Photoinduced processes in dendrimers

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Citation for published version (APA):
Chapter 2

The Photoactivity and pH Sensitivity of Methyl Orange-Functionalized Poly(propyleneamine) Dendrimers

Abstract: For the first time a pH indicator, that responds to two different external stimuli, i.e. pH and light, namely methyl orange, has been implemented in a dendrimer. Five generations (G1-G5) of methyl orange-functionalized poly(propyleneamine) dendrimers (“MO-dendrimers”) have been synthesized. The response of the MO-dendrimers towards pH changes has been monitored using UV-Vis spectroscopy and the photophysical properties have been investigated. Furthermore, the photoisomerization from E to Z and the thermal recovery from Z to E, have been studied using UV-Vis and transient-absorption spectroscopy. Interestingly, the response of the MO-units towards pH changes is found to be generation dependent. On the other hand, the photophysical properties are found to be similar for all generations, except for the ε-value, which deviates significantly from the expected value in the case of G4 and G5. Also the isomerization processes show no generation dependency within the same solvent, but different rate constants for the Z/E isomerization have been observed in different solvents.

2.1 Introduction

The interest in dendrimers has grown enormously over the past two decades, since they represent a new class of molecules with some unique properties. In particular those containing active groups, that are able to perform specific functions, are candidates for many challenging applications.\textsuperscript{1-6} Of particular interest are dendrimers functionalized with switchable moieties, where controlled interconversion between two stable states is possible using external stimuli such as light\textsuperscript{7-13}, protons\textsuperscript{14} or electrons\textsuperscript{15}.

Less common are dendrimers containing functional groups at the periphery, which can respond to two different external stimuli, \textit{i.e.} light and pH. This class of compounds can provide new information about the interactions within dendritic molecules, \textit{e.g.} among the branches, and render novel materials with unique characteristics. A suitable group able to respond to a double input is methyl orange, which is widely used as a pH indicator for titration in aqueous solutions, having a pH transition interval in water between pH 3.1 (red) and pH 4.4 (yellow) (pK\textsubscript{a} = 3.46)\textsuperscript{16}. The clear color change observed at the transition point is the result of protonation at the azo moiety, leading to an azonium ion, which is stabilized by mesomerism (Scheme 2-1).\textsuperscript{17}

Methyl orange is not only a pH-sensitive, but also a light-responsive molecule, since it contains a photoisomerizable azo moiety, which can be converted from the thermodynamically more stable \textit{E} form into the \textit{Z} form upon light excitation. Subsequently, the \textit{Z} form will transform back to the \textit{E} form either thermally or photochemically (Scheme 2-1).\textsuperscript{18}

![Scheme 2-1. The protonation to an azonium ion (right) and the E/Z-isomerization of methyl orange (left).\textsuperscript{18}](image)

It would be interesting to introduce multiple methyl orange units in large well-defined molecules, such as dendrimers. Novel materials, responsive towards light and pH, may arise as a result of cooperativity effects between the methyl orange groups. Nanosized compounds, that are able to respond to different external stimuli in a way that shape, size, color, and reactivity can be
controlled, are particularly interesting for *e. g.* data storage and the development of carrier molecules, that are able to release their content in response to a specific stimulus.

Five generations (G1-G5) of MO-dendrimers have been synthesized in the group of prof. dr. F. Vogtle at the University of Bonn (Germany) through the reaction of the sulfonic acid chloride of methyl orange with amine-functionalized poly(propyleneamine) dendrimers.\(^{19,20}\) Methyl orange itself could not be used as a model compound for this study because of its very different solubility properties as compared to the MO-dendrimers. For this purpose, G0 has been synthesized, reacting propylamine with the sulfonic acid of methyl orange, to create a good model compound containing the same sulfonamide group as the MO-dendrimers. The number of MO-units increases from 1 in G0, 3 in G1, 8 in G2, 16 in G3, 32 in G4 to 64 in G5 (Figure 2-1).

![Figure 2-1](image-url)

*Figure 2-1. A schematic representation of the MO-dendrimers bearing n MO-units (n = 1, 3, 8, 16, 32, 64); the structures of generations 1 (G1, n = 3) and 3 (G3, n = 16) are depicted in detail.\(^{19,20}\)*

The photophysical properties of the MO-dendrimers are presented. We have investigated the photoisomerization of the methyl orange groups for all generations and in particular the solvent dependency of the thermal Z to E isomerization. Also, the spectroscopic behavior as a result of the protonation at the azo moieties is presented. A different protonation behavior was observed for
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the higher generations (dendritic effects) as compared to methyl orange itself. The isomerization processes were found to be generation independent.

2.2 Results and Discussion

2.2.1 Photophysical Properties

Methyl orange belongs to the group of the so-called pseudo stilbenes, which includes both protonated azobenzenes and donor-acceptor functionalized azobenzenes. Also the MO-dendrimers (G0-G5) exhibit the characteristic photophysical properties of pseudo stilbenes. The absorption spectra of G0-G5 show a ππ* band at 305 nm and a ππ* band with charge transfer character at 445 nm (ε = 25000 M⁻¹cm⁻¹), both characteristic of the E MO-units (Figure 2-2). The nπ* band typical of azobenzene units is not observed, because the more intense ππ* band appears in the same spectral region (400-450 nm). It is interesting to notice that the molar extinction coefficients of the 445 nm band are proportional to the number of MO-units present in the dendrimer for G0-G3. However, for G4 and G5 the molar extinction coefficient shows a large deviation from the one expected, e.g. ε_{G5}(measured) = 1.09 × 10^6 M⁻¹cm⁻¹ while ε_{G5}(expected) = 1.60 × 10^6 M⁻¹cm⁻¹, while no shift in the absorption maximum is observed. This rather large discrepancy could not be attributed to impurities or defects in the dendrimer, and suggests ground state interactions between the MO-units in the case of G4 and G5.

2.2.2 Isomerization

The photoisomerization of azobenzene and its derivatives can be effected by means of light (E to Z, and Z to E) and by heat (Z to E). The E form is in all cases thermodynamically more stable than the Z form. The same holds for pseudo stilbenes, such as methyl orange.

![Figure 2-2. Absorption spectra of the E-form, the photostationary state (PSS) and the predicted spectrum of the Z-form.](image-url)
Irradiation of a solution of a MO-dendrimer in the spectral region between 440 and 480 nm results in the isomerization from the E to the Z form. The intensity of the ππ* band at 445 nm decreases, since the Z form has a weaker absorption at that position, and a shoulder appears at 382 nm, corresponding to the nπ* absorption band of the Z form (Figure 2-2).

A photostationary state is reached for each generation after the flash, i. e. within a few nanoseconds, as proven by further irradiation, which does not result in a larger decrease of the ππ* band or increase of the nπ* band. In general, for azobenzenes it is possible to evaluate the ratio between the two forms in the photostationary state by NMR spectroscopy, since in many cases the thermal back reaction is very slow (up to several hours). An accurate evaluation of the percentage of photoisomerization was not possible for our systems, since the absorption spectrum of the Z form overlaps with the one of the E form and the thermal back reaction is extremely fast. However, subtraction of the absorption spectrum of the photostationary state from the absorption spectrum of the E form gave a reasonable approximation for the absorption spectrum of the Z form (Figure 2-2). From the decrease in the ππ* band at 445 nm the conversion of the E into the Z form is estimated to be higher than 35%.

To gain more insight in the isomerization of the MO-units, both as a function of the solvent and as function of the generation, the observed isomerization rate (k_{obs} (s^{-1})) of the thermal recovery from the Z to the E form has been determined for each generation in various solvents of different polarity, namely 1:1 v/v DCM/MeOH, DMF, DMSO, and 1:1 v/v DMF/NMF (Table 2-1). The choice of solvents was limited due to the solubility properties of the MO-dendrimers. A fast thermal Z to E isomerization is expected, because of the presence of an electron donor (NMe_2-group) and an electron acceptor (SO_2-group) substituent on the azobenzene unit. The “push-pull” system has a very high dipole moment in the E form. A polar solvent will not stabilize the less polar Z isomer, and therefore favor the back reaction to the E form.

![Figure 2-3. Transient-absorption spectrum of G1 measured in 1:1 v/v DMF/NMF (λ_{exc} = 445 nm; 20 frames; incr. delay = 0.1 s).](image)
To follow the very fast Z/E isomerization in the 1:1 v/v DMF/NMF mixture transient absorption spectroscopy has been applied. The spectrum obtained just after the laser pulse clearly shows a bleaching in the 400-500 nm region due to the decrease of the ππ* band at 445 nm of the E form as a result of the isomerization to the Z form. Furthermore, an increase in the absorption is observed at 380 nm, due to the stronger ππ* absorption of the Z form (Figure 2-3).

For the other solvents a diode-array UV-Vis spectrophotometer was used to determine \( k_{\text{obs}} \). All generations show a perfectly reversible photoisomerization and thermal back reaction during several cycles. The \( k_{\text{obs}} \) values measured for all generations are of the same order of magnitude within one solvent, so no strong dendritic effects are observed (Table 2-1). Apparently, a sufficient amount of free space is available for a MO-unit to isomerize, even within the higher generations, so that the isomerization process is not hampered.

### Table 2-1. Observed isomerization rates (\( k_{\text{obs}} \) (s\(^{-1}\))) for the thermal Z/E isomerization in various solvents for G0-G5 (\( T = 20 \pm 0.5 ^\circ\text{C} \)).

<table>
<thead>
<tr>
<th>G</th>
<th>( k_{\text{obs}} ) (10(^{-3}) s(^{-1})) DCM/MeOH(^{\text{a}})</th>
<th>( k_{\text{obs}} ) (10(^{-3}) s(^{-1})) DMF(^{\text{a}})</th>
<th>( k_{\text{obs}} ) (10(^{-3}) s(^{-1})) DMSO(^{\text{a}})</th>
<th>( k_{\text{obs}} ) (s(^{-1})) DMF/NMF(^{\text{a}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>46.94 ± 2.30</td>
<td>1.60 ± 0.10</td>
<td>4.71 ± 1.03</td>
<td>1.734 ± 0.025</td>
</tr>
<tr>
<td>1</td>
<td>68.17 ± 3.28</td>
<td>3.35 ± 0.49</td>
<td>7.23 ± 0.33</td>
<td>2.079 ± 0.102</td>
</tr>
<tr>
<td>2</td>
<td>66.59 ± 0.80</td>
<td>2.92 ± 0.22</td>
<td>9.14 ± 1.31</td>
<td>1.702 ± 0.107</td>
</tr>
<tr>
<td>3</td>
<td>50.17 ± 1.63</td>
<td>2.92 ± 0.16</td>
<td>6.47 ± 0.53</td>
<td>1.938 ± 0.144</td>
</tr>
<tr>
<td>4</td>
<td>63.39 ± 3.28</td>
<td>3.64 ± 0.22</td>
<td>6.15 ± 0.19</td>
<td>1.708 ± 0.026</td>
</tr>
<tr>
<td>5</td>
<td>45.66 ± 1.42</td>
<td>3.88 ± 0.22</td>
<td>7.13 ± 0.79</td>
<td>1.141 ± 0.122</td>
</tr>
</tbody>
</table>

\(^{\text{a}}\)DCM = Dichloromethane; MeOH = Methanol; DMF = N,N'-Dimethylformamide; DMSO = Dimethylsulfoxide; NMF = N-Methylformamide.

From Table 2-1 it can be seen that the Z/E isomerization in the dark is extremely fast as compared to azobenzene itself,\(^{21,22}\) because the "push-pull" system formed by the NMe\(_2\) group and the SO\(_2\) group (\textit{vide supra}) lowers the energy barrier for the isomerization process. The double bond character of the azo-groups is reduced, facilitating rotation around the N-N bond. The increase of \( k_{\text{obs}} \) with increasing polarity of the solvent is in agreement with the findings for the isomerization rates of azobenzenes with a "push-pull" system as previously described by Wildes \textit{et al.}.\(^{23}\) Only the \( k_{\text{obs}} \) in 1:1 v/v DCM/MeOH is higher than expected. This is attributed to the protic solvent (MeOH), allowing acid-catalyzed isomerization. At the same time DCM may become slightly acidic upon irradiation with light, which would promote as well the acid-catalyzed isomerization of the MO-units.

To gain more insight in the activation energy for the thermal Z/E isomerization, the temperature dependence of the observed rate constant has been measured for all generations in DMF in the
group of prof. dr. F. Pina at the University of Lisbon (Portugal). They determined an activation energy of ~ 64 kJmol\(^{-1}\) for all generations. This value in fact is lower than the value of 94 kJmol\(^{-1}\) found for the activation energy of the Z/E isomerization of azobenzene itself, justifying the faster Z/E isomerization found for the MO-dendrimers.

### 2.2.3 pH Sensitivity

Interestingly, protonation of the MO-dendrimers at the azo moiety with trifluoroacetic acid (CF\(_3\)COOH) proceeds different for the lower generations (G\(_0\) and G\(_1\)) as compared to the higher generations (G\(_2\)-G\(_5\)). Both G\(_0\) and G\(_1\) behave like the pH indicator, methyl orange itself, which means that the addition of acid causes a decrease in the \(\pi\pi^*\) absorption band of the non-protonated form at 445 nm and an increase in the \(\pi\pi^*\) absorption band of the protonated form at 540 nm (Figure 2-4). The resulting pink color is related to the resonance structure obtained upon protonation of the azo moiety (Scheme 2-1). The isosbestic point at 485 nm shows that this conversion from the non-protonated to the protonated form is a clean reaction and that no degradation of the dendrimer takes place.

![Figure 2-4. Spectral changes in the UV-Vis absorption spectra of (a) G\(_0\) and (b) G\(_1\) upon the addition of CF\(_3\)COOH in CH\(_2\)Cl\(_2\).](attachment:image.png)

However, in the case of the higher generations (G\(_2\)-G\(_5\)), the isosbestic point as present in G\(_0\) and G\(_1\) disappears as depicted in Figure 2-5 for G\(_4\). Furthermore, the absorption band of the protonated form of the higher generations is broader and less red shifted compared to G\(_0\) (Figure 2-6). The changes in the absorption spectra of G\(_2\)-G\(_5\) compared to G\(_0\) and G\(_1\) suggest that the protonation of the individual MO-units is influenced by the accumulation of charges within one dendrimer. The addition of a large excess of acid (1.4-1.8 \times 10^3 eq. of CF\(_3\)COOH) is necessary to induce a full color change. This can be attributed to the apolar nature of the solvent in which the titration experiments were performed.
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Figure 2-5. Spectral changes in the UV-Vis absorption spectra of G4 upon the addition of CF₃COOH in CH₂Cl₂.

From literature it is known that the tertiary amines in the core are strongly basic.²⁴ The protonation of these tertiary amines is anticipated to occur prior to the protonation of the MO-units. Therefore, the presence of a large number of charges due to the protonation of the core can influence the protonation process of the MO-groups at the periphery. The broadening of the absorption spectra may also indicate sharing of protons between two MO-groups at the periphery of a dendrimer. In all cases the protonation process of the MO-dendrimers is perfectly reversible.

Figure 2-6. Absorption spectra of Gn (straight line) and GnH⁺ after addition of large excess of CF₃COOH (1000 eq.; dotted line) in DCM (n = 0, 1, 2, 3, 4, 5).
Besides the changes in the absorption spectra, it is interesting to notice that once the azo moiety of the MO-groups is protonated to an azonium ion, emission is observed for all generations at 77 K (Figure 2-7).

<table>
<thead>
<tr>
<th>G</th>
<th>τ (ns)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.80</td>
</tr>
<tr>
<td>1</td>
<td>1.55</td>
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<td>2</td>
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</tr>
<tr>
<td>4</td>
<td>1.37</td>
</tr>
<tr>
<td>5</td>
<td>1.63</td>
</tr>
</tbody>
</table>

**Figure 2-7.** Emission spectrum of G1, characteristic for all generations, (left; $\lambda_{exc} = 490 \text{ nm}$) and an overview of the excited state lifetimes of G0-G5 (right; $\lambda_{exc} = 324 \text{ nm}; \lambda_{probe} = 560 \text{ nm}$) measured at 77 K in a glass of 1:1 v/v DCM/MeOH.

The emission has maxima at 560 nm and 620 nm and decays with an excited state lifetime of about 1.5 ns for all generations (Figure 2-7). This is generally observed for pseudo stilbenes.\(^2\)

### 2.3 Conclusions

For the first time a photoresponsive pH indicator has been implemented in a dendrimer. All the described results show that the photophysical properties were found to be similar for all generations (G0-G5). Only the molar extinction coefficients of G4 and G5 show a significant deviation due to the locally high concentrations of MO-units. Both the E/Z and the Z/E isomerization rates are extremely high, as expected for pseudo stilbene molecules. The protonation behavior of the MO-units indicates clearly that the higher generations of the dendrimer do not behave like methyl orange itself. In fact, the protonation process of the MO-units is strongly influenced by the accumulation of charges within the dendrimer and the color change is not so rapid and clear as indicated by the absorption spectra. Once the MO-units are protonated, emission is observed at 77 K.
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2.4 Experimental Section

2.4.1 Materials
Dichloromethane (DCM) (Uvasol, spectroscopic grade, MERCK), methanol (MeOH) (Uvasol, spectroscopic grade, MERCK), N,N'-dimethylformamide (DMF) (Uvasol, spectroscopic grade, MERCK), dimethylsulfoxide (DMSO) (Uvasol, spectroscopic grade, MERCK), N-methylformamide (NMF) (99%, Aldrich), trifluoroacetic acid (99%, Acros Organics), and methyl orange (MERCK) were used as received.

2.4.2 Synthesis
Methyl Orange-Functionalized Dendrimers (MO-dendrimers). The MO-dendrimers were synthesized in the group of prof. dr. F. Vögtle at the University of Bonn (Germany). Details on the synthetic procedures are given in the literature.\textsuperscript{19,20}

2.4.3 UV-Vis Absorption and Fluorescence Spectroscopy
Absorption spectra were recorded on a diode-array HP8453 spectrophotometer at 298 K. Emission spectra were recorded on a SPEX fluorometer, irradiating the protonated MO-dendrimers with 490 nm light in a 1:1 v/v DCM/MeOH glass at 77 K. The concentration of the methyl-orange units was $2 \times 10^{-6}$ M for all generations. The lifetime of the emission at 77 K was determined with single photon counting using a picosecond laser ($\lambda_{\text{exc}} = 324$ nm). A detailed description of the experimental set-ups is given in the Appendix of this Thesis.

2.4.4 pH Sensitivity
To a solution of a Gn MO-dendrimer ($n = 0, 1, 2, 3, 4, 5$) in DCM a 0.05 M solution of CF$_3$COOH in DCM was added in portions of 10 µL. After the addition of 70 µL titration was continued with a 0.5 M solution of CF$_3$COOH in DCM to ensure full protonation. The concentration of methyl-orange units was $1.20 \times 10^{-5}$ M for all generations.

2.4.5 Kinetics of the Z to E Isomerization
Irradiation of the dendrimer solutions occurred in a closed spectrophotometric cell (volume 3 mL; optical path, 1 cm) using a Yashica CS-201 auto flash from a camera. The concentration of methyl-orange units was $1 \times 10^{-5}$ M. Solutions were prepared in 1/1 v/v DCM/MeOH, DMF, DMSO and 1/1 v/v DMF/NMF. The kinetics of the thermal Z to E isomerization were carried out on a HP8453 spectrophotometer in the kinetics mode (run time: 900s, steps: 1s) and were performed in triplo. Spectra were recorded every second after irradiation and from the recovery of the absorption at 445 nm, the rate of the thermal Z/E-isomerization ($k_{\text{obs}}$) could be directly determined. Very fast isomerization processes were monitored via transient absorption using a ns YAG laser with an OMA detection system. In this case the sample was irradiated using 445 nm laser light (20 frames; increment delay: 0.1 s). A detailed description of the transient absorption set-up is given in the Appendix of this Thesis.
2.5 References
