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Orthogonally Protected Diaminoterephthalate Scaffolds – Installation of Two Functional Units at the Chromophore

Leon Buschbeck and Jens Christoffers*

Dedicated to Professor Jürgen Rullkötter on the occasion of his 70th birthday

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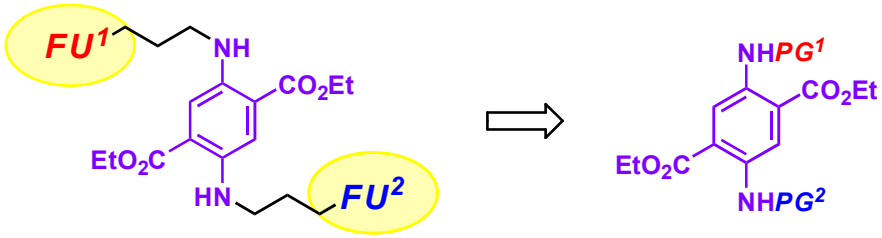
ABSTRACT:



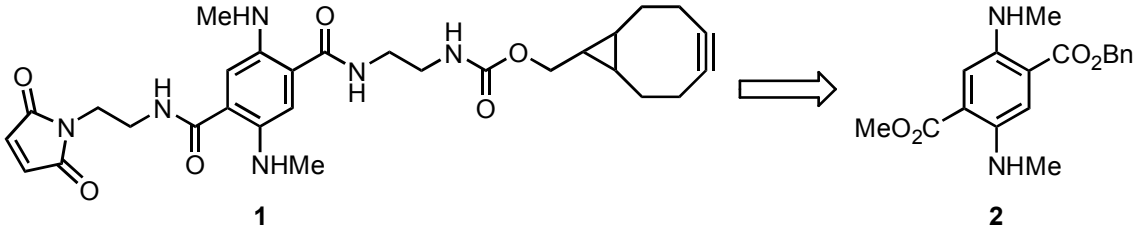
The 2,5-diaminoterephthalate structural motif is a powerful chromophore with remarkable fluorescence properties. Containing two carboxylate and two amino functions it defines a colored molecular scaffold which allows for orthogonal functionalization with different functional units. Therefore, different applications in Life Sciences and Materials Science could be addressed. In this study, the two amino functions were alkylated by reductive amination with side chains carrying amino (orthogonally protected as Boc or Alloc) and carboxylate functions (orthogonally protected as *t*Bu or allyl ester). After sequential deprotections, functional units were introduced by amidation reactions. As three examples, the chromophore was coupled to retinoic acid and fullerene C_{60} in order to obtain a triad for studying photoinduced electron transfer processes. Furthermore, cyclooctyne and azide moieties were introduced as functional units allowing for ligation by Click reactions. These two clickable groups were applied in combination with a maleimide units which are reactive towards thiol residues. The latter dyes define so called "turn on" probes, since the fluorescence quantum yields increased by an order of magnitude upon reaction with the molecular target.

INTRODUCTION

Fluorescence dyes are versatile tools for analytical applications in the Life Sciences[1] as well as Materials Science.[2] Particularly useful are chromophores holding a reactive functional unit, thus, allowing for the covalent ligation of biomolecules like proteins or other targets.[3] As functional units, for example, the maleimide moiety is suited for the conjugate addition of a thiol, e.g. a cysteine residue on the surface of a protein.[4] Furthermore, the copper-catalyzed Huisgen 1,3-dipolar cycloaddition[5] of an alkyne with an organo azide (so-called Click reaction)[6] became very popular in the recent years for binding biomolecules to dyes.[7] A newer development in this area is the use of highly reactive cyclooctyne derivatives that allow for a copper-free Click reaction.[8]

Diaminoterephthalates (DATs) are bright and colorful dyes which exhibit powerful fluorescence properties.[9] The DAT motif defines a structurally relative simple chromophore, which is in contrast to other classes of dyes, so far underrated in the literature.[10] These compounds are readily accessed by conversion of succinyl succinates with primary amines,[11] allowing a flexible introduction of side chains with various functional units. Actually, the chromophore defines a molecular scaffold,[12] which can be orthogonally equipped with different functional units,[13] thus, tailored functional materials can be prepared for addressing different applications of Life Sciences[14] and Materials Science.[15]

We have recently reported on the synthesis of bifunctional dye **1** holding a maleimide and cyclooctyne functional unit (Scheme 1).[16] We have used this probe **1** for studying protein-protein interactions. Anyhow, there are two significant problems associated with the synthesis of compound **1** from building block **2**. One carboxylate function is released from compound **2** by debenzylation (catalytic hydrogenation) which is then followed by introduction of the first functional unit by amidation. The first problem arises during the saponification of the second ester group because the respective basic reactions conditions are not fully compatible with the functional unit already installed. The second problem is the coupling of the two functional units by amidation of the aromatic carboxylate functions, which proceeded not always with satisfying results because the the electron donating amino groups at the chromophore deplete the electrophilicity of the carbonyl groups.

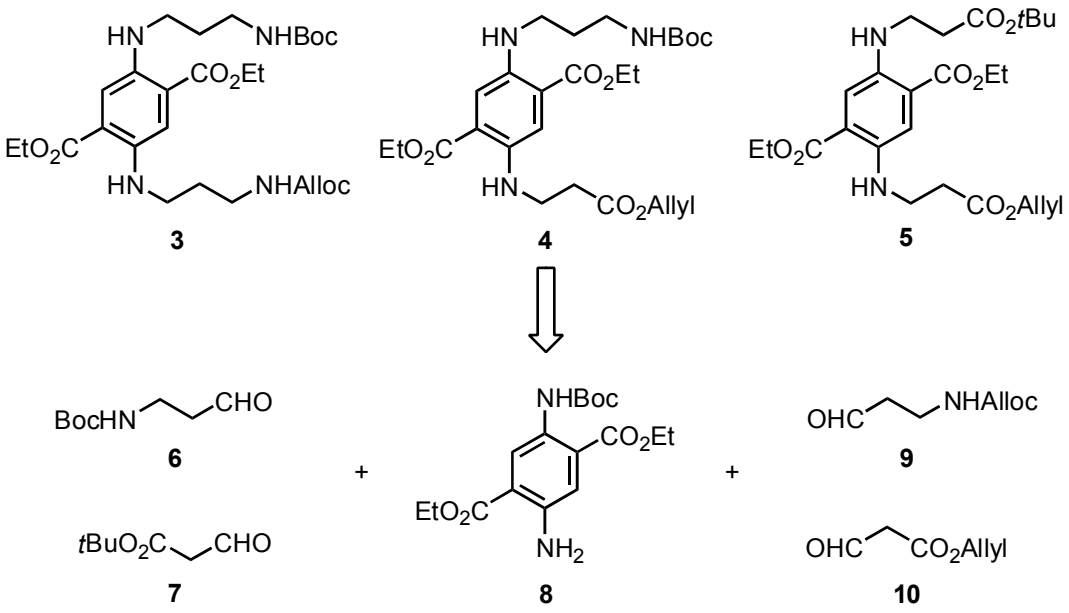


1 **2**

Scheme 1. Compound **1** as an example of the first generation of a bifunctionalized DAT

and its synthetic precursor **2**.

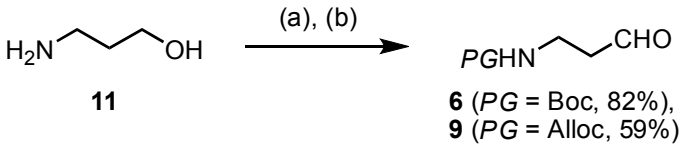
In order to overcome the above-mentioned drawbacks during synthesis of probe **1**, this manuscript suggests the next generation of bifunctionalized DATs to be prepared from the three intermediate compounds **3**, **4**, and **5** (Scheme 2). The two key advantages of the new synthetic concept are the following: (1) The functional units are sterically and electronically decoupled from the chromophore by introduction of alkyl spacers, and (2) the compounds hold either two orthogonally protected amino groups (compound **3**), two carboxylic acids (compound **5**), or a mixed amine-carboxylic acid scaffold (compound **4**), which is an enrichment of synthetic options compared to diprotected dicarboxylic acid **2**. Actually, this new concept allows for the first time to install two different functional units at the nitrogen atoms of the core structure. We are planning to introduce the spacer units by reductive aminations of aldehydes **6**, **7**, **9**, and **10** with the aromatic amine **8**. Compounds **6** and **9** are protected amines, compounds **7** and **10** protected carboxylic acids with either acid cleavable groups (BocNH, **6** and *t*BuO$_2$C, **7**) or groups cleavable by palladium catalyzed allylic substitutions (NHAlloc, **9** and CO$_2$Allyl, **10**).



Scheme 2. Concept for the second generation of functional dyes with the orthogonally protected DATs **3**, **4**, and **5** as chromophore building blocks and respective starting materials **6**–**10** for reductive aminations.

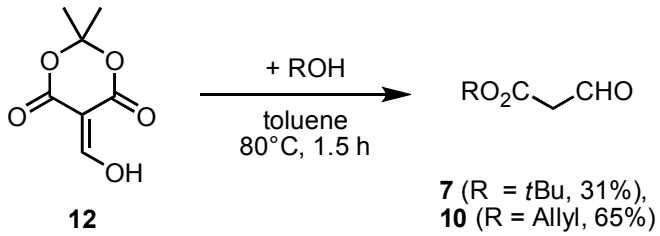
RESULTS AND DISCUSSION

The preparation of literature known aminopropanals **6**[17] and **9**[18] proceeded straightforward in two steps starting from aminopropanol **11** (Scheme 3). Standard protocols were applied for Boc-[19] and Alloc-protections[20] and the subsequent oxidation was accomplished according to the Swern-procedure.[17] After chromatographic purification, compounds **6** and **9** were obtained in 82% and 59% yields over two steps, respectively. Compound **6** slowly decomposes at ambient temperature, but is stable for at least a week at –35°C.



Scheme 3. Synthesis of protected aminopropanals **6** and **9** (yields over two steps); reagents and conditions: (a) for **6**: Boc_2O, CH_2Cl_2, 23°C, 18 h, 99%; for **9**: AllocCl, Na_2CO_3, MeCN–H_2O, 23°C, 20 h, 96%; (b) $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, –78°C→23°C, 3 h, 83% (for **6**), 61% (for **9**).

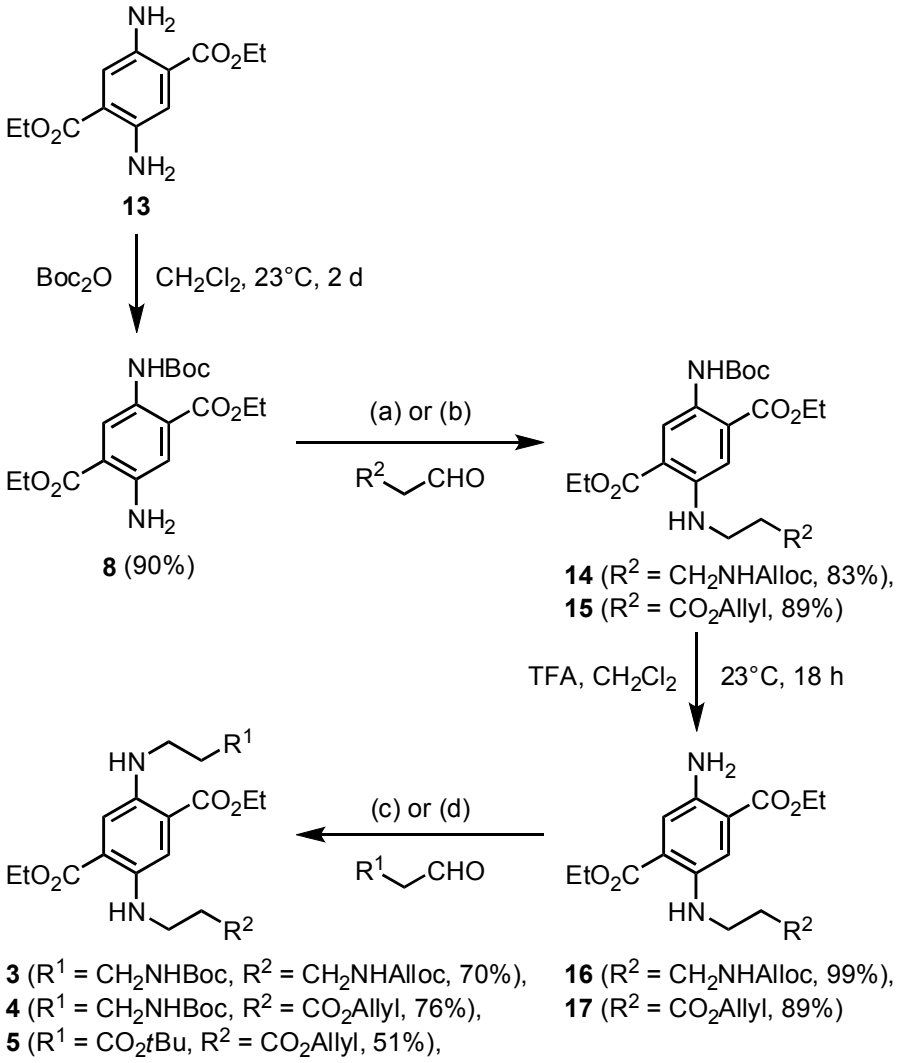
The synthesis of formyl acetic esters from formyl-Meldrums acid **12** was actually reported in the literature,[21] however, it turned out to require substantial practice when we tried to reproduce the synthesis of *tert*-butyl and allylic esters **7** and **10**. First of all, starting material **12**[22] was obtained in two steps from Meldrums acid in 68% yield. Compound **12** was then converted with *t*BuOH and allylic alcohol in toluene to furnish a crude mixture (Scheme 4), from which the products **7**[21, 23] and **10**[24] were obtained by Kugelrohr distillation in vacuum (31% and 65% yield, resp.). Both compounds are stable at –35°C at least for a week. Both decompose at ambient temperature, *tert*-butyl ester **7** faster than allyl ester **10**. In this context, we would like to point out, that a longer linker moiety, which is easier to prepare, e.g. a 3-formyl propionic ester as a C_4-unit was initially investigated, which however lead in subsequent operations to intramolecular amidations under formation of γ-butyrolactams.



Scheme 4. Synthesis of aldehydes **7** and **10** from formyl Meldrums acid **12**.

Synthesis of orthogonally protected building blocks **3**, **4**, and **5** started with DAT **13**, which

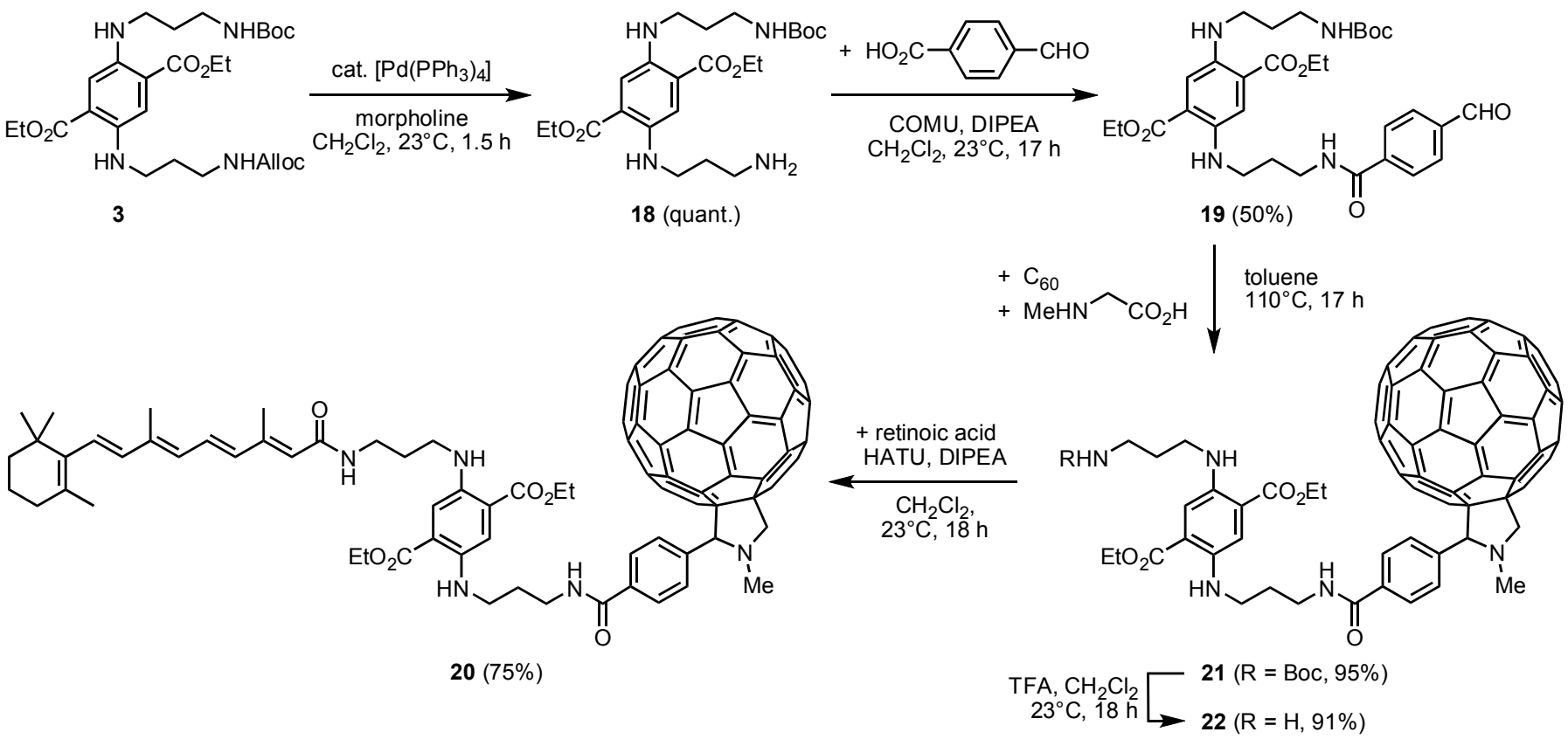
was obtained according to Sinnreich[11] from diethyl succinyl succinate[25] and then was mono-Boc protected (90% of product **8**,[26] Scheme 5). After some experimentation, two complementary procedures turned out to be optimal for the reductive aminations: For protected aminopropanals **6** and **9**, $NaBH(OAc)_3$ with or without AcOH[27] gave better results than $NaBH_3CN$ with $ZnCl_2$.[28] For protected formylacetates **7** and **10**, the choice was opposite. Accordingly, compounds **14** and **15** were obtained under different reactions conditions with 83% and 89% yield, respectively. The Boc-deprotection proceeded for both compounds under acidic conditions, although the allyl ester **17** (89% yield) showed slightly lower stability under these conditions than allyl carbamate **16** (99% yield). Finally, the second reductive amination was accomplished, again for aminopropanal **6** with $NaBH(OAc)_3$ (without AcOH, but with longer reaction times; in the presence of AcOH, the Boc group turned out to be not completely stable) and *tert*-butyl ester **7** with $NaBH_3CN$ with $ZnCl_2$. Whereas the yields with aminopropanal **6** were good if no additional AcOH was used (70% of product **3** and 76% of product **4**), the yield for the diester **5** was lower (51%). Anyhow, the overall procedures turned out to be robust and compounds **3–5** were accessed on reasonable scales, with 52% (for **3**), 54% (for **4**) and 36% (for **5**) yields over four steps, respectively. In addition to compound **4**, one might suggest a second "mixed" case with an acid cleavable carboxylate protection and an amino protection cleavable by palladium catalysis. However, such a constitution would provide no added value.



Scheme 5. Synthesis of orthogonally protected building blocks **3**, **4**, and **5**; reagents and conditions, for **14**: (a) aldehyde **9**, $R^2 = CH_2NHAlloc$, $NaBH(OAc)_3$, AcOH, CH_2Cl_2, 23°C, 1 h; for **15**: (b) aldehyde **10**, $R^2 = CO_2Allyl$, $NaBH_3CN$, $ZnCl_2$, CH_2Cl_2, 0°C→23°C, 2 d; for **3** and **4**: (c) aldehyde **6**, $R^1 = CH_2NHBoc$, $NaBH(OAc)_3$, CH_2Cl_2, 0°C→23°C, 18 h; for **5**: (d) aldehyde **7**, $R^2 = CO_2tBu$, $NaBH_3CN$, $ZnCl_2$, CH_2Cl_2, 0°C→23°C, 2 d.

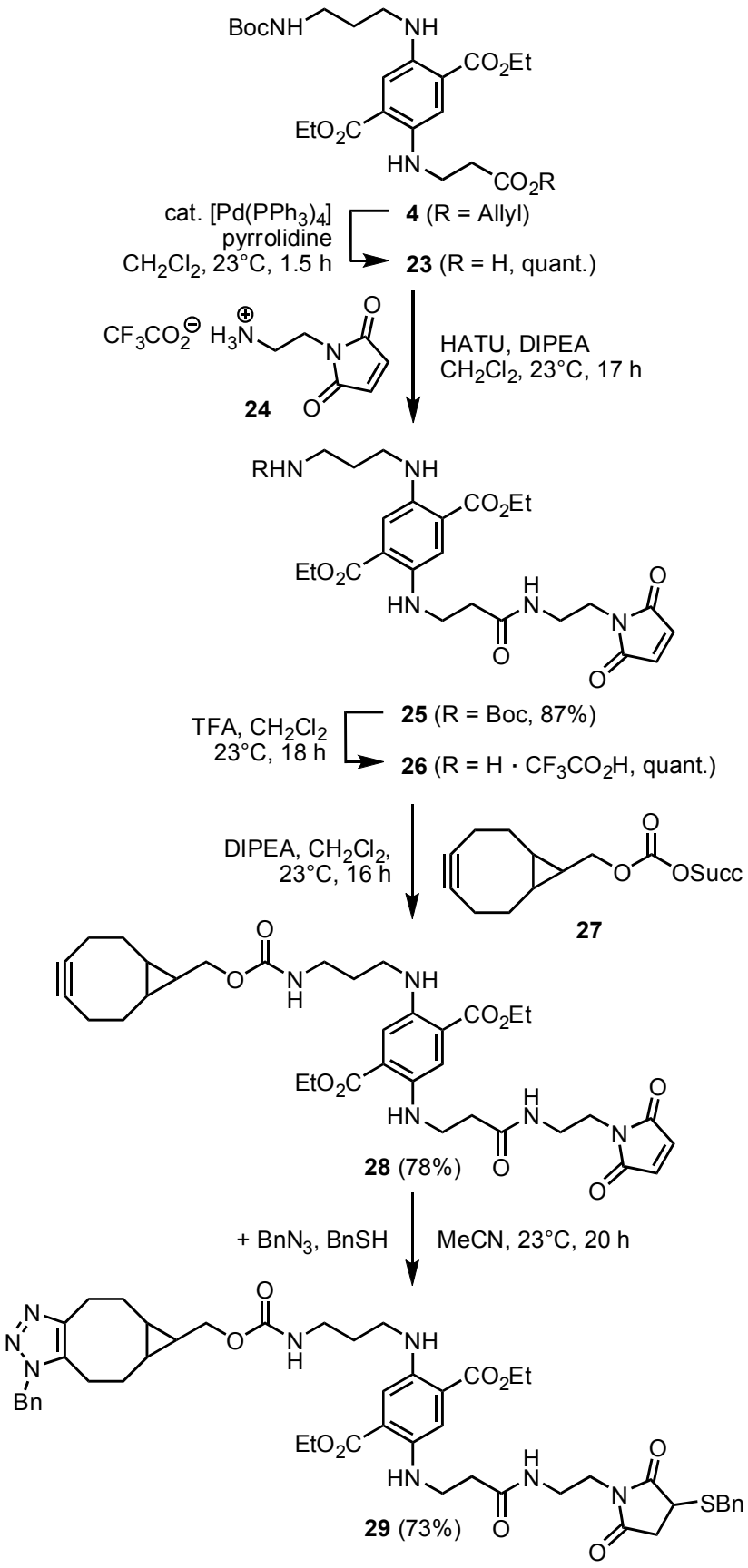
In order to mimic natural photosynthesis and to understand fundamental photoinduced electron and energy transfer processes, many photosynthetic models have been constructed and investigated in the past few decades.[29] Among the energy and electron accepting moieties, fullerene (C_{60}) has become the most promising one due to its unique physical and chemical properties. For example, it can be easily ligated to dyes and other larger molecular entities by cycloaddition reactions. Several dye-fullerene conjugates, so called dyads[15b,30] or triads,[31] have been prepared in the past years. Herein we projected the preparation of the triad **20** by

consecutive coupling of diprotected diamine **3** with retinoic acid and fullerene C_{60}. The installation of a C_{60} unit is conveniently achieved by 1,3-dipolar cycloaddition with an azomethine ylide prepared *in situ* from an aromatic aldehyde and *N*-methylglycine (sarcosine) (so-called Prato-reaction).[32] For this purpose, the allyl carbamate **3** was first deprotected in a palladium catalyzed allylic substitution reaction with morpholine as a scavenger of the allylic cation (Scheme 6).[33] The primary amine **18** was obtained in quantitative yields and further coupled with *para*-formyl benzoic acid using COMU-DIPEA[34] {COMU = 1-[1-(cyano-2-ethoxy-2-oxoethylideneaminooxy)dimethylaminomorpholino]uranium hexafluorophosphate, DIPEA = ethyldiisopropylamine} to yield the aromatic aldehyde **19** in 50% yield (as mentioned in the introduction, the coupling of benzoic acid derivatives sometimes gives not fully satisfying results). Next, the cycloaddition with C_{60} and *N*-methylglycine was accomplished and the chromophore was linked by a *N*-methyl pyrrolidine unit to the fullerene (95% of product **21**). Boc-deprotection was straightforward with TFA in CH_2Cl_2, and finally, retinoic acid was coupled with using now the HATU-DIPEA[35] [HATU = *O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate] protocol furnishing the target compound **20** (75%). The yield over five steps was from compound **3** was 32%. The major problem associated with this sequence was the extraordinary limited solubility of compounds **20**–**22** with a C_{60} moiety and their pronounced tendency to stick irreversibly to glass surfaces, which caused loss of material at every operational step. Therefore, it was important to carry out subsequent reactions always directly after isolation of the product of the previous step. Moreover, due to limited solubility and high molecular weight, signal-to-noise ratios of the carbon NMR spectra a unsatisfying; some signals could only be identified by cross-peaks of respective $^{1}H,^{13}C$-correlations. Signals in the proton spectra also appear very broad with unsatisfactory resolution, presumably due to isomerization of the C-C double bonds of the retinoate and strong associations of the molecules in solution. Anyhow, satisfactory HRMS data from compounds **20**–**22** were obtained in the MALDI and ESI spectra. As expected, the fluorescence of the DAT scaffold was quenched by introduction of the fullerene moiety. The quantum yield decreased from $\Phi = 0.02$ (compound **19**) to $\Phi = 0.001$ in compounds **20**–**22**. The photophysics of this compound is currently under investigation in cooperation with a group specialized in femtosecond spectroscopy.



Scheme 6. Five step synthesis of a retinoic acid-DAT-C_{60} triad **20** from building block **3**.

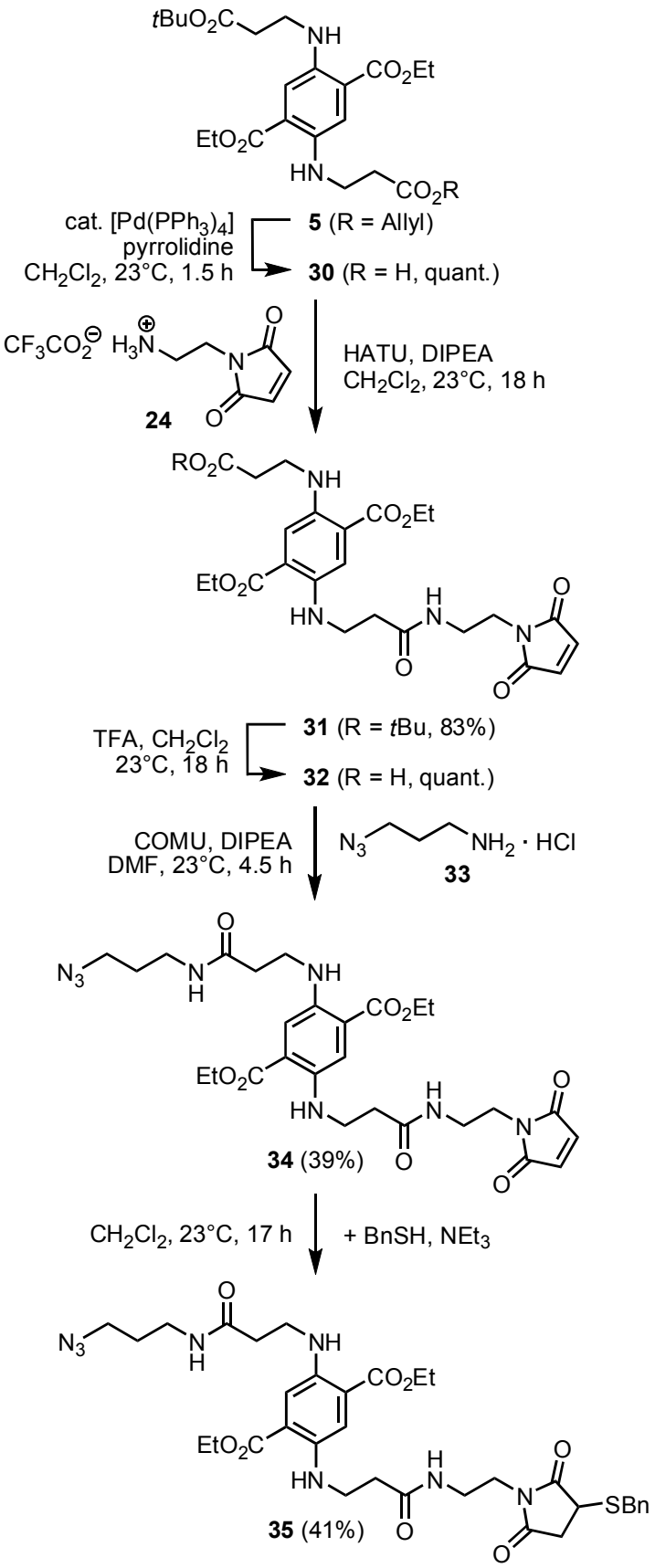
As a second target compound **28**, we aimed at the preparation of an analog of compound **1** with the functional units cyclooctyne and maleimide now bound at one 3-aminopropylamino and one to 2-carboxyethylamino moiety of scaffold **4** (Scheme 7). For this purpose, the allyl ester of compound **4** was deprotected by palladium catalyzed allylic substitution with pyrrolidine as nucleophile[36] to quantitatively furnish the acid **23**, which was subsequently amidated with maleimide building block **24**, which was accessed according to a literature procedure.[37] Compound **25** was obtained in 87% yield. The *tert*-butyl carbamate was then cleaved with TFA in CH_2Cl_2 under release of the primary amino function, which was actually reactive towards the maleimide group. For this reason, it was quantitatively isolated as the trifluoroacetate salt **26**. Finally, the reaction of *N*-hydroxysuccinimidyl active carbonate of cyclooctyne **27**, which was commercially available, in the presence of base gave to target structure **28** in 78% yield. The yield over four steps from compound **4** was 68%. Fortunately, and in contrast to fullerene derivatives **20**–**22**, all products in Scheme 7 are well-behaved organic compounds, which could easily be purified by column chromatography and spectroscopically characterized without problems. As known for other maleimide functional dyes,[14] the fluorescence of compound **28** is quenched by the maleimde moiety (quantum yield $\Phi = 0.005$). Upon reaction with a thiol, the emission was restored. As a model study to prove the "turn on" effect of fluorescence and to show its feasibility in a copper-free Click reaction, compound **28** was reacted with BnSH and BnN_3 as model substrates. Compound **29** was isolated in 73% yield and it showed efficient fluorescence ($\Phi = 0.11$).



Scheme 7. Preparation of fluorescence probe **28** with cyclooctyne and maleimide func-

tional units and its "turn on" by reaction with model azide and thiol BnN_3 and BnSH.

Finally in the last one of three case studies, dicarboxylic acid scaffold **5** was twice functionalized with organo azide and maleimide in the following sequence (Scheme 8): First of all, the allyl ester **5** was again deprotected (product **30** in quantitative yield) and amidated with the maleimide building block **24** to give compound **31** in 83%. The *tert*-butyl ester **31** was then cleaved with TFA (product **32** with quantitative yield) and the carboxylic acid **32** amidated a second time with amino azide reagent **33** (prepared according to a literature procedure)[16] to furnish target structure **34** in 39% yield. The yield over four steps from compound **5** was 32%. Similar to the above case, compound **34** ($\Phi = 0.02$) was also a "turn on" probe: Upon reaction with BnSH, compound **35** was isolated in 41% yield and it showed efficient fluorescence ($\Phi = 0.15$).



Scheme 8. Preparation of bifunctional probe **34** with azide and maleimide functional units

from dicarboxylic acid precursor **5**; "turn on" of fluorescence upon reaction with BnSH.

Spectroscopy. All compounds with diaminoterephthalate chromophore are yellow, orange or red, fluorescent materials (Table 1). As expected for a typical push-pull aromatic system, the absorption and emission wavelengths are sensitively dependent on the electron accepting or donating nature of the substituents at both nitrogen atoms bound to the aromatic ring. The prototypic compound **13** carries two NH_2 groups and shows absorption and emission at 432 nm and 532 nm, resp. (Table 1, entry 1, Stokes shift 100 nm). When introducing a single alkyl residue at only one nitrogen (compounds **16** and **17** in entries 5 and 6), both, absorption and emission receive a bathochromic shift of ca. 20 nm. With a second alkyl residue at the other nitrogen, both bands were shifted further towards the red region by ca. 20 nm. Most products in this study (compounds **3**–**5** and **18**–**35**, entries 7–24) represent this substitution pattern. They show absorption at 466–478 nm and emission band at 564–571 nm, thus, the Stokes shift is in the range of 92–106 nm. On the other hand, lowering electron density by introduction of a carbamate group resulted in hypsochromic shifts: Compound **8** (entry 2) absorbs at 408 nm and emits at 487 nm. This effect is at least partly compensated by introduction of an alkyl group at the remaining NH_2 function of compound **8**: Products **14** and **15** showed absorption at 426–430 nm and emission at 505–511 nm (entries 3 and 4). It is furthermore evident, that compounds with a *N*-Boc group show a Stokes shift of about 80 nm, whereas all others have the Stokes shift around 100 nm.

The quantum yields range between 0.02 and 0.40, apart from compounds **20**–**21** (entries 12–14), **25**–**28** (entries 16–18) and **31** (entry 21), where the fluorescence intensity is quenched by the fullerene or maleimide moiety, resp. The "turn-on" effect of fluorescence by conjugated addition of a thiol to the maleimide moiety is clearly visible for compounds **29** and **35** (entries 19 and 24), where it is higher than for the maleimide precursors **28** and **34**.

Compound **20** with two chromophors, retinoate (RA) and diaminoterephthalate (DAT), shows two absorption bands (335 nm at RA and 474 nm at DAT, entry 14), but only one emission band at 554 nm (from DAT). If irradiated at 335 nm, this compound **20** shows emission also at 554 nm due to a FRET process from RA to DAT moiety.

Table 1. Spectroscopic properties of diaminoterepthalates; solvent CH_2Cl_2.

Entry	Compound	λ_{max} / nm	lg (ε / dm^3 mol^{-1} cm^{-1})	λ_{em} / nm[a]	Φ[b]
1	**13**	432	3.75	532	0.18
2	**8**	408	3.87	487	0.21
3	**14**	430	3.86	511	0.34
4	**15**	426	3.78	505	0.40
5	**16**	455	3.77	553	0.13
6	**17**	452	3.85	551	0.10
7	**3**	478	3.75	570	0.10
8	**4**	474	3.80	567	0.10
9	**5**	472	3.99	564	0.07
10	**18**[c]	469	3.70	571	0.05
11	**19**	475	3.71	570	0.02
12	**21**	475	3.87	567	0.001
13	**22**[c]	448[d]	_[d]	552	_[d]
14	**20**	475, 335	3.49, 4.65	554	0.002
15	**23**[c]	469	3.68	571	0.05
16	**25**	474	3.67	571	0.005
17	**26**[c]	466	3.70	568	0.01
18	**28**	473	3.66	566	0.005
19	**29**	473	3.71	570	0.11
20	**30**[c]	466	3.80	571	0.05
21	**31**	470	3.66	567	0.007
22	**32**[c]	466	3.25	572	0.02
23	**34**	469	3.59	568	0.02
24	**35**	469	3.38	567	0.15

[a] Excitation at λ_{max} of the absorption band. [b] Quantum yields were determined according to the Parker Rees method[38] using rhodamine B in EtOH as standard [λ_{max} = 544 nm, lg(ε / dm^3 mol^{-1} cm^{-1}) = 3.23, λ_{em} = 569 nm, Φ = 0.46].[39] [c] Solvent MeOH. [d] Could not be determined with certainty, because the absorption it is located as a shoulder in a very broad UV-absoption of the C_{60} unit.

CONCLUSION

Diaminoterepthalates are bright and colorful dyes showing fluorescence with high quantum yields. The chromophore defines a molecular scaffold allowing a flexible introduction of side chains with various functional units. Herein we reported on the orthogonal functionalization at the two amino functions with different effector groups, thus, tailored functional materials could be prepared for addressing different applications of Life Sciences and Materials Science. In particular, the scaffold was equipped with protected amino and carboxylate functions in three different manners: (1) with two protected propylamino functions (compound **3**, *N*-Boc and *N*-Alloc), (2) with two protected carboxyethyl groups (compound **5**, *t*Bu and allyl esters) and (3) the mixed case with amino and carboxy functionalization (compound **4**, *N*-Boc and allyl ester). In all three cases, the two protective groups were orthogonally cleavable either with Brønsted acid (*N*-Boc and *t*Bu ester) or palladium catalysis (*N*-Alloc and allyl ester).

Starting from mono-*N*-Boc diethyl diaminoterephthalate **8**, side chains were introduced by reductive amination of the two amino groups with carbaldehydes, which carried the above mentioned orthogonally protected amino and carboxylate functionalities. The sequences gave the intermediate compounds **3**, **4**, and **5** in 58%, 60% and 40% yields, respectively, over three steps. As functional units, retinoic acid and fullerene C_{60} (both for studying electron transfer processes), cyclooctyne and azide (for Click reactions) and maleimide (for ligation to proteins by conjugate addition of cysteine residues) were chosen.

First of all, the *N*-Boc and *N*-Alloc protected compound **3** was elaborated towards a molecular triad equipped with an electron donating (retinoic acid) and accepting (fullerene C_{60}) moiety in order to obtain a molecular model **20** (in 32% yield over five steps) for studying photoinduced electron transfer processes. As a second example, a cyclooctyne-maleimide reactive dye **28** was prepared from the *N*-Boc allyl ester **4** (68% over four steps). This compound was designed to be conjugated by copper-free alkyne-azide Click reaction as well as conjugated addition of a thiol group to the maleimide moiety and could therefore serve as a fluorescent cross-linker for two proteins. A special feature of this compound **28** is the "turn on" effect of fluorescence, since the fluorescence quantum yield was increased by an order of magnitude upon chemical reaction with the molecular target; this feature was proven by reaction of compound **28** with benzyl azide and benzyl mercaptan as two model substrates. Finally, the scaffold **5** with *t*Bu and allyl ester functions was transformed to a reactive dye **34** (32% over four steps) with azide and maleimide moieties again for Click reaction and conjugated addition with a thiol. Just as in the above case, a "turn on" effect by reaction with benzyl mercaptan was observed.

EXPERIMENTAL SECTION

General: Preparative column chromatography was carried out using Merck SiO_2 (35–70 μm, type 60 A) with hexanes (bp. 40–60°C), *tert*-butyl methyl ether (MTBE), EtOAc or MeOH as eluents. TLC was performed on aluminum plates coated with SiO_2 F_{254}. ^{1}H- and ^{13}C-NMR spectra were recorded on 500 MHz and 300 MHz instruments. Multiplicities of carbon signals were determined with DEPT experiments. HRMS spectra were obtained with an EI spectrometer (EI and CI) with sector field analyzer, an ESI spectrometer (pos. mode) with Q-TOF analyzer or in one case with a MALDI spectrometer. IR spectra were recorded on a spectrometer equipped with a diamond ATR unit. UV/Vis spectra were recorded with a Shimadzu UV-1800, fluorescence spectra with a Shimadzu RF-5301PC spectrometer. The following compounds were prepared according to literature procedures: **6**,[17] **7**,[21] **9**,[18] **10**,[24] **12**,[22] **13**,[11] **24**,[37] and **33**.[16] All other starting materials were commercially available. Cyclooctyne derivative **27** was purchased from Synaffix BV (Oss, Netherlands).

***tert*-Butyl Formylacetate (7)**. Under exclusion of air and moisture, a solution of formyl Meldrum's acid (**12**) (15.1 mmol, 2.60 g, 1.0 eq) and *tert*-butyl alcohol (18.1 mmol, 1.34 g, 1.2 eq) in abs. toluene (25 mL) was stirred at 80°C for 1.5 h. All volatile materials were removed under reduced pressure at ambient temperature and the residue was purified by Kugelrohr destillation (70°C, 10 mbar) to yield compound **7** (667 mg, 4.63 mmol, 31%) as a colorless liquid. According to NMR spectroscopy, the compound is a mixture of an aldehyde and an enol tautomer (aldehyde/enol = 0.65/0.35).

^{1}H NMR (500 MHz, $CDCl_3$), aldehyde: δ = 1.50 (s, 9H), 3.30 (d, *J* = 2.6 Hz, 2H), 9.79 (t, *J* = 2.6 Hz, 1H) ppm; enol: δ = 1.50 (s, 9H), 4.89 (d, *J* = 6.0 Hz, 1H), 7.06 (dd, *J* = 12.7 Hz, *J* = 6.1 Hz, 1H), 11.55 (d, *J* = 12.6 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$), aldehyde: δ = 28.2 (3 CH_3), 50.0 (CH_2), 82.7 (C), 163.2 (C), 195.7 (CH) ppm; enol: δ = 28.4 (3 CH_3), 81.4 (C), 95.0 (CH), 163.1 (CH), 172.2 (C) ppm. IR (ATR): λ^{-1} = 2980 (w), 1723 (m), 1657 (w), 1153 (m), 632 (s) cm^{-1}. HRMS (ESI) m/z: [M + Na$^+$] calcd. 167.0684 for $C_7H_{12}O_3Na$; found 167.0690. $C_7H_{12}O_3$ (144.17 g mol^{-1}).

Allyl Formylacetate (10). Under exclusion of air and moisture, a solution of formyl Meldrum's acid (**12**) (10.7 mmol, 1.84 g, 1.0 eq) and allylic alcohol (12.9 mmol, 747 mg, 1.2 eq) in abs. toluene (24 mL) was stirred at 80°C for 1.5 h. All volatile materials were removed under reduced pressure at ambient temperature and the residue was purified by Kugelrohr

destillation (80°C, 3.2 mbar) to yield compound **10** (896 mg, 6.99 mmol, 65%) as a colorless liquid. According to NMR spectroscopy, the compound is a mixture of an aldehyde and two enol tautomers (aldehyde/enol1/enol2 = 0.57/0.26/0.17).

^{1}H NMR (500 MHz, $CDCl_3$), aldehyde: δ = 3.43 (d, *J* = 2.4 Hz, 2H), 4.68 (dt, *J* = 5.9 Hz, *J* = 1.3 Hz, 2H), 5.40–5.25 (m, 2H), 5.99–5.89 (m, 1H), 9.82 (t, *J* = 2.4 Hz, 1H) ppm; enol 1: δ = 4.65 (dt, *J* = 5.7 Hz, *J* = 1.4 Hz, 2H), 5.12 (d, *J* = 6.0 Hz, 1H), 5.40–5.25 (m, 2H), 5.99–5.89 (m, 1H), 7.13 (dd, *J* = 12.6 Hz, *J* = 6.0 Hz, 1H), 11.33 (d, *J* = 12.9 Hz, 1H) ppm; enol 2: δ = 4.78 (dt, *J* = 5.9 Hz, *J* = 1.3 Hz, 2H), 5.40–5.25 (m, 2H), 5.99–5.89 (m, 1H), 8.53 (s, 1H), 12.66 (br.s, 1H), 14.49 (br.s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$), aldehyde: δ = 48.6 (CH_2), 66.2 (CH_2), 119.3 (CH_2), 131.5 (CH), 166.6 (C), 194.9 (CH) ppm; enol 1: δ = 65.0 (CH_2), 93.3 (CH), 118.7 (CH_2), 132.0 (CH), 164.1 (CH), 172.5 (C) ppm; enol 2: δ = 66.7 (CH_2), 97.0 (CH), 120.0 (CH_2), 131.0 (CH), 171.8 (C), 176.8 (CH) ppm. IR (ATR): λ^{-1} = 1718 (vs), 1182 (vs), 988 (s), 932 (s) cm^{-1}. HRMS (CI) m/z: [M + H$^+$] calcd. 129.0546 (for $C_6H_9O_3$; found 129.0550. $C_6H_8O_3$ (128.13 g mol^{-1}).

Diethyl 2,5-Diamino-*N*-(*tert*-butyloxycarbonyl)terephthalate (8). A solution of Boc_2O (4.83 mmol, 1.05 g, 1.0 eq) in CH_2Cl_2 (10 mL) was added dropwise to a cooled solution (ice-water bath) of diethyl 2,5-diaminoterephthalate (**13**) (4.83 mmol, 1.22 g, 1.0 eq) in CH_2Cl_2 (15 mL). The mixture was stirred for 2 d at ambient temperature and then poured into water (50 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The residue was chromatographed (SiO_2, hexanes/EtOAc 5:1 with 1 vol% NEt_3, R_f = 0.22) to yield compound **8** (1.53 g, 4.33 mmol, 90%) as a bright yellow solid, m.p. 121–123°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.1 Hz, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.51 (s, 9H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 5.49 (br.s, 2H), 7.32 (s, 1H), 8.77 (s, 1H), 9.52 (br.s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.3 (CH_3), 14.5 (CH_3), 28.5 (3 CH_3), 61.1 (CH_2), 61.7 (CH_2), 80.1 (C), 116.1 (C), 118.7 (CH), 120.9 (C), 121.9 (CH), 130.8 (C), 144.3 (C), 153.2 (C), 167.2 (C), 167.6 (C) ppm. IR (ATR): λ^{-1} = 1690 (s), 1566 (s), 1525 (s), 1422 (m), 1367 (m), 1266 (m), 1207 (vs), 1154 (vs), 1101 (s), 792 (m) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 352 (11) [M$^+$], 296 (22), 252 (100), 233 (13), 224 (23), 206 (18), 205 (11), 178 (26), 133 (13), 132 (21), 131 (11), 57 (66), 41 (16). HRMS (EI) m/z: [M$^+$] calcd. 352.1629 for $C_{17}H_{24}N_2O_6$; found 352.1629. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 408 nm (3.87); fluorescence (CH_2Cl_2): λ_{em} = 487 nm, λ_{ex} = 408 nm, Φ = 0.21. $C_{17}H_{24}N_2O_6$ (352.34 g mol^{-1}).

Diethyl 2-[3-(Allyloxycarbonylamino)propylamino]-5-(*tert*-butoxycarbonylamino)terephthalate (14). Under exclusion of air and moisture, a solution of compound **9** (4.26 mmol, 670 mg, 1.5 eq) in abs. CH_2Cl_2 (10 mL) was added to a solution of compound **8** (2.84 mmol, 1.00 g, 1.0 eq) in abs. CH_2Cl_2 (10 mL). The mixture was stirred for 15 min at ambient temperature. Subsequently, AcOH (4.26 mmol, 256 mg, 1.5 eq) and $NaBH(OAc)_3$ (4.26 mmol, 903 mg, 1.5 eq) were added and the resulting mixture was stirred for 1 h at ambient temperature and then poured into saturated aqueous $NaHCO_3$-solution (50 mL). After extraction with CH_2Cl_2 (3 x 50 mL), the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was chromatographed (SiO_2, hexanes/EtOAc 4:1, $R_f = 0.25$) to yield compound **14** (1.16 g, 2.34 mmol, 83%) as a yellow solid, m.p. 128–130°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.1 Hz, 3H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.52 (s, 9H), 1.90 (quint, *J* = 6.8 Hz, 2H), 3.24–3.27 (m, 2H), 3.34 (q, *J* = 6.5 Hz, 2H), 4.35 (q, *J* = 7.0 Hz, 2H), 4.39 (q, *J* = 7.0 Hz, 2H), 4.56 (d, *J* = 5.0 Hz, 2H), 4.88 (br.s, 1H), 5.20 (dq *J* = 10.4 Hz, *J* = 1.3 Hz, 1H). 5.29 (dq, *J* = 17.2 Hz, *J* = 1.5 Hz, 1H), 5.91 (ddt, *J* = 17.1 Hz, *J* = 10.9 Hz, *J* = 5.7 Hz, 1H), 7.26 (s, 1H), 7.35 (br.s, 1H), 8.81 (s, 1H), 9.47 (br.s, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.4 (CH_3), 14.5 (CH_3), 28.5 (3 CH_3), 29.6 (CH_2), 39.1 (CH_2), 40.6 (CH_2), 61.1 (CH_2), 61.8 (CH_2), 65.7 (CH_2), 80.1 (C), 112.9 (CH), 115.3 (C), 117.8 (CH_2), 121.4 (CH), 122.9 (C), 129.6 (C), 133.0 (CH), 145.3 (C), 153.3 (C), 156.5 (C), 167.5 (C), 168.1 (C) ppm. IR (ATR): λ^{-1} = 1702 (s), 1677 (s), 1534 (s), 1237 (s), 1211 (vs), 1154 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 493 (17) [M^+], 437 (54), 393 (85), 379 (40), 335 (100), 291 (33), 265 (61), 245 (75), 219 (89), 57 (32). HRMS (EI) m/z: [M^+] calcd. 493.2419 for $C_{24}H_{35}N_3O_8$; found 493.2413. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 430 nm (3.86); fluorescence (CH_2Cl_2): λ_{em} = 511 nm, λ_{ex} = 430 nm, Φ = 0.34. $C_{24}H_{35}N_3O_8$ (493.56 g mol^{-1}).

Diethyl 2-[2-(Allyloxycarbonyl)ethylamino]-5-(*tert*-butoxycarbonylamino)terephthalate (15). A solution of compound **10** (0.43 mmol, 55 mg, 1.5 eq) in CH_2Cl_2 (1 mL) was added under cooling (ice-water bath) to a solution of compound **8** (0.28 mmol, 100 mg, 1.0 eq) in DCM (2 mL). The mixture was stirred for 1 h at 0°C. Then $ZnCl_2$ (0.14 mmol, 19 mg, 0.5 eq) and $NaBH_3CN$ (0.43 mmol, 27 mg, 1.5 eq) were added and the resulting mixture was stirred for 2 d at ambient temperature. It was then poured into water (30 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was chromatographed (SiO_2, hex-

anes/EtOAc 6:1, R_f = 0.46) to yield compound **15** (116 mg, 0.25 mmol, 89%) as a yellow solid, m.p. 123–125°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.1 Hz, 3H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.51 (s, 9H), 2.70 (t, *J* = 6.8 Hz, 2H), 3.55 (q, *J* = 6.7 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 4.62 (d, *J* = 5.8 Hz, 2H), 5.23 (dq, *J* = 10.4 Hz, *J* = 1.3 Hz, 1H), 5.31 (dq, *J* = 17.2 Hz, *J* = 1.4 Hz, 1H), 5.91 (ddt, *J* = 16.2 Hz, *J* = 10.5 Hz, *J* = 5.8 Hz, 1H), 7.30 (s, 1H), 7.50 (t, *J* = 5.6 Hz, 1H), 8.83 (s, 1H), 9.50 (br.s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.3 (CH_3), 14.4 (CH_3), 28.5 (3 CH_3), 34.2 (CH_2), 38.9 (CH_2), 61.1 (CH_2), 61.7 (CH_2), 65.5 (CH_2), 80.1 (C), 112.8 (CH), 115.7 (C), 118.5 (CH_2), 121.2 (C), 122.9 (CH), 129.9 (C), 132.1 (CH), 144.8 (C), 153.2 (C), 167.4 (C), 167.9 (C), 171.5 (C) ppm. IR (ATR): λ^{-1} = 1716 (s), 1687 (s), 1546 (s), 1243 (s), 1223 (vs), 1176 (s), 1155 (s), 1102 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 464 (17) [M^+], 408 (40), 365 (26), 364 (100), 363 (17), 265 (25), 263 (18), 245 (16), 219 (59), 57 (56), 41 (41). HRMS (EI) m/z: [M^+] calcd. 464.2153 for $C_{23}H_{32}N_2O_8$; found 464.2155. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 426 nm (3.78); fluorescence (CH_2Cl_2): λ_{em} = 505 nm, λ_{ex} = 426 nm, Φ = 0.40. $C_{23}H_{32}N_2O_8$ (464.52 g mol^{-1}).

Diethyl 2-[3-(Allyloxycarbonylamino)propylamino]-5-aminoterephthalate (16). TFA (25 mL) was added dropwise to a cooled (ice-water bath) solution of compound **14** (3.28 mmol, 1.62 g) in CH_2Cl_2 (25 mL). The mixture was stirred for 18 h at ambient temperature. All volatile materials were then removed under reduced pressure. The residue was suspended in aqueous KOH solution (10%, 30 mL), the mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The residue was chromatographed (SiO_2, hexanes/EtOAc 2:1 with 1 vol% NEt_3, R_f = 0.20) to yield compound **16** (1.28 g, 3.25 mmol, 99%) as an orange solid, m.p. 135–136°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.1 Hz, 3H), 1.39 (t *J* = 7.1 Hz, 3H), 1.88 (quint, *J* = 6.7 Hz, 2H), 3.21 (t, *J* = 6.6 Hz, 2H), 3.33 (q, *J* = 6.6 Hz, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.55 (d, *J* = 5.2 Hz, 2H), 4.93 (br.s, 1H), 5.04 (br.s, 2H), 5.19 (dq, *J* = 10.5 Hz, *J* = 1.3 Hz, 1H), 5.29 (dq, *J* = 17.1 Hz, *J* = 1.5 Hz, 1H), 5.91 (ddt, *J* = 16.2 Hz, *J* = 10.9 Hz, *J* = 5.6 Hz, 1H), 6.81 (br.s, 1H), 7.19 (s, 1H), 7.34 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.4 (CH_3), 14.5 (CH_3), 29.7 (CH_2), 39.2 (CH_2), 41.1 (CH_2), 60.9 (CH_2), 61.0 (CH_2), 65.6 (CH_2), 113.2 (CH), 117.0 (C), 117.7 (CH_2), 118.1 (C), 119.9 (CH), 133.1 (CH), 139.5 (C), 142.4 (C), 156.4 (C), 167.6 (C), 167.8 (C) ppm. IR (ATR): λ^{-1} = 1692 (s), 1677 (s), 1203 (vs), 1102 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 393 (36) [M^+], 335 (36), 265

(31), 259 (20), 219 (100), 191 (23), 165 (17), 73 (45), 66 (13), 57 (17). HRMS (EI) m/z: [M^+] calcd. 393.1894 for $C_{19}H_{27}N_3O_6$; found 393.1900. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 455 nm (3.77); fluorescence (CH_2Cl_2): λ_{em} = 553 nm, λ_{ex} = 455 nm, Φ = 0.13. $C_{19}H_{27}N_3O_6$ (393.44 g mol^{-1}).

Diethyl 2-[2-(Allyloxycarbonyl)ethylamino]-5-aminoterephthalate (17). TFA (6 mL) was added dropwise to a cooled (ice-water bath) solution of compound **15** (0.95 mmol, 441 mg) in CH_2Cl_2 (6 mL). The mixture was stirred for 16 h at ambient temperature. All volatile materials were then removed under reduced pressure. The residue was suspended in aqueous KOH solution (10%, 10 mL), the mixture was diluted with water (15 mL) and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The residue was chromatographed (SiO_2, hexanes/EtOAc 4:1 with 1 vol% NEt_3, R_f = 0.24) to yield compound **17** (308 mg, 0.85 mmol, 89%) as an orange solid, m.p. 96–98°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.1 Hz, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 2.69 (t, *J* = 6.8 Hz, 2H), 3.51 (t, *J* = 6.1 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 4.61 (dt, *J* = 5.6 Hz, *J* = 1.3 Hz, 2H), 5.06 (br.s, 2H), 5.22 (dq, *J* = 10.4 Hz, *J* = 1.2 Hz, 1H), 5.31 (dq, *J* = 17.2 Hz, *J* = 1.4 Hz, 1H), 5.92 (ddt, *J* = 17.2 Hz, *J* = 10.5 Hz, *J* = 5.8 Hz, 1H), 6.89 (br.s, 1H), 7.24 (s, 1H), 7.34 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.4 (CH_3), 14.5 (CH_3), 34.3 (CH_2), 39.4 (CH_2), 60.7 (CH_2), 60.9 (CH_2), 65.4 (CH_2), 113.2 (CH), 117.4 (C), 117.9 (C), 118.4 (CH_2), 120.0 (CH), 132.2 (CH), 139.7 (C), 141.7 (C), 167.57 (C), 167.58 (C), 171.8 (C) ppm. IR (ATR): λ^{-1} = 1687 (s), 1209 (vs), 1102 (s), 632 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 365 (16), 364 (77) [M^+], 265 (27), 220 (12), 219 (100), 191 (24), 173 (13), 132 (13), 41 (19). HRMS (EI) m/z: [M^+] calcd. 364.1629 for $C_{18}H_{24}N_2O_6$; found 364.1632. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 452 nm (3.85); fluorescence (CH_2Cl_2): λ_{em} = 551 nm, λ_{ex} = 452 nm, Φ = 0.10. $C_{18}H_{24}N_2O_6$ (364.40 g mol^{-1}).

Diethyl 2-[3-(Allyloxycarbonylamino)propylamino]-5-[3-(*tert*-butoxycarbonylamino)-propylamino]terephthalate (3). The transformation was performed in two parallel batches, which were executed as follows: Under exclusion of air and moisture, a solution of compound **6** (0.38 mmol, 66 mg, 1.5 eq) in abs. CH_2Cl_2 (3 mL) was added to a cooled (ice-water bath) solution of compound **16** (0.25 mmol, 100 mg, 1.0 eq) in abs. CH_2Cl_2 (3 mL). The mixture was stirred for 15 min at 0°C. Subsequently $NaBH(OAc)_3$ (0.38 mmol, 81 mg, 1.5 eq) was added and the resulting mixture was stirred for 18 h at ambient temperature. The two batches

were poured together into saturated aqueous $NaHCO_3$-solution (30 mL). After extraction with CH_2Cl_2 (3 x 30 mL), the combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The residue was chromatographed (SiO_2, hexanes/EtOAc 4:1, R_f = 0.23) to yield compound **3** (193 mg, 0.35 mmol, 70%) as a red solid, m.p. 133–134°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.1 Hz, 6 Hz), 1.43 (s, 9 H), 1.86 (quint, *J* = 6.7 Hz, 2H), 1.88 (quint, *J* = 6.7 Hz, 2H), 3.22 (q, *J* = 7.0 Hz, 4H), 3.26 (q, *J* = 6.1 Hz, 2H), 3.33 (q, *J* = 6.5 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 4H), 4.55 (d, *J* = 4.5 Hz, 2H), 4.67 (br.s, 1H), 4.91 (br.s, 1H), 5.19 (dq, *J* = 10.4 Hz, *J* = 1.4 Hz, 1H), 5.29 (dq, *J* = 17.2 Hz, *J* = 1.6 Hz, 1H), 5.91 (ddt, *J* = 17.0 Hz, *J* = 10.6 Hz, *J* = 5.6 Hz, 1H), 6.79 (br.s, 2H), 7.28 (s, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.5 (2 CH_3), 28.5 (3 CH_3), 29.7 (CH_2), 29.9 (CH_2), 38.7 (CH_2), 39.2 (CH_2), 41.3 (CH_2), 41.4 (CH_2), 61.0 (2 CH_2), 65.6 (CH_2), 79.3 (C), 87.4 (C), 114.3 (2 CH), 117.2 (C), 117.3 (C), 117.7 (CH_2), 133.1 (CH), 141.2 (C), 141.3 (C), 156.1 (C), 156.5 (C), 168.0 (C) ppm. IR (ATR): λ^{-1} = 1675 (s), 1548 (s), 1194 (vs), 1164 (s), 1110 (s), 1088 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 550 (100) [M^+], 494 (92), 476 (14), 450 (44), 406 (10), 360 (14), 302 (32), 276 (9), 219 (9), 142 (9), 57 (13). HRMS (EI) m/z: [M^+] calcd. 550.2997 for $C_{27}H_{42}N_4O_8$; found 550.3004. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 478 nm (3.75); fluorescence (CH_2Cl_2): λ_{em} = 570 nm, λ_{ex} = 478 nm, Φ = 0.10. $C_{27}H_{42}N_4O_8$ (550.65 g mol^{-1}).

Diethyl 2-[2-(Allyloxycarbonyl)ethylamino]-5-[3-(*tert*-butoxycarbonylamino)propylamino]terephthalate (4). Under exclusion of air and moisture, a solution of compound **6** (0.49 mmol, 86 mg, 1.5 eq) in abs. CH_2Cl_2 (3 mL) was added to a cooled (ice-water bath) solution of compound **17** (0.33 mmol, 119 mg, 1.0 eq) in abs. CH_2Cl_2 (3 mL). The mixture was stirred for 15 min at 0°C. Subsequently, $NaBH(OAc)_3$ (0.49 mmol, 104 mg, 1.5 eq) was added and the resulting mixture was stirred for 18 h at ambient temperature. It was then poured into saturated aqueous $NaHCO_3$-solution (15 mL). After extraction with CH_2Cl_2 (3 x 15 mL), the combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated. The residue was chromatographed (SiO_2, hexanes/EtOAc 4:1, R_f = 0.46) to yield compound **4** (131 mg, 0.25 mmol, 76%) as a red solid, m.p. 94–96°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.1 Hz, 6H), 1.42 (s, 9H), 1.84 (quint, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.8 Hz, 2H), 3.20 (t, *J* = 6.7 Hz, 2H), 3.25 (q, *J* = 6.1 Hz, 2H), 3.50 (t, *J* = 6.8 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 4H), 4.60 (d, *J* = 5.7 Hz, 2H), 4.69 (br.s, 1H), 5.21 (dd, *J* = 10.4 Hz, *J* = 1.1 Hz, 1H), 5.30 (dd, *J* = 17.2 Hz, *J* = 1.3 Hz, 1H), 5.91 (ddt, *J* = 17.1 Hz, *J* = 10.6 Hz, *J* = 5.7 Hz, 1H), 6.86 (br.s, 2H), 7.27 (s, 1H), 7.31 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.4 (2 CH_3), 28.5 (3 CH_3), 29.9 (CH_2), 34.4 (CH_2), 38.7 (CH_2), 39.5

(CH_2), 41.2 (CH_2), 60.86 (CH_2), 60.90 (CH_2), 65.4 (CH_2), 79.2 (C), 114.25 (CH), 114.27 (CH), 116.9 (C), 117.7 (C), 118.3 (CH_2), 132.2 (CH), 140.5 (C), 141.6 (C), 156.1 (C), 167.8 (C), 168.0 (C), 171.7 (C) ppm. IR (ATR): λ^{-1} = 1674 (s), 1514 (s), 1196 (s), 1164 (vs), 1106 (s), 1086 (s), 787 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 521 (100) [M^+], 465 (97), 448 (10), 421 (16), 377 (9), 331 (22), 57 (14). HRMS (EI) m/z: [M^+] calcd. 521.2732 for $C_{26}H_{39}N_3O_8$; found 521.2729. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 474 nm (3.80); fluorescence (CH_2Cl_2): λ_{em} = 567 nm, λ_{ex} = 474 nm, Φ = 0.10. $C_{26}H_{39}N_3O_8$ (521.61 g mol^{-1}).

Diethyl 2-[2-(Allyloxycarbonyl)ethylamino]-5-[2-(*tert*-butoxycarbonyl)ethylamino]terephthalate (5). A solution of compound **7** (0.74 mmol, 106 mg, 1.5 eq) in CH_2Cl_2 (3 mL) was added under cooling (ice-water bath) to a solution of compound **17** (0.49 mmol, 186 mg, 1.0 eq) in CH_2Cl_2 (2 mL). After stirring for 15 min at 0°C $ZnCl_2$ (0.25 mmol, 33 mg, 0.5 eq) was added and it was stirred for 15 min at 0°C. Subsequently, $NaBH_3CN$ (0.74 mmol, 46 mg, 1.5 eq) was added and the resulting mixture was stirred for 2 d at ambient temperature. It was then poured into water (10 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was chromatographed (SiO_2, hexanes/EtOAc 4:1, R_f = 0.33) to yield compound **5** (122 mg, 0.25 mmol, 51%) as a red solid, m.p. 59–61°C.
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.361 (t, *J* = 7.1 Hz, 3H), 1.363 (t, *J* = 7.1 Hz, 3H), 1.44 (s, 9H), 2.55 (t, *J* = 6.8 Hz, 2H), 2.67 (t, *J* = 6.8 Hz, 2H), 3.44 (t, *J* = 6.6 Hz, 2H), 3.50 (t, *J* = 6.7 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 4H), 4.59 (dt, *J* = 5.7 Hz, *J* = 1.3 Hz, 2H), 5.20 (dq, *J* = 10.5 Hz, *J* = 1.3 Hz, 1H), 5.29 (dq, *J* = 17.2 Hz, *J* = 1.5 Hz, 1H), 5.90 (ddt, *J* = 17.0 Hz, *J* = 10.6 Hz, *J* = 5.7 Hz, 1H), 6.94 (br.s, 2H), 7.30 (s, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.4 (2 CH_3), 28.1 (3 CH_3), 34.3 (CH_2), 35.6 (CH_2), 39.4 (CH_2), 39.6 (CH_2), 60.8 (2 CH_2), 65.4 (CH_2), 80.8 (C), 114.2 (CH), 114.3 (CH), 117.3 (C), 117.5 (C), 118.3 (CH_2), 132.2 (CH), 140.7 (C), 141.0 (C), 167.7 (C), 167.8 (C), 171.4 (C), 171.7 (C) ppm. IR (ATR): λ^{-1} = 1727 (s), 1676 (s), 1528 (s), 1206 (vs), 1154 (vs), 1118 (s), 1107 (s), 1094 (s), 1018 (s), 788 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 493 (13), 492 (44) [M^+], 437 (22), 436 (100), 377 (14), 331 (21), 291 (27), 245 (10), 231 (13), 199 (9), 173 (10), 57 (22). HRMS (EI) m/z: [M^+] calcd. 492.2466 for $C_{25}H_{36}N_2O_8$; found 492.2472. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 472 nm (3.99); fluorescence (CH_2Cl_2): λ_{em} = 564 nm, λ_{ex} = 472 nm, Φ = 0.07. $C_{25}H_{36}N_2O_8$ (492.57 g mol^{-1}).

Diethyl 2-[3-(Aminopropyl)amino]-5-[3-(*tert*-butoxycarbonylamino)propylamino]terephthalate (18). Morpholine (1.35 mmol, 118 mg, 5.0 eq) was added to a solution of com-

pound **3** (0.27 mmol, 146 mg, 1.0 eq) in abs. CH_2Cl_2 (4 mL). After degassing the mixture, $Pd(PPh_3)_4$ (13 µmol, 15 mg, 0.05 eq) was added under a nitrogen atmosphere and the mixture was stirred for 1.5 h at ambient temperature. Charcoal (spatula tip, ca. 2 mg) was added and the mixture was stirred for additional 5 min. After filtration, all volatile materials were evaporated. The residue was chromatographed [SiO_2, EtOAc → EtOAc/MeOH 6:1 with 1 vol% NEt_3, R_f(EtOAc/MeOH 6:1) = 0.15] to yield compound **18** (125 mg, 0.27 mmol, quant.) as a red solid, m.p. 160–161°C.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.38 (t, *J* = 7.1 Hz, 6H), 1.43 (s, 9H), 1.80 (quint, *J* = 6.7 Hz, 2H), 2.03 (quint, *J* = 6.8 Hz, 2H), 3.07–3.10 (m, 2H), 3.16 (t, *J* = 6.4 Hz, 2H), 3.18 (t, *J* = 6.6 Hz, 2H), 3.28–3.31 (m, 2H), 4.34 (q, *J* = 7.1 Hz, 4H), 7.30 (s, 1H), 7.32 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, CD_3OD): δ = 14.7 (2 CH_3), 28.3 (CH_2), 28.8 (3 CH_3), 30.7 (CH_2), 39.0 (CH_2), 39.2 (CH_2), 41.6 (CH_2), 42.1 (CH_2), 61.96 (CH_2), 61.99 (CH_2), 79.9 (C), 115.3 (CH), 115.4 (CH), 118.1 (C), 118.8 (C), 141.7 (C), 142.7 (C), 158.5 (C), 168.9 (C), 169.0 (C) ppm. IR (ATR): λ^{-1} = 1674 (s), 1199 (vs), 1176 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 466 (100) [M^+], 410 (71), 393 (9), 366 (19), 322 (14), 276 (15), 219 (9), 59 (9). HRMS (EI) m/z: [M^+] calcd. 466.2786 for $C_{23}H_{38}N_4O_6$; found 466.2789. UV/Vis (MeOH): λ_{max} (lg ε) = 469 nm (3.70); fluorescence (MeOH): λ_{em} = 571 nm, λ_{ex} = 469 nm, Φ = 0.05. $C_{23}H_{38}N_4O_6$ (466.58 g mol^{-1}).

Diethyl 2-[3-(*tert*-butoxycarbonylamino)propylamino]-5-[3-(4-formylbenzamido)propylamino]terephthalate (19). COMU (0.27 mmol, 116 mg, 1.2 eq) was added to a solution of 4-carboxybenzaldehyde (0.27 mmol, 41 mg, 1.2 eq) and DIPEA (0.27 mmol, 35 mg, 1.2 eq) in CH_2Cl_2 (2 mL). After stirring the mixture for 30 min at ambient temperature, a solution of compound **18** (0.23 mmol, 105 mg, 1.0 eq) and DIPEA (23 mmol, 30 mg, 1.0 eq) was added and the mixture was stirred for 17 h at ambient temperature. The mixture was then poured into water (25 mL) and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried over $MgSO_4$, filtered and all volatile materials were evaporated. The residue was chromatographed (SiO_2, hexanes/EtOAc 1:1, R_f = 0.28) to yield compound **19** (67 mg, 0.11 mmol, 50%) as a red solid, m.p. 125–127°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.36 (t, *J* = 7.1 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.42 (s, 9H), 1.85 (quint, *J* = 6.6 Hz, 2H), 2.02 (quint, *J* = 6.2 Hz, 2H), 3.20 (t, *J* = 6.7 Hz, 2H), 3.26 (q, *J* = 6.1 Hz, 2H), 3.31 (t, *J* = 6.1 Hz, 2H), 3.64 (q, *J* = 6.1 Hz, 2H), 4.30 (q, *J* = 7.2 Hz, 2H), 4.31 (q, *J* = 7.2 Hz, 2H), 4.72 (br.s, 1H), 6.80 (br.s, 2H), 6.91–6.94 (m, 1H), 7.26 (s, 1H), 7.30 (s, 1H), 7.85–7.89 (m, 4H), 10.03 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.4 (2

CH_3), 28.5 (3 CH_3), 28.9 (CH_2), 29.9 (CH_2), 38.7 (CH_2), 39.2 (CH_2), 41.2 (CH_2), 42.2 (CH_2), 61.03 (CH_2), 61.04 (CH_2), 79.3 (C), 114.2 (CH), 114.4 (CH), 116.9 (C), 117.5 (C), 127.8 (2 CH), 129.8 (2 CH), 138.1 (C), 139.9 (C), 140.9 (C), 141.7 (C), 156.1 (C), 166.5 (C), 167.9 (C), 168.1 (C), 191.7 (CH) ppm. IR (ATR): λ^{-1} = 1673 (s), 1524 (s), 1203 (vs), 1171 (s), 1111 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 598 (52) [M^+], 542 (40), 524 (100), 480 (16), 374 (12), 362 (16), 328 (22), 316 (36), 302 (55), 190 (16), 133 (36), 59 (14). HRMS (EI) m/z: [M^+] calcd. 598.2997 for $C_{31}H_{42}N_4O_8$; found 598.3011. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 475 nm (3.71); fluorescence (CH_2Cl_2): λ_{em} = 570 nm, λ_{ex} = 475 nm, Φ = 0.02. $C_{31}H_{42}N_4O_8$ (598.70 g mol^{-1}).

Diethyl 2-[3-(*tert*-butoxycarbonylamino)propylamino]-5-{3-[4-(1-methyl-2,3,4,5-tetrahydro[60]fullero[1',2':3,4]pyrrol-2-yl)benzamido]propylamino}terephthalate (21). Under exclusion of air and moisture, fullerene-C_{60} (127 µmol, 84 mg, 2.0 eq) and sarcosine (580 µmol, 52 mg, 10.0 eq) were added to a solution of compound **19** (58 µmol, 35 mg, 1.0 eq) in abs. toluene (100 mL). The mixture was heated to reflux for 17 h. Subsequently, the solvent was evaporated and the residue was chromatographed [SiO_2, hexanes/EtOAc 1:1 → EtOAc, R_f = 0.50 (hexanes/EtOAc 1:1)]. For further purification, it was recrystallized (CH_2Cl_2/hexanes 5:1, 200 mL) to yield compound **21** (75 mg, 557 µmol, 95%) as a brownish-black solid, m.p. > 300°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.1 Hz, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.44 (s, 9H), 1.86 (quint, *J* = 6.6 Hz, 2H), 2.01 (quint, *J* = 6.4 Hz, 2H), 2.79 (s, 3H), 3.21 (t, *J* = 6.1 Hz, 2H), 3.25–3.31 (m, 4H), 3.59–6.64 (m, 2H), 4.27 (d, *J* = 9.5 Hz, 1H), 4.32 (q, *J* = 7.2 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.66 (br.s, 1H), 4.97 (s, 1H), 4.99 (d, *J* = 9.5 Hz, 1H), 6.60 (br.s, 1H), 7.29 (s, 1H), 7.34 (s, 1H), 7.83–7.94 (m, 4H) ppm; signals for two NH-protons are not observed. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.52 (CH_3), 14.54 (CH_3), 28.6 (3 CH_3), 29.2 (CH_2), 29.8 (CH_2), 38.7 (CH_2), 38.8 (CH_2), 40.1 (CH_3), 41.4 (CH_2), 42.3 (CH_2), 61.0 (CH_2), 61.1 (CH_2), 69.2 (C), 70.2 (CH_2), 79.4 (C), 83.3 (CH), 114.4 (CH), 114.9 (CH), 117.1 (C), 117.7 (C), 127.5 (2 CH), 129.6 (2 CH), 134.8 (C), 135.8 (C), 136.1 (C), 136.6 (C), 137.1 (C), 139.7 (C), 140.1 (C), 140.3 (C), 140.4 (C), 140.8 (C), 141.7 (C), 141.8 (C), 141.97 (C), 142.00 (C), 142.12 (C), 142.16 (C), 142.19 (C), 142.24 (C), 142.27 (C), 142.31 (C), 142.4 (2 C), 142.68 (C), 142.73 (2 C), 142.9 (C), 143.15 (C), 143.24 (2 C), 143.3 (C), 144.5 (C), 144.6 (C), 144.7 (C), 144.9 (C), 145.3 (C), 145.37 (C), 145.42 (2 C), 145.49 (2 C), 145.54 (C), 145.66 (C), 145.69 (2 C), 145.9 (C), 146.0 (C), 146.09 (C), 146.10 (C), 146.26 (C), 146.30 (C), 146.33 (C), 146.37 (C), 146.41 (C), 146.46 (C), 146.52 (C), 146.7 (C), 147.5 (2 C), 152.9

(C), 153.1 (C), 154.0 (C), 156.1 (C), 156.2 (C), 167.4 (C), 167.9 (C), 168.1 (C) ppm. The signal of one quaternary bridgehead carbon atom is hidden by the $CDCl_3$ triplet, but it can be detected at ca. 77 ppm by a $^3J(^1H,^{13}C)$ crosspeak in the HMBC spectrum to the pyrrolidine proton at 4.97 ppm. IR (ATR): λ^{-1} = 1682 (s), 1531 (s), 1213 (s), 1192 (vs), 1167 (s), 1092 (s) cm^{-1}. HRMS (ESI) m/z: [M + H^+] calcd. 1346.3548 for $C_{93}H_{48}N_5O_7$; found 1346.3539. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 475 nm (3.87); fluorescence (CH_2Cl_2): λ_{em} = 567 nm, λ_{ex} = 475 nm, Φ = 0.001. $C_{93}H_{47}N_5O_7$ (1346.43 g cm^{-1}).

Diethyl 2-[3-(aminopropyl)amino]-5-{3-[4-(1-methyl-2,3,4,5-tetrahydro[60]fullero-[1',2':3,4]pyrrol-2-yl)benzamido]propylamino}terephthalate (22). TFA (5 mL) was added dropwise to a cooled (ice-water bath) solution of compound **21** (39 μmol, 52 mg) in CH_2Cl_2 (5 mL). The mixture was stirred for 18 h at ambient temperature. All volatile materials were then removed under reduced pressure. The residue was suspended in a mixture of aqueous KOH solution (10%, 20 mL) and CH_2Cl_2 (25 mL). The undissolved material was dissolved by first stirring the mixture at 40°C for 5 min in then using an ultrasonic bath (ambient temperature, 5 min). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 25 mL). The combined organic layers were dried over a small amount (400 mg) of $MgSO_4$, filtered and the solvent was evaporated to yield compound **21** (44 mg, 35 μmol, 91%) as a brownish-black solid, m.p. > 300°C.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.38 (q, *J* = 7.1 Hz, 6H), 1.83 (quint, *J* = 6.8 Hz, 2H), 1.97–2.04 (m, 2H), 2.79 (s, 3H), 2.87 (t, *J* = 7.0 Hz, 2H), 3.22–3.32 (m, 4H), 3.62 (q, *J* = 6.1 Hz, 2H), 4.26–4.37 (m, 5H), 4.97 (s, 1H), 4.99 (d, *J* = 9.4 Hz, 1H), 6.55 (br.s, 1H), 7.00 (br.s, 2H), 7.31 (s, 2H), 7.81–7.90 (m, 4H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.5 (2 CH_3), 29.3 (CH_2), 33.3 (CH_2), 38.8 (CH_2), 40.1 (CH_2), 40.2 (CH_3), 41.4 (CH_2), 42.0 (CH_2), 60.95 (CH_2), 61.03 (CH_2), 69.2 (C), 70.2 (CH_2), 83.3 (CH), 114.3 (CH), 114.4 (CH), 116.8 (C), 117.5 (C), 127.5 (2 CH), 129.6 (CH), 129.7 (CH), 134.8 (C), 135.1 (C), 136.1 (C), 136.6 (C), 137.0 (C), 139.7 (C), 140.0 (C), 140.3 (C), 140.8 (C), 140.9 (C), 141.7 (C), 141.8 (2 C), 141.96 (C), 141.98 (C), 142.15 (C), 142.17 (C), 142.23 (C), 142.26 (C), 142.29 (C), 142.4 (2 C), 142.68 (C), 142.72 (2 C), 142.84 (C), 143.1 (C), 143.2 (2 C), 143.3 (C), 144.48 (C), 144.54 (C), 144.7 (C), 144.8 (C), 145.32 (C), 145.35 (C), 145.41 (2 C), 145.48 (2 C), 145.53 (C), 145.65 (C), 145.68 (2 C), 145.9 (C), 146.0 (C), 146.1 (2 C), 146.25 (C), 146.29 (C), 146.31 (C), 146.36 (C), 146.40 (C), 146.45 (C), 146.51 (C), 146.7 (C), 147.5 (2 C), 152.9 (C), 153.1 (C), 154.0 (C), 156.2 (C), 167.4 (C), 168.03 (C), 168.14 (C) ppm. The signal of one quaternary bridgehead carbon atom is hidden by the $CDCl_3$ triplet, but it can be detected at ca.

77 ppm by a $^{3}J(^{1}H,^{13}C)$ crosspeak in the HMBC spectrum to the pyrrolidine proton at 4.97 ppm. IR (ATR): λ^{-1} = 1668 (s), 1158 (s), 1131 (vs) cm^{-1}. HRMS (ESI) m/z: $[M + H^+]$ calcd. 1246.3024 for $C_{88}H_{40}N_5O_5$; 1246.3024 found. UV/Vis (MeOH): λ_{max} = 448 nm; fluorescence (MeOH): λ_{em} = 552 nm, λ_{ex} = 448 nm. Since the absorption band is located as a shoulder in a very broad UV-absorption of the C_{60} unit, the absorption coefficient ε and the calculated quantum yield Φ could not be determined with certainty. $C_{88}H_{39}N_5O_5$ (1246.31 g mol^{-1}).

Diethyl 2-[3-(*N*-retinoylamino)propylamino]-5-{3-[4-(1-methyl-2,3,4,5-tetrahydro[60]fullero[1',2':3,4]pyrrol-2-yl)benzamido]propylamino}terephthalate (20). HATU (36 µmol, 14 mg, 2.5 eq) was added to a solution of retinoic acid (36 µmol, 13 mg, 2.5 eq) and DIPEA (49 µmol, 6.3 mg, 3.5 eq) in CH_2Cl_2 (5 mL). The mixture was stirred for 1.5 h at ambient temperature and was then added to suspension of compound **22** (14 µmol, 18 mg, 1.0 eq) in CH_2Cl_2 (5 mL). The mixture was stirred for 18 h at ambient temperature. Subsequently, the mixture was diluted with CH_2Cl_2 (40 mL) and washed with saturated aqueous $NaHCO_3$ solution (4 x 50 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated. The residue was chromatographed (SiO_2, hexanes/EtOAc 1:1 → EtOAc → CH_2Cl_2/MeOH 20:1) to yield compound **20** in two fractions [(1): R_f(CH_2Cl_2/MeOH 20:1) = 0.77, 6.5 µmol, 10.0 mg, 47%; (2): R_f(CH_2Cl_2/MeOH 20:1) = 0.46, 3.9 µmol, 6.0 mg, 28%] as a brownish black solid, m.p. 220°C (dec.).

Due to the high molecular mass, the low solubility and isomerization of the double bonds of the retinoate residue, it was not possible to get satisfactory NMR-spectra. IR (ATR): λ^{-1} = 3374 (br), 1713 (s), 1693 (s), 1660 (s), 1651 (s), 1097 (vs), 1017 (s) cm^{-1}. MS (MALDI, DCTB), *m/z* (%): 1527 (100) $[M^+]$. HRMS (ESI) m/z: $[M + H^+]$ calcd 1528.5008 for $C_{108}H_{66}N_5O_6$; found 1528.4966. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 475 nm (3.49; DAT), 335 nm (4.65; retinoate); fluorescence (CH_2Cl_2): λ_{em} = 554 nm, λ_{ex} = 475 nm, Φ = 0.002. $C_{108}H_{65}N_5O_6$ (1528.74 g mol^{-1}).

Diethyl 2-[3-(*tert*-butoxycarbonylamino)propylamino]-5-(2-carboxyethylamino)terephthalate (23). Under exclusion of air and moisture, pyrrolidine (1.0 mmol, 71 mg, 5.0 eq) was added to a solution of compound **4** (200 µmol, 106 mg, 1.0 eq), in abs. CH_2Cl_2 (7 mL). After degassing the mixture, $Pd(PPh_3)_4$ (10 µmol, 12 mg, 0.05 eq) was added under an nitrogen atmosphere and the mixture was stirred for 1.5 h at ambient temperature. Charcoal (spatula tip, ca. 2 mg) was added and the mixture was stirred for additional 5 min. After filtration, all volatile materials were evaporated. The residue was chromatographed [SiO_2, EtOAc →

EtOAc/MeOH 6:1, R_f(EtOAc/MeOH 6:1) = 0.38] to yield compound **23** (102 mg, 0.21 mmol, quant.) as a red solid, m.p. 135–137°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.377 (t, *J* = 7.1 Hz, 3H), 1.382 (t, *J* = 7.1 Hz, 3H), 1.44 (s, 9H), 1.85 (quint, *J* = 6.7 Hz, 2H), 2.69 (t, *J* = 6.7 Hz, 2H), 3.21 (t, *J* = 6.7 Hz, 2H), 3.24–3.28 (m, 2H), 3.50 (t, *J* = 6.4 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.70 (br.s, 1H), 6.31 (br.s, 2H), 7.28 (s, 1H), 7.33 (s, 1H) ppm, the signal for the carboxylate H is not observed. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.5 (2 CH_3), 28.5 (3 CH_3), 29.9 (CH_2), 34.3 (CH_2), 38.8 (CH_2), 39.6 (CH_2), 41.3 (CH_2), 60.96 (CH_2), 61.04 (CH_2), 79.4 (C), 114.4 (CH), 114.6 (CH), 116.9 (C), 118.1 (C), 140.4 (C), 141.8 (C), 156.2 (C), 167.9 (C), 168.0 (C), 176.6 (C) ppm. IR (ATR): λ^{-1} = 1674 (s), 1196 (vs), 1226 (s), 1109 (s), 817 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 481 (89) [M^+], 425 (100), 408 (11), 381 (16), 337 (18), 305 (8), 291 (42), 145 (6), 219 (8), 57 (15). HRMS (EI) m/z: [M^+] calcd. 481.2419 for $C_{23}H_{35}N_3O_8$; found 481.2417. UV/Vis (MeOH): λ_{max} (lg ε) = 469 nm (3.68); fluorescence (MeOH): λ_{em} = 571 nm, λ_{ex} = 469 nm, Φ = 0.05. $C_{23}H_{35}N_3O_8$ (481.55 g mol^{-1}).

Diethyl 2-[3-(*tert*-butoxycarbonylamino)propylamino]-5-{3-[2-(2,5-dihydro-1*H*-pyrrol-1-yl)ethylamino]-3-oxopropylamino}terephthalate (25). HATU (0.24 mmol, 91 mg, 1.2 eq), DIPEA (0.44 mmol, 57 mg, 2.2 eq) and maleimide building block **24** (0.24 mmol, 61 mg, 1.2 eq) were added to a suspension of compound **23** (0.20 mmol, 96 mg, 1.0 eq) in CH_2Cl_2 (9 mL). The mixture was stirred for 17 h at ambient temperature. Subsequently, it was diluted with CH_2Cl_2 (15 mL) and washed with saturated aqueous $NaHCO_3$ solution (4 x 25 mL). The organic layer was dried over $MgSO_4$, filtered and all volatile materials were evaporated. The residue was chromatographed (SiO_2, EtOAc/hexanes 2:1, R_f = 0.19) to yield compound **25** (105 mg, 017 mmol, 87%) as a red solid, m.p. 111–112°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.1 Hz, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.43 (s, 9H), 1.85 (quint, *J* = 6.7 Hz, 2H), 2.47 (t, *J* = 6.5 Hz, 2H), 3.20 (t, *J* = 6.0 Hz, 2H), 3.26 (q, *J* = 6.5 Hz, 2H), 3.43–3.47 (m, 4H), 3.66–3.68 (m, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.65 (br.s, 1H), 6.20 (t, *J* = 5.1 Hz, 1H), 6.64 (s, 2H), 6.80 (br.s, 2H), 7.26 (s, 1H), 7.32 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.5 (2 CH_3), 28.5 (3 CH_3), 29.9 (CH_2), 36.4 (CH_2), 37.7 (CH_2), 38.7 (CH_2), 38.9 (CH_2), 40.2 (CH_2), 41.3 (CH_2), 61.0 (2 CH), 79.3 (C), 114.2 (CH), 114.7 (CH), 116.9 (C), 118.0 (C), 134.2 (2 CH), 140.6 (C), 141.8 (C), 156.1 (C), 167.9 (C), 168.0 (C), 171.0 (2 C), 171.8 (C) ppm. IR (ATR): λ^{-1} = 1693 (s), 1677 (s), 1662 (s), 1528 (s), 1202 (vs), 1217 (vs), 1173 (s), 1105 (s), cm^{-1}. MS (EI, 70 eV), *m/z* (%): 603 (20) [M^+], 547 (21), 529 (11), 503 (13), 413 (8), 316 (8), 302 (14), 245 (8), 231

(10), 124 (9), 110 (16), 82 (7), 59 (90). HRMS (EI) m/z: [M^+] calcd. 603.2899 for $C_{29}H_{41}N_5O_9^+$; found 603.2902. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 474 nm (3.67); fluorescence (CH_2Cl_2): λ_{em} = 571 nm, λ_{ex} = 474 nm, Φ = 0.005. $C_{29}H_{41}N_5O_9$ (603.67 g mol^{-1}).

Diethyl 2-(3-ammoniopropylamino)-5-{3-[2-(2,5-dihydro-1*H*-pyrrol-1-yl)ethylamino]-3-oxopropylamino}terephthalate trifluoroacetate (26). TFA (5 mL) was added dropwise to a cooled (ice-water bath) solution of compound **25** (260 μmol, 157 mg) in CH_2Cl_2 (5 mL). The mixture was stirred for 16 h at ambient temperature. MTBE (10 mL) and hexanes (10 mL) were added. The red precipitate was isolated by filtration and washed with cold MTBE (40 mL). It was redissolved in MeOH (15 mL), filtered and the solvent was evaporated to yield compound **26** (176 mg, 28 mmol, quant.) as a red resin.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.40 (t, *J* = 7.1 Hz, 3H), 1.41 (t, *J* = 7.1 Hz, 3H), 2.13 (quint, *J* = 7.3 Hz, 2H), 2.59 (t, *J* = 6.6 Hz, 2H), 3.12 (t, *J* = 7.3 Hz, 2H), 3.34–3.37 (m, 2H), 3.46 (t, *J* = 6.6 Hz, 2H), 3.57 (t, *J* = 5.5 Hz, 2H), 3.62 (t, *J* = 5.7 Hz, 2H), 4.41 (q, *J* = 7.0 Hz, 2H), 4.42 (q, *J* = 7.0 Hz, 2H), 6.78 (s, 2H), 7.68 (s, 1H), 7.80 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, CD_3OD): δ = 14.4 (2 CH_3), 27.1 (CH_2), 34.2 (CH_2), 38.1 (CH_2), 38.3 (CH_2), 39.0 (CH_2), 44.4 (CH_2), 45.3 (CH_2), 63.0 (CH_2), 63.2 (CH_2), 117.7 (q, *J* = 292 Hz, CF_3), 120.1 (CH), 122.4 (CH), 122.5 (2 C), 135.4 (2 CH), 136.0 (C), 140.5 (C), 162.2 (q, *J* = 35 Hz, C), 167.2 (C), 167.5 (C), 172.5 (2 C), 173.1 (C) ppm. IR (ATR): λ^{-1} = 1674 (s), 1200 (s), 1174 (vs), 1142 (vs), 1106 (s) cm^{-1}. HRMS (ESI) m/z: [M – $CF_3CO_2^-$] calcd. 504.2453 (for $C_{24}H_{34}N_5O_7$; found 504.2449. UV/Vis (MeOH): λ_{max} (lg ε) = 466 nm (3.70); fluorescence (MeOH): λ_{em} = 568 nm, λ_{ex} = 466 nm, Φ = 0.01. $C_{26}H_{34}F_3N_5O_9$ (617.58 g mol^{-1}).

Diethyl 2-{3-[(1*R*,8*S*,9*s*)-(bicyclo[6.1.0]-4-nonyne-9-yl)methoxycarbonylamino]propyl-amino}-5-{3-[2-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)ethylamino]-3-oxopropylamino}-terephthalate (28). DIPEA (21 mmol, 27 mg, 2.5 eq) was added to a suspension of compound **26** (83 μmol, 51 mg, 1.0 eq) and cyclooctyne active carbonate **27** (66 μmol, 19 mg, 0.8 eq) in CH_2Cl_2 (2 mL). The mixture was stirred for 16 h at ambient temperature. Subsequently, it was diluted with CH_2Cl_2 (20 mL) and the organic layer was washed with aqueous saturated $NaHCO_3$ solution (4 x 25 mL). It was dried over $MgSO_4$, filtered and all volatile materials were evaporated. The residue was chromatographed (SiO_2, EtOAc/hexanes 2:1, R_f = 0.24) to yield compound **28** (35 mg, 51 μmol, 78%) as a red solid, m.p. 101–102°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90–0.94 (m, 2H), 1.31–1.35 (m, 1H), 1.380 (t, *J* = 7.1 Hz, 3H), 1.383 (t, *J* = 7.1 Hz, 3H), 1.52–1.60 (m, 2H), 1.88 (quint, *J* = 6.6 Hz, 2H), 2.17–2.29 (m,

6H), 2.48 (t, *J* = 6.5 Hz, 2H), 3.22 (t, *J* = 6.6 Hz, 2H), 3.32 (q, *J* = 6.2 Hz, 2H), 3.42–3.47 (m, 4H), 3.66–3.68 (m, 2H), 4.13–4.18 (m, 2H), 4.325 (q, *J* = 7.1 Hz, 2H), 4.334 (q, *J* = 7.1 Hz, 2H), 4.85 (br.s, 1H), 6.20 (t, *J* = 4.8 Hz, 1H), 6.65 (s, 2H), 6.83 (br.s, 2H), 7.26 (s, 1H), 7.32 (s, 1H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.5 (2 CH_3), 17.9 (CH), 20.2 (2 CH), 21.5 (2 CH_2), 29.2 (2 CH_2), 29.7 (CH_2), 36.4 (CH_2), 37.6 (CH_2), 38.9 (CH_2), 39.1 (CH_2), 40.2 (CH_2), 41.1 (CH_2), 60.99 (CH_2), 61.03 (CH_2), 62.8 (CH_2), 98.9 (2 C), 114.1 (CH), 114.7 (CH), 116.9 (C), 117.9 (C), 134.2 (2 CH), 140.6 (C), 141.7 (C), 156.9 (C), 167.8 (C), 168.0 (C), 171.0 (2 C), 171.8 (C) ppm. IR (ATR): λ^{-1} 1694 (s), 1678 (s), 1662 (s), 1528 (s), 1202 (vs), 1181 (vs), 1105 (s) cm^{-1}. HRMS (ESI) m/z: [M + H^+] calcd. 680.3290 for $C_{35}H_{46}N_5O_9$; found 680.3301. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 473 nm (3.66); fluorescence (CH_2Cl_2): λ_{em} = 566 nm, λ_{ex} = 473 nm, Φ = 0.005. $C_{35}H_{45}N_5O_9$ (679.77 g mol^{-1}).

Diethyl 2-{3-[((5a*R,6*S**,6a*S**)-1-benzyl-1,4,5,5a,6,6a,7,8-octahydrocyclopropa[5,6]-cycloocta[1,2-*d*][1,2,3]triazol-6-yl)methoxycarbonylamino]propylamino}-5-{3-[2-(3-benzylthio-2,5-dioxopyrrolidin-1-yl)ethylamino]-3-oxopropylamino}terephthalate (29).** A solution of BnSH (0.47 mmol, 63 mg, 10 eq) and BnN_3 (0.47 mmol, 63 mg, 10 eq) in MeCN (2 mL) was added dropwise to a solution of compound **28** (47 µmol, 32 mg, 1.0 eq) in MeCN (3 mL). The mixture was stirred for 20 h at ambient temperature. Subsequently, NEt_3 (0.71 mmol, 71 mg, 15 eq) was added and the mixture was stirred for additional 3 h at ambient temperature. All volatile materials were evaporated and the residue was chromatographed [SiO_2, CH_2Cl_2/MeOH 40:1, R_f(CH_2Cl_2/MeOH 20:1) = 0.50] to yield compound **29** (32 mg, 34 µmol, 73%) as a red solid, m.p. 55–57°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.75–0.83 (m, 1H), 0.93–1.00 (m, 1H), 1.10–1.17 (m, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.41–1.58 (m, 2H), 1.85 (quint, *J* = 6.4 Hz, 2H), 1.91–1.97 (m, 1H), 2.13–2.20 (m, 1H), 2.37 (dd, *J* = 18.6 Hz, *J* = 3.8 Hz, 1H), 2.48 (t, *J* = 6.5 Hz, 2H), 2.50–2.54 (m, 1H), 2.72–2.78 (m, 1H), 2.87–2.91 (m, 1H), 2.96 (dd, *J* = 18.7 Hz, *J* = 9.2 Hz, 1H), 3.05–3.10 (m, 1H), 3.20 (t, *J* = 6.6 Hz, 2H), 3.30 (q, *J* = 6.1 Hz, 2H), 3.40–3.46 (m, 3H), 3.48–3.54 (m, 2H), 3.61–3.71 (m, 2H), 3.82 (d, *J* = 13.5 Hz, 1H), 4.02–4.11 (m, 2H), 4.14 (d, 13.5 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 4.32 (q, *J* = 7.2 Hz, 2H), 4.85 (br.s, 1H), 5.41–5.49 (m, 2H), 6.33 (br.s, 1H), 6.91 (br.s, 2H), 7.07 (s, 1H), 7.08 (s, 1H), 7.22–7.35 (m, 10H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.46 (CH_3), 14.48 (CH_3), 17.6 (CH), 19.3 (CH), 19.5 (CH), 21.6 (CH_2), 22.3 (CH_2), 23.3 (CH_2), 26.1 (CH_2), 29.7 (CH_2), 35.5 (CH_2), 36.1 (CH_2), 36.2 (CH_2), 37.7 (CH), 38.2 (CH_2), 38.9 (CH_2), 39.1 (CH_2), 40.3 (CH_2), 41.2 (CH_2), 52.1 (CH_2), 61.0 (CH_2), 61.1 (CH_2), 62.7 (CH_2), 114.3 (CH), 114.9

(CH), 116.9 (C), 118.0 (C), 127.0 (2 CH), 127.7 (CH), 128.3 (CH), 128.8 (2 CH), 129.1 (2 CH), 129.3 (2 CH), 133.1 (C), 135.4 (C), 136.9 (C), 141.8 (C), 145.2 (C), 156.8 (C), 167.8 (C), 168.0 (C), 171.3 (C), 172.0 (C), 175.3 (C), 177.4 (C) ppm. IR (ATR): λ^{-1} = 1699 (vs), 1682 (s), 1526 (s), 1211 (vs), 1189 (vs), 1105 (s) cm^{-1}. HRMS (ESI) m/z: [M + H^+] calcd. 937.4277 for $C_{49}H_{61}N_8O_9S$; found 937.4293. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 473 nm (3.71); fluorescence (CH_2Cl_2): λ_{em} = 570 nm, λ_{ex} = 473 nm, Φ = 0.11. $C_{49}H_{60}N_8O_9S$ (937.13 g mol^{-1}).

Diethyl 2-[2-(*tert*-butoxycarbonyl)ethylamino]-5-(2-carboxyethylamino)terephthalate (30). Under exclusion of air and moisture, pyrrolidine (1.60 mmol, 114 mg, 5.0 eq) was added to a solution of compound **5** (320 µmol, 158 mg, 1.0 eq) in abs. CH_2Cl_2 (5 mL). After degassing the mixture, $Pd(PPh_3)_4$ (16 µmol, 18 mg, 0.05 eq) was added under an nitrogen atmosphere and the mixture was stirred for 1.5 h at ambient temperature. Charcoal (spatula tip, ca. 2 mg) was added and the mixture was stirred for additional 5 min. It was then filtered and all volatile materials were evaporated. The residue was chromatographed [SiO_2, EtOAc → EtOAc/MeOH 6:1, R_f(EtOAc/MeOH 6:1) = 0.67] to yield compound **30** (169 mg, 0.37 mmol, quant.) as a red solid, m.p. 124–126°C.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.38 (t, *J* = 7.1 Hz, 6H), 1.45 (s, 9H), 2.54 (t, *J* = 6.4 Hz, 2H), 2.62 (t, *J* = 6.6 Hz, 2H), 3.40–3.45 (m, 4H), 4.34 (q, *J* = 7.1 Hz, 4H), 7.34 (s, 1H), 7.36 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.6 (2 CH_3), 28.3 (3 CH_3), 34.8 (CH_2), 36.4 (CH_2), 40.5 (CH_2), 40.6 (CH_2), 61.96 (CH_2), 62.00 (CH_2), 82.1 (C), 115.5 (2 CH), 118.6 (C), 118.9 (C), 141.9 (C), 142.1 (C), 168.84 (C), 168.85 (C), 173.2 (C), 175.7 (C) ppm. IR (ATR): λ^{-1} = 1680 (s), 1207 (vs), 1239 (s), 1158 (s), 1093 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 452 (34) [M^+], 396 (100), 337 (24), 291 (49), 277 (10), 199 (4), 57 (4). HRMS (EI) m/z: [M^+] calcd. 452.2153 for $C_{22}H_{32}N_2O_8$; found 452.2157. UV/Vis (MeOH): λ_{max} (lg ε) = 466 nm (3.80); fluorescence (MeOH): λ_{em} = 571 nm, λ_{ex} = 466 nm, Φ = 0.05. $C_{22}H_{32}N_2O_8$ (452.50 g mol^{-1}).

Diethyl 2-[2-(*tert*-butoxycarbonyl)ethylamino]-5-{3-[2-(2,5-dihydro-1*H*-pyrrol-1-yl)-ethylamino]-3-oxopropylamino}terephthalate (31). HATU (280 µmol, 106 mg, 1.2 eq), DIPEA (0.51 mmol, 57 mg, 2.2 eq) and maleimide building block **24** (0.24 mmol, 65 mg, 1.2 eq) were added to a suspension of compound **30** (230 µmol, 104 mg, 1.0 eq) in CH_2Cl_2 (5 mL). The mixture was stirred for 18 h at ambient temperature. All volatile materials were evaporated, the residue was dissolved in EtOAc (25 mL) and the solution was washed with saturated aqueous $NaHCO_3$ solution (4 x 25 mL). The organic layer was dried over $MgSO_4$, filte-

red and the solvent was evaporated. The residue was chromatographed (SiO_2, EtOAc/hexanes 2:1, R_f = 0.31) to yield compound **31** (109 mg, 0.19 mmol, 83%) as a red solid, m.p. 96–98°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.360 (t, *J* = 7.1 Hz, 3H), 1.363 (t, *J* = 7.1 Hz, 3H), 1.44 (s, 9H), 2.46 (t, *J* = 6.5 Hz, 2H), 2.55 (t, *J* = 6.8 Hz, 2H), 3.42–3.45 (m, 6H), 3.64–3.66 (m, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 6.28 (t, *J* = 5.3 Hz, 1H), 6.62 (s, 2H), 6.89 (br.s, 2H), 7.28 (s, 1H), 7.30 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.40 (CH_3), 14.43 (CH_3), 28.2 (3 CH_3), 35.6 (CH_2), 36.3 (CH_2), 37.6 (CH_2), 38.8 (CH_2), 39.6 (CH_2), 40.1 (CH_2), 60.9 (CH_2), 61.0 (CH_2), 80.9 (C), 114.2 (CH), 114.7 (CH), 117.2 (C), 117.7 (C), 134.2 (2 CH), 140.6 (C), 141.2 (CH), 167.7 (C), 167.8 (C), 171.1 (2 C), 171.4 (C), 171.9 (C) ppm. IR (ATR): λ^{-1} = 1694 (s), 1677 (s), 1662 (s), 1204 (vs), 1159 (s), 1158 (s), 1106 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 574 (47) [M^+], 518 (100), 459 (10), 413 (14), 337 (10), 291 (29), 245 (7), 231 (14), 219 (6), 124 (6), 56 (22). HRMS (EI) m/z: [M^+] calcd. 574.2633 for $C_{28}H_{38}N_4O_9$; found 574.2635. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 470 nm (3.66); fluorescence (CH_2Cl_2): λ_{em} = 567 nm, λ_{ex} = 470 nm, Φ = 0.007. $C_{28}H_{38}N_4O_9$ (574.69 g mol^{-1}).

Diethyl 2-(2-carboxyethylamino)-5-{3-[2-(2,5-dihydro-1*H*-pyrrol-1-yl)ethylamino]-3-oxopropylamino}terephthalate (32). TFA (4 mL) was added dropwise to a cooled (ice-water bath) solution of compound **31** (180 μmol, 102 mg) in CH_2Cl_2 (4 mL). The mixture was stirred for 18 h at ambient temperature. All volatile materials were removed under reduced pressure. The residue was chromatographed [SiO_2, EtOAc → EtOAc/MeOH 6:1, R_f(EtOAc/MeOH 6:1) = 0.38] to yield compound **32** (98 mg, 0.19 mmol, quant.) as a red solid, m.p. 117–119°C.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.31 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 2.32 (t, *J* = 6.7 Hz, 2H), 2.54 (t, *J* = 6.5 Hz, 2H), 3.20 (q, *J* = 6.0 Hz, 2H), 3.26 (t, *J* = 6.6 Hz, 2H), 3.32 (t, *J* = 6.4 Hz, 2H), 3.45 (t, *J* = 6.0 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 6.72 (br.s, 2H), 6.96 (s, 2H), 7.22 (s, 1H), 7.23 (s, 1H), 8.04 (t, *J* = 6.1 Hz, 1H) ppm, the signal of the carboxylate-H is not observed. ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ = 14.1 (2 CH_3), 33.7 (CH_2), 34.9 (CH_2), 36.8 (CH_2), 37.1 (CH_2), 38.9 (CH_2), 39.4 (CH_2), 60.71 (CH_2), 60.74 (CH_2), 113.5 (CH), 113.6 (CH), 116.7 (C), 116.8 (C), 134.5 (2 CH), 140.0 (C), 140.2 (C), 166.88 (C), 166.95 (C), 170.7 (C), 171.0 (2 C), 173.1 (C) ppm. IR (ATR): λ^{-1} = 1674 (s), 1186 (vs), 1132 (vs) cm^{-1}. HRMS (ESI, neg. mode) m/z: [M – H^+] calcd. 517.1940 for $C_{24}H_{29}N_4O_9$; found 517.1921. UV/Vis (MeOH): λ_{max} (lg ε) = 466 nm (3.25); fluorescence (MeOH): λ_{em} = 572 nm, λ_{ex} = 466 nm, Φ = 0.02. $C_{24}H_{30}N_4O_9$ (518.52 g mol^{-1}).

Diethyl 2-[3-(3-azidopropylamino)-3-oxopropyl)amino]-5-{3-[2-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)ethylamino]-3-oxopropylamino}terephthalate (34). COMU (92 µmol, 40 mg, 1.2 eq) and DIPEA (0.27 mmol, 35 mg, 3.5 eq) were added to a solution of compound **32** (77 µmol, 40 mg, 1.0 eq) in DMF (5 mL). The mixture was stirred at ambient temperature for 1.5 h. Subsequently, compound **33** (69 µmol, 9.4 mg, 0.9 eq) was added and it was stirred for additional 3 h. The solvent was evaporated and the residue was chromatographed (SiO_2, EtOAc, R_f = 0.31) to yield compound **34**, which was then recrystallized from hexane/CH_2Cl_2 (10:1, 10 mL) to yield (16 mg, 27 µmol, 39%) as a red solid, mp 146–147°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.2 Hz, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.77 (quint, *J* = 6.6 Hz, 2H), 2.48 (t, *J* = 6.5 Hz, 2H), 2.52 (t, *J* = 6.4 Hz, 2H), 3.32–3.36 (m, 4H), 3.44–3.52 (m, 6H), 3.67–3.69 (m, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.34 (q, *J* = 7.2 Hz, 2H), 6.05 (t, *J* = 5.1 Hz, 1H), 6.16 (t, *J* = 5.1 Hz, 1H), 6.66 (s, 2H), 6.89 (br.s, 2H), 7.32 (br.s, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.5 (2 CH_3), 28.9 (CH_2), 36.4 (CH_2), 36.6 (CH_2), 37.3 (CH_2), 37.6 (CH_2), 39.0 (CH_2), 40.1 (CH_2), 40.2 (CH_2), 49.5 (CH_2), 61.09 (CH_2), 61.11 (CH_2), 114.6 (CH), 114.7 (CH), 117.6 (C), 117.7 (C), 134.3 (2 CH), 141.06 (C), 141.12 (C), 167.8 (C), 167.9 (C), 171.0 (2 C), 171.6 (C), 171.8 (C) ppm. IR (ATR): λ^{-1} = 1713 (s), 1680 (s), 1605 (s), 1526 (s), 1207 (s), 1182 (vs), 1104 (s) cm^{-1}. MS (EI, 70 eV), *m/z* (%): 600 (4) [M^+], 572 (6), 280 (10), 265 (20), 219 (59), 191 (27), 173 (17), 132 (35), 105 (18), 84 (23), 55 (100). HRMS (EI) m/z: [M^+] calcd. 600.2651 for $C_{27}H_{36}N_8O_8$; found 600.2660. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 469 nm (3.59); fluorescence (CH_2Cl_2): λ_{em} = 568 nm, λ_{ex} = 469 nm, Φ = 0.02. $C_{27}H_{36}N_8O_8$ (600.63 g mol^{-1}).

Diethyl-2-[3-(3-azidopropylamino)-3-oxopropylamino]-5-{3-[2-(3-(benzylthio)-2,5-dioxo-pyrrolidin-1-yl)ethylamino]-3-oxopropylamino}terephthalate (35). BnSH (0.27 mmol, 36 mg, 10.0 eq) and NEt_3 (0.41 mmol, 41 mg, 15.0 eq) were added to a solution of compound **34** (27 µmol, 16 mg, 1.0 eq) in CH_2Cl_2 (5 mL) and the mixture was stirred for 17 h at ambient temperature. Subsequently, the solution was directly chromatographed (SiO_2, EtOAc, R_f = 0.38) to yield compound **35** (8.0 mg, 11 µmol, 41%) as a red solid, m.p. 89–90°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.1 Hz, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.78 (quint, *J* = 6.6 Hz, 2H), 2.39 (dd, *J* = 18.7 Hz, *J* = 3.8 Hz, 1H), 2.49 (t, *J* = 6.4 Hz, 2H), 2.52 (t, *J* = 6.3 Hz, 2H), 2.98 (dd, *J* = 18.7 Hz, *J* = 9.2 Hz, 1H), 3.32–3.37 (m, 4H), 3.41–3.56 (m, 7H), 3.63–3.72 (m, 2H), 3.84 (d, *J* = 13.5 Hz, 1H), 4.16 (d, *J* = 13.5 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 5.97 (t, *J* = 5.1 Hz, 1H), 6.16 (t, *J* = 5.3 Hz, 1H), 7.03 (br.s, 2H), 7.24–7.37 (m, 7H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.5 (2 CH_3), 28.9

(CH_2), 35.6 (CH_2), 36.2 (CH_2), 36.3 (CH_2), 36.6 (CH_2), 37.3 (CH_2), 37.8 (CH), 38.3 (CH_2), 39.0 (CH_2), 40.35 (CH_2), 40.36 (CH_2), 49.5 (CH_2), 61.2 (2 CH_2), 114.7 (CH), 115.7 (CH), 117.7 (C), 118.0 (C), 127.1 (C), 128.8 (2 C), 129.3 (2 C), 136.9 (C), 141.19 (C), 141.23 (C), 167.8 (C), 167.9 (C), 171.5 (C), 171.9 (C), 175.3 (C), 177.4 (C) ppm. IR (ATR): λ^{-1} = 1692 (s), 1645 (s), 1533 (s), 1218 (vs), 1184 (s), 1105 (s) cm^{-1}. HRMS (ESI) m/z: [M + H^+] calcd. 725.3076 for $C_{34}H_{45}N_8O_8S^+$; found 725.3094. UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 469 nm (3.38); fluorescence (CH_2Cl_2): λ_{em} = 567 nm, λ_{ex} = 469 nm, Φ = 0.15. $C_{34}H_{44}N_8O_8S$ (724.83 g mol^{-1}).

ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and $^{13}C\{^1H\}$ NMR spectra of all reported products. 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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