Chapter 7: Third Generation Molecular Motors – Exploring Their Key Parameters and Limits

Herein is reported: Elucidation of the key parameters and limitations of third generation motors is essential for the design of optimized molecular machines based on light-driven rotary motion. Herein we demonstrate the thermal and photochemical rotational behaviour of a series of third generation light-driven molecular motors. The steric hindrance of the core unit exerted upon the rotors proved pivotal in controlling the speed of rotation, where a smaller size results in lower barriers. The presence of a pseudo-asymmetric carbon centre provides the motor with unidirectionality. Tuning of the steric effects of the substituents at the bridgehead allows for the precise control of the direction of disrotatory motion, illustrated by the design of two motors which show opposite rotation with respect to a methyl substituent. A third generation molecular motor with the potential to be the fastest based on overcrowded alkenes to date was used to visualize the equal rate of rotation of both its rotor units. The autonomous rotational behaviour perfectly followed the predicted model, setting the stage for more advanced motors for functional dynamic systems.

This chapter has been published as:

Introduction

Molecular motors and machines attract major attention as the introduction of dynamic properties enables a wide range of responsive functions and adaptive properties in synthetic materials.\[1–6\] Towards the design of dynamic functional systems, the use of light as an external stimulus offers particular advantages. Photochromic systems arguably have the benefit of non-invasive triggering with the potential of high spatial-temporal precision.\[7,8\] Switching between two or more states upon irradiation at different wavelengths (UV/vis) can be combined with other effectuators (temperature, pH, metal-ion binding, redox) to arrive at multiresponsive behaviour.\[9–13\] Prominent classes of photochemical switches include dithienylethenes,\[14\] stilbenes,\[15,16\] fulgides and fulgimides,\[17\] spiropyran,\[18\] DASA,\[19\] or azobenzenes\[20,21\]. Stilbenes in particular, though rather easy to prepare, suffer from the undesired thermal cis-trans isomerizing and degradation due to ring closing and oxidation towards phenanthrene (Figure 7.1a).\[15,16\] One of the major interests in our group has been the synthetic manipulation of stilbenes in order to achieve stability and increase quantum yield, control over irradiation wavelengths, and directionality of motion upon isomerization and furthermore structural modifications to prevent decomposition.\[22\]

![Figure 7.1.](image)

**Figure 7.1.** a) Stilbene cis–trans isomerization and degradation due to ring closing and oxidation. b) From left to right: stable switch, 1st generation molecular motor, 2nd generation molecular motor.

An important synthetic adjustment of a stilbene-like system (Figure 7.1b), was achieved by Feringa and Wijnberg, introducing steric overcrowding at the alkene to form thermally stable chiral forms. This was accomplished through the presence of naphthalene moieties and aliphatic rings at both sides of the central alkene to prevent ring closing.\[23\] The introduction of stereogenic centres in these systems (Figure 7.1b) originally served the purpose of proving the absolute stereochemistry of its analogues.\[24\] However, the molecules were found to have a surprising new property: they are able to undergo a 360 degrees unidirectional rotation around the
alkene bond.[25] These systems, as a result of successive alterations, became the basis of the first generation synthetic molecular motors, characterized by their $C_2$ symmetry and its principal axis at the double bond connecting upper and lower halves. Recently functional analogues of these first generation synthetic motors showed potential in asymmetric catalysis,[26] and control of dynamic chirality,[27] and as chiral hosts.[28]

![Figure 7.2. Schematic design of achiral motors. Merging of two enantiomers of motor 1 (opposite helicities ($P,M$) and central chirality ($R,S$) indicated) gives rise to symmetric double overcrowded alkenes 2-4 (pseudo-asymmetric carbon atom C2 indicated with "2").](image)

In subsequent studies one half of these new dynamic molecules was symmetrized in order to increase their speed and quantum yield as well as allowing surface assembly.[29–31] Synthetic modifications were introduced to illustrate that these motors can perform work.[32] The de-symmetrized synthetic unidirectional motors with only one stereogenic centre in the upper half and a symmetric lower half were adopted as the second generation molecular motors, in which chirality was shown essential to ensure unidirectionality (the initial ‘stilbene motive’ is continually shown in orange in all four structures in order to illustrate the predominant concept of the isomerizing alkene connecting two aromatic groups, Figure 7.1b). Not surprisingly the question regarding the necessity of a stereogenic centre for unidirectionality in rotary motion emerged. Recently, we reported a novel synthetic meso motor bearing two overcrowded alkenes and the notable absence of a stereogenic centre, although a pseudo-asymmetric centre is present.[33] In fact each individual alkene still has to experience chirality in order to perform a unidirectional rotation. This so-called third generation molecular motor (Figure 7.2) has two of such alkene moieties with identical groups that can be considered
mirror images of two separate second generation motors. This third generation motor is especially designed to maintain unidirectionality of two parallel rotors while avoiding the stereogenic element (asymmetric carbon centre) known from earlier generations of motors. Both individual alkenes experience the pseudo-asymmetry of the bridge unit (e.g. CFCH₃ in 2) and due to the opposite helicity of these alkenes with respect to the bridge unit both fluorene moieties are rotating in the same direction with respect to the core aromatic group. This symmetry property relates to a car driver moving forward on a road observing his right wheel turning anti-clockwise and his left wheel turning clockwise.

Herein is reported the investigation and characterization of the essential features of third generation molecular motors and the limits of their performance, to finally come to demonstrate the unidirectionality of the fastest third generation motor, and potentially the fastest of all molecular rotary motors based on overcrowded alkenes designed so far. We first identify the impact of the core’s size on its behaviour by a computational study followed by an experimental verification. Based on those results, we study the effect of the size of the substituents at the pseudo-asymmetric carbon atom (the indane bridgehead C2, Figure 7.2) on the behaviour of the bis-overcrowded alkenes using theoretical and experimental approaches.[34–38] After identifying the most desirable structural features, a suitable candidate is chosen as a model compound for proving the persistence of unidirectionality in ultrafast third generation molecular motors.

**Results and Discussion**

Previously, unidirectional rotation has been established for motor 2 taking advantage of its desymmetrized analogue 3.[33] For purposes of developing more advanced nanomachines offering controlled motion along surfaces, the ability to tune the rotary speed is considered highly beneficial.[32,39] We therefore instigated a theoretical study on double overcrowded alkenes with a substitution pattern of two methyl groups on C2 (R¹ = CH₃) such as 4 for maximum simplicity. Besides 4, four more structural units were selected starting with a benzene instead of xylene moiety in the core (5), a p-difluorobenzene (6), a p-dimethoxybenzene (7), and one where the core xylene moiety is replaced with a phenanthrene moiety (8) (Figure 7.3).
Theoretical study of the core-size effect

The theoretical investigation was performed using the semi-empirical PM6 model to construct a potential energy surface (PES) from two dihedrals governing the aromatic planes for compounds 4–8 (4 as example; Figure 7.4a). The resulting PES shows a two-fold symmetry with mirror planes running diagonally through the minima. The geometries of the minima and transition states (TSES) were optimized using DFT B3LYP/6-31G(d,p)\cite{40,41} and intrinsic reaction coordinates (IRC\textsubscript{s}, 4 as example; Figure 7.4b) were calculated to ensure the transition states connected the identified minima. Subsequently the geometries of the minima and transition states were optimized using DFT ωB97X-D/6-31+G(d,p)\cite{42} in dichloromethane (IEFPCM)\cite{43,44} which revealed for each compound two global minima and two metastable local minima (minima and transition states afforded zero or one imaginary frequency, respectively, and their geometries, energies and calculated barriers are shown in Table 7.1). The two redundant global minima have the desired meso geometries and are close to or have $C_\text{s}$ symmetry. The two metastable local minima were enantiomeric helical configurations and are close to or have $C_2$ symmetry and connected to the global minima by the calculated transition states which constitute the thermal helix inversions (THIs) known for overcrowded alkenes.

Figure 7.3. Double overcrowded alkenes with modified core moieties featuring; benzene (5), $p$-difluorobenzene (6), $p$-dimethoxybenzene (7) and phenanthrene (8).
Table 7.1. Optimized geometries of minima and transition states and their corresponding Gibbs free energies of 4–8 in kJ·mol⁻¹ (DFT ωB97X-D/6-31+G(d,p) in DCM).[a]

Geometries shown with methyl groups facing the reader, the H₃C–C–CH₃ bonds in the y–z plane and the five-membered ring core in the x–z plane.

<table>
<thead>
<tr>
<th></th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>4</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global minimum (C₅)[b]</td>
<td>0.0 (0.4)</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.7)</td>
<td>0.0 (1.6)</td>
<td>0.0 (0.0)</td>
</tr>
<tr>
<td>Helical minimum P/M (C₂)[b]</td>
<td>41.3 (43.9)</td>
<td>45.4 (50.5)</td>
<td>46.1 (52.2)</td>
<td>49.4 (56.3)</td>
<td>29.5 (29.5)</td>
</tr>
<tr>
<td>Transition State</td>
<td>66.9</td>
<td>96.0</td>
<td>107</td>
<td>123</td>
<td>132</td>
</tr>
<tr>
<td>THI C₂ → C₅ T at t½=1 h (°C)</td>
<td>-216</td>
<td>-121</td>
<td>-82.8</td>
<td>-46.6</td>
<td>45.5</td>
</tr>
<tr>
<td>2xTHI C₅ → C₅ T coalesc. (10 Hz) (°C)[c]</td>
<td>44.0</td>
<td>182</td>
<td>234</td>
<td>310</td>
<td>353</td>
</tr>
</tbody>
</table>

[a] Geometries shown with methyl groups facing the reader, the H₃C–C–CH₃ bonds in the y–z plane and the five-membered ring core in the x–z plane.

[b] Energies in parentheses are for the symmetrical geometries.

[c] Using $k=\pi \cdot \Delta v_0 \cdot 2^{0.5}$ to provide the rate at $T_{\text{coalescence}}$, $k$ can be used in combination with the calculated barriers to solve the Eyring equation for $T$. 

172
The redundant global minima possess $C_s$ symmetry for 6 and 8 or deviate marginally from it by twisting the rotors in 4, 5 and 7, although not detectible by NMR due to the minute barrier of isomerization ($C_s$ symmetric geometries are 0–1.6 kJ·mol$^{-1}$ higher in energy, Table 7.1). A similar phenomenon is observed for the two metastable local minima in 4–7 which deviate slightly from $C_2$ symmetry by twisting one of the methyl groups on C2 lowering the energy by 3–7 kJ·mol$^{-1}$. Again, this deviation from symmetry would not be observed by NMR since at room temperature the isomerization is very fast in which the averaged geometry is a $C_2$ symmetrical conformation. The isomerization pathway between the helical minimum and the global minimum (from now on referred to as $C_2$-x and $C_s$-x, respectively) showed increasing thermal barriers for helix inversion going from $5 < 6 < 7 < 4 < 8$ which corresponds fully with the increase in size of the aromatic
core moiety (Table 7.1). The one-hour-half-life temperature (i.e. the temperature at which the half-life is one hour, or T at t½=1 h) for THI C₂\(\rightarrow\)C₃ is a good indication of which compound would be most suitable for an NMR study. This suggests that 5–7 require very low temperatures for NMR measurements, whereas both 8 and 4 are in a temperature region where measurements can be readily performed. The two redundant meso configurations (C₄-x and C₄-x') can interconvert through C₂-x by two helix inversions (2xTHI, shown for 4 in Figure 7.4a). The barrier for this isomerization can be quantified from the approximate theoretical coalescence temperature of \(^1\)H NMR resonances (CH₃ group resonances are calculated to be separated by \(\sim\)10 Hz, *vide infra*). From the calculated coalescence temperatures (Table 7.1), compound 5 appears to be the only suitable candidate for NMR investigation. To investigate the THI and 2xTHI processes, compounds 4 and 5 as well as 9 were synthesized (Scheme 7.1). Derivative 9 was expected to have increased solubility compared with 5 and might provide insight into substituent effects for future functionalization.

Scheme 7.1. Synthesis of compounds 4, 5, and 9. Reagents and conditions: i) AlCl₃, CS₂, rt, 24 h; ii) P₄S₁₀, toluene, reflux, 18 h; iii) 1. 9-diazo-9\(^{H}\)-fluorene, toluene, 55 °C, 48 h, 2. HMPT, 120 °C, 24 h; yields C₄-4 (14% over 3 steps). R=Me: iv) K₂CO₃, RI, CH₃CN, 40 °C, overnight; v) P₄S₁₀, toluene, reflux, 18 h; vi) 9-diazo-9H-fluorene, toluene, reflux, overnight; yields C₄-5 (50% over 3 steps). R=Hexyl: iv) K₂CO₃, RI, Aliquat 336, CH₃CN, 80 °C, 24 h; iv) P₄S₁₀, Lawesson's reagent, toluene, reflux, 26 h; vi) 9-diazo-9H-fluorene, toluene/tetrahydrofuran, reflux, 20 h; yields C₄-9 (1% over three steps).
Experimental study of core-size

The synthesis of the core structure of overcrowded alkenes 4, 5, and 9 started with a double Friedel-Crafts acylation of dimethyl malonyl chloride on p-xylene afforded the bis-ketone in high yield (82%). This was transformed into the bis-thioketone by the use of phosphorous pentasulfide (97%). A Barton-Kellogg coupling of the bis-thioketone and diazofluorene followed by a desulfurization using hexamethylphosphoramide (HMPT) yielded the desired double overcrowded alkene C3-4 (17%). For compound 5, after double alkylation of indane-dione with methyl-iodide, an analogous pathway was followed where phosphorous pentasulfide was used to afford the bis-thioketone. This indanedithione underwent a Barton-Kellogg coupling with diazofluorene to give the desired product C3-5 in good overall yield (50%).[45] Double overcrowded alkene 9 caused problems in the first step, producing significant amounts of O-alkylated side-product which resulted in loss of product during purification, providing the C-alkylated product in 9% yield. The next two steps proceeded in an analogous fashion to the synthesis of 5 affording the desired C3-9.

The study of the photochemical and thermal isomerizations started with compound 4, which was irradiated with UV-light (365 nm in CH2Cl2, Figure 7.5a) and at room temperature no change was observed in the UV-vis absorption spectrum. Irradiation at −65 °C was accompanied by a bathochromic shift in the absorptionspectrum indicative of an increase in strain over the alkenes pointing to the formation of a metastable intermediate. After irradiation to the photostationary state (PSS), the sample was allowed to warm up to rt and full reversal to the original spectra was observed. Three cycles of irradiation at low temperature and heating at ambient temperatures did not reveal any signs of fatigue. During both of these processes an isosbestic point was observed at the same wavelength (459 nm), indicating the absence of side reactions during these first order reactions. 1H NMR confirmed the identity of the stable global minimum as C3-4 by the presence of three distinct methyl resonances, which is expected of a C3 symmetrical configuration of 4 but not of C2 (Figure 7.5b, H9,H10,H11; assignments in Scheme 7.1). Irradiation to PSS at low temperatures revealed the metastable state possessing a C2 symmetrical configuration, corresponding to C2-4. Following the integrals of the NMR-resonances of H1 over time at different temperatures enabled the construction of an Eyring plot (Figure 7.5c) which provided the energies of activation (Δ‡H° 63.2±1.6 kJ·mol−1, Δ‡S° −17.3±7.0 J·K−1·mol−1, Δ‡G° 68.3±0.5 kJ·mol−1, t½=1 h at T = −59.4±0.3 °C) in reasonable agreement with the calculated barrier (Δ‡H°calc. 70.3 kJ·mol−1, Δ‡S°calc −10.6 J·K−1·mol−1, Δ‡G°calc. 73.4 kJ·mol−1).
Irradiation of double alkene \( C_{2r}-5 \) in n-pentane at \(-60 ^\circ C \) did not show any shift in the UV-vis absorption spectrum (see Figure 7.6 for the UV-vis spectrum) which indicates that either \( C_{2r}-5 \) does not undergo a double bond isomerization or more likely the thermal barrier for reversion of \( C_{2}-5 \) to \( C_{2r}-5 \) is too low to observe the metastable species at that temperature. The barrier for thermal helix inversion at room temperature was calculated to be 25.6 kJ·mol\(^{-1}\) \((vide supra)\) which would allow for a lifetime of 2 ns at \(-60 ^\circ C \) and a temperature of \(-215 ^\circ C \) would be required to allow for a lifetime of 1 h. Due to the low barrier for THI, \( C_{2}-5 \) is not expected to be observed over the experimental temperature range. Photocyclization has been a problem for an overcrowded alkene without functional groups in the fjord-region,\(^{[46]}\) however, no photocyclization was observed in the case of compound 5 probably due to insufficient \( \pi \)-orbital overlap. Moreover, no other photochemistry was observed, such as described for 1,2-distyrylbenzene derivatives,\(^{[47]}\) likely due to the rigid cyclopentane. An NMR study confirms the identity of the stable global minimum \( C_{2r}-5 \) by the presence of two distinct methyl resonances, which is expected of a \( C_s \) symmetrical conformation of 5 but not of \( C_2 \).
This is corroborated by the calculated $^1$H NMR spectrum of $C_s$-$5$ (DFT giao mPW1PW91/6-311+G(2d,p) in CHCl$_3$) which strongly agrees with the experimental spectrum (Figure 7.6). Upon an increase in temperature, coalescence of the methyl resonances is observed, indicative of the two-step process in which the Me$_{\text{eq}}$ (H$^{11}$) and Me$_{\text{ax}}$ (H$^{12}$) exchange environment through a double helix inversion. The barrier determined by NMR ($\Delta^\ddagger G$ 62.5±1.0 kJ·mol$^{-1}$) is found to be lower than the computed barrier ($\Delta^\ddagger G^{\circ\text{calc}}$ 66.9 kJ·mol$^{-1}$, vide supra), probably due to a deviation in the calculated entropy term as was observed for $4$. However, it still suggests that at these temperatures the redundant isomers $C_s$-$5$ and $C_s$-$5'$ exchange through thermal processes as shown for $4$ in Figure 7.4a.

Figure 7.6. Left: Temperature dependent experimental and calculated $^1$H NMR spectra of $C_s$-$5$ and $C_s$-$9$. Right: UV-vis absorption spectra of $C_s$-$5$ (3·10$^{-5}$ M) and $C_s$-$9$ (2·10$^{-5}$ M) in DCM.

To investigate these processes in greater detail compound $9$ (Scheme 7.1) has been synthesized which is expected to show behaviour similar to $5$ but with a significantly increased solubility. Low temperature UV-vis and NMR displayed a similar absence of change under irradiation and, similar to $C_s$-$5$, presence of $C_s$ symmetry for compound $9$ was shown by NMR (Figure 7.6, see experimental section for $^{13}$C NMR resonances). An interesting pattern was observed for the $^1$H NMR resonances of the alkyl chains of $C_s$-$9$. The first methylene on each alkyl displayed a similar significant downfield shift like the methyl groups of $C_s$-$5$, but here the strongest shift was observed for the pseudo-axial methylene group (H$^{11}$) instead of the pseudo-equatorial methyl in $C_s$-$5$ (H$^{11}$). Due to their distinct chemical
environments, the two different alkyl chains follow a peculiar pattern with methylene groups of the equatorial alkyl chain exhibiting large upfield shifts. A theoretical study of several rotamers of the alkyl chains of \( \text{C}_9 \)-9 and calculation of their average \(^1\text{H}\) NMR spectrum provided a strong agreement with the experimental spectrum (\( R^2 = 0.999 \), Figure 7.6). Increasing the temperature caused coalescence of the alkyl groups most apparent for the resonances of \( \text{H}^{11–12} \) at \( \sim 2.7 \) ppm. This allowed for the determination of the barrier for thermal isomerization (\( \Delta G^\ddagger \) 59.4±1.0 kJ·mol\(^{-1}\)) which again is lower than the computed barrier (\( \Delta G_{\text{calc}}^\ddagger \) 65.7 kJ·mol\(^{-1}\), \( \Delta H_{\text{calc}}^\ddagger \) 51.7 kJ·mol\(^{-1}\)).

Conclusive information on the configuration of 9 came from X-ray crystallography. Crystals suitable for X-ray diffraction studies were grown by layered diffusion of a concentrated solution of 9 in dichloromethane on top of which volumes of, successively, pentane, heptane, and methanol were layered. The structure determination shows that there are two independent molecules in the unit cell (Figure 7.7), which have similar metrical parameters. Both have approximate \( \text{C}_s \) symmetry (meso configuration) around the core of the bis-overcrowded alkene 9. The alkyl group in the equatorial position is in both cases rotated such that the last three C-atoms of the hexyl chain are located directly above the plane of the fluorene ring, with \( C_{\text{hexyl}}-\text{fluorene} \) distances of 3.577–4.073 Å. This conformation of the equatorial alkyl group agrees with its anomalous upfield shift observed in the \(^1\text{H}\) NMR spectrum. It is unclear, however, whether this folding in the solid state is due to packing effects or represents a genuine attractive interaction.

**Figure 7.7.** Molecular structure of \( \text{C}_9 \)-9 by crystallography (only one of the two independent molecules is shown).
Conclusions on the influence of core-size

Molecular motors based on double overcrowded alkenes with a benzene moiety in the core show the potential to be significantly faster than those with a substituted benzene group. However, compounds 4–9 with \( C_\text{s} \) symmetrical stable meso states do not possess a preference for either of the two redundant geometries and therefore no preference for which of the two states undergoes a photochemical \( E\rightarrow Z \) isomerization (PEZ). The metastable helical states possess \( C_2 \) symmetry and therefore both rotors show an equal probability for undergoing a thermal helix inversion. Due to the redundancy of the stable states and the \( C_2 \) symmetry of the metastable state these rotors do not prefer a specific direction and are therefore not unidirectional.

![Diagram of molecular motors](image)

**Figure 7.8.** Rotational behaviour of 9 shown (4 and 5 behave in the same way). \( C_\text{s}-9 = C_\text{s}-9' \), produces a racemic mixture of \( C_\text{s}-(M)-9 \) and \( C_\text{s}-(P)-9 \) upon photochemical \( E\rightarrow Z \) isomerization. For \( C_\text{s}-(M)-9 \) the \( C_2 \) axis is indicated by the red dashed line and red dot on the calculated geometry on which the red arrows indicate the movement of the rotors for the two redundant thermal helix inversions.

On account of the symmetry of the stable state it is expected that a photochemical \( E\rightarrow Z \) isomerization of \( C_\text{s}-9 \) will produce a photostationary state (PSS) between \( C_\text{s}-9 \) and racemic \( C_2-9 \) (Figure 7.8). This isomerization yields a rotation of one of the rotors on \( C_\text{s}-9 \) and a rotation of one of the rotors on \( C_\text{s}-9' \), in opposite direction with respect to \( C_\text{s}-9 \). The metastable \( C_2-9 \) undergoes a thermal helix inversion of either of the rotors without preference because its \( C_2 \) symmetry as indicated in Figure 7.8, producing equal amounts of \( C_\text{s}-9 \) and \( C_\text{s}-9' \).
Figure 7.9. Structures and optimized geometries of minima and transition states of 18–22 (DFT ωB97X-D/6-31+G(d,p) in DCM). Structures shown in experimentally determined most stable isomer with numbers indicating $^1$H NMR assignments. Geometries shown with substituents facing the reader, the R–C–R bond in the y-z plane and the five-membered ring core in the x-z plane. Alkyl chains of the geometries of 18 and 20 cropped for clarity.
Over two rotational steps (PEZ–THI) the rotations sum up to a net rotation of zero due to the lack of unidirectionality. This behaviour is expected for all compounds with equally sized substituents at the bridgehead position such as 4 and 5. To achieve unidirectional rotation, a form of asymmetry has to be reintroduced like in 2 and 3, which is achieved by substituting two differently sized moieties at the indane bridgehead (carbon 2, Figure 7.3) making it a pseudo-asymmetric carbon atom.[34–38]

**Theoretical study of the substituent effect**

Several substitution patterns on the indane bridgehead were considered and investigated computationally. Certain stERICly interesting substituents such as tert-butyl (large) and hydrogen and methoxy (smaller than methyl) were disregarded on account of their synthetic demand and the expected chemically unstable nature of the resulting double overcrowded alkene. Note that for instance compound 2 (R1=H, Figure 7.2), featuring a hydrogen in a double allylic position can readily undergo 1,3-H-shift removing the pseudo-asymmetric centre. After initial calculations on multiple double overcrowded alkenes (DFT B3LYP/6-31G(d,p),) five were selected (18–22) and studied in depth (DFT ωB97X-D/6-31+G(d,p) in DCM, Figure 7.9 and Table 7.2).

**Table 7.2.** Gibbs free energies of 18–22 (corresponding structures and optimized geometries of minima and transition states see Figure 7.9. DFT ωB97X-D/6-31+G(d,p) in DCM).[a]

<table>
<thead>
<tr>
<th></th>
<th>18</th>
<th>19</th>
<th>20</th>
<th>21</th>
<th>22</th>
</tr>
</thead>
<tbody>
<tr>
<td>r (Cs)</td>
<td>0.0 (10.6)</td>
<td>0.0 (0.0)</td>
<td>12.5 (12.5)</td>
<td>6.8 (55.2)</td>
<td>0.0 (0.1)</td>
</tr>
<tr>
<td>s (Cs)</td>
<td>11.6 (19.1)</td>
<td>9.0 (9.1)</td>
<td>0.0 (15.5)</td>
<td>0.0 (0.4)</td>
<td>16.2 (17.5)</td>
</tr>
<tr>
<td>Helical minima P/M (C1)</td>
<td>48.3</td>
<td>42.0</td>
<td>39.0</td>
<td>28.6</td>
<td>37.4</td>
</tr>
<tr>
<td>TS_r P/M→r</td>
<td>67.4</td>
<td>63.5</td>
<td>66.7</td>
<td>78.9</td>
<td>54.2</td>
</tr>
<tr>
<td>TS_s P/M→s</td>
<td>74.5</td>
<td>75.6</td>
<td>71.6</td>
<td>78.8</td>
<td>67.4</td>
</tr>
</tbody>
</table>

[a] Energies in kJ·mol⁻¹. Energies in parentheses for the Cs geometries.

The three possible combinations of a methyl, an alkyl and a phenyl group (compounds 18–20) were selected because of their interesting potential balance in steric effects. Both the phenyl and the alkyl moieties have been reported to be slightly or significantly larger than the methyl group,[35,48,49] though there are instances in which the methyl group has been reported to exhibit a similar or larger steric effect.[50–53] The sterically demanding isopropyl group (compound 21) and small fluorine atom (compound 22) were selected to realize the largest difference in steric effect with respect to a methyl group. For each compound four minima were calculated, similar to 4–8 (*vide supra*), of which two were the enantiomorphic
helical metastable forms and two were found to represent the stable meso isomers with either an r or s configuration at the pseudo-asymmetric carbon atom.\textsuperscript{34–38} Note that, similar to 4–7 (vide supra, Table 7.1), the calculated minima geometries for r-18–22 and s-18–22 deviate slightly from true Cs symmetry by small twists of substituents or rotors, as can be clearly observed for s-18 and r-21. As before, this is not expected to be detectible by NMR due to the low barrier of isomerization which goes through the true Cs symmetrical geometry (energies shown in parentheses in Table 7.2).

For motors 2 and 3 it was shown that the larger substituent prefers a pseudo-axial orientation, with the rotor moieties pinching the substituent in the pseudo-equatorial orientation.\textsuperscript{33} The change from a xylene core as in 4 to a benzene core in 5 increases the pinching effect of the rotors (Table 7.1), and the preference for the larger substituent to adopt the pseudo-axial orientation is therefore expected to remain present. To exemplify, in r-18, r-19, r-21 and r-22 the pseudo-axial orientation is occupied by the methyl group. The larger substituents in 21 and 22 are the isopropyl group and the methyl group, respectively, and calculations show a preference for these groups to adopt the pseudo-axial orientation with s-21 and r-22 being lower in energy than their corresponding diastereomer (Table 7.2). The calculations presented in Table 7.2 also show a preference for r-18, r-19 and s-20 over their corresponding diastereomer, which suggest the following order for steric effects in these molecules: Me>Ph>alkyl.

The barriers for THI of metastable P/M-18–22 are calculated to be very low (19.1, 27.7, 21.6, 50.2, and 16.7 kJ·mol\(^{-1}\), respectively), which makes a PEZ–THI sequence difficult to detect by conventional UV-vis or NMR techniques. The barrier for THI for 21 might be the highest for these overcrowded alkenes, although it would still require a temperature of \(-113^\circ\text{C}\) to obtain a half-life of one hour. The calculated barrier of metastable P/M-22 to r-22 predicts it to be the fastest molecular motor to date with an expected half-life of only 109 picoseconds at room temperature. The barriers for the double inversion of s-18–22 to r-18–22 or vice versa are calculated to be measurable by coalescence in \(^1\text{H}\) NMR (62.9, 66.6, 66.7, 72.1, and 51.2 kJ·mol\(^{-1}\)) on the condition that both diastereomers are observed. The NMR spectra of r-18–22 and s-18–22 were calculated (DFT giao mPW1PW91/6-311+G(2d,p) in CHCl\(_3\), Figure 7.10) in order to be able to assign the stereoisomer of the double overcrowded alkenes which were obtained synthetically.
Experimental study of the substituent effect

The double overcrowded alkenes 18–22 were all prepared following a similar route (Scheme 7.2). In the first step a double condensation of dimethyl phthalate and symmetric ketones with the aid of sodium hydride affords the monosubstituted indandiones 10–12 in accordance with the reported literature procedures.\cite{54–56} The second alkylation using alkyl halides on the indandiones gave rise to significant amounts of O-alkylated side products. This was suppressed by the use of phase transfer reagents, such as Aliquat 336, as well as the addition of potassium fluoride immobilized on Celite to the reaction mixture. The combination of both reagents afforded the highest yield and the best C:O-alkylated product ratio of 13–16, which was finally further improved on using cesium carbonate instead of potassium carbonate. The fluorinated indandione 17 was obtained from methyl-indandione using Selectfluor.\cite{57} Bi-functionalized indandiones 13–17 were transformed to the corresponding indandithiones using phosphorous pentasulfide (or a combination with Lawesson’s reagent, see experimental section for details) of which most
products appeared to be rather stable, probably due to a lack of hydrogens at alpha carbons. Nonetheless, the indandithiones were directly submitted to double Barton-Kellogg couplings with diazofluorene to afford the desired double overcrowded alkenes 18–22 (Scheme 7.2).[57]


The ¹H NMR spectra of 18–22 were compared to the calculated spectra and were found to be in close agreement (Figure 7.10). It revealed 18–20 to be present in both isomeric forms (r- and s-isomers)[38] while 21 and 22 were only found as a single isomer. At room temperature compounds 18–20 displayed coalescence of several resonances, though at low temperature (−30 °C) the compounds entered the slow exchange region and clearly resolved ¹H NMR spectra were obtained. Using several 2D NMR techniques allowed for a complete proton and carbon assignment of the major isomers. The isomers of compound 18 were found in a 3.0 : 1.0 ratio of which the minor isomer displayed a similar effect for the hexyl chain as was observed for the pseudo-equatorially oriented hexyl chain in 9. This suggests the minor isomer to be r-18 and therefore s-18 to be the major isomer, which was confirmed by the comparison of the calculated ¹H NMR spectra to the experimental one. In this comparison, the s isomer strongly correlates to the major isomer of 18 and the r isomer correlates to the minor isomer.
The presence of coalescence was predicted by calculations, however, the asymmetry in the isomer ratio makes the use of the coalescence temperature as a tool to determine the barrier for isomerization of double helix inversion slightly unreliable. Therefore, we made use of temperature dependent 1D EXSY NMR to determine the activation parameters for the exchange process (Figure 7.11, Table 7.3, and Experimental Section for further details), which revealed a barrier of 62.0 kJ⋅mol⁻¹ for the isomerization of the major isomer s-18 to the minor isomer r-18. The isomers of compound 19 were found in a 2.0 : 1.0 ratio of which the minor isomer appeared to show five distinct signals for the phenyl substituent while the major isomer showed three signals (Figure 7.10). This suggests that the phenyl in the major isomer is free to rotate making the hydrogens ortho and meta to the indane bridgehead chemically identical, while in the minor isomer the orientation of the phenyl is fixed giving rise to five different resonances. In r-19 the phenyl is in a pseudo-equatorial orientation, placing it in between the fluorene moieties (see the geometries in Figure 7.9), whereas in s-19 it is oriented pseudo-axially giving it much more spatial freedom. This suggests the assignment of the major isomer being s-19 which corresponds fully with the calculated NMR spectra in which this assignment shows a far stronger correlation than the opposite combination does. EXSY NMR was again employed to determine the activation parameters for the double THI exchange process between the s and r isomers using the same method as was used for 18 (Table 7.3, see Experimental Section for NOESY 1D spectra
and traces), revealing a similar barrier of 63.4 kJ·mol\(^{-1}\) for the isomerization of the major isomer \(s\)-19 to the minor isomer \(r\)-19.

### Table 7.3. Gibbs free energies of 18–20 for \(r\)-\(s\) isomerization by EXSY NMR.\(^{[a]}\)

<table>
<thead>
<tr>
<th></th>
<th>18</th>
<th>19</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>(r \rightarrow s) (\Delta^\circ G^\circ / \text{kJ·mol}^{-1})</td>
<td>60.1±0.3</td>
<td>62.3±0.3</td>
<td>63.1±1.1</td>
</tr>
<tr>
<td>(s \rightarrow r) (\Delta^\circ G^\circ / \text{kJ·mol}^{-1})</td>
<td>62.0±0.3</td>
<td>63.4±0.2</td>
<td>67.3±1.1</td>
</tr>
<tr>
<td>(s - r) (\Delta G^\circ / \text{kJ·mol}^{-1})</td>
<td>1.9±0.3</td>
<td>1.0±0.1</td>
<td>4.0±0.2</td>
</tr>
</tbody>
</table>

\(^{[a]}\) Standard state: atmospheric pressure and rt (20 °C).

The isomers of compound 20 were found in an 8.9 : 1.1 ratio and for its aromatic region a nearly identical pattern is observed as was for 19, while for the aliphatic region a similar effect is seen in the exchange of a methyl group to an alkyl as was for 5 and 9 (Figure 7.10). In both 5 and 19 the pseudo-axial methyl group is shifted upfield with respect to the pseudo-equatorially oriented methyl group, while in both 9 and 20 the first methylene on the pseudo-axial alkyl group shows a downfield shift with respect to the pseudo-equatorial position. Similar to the observations for compound 9, the alkyl chains in the pseudo-equatorial orientation in \(r\)-18 and \(s\)-20 prefer conformations in which the chain is folded back onto the rotors over an anti-conformation along the entire chain as indicated by calculations and \(^1\)H NMR spectroscopy which shows the hydrogens of the fourth methylene group to exhibit the strongest upfield shift. With again a good correlation of the calculated spectra to the experimental \(^1\)H NMR spectrum, the major isomer is assigned as \(s\)-20 and the minor as \(r\)-20. EXSY NMR revealed a barrier of 67.3 kJ·mol\(^{-1}\) for the double THI exchange process going from the major isomer \(s\)-20 to the minor isomer \(r\)-20 (Table 7.3, see Experimental Section for NOESY 1D spectra and traces).

Considering the performance of overcrowded alkenes 18–20 as molecular motors, one should note that these systems feature reduced unidirectionality due to the presence of both isomers. Nonetheless, they still maintain preferential directionality of their rotary motion. For example, in 20 89% rotates in one direction (counter clockwise when observed from the left in Figure 7.9) while 11% rotates in the opposite direction resulting in a reduced unidirectional yield of 78% (determined from the \(r\)-20 : \(s\)-20 ratio at rt, \(\text{vide supra}\)). This is not an issue in 21 and 22 since they were obtained as single isomers according to \(^1\)H NMR (Figure 7.10, note that the two resonances in the aliphatic region of 22 constitute a doublet due to F-CH\(_3\) coupling, belonging to a single isomer). The size difference predicted \(s\)-21 and \(r\)-22 to be the most stable isomers with the larger isopropyl in the pseudo-axial orientation and the smaller fluorine in the equatorial orientation, respectively.
The calculated spectra were fitted to the experimental spectra which proved the expected isomers to agree the best to the experimental spectra (Figure 7.10).\textsuperscript{[58]}  

\textbf{Figure 7.12.} Molecular structures of \textit{s}-19 and \textit{s}-20 by crystallography.  

To obtain additional information on the structure and stereochemistry of the double overcrowded alkenes, crystals suitable for X-ray diffraction analysis were grown by layered diffusion of concentrated solutions of 19, 20, and 22 in dichloromethane on top of which volumes of, successively, pentane, heptane, and methanol were layered (from 18 and 21 no suitable crystals were obtained). The structure determination confirmed the expected meso configuration of the bis-overcrowded alkenes, moreover, 19 and 20 were both only found with an \textit{s} configuration at the pseudo-asymmetric carbon atom (Figure 7.12). While this clearly shows a preference for both compounds to crystallize in a single configuration, it should not be used as independent proof for the assignment of the major isomer in solution since either isomer could have possessed a stronger tendency towards crystallization. However, NMR indicates only a single isomer of 22 to be present, and its X-ray analysis confirmed the computational prediction and NMR assignment, by showing 22 to possess an \textit{r} configuration on the pseudo-asymmetric carbon atom (Figure 7.13).  

\textbf{Figure 7.13.} Molecular structure of \textit{r}-22 by crystallography.
Conclusions on the influence of substituent-size

The combined data shows the following order for steric effects of the substituents at the indane bridgehead in 18–22: i-Pr>Ph>alkyl>Me>F. However, just based on the data for 19 and 20 (Table 7.3) one might expect the methyl group to be larger than the alkyl group \((s\rightarrow r \Delta G^\circ\) being smaller for 19 than for 20) highlighting the very subtle interplay of these steric moieties with the rest of the molecule. It is also clear that this deviates from the calculated order, which predicted the steric effect of the methyl group to be larger than those of the phenyl and alkyl groups (\textit{vide supra}). The calculated barriers for the double THI exchange process of \(s\text{-}18\rightarrow20\) to \(r\text{-}18\rightarrow20\) agree well with the experimental barriers (\(\Delta \Delta^\dagger G^\circ\) 0.9, 3.2, and 4.3 kJ·mol\(^{-1}\), Table 7.2 and Table 7.3) while the agreement in the opposite process of \(r\text{-}18\rightarrow20\) to \(s\text{-}18\rightarrow20\) is much weaker (\(\Delta \Delta^\dagger G^\circ\) 14.4, 13.3, and 4.0 kJ·mol\(^{-1}\), Table 7.2 and Table 7.3). To improve the correspondence between theory and experiment it might be necessary to employ different functionals, add diffuse functions or increase the basis set. The combined experimental data also confirms that in the third generation molecular motors \(s\text{-}21\) and \(r\text{-}22\) opposite directions of rotation take place while both possess a \(\geq95\%\) unidirectional yield (since the opposite diastereomer is not observed in \(^1\)H NMR). As expected, no changes are observed in the NMR resonances at high or low temperature, or after irradiation at room or low temperature. This is due to the very low barrier for THI in combination with the symmetry of the rotors. In order to prove that these fast third generation molecular motors are able to undergo rotation of the fluorene units under photoirradiation, asymmetry has to be introduced in the rotor units.

Rotation of an ultrafast 3\textsuperscript{rd} generation motor

To unequivocally demonstrate the unidirectional rotary motion, methoxy substituents were introduced in the rotor parts of the ultrafast motor with a benzene moiety as its core. Using methoxy-diazofluorene and the indandithione of 17 in a Barton-Kellogg coupling (as in Scheme 7.2), Peter Štacko afforded the desired desymmetrized double overcrowded alkene 23 as a statistical mixture of the four isomers (isomers shown in Scheme 7.3).\(^{[57]}\) This mixture was subjected to supercritical fluid chromatography (SFC) (45% 2-propanol in CO\(_2\), Chiralpak ID at 3.5 mL·min\(^{-1}\), 40 °C, 160 bar) which allowed the isolation of each isomer (Figure 7.14, isomers sequentially numbered and corresponding to the configurations numbered in Scheme 7.3).
The four isomers are indistinguishable by UV-vis as can be seen from their nearly identical UV-vis absorption spectra (Figure 7.14). However, $^{19}$F and $^1$H NMR allowed for the assignment of the individual isomers where the enantiomers of 23 (isomers 1 and 3) displayed identical NMR spectra and were assigned based on their retention time in analogy to 3.$^{[33]}$ Irradiation of an isolated isomer of 23 is expected to allow it to undergo a photochemical $E-Z$ isomerization to be directly followed by a thermal helix inversion. This produces the two connected isomers according to Scheme 7.3 in an approximate 50:50 ratio, which go on to produce both the starting isomer as well as the final isomer connected to those isomers again in a 50:50 ratio. Finally, this last isomer is formed but at the same time undergoes isomerization producing the two intermediate isomers again. The rates presented in the kinetic scheme (Scheme 7.3) are formulated in rate equations which were solved using matrix methods$^{[59]}$ providing the following integrated rate laws (see Experimental Section for derivation and expanded formulas):

$$\begin{align*}
[(R,Z,E)-23]_t &= [(R,Z,E)-23]_e + A_1 e^{-k_v t} + A_2 e^{-k_w t} + A_3 e^{(-k_1-k_2)t} \\
[(r;E,E)-23]_t &= [(r;E,E)-23]_e + B_1 e^{-k_v t} + B_2 e^{-k_w t} \\
[(S,Z,E)-23]_t &= [(S,Z,E)-23]_e + C_1 e^{-k_v t} + C_2 e^{-k_w t} + C_3 e^{(-k_1-k_2)t} \\
[(r;Z,Z)-23]_t &= [(r;Z,Z)-23]_e + D_1 e^{-k_v t} + D_2 e^{-k_w t}
\end{align*}$$
where $[X]_e$ describes the final concentration, $k_V$ and $k_W$ are compiled rate factors including $k_1-k_4$, $A_X$–$D_x$ are compiled pre-exponential factors (including $[X]_0$ and $k_1$–$k_4$) and $t$ is time.

Concentrated solutions in CH$_2$Cl$_2$ of the individual isomers 1–4 of 23 purged with argon were placed in the autosampler of the SFC machine, in front of which a UV-lamp (365 nm) was positioned. A high concentration was used to allow the sampling to be only 4 µL, to keep the change in total volume as small as possible, and simultaneously ensuring the process lasts long enough for the collection of sufficient data. While the samples were being irradiated, aliquots for SFC analysis were taken at regular intervals, the chromatograms were integrated, and the normalized integrals were plotted against time (Figure 7.15).
In Figure 7.15 the black curves are equations 1–4 fitted against the experimental data points by least squares analysis in a single fit providing a small residual error and a high coefficient of determination ($R^2 = 0.997$) (see Experimental Section for details of fitting). The observed behaviour agrees with the proposed rate laws and proves the hypothesized connectivity as displayed in the rotational cycle in Scheme 7.3. Starting from any isomer of 23 there is an exponential decay of the initial isomer coupled with exponential formation of the two isomers directly connected to it, while the isomer across from the initial isomer experiences a delayed formation resulting in S-shaped curves (Figure 7.15). Starting from the meso isomers of 23 (isomers 2 and 4) there is no preference for either of the connected isomers, expressed in nearly identical formation curves of the two enantiomeric isomers of 23 (isomers 1 and 3), while starting from one of the enantiomers, a small preference appears to exist for the formation of isomer 2 over isomer 4. This is expressed in a deviation of the final ratios from a simple statistical 1:1:1:1 ratio to a ratio of 0.99 : 1.11 : 0.99 : 0.90 (for isomer 1:2:3:4) starting from any of the isomers. Isomers 1 and 3 of 23 are expected to behave identically on account of their enantiomeric relationship and therefore result in identical final ratios.

All experiments result in isomer 2 [(r,E,E)-23] as the major isomer and isomer 4 [(r,Z,Z)-23] as the minor isomer (this relationship is confirmed by an $^1$H NMR study, see Experimental Section for details). The origin of this behaviour is two-fold: (i) enantiomeric isomers 1 and 3 both slightly favour rotation of one rotor over the other by 2% (normalized rates $k_1=1.02$ and $k_2=0.98$), likely due to isomers 1 and 3 being chiral and therefore possessing an asymmetric potential energy surface in the excited state, and (ii) the rate of rotation is 8% smaller for isomer 2 with respect to isomer 4 (normalized rates $k_3=0.91$ and $k_4=1.08$) leading to an
accumulation of isomer 2, which could be caused by a higher quantum yield of isomer 4 with respect to isomer 2. Nonetheless, no matter what the origin of this small deviation from statistical is, it would not play a role in the third generation motors 21 and 22 with symmetric rotors. With the use of compound 23 it is shown that, even though the thermal step is too fast to be measured in a conventional way, these motors still undergo light-driven rotation and studies using ultrafast spectroscopy to identify the metastable states and quantify the barriers involved are currently ongoing.

**Conclusion**

We have demonstrated the thermal and photochemical rotational behaviour of a series of third generation light-driven molecular motors. The steric hindrance around the core proved to be decisive in the tuning of the potential speed of double overcrowded alkenes. Computational prediction of $^1$H NMR spectra was used to support the assignment of experimental spectra as well as the relative configurations. The presence of a pseudo-asymmetric centre has been shown to be essential to achieve unidirectional rotation. Careful modification of the steric bulk of the substituents on the bridgehead allows for the precise control over the direction of rotation, as clearly illustrated by the opposite directionality with respect to the methyl substituent taking place in motors 21 and 22. Motor 22 has the potential to be the fastest unidirectional motor based on overcrowded alkenes to date, and its desymmetrization into motor 23 allowed for the visualization of the equal rate of rotation of the two rotor units, which perfectly followed the predicted model for their rotational behaviour. This detailed study on elucidating key parameters for control of rotary motion of third generation molecular motors is essential for the design of more-advanced molecular machines based on light-driven rotary motion.

**Acknowledgements**

Peter Štacko, Diederik Roke, Alexander Wolters, Henrieke Heideman and Johan Visser all contributed to the synthesis and characterization of third generation molecular motors. Pieter van der Meulen aided with NMR spectroscopy and kinetics of the EXSY experiments. X-Ray spectroscopy was performed by Mu-Chieh Chang and Edwin Otten. Thom Pijper is thanked for fruitful discussions regarding calculations and Thomas Neubauer for his help with the SFC spectrometer.
Experimental Section

General remarks

Reagents were purchased from Aldrich, Merck or Fluka and were used as provided unless otherwise stated. The solvents were distilled and dried, if necessary, by standard methods. Column chromatography was performed on silica gel (Grace Reveileris or Merck type 9385 230–400 mesh) using positive pressure, TLC: silica gel 60, Merck, 0.25 mm. High Resolution Mass spectra (HRMS) were recorded on an LTQ Orbitrap XL. NMR spectra were obtained using a Varian Gemini-200 (1'H: 200 MHz, 13C: 50 MHz), a Varian Mercury Plus (1'H: 400 MHz, 19F: 376 MHz, 13C: 100 MHz), a Varian Unity Plus (1'H: 500 MHz, 19F: 470 MHz, 13C: 125 MHz) or a Varian Innova (1'H: 600 MHz, 19F: 564 MHz) in CDCl3 or CD2Cl2. Chemical shifts are reported in δ units (ppm) relative to the residual deuterated solvent signal of CDCl3 (1'H NMR, δ 7.26 ppm; 13C NMR, δ 77.0 ppm) or CD2Cl2 (1'H NMR, δ 5.32 ppm; 13C NMR, δ 54.0 ppm). The splitting patterns are designated as follows: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), td (triplet of doublets), qt (quartet of triplets), m (multiplet) and br (broad). SFC was performed on a Thar SFC system consisting of a fluid delivery module (FDM10-1), an autosampler (a modified Alias 840), a semi-prep column oven, PDA detector, a back pressure regulator (ABPR20), heat-exchanger, and a fraction collector (modified Thar SFC-FC). UV-vis absorption spectra were measured on a Jasco V-630 or a Hewlett-Packard 8453 spectrometer. CD spectra were measured on a Jasco J-815 CD spectrometer. Dichloromethane used for spectroscopic studies was of spectroscopic grade (UVASOL Merck). Irradiations were performed using a spectroline ENB-280C/FE lamp (λmax = 365 nm), a Lot-Oriel 75 W ozone free Xenon lamp coupled to a Zolix 150 monochromator with slit widths set to 20 microns (monochromated light was focused on the sample using a 5 cm diameter lens (F 15 mm, Thorlabs)), or an LED (5 W, 365 nm, 10 nm width at half-height), mounted in a modified Nalorac Z-Spec probe in the Varian Innova-600 NMR.

Synthesis

2,2,4,7-tetramethyl-1H-indene-1,3(2H)-dione (S1). A 100 mL three necked flask was dried and put under nitrogen atmosphere and charged with 2,2-dimethylmalonyl dichloride[60] (1.0 g, 6.25 mmol), p-xylene (2 mL, 16 mmol) and 15 mL CS2. The mixture was cooled to 0 °C and AlCl3 (1.9 g, 13.4 mmol) was added carefully. The reaction mixture was stirred for 17 h at room temperature followed by quenching with 200 g ice. The organic layer was separated and the water layer was extracted four times with 100 mL CH2Cl2. The combined organic layers were dried with MgSO4 and filtrated. The solvent was removed under reduced pressure. The product was purified by column chromatography over silica using pentane and CH2Cl2 as eluent. Pure product was obtained as a yellow solid (1.07 g, 82%). M.p. 98–102 °C; 1H-NMR (200 MHz, CDCl3) δ: 7.44 (s, 2H), 2.70 (s, 6H), 1.26 (s, 6H); 13C-NMR (200 MHz, CDCl3) δ: 206.0 (2C), 137.8 (2C), 137.4 (2CH), 136.4 (2C), 49.9 (1C), 20.5 (2CH3), 18.5 (2CH3); HRMS (APCI+): calcd for C13H15O2+(M + H+) 203.1072 found 203.1065.
2,2,4,7-tetramethyl-1H-indene-1,3(2H)-dithione (S2). A solution of compound S1 (1.12 g, 5.5 mmol) in 10 mL dry toluene was stirred and heated to 40 °C. P2S5 (3.30 g, 7.4 mmol) was added and the reaction mixture was heated to reflux for 18 h. After cooling to room temperature the mixture was concentrated in vacuo and directly subjected to column chromatography on silica gel (pentane). Pure product was obtained as a blue solid (1.03 g, 97%). M.p. 65–68 °C; 1H-NMR (200 MHz, CDCl3) δ: 7.49 (s, 2H), 2.82 (s, 6H), 1.43 (s, 6H); 13C-NMR (200 MHz, CDCl3) δ: 248.5 (2C), 143.3 (2C) 137.5 (2CH), 137.5 (2C), 71.7 (1C), 28.9 (2CH3), 22.4 (2CH3); HRMS (APCI-Ion trap): calc for C13H15S2+[M + H]+ 235.0610 found 235.0610.

9,9’-(2,2,4,7-tetramethyl-1H-indene-1,3(2H)-diylidene)bis(9H-fluorene) (4). A 100 mL three necked flask was charged with a solution of compound S2 (408 mg, 1.7 mmol) in 10 mL dry toluene and heated to 55 °C under an atmosphere of nitrogen. A solution of 9-diazo-9H-fluorenone[52] (1.63 g, 8.5 mmol) in 20 mL dry toluene, was added over 20 h after which the reaction mixture was stirred for another 28 h. It was cooled to room temperature and concentrated in vacuo. The mixture was run over a plug of silica (pentane/CH2Cl2; 2%) and the resulting dark-orange solution was concentrated in vacuo and dissolved in 2 mL hexamethylphosphanetriamine. The solution was heated at 120 °C and stirred for 24 h under an argon atmosphere. The product was purified by column chromatography over silicagel (pentane / CH2Cl2 gradient). Further purification by recrystallization from methanol afforded the product as a red solid (154 mg, 17%). M.p. 308–309 °C; 1H-NMR (500 MHz, CD2Cl2) δ: 7.85 (m, 2H), 7.69 (m, 2H), 7.64 (d, J = 7.5 Hz, 2H), 7.41 (d, J = 7.9 Hz, 2H), 7.25 (m, 4H), 7.17 (td, J1 = 7.5 Hz, J2 = 0.9 Hz, 2H), 7.15 (s, 2H), 7.02 (td, J1 = 8.0 Hz, J2 = 1.1 Hz, 2H), 2.08 (s, 3H), 2.04 (s, 6H), 1.93 (s, 3H); 13C-NMR (500 MHz, CD2Cl2) δ: 161.3 (2C), 149.2 (2C), 143.3 (2C), 143.0 (2C), 141.4 (2C), 140.1 (2C), 138.1 (2C), 136.6 (2C), 135.4 (2CH), 129.9 (2CH), 129.7 (4CH), 129.5 (2CH), 128.7 (2CH), 125.4 (2CH), 122.3 (2CH), 121.8 (2CH), 68.6 (1C), 27.6 (1CH3), 27.4 (1CH3), 24.4 (2CH3); HRMS (APCI-Ion trap): calc for C39H31+[M + H]+ 499.2426 found 499.2410; Anal calc. C 93.94, H 6.06, found C 86.72, H 5.80.

2,2-dimethyl-2H-indene-1,3-dione (S3). To a solution of indane-1,3-dione (212.7 mg, 1.46 mmol) in acetonitrile (10 mL) 5 equiv of potassium carbonate (838 mg) were added, after which the solution turned dark red, due to the formation enolate ion of indane-1,3-dione formation. 3 equiv of iodomethane (622 mg) were added dropwise which allowed the solution to turn yellow again. The mixture was stirred overnight in a sealed flask at room temperature. The volatiles were removed under vacuum and the resulting solid was redissolved in dichloromethane (10 mL) and filtered over a glass filter (type 4). The volatiles were removed from the filtrate. Short white needles, yield: 241 mg, 95%. 1H NMR (200 MHz, CDCl3) δ: 7.91 (ddd, 2H), 7.80 (ddd, 2H), 1.22 (s, 6H); 13C NMR (50 MHz, CDCl3) δ: 205.5, 142.7, 135.8, 123.1, 50.0, 21.1.
2,2-dimethyl-2H-indene-1,3-dithione (S4). A solution of compound S3 (250 mg, 1.44 mmol) in toluene (10 mL) was warmed to 40 °C while stirring after which 2 equiv of P4S10 (0.6 g, 2.7 mmol) were added and the mixture was then heated to reflux for 18 h. The yellow suspension turns red after 1 h and slowly turns more towards blue. The reaction can be followed with TLC, but the fastest running spot (strong blue/green color) hydrolyses within several minutes in air. The resulting dark blue suspension was cooled to rt and stirring was stopped. A yellow/white precipitate was formed at the bottom. The dark blue solution was taken from the top and was directly subjected to a short SiO2 column with toluene as eluent. Collecting of the green fraction, subsequent removal of volatiles under vacuum retrieved a turquoise compound as a result. Preferably for the use in the next step the green fraction was only concentrated under vacuum. 1H NMR (300 MHz, CDCl3) δ 8.03 (ddd, 2H), 7.78 (ddd, 2H), 1.48 (s, 6H); 13C NMR (50 MHz, CDCl3) δ 245.2, 145.6, 135.6, 123.9, 70.4, 27.9.

9-(3-(9H-fluoren-9-ylidene)-2,2-dimethyl-2,3-dihydroinden-1-ylidene)-9H-fluorene (5). A solution of 9-diazofluorene (408 mg, 2.0 mmol) and S4 (102 mg, 0.5 mmol) was heated to reflux in toluene under nitrogen. Immediately after addition of 9-diazofluorene a yellow vapour was observed and the solution turns red. The reaction was kept refluxing overnight and the mixture was allowed to cooled to room temperature. After concentrating the mixture under vacuum, it was subjected to column chromatography (SiO2, pentane/toluene 20:1) gave 2 major fractions. Product 5 (orange) with Rf=0.40 and bisfluorenylidene (red) with Rf=0.70. No mono coupled product or episulfides were found in the crude mixture. Yellow solid, yield: 153 mg, 65%. 1H NMR (300 MHz, CDCl3, 20 °C) δ: 8.40 (d, J=7.6 Hz, 2H), 8.19 (m, 2H) 8.10 (m, 2H), 7.80 (m, 2H), 7.75 (d, J=7.6 Hz, 2H), 7.37 (m, 4H), 7.30 (t, J=7.6 Hz, 2H), 7.23 (m, 2H), 7.14 (t, 7.6 Hz, 2H), 2.29 (br s, 3H), 2.08 (br s, 3H); 13C NMR (50 MHz, CDCl3) δ: 159.4, 145.9, 141.0, 140.1, 139.1, 131.9, 130.1, 129.3, 127.9, 127.6, 127.2, 126.6, 126.4, 124.4, 112.0, 119.6, 110.0, 59.9, 24.7. Anal. calcd. for C37H26: C, 94.43; H, 5.57, found: C, 94.41; H, 5.59. m/z (EI, %) = 470 (M+, 100), 455 (M-CH3, 99.9).

2,2-bis hexyl-1,3-indandione (S5). A mixture of 97% 1,3-indandione (3.09 g, 20.5 mmol), 1-bromohexane (7.12 g, 43.1 mmol 2.1 equiv) methyltrioctylammonium chloride (0.15 g, 1–2 mol%), acetonitrile (0.1 M, 205 mL) and an excess of K2CO3 (28.4 g, 205.8 mmol 10 equiv) was heated to 80 °C for 24 h under nitrogen atmosphere. The mixture was extracted with ether. The organic layer was washed with 1 M aqueous NaOH (100 mL) 5x, 1 M aqueous HCl (100 mL), brine (100 mL), H2O (100 mL) and dried over MgSO4. The solvent was removed in vacuo and the crude product was purified by column chromatography (SiO2, pentane: CH2Cl2 gradient from pure pentane to 50% CH2Cl2) yielding 1 (=0.57 g, 9%) as a white solid. 1H NMR (200 MHz, CDCl3) δ: 7.97 (m, 2H), 7.85 (m, 2H), 1.79 (m, 4H), 1.31–0.87 (m, 16H), 0.79 (t, J=6.6 Hz, 6H); 13C NMR (75 MHz, CDCl3) δ: 205.3, 142.6, 135.6, 122.9, 58.7, 35.6, 31.4, 29.7, 25.8, 22.5, 14.0; HRMS (ESI-pos): calcd for C23H31O2+ [M + H]+ 315.23186 found 315.23223.
2,2-dihexyl-1H-indene-1,3-2H-dithione (S6). A mixture of 2,2-bis hexyl-1,3-indandione (S5) (0.48 g, 1.52 mmol), P4S10 (2.84 g, 12.8 mmol 8 equiv), Lawesson’s reagent (2.58 g, 6.38 mmol 4 equiv) and dry toluene (0.05 M, 35 mL) was heated to 110 °C for 26 h under nitrogen atmosphere. The solvent was removed in vacuo. The deep blue mixture was dissolved in CH2Cl2 and filtered over silica to remove the excess of Lawesson’s reagent and P2S5. The crude product was purified by column chromatography (SiO2, pentane: CH2Cl2 (5 % CH2Cl2)) yielding S6 (0.23 g, 43%) as a deep blue oil. 1H NMR (200 MHz, CDCl3) δ: 8.07–7.96 (m, 2H), 7.83–7.71 (m, 2H), 2.15–1.98 (m, 4H), 1.23–0.91 (m, 12H), 0.86–0.59 (m, 10H); 13C NMR (101 MHz, CDCl3) δ: 246.5, 148.0, 135.4, 123.1, 79.2, 42.6, 31.3, 29.6, 23.6, 22.6, 14.1.

9,9’-(2,2-dihexyl-1H-indene-1,3-2H-diylidene)bis(9H-fluorene) (9). A mixture of 2,2-dihexyl-1H-indene-1,3-2H-dithione (S6) (220 mg, 0.63 mmol), 7.5 mL dry toluene and 7.5 mL distilled THF was heated to 130 °C under nitrogen atmosphere. A mixture of 9-diazofluorene (1.27 g, 6.61 mmol, 10 equiv) 7.5 mL toluene and 7.5 mL THF was added over 16 h (2 equiv 9-diazofluorene was added at once and the other 8 equiv was added over time). The mixture was stirred and heated for another 4 h. The solvent was removed in vacuo and the crude product was purified three times by column chromatography (SiO2, pentane: CH2Cl2 gradient from pure pentane to 100% CH2Cl2) and subsequently washed three times with hot acetonitrile and filtered to provide 9 as an orange solid (98.9 mg, 26%). M.p. 196.3–198.2 °C (deg); 1H NMR (500 MHz, CDCl3, −30 °C) δ: 8.42 (d, J = 8.0 Hz, 2H), 8.13 (dd, J = 6.0, 3.2 Hz, 2H), 8.03 (d, J = 7.2 Hz, 2H), 7.83–7.77 (m, 2H), 7.74 (d, J = 7.5 Hz, 2H), 7.35 (p, J = 7.2 Hz, 4H), 7.28 (t, J = 7.3 Hz, 2H), 7.17 (dd, J = 6.0, 3.1 Hz, 2H), 7.12 (t, J = 7.4 Hz, 2H), 2.80–2.70 (m, 2H), 2.70–2.61 (m, 2H), 1.12–1.04 (m, 2H), 1.04–0.99 (m, 2H), 0.97 (dd, J = 9.3, 5.1 Hz, 2H), 0.80 (d, J = 7.8 Hz, 2H), 0.74 (dd, J = 14.8, 7.6 Hz, 2H), 0.69 (t, J = 7.1 Hz, 3H), 0.56 (p, J = 7.0 Hz, 2H), 0.48 (dd, J = 15.0, 7.3 Hz, 2H), 0.40–0.28 (m, 2H), 0.23 (t, J = 7.2 Hz, 3H); 13C NMR (126 MHz, CDCl3) δ: 156.1, 148.0, 140.5, 139.5, 138.7, 137.2, 132.3, 129.2, 128.9, 127.4, 127.2, 126.8, 126.4, 126.2, 124.1, 119.8, 119.4, 69.5, 38.7, 35.2, 31.6, 30.4, 29.9, 29.0, 26.4, 26.1, 22.9, 22.1, 14.3, 14.1; HRMS (ESI-pos): calcd for C47H46+[M + H]+ 610.35940 found 610.35908.

2-methyl-1H-indene-1,3(2H)-dione (10).[55] A solution of pentan-3-one (20.5 g, 238 mmol) and dimethyl phthalate (50.0 g, 257 mmol) in dry toluene (100 mL) was added to a suspension of sodium hydride on oil (12.0 g, 50 wt%, 250 mmol) in dry toluene (150 mL) and heated at reflux overnight. The residue was filtered, washed with toluene (100 mL), dried in vacuo and dissolved in water. The aqueous layer was acidified dropwise with 35% HCl. The residue was filtered and dried in vacuo to give the pure product as an light orange solid (24 g, 63%); 1H NMR (400 MHz, CDCl3) δ: 7.98 (dd, J = 5.7, 3.0 Hz, 2H), 7.85 (dd, J = 5.7, 3.1 Hz, 2H), 3.05 (q, J = 7.7 Hz, 1H), 1.42 (d, J = 7.7 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ: 201.2, 142.1, 135.8, 123.4, 48.9, 10.6; HRMS (APCI-Ion trap); calcd for C10H10O2 [M + H] + 161.0603 found 161.0807.
2-phenyl-1H-indene-1,3(2H)-dione (11).

A solution of 1,3-diphenylpropan-2-one (10.1 g, 48.1 mmol) in dry toluene (100 mL) was added to a suspension of dimethyl phthalate (7.70 mL, 47.2 mmol) and sodium hydride on oil (2.00 g, 60 wt%, 50.0 mmol) in dry toluene (350 mL) and heated at reflux overnight. The residue was filtered, washed with toluene (200 mL) and dissolved in water. The aqueous layer was washed with CH$_2$Cl$_2$ (200 mL) and ether (200 mL) and acidified dropwise with 35% HCl. The residue was filtered, washed with 1 M HCl (200 mL) and water (200 mL), dissolved in CHCl$_3$ and dried over MgSO$_4$. The volatiles were evaporated under reduced pressure, 90% ethanol (~100 mL) was added, the mixture was heated to reflux and filtered hot. The residue provided the pure product as a white solid (3.2 g, 31%). M.p. 147.9–150.3 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ: 8.05 (m, 2H), 7.89 (m, 2H), 7.33 (m, 3H), 7.18 (m, 2H), 4.26 (s, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ: 198.4, 142.8, 136.1, 133.3, 129.2, 128.9, 128.0, 123.9, 60.0; HRMS (ESI-pos): calcd for C$_{15}$H$_{11}$O$_2$+ [M + H]$^+$ 223.07536 found 223.07545.

2-isopropyl-1H-indene-1,3(2H)-dione (12).

A solution of 2,6-dimethylheptan-4-one (4.50 g, 31.6 mmol) in dry toluene (50 mL) was added to a suspension of dimethyl phthalate (5.0 mL, 31 mmol) and sodium hydride on oil (1.30 g, 60 wt%, 32.5 mmol) in dry toluene (250 mL) and heated at reflux overnight. The residue was filtered, washed with toluene (100 mL) and dissolved in water. The aqueous layer was washed with CH$_2$Cl$_2$ (100 mL) and ether (100 mL) and acidified dropwise with 35% HCl. The residue was filtered, washed with 1 M HCl (100 mL) and water (100 mL), dissolved in CHCl$_3$ and dried over MgSO$_4$. The volatiles were evaporated under reduced pressure while the residue was adsorbed on celite and purified by column chromatography on silica gel (gradient pentane/CH$_2$Cl$_2$; 10–20%) to give the pure product as an off-white wax (5.2 g, 87%). $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.96 (app. dd, $J$ = 5.6, 3.1 Hz, 2H), 7.83 (app. dd, $J$ = 5.7, 3.1 Hz, 2H), 2.89 (d, $J$ = 3.8 Hz, 1H), 2.58 (pd, $J$ = 7.0, 3.9 Hz, 1H), 1.07 (d, $J$ = 6.9 Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ: 201.3, 143.0, 135.7, 123.0, 58.8, 29.5, 19.7; HRMS (APCI-Ion trap): calcd for C$_{12}$H$_{12}$FO$_2$+ [M + H]$^+$ 207.0816 found 207.0815.

2-hexyl-2-methyl-1H-indene-1,3(2H)-dione (13).

Under an atmosphere of nitrogen acetonitrile (50 mL) was added to a mixture of diketone 10 (0.80 g, 5.00 mmol), cesium carbonate (1.95 g, 6.00 mmol), $N$-methyl-$N$-$N$,$N$-trioctyloctan-1-amonium chloride (0.2 mL, 0.45 mmol) and potassium fluoride on celite (0.16 g, 50 wt%, 0.45 mmol). After stirring for 10 min the temperature was raised to 80 °C and iodohexane (0.81 mL, 5.5 mmol) was added over 5 min. The mixture was heated at reflux overnight after which it was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The residue was partitioned between diethyl ether (100 mL) and water (100 mL). The organic layer was separated, washed with 1 M NaOH (2 x 100 mL), 1 M HCl (100 mL), sat. NaHCO$_3$ (100 mL), water (100 mL), brine (100 mL) and dried over MgSO$_4$. The volatiles were evaporated under reduced pressure while the residue was adsorbed on celite and purified by column chromatography on silica gel (gradient pentane/CH$_2$Cl$_2$; 0 – 30%) yielding the product as a pale yellow oil (0.49 g, 40%). $^1$H NMR (400 MHz, CHCl$_3$) δ: 8.01–7.95 (m, 2H), 7.88–7.82 (m, 2H), 1.85–1.77 (m, 2H),
1.26 (s, 3H), 1.23–1.08 (m, 6H), 1.07–0.97 (m, 2H), 0.80 (t, \( J = 6.8 \text{ Hz} \), 3H); \(^{13}\text{C-NMR}\) (100 MHz, CHCl\(_3\)) \( \delta \): 204.9, 141.4, 135.7, 123.3, 54.1, 35.8, 31.3, 29.6, 25.0, 22.4, 19.8, 13.9; HRMS (ESI-pos, \( m/z \)) calcd for C\(_{16}\)H\(_{21}\)O\(_2\), [M + H]\(^+\) 245.15361 found: 245.15363.

2-methyl-2-phenyl-1\(\text{H}\)-indene-1,3(2\(\text{H}\))-dione (14). Under an atmosphere of nitrogen acetonitrile (60 mL) was added to a mixture of diketone 11 (1.31 g, 5.89 mmol), potassium carbonate (0.98 g, 7.07 mmol), \( N,N,N,N\)-trioctyloctan-1-amonium chloride (0.21 g, 0.53 mmol) and potassium fluoride on celite (0.19 g, 50 wt%, 0.53 mmol). After stirring for 10 min the temperature was raised to 80 °C and iodomethane (0.41 mL, 6.58 mmol) was added over 5 min. The mixture was heated at reflux for 3 h after which it was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The residue was partitioned between diethyl ether (100 mL) and water (100 mL). The organic layer was separated, washed with 1 M NaOH (2 x 100 mL), 1M HCl (100 mL), sat. NaHCO\(_3\) (100 mL), water (100 mL), brine (100 mL) and dried over MgSO\(_4\). The volatiles were evaporated under reduced pressure while the residue was adsorbed on celite and purified by column chromatography on silica gel (gradient pentane/CH\(_2\)Cl\(_2\); 0–30%) yielding the product as a pale yellow solid (1.15 g, 83%). Mp: 158.0–159.5 °C; \(^{1}H\)-NMR (400 MHz, CDCl\(_3\)) \( \delta \): 8.08–8.02 (m, 2H), 7.91–7.85 (m, 2H), 7.37–7.22 (m, 5H), 1.72 (s, 3H); \(^{13}\text{C-NMR}\) (100 MHz, CDCl\(_3\)) \( \delta \): 201.9, 141.3, 137.7, 136.0, 128.8, 127.6, 126.7, 123.9, 57.9, 20.0; HRMS (ESI-pos, \( m/z \)) calcd for C\(_{16}\)H\(_{13}\)O\(_2\), [M + H]\(^+\) 237.09101 found: 237.09095

2-decyl-2-phenyl-1\(\text{H}\)-indene-1,3(2\(\text{H}\))-dione (15). Under an atmosphere of nitrogen acetonitrile (80 mL) was added to a mixture of diketone 11 (1.72 g, 7.72 mmol), potassium carbonate (1.25 g, 9.04 mmol), \( N,N,N,N\)-trioctyloctan-1-amonium chloride (0.28 g, 0.69 mmol) and potassium fluoride on celite (0.25 g, 50 wt%, 2.2 mmol). After stirring for 10 min the temperature was raised to 80 °C and 1-iododecane (1.8 mL, 8.4 mmol) was added over 5 min. The mixture was heated at reflux overnight after which it was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The residue was partitioned between diethyl ether (100 mL) and water (100 mL). The organic layer was separated, washed with 1 M NaOH (2 x 100 mL), 1M HCl (100 mL), saturated bicarbonate solution (100 mL), water (100 mL), brine (100 mL) and dried over MgSO\(_4\). The volatiles were evaporated under reduced pressure while the residue was adsorbed on celite and purified by column chromatography on silica gel thrice (gradient pentane/CH\(_2\)Cl\(_2\); 0–20%) yielding a mixture of 17:1 of the C:O alkylated products as an off white wax (1.0 g, 36%). \(^{1}H\) NMR (300 MHz, CDCl\(_3\)) \( \delta \): 8.03 (m, 2H), 7.86 (m, 2H), 7.40 (m, 2H), 7.28 (m, 3H), 2.25 (m, 2H), 1.18 (m, 16H), 0.85 (d, \( J = 6.2 \text{ Hz} \), 3H); \(^{13}\text{C-NMR}\) (75 MHz, CDCl\(_3\)) \( \delta \): 202.2, 142.2, 137.4, 136.0, 128.9, 127.7, 127.0, 123.7, 62.5, 36.5, 32.0, 30.1, 29.6, 29.4, 29.3, 25.4, 22.8, 14.3; HRMS (ESI-pos): calcd for C\(_{25}\)H\(_{31}\)O\(_2\), [M + H]\(^+\) 363.23186 found 363.23234.
2-isopropyl-2-methyl-1H-indene-1,3(2H)-dione (16). Under an atmosphere of nitrogen acetonitrile (56 mL) was added to a mixture of diketone 12 (1.06 g, 5.63 mmol), potassium carbonate (1.17 g, 8.44 mmol), N-methyl-N,N,N-trioctyloctan-1-amonium chloride (0.10 g, 0.25 mmol) and potassium fluoride on celite (0.13 g, 50 wt%, 1.1 mmol). After stirring for 10 min the temperature was raised to 80 °C and iodomethane (440 μl, 6.04 mmol) was added over 5 min. The mixture was heated at reflux overnight after which it was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The residue was partitioned between diethyl ether (50 mL) and water (50 mL). The organic layer was separated, washed with 1 M NaOH (2 x 50 mL), 1M HCl (50 mL), saturated bicarbonate solution (50 mL), water (50 mL), brine (50 mL) and dried over MgSO4. The volatiles were evaporated under reduced pressure while the residue was adsorbed on celite and purified by column chromatography on silica gel (gradient pentane/CH2Cl2; 0–20%) yielding a mixture of the carbon and oxygen alkylated products which were separated using column chromatography on silica gel twice (gradient pentane/CH2Cl2; 8–18%) to give the pure product as a slightly yellow liquid (956 mg, 84%). 1H NMR (201 MHz, CDCl3) δ: 7.93 (m, 2H), 7.82 (m, 2H), 2.15 (hept, J = 6.9 Hz, 1H), 1.26 (s, 3H), 0.92 (d, J = 6.9 Hz, 6H); 13C NMR (50 MHz, CDCl3) δ: 205.2, 135.8, 123.1, 34.3, 18.2, 17.5; HRMS (APCI-Ion trap): calcd for C13H14O2+ [M + H]+ 203.1067 found 203.1065.

2-hexyl-2-methyl-1H-indene-1,3(2H)-dithione (S7). A solution of diketone 13 (0.43 g, 1.74 mmol), P4S10 (1.46 g, 6.58 mmol) and Lawesson’s reagent (2.66 g, 6.58 mmol) in toluene (15 mL) was heated at reflux under a nitrogen atmosphere until full conversion to the bisthioketone as monitored by TLC. The volatiles were evaporated under reduced pressure and the resulting mixture was dissolved in pentane/CH2Cl2 1:1 and filtered over layered celite on silica gel. After removal of the volatiles under reduced pressure the solid was purified by column chromatography on silica gel (gradient pentane/CH2Cl2; 0–20%) yielding the product as a blue oil (408 mg, 85%). 1H NMR (400 MHz, CDCl3) δ: 8.05–8.00 (m, 2H), 7.81–7.75 (m, 2H), 2.13–2.06 (m, 2H), 1.44 (s, 3H), 1.18–1.00 (m, 6H), 0.81–0.70 (m, 5H); 13C NMR (100 MHz, CDCl3) δ: 246.6, 146.5, 135.3, 123.3, 74.4, 41.9, 31.2, 29.4, 28.1, 24.1, 22.4, 13.9; HRMS (ESI-pos, m/z) calcd for C16H21OS+ [M + OH −S]+ 261.13076 found: 261.13074.

2-methyl-2-phenyl-1H-indene-1,3(2H)-dithione (S8) A solution of diketone 14 (1.10 g, 4.70 mmol), P4S10 (3.7 g, 16.8 mmol) and Lawesson’s reagent (6.8 g, 16.8 mmol) in toluene (40 mL) was heated at reflux under a nitrogen atmosphere until full conversion to the bisthioketone as monitored by TLC. The volatiles were evaporated under reduced pressure and the resulting mixture was dissolved in pentane/CH2Cl2 1:1 and filtered over layered celite on silica gel. After removal of the volatiles under reduced pressure the solid was purified by column chromatography on silica gel (gradient pentane/CH2Cl2; 0–20%) which afforded the product as a blue solid (515 mg, 41%). Mp: 120 °C; 1H NMR (400 MHz, CDCl3) δ: 8.11–8.06 (m, 2H), 7.87–7.81 (m, 2H), 7.25–7.17 (m, 5H), 1.94 (s, 3H); 13C-NMR (100 MHz, CDCl3) δ: 244.7, 146.6, 142.1, 135.6,
128.3, 127.3, 126.8, 124.0, 77.1, 25.8; HRMS (ESI-pos, m/z) calcd for C₁₆H₁₃S₂⁺ [M + H]⁺ 269.04532 found: 269.04522.

2-decyl-2-phenyl-1H-indene-1,3(2H)-dithione (S9). A solution of the diketone 15 (2.8 g, 7.7 mmol), P₄S₁₀ (6.12 g, 27.5 mmol) and Lawesson’s reagent (11.3 g, 27.9 mmol) in toluene (77 mL) was heated at reflux under a nitrogen atmosphere until full conversion to the bisthioketone as monitored by TLC. The volatiles were evaporated under reduced pressure and the resulting mixture was dissolved in 10% CH₂Cl₂ in pentane and filtered over layered celite on silica gel. After removal of the volatiles under reduced pressure the oil was purified by column chromatography on silica gel (gradient pentane/CH₂Cl₂; 0–5%) which afforded the product as a blue oil (1.7 g, 56%).¹H NMR (400 MHz, CDCl₃) δ: 8.08 (dd, J = 5.8, 3.1 Hz, 2H), 7.84 (dd, J = 5.8, 3.1 Hz, 2H), 7.20 (s, 5H), 2.67 (m, 2H), 1.18 (m, 14H), 0.91 (m, 2H), 0.87 (t, J = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ: 244.4, 148.1, 142.9, 135.6, 128.4, 127.4, 127.0, 123.8, 81.5, 38.9, 32.0, 30.1, 29.6, 29.4, 29.2, 23.7, 14.3; HRMS (ESI-pos): calcd for C₂₅H₃₁S₂⁺ [M + H]⁺ 395.18617 found 395.18649.

2-isopropyl-2-methyl-1H-indene-1,3(2H)-dithione (S10). A solution of the diketone 16 (500 mg, 2.47 mmol), P₄S₁₀ (2.2 g, 9.9 mmol) and Lawesson’s reagent (4.0 g, 9.9 mmol) in toluene (25 mL) was heated at reflux under a nitrogen atmosphere until full conversion to the bisthioketone as monitored by TLC. The volatiles were evaporated under reduced pressure and the resulting mixture was dissolved in 10% CH₂Cl₂ in pentane and filtered over layered celite on silica gel. After removal of the volatiles under reduced pressure the oil was purified by column chromatography on silica gel (gradient pentane/CH₂Cl₂; 0–5%) which afforded the product as a blue oil (283 mg, 49%).¹H NMR (400 MHz, CDCl₃) δ: 7.97 (m, 1H), 7.73 (m, 2H), 2.45 (hept, J = 6.9 Hz, 1H), 1.52 (s, 3H), 0.88 (d, J = 6.9 Hz, 6H); ¹³C NMR (50 MHz, CDCl₃) δ: 246.9, 246.9, 146.8, 146.8, 135.2, 123.1, 76.4, 76.4, 39.9, 24.9, 17.9; HRMS (APCI-Ion trap); calcd for C₁₃H₁₄S₂⁺ [M + H]⁺ 235.0610 found 235.0610.

9,9’-(2-hexyl-2-methyl-1H-indene-1,3(2H)-diylidene)bis(9H-fluorene) (18). A solution of dithioketone S7 (360 mg, 1.30 mmol) and 9-diazo-9H-fluorenone (625 mg, 3.25 mmol) in toluene (25 mL) was stirred for 4 h at room temperature. Hexamethylphosphoramidetamine (0.26 mL, 1.43 mmol) was then added and the mixture was stirred overnight. The volatiles were evaporated under reduced pressure. The residue was adsorbed on celite and purified by column chromatography on silica gel (gradient pentane/CH₂Cl₂; 0–20%) to give the product as an orange solid (543 mg, 77%). Mp: 162–170 °C; ¹H-NMR (60 °C, 400 MHz, CDCl₃) δ: 8.42 (d, J = 8.0 Hz, 2H), 8.23–8.15 (m, 2H), 8.15–8.09 (m, 2H), 7.83–7.77 (m, 2H), 7.74 (d, J = 7.7 Hz, 2H), 7.40–7.32 (m, 4H), 7.32–7.24 (m, 2H), 7.23–7.18 (m, 2H), 7.13 (t, J = 7.7 Hz, 2H), 2.92–2.79 (m, 2H), 2.24 (s, 3H), 1.19–0.30 (m, 11H); ¹³C NMR (60 °C, 100 MHz, CDCl₃) δ: 158.3, 156.7, 147.2, 146.0, 140.4, 140.3, 139.4, 139.2, 138.7, 138.5, 137.1, 136.9, 131.6, 129.7, 128.9, 128.6, 127.4, 127.3, 127.1,
127.1, 126.9, 126.6, 126.3, 126.1, 126.0, 123.9, 123.8, 119.6, 119.3, 119.2, 77.2, 64.6, 63.7, 38.5, 33.6, 31.4, 30.3, 29.7, 28.9, 26.6, 26.1, 25.5, 23.7, 22.5, 21.9, 14.1, 13.8; HRMS (ESI-pos, m/z) calcd for C₄₂H₃₇⁺ [M + H]⁺ 541.28898 found: 541.28755.

9,9’-(2-methyl-2-phenyl-1H-indene-1,3(2H)-diyliadene)bis(9H-fluorene) (19). A solution of dithioketone S₈ (400 mg, 1.49 mmol) and 9-diazo-9H-fluorenone (717 mg, 3.73 mmol) in toluene (30 mL) was stirred for 2 h at room temperature. Hexamethylphosphanetriamine (0.3 mL, 1.65 mmol) was then added and the mixture was stirred overnight. The volatiles were evaporated under reduced pressure. The residue was adsorbed on celite and purified by column chromatography on silica gel (gradient pentane/CH₂Cl₂: 0–100%). The resulting orange solid was further purified by layered crystallization from CHCl₃ and heptane (40 and 20 mL) to give the product as an orange solid (442 mg, 56%). M.p. 330 °C (deg); ¹H-NMR (90 °C, 400 MHz, tetrachloroethane-d₂) δ: 8.45 (d, J = 8.0 Hz, 2H), 8.22 (dd, J = 5.9, 3.2 Hz, 2H), 7.51 (bs, 2H), 7.77 (d, J = 7.9 Hz, 2H), 7.69 (d, J = 7.6 Hz, 2H), 7.65 (d, J = 7.6 Hz, 2H), 7.37 (dd, J = 6.0, 3.2 Hz, 2H), 7.31 (t, J = 7.4 Hz, 2H), 7.25 (t, J = 7.4 Hz, 2H), 7.23 (bs, 1H), 7.17 (t, J = 7.6 Hz, 2H), 7.13 (bs, 2H), 7.11 (t, J = 7.7 Hz, 2H), 2.43 (s, 3H); ¹³C-NMR (−30 °C, 100 MHz, CDCl₃) δ: 160.3, 157.2, 148.2, 145.6, 141.6, 141.6, 140.5, 140.2, 140.2, 140.0, 139.8, 139.3, 137.6, 135.9, 133.1, 132.7, 132.0, 130.6, 130.0, 129.4, 129.1, 128.6, 127.8, 127.7, 127.6, 127.6, 127.4, 127.3, 127.2, 126.7, 126.3, 126.1, 126.1, 125.5, 125.2, 123.8, 123.6, 119.6, 119.4, 118.9, 70.8, 68.6, 19.9, 19.3; HRMS (ESI-pos, m/z) calcd for C₄₂H₂₉⁺ [M + H]⁺ 533.22638 found: 533.22510.

9,9’-(2-decyl-2-phenyl-1H-indene-1,3(2H)-diyliadene)bis(9H-fluorene) (20). A solution of dithioketone S₉ (420 mg, 1.06 mmol) and 2 equiv of 9-diazo-9H-fluorenone[52] (409 mg, 2.13 mmol) in toluene (10 mL) was heated at reflux under a nitrogen atmosphere while over 20 h additional 6.85 equiv of 9-diazo-9H-fluorenone[52] (1.40 g, 7.29 mmol) in toluene (15 mL) were added, heating and stirring continued overnight. After cooling to room temperature hexamethylphosphanetriamine (0.2 mL, 1.1 mmol) was added and stirred overnight. The volatiles were evaporated under reduced pressure. The residue was adsorbed on celite and purified by column chromatography on silica gel (gradient pentane/CH₂Cl₂; 0–20%). The resulting orange solid was further purified by layered crystallization from CHCl₃ and heptane (40 and 20 mL) to give the product as an orange solid (442 mg, 56%). M.p: 330 °C (deg); ¹H-NMR (90 °C, 400 MHz, tetrachloroethane-d₂) δ: 8.46 (d, J = 8.0 Hz, 2H), 8.25 (m, 2H), 7.72 (m, 5H), 7.47 (d, J = 7.8 Hz, 2H), 7.32 (m, 10H), 7.15 (t, J = 7.6 Hz, 2H), 7.10 (t, J = 7.7 Hz, 2H), 3.04 (m, 2H), 1.18 (m, 10H), 1.04 (m, 2H), 0.92 (m, 2H), 0.85 (t, J = 7.3 Hz, 3H), 0.81 (m, 2H), 0.70 (m, 2H), 0.66 (m, 2H), 0.51 (m, 2H), 0.42 (m, 2H); ¹³C-NMR (APT/HMBC, 101 MHz, CDCl₃, −30 °C) δ: 155.3, 148.8, 141.5, 140.2, 140.0, 139.0, 137.6, 133.6, 130.6, 129.1, 128.5, 127.6, 127.5, 127.5, 127.4, 126.9, 126.2, 126.0, 123.6, 119.4, 119.3, 72.3, 32.0, 31.2, 29.5, 29.2, 29.2, 29.0, 28.1, 25.0, 22.9, 14.4; HRMS (ESI-pos): calcd for C₅₁H₄₇⁺ [M + H]⁺ 659.36723 found 659.36585.
9,9’-(2-isopropyl-2-methyl-1H-indene-1,3(2H)-diylidene)bis(9H-fluorene) (21). A solution of dithioketone S10 (283 mg, 1.21 mmol) and 2 equiv of 9-diazo-9H-fluorenone [52] (465 mg, 2.42 mmol) in toluene (30 mL) and tetrahydrofuran (30 mL) was heated at reflux under a nitrogen atmosphere while over 20 h additional 10 equiv of 9-diazo-9H-fluorenone [52] (2.33 g, 12.1 mmol) in toluene-tetrahydrofuran (20 mL) were added, heating and stirring continued overnight. The volatiles were evaporated under reduced pressure. The residue was adsorbed on celite and purified by column chromatography on silica gel (gradient pentane/CH2Cl2; 0–20%). The resulting red solid was washed with hot acetonitrile (3 x 15 mL) and further purified by layered crystallization from CH2Cl2, heptane (3 and 20 mL). The resulting solid was adsorbed on celite and purified by column chromatography on silica gel (gradient pentane/CHCl3; 0–20%) to give the pure product as an orange solid (32 mg, 5.3%). M.p. 228.0–228.5 °C (deg.); 1H NMR (400 MHz, CDCl3) δ: 8.32 (d, J = 8.0 Hz, 2H), 8.08 (dd, J = 5.9, 3.2 Hz, 2H), 8.04 (dd, J = 6.6, 2.0 Hz, 2H), 7.80 (dd, J = 6.4, 2.4 Hz, 2H), 7.75 (d, J = 7.1 Hz, 2H), 7.37 (p, J = 7.3, 5.8 Hz, 4H), 7.28 (dt, J = 7.4, 0.9 Hz, 4H), 7.25 (m, 2H), 7.12 (ddd, J = 8.3, 7.3, 1.2 Hz, 2H), 3.03 (p, J = 6.8 Hz, 2H), 2.38 (s, 3H), 1.04 (d, J = 6.8 Hz, 6H); 13C NMR (101 MHz, CDCl3) δ: 158.8, 148.7, 141.1, 139.8, 139.4, 137.1, 132.4, 129.4, 129.0, 127.6, 127.5, 127.2, 126.3, 126.2, 124.3, 119.7, 119.4, 70.8, 39.7, 27.5, 23.6; HRMS (APCI-Ion trap): calcd for C39H31+ [M + H]+ 499.2426 found 499.2410.

9,9’-(2-fluoro-2-methyl-1H-indene-1,3(2H)-diylidene)bis(9H-fluorene) (22). Compound 22 was synthesized from 10 by Peter Stacko and obtained as a bright yellow solid as reported in [57]. Mp >187 °C (decomp.). 1H NMR (400 MHz, CD2Cl2) δ: 8.43 (d, 2H, J = 8.0 Hz), 7.34–7.36 (m, 2H), 8.18 (dd, J1 = 5.9 Hz, J2 = 3.2 Hz), 7.74–7.89 (m, 4H), 7.33–7.41 (m, 8H), 7.17 (dd, 2H, J = 7.7 Hz, J2 = 7.7 Hz), 2.21 (d, 3H, J = 15.7 Hz). 13C NMR (100 MHz, CD 2Cl2) δ: 146.0, 145.8, 142.0 (d, J = 5.7 Hz), 141.1 (d, J = 8.2 Hz), 138.1, 137.6, 131.5, 130.0, 129.0, 128.9 (d, J = 2.0 Hz), 128.4, 127.7, 126.7, 127.4 (d, J = 2.4 Hz), 126.7, 124.5, 119.8 (d, J = 3.8 Hz), 106.7 (d, J = 200.9 Hz), 20.3 (d, J = 23.2 Hz). 19F NMR (376 MHz, CD2Cl2) δ: −140.4 (q, J = 15.8 Hz). HRMS (ESI): calcd for C36H23+ (M – F-) 455.1794 found 455.17691.

9,9’-(2-fluoro-2-methyl-1H-indene-1,3(2H)-diylidene)bis(2-methoxy-9H-fluorene) (23). Compound 23 was synthesized from 10 by Peter Stacko and obtained as a bright yellow solid as reported in [57]. Mp >180 °C (decomp.). 1H NMR (400 MHz, CDCl3) δ: 8.39 (dd, 1H, J1 = 7.2 Hz, J2 = 7.2 Hz), 8.24–8.30 (m, 2H), 8.18–8.20 (m, 1H), 8.03 (dd, 1H, J = 8.8 Hz, J2 = 2.2 Hz), 7.91 (1H, m), 7.62–7.68 (m, 4H), 7.30–7.36 (m, 5H), 7.10 (dd, 2H, J = 7.5 Hz, J2 = 7.5 Hz), 6.98 (dd, 2H, J = 8.3 Hz, J2 = 2.2 Hz), 6.98 (dd, 2H, J = 8.3 Hz, J2 = 2.2 Hz), 6.93 (m, 1H), 3.96–3.97 (s, 3H), 3.79 (m, 3H), 2.17–2.25 (m, 3H). 13C/HSQC/HMBC NMR (100/400/400 MHz, CD2Cl2) δ: 159.5, 145.9, 145.7 141.5, 141.5, 139.8, 139.8, 137.7, 134.7, 134.7, 134.6, 130.4, 130.2, 130.2, 130.0, 129.4, 129.2, 129.2, 128.9, 128.9, 128.8, 127.9, 127.8, 127.7, 127.6, 126.6, 126.6, 126.5, 125.7, 125.8, 124.7, 124.7, 120.7, 120.6, 120.5, 119.3, 119.3, 115.6,
115.6, 114.6, 114.5, 113.9, 110.6, 110.4, 107.7, 105.7, 56.2, 56.1, 56.0, 20.4, 20.4, 20.2, 20.2. <sup>19</sup>F NMR (376 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ: −139.5 (<sup>q</sup>, <i>J</i> = 15.7 Hz), −134.0 (<sup>q</sup>, <i>J</i> = 16.0 Hz), −140.3 (<i>J</i> = 15.8 Hz). HRMS (ESI): calcd for C<sub>38</sub>H<sub>27</sub>O<sub>2</sub>− (<M − F−) 515.2006 found 515.19865.

9,9′-((R,1-(Z,M),3-(E,P))-2-fluoro-2-methyl-1H-indene-1,3(2H)-dilylidene)bis(2-methoxy-9H-fluorene) (1:(R,(Z,M),(E,P))-23). A solution of a mixture of isomers of 23 was subjected to SFC (Chiralpak®IA, 32% IPA, 394 nm, 3.5 mL·min<sup>−1</sup>, T = 40 °C, 180 bar) <i>t</i><sub>R</sub> = 8.2 min. The collected solution was kept in the dark and concentrated in vacuo. The residue was subjected to column chromatography on silica gel in the dark (pentane/CH<sub>2</sub>Cl<sub>2</sub>; 4:1) affording (R,(Z,M),(E,P))-23. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ: 8.39 (d, <i>J</i> = 7.9 Hz, 1H), 8.27 – 8.21 (m, 2H), 8.21 – 8.14 (m, 1H), 8.01 (d, <i>J</i> = 2.3 Hz, 1H), 7.89 (t, <i>J</i> = 2.0 Hz, 1H), 7.68 – 7.60 (m, 4H), 7.38 – 7.27 (m, 5H), 7.09 (t, <i>J</i> = 7.7 Hz, 1H), 6.97 (dd, <i>J</i> = 8.3, 2.3 Hz, 1H), 6.92 (dd, <i>J</i> = 8.3, 2.3 Hz, 1H), 3.96 (s, 3H), 3.77 (s, 3H), 2.18 (d, <i>J</i> = 15.8 Hz, 3H). <sup>19</sup>F NMR (376 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ: −139.96 (<sup>q</sup>, <i>J</i> = 15.6 Hz).

9,9′-((r,1-(E,M),3-(E,P))-2-fluoro-2-methyl-1H-indene-1,3(2H)-dilylidene)bis(2-methoxy-9H-fluorene) (2:(r,E,E)-23). A solution of a mixture of isomers of 23 was subjected to SFC (Chiralpak®IA, 32% IPA, 394 nm, 3.5 mL·min<sup>−1</sup>, T = 40 °C, 180 bar) <i>t</i><sub>R</sub> = 9.4 min. The collected solution was kept in the dark and concentrated in vacuo. The residue was subjected to column chromatography on silica gel in the dark (pentane/CH<sub>2</sub>Cl<sub>2</sub>; 4:1) affording (r,E,E)-23. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ: 8.31 – 8.22 (m, 4H), 8.03 (d, <i>J</i> = 2.3 Hz, 2H), 7.67 – 7.60 (m, 4H), 7.39 – 7.27 (m, 6H), 6.92 (dd, <i>J</i> = 8.3, 2.3 Hz, 2H), 3.78 (s, 6H), 2.18 (d, <i>J</i> = 15.6 Hz, 3H). <sup>19</sup>F NMR (376 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ: −140.28 (<sup>q</sup>, <i>J</i> = 15.8 Hz).

9,9′-((S,1-(Z,P),3-(E,M))-2-fluoro-2-methyl-1H-indene-1,3(2H)-dilylidene)bis(2-methoxy-9H-fluorene) (3:(S,(Z,P),(E,M))-23). A solution of a mixture of isomers of 23 was subjected to SFC (Chiralpak®IA, 32% IPA, 394 nm, 3.5 mL·min<sup>−1</sup>, T = 40 °C, 180 bar) <i>t</i><sub>R</sub> = 13.3 min. The collected solution was kept in the dark and concentrated in vacuo. The residue was subjected to column chromatography on silica gel in the dark (pentane/CH<sub>2</sub>Cl<sub>2</sub>; 4:1) affording (S,(Z,P),(E,M))-23. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ: 8.39 (dt, <i>J</i> = 8.0, 0.8 Hz, 1H), 8.29 – 8.21 (m, 2H), 8.21 – 8.14 (m, 1H), 8.01 (d, <i>J</i> = 2.3 Hz, 1H), 7.89 (t, <i>J</i> = 1.9 Hz, 1H), 7.68 – 7.60 (m, 4H), 7.38 – 7.27 (m, 5H), 7.09 (t, <i>J</i> = 7.7 Hz, 1H), 6.97 (dd, <i>J</i> = 8.3, 2.3 Hz, 1H), 6.92 (dd, <i>J</i> = 8.4, 2.3 Hz, 1H), 3.96 (s, 3H), 3.77 (s, 3H), 2.18 (d, <i>J</i> = 15.8 Hz, 3H). <sup>19</sup>F NMR (376 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ: −139.96 (<i>J</i> = 15.6 Hz).
9,9’-((r,1-(Z,M),3-(Z,P))-2-fluoro-2-methyl-1H-indene-1,3(2H)-dilidenedi)bis(2-methoxy-9H-fluorene) (4:\(r,Z,Z\)-23). A solution of a mixture of isomers of 23 was subjected to SFC (Chiralpak®IA, 32% IPA, 394 nm, 3.5 mL·min⁻¹, T = 40 °C, 180 bar) \(t_R = 14.7\) min. The collected solution was kept in the dark and concentrated \textit{in vacuo}. The residue was subjected to column chromatography on silica gel in the dark (pentane/CH₂Cl₂; 4:1) affording \((r,Z,Z)\)-23. \(^1\)H NMR (400 MHz, CD₂Cl₂) δ: 8.37 (dt, \(J = 8.0, 0.9\) Hz, 2H), 8.18 (dd, \(J = 5.9, 3.2\) Hz, 2H), 7.89 (t, \(J = 1.9\) Hz, 2H), 7.68 – 7.61 (m, 4H), 7.37 – 7.28 (m, 4H), 7.09 (dd, \(J = 7.9, 7.3, 1.2\) Hz, 2H), 6.97 (dd, \(J = 8.3, 2.3\) Hz, 2H), 3.95 (s, 6H), 2.20 (d, \(J = 15.8\) Hz, 3H). \(^19\)F NMR (376 MHz, CD₂Cl₂) δ: −139.51 (q, \(J = 15.4\) Hz).

**Kinetics Experiment of 4**

NMR samples were irradiated in a Varian Innova-600 NMR using an LED (5 W, 365 nm, 10 nm width at half-height), mounted in a modified Nalorac Z-Spec probe, to PSS at controlled temperatures measured with a PT-100 resistance thermometer. \(^1\)H NMR absorptions were followed over time and least square fitting of the trace to a first order formation afforded the reaction rates from which an Eyring plot was constructed. A least squares analysis was performed on the original form of the Eyring equation:

\[
k = \frac{k_B \cdot T}{h} \cdot \exp \left( -\frac{\Delta H}{RT} + \frac{\Delta S}{R} \right)
\]

with appropriate weighing \((1/k^2)\) while the standard errors were determined by a Monte Carlo calculation on the linearized Eyring equation:

\[
T \cdot \ln \left( \frac{k}{T} \right) = T \cdot \left( \ln \left( \frac{k_B}{h} \right) + \frac{\Delta S}{R} \right) - \frac{\Delta H}{R}
\]

using \(3\sigma_T = 0.5\) K and \(\sigma_k\) given by the individual least square fits. For the determination of the one-hour-half-life temperature (T at \(t_{1/2} = 1\) h) the Eyring equation was solved for T:

\[
T_{t_{1/2}=1h} = \frac{\Delta H}{R \cdot W \left( \frac{3600 \cdot k_B \cdot \Delta H \cdot \exp \left( \frac{\Delta S}{R} \right)}{h \cdot R \cdot \log(2)} \right)}
\]

in which \(W\) denotes the Lambert W function.

**EXSY NMR Experiments**

NOESY 1D \(^1\)H NMR spectra were recorded of samples of 18-20 in CDCl₃ over a range of mixing times and temperatures in either a 400 or 600 MHz NMR machine (Figure 7.16). Temperature calibration was performed using a PT-100 resistance thermometer. \(^1\)H NMR absorptions of the exchange peaks were recorded at different mixing times (Figure 7.16) and least square fitting of the normalized fractions of a single isomer to a first order formation:

\[
[r-x] = y + A(1 - e^{-t \cdot k_{tot}})
\]
afforded the total reaction rates ($k_{tot}$) for the following reaction:

\[ \frac{k_f}{k_b} \quad \text{s isomer of } x \quad \text{r isomer of } x \]

for which:

\[ k_{tot} = k_f + k_b \quad \text{(9)} \]

from which the forward and backward reaction rates ($k_f$ and $k_b$) were derived using the following equation:

\[ \frac{[B]_e}{[A]_e} = \frac{k_f}{k_b} \quad \text{(10)} \]

which solves to:

\[ k_f = \frac{k_{tot}}{1+K^{-1}} = \frac{[B]_e}{[A]_e}[B]_e \\ k_b = \frac{[A]_e}{[A]_e+[B]_e} \quad \text{(11)} \]

From the resulting rates Eyring plots were constructed. A least squares analysis was performed on the original forms of the Eyring and Van ‘t Hoff equations:

\[ k = \frac{k_B}{h} \cdot T \cdot \exp\left(-\frac{\Delta H}{RT} + \frac{\Delta S}{R}\right) \quad \text{and } K = \exp\left(-\frac{\Delta H}{RT} + \frac{\Delta S}{R}\right) \quad \text{(12)} \]

with appropriate weighting ($1/k^2$) while the standard errors were determined by a Monte Carlo calculation on the linearized Eyring and Van ‘t Hoff equations:

\[ T \cdot \ln\left(\frac{k}{T}\right) = T \cdot \left(\ln\left(\frac{k_B}{h}\right) + \frac{\Delta S}{R}\right) - \frac{\Delta H}{R} \quad \text{and } T \cdot \ln(K) = T \cdot \left(\frac{\Delta S}{R}\right) - \frac{\Delta H}{R} \quad \text{(13)} \]

using $3\sigma_T = 0.5$ K and $\sigma_k$ given by the individual least square fits. This provided the activation parameters for the equilibria of 18–20 (Table 7.4).

**Figure 7.16.** EXSY NMR of 19 and 20. Top: NOESY 1D 1H NMR spectrum of 19 (400 MHz, CDCl3, 0.5 °C, 0.95 s mixing time) and 20 (400 MHz, CDCl3, −3.6 °C, 0.9 s mixing time). Bottom: normalized integral of r-19 (left) and r-20 (right) at various mixing times and temperatures.
Table 7.4. Activation parameters of 18–20 for r–s isomerization by EXSY NMR.[a]

<table>
<thead>
<tr>
<th></th>
<th>18</th>
<th>19</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Δ‡H°</td>
<td>Δ‡S°</td>
<td>Δ‡H°</td>
</tr>
<tr>
<td>r → s</td>
<td>56.0±2.2</td>
<td>−14.0±8.6</td>
<td>73.6±2.6</td>
</tr>
<tr>
<td>s → r</td>
<td>59.7±2.3</td>
<td>−7.7±8.7</td>
<td>77.5±1.9</td>
</tr>
<tr>
<td>s − r</td>
<td>3.7±2.1</td>
<td>6.3±7.9</td>
<td>3.9±0.4</td>
</tr>
</tbody>
</table>

[a] Δ‡H° in kJ·mol⁻¹, Δ‡S° in J·mol⁻¹·K⁻¹.

Kinetic Behavior of 23

Integrated Rate Laws Derivation

The kinetic scheme for the rotational cycle of 23 is shown in Scheme 7.3. Isomer 1 is chiral and might therefore exhibit an asymmetry in its reactivity towards isomer 2 and isomer 4, and is therefore assigned distinct rates towards either product (k₁ and k₂, respectively). Isomer 3 is expected to show identical behaviour as isomer 1, being its enantiomer, and is assigned the same rates for reactions leading to the same products. Isomer 2 is meso and should therefore not possess a preference for either product (isomer 1 and isomer 3) and both processes are assigned the same rate correspondingly (k₃). The same reasoning holds for isomer 4, which has therefore been assigned a single rate (k₄) for both processes leading to isomer 1 and isomer 3. From the kinetic scheme the following differential rate equations can be derived:

\[
\frac{d[1-23]}{dt} = -k_1[1-23] - k_2[1-23] + k_3[2-23] + k_4[4-23]
\]

(14)

\[
\frac{d[2-23]}{dt} = k_1[1-23] - 2k_3[2-23] + k_1[3-23]
\]

(15)

\[
\frac{d[3-23]}{dt} = k_3[2-23] - k_1[3-23] - k_2[3-23] + k_4[4-23]
\]

(16)

\[
\frac{d[4-23]}{dt} = k_2[1-23] + k_2[3-23] - 2k_4[4-23]
\]

(17)

With its associated rate matrix \(K\), state vector \(X\), and differential rate equation:

\[
K = \begin{bmatrix}
-k_1 & k_2 & k_3 & 0 & 0 \\
0 & -k_1 & -k_2 & k_4 & 0 \\
k_2 & 0 & -k_3 & 0 & -2k_4
\end{bmatrix}, \quad X = \begin{bmatrix}
[1-23] \\
[2-23] \\
[3-23] \\
[4-23]
\end{bmatrix}, \quad \frac{dx}{dt} = KX
\]

Solving the differential provides the integrated rate laws for the isomers of 23:

\[
[1-23]_e = [1-23]_e + A_1e^{-k_1t} + A_2e^{-k_2t} + \frac{1}{2}([1-23]_0 - [3-23]_0)e^{-k_1-k_2t}
\]

(18)

\[
[2-23]_e = [2-23]_e + B_1e^{-k_1t} + B_2e^{-k_2t}
\]

(19)

\[
[3-23]_e = [3-23]_e + C_1e^{-k_1t} + C_2e^{-k_2t} + \frac{1}{2}([3-23]_0 - [1-23]_0)e^{-k_1-k_2t}
\]

(20)

\[
[4-23]_e = [4-23]_e + D_1e^{-k_1t} + D_2e^{-k_2t}
\]

(21)

Where:
\[ k_V = \frac{1}{2}k_1 + k_2 + 2k_3 + 2k_4 + Z \quad (22) \]
\[ k_W = \frac{1}{2}k_1 + k_2 + 2k_3 + 2k_4 - Z \quad (23) \]
\[ Z = \sqrt{(k_1 + k_2 + k_3 + 2k_4)^2 - 8(k_3(k_2 + 2k_4) + k_1k_4)} \quad (24) \]

And \([X]_0\) is the concentration at \(t=0\), and the final concentration at photoequilibrium \([X]_e\) – is derived as follows:

\[ [1-23]_e = \frac{k_3k_4[X]_0}{k_3(2k_4 + k_2 + k_1)} \quad (25) \]
\[ [2-23]_e = \frac{k_1k_4[X]_0}{k_3(2k_4 + k_2 + k_1)} \quad (26) \]
\[ [3-23]_e = \frac{k_3k_4[X]_0}{k_3(2k_4 + k_2 + k_1)} \quad (27) \]
\[ [4-23]_e = \frac{k_3k_4[X]_0}{k_3(2k_4 + k_2 + k_1)} \quad (28) \]

And the pre-exponential factors are as follows:

\[ A_1 = (-2k_3^2(2[-123]_0 + 2[2-23]_0 + [3-23]_0 + 2k_4(2[-23]_0 - [4-23]_0)) + k_4k_1((-123)_0 - [3-23]_0)(k_2 + k_1) - 2k_4([1-23]_0 + [3-23]_0 + 2[4-23]_0) + [123]_0Z + [323]_0Z + k_3(4k_4^2([2-23]_0 - [4-23]_0) + k_2([1-23]_0 + [3-23]_0)(k_2 + k_1 + Z) + 2k_1([1-23]_0(k_2 + k_1) + k_5([2-23]_0 + [3-23]_0 - [4-23]_0) + k_1([-2-23]_0 + [3-23]_0 + [4-23]_0) + k_1(-[2-23]_0 + [3-23]_0 + [4-23]_0) - [2-23]_0Z - [4-23]_0Z) / (4(k_3(2k_4 + k_2) + k_4k_1)Z) \quad (29) \]

\[ A_2 = (2k_3^2(2[1-23]_0 + 2[2-23]_0 + [3-23]_0 + 2k_4(2[-23]_0 - [4-23]_0)) + k_4k_1((-123)_0 - [3-23]_0)(k_2 + k_1) + 2k_4([1-23]_0 + [3-23]_0 + 2[4-23]_0) + [123]_0Z + [323]_0Z - k_3(4k_4^2([2-23]_0 - [4-23]_0) + k_2([1-23]_0 + [3-23]_0)(k_2 + k_1 - Z) + 2k_4([1-23]_0(k_2 + k_1) + k_5([2-23]_0 + [3-23]_0 - [4-23]_0) + k_1([-2-23]_0 + [3-23]_0 + [4-23]_0) + [2-23]_0Z + [4-23]_0Z) / (4(k_3(2k_4 + k_2) + k_4k_1)Z) \quad (30) \]

\[ A_3 = \frac{1}{2}([123]_0 - [323]_0) \quad (31) \]

\[ B_1 = ((k_1 + k_2 - 2k_3 - 2k_4)^2 - Z^2) \left( k_1k_4((-123)_0 + [3-23]_0)(-k_1 + k_2 - 2k_3 + 2k_4 - Z) + [4-23]_0(k_1 + k_2 + 2k_3 + 2k_4 - Z)) + k_3 \left( 2[2-23]_0(k_4(k_1 - 2k_3 + 2k_3 - 2k_4 + Z) + k_2(-k_1 - k_2 + 2k_3 + Z) - 2k_1k_4([1-23]_0 + [3-23]_0)) \right) / (16(2k_3k_4 - k_2k_4 - k_1k_3)(k_3(2k_4 + k_2) + k_4k_1)Z) \quad (32) \]

\[ B_2 = -((k_1 + k_2 - 2k_3 - 2k_4)^2 - Z^2) \left( k_1k_4((-123)_0 + [3-23]_0)(-k_1 + k_2 - 2k_3 + 2k_4 + Z) + [4-23]_0(k_1 + k_2 + 2k_3 + 2k_4 + Z)) + k_3 \left( 2[2-23]_0(k_4(k_1 - 2k_3 + 2k_3 - 2k_4 - Z) + k_2(-k_1 - k_2 + 2k_3 - Z) - 2k_1k_4([-123]_0 + [3-23]_0)) \right) / (16(2k_3k_4 - k_2k_4 - k_1k_3)(k_3(2k_4 + k_2) + k_4k_1)Z) \quad (33) \]

\[ C_1 = -2k_3^2(2[1-23]_0 + 2[2-23]_0 + [3-23]_0 + 2k_4(2[-23]_0 - [4-23]_0)) - k_4k_1((-123)_0 - [3-23]_0)(k_2 + k_1) + 2k_4([1-23]_0 + [3-23]_0 + 2[4-23]_0) - [123]_0Z - [3-23]_0Z - k_3(4k_4^2([2-23]_0 + [4-23]_0) - k_2([1-23]_0 + [3-23]_0)(k_2 + k_1 + Z) - 2k_4([1-23]_0(k_2 + k_1) + 2k_4([1-23]_0 + [3-23]_0) + k_2([1-23]_0 + [3-23]_0)(k_2 + k_1) + 2k_4([1-23]_0 + [3-23]_0) - [123]_0Z - [3-23]_0Z) / (4(k_3(2k_4 + k_2) + k_4k_1)Z) \quad (34) \]
Therefore, each sample was fitted an individual set of initial concentrations corresponding initial isomer, however, small amounts of other isomers are present. This rate is fully dependent on the concentration (which were roughly equal) and the intensity of the light source which varied due to the setup of its final concentration, which occurs at 39 h, 40 h, 29 h and 19 h for the described samples. All other parameters follow which are reported for completeness (Table 7.6). From the rates one can determine the average amount of rotor turns in a specific period of isomerization. During the period in which it takes the isomer with delayed formation to reach 95% (t95%) of its final concentration, which occurs at 39 h, 40 h, 29 h and 19 h for the described samples of isomers 1–4 of 23, respectively, each motor molecule on average undergoes 2.9 isomerizations of their rotor units. This rate is fully dependent on the concentration (which were roughly equal) and the intensity of the light source which varied due to the setup (isomer 4: (r, Z, Z)-23 was closest to the lamp in the autosampler reflected by the lowest t95%).

Samples of low concentration and close to the lamp reached equilibrium conditions in the duration of a single SFC analysis (~10 min). Normalized rates are presented in Table 7.5 for clarity, see Table 7.6 for rates of individual experiments.

\[ k_2([2-23]_0 + [3-23]_0 - [4-23]_0) + k_1([-2-23]_0 + [3-23]_0 + [4-23]_0) - [2-23]_0Z - [4-23]_0Z) \right) / (4(k_2k_4 + k_2 + k_1k_4)Z) \]  \hspace{1cm} (34)

\[ C_2 = (2k_3^2([1-23]_0 + 2[2-23]_0 + [3-23]_0) + 2k_4([-2-23]_0 - [4-23]_0)) - k_4k_1([1-23]_0 + [3-23]_0)(k_2 + k_1) - 2k_4([1-23]_0 + [3-23]_0) - [1-23]_0Z - [3-23]_0Z - k_3(4k_4^2([2-23]_0 - [4-23]_0) + k_2([1-23]_0 + [3-23]_0)(k_2 + k_1 - Z) + 2k_4([1-23]_0(k_2 + k_1) + k_3([2-23]_0 + [3-23]_0 - [4-23]_0) + k_1([-2-23]_0 + [3-23]_0 + [4-23]_0) + [2-23]_0Z) \right) / (4(k_3(2k_4 + k_2) + k_4k_1)Z) \]  \hspace{1cm} (35)

\[ D_1 = -\left( ((k_1 + k_2 - 2k_3 - 2k_4)Z^2) - k_2k_3([1-23]_0 + [3-23]_0)(k_1 - k_2 + 2k_3 - 2k_4 - Z) + [2-23]_0(k_1 + k_2 + 2k_3 + 2k_4 - Z) + k_4 (4[23]_0)(2k_3(-2k_1 + k_2 - 2k_3 + 2k_4 + Z) - k_1(k_1 + k_2 - 2k_4 - Z)) - 2k_2k_3([1-23]_0 + [3-23]_0) \right) / (16(2k_3k_4 - k_2k_4 - k_1k_3)(k_3(2k_4 + k_2) + k_1k_4)Z) \]  \hspace{1cm} (36)

\[ D_2 = -\left( ((k_1 + k_2 - 2k_3 - 2k_4)Z^2) - k_2k_3([1-23]_0 + [3-23]_0)(k_1 - k_2 + 2k_3 - 2k_4 + Z) + [2-23]_0(k_1 + k_2 + 2k_3 + 2k_4 + Z) + k_4 (4[23]_0)(2k_3(-2k_1 + k_2 - 2k_3 + 2k_4 - Z) - k_1(k_1 + k_2 - 2k_4 + Z)) - 2k_2k_3([1-23]_0 + [3-23]_0) \right) / (16(2k_3k_4 - k_2k_4 - k_1k_3)(k_3(2k_4 + k_2) + k_1k_4)Z) \]  \hspace{1cm} (37)

Details on SFC measurements of 23 and fitting of rate equations:

A single set of variable rates (k1–k4) was provided for a global fit. Each sample experiences different overall rates due to differences in light intensity, though the relative rates should stay constant; therefore, a scaling factor (sF) for each sample was used. Each sample possesses a unique initial composition, approximating maximum concentration of the corresponding initial isomer, however, small amounts of other isomers are present. Therefore, each sample was allowed to be fitted an individual set of initial concentrations ([X]0). All other parameters follow from these rates, scaling factors and initial concentrations according to the equations above. The free variables were optimized by a reduction of the squared error of the normalized integrals and the predicted concentrations resulting in an R² of 0.997 and an average absolute residual error of 0.0073 per point. The optimization provided the following set of rates from which the concentrations at photoequilibrium ([X]₀) follow (Table 7.5), as well as the set of initial concentrations and scaling factors from which all other parameters follow which are reported for completeness (Table 7.6). From the rates one can determine the average amount of rotor turns in a specific period of isomerization.

During the period in which it takes the isomer with delayed formation to reach 95% (t95%) of its final concentration, which occurs at 39 h, 40 h, 29 h and 19 h for the described samples of isomers 1–4 of 23, respectively, each motor molecule on average undergoes 2.9 isomerizations of their rotor units. This rate is fully dependent on the concentration (which were roughly equal) and the intensity of the light source which varied due to the setup (isomer 4: (r, Z, Z)-23 was closest to the lamp in the autosampler reflected by the lowest t95%). Samples of low concentration and close to the lamp reached equilibrium conditions in the duration of a single SFC analysis (~10 min). Normalized rates are presented in Table 7.5 for clarity, see Table 7.6 for rates of individual experiments.
### Table 7.5. Fitted rates and photoequilibrium concentrations.

<table>
<thead>
<tr>
<th>$k_1$</th>
<th>$k_2$</th>
<th>$k_3$</th>
<th>$k_4$</th>
<th>[1-23]$_p$</th>
<th>[2-23]$_p$</th>
<th>[3-23]$_p$</th>
<th>[4-23]$_p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.228</td>
<td>0.270</td>
<td>0.246</td>
<td>0.256</td>
<td>0.248</td>
<td>0.278</td>
<td>0.248</td>
<td>0.225</td>
</tr>
</tbody>
</table>

### Table 7.6. Fitted initial concentrations and scaling factors. Samples correlate to major starting isomer as shown in Figure 7.15 and Figure 7.17.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>[1-23]$_p$</td>
<td>1.001</td>
<td>0.098</td>
<td>0.126</td>
<td>-0.109</td>
</tr>
<tr>
<td>[2-23]$_p$</td>
<td>0.004</td>
<td>1.100</td>
<td>0.094</td>
<td>0.075</td>
</tr>
<tr>
<td>[3-23]$_p$</td>
<td>0.040</td>
<td>0.092</td>
<td>1.096</td>
<td>-0.103</td>
</tr>
<tr>
<td>[4-23]$_p$</td>
<td>-0.010</td>
<td>0.128</td>
<td>0.058</td>
<td>1.124</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>$sF$</th>
<th>$k_1$</th>
<th>$k_2$</th>
<th>$k_3$</th>
<th>$k_4$</th>
<th>$k_V$</th>
<th>$k_W$</th>
<th>$Z$</th>
<th>$A_1$</th>
<th>$A_2$</th>
<th>$A_3$</th>
<th>$B_1$</th>
<th>$B_2$</th>
<th>$C_1$</th>
<th>$C_2$</th>
<th>$C_3$</th>
<th>$D_1$</th>
<th>$D_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4.35·10$^{-5}$</td>
<td>4.14·10$^{-5}$</td>
<td>5.18·10$^{-5}$</td>
<td>9.69·10$^{-5}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_1$</td>
<td>9.92·10$^{-6}$</td>
<td>9.44·10$^{-6}$</td>
<td>1.12·10$^{-5}$</td>
<td>2.21·10$^{-5}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_2$</td>
<td>1.18·10$^{-5}$</td>
<td>1.12·10$^{-5}$</td>
<td>1.40·10$^{-5}$</td>
<td>2.62·10$^{-5}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_3$</td>
<td>1.07·10$^{-5}$</td>
<td>1.02·10$^{-5}$</td>
<td>1.27·10$^{-5}$</td>
<td>2.38·10$^{-5}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_4$</td>
<td>1.11·10$^{-5}$</td>
<td>1.06·10$^{-5}$</td>
<td>1.32·10$^{-5}$</td>
<td>2.48·10$^{-5}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_V$</td>
<td>-4.36·10$^{-5}$</td>
<td>-4.15·10$^{-5}$</td>
<td>-5.19·10$^{-5}$</td>
<td>-9.72·10$^{-5}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_W$</td>
<td>-2.16·10$^{-5}$</td>
<td>-2.05·10$^{-5}$</td>
<td>-2.57·10$^{-5}$</td>
<td>-4.81·10$^{-5}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$Z$</td>
<td>2.20·10$^{-5}$</td>
<td>2.10·10$^{-5}$</td>
<td>2.62·10$^{-5}$</td>
<td>4.91·10$^{-5}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$A_1$</td>
<td>2.61·10$^{-1}$</td>
<td>-2.18·10$^{-1}$</td>
<td>2.67·10$^{-1}$</td>
<td>-3.95·10$^{-1}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$A_2$</td>
<td>3.08·10$^{-3}$</td>
<td>-3.87·10$^{-2}$</td>
<td>2.93·10$^{-3}$</td>
<td>4.41·10$^{-2}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$A_3$</td>
<td>4.80·10$^{-1}$</td>
<td>2.89·10$^{-3}$</td>
<td>-4.85·10$^{-1}$</td>
<td>-2.75·10$^{-3}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$B_1$</td>
<td>-2.44·10$^{-1}$</td>
<td>2.04·10$^{-1}$</td>
<td>-2.50·10$^{-1}$</td>
<td>3.70·10$^{-1}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$B_2$</td>
<td>-3.99·10$^{-2}$</td>
<td>5.01·10$^{-1}$</td>
<td>-3.79·10$^{-2}$</td>
<td>-5.70·10$^{-1}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_1$</td>
<td>2.61·10$^{-1}$</td>
<td>-2.18·10$^{-1}$</td>
<td>2.67·10$^{-1}$</td>
<td>-3.95·10$^{-1}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_2$</td>
<td>3.08·10$^{-3}$</td>
<td>-3.87·10$^{-2}$</td>
<td>2.93·10$^{-3}$</td>
<td>4.41·10$^{-2}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_3$</td>
<td>-4.80·10$^{-1}$</td>
<td>-2.89·10$^{-3}$</td>
<td>4.85·10$^{-1}$</td>
<td>2.75·10$^{-3}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$D_1$</td>
<td>-2.77·10$^{-1}$</td>
<td>2.32·10$^{-1}$</td>
<td>-2.84·10$^{-1}$</td>
<td>4.20·10$^{-1}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$D_2$</td>
<td>3.37·10$^{-2}$</td>
<td>-4.23·10$^{-1}$</td>
<td>3.20·10$^{-2}$</td>
<td>4.82·10$^{-1}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 7.17. Photochemical/thermal behavior of isolated isomers of 23 (in CD<sub>2</sub>Cl<sub>2</sub>, rt, 365 nm). Stacked original SFC traces (Chiralpak<sup>®</sup>IA, 32% IPA, 394 nm, 3.5 mL·min<sup>−1</sup>, T = 40 °C, 180 bar). For the integrals over time see Figure 7.15.

The final ratios determined from the integrals of the SFC chromatograms (Figure 7.15 and Figure 7.17) are tabulated in Table 7.7 and were controlled by an individual experiment. A solution of 23 in CD<sub>2</sub>Cl<sub>2</sub> was irradiated with 365 nm overnight (~10 h) of which <sup>1</sup>H and <sup>19</sup>F NMR spectra were recorded (Figure 7.18). Only of the <sup>19</sup>F NMR absorptions could distinct
peaks be integrated affording a ratio of 0.24 : 0.29 : 0.24 : 0.23 for isomer 1:2:3:4, respectively (with isomers 1 and 3 being enantiomers and identical by NMR). The $^{19}$F NMR spectrum does show a significant amount of noise even using an almost saturated solution, therefore peak fitting was performed on both spectra indicated by the blue peaks (with a residual line in bright red). The line fitting afforded the same ratio for the $^{19}$F NMR absorptions as was found by integration, while $^1$H NMR slightly deviates (Table 7.7). For the discussion regarding the asymmetric reaction profile only the ratio between isomers 2 and 4 matter. This ratio consistently indicates isomer 2 to be the major product and isomer 4 as the minor product, although the specific ratios do vary by which method is used to determine them, which indicates there is some error involved in the determination. Due to the high level of noise in the NMR spectra, the SFC integration is assumed to be superior being able to quantitatively identify each isomer, and the fitting method to be best, relying on the largest amount of data.

Table 7.7. Final ratios starting from a single isomer according to SFC integration, fitting and NMR.

<table>
<thead>
<tr>
<th></th>
<th>1-23</th>
<th>2-23</th>
<th>3-23</th>
<th>4-23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting from isomer 1</td>
<td>0.242</td>
<td>0.278</td>
<td>0.249</td>
<td>0.232</td>
</tr>
<tr>
<td>Starting from isomer 2</td>
<td>0.253</td>
<td>0.266</td>
<td>0.250</td>
<td>0.232</td>
</tr>
<tr>
<td>Starting from isomer 3</td>
<td>0.238</td>
<td>0.281</td>
<td>0.246</td>
<td>0.235</td>
</tr>
<tr>
<td>Starting from isomer 4</td>
<td>0.254</td>
<td>0.280</td>
<td>0.249</td>
<td>0.217</td>
</tr>
<tr>
<td>Average ratio by SFC integral</td>
<td>0.246</td>
<td>0.276</td>
<td>0.249</td>
<td>0.229</td>
</tr>
<tr>
<td>Ratio by fitting (Table 7.5)</td>
<td>0.248</td>
<td>0.278</td>
<td>0.248</td>
<td>0.225</td>
</tr>
<tr>
<td>Ratio by $^{19}$F NMR</td>
<td>0.239</td>
<td>0.290</td>
<td>0.239</td>
<td>0.232</td>
</tr>
<tr>
<td>Ratio by $^1$H NMR</td>
<td>0.262</td>
<td>0.258</td>
<td>0.262</td>
<td>0.218</td>
</tr>
</tbody>
</table>

Figure 7.18. NMR spectra of 23 after 10 h of irradiation (365 nm, CD$_2$Cl$_2$) with peak fitting. Left: $^1$H NMR. Right: $^{19}$F NMR.
References


[38] IUPAC: “Pseudo-asymmetric carbon atom is the traditional name for a tetrahedrally coordinated carbon atom bonded to four different entities, two and only two of which have the same constitution but opposite chirality sense. The r/s descriptors of pseudo-asymmetric carbon atoms are invariant on reflection in a mirror (i.e. r remains r, and s remains s), but are reversed by the exchange of any two entities (i.e. r becomes s, and s becomes r).”


[58] Sum of squared residuals six times smaller for s-21 than for r-21 and four times smaller for r-22 than for s-22.


THIRD GENERATION MOTORS – KEY PARAMETERS AND LIMITS