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Amine Detection with Distyrylbenzenedialdehyde-Based Knoevenagel Adducts

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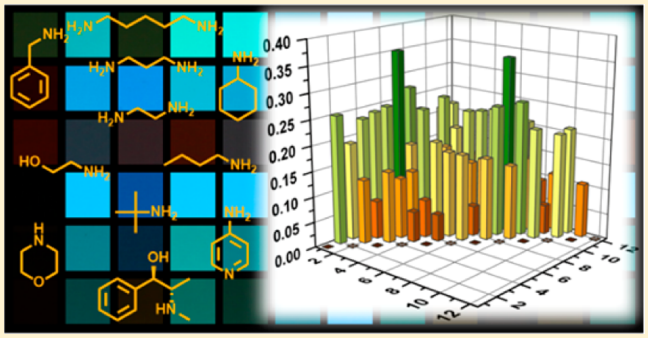
Supporting Information

ABSTRACT: Eight acceptor-substituted distyrylbenzene (DSB) derivatives were obtained by postfunctionalization of dialdehyde precursor **1** using Knoevenagel condensation. Solubility in a water/THF 9:1 mixture was achieved through the addition of branched oligoethylene glycol side chains. The acceptor compounds discriminate primary and secondary amines in aqueous solution. The fluorescence responses were analyzed by the multivariate analysis of variance (MANOVA) protocol, a statistical tool. In contrast to **1**, the adducts show reactivity toward secondary and aromatic amines. Nitroolefin **2f** is the most active dosimeter molecule. Reaction with amines is completed after less than 3 min, and the limit of detection (LOD) is improved by a factor of 10. Propylenediamine can be detected at 75 μM. This is a 10-fold improvement for the detection limit when compared to the detection limit of the starting dialdehyde.



INTRODUCTION

The sensing of amines is an important task. Amines are part of industrial effluvia, food spoilage in fish and shellfish, but they can also be found as indicators for specific disease states in the breath of afflicted subjects.[1] Therefore, sensing of amines has generated a number of different concepts based on antibodies[2] or enzymes,[3] but most commonly upon complicated chromatographic methods.[4] Some of these methods, including mass spectrometry, have a very low detection limit, but often such instrument-intensive methods are cost intensive and need the presence of a machine park. In addition, antibody-based and enzyme-based essays often involve materials that are chemically and temperature sensitive; In addition, the antibodies have to be raised. All these facts make the use of these powerful methods a bit more complex. There is a fundamental question, if one can use simple, dye-based systems to discern and detect amines and at which levels can this be achieved. Indicator sensing approaches are a more simple alternative. They reach from proton-transfer-type reactions of conjugated polymers[5] and phenolic cruciform fluorophores[6] to the reaction of acceptor-substituted aromatic ketones[7] under formation of imines and hemiaminals or the use of nonspecific indicator and dye arrays as reported by Suslick;[8] such sensors and/or dosimeters function for amines in solution or in the gas phase or sometimes for both.

While our best sensor has a detection limit of 0.075 mM, it is no match for detection of amines using HPLC (0.05 nM),[4d] but it has a better sensitivity than that of Lavigne[5b] and is similar to that of Zimmerman et al.[7b] His dosimeter reached a detection limit of 20 μM but used THF as solvent instead of water. If one uses vapor-phase detection, the concentration of amines that can be detected by colorimetric sensor arrays can be less than 1 ppm (vol).[1c] If MOFs are employed, amines can be detected at 0.1 mM concentration.[4e] While the presence of amines is never beneficial, species such as histamine lead to fish poisoning at concentrations of around 500 ppm, while cadaverine (diaminopentane) and putresceine (diaminobutane) have toxicity levels of around 2000 ppm (2 g L^{-1}, 19 mM concentration).[4f] As a consequence, even relatively simple sensory systems should be viable for their detection in meaningful concentrations.

We have developed a sensor, or better dosimeter platform, with the water-soluble DSB-dialdehyde **1**, which detects amines in water and in vapors when sprayed onto a solid surface. The detection scheme rests on the conversion of the dialdehyde into a bis-imine or into a bis-aminal, when diamines, such as propylenediamine or ethylenediamine, are the model analytes, which are detected at concentrations of less than 1 mM L^{-1} in water.[9] While **1** and its alkoxy derivatives have been fairly successful as amine dosimeters, we want to modulate the amine sensing capabilities of **1** by postfunctionalization. Aldehydes convert into Michael systems by a Knoevenagel condensation with C−H-active compounds. Depending upon the electronic nature of the C−H-active compound, such Michael systems show varying degrees of electron-accepting character and therefore should display a differential reactivity toward amines. The Knoevenagel approach has the advantage that it is a late-stage functionalization. We condense one module into an array of amine-sensitive Knoevenagel adducts, some of

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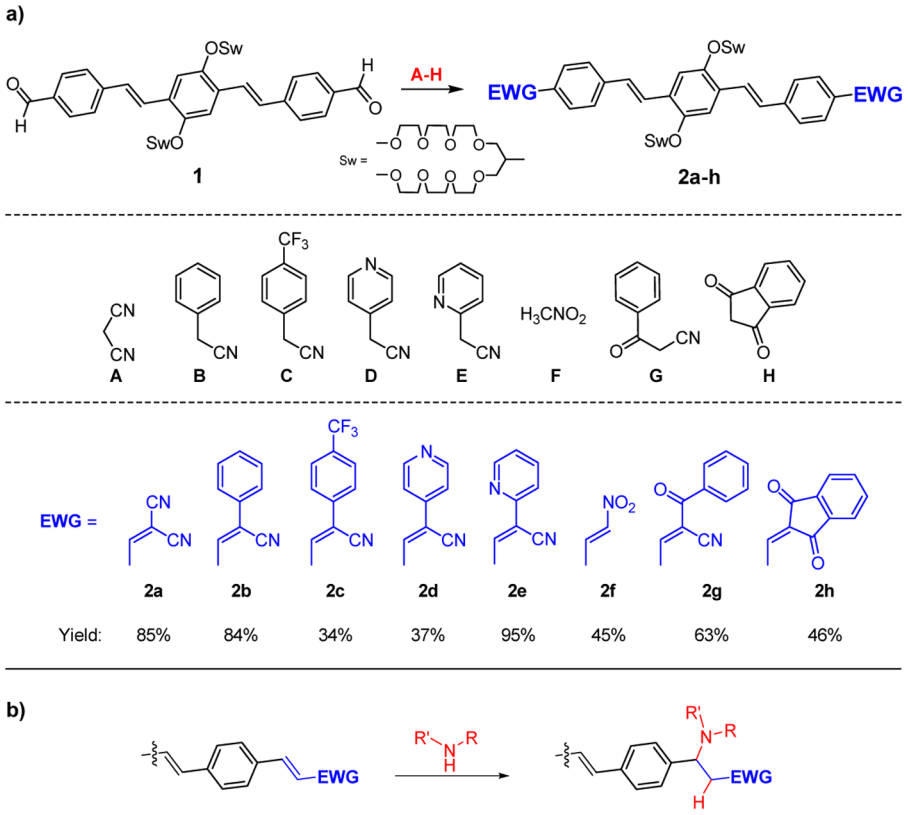
Scheme 1. (a) Synthesis of Compounds 2a–h.[a] (b) Detection Mechanism of the Amines



[a]Conditions for **2a**: piperidine, AcOH, MeCN, rt. Conditions for **2b,c**: NaOMe, MeOH, reflux. Conditions for **2d,e,h**: piperidine, AcOH, EtOH, rt. Compound **2f**: $MeNO_2$, NH_4OAc, reflux. Compound **2g**: *S*-proline, EtOH, rt.

which are employed in the detection and identification of amines in water.

RESULTS AND DISCUSSION

The dialdehyde **1** reacts smoothly with the C–H-active compounds **A**–**H** in the presence of a base to give the Knoevenagel adducts **2a**–**h** in yields ranging from 37 to 85% after workup and purification. Depending upon the coupling partner, different bases were applied to complete the condensation (Scheme 1a).

Figure 1 shows photographs of solutions of **2a**–**h** in dichloromethane (DCM) under irradiation with black light

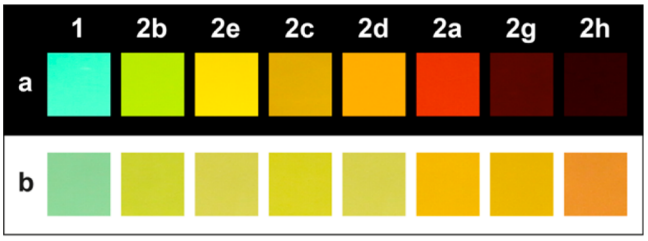


Figure 1. (a) Photographs of solutions (DCM, c = 20 μM) of **1**–**2h** under irradiation with a hand-held UV lamp at an emission wavelength of 365 nm. (b) Photographs of the same solutions taken under daylight.

(λ_{max} 365 nm) arranged according to their emission color and the corresponding photographs taken by daylight. Compound **2f** is non-fluorescent and therefore not included in this panel. Compounds **2a–c,e** are quite fluorescent in DCM, while **2d,f–h** are much less so. Under daylight, solutions of the adducts **2** are yellow to deeply orange in color.

Figure 2 displays the respective spectroscopic data; **2h** is the most red-shifted chromophore both in absorption as well as in emission, followed by **2a,g**. The adducts **2b–e** are structurally similar and show the expected change in the emission colors; i.e., with higher acceptor character of the benzene ring of the benzyl cyanide, both absorption and emission are more red-shifted. In Table 1 the photophysical properties of the adducts **2** (in DCM) are presented. As expected, quantum yields drop for the adducts with more red-shift in emission.

Compound **2a** is extremely reactive to nucleophiles and is not stable in water. Hydrolysis is almost complete at low concentrations when **2a** is used ($<10^{-5}$ M), and therefore, **2a** reverts back into **1** and malodinitrile **A**.[10] We did not investigate **2a** further for water-based sensing approaches as it is too reactive; **2b** and **2c** do not react with amines in water at ambient temperature. The adducts **2d** and **2e** react slowly, while **2f**, **2g**, and **2h** react directly after addition of amines to the aqueous solution. Compound **2f** detects morpholine (**9**) and 4-aminopyridine (**11**), which is not observed for the dialdehyde **1**.

Figure 3 shows the emission colors of the amine-sensitive adducts **2d–h** in aqueous/THF (9:1) solution and after their reaction with the amines **2**–**12**. While **1** is non-reactive toward **9**–**12**, **2d** and **2f** react with both morpholine (**9**) and 4-aminopyridine (**11**). Only ephedrine (**10**) does not elicit any reaction with the offered fluorogenic probes. As the adducts are also highly colored (Figure 4) in water/THF, we investigated

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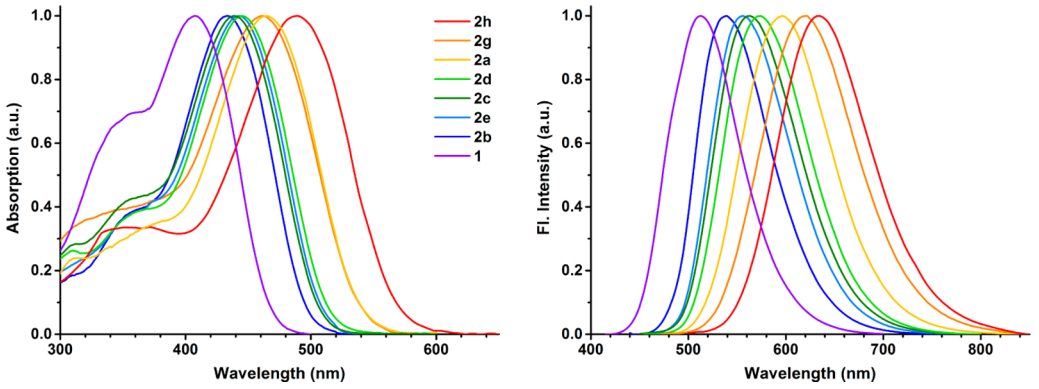

Figure 2. Absorption (left) and emission spectra (right) of **1**−**2h** in DCM.

Table 1. Photophysical Properties of 2a−h Recorded in DCM

compd	$\lambda_{max,\ abs}$ (nm)	$\lambda_{max,\ em}$ (nm)	Stokes shift (cm^{-1})	$\Phi_f \pm 5$ (%)	τ_f (ns)
2a	465	596	4727	53	1.7
2b	433	539	4542	72	1.6
2c	439	563	5017	55	1.6
2d	445	574	5050	45	1.7
2e	443	556	4588	64	1.6
2f	447	n/a	n/a	n/a	n/a
2g	461	621	5589	23	1.0
2h	489	635	4702	23	0.9

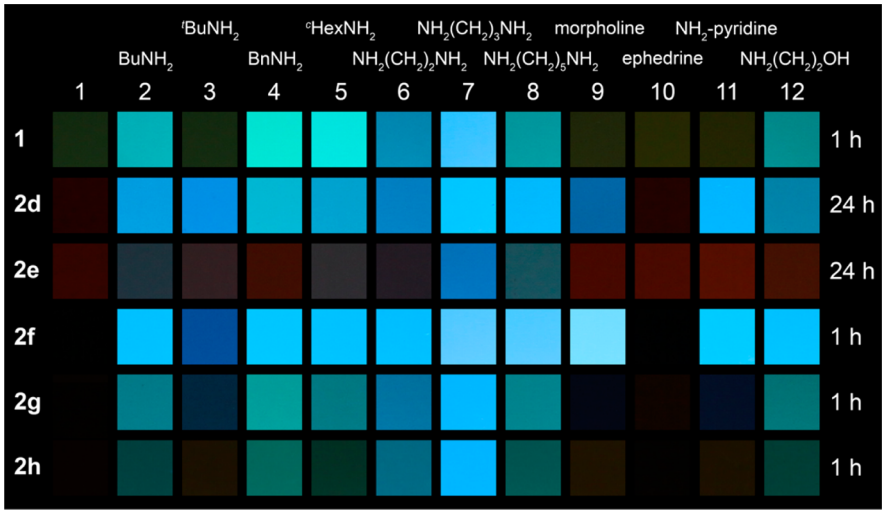

Figure 3. Photographs of solutions (water/THF = 9:1, c = 4.4 μM) of **1** and **2d**−**h** upon addition of amines **2**−**12** (left to right). Columns: (1) fluorophore reference, (2) butylamine, (3) *tert*-butylamine, (4) benzylamine, (5) cyclohexylamine, (6) ethylenediamine, (7) propylenediamine, (8) cadaverine, (9) morpholine, (10) ephedrine, (11) 4-aminopyridine, (12) ethanolamine. The samples were excited using a hand-held UV lamp at an emission wavelength of 365 nm. Photographs were taken with fixed settings of the camera (JPEG format, shutter speed 125 ms, ISO value 100, aperture F2.8, white balance 6500K, and Adobe RGB 1986 color space).

their use as colorimetric amine dosimeters, employing propylenediamine as model analyte. This dosimeter type works, but the amount of propylenediamine needed to effect a color change is considerably higher than the amount leading to a change in the emission color, so we did not pursue colorimetric dosimetry further.

Figure 5 shows the changes in emission of **1** and **2d**−**h** in aqueous solution after addition of different amines. The adducts and **1** are mostly non-fluorescent in water, and the addition of amines leads to a large fluorescence turn-on. As in the case of **1**, propylenediamine gives the highest turn-on factor, followed by other amines. In the case of **2h**, propylenediamine is almost the only amine that leads to significant fluorescence turn-on, while the nitromethane adduct **2f** is the most reactive adduct that reacts with almost all amines **2**−**12** under similar turn-on factors. Interestingly enough, the isomeric adducts **2d**,**e** show different behavior toward the amines. In addition, **2e** is the only ratiometric species in this series that reacts strongly with propylenediamine and cadaverine. The reactivity and the sensitivity of our adducts for different amines changes with the chemical nature of these condensation product. That is perhaps not unexpected.

Figure 6 displays the reaction rate and the sensitivity of the adducts **2f**−**h** toward the model analyte propylenediamine (**7**).

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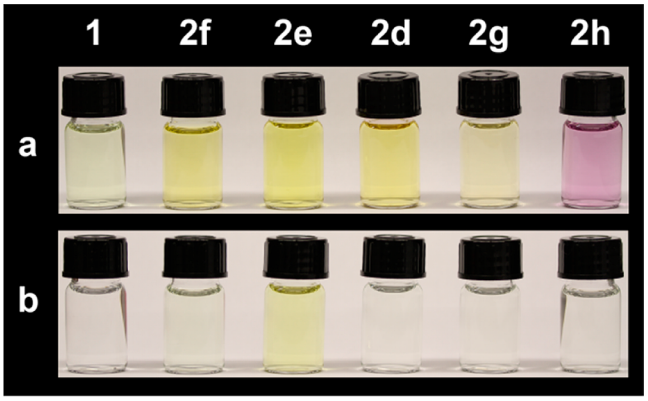

Figure 4. (a) Photographs of solutions (water/THF = 9:1, c = 4.4 μM) of **1** and **2d**–**h** by natural light before and (b) and 1 h after addition propylenediamine.

While **2f** reacts to completion in 2 min, adducts **2g**,**h** need 30–40 min for reaction completion. Thus, **2f** reacts in the presence of (7, 0.012 vol %) distinctly faster than **1** (completion after 30 min), while **2g**,**h** take around the same time as **1** to complete the reaction.

Compound **2f** detects propylenediamine (7) at a concentration of 5.5 ppm (75 μM), which is by a factor of 10 better than the detection limit of (7) using the dialdehyde **1** (c = 750 μM, see the Supporting Information). Adducts **2g** and **2h** show a turn-on only at 55 ppm; i.e., they are just as sensitive as **1**. To evaluate **2f** further, we determined the reaction rate and detection limit of butylamine (**2**, finished after 3 min) and morpholine (**9**, finished after 1 min). The limit of detection for butylamine (**2**) and morpholine (**9**) is at 750 μM, less sensitive than the detection of propylene diamine (7). In comparison, dialdehyde **1** is much less sensitive toward butylamine (**2**) and shows a distinct signal at a 7.5 mM concentration. In the presence of morpholine (**9**), no reaction with **1** could be observed. The mechanism of the detection reaction, we presume, to be in all cases the Michael addition of the amine to the Knoevenagel adduct. This

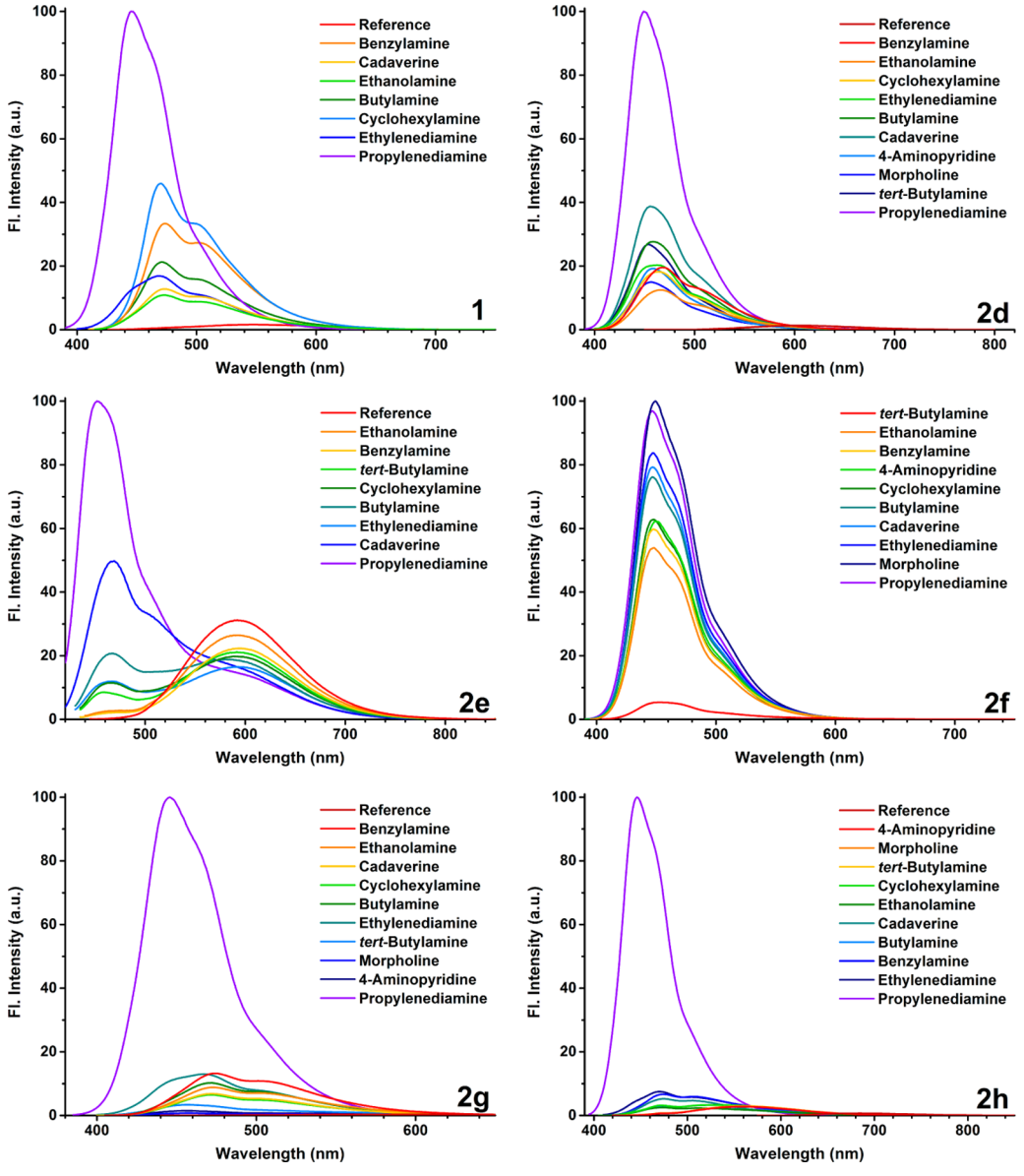

Figure 5. Non-normalized emission spectra of solutions of **1** and **2d**–**h** in a water/THF = 9:1 mixture upon addition of different amines.

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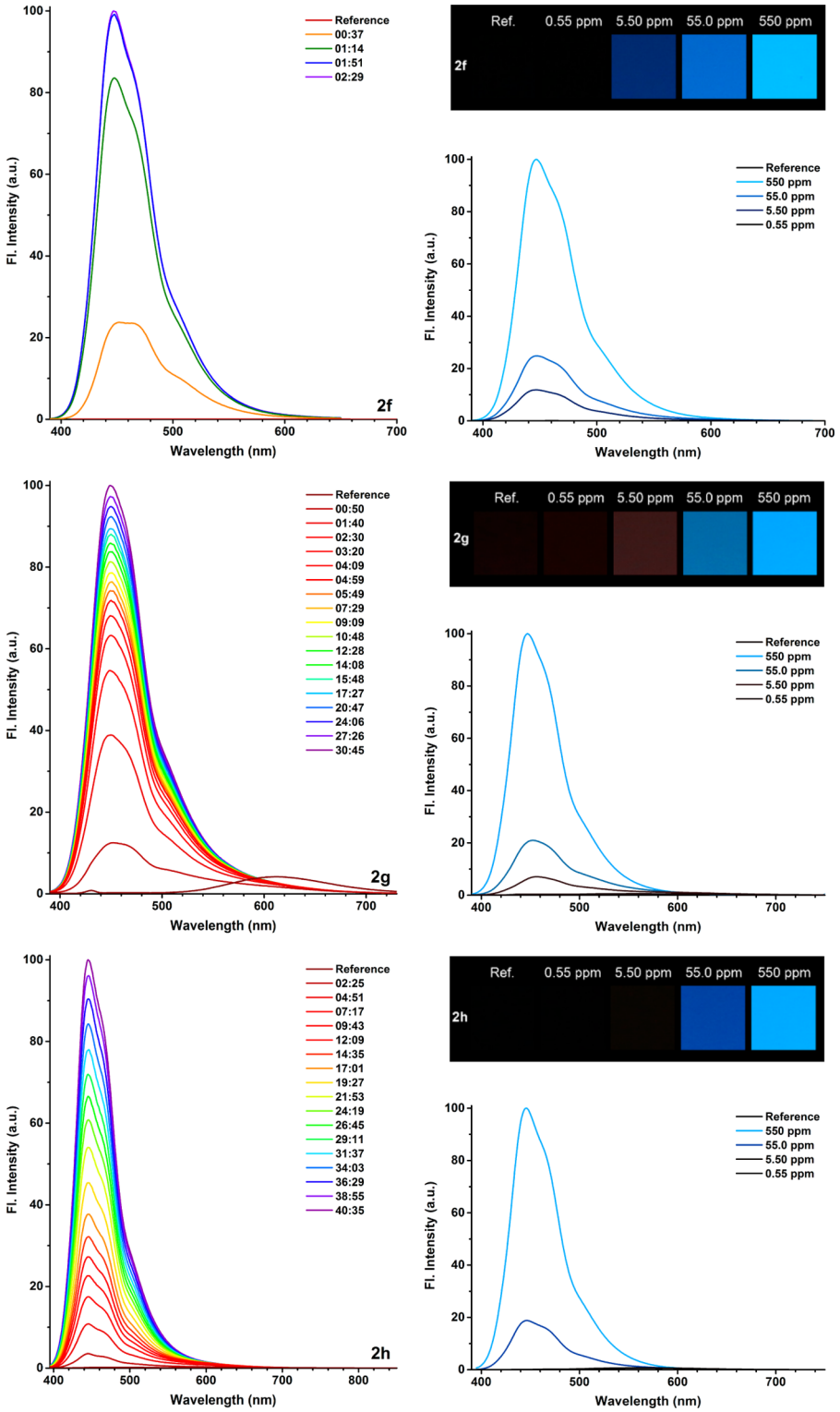

Figure 6. Left: Time-dependent evolution (mm:ss) of the emission wavelength and emission intensity for the reactions of **2f** (top), **2g** (middle), and **2h** (bottom) in water/THF = 9:1 (c = 0.9 μM) after addition of propylenediamine (0.012 vol %). Right: Photographs and fluorescence spectra of solutions (water/THF = 9:1, c = 4.4 μM) of **2f** (top), **2g** (middle), and **2h** (bottom) at the concentrations of propylenediamine specified in the panels.

reaction reforms the simple distyrylbenzene fluorophore, and that leads to a turn-on of the fluorescence (Scheme 1b), as the quenching nitrovinyl (or other Michael system) is destroyed.

For the discrimination of the amines **1**−**12** we determined autocorrelation plots of their combined (**2a**−**h**) emission color changes. For these plots, we used color coordinates *rgL* of the RAW RGB data obtained by photography.[11] *L* encodes the brightness, and *r* and *g* are chromaticity coordinates of the emission color. These rgL values were treated with MANOVA statistics, and the deviation σ of the different response fields generated from **2a**−**h** was calculated:[12,13]

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$$\sigma_{m,n}(\mathrm{r,\ g,\ L}) = \sqrt{\frac{\sum_{\mathrm{dye6}}^{\mathrm{dye1}} (r_n - r_m)^2 + (g_n - g_m)^2 + (L_n - L_m)^2}{3 \cdot 6}}$$

$$r = \frac{R}{R + G + B}$$

$$g = \frac{G}{R + G + B}$$

$$L = \sqrt{\frac{R^2 + G^2 + B^2}{3}}$$

In this correlation, the sensor system was built out of six fluorophores **1** and **2d**–**h** in water/THF = 9:1. Figure 7 shows

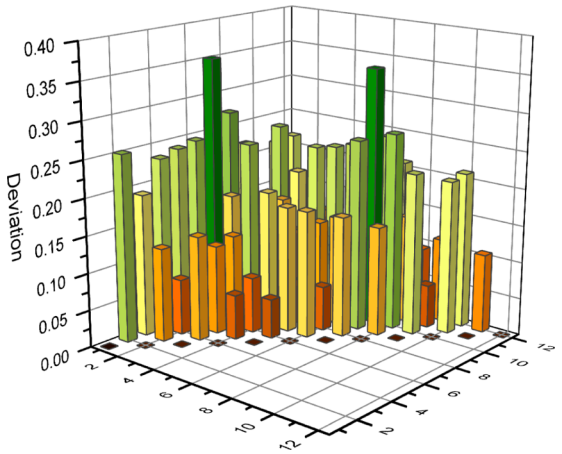

Figure 7. Autocorrelation plot (RAW rgL values) of solutions (water/THF = 9:1, c = 4.4 μM) of fluorescent dyes **1** and **2d**–**h** upon addition of amines recorded with a digital camera. When color information on identical amines + dyes is correlated, the deviation $\sigma_{n,m}$ disappears (dark red squares on the diagonal). Green columns represent an excellent and orange columns a good discrimination.

the autocorrelation plot for all amines. The amines are distinguishable from each other, and the deviation always exceeds 0.034. Having different combinations of color appearances, amine (**3**), (**7**), (**9**), and (**11**) are easily discriminated. Ephedrine (**10**) shows almost no reaction with any of the fluorophores. Therefore, the deviation to all amines is bigger than 0.188. Differentiation is seen between the amines (**4**), (**5**), (**2**), and (**8**) ($\sigma_{4,5}$ = 0.060, $\sigma_{2,8}$ = 0.036), although these combinations seem to have similar emission colors (Figure 3). MANOVA analysis provided a similar deviation using spectroscopic data from Figure 5 (relative intensity, full width at have maximum and wavenumber of emission maximum).

CONCLUSIONS

In conclusion, the sensor-active dialdehyde **1** and its easy postfuntionalization gives adducts **2a**–**h** that are soluble in a water/THF mixture that shows differential reactivities to amines. The nitrovinyl adduct is a reasonably sensitive dosimeter that reacts with aqueous propylenediamine solutions at less than 0.1 mM L^{-1} concentrations under change of the emission color. Postfunctionalization of **1** is therefore a good way to tune the activity of this amine detection system. If the reactivity of an adduct is too high, such as with the malodinitrile adduct **2a**, water already interferes as nucleophile. Adduct **2a** is so reactive that it hydrolyzes in water. The nitrovinyl **2f** is our best performer and reacts much faster with amines than **1**. Adduct **2f** also detects amines at much lower (1/10th) concentration than **1** does. Some of the other condensation products are not active at all (**2a**–**c**), react only sluggishly with amines (**2d**,**e**), or are of similar reactivity as **1** (**2g**,**h**). The identification of the different amines is possible using a MANOVA tool, yet the developed system is not ideal, as the limit of detection of 5.5 ppm is still too high to detect trace analytes of amines in water but it suffices to detect diaminoalkanes at reasonable levels where they are not yet poisonous. Nitroolefin **2f** improves the detection limit of amines substantially, making it a much superior dosimeter in comparison to the dialdehyde **1**. The "mutagenesis" of **1** into Knoevenagel adducts allows the powerful fine-tuning and an increase of the sensing prowess of this modular system for utilization in chemical tongue/nose approaches. Generally, these chemodosimeters are considerably more simple and less involved with respect to instrumentation than the established chromatographic methods. Further developments will be the inspection of the formed adducts as sprayed on.

EXPERIMENTAL SECTION

All reagents and solvents were obtained from commercial suppliers and were used without further purification unless otherwise noted. Compound **1** was prepared as reported.[9c] ^{1}H NMR spectra were recorded on a 300, 400, or 600 MHz spectrometer, and ^{13}C NMR spectra were recorded on a 75, 100, or 150 MHz spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) relative to traces of $CHCl_3$.[14] MS spectra were recorded using fast atom bombardment, electronspray ionization, direct analysis in real-time, or electron impact detected by magnetic sector and FT-ICR techniques, respectively. Infrared (IR) spectra are reported in wavenumbers (cm^{-1}) and were recorded neat. Absorption and emission spectra were recorded in dichloromethane or water/THF = 9:1 solutions. Quantum yields Φ were obtained by the absolute method using an Ulbricht sphere.[15] Time-correlated single photon counting lifetime measurements were carried out with a pulsed laser diode.

General Procedure (GP1) for preparation of compounds 2a,d,e,h. To a solution of **1** (1.00 equiv) and the C–H-active compound **A**–**H** (2.20 equiv) in the appropriate solvent (3 mL) were added catalytic amounts of acetic acid and piperidine. The reaction mixture was stirred at rt overnight and quenched with water (10 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (4 × 20 mL). The combined organic layers were dried over $MgSO_4$, and the solvents were evaporated.

*2,2′-[[2,5-Bis(2,5,8,11,15,18,21,24-octaoxapentacosan-13-yloxy)-benzene-1,4-diyl]bis[(E)-ethene-2,1-diylbenzene-4,1-diylmethylylidene]]-dipropanedinitrile (**2a**).* According to GP1, dialdehyde **1** (200 mg, 181 μmol) and malononitrile (26.4 mg, 396 μmol) were reacted in acetonitrile (3 mL). Column chromatography (silica gel, petroleum ether/dichloromethane/ethyl acetate/methanol = 5:3:1:0.6, R_f = 0.12) afforded the desired compound as a dark red wax (185 mg, 154 μmol, 85%). IR (cm^{-1}): 2868, 2223, 1599, 1568, 1544, 1511, 1487, 1453, 1421, 1350. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, J = 8.5 Hz, 4H), 7.72 (d, J = 16.8 Hz, 4H), 7.68 (d, J = 8.5 Hz, 4H), 7.39(s, 2H), 7.16 (d, J = 16.5 Hz, 2H), 4.55 (quin, J = 5.0 Hz, 2H), 3.81–3.76 (m, 8H), 3.70–3.58 (m, 40H), 3.51–3.49 (m, 8H), 3.34 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 151.6, 144.5, 131.6, 130.0, 129.1, 127.9, 127.8, 127.6, 114.6, 114.3, 113.2, 81.0, 79.9, 72.0, 71.2, 70.9, 70.7–70.6 (m), 59.2. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{64}H_{86}N_4O_{18}Na$ 1221.5835, found 1221.5861, m/z $[M + K]^+$ calcd for $C_{64}H_{86}N_4O_{18}K$ 1237.5574, found 1237.5596.

*(2Z,2′Z)-3,3′-[[2,5-Bis(2,5,8,11,15,18,21,24-octaoxapentacosan-13-yloxy)benzene-1,4-diyl]bis[(E)-ethene-2,1-diylbenzene-4,1-diyl]]-bis(2-phenylprop-2-enenitrile) (**2b**).* To a solution of **1** (200 mg, 181 μmol, 1.00 equiv) and phenylacetonitrile (44.0 μL, 381 μmol, 2.10 equiv) in methanol (3 mL) was added NaOMe (100 μL of a 25 wt % solution in MeOH, 435 μmol, 2.40 equiv) dropwise. The reaction

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mixture was refluxed overnight (65 °C) (end of reaction monitored by TLC), cooled to rt, and diluted with ethyl acetate/hexanes = 1:1 (5 mL). The solution was washed with water (2 × 10 mL) and brine (2 × 10 mL) and dried over $MgSO_4$, and the solvents were evaporated. Purification by column chromatography (silica gel, petroleum ether/dichloromethane/ethyl acetate/methanol = 5:3:1:0.5, R_f = 0.15) afforded the desired product as an orange oil (198 mg, 152 μmol, 84%). IR (cm^{-1}): 2868, 2211, 1586, 1487, 1449, 1417. ^1H NMR (400 MHz, $CDCl_3$): δ 7.92, (d, J = 8.4 Hz, 4H), 7.71−7.69 (m, 4H), 7.64−7.60 (m, 6H), 7.53 (s, 2H), 7.48−7.44 (m, 4H), 7.41−7.38 (m, 4H), 7.14 (d, J = 16.4 Hz, 2H), 4.56 (quin, J = 5.0 Hz, 2H), 3.84−3.77 (m, 8H), 3.72−3.58 (m, 40H), 3.51−3.49 (m, 8H), 3.34 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4, 141.8, 140.4, 134.8, 132.9, 129.9, 129.24, 129.21, 129.0, 128.3, 127.2, 126.1, 125.5, 118.4, 114.4, 110.9, 79.9, 72.1, 71.3, 70.9−70.6 (m), 59.1. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{74}H_{96}N_2O_{18}Na$ 1323.6556, found 1323.6579, m/z $[M + K]^+$ calcd for $C_{74}H_{96}N_2O_{18}K$ 1339.6295, found 1339.6303. Anal. Calcd for $C_{74}H_{96}N_2O_{18}$: C, 68.29; H, 7.43; N, 2.15. Found: C, 68.03; H, 7.53; N, 1.88.

*(2Z,2′Z)-3,3′-[[2,5-Bis(2,5,8,11,15,18,21,24-octaoxapentacosan-13-yloxy)benzene-1,4-diyl]bis[(E)-ethene-2,1-diylbenzene-4,1-diyl]]-bis[2-[4-(trifluoromethyl)phenyl]prop-2-enenitrile] (**2c**).* To a solution of **1** (100 mg, 90.6 μmol, 1.00 equiv) and 4-(trifluoromethyl)-phenylacetonitrile (35.2 mg, 190 μmol, 2.10 equiv) in methanol (2 mL) was added NaOMe (50 μL of a 25 wt % solution in methanol, 218 μmol, 2.40 equiv) dropwise. The reaction mixture was refluxed overnight (65 °C), cooled to rt, and diluted with ethyl acetate/hexanes = 1:1 (5 mL). The solution was washed with water (10 mL) and brine (10 mL) and dried over $MgSO_4$, and the solvents were evaporated. Purification by column chromatography on silica gel (petroleum ether/dichloromethane/ethyl acetate/methanol = 5:3:1:0.5, R_f = 0.14) afforded the desired product as an orange oil (44 mg, 30,6 μmol, 34%). IR (cm^{-1}): 2871, 2358, 2214, 1585, 1488, 1417, 1323, 1253. ^1H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, J = 8.4 Hz, 4H), 7.81 (d, J = 8.4 Hz, 4H), 7.71 (d, J = 8.4 Hz, 4H), 7.67−7.60 (m, 8H), 7.39 (s, 2H), 7.14 (d, J = 16.4 Hz, 2H), 4.56 (quin, J = 5.0 Hz, 2H), 3.81−3.79 (m, 8H), 3.72−3.57 (m, 40H), 3.53−3.49 (m, 8H), 3.34 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 151.4, 143.7, 141.0, 138.2, 132.3, 131.0 (q, J = 32.8 Hz), 130.2, 129.0, 128.1, 127.3, 126.4, 126.2 (q, J = 3.7 Hz), 125.8, 123.9 (q, J = 272.0 Hz), 117.9, 114.4, 109.2, 79.8, 72.0, 71.2, 70.9, 70.7−70.6, 59.1. ^{19}F NMR (470 MHz, $CDCl_3$): δ −62.69. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{76}H_{95}F_6N_2O_{18}$ 1437.6484, found 1437.6491, m/z $[M + Na]^+$ calcd for $C_{76}H_{94}F_6N_2O_{18}Na$ 1459.6304, found 1459.6347.

*(2Z,2′Z)-3,3′-[[2,5-Bis(2,5,8,11,15,18,21,24-octaoxapentacosan-13-yloxy)benzene-1,4-diyl]bis[(E)-ethene-2,1-diylbenzene-4,1-diyl]]-bis[2-(pyridin-4-yl)prop-2-enenitrile] (**2d**).* According to GP1, dialdehyde **1** (100 mg, 90.6 μmol) and 4-pyridylacetonitrile hydrochloride (30.9 mg, 200 μmol) were reacted in ethanol (3 mL). Purification by column chromatography (silica gel, petroleum ether/dichloromethane/ethyl acetate/methanol = 5:3:1:1.2, R_f = 0.13) yielded the desired compound as a dark orange colored oil (44.0 mg, 33.8 μmol, 37%). IR (cm^{-1}): 2872, 2209, 1578, 1551, 1487, 1418, 1338. ^1H NMR (600 MHz, $CDCl_3$): δ 8.70 (d, J = 5.9 Hz, 4H), 7.97 (d, J = 8.2 Hz, 4H), 7.71 (s, 2H), 7.66−7.64 (m, 6H), 7.58 (d, J = 5.8 Hz, 4H), 7.39 (s, 2H), 7.14 (d, J = 16.4 Hz, 2H), 4.56 (quin, J = 4.9 Hz, 2H), 3.82−3.77 (m, 8H), 3.70−3.58 (m, 40H), 3.51−3.49 (m, 8H), 3.33 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 151.3, 150.6, 144.5, 142.0, 141.4, 131.8, 130.4, 128.9, 127.9, 127.2, 126.0, 119.9, 117.2, 114.3, 108.0, 79.7, 71.9, 71.1, 70.7−70.5 (m), 59.0. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{72}H_{94}N_4O_{18}Na$ 1325.6461, found 1325.6476, m/z $[M + K]^+$ calcd for $C_{72}H_{94}N_4O_{18}K$ 1341.6200, found 1341.6218.

*(2Z,2′Z)-3,3′-[[2,5-Bis(2,5,8,11,15,18,21,24-octaoxapentacosan-13-yloxy)benzene-1,4-diyl]bis[(E)-ethene-2,1-diylbenzene-4,1-diyl]]-bis[2-(pyridin-2-yl)prop-2-enenitrile] (**2e**).* According to GP1, dialdehyde **1** (100 mg, 90.6 μmol) and 2-pyridylacetonitrile (23.0 μL, 200 μmol) were reacted in ethanol (3 mL). Purification by column chromatography (silica gel, petroleum ether/dichloromethane/ethyl acetate/methanol = 5:3:1:0.6, R_f = 0.10) afforded the desired compound as a dark orange oil (112 mg, 85.9 μmol, 95%). IR (cm^{-1}): 2867, 2211, 1579, 1563, 1550, 1515, 1488, 1466, 1432, 1422, 1350, 1324, 1312, 1299, 1251. ^1H NMR (600 MHz, $CDCl_3$): δ 8.65 (d, J = 4.5 Hz, 2H), 8.47 (s, 2H), 8.02 (d, J = 8.3 Hz, 4H), 7.81−7.76 (m, 4H), 7.65−7.63 (m, 6H), 7.39 (s, 2H), 7.29−7.27 (m, 2H), 7.14 (d, J = 16.4 Hz, 2H), 4.56 (quin, J = 5.0 Hz, 2H), 3.82−3.77 (m, 8H), 3.71−3.58 (m, 40H), 3.51−3.49 (m, 8H), 3.33 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 151.4, 151.3, 149.8, 144.6, 141.0, 137.5, 132.5, 130.7, 129.0, 128.2, 127.2, 125.7, 123.5, 121.4, 118.2, 114.4, 109.2, 79.8, 72.8, 71.2, 70.9−70.6 (m), 59.1. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{72}H_{95}N_4O_{18}$ 1303.6641, found 1303.6743, m/z $[M + Na]^+$ calcd for $C_{72}H_{94}N_4O_{18}Na$ 1325.6461, found 1325.6537.

*13,13′-[[2,5-Bis[(E)-2-[4-[(E)-2-nitroethenyl]phenyl]ethenyl]-benzene-1,4-diyl]bis(oxy)]bis(2,5,8,11,15,18, 21,24-octaoxapentacosane) (**2f**).* To a mixture of dialdehyde **1** (100 mg, 90.6 μmol, 1.00 equiv) and nitromethane (1.5 mL) was added ammonium acetate (3.50 mg, 45.3 μmol, 0.50 equiv). The reaction mixture was refluxed for 48 h. The excess nitromethane was removed under reduced pressure, and purification by column chromatography (silica gel, petroleum ether/dichloromethane/ethyl acetate/methanol = 5:3:1:0.6, R_f = 0.14) afforded the desired compound as an orange wax (48.0 mg, 40.4 μmol, 45%). IR (cm^{-1}): 2869, 2359, 1628, 1597, 1494, 1407, 1329, 1268, 1182, 1100, 1039, 962, 850, 830, 813, 730, 528. ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J = 13.6 Hz, 2H), 7.65−7.60 (m, 8H), 7.55 (d, J = 8.4 Hz, 4H), 7.37 (s, 2H), 7.12 (d, J = 16.4 Hz, 2H), 4.53 (quin, J = 5.0 Hz, 2H), 3.80−3.78 (m, 8H), 3.70−3.58 (m, 40H), 3.51−3.49 (m, 8H), 3.34 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.5, 142.1, 138.8, 136.7, 129.9, 129.2, 129.0, 128.1, 127.6, 126.2, 114.6, 79.9, 72.1, 71.2, 70.9−70.7 (m), 59.1. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{60}H_{88}N_2O_{22}Na$ 1211.5726, found 1211.5744, m/z $[M + K]^+$ calcd for $C_{60}H_{88}N_2O_{22}K$ 1227.5466, found 1227.5477.

*(2E,2′E)-3,3′-[[2,5-Bis(2,5,8,11,15,18,21,24-octaoxapentacosan-13-yloxy)benzene-1,4-diyl]bis[(E)-ethene-2,1-diylbenzene-4,1-diyl]]-bis(2-benzoylprop-2-enenitrile) (**2g**).* To a solution of benzoylacetonitrile (28.9 mg, 199 μmol, 2.20 equiv) and dialdehyde **1** (100 mg, 90.6 μmol, 1.00 equiv) in ethanol was added *S*-proline (4.20 mg, 36.3 μmol, 0.40 equiv). The reaction mixture was stirred at rt for 24 h and then concentrated in vacuo. The crude product was purified by column chromatography (silica gel, petroleum ether/dichloromethane/ethyl acetate/methanol = 5:3:1:0.6, R_f = 0.12) to yield the desired compound as a dark red oil (78.0 mg, 57.5 μmol, 63%). IR (cm^{-1}): 2869, 2360, 1655, 1577, 1544, 1489, 1448, 1418, 1349, 1317, 1261. ^1H NMR (300 MHz, $CDCl_3$): δ 8.07−8.05 (m, 6H), 7.92−7.89 (m, 4H), 7.73−7.61 (m, 8H), 7.56−7.51 (m, 4H), 7.40 (s, 2H), 7.16 (d, J = 16.4 Hz, 2H), 4.56 (quin, J = 4.9 Hz, 2H),3.80−3.79 (m, 8H), 3.72−3.57 (m, 40H), 3.52−3.48 (m, 8H), 3.34 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.2, 155.0, 151.6, 143.4, 136.3, 133.4, 132.0, 130.9, 129.4, 129.1, 128.8, 128.1, 127.4, 127.2, 117.5, 114.6, 109.0, 79.9, 72.1, 71.3−70.7 (m), 59.1. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{76}H_{96}N_2O_{20}Na$ 1379.6454, found 1379.6523, m/z $[M + K]^+$ calcd for $C_{76}H_{96}N_2O_{20}K$ 1395.6194, found 1395.6250.

*2,2′-[[2,5-Bis(2,5,8,11,15,18,21,24-octaoxapentacosan-13-yloxy)-benzene-1,4-diyl]bis[(E)-ethene-2,1-diylbenzene-4,1-diylmethylylidene]]-bis(1H-indene-1,3-(2H)-dione) (**2h**).* According to GP1, dialdehyde **1** (100 mg, 90.6 μmol) and 1,3-indandione (29.1 mg, 200 μmol) were reacted in ethanol (3 mL). Purification by column chromatography (silica gel, ethyl acetate/methanol = 20:1, R_f = 0.13) yielded the desired product as a dark red wax (57 mg, 41.9 μmol, 46%). IR (cm^{-1}): 2867, 1722, 1682, 1615, 1562, 1537, 1513, 1424, 1380, 1348, 1320, 1252, 1205, 1180, 1080, 1018,. ^1H NMR (600 MHz, $CDCl_3$): δ 8.51 (d, J = 8.3 Hz, 4H), 8.02−8.00 (m, 4H), 7.88 (s, 2H), 7.83−7.80 (m, 4H), 7.70 (d, J = 16.4 Hz, 2H), 7.67 (d, J = 8.4 Hz, 4H), 7.41 (s, 2H), 7.18 (d, J = 16.4 Hz, 2H), 4.57 (quin, J = 4.9 Hz, 2H), 3.83−3.78 (m, 8H), 3.72−3.58 (m, 40H), 3.50−3.49 (m, 8H), 3.33 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 190.6, 189.3, 151.5, 146.4, 143.1, 142.7, 140.2, 135.4, 135.2, 135.1, 132.5, 129.1, 128.6, 128.4, 127.0, 126.8, 123.4, 114.5, 79.9, 72.0, 71.2, 70.9, 70.7−70.6 (m), 59.1. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{76}H_{94}O_{22}Na$ 1381.6134, found

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1381.6151, m/z $[M + K]^+$ calcd for $C_{76}H_{94}O_{22}K$ 1397.5874, found 1397.5898.

■ ASSOCIATED CONTENT

Supporting Information

Additional emission spectra in the presence of amines, data treatment for the autocorrelation plot, and ^1H NMR and ^{13}C NMR spectra of all newly synthesized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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