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Tetrapodal Molecular Switches and Motors: Synthesis and Photochemistry

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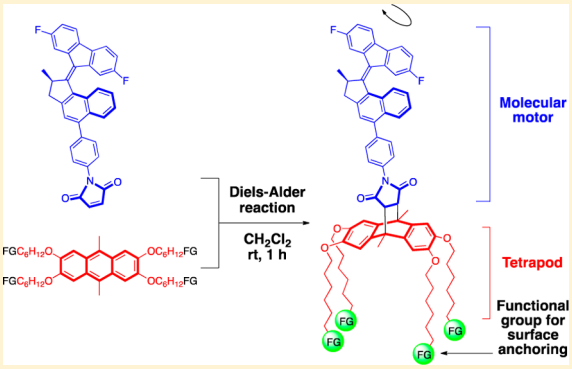
Supporting Information

ABSTRACT: The design, synthesis, and dynamic behavior of a series of novel tetrapodal molecular switches and motors containing common functional groups for attachment to various inorganic and organic surfaces are presented. Using a Diels–Alder reaction, an anthracene unit with four functionalized alkyl substituents ("legs") was coupled to maleimide-functionalized molecular switches or motors under ambient conditions. Terminal functional groups at the "legs" include thioacetates and azides, making these switches and motors ideal candidates for attachment to metallic or alkyne-functionalized surfaces. UV/vis absorption spectroscopy shows that the molecular switches and motors retain their ability to undergo reversible photoinduced and/or thermally induced structural changes after attachment to the tetrapodal anthracene.



INTRODUCTION

Achieving molecular-level control over macroscopic phenomena is a key challenge in nanotechnology.[1−9] Tuning the surface properties of a material, including wettability,[10,11] optical properties,[12,13] and conductance,[14−17] without modifying the bulk properties is of particular interest. One approach toward this goal is to attach photochromic molecules,[4,18,19] which are capable of undergoing reversible structural changes upon application of external stimuli, e.g. light, to the interfaces. Azobenzenes,[18,20,21] dithienylethenes,[18,22,23] and molecular motors based on overcrowded alkenes[24,25] have proven to be particularly versatile photochromic molecules in surface-immobilized systems.[17,26−31]

The origin of the popularity of azobenzene in these applications is their relatively facile synthesis and fatigue-resistant *trans* → *cis* photoisomerization (Scheme 1a), which is accompanied by large changes in geometry and dipole moment.[20,32] Dithienylethenes can undergo a reversible photocyclization between a ring-opened and ring-closed form by irradiation with UV and visible light (Scheme 1b). In comparison to other photochromic compounds, dithienylethenes display excellent thermal stability for both isomers as well as high fatigue resistance.[22,23] Molecular motors based on overcrowded alkenes are a unique group of photoresponsive organic molecules that are capable of converting light energy into repetitive unidirectional rotation and are promising candidates in photochemically driven systems and as multistage switches (Scheme 1c).[24,25,31]

Although the key components of surface-bound systems are the photochromic moieties that undergo structural changes upon the absorption of light, in most cases, the anchoring strategy can have a considerable impact on their switching efficiencies and performances. Their proper assembly on the surface is essential for the dynamic control of surface properties by light. The two foremost reasons for inefficient switching of monolayers of photoisomerizable chromophores are steric crowding (often observed with azobenzenes[33−39] and molecular motors[40,41]) and electronic effects (most often observed with dithienylethenes[42,43]).

A general approach to deal with the disadvantages of tight packing is to provide photochromic units with sufficient free volume to undergo the desired conformational changes. Photoresponsive azobenzene-based monolayers have been prepared using bulky anchoring groups[33,35] or substituents[36,38] as well as in mixed monolayer environments[34,39] applying alkyl thiols or silanes as diluents to ensure efficient performance. Previous studies in our group have shown that the photochemical and thermal isomerization behaviors of altitudinal bipodal molecular motors (Figure 1, left, R = H) were obstructed by intermolecular interactions when they were confined to a crowded monolayer, in comparison to the motor molecules in solution.[40]

To address this problem, we recently developed a tripodal surface-attached altitudinal rotary molecular motor system (Figure 1, right) that is able to undergo photoisomerization, which is accompanied by changes in surface wettability, on irradiation with UV light.[31] In comparison, a related bipodal

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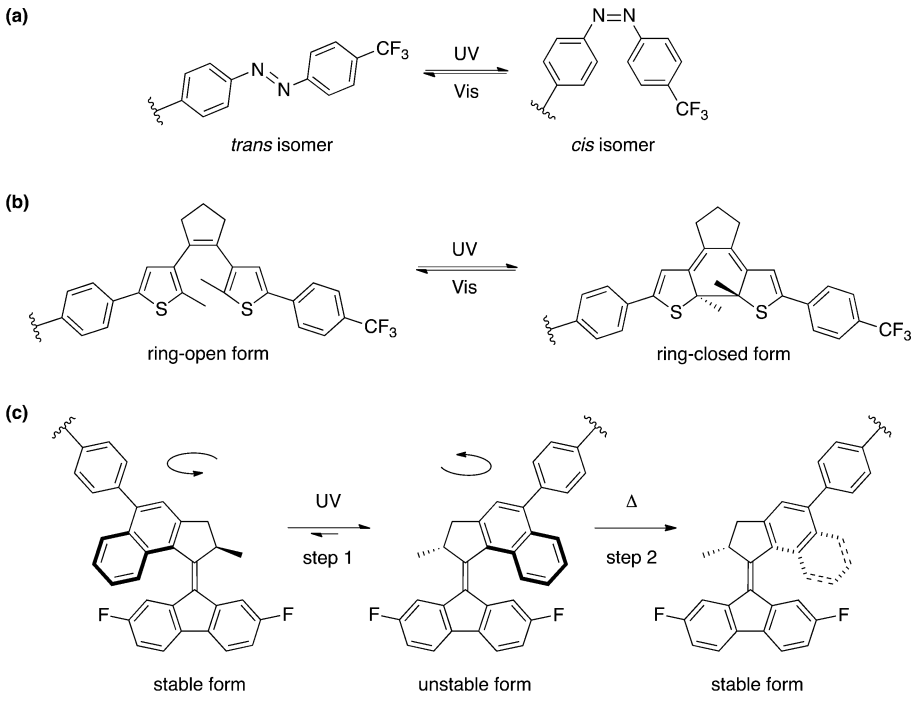
Scheme 1. Photoisomerization of (a) Azobenzenes and (b) Dithienylethenes and (c) Photochemical and Thermal Isomerization of Molecular Motors



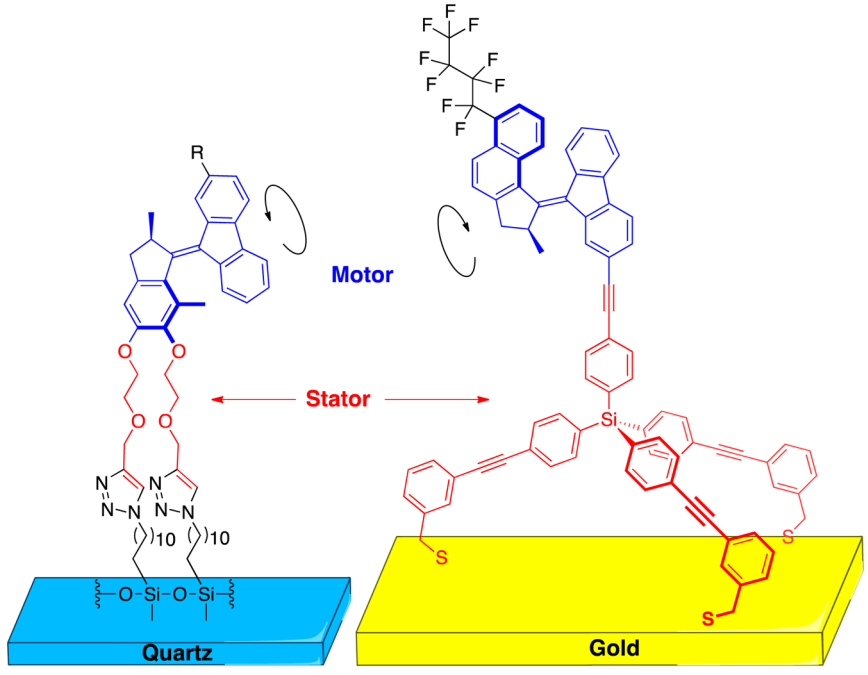


Figure 1. Bipodal (left; R = H, C_4F_9) and tripodal (right) molecular motors.

system was unable to alter surface wettability upon UV irradiation (Figure 1, left; R = C_4F_9).[41] The extra free volume between the surface-bound motors in the tripodal system resulted in enhanced switching behavior, whereas intermolecular interactions in the bipodal system interfered with isomerization, resulting in negligible changes in surface wettability upon UV irradiation.

Driven by our interest in surface-bound dynamic molecular systems for nanoscale applications and control over assembly and dynamic functions, we envisioned novel anchoring strategies for molecular switches and motors, as are shown in Scheme 2.

The tetrapodal portion of the molecules **1**–**6** consists of an anthracene-derived core with four pendant alkyl chains terminated with surface-reactive groups for attachment to metallic or organic interfaces (Scheme 2). Terminal thioacetate (SAc) functional groups at the "legs" allow for the attachment to metallic surfaces such as copper, silver, and gold,[44,45] while terminal azide (N_3) functional groups were incorporated for attachment to organic surfaces containing alkynes[40] via a Cu(I)-

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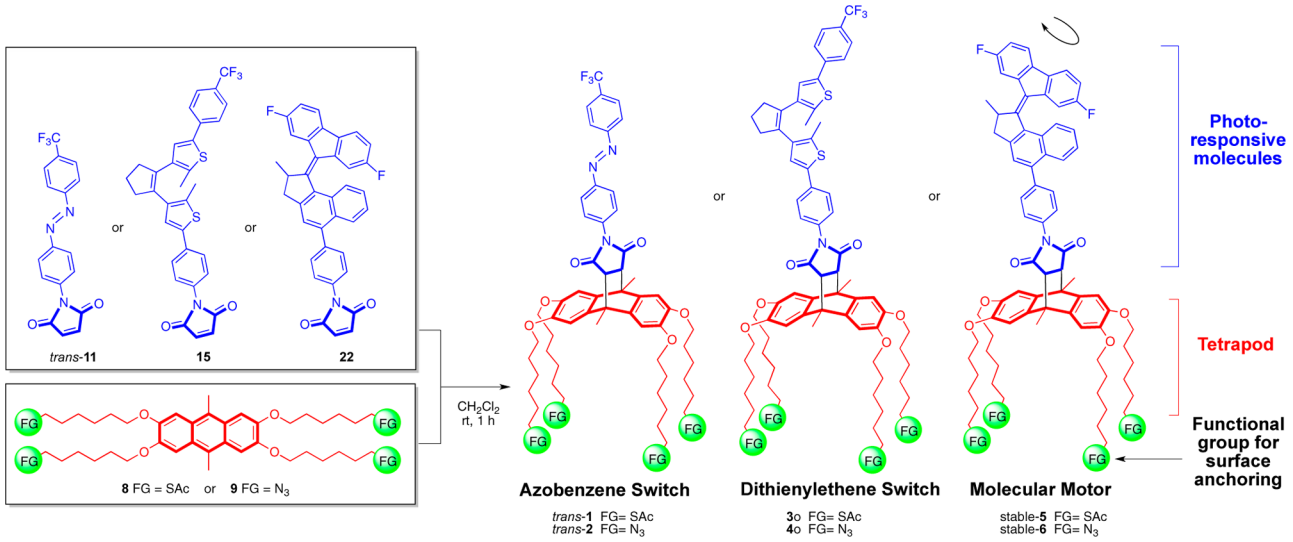
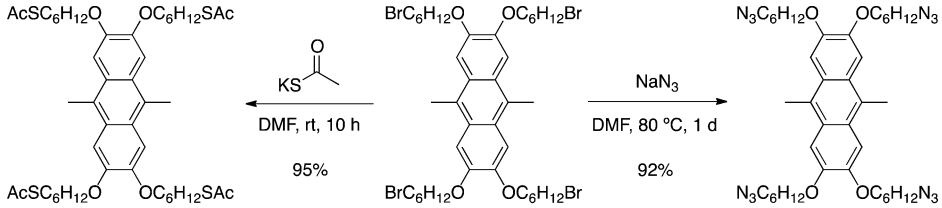
Scheme 2. Synthetic Route toward Tetrapodal Molecular Switches and Motors via a Diels–Alder Reaction[a]

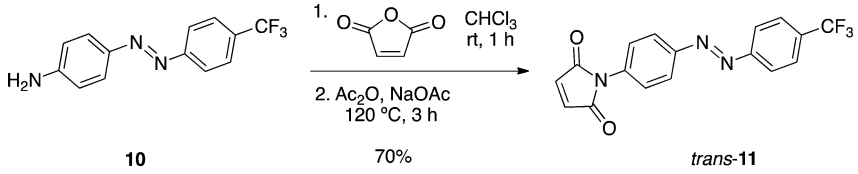


[a]For the calculated energy-minimized geometries of the Diels–Alder adducts, see the Supporting Information.

Scheme 3. Synthesis of Tetrapods 8 and 9



Scheme 4. Synthesis of the Maleimide-Functionalized Azobenzene *trans*-11



catalyzed azide–alkyne cycloaddition (1,3-dipolar cycloaddition).[46] Note that although the latter reaction requires that alkynes be introduced at the interfaces, it has been shown to be a very versatile approach for modifying the surface of a variety of materials, including Si wafers,[40] quartz,[47] polymer films,[48] and nanoparticles.[49] The anthracene core in **8** and **9** provides a stable diene moiety[50] which can react with molecular switches or motors containing dienophiles.

Here, we report a new synthetic route to produce six unique photoresponsive tetrapodal molecules suitable for surface attachment by reacting three different maleimide-functionalized molecular switches or motors with two different anthracene-based tetrapods via a Diels–Alder cycloaddition (Scheme 2). Construction of these tetrapodal photochromes is more versatile than that of our recently reported tripodal molecular motors (Figure 1, right),[31] and after surface assembly it is expected to maintain sufficient free volume, allowing for photochemical and/or thermal isomerization to occur with minimal, if any, interference from neighboring molecules.

RESULTS AND DISCUSSION

Synthesis of the Tetrapodal Molecular Switches and Motors. The synthetic approach toward tetrapod scaffolds **8** and **9** is shown in Scheme 3. The tetrapod contains four functionalized alkyl chains suitable for surface attachment and an anthracene moiety that provides a diene to react with maleimide-functionalized photochromes via a Diels–Alder reaction. The four bromide substituents of compound **7**[51] were replaced either with thioacetate groups via reaction with potassium thioacetate in DMF or with azide groups using sodium azide in DMF to afford tetrapods **8** and **9** in 95% and 92% yields, respectively.

The molecular switches and motor used in this study (i.e. *trans*-**11**, **15**, and **22**; Scheme 2) were modified with a maleimide group, allowing them to react with anthracene **8** or **9** via a Diels–Alder reaction. Note that the synthetic procedure includes the introduction of fluorine atoms into each photochromic moiety in order to facilitate the future characterization of the surface when water contact angle[52] and X-ray photoelectron spectroscopy (XPS)[53] measurements are performed.

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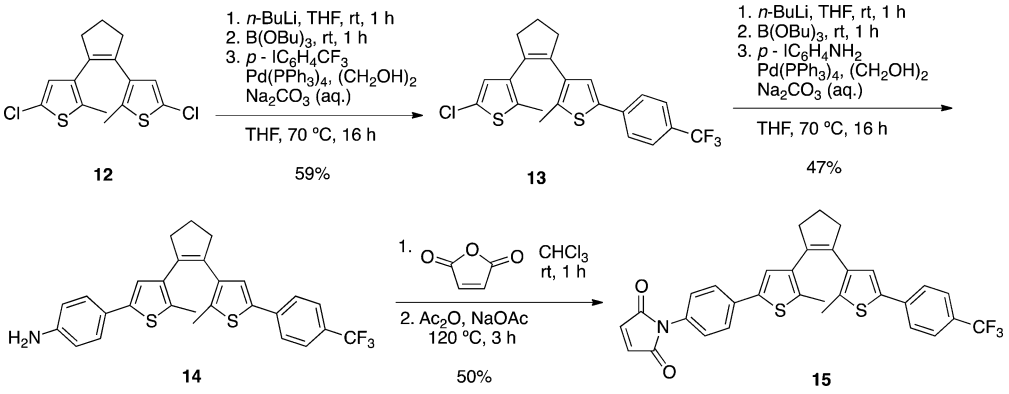
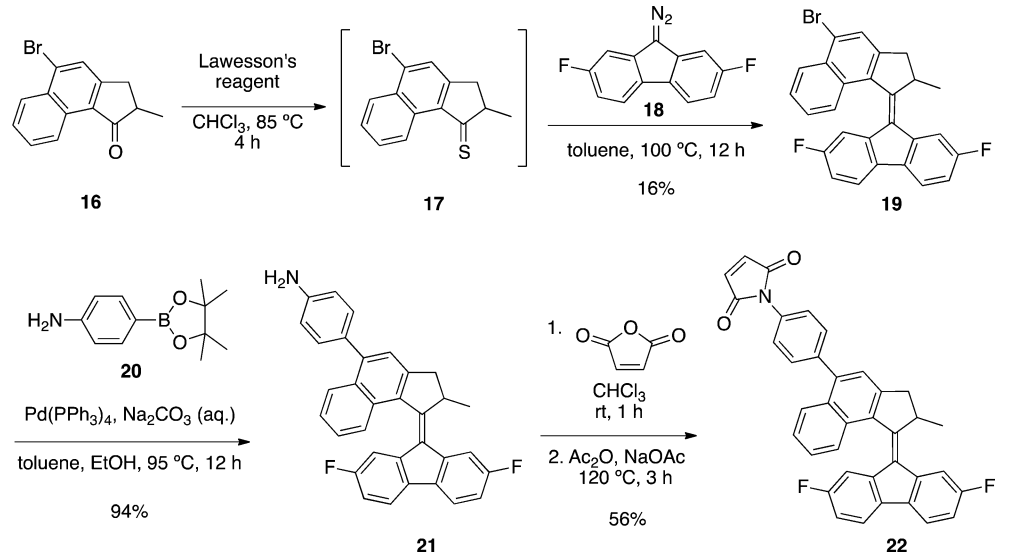
Scheme 5. Synthesis of the Maleimide-Functionalized Dithienylethene 15



Scheme 6. Synthesis of the Maleimide-Functionalized Molecular Motor 22



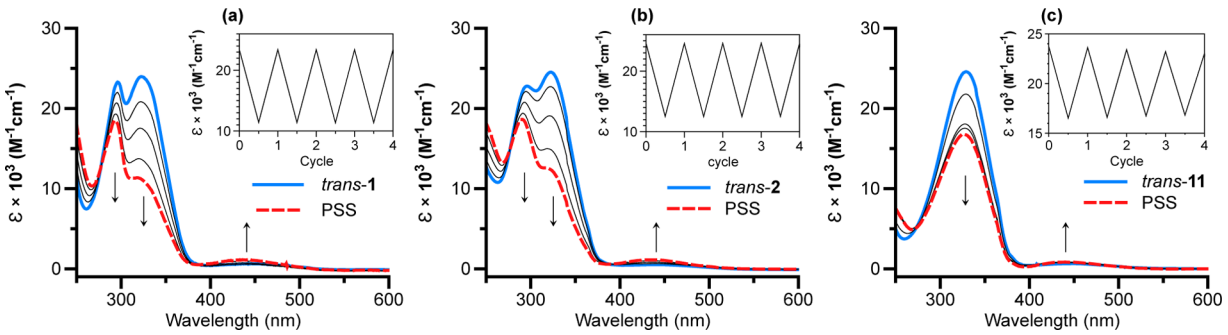


Figure 2. UV/vis absorption spectra (CH_2Cl_2, 283 K) of *trans*-**1** (a), *trans*-**2** (b), and *trans*-**11** (c) before UV irradiation (solid bold line) and at the photostationary state (PSS) (dashed line). Inserts show changes in molar absorptivity (ε) at 322 nm upon alternating irradiation with UV light and visible light over several cycles.

The maleimide-functionalized azobenzene *trans*-**11** was synthesized by treating aniline **10**[54] with maleic anhydride in chloroform followed by cyclization using a solution of sodium acetate in acetic anhydride (Scheme 4).

Dithienylethene **15** was synthesized as depicted in Scheme 5. The dichloro compound **12**[55] was first monofunctionalized with a trifluoromethylbenzene group through a Suzuki cross-coupling, affording the monochloro compound **13**. A second Suzuki cross-coupling with commercially available *p*-$IC_6H_4NH_2$ yielded intermediate **14**. The maleimide-functionalized dithienylethene **15** was then obtained using a procedure similar to that described above for the synthesis of *trans*-**11**.

The molecular motor **22** was synthesized according to the route depicted in Scheme 6. Ketone **16**[56] was treated with Lawesson's reagent in chloroform to give the thioketone intermediate **17**. The highly sterically hindered olefin in **19** was formed using a Barton–Kellogg diazo–thioketone coupling by heating thioketone **17** and the known diazo compound **18**[57] at 100 °C in toluene. A subsequent palladium-catalyzed cross coupling was used to attach the aniline group in **21**, followed by

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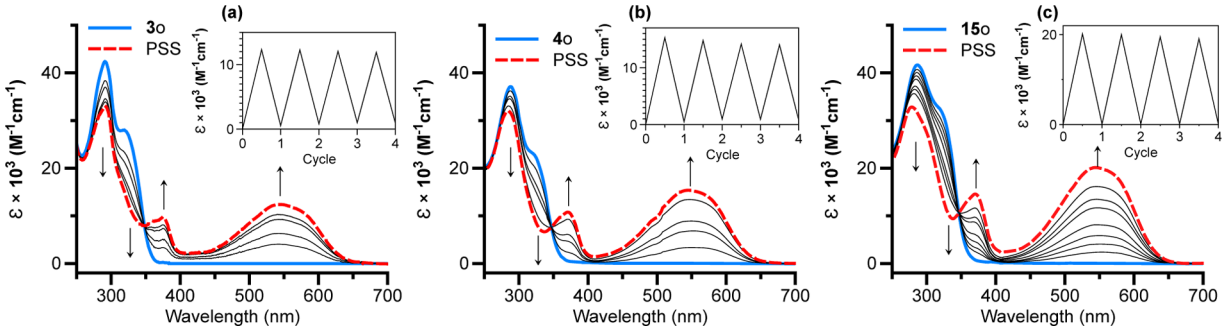

Figure 3. UV/vis absorption spectra (CH_2Cl_2, 283 K) of **3**o (a), **4**o (b), and **15**o (c) before UV irradiation (solid bold line) and at the PSS (dashed line). Inserts show changes in molar absorptivity (ε) at 550 nm upon alternating irradiation with UV and visible light over several cycles.

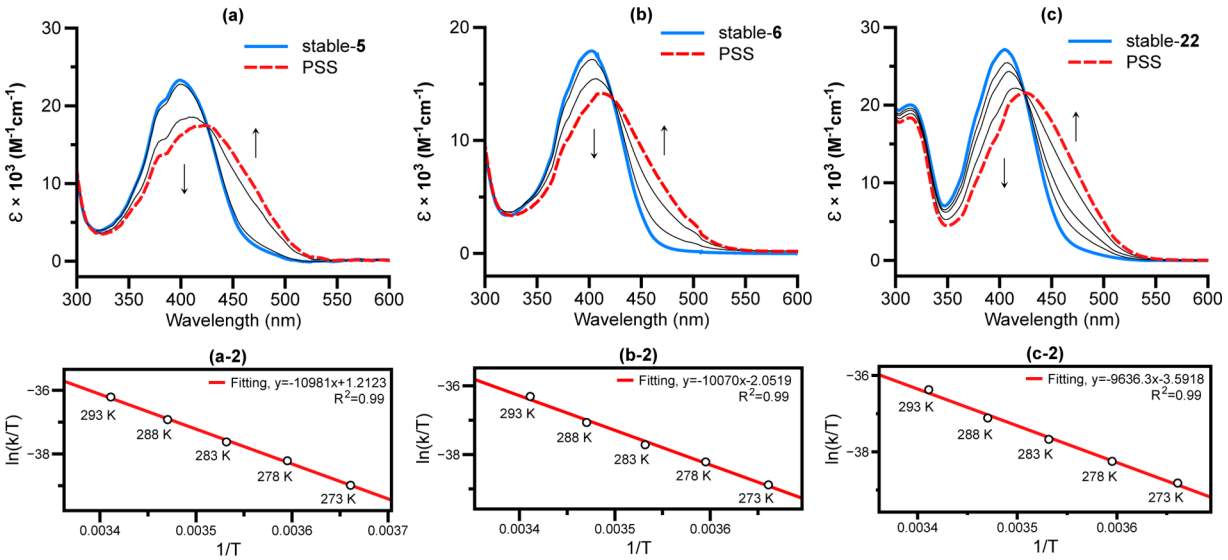

Figure 4. UV/vis absorption spectra (CH_2Cl_2, 283 K) of stable-**5** (a), stable-**6** (b), and stable-**22** (c) before irradiation (solid bold line) and at the PSS (dashed line); Eyring plot of the conversion of unstable-**5** → stable-**5** (a-2), unstable-**6** → stable-**6** (b-2), and unstable-**22** → stable-**22** (c-2) via thermal isomerization at different temperatures.

the introduction of the maleimide group to afford molecular motor **22**.

The Diels–Alder strategy toward tetrapodal compounds **1**–**6** ultimately to be used for surface modification was tested by mixing diene **8** or **9** with *trans*-**11**, **15**, or **22** in CH_2Cl_2 under ambient conditions, yielding *trans*-**1**, *trans*-**2**, **3**o, **4**o, stable-**5**, and stable-**6** (Scheme 2). By monitoring the reaction by TLC and ^{1}H NMR, we observed full conversion in 1 h and the desired products were obtained in excellent isolated yield (>95%). Although Diels–Alder reactions are known to be thermally reversible,[58] no retro Diels–Alder reaction was observed upon standing of the NMR solutions at room temperature for 72 h, showing the thermal stability of the Diels–Alder adducts. See also S9 in the Supporting Information for further discussions.

Photochemical Behavior of Tetrapodal Azobenzenes. The photochemical behavior of azobenzenes **1**, **2**, and **11** was analyzed by UV/vis absorption spectroscopy. The UV/vis absorption spectra of azobenzenes *trans*-**1** and *trans*-**2** in CH_2Cl_2 showed absorption bands centered at 296 and 322 nm (Figure 2a,b, solid bold line). For *trans*-**11** the maximum absorption was centered at 329 nm (Figure 2c, solid bold line). Upon irradiation with UV light (λ_{max} 365 nm), the major bands decreased in intensity and new bands centered at 437 nm appeared. This spectral change is indicative of the photochemically induced formation of the *cis* isomer (Scheme 1a; *cis*-**1**, *cis*-**2**, and *cis*-**11**).[20]

During the irradiation of each compound, clear isosbestic points were observed, and each sample was irradiated until no further changes were noted: i.e., the photostationary state (PSS) was reached (Figure 2, dashed lines). Irradiation of the PSS mixture of *trans*-**1**/*cis*-**1**, *trans*-**2**/*cis*-**2**, or *trans*-**11**/*cis*-**11** with visible light (>500 nm) resulted in the recovery of the original spectra, which is indicative of photoisomerization back to the original *trans* isomers. These switching cycles could be repeated several times without observing any sign of fatigue (Figure 2, insert).

Photochemical Behavior of Tetrapodal Dithienylethenes. The photochemical behavior of dithienylethenes **3**, **4**, and **15** was analyzed in a similar manner. UV/vis absorption spectra of dithienylethenes **3**o, **4**o, and **15**o (o, ring-opened form of the dithienylethenes) in CH_2Cl_2 showed absorption bands with maxima around 290 and 325 nm (Figure 3, solid bold line). Upon UV irradiation (λ_{max} 312 nm), both major bands decreased in intensity and two new bands centered around 370 and 544 nm appeared simultaneously, which is indicative of the photochemically induced formation of the isomers in the ring-closed form (Scheme 1b, **3**c, **4**c and **15**c; c denotes the ring-closed form of the dithienylethenes).[22]

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Isosbestic points were clearly visible during the irradiation, and the PSS (Figure 3, dashed lines) was reached after 5 min. Irradiation of the PSS mixture of **3**o/**3**c, **4**o/**4**c, or **15**o/**15**c with visible light (>500 nm) regenerated the original spectra, indicating formation of the isomers in the ring-opened form. The inserts in Figure 3 show that the switching cycles could be repeated several times without the observation of any fatigue: i.e., the tetrapodal dithienylethene switches are highly stable under photochemical conditions.

Photochemical and Thermal Behavior of Tetrapodal Molecular Motors. Finally, the photochemical and thermal behavior of molecular motors **5**, **6**, and **22** were studied. The UV/vis absorption spectra of the stable form of molecular motors **5**, **6**, and **22** in CH_2Cl_2 show absorption bands centered at 405 nm (Figure 4, solid bold line). Irradiation of the samples with UV light (λ_{max} 365 nm) led to a red shift of the bands at 405 nm, indicating the photochemically induced formation of the unstable isomer (Scheme 1c, step 1; unstable-**5**, unstable-**6**, and unstable-**22**). This shift is consistent with increased strain at the central double bond and the generation of a higher energy isomer.[59]

During irradiation, clear isosbestic points were maintained in each case and samples were irradiated until no further changes were observed: i.e., the PSS (Figure 4, dashed lines) was reached. Warming the PSS mixtures to room temperature resulted in a blue shift of the bands back to their original position, which is consistent with thermal isomerization back to the corresponding stable isomers (Scheme 1c, step 2). The thermal isomerization steps (Scheme 1c, step 2) were followed over a range of temperatures, and from these data the Eyring plots were obtained (Figure 4, lower panels; see the Experimental Section for details). For unstable-**5** → stable-**5**, the Gibbs free energy of activation ($\Delta G^{\ddagger\circ}$) was calculated to be 88.5 kJ/mol (half-life $t_{1/2}$ = 625 s at room temperature), and for unstable-**6** → stable-**6**, $\Delta G^{\ddagger\circ}$ = 89.1 kJ/mol ($t_{1/2}$ = 731 s at room temperature). These values are similar to the half-life of their parent motor **22** (unstable-**22** → stable-**22**, $\Delta G^{\ddagger\circ}$ = 89.2 kJ/mol; $t_{1/2}$ = 777 s at room temperature).

In summary, by studying the photochemical and thermal behavior of **5**, **6**, and **22** in solution by UV/vis absorption spectroscopy, and by analogy with similar motor systems reported previously,[31,59,60] it is anticipated that **5**, **6**, and **22** function as light-driven rotary motors in solution. The photochemical studies and the Eyring analyses show that the Diels–Alder adduct does not have a significant influence on the photochemical and thermal behaviors of the motors.

CONCLUSION

In conclusion, we have described a new surface attachment strategy for molecular switches and motors based on a Diels–Alder transformation. To achieve this, we have developed tetrapodal anthracene units as dienes containing either thioacetate or azide pendant functional groups. These dienes were coupled to maleimide-functionalized molecular switches as well as a molecular motor. The tetrapodal molecular switches and motors produced by this method retained their ability to undergo photoisomerization in solution upon irradiation, as was demonstrated by UV/vis absorption spectroscopy. The design and synthesis of these novel tetrapod-functionalized photochromophores described herein will allow us to develop highly functional and photoresponsive surfaces for application in smart materials and nanotechnology research. Studies on the behavior of the systems on attachment to surfaces are currently ongoing.

EXPERIMENTAL SECTION

General Remarks. All reactions were performed in oven-dried glassware under a nitrogen atmosphere, unless stated otherwise; solvents were reagent grade, and commercially available reagents were used without purification. UVASOL grade solvents were used for spectroscopic measurements. UV irradiation experiments were performed using an UV lamp (λ_{max} 312 or 365 nm) and visible irradiation using a high-intensity fiber optic white light source combined with a 500 nm long-pass filter. Kinetic analyses of the thermal isomerization steps of the motors (unstable-**5** → stable-**5**, unstable-**6** → stable-**6**, and unstable-**22** → stable-**22**) were performed by UV/vis absorption spectroscopy. A long-pass filter was mounted between the UV light source and the sample to cut off light with wavelengths below 460 nm to minimize photochemical isomerization occurring upon data recording. The thermal isomerization was followed by monitoring the change in absorption at 470 nm as a function of time at 273, 278, 283, 288, and 293 K. From the obtained data the rate constants (k) for the thermal isomerization steps were obtained and Eyring plots were drawn for the data.

Synthesis. *Compound* ***8***. A suspension of 2,3,6,7-tetrakis(6-bromohexyloxy)-9,10-dimethylanthracene (**7**;[51] 1.00 g, 1.08 mmol) and potassium thioacetate (656 mg, 5.75 mmol) in DMF (130 mL) was stirred for 10 h at room temperature. The mixture was treated with water (90 mL), and the water layer was extracted with CH_2Cl_2 (3 × 45 mL). The combined organic layers were washed with water (75 mL) and brine (75 mL), dried over $MgSO_4$, and concentrated. Flash column chromatography (SiO_2, CH_2Cl_2) gave **8** as a pale yellow solid (930 mg, 1.03 mmol, 95%): mp 116.8–118.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 4H), 4.17 (t, J = 6.5 Hz, 8H), 2.90 (m, 14H), 2.33 (s, 12H), 1.99–1.87 (m, 8H), 1.69–1.43 (m, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) 195.9, 148.5, 125.8, 123.6, 104.3, 68.5, 30.6, 29.5, 29.0, 28.6, 25.7, 14.7; UV/vis (CH_2Cl_2, 293 K) λ_{max} (ε) 278 nm (143517 M^{-1} cm^{-1}); HRMS (ESI-ion trap) m/z: $[M]^+$ calcd for $C_{48}H_{70}O_8S_4$ 902.3948, found 902.3922.

Compound ***9***. A mixture of 2,3,6,7-tetrakis(6-bromohexyloxy)-9,10-dimethylanthracene (**7**;[51] 85 mg, 0.092 mmol) and sodium azide (36 mg, 0.55 mmol) was heated to 80 °C in DMF (30 mL) for 24 h. The solvent was evaporated, and the residue was dissolved in CH_2Cl_2 (50 mL) and washed with water (50 mL). The organic phase was dried over $MgSO_4$ and filtered over a silica plug, and then the residue was concentrated in vacuo, affording **9** as a pale yellow solid (65 mg, 0.085 mmol, 92%): mp 105.4–107.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (s, 4H), 4.18 (t, J = 6.4 Hz), 3.31 (t, J = 6.8 Hz), 2.91 (s, 6H), 2.03–1.88 (m, 8H), 1.75–1.43 (m, 24H); ^{13}C NMR δ (75 MHz, $CDCl_3$) 148.8, 126.1, 123.8, 104.7, 68.7, 51.6, 29.3, 29.1, 26.8, 26.0, 14.9; UV/vis (CH_2Cl_2, 293 K) λ_{max} (ε) 277 nm (100717 M^{-1} cm^{-1}); HRMS (ESI-ion-trap) m/z $[M]^+$ calcd for $C_{40}H_{58}N_{12}O_4$ 770.4698, found 770.4695.

Compound ***11***. (*E*)-4-((4-(Trifluoromethyl)phenyl)diazenyl)-benzeneamine **10** (2.36 g, 24.1 mmol) in $CHCl_3$ (200 mL) was added dropwise to a stirred solution of maleic anhydride (6.39 g, 24.1 mmol) in $CHCl_3$ (40 mL) at room temperature, after which stirring was continued for 1 h. The solvent was evaporated and the residue was added to a solution of sodium acetate (3.95 g, 48.2 mmol) in acetic anhydride (2 mL). The resulting mixture was heated at 120 °C for 3 h, cooled to room temperature and concentrated in vacuo. Flash column chromatography (SiO_2, CH_2Cl_2) provided *trans*-**11** as an orange solid (5.82 g, 16.9 mmol, 70%): mp 174.4–175.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08–7.98 (m, 4H), 7.79 (d, J = 8.3 Hz, 2H), 7.62–7.57 (m, 2H), 6.90 (s, J = 3.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 151.0, 134.4, 134.2, 126.3, 126.3, 126.2, 123.8, 123.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.60; UV/vis (CH_2Cl_2, 283 K) λ_{max} (ε) = 445 (643), 329 nm (24648 M^{-1} cm^{-1}); HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{17}H_{11}F_3N_3O_2$ 346.0798, found 346.0787.

Compound ***13***. *n*-BuLi (1.6 M solution in hexane, 3.99 mL, 6.38 mmol) was added dropwise to a stirred solution of 1,2-bis(5-chloro-2-

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methylthiophen-3-yl)cyclopent-1-ene (**12**;[55] 2.00 g, 6.07 mmol) at room temperature in THF (80 mL), after which stirring was continued for 1 h. Subsequently, tributyl borate (1.96 g, 8.50 mmol) was added dropwise and the resulting mixture was deoxygenated by purging with argon for 5 min and then stirred for an additional 1 h (flask A). Meanwhile, in a separate flask (flask B), a stirred mixture of *p*-$IC_6H_4CF_3$ (2.48 g, 9.11 mmol), $Pd(PPh_3)_4$ (0.19 g, 0.18 mmol), ethylene glycol (0.8 mL), and aqueous Na_2CO_3 (2 M, 32 mL) in THF (50 mL) was deoxygenated by purging with argon for 5 min and then heated to 70 °C. The suspension in flask A was transferred to flask B by cannula, and the combined mixture was heated at 70 °C for 16 h under an argon atmosphere. The mixture was diluted with Et_2O (200 mL) and washed with water (2 × 100 mL). The combined aqueous layers were extracted with Et_2O (100 mL), after which the combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. Flash column chromatography (SiO_2, pentane) provided **13** as a light brown solid (1.56 g, 3.55 mmol, 59%): mp 84.5−85.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 4H), 7.06 (s, 1H), 6.62 (s, 1H), 2.85−2.72 (m, 4H), 2.11−2.00 (m, 5H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1, 137.8, 136.8, 136.1, 135.0, 135.0, 134.3, 133.29, 126.8, 125.9, 125.8, 125.8, 125.7, 125.3, 125.3, 125.2, 118.5, 115.8, 38.4, 38.4, 22.9, 14.5, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.50 (d, J = 8.5 Hz); HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{22}H_{19}ClF_3S_2$ 439.0563, found 439.0567.

Compound ***14***. *n*-BuLi (1.6 M solution in hexane, 2.30 mL, 3.68 mmol) was added dropwise to a stirred solution of **13** (1.54 g, 3.51 mmol) at room temperature in THF (50 mL), after which stirring was continued for 1 h. Tributyl borate (1.13 g, 4.91 mmol) was added dropwise, and the resulting mixture was deoxygenated by purging with argon for 5 min and then stirred for an additional 1 h (flask A). Meanwhile, in a separate flask (flask B), a stirred mixture of *p*-$IC_6H_4NH_2$ (1.54 g, 7.02 mmol), $Pd(PPh_3)_4$ (109 mg, 0.11 mmol), ethylene glycol (0.8 mL), and aqueous Na_2CO_3 (2 M, 18 mL) in THF (30 mL) was deoxygenated by purging with argon for 5 min and then heated to 70 °C. The suspension in flask A was transferred to flask B by cannula, and the resulting mixture was heated at 70 °C for 16 h under an argon atmosphere. The mixture was diluted with Et_2O (100 mL) and washed with water (2 × 100 mL). The combined aqueous layers were extracted with Et_2O (50 mL), after which the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Flash column chromatography (SiO_2, 17/3 pentane/Et_2O) provided **14** as an orange viscous oil (813 mg, 1.64 mmol, 47%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 4H), 7.31 (d, J = 8.5 Hz, 2H), 7.11 (s, 1H), 6.87 (s, 1H), 6.66 (d, J = 8.6 Hz, 2H), 3.71 (br s, 2H), 2.84 (t, J = 7.4 Hz, 4H), 2.15−1.98 (m, 5H), 1.96 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.5, 140.4, 137.9, 137.7, 137.2, 136.2, 136.1, 135.4, 133.9, 132.6, 128.7, 128.4, 126.5, 125.8, 125.8, 125.7, 125.7, 125.6, 125.3, 125.2, 122.9, 122.0, 115.3, 38.5, 38.4, 23.0, 14.6, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.45; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{28}H_{25}F_3NS_2$ 496.1375, found 496.1361.

Compound ***15***. Compound **14** (300 mg, 0.61 mmol) in $CHCl_3$ (1 mL) was added dropwise to a stirred solution of maleic anhydride (60 mg, 0.61 mmol) in $CHCl_3$ (0.2 mL) at room temperature, after which stirring was continued for 1 h. The solution was concentrated, and to the residue were added acetic anhydride (5 mL) and sodium acetate (99 mg, 1.21 mmol). The resulting mixture was heated to 120 °C for 3 h, cooled to room temperature, and concentrated in vacuo. Flash column chromatography (SiO_2, CH_2Cl_2) provided **15** as a yellow solid (173 mg, 0.30 mmol, 50%): mp 186.0−187.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60−7.54 (m, 6H), 7.32 (d, J = 8.5 Hz, 2H), 7.11 (s, 1H), 7.03 (s, 1H), 6.85 (s, 2H), 2.86 (t, J = 7.4 Hz, 4H), 2.15−2.05 (m, 2H), 2.02 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 138.6, 137.9, 137.8, 137.0, 136.7, 136.1, 135.2, 135.0, 134.5, 134.2, 134.2, 129.8, 128.8, 128.5, 128.1, 126.3, 125.9, 125.8, 125.8, 125.8, 125.7, 125.5, 125.4, 125.2, 124.6, 122.8, 38.4, 23.0, 14.5, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.47; UV/vis (CH_2Cl_2, 283 K) λ_{max} (ε) 325 (30568), 287 nm (41446 M^{-1} cm^{-1}); HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{32}H_{25}F_3NO_2S_2$ 576.1273, found 576.1257.

Compound ***19***. To a solution of 5-bromo-2-methyl-2,3-dihydro-1*H*-cyclopenta[*a*]naphthalen-1-one (**16**;[56] 2.30 g, 8.4 mmol) in toluene (30 mL) was added Lawesson's reagent (4.15 g, 10.3 mmol). The mixture was heated to 90 °C for 4 h. The solution was concentrated, and the residue was purified by flash column chromatography (SiO_2, 1/1 pentane/CH_2Cl_2). The first wine red band was collected (1.28 g), concentrated in vacuo, and added immediately to a solution of 9-diazo-2,7-difluoro-9*H*-fluorene (**18**;[57] 1.00 g, 4.4 mmol) in toluene (30 mL). The mixture was heated at 90 °C for 12 h, cooled to room temperature, and concentrated in vacuo. Flash column chromatography (SiO_2, 19/1 pentane/MTBE) afforded **19** as a viscous orange oil (330 mg, 0.72 mmol, 16%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 8.5 Hz, 1H), 7.93 (s, 1H), 7.77−7.66 (m, 2H), 7.65−7.56 (m, 3H), 7.43 (dd, J = 11.2, 4.0 Hz, 1H), 7.10 (td, J = 8.6, 2.2 Hz, 1H), 6.92 (td, J = 8.6, 2.3 Hz, 1H), 6.27 (dd, J = 10.7, 2.3 Hz, 1H), 4.32−4.21 (m, 1H), 3.58 (dd, J = 15.3, 5.6 Hz, 1H), 2.77 (d, J = 15.3 Hz, 1H), 1.39 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 162.7, 161.2, 160.3, 152.4, 147.9, 141.3, 141.3, 141.2, 138.7, 138.7, 138.6, 138.6, 135.6, 135.4, 135.4, 135.0, 135.0, 130.9, 130.8, 130.3, 129.9, 129.6, 128.3, 128.2, 127.8, 127.4, 127.3, 127.1, 126.9, 126.4, 125.3, 120.2, 120.1, 119.5, 119.4, 114.3, 114.0, 112.9, 112.7, 111.4, 111.2, 72.8, 49.5, 45.5, 45.2, 41.6, 27.0, 19.1; HRMS (APCI) m/z $[M + H]^+$ calcd for $C_{27}H_{18}BrF_2$ 459.0554, found 459.0547.

Compound ***21***. An aqueous solution of Na_2CO_3 (2 M, 1.36 mL), EtOH (1.5 mL), and 4-aminophenylboronic acid pinacol ester **20** (143 mg, 0.65 mmol) were added to a solution of **19** (250 mg, 0.55 mmol) and $Pd(PPh_3)_4$ (28 mg, 27 μmol) in toluene (5 mL). The reaction mixture was deoxygenated by purging with argon for 5 min and stirred at 95 °C for 12 h. The mixture was diluted with water (20 mL) and EtOAc (20 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Flash column chromatography (SiO_2, 1/1 pentane/CH_2Cl_2) provided **21** as an orange sticky oil (173 mg, 0.30 mmol, 50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.3 Hz, 1H), 7.78−7.59 (m, 4H), 7.52 (s, 1H), 7.48−7.33 (m, 4H), 7.10 (td, J = 8.7, 2.2 Hz, 1H), 6.96−6.91 (m, 1H), 6.91−6.85 (m, 2H), 6.43 (dd, J = 10.9, 2.3 Hz, 1H), 4.29 (quin, J = 6.5 Hz, 1H), 3.98 (brs, 2H), 3.60 (dd, J = 15.1, 5.6 Hz, 1H), 2.81 (d, J = 15.2 Hz, 1H), 1.43 (d, J = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 165.2, 164.1, 163.3, 156.8, 150.4, 148.4, 146.9, 144.2, 144.1, 141.6, 141.6, 137.9, 137.4, 137.4, 137.3, 137.2, 137.1, 136.7, 133.9, 133.5, 132.9, 132.7, 131.3, 130.5, 130.5, 130.4, 130.4, 130.2, 130.0, 129.4, 128.2, 127.4, 122.8, 122.7, 122.0, 121.9, 117.8, 116.5, 116.3, 115.7, 115.5, 114.0, 113.8, 105.0, 47.8, 44.6, 22.1; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{33}H_{24}F_2N$ 472.1871, found 472.1865.

Compound ***22***. Compound **21** (100 mg, 0.21 mmol) in $CHCl_3$ (1 mL) was added dropwise to a stirred solution of maleic anhydride (20.1 mg, 0.21 mmol) in $CHCl_3$ (0.2 mL) at room temperature, after which stirring was continued for 1 h. The solution was concentrated, and the residue was treated with acetic anhydride (2 mL) and sodium acetate (34.8 mg, 0.42 mmol). This mixture was heated at 120 °C for 3 h, cooled to room temperature, and concentrated in vacuo. Flash column chromatography (SiO_2, CH_2Cl_2) provided **22** as a yellow solid (65 mg, 0.12 mmol, 56%): mp 300.5−301.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 8.6 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.78−7.63 (m, 5H), 7.58 (d, J = 7.6 Hz, 3H), 7.49 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.4 Hz, 1H), 7.29 (s, 1H), 7.13 (t, J = 8.3 Hz, 1H), 7.00−6.93 (m, 3H), 6.46 (d, J = 10.7 Hz, 1H), 4.41−4.28 (m, 1H), 3.65 (dd, J = 15.3, 5.3 Hz, 1H), 2.86 (d, J = 15.1 Hz, 1H), 1.47 (d, J = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 166.0, 165.2, 164.1, 163.3, 156.3, 150.1, 145.4, 144.1, 144.1, 142.9, 141.5, 141.5, 138.0, 137.9, 137.6, 137.0, 133.5, 133.5, 133.4, 132.5, 131.9, 130.0, 129.9, 129.7, 128.6, 128.6, 127.8, 122.8, 122.7, 122.1, 122.0, 116.7, 116.5, 115.8, 115.6, 114.1, 113.9, 47.9, 44.6, 22.0; UV/vis (CH_2Cl_2, 283 K) λ_{max} (ε) 405 (27161), 314 nm (20017 M^{-1} cm^{-1}); HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{37}H_{23}F_2NO_2$ 551.1691, found 551.1681.

General Method for the Synthesis of *trans*-1, *trans*-2, 3o, 4o, stable-5, and stable-6. A solution of diene (**8** or **9**, 25 mg) and dienophile (**11**, **15**, or **22**, 1.1 equiv) in CH_2Cl_2 (0.02 M) was stirred at room temperature until TLC and ^{1}H NMR indicated complete conversion. The solvent was evaporated to yield the crude product.

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The products were obtained after filtration of the crude material through a short plug of SiO_2 with CH_2Cl_2 as eluent to remove the unreacted dienophile and subsequently using EtOAc to collect the product.

*Compound trans-**1**.* Following the general method, *trans*-**1** was obtained (33 mg, 0.027 mmol, 96%) as an orange oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.3 Hz, 2H), 7.88 (d, J = 8.6 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H), 6.98 (s, 2H), 6.89 (s, 2H), 6.82 (d, J = 8.6 Hz, 2H), 4.05−3.86 (m, 8H), 3.04 (s, 2H), 2.86 (dt, J = 12.0, 7.3 Hz, 8H), 2.32 (s, 6H), 2.29 (s, 6H), 2.26 (s, 6H), 1.84−1.71 (m, 8H), 1.65−1.35 (m, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 195.9, 174.7, 154.2, 151.6, 147.8, 147.5, 138.0, 134.5, 134.3, 127.2, 126.3, 126.3, 123.7, 123.2, 109.7, 109.3, 69.8, 69.8, 52.8, 44.1, 30.6, 30.6, 29.5, 29.5, 29.3, 29.2, 29.0, 28.99, 28.5, 28.5, 25.6, 25.5, 16.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.60; UV/vis (CH_2Cl_2, 283 K) λ_{max} (ε) 454 (964), 322 (24068), 296 nm (23343 M^{-1} cm^{-1}); HRMS (ESI-ion trap) m/z [M + Na]$^+$ calcd for $C_{65}H_{80}F_3N_3O_{10}S_4Na$ 1270.4570, found 1270.4573.

*Compound trans-**2**.* Following the general method, *trans*-**2** was obtained (34 mg, 0.031 mmol, 95%) as an orange oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.3 Hz, 2H), 7.88 (d, J = 8.7 Hz, 2H), 7.78 (d, J = 8.5 Hz, 2H), 6.99 (s, 2H), 6.90 (s, 2H), 6.83 (d, J = 8.7 Hz, 2H), 4.07−3.87 (m, 8H), 3.27 (dt, J = 14.1, 6.9 Hz, 8H), 3.05 (s, 2H), 2.27 (s, 6H), 1.87−1.71 (m, 8H), 1.69−1.38 (m, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 151.6, 147.8, 147.5, 138.0, 134.6, 134.3, 127.2, 126.3, 123.7, 123.1, 109.7, 109.3, 69.7, 52.8, 51.4, 51.3, 44.1, 29.3, 29.2, 28.8, 28.8, 26.5, 26.4, 25.7, 25.6, 16.0; UV/vis (CH_2Cl_2, 283 K) λ_{max} (ε) 454 (1394), 322 (24559), 297 nm (23851 M^{-1} cm^{-1}); HRMS (ESI-ion trap) m/z [M + H]$^+$ calcd for $C_{57}H_{69}F_3N_{15}O_6$ 1116.5502, found 1116.5507.

*Compound **3o**.* Following the general method, **3o** was obtained (39 mg, 0.026 mmol, 94%) as a beige oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 4H), 7.40 (d, J = 8.5 Hz, 2H), 7.08 (s, 1H), 6.97 (br s, 3H), 6.87 (s, 2H), 6.56 (d, J = 8.5 Hz, 2H), 4.03−3.85 (m, 8H), 3.01 (s, 2H), 2.91−2.79 (m, 12H), 2.32 (s, 6H), 2.30 (s, 6H), 2.25 (s, 6H), 2.15−2.03 (m, 2H), 1.99 (s, 3H), 1.98 (s, 3H), 1.84−1.69 (m, 8H), 1.66−1.35 (m, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 195.9, 175.0, 147.8, 147.5, 138.6, 138.1, 137.9, 137.8, 137.0, 136.7, 136.1, 135.2, 135.0, 134.8, 134.6, 134.5, 130.1, 128.7, 128.4, 128.2, 128.1, 126.8, 125.8, 125.8, 125.8, 125.7, 125.5, 125.4, 125.2, 124.5, 122.8, 109.6, 109.3, 69.8, 69.8, 52.7, 44.0, 38.4, 30.6, 30.6, 29.5, 29.5, 29.3, 29.2, 29.0, 28.5, 28.5, 25.6, 25.5, 23.0, 16.0, 14.5, 14.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.45; UV/vis (CH_2Cl_2, 283 K) λ_{max} (ε) 325 (34875), 290 nm (42534 M^{-1} cm^{-1}); HRMS (ESI-ion trap) m/z [M + Na]$^+$ calcd for $C_{80}H_{94}F_3NO_{10}S_6Na$ 1500.5046, found 1500.5050.

*Compound **4o**.* Following the general method, **4o** was obtained (43 mg, 0.032 mmol, 98%) as a beige oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 4H), 7.39 (d, J = 8.5 Hz, 2H), 7.07 (s, 1H), 6.97 (s, 2H), 6.96 (s, 1H), 6.88 (s, 2H), 6.56 (d, J = 8.6 Hz, 2H), 4.05−3.84 (m, 8H), 3.26 (dt, J = 14.1, 6.9 Hz, 8H), 3.01 (s, 2H), 2.83 (s, 4H), 2.25 (s, 6H), 2.14−2.04 (m, 2H), 1.99 (s, 3H), 1.98 (s, 3H), 1.86−1.70 (m, 8H), 1.68−1.34 (m, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.0, 174.9, 147.7, 147.4, 138.6, 138.1, 137.9, 137.8, 136.9, 136.7, 136.1, 135.3, 134.9, 134.8, 134.6, 134.5, 130.1, 126.8, 125.8, 125.8, 125.4, 125.2, 124.6, 109.6, 109.3, 69.7, 69.7, 52.7, 51.4, 51.3, 44.0, 38.4, 29.3, 29.2, 28.8, 28.8, 26.5, 26.4, 25.7, 25.6, 23.0, 16.0, 14.4, 14.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.45; UV/vis (CH_2Cl_2, 283 K) λ_{max} (ε) 325 (21568), 290 nm (36490 M^{-1} cm^{-1}); HRMS (ESI-ion trap) m/z [M + H]$^+$ calcd for $C_{72}H_{83}F_3N_{13}O_6S_2$ 1346.5977, found 1346.5992.

*Compound stable-**5**.* Following the general method, stable-**5** was obtained (39 mg, 0.027 mmol, 97%) as a yellow oil: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.96 (d, J = 8.4 Hz, 1H), 7.81−7.73 (m, 2H), 7.72−7.64 (m, 2H), 7.59 (d, J = 8.2 Hz, 2H), 7.55 (s, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.2 Hz, 1H), 7.13 (td, J = 8.7, 2.2 Hz, 1H), 7.04 (s, 2H), 7.00−6.91 (m, 3H), 6.83 (d, J = 8.3 Hz, 2H), 6.43 (dd, J = 10.9, 2.3 Hz, 1H), 4.33 (quin, J = 6.6 Hz, 1H), 4.09−3.88 (m, 8H), 3.64 (dd, J = 15.1, 5.6 Hz, 1H), 3.11 (s, 2H), 2.92−2.79 (m, 9H), 2.32 (s, 6H), 2.30 (s, 6H), 2.27 (s, 3H), 2.25 (s, 3H), 1.85−1.70 (m, 8H), 1.68−1.25 (m, 24 + 3H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ 195.5, 195.4, 174.9, 163.5, 162.7, 161.1, 160.3, 153.9, 147.9, 147.8, 147.5, 142.7, 141.4, 140.8, 138.8, 138.2, 135.2, 134.9, 131.4, 130.7, 130.6, 129.8, 129.0, 127.2, 127.0, 126.8, 126.6, 125.8, 125.2, 120.1, 119.4, 113.9, 113.6, 112.8, 111.3, 110.0, 109.4, 70.0, 69.8, 45.2, 44.0, 41.9, 30.4, 30.4, 29.5, 29.5, 29.4, 29.3, 28.9, 28.9, 28.5, 28.5, 25.6, 25.5, 25.5, 19.0, 15.8; UV/vis (CH_2Cl_2, 283 K) λ_{max} (ε) 402 nm (23194 M^{-1} cm^{-1}); HRMS (ESI-ion trap) m/z [M + Na]$^+$ calcd for $C_{85}H_{93}F_2NO_{10}S_4Na$ 1476.5542, found 1476.5531.

*Compound stable-**6**.* Following the general method, stable-**6** was obtained (42 mg, 0.031 mmol, 97%) as a yellow oil: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.95 (d, J = 7.9 Hz, 1H), 7.79−7.72 (m, 2H), 7.71−7.64 (m), 7.61−7.56 (m, 2H), 7.55 (s, 1H), 7.46 (dd, J = 11.2, 4.2 Hz, 1H), 7.42−7.36 (m, 2H), 7.13 (td, J = 8.8, 2.2 Hz, 1H), 7.03 (s, 2H), 6.99−6.92 (m, 2H), 6.82 (d, J = 8.5 Hz, 2H), 6.42 (dd, J = 10.9, 2.3 Hz, 1H), 4.36−4.28 (m, 1H), 4.09−3.90 (m, 8H), 3.63 (dd, J = 15.2, 5.5 Hz, 1H), 3.35−3.16 (m, 8H), 3.11 (s, 2H), 2.85 (d, J = 15.3 Hz, 1H), 2.30 (s, 6H), 1.89−1.71 (m, 8H), 1.71−1.23 (m, 24 + 3H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ 174.9, 163.6, 162.7, 161.2, 160.3, 153.9, 147.9, 147.8, 147.5, 142.6, 141.5, 141.4, 140.9, 138.9, 138.8, 138.2, 135.3, 135.2, 135.0, 134.9, 131.4, 130.7, 130.6, 129.8, 129.0, 127.3, 127.0, 126.8, 126.6, 125.8, 125.2, 120.2, 120.1, 119.5, 119.4, 113.9, 113.6, 112.8, 112.5, 111.3, 111.1, 110.0, 109.4, 69.9, 69.8, 51.4, 51.4, 51.3, 45.2, 44.0, 41.9, 29.4, 28.8, 26.47, 26.43, 25.63, 18.99, 15.82; UV/vis (CH_2Cl_2, 283 K) λ_{max} (ε) 402 nm (18104 M^{-1} cm^{-1}); HRMS (ESI-ion trap) m/z [M + H]$^+$ calcd for $C_{77}H_{81}F_2N_{13}O_6$ 1322.6474, found 1322.6489.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text, figures, and tables giving ^{1}H and ^{13}C NMR spectra for new compounds and DFT B3LYP/6-31G(d,p) geometry optimized structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Saha, S.; Stoddart, J. F. *Chem. Soc. Rev.* **2006**, *36*, 77−92.

(2) Browne, W. R.; Feringa, B. L. *Nat. Nanotechnol.* **2006**, *1*, 25−35.

(3) Kay, E. R.; Leigh, D. A.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 72−191.

(4) *Molecular Devices and Machines: Concepts and Perspectives for the Nanoworld*; Balzani, V., Credi, A., Venturi, M.; Wiley-VCH: Weinheim, Germany, 2008.

(5) *From Non-Covalent Assemblies to Molecular Machines*; Sauvage, J.-P., Gaspard, P., Eds.; Wiley-VCH: Weinheim, Germany, 2010.

(6) Coskun, A.; Banaszak, M.; Astumian, R. D.; Stoddart, J. F.; Grzybowski, B. A. *Chem. Soc. Rev.* **2012**, *41*, 19−30.

(7) Silvi, S.; Venturi, M.; Credi, A. *J. Mater. Chem.* **2009**, *19*, 2279−2294.
(8) Perera, U. G. E.; Ample, F.; Kersell, H.; Zhang, Y.; Vives, G.; Echeverria, J.; Grisolia, M.; Rapenne, G.; Joachim, C.; Hla, S.-W. *Nat. Nanotechnol.* **2012**, *8*, 46−51.
(9) Lemouchi, C.; Iliopoulos, K.; Zorina, L.; Simonov, S.; Wzietek, P.; Cauchy, T.; Rodríguez-Fortea, A.; Canadell, E.; Kaleta, J.; Michl, J.; Gindre, D.; Chrysos, M.; Batail, P. *J. Am. Chem. Soc.* **2013**, *135*, 9366−9376.
(10) Berná, J.; Leigh, D. A.; Lubomska, M.; Mendoza, S. M.; Pérez, E. M.; Teobaldi, G.; Zerbetto, F. *Nat. Mater.* **2005**, *4*, 704−710.
(11) Tian, D.; Song, Y.; Jiang, L. *Chem. Soc. Rev.* **2013**, *42*, 5184−5209.
(12) Hutchison, J. A.; Uji-i, H.; Deres, A.; Vosch, T.; Rocha, S.; Müller, S.; Bastian, A. A.; Enderlein, J.; Nourouzi, H.; Li, C.; Herrmann, A.; Müllen, K.; De Schryver, F.; Hofkens, J. *Nat. Nanotechnol.* **2014**, *9*, 131−136.
(13) Klajn, R. *Chem. Soc. Rev.* **2014**, *43*, 148−184.
(14) Donhauser, Z. J.; Mantooth, B. A.; Kelly, K. F.; Bumm, L. A.; Monnell, J. D.; Stapleton, J. J.; Price, D. W., Jr.; Rawlett, A. M.; Allara, D. L.; Tour, J. M.; Weiss, P. S. *Science* **2001**, *292*, 2303−2307.
(15) Katsonis, N.; Kudernac, T.; Walko, M.; van der Molen, S. J.; van Wees, B. J.; Feringa, B. L. *Adv. Mater.* **2006**, *18*, 1397−1400.
(16) Moore, A. M.; Dameron, A. A.; Mantooth, B. A.; Smith, R. K.; Fuchs, D. J.; Ciszek, J. W.; Maya, F.; Yao, Y.; Tour, J. M.; Weiss, P. S. *J. Am. Chem. Soc.* **2006**, *128*, 1959−1967.
(17) Nakanishi, H.; Bishop, K. J. M.; Kowalczyk, B.; Nitzan, A.; Weiss, E. A.; Tretiakov, K. V.; Apodaca, M. M.; Klajn, R.; Stoddart, J. F.; Grzybowski, B. A. *Nature* **2009**, *460*, 371−375.
(18) Göstl, R.; Senf, A.; Hecht, S. *Chem. Soc. Rev.* **2014**, *43*, 1982−1996.
(19) *Molecular Switches*, 2nd ed.; Browne, W. R., Feringa, B. L., Eds.; Wiley-VCH: Weinheim, Germany, 2011.
(20) Klajn, R. *Pure Appl. Chem.* **2010**, *82*, 2247−2279.
(21) Dri, C.; Peters, M. V.; Schwarz, J.; Hecht, S.; Grill, L. *Nat. Nanotechnol.* **2008**, *3*, 649−653.
(22) Irie, M.; Mohri, M. *J. Org. Chem.* **1988**, *53*, 803−808.
(23) Castellanos, S.; Vieira, A. A.; Illescas, B. M.; Sacchetti, V.; Schubert, C.; Moreno, J.; Guldi, D. M.; Hecht, S.; Martín, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 13985−13990.
(24) Kudernac, T.; Ruangsupapichat, N.; Parschau, M.; Maciá, B.; Katsonis, N.; Harutyunyan, S. R.; Ernst, K.-H.; Feringa, B. L. *Nature* **2011**, *479*, 208−211.
(25) Wang, J.; Feringa, B. L. *Science* **2011**, *331*, 1429−1432.
(26) Hugel, T.; Holland, N. B.; Cattani, A.; Moroder, L.; Seitz, M.; Gaub, H. E. *Science* **2002**, *296*, 1103−1106.
(27) Liu, Y.; Flood, A. H.; Bonvallet, P. A.; Vignon, S. A.; Northrop, B. H.; Tseng, H.-R.; Jeppesen, J. O.; Huang, T. J.; Brough, B.; Baller, M.; Magonov, S.; Solares, S. D.; Goddard, W. A.; Ho, C.-M.; Stoddart, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 9745−9759.
(28) Ferri, V.; Elbing, M.; Pace, G.; Dickey, M. D.; Zharnikov, M.; Samorì, P.; Mayor, M.; Rampi, M. A. *Angew. Chem., Int. Ed.* **2008**, *47*, 3407−3409.
(29) Balzani, V.; Credi, A.; Venturi, M. *ChemPhysChem* **2008**, *9*, 202−220.
(30) Browne, W. R.; Feringa, B. L. *Annu. Rev. Phys. Chem.* **2009**, *60*, 407−428.
(31) Chen, K.-Y.; Ivashenko, O.; Carroll, G. T.; Robertus, J.; Kistemaker, J. C. M.; London, G.; Browne, W. R.; Rudolf, P.; Feringa, B. L. *J. Am. Chem. Soc.* **2014**, *136*, 3219−3224.
(32) Sun, R.; Xue, C.; Ma, X.; Gao, M.; Tian, H.; Li, Q. *J. Am. Chem. Soc.* **2013**, *135*, 5990−5993.
(33) Ichimura, K.; Oh, S. K.; Nakagawa, M. *Science* **2000**, *288*, 1624−1626.
(34) Kumar, A. S.; Ye, T.; Takami, T.; Yu, B. C.; Flatt, A. K.; Tour, J. M.; Weiss, P. S. *Nano Lett.* **2008**, *8*, 1644−1648.
(35) Han, M.; Ishikawa, D.; Honda, T.; Ito, E.; Hara, M. *Chem. Commun.* **2010**, *46*, 3598−600.
(36) Lim, H. S.; Lee, W. H.; Lee, S. G.; Lee, D.; Jeon, S.; Cho, K. *Chem. Commun.* **2010**, *46*, 4336−4338.
(37) Min, M.; Bang, G. S.; Lee, H.; Yu, B. C. *Chem. Commun.* **2010**, *46*, 5232−5234.
(38) Han, M. N.; Honda, T.; Ishikawa, D.; Ito, E.; Hara, M.; Norikane, Y. *J. Mater. Chem.* **2011**, *21*, 4696−4702.
(39) Valley, D. T.; Onstott, M.; Malyk, S.; Benderskii, A. V. *Langmuir* **2013**, *29*, 11623−11631.
(40) Carroll, G. T.; London, G.; Landaluce, T. F.; Rudolf, P.; Feringa, B. L. *ACS Nano* **2011**, *5*, 622−630.
(41) London, G.; Chen, K.-Y.; Carroll, G. T.; Feringa, B. L. *Chem. Eur. J.* **2013**, *19*, 10690−10697.
(42) Pijper, T. C.; Kudernac, T.; Browne, W. R.; Feringa, B. L. *J. Phys. Chem. C* **2013**, *117*, 17623−17632.
(43) Zhang, J.; Zou, Q.; Tian, H. *Adv. Mater.* **2013**, *25*, 378−399.
(44) Love, J. C.; Estroff, L. A.; Kriebel, J. K.; Nuzzo, R. G.; Whitesides, G. M. *Chem. Rev.* **2005**, *105*, 1103−1169.
(45) Shirai, Y.; Cheng, L.; Chen, B.; Tour, J. M. *J. Am. Chem. Soc.* **2006**, *128*, 13479−13489.
(46) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004−2021.
(47) Vachon, J.; Carroll, G. T.; Pollard, M. M.; Mes, E. M.; Brouwer, A. M.; Feringa, B. L. *Photochem. Photobiol. Sci.* **2014**, *13*, 241−246.
(48) Such, G. K.; Quinn, J. F.; Quinn, A.; Tjipto, E.; Caruso, F. *J. Am. Chem. Soc.* **2006**, *128*, 9318−9319.
(49) Ranjan, R.; Brittain, W. J. *Macromolecules* **2007**, *40*, 6217−6223.
(50) Bova, S.; Saponara, S.; Rampa, A.; Gobbi, S.; Cima, L.; Fusi, F.; Sgaragli, G.; Cavalli, M.; de los Rios, C.; Striessnig, J.; Bisi, A. *Org. Lett.* **2009**, *52*, 1259−1262.
(51) Han, T.; Chen, C.-F. *J. Org. Chem.* **2008**, *73*, 7735−7742.
(52) Yoshimitsu, Z.; Nakajima, A.; Watanabe, T.; Hashimoto, K. *Langmuir* **2002**, *18*, 5818−5822.
(53) Fluorine atom(s) will be an important marker for monitoring the progress of the interfacial Diels−Alder reactions between the molecular switches/motors and an anthracene-functionalized surface by using XPS, a surface-sensitive technique.
(54) Yu, B.-C.; Shirai, Y.; Tour, J. M. *Tetrahedron* **2006**, *62*, 10303−10310.
(55) Lucas, L. N.; van Esch, J.; Kellogg, R. M.; Feringa, B. L. *Chem. Commum.* **1998**, 2313−2314.
(56) Ruangsupapichat, N. *Controlling the Motion of Molecular Machines at the Nanoscale*; Ph.D. Thesis, University of Groningen, April 2012; p 76.
(57) DuPriest, M. T.; Griffin, B. W.; Kuzmich, D.; McNatt, L. G. *J. Med. Chem.* **1991**, *34*, 3229−3234.
(58) Foster, R. A. A.; Willis, M. C. *Chem. Soc. Rev.* **2012**, *42*, 63−76.
(59) The term "unstable" does not refer to chemical instability or degradation but to the fact that in the photochemically generated species the stereogenic methyl group is forced to adopt a conformationally unfavored pseudo-equatorial orientation. See: ter Wiel, M. K. J.; van Delden, R. A.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc.* **2005**, *127*, 14208−14222.
(60) Cnossen, A.; Hou, L.; Pollard, M. M.; Wesenhagen, P. V.; Browne, W. R.; Feringa, B. L. *J. Am. Chem. Soc.* **2012**, *134*, 17613−17619.