Supplementary Material (ESI) for *PCCP*

Supporting Information

Alkoxy-Styryl DCDHF Fluorophores

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General

The chemical reagents were purchased reagent-grade and were used without further purification unless otherwise stated. The synthesis of compounds ***trans*-1** and ***trans*-2** has been previously described.[1] All solvents were purified using standard procedures. Column chromatography was performed on silica gel 60 (40-63 μm). TLC plates coated with SiO_2 60F254 were visualized by UV light. ^{1}H-NMR and ^{13}C-NMR were recorded in a Bruker AC 300 MHz and in a Bruker AVANCE DRX-500 using $CDCl_3$ as solvent, unless otherwise stated; chemical shifts (δ) are reported in ppm relative to TMS, and the coupling constants (*J*) are in hertz (Hz). UV-vis spectra were recorded with a Helios Gamma spectrophotometer, and IR spectra with a Nicolet Impact 400D spectrophotometer. Fluorescence spectra were obtained in a Perkin Elmer LS 55 Luminiscence spectrophotometer. Quantum yields were calculated using quinine as reference. Mass spectra (EI) were measured in Servicios Técnicos de Investigación (STI) from Universidad de Alicante, Spain.

Synthesis of 3-cyano-4-{(*E*)-2'-[3''-hexyloxy-4''-(6'''-hydroxyhexyloxy)phenyl]-1'-ethenyl}-5,5-dimethyl-2-propanylidendinitrile-2,5-dihydrofuran (*trans*-3).

Synthesis of 4-bromo-2-hexyloxyphenol. To a cooled solution (0 ºC) of 2-hexyloxyphenol[2] (4.5 g, 23.20 mmol) in 100 mL of dichloromethane was added dropwise a solution of bromine (3.7 g, 23.15 mmol) in 50 mL of dichloromethane. After addition, the reaction was stirred at room temperature for one hour, then was washed with 10% sodium hydroxide and dried with magnesium sulfate; the solvent was distilled off under reduced pressure. The crude product was purified by chromatography on silica gel (hexane/ethyl acetate, 9/1) to give an oil (4.94 g, 78%). ^{1}H NMR ($CDCl_3$): δ 6.97 (d, 1H, *J* = 8.8 Hz), 6.96 (s, 1H), 6.80 (d, 1H, *J* = 8.8 Hz), 3.99 (t, 2H, *J* = 6.6 Hz), 1.72-1.80 (m, 2H), 1.26-1.46 (m, 6H), 0.91 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR ($CDCl_3$): δ 146.6, 144.9, 123.8, 115.6, 114.8, 111.4, 69.1, 31.4, 28.9, 25.5, 22.5, 13.9; MS (EI) m/z: 272 (M^+, 38), 274 (37), 190 (99), 188 (100); IR (KBr): 3541 cm^{-1}. Anal Calcd for $C_{12}H_{17}BrO$: C, 52.76; H, 6.27, found: C, 52.75; H, 6.42 %.

Synthesis of 6-(4'-bromo-2'-hexyloxyphenoxy)hexan-1-ol. To a mixture of 4-bromo-2-hexyloxyphenol (9 g, 33 mmol) and sodium hydride 60% (1.5 g, 36.7 mmol) in DMF (100 mL) under argon atmosphere, was added potassium iodide (1 g, 6 mmol), 6-chlorohexanol (6 g, 36.6 mmol) and was heated at 120 ºC for 4 hours. The reaction mixture was cooled in an ice bath.

Hydrochloric acid (10%, 40 mL) and diethyl ether (50 mL) were added and the two phases were separated. The water phase was extracted twice with diethyl ether. The resulting organic phases were combined and washed with water. The organic extracts were dried over sodium sulfate an evaporated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate, 2/1) to give an oil (8.10 g, 66%). ^{1}H NMR ($CDCl_3$): δ 6.93 (s, 1H), 6.92 (d, 1H, *J* = 9.0 Hz), 6.67 (d, 1H, *J* = 9.0 Hz), 3.90 (t, 2H, *J* = 6.3 Hz), 3.89 (t, 2H, *J* = 6.3 Hz), 3.56 (t, 2H, *J* = 6.3 Hz), 2.48 (s, 1H), 1.28-1.77 (m, 16H), 0.86 (t, 3H, *J* = 7.0 Hz) ^{13}C NMR ($CDCl_3$): δ 149.9, 148.2, 123.4, 116.9, 115.1, 112.9, 69.3, 62.8, 32.6, 31.5, 29.1, 29.0, 25.8, 25.6, 25.5, 22.6, 13.9; MS (EI) m/z: 372 (M^+, 16), 374 (16), 190 (97), 188 (100); IR (KBr): 3327, 2928 cm^{-1}; HRMS calcd for $C_{18}H_{29}BrO_3$: 372.1300, found 372.1287.

Synthesis of 3-hexyloxy-4-(6'-hydroxyhexyloxy)benzaldehyde. To a solution of 6-(4'-bromo-2'-hexyloxyphenoxy)hexan-1-ol (3.3 g, 12.10 mmol) in tetrahydrofuran (50 mL) at -78 ºC under nitrogen atmosphere was added butillithium (12 mL of a 2.5 M solution in hexanes) and the reaction mixture was stirred one hour. Then, 3.4 g of *N*-formylpiperidine were added, and the reaction was kept at room temperature for 24 hours. After cooling in an ice bath, hydrochloric acid (10%, 40 mL) was added. The crude was extracted with diethyl ether and the organic extracts were washed and dried with anhydrous sodium sulfate. Solvent was removed, and the residue was purified by chromatography on silica gel (hexane/ethyl acetate, 2/1) to yield a solid (1.44 g, 37%). ^{1}H NMR ($CDCl_3$): δ 9.75 (s, 1H), 7.35 (d, 1H, *J* = 8.1 Hz), 9.32 (s, 1H), 6.88 (d, 1H, *J* = 8.1 Hz), 4.01 (t, 2H, *J* = 6.3 Hz), 3.98 (t, 2H, *J* = 6.3 Hz), 3.58 (t, 2H, *J* = 6.3 Hz), 2.27 (s, 1H), 1.27-1.80 (m, 16H), 0.84 (t, 3H, *J* = 7.0 Hz) ^{13}C NMR ($CDCl_3$): δ 190.9, 154.5, 149.3, 129.8, 126.5, 111.7, 110.8, 69.0, 68.9, 62.7, 32.5, 31.4, 28.9, 28.8, 25.7, 25.6, 25.4, 22.5, 13.9; MS (EI) m/z: 322 (M^+, 23), 138 (100); IR (KBr): 3342, 1687 cm^{-1}; Mp: 47-48 ºC. HRMS calcd for $C_{19}H_{30}O_4$: 322.2144, found 322.2157.

Synthesis of ***trans-3***. A mixture of 3-hexyloxy-4-(6'-hydroxyhexyloxy)benzaldehyde (1.65 g, 5.12 mmol), 3-cyano-4,5,5-trimethyl-2-propanylidendinitrile-2,5-dihydrofuran [3] (1.4 g, 7.03 mmol), sodium hydride (0.005 g, 0.21 mmol) and dry DMF (25 mL) was refluxed for 24 hours under inert atmosphere. The mixture was poured into water (25 mL) followed by extraction with dichloromethane. The organic extract was washed with water and dried. After removal of solvent under reduced pressure, the residue was purified by chromatography on silica gel (hexane/ethyl acetate, 1/3) to afford a red solid (1.25 g, 55%). ^{1}H NMR ($CDCl_3$): δ 7.57(d, 1H, *J* = 16.1 Hz),

7.25 (dd, 1H, J_1 = 8.5 Hz, J_2 = 1.7 Hz), 7.05 (d, 1H, J = 1.7 Hz), 6.90 (s, 1H, J = 8.5 Hz), 6.85 (d, 1H, J = 16.1 Hz), 4.06 (m, 4H), 2.36 (s, 1H), 1.33-1.90 (m, 16H), 0.90 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$): δ 175.6, 174.2, 154.1, 149.6, 147.9, 126.7, 125.3, 112.7, 112.3, 112.2, 111.9, 111.1, 110.6, 97.9, 97.4, 69.6, 69.0, 62.7, 56.7, 32.6, 31.5, 29.1, 26.6, 25.7, 25.6, 25.4, 24.3, 22.5, 13.9; HRMS calcd for $C_{30}H_{37}N_3O_4$: 503.2784, found 503.2784; IR (KBr): 3430, 2226 cm^{-1}; Mp: 128-129 ºC. Anal. Calcd for $C_{30}H_{37}N_3O_4 \cdot ½H_2O$: C, 70.29; H, 7.47; N, 8.20. Found: C, 70.57 ; H, 7.38 ; N, 8.26 %.

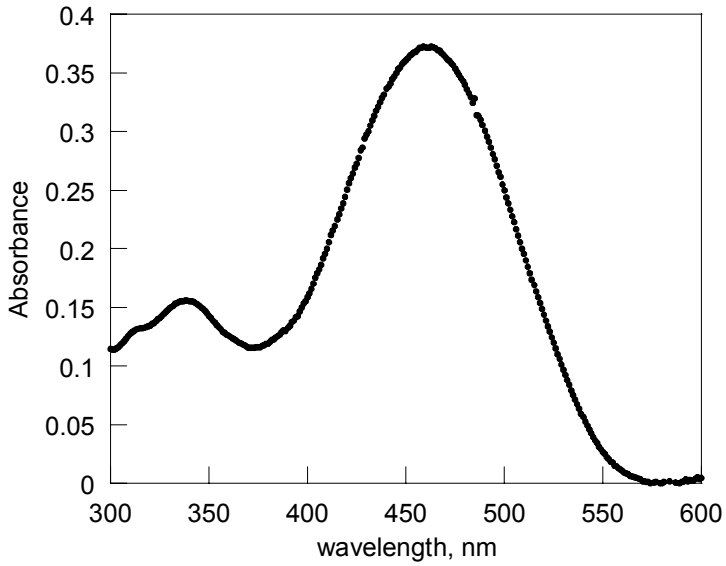

Figure S1: Absorbance spectrum of compound ***trans*-1** in methanol.

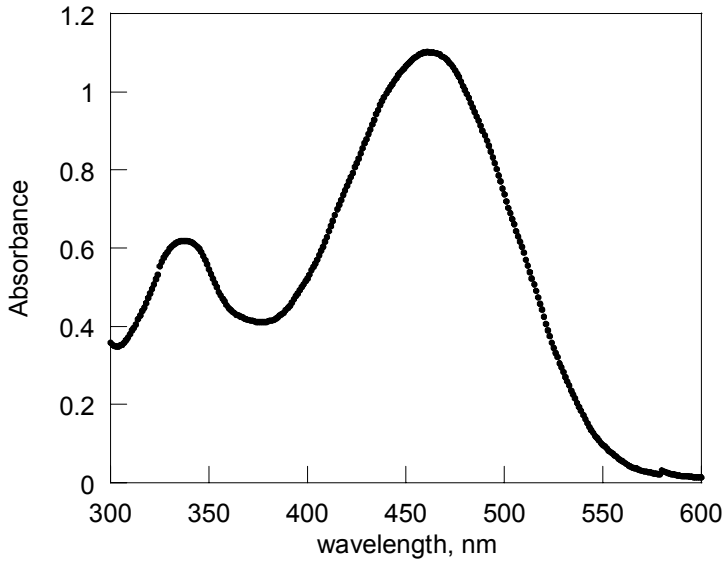

Figure S2: Absorbance spectrum of compound ***trans*-3** in methanol.

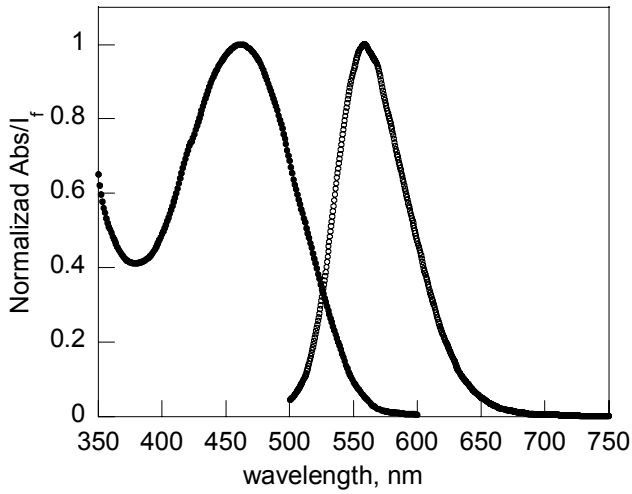

Figure S3: Normalised absorbance and fluorescence intensity of compound ***trans*-1** in methanol.

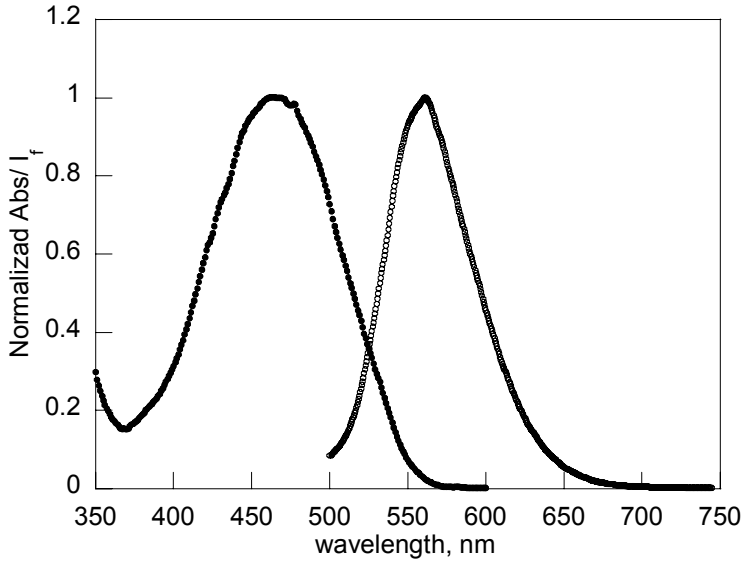

Figure S4: Normalised absorbance and fluorescence intensity of compound ***trans*-2** in methanol.

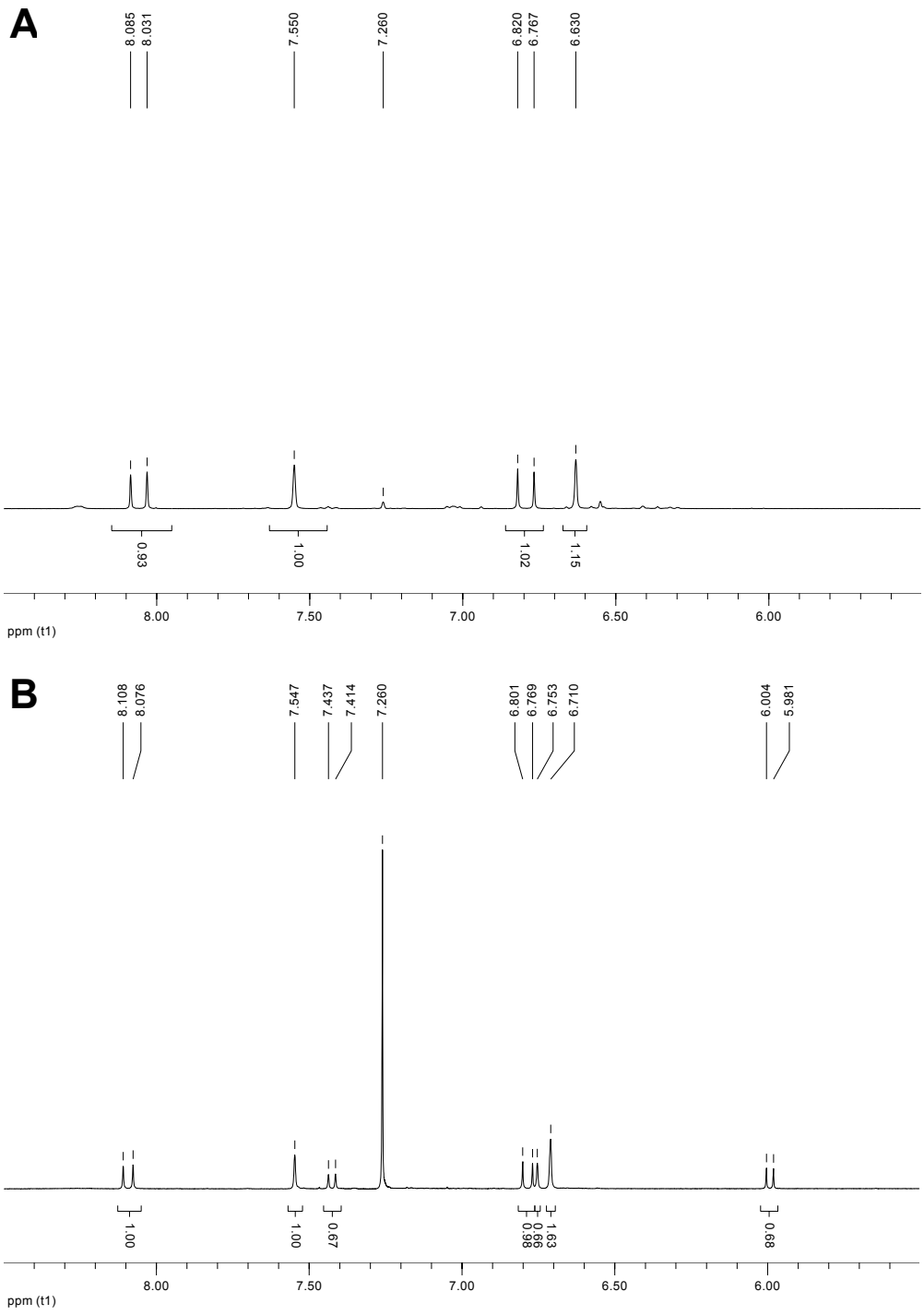

Figure S5: (A) ^{1}H-NMR spectrum of compound ***trans*-1** in $CDCl_3$. (B) ^{1}H-NMR spectrum obtained after irradiation of ***trans*-1** in methanol for 1 h.

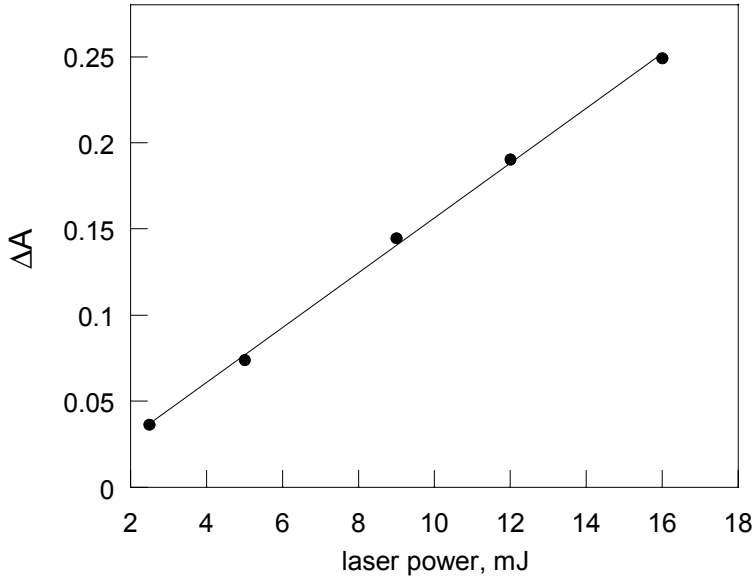

Figure S6: Laser (355 nm) power dependence of the transient absorbance for compound ***trans*-3** in methanol, monitored at 460 nm.

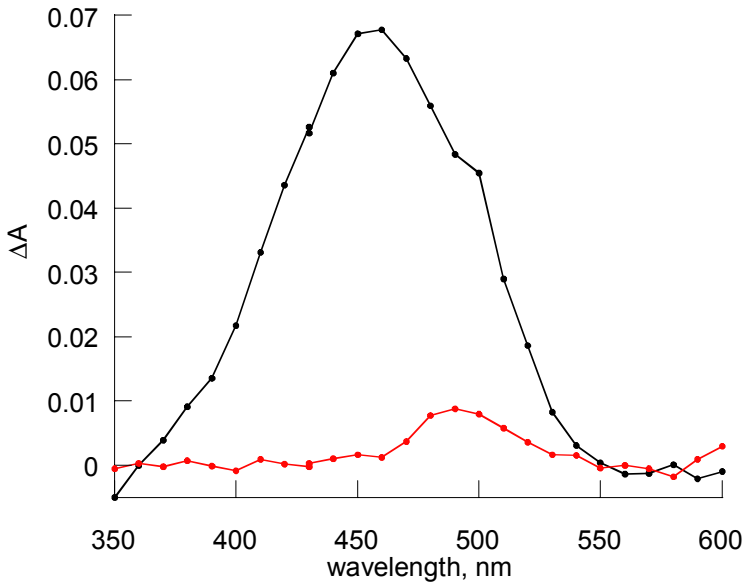

Figure S7: Transient absorption spectra of ***trans-3*** in methanol (●) and glycerol/methanol (9:1) mixture (■) recorded 50μs after the laser pulse of 355 nm.

Theoretical study

Computational Methods. Density functional theory (DFT) were carried out using the B3LYP [4] exchange-correlation functionals, together with the standard 6-31G(d) basis set.[5] Optimizations were carried out using the Berny analytical gradient optimization method.[6] Vertical energies of the singlet-excited state were calculated using the time-dependent (TD)[7] DFT methods at the B3LYP/6311+G** level. The electronic structures of stationary points were analyzed by the natural bond orbital (NBO) method.[8] All calculations were carried out with the Gaussian 03 suite of programs.[9]

A conformational analysis of the methoxy and the dimethylamino derivatives **A** and **F** (see Chart 2) was performed. These compounds can adopt a second planar conformation by rotation around the C3–C4 single bond, namely **B** and **G**. Conformers **B** and **G** are only 0.4 and 0.2 kcal/mol more energetic than the minimum **A** and **F**, respectively. These planar conformations allow to extend the conjugation between the electron-rich aryl and the electron-deficient dihydrofuran rings through the C2–C3 double bond.

The barriers for the equilibration between these conformers *via* conformations **C** and **H**, in which dihydrofuran rings are twisted 90 degrees, are 10.1 and 11.3 kcal/mol. respectively. These barriers can be related to the lost of the conjugation present in the planar conformations. The relative energy between these conformations at the S_1 singlet excited state, i.e. between ^{1}A and ^{1}B for *O*-DCDHF and between ^{1}F and ^{1}G for *N*-DCDHF, were not substantially different from those at the ground state (see Table S1). Therefore, for both compounds, the rotational barrier does not prevent the equilibration between the two planar conformers at the ground state, but it is too high for the time scale of the excited state

Next we analyzed the energies involved in the rotation around the C–O and C–N single bonds at **A** and **F**, *i.e.* conformations **D** and **I**, and the energy for the perpendicular disposition of the $C(CN)_2$ moiety, structures **E** and **J** (see Chart 2). At the ground state, the conformations **D** and **I** are 4.9 and 13.9 kcal/mol higher in energy than the planar structures **A** and **F**, respectively. The larger energy involved in the rotation around the C–N single bond is in agreement with the larger electron-releasing character of the Me_2N- group compared with the MeO- one. Note that these conformations are maxima on the C–O(N)

single bond rotation. TD-DFT calculations at the S_1 singlet excited state indicated that conformation ^{1}**D** is located 6.0 kcal/mol above the planar conformer ^{1}**A**, while the twisted conformation ^{1}**I** is 4.5 kcal/mol lower in energy than the planar conformer ^{1}**F**. That is, at the excited state, conformation ^{1}**I** is a minimum. A similar behavior was found for the twisted structures **E** and **J**. While at the ground state they are 38.5 and 37.2 kcal/mol above **A** and **F**, ^{1}**E** and ^{1}**J** are more stable than the planar conformers ^{1}**A** and ^{1}**F** (–10.9 and –9.2 kcal/mol, respectively). Consequently ^{1}**E** and ^{1}**J** are stationary points at the excited state.

In order to prove the unlike energy results obtained for the twisted **D** and **I** conformations, we performed a conformational analysis for the C–O(N) single bond rotation in the methoxy- and dimethylaminobenzonitrile derivatives **K** and **M** (see Chart S1). In conformations **L** and **N**, the methoxy and dimethylamino substituents, repectively, are twisted 90 degrees relative to the benzene ring. At the ground state, the planar conformations **K** and **M** are more stable than the corresponding perpendicular ones (**L**: 4.4 kcal/mol; **N**: 11.0 kcal/mol), see Table S2. Note that these relative energies are close to those obtained for **D** and **I**. However, at the S_1 singlet excited state, for the dimethylamino derivative, the perpendicular conformation ^{1}**N** is found 16.0 kcal/mol below the planar one ^{1}**M**. Although these S_1 singlet excited states were not optimized, these energy results indicated that ^{1}**N** can be also a minimum at the excited state. These energy results point out to the preferential perpendicular arrangement of the amino substituent at the excited state. By contrast, in the case of the methoxy derivative, the planar conformation ^{1}**K** is 7.5 kcal/mol more stable than the perpendicular one ^{1}**L.**

The presence of an electron-rich benzene and an electron-deficient dihydrofuran at the extremes of the C2–C3 double bond in **A** and **F** turns these compounds into push-pull ethylenes. This opposite substitution favors an asymmetric charge distribution in these molecules along the planar conjugated system, which could favor the formation of electronically stabilized sandwich dimers. This behavior is supported by the large dipole moment of these molecules, 14.6 (**A**) and 18.7 (**F**) Debye. In order to verify the suitability of the formation of dimeric species, we optimized the dimers of the methoxy and dimethylamino derivatives **A** and **F**, namely dimers **O** and **P**, respectively (see Chart 2).

Full geometrical optimizations at the B3LYP/6-31G* level afforded dimers **O** and **P**, which are 10.2 and 13.0 kcal/mol more stable than the separated monomeric species (see Table S3). Note that the dimer of the more polar amino derivative **F** is more stabilized. In spite of this large electronic stabilization, the unfavorable entropy associated with the formation of dimers, around –43.0 (**O**) and –47.5 (**P**) eu, makes the formation of these species endergonic processes by 4.0 (**O**) and 2.8 (**P**) kcal/mol (see Table S4).

TD DFT calculations for the dimer ^{1}**O** yielded an energy 18.9 kcal/mol lower than that of the monomer ^{1}**A**. That is, formation of the excited dimer ^{1}**O** is *ca.* 8 kcal/mol more favorable than the ground state dimer **O**. Since at room temperature the unfavorable entropic factor can be estimated in 13 kcal/mol, formation of the dimer ^{1}**O** could be exergonic by *ca.* 5 kcal/mol. TD calculationsfor the formation of the dimer ^{1}**P** from the amino derivative ^{1}**F** afforded a stabilization around 7 kcal/mol. In this case we estimated that at the excited state the perpendicular conformer ^{1}**I**, in which the dimethylamino is twisted 90 degree relative to the benzene ring, is 5 kcal/mol more stable than the planar one. In addition, the dimer ^{1}**Q**, in which the dimethylamino group is twisted 90 degrees, is 7.3 kcal/mol higher in energy than the dimer ^{1}**P**, in which the two monomers are in the planar conformation (see Chart S2 and Tables S3 and S4). Consequently while formation of the dimer ^{1}**P** is exergonic, formation of the dimer ^{1}**Q**, arising from the relaxed twisted conformation ^{1}**I**, is thermodynamically unfavourable.

Table S1. Total (E, in au) and relative (ΔE, in kcal/mol) energies at the S_0 and S_1[a] states of the planar and twisted conformations of ***trans*-5** and ***trans*-6**.

	B3LYP/6–31G*			B3LYP/6–311+G**	
	E	ΔE		E	ΔE
			***trans*-5**		
A	–1047.673273		(S_0)	–1047.947589	
			(S_1)	–1047.842990	65.6
B	–1047.672609	0.4	(S_0)	–1047.946723	0.5
			(S_1)	–1047.844986	64.4
C	–1047.657132	10.1	(S_0)	–1047.932365	9.6
			(S_1)	–1047.827791	75.2
D	–1047.665452	4.9	(S_0)	–1047.939989	4.8
			(S_1)	–1047.833523	71.6
E	–1047.611981	38.5	(S_0)	–1047.888605	37.0
			(S_1)	–1047.860469	54.7
			***trans*-6**		
F	–1067.121982		(S_0)	–1067.398979	
			(S_1)	–1067.301037	61.5
G	–1067.121760	0.1	(S_0)	–1067.398601	0.2
			(S_1)	–1067.302129	60.8
H	–1067.103913	11.3	(S_0)	–1067.381653	10.9
			(S_1)	–1067.296663	64.2
I	–1067.099908	13.9	(S_0)	–1067.376699	14.0
			(S_1)	–1067.308116	57.0
J	–1067.062711	37.2	(S_0)	–1067.342251	35.6
			(S_1)	–1067.315618	52.3

a) Energies at the S_1 singlet excited states were computed using time dependent (TD) calculations.

Table S2. Total (E, in au) and relative (ΔE, in kcal/mol) energies at the S_0 and S_1 [a] states of the planar and twisted conformations **K** – **N**.

	B3LYP/6–31G*			B3LYP/6–311+G**	
	E	ΔE		E	ΔE
K	–439.016826		(S_0)	–439.135779	
			(S_1)	–438.957968	111.6
L	–439.009841	4.4	(S_0)	–439.129512	3.9
			(S_1)	–438.946011	119.1
M	–458.463485		(S_0)	–458.585045	
			(S_1)	–458.424563	100.7
N	–458.445893	11.0	(S_0)	–458.567151	11.2
			(S_1)	–458.450137	84.7

a) Energies at the S_1 singlet excited states were computed using time dependent (TD) calculations.

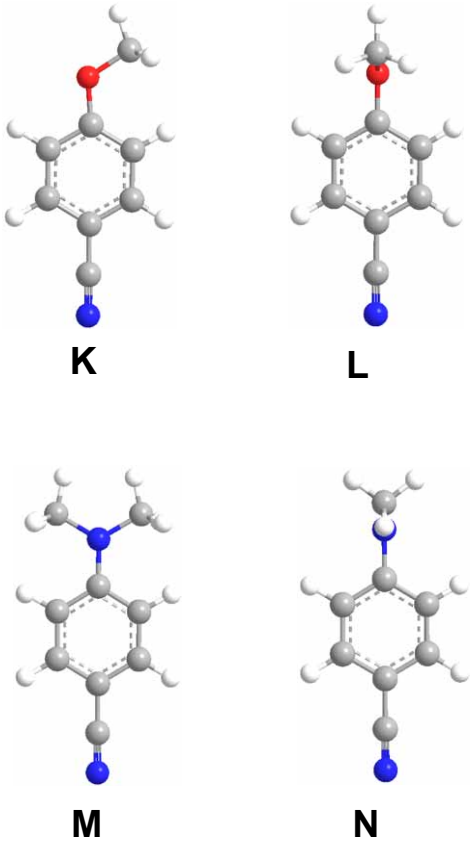

Chart S1

Table S3. Total (E, in au) and relative (ΔE,[a] in kcal/mol), in kcal/mol) energies at the S_0 and S_1[b] for the formation of the dimers **O**, **P** and **Q**.

	B3LYP/6–31G*		B3LYP/6–311+G*		
	E	ΔE		E	ΔE
O	–2095.362777	–10.2	(S_0)	–2095.907933	–8.0
			(S_1)	–2095.820692	46.7
P	–2134.264606	–13.0	(S_0)	–2134.813762	–9.9
			(S_1)	–2134.737738	37.8
Q	–2134.240975	1.9	(S_0)	–2134.790453	4.7
			(S_1)	–2134.726122	45.1

a) Relative to the monomer (see Table S1)
b) Energies at the S_1 singlet excited states were computed using time dependent (TD) calculations.

Table S4. B3LYP/6–31G* thermodynamic data at the S_0 ground state for the formation of the dimers **O** and **P**.

	H au	ΔH kcal/mol	S eu	ΔS eu	G au	ΔG kcal/mol
A	–1047.351583		163.0		–1047.429037	
O	–2094.717280	–8.9	283.0	–43.0	–2094.851754	4.0
F	–1066.757734		173.8		–1066.840297	
P	–2133.533591	–11.4	300.0	–47.5	–2133.676141	2.8

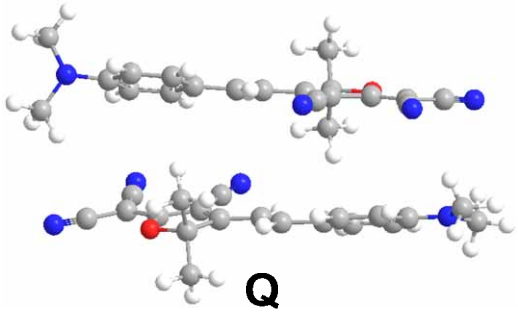

Chart S2

References

[1] E. Font-Sanchis, F. J. Céspedes-Guirao, A. Sastre-Santos, B. Villacampa, J. Orduna, R. Alicante and F. Fernández-Lázaro, *Tetrahedron* 2009, **65**, 4513.

[2] N. Boden, R. J. Bushby, A. N. Cammidge, *J. Am. Chem. Soc.* 1995, **117**, 924-927.

[3] D. Villemin, L. Liao, *Synth. Commun.* 2001, **31**, 1771-1780.

[4] (a) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785-789. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648-5652.

[5] Hehre, W. J.; L. Radom, L.; Schleyer, P.v.R.; J. A. Pople, *Ab initio Molecular Orbital Theory*, Wiley, New York, **1986**.

[6] (a) Schlegel, H. B. *J. Comput. Chem.* **1982**, *3*, 214-218. (b) Schlegel, H. B. *"Geometry Optimization on Potential Energy Surface," in Modern Electronic Structure Theory.* D.R. Yarkony ed., World Scientific Publishing: Singapore, **1994**.

[7] (a) Bauernschmitt, R, Ahlrichs, R. *Chem. Phys. Lett.* **1996**, *256*, 454-464. (b) Casida, M. E.; Jamorski, C.; Casida, K. C.; Salahud, D.R.; *J. Chem. Phys.* **1998**, *108*, 4439-4449.

[8] Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735-746.

[9] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J .R.; Montgomery, J. A. Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G.A. ; Nakatsuji, H. ; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H.P.; Cross, J.B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R.E.; Yazyev, O.; Austin, A.J.; Cammi, R.; Pomelli, C.; Ochterski, J.W.; Ayala, P.Y.; Morokuma, K.; Voth, G.A.; Salvador, P.; Dannenberg, J.J.; Zakrzewski, V.G.; Dapprich, S.; Daniels, A.D.; Strain, M.C.; Farkas, O.; Malick, D.K.; Rabuck, A.D.; Raghavachari, K.; Foresman, J.B.; Ortiz, J.V.; Cui, Q.; Baboul, A.G.; Clifford, S.; Cioslowski, J.; Stefanov, B.B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R.L.; Fox, D.J.; Keith, T.; Al-Laham, M. A.; Peng, C.Y.; Nanayakkara, A.; Challacombe, M.; Gill, P.M. W.; Johnson, B.; Chen, W.; Wong, M.W.; Gonzalez, C.; Pople, J.A. *Gaussian 03, Revision C.02*, Gaussian, Inc., Wallingford CT, **2004**.