Turn-On Sulfide π Donors: An Ultrafast Push for Twisted Mechanophores

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S *Supporting Information*

ABSTRACT: Attached to electron-rich aromatic systems, sulfides are very weak acceptors; however, attached to electron-poor aromatics, they turn into quite strong donors. Here, we show that this underappreciated dual nature of sulfides deserves full consideration for the design of functional systems. Tested with newly designed and synthesized planarizable push−pull mechanophores, sulfide acceptors in the twisted ground state are shown to prevent oxidative degradation and promote blue-shifting deplanarization. Turned on in the planar excited state, sulfide donors promote red-shifting polarization. Impressive Stokes shifts are the result. Demonstrating the usefulness of time-resolved broadband emission spectra to address significant questions, direct experimental evidence for the ultrafast (3.5 ps), polarity-independent and viscosity-dependent planarization from the twisted Franck−Condon S_1 state to the relaxed S_1 state could be secured.
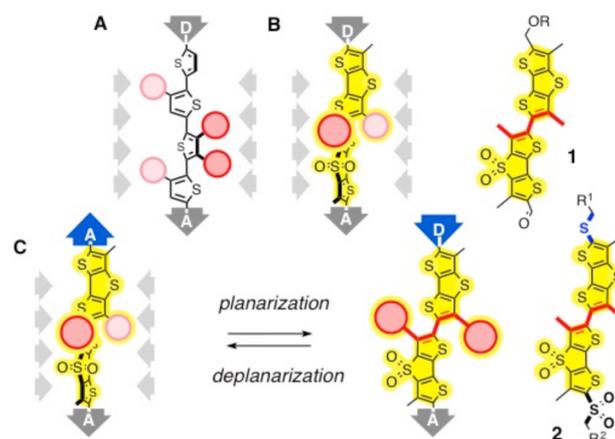
Figure 1. (A) Planarizable push−pull probes, designed to report on lateral pressure and parallel potentials with shifts in excitation. (B) Fluorescent flippers, i.e., large and shiny monomers, added to maximize mechanosensitivity and lifetime (R = -COCH$_2$OCH$_2$COOH). (C) The concept of turn-on sulfide π donors (blue).

Sulfide substituents on electron-rich aromatic systems are weak electron acceptors, whereas on electron-poor aromatic systems, they are quite strong electron donors.[1] The very weakly accepting nature of sulfides with electron-rich aromatics is best appreciated with the Hammett σ_p = +0.03 of ethyl sulfides, a value referring to benzoic acids.[2] This compares to σ_p = −0.83 for dimethylamino and σ_p = −0.27 for methoxy donors, and to σ_p = +0.66 for cyano and σ_p = +0.77 for ethylsulfone acceptors. The strongly donating nature of sulfides to electron-poor aromatics is best appreciated by the deep red color of naphthalenediimides (NDIs) with two sulfides in the core,[3] halfway between the yellow NDIs with two alkoxy and the blue NDIs with two alkylamino substituents in the core.[4] The conversion of sulfides into strong donors for electron-poor aromatics is also well reflected in the σ_p^+ = −0.60 of methyl sulfides (for cyano acceptors, e.g., $\sigma_p = \sigma_p^+$ = +0.66).[2]

Here, the switch of sulfide substituents from very weak acceptors to strong donors with decreasing electron deficiency of the aromatic system is used to tackle an intriguing challenge with planarizable push−pull probes.[5,6] The design of these probes was inspired by the color change of lobsters during cooking and the origin of color vision.[7] Namely, the combination of planarization and polarization in the ground state was envisioned to afford mechanosensitive fluorescent membrane probes[8] that operate with changes in excitation rather than emission.[5,6] Evolving from twisted[9] push−pull[8,10−12] oligothiophenes[8,10] (Figure 1A),[13] the

best probes currently operate with fluorescent flippers. Fluorescent flippers are monomers with large surface area to better feel the environment and to keep on shining also when twisted out of conjugation (Figure 1B).[6] In flipper probe **1**, one bithiophene was bridged with a "sulfide donor" and the other with a "sulfone acceptor." The highly fluorescent dithienothiophene *S,S*-dioxide[14] acceptor is further strengthened with an aldehyde. Repulsion between methyl substituents and the chalcogenic σ holes[15] of the endocyclic sulfur atoms next to the connecting bond is used to twist the two aromatic planes out of coplanarity. In mixed membranes, disordered domains could be imaged by excitation of deplanarized flippers **1** at shorter wavelength, whereas more ordered domains emitted upon excitation of planarized probes at longer wavelength.[6] However, considering the concept of planarizable push−pull probes, flipper probe **1** contains a strong aldehyde acceptor but fails to integrate a strong donor. This failure is not accidental. In conjugated push−pull systems, the electron density injected by the donor is delocalized toward the acceptor. However, when twisted out of conjugation, the electron density injected by the donor accumulates on the first aromatic system, a situation that inevitably leads to oxidative degradation.[13,10d] Ideally, strong

Table 1. Structure and Spectroscopic Properties of Twisted Push−Pull Probes in Solution[a]

cpd[b]	donor[b]	acceptor[b]	λ_{abs} (nm)[c]	λ_{em} (nm)[d]	$\Delta\lambda$ (nm)[e]	$\Delta\nu$ (cm^{-1})[f]	$\Delta\Delta\nu$ (cm^{-1})[g]	QY (%)[h]
1	-CH$_2$OR^1	-CHO	422	621	199	7800	−	−
2	-SEt	-SO$_2$Et	403	635	232	9300	+1500	29
3	-OMe	-SO$_2$Et	418	648	230	8700	+900	22
4	-SEt	-CN	411	650	239	9400	+1600	33
5	-OMe	-CN	428	681	253	9000	+1200	23
6	-H	-CN	396	543	147	7000	−800	−

[a]Reported for EtOAc because of the similarity to emission in membranes (Figure 3A), other solvents gave the same trends. [b]For structures, see Figure 1, Schemes 1 and S2 (7: A = -CN, D = -N(n-Pr)$_2$); 8: A = -COR^2, D = -N(n-Pr)$_2$). [c]Wavelength λ_{abs} of absorption maximum (2: ε = 19.7 mM^{-1} cm^{-1}, 3: ε = 15.9 mM^{-1} cm^{-1}). [d]Wavelength λ_{em} of emission maximum (excitation at λ_{abs}). [e]Stokes shift in wavelength (nm, $\lambda_{em} - \lambda_{abs}$). [f]Stokes shift in frequency (wavenumbers, $\nu_{abs} - \nu_{em}$). [g]Change of Stokes shift compared to original 1. [h]Fluorescence quantum yield in CHCl$_3$ relative to rhodamine G (94% in EtOH). QYs are unrelated to planarization kinetics from FC to the relaxed S$_1$ excited state.

donors in planarizable push−pull probes would turn on only upon planarization of the aromatic system (Figure 1C). Turn-on sulfides appeared just perfect to meet this subtle challenge.

To elaborate on the concept of turn-on sulfide donors comprehensively, we decided to prepare a series of push−pull flippers 2−8 (Table 1, Scheme 1). "Turn-on" probes 2 and 4
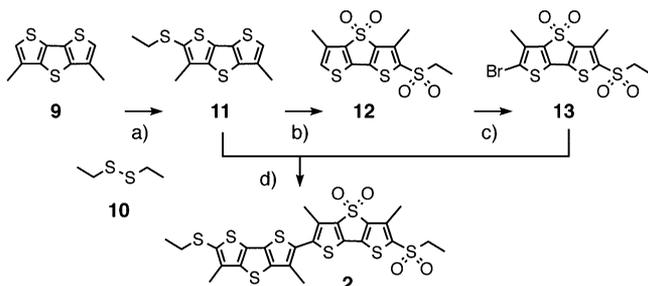
Scheme 1[a]

[a](a) 1. LDA, THF, −78 °C, 30 min; 2. 10, THF, rt, 12 h, 70%; (b) mCPBA, CH$_3$Cl, rt, 12 h, 53%; (c) NBS, AcOH, CH$_2$Cl$_2$, reflux, 24 h, 66%; (d) 1. LDA, SnCl(Bu)$_3$, THF, −78 °C, 1 h; 2. Pd(PPh$_3$)$_4$, DMF, 70 °C, 2 d, 38%.

contain sulfide substituents that should "turn on" as donors only in response to planarization and conjugation with sulfone and cyano acceptors (Figure 1C). In control probes 3 and 5, the turn-on sulfides are replaced by conventional methoxy donors. Turn-on probe 2, the key target, was readily accessible[6] from dithienothiophene 9. The critical sulfide substituent could be introduced with disulfide 10 after deprotonation of the substrate 9 with LDA. Simultaneous oxidation of dithienothiophene and the turn-on sulfide donor of 11 with mCPBA afforded dithienothiophene S,S-oxide 12 with a sulfone acceptor. The activated sulfone 13 was obtained by bromination with NBS, and Stille coupling with sulfide 11 afforded flipper 2 in overall four straightforward steps only. For future probe development, it is important to note that the introduction of sulfide turn-on donors from their respective disulfides is compatible with a broad variety of functional groups. Flippers 3−8 were prepared analogously, details on their synthesis can be found in the Supporting Information (Schemes S1−S2).

In the ^{1}H NMR spectrum of 5, the signals of the methyl protons next to the cyano acceptor and the methoxy donor appeared downfield and upfield of the methyl protons in the middle of the fluorophore, respectively (Figure 2C), and the spectrum changed completely within hours (Figure 2D). Consistent with the sulfide acting as stabilizing acceptor in the twisted ground state of 2, the proximal methyl protons were
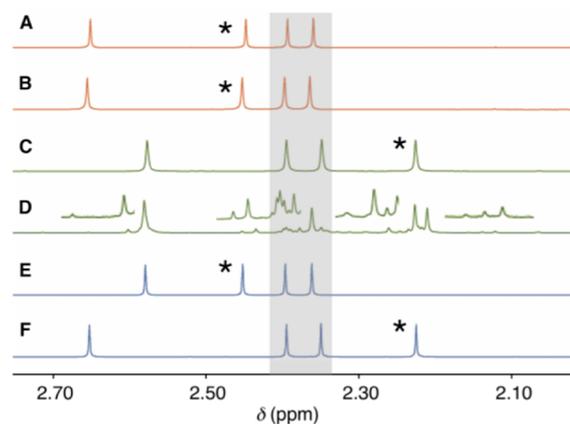
Figure 2. Part of the ^{1}H NMR spectra of 2 (A; remeasured after 6 days, B), 5 (C; remeasured after 6 h, D), 4 (E), and 3 (F). The signals of the methyls next to sulfide (*, A, B, E) and methoxy substituents (*, C, F) and the region of those in the middle of the chromophores (gray area) are highlighted. (D) Peak patterns from degradation side products are reproduced in magnified form just above the original spectrum.

downfield shifted (Figure 2A), and the fluorophore remained intact for more than a week under ambient conditions, in solution and in the light (Figure 2B). Identical trends were found with regard to photostability. Under constant irradiation at 435 nm for long time, the initial decrease of emission intensity of probe 2 with turn-on sulfide donors with time was 8.2 times slower than that of carboxyfluorescein and 37.8 times slower than that of the unstable probe 3 with conventional methoxy donors.

The emission maximum of the original probe 1 in membranes is close to that in EtOAc (Figure 3A, solid). The large difference
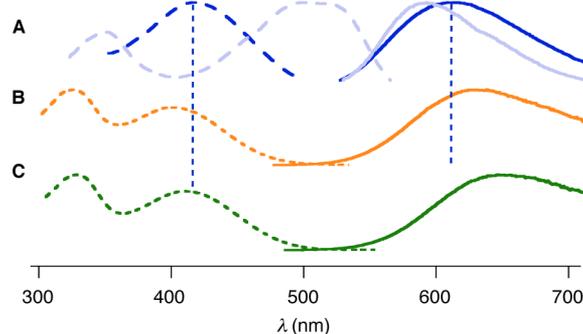
Figure 3. Absorption (left) and emission spectra (right) of 1 (A), 2 (B), and 3 (C) in EtOAc and 1 in solid-ordered membranes (DPPC vesicles at 25 °C; A, light blue). Spectra in A are from ref 6.

between the absorption maxima of **1** in EtOAc (and all other solvents) and solid-ordered membranes is thought to originate from ground-state planarization (Figure 3A, dashed).[6] The absorption maximum of turn-on probe **2** in EtOAc was found at λ_{abs} = 403 nm (Figure 3B, dashed, Table 1). This compared to **1** blue-shifted absorption was in agreement with an increased ground-state deplanarization in the absence of a strong push–pull dipole, i.e., with a weakly withdrawing sulfide acceptor at the partially decoupled, electron-rich dithienothiophene. The emission of turn-on probe **2** at λ_{em} = 635 nm was red-shifted compared to **1** (Figure 3B, solid, Table 1). This red shift was in agreement with a strengthened push–pull dipole in the planar S_1 state, i.e., the presence of turned-on sulfide donors. Blue shift in absorption and red shift in emission added up to a large Stokes shift, increasing by $\Delta\Delta\nu$ = +1500 cm^{-1} from original **1** to $\Delta\nu$ = 9300 cm^{-1} for turn-on probe **2** (Table 1, entry 2).[16]

Compared to original **1**, the presence of conventional methoxy donors in **3** shifted the emission to the red but failed to shift the absorption significantly to the blue (Figure 3C, Table 1). An increased Stokes shift by only $\Delta\Delta\nu$ = +900 cm^{-1} was the result; that is not much more than half the $\Delta\Delta\nu$ = +1500 cm^{-1} obtained with turn-on donors in **2** (Figure 3C, Table 1). Cyano instead of sulfone acceptors caused global red shifts (Table 1, entries 2–5). These uniform shifts implied slightly increased ground-state planarization and excited-state polarization. Despite their smaller σ_p, cyano groups are thus slightly stronger acceptors than sulfones in these systems. Partially preserved blue-shifted absorption in **4** compared to **1** showed that the stronger cyano acceptors are insufficient to turn on sulfide donors in the twisted ground state. As a result, the Stokes shift with turn-on donors combined with cyano acceptors in **4** was with $\Delta\nu$ = +9400 cm^{-1}; the largest found in this series. However, compared to conventional methoxy donors in **3** and **5**, the increase of the Stokes shift with turn-on sulfide donors was more pronounced in combination with sulfones in **2** (+600 cm^{-1}) than with cyano acceptors in **4** (+400 cm^{-1}, Table 1).

Controls **6** without any substituent in the donating position gave the expected large blue shifts in absorption and emission with significantly reduced Stokes shift ($\Delta\Delta\nu$ = −800 cm^{-1}, Table 1, entry 6). Amino donors combined with cyano and ketone acceptors in **7** and **8**, respectively, removed essentially all fluorescence in EtOAc. Appreciable emission only in the least polar solvents such as hexane (**7**: λ_{abs} = 445 nm, λ_{em} = 635 nm, $\Delta\nu$ = 6900 cm^{-1}; **8**: λ_{abs} = 420 nm, λ_{em} = 642 nm, $\Delta\nu$ = 8400 cm^{-1}) implied that fluorescence quenching occurs by photoinduced intramolecular electron transfer from the amino donor,[8d] independent of the nature of the acceptor.

A novel, extremely versatile broadband fluorescence up-conversion technique,[17] unrivaled in photometric precision, was applied to gain direct insight into the conformational and energetic relaxation processes in real-time. Contrary to the monomeric control **12** (Figure 4A), the time-resolved emission spectra of **2** and **3** in EtOAc showed a large red shift with time (using times larger than 0.2 ps, Figure 4B,C). The time-resolved emission spectra of **2** with turn-on and **3** with conventional donors were quite similar. In EtOAc, the characteristic instability of **3** was nicely visible with the mismatch at the transition from the linear to the logarithmic recording range at 2 ps (30 min delay between the two measurements; Figure 4C, compare to 2D). Persistent red shifts of almost 1500 cm^{-1} (t_{1e} > 0.2 ps) in apolar solvents and their slowing-down with increasing solvent viscosity supported that the spectral-shift dynamics in apolar solvents report on the planarization of **2** in the excited state (Figure 4D).
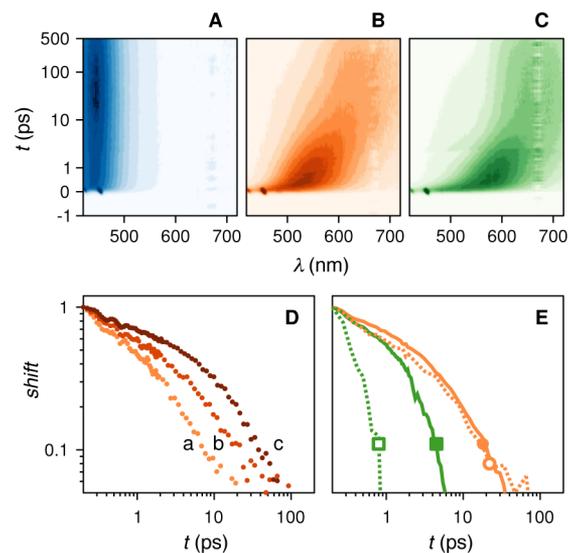

Figure 4. Time-resolved broadband emission spectra of **12** (A), **2** (B), and **3** (C) in EtOAc. (D) Normalized shift of the position of the emission maximum with time, shift = $[\nu(t) - \nu(\infty)]/[\nu(0.2\ ps) - \nu(\infty)]$, with ν being the frequency of the fluorescence maximum,[19b] after excitation at 400 nm (100 fs pulse) for **2** in alkanes of different viscosity (a, *n*-hexane, 0.3 cP; b, *c*-hexane, 0.9 cP; c, *n*-hexadecane, 2.8 cP). (E) Same for **2** (○, ●) and **3** (□, ■) in solvents of different polarity (ethyl acetate (●, ■), cyclohexane (○, □)).

The 1/e time associated with the planarization of **2** in the S_1 state increased from t_{1e} = 1.5 ps at 0.3 cP in *n*-hexane (Figure 4D, a) to t_{1e} = 8.0 ps at 2.8 cP in *n*-hexadecane (Figure 4D, c).

In going from apolar cyclohexane to moderately polar EtOAc, the time constant of the red-shift dynamics for **3** with the methoxy group as donor increased from t_{1e} = 0.45 ps up to t_{1e} = 1.8 ps (Figure 4E, □, ■). This is in clear contrast to the red-shift dynamics for **2**, with turn-on sulfides, which showed basically no dependence on the solvent polarity and was distinctly slower than for **3** in apolar and polar solvents ($t_{1e} \approx$ 3.5 ps, Figure 4E, ○, ●).

These observations allow for two conclusions. First, the excited-state planarization (the exclusive dynamics being monitored in apolar solvents) is distinctly slower for **2** than for **3**. The conventional strong donor in **3** thus supports planarization already in ground state, as expected for push–pull systems and demonstrated by red-shifted absorption. Thus, planarization from the less twisted Franck–Condon (FC) S_1 state to the planar relaxed S_1 state requires little structural rearrangement. In clear contrast, turn-on donors in **2** support deplanarization while acting as acceptors in the ground state, as expected for pull–pull systems and demonstrated by blue-shifted absorption. As a result, they need correspondingly larger amplitude motion, and thus more time, to planarize from the more twisted FC state to the relaxed S_1 state while transforming from weak acceptors to strong donors.

Second, when moving toward polar solvents, the slower diffusive solvent relaxation starts to dominate the relaxation dynamics of the S_1 state of **3**. In clear contrast, planarization of **2** is slower than solvent relaxation, and thus the excited-state dynamics of **2** are independent of solvent polarity. This could indicate that in **2**, planarization is a prerequisite for the excited-state charge transfer, which may be interpreted as a direct experimental support of the concept of turn-on sulfide donors. These insights could be secured only with ultrafast broadband

fluorescence in a judicious choice of solvents, thus allowing us to assign the time scales of the different relevant relaxation processes without the complications arising from overlapping spectral contributions when using transient absorption spectroscopy[18] or the limited access to spectral lineshapes in single wavelength fluorescence measurements.[19,20]

Direct evidence for a twisted FC S_1 state from time-resolved emission spectra was in agreement with strong positive solvatochromism of the emission but not the absorption maxima (Figures S1−S6). This key characteristic of planarizable push−pull probes[5,6] contrasts clearly with positive solvatochromism in both absorption and emission found for standard push−pull fluorophores with planar ground and excited states.[11] The dependence of emission maxima on polarity index was linear and similar for all push−pull probes (slope ν_f = 13,300−17,400 cm^{-1}, **2** < **4** ≤ **3** < **5**). As with the Stokes shifts, solvatochromism of **6** without additional donor was much weaker (ν_f = 7600 cm^{-1}, Figure S6).

In summary, turn-on donors provide access to twisted push−pull probes that, most importantly, are stable and, moreover, have maximal Stokes shifts, reasonable quantum yields, and mechanosensitive excited-state dynamics that are controlled by planarization rather than by solvation.[16] These findings became possible with the concept of turn-on sulfides, i.e., their conversion from very weak acceptors for electron-rich aromatics[2] to strong donors for electron-poor aromatics.[1,3] Compared to isostructural sulfur redox switches,[3,6,12] the more subtle concept of turn-on sulfide donors has attracted much less attention for the design of functional systems. The reported results suggest that it certainly could, maybe should.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b10879.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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(16) As an amorphous solid, turn-on probe **2** is highly fluorescent, whereas π-stacked in single crystals, **2** is fully planarized and does not fluoresce. Studies on ground-state planarization in confined space are ongoing and will be reported in due course.

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(20) Involvement of a twisted intramolecular charge-transfer (TICT) state can be excluded because of, *inter alia*, the substantial red shift of the fluorescence observed in apolar solvents and the polarity-independent excited-state dynamics of **2**.