Property-selected Asymmetric Azobenzenes for Photoswitchable Ligands[†]

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Abstract

Suitable designed photoswitches based on azobenzenes are essential structural features for photopharmacological compounds. Optimized azobenzenes are important for serving as building blocks in „azo extension“ strategies, and for designing photodrugs with tailored properties. Herein we present the synthesis and characterization of a variety of asymmetric azobenzenes by addressing selected structural features of the diazene core, such as polarity, steric demand, and electronical properties. Systematic exploration led to photoswitches with a relaxation half-life of seconds, minutes, hours, or days. Furthermore, the influence of different substitution pattern on the photophysical properties was charted. For analysis of all switches, robust characterization as well as examination under near-to physiological conditions was established, in order to assist with photoswitch choice for specific biological applications.

INTRODUCTION

Influencing biological systems by light is non-invasive and offers high temporal and spatial resolution, which can be used for studying living organisms in functional detail. In photopharmacology¹ the reported application possibilities grow constantly including the manipulation of peptides and proteins², ion channels³, enzymes,¹ or the cytoskeleton.^{4,5} Photoswitching biologically active molecules can be realized by using several photoexcitable molecules, for example diarylethanes,⁶ spiropyrans,⁷ or hemithioindigo,⁸ all of which offer distinct property profiles.⁹ However, due to ease of synthesis, favorable absorption properties, and useful structural reorganization upon photoswitching, “azobenzenes” (i. e. diaryldiazenes) are most frequently applied.^{1-3,10} Their photophysical properties, such as quantum yield, bleaching propensity, or thermal relaxation rate, have been reported to respond to changes in chemical structure.¹⁰⁻¹⁴

Azobenzenes can serve as a photoswitches, because the diazene bond is configurationally bistable. Its two possible configurational isomers differ in shape and in their dipole moments (Figure 1A). The *E*-isomer (*trans*) has an extended, linear shape, and co-planar aryl substituents, compared to the *Z*-isomer (*cis*), which adopts a curled, bent shape, with twisted aryl rings.¹⁴ Isomerization can be triggered by excitation of the strong $\pi \rightarrow \pi^*$ transition of the *E*-isomer, leading to configurational relaxation to the metastable *Z*-isomer.^{15, 16} The $\pi \rightarrow \pi^*$ transition of the *Z*-isomer that induces back-isomerization to *E*-configuration is typically weaker and more blue shifted, but both absorption spectra often overlap considerably. Hence, a so called photostationary state (PSS) is reached upon irradiation, i. e. a constant ratio of both forms is established by simultaneously exciting both *E*- and *Z*-isomers at the same time with a ratio depending on the absorption band intensity at the particular wavelength.^{15,17} Back isomerization to the thermodynamically favored *E*-isomer also takes place spontaneously, leading to an exclusive recovery of the *E*-isomer over time in the dark.¹¹ Alternatively, excitation of the less favoured $n \rightarrow \pi^*$ transition, which is stronger in the nonplanar *Z*-isomer, might lead to a PSS with excess of *E*-isomer (Figure 1B), depending on excitation wavelength and intensity.¹⁸

The maximum of the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, photoswitch geometry, as well as the thermal relaxation rate are important factors for tuning the activity and function of a biological active photoswitch. In small molecules, azobenzene moieties may serve as isosteric motifs (“azalogs”) like in **VUF 14738**¹⁹ or in the photostatins.⁴ Alternatively, attached switches like in **optojasp-1** may render bioactive ligands susceptible to light.^{5,20} Furthermore, asymmetric azobenzenes may be utilized for switching chain geometry (**L-MAG-0₄₆₀**)²¹ or sidechain presentation (**9c-8azo**)²² in larger biomolecules or ligands (Figure 1C). Finally, they may connect peptide chains or other polymers mechanically and making them reactive to light-induced conformational switching.^{10,23,24}

For any of these molecular designs, the unimolecular thermal reversion rate of the switch is a structural property of high importance for applications, as biological response may occur on variable time scales, depending on the particular application (ms – days).¹ However, with the exception of “azalogs”, the majority of azobenzene switches for biological are based on simple monosubstituted azobenzenes.^{1,25-27} These contain push-pull substitution, frequently amines or anilines, displaying either very fast (<1s) or very slow (~hours) thermal kinetics.^{28,29} Structural variations such as *ortho* substitutions were mainly investigated for addressing the activation wavelength, and for state control.^{2,10,29-32} In order to optimize properties of the optojasp actin photoswitches, we have conducted a systematic study which led to a photoswitch design with thermal relaxation properties fitting to the practically important sec-mins range.

Figure 1. **A:** *E*-*Z*-isomerization and resulting structural change of azobenzene photoswitches. **B:** Absorption spectra of azobenzene depending on configuration. **C:** Azobenzene-based photoswitches applied in biologically active ligands.

RESULTS AND DISCUSSION

Research Design

We aimed for structures where any ligand of interest could be possibly attached to the structural ring “A”, while the exposed “B”-ring, that would change its relative orientation upon photoswitching, allows for suitable modifications or elongations (Figure 2). This asymmetric switch design is also inspired by structural biology data we²⁰ and others³³ have recently been able to obtain on target-bound azobenzene photoswitches. To generate asymmetric azobenzenes straightforwardly, an azo coupling of diazonium salt intermediates to phenols may be used.³⁴ The phenolic hydroxyl group enables further functionalization or could become later part of either the “A”-, or the “B”-ring substructure. Thereby 4,4'-substituted azobenzenes with electron donating groups are obtained, related to the photostatins and the optojasps.^{4,5}

Figure 2. Asymmetric azobenzene design for biological applications.

Synthesis

To systematically study structural-function relationship a panel of differently shaped azobenzenes was prepared. This collection featured azobenzenes with phenol being either part of the “A”- or the “B”-ring, and being connected to a potential ligand in *para*- or *ortho*- position of the diazene (Scheme 1 – 3). A carboxylic acid should enable ligand attachment or coupling to biomolecules of interest.

A diazo coupling was used to form phenolic azobenzenes. 4-Methoxyanilin (**1a**), 4-bromoanilin (**1b**), 3,5-dimethoxyanilin (**2**), 3,4,5-trimethoxyanilin (**3**), and known³⁵ oxazin **4** were efficiently converted into diazonium salts by using isoamyl nitrite.^{4,36} Protected aniline precursors **5** and **6** were deprotected in situ before forming the diazonium salts. During transformation of oxazin **4** an excess of isoamyl nitrite had to be used because the secondary amine became transiently nitrosylated as well (evident from LC-MS). The following coupling of the diazonium salts was performed with several phenols **7a-c**, **8**, **9**, **10a-e**, 8-hydroxy-quinoline (**11a**) and naphthol **11b-d**, **12**. In general, designs for *para* attached azobenzenes (Scheme 1 and 3) were coupled in rewarding yields, accessing a broad variety of phenolic azobenzenes

(**13**, **14**, **15**, **16a-c**, **18**, **21a-e**, **22a-d**, **23**). The *N*-nitrosylation of oxazine **4** was removed by treating the crude diazo coupling product with anhydrous HCl in dioxane/MeOH (Scheme 1A). Basic conditions during diazo couplings with Boc-protected aniline **5** in MeOH led to transesterification in some cases (Scheme 1B). Diazo couplings of *ortho* substituted derivatives **6** and **8** that contained a succinimidyl residue lead to reaction mixtures of imide, methyl ester and carboxylic acid of compounds **17a,b**, **19b,c** and **20** (Scheme 2). However, the mixture of imid and ester could be used for further steps (combined yields approx. 60%). Alternatively, the succinimidyl residue was introduced at the end. From Boc-protected hydroxyaniline **9** azobenzene **18** was obtained by azo coupling. After ether formation ($\rightarrow$ **24**) and Boc-deprotection, a succinyl acid sidechain was introduced by using succinic anhydride to obtain azobenzene **25** in good yield (Scheme 2A).

Scheme 1. Synthesis of *para* attached linkers with "B"-ring modifications. **A:** Phenol part of the "A"-ring. **B:** Phenol part of the "B"-ring. Conditions: a) 1. Isoamyl nitrite, HCl*aq, MeOH, 0 °C; 2. NaOH*aq, MeOH, phenol, 0°C; b) EtOOCCH₂Br, K₂CO₃, Me₂CO, rfx; c) amine, Cs₂CO₃, Pd(dpa)₂, RuPhos, CH₃CN, 100°C; d) CuI, K-phthalimide, DMF, 160 °C; e) THF/aq. 2M LiOH, r.t.; f) aldehyde, NaCNBH₃, AcOH/EtOH 1:9; g) alkyl halide, K₂CO₃, Me₂CO, rfx; h) K₂CO₃, *N*-methylpiperazine, CH₃CN, 140 °C,))) Substituents: **26**, **38 a**: R¹ = Br; **b**: R¹ = NMe₂; **c**: R¹ = morpholino; **d**: R¹ = *N*-methylpiperazino; **e**: R¹ = NHAc; **f**: R¹ = NPhth; **36**, **39 a**: R² = Me; **b**: R² = Bn; **7**, **16**, **32**, **40 a**: R³ = H, R⁴ = H, R⁵ = Me; **b**: R³ = OMe, R⁴ = H, R⁵ = Me; **c**: R³ = OMe, R⁴ = OMe, R⁵ = Me; **d**: R³ = OMe, R⁴ = OMe, R⁵ = 2-hydroxyethoxy; **e**: R³ = OMe, R⁴ = OMe, R⁵ = 2-bromoethoxy; **f**: R³ = OMe, R⁴ = OMe, R⁵ = 2-(4-methylpiperazino)ethoxy.

Scheme 2. Synthesis of *ortho* attached linkers with "B"-ring modifications. **A:** Phenol part of the "A"-ring. **B:** Phenol part of the "B"-ring. Conditions: a) 1. Pd/C, H₂, EtOH/EtOAc/AcOH 2. Isoamyl nitrite, HCl*aq, MeOH, 0 °C 3. NaOH*aq, MeOH, phenol, 0°C; b) MeI, K₂CO₃, Me₂CO, rfx; c) Amine, Cs₂CO₃, Pd(dba)₂, RuPhos, CH₃CN, 100°C; d) THF/aq., 2M LiOH, r.t.; e) 1. 4M HCl in 1,4-dioxane, MeOH 2. succinic anhydride, K₂CO₃, DMF, 70°C; f) alkyl halide, K₂CO₃, Me₂CO, rfx; g) K₂CO₃, *N*-methylpiperazine, CH₃CN, 140 °C,)); Substituents: **1, 17, 33, 37, 41, 42 a:** R¹ = OMe; **b:** R¹ = Br; **c:** R¹ = NMe₂; **d:** R¹ = morpholino; **e:** R¹ = *N*-methylpiperazino; **7, 19, 34, 42 b:** R² = H, R³ = Me; **c:** R² = OMe, R³ = Me; **d:** R² = OMe, R³ = 2-bromoethoxy; **e:** R² = OMe, R³ = 2-(4-methylpiperazino)ethoxy.

All azobenzene phenols were next converted to ethers. *Para*-attached derivatives with the phenol in ring "A" were synthesized with ethyl bromoacetate in dry acetone and K₂CO₃, providing ethers **26a**, **27**, **28**, **29a-e**, **30a-d** and **31** in good to excellent yields (Scheme 1A, Scheme 3). For TBS-protected phenol **21b** the ether **29b** was formed by using sodium hydride in dry THF at -20 °C to prevent silyl group cleavage. All other phenolic azobenzenes were methylated by using methyl iodide, providing ethers **32a-c**, **33a,b**, **34b,c** and **35** in excellent yields (Scheme 1B, Scheme 2). For additional modifications in the "B"-ring phenolic azobenzenes **16c** and **19c** were alternatively converted by alkylation with 2-bromethanol or 1,2-dibromethane to azobenzenes **32d,e** and **34d** in good yields.

The 4,4'-substituted azobenzenes such obtained were further modified (Scheme 1 – 3). Amine **28** was converted by reductive amination with paraformaldehyde or benzaldehyde to ester **36a** and **36b** in good yields. The arylbromides **26a**, **29d** and **33b** were derivatized in good to excellent yields by *Buchwald-Hartwig* amination^{37,38} to introduce amino (**26b-d**, **29f**, **37c-e**) or amide substituents (**26e**). To obtain phthalimide **26f**, an *Ullmann*-type coupling with potassium phthalimide was performed instead, because *Buchwald-Hartwig* conditions failed to provide clean material. Alkylbromides **32e** and **34d** offer a handle for attaching additional groups or to elongate to a chain. As an example, they were converted in a microwave assisted nucleophilic substitution reaction with *N*-methylpiperazine to the polar azobenzenes **32f** and **34e** (Scheme 1 and 2). Finally, the free Carboxylic acids were liberated by hydrolysis of ester or succinimidyl residue with aq. LiOH in THF in good to excellent yields (Scheme 1 – 3), giving carboxylic acids **5b-d**, **10a,b**, **15a-d,f**, **21b-e**, **26a-c,e**, **31a,c,g** and **35a-d** for conjugation.

Scheme 3. Modifications at the “A”-ring. Conditions: a) 1. Isoamyl nitrite, HCl*aq, MeOH, 0 °C 2. NaOH*aq, MeOH, phenol, 0°C; b) EtOOCCH₂Br, K₂CO₃, Me₂CO, rfx; c) EtOOCCH₂Br, NaH, THF, -20°C; d) amine, Cs₂CO₃, Pd(dba)₂, RuPhos, CH₃CN, 100°C; e) THF/aq., 2M LiOH, r.t.; substituents: **10**, **21**, **29**, **44 a**: X = H, Y = H; **b**: X = OTBS, Y = H; **c**: X = H, Y = OH; **d**: X = Br, Y = H; **e**: X = H, Y = Br; **f**: X = morpholino, Y = H; **g**: X = OH, Y = H; **11**, **22**, **30**, **45 a**: R¹ = H, R² = H, R³ = H, X = N; **b**: R¹ = H, R² = H, R³ = H, X = CH; **c**: R¹ = OMe, R² = H, R³ = H, X = CH; **d**: R¹ = H, R² = OMe, R³ = OMe, X = CH.

Photophysical characterization

Absorption maxima (λ_{max}) and the thermal $Z \rightarrow E$ relaxation half-life ($\tau_{1/2}$) were determined by using UV-Vis spectroscopy. Surprisingly, thermal half-life seemed to vary in pure organic solvent (acetonitrile), and literature data seemed to be variable, too, especially for aniline derivatives.³⁹ A brief examination was hence undertaken (Table 1). HPLC grade acetonitrile showed changing relaxation half-life over time after bottle opening (Table 1, entry 1-3), independent of water content (Table 1, entry 4-6). After treatment with activated Al_2O_3 a significant change was observed, indicating that traces of protic acid(s) may be involved (Table 1, entry 6-8). Indeed, air purging (20 min) led to variations of $\tau_{1/2}$ depending on water content, suggesting carbonic acid to be formed. Indeed, by adding 0.5% piperidine the relaxation kinetics data became reproducible. The absorption spectrum of the azobenzene **26c** did not change under the different conditions, excluding the presence of azonium ions.⁴⁰ This property notwithstanding, azobenzene photoswitch properties may still be dependent on local pH or on its binding environment.

To determine the photostationary state (PSS) ratio at different wavelengths of irradiation, the method developed by *Fischer* was implemented.⁴¹ It allows computing the ratio of the isomers in the PSS after irradiation at two different wavelengths when the absorption spectrum of the pure *E*-isomer is known. The spectrum of the pure *Z*-isomer can additionally be computed from these data. This method is fast and reliable for azobenzenes with a half-life long enough to complete the measurement. When comparing it to NMR methods (Figure 3), the PSS ratio is easily extracted at several wavelengths and its determination is not compromised by potentially overlapping NMR signals.

We then studied the influence of the solvent. Solvent polarity did not strongly affect the absorption spectra of the investigated azobenzenes. The absorption maxima of the $\pi \rightarrow \pi^*$ transition remained constant (Table 2). Depending on the solvent, the $n \rightarrow \pi^*$ transition was found somewhat modulated. Under aqueous conditions the absorption was broader, resulting in measurable changes of the PSS between 420 nm and 470 nm (Table 2, Figure S1) especially for aniline derivatives. In general, the maximal achievable PSS for PBS-buffer compared to acetonitrile was not significantly different.

Table 1 Thermal relaxation influence of solvent on azobenzene **26c**.

Entry	Solvent	$t_{1/2}$ [min] at 37 °C		
		Pure	Air purge	+ 0.5% piperidine
1	CH ₃ CN (new bottle)	29.4	-	30.4
2	CH ₃ CN (2 months old)	24.4	-	-
3	CH ₃ CN (5 months old)	13.6	-	31.2
4	CH ₃ CN (0.0001% H ₂ O)	28.1	29.1	29.8
5	CH ₃ CN (0.01% H ₂ O)	29.7	-	-
6	CH ₃ CN (1.0% H ₂ O)	29.1	12.9	31.5
7	CH ₃ CN (basic Al ₂ O ₃)	28.8	-	32.1
8	CH ₃ CN (neutral Al ₂ O ₃)	26.3	-	32.0
9	CH ₃ CN (acidic Al ₂ O ₃)	sec.	-	29.9

Figure 3. *E*- to *Z*-isomer ratio determination in the PSS of azobenzene **32c** in methanol. **A:** UV-Vis spectra by using the method of *E. Fischer*⁴¹ indicate an *E*- to *Z*-isomer ratio of 90% *Z*-isomer at 390 nm irradiation. **B:** 400 MHz ¹H-NMR of dark (all "*E*") and irradiated (390 nm) azobenzene **32c** in MeOH-*d*₄, indicating 91% *Z*-isomer at 390 nm irradiation.

Table 2 PSS of **32c** in different solvents.

Solvent	PSS [%] ^[a]								$\lambda_{\text{max, E}}$ [nm]	$\lambda_{\text{max, Z}}$ [nm]
	370 nm	380 nm	390 nm	400 nm	420 nm	450 nm	470 nm	520 nm		
PBS ^[b]	96	94	90	71	49	36	30	18	360	439
CH ₃ CN	97	95	91	72	44	33	29	18	360	442
CH ₃ CN ^[c]	97	95	91	72	45	34	28	18	360	442
CHCl ₃	95	94	91	73	48	35	29	18	361	447
MeOH	96	94	90	69	41	30	25	15	358	443
toluene	96	96	92	73	44	31	25	14	362	448

[a] amount of *Z*-isomer after irradiation at referred wavelength. [b] 1xPBS buffer/CH₃CN, 2:1. [c] CH₃CN + 0.5% piperidine.

Acetonitrile was used to compare the PSS ratio of all synthesized azobenzenes overall, as thermal relaxation of some azobenzenes was very fast in PBS-buffer (Table 3, PSS in PBS: Table S1). The absorption maxima (λ_{max}) belonging to the strong $\pi \rightarrow \pi^*$ band are given for the solvent in which the PSS is measured. Absorption spectra of all azobenzenes are depicted in the ESI.

Table 3 PSS and photophysical data of azobenzenes.

Entry	PSS [%] ^[a]								λ_{max} [nm]	ϵ [l·mol ⁻¹ ·cm ⁻¹]	$t_{1/2}^{[b]}$ in CH ₃ CN ^[c] [h]	$t_{1/2}^{[b]}$ in PBS ^[d] [min]
	370 nm	380 nm	390 nm	400 nm	420 nm	450 nm	470 nm	520 nm				
13	-	-	-	-	-	-	-	-	350	23800	fast	fast
14	-	-	-	-	-	-	-	-	355	21900	fast	fast
15	-	-	-	-	-	-	-	-	406	24000	fast	fast
16a	-	-	-	-	-	-	-	-	359	16500	fast	fast
16b	-	-	-	-	-	-	-	-	376	19000	fast	fast
16c	-	-	-	-	-	-	-	-	384	20000	fast	fast
17a	-	-	-	-	-	-	-	-	390	23000	fast	fast
17b	-	-	-	-	-	-	-	-	464	19800	fast	fast
18	-	-	-	-	-	-	-	-	473	27300	fast	fast
19b	-	-	-	-	-	-	-	-	394	16500	fast	fast
19c	-	-	-	-	-	-	-	-	401	24100	fast	fast
20	-	-	-	-	-	-	-	-	515	19100	fast	fast
21a	-	-	-	-	-	-	-	-	362	24600	fast	fast
21b	-	-	-	-	-	-	-	-	375	17300	fast	fast
21c	-	-	-	-	-	-	-	-	350	23800	fast	fast
21d	-	-	-	-	-	-	-	-	458	28600	fast	fast
21e	-	-	-	-	-	-	-	-	458	28300	fast	fast
22a	-	-	-	-	-	-	-	-	494	17400	fast	fast
22b	-	-	-	-	-	-	-	-	517	18000	fast	fast
22c	-	-	-	-	-	-	-	-	519	25200	fast	fast
22d	-	-	-	-	-	-	-	-	517	23000	fast	fast
23	-	-	-	-	-	-	-	-	469	26300	fast	fast
24	95	96	95	84	59	41	33	19	372	22100	21.7	132
25	96	97	96	85	62	42	32	18	373	22600	16.3	204
26a	-	-	-	-	-	-	-	-	470	20900	fast	fast
26b	68	84	-	93	87	77	66	19	409	24700	2.36	fast
26c	86	92	94	91	79	63	57	15	392	26200	4.05	0.065
26d	82	90	93	92	83	68	62	22	396	27300	3.58	0.046
26e	97	96	93	71	41	31	27	17	361	25700	2.15	144
26f	97	95	87	55	32	28	28	24	351	25300	12.5	834
27	96	89	78	44	30	29	31	28	345	20100	17,03	slow
28	-	-	-	-	-	-	-	-	408	24000	fast	fast
29a	97	95	91	72	45	34	28	18	360	22100	37.0	313
29b	96	95	-	77	52	35	29	18	369	21300	43.1	314
29c	-	-	-	-	-	-	-	-	390	27300	fast	fast
29d	96	95	93	77	44	29	24	13	364	25700	37.3	216
29e	94	95	93	81	48	35	33	31	369	23000	43.0	330
29f	91	92	91	82	62	44	34	18	368	22000	24.7	245
30a	88	91	92	87	71	50	38	25	389	20900	0.63	9.45
30b	86	92	93	90	78	62	49	32	397	20100	0.71	8.46
30c	78	77	75	59	49	44	43	44	388	20300	5.53	256
30d	84	90	92	91	84	72	59	40	408	21300	0.63	6.71
31	77	82	80	61	41	35	40	55	370	26800	slow	slow
32a	99	96	-	68	37	30	25	15	354	26000	33.3	231
32b	98	98	-	81	51	34	26	16	368	20100	35.4	126
32c	97	95	91	72	45	34	28	18	360	22100	37.0	313
32d	97	95	-	69	44	34	30	20	360	19800	76.5	116
32e	97	95	-	72	43	33	30	23	360	27200	53.2	322
32f	97	95	-	72	49	36	31	21	362	21600	35.3	17.7
33a	94	96	96	89	72	50	30	5	384	24500	0.46	17.2
33b	90	93	93	86	71	51	38	19	383	19100	0.56	26.8

[a] amount of Z-isomer after irradiation at referred wavelength. [b] "fast" means $t_{1/2} < 1$ s, "slow" means $t_{1/2} > 72$ h. [c] measured at 20 °C in CH₃CN + 0.5% piperidine. [d] measured at 37 °C in PBS-buffer/ CH₃CN (2:1) mixture.

Table 3 continued

Entry	PSS [%] ^[a]								$\lambda_{\max}$ [nm]	ϵ [l·mol ⁻¹ ·cm ⁻¹]	$t_{1/2}^{[b]}$ in CH ₃ CN ^[c] [h]	$t_{1/2}^{[b]}$ in PBS ^[d] [min]
	370 nm	380 nm	390 nm	400 nm	420 nm	450 nm	470 nm	520 nm				
34c	94	95	-	84	58	38	27	13	374	20600	6.25	60.2
34d	97	97	94	76	48	31	27	19	368	24200	6.78	82.2
34e	93	93	-	79	54	35	28	18	371	26400	9.81	23.1
35	85	87	87	81	74	68	64	46	361	17100	1.74	86.7
36a	61	71	-	86	85	78	67	26	419	26800	1.12	fast
36b	56	68	-	85	84	76	65	27	420	25300	1.23	fast
37c	55	67	-	89	86	78	66	26	421	22400	1.25	fast
37d	72	84	-	90	81	66	49	10	404	24300	3.24	0.108
37e	72	84	-	92	87	74	52	16	409	21000	2.31	0.061
38b	71	86	-	93	88	78	61	17	408	24400	1.24	fast
38c	89	94	94	92	82	65	46	22	392	26200	3.10	0.069
38d	84	92	94	92	84	66	50	26	395	26200	2.28	0.042
39a	66	75	-	89	86	77	65	25	417	26600	0.70	fast
39b	63	74	-	88	86	78	65	22	418	22700	0.74	fast
40a	99	98	-	71	43	30	29	15	360	25000	19.9	171
40b	97	97	93	85	60	39	30	13	372	25300	33.7	78.6
40c	97	97	95	81	53	37	30	16	368	20800	17.1	193
40d	99	98	-	80	56	40	34	26	369	22000	25.8	148
40f	97	97	-	81	56	39	31	17	368	22900	25.8	12.4
41c	39	55	-	82	80	76	69	24	450	21300	0.11	fast
41d	69	80	-	90	86	77	67	31	414	28000	0.23	0.088
41e	62	77	-	90	87	80	71	33	417	19300	0.22	0.062
42a	93	97	97	90	75	51	32	7	386	21400	1.58	10.7
42b	89	93	95	91	82	63	41	8	395	24700	0.91	8.10
42c	92	95	95	91	78	62	46	24	393	20600	1.34	10.6
42e	89	93	94	90	76	59	42	22	393	24100	1.03	3.51
43	83	86	85	81	75	70	68	58	360	19800	4.86	85.3
44a	97	97	95	81	53	37	30	16	368	20800	17.1	193
44c	-	-	-	-	-	-	-	-	394	19300	fast	fast
44g	90	89	-	70	50	35	30	21	367	21100	25.2	318
45a	79	89	91	87	74	53	40	24	393	25500	0.50	4.75
45b	68	86	90	90	83	70	57	31	409	23300	0.32	4.17
45c	78	84	82	71	60	54	53	44	398	22000	slow	200
45d	69	83	88	91	87	77	67	34	419	26000	0.52	3.49
44a	97	97	95	81	53	37	30	16	368	20800	17.1	193
44c	-	-	-	-	-	-	-	-	394	19300	fast	fast
44g	90	89	-	70	50	35	30	21	367	21100	25.2	318
45a	79	89	91	87	74	53	40	24	393	25500	0.50	4.75
45b	68	86	90	90	83	70	57	31	409	23300	0.32	4.17
45c	78	84	82	71	60	54	53	44	398	22000	slow	200
45d	69	83	88	91	87	77	67	34	419	26000	0.52	3.49

[a] amount of Z-isomer after irradiation at referred wavelength. [b] "fast" means $t_{1/2} < 1$ s, "slow" means $t_{1/2} > 72$ h. [c] measured at 20 °C in CH₃CN + 0.5% piperidine. [d] measured at 37 °C in PBS-buffer/ CH₃CN (2:1) mixture.

Interesting trends are obtained for tuning photoswitch properties. In general, a more delocalized diazene provides a more redshifted $\pi \rightarrow \pi^*$ transition and faster thermal relaxation kinetics under physiological conditions. To investigate this property, a first set of compounds with *para* attached linkers was tuned by changing electron density in the “B”-ring. Electron withdrawing groups (EWGs) such as bromine ($\rightarrow$ **26a**) result in a push-pull system with red shifted absorption and short half-life (< 1 s), compared to azobenzene. In contrast, substituents with electron donating groups (EDGs) like in the anilines **26b-d** and **36a,b** only show a polarization of the diazene bond. A thermal relaxation half-life in the range of several seconds was observed for them. As expected,^{2,10,29} this measure led to a weaker redshift of the absorption maximum as for derivative **26a**. By attaching functional groups with decreasing electron donating properties the thermal relaxation gets retarded, as illustrated by methylether **32a** and amide **26e** ($\tau_{1/2} = 2$ -3h) and imide **26f** ($\tau_{1/2} = 12$ -14h). Thermal relaxation of derivative **27**, without an EDG, occurs in the range of several days. Along with prolonged thermal relaxation rate, the absorption maximum is shifted to shorter wavelengths.

Hence, azobenzenes with very fast or very slow relaxation are easily accessed. However, obtaining azobenzenes with thermal relaxation in the minutes range in aqueous environment, as necessary for cell biology and photopharmacology, would be highly desirable. By implementing quinoline as “A”-ring motif (**30a**) a half-life of around 10 minutes was achieved, accompanied by a significant bathochromic shift of nearly 30 nm compared to the benzyl derivative **29a**. Increasing the electron density even more by using a naphthalene core (**30b**) and by electron donating substituents (OMe, **30d**) this effect becomes more prominent. For derivative **30c** the methoxy group in 8-position seemed to stabilize the *Z*-isomer. The resulting blueshift of the transitions however leads to an unfavorable PSS for this compound.

With an EDG in the *ortho* position (e. g. methoxy, amines), the *Z*-isomer gets destabilized.^{2,29,30} By introducing an amide in *ortho* position of 4,4'-substituted ethers, switches with relaxation rate in the minute range were obtained (**42a-c,e**). Thereby, the absorbance of the *E*-conjugated form was shifted to longer wavelengths by approximately 25 nm. In addition, the amide structure was used to introduce an attachment point for potential ligands in *ortho* position. The general trends of the photophysical properties for *ortho* attached linkers by modifications at the “B”-ring were identical compared to the *para* attached linkers, like anilines **41c-e** compared to **38b-d**, or the methoxy substituted compounds **42a-c, e** compared to **40a-f**. Hydrogen bond donors in the *ortho* position (e.g. compounds **23** or **29c**) destabilize the *Z*-configured diazene bond even more, resulting in a very short thermal half-life.⁴² Interestingly, multiple *ortho* substitutions were reported to interfere with bond, slowing down isomerization kinetics.² Retarding thermal relaxation rate excessively creates persistent switches, approaching properties of a caged compound. In this set this was observed for weakly polarized diazene bonds obtained from removing one *para* substituent, shown for compounds **27** and **31**.

The design of any photoswitch needs to additionally consider interactions of the switch with the ligand and/or the target.²⁰ In order to study such variations, e. g. in optojasps,⁵ derivatives with different steric demands and polarity are required, but with absorption and thermal relaxation properties unchanged. In this regard, a methoxy substitution in *meta* position to the diazene was having only minor influence on photophysical properties, as seen for monomethoxy compound **32a** compared to trimethoxy compound **32c**. Asymmetric substitution patterns in the “B”-ring, such shown by compounds **32b** or **36a**, have a twofold reduced thermal relaxation rate and a absorption maximum redshifted by 10 nm, compared to their symmetric analogues **32a** or **26b**. This applies also to *meta* substituents in the “A”-ring (**29b,d,f**).

The residue introduced by reductive amination to aniline **28** does not modify the absorption spectra significantly, allowing to modify this position (**36**, **39**). Similarly, extension of the *para*-methoxy group also did not affect photophysical properties, as shown by compounds **32d** and **32f**. However, depending on the polarity of the residue, the thermal relaxation time was modified ($\rightarrow$ **32f**). The same was true for the free acid analogues compared to their corresponding esters, which generally relax faster. Furthermore, attachment of large ligands may also modify this property. For example, a significant increase in the thermal relaxation kinetics was observed for the switches attached to jasplakinolide analogues.⁵

A 4,4'-substitution with an EDG was an important factor for advantageous PSS ratios, because the band overlap of the *E*- and *Z*-isomers UV spectra gets reduced. As a result, high ratios of over 95% of *Z*-isomer could be achieved for most derivatives through exposure to blue or violet light. For amines, the ratio in the PSS drops to around 90% of *Z*-isomer because of more strongly overlapping $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions. A similar trend is observed for *ortho* attachment, compared to the *para* isomers. In general, the achieved PSS ratios are sufficient for applications as photoswitches.²⁶ Without a 4,4'-substitution pattern, the ratio in the PSS dropped (e. g. **31**). In general, the PSS observed for *meta* substituted compounds in the “B”-ring was minimal decreased. This applied also to *meta* modifications in the “A”-ring (**29b-f**) or to the attachment of a linker in *meta* position (**25**). Extension of the residues with additional groups or linkers did not influence the PSS (e. g. **32f**).

CONCLUSIONS

A set of >50 azobenzenes with a wide range of thermal relaxation kinetics, steric demand, and varying polarity was synthesized. The influence of various symmetrical and asymmetrical substitutions at different positions on the photophysical properties was investigated, extending the knowledge of azobenzene photoswitches.^{2,29,30} This was achieved by establishing a reproducible UV-Vis characterization for thermal relaxation kinetics and by uniform determination of photostationary state ratios. Different electron donating groups in *para* position were found to polarize the diazene bond and

lower the energy of the $\pi \rightarrow \pi^*$ transition, resulting in shortened relaxation rates and a red shifted absorption maximum. This polarization can be modulated by varying the electron density in the two aromatic rings providing half-life from several hours to milliseconds (Figure 4). Polar interactions from *ortho* substituents with the diazene bond reduce the half-life and strongly influence kinetics. On the other hand, modifications in the *meta* position only show marginal modulation on the photophysical properties. Furthermore, asymmetric substitution of the aromatic rings induces a slight bathochromic shift, to go along with a reduced half-life. In general, photophysical properties are not affected by extension of the residues, but may depend on polarity and compound size (Figure 4).

Modulation of thermal relaxation half-life ($\tau_{1/2}$) by polarization of Diazene Bond

"push-pull": $\tau_{1/2} \leq \text{ms}$
 Amines: $\tau_{1/2} = \text{ms to s}$
 PAHs: $\tau_{1/2} = \text{min}$
 Ethers/Amides: $\tau_{1/2} = \text{min to hrs}$
 unsubstituted: $\tau_{1/2} = \text{days}$

Modulation of thermal relaxation half-life ($\tau_{1/2}$) by *ortho* substitution

- polar interactions with diazene bond **reduce** $\tau_{1/2}$
- steric effects impede the rotation and **increase** $\tau_{1/2}$
- $R^1 \neq R^2$ decrease of $\tau_{1/2}$

Influence of *meta* substitution on $\tau_{1/2}$

- $R^3 = R^4$ no influence on $\tau_{1/2}$
- $R^3 \neq R^4$ decrease of $\tau_{1/2}$

Figure 4. General influence of azobenzene substitution patterns on thermal relaxation half-life.

Individual photoswitch design is certainly depending on the individual activities of the *Z*- and *E*-isomers, as well as their target engagement and pharmacokinetics. The extensive range of the thermal half-life that is now available for azobenzene photoswitches offers diverse application possibilities in biology and pharmacology on different time scales (sub-second to days), fitting to neuronal and cellular signaling, cell division, or tissue development. Positions to be modified without substantial property change were identified. Therefore, this panel of compounds may provide cues and structural leads for future "azo extension" strategies of ligands, or for linking designs in proteins, peptides, or other biomolecules. The molecular structures also allow further modifications while maintaining excellent photophysical properties. These data expand the understanding of the molecular structure of azobenzenes and allow the improvement of azobenzene-based systems in biological applications.

Conflicts of interest

There are no conflicts to declare.

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Property-selected Asymmetric Azobenzenes for Photoswitchable Ligands[†]

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- Supplemental Information -

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Supplementary Figures

Figure S1. UV-Vis spectra of **32c** (left) and **26c** (right) in different solvents.

Table S1. PSS of azobenzenes in PBS-buffer.^[a]

Entry	PSS [%] ^[b]								λ_{max} [nm]
	370 nm	380 nm	390 nm	400 nm	420 nm	450 nm	470 nm	520 nm	
24	93	93	91	80	62	46	35	16	373
25	96	94	88	67	44	32	26	15	370
26e	96	94	88	67	44	32	26	15	360
26f	93	87	79	46	32	28	26	21	352
29a	96	94	90	71	49	36	30	18	360
29b	95	96	-	79	55	37	28	13	369
29d	95	94	89	71	48	34	27	15	363
29e	93	92	88	72	50	40	37	33	368
29f	81	86	83	71	54	41	32	16	368
30a	86	90	90	82	66	49	38	24	388
30b	85	90	92	90	80	66	55	32	400
30c	77	78	75	64	54	51	50	45	388
30d	83	88	90	88	81	70	59	30	407
32a	97	94	-	60	41	29	22	10	356
32b	94	95	-	81	61	42	29	13	368
32c	96	94	90	71	49	36	30	18	360
32d	93	91	-	69	46	34	27	14	361
32e	95	94	-	72	47	34	27	14	360
32f	94	92	-	70	49	36	28	16	361
33b	89	89	85	74	57	42	35	20	368
33a	96	96	94	86	71	53	39	14	380
34b	91	94	94	84	67	50	36	15	381
34d	94	94	91	74	48	32	25	16	368
34e	92	93	-	74	54	39	31	18	373
35	82	82	78	64	47	39	38	34	360
40a	99	97	-	74	51	35	25	10	361
40b	93	93	91	79	61	40	26	8	370
40c	94	95	91	75	55	40	30	15	365
40d	96	96	-	81	62	46	35	18	368
40f	96	95	-	76	57	42	33	17	366
42a	94	95	93	84	69	51	36	12	380
42b	90	93	93	87	75	61	45	15	390
42c	92	94	93	86	72	57	44	20	384
42e	91	93	92	83	70	56	43	17	384
43	81	80	77	67	55	49	48	40	360
44a	94	95	91	75	55	40	30	15	365
44g	90	91	-	80	60	41	28	7	373
45a	82	88	89	83	68	52	41	24	392
45b	78	85	88	87	79	67	58	32	406
45c	68	76	74	66	57	53	53	45	394
45d	75	83	87	88	83	73	64	32	415

[a] measured at 37 °C in PBS-buffer/ CH₃CN (2:1) mixture. [b] amount of Z-isomer after irradiation at referred wavelength.

Materials and Methods

Synthetic protocols

The Boc-protected anilines **5** and **9**, mono protected catechol **7b** and phenol **8** were synthesized using standard procedures.¹ TBS-protected catechol **10b** was synthesised following literature procedure of Stein.² Naphtols **11c** and **11d** were synthesized according to literature procedures of Deyris³ and Ramkumar.⁴ Oxazine **4** was synthesised according to literature procedures of Mofford⁵ and Doherty.⁶ All other reagents and solvents were purchased from vendors (Acros, Alfa Aesar, ChemPur, Fluka, Fluorochem, Sigma-Aldrich, Strem Chemicals, TCI Europe N.V., VWR) and were used without further purification unless noted otherwise.

All solvents, when not purchased in suitable purity or dryness, were distilled using standard methods,⁷ or suitable dehydration procedures: tetrahydrofuran (THF) was distilled under a N₂ atmosphere from Na/benzophenone before use; dichloromethane (CH₂Cl₂) was distilled under a N₂ atmosphere from CaH₂ before use. Other anhydrous solvents such as toluene and dimethylformamide (DMF) were obtained in HPLC quality and passed through a solvent purification system equipped with Al₂O₃ (toluene) or molecular sieves 3 Å (DMF, Pure Solv, Innovative Technology, Inc., USA) by applying N₂ overpressure immediately before use. Commercial-grade distilled (*i*Pr)₂NEt (99%) was used without additional distillation. The petroleum ether used had a boiling range of 40-60 °C. Phosphate buffer (pH = 7) was prepared by dissolving Na₃PO₄ × 12 H₂O (54.8 g, 0.14 mol) und NaH₂PO₄ (42.7 g, 0.36 mol) in water (1.0 L). Deionized water was used for all experiments.

Chromatography

Reaction progress was monitored by TLC on precoated, Merck Silica gel 60 F254 alumina-backed plates. TLC chromatograms were first visualized by UV irradiation at 254 nm or 320 nm, followed by staining with aqueous KMnO₄ (2 g KMnO₄, 13.2 g K₂CO₃, 165 mg NaOH, 200 mL H₂O) or ceric ammonium molybdate solution (0.5 g of Ce(NH₄)₄(SO₄)₄ × 2H₂O, 12 g (NH₄)₆Mo₇O₂₄ × 4H₂O, 15 mL H₂SO₄, 235 mL H₂O) followed by gentle heating on air for detection. Primary and secondary amines were detected with ninhydrin (6% in EtOH).

Flash chromatography was performed using silica gel (SiO₂, particle size 40 – 63 µm) purchased from Macherey & Nagel, Düren (Germany) under a pressure of 0.3 – 0.5 bar. Preparative HPLC purification was performed on a Varian system consisting of a ProStar 215 (pump), ProStar 340 (UV/VIS-detector) and a ProStar 701 (collector). A VP250/21 Nucleodur C18 Gravity 5µm column was used. A gradient of Water and Acetonitrile was applied as mobile phase.

NMR spectra

¹H- and ¹³C-NMR spectra were recorded on Bruker Avance I 250 (250 MHz (¹H) and 63 Hz (¹³C)), Bruker Fourier 300 (300 MHz (¹H) and 75 Hz (¹³C)), Bruker Avance III 400 (400 MHz (¹H) and 100 MHz (¹³C)), Bruker Avance III HD 500 (500 MHz (¹H) and 100 MHz (¹³C)), and Bruker AC 600 (600 MHz (¹H) and 150 MHz (¹³C)) spectrometers. Chemical shifts are expressed in parts per million (ppm). The spectra were calibrated to residual solvent signals of CHCl₃ (7.26 ppm (¹H) and 77.0 ppm (¹³C)), DMSO-*d*₅ (2.50 ppm (¹H) and 39.43 ppm (¹³C)), CHD₂OD (3.31 ppm (¹H) and 49.0 ppm (¹³C)), DHO (4.79 ppm (¹H)), respectively. Coupling constants are given in Hertz (Hz) and the following notations indicate the multiplicity of the signals: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad signal). Owing to the *E/Z* equilibrium of some compounds containing an azobenzene functionality, more signals were observed in the ¹H and ¹³C spectra than would be expected for a single isomer. Signals for the major *E*- isomer are reported. Signal identity and peak assignments were verified by 2D-NMR experiments (COSY, TOCSY, HSQC and HMBC) whenever necessary. NMR spectra are displayed in Supplementary Note 2.

UV–Vis analysis

UV-Vis spectra were recorded using a JASCO V-730 UV–Visible Spectrophotometer with Helma SUPRASIL precision cuvettes (5 mm light path). All compounds were dissolved as 10–30 mM stock solutions in DMF and diluted to the given concentrations using cosolvents and buffers as indicated. Switching was achieved by irradiating the cuvettes at 0.2 to 0.5 cm within the spectrometer for 10 to 30 s. For irradiation high power single chip SMD LEDs from Roithner Lasertechnik GmbH with a current of 350 mA were used. The LEDs show their

main intensity at the specified wavelength with a width of ± 5 nm. UV-spectra of all compounds are reproduced in Supplementary Note 1.

Table S2. LEDs from Roithner Lasertechnik GmbH used in this paper

Entry	λ [nm]	LED code
1	370	VL370-5050
2	380	VL380-5050
3	390	VL390-5050
4	400	VL400-5050
5	420	SMB1N-420H
6	450	SMB1N-D450
7	470	SMD1N-D470
8	520	SMD1N-D520

Relaxation rates were evaluated assigning first order kinetics of the *E-Z*-isomerization reaction. Samples were measured under dark (*E*) conditions at their absorption maximum, irradiated (*Z*) to reach photostationary equilibrium, followed by measuring the changing absorbance over time according to first order kinetics. Data were evaluated by fitting the rate equation $[A] = [A]_0 e^{(-kt)}$ using the Excel program. Half-lives were obtained by: $t_{1/2} = \ln(2)/k$.

To determine the ratio α of the two isomers in the PSS *Fischer's* method was applied.⁸ The absorbance (*A*) of the pure *E*- isomer (dark) and mixed spectra of *E*- and *Z*- isomer after irradiation with two different wavelengths (λ_1 and λ_2) are required. According to *Fischer's* formula:

$$\alpha_{\lambda 1} = \frac{\frac{\Delta A_{\lambda 1}}{A_{\lambda 1, \lambda 1}} - \frac{\Delta A_{\lambda 2}}{A_{\lambda 2, \lambda 2}}}{1 + \frac{\Delta A_{\lambda 1}}{A_{\lambda 1, \lambda 1}} - n \left(1 + \frac{\Delta A_{\lambda 2}}{A_{\lambda 2, \lambda 2}}\right)} \quad \text{with} \quad n = \frac{A_{\text{dark}, \lambda 1} - A_{\lambda 1, \lambda 1}}{A_{\text{dark}, \lambda 1} - A_{\lambda 2, \lambda 1}}$$

the PSS (PSS = $\alpha \cdot 100$) at the irradiated wavelengths can be determined. In this work, irradiation was carried out at seven to eight different wavelengths. To determine the PSS, the wavelength that provided the largest percentage of (*Z*) isomers was chosen as the basis and the ratio α was determined with the other wavelengths. For this wavelength, the PSS was determined from the mean value of all received α . The other wavelengths were specified relative to it. The determined α values generally had a standard deviation of $\pm 0.01 - 0.03$, for some aniline derivatives the deviation was up to ± 0.05 . Based on the obtained ratio α , the absorbance of the pure (*Z*) isomer can be calculated using the formula:

$$A_{Z\text{-Isomer}, \lambda} = A_{\text{dark}, \lambda} + \frac{A_{\lambda 1, \lambda} - A_{\text{dark}, \lambda}}{\alpha_{\lambda 1}}$$

Infrared (IR) spectra

Fourier transform infrared spectroscopy (FT-IR) spectra were obtained by using an IR-Affinity-1 from Shimadzu (ATR, neat or as a thin film). Wave numbers are reported in cm^{-1} .

Microwave reactor

A Biotage Initiator Sixty microwave reactor with sealed glass vessels was used for the irradiation with microwaves. The temperature was measured using an IR sensor (accuracy $\pm 2\%$). Reaction times indicate how long the mixture was stirred at the specified temperature, not how long the mixture was irradiated overall.

Melting points

The melting points were measured on a Stuart Melting Point SMP 3 device.

Low- and high-resolution ESI mass spectra

Low- and high-resolution ESI **mass spectra** were obtained on Thermo-Finnigan LCQ (LR) and Bruker Maxis Impact (HR) spectrometers operating in either positive or negative ionization modes, respectively, fitted to Shimadzu AL-10 (LR-ESI-MS) or Dionex Ultima 3000 HPLC systems (HR-ESI-MS).

Chemical Synthesis and Characterisation

Standard Procedures

For Standard Procedures, the conditions and ratios of reactants/reagents employed were kept constant. Solvent volumes refer to 1.0 equiv. In general, the *E*- and *Z*- isomers of the azobenzenes were separable by silica-gel chromatography and on TLC when the thermal relaxation half-life time was in the range of minutes or longer. For improving separation, yields and purity of the desired product the crude materials were kept in the dark at room temperature overnight after isolation and protected from UV light during chromatographic separation (i.e. work under red light, wrapped/shielded column wherever possible).

Standard Procedure A: Diazo Coupling using isoamyl nitrite

To a solution of the aniline (1.0 equiv.) in MeOH (5.0 mL/mmol) conc. HCl (6.0 equiv.) was added and cooled to 0 °C (icebath). In case of Boc-protected anilines the amount of HCl was doubled and the solution was stirred at room temperature until TLC showed full deprotection before cooling down (approx. 2 h). A solution of isoamyl nitrite (1.02 equiv.) in methanol (1.0 mL/mmol) was added slowly and the mixture was stirred for 30 min in the cold.

A1: A cold solution of the phenol (1.05 equiv.) in methanol (2.0 mL/mmol) was added followed by addition of NaOH (2.0 M) until pH = 11 was reached (characteristic color change from yellow to deep red).

A2: A solution of the phenol (1.05 equiv.) in methanol (2.0 mL/mmol) was basified with NaOH (2.0 M, 7.2 equiv.) and cooled in an icebath. To it was added the solution of the diazonium salt prepared above dropwise over 1 minute.

After 30 minutes stirring at 0 °C, the pH was adjusted to 7 with phosphate buffer (30 mL/mmol) and CHCl₃ (30 mL/mmol) was added. The organic layer was separated followed by extraction of the aqueous layer with CHCl₃ (3 – 5 × 20 mL/mmol). The combined organic extracts were dried with Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography or recrystallization provided the pure azobenzene.

Standard Procedure B: Phenol etherification in acetone

To a solution of the phenol (1.0 equiv.) and K_2CO_3 (4.0 equiv.) in anhydrous acetone (10 mL/mmol) the alkylhalogenide (1.0 – 10.0 equiv.) was added and stirred at reflux for 2 – 18 h until TLC indicated satisfactory conversion. The reaction mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (20 mL/mmol) and phosphate buffer (pH = 7, 30 mL/mmol). The organic layer was separated followed by extraction of the aqueous layer with EtOAc (3 × 20 mL/mmol). The combined organic extracts were dried with Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography or recrystallization provided the arylether.

Standard Procedure C: Ester or Imine cleavage with LiOH

Ester or Imine (1.0 equiv.) was dissolved in THF (20 mL/mmol), treated with aqueous LiOH (2 M, 10.0 equiv.), and stirred for 2 h at room temperature. The solution was neutralized with aqueous HCl (1 M). Most of the THF was removed under reduced pressure and $CHCl_3$ (20 mL/mmol) was added. The organic layer was separated followed by extraction of the aqueous layer with $CHCl_3$ or EtOAc (3 – 12 × 20 mL/mmol). The combined organic extracts were dried with Na_2SO_4 , filtered, and concentrated under reduced pressure. If necessary, the residue was purified by silica-gel chromatography or prep. HPLC to obtain the carboxylic acid.

Standard Procedure D: Buchwald – Hartwig amination

A solution of bromoaryl azobenzene (1.0 equiv.) and Cs_2CO_3 (4.0 equiv.) in anhydrous acetonitrile (25 mL/mmol) was purged with N_2 in a microwave reaction vial over 20 minutes. Amine (2.0 equiv.), $Pd(dba)_2$ (0.1 equiv.) and RuPhos (0.2 equiv.) were added and the vial was capped under nitrogen flow. The resulting suspension was heated with stirring to 100 °C and kept at this temperature until TLC indicated satisfactory conversion (typically 16 h). The mixture was cooled to RT, filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography provided the aminated azobenzene.

Standard Procedure E: Reductive amination

To a solution of amine (1.0 equiv.) in a mixture of AcOH and EtOH (1:9, 25 mL/mmol) aldehyde (3.0 equiv.) was added and stirred for 2 hours at room temperature. The mixture was cooled to 0 °C (icebath) and NaCNBH₃ (4.5 equiv.) was added. The icebath was removed and stirring was continued until TLC indicated satisfactory conversion (16 – 38 h). The solution was neutralized with aqueous NaOH (2 M) and most of the EtOH was removed under reduced pressure followed by extraction of the aqueous phase with CHCl₃ (3 × 20 mL/mmol). The combined organic extracts were dried with Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography provided the pure azobenzene.

Standard Procedure F: Reduction of nitroaryl compounds

Nitrobenzene (1.0 equiv.) was dissolved in a mixture of EtOH, EtOAc and AcOH (5:10:1, 50 mL/mmol). Pd/C (10 m%, 55 mg/mmol) was added and H₂ was bubbled through the solution until TLC indicates satisfactory conversion (6 – 24 h). The mixture was filtered through a pad of celite and the filter cake was washed with EtOH (~100 mL/mmol). Toluene (5 mL/mmol) was added and the mixture was concentrated under reduced pressure. The resulting crude product was dried under vacuum and used without further purification.

Syntheses

N-(5'-Methoxy-2'-nitrophenyl)succinimide **p-6**

Under an atmosphere of nitrogen 5-methoxy-2-nitroaniline (2.00 g, 11.9 mmol, 1.0 equiv.) and K_2CO_3 (4.11 g, 29.7 mmol, 2.5 equiv.) were suspended in dry THF (160 mL). Succinylchloride (1.31 mL, 11.9 mmol, 1.0 equiv.) was added dropwise and the reaction mixture was heated to 45 °C for 16 h. The reaction mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (100 mL) and washed with water (2×30 mL). The combined extracts were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography (EtOAc/petroleum ether, 1:1) provided succinimide **p-6** (1.95 g, 66%) as a yellow solid. R_f = 0.34 (EtOAc/petroleum ether, 1:1); m.p. 176 °C; 1H -NMR (250 MHz, $CDCl_3$): δ = 8.27 (d, J = 9.3 Hz, 1 H), 7.07 (dd, J = 2.7, 9.1 Hz, 1 H), 6.83 (d, J = 2.6 Hz, 1 H), 3.94 (s, 3 H), 3.16 - 2.82 (m, 4 H); ^{13}C -NMR (63 MHz, $CDCl_3$): δ = 176.3, 164.9, 139.0, 129.3, 129.2, 116.9, 115.7, 57.2, 29.8; IR: $\tilde{\nu}$ = 3356, 2839, 1786, 1701, 1585, 1489, 1280, 1173, 1092, 825; HRMS (ESI): m/z calcd for $C_{11}H_{11}N_2O_5$: 251.0662 $[M+H]^+$; found: 251.0666.

N-(4'-Methoxy-2'-nitrophenyl)succinimide **m-6**

Under an atmosphere of nitrogen 5-methoxy-2-nitroaniline (2.00 g, 11.9 mmol, 1.0 equiv.) and K_2CO_3 (4.11 g, 29.7 mmol, 2.5 equiv.) were suspended in dry THF (160 mL). Succinylchloride (1.31 mL, 11.9 mmol, 1.0 equiv.) was added dropwise and the reaction mixture was heated to 45 °C for 16 h. The reaction mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (100 mL) and washed with water (2×30 mL). The combined organic extracts were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography (EtOAc/petroleum ether, 1:1) provided succinimide **m-6** (1.94 g, 65%) as a yellow solid. R_f = 0.32 (EtOAc/petroleum ether, 1:1); m.p. 176 °C; 1H -NMR (300 MHz, $CDCl_3$): δ = 7.70 (dd, J = 1.2, 1.8 Hz, 1 H), 7.28 - 7.25 (m, 2 H), 3.92 (s, 3 H), 2.94 (d, J = 5.2 Hz, 4 H); ^{13}C -NMR (75 MHz, $CDCl_3$): δ = 175.7, 160.3, 145.7, 131.3, 120.3,

118.3, 110.9, 56.2, 28.7; IR: $\tilde{\nu}$ = 3348, 3089, 2939, 1774, 1705, 1539, 1357, 1280, 1171, 1030, 887, 664; HRMS (ESI): m/z calcd for $C_{11}H_{11}N_2O_5$: 251.0662 $[M+H]^+$; found: 251.0666.

4-((4'-bromophenyl)diazenyl)phenol **13**

Standard Procedure **A1** with *p*-bromaniline (5.00 g, 29.1 mmol, 1.0 equiv.) and phenol (2.87 g, 30.5 mmol, 1.05 equiv.) gave azobenzene **13** (6.28 g, 78 %) as an ocher solid after recrystallisation (toluene/petroleum ether, 1:3). R_f = 0.40 (EtOAc/petroleum ether, 1:4); m.p. 160 °C; 1H -NMR (300 MHz, $CDCl_3$): δ = 7.88 (d, J = 8.8 Hz, 2 H), 7.77 (d, J = 8.8 Hz, 2 H), 7.63 (d, J = 8.8 Hz, 2 H), 6.96 (d, J = 8.8 Hz, 2 H), 5.19 (br s, 1 H); ^{13}C -NMR (75 MHz, $CDCl_3$): δ = 158.4, 151.4, 147.0, 132.3, 125.1, 124.7, 124.1, 115.9; IR: $\tilde{\nu}$ = 3159, 2951, 2854, 1739, 1601, 1462, 1366, 1253, 837, 671; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 350 nm ($23800\text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $C_{12}H_{10}BrN_2O$: 276.9971/278.9951 $[M+H]^+$; found: 276.9975/278.9954.

4-((3',5'-dimethoxyphenyl)diazenyl)phenol **14**

Standard Procedure **A1** with 3,5-trimethoxyaniline (307 mg, 2.0 mmol, 1.0 equiv.) and phenol (198 mg, 2.1 mmol, 1.05 equiv.) gave azobenzene **14** (215 mg, 42 %) as an orange solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4). R_f = 0.38 (EtOAc/petroleum ether, 1:2); m.p. 129 °C; 1H -NMR (300 MHz, $CDCl_3$): δ = 7.89 (d, J = 8.8 Hz, 2 H), 7.10 (d, J = 2.2 Hz, 2 H), 6.95 (d, J = 8.8 Hz, 2 H), 6.59 (t, J = 2.2 Hz, 1 H), 3.88 (s, 6 H); ^{13}C -NMR (101 MHz, $CDCl_3$): δ = 161.1, 158.4, 154.5, 147.0, 125.1, 115.8, 103.4, 100.7, 55.6; IR: $\tilde{\nu}$ = 3062, 2935, 1585, 1416, 1281, 1207, 1151, 1053, 942, 667; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 355 nm ($21900\text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $C_{14}H_{15}N_2O_3$: 259.1077 $[M+H]^+$; found: 259.1082.

4-((3',4'-dihydro-2H-benzo[b][1',4']oxazin-7'-yl)diazenyl)phenol **15**

Standard Procedure **A1** with aniline **4** (156 mg, 1.04 mmol, 1.0 equiv.), phenol (103 mg, 1.09 mmol, 1.05 equiv.), and isoamyl nitrite (256 mg, 2.18 mmol, 2.1 equiv.) were converted to give a yellow solid (229 mg) that was dissolved in dry MeOH (12 mL), and HCl (4M in dioxane), and stirred at room temperature for 18 h. All solvents were removed under reduced pressure, and aq. NaHCO₃ (15 mL), CHCl₃ (20 mL), and acetone (2 mL) were added. The organic layer was separated, and the aqueous phase was extracted with CHCl₃ (3 × 20mL). The combined organic extracts were dried with Na₂SO₄, filtered, and concentrated under reduced pressure. Azobenzene **15** (145 mg, 55 %) was isolated as a brown oil after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4 → 1:1). *R_f* = 0.45 (EtOAc/petroleum ether, 1:1); ¹H-NMR (400 MHz, DMSO-*d*₆): δ = 10.00 (br s, 1 H), 7.65 (d, *J* = 8.8 Hz, 2 H), 7.30 (dd, *J* = 2.0, 8.5 Hz, 1 H), 7.15 (d, *J* = 2.3 Hz, 1 H), 6.88 (d, *J* = 9.1 Hz, 2 H), 6.66 (d, *J* = 8.5 Hz, 1 H), 4.15 (t, *J* = 4.4 Hz, 2 H); ¹³C-NMR (101 MHz, DMSO-*d*₆): δ = 159.8, 145.9, 143.6, 143.2, 138.7, 124.2, 120.1, 116.2, 113.8, 108.2, 64.6, 40.1; IR: $\tilde{\nu}$ = 3360, 2920, 2851, 1740, 1582, 1501, 1211, 840, 810; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 406 nm (24000 l·mol⁻¹·cm⁻¹); HRMS (ESI): *m/z* calcd for C₁₄H₁₄N₃O₂: 256.1081 [M+H]⁺; found: 256.1081.

2-(4'-((4''-hydroxyphenyl)diazenyl)phenoxy)acetic acid **16a**

Standard Procedure **A1** with Boc-protected aniline **5** (100 mg, 0.34 mmol, 1.0 equiv.) and phenol (33.5 mg, 0.35 mmol, 1.05 equiv.) gave azobenzene **16a** (47 mg, 51 %) as an orange solid after silica-gel chromatography (CH₂Cl₂/MeOH, 98:2 + 1.0 % formic acid). *R_f* = 0.17 (CH₂Cl₂/MeOH, 98:2 + 1.0 %

formic acid); m.p. 186 °C; $^1\text{H-NMR}$ (300 MHz, CD_3OD): δ = 7.83 (d, J = 8.9 Hz, 2 H), 7.77 (d, J = 8.8 Hz, 2 H), 7.06 (d, J = 8.9 Hz, 2 H), 6.90 (d, J = 8.8 Hz, 2 H), 4.75 (s, 2 H); $^{13}\text{C-NMR}$ (101 MHz, CD_3OD): δ = 171.0, 160.2, 159.9, 147.4, 146.1, 124.2, 123.7, 115.3, 114.6, 64.7; IR: $\tilde{\nu}$ = 3406, 2924, 1728, 1585, 1497, 1435, 1215, 1146, 1080, 837; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 359 nm ($16500 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{O}_4$: 273.0870 $[\text{M}+\text{H}]^+$; found: 273.0874.

Methyl-2-(4'-((4''-hydroxy-3''-methoxyphenyl)diazenyl)phenoxy)acetate **16b**

Standard Procedure **A1** with Boc-protected aniline **5** (200 mg, 0.68 mmol, 1.0 equiv.) and 2-methoxyphenol (88.3 mg, 0.71 mmol, 1.05 equiv.) gave after extraction, and evaporation of the solvent a residue that was redissolved in anhydrous MeOH (20 mL). Thionylchloride (1 mL) was added, and the mixture was stirred at room temperature for 2 h. The pH was adjusted to 7 with phosphate buffer, and CHCl_3 (30 mL) was added. The organic layer was separated followed by extraction of the aqueous layer with CHCl_3 ($3 \times 20 \text{ mL}$). The combined organic extracts were dried with Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2) provided azobenzene **16b** (146 mg, 68 %) as an ocher solid. R_f = 0.47 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2 + 1.0 % formic acid); m.p. 133 °C; $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 7.99 (d, J = 8.7 Hz, 2 H), 7.67 (dd, J = 2.1, 8.4 Hz, 1 H), 7.60 (d, J = 2.1 Hz, 1 H), 7.16 (d, J = 8.6 Hz, 1 H), 7.13 (d, J = 9.1 Hz, 2 H), 6.06 (br s, 1 H), 4.83 (s, 2 H), 4.10 (s, 3 H), 3.95 (s, 3 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 169.0, 159.5, 148.5, 147.6, 147.1, 146.7, 124.3, 121.0, 114.9, 114.2, 101.8, 65.4, 56.1, 52.4; IR: $\tilde{\nu}$ = 3190, 2916, 2851, 1771, 1582, 1501, 1207, 1022, 837; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 376 nm ($19000 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_2\text{O}_5$: 317.1132 $[\text{M}+\text{H}]^+$; found: 317.1135.

Methyl-2-(4'-((4''-hydroxy-3'',5''-dimethoxyphenyl)diazenyl)phenoxy)acetate **16c**

Standard Procedure **A1** with Boc-protected aniline **5** (500 mg, 1.69 mmol, 1.0 equiv.) and 2,6-dimethoxyphenol (274 mg, 1.78 mmol, 1.05 equiv.) gave after extraction and evaporation of the solvent a residue that was redissolved in dry MeOH (20 mL). Thionylchloride (1 mL) was added and the mixture was stirred at room temperature for 2 h. The pH was adjusted to 7 with phosphate buffer, and CHCl₃ (30 mL) was added. The organic layer was separated followed by extraction of the aqueous layer with CHCl₃ (3 × 20 mL). The combined organic extracts were dried with Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography (EtOAc/petroleum ether, 1:1) provided azobenzene **16c** (397 mg, 68 %) as an ocher solid. R_f = 0.53 (EtOAc/petroleum ether, 1:1); m.p. 122 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 7.89 (d, J = 8.9 Hz, 2 H), 7.28 (s, 2 H), 7.03 (d, J = 8.9 Hz, 2 H), 5.82 (s, 1 H), 4.73 (s, 2 H), 4.01 (s, 6 H), 3.84 (s, 3 H); ¹³C-NMR (63 MHz, CDCl₃): δ = 169.0, 159.6, 147.5, 147.2, 145.5, 137.5, 124.3, 114.9, 100.2, 65.4, 56.4, 52.4; IR: $\tilde{\nu}$ = 3453, 2951, 1751, 1585, 1497, 1315, 1200, 1107, 841; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 384 nm (20000 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₇H₁₉N₂O₆: 347.1238 [M+H]⁺; found: 347.1242.

Methyl-*N*-(5'-hydroxy-2'-((4''-methoxyphenyl)diazenyl)phenyl)succinamate **17a**

Standard Procedure **A1** with *p*-anisidine (123 mg, 1.00 mmol, 1.0 equiv.) and phenol **8** (201 mg, 1.05 mmol, 1.05 equiv.) gave after extraction and evaporation of the solvent a residue that was redissolved in anhydrous MeOH (20 mL). Thionylchloride (1 mL) was added and the mixture was stirred at room temperature for 2 h. The pH was adjusted to 7 with phosphate buffer and EtOAc (30 mL) was added. The organic layer was separated followed by extraction of the aqueous layer with EtOAc (3 × 20 mL). The combined organic extracts were dried with Na₂SO₄, filtered, and concentrated under reduced

pressure. Purification by silica-gel chromatography (EtOAc/petroleum ether, 1:2) provided azobenzene **17a** (201 mg, 56 %) as a yellow solid. $R_f = 0.21$ (EtOAc/petroleum ether, 1:2); m.p. 189 °C; $^1\text{H-NMR}$ (300 MHz, DMSO- d_6): $\delta = 10.28$ (br s, 1 H), 10.19 (s, 1 H), 7.95 (d, $J = 8.9$ Hz, 2 H), 7.86 (d, $J = 2.5$ Hz, 1 H), 7.64 (d, $J = 8.9$ Hz, 1 H), 7.10 (d, $J = 9.0$ Hz, 2 H), 6.57 (dd, $J = 2.6, 8.9$ Hz, 1 H), 3.85 (s, 3 H), 3.59 (s, 3 H), 2.80 (t, $J = 6.5$ Hz, 2 H), 2.63 (t, $J = 6.9$ Hz, 2 H); $^{13}\text{C-NMR}$ (126 MHz, DMSO- d_6): $\delta = 173.4, 170.8, 161.7, 161.7, 146.9, 138.6, 134.0, 125.0, 119.6, 114.9, 111.8, 107.6, 56.0, 51.9, 31.9, 29.1$; IR: $\tilde{\nu} = 3113, 2951, 2839, 1720, 1663, 1597, 1454, 1242, 1172, 1111, 841$; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 390 nm (23000 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₈H₂₀N₃O₅: 358.1397 [M+H]⁺; found: 358.1401.

Methyl-*N*-(2'-((4'-bromophenyl)diazenyl)-5'-hydroxyphenyl)succinamate **17b**

Standard Procedure **A1** with *p*-bromaniline (400 mg, 2.33 mmol, 1.0 equiv.), and phenol **8** (467 mg, 2.44 mmol, 1.05 equiv.) gave azobenzene **17b** (651 mg, 67 %) as an orange solid after recrystallization (toluene/petroleum ether, 3:1). $R_f = 0.30$ (CH₂Cl₂/MeOH, 95:5); m.p. 192 °C; $^1\text{H-NMR}$ (400 MHz, DMSO- d_6): $\delta = 10.55$ (br s, 1 H), 10.24 (s, 1 H), 7.92 (d, $J = 8.8$ Hz, 2 H), 7.89 (d, $J = 2.6$ Hz, 1 H), 7.77 (d, $J = 8.5$ Hz, 2 H), 7.70 (d, $J = 8.8$ Hz, 1 H), 6.61 (dd, $J = 2.5, 8.9$ Hz, 1 H), 3.61 (s, 3 H), 2.82 (t, $J = 6.7$ Hz, 2 H), 2.64 (t, $J = 6.4$ Hz, 2 H); $^{13}\text{C-NMR}$ (101 MHz, DMSO- d_6): $\delta = 173.4, 170.9, 162.9, 151.6, 139.5, 134.1, 132.7, 125.0, 124.1, 120.0, 112.1, 107.7, 51.9, 31.9, 29.0$; IR: $\tilde{\nu} = 3012, 2951, 2322, 1736, 1458, 1366, 1207, 833$; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 464 nm (19800 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₇H₁₇BrN₃O₄: 406.0397/408.0379 [M+H]⁺; found: 406.0393/408.0375.

tert-Butyl-2-hydroxy-5-((3',4',5'-trimethoxyphenyl)diazenyl)phenylcarbamate **18**

Standard Procedure **A2** with 3,4,5-trimethoxyaniline (1.0 g, 5.46 mmol, 1.0 equiv.) and phenol **9** (1.20 g, 5.73 mmol, 1.05 equiv.) gave azobenzene **18** (1.36 g, 62 %) as red solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4). R_f = 0.52 (EtOAc/petroleum ether, 1:4); m.p. 80 °C; ^1H -NMR (300 MHz, CDCl_3): δ = 8.73 (br s, 1 H), 7.76 (d, J = 1.6 Hz, 1 H), 7.68 (dd, J = 2.0, 8.7 Hz, 1 H), 7.20 (s, 2 H), 7.08 (d, J = 8.8 Hz, 1 H), 6.79 (br s, 1 H), 3.96 (s, 6 H), 3.94 (s, 3 H), 1.56 (s, 9 H); ^{13}C -NMR (101 MHz, CDCl_3): δ = 154.8, 153.6, 148.4, 140.6, 129.9, 126.8, 122.1, 118.8, 112.6, 105.2, 100.2, 82.4, 61.1, 56.3, 28.2; IR: $\tilde{\nu}$ = 3260, 2970, 2361, 1736, 1597, 1493, 1366, 1219, 1123, 999; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 473 nm ($27300 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{20}\text{H}_{26}\text{N}_3\text{O}_6$: 404.1816 $[\text{M}+\text{H}]^+$; found: 404.1824.

Methyl-*N*-(2'-((4''-hydroxy-3''-methoxyphenyl)diazenyl)-5'-methoxyphenyl) succinamate **19b**

Nitrobenzene **p-6** (250 mg, 1.14 mmol, 1.0 equiv.) was reduced to the corresponding aniline (quant.) following Standard Procedure **F**. The crude material was converted according to Standard Procedure **A1** with 2-methoxyphenol (176 mg, 1.42 mmol, 1.05 equiv.) to give azobenzene **19b** (128 mg, 30 %) as chartreuse solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 7:3 $\rightarrow$ EtOAc). R_f = 0.39 (EtOAc/petroleum ether, 7:3); m.p. 104 °C; ^1H -NMR (300 MHz, CDCl_3): δ = 10.85 (s, 1 H), 8.31 (d, J = 2.8 Hz, 1 H), 7.81 (d, J = 9.0 Hz, 1 H), 7.52 - 7.44 (m, 2 H), 7.06 (d, J = 8.9 Hz, 1 H), 6.71 (dd, J = 2.7, 9.0 Hz, 1 H), 4.01 (s, 3 H), 3.90 (s, 3 H), 3.71 (s, 3 H), 2.80 (s, 4 H); ^{13}C -NMR (63 MHz, CDCl_3): δ = 174.1, 171.2, 163.6, 149.3, 148.1, 147.3, 137.5, 134.2, 125.5, 120.6, 115.3, 111.7, 104.6, 103.0, 57.0, 56.6, 52.9, 33.8, 30.1; IR: $\tilde{\nu}$ = 3348, 2940, 2322, 1728, 1585, 1431, 1200, 1157, 1111, 1022,

848, 806; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\max}$ (ϵ) = 401 nm (24100 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₉H₂₁N₃O₆: 388.1503 [M+H]⁺; found: 388.1511.

N-(2'-((4''-Hydroxy-3'',5''-dimethoxyphenyl)diazenyl)-5'-methoxyphenyl)succinimide **19c**

Nitrobenzene **p-6** (751 mg, 3.00 mmol, 1.0 equiv.) was reduced to the corresponding aniline (quant.) following Standard Procedure **F**. The crude material was converted according to Standard Procedure **A1** with 2,6-dimethoxyphenol (486 mg, 3.15 mmol, 1.05 equiv.) to give azobenzene **19c** (495 mg, 43 %) as a red solid after purification by silica-gel chromatography (CH₂Cl₂/MeOH, 98:2 → 95:5). R_f = 0.48 (CH₂Cl₂/MeOH, 97:3); m.p. 76 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 7.88 (d, J = 9.0 Hz, 1 H), 7.09 (s, 2 H), 7.06 (dd, J = 2.6, 9.1 Hz, 1 H), 6.85 (d, J = 2.6 Hz, 1 H), 3.95 (s, 6 H), 3.90 (s, 3 H), 3.02 - 2.87 (m, 4 H); ¹³C-NMR (101 MHz, CDCl₃): δ = 176.1, 162.0, 147.1, 146.0, 141.1, 137.8, 132.3, 118.8, 116.3, 113.5, 100.3, 56.2, 55.8, 28.8; IR: $\tilde{\nu}$ = 2940, 2839, 1705, 1604, 1508, 1377, 1234, 1176, 1026, 818; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\max}$ (ϵ) = 394 nm (16500 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₉H₂₀N₃O₆: 386.1347 [M+H]⁺; found: 386.1351.

Methyl-*N*-(2'-((4''-hydroxy-3'',5''-dimethoxyphenyl)diazenyl)-4'-methoxyphenyl) succinamate **20**

Nitrobenzene **m-6** (1.14 g, 4.56 mmol, 1.0 equiv.) was reduced to the corresponding aniline (quant.) following Standard Procedure **F**. The crude material was further converted according to Standard Procedure **A1** with 2,6-dimethoxyphenol (738 mg, 4.80 mmol, 1.05 equiv.). The resulting crude material was dissolved in anhydrous MeOH (20 mL). Thionylchloride (1 mL), was added and the mixture was stirred at room temperature for 2 h. The pH was adjusted to 7 with phosphate buffer, and CHCl₃ (40 mL) was added. The organic layer was separated followed by extraction of the aqueous layer with CHCl₃ (3 × 30 mL). The combined organic extracts were dried with Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography (EtOAc/petroleum ether, 2:1 → EtOAc) provided azobenzene **20** (829 mg, 44 %) as an ocher solid. R_f = 0.21 (EtOAc/petroleum ether, 1:2); m.p. 159 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 9.67 (br s, 1 H), 8.54 (d, J = 9.1 Hz, 1 H), 7.32 (s, 2 H), 7.27 (s, 1 H), 7.03 (dd, J = 3.0, 9.1 Hz, 1 H), 5.98 (s, 1 H), 4.03 (s, 6 H), 3.86 (s, 3 H), 3.67 (s, 3 H), 2.84 - 2.72 (m, 4 H); ¹³C-NMR (75 MHz, CDCl₃): δ = 173.4, 169.3, 155.8, 147.3, 145.5, 140.0, 138.4, 130.4, 121.6, 119.3, 101.4, 100.7, 56.5, 55.6, 52.0, 32.8, 29.5; IR: $\tilde{\nu}$ = 3360, 2947, 2361, 1732, 1609, 1504, 1462, 1308, 1107, 1033, 814; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 515 nm (19100 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₀H₂₄N₃O₇: 418.1609 [M+H]⁺; found: 418.1622.

4-((3',4',5'-Trimethoxyphenyl)diazenyl)phenol **21a**

Standard Procedure **A1** with 3,4,5-trimethoxyaniline (1.09 g, 5.0 mmol, 1.0 equiv.) and phenol (500 mg, 5.25 mmol, 1.05 equiv.) gave azobenzene **21a** (1.25 g, 87 %) as an ocher solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:2). R_f = 0.32 (EtOAc/petroleum ether, 1:2); m.p. 165 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 7.87 (d, J = 8.8 Hz, 2 H), 7.22 (s, 2 H), 6.96 (d, J = 8.9 Hz, 2 H), 5.38

(br s, 1 H), 3.97 (s, 6 H), 3.94 (s, 3 H); ^{13}C -NMR (63 MHz, CDCl_3): δ = 158.3, 153.4, 148.6, 146.9, 140.0, 124.8, 115.8, 100.0, 61.0, 56.2; IR: $\tilde{\nu}$ = 3283, 2947, 2839, 1740, 1585, 1227, 1126, 991, 845; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 362 nm ($24600 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_4$: 289.1183 $[\text{M}+\text{H}]^+$; found: 289.1184.

2-((*tert*-Butyldimethylsilyl)oxy)-4-((3',4',5'-trimethoxyphenyl)diazenyl)phenol **21b**

Standard Procedure **A1** with 3,4,5-trimethoxyaniline (366 mg, 2.0 mmol, 1.0 equiv.) and phenol **10b** (471 mg, 2.1 mmol, 1.05 equiv.) gave azobenzene **21b** (264 mg, 32 %) as a red oil after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4). R_f = 0.44 (EtOAc/petroleum ether, 1:4); ^1H -NMR (250 MHz, CDCl_3): δ = 7.57 (dd, J = 2.2, 8.6 Hz, 1 H), 7.45 (d, J = 2.2 Hz, 1 H), 7.20 (s, 2 H), 7.06 (d, J = 8.6 Hz, 1 H), 5.81 (s, 1 H), 3.98 (s, 6 H), 3.93 (s, 3 H), 1.06 (s, 9 H), 0.36 (s, 6 H); ^{13}C -NMR (63 MHz, CDCl_3): δ = 153.5, 150.3, 148.5, 147.8, 146.5, 142.8, 119.6, 117.5, 110.7, 100.1, 61.0, 56.2, 25.7, 18.2, -4.3; IR: $\tilde{\nu}$ = 2932, 2859, 2361, 1740, 1593, 1493, 1258, 1219, 1126, 829, 783; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 375 nm ($17300 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{21}\text{H}_{31}\text{N}_2\text{O}_5\text{Si}$: 419.1997 $[\text{M}+\text{H}]^+$; found: 419.2004.

4-((3',4',5'-Trimethoxyphenyl)diazenyl)resorcin **21c**

Standard Procedure **A1** with 3,4,5-trimethoxyaniline (366 mg, 2.0 mmol, 1.0 equiv.) and resorcin (231 mg, 2.1 mmol, 1.05 equiv.) gave azobenzene **21c** (347 mg, 57 %) as a red solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4 $\rightarrow$ 1:2). R_f = 0.42 (EtOAc/petroleum ether, 1:2); m.p. 95 °C; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 13.83 (br s, 1 H), 7.76 (d, J = 8.8 Hz, 1 H), 7.10 (s, 2 H), 6.58 (dd, J = 2.5, 8.6 Hz, 1 H), 6.46 (d, J = 2.6 Hz, 1 H), 3.97 (s, 6 H), 3.95 (s, 3 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 160.7, 156.6, 153.7, 145.9, 139.7, 135.1, 132.9, 108.9, 103.8, 99.0, 61.1, 56.3; IR: $\tilde{\nu}$ = 3360, 2940, 2832, 1724, 1597, 1215, 1115, 1006, 826, 783; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 350 nm (23800 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_5$: 305.1132 $[\text{M}+\text{H}]^+$; found: 305.1133.

2-Bromo-4-((3',4',5'-trimethoxyphenyl)diazenyl)phenol **21d**

Standard Procedure **A1** with 3,4,5-trimethoxyaniline (366 mg, 2.0 mmol, 1.0 equiv.) and 2-bromophenol (363 mg, 2.1 mmol, 1.05 equiv.) gave azobenzene **21d** (402 mg, 55 %) as an ocher solid after purification by silica-gel chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 95:5 + 1.0 % formic acid). R_f = 0.45 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 95:5 + 1.0 % formic acid); m.p. 161 °C; $^1\text{H-NMR}$ (250 MHz, CDCl_3): δ = 8.11 (d, J = 2.2 Hz, 1 H), 7.88 (dd, J = 2.3, 8.7 Hz, 1 H), 7.23 (s, 2 H), 7.17 (d, J = 8.6 Hz, 1 H), 5.83 (s, 1 H), 3.97 (s, 6 H), 3.95 (s, 3 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 154.4, 153.5, 148.2, 147.2, 140.6, 125.5, 116.1, 111.1, 100.3, 61.1, 56.2; IR: $\tilde{\nu}$ = 3325, 2955, 1740, 1597, 1334, 1207, 1130, 991; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 458 nm (28600 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{16}\text{BrN}_2\text{O}_4$: 367.0288/369.0267 $[\text{M}+\text{H}]^+$; found: 367.0296/369.0275.

3-Bromo-4-((3',4',5'-trimethoxyphenyl)diazenyl)phenol **21e**

Standard Procedure **A1** with 3,4,5-trimethoxyaniline (366 mg, 2.0 mmol, 1.0 equiv.) and 3-bromophenol (363 mg, 2.1 mmol, 1.05 equiv.) gave azobenzene **21e** (516 mg, 70 %) as a dark green solid after purification by silica-gel chromatography (CH₂Cl₂/MeOH, 95:5 + 1.0 % formic acid). R_f = 0.45 (CH₂Cl₂/MeOH, 95:5 + 1.0 % formic acid); m.p. 221 °C; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 7.64 (d, J = 8.9 Hz, 1 H), 7.21 (s, 2 H), 7.21 (d, J = 2.5 Hz, 1 H), 6.88 (dd, J = 2.5, 8.9 Hz, 1 H), 3.86 (s, 6 H), 3.75 (s, 3 H); ¹³C-NMR (75 MHz, DMSO-*d*₆): δ = 162.1, 153.8, 148.5, 141.8, 140.5, 127.8, 120.0, 119.1, 116.4, 100.6, 60.7, 56.4; IR: $\tilde{\nu}$ = 3237, 2940, 1740, 1593, 1458, 1227, 1123, 984, 856; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 458 nm (28300 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₅H₁₆BrN₂O₄: 367.0288/369.0267 [M+H]⁺; found: 367.0295/369.0274.

8-Hydroxy-5-((3',4',5'-trimethoxyphenyl)diazenyl)quinolin **22a**

Standard Procedure **A1** with 3,4,5-trimethoxyaniline (366 mg, 2.0 mmol, 1.0 equiv.) and 8-hydroxyquinoline (305 mg, 2.1 mmol, 1.05 equiv.) gave azobenzene **22a** (419 mg, 62 %) as a dark green solid after purification by silica-gel chromatography (CH₂Cl₂/MeOH, 95:5 + 1.0 % formic acid). R_f = 0.46 (CH₂Cl₂/MeOH, 95:5 + 1.0 % formic acid); m.p. 180 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 9.22 (dd, J = 1.6, 8.5 Hz, 1 H), 8.84 (dd, J = 1.5, 4.1 Hz, 1 H), 7.98 (d, J = 8.5 Hz, 1 H), 7.59 (dd, J = 4.2, 8.6 Hz, 1 H), 7.23 (d, J = 8.5 Hz, 1 H), 7.22 (s, 2 H), 3.96 (s, 6 H), 3.91 (s, 3 H); ¹³C-NMR (101 MHz, CDCl₃): δ = 155.2, 153.6, 149.1, 148.5, 140.5, 139.9, 137.8, 132.8, 127.0, 122.8, 115.6, 110.0, 100.4, 61.1, 56.3; IR: $\tilde{\nu}$ = 2940, 2322, 1740, 1574, 1493, 1458, 1312, 1215, 1126, 999, 787; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 494 nm (17400 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₈H₁₈N₃O₄: 340.1292 [M+H]⁺; found: 340.1298.

4-((3',4',5'-Trimethoxyphenyl)diazenyl)naphth-1-ol **22b**

Standard Procedure **A1** with 3,4,5-trimethoxyaniline (366 mg, 2.0 mmol, 1.0 equiv.) and 1-naphthol (302 mg, 2.1 mmol, 1.05 equiv.) gave azobenzene **22b** (422 mg, 62 %) as an ocher solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4 $\rightarrow$ 1:2). R_f = 0.59 (EtOAc/petroleum ether, 1:4); m.p. 185 °C; $^1\text{H-NMR}$ (300 MHz, DMSO- d_6): δ = 8.89 (d, J = 8.4 Hz, 1 H), 8.23 (d, J = 8.2 Hz, 1 H), 7.87 (d, J = 8.5 Hz, 1 H), 7.71 (ddd, J = 1.3, 6.9, 8.3 Hz, 1 H), 7.59 (ddd, J = 1.1, 7.0, 8.2 Hz, 1 H), 7.30 (s, 2 H), 7.00 (d, J = 8.6 Hz, 1 H), 3.93 (s, 6 H), 3.76 (s, 3 H); $^{13}\text{C-NMR}$ (75 MHz, DMSO- d_6): δ = 157.8, 153.4, 148.3, 139.3, 132.6, 127.9, 125.5, 124.6, 122.7, 122.5, 114.4, 108.9, 99.7, 79.2, 60.2, 56.0; IR: $\tilde{\nu}$ = 3244, 2997, 2322, 1740, 1593, 1551, 1477, 1188, 1123, 1014, 814, 752; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 517 nm (18000 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₉H₁₉N₂O₄: 339.1339 [M+H]⁺; found: 339.1342.

4-((3',4',5'-Trimethoxyphenyl)diazenyl)-6,7-dimethoxynaphth-1-ol **22d**

Standard Procedure **A1** with 3,4,5-trimethoxyaniline (366 mg, 2.0 mmol, 1.0 equiv.) and naphthol **11d** (429 mg, 2.1 mmol, 1.05 equiv.) gave azobenzene **22d** (488 mg, 62 %) as a dark red solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:2 $\rightarrow$ 1:1). R_f = 0.45 (EtOAc/petroleum ether, 1:2); m.p. 191 °C; $^1\text{H-NMR}$ (600 MHz, DMSO- d_6): δ = 8.22 (br s, 1 H), 7.73 (d,

$J = 8.3$ Hz, 1 H), 7.49 (s, 1 H), 7.28 (br s, 2 H), 6.86 (d, $J = 8.4$ Hz, 1 H), 3.98 (s, 3 H), 3.92 (s, 3 H), 3.91 (s, 6 H), 3.75 (s, 3 H); ^{13}C -NMR (151 MHz, DMSO- d_6): $\delta = 157.0, 153.8, 150.9, 149.3, 139.6, 138.7, 129.7, 120.2, 112.8, 108.0, 102.1, 101.8, 100.1, 79.6, 60.7, 56.3, 55.8, 55.6$; IR: $\tilde{\nu} = 2940, 2839, 1736, 1593, 1543, 1458, 1373, 1226, 1122, 1003, 779$; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\text{max}} (\epsilon) = 517$ nm (23000 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₁H₂₃N₂O₆: 399.1551 [M+H]⁺; found: 399.1561.

1-((3',4',5'-trimethoxyphenyl)diazenyl)naphth-2-ol **23**

Standard Procedure **A1** with 3,4,5-trimethoxyaniline (366 mg, 2.0 mmol, 1.0 equiv.) and 2-naphthol (302 mg, 2.1 mmol, 1.05 equiv.) gave azobenzene **23** (574 mg, 85 %) as a red solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4 → 1:2). $R_f = 0.41$ (EtOAc/petroleum ether, 1:4); m.p. 114 °C; ^1H -NMR (600 MHz, CDCl₃): $\delta = 8.58$ (d, $J = 8.3$ Hz, 1 H), 7.74 (d, $J = 9.4$ Hz, 1 H), 7.65 (d, $J = 7.9$ Hz, 1 H), 7.58 (ddd, $J = 1.1, 7.2, 8.3$ Hz, 1 H), 7.41 (ddd, $J = 0.9, 7.2, 7.9$ Hz, 1 H), 7.04 (s, 2 H), 6.96 (d, $J = 9.4$ Hz, 1 H), 3.98 (s, 6 H), 3.93 (s, 3 H); ^{13}C -NMR (151 MHz, CDCl₃): $\delta = 166.7, 154.0, 142.2, 138.6, 138.5, 133.3, 129.8, 128.6, 128.1, 125.4, 123.5, 121.5, 96.9, 61.1, 56.3$; IR: $\tilde{\nu} = 2970, 2820, 1748, 1597, 1450, 1215, 1123, 991, 818, 752$; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\text{max}} (\epsilon) = 469$ nm (26300 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₉H₁₉N₂O₄: 339.1339 [M+H]⁺; found: 339.1344.

tert-Butyl-2-methoxy-5-((3',4',5'-trimethoxyphenyl)diazenyl)phenylcarbamate **24**

Standard Procedure **B** with azobenzene **18** (1.25 g, 3.10 mmol, 1.0 equiv.) and MeI (386 μ L, 6.20 mmol, 2.0 equiv.) gave azobenzene **24** (1.18 g, 91 %) as a yellow solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4). R_f = 0.27 (EtOAc/petroleum ether, 1:4); m.p. 132 °C; ^1H -NMR (300 MHz, CDCl_3): δ = 8.72 (s, 1 H), 7.62 (dd, J = 2.4, 8.6 Hz, 1 H), 7.26 (s, 2 H), 7.17 (s, 1 H), 6.98 (d, J = 8.7 Hz, 1 H), 3.97 (s, 9 H), 3.93 (s, 3 H), 1.57 (s, 9 H); ^{13}C -NMR (75 MHz, CDCl_3): δ = 153.4, 152.5, 149.7, 148.6, 146.9, 139.9, 128.7, 119.0, 111.1, 109.6, 100.1, 80.6, 61.0, 56.2, 56.0, 28.3; IR: $\tilde{\nu}$ = 2970, 2836, 2361, 1720, 1593, 1520, 1366, 1219, 1119, 992; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 372 nm (22100 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{21}\text{H}_{28}\text{N}_3\text{O}_6$: 418.1973 $[\text{M}+\text{H}]^+$; found: 418.1978.

N-(2-Methoxy-5-((3',4',5'-trimethoxyphenyl)diazenyl)phenyl)succinamic acid **25**

Azobenzene **24** (585 mg, 1.40 mmol, 1.0 equiv.) dissolved in a mixture of 1,4-dioxane and methanol (1:1, 10 mL) was treated with HCl (8.0 mL, 4 M in dioxan) and stirred at room temperature for 4 h. After evaporation of all solvents, K_2CO_3 (2.17 g, 15.7 mmol, 11.2 equiv.) and succinic anhydride (631 mg, 6.31 mmol, 4.5 equiv.) were added followed by DMF (8.0 mL). The resulting mixture was stirred for 16 h at 85 °C. After cooling water (30 mL) and EtOAc (20 mL) were added and the pH was adjusted to 10 with sat. NaHCO_3 . The organic layer was discarded. The pH of the aqueous phase was adjusted to 3 with HCl (1 M), followed by extraction of the aqueous layer with EtOAc (3 $\times$ 150 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid) to provide azobenzene **25**

(317 mg, 54 %) as an orange solid. $R_f = 0.20$ (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 88 °C; $^1\text{H-NMR}$ (300 MHz, DMSO- d_6): $\delta = 12.12$ (br s, 1 H), 9.36 (s, 1 H), 8.62 (d, $J = 2.1$ Hz, 1 H), 7.71 (dd, $J = 2.4, 8.7$ Hz, 1 H), 7.24 (d, $J = 8.9$ Hz, 1 H), 7.22 (s, 2 H), 3.95 (s, 3 H), 3.89 (s, 6 H), 3.75 (s, 3 H), 2.69 (t, $J = 6.9$ Hz, 2 H), 2.57 - 2.52 (m, 2 H); $^{13}\text{C-NMR}$ (101 MHz, DMSO- d_6): $\delta = 174.4, 171.2, 153.8, 152.2, 148.3, 145.9, 140.2, 128.7, 122.1, 113.6, 111.5, 100.3, 60.7, 56.6, 56.4, 31.4, 29.3$; IR: $\tilde{\nu} = 3329, 2920, 2851, 1740, 1705, 1593, 1531, 1408, 1250, 1123, 991$; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\text{max}} (\epsilon) = 373$ nm (22600 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₀H₂₄N₃O₇: 418.1609 [M+H]⁺; found: 418.1610.

Ethyl-2-(4'-((4''-bromophenyl)diazenyl)phenoxy)acetate **26a**

Standard Procedure **B** with azobenzene **3** (1.10 g, 4.0 mmol, 1.0 equiv.) and ethyl bromoacetate (1.45 mL, 13.1 mmol, 3.3 equiv.) gave azobenzene **26a** (1.20 g, 83 %) as a yellow solid after recrystallization (toluene/petroleum ether, 1:4). $R_f = 0.55$ (EtOAc/petroleum ether, 1:4); m.p. 203 °C; $^1\text{H-NMR}$ (300MHz, CDCl₃): $\delta = 7.92$ (d, $J = 9.0$ Hz, 2 H), 7.77 (d, $J = 8.6$ Hz, 2 H), 7.64 (d, $J = 8.5$ Hz, 2 H), 7.03 (d, $J = 9.0$ Hz, 2 H), 4.71 (s, 2 H), 4.31 (q, $J = 7.1$ Hz, 2 H), 1.32 (t, $J = 7.1$ Hz, 3 H); $^{13}\text{C-NMR}$ (75MHz, CDCl₃): $\delta = 168.4, 160.3, 151.4, 147.4, 132.2, 124.9, 124.8, 124.1, 115.0, 65.5, 61.6, 14.2$; IR: $\tilde{\nu} = 3167, 3024, 2816, 1740, 1570, 1473, 1409, 1219, 1060, 834$; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\text{max}} (\epsilon) = 464$ nm (19800 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₆H₁₆BrN₂O₃: 363.0339/365.0320 [M+H]⁺; found: 363.0344/365.0327.

Ethyl-2-(4'-((4''-(dimethylamino)phenyl)diazenyl)phenoxy)acetate **26b**

Standard Procedure **D** with azobenzene **26a** (50.0 mg, 0.14 mmol, 1.0 equiv.), dimethylamine hydrochloride (22.5 mg, 0.28 mmol, 2.0 equiv.) and Cs_2CO_3 (269 mg, 0.83 mmol, 6.0 equiv.) gave azobenzene **26b** (39.1 mg, 87 %) as a scarlet solid after silica-gel chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 20:1). $R_f = 0.26$ ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 20:1); m.p. 142 °C; $^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 7.86$ (d, $J = 3.3$ Hz, 2 H), 7.83 (d, $J = 3.1$ Hz, 2 H), 7.00 (d, $J = 8.9$ Hz, 2 H), 6.77 (d, $J = 9.1$ Hz, 2 H), 4.69 (s, 2 H), 4.30 (q, $J = 7.2$ Hz, 2 H), 3.09 (s, 6 H), 1.32 (t, $J = 7.1$ Hz, 3 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): $\delta = 168.7, 158.9, 152.1, 148.1, 143.6, 124.6, 123.3, 114.8, 111.5, 65.6, 61.5, 40.3, 14.2$; IR: $\tilde{\nu} = 3460, 3082, 2961, 2820, 1738, 1597, 1366, 1207, 1083, 838$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): λ_{max} (ϵ) = 409 nm (24700 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{22}\text{N}_3\text{O}_3$: 328.1656 $[\text{M}+\text{H}]^+$; found: 328.1658.

Ethyl-2-(4'-((4'-morpholinophenyl)diazenyl)phenoxy)acetate **26c**

Standard Procedure **D** with azobenzene **26a** (50.0 mg, 0.14 mmol, 1.0 equiv.) and morpholine (24.0 mg, 0.28 mmol, 2.0 equiv.) gave azobenzene **26c** (40.2 mg, 79 %) as an orange solid after silica-gel chromatography (EtOAc /petroleum ether, 1:4 $\rightarrow$ 1:2). $R_f = 0.28$ (EtOAc /petroleum ether, 1:4); m.p. 160 °C; $^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 7.87$ (d, $J = 9.0$ Hz, 2 H), 7.87 (d, $J = 9.0$ Hz, 2 H), 7.01 (d, $J = 9.1$ Hz, 2 H), 6.98 (d, $J = 9.1$ Hz, 2 H), 4.70 (s, 2 H), 4.30 (q, $J = 7.2$ Hz, 2 H), 3.95 - 3.82 (m, 4 H), 3.35 - 3.28 (m, 4 H), 1.32 (t, $J = 7.2$ Hz, 3 H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = 168.6, 159.3, 152.8, 147.9, 145.8, 124.3, 124.1, 114.9, 114.5, 66.7, 65.5, 61.5, 48.2, 14.2$; IR: $\tilde{\nu} = 3464, 2963, 2843, 1759, 1578, 1366, 1246, 1153, 921, 841$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): λ_{max} (ϵ) = 392 nm (26200 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{20}\text{H}_{24}\text{N}_3\text{O}_4$: 370.1761 $[\text{M}+\text{H}]^+$; found: 370.1766.

Ethyl-2-(4'-((4''-(4'''-methylpiperazin-1-yl)phenyl)diazenyl)phenoxy)acetate **26d**

Standard Procedure **D** with azobenzene **26a** (100.0 mg, 0.28 mmol, 1.0 equiv.) and 1-methylpiperazine (55.2 mg, 0.55 mmol, 2.0 equiv.) gave azobenzene **26d** (89.0 mg, 85 %) as a yellow solid after silica-gel chromatography (CH₂Cl₂/MeOH, 80:1 → 20:1). *R_f* = 0.25 (CH₂Cl₂/MeOH, 20:1); m.p. 150 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 7.87 (d, *J* = 3.4 Hz, 2 H), 7.84 (d, *J* = 3.4 Hz, 2 H), 7.01 (d, *J* = 8.2 Hz, 2 H), 6.98 (d, *J* = 8.2 Hz, 2 H), 4.70 (s, 2 H), 4.30 (q, *J* = 7.2 Hz, 2 H), 3.43 - 3.34 (m, 4 H), 2.64 - 2.55 (m, 4 H), 2.38 (s, 3 H), 1.32 (t, *J* = 7.1 Hz, 3 H); ¹³C-NMR (75 MHz, CDCl₃): δ = 168.6, 159.2, 152.8, 148.0, 145.4, 124.3, 124.1, 114.8, 114.7, 65.5, 61.5, 54.9, 47.9, 46.1, 14.2; IR: $\tilde{\nu}$ = 3460, 2931, 2839, 2793, 1751, 1736, 1581, 1497, 1443, 1377, 1220, 834; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 396 nm (27300 l·mol⁻¹·cm⁻¹); HRMS (ESI): *m/z* calcd for C₂₁H₂₇N₄O₃: 383.2078 [M+H]⁺; found: 383.2084.

Ethyl-2-(4'-((4''-acetamidophenyl)diazenyl)phenoxy)acetate **26e**

Standard Procedure **D** with azobenzene **26a** (100.0 mg, 0.28 mmol, 1.0 equiv.), and acetamide (32.5 mg, 0.55 mmol, 2.0 equiv.) gave azobenzene **26e** (61.2 mg, 65 %) as an orange solid after silica-gel chromatography (CH₂Cl₂/MeOH, 9:1). *R_f* = 0.40 (CH₂Cl₂/MeOH, 9:1); m.p. 192 °C; ¹H-NMR (400 MHz, CDCl₃): δ = 7.92 (d, *J* = 6.7 Hz, 2 H), 7.90 (d, *J* = 6.7 Hz, 2 H), 7.68 (d, *J* = 8.5 Hz, 2 H), 7.34 (s, 1 H), 7.04 (d, *J* = 8.8 Hz, 2 H), 4.72 (s, 2 H), 4.32 (q, *J* = 7.2 Hz, 2 H), 2.25 (s, 3 H), 1.34 (t, *J* = 7.2 Hz, 3 H); ¹³C-NMR (101 MHz, CDCl₃): δ = 168.5, 168.2, 159.9, 149.1, 147.7, 140.0, 124.6, 123.7, 119.7, 114.9,

65.5, 61.6, 24.8, 14.2; IR: $\tilde{\nu}$ = 3005, 2913, 2322, 1717, 1601, 1504, 1377, 1203, 1076, 837, 714; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 361 nm (25700 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₈H₂₀N₃O₄: 342.1448 [M+H]⁺; found: 342.1451.

Ethyl-2-(4'-((4''-(1''',3'''-dioxoisindolin-2'''-yl)phenyl)diazenyl)phenoxy)acetate **26f**

Bromaryl azobenzene **26a** (50.0 mg, 0.14 mmol, 1.0 equiv.) CuI (39.3 mg, 0.21 mmol, 1.5 equiv.), and potassium phthalimide (38.3 mg, 0.21 mmol, 1.5 equiv.) were placed in a microwave reaction vial. The vial was sealed, and the atmosphere replaced by nitrogen. The solids were suspended in dry DMF (4 mL), and the vial was heated for 9 h to 160 °C. After cooling aqueous HCl (1 M, 3 mL) was added, followed by extraction with CHCl₃ (3 × 10 mL). The combined organic extracts were washed with H₂O (20 mL), and brine (20 mL), dried with Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography (EtOAc/petroleum ether, 1:9 → 1:1) provided pure azobenzene **26f** (42.0 mg, 71 %) as an ocher solid. R_f = 0.39 (EtOAc/petroleum ether, 1:2); m.p. 189 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 8.06 - 7.92 (m, 6 H), 7.84 - 7.80 (m, J = 3.1, 5.5 Hz, 2 H), 7.64 (d, J = 8.8 Hz, 2 H), 7.04 (d, J = 9.0 Hz, 2 H), 4.72 (s, 2 H), 4.31 (q, J = 7.2 Hz, 2 H), 1.33 (t, J = 7.2 Hz, 3 H); ¹³C-NMR (75 MHz, CDCl₃): δ = 168.4, 167.1, 160.3, 151.5, 147.6, 134.6, 133.5, 131.7, 126.8, 124.9, 123.9, 123.3, 114.9, 65.5, 61.6, 14.2; IR: $\tilde{\nu}$ = 3375, 2990, 2322, 1740, 1694, 1524, 1223, 1153, 1080, 841; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 351 nm (25300 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₄H₂₀N₃O₅: 430.1397 [M+H]⁺; found: 430.1410.

Ethyl-2-(4'-((3'',5''-trimethoxyphenyl)diazenyl)phenoxy)acetate **27**

Standard Procedure **B** with azobenzene **14** (199 mg, 0.77 mmol, 1.0 equiv.) and ethyl bromoacetate (282 μ L, 13.4 mmol, 3.3 equiv.) gave azobenzene **27** (241 mg, 91 %) as an orange solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4). R_f = 0.40 (EtOAc/petroleum ether, 1:4); m.p. 93 °C; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 7.94 (d, J = 9.1 Hz, 2 H), 7.11 (d, J = 2.3 Hz, 2 H), 7.05 (d, J = 9.1 Hz, 2 H), 6.60 (t, J = 2.3 Hz, 1 H), 4.72 (s, 2 H), 4.32 (q, J = 7.0 Hz, 2 H), 3.89 (s, 6 H), 1.33 (t, J = 7.2 Hz, 3 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 168.5, 161.1, 160.2, 154.5, 147.4, 124.8, 114.9, 103.5, 100.7, 65.5, 61.6, 55.6, 14.2; IR: $\tilde{\nu}$ = 3062, 2908, 1762, 1582, 1412, 1210, 1145, 852, 829, 675; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 345 nm (20100 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_5$: 345.1445 $[\text{M}+\text{H}]^+$; found: 345.1450.

Ethyl-2-(4'-((3'',4''-dihydro-2''*H*-benzo[b][1'',4'']oxazin-7''-yl)diazenyl)phenoxy) acetate **28**

Standard Procedure **B** with azobenzene **15** (100 mg, 0.39 mmol, 1.0 equiv.), and ethyl bromoacetate (46 μ L, 0.41 mmol, 1.05 equiv.) gave azobenzene **28** (124 mg, 93 %) as an orange solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4 $\rightarrow$ 1:1). R_f = 0.35 (EtOAc/petroleum ether, 1:2); m.p. 76 °C; $^1\text{H-NMR}$ (400 MHz, $\text{DMSO}-d_6$): δ = 7.73 (d, J = 9.1 Hz, 2 H), 7.34 (dd, J = 2.0, 8.5 Hz, 1 H), 7.18 (d, J = 2.0 Hz, 1 H), 7.06 (d, J = 9.1 Hz, 2 H), 6.80 - 6.76 (m, 1 H), 6.68 (d, J = 8.5 Hz, 1 H), 4.87 (s, 2 H), 4.19 (q, J = 7.1 Hz, 2 H), 4.16 (t, J = 4.4 Hz, 2 H), 3.43 - 3.37 (m, J = 2.3 Hz, 2 H), 1.23 (t, J = 7.2 Hz, 3 H); $^{13}\text{C-NMR}$ (101 MHz, $\text{DMSO}-d_6$): δ = 168.5, 158.8, 146.9, 143.0, 142.7, 138.8, 123.4, 120.2, 115.0, 113.2, 107.8, 64.8, 64.1, 60.7, 40.0, 14.0; IR: $\tilde{\nu}$ = 3356, 2970, 2928, 2870, 1751, 1597, 1500, 1315, 1261, 1080, 837, 810; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 408 nm (24000 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{20}\text{N}_3\text{O}_4$: 342.1448 $[\text{M}+\text{H}]^+$; found: 342.1452.

Ethyl-2-(4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenoxy)acetate **29a**

Standard Procedure **B** with azobenzene **21a** (1.17 g, 4.05 mmol, 1.0 equiv.) and ethyl bromoacetate (1.48 mL, 13.4 mmol, 3.3 equiv.) gave azobenzene **29a** (1.39 g, 91 %) as an orange solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4). R_f = 0.52 (EtOAc/petroleum ether, 1:2); m.p. 51 °C; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 7.92 (d, J = 8.5 Hz, 2 H), 7.23 (s, 2 H), 7.04 (d, J = 8.8 Hz, 2 H), 4.72 (s, 2 H), 4.31 (q, J = 7.2 Hz, 2 H), 3.98 (s, 6 H), 3.95 (s, 3 H), 1.33 (t, J = 7.9 Hz, 3 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 168.4, 159.9, 153.5, 148.5, 147.4, 140.2, 124.5, 114.9, 100.1, 65.4, 61.5, 61.0, 56.1, 14.1; IR: $\tilde{\nu}$ = 2940, 2913, 2839, 1759, 1578, 1215, 1123, 1003, 845, 829; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 360 nm (22100 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_6$: 375.1551 $[\text{M}+\text{H}]^+$; found: 375.1563.

Ethyl-2-(2'-(*tert*-butyldimethylsilyl)oxy-4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenoxy) acetate **29b**

A solution of phenol **21b** (100 mg, 0.24 mmol, 1.0 equiv.) in dry THF (10 mL) was cooled to -20 °C under an atmosphere of argon. Solid NaH (8.6 mg, 0.36 mmol, 1.5 equiv.) was added and stirred for 10 min followed by addition of ethyl bromoacetate (133 μL , 1.19 mmol, 5.0 equiv.). The reaction mixture was stirred at 0°C for 1.5 h. After stirring for additional 1h at 20°C the pH was adjusted to 7 with phosphate buffer, and CHCl_3 (20 mL) was added. The aqueous layer was separated and extracted with CHCl_3 (3 $\times$ 10 mL). The combined organic extracts were dried with Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4) provided

azobenzene **29b** (75 mg, 62 %) as a yellow solid. $R_f = 0.42$ (EtOAc/petroleum ether, 1:4); m.p. 101 °C; $^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 7.54$ (dd, $J = 2.3, 8.5$ Hz, 1 H), 7.47 (d, $J = 2.3$ Hz, 1 H), 7.21 (s, 2 H), 6.90 (d, $J = 8.5$ Hz, 1 H), 4.70 (s, 2 H), 4.29 (q, $J = 7.1$ Hz, 2 H), 3.98 (s, 6 H), 3.93 (s, 3 H), 1.31 (t, $J = 7.2$ Hz, 3 H), 1.09 - 1.03 (m, 9 H), 0.26 (s, 6 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): $\delta = 168.4, 153.5, 151.9, 148.5, 147.8, 145.9, 140.2, 118.6, 114.2, 113.3, 100.2, 66.1, 61.4, 61.0, 56.2, 25.7, 18.4, 14.2, -4.6$; IR: $\tilde{\nu} = 2932, 1759, 1593, 1493, 1416, 1277, 1192, 1122, 837, 783$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\text{max}} (\epsilon) = 369$ nm ($21300 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{25}\text{H}_{37}\text{N}_2\text{O}_7\text{Si}$: 505.2365 $[\text{M}+\text{H}]^+$; found: 505.2359.

Ethyl-2-(3'-hydroxy-4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenoxy)acetate **29c**

Standard Procedure **B** with azobenzene **21c** (115 mg, 0.38 mmol, 1.0 equiv.) and ethyl bromoacetate (42 μL , 0.38 mmol, 1.0 equiv.) gave azobenzene **29c** (110 mg, 75 %) as an orange solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4 $\rightarrow$ 1:2). $R_f = 0.64$ (EtOAc/petroleum ether, 1:2); m.p. 121 °C; $^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 13.57$ (br s, 1 H), 7.82 (d, $J = 8.8$ Hz, 1 H), 7.11 (s, 2 H), 6.66 (dd, $J = 2.7, 8.9$ Hz, 1 H), 6.45 (d, $J = 2.7$ Hz, 1 H), 4.68 (s, 2 H), 4.30 (q, $J = 7.1$ Hz, 2 H), 3.96 (s, 6 H), 3.93 (s, 3 H), 1.32 (t, $J = 7.1$ Hz, 3 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): $\delta = 168.1, 161.6, 155.7, 153.8, 146.1, 140.2, 134.6, 133.2, 108.2, 102.3, 99.2, 65.3, 61.6, 61.1, 56.3, 14.2$; IR: $\tilde{\nu} = 2940, 2639, 1724, 1597, 1423, 1280, 1219, 1114, 1006, 856, 825, 795$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\text{max}} (\epsilon) = 390$ nm ($27300 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_7$: 391.1500 $[\text{M}+\text{H}]^+$; found: 391.1503.

Ethyl-2-(2'-bromo-4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenoxy)acetate **29d**

Standard Procedure **B** with azobenzene **21d** (305 mg, 0.83 mmol, 1.0 equiv.), and ethyl bromoacetate (0.37 mL, 3.33 mmol, 4.0 equiv.) gave azobenzene **29d** (338 mg, 89 %) as a yellow solid after silica-gel chromatography (EtOAc/petroleum ether, 1:4 $\rightarrow$ 1:2). R_f = 0.60 (EtOAc/petroleum ether, 1:2); m.p. 112 °C; $^1\text{H-NMR}$ (250 MHz, CDCl_3): δ = 8.19 (d, J = 2.4 Hz, 1 H), 7.88 (dd, J = 2.4, 8.8 Hz, 1 H), 7.23 (s, 2 H), 6.92 (d, J = 8.8 Hz, 1 H), 4.80 (s, 2 H), 4.31 (q, J = 7.1 Hz, 2 H), 3.97 (s, 6 H), 3.94 (s, 3 H), 1.32 (t, J = 7.1 Hz, 3 H); $^{13}\text{C-NMR}$ (63 MHz, CDCl_3): δ = 167.9, 156.2, 153.5, 148.2, 147.6, 140.7, 126.5, 125.0, 113.2, 112.7, 100.4, 66.3, 61.7, 61.0, 56.2, 14.1; IR: $\tilde{\nu}$ = 2943, 2832, 1763, 1593, 1485, 1411, 1200, 1119, 1011, 849; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 364 nm (25700 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{22}\text{BrN}_2\text{O}_6$: 453.0656/455.0635 $[\text{M}+\text{H}]^+$; found: 453.0662/455.0642.

Ethyl-2-(3'-bromo-4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenoxy)acetate **29e**

Standard Procedure **B** with azobenzene **21e** (453 mg, 1.24 mmol, 1.0 equiv.) and ethyl bromoacetate (0.55 mL, 4.94 mmol, 4.0 equiv.) gave azobenzene **29e** (471 mg, 84 %) as an orange solid after silica-gel chromatography (EtOAc/petroleum ether, 1:4 $\rightarrow$ 1:2). R_f = 0.57 (EtOAc/petroleum ether, 1:2); m.p. 93 °C; $^1\text{H-NMR}$ (250 MHz, CDCl_3): δ = 7.75 (d, J = 9.0 Hz, 1 H), 7.30 (d, J = 3.1 Hz, 3 H), 6.98 (dd, J = 2.7, 9.0 Hz, 1 H), 4.71 (s, 2 H), 4.33 (q, J = 7.1 Hz, 2 H), 3.99 (s, 6 H), 3.96 (s, 3 H), 1.35 (t, J = 7.1 Hz, 3 H); $^{13}\text{C-NMR}$ (63 MHz, CDCl_3): δ = 168.0, 160.0, 153.5, 148.6, 144.2, 140.8, 127.4, 118.9, 118.6, 114.8, 100.7, 65.5, 61.7, 61.0, 56.1, 14.1; IR: $\tilde{\nu}$ = 2982, 2839, 1763, 1589, 1416, 1200, 1126, 1076, 991, 841; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 369 nm (23000 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{22}\text{BrN}_2\text{O}_6$: 453.0656/455.0635 $[\text{M}+\text{H}]^+$; found: 453.0660/455.0639.

Ethyl-2-(2'-morpholino-4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenoxy)acetate **29f**

Standard Procedure **D** with azobenzene **29d** (30.0 mg, 0.66 mmol, 1.0 equiv.) and morpholine (13.1 μ L, 0.132 mmol, 2.0 equiv.) gave azobenzene **29f** (14.0 mg, 45 %) as an orange wax after silica-gel chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1). R_f = 0.40 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1); $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 7.62 (dd, J = 2.3, 8.5 Hz, 1 H), 7.57 (d, J = 2.2 Hz, 1 H), 7.23 (s, 2 H), 6.90 (d, J = 8.6 Hz, 1 H), 4.78 (s, 2 H), 4.31 (q, J = 7.1 Hz, 2 H), 3.98 (s, 6 H), 3.94 (s, 3 H), 3.99 - 3.92 (m, 4 H), 3.25 (t, J = 4.4 Hz, 4 H), 1.33 (t, J = 7.2 Hz, 3 H); $^{13}\text{C-NMR}$ (75MHz, CDCl_3): δ = 168.3, 153.5, 152.6, 148.5, 147.7, 142.2, 140.3, 120.1, 112.4, 111.2, 100.1, 67.2, 65.6, 61.6, 61.0, 56.2, 51.1, 14.2; IR: $\tilde{\nu}$ = 3460, 2963, 2842, 1752, 1581, 1345, 1241, 1163, 911, 840; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 368 nm (22000 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{30}\text{N}_3\text{O}_7$: 460.2079 $[\text{M}+\text{H}]^+$; found: 460.2090.

Ethyl-2-((5'-((3'',4'',5''-trimethoxyphenyl)diazenyl)quinolin-8'-yl)oxy)acetate **30a**

Standard Procedure **B** with azobenzene **22a** (359 mg, 1.06 mmol, 1.0 equiv.) and ethyl bromoacetate (0.47 mL, 4.23 mmol, 4.0 equiv.) gave azobenzene **30a** (362 mg, 80 %) as an orange solid after silica-gel chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1). R_f = 0.41 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 95:5); m.p. 114 $^{\circ}\text{C}$; $^1\text{H-NMR}$ (250 MHz, CDCl_3): δ = 9.27 (d, J = 8.2 Hz, 1 H), 9.07 (d, J = 2.4 Hz, 1 H), 7.91 (d, J = 8.6 Hz, 1 H), 7.64 (dd, J = 3.8, 8.3 Hz, 1 H), 7.32 (s, 2 H), 7.05 (d, J = 8.6 Hz, 1 H), 5.06 (s, 2 H), 4.30 (q, J = 7.1 Hz, 2 H),

4.01 (s, 6 H), 3.96 (s, 3 H), 1.29 (t, $J = 7.1$ Hz, 3 H); ^{13}C -NMR (63 MHz, CDCl_3): $\delta = 168.3, 156.1, 153.6, 150.1, 148.9, 141.6, 140.7, 139.8, 132.1, 127.9, 122.5, 113.1, 108.9, 100.5, 66.2, 61.6, 61.1, 56.2, 14.1$; IR: $\tilde{\nu} = 2970, 2835, 1732, 1566, 1493, 1308, 1199, 1126, 999, 840$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\text{max}} (\epsilon) = 389 \text{ nm}$ ($20900 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{24}\text{N}_3\text{O}_6$: 426.1660 $[\text{M}+\text{H}]^+$; found: 426.1666.

Ethyl-2-((4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)naphth-1'-yl)oxy)acetate **30b**

Standard Procedure **B** with azobenzene **22b** (363 mg, 1.07 mmol, 1.0 equiv.) and ethyl bromoacetate (0.48 mL, 4.30 mmol, 4.0 equiv.) gave azobenzene **30b** (436 mg, 96 %) as an orange solid after silica-gel chromatography (EtOAc/petroleum ether, 1:4 $\rightarrow$ 1:2). $R_f = 0.23$ (EtOAc/petroleum ether, 1:4); m.p. 99 °C; ^1H -NMR (250 MHz, CDCl_3): $\delta = 8.93$ (d, $J = 8.1$ Hz, 1 H), 8.47 (d, $J = 7.9$ Hz, 1 H), 7.84 (d, $J = 8.4$ Hz, 1 H), 7.73 (ddd, $J = 1.3, 6.8, 8.1$ Hz, 1 H), 7.65 (ddd, $J = 1.3, 7.0, 8.2$ Hz, 1 H), 7.37 (s, 2 H), 6.83 (d, $J = 8.4$ Hz, 1 H), 4.92 (s, 2 H), 4.35 (q, $J = 7.1$ Hz, 2 H), 4.04 (s, 6 H), 3.98 (s, 3 H), 1.35 (t, $J = 7.1$ Hz, 3 H); ^{13}C -NMR (101 MHz, CDCl_3): $\delta = 168.4, 156.3, 153.6, 149.2, 142.5, 140.4, 132.5, 127.7, 126.2, 125.7, 123.0, 122.4, 112.5, 104.8, 100.4, 65.8, 61.6, 61.1, 56.3, 14.2$; IR: $\tilde{\nu} = 2940, 2835, 1755, 1578, 1470, 1207, 1107, 991, 845, 768$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\text{max}} (\epsilon) = 397 \text{ nm}$ ($20100 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_6$: 425.1707 $[\text{M}+\text{H}]^+$; found: 425.1711.

Ethyl-2-((4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)-5'-methoxynaphth-1-yl)oxy)acetate **30c**

Standard Procedure **A1** with 3,4,5-trimethoxyaniline (183 mg, 1.0 mmol, 1.0 equiv.) and naphthol **11c** (183 mg, 1.05 mmol, 1.05 equiv.) gave crude azobenzene **22c** (185 mg) after evaporation of the solvent. The crude material was directly converted according to Standard Procedure **B** with ethyl bromoacetate (89 μ L, 2.0 mmol, 4.0 equiv.). Azobenzene **30c** (61 mg, 13 %) was isolated as an orange solid after silica-gel chromatography (EtOAc/petroleum ether, 1:2). R_f = 0.64 (EtOAc/petroleum ether, 1:2); m.p. 143 °C; $^1\text{H-NMR}$ (250 MHz, CDCl_3): δ = 8.10 (d, J = 7.9 Hz, 1 H), 7.53 (t, J = 8.1 Hz, 1 H), 7.36 (s, 2 H), 7.27 (d, J = 8.4 Hz, 1 H), 7.08 (d, J = 7.7 Hz, 1 H), 6.79 (d, J = 8.4 Hz, 1 H), 4.87 (s, 2 H), 4.34 (q, J = 7.1 Hz, 2 H), 4.02 (s, 6 H), 3.98 (s, 3 H), 3.97 (s, 3 H), 1.34 (t, J = 7.1 Hz, 3 H); $^{13}\text{C-NMR}$ (63 MHz, CDCl_3): δ = 169.4, 157.6, 155.7, 154.5, 150.0, 147.1, 141.0, 128.8, 127.4, 122.6, 116.1, 113.8, 109.7, 106.2, 101.4, 66.8, 62.4, 62.0, 57.4, 57.1, 15.1; IR: $\tilde{\nu}$ = 2909, 2839, 1759, 1593, 1412, 1207, 1084, 1002, 760; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 388 nm (20300 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{27}\text{N}_2\text{O}_7$: 455.1813 $[\text{M}+\text{H}]^+$; found: 455.1824.

Ethyl-2-((4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)-6',7'-dimethoxynaphth-1'-yl)oxy) acetate **30d**

Standard Procedure **B** with azobenzene **22d** (422 mg, 1.06 mmol, 1.0 equiv.) and ethyl bromoacetate (0.47 mL, 4.24 mmol, 4.0 equiv.) gave azobenzene **30d** (424 mg, 83 %) as an orange solid after silica-gel chromatography (EtOAc/petroleum ether, 1:2 $\rightarrow$ 1:1). R_f = 0.53 (EtOAc/petroleum ether, 1:2); m.p. 123 °C; $^1\text{H-NMR}$ (250 MHz, CDCl_3): δ = 8.25 (s, 1 H), 7.70 (s, 1 H), 7.71 (d, J = 8.4 Hz, 1 H), 7.32 (s, 2 H), 6.70 (d, J = 8.6 Hz, 1 H), 4.89 (s, 2 H), 4.32 (q, J = 7.1 Hz, 2 H), 4.09 (s, 3 H), 4.09 (s, 3 H), 4.00 (s, 6 H),

3.96 (s, 3 H), 1.33 (t, $J = 7.1$ Hz, 3 H); ^{13}C -NMR (101 MHz, CDCl_3): $\delta = 168.5, 155.4, 153.5, 150.5, 149.6, 149.3, 141.5, 140.3, 129.0, 121.2, 111.5, 104.0, 101.9, 101.2, 100.3, 65.8, 61.5, 61.1, 56.1, 55.9, 55.7, 14.2$; IR: $\tilde{\nu} = 2940, 2828, 1732, 1585, 1485, 1211, 1118, 1038, 1011, 818$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\text{max}} (\epsilon) = 408 \text{ nm} (21300 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1})$; HRMS (ESI): m/z calcd for $\text{C}_{25}\text{H}_{29}\text{N}_2\text{O}_8$: 485.1918 $[\text{M}+\text{H}]^+$; found: 485.1927.

Ethyl-2-((1'-((3'',4'',5''-trimethoxyphenyl)diazenyl)naphth-2'-yl)oxy)acetate **31**

Standard Procedure **B** with azobenzene **23** (502 mg, 1.48 mmol, 1.0 equiv.) and ethyl bromoacetate (0.66 mL, 5.92 mmol, 4.0 equiv.) gave azobenzene **31** (449 mg, 71 %) as an orange solid after silica-gel chromatography (EtOAc /petroleum ether, 1:4 $\rightarrow$ 1:2). $R_f = 0.30$ (EtOAc /petroleum ether, 1:4); m.p. 126°C ; ^1H -NMR (300 MHz, CDCl_3): $\delta = 8.33$ (d, $J = 8.6$ Hz, 1 H), 7.85 (d, $J = 8.7$ Hz, 2 H), 7.54 (ddd, $J = 1.4, 6.8, 8.4$ Hz, 1 H), 7.47 (ddd, $J = 1.3, 6.7, 8.1$ Hz, 1 H), 7.37 (s, 2 H), 7.36 (d, $J = 8.8$ Hz, 1 H), 4.79 (s, 2 H), 4.23 (q, $J = 7.1$ Hz, 2 H), 4.00 (s, 6 H), 3.97 (s, 3 H), 1.25 (t, $J = 7.1$ Hz, 3 H); ^{13}C -NMR (75 MHz, CDCl_3): $\delta = 168.8, 153.6, 149.3, 146.8, 140.8, 137.8, 130.6, 130.2, 128.2, 127.9, 127.7, 125.1, 123.4, 117.6, 100.4, 68.7, 61.3, 61.1, 56.3, 14.1$; IR: $\tilde{\nu} = 2940, 2835, 1755, 1593, 1415, 1311, 1199, 1103, 991, 810$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\text{max}} (\epsilon) = 370 \text{ nm} (26800 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1})$; HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_6$: 425.1707 $[\text{M}+\text{H}]^+$; found: 425.1713.

Methyl-2-(4'-((4''-methoxyphenyl)diazenyl)phenoxy)acetate **32a**

Standard Procedure **B** with azobenzene **16a** (30 mg, 0.10 mmol, 1.0 equiv.) and MeI (104 mg, 0.73 mmol, 7.0 equiv.) gave azobenzene **32a** (26 mg, 83 %) as a yellow solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:2). R_f = 0.58 (EtOAc/petroleum ether, 1:2); m.p. 149 °C; $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 7.86 (dd, J = 1.1, 9.0 Hz, 4 H), 6.99 (dd, J = 1.9, 8.9 Hz, 4 H), 4.70 (s, 2 H), 3.87 (s, 3 H), 3.81 (s, 3 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 169.0, 161.7, 159.5, 147.8, 147.0, 124.5, 124.4, 114.9, 114.2, 65.4, 55.6, 52.4; IR: $\tilde{\nu}$ = 2955, 2322, 1766, 1578, 1493, 1211, 1026, 840; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 354 nm (26000 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_2\text{O}_4$: 301.1183 $[\text{M}+\text{H}]^+$; found: 301.1183.

Methyl-2-(4'-((3'',4''-dimethoxyphenyl)diazenyl)phenoxy)acetate **32b**

Standard Procedure **B** with azobenzene **16b** (100 mg, 0.32 mmol, 1.0 equiv.), and MeI (94 mg, 0.66 mmol, 2.1 equiv.) gave azobenzene **32b** (83 mg, 80 %) as a yellow solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:2). R_f = 0.62 (EtOAc/petroleum ether, 1:2); m.p. 141 °C; $^1\text{H-NMR}$ (250 MHz, CDCl_3): δ = 7.92 (d, J = 9.0 Hz, 2 H), 7.62 (dd, J = 2.2, 8.4 Hz, 1 H), 7.52 (d, J = 2.0 Hz, 1 H), 7.09 - 6.98 (m, 3 H), 4.75 (s, 2 H), 4.01 (s, 3 H), 4.00 (s, 3 H), 3.86 (s, 3 H); $^{13}\text{C-NMR}$ (63 MHz, CDCl_3): δ = 169.9, 160.5, 152.5, 150.5, 148.5, 147.8, 125.3, 121.4, 115.8, 111.3, 102.8, 66.3, 57.0, 56.9, 53.3; IR: $\tilde{\nu}$ = 2959, 2612, 1751, 1578, 1497, 1439, 1188, 1111, 1018, 856, 817; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 376 nm (19000 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_5$: 331.1288 $[\text{M}+\text{H}]^+$; found: 311.1295.

Methyl-2-(4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenoxy)acetate **32c**

Standard Procedure **B** with azobenzene **16c** (222 mg, 0.64 mmol, 1.0 equiv.), and MeI (188 mg, 1.32 mmol, 2.1 equiv.) gave azobenzene **32c** (206 mg, 89 %) as a yellow solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:2). R_f = 0.62 (EtOAc/petroleum ether, 1:2); m.p. 51 °C; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 7.92 (d, J = 8.5 Hz, 2 H), 7.23 (s, 2 H), 7.04 (d, J = 8.8 Hz, 2 H), 4.72 (s, 2 H), 4.31 (q, J = 7.2 Hz, 2 H), 3.98 (s, 6 H), 3.95 (s, 3 H), 1.33 (t, J = 7.9 Hz, 3 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 168.4, 159.9, 153.5, 148.5, 147.4, 140.2, 124.5, 114.9, 100.1, 65.4, 61.5, 61.0, 56.1, 14.1; IR: $\tilde{\nu}$ = 2940, 2913, 2839, 1759, 1578, 1215, 1123, 1003, 845, 829; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 360 nm (22100 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_6$: 375.1551 $[\text{M}+\text{H}]^+$; found: 375.1563.

Methyl-2-(4'-((4''-(2'''-hydroxyethoxy)-3'',5''-dimethoxyphenyl)diazenyl)phenoxy) acetate **32d**

Standard Procedure **B** with azobenzene **16c** (100 mg, 0.28 mmol, 1.0 equiv.) and 2-bromoethanol (59 μL , 0.83 mmol, 1.0 equiv.) gave azobenzene **32d** (82 mg, 76 %) as a yellow solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:1). R_f = 0.38 (EtOAc/petroleum ether, 1:1); m.p. 91 °C; $^1\text{H-NMR}$ (250 MHz, CDCl_3): δ = 7.91 (d, J = 8.6 Hz, 2 H), 7.24 (s, 2 H), 7.03 (d, J = 8.6 Hz, 2 H), 4.73 (s, 2 H), 4.22 (t, J = 3.9 Hz, 2 H), 3.98 (s, 6 H), 3.84 (s, 3 H), 3.76 (t, J = 4.0 Hz, 2 H); $^{13}\text{C-NMR}$ (63 MHz, CDCl_3): δ = 169.8, 160.9, 154.5, 149.7, 148.3, 139.3, 125.6, 115.8, 101.0, 76.5, 66.3, 62.3, 57.2, 53.3; IR: $\tilde{\nu}$ = 3510, 2951, 2322, 1751, 1582, 1497, 1207, 1126, 1072, 841; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 360 nm (19800 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_7$: 391.1500 $[\text{M}+\text{H}]^+$; found: 391.1503.

Methyl-2-(4'-((4''-(2'''-bromoethoxy)-3'',5''-dimethoxyphenyl)diazenyl)phenoxy) acetate **32e**

Standard Procedure **B** with azobenzene **16c** (100 mg, 0.28 mmol, 1.0 equiv.) and 1,2-dibromoethane (249 μ L, 2.89 mmol, 10.0 equiv.) in anhydrous acetone (20 mL) gave azobenzene **32e** (119 mg, 91 %) as a chartreuse solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4). R_f = 0.57 (EtOAc/petroleum ether, 1:4); m.p. 179 $^{\circ}$ C; 1 H-NMR (300 MHz, CDCl_3): δ = 7.90 (d, J = 8.7 Hz, 2 H), 7.21 (s, 2 H), 7.03 (d, J = 8.8 Hz, 2 H), 4.73 (s, 2 H), 4.34 (t, J = 7.0 Hz, 2 H), 3.96 (s, 6 H), 3.84 (s, 3 H), 3.64 (t, J = 7.0 Hz, 2 H); 13 C-NMR (75 MHz, CDCl_3): δ = 168.9, 160.0, 153.5, 148.9, 147.5, 138.4, 124.7, 114.9, 100.0, 72.7, 65.3, 56.2, 52.4, 29.6; IR: $\tilde{\nu}$ = 2062, 2835, 1759, 1597, 1501, 1439, 1408, 1211, 1130, 1076, 991, 810; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 360 nm (27200 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{22}\text{BrN}_2\text{O}_6$: 453.0656/455.0638 $[\text{M}+\text{H}]^+$; found: 453.0658/455.0640.

Methyl-2-(4'-((3'',5''-dimethoxy-4''-(2'''-(4''''-methylpiperazin-1''''-yl)ethoxy)phenyl) diazenyl)-phenoxy)acetate **32f**

A microwave vial charged with azobenzene **32e** (60 mg, 0.13 mmol, 1.0 equiv.), 1-methylpiperazine (19 μ L, 0.17 mmol, 1.3 equiv.), K_2CO_3 (24 mg, 0.17 mmol, 1.3 equiv.), and CH_3CN (4 mL) was heated to 140 $^{\circ}$ C for 10 min. in a microwave. After cooling the solvent was removed under reduced pressure, and the residue was redissolved in CHCl_3 (30 mL). The organic phase was washed with water (20 mL), and brine (20 mL), dried with Na_2SO_4 , filtered, and concentrated under reduced pressure. Azobenzene **32f** (45 mg, 72 %) was obtained as an orange oil without further purification. R_f = 0.31 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1); 1 H-NMR (300 MHz, CDCl_3): δ = 7.87 (d, J = 8.9 Hz, 2 H), 7.18 (s, 2 H), 7.00 (d, J = 8.9 Hz, 2 H), 4.70

(s, 2 H), 4.16 (t, $J = 5.8$ Hz, 2 H), 3.91 (s, 6 H), 3.81 (s, 3 H), 2.79 (t, $J = 6.1$ Hz, 2 H), 2.63 (br s, 4 H), 2.49 (br s, 4 H), 2.27 (s, 3 H); ^{13}C -NMR (75 MHz, CDCl_3): $\delta = 168.8, 159.8, 153.6, 148.5, 147.4, 139.3, 124.5, 114.8, 100.0, 70.6, 65.3, 57.9, 56.0, 55.0, 53.4, 52.3, 46.0$; IR: $\tilde{\nu} = 2940, 2797, 2361, 1740, 1597, 1497, 1204, 1123, 1003, 841$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\text{max}} (\epsilon) = 362$ nm ($21600 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{33}\text{N}_4\text{O}_6$: 473.2395 $[\text{M}+\text{H}]^+$; found: 473.2398.

Methyl-*N*-(5'-methoxy-2'-((4''-methoxyphenyl)diazenyl)phenyl)succinamate 33a

Standard Procedure **B** with azobenzene **17a** (70.0 mg, 0.20 mmol, 1.0 equiv.) and MeI (24.4 μL , 0.39 mmol, 2.0 equiv.) gave azobenzene **33a** (66 mg, 91 %) as an ocher solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:4 $\rightarrow$ 1:2). $R_f = 0.46$ (EtOAc/petroleum ether, 1:2); m.p. 126°C ; ^1H -NMR (300 MHz, CDCl_3): $\delta = 10.74$ (br s, 1 H), 8.36 (d, $J = 2.7$ Hz, 1 H), 7.90 (d, $J = 8.9$ Hz, 2 H), 7.87 (d, $J = 9.0$ Hz, 1 H), 7.09 (d, $J = 9.0$ Hz, 2 H), 6.76 (dd, $J = 2.7, 9.0$ Hz, 1 H), 3.96 (s, 3 H), 3.95 (s, 3 H), 3.78 (s, 3 H), 2.87 (br. s, 4 H); ^{13}C -NMR (101 MHz, CDCl_3): $\delta = 173.2, 170.1, 162.8, 161.7, 146.7, 136.9, 133.4, 124.1, 123.7, 114.4, 110.9, 103.5, 55.7, 55.6, 52.0, 32.8, 29.1$; IR: $\tilde{\nu} = 3337, 2932, 2835, 1744, 1670, 1582, 1470, 1227, 1168, 1034, 837$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\text{max}} (\epsilon) = 384$ nm ($24500 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{22}\text{N}_3\text{O}_5$: 372.1554 $[\text{M}+\text{H}]^+$; found: 372.1563.

Methyl-*N*-(2'-((4''-bromophenyl)diazenyl)-5'-methoxyphenyl)succinamate 33b

Standard Procedure **B** with azobenzene **17b** (555 mg, 1.37 mmol, 1.0 equiv.) and MeI (170 μ L, 2.73 mmol, 2.0 equiv.) gave azobenzene **33b** (520 mg, 91 %) as a yellow solid after purification by silica-gel chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2). R_f = 0.31 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2); m.p. 140 $^\circ\text{C}$; $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 10.66 (br s, 1 H), 8.32 (d, J = 2.7 Hz, 1 H), 7.84 (d, J = 9.0 Hz, 1 H), 7.74 (d, J = 8.8 Hz, 2 H), 7.65 (d, J = 8.8 Hz, 2 H), 6.72 (dd, J = 2.7, 9.1 Hz, 1 H), 3.91 (s, 3 H), 3.72 (s, 3 H), 2.81 (s, 4 H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = 173.2, 170.3, 163.8, 151.2, 137.5, 133.4, 132.4, 124.7, 124.4, 123.8, 111.1, 103.5, 55.8, 52.0, 32.8, 29.0; IR: $\tilde{\nu}$ = 3329, 2943, 2322, 1732, 1604, 1527, 1474, 1219, 1157, 833; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 383 nm (19100 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{19}\text{BrN}_3\text{O}_4$: 420.0553/422.0535 $[\text{M}+\text{H}]^+$; found: 420.0555/422.0537.

N-(2'-((3'',4''-Dimethoxyphenyl)diazenyl)-5'-methoxyphenyl)succinimide **34b**

Standard Procedure **B** with azobenzene **19b** (69.4 mg, 0.19 mmol, 1.0 equiv.) and MeI (25.4 μ L, 0.41 mmol, 2.1 equiv.) gave azobenzene **34b** (47 mg, 68 %) as an orange solid after purification by silica-gel chromatography ($\text{EtOAc}/\text{petroleum ether}$, 1:1 $\rightarrow$ EtOAc). R_f = 0.50 (EtOAc); m.p. 89 $^\circ\text{C}$; $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 7.91 (d, J = 9.0 Hz, 1 H), 7.46 (dd, J = 2.2, 8.5 Hz, 1 H), 7.29 (d, J = 2.1 Hz, 1 H), 7.07 (dd, J = 2.8, 9.1 Hz, 1 H), 6.97 (d, J = 8.6 Hz, 1 H), 6.86 (d, J = 2.8 Hz, 1 H), 3.97 (s, 3 H), 3.93 (s, 3 H), 3.90 (s, 3 H), 3.03 - 2.90 (m, 4 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 176.2, 162.0, 151.8, 149.4, 147.3, 141.2, 132.2, 119.4, 119.1, 116.3, 113.5, 110.5, 102.9, 56.2, 55.8, 55.7, 28.8; IR: $\tilde{\nu}$ = 2943, 2322, 1713, 1504, 1373, 1234, 1177, 1015, 814; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 374 nm (20600 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{20}\text{N}_3\text{O}_5$: 370.1403 $[\text{M}+\text{H}]^+$; found: 370.1404.

N-(2'-((4''-(2'''-Bromoethoxy)-3'',5''-dimethoxyphenyl)diazenyl)-5'-methoxyphenyl)succinimide **34d**

Standard Procedure **B** with azobenzene **19c** (200 mg, 0.52 mmol, 1.0 equiv.) and 1,2-dibromoethane (447 μ L, 5.19 mmol, 10.0 equiv.) in anhydrous acetone (50 mL) gave azobenzene **34d** (108 mg, 43 %) as a red solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 1:2 $\rightarrow$ 2:1). R_f = 0.23 (EtOAc/petroleum ether, 1:1); m.p. 126 $^{\circ}$ C; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 7.91 (d, J = 9.1 Hz, 1 H), 7.09 (dd, J = 2.6, 9.1 Hz, 1 H), 7.06 (s, 2 H), 6.89 (d, J = 2.6 Hz, 1 H), 4.35 (t, J = 7.2 Hz, 2 H), 3.93 (s, 6 H), 3.92 (s, 3 H), 3.65 (t, J = 7.3 Hz, 2 H), 3.06 - 2.87 (m, 4 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 176.1, 162.5, 153.4, 149.2, 141.0, 138.7, 132.8, 118.8, 116.3, 113.5, 100.1, 72.8, 56.1, 55.9, 29.6, 28.8; IR: $\tilde{\nu}$ = 2936, 2835, 2318, 1709, 1377, 1234, 1177, 1123, 856, 822; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 368 nm (24200 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{21}\text{H}_{23}\text{BrN}_3\text{O}_6$: 492.0765/494.0747 $[\text{M}+\text{H}]^+$; found: 492.0769/494.0750.

N-(2'-((3'',5''-Dimethoxy-4''-(2'''-(4''''-methylpiperazin-1''''-yl)ethoxy)phenyl)diazenyl)-5'-methoxyphenyl)succinimide **34e**

A microwave vial charged with azobenzene **34d** (64 mg, 0.13 mmol, 1.0 equiv.), 1-methylpiperazine (20 μ L, 0.18 mmol, 1.3 equiv.), K_2CO_3 (25 mg, 0.18 mmol, 1.3 equiv.), and CH_3CN (4 mL) was heated to 140 $^{\circ}$ C for 10 min. in a microwave. After cooling the solvent was removed under reduced pressure, and the residue was redissolved in CHCl_3 (10 mL). The organic phase was washed with water (5 mL), brine (5 mL), dried with Na_2SO_4 , filtered, and concentrated under reduced pressure. Azobenzene **34e** (43 mg, 65 %) was obtained as an orange oil after purification by silica-gel chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 95:5 $\rightarrow$ 90:10). R_f = 0.35 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1); $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 7.89 (d, J = 9.0 Hz, 1 H),

7.07 (dd, $J = 2.7, 9.1$ Hz, 1 H), 7.03 (s, 2 H), 6.87 (d, $J = 2.7$ Hz, 1 H), 4.17 (t, $J = 5.8$ Hz, 2 H), 3.90 (s, 3 H), 3.90 (s, 6 H), 3.03 - 2.87 (m, 4 H), 2.82 (t, $J = 5.8$ Hz, 2 H), 2.69 (br s, 4 H), 2.56 (br s, 4 H), 2.34 (s, 3 H); ^{13}C -NMR (75 MHz, CDCl_3): $\delta = 176.1, 162.3, 153.6, 148.9, 141.0, 139.7, 132.7, 118.8, 116.3, 113.5, 100.2, 70.6, 57.9, 56.0, 55.8, 55.0, 53.3, 46.0, 28.8$; IR: $\tilde{\nu} = 2936, 2797, 1713, 1601, 1454, 1223, 1123, 1003, 822$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\text{max}} (\epsilon) = 371$ nm ($26400 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{26}\text{H}_{34}\text{N}_5\text{O}_6$: 512.2504 $[\text{M}+\text{H}]^+$; found: 512.2510.

Methyl-*N*-(4'-methoxy-2'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenyl)succinamate **35**

Standard Procedure **B** with azobenzene **20** (160 mg, 0.38 mmol, 1.0 equiv.) and MeI (47.7 μL , 0.77 mmol, 2.0 equiv.) gave azobenzene **35** (147 mg, 89 %) as a yellow solid after purification by silica-gel chromatography (acetone/petroleum ether, 1:4). $R_f = 0.38$ (acetone/petroleum ether, 1:3); m.p. 129°C ; ^1H -NMR (300 MHz, CDCl_3): $\delta = 9.66$ (br s, 1 H), 8.53 (d, $J = 9.1$ Hz, 1 H), 7.31 (d, $J = 3.0$ Hz, 1 H), 7.25 (s, 2 H), 7.04 (dd, $J = 3.0, 9.2$ Hz, 1 H), 3.97 (s, 6 H), 3.94 (s, 3 H), 3.84 (s, 3 H), 3.65 (s, 3 H), 2.81 - 2.68 (m, 4 H); ^{13}C -NMR (101 MHz, CDCl_3): $\delta = 173.4, 169.4, 155.8, 153.7, 148.4, 141.1, 139.9, 130.7, 121.7, 119.9, 101.5, 100.6, 61.1, 56.3, 55.6, 52.0, 32.8, 29.5$; IR: $\tilde{\nu} = 3306, 2940, 2835, 1744, 1597, 1508, 1215, 1119, 1007, 845, 818$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\text{max}} (\epsilon) = 409$ nm ($23300 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{21}\text{H}_{26}\text{N}_3\text{O}_7$: 432.1765 $[\text{M}+\text{H}]^+$; found: 432.1773.

Ethyl -2-(4'-((4''-methyl-3'',4''-dihydro-2''*H*-benzo[b][1'',4'']oxazin-7-yl)diazenyl)phenoxy)acetate **36a**

Standard Procedure **E** with azobenzene **28** (66 mg, 0.19 mmol, 1.0 equiv.) and paraformaldehyde (17 mg, 0.58 mmol, 3.0 equiv.) gave azobenzene **36a** (57 mg, 83 %) as an orange solid after purification by silica-

gel chromatography (CHCl₃). R_f = 0.31 (CH₂Cl₂); m.p. 112 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 7.83 (d, J = 9.0 Hz, 2 H), 7.52 (dd, J = 2.2, 8.6 Hz, 1 H), 7.40 (d, J = 2.1 Hz, 1 H), 7.00 (d, J = 9.0 Hz, 2 H), 6.72 (d, J = 8.7 Hz, 1 H), 4.69 (s, 2 H), 4.36 - 4.24 (m, 4 H), 3.43 - 3.37 (m, 2 H), 3.02 (s, 3 H), 1.32 (t, J = 7.2 Hz, 3 H); ¹³C-NMR (101 MHz, CDCl₃): δ = 168.6, 159.0, 148.0, 144.8, 144.0, 139.1, 124.0, 120.6, 114.8, 110.8, 107.7, 65.6, 64.4, 61.5, 48.9, 38.5, 14.2; IR: $\tilde{\nu}$ = 3460, 2075, 2972, 1739, 1582, 1520, 1377, 1203, 810; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 419 nm (26800 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₉H₂₂N₃O₄: 356.1605 [M+H]⁺; found: 356.1606.

Ethyl-2-(4'-((4''-benzyl-3'',4''-dihydro-2''*H*-benzo[b][1'',4'']oxazin-7-yl)diazenyl) phenoxy)acetate
36b

Standard Procedure **E** with azobenzene **28** (124 mg, 0.36 mmol, 1.0 equiv.) and benzaldehyde (116 mg, 1.09 mmol, 3.0 equiv.) gave azobenzene **36b** (105 mg, 68 %) as an orange solid after purification with silica-gel chromatography (CH₂Cl₂/petroleum ether, 1:1 → 2:1). R_f = 0.14 (CH₂Cl₂); m.p. 193 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 7.83 (d, J = 9.0 Hz, 2 H), 7.46 (qd, J = 2.3, 4.6 Hz, 2 H), 7.40 - 7.26 (m, 5 H), 7.00 (d, J = 9.0 Hz, 2 H), 6.74 (d, J = 9.2 Hz, 1 H), 4.69 (s, 2 H), 4.59 (s, 2 H), 4.36 - 4.25 (m, 4 H), 3.54 - 3.46 (m, 3 H), 1.32 (t, J = 7.1 Hz, 3 H); ¹³C-NMR (75 MHz, CDCl₃): δ = 168.6, 159.0, 148.0, 144.6, 143.8, 138.3, 137.1, 128.8, 127.4, 126.9, 124.0, 120.6, 114.8, 111.1, 108.5, 65.6, 64.3, 61.5, 54.5, 47.4, 14.2; IR: $\tilde{\nu}$ = 3460, 2909, 2870, 2326, 1763, 1582, 1246, 1080, 880, 810; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 420 nm (25300 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₅H₂₆N₃O₄: 432.1918 [M+H]⁺; found: 432.1921.

N-(2'-((4''-(Dimethylamino)phenyl)diazenyl)-5'-methoxyphenyl)succinimide **37c**

Standard Procedure **D** with azobenzene **33b** (100.0 mg, 0.24 mmol, 1.0 equiv.) and dimethylamine (92 μ L, 5.2 M in EtOH, 0.48 mmol, 2.0 equiv.) gave azobenzene **37c** (73 mg, 88 %) as a yellow solid after silica-gel chromatography (EtOAc/petroleum ether, 1:4 $\rightarrow$ EtOAc). R_f = 0.29 (EtOAc/petroleum ether, 2:1); m.p. 94 $^{\circ}$ C; $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 7.89 (d, J = 9.1 Hz, 1 H), 7.69 (d, J = 9.0 Hz, 2 H), 7.05 (dd, J = 2.7, 9.1 Hz, 1 H), 6.82 (d, J = 2.7 Hz, 1 H), 6.72 (d, J = 9.1 Hz, 2 H), 3.88 (s, 3 H), 3.08 (s, 6 H), 2.97 (s, 4 H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 176.4, 161.1, 152.3, 144.0, 141.8, 131.5, 124.7, 118.8, 116.3, 113.3, 111.5, 55.7, 40.3, 28.8; IR: $\tilde{\nu}$ = 2920, 2361, 1717, 1601, 1369, 1146, 826; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 421 nm (22400 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{21}\text{N}_4\text{O}_3$: 353.1608 $[\text{M}+\text{H}]^+$; found: 353.1610.

N-(5'-Methoxy-2'-((4''-morpholinophenyl)diazenyl)phenyl)succinimide **37d**

Standard Procedure **D** with azobenzene **33b** (80.0 mg, 0.19 mmol, 1.0 equiv.) and morpholine (33 μ L, 0.38 mmol, 2.0 equiv.) gave azobenzene **37d** (76 mg, 94 %) as a dark red solid after silica-gel chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2). R_f = 0.46 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2); m.p. 85 $^{\circ}$ C; $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 7.90 (d, J = 9.1 Hz, 1 H), 7.69 (d, J = 9.0 Hz, 2 H), 7.06 (dd, J = 2.7, 9.1 Hz, 1 H), 6.92 (d, J = 9.1 Hz, 2 H), 6.83 (d, J = 2.7 Hz, 1 H), 3.91 - 3.84 (m, 8 H), 3.33 - 3.26 (m, 4 H), 2.97 (s, 4 H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = 176.3, 161.6, 153.0, 146.0, 141.6, 132.0, 124.4, 118.9, 116.3, 114.4, 113.4, 66.6, 55.8, 48.1, 28.8; IR: $\tilde{\nu}$ = 2928, 2851, 2322, 1708, 1593, 1377, 1146, 926, 826; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 404 nm (24300 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{21}\text{H}_{23}\text{N}_4\text{O}_4$: 395.1714 $[\text{M}+\text{H}]^+$; found: 395.1714.

N-(5'-Methoxy-2'-((4''-(4'''-methylpiperazin-1'''-yl)phenyl)diazenyl)phenyl) succinimide **37e**

Standard Procedure **D** with azobenzene **33b** (100.0 mg, 0.24 mmol, 1.0 equiv.) and 1-methylpiperazine (53 μ L, 0.48 mmol, 2.0 equiv.) gave azobenzene **37e** (94 mg, 97 %) as an ocher solid after silica-gel chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2 $\rightarrow$ 93:7). R_f = 0.32 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 95:5); m.p. 86 $^\circ\text{C}$; ^1H -NMR (400 MHz, MeOD): δ = 7.85 (d, J = 9.1 Hz, 1 H), 7.69 (d, J = 9.1 Hz, 2 H), 7.12 (dd, J = 2.6, 9.1 Hz, 1 H), 7.03 (d, J = 9.1 Hz, 2 H), 6.96 (d, J = 2.9 Hz, 1 H), 3.89 (s, 3 H), 3.46 - 3.39 (m, 4 H), 2.96 (s, 4 H), 2.79 (t, J = 4.4 Hz, 4 H), 2.48 (s, 3 H); ^{13}C -NMR (101 MHz, MeOD): δ = 177.7, 161.8, 152.8, 145.7, 141.7, 132.4, 124.0, 117.9, 115.7, 114.7, 113.5, 55.0, 53.9, 46.7, 44.0, 28.3; IR: $\tilde{\nu}$ = 2932, 2839, 1709, 1597, 1373, 1234, 1138, 1007, 822; UV-VIS (CH_3CN + 0.5 % piperidine): λ_{max} (ϵ) = 409 nm (21000 $\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{26}\text{N}_5\text{O}_3$: 408.2030 $[\text{M}+\text{H}]^+$; found: 408.2034.

2-(4'-((4''-(dimethylamino)phenyl)diazenyl)phenoxy)acetic acid **38b**

Standard Procedure **C** with ester **26b** (50.0 mg, 0.15 mmol, 1.0 equiv.) gave carboxylic acid **38b** (35.6 mg, 78 %) as an ocher solid after evaporation of the solvent. R_f = 0.19 (MeOH); m.p. 279 $^\circ\text{C}$; ^1H -NMR (500 MHz, CD_3OD): δ = 7.77 (t, J = 7.6 Hz, 4 H), 7.03 (d, J = 8.2 Hz, 2 H), 6.82 (d, J = 8.5 Hz, 2 H), 4.45 (s, 2 H), 3.07 (s, 6 H); ^{13}C -NMR (126 MHz, CD_3OD): δ = 176.3, 161.8, 154.0, 148.8, 145.0,

125.6, 124.7, 116.1, 112.9, 68.7, 40.6; IR: $\tilde{\nu}$ = 3460, 2943, 2789, 1740, 1597, 1420, 1366, 1231, 1034, 826; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\max}$ (ϵ) = 408 nm (24400 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₆H₁₈N₃O₃: 300.1343 [M+H]⁺; found: 300.1342.

2-(4'-((4''-morpholinophenyl)diazenyl)phenoxy)acetic acid **38c**

Standard Procedure **C** with ester **26c** (70.0 mg, 0.19 mmol, 1.0 equiv.) gave carboxylic acid **38c** (54.2 mg, 84 %) as a yellow solid after evaporation of the solvent. R_f = 0.20 (MeOH); m.p. 312 °C; ¹H-NMR (500 MHz, DMSO-*d*₆): δ = 7.76 (d, J = 9.2 Hz, 2 H), 7.73 (d, J = 9.2 Hz, 2 H), 7.08 (d, J = 9.2 Hz, 2 H), 6.90 (d, J = 8.8 Hz, 2 H), 4.14 (s, 2 H), 3.78 - 3.74 (m, 4 H), 3.30 - 3.27 (m, 4 H); ¹³C-NMR (126 MHz, DMSO-*d*₆): δ = 169.1, 161.9, 153.0, 146.1, 145.0, 124.2, 123.9, 115.4, 114.6, 68.9, 66.4, 47.8; IR: $\tilde{\nu}$ = 3464, 3205, 2970, 2851, 1740, 1574, 1423, 1377, 1346, 1227, 1123, 926, 841; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\max}$ (ϵ) = 392 nm (26200 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₈H₂₀N₃O₄: 342.1448 [M+H]⁺; found: 342.1454.

2-(4'-((4''-(4'''-methylpiperazin-1'''-yl)phenyl)diazenyl)phenoxy)acetic acid **38d**

Standard Procedure **C** with ester **26d** (70.0 mg, 0.18 mmol, 1.0 equiv.) gave carboxylic acid **38d** (38.2 mg, 59 %) as a yellow solid after evaporation of the solvent. R_f = 0.20 (MeOH); m.p. 255 °C (decomp.); ¹H-NMR (500 MHz, D₂O): δ = 7.67 (d, J = 8.5 Hz, 2 H), 7.64 (d, J = 8.8 Hz, 2 H), 7.04 (d, J = 8.5 Hz, 2 H), 6.99 (d, J = 8.2 Hz, 2 H), 4.47 (s, 2 H), 3.22 (br s, 4 H), 2.55 (br s, 4 H), 2.24 (s, 3 H); ¹³C-NMR (126 MHz, D₂O): δ = 176.2, 160.0, 152.9, 146.5, 145.4, 124.0, 123.9, 116.4, 115.0, 66.8, 53.4,

48.0, 44.4; IR: $\tilde{\nu}$ = 3460, 2947, 2843, 2681, 2596, 1744, 1597, 1234, 1080, 840; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\max}$ (ϵ) = 395 nm (26200 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₉H₂₃N₄O₃: 355.1765 [M+H]⁺; found: 355.1769.

2-(4'-((4''-methyl-3'',4''-dihydro-2''*H*-benzo[b][1'',4'']oxazin-7''-yl)diazenyl)phenoxy) acetic acid **39a**

Standard Procedure **C** with ester **36a** (45.0 mg, 0.13 mmol, 1.0 equiv.) gave carboxylic acid **39a** (34 mg, 76 %) as a red solid after purification by silica-gel chromatography (CH₂Cl₂/MeOH, 10:1). R_f = 0.10 (CH₂Cl₂/MeOH, 10:1); m.p. 172 °C; ¹H-NMR (400 MHz, DMSO-*d*₆): δ = 13.11 (br s, 1 H), 7.75 (d, J = 9.1 Hz, 2 H), 7.43 (dd, J = 2.3, 8.5 Hz, 1 H), 7.19 (d, J = 2.0 Hz, 1 H), 7.04 (d, J = 8.8 Hz, 2 H), 6.80 (d, J = 8.8 Hz, 1 H), 4.76 (s, 2 H), 4.29 - 4.19 (m, 2 H), 3.42 - 3.37 (m, 2 H), 2.98 (s, 3 H); ¹³C-NMR (101 MHz, DMSO-*d*₆): δ = 170.4, 159.7, 147.2, 144.1, 143.9, 140.0, 124.0, 121.3, 115.4, 111.4, 106.7, 65.2, 64.5, 48.5, 38.4; IR: $\tilde{\nu}$ = 2916, 2851, 2326, 1736, 1520, 1215, 1080, 829, 795; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\max}$ (ϵ) = 417 nm (26600 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₇H₁₈N₃O₄: 328.1292 [M+H]⁺; found: 328.1296.

2-(4'-((4''-benzyl-3'',4''-dihydro-2''*H*-benzo[b][1'',4'']oxazin-7''-yl)diazenyl)phenoxy) acetic acid **39b**

Standard Procedure **C** with ester **36b** (80.0 mg, 0.19 mmol, 1.0 equiv.) gave carboxylic acid **39b** (67 mg, 89 %) as an orange solid after purification by silica-gel chromatography (CH₂Cl₂/MeOH, 10:1). R_f = 0.31 (CH₂Cl₂/MeOH, 10:1); m.p. 87 °C; ¹H-NMR (400 MHz, DMSO-*d*₆): δ = 13.11 (br s, 1 H), 7.74 (d, J = 9.1 Hz, 2 H), 7.40 - 7.25 (m, 6 H), 7.24 (d, J = 2.3 Hz, 1 H), 7.04 (d, J = 9.1 Hz, 2 H), 6.80 (d, J = 8.8 Hz, 1 H), 4.76 (s, 2 H), 4.66 (s, 2 H), 4.28 (t, J = 4.4 Hz, 2 H), 3.55 (t, J = 4.4 Hz, 2 H); ¹³C-NMR (101 MHz,

DMSO-*d*₆): δ = 170.4, 159.6, 147.2, 143.9, 143.6, 138.8, 138.0, 129.1, 127.5, 127.4, 124.0, 121.3, 115.4, 111.5, 107.3, 65.2, 64.3, 54.0, 47.5; IR: $\tilde{\nu}$ = 3460, 2920, 2866, 2578, 1736, 1597, 1315, 1234, 844, 725; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 418 nm (22700 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₃H₂₂N₃O₄: 404.1605 [M+H]⁺; found: 404.1608.

2-(4'-((4''-methoxyphenyl)diazenyl)phenoxy)acetic acid **40a**

Standard Procedure **C** with ester **32a** (24 mg, 0.08 mmol, 1.0 equiv.) gave carboxylic acid **40a** (22 mg, 96 %) as a yellow solid after evaporation. R_f = 0.22 (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 104 °C; ¹H-NMR (400 MHz, DMSO-*d*₆): δ = 13.10 (br s, 1 H), 7.84 (t, J = 7.9 Hz, 4 H), 7.11 (t, J = 9.8 Hz, 4 H), 4.80 (s, 2 H), 3.86 (s, 3 H); ¹³C-NMR (101 MHz, DMSO-*d*₆): δ = 170.3, 162.0, 160.4, 146.9, 146.6, 124.7, 124.5, 115.5, 115.0, 65.2, 56.1; IR: $\tilde{\nu}$ = 2916, 2569, 1736, 1705, 1597, 1578, 1497, 1234, 1146, 841; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 360 nm (25000 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₅H₁₅N₂O₄: 287.1026 [M+H]⁺; found: 287.1027.

2-(4'-((3'',4''-dimethoxyphenyl)diazenyl)phenoxy)acetic acid **40b**

Standard Procedure **C** with ester **32b** (60 mg, 0.18 mmol, 1.0 equiv.) gave carboxylic acid **40b** (56 mg, 98 %) as a yellow solid after evaporation. R_f = 0.22 (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 190 °C; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 7.83 (d, J = 9.0 Hz, 2 H), 7.53 (dd, J = 2.2, 8.5 Hz, 1 H), 7.42 (d, J = 2.2 Hz, 1 H), 7.14 (d, J = 8.7 Hz, 1 H), 7.07 (d, J = 8.8 Hz, 2 H), 4.77 (s, 2 H), 3.85 (s, 3 H), 3.84 (s, 3 H); ¹³C-NMR (101 MHz, CDCl₃): δ = 170.4, 160.3, 152.0, 149.9, 146.9, 146.5, 124.5, 120.2, 115.5, 111.7, 102.3, 65.2, 56.2, 55.9; IR: $\tilde{\nu}$ = 2916, 2851, 2577, 1736, 1705, 1578, 1497, 1231,

1018, 845; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 372 nm (25300 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₆H₁₇N₂O₅: 317.1132 [M+H]⁺; found: 317.1134.

2-(4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenoxy)acetic acid **40c**

Standard Procedure **C** with ester **32c** (135 mg, 0.37 mmol, 1.0 equiv.) gave carboxylic acid **40c** (106 mg, 82 %) as an orange solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid). R_f = 0.22 (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 110 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 7.93 (d, J = 9.0 Hz, 2 H), 7.23 (s, 2 H), 7.06 (d, J = 9.0 Hz, 2 H), 4.79 (s, 2 H), 3.98 (s, 6 H), 3.94 (s, 3 H); ¹³C-NMR (101 MHz, CDCl₃): δ = 172.6, 159.4, 153.5, 148.5, 147.7, 140.4, 124.6, 114.9, 100.2, 64.8, 61.0, 56.2; IR: $\tilde{\nu}$ = 2943, 2839, 2573, 1732, 1585, 1416, 1219, 1126, 991, 845; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 368 nm (22100 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₇H₁₉N₂O₆: 347.1238 [M+H]⁺; found: 347.1241.

2-(4'-((4''-(2'''-hydroxyethoxy)-3'',5''-dimethoxyphenyl)diazenyl)phenoxy)acetic acid **40d**

Standard Procedure **C** with ester **32d** (68 mg, 0.17 mmol, 1.0 equiv.) gave carboxylic acid **40d** (36 mg, 57 %) as a yellow solid after purification by preparative HPLC (H₂O/CH₃CN, 70:30 → 0:100). R_f = 0.31 (CH₂Cl₂/MeOH, 8:2); m.p. 183 °C; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 7.86 (d, J = 9.0 Hz, 2 H), 7.21 (s, 2 H), 7.09 (d, J = 8.9 Hz, 2 H), 4.79 (s, 2 H), 3.96 (t, J = 5.6 Hz, 2 H), 3.87 (s, 6 H), 3.64 (t, J = 5.6 Hz, 2 H); ¹³C-NMR (126 MHz, DMSO-*d*₆): δ = 170.4, 160.8, 153.8, 148.2, 146.8, 139.6, 124.8, 115.6, 100.5, 74.8, 65.3, 60.7, 56.5; IR: $\tilde{\nu}$ = 3410, 2932, 1593, 1493, 1258, 1126, 984, 826; UV-VIS (CH₃CN + 0.5 %

piperidine): $\lambda_{\max} (\epsilon) = 369 \text{ nm}$ ($22000 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_7$: 377.1343 $[\text{M}+\text{H}]^+$; found: 377.1347.

2-(4'-((3'',5''-dimethoxy-4''-(2'''-(4''''-methylpiperazin-1''''-yl)ethoxy)phenyl)diazenyl)-phenoxy)acetic acid **40f**

Standard Procedure **C** with ester **32f** (35 mg, 0.074 mmol, 1.0 equiv.) gave carboxylic acid **40f** (26 mg, 77 %) as a yellow solid after purification by preparative HPLC ($\text{H}_2\text{O}/\text{CH}_3\text{CN}$, 90:10 $\rightarrow$ 0:100). $R_f = 0.22$ ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 8:2); m.p. 128°C ; $^1\text{H-NMR}$ (300 MHz, D_2O): $\delta = 7.26$ (d, $J = 7.9 \text{ Hz}$, 2 H), 6.70 (d, $J = 8.0 \text{ Hz}$, 2 H), 6.39 (s, 2 H), 4.31 (s, 2 H), 3.70 (s, 2 H), 3.45 (s, 6 H), 3.15 (br s, 4 H), 2.77 (s, 3 H), 2.88 - 2.66 (br s, 4 H); $^{13}\text{C-NMR}$ (101 MHz, D_2O): $\delta = 175.7, 160.4, 152.4, 147.8, 145.7, 137.3, 124.3, 114.7, 99.6, 68.8, 66.7, 56.1, 55.6, 52.4, 49.6, 42.9$; IR: $\tilde{\nu} = 3422, 2997, 2634, 2361, 1597, 1412, 1219, 1126, 1042, 941, 840$; UV-VIS ($\text{CH}_3\text{CN} + 0.5\%$ piperidine): $\lambda_{\max} (\epsilon) = 368 \text{ nm}$ ($22900 \text{ l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$); HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{31}\text{N}_4\text{O}_6$: 459.2238 $[\text{M}+\text{H}]^+$; found: 459.2243.

N-(2'-((4''-(Dimethylamino)phenyl)diazenyl)-5'-methoxyphenyl)succinamic acid **41c**

Standard Procedure **C** with ester **37c** (38 mg, 0.11 mmol, 1.0 equiv.) gave carboxylic acid **41c** (33 mg, 83 %) as an orange solid after purification by preparative HPLC ($\text{H}_2\text{O}/\text{CH}_3\text{CN}$, 70:30 $\rightarrow$ 0:100). $R_f = 0.18$ ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 8:2); m.p. 286°C ; $^1\text{H-NMR}$ (300 MHz, $\text{DMSO}-d_6$): $\delta = 11.75$ (s, 1 H), 8.16 (d, $J = 2.7 \text{ Hz}$, 1 H), 8.10 (d, $J = 9.0 \text{ Hz}$, 2 H), 7.66 (d, $J = 9.0 \text{ Hz}$, 1 H), 6.79 (d, $J = 9.1 \text{ Hz}$, 2 H), 6.66 (dd, $J = 2.8, 9.0 \text{ Hz}$, 1 H), 3.79 (s, 3 H), 3.05 (s, 6 H), 2.50 - 2.48 (m, 2 H), 2.25 - 2.19 (m, 2 H); $^{13}\text{C-NMR}$ (101 MHz,

DMSO-*d*₆): δ = 174.6, 173.8, 161.4, 152.3, 143.9, 139.2, 135.3, 126.0, 117.1, 112.0, 109.4, 105.5, 55.8, 39.4, 36.2, 34.8; IR: $\tilde{\nu}$ = 3345, 2920, 1654, 1589, 1362, 1280, 1141, 1030, 822; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\max}$ (ϵ) = 450 nm (21300 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₉H₂₃N₄O₄: 371.1714 [M+H]⁺; found: 371.1718.

N-(5'-Methoxy-2'-((4''-morpholinophenyl)diazenyl)phenyl)succinamic acid **41d**

Standard Procedure **C** with ester **37d** (25 mg, 0.06 mmol, 1.0 equiv.) gave carboxylic acid **41d** (18 mg, 69 %) as a yellow solid after purification by preparative HPLC (H₂O/CH₃CN, 70:30 → 0:100). R_f = 0.22 (CH₂Cl₂/MeOH, 8:2); m.p. 207 °C; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 10.23 (s, 1 H), 8.02 (d, J = 2.6 Hz, 1 H), 7.90 (d, J = 8.9 Hz, 2 H), 7.70 (d, J = 9.0 Hz, 1 H), 7.09 (d, J = 9.0 Hz, 2 H), 6.76 (dd, J = 2.6, 9.0 Hz, 1 H), 3.82 (s, 3 H), 3.79 - 3.72 (m, 4 H), 3.30 - 3.27 (m, 4 H), 2.76 (t, J = 6.2 Hz, 2 H), 2.56 (t, J = 6.8 Hz, 2 H); ¹³C-NMR (101 MHz, DMSO-*d*₆): δ = 173.8, 170.7, 161.5, 152.7, 144.6, 137.6, 134.5, 124.5, 118.8, 114.0, 109.8, 105.3, 65.9, 55.5, 47.2, 31.7, 28.9; IR: $\tilde{\nu}$ = 3375, 2970, 1701, 1589, 1234, 1111, 1038, 918, 818; UV-VIS (CH₃CN + 0.5 % piperidine): $\lambda_{\max}$ (ϵ) = 414 nm (28000 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₁H₂₅N₄O₅: 413.1819 [M+H]⁺; found: 413.1825.

N-(5'-Methoxy-2'-((4''-(4'''-methylpiperazin-1'''-yl)phenyl)diazenyl)phenyl)succinamic acid **41e**

Standard Procedure **C** with ester **37e** (25 mg, 0.06 mmol, 1.0 equiv.) gave carboxylic acid **41e** (13 mg, 38 %) as a yellow solid after purification by preparative HPLC (H₂O/CH₃CN, 70:30 → 0:100). R_f = 0.12

(CH₂Cl₂/MeOH, 8:2); m.p. 160 °C; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 10.26 (s, 1 H), 8.03 (d, *J* = 2.6 Hz, 1 H), 7.88 (d, *J* = 8.9 Hz, 2 H), 7.70 (d, *J* = 9.0 Hz, 1 H), 7.07 (d, *J* = 9.0 Hz, 2 H), 6.75 (dd, *J* = 2.7, 9.0 Hz, 1 H), 3.81 (s, 3 H), 3.40 - 3.27 (m, 4 H), 2.75 (t, *J* = 6.6 Hz, 2 H), 2.56 (t, *J* = 6.9 Hz, 2 H), 2.48 - 2.41 (m, 4 H), 2.23 (s, 3 H); ¹³C-NMR (101 MHz, DMSO-*d*₆): δ = 173.9, 170.8, 161.4, 152.6, 144.3, 137.5, 134.5, 124.6, 118.7, 114.1, 109.7, 105.3, 55.5, 54.3, 46.9, 45.7, 31.8, 29.0; IR: $\tilde{\nu}$ = 3368, 2967, 2839, 1682, 1585, 1508, 1285, 1238, 1150, 1033, 829; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 417 nm (19300 l·mol⁻¹·cm⁻¹); HRMS (ESI): *m/z* calcd for C₂₂H₂₈N₅O₄: 426.2136 [M+H]⁺; found: 426.2139.

N-(5'-Methoxy-2'-((4''-methoxyphenyl)diazenyl)phenyl)succinamic acid **42a**

Standard Procedure C with ester **33a** (60.0 mg, 0.16 mmol, 1.0 equiv.) gave carboxylic acid **42a** (57 mg, 99 %) as a chartreuse solid after evaporation of the solvent. *R_f* = 0.23 (CH₂Cl₂/MeOH, 95:5); m.p. 167 °C; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 12.19 (s, 1 H), 10.22 (s, 1 H), 8.04 (d, *J* = 2.8 Hz, 1 H), 8.00 (d, *J* = 8.9 Hz, 2 H), 7.74 (d, *J* = 9.0 Hz, 1 H), 7.13 (d, *J* = 9.0 Hz, 2 H), 6.78 (dd, *J* = 2.8, 9.1 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 2.79 (t, *J* = 6.5 Hz, 2 H), 2.58 (t, *J* = 6.7 Hz, 2 H); ¹³C-NMR (101 MHz, DMSO-*d*₆): δ = 174.3, 171.3, 162.5, 162.0, 146.9, 138.6, 134.9, 125.2, 119.1, 114.9, 110.4, 105.9, 56.1, 56.0, 32.1, 29.3; IR: $\tilde{\nu}$ = 3368, 2924, 2592, 1713, 1578, 1470, 1231, 1146, 1026, 833; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 386 nm (21400 l·mol⁻¹·cm⁻¹); HRMS (ESI): *m/z* calcd for C₁₈H₂₀N₃O₅: 358.1397 [M+H]⁺; found: 358.1402.

N-(2'-((3'',4''-Dimethoxyphenyl)diazenyl)-5'-methoxyphenyl)succinamic acid **42b**

Standard Procedure **C** with ester **34b** (40.0 mg, 0.11 mmol, 1.0 equiv.) gave carboxylic acid **42b** (41 mg, 98 %) as a yellow solid after purification by silica-gel chromatography (CH₂Cl₂/MeOH, 98:2 → 95:5). *R_f* = 0.13 (CH₂Cl₂/MeOH, 95:5); m.p. 158 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 11.00 (s, 1 H), 8.32 (d, *J* = 2.6 Hz, 1 H), 7.85 (d, *J* = 9.0 Hz, 1 H), 7.51 (dd, *J* = 2.3, 8.5 Hz, 1 H), 7.47 (d, *J* = 2.1 Hz, 1 H), 7.03 (d, *J* = 8.5 Hz, 1 H), 6.76 (dd, *J* = 2.7, 9.0 Hz, 1 H), 4.01 (s, 3 H), 4.01 (s, 3 H), 3.93 (s, 3 H), 2.91 - 2.79 (m, 4 H); ¹³C-NMR (101 MHz, CDCl₃): δ = 175.8, 170.3, 162.7, 151.6, 149.8, 146.6, 136.2, 133.3, 125.3, 119.4, 111.0, 110.6, 103.8, 102.0, 56.2, 56.0, 55.7, 32.5, 29.0; IR: $\tilde{\nu}$ = 2940, 2839, 2322, 1717, 1585, 1504, 1420, 1231, 1107, 1022, 856, 810; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 395 nm (24700 l·mol⁻¹·cm⁻¹); HRMS (ESI): *m/z* calcd for C₁₉H₂₂N₃O₆: 388.1503 [M+H]⁺; found: 388.1512.

N-(5'-Methoxy-2'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenyl)succinamic acid **42c**

Standard Procedure **B** with azobenzene **19c** (100 mg, 0.26 mmol, 1.0 equiv.) and MeI (32.3 μL, 0.52 mmol, 2.0 equiv.) gave crude azobenzene **34c** (99 mg) after evaporation of the solvent. The crude material was directly converted according to Standard Procedure **C** to give carboxylic acid **42c** (77 mg, 71 %) as a yellow solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid). *R_f* = 0.19 (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 165 °C; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 8.02 (d, *J* = 2.7 Hz, 1 H), 7.75 (d, *J* = 9.1 Hz, 1 H), 7.38 (s, 2 H), 6.79 (dd, *J* = 2.8, 9.1 Hz, 1 H), 3.91 (s, 6 H), 3.84 (s, 3 H), 3.75 (s, 3 H), 2.75 (t, *J* = 6.6 Hz, 2 H), 2.56 (t, *J* = 6.6 Hz, 2 H); ¹³C-NMR (101 MHz, DMSO-*d*₆): δ = 174.4, 171.5, 163.0, 153.7, 148.6, 140.2, 139.3, 134.9, 118.5, 110.6, 106.1, 101.1, 60.7, 56.5, 56.1, 32.3, 29.7; IR: $\tilde{\nu}$ = 3291, 2940, 2361, 1732, 1597, 1458, 1231, 1119,

1006, 821; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 393 nm (20600 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₀H₂₄N₃O₇: 418.1609 [M+H]⁺; found: 418.1617.

N-(2'-((3'',5''-Dimethoxy-4''-(2'''-(4''''-methylpiperazin-1''''-yl)ethoxy)phenyl)diazenyl)-5'-methoxyphenyl)succinamic acid **42e**

Standard Procedure **C** with ester **34e** (36 mg, 0.07 mmol, 1.0 equiv.) gave carboxylic acid **42e** (35 mg, 94 %) as an orange solid after purification by preparative HPLC (H₂O/CH₃CN, 90:10 → 0:100). R_f = 0.24 (CH₂Cl₂/MeOH, 8:2); m.p. 208 °C; ¹H-NMR (500 MHz, DMSO-*d*₆): δ = 10.37 (s, 1 H), 8.02 (d, J = 2.7 Hz, 1 H), 7.75 (d, J = 9.2 Hz, 1 H), 7.38 (s, 2 H), 6.79 (dd, J = 2.7, 9.2 Hz, 1 H), 4.04 (t, J = 6.0 Hz, 2 H), 3.90 (s, 6 H), 3.84 (s, 3 H), 2.75 (t, J = 6.6 Hz, 2 H), 2.64 (t, J = 6.0 Hz, 2 H), 2.56 (t, J = 6.6 Hz, 2 H), 2.46 (br. s, 4 H), 2.33 (br s, 4 H), 2.16 (s, 3 H); ¹³C-NMR (126 MHz, DMSO-*d*₆): δ = 174.0, 171.1, 162.6, 153.4, 148.1, 138.9, 138.8, 134.5, 118.1, 110.1, 105.6, 100.7, 70.5, 57.4, 56.1, 55.6, 54.6, 52.8, 45.6, 32.0, 29.3; IR: $\tilde{\nu}$ = 3379, 2940, 2835, 1736, 1694, 1593, 1385, 1215, 1126, 1030, 845; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 393 nm (24100 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₆H₃₆N₅O₇: 530.2609 [M+H]⁺; found: 530.2613.

N-(4'-Methoxy-2'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenyl)succinamic acid **43**

Standard Procedure **C** with ester **35** (80 mg, 0.19 mmol, 1.0 equiv.) gave carboxylic acid **43** (58 mg, 75 %) as a yellow solid after purification by silica-gel chromatography (CH₂Cl₂/MeOH, 98:2 → 95:5). R_f = 0.11 (CH₂Cl₂/MeOH, 95:5); m.p. 163 °C; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 10.03 (br s, 1 H), 8.05

(d, $J = 9.0$ Hz, 1 H), 7.40 (s, 2 H), 7.20 (d, $J = 3.0$ Hz, 1 H), 7.10 (dd, $J = 3.0, 9.0$ Hz, 1 H), 3.88 (s, 6 H), 3.77 (s, 3 H), 3.74 (s, 3 H), 2.66 (t, $J = 6.7$ Hz, 2 H), 2.51 (t, $J = 6.5$ Hz, 2 H); ^{13}C -NMR (101 MHz, DMSO- d_6): $\delta = 175.0, 170.9, 156.2, 153.7, 148.5, 142.3, 140.9, 131.8, 124.9, 119.7, 101.6, 98.9, 60.7, 56.5, 55.9, 29.8, 28.3$; IR: $\tilde{\nu} = 3310, 2936, 2832, 1721, 1655, 1531, 1404, 1304, 1215, 1007, 833$; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 393 nm (25500 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₀H₂₄N₃O₇: 418.1609 [M+H]⁺; found: 418.1620.

2-(4'-((3'',4'',5''-Trimethoxyphenyl)diazenyl)phenoxy)acetic acid **44a**

Standard Procedure C with ester **29a** (151 mg, 0.41 mmol, 1.0 equiv.) gave carboxylic acid **44a** (123 mg, 85 %) as an orange solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid). $R_f = 0.22$ (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 110 °C; ^1H -NMR (300 MHz, CDCl₃): $\delta = 7.93$ (d, $J = 9.0$ Hz, 2 H), 7.23 (s, 2 H), 7.06 (d, $J = 9.0$ Hz, 2 H), 4.79 (s, 2 H), 3.98 (s, 6 H), 3.94 (s, 3 H); ^{13}C -NMR (101 MHz, CDCl₃): $\delta = 172.6, 159.4, 153.5, 148.5, 147.7, 140.4, 124.6, 114.9, 100.2, 64.8, 61.0, 56.2$; IR: $\tilde{\nu} = 2943, 2839, 2573, 1732, 1585, 1416, 1219, 1126, 991, 845$; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 368 nm (22100 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₇H₁₉N₂O₆: 347.1238 [M+H]⁺; found: 347.1241.

2-(3'-Hydroxy-4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenoxy)acetic acid **44c**

Standard Procedure **C** with ester **29c** (100 mg, 0.26 mmol, 1.0 equiv.) gave carboxylic acid **44c** (80 mg, 86 %) as a red solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 3:7 → EtOAc + 0.5 % formic acid). R_f = 0.17 (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 204 °C; $^1\text{H-NMR}$ (300 MHz, DMSO- d_6): δ = 11.88 (br s, 1 H), 7.73 (d, J = 9.0 Hz, 1 H), 7.31 (s, 2 H), 6.60 (dd, J = 2.7, 9.0 Hz, 1 H), 6.50 (d, J = 2.6 Hz, 1 H), 4.71 (s, 2 H), 3.88 (s, 6 H), 3.74 (s, 3 H); $^{13}\text{C-NMR}$ (75 MHz, DMSO- d_6): δ = 169.7, 162.2, 156.0, 153.4, 146.9, 139.6, 132.9, 126.9, 108.1, 102.2, 99.8, 65.2, 60.2, 56.1; IR: $\tilde{\nu}$ = 3545, 2943, 2839, 2530, 1751, 1600, 1226, 1130, 1060, 825; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 390 nm (27300 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₇H₁₉N₂O₇: 363.1187 [M+H]⁺; found: 363.1184.

2-(2'-Hydroxy-4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)phenoxy)acetic acid **44g**

Standard Procedure **C** with ester **29b** (60 mg, 0.12 mmol, 1.0 equiv.) gave carboxylic acid **44g** (40 mg, 94 %) as an orange solid after purification by silica-gel chromatography (EtOAc/petroleum ether, 3:7 → EtOAc + 0.5 % formic acid). R_f = 0.15 (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 132 °C; $^1\text{H-NMR}$ (400 MHz, DMSO- d_6): δ = (br s, 1 H), 7.41 (dd, J = 2.3, 8.5 Hz, 1 H), 7.34 (d, J = 2.0 Hz, 1 H), 7.18 (s, 2 H), 7.00 (d, J = 8.5 Hz, 1 H), 4.77 (s, 2 H), 3.88 (s, 6 H), 3.75 (s, 3 H); $^{13}\text{C-NMR}$ (101 MHz, DMSO- d_6): δ = 170.1, 153.3, 149.5, 147.8, 147.5, 146.7, 139.8, 118.3, 113.4, 106.2, 99.9, 65.5, 60.2, 56.0; IR: $\tilde{\nu}$ = 3507, 3005, 2360, 1748, 1597, 1493, 1207, 1114, 995, 806; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 367 nm (21100 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₁₇H₁₉N₂O₇: 363.1187 [M+H]⁺; found: 363.1194.

2-((5'-((3'',4'',5''-Trimethoxyphenyl)diazenyl)quinolin-8'-yl)oxy)acetic acid **45a**

Standard Procedure **C** with ester **30a** (190 mg, 0.46 mmol, 1.0 equiv.) gave carboxylic acid **45a** (176 mg, 97 %) as a yellow solid after evaporation of the solvent. $R_f = 0.20$ (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 310 °C decomp.; $^1\text{H-NMR}$ (300 MHz, DMSO- d_6): $\delta = 9.33$ (dd, $J = 1.7, 8.6$ Hz, 1 H), 9.01 (dd, $J = 1.7, 4.1$ Hz, 1 H), 7.93 (d, $J = 8.7$ Hz, 1 H), 7.77 (dd, $J = 4.1, 8.6$ Hz, 1 H), 7.37 (s, 2 H), 7.29 (d, $J = 8.8$ Hz, 1 H), 5.05 (s, 2 H), 3.94 (s, 6 H), 3.78 (s, 3 H); $^{13}\text{C-NMR}$ (126 MHz, , DMSO- d_6): $\delta = 171.5, 157.1, 153.8, 150.0, 148.9, 140.4, 139.8, 138.9, 132.8, 127.7, 123.7, 114.5, 109.6, 100.7, 68.5, 60.9, 56.5$; IR: $\tilde{\nu} = 2936, 2835, 1624, 1408, 1312, 1107, 991, 783$; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 393 nm (25500 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₀H₂₀N₃O₆: 398.1347 [M+H]⁺; found: 398.1357.

2-((4'-((3'',4'',5''-Trimethoxyphenyl)diazenyl)naphth-1'-yl)oxy)acetic acid **45b**

Standard Procedure **C** with ester **30b** (166 mg, 0.39 mmol, 1.0 equiv.) gave carboxylic acid **45b** (150 mg, 97 %) as an orange solid after evaporation of the solvent. $R_f = 0.24$ (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 295 °C; $^1\text{H-NMR}$ (300 MHz, DMSO- d_6): $\delta = 8.91$ (d, $J = 8.3$ Hz, 1 H), 8.32 (d, $J = 8.2$ Hz, 1 H), 7.84 (d, $J = 8.6$ Hz, 1 H), 7.71 (ddd, $J = 0.9, 7.0, 8.4$ Hz, 1 H), 7.61 (ddd, $J = 0.9, 7.0, 8.4$ Hz, 1 H), 7.33 (s, 2 H), 6.87 (d, $J = 8.7$ Hz, 1 H), 4.42 (s, 2 H), 3.93 (s, 6 H), 3.76 (s, 3 H); $^{13}\text{C-NMR}$ (75 MHz, DMSO- d_6): $\delta = 169.1, 158.8, 153.8, 149.1, 140.1, 140.1, 132.4, 128.0, 126.0, 125.6, 123.1, 122.9, 113.8, 106.0, 100.5, 69.2, 60.7, 56.5$; IR: $\tilde{\nu} = 3449, 2936, 2835, 1609, 1404, 1219, 1130, 984, 814, 760$; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 409 nm (23300 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₁H₂₁N₂O₆: 397.1394 [M+H]⁺; found: 397.1398.

2-((4'-((3'',4'',5''-Trimethoxyphenyl)diazenyl)-5'-methoxynaphthalen-1'-yl)oxy)acetic acid **45c**

Standard Procedure **C** with ester **30c** (45 mg, 0.10 mmol, 1.0 equiv.) gave carboxylic acid **45c** (38 mg, 90 %) as an orange solid after evaporation of the solvent. $R_f = 0.22$ (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 196 °C; $^1\text{H-NMR}$ (300 MHz, DMSO- d_6): $\delta = 7.94$ (d, $J = 8.4$ Hz, 1 H), 7.55 (t, $J = 8.1$ Hz, 1 H), 7.30 (s, 2 H), 7.29 (d, $J = 7.7$ Hz, 1 H), 7.21 (d, $J = 7.7$ Hz, 1 H), 6.99 (d, $J = 8.5$ Hz, 1 H), 4.93 (s, 2 H), 3.92 (s, 3 H), 3.91 (s, 6 H), 3.77 (s, 3 H); $^{13}\text{C-NMR}$ (75 MHz, DMSO- d_6): $\delta = 169.8, 156.4, 154.7, 153.3, 148.5, 144.3, 139.5, 127.0, 126.6, 121.0, 114.4, 113.0, 109.1, 105.6, 100.1, 65.4, 60.2, 56.4, 55.9$; IR: $\tilde{\nu} = 2970, 2835, 1751, 1593, 1408, 1215, 1123, 1084, 748$; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 398 nm (22000 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₂H₂₃N₂O₇: 427.1500 [M+H]⁺; found: 427.1505.

2-((4'-((3'',4'',5''-trimethoxyphenyl)diazenyl)-6',7'-dimethoxynaphth-1'-yl)oxy)acetic acid **45d**

Standard Procedure **C** with ester **30d** (160 mg, 0.33 mmol, 1.0 equiv.) gave carboxylic acid **45d** (149 mg, 99 %) as an ochre solid after evaporation of the solvent. $R_f = 0.23$ (EtOAc/petroleum ether, 3:7 + 0.5 % formic acid); m.p. 235 °C; $^1\text{H-NMR}$ (250 MHz, DMSO- d_6): $\delta = 8.26$ (s, 1 H), 7.73 (d, $J = 8.6$ Hz, 1 H), 7.58 (s, 1 H), 7.35 (s, 2 H), 6.91 (d, $J = 8.6$ Hz, 1 H), 4.99 (s, 2 H), 4.00 (s, 3 H), 3.95 (s, 3 H), 3.94 (s, 6 H), 3.78 (s, 3 H); $^{13}\text{C-NMR}$ (63 MHz, DMSO- d_6): $\delta = 171.3, 156.8, 154.7, 151.8, 150.7, 150.0, 141.1,$

129.8, 121.6, 112.7, 105.8, 103.0, 102.1, 101.4, 66.5, 61.6, 57.3, 56.7, 56.6; IR: $\tilde{\nu}$ = 2932, 2832, 2361, 1732, 1481, 1312, 1211, 1168, 1111, 1002, 810; UV-VIS (CH₃CN + 0.5 % piperidine): λ_{max} (ϵ) = 419 nm (26000 l·mol⁻¹·cm⁻¹); HRMS (ESI): m/z calcd for C₂₃H₂₅N₂O₈: 457.1605 [M+H]⁺; found: 457.1611.

Supplementary Note 1.

Supplementary Note 2.

¹H-NMR (250 MHz, CDCl₃) and ¹³C-NMR (63MHz, CDCl₃) spectrum of compound **p-6**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound *m*-6. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **13**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **14**. * = NMR-solvent

¹H-NMR (400 MHz, DMSO-*d*₆) and ¹³C-NMR (101 MHz, DMSO-*d*₆) spectrum of compound **15**. * = H₂O

¹H-NMR (300 MHz, CD₃OD) and ¹³C-NMR (101 MHz, CD₃OD) spectrum of compound **16a**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **16b**. * = NMR-solvent, grease

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (63 MHz, CDCl₃) spectrum of compound **16c**. * = NMR-solvent

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (126 MHz, DMSO-*d*₆) spectrum of compound **17a**. * = NMR-solvent, H₂O

¹H-NMR (400 MHz, DMSO-*d*₆) and ¹³C-NMR (101 MHz, DMSO-*d*₆) spectrum of compound **17b**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **18**. * = NMR-solvent

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (63 MHz, CDCl₃) spectrum of compound **19b**. * = NMR-solvent

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **19c**. * = NMR-solvent, CH₃CN

^1H -NMR (300 MHz, CDCl_3) and ^{13}C -NMR (75 MHz, CDCl_3) spectrum of compound **20**. * = NMR-solvent

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (63 MHz, CDCl₃) spectrum of compound **21a**. * = NMR-solvent, H₂O

¹H-NMR (250 MHz, CDCl₃) and ¹³C-NMR (63 MHz, CDCl₃) spectrum of compound **21b**. * = NMR-solvent

¹H-NMR (400 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **21c**. * = NMR-solvent, H₂O

¹H-NMR (250 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **21d**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (75 MHz, DMSO-*d*₆) spectrum of compound **21e**.

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **22a**. * = NMR-solvent

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (75 MHz, DMSO-*d*₆) spectrum of compound **22b**. * = NMR-solvent

¹H-NMR (600 MHz, DMSO-*d*₆) and ¹³C-NMR (151 MHz, DMSO-*d*₆) spectrum of compound **22d**. * = NMR-solvent

¹H-NMR (600 MHz, CDCl₃) and ¹³C-NMR (151 MHz, CDCl₃) spectrum of compound **23**. * = NMR-solvent, CH₃CN, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **24**. * = NMR-solvent

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (101 MHz, DMSO-*d*₆) spectrum of compound **25**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **26a**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **26b**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **26c**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **26d**. * = NMR-solvent

¹H-NMR (400 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **26e**. * = NMR-solvent, H₂O, grease

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **26f**. * = NMR-solvent

¹H-NMR (400 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **27**. * = NMR-solvent, H₂O

¹H-NMR (400 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **29a/32c**. * = NMR-solvent

¹H-NMR (400 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **29b**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **29c**. * = NMR-solvent

¹H-NMR (250 MHz, CDCl₃) and ¹³C-NMR (63 MHz, CDCl₃) spectrum of compound **29d**. * = NMR-solvent, H₂O

¹H-NMR (250 MHz, CDCl₃) and ¹³C-NMR (63 MHz, CDCl₃) spectrum of compound **29e**. * = NMR-solvent, H₂O

¹H-NMR (250 MHz, CDCl₃) and ¹³C-NMR (63 MHz, CDCl₃) spectrum of compound **29f**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (63 MHz, CDCl₃) spectrum of compound **30a**. * = NMR-solvent

¹H-NMR (250 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **30b**. * = NMR-solvent, H₂O

¹H-NMR (250 MHz, CDCl₃) and ¹³C-NMR (63 MHz, CDCl₃) spectrum of compound **30c**. * = NMR-solvent

¹H-NMR (250 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **30d**. * = NMR-solvent

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **31**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **32a**. * = NMR-solvent, H₂O

^1H -NMR (250 MHz, CDCl_3) and ^{13}C -NMR (63 MHz, CDCl_3) spectrum of compound **32b**. * = NMR-solvent, grease

¹H-NMR (250 MHz, CDCl₃) and ¹³C-NMR (63 MHz, CDCl₃) spectrum of compound **32d**. * = NMR-solvent

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **32e**. * = NMR-solvent, grease

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **32f**. * = NMR-solvent, H₂O, grease

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **33a**. * = NMR-solvent, H₂O

^1H -NMR (300 MHz, CDCl_3) and ^{13}C -NMR (75 MHz, CDCl_3) spectrum of compound **33b**. * = NMR-solvent, H_2O , grease

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **34b**. * = NMR-solvent, H₂O

¹H-NMR (400 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **34d**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **34e**. * = NMR-solvent

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **35**. * = NMR-solvent, grease

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **36a**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **36b**. * = NMR-solvent, grease

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **37c**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (75 MHz, CDCl₃) spectrum of compound **37d**. * = NMR-solvent, H₂O

¹H-NMR (400 MHz, CD₃OD) and ¹³C-NMR (101 MHz, CD₃OD) spectrum of compound **37e**. * = NMR-solvent, H₂O

¹H-NMR (500 MHz, CD₃OD) and ¹³C-NMR (126 MHz, CD₃OD) spectrum of compound **38b**. * = NMR-solvent, H₂O

^1H -NMR (500 MHz, $\text{DMSO}-d_6$) and ^{13}C -NMR (126 MHz, $\text{DMSO}-d_6$) spectrum of compound **38c**. * = NMR-solvent, H_2O

¹H-NMR (500 MHz, D₂O) and ¹³C-NMR (126 MHz, D₂O) spectrum of compound **38d**. * = NMR-solvent

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^1H -NMR (400 MHz, DMSO- d_6) and ^{13}C -NMR (101 MHz, DMSO- d_6) spectrum of compound **39b**. * = NMR-solvent, H_2O

¹H-NMR (400 MHz, DMSO-*d*₆) and ¹³C-NMR (101 MHz, DMSO-*d*₆) spectrum of compound **40a**. * = NMR-solvent, H₂O, grease

$^1\text{H-NMR}$ (300 MHz, $\text{DMSO-}d_6$) and $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) spectrum of compound **40b**. * = NMR-solvent, H_2O

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **40c/44a**. * = NMR-solvent

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (126 MHz, DMSO-*d*₆) spectrum of compound **40d**. * = NMR-Solvent

¹H-NMR (300 MHz, D₂O) and ¹³C-NMR (101 MHz, D₂O) spectrum of compound **40f**. * = NMR-Solvent

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (101 MHz, DMSO-*d*₆) spectrum of compound 41c. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (101 MHz, DMSO-*d*₆) spectrum of compound **41d**. * = NMR-solvent, H₂O, grease

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (101 MHz, DMSO-*d*₆) spectrum of compound **41f**. * = NMR-solvent

^1H -NMR (300 MHz, $\text{DMSO}-d_6$) and ^{13}C -NMR (101 MHz, $\text{DMSO}-d_6$) spectrum of compound **42a**. * = NMR-solvent, H_2O , grease

¹H-NMR (300 MHz, CDCl₃) and ¹³C-NMR (101 MHz, CDCl₃) spectrum of compound **42b**. * = NMR-solvent

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (101 MHz, DMSO-*d*₆) spectrum of compound **42c**. * = NMR-solvent, H₂O

^1H -NMR (500 MHz, $\text{DMSO}-d_6$) and ^{13}C -NMR (126 MHz, $\text{DMSO}-d_6$) spectrum of compound **42e**. * = NMR-solvent, H_2O

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (101 MHz, DMSO-*d*₆) spectrum of compound **43**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (75 MHz, DMSO-*d*₆) spectrum of compound **44c**. * = NMR-solvent, H₂O

¹H-NMR (400 MHz, DMSO-*d*₆) and ¹³C-NMR (101 MHz, DMSO-*d*₆) spectrum of compound **44g**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (126 MHz, DMSO-*d*₆) spectrum of compound **45a**. * = NMR-solvent, H₂O

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (75 MHz, DMSO-*d*₆) spectrum of compound **45b**. * = NMR-solvent

¹H-NMR (300 MHz, DMSO-*d*₆) and ¹³C-NMR (75 MHz, DMSO-*d*₆) spectrum of compound **45c**. * = NMR-solvent

¹H-NMR (250 MHz, DMSO-*d*₆) and ¹³C-NMR (63 MHz, DMSO-*d*₆) spectrum of compound **45d**. * = NMR-solvent

Supplemental References

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