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Fluorescent Donor-Acceptor-Psoralen Cruciforms by Consecutive Suzuki-Suzuki and Sonogashira-Sonogashira One-pot Syntheses

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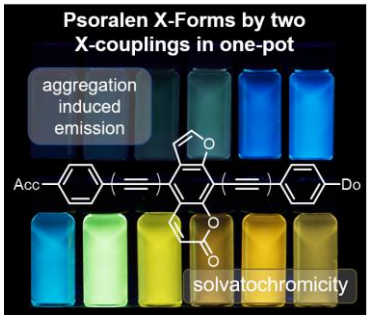
Supporting Information Placeholder



ABSTRACT: Two novel donor-acceptor cruciform topologies are efficiently synthesized by site-selective Suzuki-Suzuki and Sonogashira-Sonogashira multicomponent reactions starting from a bromo-triflato functionalized psoralen scaffold. Besides tunability of photophysical properties, such as absorption and emission, many derivatives possess partially high relative fluorescence quantum yields in solution and fluoresce strongly in the solid state. Additionally, the promising compounds show solvatochromism and acidochromic effects. Besides, 8-*p*-anisyl-5-*p*-cyanophenyl substituted psoralen exhibits aggregation induced emission properties. Experimentally (applying the Lippert-Mataga model) and computationally (TD-DFT calculations), the pronounced charge transfer character of longest wavelength absorption band was confirmed.

Introduction

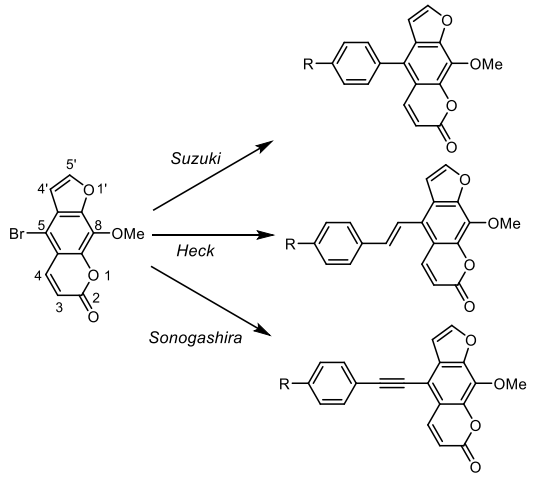
Functional π-systems are particularly valuable in modern applications, such as molecular electronics and photonics.[1] Especially, in the field of life sciences certain representatives of such chromophores are highly attractive for therapy and diagnostic applications (theranostics) due to their electronic properties.[2] X-shaped molecules with frontier orbitals that are localized on orthogonally arranged branches, so called cruciforms, enable the design of functional chromophores with interesting properties stemming from significant changes of the transition dipole vector's orientation.[3] As a modern approach, we have disclosed modular syntheses of functional chromophores with tunable electronic characteristics by consecutive and diversity-oriented multicomponent reactions.[4] In particular, novel systems showing distinctive properties, such as strong emission solvatochromism and aggregation-induced behavior, became accessible and structure-property relationships were established.[5] Furthermore, the concept of sequentially palladium-catalyzed processes has often adopted a pivotal role, several consecutive reactions are conducted in the same reaction vessel using a sole, suitable catalyst.[6]

Psoralen, furo[3,2-*g*]chromen-7-one, is a tricyclic donor-acceptor heterocycle with ligation of electron-rich furan and electron-poor α-pyrone to a central benzene core. It occurs naturally in Psoralea corylifolia, which has already been used as a medicinal plant for thousands of years, without exactly knowing its mode of action.[7] Psoralen was mainly used to treat various skin diseases such as vitiligo or psoriasis.[8] Therefore, the substance is applied on the skin and the affected areas were exposed to sunlight, whereby a pigmentation of the skin appears.[7a] Today the accepted mode of action is based on the PUVA mechanism.[9] A double [2+2]-cycloaddition between the psoralen and the DNA bases is supposed to cause apoptosis inducing crosslinks.[10] Recent studies also suggest that, depending on the psoralen derivative and directly adjacent base pair in the DNA helix, a photo-induced electron transfer takes place as a competitive process.[11]

Most research areas are focused on the synthesis of naturally occurring psoralen derivatives,[12] such as 8-methoxypsoralen or its related compounds.[13] Recently, starting from 5-bromo-8-methoxypsoralen we successfully disclosed diversity-oriented cross-coupling reactions to 5-arylated, 5-styrylated and 5-arylalkynylated 8-methoxypsoralens with fine-tunable absorption and emission maxima (Scheme 1).[14] Due to the inherent donor-acceptor chromophore structure of psoralen we reasoned that placing donor and acceptor moieties in positions 5 and 8 could result in orthogonal bis(donor-acceptor) cruciforms. These X-shaped chromophores presumably will possess distinct spatially separated frontier molecular orbitals (FMO).[3a,15] These features are particularly interesting beyond psoralen-typical applications as absorbers or emitters in molecular photonics.[15b,16]

Here, we report consecutive three-component syntheses of psoralen cruciforms based upon site-selective Suzuki arylation and Sonogashira alkynylation giving rise to unsymmetrically functionalized donor-acceptor psoralens in a one-pot fashion. The electronic structure is investigated by absorption and emission spectroscopy,

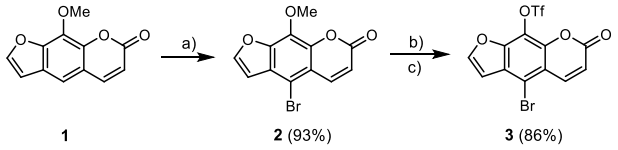
as well as by (TD)DFT calculations. In addition, attractive photonic characteristics, such as emission solvatochromism, acidochromism, and aggregation-induced emission, can be identified.



Scheme 1. Suzuki, Heck and Sonogashira approach to 5-substituted 8-methoxypsoralens with conjugated aryl, styryl, and arylethynyl substituents (R = CN, NO_2, CHO, NMe_2 etc.).

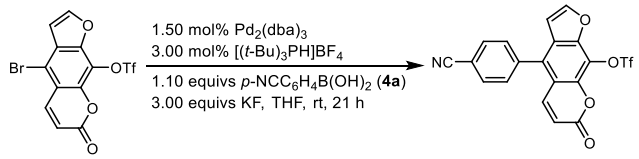
Results and Discussion

Synthesis. For envisioning twofold site-selective stepwise cross-coupling in the sense of a sequentially Pd-catalyzed process[17] two different (pseudo)halogen functionalities are prerequisite. Starting from 8-methoxypsoralen (**1**), convenient selective monobromination was performed in 5-position to give 5-bromo-8-methoxypsoralen (**2**) in excellent yield (Scheme 2).[14,18] Then, after demethylation of compound **2** with boron tribromide[19] followed by triflation with trifluoromethanesulfonic acid anhydride the proposed 5-bromo-8-triflatopsoralen (**3**) was obtained in 86% over two steps.[20]



Scheme 2. Synthesis of 5-bromo-8-triflatopsoralen (**3**). a) 3.00 equivs HBr, 3.00 equivs DMSO, EtOAc, 60 °C, 16 h. b) 4.00 equivs BBr_3 (1.00 m in CH_2Cl_2), CH_2Cl_2, 0 °C, 3 h. c) 2.00 equivs Tf_2O, 3.60 equivs pyridine, CH_2Cl_2, 0 °C, 2 h.

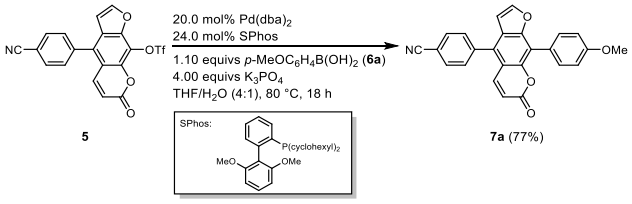
For selectively introducing acceptor and donor units, Suzuki coupling was performed according to Fu's conditions.[21] In the presence of $Pd_2(dba)_3$ as a catalyst, potassium fluoride as a base, tri-*tert*-butylphosphonium tetrafluoroborate was used as a ligand in THF as a solvent at room temperature (Scheme 3).



Scheme 3. Suzuki synthesis of the 5-(*p*-cyanophenyl) substituted 8-psoralen triflate **5**.

Under these conditions, 5-bromo-8-triflatopsoralen (**3**) was selectively coupled with *p*-cyanophenyl boronic acid (**4a**) to give the 5-(*p*-cyanophenyl) substituted 8-psoralen triflate **5** in a good yield of 67% after flash chromatography. The structure of product **5** was unambiguously assigned by ^1H, ^{19}F, and ^{13}C NMR spectroscopy as well as mass spectrometry.

For coupling the triflate functionality with a donor boronic acid, several conditions were tested. Suzuki coupling of triflate **5** with *p*-methoxyphenyl boronic acid (**6a**) in the presence of $Pd(PPh_3)_4$ as a catalyst and cesium carbonate as base in DMF was unsuccessful and resulted in a cleavage of the triflate. Neither conditions applied for the formation of educt **5** (Scheme 3), nor $Pd(dppf)Cl_2$ and dry cesium acetate in tetrahydrofuran[22] led to the targeted product. However, using $Pd(dba)_2$ and SPhos as a catalyst system and potassium phosphate as a base in THF/water finally gave rise to the formation of the donor-acceptor system **7a** in 77% yield after flash chromatography (Scheme 4).



Scheme 4. Suzuki synthesis of 5-donor-8-acceptor psoralen **7a**.

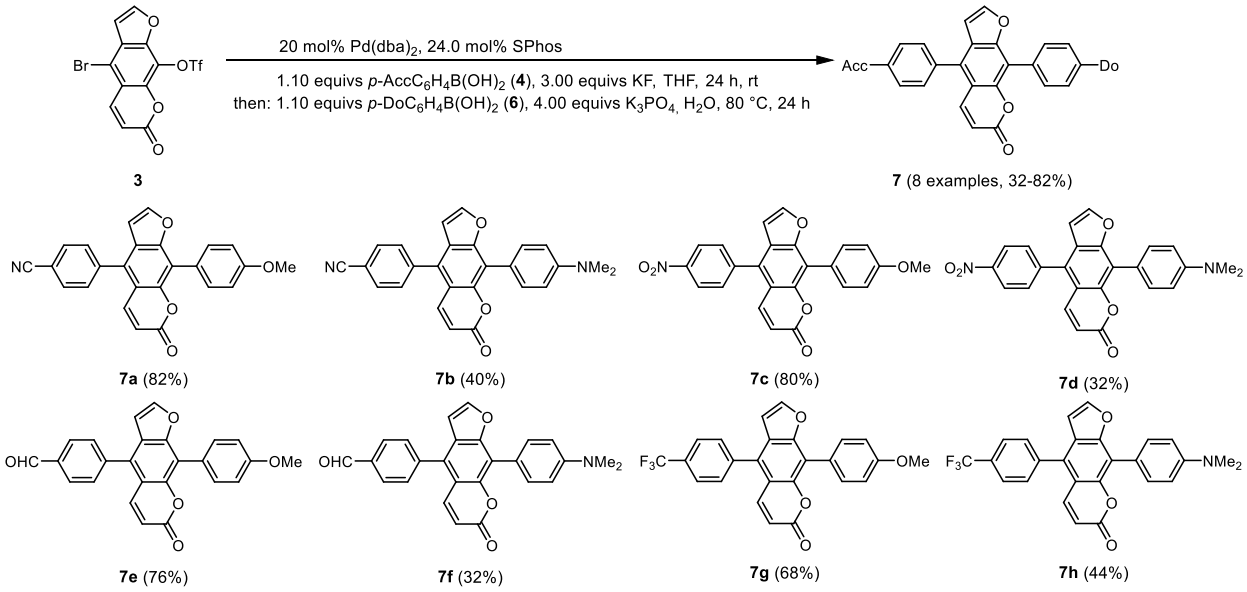
Applying the conditions outlined in Scheme 4 to the coupling of 5-bromo-8-triflatopsoralen (**3**) with *p*-cyanophenyl boronic acid (**4a**) to furnish intermediate **5** gave a yield of 59% after isolation. Interestingly, performing consecutively both couplings with boronic acids **4a** and **6a** with $Pd(dba)_2$ and SPhos as the initially employed catalyst system resulted in formation of the donor-acceptor psoralen **7a**, which was isolated after flash chromatography in 82% yield. This is a significantly higher yield of the one-pot process in comparison to the combined stepwise processes furnishing compound **7a** only in 52% yield after isolation. These conditions were applied to illustrate the novel consecutive three-component synthesis of donor-acceptor psoralens **7** in 8 examples with yields in a range of 32-82% (Scheme 5, for experimental details see Table 1). The structures of the compounds **7** were unambiguously assigned by ^1H and ^{13}C NMR spectroscopy as well as mass spectrometry.

Besides *p*-cyanophenyl boronic acid (**4a**) *p*-nitro- (**4b**), *p*-formyl- (**4c**), and *p*-trifluoromethyl (**4d**) derivatives were employed as acceptor substrates, whereas *p*-methoxyphenyl (**6a**) and *p*-dimethylaminophenyl (**6b**) boronic acids were chosen as donor reactants. This one-pot synthesis specifically takes advantage of the concept of sequentially Pd-catalyzed processes where a single catalyst system is operating in a one-pot fashion without further addition of catalyst.[17]

With this concise consecutive Suzuki-Suzuki three-component synthesis of 5-donor substituted 8-acceptor psoralens in hand, we reasoned that a similar process based of a consecutive Sonogashira-Sonogashira sequence could lead to alkynyl-expanded 5-donor substituted 8-acceptor psoralens. However, site selective Sonogashira coupling turned out to be more challenging and three optimization studies were performed, where Pd-catalyst systems, bases, solvents, and reaction temperatures and times had to be identified (see Supp. Inf., chpt 1.1.). First, $Pd_2(dba)_3$ and cataCXium® ABn · HBr as a catalyst system[23] with NEt_3 as a base in 1,4-dioxane at 75 °C for 24 h were identified as best conditions for coupling an acceptor substituted alkyne selectively at the 5-bromo position of 5-bromo-8-triflatopsoralen (**3**) (for details, see Supp. Inf., Table S1). Then, the site-selective coupling with a donor substituted alkyne at the 8-triflato position of this intermediate was found to occur optimally with $Pd(PPh_3)_4$ as a catalyst in DMSO at 90 °C for 20 h (for details, see Supp. Inf., Table S2).

Finally, the complete one-pot sequence with two consecutive Sonogashira alkynylations, starting 5-bromo-8-triflatopsoralen (**3**)

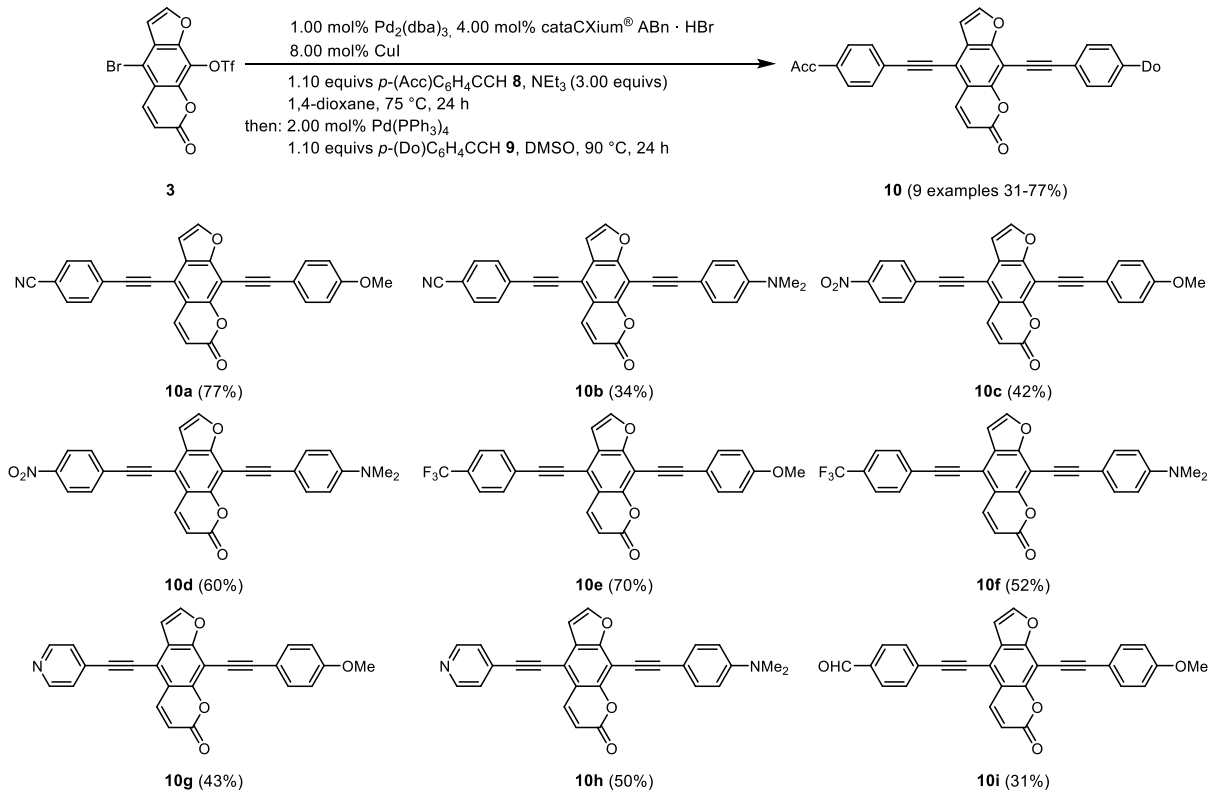
proceeds optimally, indeed, with two different catalyst systems in each step. The first alkynylation takes place with $Pd_2(dba)_3$ and cataCXium® ABn · HBr as a catalyst system in 1,4-dioxane at 75 °C for 24 h, followed by addition of $Pd(PPh_3)_4$ and DMSO for the second alkynylation at 90 °C for 18 h (for details, see Supp. Inf., Table S3). These conditions were then applied to 5-bromo-8-triflatopsoralen (**3**), *p*-(acceptor)phenylacetylenes **8**, (**8a**: *p*-Acc = CN; **8b**: *p*-Acc = NO_2; **8c**: *p*-Acc = CF_3; **8d**: *p*-(Acc)C_6H_4 = 4-pyridyl; **8e**: *p*-Acc = CHO), and *p*-(donor)phenylacetylenes **9** (**9a**: *p*-Do = OMe; **9b**: *p*-Do = NMe_2). This novel consecutive three-component synthesis of alkynyl-expanded 5-donor substituted 8-acceptor psoralens **10** is illustrated in nine examples with yields in a range of 31-77% (Scheme 6, , for experimental details see Table 2). The structures of the compounds **10** were unambiguously assigned by ^1H and ^{13}C NMR spectroscopy as well as mass spectrometry.



Scheme 5. Selective consecutive sequentially Pd-catalyzed Suzuki-Suzuki three-component synthesis of 5-donor substituted 8-acceptor psoralens **7**.

Table 1. Experimental details of the selective Suzuki-Suzuki three-component synthesis of 5-acceptor-8-donor psoralens **7**.

5-Bromo-8-triflatopsoralen (**3**) [mg] ([mmol])	*p*-(Acc)$C_6H_4B(OH)_2$ **4** [mg] ([mmol])	$Pd(dba)_2$ / SPhos [mg] ([mmol])	KF [mg] ([mmol])	THF [mL]	*p*-(Do)$C_6H_4B(OH)_2$ **6** [mg] ([mmol])	K_3PO_4 [mg] ([mmol])	Product **7** (yield) [mg] (%)
510 (1.23)	198 (1.35) of **4a**	142 (0.247) / 121 (0.295)	214 (3.69)	5.00	205 (1.35) of **6a**	1040 (4.92)	386 (80) of **7a**
250 (0.605)	103 (0.700) of **4a**	69.6 (0.121) / 67.1 (0.163)	106 (1.82)	2.50	116 (0.700) of **6b**	513 (2.42)	98.4 (40) of **7b**
150 (0.363)	66.7 (0.400) of **4b**	41.7 (0.0726) / 40.2 (0.0980)	63.2 (1.09)	1.75	62.0 (0.408) of **6a**	308 (1.45)	120 (80) of **7c**
250 (0.605)	111 (0.666) of **4b**	69.6 (0.121) / 67.1 (0.163)	106 (1.82)	2.50	116 (0.700) of **6b**	513 (2.42)	82.1 (32) of **7d**
150 (0.363)	61.2 (0.408) of **4c**	41.7 (0.0726) / 40.2 (0.0980)	63.2 (1.09)	1.75	62.0 (0.408) of **6a**	308 (1.45)	137 (76) of **7e**
250 (0.605)	100 (0.666) of **4c**	69.6 (0.121) / 67.1 (0.163)	106 (1.82)	2.50	110 (0.666) of **6b**	513 (2.42)	86.7 (32) of **7f**
200 (0.484)	106 (0.558) of **4d**	55.7 (0.0968) / 47.7 (0.116)	84.4 (1.45)	2.00	80.9 (0.532) of **6a**	411 (1.94)	143 (68) of **7g**
250 (0.605)	133 (0.668) of **4d**	69.6 (0.121) / 67.1 (0.163)	106 (1.82)	2.50	110 (0.666) of **6b**	513 (2.42)	130 (44) of **7h**



Scheme 6. Selective consecutive Sonogashira-Sonogashira three-component synthesis of alkynyl-expanded 5-donor substituted 8-acceptor psoralens **10**.

Table 2. Experimental details of the selective Sonogashira coupling of alkynyl expanded 5-donor substituted 8-acceptor psoralens **10**.

5-Bromo-8-tri-flatopsoralen (**3**) [mg] ([mmol])	*p*-Acc-$C_6H_4BC{\equiv}CH$ **8** [mg] ([mmol])	$Pd_2(dba)_3$/ cat-aCXium ABn® · HBr [mg] ([µmol])	NEt_3 / CuI [mg] ([mmol])	1,4-di-oxane [mL]	*p*-Do-$C_6H_4C{\equiv}CH$ **9** [mg] ([mmol])	$Pd(PPh)_4$ / DMSO [mg] ([µmol]) / [mL]	Product **10** (%) [mg]
274 (0.664)	93.1 (0.732) of **8a**	6.08 (6.65) / 11.4 (24.1)	202 (2.00) / 10.1 (0.0531)	3.00	96.6 (0.732) of **9a**	14.4 (12.5) / 3.00	196 (77) of **10a**
100 (0.242)	33.8 (0.266) of **8a**	2.21 (2.42) / 4.58 (9.68)	73.5 (0.726) / 3.69 (0.0194)	1.50	38.1 (0.266) of **9b**	5.60 (4.84) / 1.50	40.1 (34) of **10b**
85.9 (0.208)	33.7 (0.229) of **8b**	1.90 (2.08) / 3.55 (7.51)	63.1 (0.624) / 3.16 (0.0166)	1.00	30.3 (0.229) of **9a**	4.80 (4.16) / 1.00	40.0 (43) of **10c**
85.9 (0.208)	33.7 (0.229) of **8b**	1.90 (2.08) / 3.55 (7.51)	63.1 (0.624) / 3.16 (0.0166)	1.00	33.2 (0.229) of **9b**	4.80 (4.16) / 1.00	59.2 (60) of **10d**
103 (0.250)	46.8 (0.275) of **8c**	2.29 (2.50) / 4.73 (10.0)	75.9 (0.75) / 3.80 (2.00)	1.00	36.3 (0.275) of **9a**	5.78 (5.00) / 1.00	84.1 (70) of **10e**
103 (0.250)	46.8 (0.275) of **8c**	2.29 (2.50) / 4.73 (10.0)	75.9 (0.75) / 3.80 (2.00)	1.00	40.0 (0.275) of **9b**	5.78 (5.00) / 1.00	64.0 (52) of **10f**
103 (0.250)	38.4 (0.275) of **8d**	2.29 (2.50) / 4.73 (10.0)	75.9 (0.75) / 3.80 (2.00)	1.00	36.3 (0. 275) of **9a**	5.78 (5.00) / 1.00	45.0 (43) of **10g**
436 (1.06)	124 (1.20) of **8d**	9.70 (10.6) / 20.0 (42.4)	322 (3.18) / 16.1 (8.48)	4.00	158 (1.20) of **9a**	24.5 (21.2) / 4.00	177 (40) of **10g**
103 (0.250)	38.4 (0.275) of **8d**	2.29 (2.50) / 4.73 (10.0)	75.9 (0.75) / 3.80 (0.0200)	1.00	40.0 (0.275) of **9b**	5.78 (5.00) / 1.00	53.8 (50) of **10h**
103 (0.250)	35.7 (0.275) of **8a**	2.29 (2.50) / 4.73 (10.0)	75.9 (0.75) / 3.80 (2.00)	1.00	36.3 (0. 275) of **9a**	5.78 (5.00) / 1.00	34.0 (31) of **10i**

Photophysical properties. All cruciforms **7** and **10** are colorless to red solids, depending on the substitution pattern. Moreover, with exception of the nitro derivatives **7c,d** and **10c,d**, all dyes are emissive in solution and in the solid state upon excitation with the hand-held UV lamp (Figures 1 and 2). Therefore, a comprehensive quantitative photophysical characterization by measuring absorption and emission spectra, and determining relative fluorescence quantum yields Φ_F with Coumarin 30 as a standard[24] was conducted for all cruciforms **7** and **10** (Tables 3 and 4).

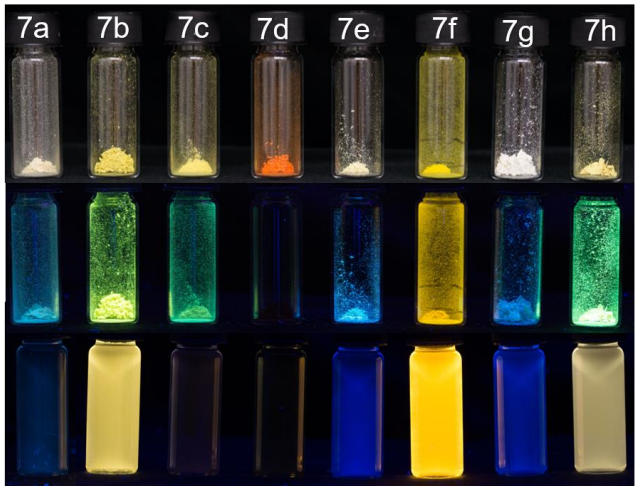


Figure 1. Psoralen derivatives **7** in solid state in daylight (top row) and in UV-light (center row), and in dichloromethane (bottom row, c(**7**) = 10^{-7} M, hand-held UV-lamp, λ_{exc} = 365 nm).

Table 3. Selected photophysical properties of 5-substituted 5-acceptor-8-donor psoralens **7**.

compound	$\lambda_{max,abs}$ [nm][a] (ε [$M^{-1}cm^{-1}$])	$\lambda_{max,em}$ [nm][b] (Φ_F [a.u.])	Stokes shift $\Delta\tilde{\nu}$ [cm^{-1}][c]
7a	313 (21000) 359 (6300sh)	-	-
7b	308 (25300) 345 (14300sh) 388 (7300sh)	586 (0.10)	8700
7c	325 (16000) 376 (8100sh)	-	-
7d	305 (24900) 402 (7200sh)	-	-
7e	317 (17900) 367 (5400sh)	455 (0.05)	5300
7f	302 (29000) 343 (16700sh) 393 (8800sh)	600 (0.17)	8900
7g	287 (27700) 314 (23200sh) 360 (6100sh)	452 (0.01)	5600
7h	304 (25800) 340 (14400sh) 384 (5600sh)	573 (0.07)	8600

[a] Recorded in CH_2Cl_2, c(**7**) = 10^{-5} M at T = 293 K. [b] Recorded in CH_2Cl_2, c(**7**) = 10^{-7} M at T = 293 K, relative quantum yields were determined with Coumarin 30 as a standard in acetonitrile (Φ_F = 0.67[24]). [c] $\Delta\tilde{\nu} = \frac{1}{\lambda_{max,abs}} - \frac{1}{\lambda_{max,em}}$.

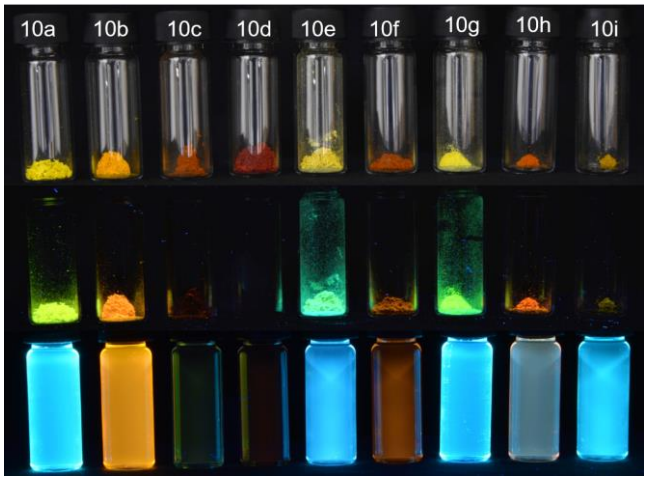


Figure 2. Psoralen derivatives **10** in solid state in daylight (top row) and in UV-light (center row), and in dichloromethane (bottom row, c(**10**) = 10^{-7} M, hand-held UV-Lamp, λ_{exc} = 365 nm).

Table 4. Selected photophysical properties of alkynyl expanded 5-acceptor-8-donor psoralens **10**.

compound	$\lambda_{max,abs}$ [nm][a] (ε [$M^{-1}cm^{-1}$])	$\lambda_{max,em}$ [nm][b] (Φ_F [a.u.])	Stokes shift $\Delta\tilde{\nu}$ [cm^{-1}][c]
10a	304 (20300) 365 (29200) 393 (22300)	492 (0.38)	5100
10b	273 (26200) 331 (36000) 432 (27200)	620 (0.32)	7000
10c	308 (30000) 372 (35300) 404 (34700)	-	-
10d	280 (29800) 332 (42200) 443 (31200)	-	-
10e	318 (28100) 360 (40700) 388 (27400)	480 (0.08)	4900
10f	275 (21100) 331 (35000) 412 (19900)	602 (0.06)	7700
10g	315 (28500) 360 (40800) 389 (29600)	478 (0.08)	4800
10h	275 (24600) 331 (39000) 429 (27500)	618 (0.05)	7100
10i	310 (24400) 367 (33300) 397 (27221)	487 (0.08)	4700

[a] Recorded in CH_2Cl_2, c(**10**) = 10^{-5} M at T = 293 K. [b] Recorded in CH_2Cl_2, c(**10**) = 10^{-7} M at T = 293 K, relative quantum yields were determined with Coumarin 30 as a standard in acetonitrile (Φ_F = 0.67[24]). [c] $\Delta\tilde{\nu} = \frac{1}{\lambda_{max,abs}} - \frac{1}{\lambda_{max,em}}$.

For all (hetero)aryl substituted compounds **7** the longest wavelength absorption band in dichloromethane is just discernible as a shoulder (Figure 3). These psoralen derivatives exhibit relatively low molar absorption coefficients ε between 5600 and 8800 $M^{-1}cm^{-1}$ (Table 3). Changing the donor substituent from *p*-methoxy to *p*-dimethylamino for the same acceptor moiety causes a significant

bathochromic shift of the longest wavelength absorption maxima between 1720 and 2082 cm^{-1}. Even more pronounced is the redshift of the emission maxima upon changing from *p*-methoxy (**7e**: 455 nm) to *p*-dimethylamino substitution (**7f**: 600 nm). This reflects also in the Stokes shifts, which appear for *p*-dimethylamino derivatives **7b**, **7f**, and **7h** between 8600 and 8900 cm^{-1} and for *p*-methoxy derivatives **7e** and **7g** between 5300 and 5600 cm^{-1}. The fluorescence quantum yields Φ_F of the cruciforms **7** range between 1 and 17% and are mainly related to the donor strength of the substituents. Thus, directly linked *p*-dimethylaminophenyl-substituted psoralens tend to show higher relative fluorescence quantum yields, while anisyl-functionalized psoralens 7 show no or only low relative fluorescence quantum yields of up to 5 %. As mentioned above the nitro derivatives **7c-d** do not fluoresce as a consequence of a common competitive deactivation of the excited state by predissociation.[25] With exception of compound **7d** all (hetero)aryl psoralen cruciforms **7** fluoresce in the solid state with tunable emission color from blue over green to yellow and orange (Figure 1, center).

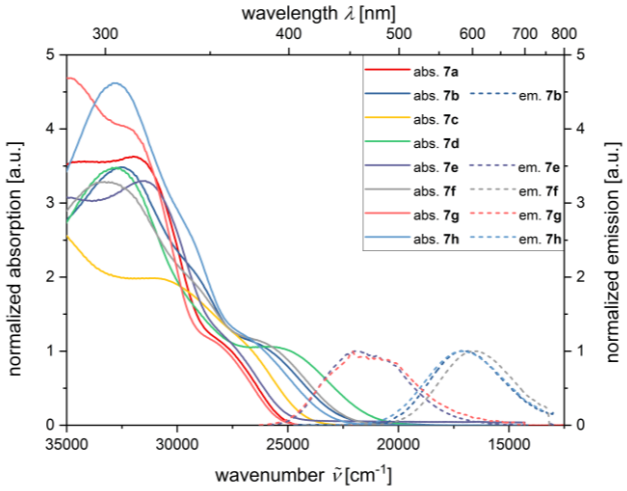


Figure 3. Normalized UV/Vis absorption (recorded in CH_2Cl_2, T = 293 K, c(**7**) = 10^{-5} M, bold lines) and emission bands (recorded in CH_2Cl_2, T = 293 K, c(**7**) = 10^{-7} M, dashed lines) of compounds **7**.

Compared to 5-donor substituted 8-acceptor psoralens **7** their alkynyl-expanded congeners **10** in dichloromethane solutions clearly exhibit pronounced maxima of the longest wavelength absorption bands, as a consequence of the extended π-conjugation, in a range between 388 and 443 nm with intense molar absorption coefficients between 22300 and 34700 $Lmol^{-1}cm^{-1}$ (Figure 4, Table 4). The emission maxima of cruciforms **10** with similar substituent patterns are redshifted as well and appear between 480 and 620 nm with Stokes shifts of 4700 to 5100 cm^{-1} for *p*-methoxy derivatives and 7000 to 7700 for *p*-dimethylamino systems. Furthermore, their fluorescence quantum yields Φ_F (between 5 and 38%) are significantly higher than the corresponding (hetero)aryl substituted cruciforms **7**, being no longer dependent on the donor strength of the aryl acetylene in position 8. Here, the acceptor strength seems to have a more significant effect, since especially the strongly electron-withdrawing cyano group leads to a very high relative fluorescence quantum yield. Again, the nitro derivatives **10c-d** do not fluoresce in solution due to deactivation (Figure 2, bottom).

The weak fluorescence of compound **7a** in solution and its intense emission in the solid state (Figure 1, center and bottom) caught our interest to study its aggregation induced emission[26] behavior in water/acetonitrile mixtures (Figure 5, top). While a pure acetonitrile solution of compound **7a** is essentially nonluminescent, increasing water/acetonitrile ratios at constant cruciform concentration causes a constant increase in emission intensity (Figure 5, bottom). At a water/acetonitrile ratio of 50% a significant increase of fluorescence intensity with a concomitant solvatochromic effect occurs up to 70%. At higher water content the color shifts to sky blue (for further details, see Supp. Inf. Figure S15).

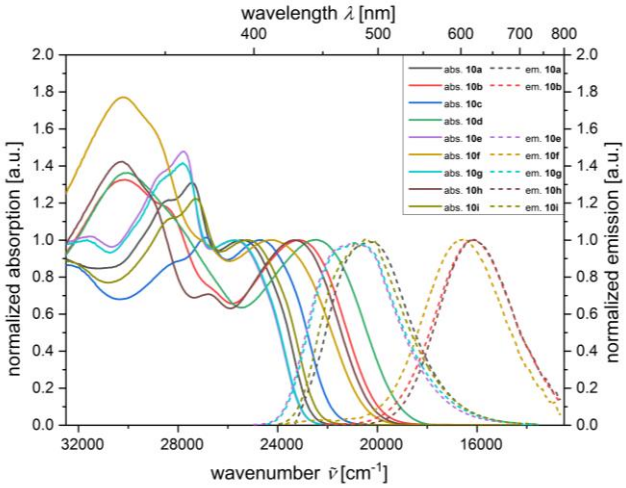


Figure 4. Normalized UV/Vis absorption (recorded in CH_2Cl_2, T = 293 K, c(**10**) = 10^{-5} M, bold lines) and emission bands (recorded in CH_2Cl_2, T = 293 K, c(**10**) = 10^{-7} M, dashed lines) of compounds **10**.

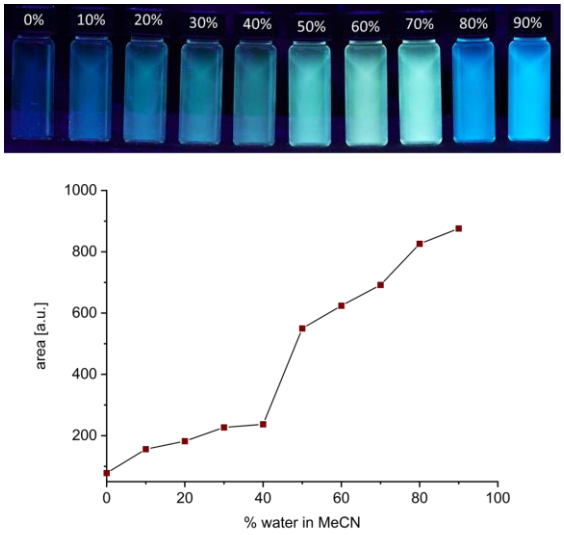


Figure 5. Top: Cruciform **7a** in different MeCN/H_2O mixtures (from left to right the ratio of H_2O increases) (hand-held UV-Lamp, λ_{exc} = 365 nm). Bottom: Aggregation induced emission of **7a** in solution measured in MeCN/H_2O (recorded at T = 293 K, c(**7a**) = 2.41 · 10^{-4} M , λ_{exc} = 359 nm).

The combination of large Stokes shifts and donor-acceptor substitution pattern accounts for significant excited state polarity. Therefore, we performed solvatochromism studies with selected cruciforms **7** and **10**. First, absorption and emission spectra of 5-(*p*-dimethylaminophenyl)-8-(*p*-trifluoromethylphenyl)psoralen (**7h**) were recorded in solvents of different polarity, indicating a pronounced positive emission solvatochromism (Figure 6, top), whereas the absorption maxima essentially remained unchanged (for details, see Supp. Inf., Table S4). The emission color shifts from blue in cyclohexane to orange in dichloromethane (Figure 6). The positive emission solvatochromicity accounts for a large dipole moment of the vibrationally relaxed S_1 state, which is stabilized by increasing solvent polarity.[27]

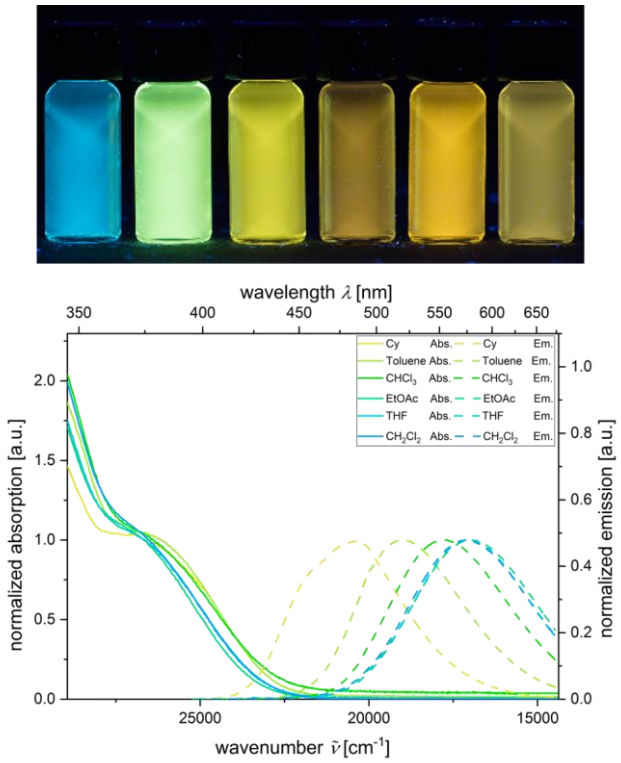


Figure 6. Top: Fluorescence of compound **7h** in solvents of different polarity (from left to right: cyclohexane, toluene, chloroform, ethyl acetate, tetrahydrofuran, dichloromethane; λ_{exc} = 365 nm). Bottom: UV/Vis absorption (bold lines) and emission (dashed lines) spectra of compound **7h** measured in six solvents of different polarity recorded at T = 293 K.

Applying the Lippert-Mataga model[28] the change of dipole moment from ground to vibrationally relaxed excited state for compound **7h** is calculated by plotting the Stokes shifts of the solvent against the corresponding orientation polarizability Δf to give $\Delta\mu$ = 13 D ($4.20 \cdot 10^{-29}$ Cm), indicating a significant charge transfer character (for details, see Supp. Inf., Table S4 and Figure S2).

Likewise, the solvatochromism of two ethynyl-expanded cruciforms **10a-b** was studied in detail. Expectedly, the weaker donor methoxy in cruciform **10a** results in considerably lower absorption and emission solvatochromicity (Figure 7, top) than the stronger donor dimethylamine in cruciform **10b** (Figure 7, bottom). However, the effect of the stronger donor on the polarity of the excited state becomes apparent by magnitude of the corresponding Stokes shift in the same solvent, e.g. ethyl acetate (**10a**: 4300 cm^{-1}; **10b**: 7300 cm^{-1}). This is also supported by the ensuing values for the change of dipole moments applying the Lippert-Mataga model[28] giving $\Delta\mu$ = 11 D ($3.57 \cdot 10^{-29}$ Cm) for compound **10a** and $\Delta\mu$ = 17 D ($5.50 \cdot 10^{-29}$ Cm) for compound **10b** (for details, see Supp. Inf., Table S5 and S6, and Figures S4 and S6). From the three studied cruciforms **7h**, **10a** and **10b** it becomes apparent that the charge transfer character of the excited state is governed by the donor-acceptor substitution at positions 5 and 8, where the longest chromophore axes are embedded.

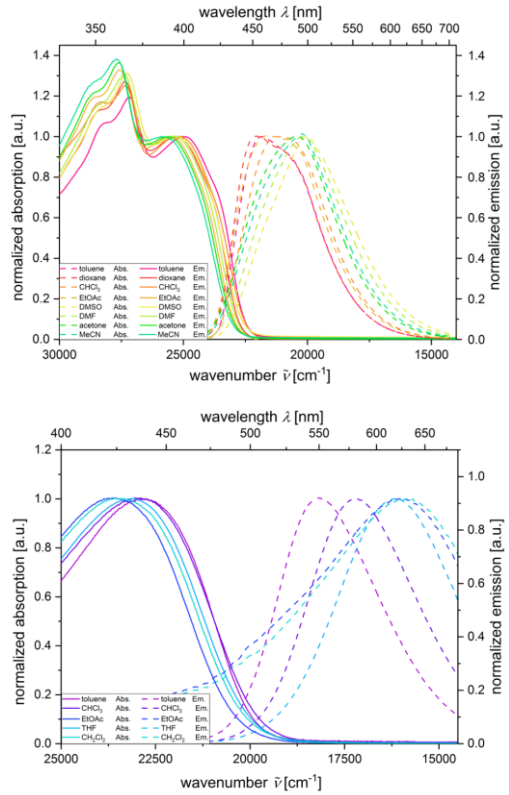


Figure 7. UV/Vis absorption (bold lines) and emission (dashed lines) spectra of compound **10a** (top) and **10b** (bottom) measured in solvents of different polarity recorded at T = 293 K.

Dimethylamino substituted cruciforms will change the donor effect to an inductive acceptor upon protonation[29] and should cause for psoralen cruciforms significant changes of their photophysical properties. Upon adding trifluoroacetic acid to dichloromethane solutions of the dimethylamino-substituted cruciforms **7b** and **10b**, the apparent fluorescence disappeared (compound **7b**) or decreased (compound **10b**) (Figure 8). Upon addition of triethylamine as a base, the acidochromicity can be reversed.

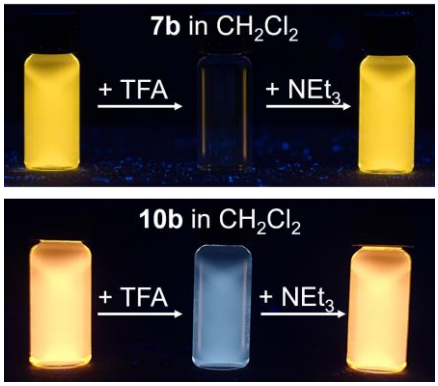


Figure 8. Cruciforms **7b** (top) and **10b** (bottom) in dichloromethane and by addition of trifluoroacetic acid (TFA) and subsequently by addition of triethylamine under the hand-held UV lamp (c = 10^{-5} M, λ_{exc} = 365 nm).

The acidochromicity can be monitored by absorption and emission spectroscopy as shown for cruciform **10b** (Figure 9). Upon addition of aliquots of trifluoroacetic acid the longest wavelength absorption maximum at 432 nm steadily decreases to a shoulder while the absorption band at 331 nm redshifts to 363 nm by the occurrence of isosbestic points. Upon plotting the spectral changes

the pK_a value of **10b+H$^+$** is determined to 2.78 (for experimental details, see Supp. Inf., Figure S10). Likewise, a pK_a value of 3.65 is determined for **7b+H$^+$**.

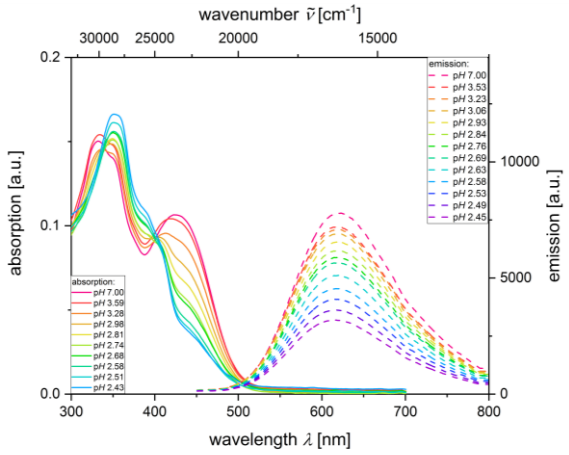


Figure 9. Absorption and emission spectra of **10b** in the presence of increasing amounts of trifluoroacetic acid (recorded in CH_2Cl_2, c(**10b**) = 9.46 · 10^{-5} M (absorption), c(**10b**) = 9.24 · 10^{-9} M (emission; the decrease of the fluorescence signal at 618 nm (λ_{exc} = 432 nm) was monitored); T = 293 K).

In addition, the pK_a value can also be determined by emission quenching using the Stern-Volmer model.[30] In this case, the Stern-Volmer constant upon protonation with trifluoroacetic acid corresponds to the pK_a values (for experimental details, see Supp. Inf., chpts. 5.2.3 and 5.2.4). The corresponding pK_a values of 2.62 (**10b+H$^+$**) and 3.90 (**7b+H$^+$**) are in good agreement with the values determined by absorption measurements.

Calculated electronic structure. For assigning the nature of the longest wavelength absorption bands of these novel cruciforms, TD-DFT calculations were performed for all psoralen chromophores **7** and **10** (for details, see Supp. Inf., chpt. 7). The geometry of the electronic ground state structures was optimized by Gaussian 09,[31] with the PBE1PBE[32] functional, taking into account significant contributions of charge transfer character,[33] and the Pople 6-311G(d,p)[34] basis set. For comparison with the experimental data, the polarizable continuum model (PCM) with dichloromethane as solvent was chosen.[35] For comparing the general tendency, the methoxy (**7a** and **10a**) and dimethylamino (**7b** and **10b**) donor systems bearing a cyano substituent as an acceptor are briefly discussed. Starting from the geometry-optimized structures the lowest energy Franck-Condon singlet configurations of cruciforms **7a-b** and **10a-b** were computed on the level of TD-DFT theory using the Pople 6-3-11G(d,p) basis set (Table 5).[36] As the experimental spectra reveal broad shoulders (compounds **7**) and broad maxima (compounds **10**) for the longest wavelength absorption maxima, deviations to the calculated maxima of the lowest energy Franck-Condon singlet configurations to longer wavelengths are often found. Nevertheless, the significant oscillatory strengths indicate that they represent dominant, allowed transitions. In all cases, the longest wavelength absorption maxima can be interpreted as HOMO-LUMO transitions.

As can be seen from the Kohn-Sham frontier molecular orbitals the coefficient densities of the HOMOs of the methoxy-substituted cruciforms **7a** and **10a** are located on the *p*-methoxy-*p*-cyano donor-acceptor axes and the benzofuran moiety of the psoralen core (Figure 10). The electronic structure of the dimethylamino-substituted chromophores **7b** and **10b** are exclusively located on the *p*-dimethylamino-*p*-cyano donor-acceptor axes without any contribution of the benzofuran part. Therefore, the HOMO energy differences roughly amount to 0.5 to 0.6 eV in the corresponding consanguineous pair. In contrast, the LUMO structures reveal that coefficient density is distributed over *p*-cyanophenyl(ethynyl) acceptor part and the complete psoralen, α-pyrone and benzofuran. The remote donor substituent affects neither the electronic structure nor the LUMO energies, which only deviate by 0.06 eV within the consanguineous pairs.

The electronic structure of the HOMO-LUMO contributed longest wavelength absorption band clearly reveals a charge transfer character from the remote *p*-(donor)phenyl moiety to the T-shaped *p*-(acceptor)phenyl-substituted psoralen, i.e. a deviation from the main *p*-(donor)phenyl(ethynyl)-*p*-(acceptor)phenyl axis to a more diffuse transfer in the psoralen-acceptor part. The charge transfer character is in good agreement with the experimental findings of emission solvatochromicity of these novel psoralen cruciforms.

Table 5. Selected photophysical properties of alkynyl expanded 5-acceptor-8-donor psoralens **10**. TD-DFT calculations (PBE1PBE/6-311G(d,p) of the UV/Vis absorption maxima of **7a-b**, **10a-b** using PCM with dichloromethane as solvent.

compound	$\lambda_{max,abs}$ [nm][a] (ε [M^{-1}cm^{-1}])	$\lambda_{max,calcd}$ [nm]	dominant contributions	oscillator strength
7a	359 (6300sh)	371	HOMO→LUMO (96%)	0.3226
	313 (21000)	322	HOMO-1→LUMO (44%), HOMO→LUMO+1 (45%)	0.2018
		314	HOMO-1→LUMO (48%)	0.1254
7b	388 (7300sh)	444	HOMO→LUMO (97%)	0.2613
	345 (14300sh)	368	HOMO→LUMO+1 (94%)	0.1252
		334	HOMO-1→LUMO (93%)	0.1029
	308 (25300)	312	HOMO→LUMO+2 (83%)	0.3384
10a	393 (22300)	460	HOMO→LUMO (98%)	1.4820
	365 (29200)	361	HOMO-1→LUMO (58%)	0.1704
		347	HOMO-2→LUMO (41%)	0.4030
10b	432 (27200)	530	HOMO→LUMO (99%)	1.2437
	331 (36000)	380	HOMO-1→LUMO (48%)	0.7760
		347	HOMO-2→LUMO (76%)	0.3515
		335	HOMO→LUMO+2 (79%)	0.2726

[a] Recorded in CH_2Cl_2, c(**7**), c(**10**) = 10^{-5} M at T = 293 K.

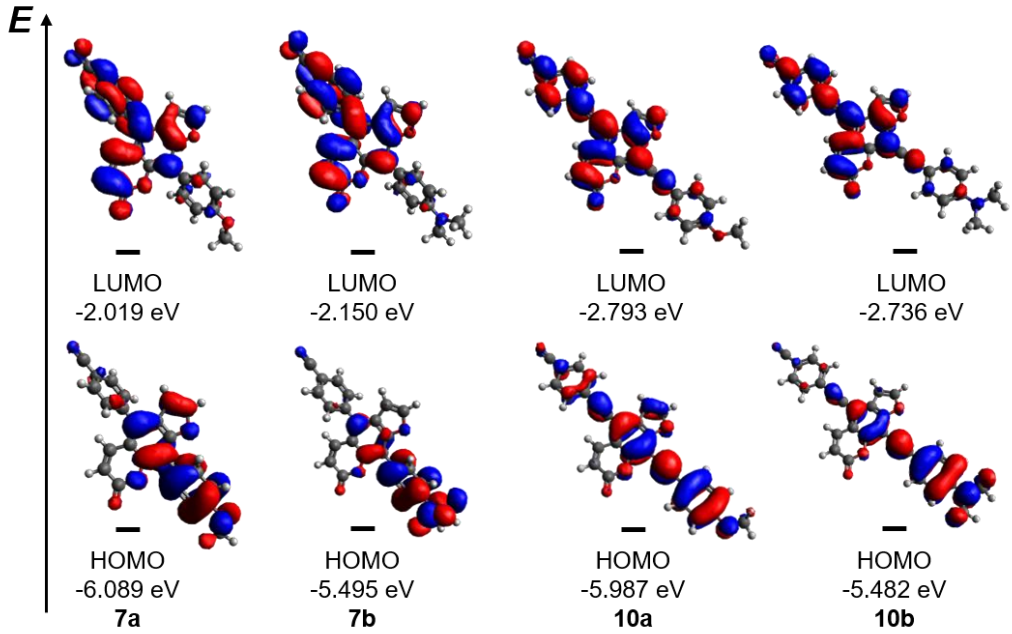


Figure 10. Selected Kohn-Sham frontier molecule orbitals (FMOs) of psoralens **7a-b** and **10a-b** (with PBE1PBE/6-311G(d,p) and PCM with dichloromethane as solvent).

Conclusion

In summary, two site-selective and efficient one-pot syntheses combining Suzuki-Suzuki and Sonogashira-Sonogashira sequentially Pd-catalyzed processes have been disclosed employing 5-bromo-8-triflatopsoralen as a versatile substrate. By implementing donor- and acceptor-substituted coupling partners as substrates novel orthogonally oriented cruciforms were formed, with the newly installed donor-acceptor axis and psoralen, a donor-acceptor composite by its own virtue. The title compounds reveal interesting tunable photophysical properties, such as bright emission colors in a range from sky-blue to deep orange, large Stokes shifts and partially high fluorescence quantum yields of up to 38%. Particularly promising are also aggregation induced emission of a solution nonemissive derivative, solvatochromism and acidochromism of several cruciforms. The experimentally determined change of dipole moments and pK_a values additionally indicate that these novel chromophores also have a potential as molecular sensors. Finally, accompanying TD-DFT calculations assign and rationalize the electronic structure of the longest wavelength absorption bands. This novel type of psoralen derivatives tunable in their electronic properties can as well be considered for PUVA therapy, since they absorb efficiently in the range of visible light.[14] As for other cruciforms sensory applications and responsive materials[3a] lie at hand. Further studies directed to an extension of the synthetic concept to other orthogonally attached chromophore branches, their electronic properties and applications are currently underway.

Experimental Section

General Considerations. Reactions were carried out in nitrogen atmosphere by in heat-gun dried Schlenk glassware. Oil baths were used as heating source for all thermal reactions. Dry solvents were obtained from a solvent drying system. Commercially available reagents, catalysts and ligands were purchased and employed without further purification. 5-Bromo-8-methoxy-psoralen (**2**)[14] and terminal alkynes **8**[37] and **9**[38] were synthesized according to literature. The purification of the crude products was carried out by column chromatography with silica gel 60 (particle size 0.04-0.063 mm) from Macherey and Nagel. A chromatograph apparatus used for purification by adsorption of the crude products on Celite®. The reaction progress was observed qualitatively using TLC silica gel 60 F254 aluminum sheets. The spots were detected with UV light at 254 and 365 nm and with iodine vapor. Chemical shifts δ in the ^{1}H and ^{13}C{^{1}H} NMR spectra are reported in ppm relative to the signal of the remaining proton resonances of the deuterated solvent. The assignments of C_{quat}, CH, CH_2, and CH_3 signals were made by using DEPT spectra. Melting points (uncorrected values) were measured using a Büchi Melting Point B-535 apparatus.

*5-Bromo-8-triflatopsoralen (**3**).* In a two-necked 100 mL round-bottom flask with magnetic stir bar 5-bromo-8-methoxypsoralen[14] (**2**) (1.59 g, 5.39 mmol) was solved in dichloromethane (19 mL) and cooled down to 0 °C. Boron tribromide (1.00 M in dichloromethane, 21.6 mL, 21.6 mmol) was added to the reaction solution and stirred at 0 °C for 3 h. Then, ice water was added and the precipitated intermediate product was dried in vacuo. The resulting solid (1.51 g, 5.37 mmol) was dissolved in dichloromethane (25 mL) and pyridine (1.56 mL, 19.28 mmol) and cooled to 0 °C. After addition of trifluoromethanesulfonic anhydride (1.79 mL, 10.62 mmol) the solution was stirred for at 0 °C for 2 h. The reaction was then terminated by adding ice water (20 mL) and extracted with dichloromethane (3 × 20 mL). The organic phases were combined, dried (anhydrous sodium sulfate) and absorbed on Celite® before purification by column chromatography (petroleum ether/ethyl acetate 1:1). Yield: 1.91 g (4.62 mmol, 86%), colorless crystals, R_f = 0.47 (petroleum ether/ethyl acetate, 3:1), Mp 135 °C. ^{1}H NMR: (300 MHz, $CDCl_3$) δ = 8.13 (d, J = 10.0 Hz, 1 H), 7.83 (d, J = 2.3 Hz, 1 H), 6.97 (d, J = 2.2 Hz, 1 H), 6.51 (d, J = 10.0 Hz, 1 H). ^{13}C{^{1}H} NMR: (75 MHz, $CDCl_3$) δ = 157.6 (C_{quat}), 148.3 (CH), 146.5 (C_{quat}), 144.4 (C_{quat}), 141.9 (CH), 128.3 (C_{quat}), 120.6 (C_{quat}), 118.6 (C_{quat}, q, $^1J_{CF}$ = 320.8 Hz), 116.6 (CH), 115.9 (C_{quat}), 113.4 (C_{quat}), 107.9 (CH). MS (EI) (*m*/*z* (%)): 412 ([$C_{12}H_4{}^{79}BrF_3O_6S$]$^+$, 20), 279 ([$C_{11}H_4{}^{79}BrO_4$]$^+$, 100). IR: $\tilde{\nu}$ [cm^{-1}] 3170 (w), 3115 (w), 1734 (vs), 1636 (w), 1581 (m), 1460 (m), 1422 (s), 1391 (m), 1263 (w), 1321 (m), 1298 (m), 1238 (m), 1209 (vs), 1186 (m), 1132 (s), 1067 (s), 1026 (m), 989 (m), 887 (s), 797 (vs), 756 (s), 727 (w), 689 (w), 652 (w), 631 (m). Anal. calcd. for $C_{12}H_4BrF_3O_6S$ [411.89]: C 34.89, H 0.98, S 7.76. Found: C 34.87, H 0.81, S 7.77.

General procedure GP1 of the selective consecutive Suzuki-Suzuki three-component synthesis of 5-donor substituted 8-acceptor psoralens 7. 5-Bromo-8-triflatopsoralen (3, 1.00 equivs) was placed in dry THF (4.50 mL/mmol) under nitrogen atmosphere in a screw-cap Schlenk tube with magnetic stir bar (for experimental details, see Table 1). The *p*-(acceptor)phenyl boronic acid 4 (1.10 equivs), bis(dibenzylidene-acetone)palladium(0) (0.20 equivs), SPhos (0.24 equivs) and potassium fluoride (3.00 equivs) were added and the solution was then degassed with nitrogen for 5 min. The reaction mixture was stirred at room temp for 24 h. Subsequently, the *p*-(donor)phenyl boronic acid 6 (1.10 equivs), potassium phosphate (4.00 equivs) and water (1 mL) were added and stirred at 80 °C for further 24 h. After cooling, water was added (10 mL) and the aqueous phase extracted with dichloromethane (3 x 30 mL). The organic layers were combined and dried (anhydrous sodium sulfate). The mixture was adsorbed on Celite® and purified by column chromatography (petroleum ether/ethyl acetate or petroleum ether/acetone). *4-(9-(4-Methoxyphenyl)-7-oxo-7H-furo[3,2-g]chromen-4-yl)benzonitrile (7a).* According to GP1 and after purification by flash chromatography on silica gel (petroleum ether/acetone 3:1) and after crystallization from ethanol/dichloromethane (4:1) compound 7a (395 mg, 82%) was obtained as a yellowish solid, R_f = 0.25 (petroleum ether/ethyl acetate, 3:1). Mp 289 °C. ^{1}H NMR: (300 MHz, $CDCl_3$) δ = 7.91 – 7.86 (m, 2 H), 7.77 – 7.69 (m, 4 H), 7.62 – 7.57 (m, 2 H), 7.14 – 7.07 (m, 2 H), 6.63 (d, *J* = 2.3 Hz, 1 H), 6.36 (d, *J* = 9.9 Hz, 1 H), 3.90 (s, 3 H).^{13}C{^{1}H} NMR: (75 MHz, $CDCl_3$) δ = 160.4 (C_{quat}), 160.0 (C_{quat}), 153.8 (C_{quat}), 149.1 (C_{quat}), 147.6 (CH), 141.6 (CH), 140.8 (C_{quat}), 132.8 (CH), 132.0 (CH), 131.2 (CH), 129.5 (C_{quat}), 124.5 (C_{quat}), 121.9 (C_{quat}), 118.4 (C_{quat}), 115.1 (CH), 114.8 (C_{quat}), 114.2 (CH), 113.7 (C_{quat}), 112.7 (C_{quat}), 105.9 (CH), 55.5 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 2901 (w), 2228 (w), 1724 (s), 1605 (w), 1582 (m), 1516 (m), 1458 (w), 1429 (w), 1408 (w), 1356 (w), 1290 (m), 1254 (s), 1179 (m), 1136 (s), 1109 (m), 1028 (s), 926 (w), 901 (w), 868 (m), 826 (s), 802 (m), 754 (m), 719 (w). ESI-MS (*m*/*z*): 394.5 ([M+H]$^+$, 100%). HR-MS (ESI) (*m*/*z*) calcd. for ($C_{25}H_{15}NO_4$+H)$^+$: 394.1074; Found: 394.1073. HPLC (acetonitrile/acetone): 99% (RT = 4.7 min).

*4-(9-(4-(Dimethylamino)phenyl)-7-oxo-7H-furo[3,2-g]chromen-4-yl)benzonitrile (**7b**).* According to GP1 and after purification by flash chromatography on silica gel (petroleum ether/acetone 3:1) and after crystallization from dichloromethane compound **7b** (98.4 mg, 40%) was obtained as an orange solid, R_f = 0.25 (petroleum ether/ethyl acetate, 3:1). Mp 295 °C (dec). ^{1}H NMR: (500 MHz, $CDCl_3$) δ = 7.93 – 7.82 (m, 2 H), 7.78 – 7.68 (m, 4 H), 7.62 – 7.55 (m, 2 H), 7.03 (s, 2 H), 6.61 (d, *J* = 2.2 Hz, 1 H), 6.35 (d, *J* = 9.8 Hz, 1 H), 3.08 (s, 6 H). ^{13}C{^{1}H} NMR: (126 MHz $CDCl_3$) δ = 160.6 (C_{quat}), 154.1 (C_{quat}), 149.4 (C_{quat}), 147.8 (CH), 141.8 (CH), 141.2 (C_{quat}), 133.0 (CH), 132.0 (CH), 132.0 (C_{quat}), 131.5 (CH), 129.2 (C_{quat}), 124.7 (C_{quat}), 118.6 (C_{quat}), 115.3 (CH), 114.0 (C_{quat}), 112.9 (C_{quat}), 112.9 (C_{quat}), 106.1 (CH) 44.0 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 2226 (w), 1720 (vs), 1603 (m), 1578 (m), 1526 (m), 1449 (w), 1410 (m), 1360 (m), 1302 (m), 1229 (w), 1202 (w), 1144 (vs), 1111 (m), 1092 (w), 1065 (w), 1040 (s), 1020 (w), 991 (m), 949 (w), 924 (w), 903 (w), 868 (m), 833 (m), 820 (s), 793 (m), 770 (m), 750 (w), 725 (s). ESI-MS (*m*/*z*): 407.5 ([M]$^+$, 100%). HR-MS (ESI) (*m*/*z*) calcd. for ($C_{26}H_{18}N_2O_3$+H)$^+$: 407.1390; Found: 407.1384. HPLC (acetonitrile): 98% (RT = 6.9 min).

*9-(4-Methoxyphenyl)-4-(4-nitrophenyl)-7H-furo[3,2-g]chromen-7-one (**7c**).* According to GP1 and after purification by flash chromatography on silica gel (petroleum ether/acetone 3:1) and after crystallization from ethanol (3:1) compound **7c** (120 mg, 80%) was obtained as a yellow solid, R_f = 0.25 (petroleum ether/ethyl acetate, 3:1). Mp 304 °C dec. ^{1}H NMR: (600 MHz, $CDCl_3$) δ = 8.52 – 8.36 (m, 2 H), 7.77 – 7.72 (m, 4 H), 7.67 (d, *J* = 8.6 Hz, 2 H), 7.13 – 7.08 (m, 2 H), 6.64 (d, *J* = 2.2 Hz, 1 H), 6.38 (d, *J* = 9.9 Hz, 1 H), 3.91 (s, 3 H). ^{13}C{^{1}H} NMR: (151 MHz, $CDCl_3$) δ = 160.2 (C_{quat}), 159.9 (C_{quat}), 153.7 (C_{quat}), 149.0 (C_{quat}), 147.9 (C_{quat}), 147.6 (CH), 142.6 (C_{quat}), 141.4 (CH), 131.8 (CH), 131.3 (CH), 128.9 (C_{quat}), 124.4 (C_{quat}), 124.1 (CH), 121.7 (C_{quat}), 115.1 (CH), 114.8 (C_{quat}), 114.1 (CH), 113.7 (C_{quat}), 105.7 (CH), 55.4 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1724 (s), 1581 (m), 1541 (w), 1510 (vs), 1456 (w), 1410 (w), 1342 (s), 1305 (w), 1251 (m), 1219 (w), 1184 (m), 1146 (s), 1130 (s), 1028 (s), 1011 (w), 924 (w), 903 (w), 870 (w), 852 (m), 831 (vs), 785 (m), 760 (s), 750 (s), 721 (m), 700 (m). MS (EI) (*m*/*z* (%)): 414 (25), 413 ([M]$^+$, 100). HR-MS (ESI) (*m*/*z*) calcd. for ($C_{24}H_{16}NO_6$+H)$^+$: 414.0972; Found: 414.0976. HPLC (acetonitrile): 99% (RT = 7.3 min).

*9-(4-(Dimethylamino)phenyl)-4-(4-nitrophenyl)-7H-furo[3,2-g]chromen-7-one (**7d**).* According to GP1 and after purification by flash chromatography on silica gel (petroleum ether/acetone 1:1) and after crystallization from acetone compound **7d** (82.1 mg, 32%) was obtained as a red solid, R_f = 0.15 (petroleum ether/ethyl acetate, 3:1). Mp 225 °C (dec). ^{1}H NMR: (500 MHz, CD_2Cl_2) δ = 8.48 – 8.37 (m, 2 H), 7.80 – 7.72 (m, 2 H), 7.73 – 7.63 (m, 4 H), 7.01 (s, 2 H), 6.67 (d, *J* = 2.3 Hz, 1 H), 6.32 (d, *J* = 9.9 Hz, 1 H), 3.08 (s, 6 H). ^{13}C{^{1}H} NMR: (126 MHz, CD_2Cl_2) δ = 160.7 (C_{quat}), 154.5 (C_{quat}), 149.8 (C_{quat}), 148.6 (C_{quat}), 148.1 (CH), 143.4 (C_{quat}), 142.1 (CH), 132.1 (CH), 132.1 (CH), 129.3 (C_{quat}), 125.0 (C_{quat}), 124.6 (CH), 117.8 (C_{quat}), 113.4 (C_{quat}), 115.4 (CH), 115.7 (C_{quat}), 113.4 (C_{quat}), 106.4 (CH), 41.3 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1719 (s), 1609 (m), 1570 (m), 1508 (s), 1449 (w), 1408 (w), 1368 (w), 1340 (m), 1300 (m), 1233 (w), 1200 (m), 1144 (s), 1107 (m), 1067 (w), 1040 (s), 1015 (w), 989 (m), 951 (w), 923 (w), 851 (w), 829 (m), 818 (s), 791 (w), 768 (s), 748 (w), 700 (w), 615 (w). MS (EI) (*m*/*z* (%)): 427 (35), 426 ([M]$^+$,100). HR-MS (ESI) (*m*/*z*) calcd. for ($C_{25}H_{18}N_2O_5$+H)$^+$: 427.1288; Found: 427.1289. HPLC (acetonitrile): 98% (RT = 7.4 min).

*4-(9-(4-Methoxyphenyl)-7-oxo-7H-furo[3,2-g]chromen-4-yl)benzaldehyde (**7e**).* According to GP1 and after purification by flash chromatography on silica gel (petroleum ether/acetone 3:1) and after crystallization from acetone compound **7e** (137 mg, 76%) was obtained as a yellow solid, R_f = 0.38 (petroleum ether/ethyl acetate, 3:1). Mp 257 °C (dec). ^{1}H NMR: (600 MHz, $CDCl_3$) δ = 10.16 (s, 1 H), 8.15 – 8.02 (m, 2 H), 7.80 (d, *J* = 9.9 Hz, 1 H), 7.75 – 7.72 (m, 2 H), 7.70 (d, *J* = 2.3 Hz, 1 H), 7.67 – 7.63 (m, 2 H), 7.15 – 7.05 (m, 2 H), 6.66 (d, *J* = 2.3 Hz, 1 H), 6.35 (d, *J* = 9.9 Hz, 1 H), 3.90 (s, 3 H). ^{13}C{^{1}H} NMR: (151 MHz, $CDCl_3$) δ = 191.6 (CH), 160.4 (C_{quat}), 159.8 (C_{quat}), 153.7 (C_{quat}), 149.0 (C_{quat}), 147.3 (CH), 142.0 (C_{quat}), 141.9 (CH), 136.1 (C_{quat}), 131.8 (CH), 131.0 (CH), 130.2 (C_{quat}), 130.1 (CH), 124.4 (C_{quat}), 121.9 (C_{quat}), 114.7 (CH), 114.4 (C_{quat}), 114.1 (CH), 113.7 (C_{quat}), 106.0 (CH), 55.4 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1719 (vs), 1692 (vs), 1603 (m), 1582 (s), 1541 (w), 1514 (m), 1460 (w), 1410 (w), 1358 (w), 1304 (m), 1250 (m), 1204 (w), 1173 (m), 1144 (vs), 1113 (s), 1096 (w), 1031 (s), 993 (m), 925 (w), 903 (m), 867 (m), 825 (s), 794 (m), 763 (s), 731 (w), 675 (w), 615 (m). ESI-MS (*m*/*z*): 397.3 ([M+H]$^+$, 100%). HR-MS (ESI) (*m*/*z*) calcd. for ($C_{25}H_{16}O_5$+H)$^+$: 397.1071; Found: 397.1069. HPLC (acetonitrile): 98% (RT = 7.0 min).

*4-(9-(4-(Dimethylamino)phenyl)-7-oxo-7H-furo[3,2-g]chromen-4-yl)benzaldehyde (**7f**).* According to GP1 and after purification by flash chromatography on silica gel (petroleum ether/acetone 2:1) and after crystallization from dichloromethane compound **7f** (86.7 mg, 32%) was obtained as an orange solid, R_f = 0.38 (petroleum ether/ethyl acetate, 3:1). Mp 269 °C. ^{1}H NMR: (500 MHz, $CDCl_3$) δ = 10.44 (s, 1 H), 8.39 – 8.35 (m, 2 H), 8.07 (d, *J* = 9.8 Hz, 1 H), 8.04 – 8.00 (m, 2 H), 7.99 (d, *J* = 2.3 Hz, 1 H), 7.95 – 7.92 (m, 2 H), 7.25 (s, 2 H), 6.93 (d, *J* = 2.3 Hz, 1 H), 6.63 (d,
J = 9.8 Hz, 1 H), 3.35 (s, 6 H). ^{13}C{^{1}H} NMR: (126 MHz, $CDCl_3$) δ = 191.8 (CH), 160.8 (C_{quat}), 154.2 (C_{quat}), 149.4 (C_{quat}), 147.5 (CH), 142.6 (C_{quat}), 142.2 (CH), 136.5 (C_{quat}), 131.9 (CH), 131.4

(CH), 130.4 (CH), 130.4 (C_{quat}), 130.4 (C_{quat}), 124.7 (C_{quat}), 124.7 (C_{quat}), 115.1 (CH), 114.1 (C_{quat}), 106.3 (CH), 77.6 (C_{quat}), 53.7 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1717 (m), 1690 (m), 1601 (m), 1577 (m), 1558 (s), 1526 (w), 1452 (w), 1410 (w), 1368 (w), 1304 (w), 1202 (w), 1179 (w), 1038 (m), 991 (m), 951 (w), 924 (w), 903 (w), 868 (w), 839 (m), 820 (s), 795 (w), 767 (m), 675 (w). MS (EI) (*m*/*z* (%)): 410 (30), 409 ($[M]^+$, 100). HR-MS (ESI) (*m*/*z*) calcd. for $(C_{26}H_{19}NO_4+H)^+$: 410.1387; Found: 410.1386 (100%). HPLC (acetonitrile): 97% (RT = 7.0 min).

*9-(4-Methoxyphenyl)-4-(4-(trifluoromethyl)phenyl)-7H-furo[3,2-g]chromen-7-one (**7g**).* According to GP1 and after purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) and after crystallization from ethanol/dichloromethane (4:1) compound **7g** (143 mg, 68%) was obtained as a colorless solid, R_f = 0.68 (petroleum ether/ethyl acetate, 2:1). Mp 280 °C (dec). ^{1}H NMR: (300 MHz, $CDCl_3$) δ = 7.87 – 7.68 (m, 6 H), 7.62 – 7.56 (m, 2 H), 7.14 – 7.07 (m, 2 H), 6.65 (d, J = 2.3 Hz, 1 H), 6.35 (d, J = 9.9 Hz, 1 H), 3.91 (s, 3 H). $^{13}C\{^1H\}$ NMR: (75 MHz, $CDCl_3$) δ = 160.5 (C_{quat}), 159.8 (C_{quat}), 153.7 (C_{quat}), 148.9 (C_{quat}), 147.3 (CH), 141.8 (CH), 139.5 (C_{quat}), 131.8 (CH), 130.7 (CH), 130.0 (C_{quat}), 125.9 (q, $^3J_{CF}$ = 3.95 Hz, CH), 124.5 (C_{quat}), 121.9 (C_{quat}), 114.7 (CH), 114.3 (C_{quat}), 114.1 (CH), 113.8 (C_{quat}), 106.0 (CH), 77.2 (C_{quat}), 55.4 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1740 (s), 1724 (s), 1589 (m), 1545 (w), 1512 (m), 1460 (w), 1431 (w), 1406 (w), 1323 (s), 1287 (w), 1250 (m), 1167 (m), 1144 (m), 1109 (s), 1065 (s), 1018 (s), 993 (m), 926 (w), 903(w), 870 (m), 833 (s), 810 (w), 768 (m), 754 (m).MS (EI) (*m*/*z* (%)): 438 (27), 437 ($[M+H]^+$, 100). HR-MS (ESI) (*m*/*z*) calcd. for $(C_{25}H_{15}F_3O_4+H)^+$: 437.0995; Found: 437.0995. HPLC (acetonitrile): 98% (RT = 7.8 min).

*9-(4-(Dimethylamino)phenyl)-4-(4-(trifluoromethyl)phenyl)-7H-furo[3,2-g] chromen-7-one (**7h**).* According to GP1 and after purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 2:1) and after crystallization from ethanol/dichloromethane (4:1) compound **7h** (130 mg, 44%) was obtained as a yellow solid, R_f = 0.38 (petroleum ether/ethyl acetate, 3:1). Mp 296 °C (dec.). ^{1}H NMR: (300 MHz, $CDCl_3$) δ = 7.88 – 7.66 (m, 6 H), 7.59 (m, 2 H), 6.97 (s, 2 H), 6.64 (d, *J* = 2.3 Hz, 1 H), 6.34 (d, *J* = 9.9 Hz, 1 H), 3.07 (s, 6 H). $^{13}C\{^1H\}$ NMR: (75 MHz, $CDCl_3$) δ = 160.6 (C_{quat}), 158.8 (C_{quat}), 153.7 (C_{quat}), 153.3 (C_{quat}), 148.9 (C_{quat}), 147.9 (C_{quat}), 147.1 (CH), 141.9 (CH), 139.7 (C_{quat}), 137.8 (C_{quat}), 131.5 (CH), 130.7 (CH), 125.8 (q, $^3J_{CF}$ = 3.90 Hz CH), 124.4 (C_{quat}), 114.6 (CH), 113.8 (C_{quat}), 105.9 (CH), 77.2 (C_{quat}), 40.8 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1735 (s), 1608 (m), 1585 (m), 1525 (m), 1449 (s), 1408 (m), 1357 (m), 1321 (s), 1227 (w), 1194 (w), 1163 (s), 1142 (s), 1123 (s), 1109 (s), 1065 (s), 1036 (m), 1016 (s), 993 (m), 949 (w), 924 (w), 903 (w), 867 (w), 837 (m), 822 (s), 795 (w), 756 (s), 721 (w), 619 (m). MS (EI) (*m*/*z* (%)): 451 (28), 450 ($[M+H]^+$, 100). HR-MS (ESI) (*m*/*z*) calcd. for $(C_{26}H_{18}F_3NO_3+H)^+$: 450.1312; Found: 450.1305. HPLC (acetonitrile): 98% (RT = 8.0 min).

General procedure GP2 of the one-pot synthesis of alkynyl expanded 5-donor substituted 8-acceptor psoralens 10. 5-Bromo-8-triflatopsoralen (**3**, 1.00 equivs) was placed in dry 1,4-dioxane (4.00 mL/mmol) under nitrogen atmosphere in a screw-cap Schlenk tube with a magnetic stir bar (for experimental details, see Table 2). *p*-(Acceptor)arylalkyne **8** (1.10 equivs), tris(dibenzylideneacetone)dipalladium(0) (0.01 equivs), cataCXium ABn® (0.04 equivs), copper iodide (0.08 equivs), and triethylamine (3.00 equivs) were added and the solution was then degassed with nitrogen for 5 min. The reaction mixture was stirred at 75 °C for 48 h. Subsequently, *p*-(donor)arylalkyne **9** (1.10 equivs), tetrakis(triphenylphosphane)palladium(0) (0.02 equivs), and dimethyl sulfoxide (4.00 mL/mmol) were added and stirred at 90 °C for further 24 h. After cooling to room temp, water was added (10 mL) and the aqueous phase extracted with dichloromethane (3 x 30 mL). The organic layers were combined and dried (anhydrous sodium sulfate). The mixture was adsorbed on Celite® and purified by column chromatography (petroleum ether/ethyl acetate).

*4-((9-((4-Methoxyphenyl)ethynyl)-7-oxo-7H-furo[3,2-g]chromen-4-yl)ethynyl) benzonitrile (**10a**).* According to GP2 and after purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) and after crystallization from ethanol compound **10a** (196 mg, 77%) was obtained as a yellow solid, R_f = 0.31 (petroleum ether/ethyl acetate, 3:1). Mp 254 °C (dec). ^{1}H NMR: (500 MHz, CD_2Cl_2) δ = 8.20 (d, J = 9.8 Hz, 1 H), 7.78 (d, J = 2.2 Hz, 1 H), 7.70 – 7.63 (m, 4 H), 7.58 – 7.51 (m, 2 H), 7.01 (d, J = 2.3 Hz, 1 H), 6.91 – 6.85 (m, 2 H), 6.41 (d, J = 9.7 Hz, 1 H), 3.78 (s, 3 H). $^{13}C\{^1H\}$ NMR: (126 MHz, CD_2Cl_2) δ = 161.5 (C_{quat}), 160.3 (C_{quat}), 156.1 (C_{quat}), 152.8 (C_{quat}), 148.6 (CH), 142.3 (CH), 134.3 (CH), 133.1 (CH), 133.0 (CH), 127.6 (C_{quat}), 127.5 (C_{quat}), 118.9 (C_{quat}), 117.5 (C_{quat}), 116.4 (CH), 115.0 (CH), 113.5 (C_{quat}), 112.5 (C_{quat}), 107.4 (CH), 102.9 (C_{quat}), 99.8 (C_{quat}), 99.0 (C_{quat}), 87.7 (C_{quat}), 77.3 (C_{quat}), 56.2 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 2961 (w), 2226 (w), 1747 (s), 1728 (s), 1601 (m), 1581 (m), 1508 (s), 1464 (m), 1375 (m), 1294 (m), 1250 (s), 1169 (m), 1140 (m), 1123 (m), 1090 (m), 1022 (s), 980 (m), 793 (s), 756 (m), 691 (w), 615 (w). MALDI (*m*/*z* (%)): 441.029 ($[M^+]$). HR-MS (ESI) *m*/*z* calcd. for $(C_{29}H_{15}NO_4+H)^+$: 442.1074 ; Found: 442.1067. HPLC (acetone): 98% (RT = 6.0 min).

*4-((9-((4-(Dimethylamino)phenyl)ethynyl)-7-oxo-7H-furo[3,2-g]chromen-4-yl) ethynyl)benzonitrile (**10b**).* According to GP2 and after purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) and after crystallization from dichloromethane compound **10b** (40.1 mg, 34%) was obtained as an orange solid, R_f = 0.27 (petroleum ether/ethyl acetate, 3:1). Mp 246 °C (dec). ^{1}H NMR: (500 MHz, DMSO-d_6) δ = 8.48 (d, *J* = 9.8 Hz, 1 H), 8.32 (d, *J* = 2.2 Hz, 1 H), 8.04 – 7.94 (m, 4 H), 7.45 (d, *J* = 8.8 Hz, 2 H), 7.40 (d, *J* = 2.2 Hz, 1 H), 6.80 – 6.74 (m, 2 H), 6.60 (d, *J* = 9.7 Hz, 1 H), 3.00 (s, 6 H). $^{13}C\{^1H\}$ NMR: (126 MHz, DMSO-d_6) δ = 159.6 (C_{quat}), 154.6 (C_{quat}), 151.5 (C_{quat}), 151.2 (C_{quat}), 149.5 (CH), 142.5 (CH), 133.1 (CH), 133.0 (CH), 132.9 (CH), 126.9 (C_{quat}), 126.7 (C_{quat}), 118.7 (C_{quat}), 117.0 (C_{quat}), 116.1 (CH), 112.3 (CH), 112.1 (C_{quat}), 111.0 (C_{quat}), 107.7 (C_{quat}), 107.2 (CH), 103.9 (C_{quat}), 99.8 (C_{quat}), 98.9 (C_{quat}), 98.7 (C_{quat}), 87.3 (C_{quat}), 76.7 (C_{quat}), 40.6 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 2195 (w), 1719 (s), 1599 (m), 1578 (s), 1522 (s), 1445 (w), 1364 (m), 1254 (w), 1225 (w), 1184 (w), 1140 (s), 1078 (w), 1030 (m), 989 (w), 941 (w), 835 (s), 816 (s), 787 (w), 762 (m).ESI-MS (*m*/*z* (%)): 440.3 (55%), 455.2 ($[M+H]^+$, 100%). HR-MS (ESI) *m*/*z* calcd. for $(C_{30}H_{18}N_2O_3+H)^+$: 455.1390; Found: 455.1383. HPLC (acetonitrile): 99% (RT = 8.3 min).

*9-((4-Methoxyphenyl)ethynyl)-4-((4-nitrophenyl)ethynyl)-7H-furo[3,2-g]chromen-7-one (**10c**).* According to GP2 and after purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) and after crystallization from acetone/ethanol (1:1) compound **10c** (40 mg, 42%) was obtained as a yellow solid, R_f = 0.63 (petroleum ether/ethyl acetate, 3:1). Mp 281 °C (dec). ^{1}H NMR: (300 MHz, $CDCl_3$) δ = 8.37 – 8.22 (m, 3 H), 7.87 – 7.73 (m, 3 H), 7.70 – 7.59 (m, 2 H), 7.06 (d, *J* = 2.3 Hz, 1 H), 6.96 – 6.88 (m, 2 H), 6.54 (d, *J* = 9.7 Hz, 1 H), 3.87 (s, 3 H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ = 192.1 (C_{quat}), 167.9 (C_{quat}), 165.1 (C_{quat}), 163.8 (C_{quat}), 160.5 (C_{quat}), 159.9 (C_{quat}), 147.8 (CH), 147.7 (C_{quat}), 133.8 (CH), 132.5 (CH), 132.0 (C_{quat}), 128.8 (C_{quat}), 126.9 (C_{quat}), 123.9 (CH), 116.7 (C_{quat}), 115.9 (CH), 114.1 (CH), 111.1 (C_{quat}), 107.8 (C_{quat}), 106.7 (CH), 88.1 (C_{quat}), 77.4 (CH), 37.7 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1728 (s), 1593 (w), 1578 (m), 1509 (s), 1441 (w), 1377 (w), 1341 (s), 1310 (w), 1292 (m), 1248 (s), 1175 (m), 1143 (s), 1130 (s), 1105 (s), 1022 (m), 986 (m), 885 (w), 854 (s), 835 (s), 812 (w), 756 (s), 746 (s), 723 (w), 687 (m), 662 (m). MALDI (*m*/*z* (%)): 461.256 ($[M]^+$, 100%). HR-MS (ESI *m*/*z* calcd.

for $(C_{28}H_{15}NO_6+H)^+$: 462.0972; Found: 462.0973. HPLC (acetonitrile): 98% (RT = 8.5 min).

*9-((4-(Dimethylamino)phenyl)ethynyl)-4-((4-nitrophenyl)-ethynyl)-7H-furo[3,2-g] chromen-7-one (**10d**)*. According to GP2 and after trituration with hot dichloromethane compound **10d** (59.2 mg, 60%) was obtained as a red solid, R_f = 0.50 (petroleum ether/ethyl acetate, 3:1). Mp 301 °C (dec). ^{1}H NMR: (600 MHz, DMF-d_7) δ = 8.61 (d, J = 9.7 Hz, 1 H), 8.41 – 8.37 (m, 2 H), 8.30 (d, J = 2.2 Hz, 1 H), 8.18 – 8.13 (m, 2 H), 7.57 – 7.52 (m, 2 H), 7.43 (d, J = 2.2 Hz, 1 H), 6.89 – 6.82 (m, 2 H), 6.64 (d, J = 9.7 Hz, 1 H), 3.07 (s, 6 H). ^{13}C{^{1}H} NMR: (151 MHz, DMF-d_7) δ = 159.3 (C_{quat}), 155.0 (C_{quat}), 151.9 (C_{quat}), 151.5 (C_{quat}), 149.1 (CH), 148.1 (C_{quat}), 142.1 (CH), 133.2 (CH), 133.0 (CH), 128.9 (C_{quat}), 127.0 (C_{quat}), 123.9 (CH), 117.2 (C_{quat}), 115.9 (CH), 112.2 (CH), 111.0 (C_{quat}), 108.4 (C_{quat}), 106.9 (CH), 104.1 (C_{quat}), 98.3 (C_{quat}), 87.9 (C_{quat}), 76.3 (C_{quat}), 39.4 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1717 (s), 1605 (m), 1578 (s), 1512 (s), 1443 (w), 1364 (s), 1339 (s), 1310 (w), 1287 (w), 1253 (w), 1224 (w), 1180 (w), 1138 (s), 1076 (w), 1028 (s), 984 (m), 941 (w), 853 (s), 831 (s), 814 (s), 758 (s), 750 (s), 725 (w), 687 (w). ESI-MS (*m*/*z* (%)): 475.4 ([M+H]$^+$, 100%). HR-MS (ESI) *m*/*z* calcd. for $(C_{29}H_{18}N_2O_5+H)^+$: 475.1288; Found: 475.1287. HPLC (acetonitrile/DMF): 98% (RT = 7.8 min).

*9-((4-Methoxyphenyl)ethynyl)-4-((4-(trifluoromethyl)phenyl)-ethynyl)-7H-furo[3,2-g]chromen-7-one (**10e**)*. According to GP2 and after purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 5:1) and after crystallization from ethanol compound **10e** (84.1 mg, 70%) was obtained as a yellow solid, R_f = 0.25 (petroleum ether/ethyl acetate, 3:1). Mp 213 °C. ^{1}H NMR: (300 MHz, $CDCl_3$) δ = 8.28 (d, J = 9.7 Hz, 1 H), 7.82 (d, J = 2.3 Hz, 1 H), 7.79 – 7.51 (m, 7 H), 7.04 (d, J = 2.2 Hz, 1 H), 6.92 (d, J = 8.9 Hz, 1 H), 6.51 (d, J = 9.8 Hz, 1 H), 3.86 (s, 3 H). ^{13}C{^{1}H} NMR: (75 MHz, $CDCl_3$) δ = 160.4 (C_{quat}), 160.0 (C_{quat}), 155.3 (C_{quat}), 152.0 (C_{quat}), 147.5 (CH), 141.7 (CH), 133.7 (CH), 132.0 (CH), 131.2 (C_{quat}), 130.8 (C_{quat}), 126.7 (C_{quat}), 125.6 (C_{quat}), 125.6 (q, $^3J_{CF}$ = 3.91 Hz, CH), 116.6 (C_{quat}), 115.6 (CH), 114.5 (C_{quat}), 114.1 (CH), 111.8 (C_{quat}), 106.7 (CH), 102.4 (C_{quat}), 99.2 (C_{quat}), 98.4 (C_{quat}), 85.4 (C_{quat}), 77.3 (C_{quat}), 55.4 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1724 (s), 1604 (w), 1582 (m), 1510 (m), 1406 (w), 1375 (w), 1321 (s), 1295 (m), 1250 (m), 1190 (m), 1144 (s), 1123 (s), 1105 (s), 1080 (w), 1063 (s), 1030 (s), 986 (m), 883 (w), 856 (s), 787 (w), 756 (s), 745 (m), 721 (w), 640 (w). ESI-MS (*m*/*z*): 986.1 ([M_2+H_2O]$^+$). HR-MS (ESI) *m*/*z* calcd. for $(C_{29}H_{15}F_3O_4+H)^+$: 485.0995; Found: 485.0996. HPLC (acetonitrile): 99% (RT = 8.7 min).

*9-((4-(Dimethylamino)phenyl)ethynyl)-4-((4-(trifluoromethyl)-phenyl)ethynyl)-7H-furo[3,2-g]chromen-7-one (**10f**)*. According to GP2 and after purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 5:1) and after crystallization from dichloromethane/ethanol compound **10f** (64 mg, 52%) was obtained as a yellow solid, R_f = 0.33 (petroleum ether/ethyl acetate, 5:1). Mp 202 °C (dec). ^{1}H NMR: (300 MHz, $CDCl_3$) δ = 8.29 (d, J = 9.8 Hz, 1 H), 7.82 (d, J = 2.2 Hz, 1 H), 7.79 – 7.56 (m, 6 H), 7.04 (d, J = 2.3 Hz, 1 H), 6.78 (d, J = 8.3 Hz, 2 H), 6.52 (d, J = 9.7 Hz, 1 H), 3.05 (s, 6 H). ^{13}C{^{1}H} NMR: (75 MHz, $CDCl_3$) δ = 160.2 (C_{quat}), 155.1 (C_{quat}), 151.7 (C_{quat}), 150.7 (C_{quat}), 147.4 (CH), 146.3 (C_{quat}), 141.8 (CH), 133.4 (CH), 132.0 (CH), 128.2 (CH), 127.3 (C_{quat}), 126.7 (C_{quat}), 125.6 (q, $^3J_{CF}$ = 3.85 Hz, CH), 116.6 (C_{quat}), 115.6 (CH), 111.6 (CH), 110.0 (C_{quat}), 108.9 (C_{quat}), 106.7 (CH), 104.4 (C_{quat}), 100.0 (C_{quat}), 98.1 (C_{quat}), 85.6 (C_{quat}), 77.2 (C_{quat}), 40.2 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1728 (s), 1607 (s), 1582 (m), 1526 (s), 1447 (w), 1361 (s), 1319 (s), 1227 (w), 1180 (w), 1163 (m), 1140 (s), 1124 (s), 1105 (m), 1020 (m), 1063 (m), 1030 (m), 989 (w), 943 (w), 883 (w), 841 (m), 916 (s), 760 (m), 743 (w), 723 (w). ESI-MS (*m*/*z* (%)): 498.5 ([M+H]$^+$, 100%). HR-MS (ESI) *m*/*z* calcd. for $(C_{30}H_{18}F_3NO_3+H)^+$: 498.1312; Found: 498.1313. HPLC (acetonitrile): 99% (RT = 8.7 min).

*9-((4-Methoxyphenyl)ethynyl)-4-(pyridin-4-ylethynyl)-7H-furo[3,2-g]chromen-7-one (**10g**)*. According to GP2 and after purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:2) and after crystallization from ethanol compound **10g** (45 mg, 43%) was obtained as a yellowish solid, R_f = 0.63 (petroleum ether/ethyl acetate, 1:2). Mp 267 °C (dec). ^{1}H NMR: (300 MHz, CD_2Cl_2) δ = 8.68 (d, J = 5.5 Hz, 2 H), 8.30 (d, J = 9.7 Hz, 1 H), 7.88 (d, J = 2.3 Hz, 1 H), 7.66 – 7.60 (m, 2 H), 7.57 – 7.48 (m, 2 H), 7.10 (d, J = 2.3 Hz, 1 H), 6.98 – 6.94 (m, 2 H), 6.51 (d, J = 9.7 Hz, 1 H), 3.87 (s, 3 H). ^{13}C{^{1}H} NMR: (75 MHz, CD_2Cl_2) δ = 161.0 (C_{quat}), 160.0 (C_{quat}), 155.7 (C_{quat}), 152.4 (C_{quat}), 150.3 (CH), 148.3 (CH), 142.0 (CH), 133.9 (CH), 130.6 (C_{quat}), 127.8 (C_{quat}), 125.8 (CH), 117.2 (C_{quat}), 116.1 (CH), 114.6 (CH), 114.5 (C_{quat}), 111.9 (C_{quat}), 107.0 (CH), 102.5 (C_{quat}), 99.5 (C_{quat}), 97.4 (C_{quat}), 87.6 (C_{quat}), 76.9 (C_{quat}), 55.9 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1728 (s), 1595 (m), 1582 (m), 1558 (w), 1508 (m), 1441 (w), 1373 (w), 1292 (w), 1256 (s), 1225 (w), 1167 (m), 1130 (s), 1105 (w), 1026 (m), 988 (m), 881 (w), 822 (s), 791 (w), 750 (w), 637 (m). ESI-MS (*m*/*z* (%)): 418.4 ([M+H]$^+$, 100%). HR-MS (ESI) *m*/*z* calcd. for $(C_{27}H_{15}NO_4+H)^+$: 418.1074; Found: 418.1080. HPLC (acetonitrile): 99% (RT = 7.4 min).

*9-((4-(Dimethylamino)phenyl)ethynyl)-4-(pyridin-4-ylethynyl)-7H-furo[3,2-g] chromen-7-one (**10h**)*. According to GP2 and after purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 1:2) and after crystallization from acetone compound **10h** (53.8 mg, 50%) was obtained as a red solid. R_f = 0.45 (petroleum ether/ethyl acetate, 1:2). Mp 221 °C (dec). ^{1}H NMR: (300 MHz, $CDCl_3$) δ = 8.72 (s, 2 H), 8.25 (dd, J = 9.7, 1.0 Hz, 1 H), 7.82 (d, J = 2.1 Hz, 1 H), 7.61 – 7.53 (m, 2 H), 7.49 (s, 2 H), 7.03 (d, J = 2.1 Hz, 1 H), 6.68 (d, J = 8.6 Hz, 2 H), 6.52 (dd, J = 9.7, 1.0 Hz, 1 H), 3.03 (d, J = 1.1 Hz, 6 H). ^{13}C{^{1}H} NMR: (75 MHz, $CDCl_3$) δ = 160.1 (C_{quat}), 155.1 (C_{quat}), 151.6 (C_{quat}), 150.7 (C_{quat}), 150.0 (CH), 147.6 (CH), 141.6 (CH), 136.0 (C_{quat}), 133.5 (CH), 126.8 (C_{quat}), 116.8 (C_{quat}), 115.8 (CH), 111.6 (CH), 110.3 (C_{quat}), 108.8 (C_{quat}), 106.6 (CH), 104.7 (C_{quat}), 100.4 (C_{quat}), 96.6 (C_{quat}), 87.6 (C_{quat}), 76.1 (C_{quat}), 40.2 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 1720 (s), 1605 (m), 1522 (m), 1489 (w), 1445 (w), 1404 (m), 1364 (m), 1327 (w), 1256 (w), 1182 (w), 1138 (s), 1080 (w), 1028 (m), 988 (m), 939 (w), 881 (w), 858 (w), 837 (m), 816 (s), 787 (w), 760 (s), 727 (w), 698 (w), 635 (m). ESI-MS (*m*/*z* (%)): 431.4 ([M+H]$^+$,100%). HR-MS (ESI) *m*/*z* calcd. for $(C_{28}H_{18}N_2O_3+H)^+$: 431.1390; Found: 431.1399. HPLC (acetonitrile): 98% (RT = 8.0 min).

*4-((9-((4-Methoxyphenyl)ethynyl)-7-oxo-7H-furo[3,2-g]chromen-4-yl)ethynyl) benzaldehyde (**10i**)*. According to GP2 and after purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 3:1) and after crystallization from acetone/dichloromethane/ethanol (4:1:1) compound **10i** (34 mg, 31%) was obtained as a yellow solid, R_f = 0.31 (petroleum ether/ethyl acetate, 3:1). Mp 225 °C (dec). ^{1}H NMR: (300 MHz, $CDCl_3$) δ = 10.07 (s, 1 H), 8.30 (d, J = 9.7 Hz, 1 H), 8.00 – 7.91 (m, 2 H), 7.86 – 7.74 (m, 3 H), 7.72 – 7.58 (m, 2 H), 7.06 (d, J = 2.3 Hz, 1 H), 6.98 – 6.87 (m, 2 H), 6.53 (d, J = 9.7 Hz, 1 H), 3.86 (s, 3 H). ^{13}C{^{1}H} NMR: (75 MHz, $CDCl_3$) δ = 191.2 (CH), 160.4 (C_{quat}), 160.0 (C_{quat}), 155.3 (C_{quat}), 152.0 (C_{quat}), 147.6 (CH), 141.7 (CH), 136.2 (C_{quat}), 133.7 (CH), 132.3 (CH), 129.8 (CH), 128.1 (C_{quat}), 126.8 (C_{quat}), 116.7 (C_{quat}) , 115.7 (CH), 114.5 (C_{quat}), 114.1 (CH), 111.7 (C_{quat}), 106.7 (CH), 102.6 (C_{quat}), 99.4 (C_{quat}), 98.9 (C_{quat}), 86.9 (C_{quat}), 77.2 (C_{quat}), 55.4 (CH_3). IR: $\tilde{\nu}$ [cm^{-1}] = 2922 (m), 1719 (s), 1597 (m), 1578 (m), 1503 (s), 1375 (w), 1292 (m), 1247 (m), 1207 (m), 1169 (m), 1144 (s), 1126 (m), 1101 (w), 1070 (w), 1022 (m), 984 (w), 883 (w), 820 (s), 795 (m), 752 (m), 752 (w), 621 (m). ESI-MS (*m*/*z* (%)): 445.3 ([M+H]$^+$, 15%), 889.6 ([M_2+H]$^+$, 100%). HR-MS (ESI) *m*/*z* calcd. for $(C_{29}H_{16}O_5+H)^+$: 445.1071; Found: 445.1074. HPLC (acetonitrile): 99% (RT = 4.7 min).

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Optimization studies of the selective consecutive Sonogashira-Sonogashira three-component synthesis, HPLC of compounds **7** and **10**, and all ^{1}H and ^{13}C NMR spectra of compounds **3**, **7** and **10**, absorption and emission spectra, aggregation induced emission enhancement, solvatochromicity and acidochromicity studies as well as TD-DFT calculations are compiled in the Supporting Information.

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Notes

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