Organic Compounds with Large and High-Contrast pH-Switchable Nonlinear Optical Response

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ABSTRACT: Measurements of the nonlinear optical (NLO) response (molecular first hyperpolarizability, \( \beta \)) of two pH-switchable dyes were performed by means of hyper-Rayleigh scattering (HRS) over a wide range of laser wavelengths and pH values. The extensive wavelength-dependent NLO data combined with linear optical spectroscopy allow the results to be related to the electronic structures of the push–pull systems and the NLO switching contrast to be optimized. The results are modeled theoretically using a vibronic \( \beta \) dispersion model including both homogeneous and inhomogeneous broadening, yielding a full wavelength dependence of \( \beta \), as well as of its switching contrast. The hyperpolarizabilities measured for the basic “on”-states are the highest ever reported for such compounds, reaching over \( 200 \times 10^{-30} \) esu in the static limit and over \( 2700 \times 10^{-30} \) esu at resonance. By combining a high intrinsic contrast in the static hyperpolarizability \( \beta_0 \) with a large shift in resonance, an extremely large range in contrasts of the HRS signal is reached of more than 2 orders of magnitude at wavelengths accessible with the widely used Ti:sapphire laser and moreover within a biologically compatible pH range.

INTRODUCTION

Organic compounds with large molecular second-order nonlinear optical (NLO) polarizability (first hyperpolarizability \( \beta \)) are of interest for their use as active components in electro-optical devices, wavelength conversion of lasers, and as labels for second harmonic imaging. A second-order NLO response requires an asymmetrically polarizable system, typically obtained by combining a long conjugated bridge with strong electron donor and acceptor end groups to form a “push–pull” chromophore. Larger hyperpolarizabilities can be achieved by optimizing either the conjugated chain and/or the donor or acceptor groups. For some compounds this response can be reversibly switched, using redox-reactions, photoconversion, or pH changes, a property that has been broadly investigated since the 1990s as it opens a new range of possible applications for NLO materials.

Because efficient NLO molecules exhibit intramolecular charge-transfer transitions at long wavelengths, experimentally measured \( \beta \)-values are very often enhanced by (two-photon) resonance, which complicates direct comparison of different compounds. This enhancement effect can be removed by extrapolation of the experimental values to zero frequency, yielding the static hyperpolarizability \( \beta_0 \). To determine this parameter reliably, one should measure the NLO response at several wavelengths, preferably both on- and off-resonance (requiring state-of-the-art tunable laser systems), and make use of suitable dispersion models for extrapolation, which is why detailed studies are scarce in the literature. If such data is available, the practical vibronic \( \beta \) dispersion model that we developed can be used, which takes into account both homogeneous and inhomogeneous broadening but restrains the dispersion to be fully consistent with the experimental absorption spectrum, such that an accurate dispersion can be obtained while involving only a single shape-determining free parameter.

Because of their noncentrosymmetric crystallization, both compounds shown in Scheme 1 have previously been investigated for their macroscopic second-order NLO properties, with crystals of 2 already finding their way to commercialization for terahertz generation and detection. In those previous studies, only the protonated forms were considered, and also in a measurement of the molecular \( \beta \) of 2 (at 800 nm in methanol), a pH sensitivity of the compound was not reported, and presumably only the response of the protonated form was measured. Here we find that the compounds show a pronounced pH dependence near neutral pH, and for the first time for any pH-switchable compound, we study the complete pH and wavelength dependence of their linear and NLO response, including accurate modeling of the \( \beta \) dispersion and consequently reliable extrapolation to \( \beta_0 \). In this way, we aim at understanding the origin of the NLO switching behavior and at optimizing the switching contrast.

EXPERIMENTAL METHODS

Hyperpolarizabilities were determined using hyper-Rayleigh scattering (HRS), i.e., incoherent second-harmonic light
scattering, from molecules in solution. The highly sensitive and wavelength-tunable setup used for this study has been described before. Briefly, a Ti:sapphire chirped-pulse regenerative laser amplifier pumps a dual-stage optical parametric amplifier to provide 2 ps pulses at a 1 kHz repetition rate with a continuously tunable wavelength. The output beam is focused into a cuvette containing the solution under investigation, and the generated HRS light is detected using a spectrograph coupled to a nitrogen-cooled, silicon CCD, which ensures the parallel detection of a narrow spectral range around the second harmonic wavelength. This spectral analysis is essential for systematic and complete subtraction of any multiphoton fluorescence contributions that often occur and are easily distinguished as a broad background. All hyperpolarizabilities are determined by reliable, internal calibration against the HRS signal of the pure solvent itself, which we extensively calibrated before against CHCl₃. Values are given as the βzzz-component, which is the dominant component for elongated push–pull compounds such as those considered here, in which case βHRS = (6/35)1/2βzzz. For D₂O, which was used for all measurements above 1200 nm because of its infrared (IR) transparency, the previously determined β-dispersion of H₂O was used, as the β of H₂O and D₂O were found to be the same within experimental error, in accordance with Kaatz et al.

The obtained β values were accurately fitted using the practical vibronic β dispersion model developed in ref 18, taking into account both homogeneous and inhomogeneous broadening, yet fully consistent with the experimental absorption spectrum and involving only a single shape-determining free parameter, the inhomogeneous line broadening Ginhom. This model is in fact an intermediate model between two extreme cases that were developed before involving only homogeneous or inhomogeneous broadening, and Ginhom determines the contribution of both classes of broadening mechanisms. Ginhom values used in the dispersion models of the compounds are as follows: in water, 1020 cm⁻¹ (1b); in acetonitrile, 1500 cm⁻¹ (1a), 570 cm⁻¹ (1b), 1400 cm⁻¹ (2a), and 1730 cm⁻¹ (2b). For compound 1a (in water), the best fit is obtained with the purely homogeneous vibronic model (which corresponds to the homogeneous limit of the more general model, i.e., Ginhom = 0). Uncertainties on the Ginhom values are large (up to 500 cm⁻¹), but in most cases the improvement of the fits with this intermediate model compared to either extreme case was significant, and the uncertainties on Ginhom did not translate into large errors in calculated static hyperpolarizabilities. Error margins on β₀ reported below include the effect of the uncertainty on the fitted Ginhom.

For the water-soluble compound 1, common buffer solutions (phosphate (pH < 7.5) and TRIS (pH > 7.5)) could be used to stabilize the pH for the pH-dependent absorption spectra shown in Figure 1, as well as for the pH-sensitive HRS measurements at 1550 nm in D₂O depicted in Figure 2. All given pH values were measured using a glass electrode pH meter (Lab 850 from Schott Instruments). The used buffers were found to exhibit negligible HRS signals (i.e., the HRS signals of the buffer solutions were identical to those of pure water). For the other HRS measurements (both in water and acetonitrile), the pure acidic and basic forms of the dyes were obtained by the addition of small amounts of 37% HCl/H₂O and 50% NaOH/H₂O stock solutions. As NaOH does not dissolve in pure acetonitrile, 5 vol % of H₂O (D₂O for λ > 1200 nm) was added to all solutions (including the acidic ones, as

![Scheme 1. Investigated Compounds 1 and 2 in Acidic (a) and Basic (b) Environments, the Latter with Their Two Resonance Forms](image)

![Figure 1. Left panel: Absorption spectra of 1 in H₂O for a range of pH values. Isosbestic points are found at 448, 349, and 315 nm. Right panel: Solvatochromism of 1b, where black dots are plotted with respect to the dielectric constant and red dots with respect to the empirical ET-N(30) scale.](image)

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well as the reference samples), which did not influence the HRS signal beyond experimental error. Ultraviolet−visible absorption spectra were measured using a Varian Cary 5E absorption spectrometer.

### RESULTS AND DISCUSSION

Compound 1 is water-soluble, which is an interesting feature for biological purposes, and allowed us to measure its hyperpolarizability over a wide range of pH values. To first determine in which pH range its switching occurs, absorption spectra were taken as a function of pH (Figure 1, left panel). The spectra show a clear shift of intensity from the longest wavelength absorption band maximum at $\lambda_{\text{max}} = 418$ nm to one at $\lambda_{\text{max}} = 520$ nm upon increasing pH (with well-defined isosbestic points at 448, 349, and 315 nm, confirming that only two forms of the dye are involved, without any decomposition). From these spectra a $pK_a$ of $7.9 \pm 0.1$ in H$_2$O was established.

From similar spectra in D$_2$O (that was used in some HRS measurements for its IR transparancy) a $pK_a^D$ of $8.3 \pm 0.1$ was observed, the difference of 0.4 resulting from the use of a glass probe pH meter (this constant offset was corrected for in the pH-dependent HRS measurements).

For the basic form of 1, both a neutral and zwitterionic resonance structure might be important (see Scheme 1), where the latter is stabilized by the gain in aromaticity. To verify which resonance structure dominates in this compound, we recorded absorption spectra in different polarity solvents to reveal its solvatochromism, which is governed by the ground- and excited-state dipole moments. While the solvatochromism data shows somewhat more scatter when plotted versus dielectric constant, the shift is even more systematic when the empirical $E_T(30)$ polarity scale is used that runs from 0 for gas-phase to 1 for water, and which is particularly suitable here, as it was set up using a zwitterionic compound with rather similar structural features as 1b. The negative solvatochromism of the compound (Figure 1, right panel) indicates that indeed its ground state is dominated by the zwitterionic structure, and the excited state by the neutral one, and thus places this compound in the right-hand side of the well-known bond-length alternation (BLA) diagram (or its generalization, the “MIX” model, providing a very general description of the NLO behavior of conjugated molecules), i.e., beyond the cyanine limit. Such “right-hand side” molecules can have hyperpolarizabilities of equally large magnitude (but opposite sign) as the more common “left-hand side” molecules with the same conjugation length and have the added benefit of very large dipole moments, $\mu$. This makes them also particularly interesting for NLO devices based on poled polymer films (the figure of merit for these being $\mu \beta$). Likewise, the ground state of the basic form of 2 can also be expected to be dominated by the aromatic resonance structure. This results, for the basic forms of both compounds, in strong push−pull systems formed by a strong electron acceptor (quinolinium or dicyanomethylene) and a strong donor ($\sim$O) for which a high optical

![Figure 2. pH dependence of the effective (i.e., root-mean-square) first hyperpolarizability of 1 at 1550 nm (measured in D$_2$O, but pH values were corrected for the isotope effect to their equivalent in H$_2$O).](image)

![Figure 3. a–c: Experimental wavelength-dependent HRS results (symbols) with $\beta$-dispersion models (solid curves) and normalized absorption spectra (dashed curves) of the acidic (blue) and basic (red) form of 1 in water (a) and acetonitrile (b), and of 2 in acetonitrile (c). d–f: Dispersion of the corresponding $\beta$ contrast.](image)
nonlinearity can be anticipated. In contrast, the acidic forms have a much weaker OH electron donor.

To examine the NLO switching of compound 1, its hyperpolarizability was first measured over a range of pH values at 1550 nm in D$_2$O (Figure 2). A very good fit to the experimental data is obtained using the well-known Henderson–Hasselbalch equation for the concentrations of both forms and calculating the root-mean-square of the hyperpolarizabilities of the components of a binary mixture, which is the observable in HRS:

$$\beta_{\text{eff}} = \sqrt{\frac{N_a \beta_a^2 + N_b \beta_b^2}{N_a + N_b}}$$

(1)

where $N_a$ ($N_b$) are the concentrations of the acidic (basic) form and $\beta^a$ ($\beta^b$) are their second-order polarizabilities; the usual assumption is made that the hyperpolarizability is dominated by a single diagonal tensor component along the long axis of the conjugated chain. This fit yields a first hyperpolarizability of $(131 \pm 6.6) \times 10^{-30}$ esu for the pure acidic form ($\beta_a$) and $(431 \pm 22) \times 10^{-30}$ esu for the pure basic form ($\beta_b$), which amounts to a $\beta$ contrast ($\beta_a/\beta_b$) of 3.30 at 1550 nm.

To determine the dispersion of the hyperpolarizability of both the protonated and deprotonated forms of compounds 1 and 2, and to allow for reliable extrapolation to the static limit, the $\beta$-values of both compounds were determined over a wide range of wavelengths, at both extremely acidic and basic pH (Figure 3). Compound 2, not being water-soluble, was measured in acetonitrile solution, while 1 was measured in both H$_2$O (D$_2$O for $\lambda > 1200$ nm) and acetonitrile, to allow for direct comparison with 2. These $\beta$ values were then accurately fitted using the aforementioned vibronic $\beta$ dispersion model\textsuperscript{18} (Figure 3a–c). The large deviation of the shortest-wavelength data-point of the basic form of compound 1 in water is likely to be caused by contributions from higher-energy transitions visible in the absorption spectrum that are not taken into account in this model; therefore, this data point was omitted in the fitting procedure. For the same reason, the two shortest-wavelength data points of the basic form of both compounds in acetonitrile were omitted. By dividing the $\beta$-dispersion curve obtained for the basic form by the one obtained for the acidic form, the wavelength dependence of the $\beta$ switching contrast is obtained (Figure 3d–f). Note that for our compounds, the contrast drops below unity in some wavelength ranges; hence, the terminology “on” and “off” sometimes used in the literature for either state of a switchable compound does not strictly apply at all wavelengths.

An overview of relevant figures of merit for the compounds under study is given in Table 1. While for both 1 and 2 only the acidic compounds have been crystallized (and used for frequency doubling and terahertz pulse generation), here we reveal much larger hyperpolarizabilities for the basic forms. The $\lambda_{\text{max}}$ of the basic forms being significantly red-shifted and the extinction coefficient increased compared to the corresponding acidic forms, this result correlates well with the two-level model.\textsuperscript{34} Also, the basic form of 1 shows static hyperpolarizabilities larger than those of the already commercialized compound 2. In fact, the resonantly enhanced $\beta$-values for the basic forms are significantly higher than for any pH-switchable compound reported before. Only the pH-sensitive product measured on resonance by Asselberghs et al.\textsuperscript{9} is comparable, with a $\beta_{ approaching 0.258 \times 10^{-30}$ esu (recalculated using the more recent $\beta$ value\textsuperscript{35} for their calibration compound), and Mancois et al.\textsuperscript{36} also reported a very large value (≈42% of the hyperpolarizability of compound 1b), [in ref 36, $\beta_{HRS,1064 \text{ nm}} = (|\langle \beta_{ZZZ} \rangle|^2 + |\langle \beta_{ZZZ} \rangle|^2)^{1/2} = 475 \times 10^{-30}$ esu (rescaled for the different reference value used for acetonitrile $\beta_{HRS,1064 \text{ nm}} = 0.284 \times 10^{-30}$ esu (ref 37) instead of 0.258 $\times 10^{-30}$ esu (ref 26)), to be compared with $\beta_{HRS,1064 \text{ nm}} = 1143 \times 10^{-30}$ esu for our compound 1b.]

Also, the maximum $\beta$ contrasts, occurring slightly red-shifted from the $\lambda_{\text{max}}$ of the basic state, are very high (up to 13.9, see Table 1) and correspond to huge contrasts in HRS signal (proportional to $\beta^2$), reaching almost 200 for 1 in acetonitrile at 1240 nm and almost 100 in water at 1125 nm, rendering the signal coming from the acidic state virtually negligible. Only one compound reported by Mancois et al.\textsuperscript{7} has a higher maximum $\beta$ contrast (≈26; albeit with lower absolute $\beta$), which may be attributed to a larger separation of the longest wavelength band of the two states, so that an increase in contrast due to resonant enhancement in one form is not opposed by resonant enhancement in the other.

### CONCLUSION

For the first time for pH-sensitive compounds, the first hyperpolarizability $\beta$ was measured over a wide range of wavelengths and pH values, and the obtained experimental results were used to model the $\beta$ dispersion behavior, which not only allows for understanding the results but also is a valuable tool for practical purposes, e.g., in optimizing the $\beta$ contrast. The responses of the basic forms are the highest ever measured for the “on”-state of pH-sensitive NLO compounds, with 1 showing higher responses than 2. Both compounds show very high contrasts both at and off-resonance that are more than suitable for practical applications. The fact that the switching range of 1 is within biological pH limits (which is another feature that has never been reported before), while a $\beta$ contrast of unity is reached at ~800 nm and a high maximum contrast at ~1100 nm, both within reach of the common Ti:sapphire laser, makes compound 1 highly promising for pH sensing through ratiometric second harmonic generation imaging.

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#### Notes

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