10^3$
NH_O_CN_CN_H	$7.81  imes 10^{-1}$	$6.92 \times 10^3$	$6.92 \times 10^3$
$S\_S\_CN\_CN\_NH_2$	$1.59 \times 10^{3}$	$1.08 \times 10^4$	$6.84 \times 10^3$
NH_S_CN_CN_H	$2.83 \times 10^{-2}$	$6.82 \times 10^3$	$6.82 \times 10^3$
$\rm NH_O_H_F_NO_2$	$5.88 \times 10^2$	$8.41 \times 10^{3}$	$6.80 \times 10^{3}$
O_NH_CN_CN_F	$7.11  imes 10^{-1}$	$6.80 \times 10^3$	$6.80 \times 10^3$
NH_S_H_CN_CN	$7.42\times10^{-2}$	$6.77 \times 10^3$	$6.77 \times 10^3$
$\rm NH\_S\_CH_3\_CN\_NH_2$	$1.02 \times 10^0$	$6.77 \times 10^3$	$6.76 \times 10^3$
NH_NH_H_CN_CN	$1.00 \times 10^{-1}$	$6.72 \times 10^3$	$6.72 \times 10^3$

Table 5: Collection of the dataset generated during the BFS and prestudy containing the individual first hyperpolarizabilities of the OFF- and ON-state, NLO contrast of the  $28R \Rightarrow 30R$  switch pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

$X_{-}Y_{-}R_{1,4}-R_{2,5}-R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
$\rm NH\_Se\_H\_CN\_NH_2$	$3.28\times 10^{-2}$	$6.71 \times 10^3$	$6.71 \times 10^3$
NH_O_OH_CN_F	$1.85 \times 10^1$	$6.71 \times 10^3$	$6.66  imes 10^3$
NH_S_CN_H_F	$1.10\times 10^{-2}$	$6.59  imes 10^3$	$6.59  imes 10^3$
$O_NH_NH_2_CN_NH_2$	$2.18 \times 10^0$	$6.58  imes 10^3$	$6.57  imes 10^3$
$NH_S_F_CN_NH_2$	$2.56 \times 10^0$	$6.57 \times 10^3$	$6.56  imes 10^3$
$\rm NH_O_CN_NO_2_F$	$5.56  imes 10^2$	$8.09 \times 10^3$	$6.56  imes 10^3$
$O_Se_NH_2_F_NO_2$	$3.39 \times 10^0$	$6.55 \times 10^3$	$6.54 \times 10^3$
$NH_S_CN_NH_2_F$	$1.00 \times 10^0$	$6.53  imes 10^3$	$6.53  imes 10^3$
$\rm NH_S_NH_2_CN_H$	$4.31\times10^{-2}$	$6.52 \times 10^3$	$6.52 \times 10^3$
$\rm NH_O_NO_2_OH_NH_2$	$1.11 \times 10^3$	$9.37 \times 10^3$	$6.51  imes 10^3$
$\rm NH\_Se\_CH_3\_CN\_NH_2$	$1.15 \times 10^0$	$6.51  imes 10^3$	$6.51  imes 10^3$
$\rm NH_S_NH_2_CN_OH$	$0.00 \times 10^0$	$6.50  imes 10^3$	$6.50  imes 10^3$
$NH_NH_H_NO_2$	$4.23 \times 10^{0}$	$6.41 \times 10^3$	$6.40  imes 10^3$
NH_S_NH <sub>2</sub> _NO <sub>2</sub> _NO <sub>2</sub>	$0.00 \times 10^0$	$6.40 \times 10^3$	$6.40 \times 10^3$
$O_NH_CN_CN_CH_3$	$5.12  imes 10^{-1}$	$6.36 \times 10^3$	$6.36  imes 10^3$
$O_O_NH_2_CN_NH_2$	$3.99 \times 10^2$	$7.47 \times 10^3$	$6.36 \times 10^3$
$NH_S_CN_CH_3_F$	$6.03 imes10^{-1}$	$6.36 \times 10^3$	$6.36  imes 10^3$
$NH_S_NH_2_CN_CH_3$	$8.02 \times 10^0$	$6.37 \times 10^3$	$6.34 \times 10^3$
$\rm NH_O_F_CN_NH_2$	$1.33 \times 10^0$	$6.25 \times 10^3$	$6.24 \times 10^3$
$NH_S_NH_2_CN_F$	$1.03  imes 10^1$	$6.27 \times 10^3$	$6.24 \times 10^3$
$\rm NH\_Se\_F\_CN\_NH_2$	$2.24 \times 10^0$	$6.23 \times 10^3$	$6.23 \times 10^3$
$NH_Se_H_CN_NO_2$	$3.27  imes 10^{-1}$	$6.20 \times 10^3$	$6.20 \times 10^3$
$\rm NH_O_H_CN_NH_2$	$1.58 \times 10^0$	$6.18 \times 10^3$	$6.17 \times 10^3$
$\rm NH_O_H_NH_2_NO_2$	$1.12 \times 10^3$	$9.02 \times 10^3$	$6.16  imes 10^3$
$O_O_H_CN_NO_2$	$0.00 \times 10^0$	$6.13 \times 10^3$	$6.13 \times 10^3$
$\rm NH_O_CH_3_CN_NH_2$	$9.78  imes 10^{-1}$	$6.10 \times 10^3$	$6.10 \times 10^3$
NH_O_H_H_CN	$7.07  imes 10^{-1}$	$5.97 \times 10^3$	$5.97 \times 10^3$
$\rm NH_O_OH_CH_3_NO_2$	$2.23 \times 10^3$	$1.12 \times 10^4$	$5.97 \times 10^3$
NH_S_CN_F_F	$2.17 \times 10^0$	$5.95  imes 10^3$	$5.95  imes 10^3$
$\rm NH_O_OH_NO_2_NO_2$	$1.37  imes 10^{-1}$	$5.86 \times 10^3$	$5.85  imes 10^3$
$\rm NH\_Se\_NH_2\_CN\_H$	$2.85\times10^{-2}$	$5.81 \times 10^3$	$5.81 \times 10^3$
$S_O_H_NO_2$	$5.88 \times 10^2$	$7.34 \times 10^3$	$5.75 \times 10^3$

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$X_Y_R_{1,4}R_{2,5}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
NH_Se_NH <sub>2</sub> _CN_CH <sub>3</sub>	$1.64\times 10^{-1}$	$5.67 \times 10^3$	$5.67 \times 10^3$
$\rm NH_Se_NH_2_NO_2_NO_2$	$1.86  imes 10^2$	$6.20 \times 10^3$	$5.67  imes 10^3$
$\rm NH\_Se\_NH_2\_CN\_F$	$8.36 \times 10^0$	$5.68  imes 10^3$	$5.65  imes 10^3$
O_O_NH <sub>2</sub> _CN_OH	$2.79  imes 10^2$	$6.43 \times 10^3$	$5.64  imes 10^3$
$\rm NH_S_OH_CN_NH_2$	$6.42 \times 10^2$	$7.32 \times 10^3$	$5.61  imes 10^3$
$O_NH_CN_F_NH_2$	$1.12 \times 10^3$	$8.43 \times 10^3$	$5.59  imes 10^3$
$O_NH_CN_OH_NH_2$	$1.15 \times 10^3$	$8.46 \times 10^3$	$5.57  imes 10^3$
$\rm NH_S_H_H_NO_2$	$1.09 \times 10^0$	$5.51 \times 10^3$	$5.50  imes 10^3$
$\rm NH_O_CN_NH_2_NH_2$	$1.14 \times 10^3$	$8.38 \times 10^3$	$5.49  imes 10^3$
$\rm NH_O_NO_2$ $\rm CN_NH_2$	$2.80 \times 10^3$	$1.17 \times 10^4$	$5.48  imes 10^3$
$\rm NH_O_H_CH_3_NO_2$	$1.03 \times 10^3$	$8.00 \times 10^3$	$5.38  imes 10^3$
$\rm NH_O_CH_3_CN_NO_2$	$8.08 \times 10^2$	$7.47 \times 10^3$	$5.36  imes 10^3$
$\rm NH_NH_CN_NO_2_F$	$2.57 \times 10^2$	$5.98 \times 10^3$	$5.26 \times 10^3$
$\rm NH\_Se\_OH\_CN\_NH_2$	$6.43 \times 10^2$	$6.90 \times 10^3$	$5.19  imes 10^3$
$NH_S_NH_2_NO_2_F$	$1.46 \times 10^2$	$5.61 \times 10^3$	$5.19  imes 10^3$
$O_NH_CN_CH_3_NH_2$	$1.44 \times 10^3$	$8.65  imes 10^3$	$5.15  imes 10^3$
$O_NH_CN_NH_2_NH_2$	$1.16 \times 10^3$	$8.03 \times 10^3$	$5.14 \times 10^3$
O_NH_CN_CN_H	$8.95  imes 10^{-1}$	$5.11 \times 10^3$	$5.11 \times 10^3$
$Se\_S\_CN\_CN\_NH_2$	$1.96 \times 10^3$	$9.62 \times 10^3$	$5.06 \times 10^3$
$S_Se_NH_2_CN_NO_2$	$6.85 \times 10^2$	$6.76 \times 10^3$	$4.96 \times 10^{3}$
$O_NH_OH_CN_NH_2$	$2.02 \times 10^2$	$5.53 \times 10^3$	$4.95 \times 10^3$
$\rm NH_S_NO_2\_CN\_CH_3$	$1.72 \times 10^3$	$8.99 \times 10^3$	$4.94 \times 10^3$
NH_NH_CN_H_H	$5.15  imes 10^{-1}$	$4.83 \times 10^3$	$4.83 \times 10^{3}$
NH_NH_H_H_CN	$4.05\times10^{-1}$	$4.83 \times 10^3$	$4.83 \times 10^{3}$
$\rm NH\_Se\_NH_2\_CN\_OH$	$5.19 \times 10^2$	$6.07 \times 10^3$	$4.67 \times 10^{3}$
$NH_Se_H_H_NO_2$	$2.00 \times 10^0$	$4.66 \times 10^{3}$	$4.66 \times 10^{3}$
$O_NH_CN_NO_2_F$	$2.29 \times 10^2$	$5.20 \times 10^3$	$4.56 \times 10^{3}$
NH_S_CN_OH_F	$7.18 \times 10^2$	$6.41 \times 10^{3}$	$4.54 \times 10^{3}$
$Se_O_H_ON_2$	$7.12 \times 10^2$	$6.33 \times 10^3$	$4.48 \times 10^3$
$\rm NH_O_NH_2_CN_NO_2$	$3.96 \times 10^3$	$1.24 \times 10^4$	$4.34 \times 10^3$
$NH_S_CN_CN_NO_2$	$8.96  imes 10^{-1}$	$4.33 \times 10^3$	$4.33 \times 10^{3}$
$\rm NH\_Se\_CN\_CN\_NO_2$	$8.32  imes 10^{-1}$	$4.30 \times 10^3$	$4.30 \times 10^{3}$
$\rm NH_O_CN_NO_2$	$0.00 \times 10^0$	$4.29 \times 10^3$	$4.29 \times 10^3$

Table 5: Collection of the dataset generated during the BFS and prestudy containing the individual first hyperpolarizabilities of the OFF- and ON-state, NLO contrast of the  $28R \Rightarrow 30R$  switch pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

$X_Y_R_{1,4}R_{2,5}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
S_Se_NO <sub>2</sub> _CN_NH <sub>2</sub>	$2.78 \times 10^3$	$1.01 \times 10^4$	$4.13 \times 10^{3}$
$S_O_CN_CN_NH_2$	$2.17 \times 10^3$	$8.94 \times 10^3$	$4.12 \times 10^3$
$S_Se_NH_2_F_NO_2$	$7.95  imes 10^{-1}$	$4.08 \times 10^3$	$4.08 \times 10^3$
$\rm NH\_Se\_NO_2\_CN\_CN$	$0.00 \times 10^0$	$4.03 \times 10^3$	$4.03 \times 10^3$
$S_S_NO_2_CN_NH_2$	$2.84 \times 10^3$	$1.00 \times 10^4$	$4.01 \times 10^3$
NH_S_CH <sub>3</sub> _NO <sub>2</sub> _F	$1.66  imes 10^2$	$4.40 \times 10^3$	$3.93 \times 10^3$
NH_NH_H_CN_H	$4.62\times 10^{-4}$	$3.88 \times 10^3$	$3.88 \times 10^3$
$S_O_NH_2_F_NO_2$	$3.27 \times 10^3$	$1.06 \times 10^4$	$3.88 \times 10^3$
$Se_O_CN_CN_NH_2$	$2.36 \times 10^3$	$8.96  imes 10^3$	$3.85 \times 10^3$
$\rm NH_NH_NO_2\_CN\_NH_2$	$2.92 \times 10^3$	$9.86  imes 10^3$	$3.77 \times 10^3$
$Se_Se_NH_2_F_NO_2$	$0.00 \times 10^0$	$3.77 \times 10^3$	$3.77 \times 10^3$
O_NH_H_H_CN	$2.81\times10^{-1}$	$3.70 \times 10^3$	$3.70 \times 10^3$
NH_O_CN_CN_CN	$5.66\times10^{-1}$	$3.55 \times 10^3$	$3.55 \times 10^3$
$\rm NH_NH_H_H_NH_2$	$1.04 \times 10^{-1}$	$3.49 \times 10^3$	$3.49 \times 10^3$
$\rm NH_NH_NH_2_H_H$	$4.56\times10^{-1}$	$3.49 \times 10^3$	$3.49 \times 10^3$
$S_O_OH_CN_NO_2$	$1.57 \times 10^3$	$6.94 \times 10^3$	$3.38 \times 10^3$
$O_NH_CN_CN_NO_2$	$2.43 \times 10^0$	$3.38 \times 10^3$	$3.37 \times 10^3$
$NH_S_F_NO_2_F$	$2.78 \times 10^2$	$4.14 \times 10^3$	$3.37 \times 10^3$
NH_S_CN_CN_CN	$6.06 imes10^{-1}$	$3.31 \times 10^3$	$3.31 \times 10^3$
$S_O_NH_2_F_N$	$1.99 \times 10^3$	$7.56  imes 10^3$	$3.25 \times 10^3$
$Se\_Se\_NO_2\_CN\_NH_2$	$3.00 \times 10^3$	$9.27 \times 10^3$	$3.20 \times 10^3$
O_NH_CN_CN_CN	$5.68 imes10^{-1}$	$3.13 \times 10^3$	$3.13 \times 10^3$
O_O_CN_CN_CN	$1.00 \times 10^0$	$3.07 \times 10^3$	$3.07 \times 10^3$
$NH_S_H_NO_2_F$	$2.65 \times 10^2$	$3.74 \times 10^3$	$3.01 \times 10^3$
$Se_S_NO_2_CN_NH_2$	$3.03 \times 10^3$	$9.04 \times 10^3$	$2.99 \times 10^3$
NH_NH_H_H_OH	$9.93  imes 10^{-1}$	$2.96 \times 10^3$	$2.96 \times 10^3$
$\rm NH_S_NO_2_CN_NO_2$	$6.26 \times 10^2$	$4.38 \times 10^3$	$2.81 \times 10^3$
$\rm NH\_Se\_NO_2\_CN\_NO_2$	$6.32 \times 10^2$	$4.38 \times 10^3$	$2.80 \times 10^3$
$Se_O_OH_CN_NO_2$	$1.67 \times 10^3$	$6.44 \times 10^3$	$2.80 \times 10^3$
$S_NH_CN_CN_NH_2$	$3.47 \times 10^3$	$9.30 \times 10^3$	$2.66 \times 10^3$
NH_NH_H_H_F	$3.24 \times 10^0$	$2.62 \times 10^3$	$2.61 \times 10^3$
$\rm NH\_NH\_H\_H\_CH_3$	$1.32 \times 10^0$	$2.53 \times 10^3$	$2.53 \times 10^3$
$\rm NH_O_H_OH_NH_2$	$9.88  imes 10^{-1}$	$2.48 \times 10^3$	$2.48 \times 10^3$

Table 5: Collection of the dataset generated during the BFS and prestudy containing the individual first hyperpolarizabilities of the OFF- and ON-state, NLO contrast of the  $28R \Rightarrow 30R$  switch pattern. The static hyper-Rayleigh scattering first hyperpolarizability values of the [28]hexaphyrins and [30]hexaphyrins are given in a.u.

$X_{-}Y_{-}R_{1,4}_{-}R_{2,5}_{-}R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30\mathrm{R})$	NLO contrast
NH_O_H_H_H	$5.67  imes 10^{-1}$	$2.47 \times 10^3$	$2.47 \times 10^3$
S_O_H_F_NO <sub>2</sub>	$1.23 \times 10^3$	$5.06 \times 10^3$	$2.33 \times 10^3$
$S_O_F_F_NO_2$	$1.63 \times 10^3$	$5.79  imes 10^3$	$2.33 \times 10^3$
$O_O_NO_2_CN_CN$	$3.38 \times 10^2$	$3.18 \times 10^3$	$2.30 \times 10^3$
NH_O_H_NO_NO2	$1.29 \times 10^3$	$5.02 \times 10^3$	$2.21 \times 10^3$
NH_O_CH <sub>3</sub> _OH_NH <sub>2</sub>	$8.50 imes10^{-1}$	$2.20 \times 10^3$	$2.19  imes 10^3$
NH_NH_H_H_H	$5.04 \times 10^{-3}$	$2.18 \times 10^3$	$2.18 \times 10^3$
Se_NH_H_H_H	$5.72  imes 10^{-3}$	$2.17 \times 10^3$	$2.17  imes 10^3$
$S_O_OH_F_NO_2$	$2.47 \times 10^3$	$6.98 \times 10^3$	$2.15 \times 10^3$
O_NH_H_H_H	$1.09  imes 10^{-2}$	$2.09 \times 10^3$	$2.09 \times 10^3$
NH_O_NO2_CN_NO2	$5.88  imes 10^2$	$3.49 \times 10^3$	$2.06 \times 10^3$
S_NH_H_H_H	$2.82  imes 10^{-1}$	$2.06 \times 10^3$	$2.06 \times 10^3$
Se_Se_H_H_H	$3.07  imes 10^{-1}$	$2.05  imes 10^3$	$2.05 \times 10^3$
O_O_H_H_H	$1.52 \times 10^0$	$2.03 \times 10^3$	$2.03 \times 10^3$
NH_S_H_H_H	$2.25 \times 10^{0}$	$2.02 \times 10^3$	$2.01 \times 10^3$
$NH_O_F_OH_NH_2$	$2.75 \times 10^0$	$2.01 \times 10^3$	$2.00 \times 10^3$
$\rm NH_O_NH_2_OH_NH_2$	$9.16 imes10^{-1}$	$2.00 \times 10^3$	$2.00 \times 10^3$
$Se_NH_CN_CN_NH_2$	$3.23 \times 10^3$	$7.92 \times 10^3$	$1.97 \times 10^3$
$S_O_CH_3_F_NO_2$	$1.67 \times 10^3$	$5.39 \times 10^3$	$1.97  imes 10^3$
S_S_H_H_H	$7.24  imes 10^{-1}$	$1.96 \times 10^3$	$1.96  imes 10^3$
$S_NH_CN_NO_2_F$	$1.32 \times 10^3$	$4.74 \times 10^3$	$1.93  imes 10^3$
$\rm NH_O_CN_NO_2_NH_2$	$1.31 \times 10^3$	$4.70 \times 10^3$	$1.91 \times 10^3$
NH_Se_H_H_H	$3.80 \times 10^0$	$1.92 \times 10^3$	$1.91 \times 10^3$
NH_NH_F_F_F	$2.58  imes 10^{-3}$	$1.87 \times 10^3$	$1.87  imes 10^3$
$Se_Se_NH_2_CN_NO_2$	$2.00 \times 10^3$	$5.76 \times 10^3$	$1.82 \times 10^3$
$\rm NH\_Se\_NH_2\_OH\_NH_2$	$8.24 \times 10^2$	$3.67 \times 10^3$	$1.81  imes 10^3$
$\rm NH_S_NO_2_CN_CN$	$1.08 \times 10^3$	$4.15 \times 10^3$	$1.79 \times 10^3$
$\rm NH\_S\_OH\_NO_2\_F$	$1.56  imes 10^3$	$4.97 \times 10^3$	$1.77 \times 10^3$
$Se_NH_CN_NO_2\_F$	$1.60 \times 10^3$	$4.92 \times 10^3$	$1.70 \times 10^3$

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$X_{-}Y_{-}R_{1,4}-R_{2,5}-R_{3,6}$	$eta_{HRS}(28\mathrm{R})$	$eta_{HRS}(30{ m R})$	NLO contrast
NH_NH_OH_OH_OH	$2.68\times 10^{-1}$	$1.67 \times 10^3$	$1.67 \times 10^3$
NH_S_NH <sub>2</sub> _OH_NH <sub>2</sub>	$7.67  imes 10^2$	$3.27 \times 10^3$	$1.55 \times 10^3$
$\rm NH_NH_H_NH_2_H$	$1.64 \times 10^0$	$1.32 \times 10^3$	$1.31 \times 10^3$
NH_NH_NO2_NO2_NO2	$8.78  imes 10^2$	$3.18 \times 10^3$	$1.30 \times 10^3$
NH_NH_CN_CN_CN	$1.16 \times 10^3$	$3.52 \times 10^3$	$1.19 \times 10^3$
$S_O_CN_F_NO_2$	$1.42 \times 10^3$	$3.68 \times 10^3$	$1.00 \times 10^3$
$S_O_NH_2_F_H$	$1.35 \times 10^3$	$3.46 \times 10^3$	$9.22 \times 10^2$
$\rm NH_O_OH_OH_NH_2$	$7.64  imes 10^2$	$2.33 \times 10^3$	$7.94  imes 10^2$
$S_O_NH_2_F_F$	$1.24 \times 10^3$	$2.98 \times 10^3$	$7.16  imes 10^2$
$S_S_NH_2_F_NO_2$	$2.44 \times 10^3$	$4.66 \times 10^3$	$6.94  imes 10^2$
$\rm NH_NH_NH_2-OH_NH_2$	$1.12 \times 10^3$	$2.60 \times 10^3$	$5.94  imes 10^2$
$S_O_NH_2_F_CH_3$	$1.55 \times 10^3$	$3.14 \times 10^3$	$5.38  imes 10^2$
$S_O_NO_2_F_NO_2$	$1.36 \times 10^3$	$2.86 \times 10^3$	$5.31  imes 10^2$
$S_O_NH_2_F_NH_2$	$1.57 \times 10^3$	$2.65 \times 10^3$	$2.76 \times 10^2$
$S_O_NH_2_F_OH$	$1.47 \times 10^3$	$2.47 \times 10^3$	$2.53  imes 10^2$
$S_O_NH_2_OH_NH_2$	$2.60 \times 10^3$	$1.71 \times 10^3$	$1.84 \times 10^2$
NH_NH_CH <sub>3</sub> _CH <sub>3</sub> _CH <sub>3</sub>	$1.52 \times 10^3$	$2.19 \times 10^3$	$1.22 \times 10^2$
$Se_O_NH_2_OH_NH_2$	$2.85 \times 10^3$	$2.35 \times 10^3$	$4.65  imes 10^1$
$O_O_NH_2_OH_NH_2$	$2.55 \times 10^3$	$2.21 \times 10^3$	$2.40 \times 10^1$
NH_NH_NH2_NH2_NH2	$2.72 \times 10^3$	$2.88 \times 10^3$	$5.11 \times 10^0$
$S_NH_NH_2_F_NO_2$	$2.89 \times 10^3$	$2.91 \times 10^3$	$7.20\times10^{-2}$