Synthesis of Cyclic Peptides by Photochemical Decarboxylation of *N*-Phthaloyl Peptides in Aqueous Solution

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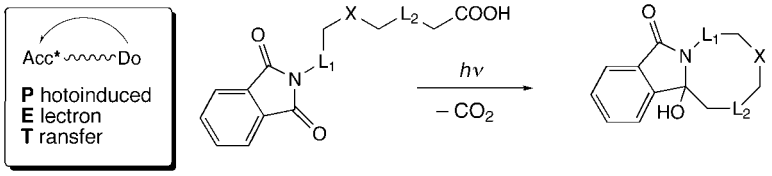
This paper is dedicated to Professor *Dieter Seebach* on the occasion of this 65th birthday

The synthesis of a variety of cyclic peptides from *N*-phthaloyl-protected di-, tri-, tetra-, and pentapeptides with different aminocarboxylic acid tethers by photodecarboxylation – initiated by intramolecular electron transfer – has been explored in aqueous media. The progress and the chemoselectivity of the follow-up processes after CO_2 extrusion were traced by the respective pH/time-profiles, as well as by the overall change in pH after completion of the reaction. The competition between cyclization and simple oxidative decarboxylation depends on spacer length and geometry, H-bonding interaction between the electron accepting phthalimide C=O groups and amide H-atoms, as well as the geometric reorganization coupled with the radical combination step and the formation of the lactam rings. With progressing reaction, hydrolysis of the phthalimide chromophore becomes an increasingly important side reaction due to the constant increase in pH. The use of phosphate-buffered aqueous media consequently improved the cyclization yields. The ground-state interactions between amide groups and the terminal COO^- group with the imide C=O groups were studied for the model system [*N*-(phthaloyl)glycyl]sarcosine (**1**) by NMR spectroscopy where the amide (*E*/*Z*)-equilibrium depends on the presence of carboxylate *vs.* free carboxylic acid, demonstrating the role of H-bonding and metal coordination.

1. Introduction. – In the last years, we have elaborated the synthetic applicability of the *intra*molecular photoinduced decarboxylation of electronically excited phthalimides, originally described in 1991 [1]. In a first attempt to evaluate the scope and limitation of this reaction with respect to the dimension of a flexible hydrocarbon chain linking the electron acceptor with the electron donor (phthalimide and carboxylate, respectively), we discovered that macrocyclic amines can be prepared in high yields even without the use of dilution conditions (*Scheme 1*) [2]. The *inter*molecular version of this reaction was subsequently discovered and proceeds with high efficiency and

Scheme 1. *Photoinduced Electron-Transfer Decarboxylation/Cyclization Reaction of ω-Phthalimido-substituted Alkylcarboxylates with Divergent Linker Chains L_1 and L_2 and Spacer Functional Groups X*



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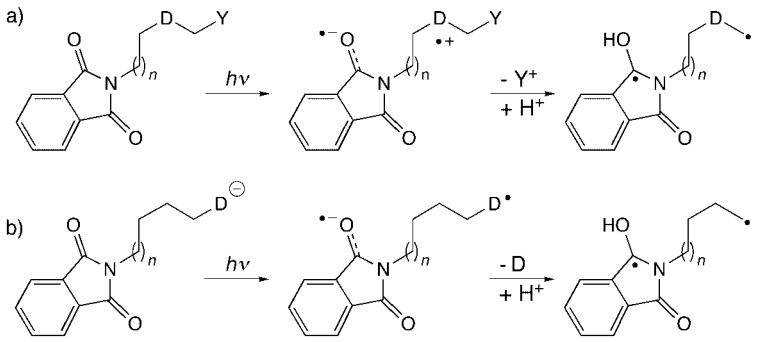
flexibility when potassium alkylcarboxylates are used as the electron-donor components and *N*-alkylated phthalimides as the acceptors [3]. Laser flash photolysis studies revealed that triplet-excited states are responsible for the photochemistry of the electronically excited phthalimides, with a substantial participation of the second excited triplet state T_2 [4]. From the results of time-resolved conductivity measurements, we concluded that the intramolecular *photoinduced electron transfer* (PET) [5] step is complete within less than 20 ns [6].

Substrates with a thioether moiety as the internal functional group X in *Scheme 1* are prone to one-electron oxidation at the S-atom. This primary PET is followed by decarboxylation in case of mercaptoacetic acid derivatives [7]. This approach (*Scheme 2,a* D = S, Y = CO_2^-) to medium-sized and macrocyclic thioethers is analogous to the α-trialkylsilyl pathway developed by *Yoon* and *Mariano* (D = O, S, or NR; Y = SiR_3) [8]. The principal difference between these two approaches is the position and the function of the primary electron donor: in *Scheme 2,a*, the primary electron donor is part of the spacer, and a biradical is generated by mesolytic[3]) cleavage of an α-CY bond (Y = H, CO_2, SiR_3, SnR_3); in *Scheme 2,b*, as a consequence of PET, the primary electron donor D is converted to a leaving group and, thus, does not become part of the new ring structure. We have recently applied this PET decarboxylation to the synthesis of benzopyrrolizidines [10], macrocyclic lactones, and benzodiazepines [11].

Scheme 2. *Pathways* a) *and* b) *to Biradicals Initiated by Photoinduced Electron-Transfer of Phthalimides in the Presence of Electron-Donor Groups* (D)

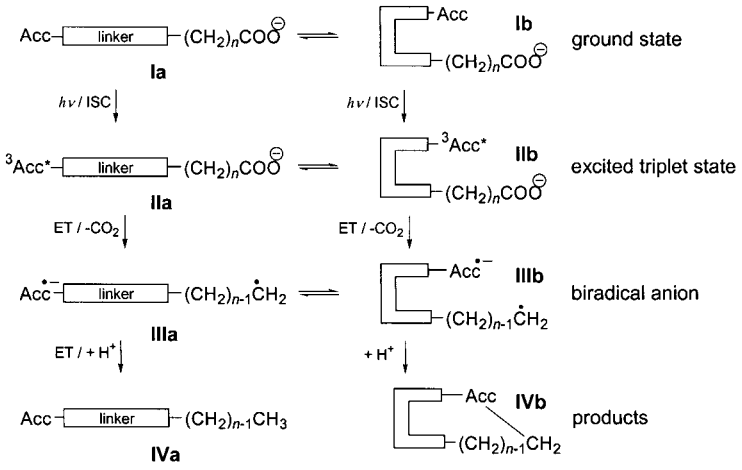


We now report the application of this new type of photo-initiated biradical generation for the synthesis of various cyclopeptides from terminally *N*-phthaloyl-protected peptides and discuss the influence of ground-state properties on the efficiency of the cyclization step [12].

2. Results and Discussion. – 2.1. *Mechanistic Studies on Electron-Transfer Geometries.* In *Scheme 3*, the possible pathways for the PET decarboxylation are summarized, taking into account different conformational situations in the ground states, electronically excited states, radical ions, as well as the precyclization states (*i.e.*, the 1,*n*-biradical or biradical anion, respectively). Among numerous conformational

[3]) The term mesolytic was introduced by *Maslak et al.* [9].

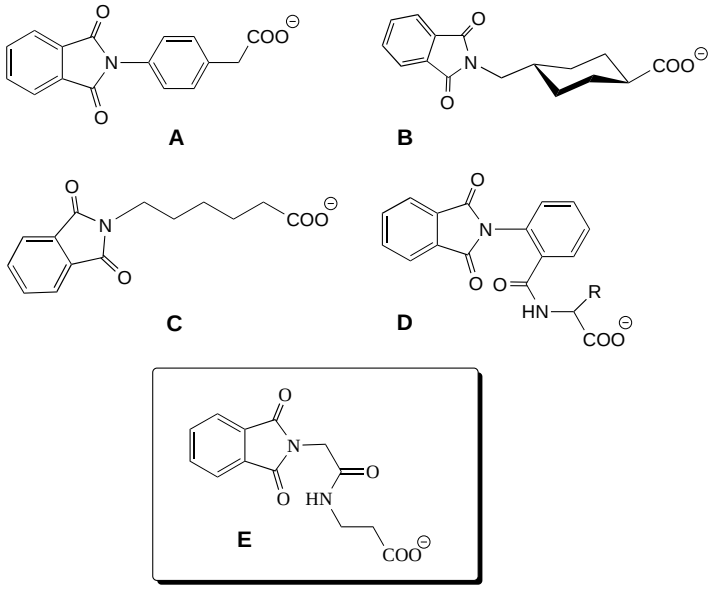
Scheme 3. *General Mechanistic Pathways for Photodecarboxylations*



local minima, only two states are discussed here: the remote conformations **Ia**–**IIIa**, where radical combination is geometrically impossible, and the proximate conformations **Ib**–**IIIb**, which are likely to preceed the biradical combination.

It appears obvious, by chemical intuition, that the proximate states should favor also the electron-transfer step due to the distance dependence of this reaction. Taking into account the relatively long lifetimes of the T_1 state (in the microsecond range), conformational rearrangement at this stage is possible, however, less feasible at the stage of the short-lived T_2 state. From time-resolved laser flash conductivity studies with the tranexamic acid derivative **B**, we concluded that the PET is rapid and should proceed at the stage of the chair conformer and, preferentially, *via* the T_2 state [6]. The distance for electron transfer is *ca.* 6–7 Å, and subsequent extrusion of CO_2, chair-boat interconversion, and biradical combination are all time-delayed. Thus, the photochemistry of this conformationally flexible but ground-state-remote substrate is initiated at the acceptor side of **Ia**, proceeds *via* the biradical anion **IIIa** to give the cyclization product **IVb** [2][6]. The 4-aminobenzoic acid derivative **A** cannot adopt a proximate conformation, but the photoinduced decarboxylation still proceeds, however, with clean formation of *N*-phthaloyltoluidine (**F**) (oxidative decarboxylation product **IVa** in *Scheme 3*). In order to be readily comparable, the model substrates **A** and **B**, as well as the more-elaborate substrates **C**–**E**, possess identical numbers of linker atoms: in **A**–**C** five C-atoms separate the phthalimide from the carboxylate group, while **D** and **E** exhibit an additional (*Z*)-configured amide functionality.

The ε-aminocaproic acid derived substrate **C**, upon PET, gives the corresponding cyclization product **H** in high yields (*Scheme 4*) [1][2]. Due to the conformationally flexible hydrocarbon chain, both the remote and proximate states **Ia**,**b** can be involved in the excitation and electron transfer steps. A U-shaped conformation **Ib** is present in the anthranilic acid derivatives of type **D**, which were investigated as precursors to the benzodiazepines **I** [11]. These substrates efficiently photocyclize only when substituted amino acids are applied (R ≠ H). The parent substrate (R = H) gives rise to complete



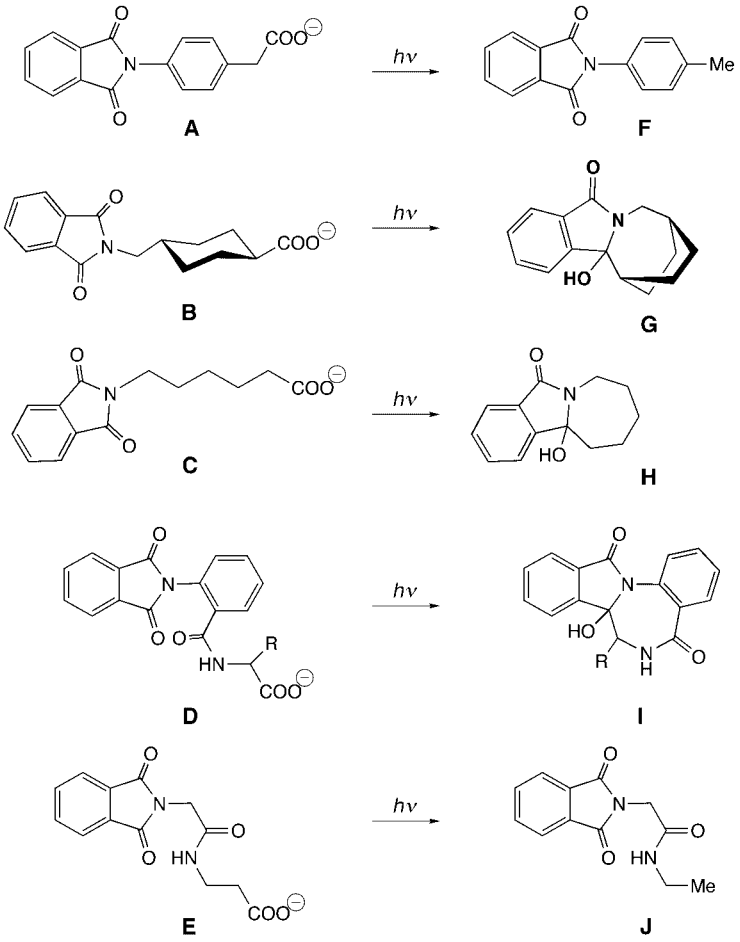
oxidative decarboxylation. This behavior can be rationalized by assuming the presence of a H-bond between the amide NH and one of the imide C=O groups. Likewise, open-chain [*N*-(phthaloyl)glycyl]-β-alanin (**E**) decomposes to **J**, and no cyclization product could be observed.

Whether the reaction of **E** → **J** is really due to an internal H-bond deactivation was investigated by comparison with the corresponding transformation of **1** (*Scheme 5*). This substrate, when irradiated in aqueous acetone, gave upon 50% conversion the δ-lactam **2** in 20% yield besides simple photodecarboxylation. Additionally, this substrate enabled us to observe by NMR spectroscopy a competing cooperative phenomenon, *i.e.*, a potassium-mediated donor-acceptor interaction (corresponding to **Ib** in *Scheme 3*).

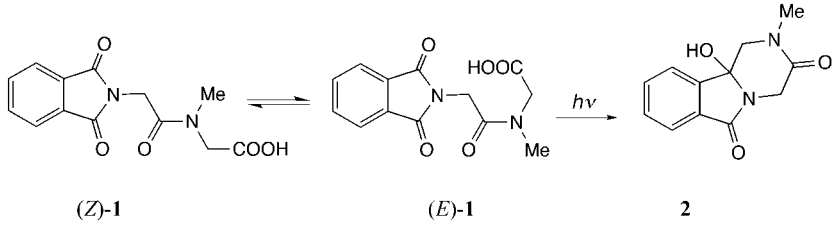
In acetone/D_2O solution, the (*Z*)-isomer of the free acid **1** dominated with *ca.* 75% relative proportion. When 0.5 equiv. of K_2CO_3 was added, the (*E*)/(*Z*)-ratio changed from 1:3 to 0.9:1, indicating that noncovalent interactions operate in favor of the (*E*)-isomer (*Fig. 1*).

The assumption of a metal-chelate facilitating the electron transfer step is reasonable and in analogy to H-bonding interactions in ω-phthalimido-containing alkylcarboxylates as detected by X-ray analyses and cyclic voltammetry [13]. From these results and by comparing photochemical behavior with ground-state properties, we conclude that, in the case of *N*-(phthaloyl)dipeptides (and higher homologues thereof), an appreciable amount of proximate conformation **Ib** exists in the ground state, which favorably conducts both the PET and the cyclization steps after electronic excitation. This type of PET-promoting interaction can compete with intramolecular H-bonds or exist independently when the linker chain is long and flexible enough to enable both types of interactions. Thus, we expected a pronounced influence of the amino acid structure and the total peptide length on the electron transfer as well as the cyclization efficiency.

Scheme 4. *Photolysis of the Model Substrates* **A**–**E** *in Aqueous Acetone at 300 nm*



Scheme 5. *(*E/Z*)-Equilibrium of the Peptide Bond of* N*-(Pht)Gly-Sar* (**1**) *and Subsequent Photoreaction*



2.2. *Reactivity Studies of* N*-Phthaloyl-Protected Dipeptides.* In a first series of photochemically active dipeptides, we prepared compounds **3a**–**f** (*N*(Pht)Gly-AA^2) with increasing chain length of the second amino acid (AA^2) component. The diglycine and the glycyl-β-alanine substrates **3a**,**b** (not shown) have already been described as

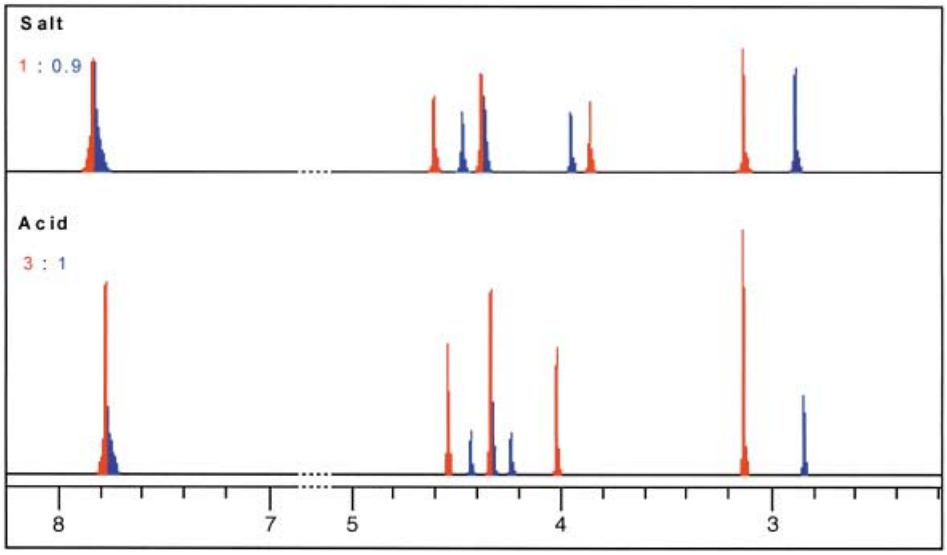


Fig. 1. *^{1}H-NMR Spectrum of peptide* **1** *in (D_6)acetone/D_2O as the potassium salt* (upper spectrum) *and the free acid* (lower spectrum). The red color refers to signals arising from the (*Z*)-isomer, blue signals belong to the corresponding (*E*)-isomer of **1** with respect to the peptide bond.

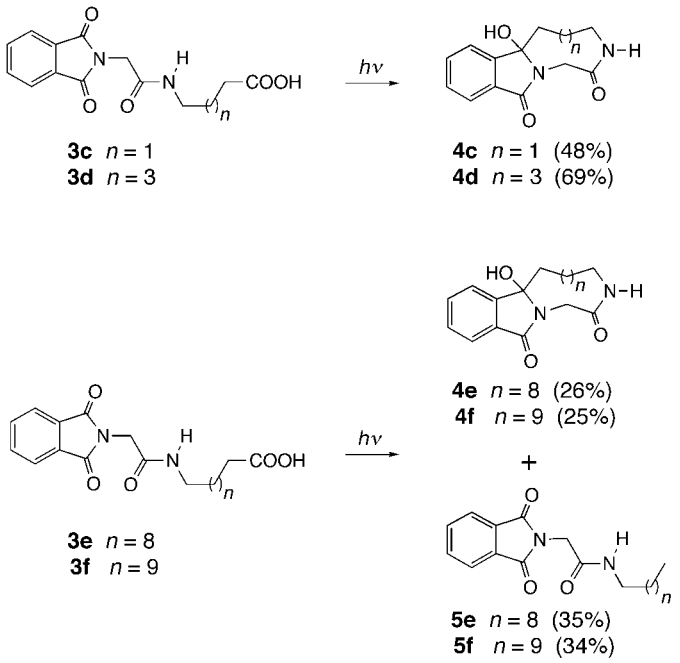
photochemically active but only gave decomposition and simple decarboxylation products [2]. From the elongated starting materials **3c**–**3f**, however, we obtained the lactams **4c**–**4f** in medium yields through photolysis in H_2O in the presence of small amounts of acetone and 0.5 equiv. of K_2CO_3 (*Scheme 6*). The eight- and ten-membered lactams **4c**,**d** could be isolated in 48% and 69% yield, respectively, without detection of simple decarboxylation products. In contrast to these two reactions, the more-elongated substrates **3e**,**f** gave, in addition to the desired 15- and 16-membered lactams **4e**,**f**, the simple oxidative decarboxylation products **5e**,**f**, respectively.

With a second series of substrates (**6a**–**c**), we investigated the influence of the hydrocarbon chain-length of the N-terminal amino acid on the efficiency of the reaction (*Scheme 7*). These substrates were of special interest for another (mechanistic) reason: the arrangement of amide bond and the terminal COOH group corresponds to the situation shown in *Scheme 2*,*a*, *i.e.*, the primary electron transfer can also involve oxidation of the amide N-atom followed by decarboxylation. Analysis of the relative rate of decarboxylation (*vide infra*) and the yields of the cyclization products **7a**–**c** revealed, however, that this approach is not superior to the unmediated direct one-electron oxidation of the carboxylate anion in contrast to the results obtained from the mercaptoacetic acid derivatives [7].

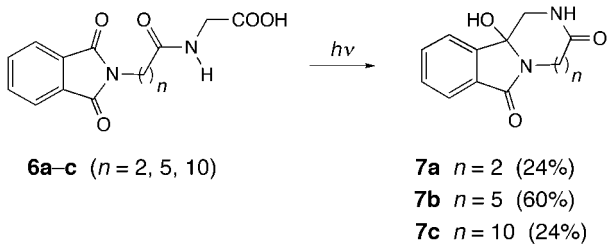
Next, the tripeptides **8a**–**d** were investigated (*Scheme 8*). These substrates differ in the position of the diglycine motif within the sequence. Here, no substantial effects were detected from the terminal glycyl electron donor group (in **8a**,**b**) in comparison with an elongated terminal amino acid spacer (in **8c**,**d**).

Similar to the diglycine derivative, the homologous triglycine substrate was reluctant in the photocyclization step and yielded solely its decarboxylation product in

Scheme 6



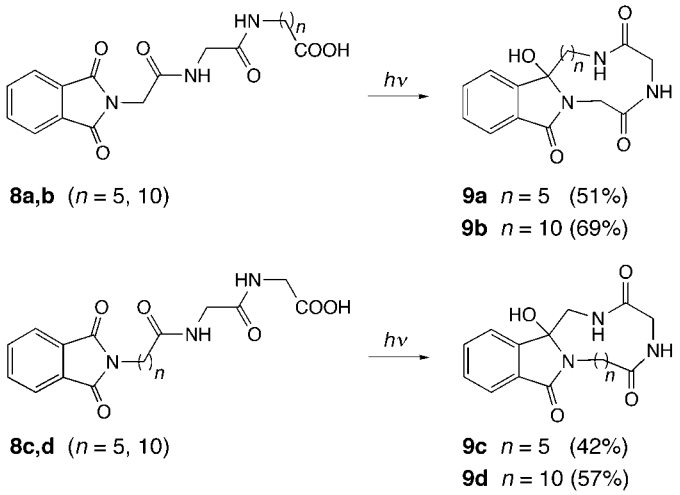
Scheme 7



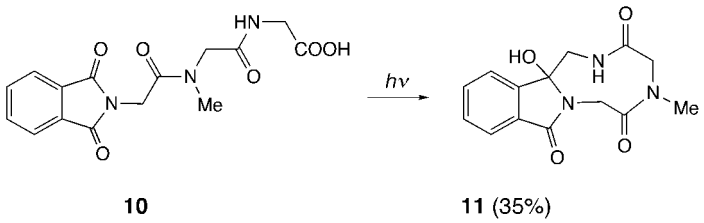
28% yield. Likewise, as described for the *N*-protected glycylsarcosine **1**, incorporation of sarcosine as the second amino acid component led to peptide **10**, which was photocyclized in 35% yield to the nine-membered tricyclic system **11** (*Scheme 9*).

Following the above approach, we also investigated two tetrapeptide derivatives, *N*-phthaloyl-protected Gly-Sar-Gly-Gly (**12**) and Gly-Pro-Gly-Gly (**14**), respectively. Except for small amounts of decarboxylation and hydrolysis products (*vide infra*), the cyclopeptides **13** and **15** were formed in 31 and 44% yields, respectively (*Scheme 10*). Only one diastereoisomeric product was obtained from the chiral substrate **14**, which we assigned the *trans*-configuration based on ^{1}H-NMR analysis and by comparison with benzodiazepines obtained stereoselectively by a similar approach [11].

Scheme 8



Scheme 9

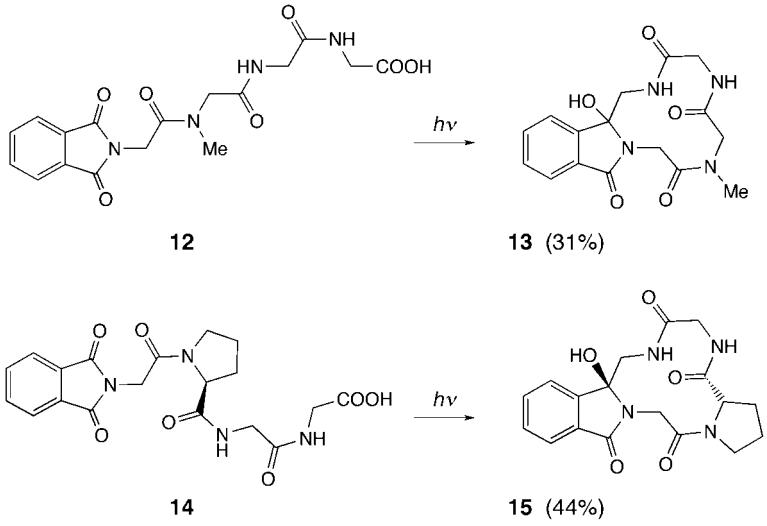


Finally, to evaluate the limitations of this cyclization protocol, we investigated the photochemistry of the phthaloyl-protected pentapeptide Gly-Pro-Gly-Pro-Gly (**16**). Here, the proline residues were incorporated to avoid a deactivating H-bond (as for the corresponding oligo glycines) and, additionally, to induce a hairpin structure that might facilitate the donor/acceptor approach (*Scheme 11*).

The pH/time profile showed a constant increase in pH during the photolysis of **16** in a H_2O/acetone 4:1, as well as a desymmetrization of the NMR-pattern of the phthalimide electrophore. The resulting product **17** had the expected molecular weight (as shown by high-resolution MS), but consisted of an inseparable mixture of at least four isomers, most probably diastereoisomers with different amide-bond configurations of the prolyl residues, a known phenomenon for flexible, proline-containing peptides and cyclopeptides [14].

2.3. *Analysis of the pH-Profile as an Analytical Tool.* In our recent time-resolved conductivity study, we detected a rapid conductivity increase after the laser pulse, which slowly decays when the reaction is initiated at low or neutral pH. Correspondingly, we used the pH/time profile to follow the course of the reaction [15]. To obtain tentative information about the nature of the photoreaction, it was sufficient to measure and compare the changes in pH after a constant reaction time for different

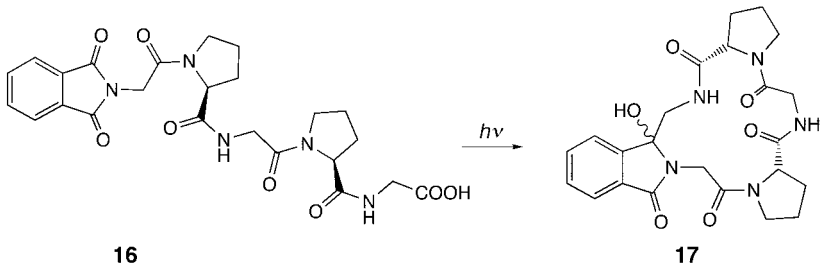
Scheme 10



12 **13** (31%)

14 **15** (44%)

Scheme 11



16 **17**

substrates. The values given in the *Table* show pH-changes after constant irradiation times (3 h) at identical initial substrate concentrations (10 mM).

Table. *Representative pH-Changes* ($\Delta pH_{h\nu}$) *upon Irradiation of Aqueous Solutions of Selected Oligopeptides.* The substrates were irradiated for 3 h at $\lambda = 300$ nm at an initial pH of 6.8–7.3.

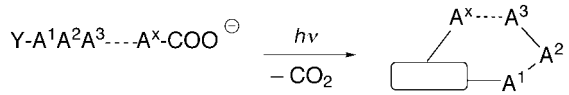
Entry	Peptide[a])	$\Delta pH_{h\nu}$	$\Delta pH_{control}$
1	(Pht)Gly-Gly	+0.34	−0.42
2	(Pht)ε-Acs-Gly (**6b**)	+2.60	0.00
3	(Pht)Gly-Gly-Gly	−1.88	−0.53
4	(Pht)Gly-Gly-ε-Acs (**8b**)	+1.30	−0.16
5	(Pht)ε-Acs-Gly-Gly (**8c**)	+2.20	+0.17
6	(Pht)Gly-Sar-Gly (**10**)	+2.03	+0.13
7	(Pht)Gly-Gly-Gly-Gly	+0.54	−0.29
8	(Pht)Gly-Sar-Gly-Gly (**12**)	+1.85	−0.21
9	(Pht)Gly-Pro-Gly-Gly (**14**)	+2.90	+0.12

[a]) (Pht) = *N*-Phthaloyl.

All oligoglycine derivatives (*Entries 1*, *2*, and *7* in the *Table*) showed a significant decrease in pH under control conditions, indicating thermal hydrolysis with formation of the corresponding phthalic monoacid. This hydrolysis was photochemically accelerated with triglycine (*Entry 3*). The two other substrates, di- (*Entry 1*) and tetraglycine (*Entry 7*) underwent decarboxylation without cyclization, which is indicated by a small increase in pH. An efficient cyclization corresponds to a strong increase in pH (1.5 to 2.5 units), resulting from the protonation of the alkoxide formed after PET and biradical combination. With increasing pH, however, thermal hydrolysis starts to interfere, and substantial amounts of nonabsorbing phthalic monoacid is formed as a product. To suppress this unwanted side reaction, we performed the cyclization in phosphate-buffer solution (pH 7.0) and, in the case of **6b**, indeed detected a 20% increase in the yield of **7b** to 80%. It can be safely expected that this change in reaction conditions will generally improve the yields of these reactions.

3. Conclusions. – Photodecarboxylation cyclization is an attractive route to synthetic cyclic oligopeptides that can potentially mimic conformational motifs of bioactive oligopeptides [16], and are, thus, currently investigated as peptidomimetics [17], pharmaceutically active low-molecular-weight peptide analogues [18], or artificial arrays with defined nanostructures [19]. The classical pathways to these target structures are numerous and take advantage of the highly developed techniques in peptide synthesis [20]. Nevertheless, due to the observation that most of these compounds are macrocyclic polylactams, the fundamental restrictions in (thermal) macrocyclization chemistry have to be considered [21]. Photochemical macrocyclizations constitute an alternative class of reactions that are often controlled by excited-state rather than ground-state properties [22]. The advantage of the concept described herein is its simplicity and the obvious applicability to polypeptide structures where distinct peptide motifs [23] can be incorporated into cyclic systems (*Scheme 12*).

Scheme 12. *Photodecarboxylation/Cyclization Concept for Peptide Motifs*



Y = Chromophore, electrophore
A = Amino acid

In the course of our investigations, we were repeatedly confronted with the question of donor/acceptor geometries (*cf. Scheme 3*). The electron transfer is expected to be fast due to the lifetime properties of the excited phthalimide triplet states, which is in good agreement with time-resolved conductivity measurements [6] and the observation that no dimers were obtained during photolysis even at relatively high concentrations up to 50 mM. Thus, we assume that there are already ground-state donor/acceptor interactions that facilitate electron transfer and subsequent biradical combination. The geometric prerequisites for electron transfer are, however, less stringent compared to biradical combination. Electron transfer can be conducted *via* a π-system as, *e.g.*, in substrate **A** (*Scheme 4*). Obviously, subsequent bond-formation is prohibited here. But, also in polyglycine substrates that are PET-reactive, bond-formation seems to be

prohibited. Due to the linker geometry, a H-bond interaction between the phthalimide chromophore and a proximate secondary amide can generate an unfavorable situation. If this H-bond is excluded, biradical combination reactivity is restored (*e.g.*, *N*(Pht)Gly-Gly *vs.* *N*(Pht)Gly-Sar or *N*(Pht)Ala-Pro [24]). Alternatively, by elongating the second amino acid component, the electron-donating carboxylate can 'return' to the electron acceptor and consequently C–C bond-formation starts to compete with other processes (*Fig. 2*). Analogously, approach-favoring linkers like the *ortho*-phenylene group in substrates of type **D** (*Scheme 4*) are unfavorable when the second amino acid component spatially separates the donor from the acceptor. In this case, the electron transfer is followed by an 'exit' process (decarboxylation, second electron transfer, and protonation leading to 'simple' decarboxylation) [25]. Naturally, 'return' and 'exit' geometries take into account neither solvent effects nor the exact structure of the amphiphilic substrates in aqueous solutions, which might additionally influence the geometry of the electronic ground and excited states.

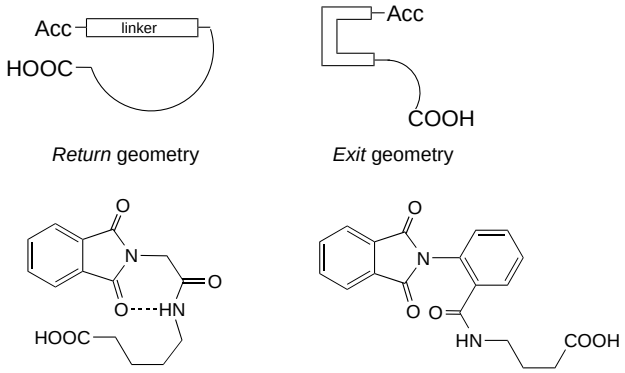


Fig. 2. *'Return' and 'exit' geometries in* N-*Phthaloylpeptides*

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Experimental Part

General. Substrates, reagents and products for/of peptide syntheses are abbreviated by standard amino-acid terminology; Pht = phthaloyl, Sar = sarcosine, β-Ala = β-alanine, γ-Aba = γ-aminobutyric acid, ε-Aca = ε-aminocaproic acid, Auda = 11-aminoundecanoic acid. Column chromatography (CC) was performed on *Merck* silica gel *60* (230 mesh) with AcOEt/petroleum ether (PE) mixtures. Melting points (m.p.): *Büchi 535* melting point apparatus; uncorrected. IR: *Perkin-Elmer Paragon-1000* spectrophotometer; in cm^{-1}. ^{1}H-NMR and ^{13}C-NMR: *Bruker AC-250*, *DPX-300*, and *DRX-500*; in $CDCl_3$, (D_6)DMSO, (D_6)acetone, and (CF_3)COOD (TFA); coupling constants J in Hz, chemical shifts δ in ppm relative to Me_4Si as internal standard; carbon multiplicities determined by DEPT. Electron-impact mass spectroscopy (EI-MS): *Finnigan MAT-8200* and *MAT-312*. Electrospray-ionization mass spectra (ESI-MS) were recorded with methanolic peptide samples at concentrations of *ca.* 3×10^{-8} mol ml^{-1} and at 3.6 kV. Elemental analyses: *Elementar Vario EL Rayonet*. Irradiation experiments: chamber photoreactors *RPR-208* (8×3000 Å lamps, *ca.* 800 W, $\lambda = 300 \pm 10$ nm) and *RPR-100* (16×3500 Å lamps, *ca.* 400 W, $\lambda = 350 \pm 20$ nm), and immersion-wall reactors ($\lambda > 280$ nm).

Synthesis of Unfunctionalized N-*Phthaloyl-containing Peptides.* All substrates were synthesized following published routes by coupling reactions of the appropriate *N*-phthaloylamino acids with the corresponding amino acid benzyl esters following the DCC/HOBt (dicyclohexylcarbodiimide/1-hydroxy-1*H*-benzotriazole) protocol

[2][11b][25]. Subsequent hydrogenolysis of the benzyl ester groups were performed in MeOH with Pd·C under a H_2 atmosphere (standard pressure and temp.).

General Procedure (*GP*) *for the Photolysis of* N-*Phthaloyl Peptides.* Preparative photolyses were performed in *Pyrex* vessels containing 20–40 ml of solvent while purging with a stream of N_2 and cooling to 15° in H_2O/acetone mixtures. In exploratory experiments, photolyses with continous pH and sequential NMR control were performed in 2 ml of a D_2O/(D_6)acetone. Preparative photolyses were performed until completion was indicated by thin-layer chromatography (TLC). The resulting soln. was extracted with CH_2Cl_2 (3 × 20 ml); the aq. phase was acidified to pH 1 and extracted with AcOEt (3 × 20 ml). The combined org. phases were dried, the solvent was evaporated, and the residue was purified by CC.

*(*N-*Phthaloylglycyl)sarcosine* (**1**). Following the *GP*, starting from 32.0 g (87.0 mmol) of *N*-(Pht)Gly-Sar-OBn, 15.7 g (65%) of **1** was obtained as a colorless solid. M.p. 128–129°. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 3.11 (*s*, Me); 3.97 (*s*, NCH_2CO_2); 4.48 (*s*, NCH_2); 7.68 (*m*, 2 arom. H); 7.77 (*m*, 2 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 35.0 (*q*, Me); 38.7 (*t*, NCH_2); 49.1 (*t*, NCH_2CO_2); 122.8 (*d*, 2 arom. CH); 131.6 (*d*, 2 C_q); 133.8 (*s*, 2 arom. CH); 165.8 (*s*, 2 CON); 167.2 (*s*, *C*ONMe); 170.0 (*s*, CO_2).

*4-[(*N-*Phthaloylglycyl)amino]butyric Acid* (**3c**). Following the *GP*, starting from 2.00 g (5.30 mmol) of *N*(Pht)Gly-γ-Abu-OBn, 1.40 g (91.5%) of **3c** was obtained as a colorless solid. M.p. 213–214°. IR (CsI): 3297, 2930, 1778, 1729, 1714, 1658, 1461, 1421, 1089, 807, 722, 716, 676. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 1.60 (*quint.*, CH_2); 2.11 (*t*, ^3J = 7.3, CH_2CO_2); 3.04 (*dt*, ^3J = 5.1, 6.6, $NHCH_2$); 4.11 (*s*, NCH_2); 7.41 (*t*, ^3J = 5.1, NH); 7.53 (*m*, 2 arom. H); 7.65 (*m*, 2 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 23.6 (*t*, CH_2); 30.4 (*t*, CH_2CO_2); 32.9 (*t*, $NHCH_2$); 37.7 (*t*, NCH_2); 122.2 (*d*, 2 arom. CH); 131.2 (*s*, 2 arom. C_q); 133.1 (*d*, 2 arom. H); 165.4 (*s*, 2 CON); 166.7 (*s*, CONH); 173.9 (*s*, CO_2).

*6-[*N-*(Phthaloylglycyl)amino]hexanoic Acid* (**3d**). Following the *GP*, starting from 2.00 g (4.88 mmol) of *N*-(Pht)Gly-ε-Aca-OBn, 1.25 g (80.5%) of **3d** was obtained as a colorless solid. M.p. 140–141°. IR: (CsI) : 3293, 2936, 1777, 1733, 1711, 1656, 1627, 1564, 1468, 1421, 1089, 803, 745, 716, 686. ^{1}H-NMR (300 MHz, D_2O/(D_6)acetone): 1.30 (*m*, CH_2); 1.45–1.64 (*m*, 2 CH_2); 2.22 (*t*, ^3J = 7.4, CH_2CO_2); 4.13 (*t*, ^3J = 7.4, $NHCH_2$); 4.46 (*s*, NCH_2); 7.88 (br. *m*, 4 arom. H). ^{13}C-NMR: (75.5 MHz, D_2O/(D_6)acetone): 24.4 (*t*, CH_2); 25.2 (*t*, 2 CH_2); 30.0 (*t*, CH_2CO_2); 34.0 (*t*, $NHCH_2$); 39.3 (*t*, NCH_2); 124.1 (*d*, 2 arom CH); 131.6 (*s*, 2 arom C_q); 135.6 (*d*, 2 arom. CH); 168.9 (*s*, 2 CON); 169.0 (*s*, CONH); 177.7 (*s*, CO_2). Anal. calc. for $C_{16}H_{18}N_2O_5$ (318.1): C 60.37, H 5.70, N 8.80; found: C 60.76, H 5.82, N 7.11.

*11-[*N-*(Phthaloylglycyl)amino]undecanoic Acid* (**3e**). Following the *GP*, starting from 1.30 g (2.70 mmol) of *N*-(Pht)Gly-Auda-OBn, 1.02 g (97%) of **3e** was obtained as a colorless solid. M.p. 160–162°. ^{1}H-NMR: (300 MHz, $CDCl_3$/(D_6)DMSO): 1.20–1.56 (br. *m*, 8 CH_2); 2.13 (*t*, ^3J = 7.4, CH_2CO_2); 3.37 (*dt*, ^3J = 6.2, 6.8, $NHCH_2$); 4.17 (*s*, NCH_2); 7.72 (*m*, 2 arom. H); 7.80 (*m*, 2 arom. H); 7.94 (*t*, ^3J = 6.4, NH). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 25.2 (*t*, CH_2); 26.3 (*t*, CH_2); 28.4 (*t*, CH_2); 28.5 (*t*, CH_2); 28.6 (*t*, CH_2); 28.7 (*t*, CH_2); 28.8 (*t*, CH_2); 28.9 (*t*, CH_2); 33.5 (*t*, CH_2CO_2); 33.3 (*t*, $NHCH_2$); 38.8 (*t*, NCH_2); 122.7 (*d*, 2 arom. CH); 133.7 (*d*, 2 C_q); 135.5 (*d*, arom. H); 167.2 (*s*, 2 CON); 172.4 (*s*, CONH); 174.6 (*s*, CO_2).

N-*(3-Phthalimidopropanoyl)glycine* (**6a**). Following the *GP*, starting from 2.00 g (5.45 mmol) of *N*-(Pht)β-Ala-Gly-OBn, 1.45 g (96%) of **6a** was obtained as a colorless solid. M.p. 200–202°. ^{1}H-NMR (300 MHz, $CDCl_3$/TFA): 2.87 (*t*, ^3J = 6.7, CH_2CON); 4.06 (*t*, ^3J = 6.7, NCH_2); 4.14 (*d*, ^3J = 5.2, $NHCH_2$); 7.17 (br. *t*, NH); 7.77 (*m*, 2 arom. H); 7.85 (*m*, 2 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/TFA): 32.5 (*t*, CH_2CON); 34.4 (*t*, $NHCH_2$); 41.5 (*t*, NCH_2); 124.1 (*d*, 2 arom. CH); 131.1 (*s*, 2 C_q); 135.1 (*d*, 2 arom. CH); 169.7 (*s*, 2 CON); 174.9 (*s*, CONH); 175.0 (s, CO_2).

N-*(6-Phthalimidohexanoyl)glycine* (**6b**). Following the *GP*, starting from 2.00 g (4.89 mmol) of *N*-(Pht)ε-Aca-Gly-OBn, 1.42 g (91%) of **6b** was obtained as a colorless solid. M.p. 142–144°. IR: (CsI): 3301, 2940, 1774, 1722, 1647, 1547, 1460, 1439, 1075, 796, 723, 712, 622. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 1.30 (*m*, CH_2); 1.58 (*m*, 2 CH_2); 2.12 (*t*, ^3J = 7.4, CH_2CO_2); 3.56 (*t*, ^3J = 7.4, $NHCH_2$); 3.73 (*d*, ^3J = 7.7, NCH_2); 7.69 (*m*, 2 arom. H); 7.75 (*m*, 2 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 24.5 (*t*, CH_2); 25.8 (*t*, CH_2); 27.7 (*t*, CH_2); 35.0 (*t*, CH_2CO_2); 37.1 (*t*, NCH_2); 40.4 (*t*, $NHCH_2$); 122.5 (*d*, 2 arom. CH); 131.4 (*d*, 2 arom. C_q); 133.6 (*s*, 2 arom. CH); 167.5 (*s*, 2 CON); 171.2 (*s*, CONH); 172.6 (*s*, CO_2). Anal. calc. for $C_{16}H_{18}N_2O_5$ (318.1): C 60.37, H 5.70, N 8.80; found: C 60.81, H 6.16, N 9.11.

N-*(6-Phthalimidoundecanoyl)glycine* (**6c**). Following the *GP*, starting from 2.00 g (4.18 mmol) of *N*-(Pht)Auda-Gly-OBn, 1.55 g (96%) of **6c** was obtained as a colorless solid. M.p. 83–84°. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.24–1.29 (br. *m*, 6 CH_2); 1.59–1.63 (*m*, 2 CH_2); 2.27 (*t*, ^3J = 7.5, CH_2CO_2); 3.64 (*t*, ^3J = 7.2, NCH_2); 4.05 (*d*, ^3J = 4.9, $NHCH_2$); 6.44 (br. *t*, NH); 7.68 (*m*, 2 arom. H); 7.82 (*m*, 2 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 24.6 (*t*, CH_2); 25.5 (*t*, CH_2); 26.7 (*t*, CH_2); 28.5 (*t*, CH_2); 28.9 (*t*, CH_2); 29.0 (*t*, CH_2); 29.0 (*t*, CH_2); 29.1 (*t*, CH_2);

36.1 (*t*, *C*H_2CON); 38.1 (*t*, NHCH$_2$); 41.5 (*t*, NCH$_2$); 123.2 (*d*, 2 arom. CH); 132.1 (*s*, 2 arom. C$_q$); 133.9 (*d*, 2 arom. CH); 168.6 (*s*, 2 CON); 172.2 (*s*, CONH); 175.3 (*s*, CO$_2$).

*6-{[(*N*-Phthaloylglycyl)glycyl]amino}hexanoic Acid* (**8a**). Following the *GP*, starting from 2.00 g (4.30 mmol) of *N*-(Pht)Gly-Gly-ε-Aca-OBn, 1.56 g (97%) of **8a** was obtained as a colorless solid. M.p. 191–192°. IR: (CsI): 3318, 2927, 1775, 1721, 1707, 1684, 1634, 1562, 1469, 1426, 1090, 916, 716, 663. ^{1}H-NMR (300 MHz, CDCl$_3$/(D$_6$)DMSO): 1.21–1.40 (*m*, CH$_2$); 1.45 (*m*, 2 CH$_2$); 2.16 (*t*, ^3J = 7.4, CH$_2$CO$_2$); 3.05 (*dt*, ^3J = 6.2, 6.5, NHC*H*$_2$); 3.71 (*d*, ^3J = 5.6, NHC*H*$_2$CO); 4.30 (*s*, NCH$_2$); 7.73 (*t*, ^3J = 5.3, NH); 7.79 (*m*, 2 arom. H); 7.85 (*m*, 2 arom. H); 8.52 (*t*, ^3J = 5.6, NH). ^{13}C-NMR (75.5 MHz, CDCl$_3$/(D$_6$)DMSO): 24.2 (*t*, CH$_2$); 25.9 (*t*, CH$_2$); 28.8 (*t*, CH$_2$); 33.6 (*t*, *C*H$_2$CO$_2$); 38.5 (*t*, NHCH$_2$); 40.1 (*t*, NH*C*H$_2$CO); 42.2 (*t*, NCH$_2$); 123.0 (*d*, 2 arom. CH); 131.7 (*d*, 2 arom. C$_q$); 134.3 (*s*, 2 arom. CH); 166.4 (*s*, 2 CON); 167.4 (*s*, CONH); 168.2 (*s*, CONH); 174.4 (*s*, CO$_2$).

*11-{[(*N*-Phthaloylglycyl)glycyl]amino}undecanoic Acid* (**8b**). Following the *GP*, starting from 2.00 g (3.73 mmol) of *N*-(Pht)Gly-Gly-Auda-OBn, 1.55 g (93%) of **8b** was obtained as a colorless solid. M.p. 170–172°. ^{1}H-NMR (300 MHz, CDCl$_3$/(D$_6$)DMSO): 1.20 (br. *m*, 6 CH$_2$); 1.38–1.48 (br. *m*, 4 CH$_2$); 2.14 (*t*, ^3J = 7.4, 2 CH$_2$CO$_2$); 3.08 (*dt*, ^3J = 6.0, 6.8, 2 NHC*H*$_2$); 3.73 (*d*, ^3J = 5.7, NHC*H*$_2$CO); 4.30 (*s*, 2 NCH$_2$); 7.72 (*m*, 2 arom. H); 7.79 (*m*, 2 arom. H); 8.52 (*t*, ^3J = 5.6, NH); 8.79 (*t*, ^3J = 6.2, NH). ^{13}C-NMR (75.5 MHz, CDCl$_3$/(D$_6$)DMSO): 23.5 (*t*, CH$_2$); 25.4 (*t*, CH$_2$); 27.6 (*t*, CH$_2$); 27.8 (*t*, CH$_2$); 27.9 (*t*, CH$_2$); 28.0 (*t*, CH$_2$); 28.8 (*t*, CH$_2$); 32.7 (*t*, CH$_2$); 33.6 (*t*, *C*H$_2$CO$_2$); 39.1 (*t*, NHCH$_2$); 40.0 (*t*, NH*C*H$_2$CO); 42.4 (*t*, NCH$_2$); 121.9 (*d*, 2 arom. CH); 130.8 (*d*, 2 arom. C$_q$); 132.9 (*s*, 2 arom. CH); 165.5 (*s*, 2 CON); 166.3 (*s*, CONH); 167.8 (*s*, CONH); 173.9 (*s*, CO$_2$). Anal. calc. for C$_{23}$H$_{31}$N$_3$O$_6$ · 0.5 H$_2$O (454.2): C 60.78, H 7.10, N 9.25; found: C 60.29, H 7.51, N 9.12.

*[*N*-(6-Phthalimidohexanoyl)glycyl]glycine* (**8c**). Following the *GP*, starting from 2.00 g (4.59 mmol) of *N*-(Pht)ε-Aca-Gly-Gly-OBn, 1.64 g (95%) of **8c** was obtained as a colorless solid. M.p. 158–159°. ^{1}H-NMR (300 MHz, CDCl$_3$/(D$_6$)DMSO): 1.30 (*m*, 2 CH$_2$); 1.59 (*m*, 2 CH$_2$); 2.14 (*t*, ^3J = 7.4, CH$_2$CON); 3.56 (*t*, ^3J = 7.2, NCH$_2$); 3.78 (*t*, ^3J = 5.4, 2 NHC*H*$_2$); 7.68 (*m*, 2 arom. H); 7.75 (*m*, 2 arom. H); 7.7 (*t* (obscured), ^3J = 5.4, 2 NH). ^{13}C-NMR (75.5 MHz, CDCl$_3$/(D$_6$)DMSO): 24.5 (*t*, CH$_2$); 26.9 (*t*, CH$_2$); 27.7 (*t*, CH$_2$); 34.3 (*t*, *C*H$_2$CON); 37.1 (*t*, NCH$_2$); 40.5 (*t*, NHCH$_2$); 41.2 (*t*, NH*C*H$_2$CO$_2$); 65.9 (*t*, PhCH$_2$); 12.7 (*d*, 2 arom. CH); 130.6 (*d*, 2 arom. C$_q$); 132.7 (*s*, 2 arom. CH); 166.7 (*s*, 2 CON); 169.1 (*s*, CONH); 169.5 (*s*, CONH); 171.8 (*s*, CO$_2$).

*[*N*-(11-Phthalimidoundecanoyl)glycyl]glycine* (**8d**). Following the *GP*, starting from 2.00 g (3.55 mmol) of *N*-(Pht)Auda-Gly-Gly-OBn, 1.38 g (58%) of **8d** was obtained as a colorless solid. M.p. 180–181°. IR (CsI): 3411, 3376, 3336, 2928, 2851, 1698, 1667, 1631, 1530, 1467, 1401, 1088, 1018, 725. ^{1}H-NMR (300 MHz, CDCl$_3$/(D$_6$)DMSO): 1.20 (br. *m*, 6 CH$_2$); 1.47–1.59 (br. *m*, 2 CH$_2$); 2.12 (*t*, ^3J = 7.4, CH$_2$CON); 3.56 (*t*, ^3J = 7.1, NCH$_2$); 3.78 (*d*, ^3J = 5.7, 2 NHC*H*$_2$); 7.70 (*m*, arom. H); 7.77 (*m*, 2 arom. H); 7.80 (*t* (partly obscured), ^3J = 5.6, NH); 8.05 (*t*, ^3J = 5.8, NH). ^{13}C-NMR (75.5 MHz, CDCl$_3$/(D$_6$)DMSO): 24.4 (*t*, CH$_2$); 25.0 (*t*, CH$_2$); 26.2 (*t*, CH$_2$); 27.9 (*t*, CH$_2$); 28.5 (*t*, CH$_2$); 28.6 (*t*, CH$_2$); 28.7 (*t*, CH$_2$); 33.3 (*t*, CH$_2$); 35.3 (*t*, *C*H$_2$CON); 37.2 (*t*, NCH$_2$); 40.5 (*t*, NHCH$_2$); 41. 9 (*t*, NH*C*H$_2$CO$_2$); 121.4 (*d*, 2 arom. CH); 130.3 (*d*, 2 C$_q$); 132.5 (*d*, 2 arom. CH); 167.6 (*s*, 2 CON); 169.1 (*s*, CONH); 169.6 (*s*, CONH); 173.6 (*s*, CO$_2$). Anal. calc. for C$_{23}$H$_{31}$N$_3$O$_6$ · 3 H$_2$O (499.2): C 55.30, H 7.47, N 8.41; found: C 55.21, H 7.62, N 9.02.

*[(*N*-Phthaloylglycyl)sarcosyl]glycine* (**10**). Following the *GP*, starting from 2.10 g (5.00 mmol) of *N*-(Pht)Gly-Sar-Gly-OBn, 1.30 g (78%) of **10** was obtained as a colorless solid. M.p. 69–70°. IR (CsI): 3330, 2935, 1775, 1721, 1665, 1572, 1547, 1468, 1431, 1115, 958, 795, 716. ^{1}H-NMR (300 MHz, CDCl$_3$/(D$_6$)DMSO): 2.88 (*d*, Me); 3.74–4.09 (*m*, MeNC*H*$_2$, NHC*H*$_2$); 4.51 (*d*, NCH$_2$); 7.71 (*m*, arom. H); 7.79 (*m*, 2 arom. H); 7.96 (*t*, ^3J = 5.4, NH). ^{13}C-NMR (75.5 MHz, CDCl$_3$/(D$_6$)DMSO): 35.0 (*q*, Me); 38.8 (*t*, NCH$_2$); 41.0 (*t*, NHCH$_2$); 50.2 (*t*, MeN*C*H$_2$); 122.8 (*d*, 2 arom. CH); 131.6 (*d*, 2 arom. C$_q$); 133.8 (*s*, 2 arom. CH); 165.9 (*s*, 2 CON); 166.2 (*s*, *C*ONMe); 167.1 (*s*, NHCO); 167.8 (*s*, CO$_2$).

*{[(*N*-Phthaloylglycyl)sarcosyl]glycyl}glycine* (**12**). Following the *GP*, starting from 5.00 g (10.0 mmol) of *N*-(Pht)Gly-Sar-Gly-Gly-OBn, 3.33 g (84.5%) of **12** was obtained as a yellowish solid. M.p. 96–97°. IR (CsI): 3646, 3628, 3329, 2934, 2852, 1772, 1717, 1700, 1652, 1627, 1575, 1559, 1436, 1089, 959, 893, 717. ^{1}H-NMR (300 MHz, CDCl$_3$/(D$_6$)DMSO): 2.85 (*s*, Me); 3.72–4.11 (*m*, MeNC*H*$_2$, 2 NHC*H*$_2$); 4.52 (*s*, NCH$_2$); 7.72 (*m*, 2 arom. H); 7.79 (*m*, 2 arom. H); 7.98 (*t*, ^3J = 5.6, NH); 8.14 (*t*, ^3J = 5.7, NH). ^{13}C-NMR (75.5 MHz, CDCl$_3$/(D$_6$)DMSO): 35.8 (*q*, Me); 38.9 (*t*, NCH$_2$); 40.5 (*t*, NHCH$_2$); 41.9 (*t*, NHCH$_2$); 47.5 (*t*, MeN*C*H$_2$); 122.8 (*d*, 2 arom. CH); 131.6 (*d*, 2 arom. C$_q$); 133.8 (*s*, 2 arom. CH); 166.1 (*s*, 2 CON); 167.2 (*s*, *C*ONMe); 167.7 (*s*, NHCO); 168.1 (*s*, NHCO); 168.9 (*s*, CO$_2$).

*{[(*N*-Phthaloylglycyl)-*L*-prolyl]glycyl}glycine* (**14**). Following the *GP*, starting from 6.90 g (14.0 mmol) of *N*-(Pht)Gly-Pro-Gly-Gly-OBn, 2.95 g (51%) of **14** was obtained as a yellowish solid. M.p. 95–96°. $[\alpha]_D^{20}$: –77.9 (*c* = 1, MeOH). IR (CsI): 3808, 3328, 2935, 2362, 1777, 1721, 1659, 1650, 1562, 1547, 1536, 1449, 1090, 958, 717. ^{1}H-NMR (300 MHz, CDCl$_3$): 2.00 (*m*, 2 CH$_2$); 3.55–3.93 (*m*, CH$_2$, 2 NHC*H*$_2$); 4.44 (*s*, NCH$_2$); 4.38–4.50

(*m*, CH); 7.40 (br. *t*, NH); 7.7 (*t* (partly obscured), NH); 7.66 (*m*, 2 arom. H); 7.77 (*m*, 2 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 25.0 (*t*, CH_2); 28.7 (*t*, CH_2); 39.9 (*t*, CH_2); 41.1 (*t*, $NHCH_2$); 42.7 (*t*, $NHCH_2$); 46.9 (*t*, NCH_2); 61.1 (*d*, CH); 123.5 (*d*, 2 arom. CH); 131.8 (*d*, 2 arom. C_q); 134.2 (*s*, 2 arom. CH); 166.2 (*s*, 2 CON); 167.9 (*s*, CONH); 170.6 (*s*, CONH); 170.9 (*s*, CONCH); 171.9 (*s*, CO_2). Anal. calc. for $C_{19}H_{20}N_4O_7$ (416.1): C 54.81, H 4.84, N 13.46; found: C 56.77, H 5.54, N 11.39.

*([[(*N*-Phthaloylglycyl)-*L*-prolyl]glycyl]-*L*-prolyl)glycine* (**16**). Following the *GP*, starting from 3.18 g (5.3 mmol) of *N*-(Pht)Gly-Pro-Gly-Gly-OBn, 2.29 g (85%) of **16** was obtained as a yellow solid. M.p. 128–130°. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.73–2.19 (*m*, 4 CH_2); 3.30–4.07 (*m*, 8 H, 4 CH_2); 4.31–4.62 (*m*, 2 NCH_2); 7.68 (*dd*, $J = 8.5$, 2 arom. H); 7.80 (*dd*, $^3J = 8.5$, 2 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 24.6 (*t*, CH_2); 24.5 (*t*, CH_2); 28.7 (*t*, CH_2); 28.8. (*t*, CH_2); 39.8 (*t*, NCH_2CO); 41.2 (*t*, NCH_2CO); 42.1 (*t*, NCH_2CO); 46.6 (*t*, NCH_2); 46.7 (*t*, NCH_2); 60.3 (*d*, NCH); 60.4 (*d*, NCH); 123.5 (*d*, 2 arom. CH); 132.0 (*s*, 2 arom. C_q); 134.2 (*d*, 2 arom. CH); 162.7 (*s*, 2 NCO); 165.6 (*s*, CO); 167.8 (*s*, CO); 168.5 (*s*, CO); 171.7 (*s*, CO); 172.0 (*s*, COOH). ESI-HR-MS (peak matching, reference ion: PPG 505, resolution > 7000): 536.174 ($[M+Na]^+$, $C_{24}H_{27}N_5O_8Na$; calc.: 536.176). Anal. calc. for $C_{24}H_{27}N_5O_8 \cdot H_2O$ (531.2): C 54.23, H 5.50, N 13.18; found: C 53.64, H 5.89, N 13.74.

*1,10b-Dihydro-10b-hydroxy-2-methylpyrazino[2,1-*a*]isoindole-3,6(2*H*,4*H*)-dione* (**2**). Following the general photolysis procedure, a mixture of 280 mg (1.00 mmol) of **1** and 70.0 mg (0.50 mmol) of K_2CO_3 in 100 ml of H_2O/acetone 1:1 was irradiated for 18 h. After extraction with CH_2Cl_2, acidification of the aq. phase and extraction with AcOEt, the crude product was purified by CC (AcOEt/hexane 10:1), resulting in 74 mg (20%) of **2** as a colorless oil (50% conversion). ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 2.78 (*s*, NMe); 3.19 (*d*, $^2J =$ 12.3, $MeNCH_2$); 3.57 (*d*, $^2J = 12.3$, $MeNCH_2$); 3.68 (*d*, $^2J = 18.2$, NCH_2); 4.34 (*d*, $^2J = 18.2$, NCH_2); 6.48 (br. *s*, COH); 7.22–7.56 (*m*, 4 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 34.6 (*q*, NMe); 40.5 (*t*, $MeNCH_2$); 56.7 (*t*, NCH_2); 82.4 (*s*, COH); 121.5 (*d*, arom. CH); 123.0 (*d*, arom. CH); 129.5 (*d*, arom. CH); 130.7 (*s*, arom. C_q); 131.9 (*d*, arom. CH); 144.8 (*s*, arom. C_q); 163.7 (*s*, CON); 168.6 (*s*, CONH).

*4,5,6,6a-Tetrahydro-6a-hydroxy[1,4]diazocino[8,1-*a*]isoindole-2,11(1*H*,3*H*)-dione* (**4c**). Following the general photolysis procedure, a mixture of 116 mg (0.40 mmol) of **3c** and 14.0 mg (0.10 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 10:1 was irradiated for 3 h. After extraction with CH_2Cl_2, acidification of the aq. phase, and extraction with AcOEt, the crude product was purified by CC (MeOH/CH_2Cl_2 1:7), resulting in 46.8 mg (48%) of **4c** as a yellow oil. $\Delta pH_{control} = -0.06$; $\Delta pH_{h\nu} = +1.22$. IR (CsI): 3387, 2957, 2357, 1652, 1578, 1551, 1497, 1295, 1150, 1049, 1026. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 1.47–1.57 (br. *m*, CH_2); 2.26 (*t*, $^3J = 4.1$, CH_2COH); 3.09–3.21 (br. *m*, $NHCH_2$); 3.88 (*d*, $^3J = 17.9$, 1 H, NCH_2); 4.79 (*d*, $^3J = 17.9$, 1 H, NCH_2); 6.21 (*s*, OH); 6.96 (*t*, $^3J = 7.1$, NH); 7.34 (*m*, 1 arom. H); 7.43 (*m*, 1 arom. H); 7.45 (*m*, 1 arom. H); 7.93 (*m*, 1 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 32.3 (*t*, CH_2); 37.2 (*t*, CH_2COH); 39.8 (*t*, $NHCH_2$); 40.4 (*t*, NCH_2); 89.5 (*s*, COH); 121.3 (*d*, arom. CH); 122.7 (*d*, 1 arom. CH); 128.9 (*d*, arom. CH); 130.4 (*d*, arom. CH); 132.3 (*s*, 1 arom. C_q); 146.3 (*s*, arom. C_q); 168.4 (*s*, CON); 170.6 (s, CH_2CO). Anal. calc. for $C_{13}H_{14}N_2O_3$ (246.1): C 63.40, H 5.73, N 11.38; found: C 62.96, H 5.51, N 11.67.

*4,5,6,7,8,8a-Hexahydro-8a-hydroxy[1,4]diazecino[10,1-*a*]isoindole-2,13(1*H*,3*H*)-dione* (**4d**). Following the general photolysis procedure, a mixture of 130 mg (0.40 mmol) of **3c** and 14.0 mg (0.10 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 10:1 was irradiated for 3 h. After extraction with CH_2Cl_2, acidification of the aq. phase, and extraction with AcOEt, the crude product was purified by CC (MeOH/CH_2Cl_2 1:5), resulting in 76.8 mg (69%) of **4c** as a yellow oil. $\Delta pH_{control} = 0.0$; $\Delta pH_{h\nu} = +2.60$. IR (CsI): 3409, 2954, 2257, 1651, 1568, 1557, 1397, 1295, 1152, 1049, 1026, 1004, 824, 764. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 0.93 (*m*, CH_2); 1.38 (*m*, CH_2); 1.41 (*m*, 1 H, $NHCH_2CH_2$); 1.43 (*m*, 1 H, CH_2); 1.79 (*m*, 1 H, CH_2COH); 1.93 (*m*, 1 H, $NHCH_2CH_2$); 2.10 (*m*, 1 H, CH_2COH); 3.71 (*dt*, $^3J = 11.3$, 1 H, $NHCH_2$); 3.75 (*d*, $^3J = 17.1$, 1 H, NCH_2); 4.49 (*d*, $^3J = 17.2$, 1 H, NCH_2); 4.80 (*dt*, $^3J = 11.0$, 1 H, $NHCH_2$); 7.47 (*m*, arom. H); 7.51 (*m*, arom. H); 7.58 (*m*, arom. H); 7.71 (*m*, arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 22.1 (*t*, CH_2); 23.6 (*t*, $NHCH_2CH_2$); 25.3 (*t*, CH_2); 31.3 (*t*, CH_2COH); 39.7 (*t*, NCH_2); 67.0 (*t*, $NHCH_2$); 91.5 (*s*, COH); 121.9 (*d*, arom. CH); 123.6 (*d*, arom. CH); 129.7 (*d*, arom. CH); 130.6 (*s*, arom. C_q); 132.8 (*d*, arom. CH); 146.0 (*s*, arom. C_q); 166.9 (*s*, CON); 169.0 (*s*, CH_2CO). Anal. calc. for $C_{15}H_{18}N_2O_3$ (274.1): C 65.68, H 6.61, N 10.21; found: C 65.33, H 6.44, N 10.49.

*3,4,5,6,7,8,9,10,11,12,13,13a-Dodecahydro-13a-hydroxy-1*H*-[1,4]diazacyclopentadecino[15,1-*a*]isoindole-2,18- dione* (**4e**) *and* N*-Decyl-2,3-dihydro-1,3-dioxo-1*H*-isoindole-2-acetamide* (**5e**). Following the general photolysis procedure, a mixture of 155 mg (0.40 mmol) of **3e** and 14.0 mg (0.10 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 1:1 was irradiated for 5 h. After extraction with CH_2Cl_2, acidification of the aq. phase, and extraction with AcOEt, the crude product was purified by CC (SiO_2; MeOH/CH_2Cl_2 1:10), resulting in 34.4 mg (26%) of **4e** and 48.2 mg (35%) of **5e** as oils. $\Delta pH_{control} = +0.14$; $\Delta pH_{h\nu} = +1.30$.

Data of **4e**: ^{1}H-NMR (300 MHz, $CDCl_3$): 1.10–1.69 (br. *m*, 8 CH_2); 1.84 (*m*, 1 H, CH_2COH); 1.88 (*m*, 1 H, CH_2COH); 3.36 (*m*, $NHCH_2$); 3.90 (*d*, $^3J = 16.0$, 1 H, NCH_2); 4.15 (*d*, $^3J = 16.0$, 1 H, NCH_2); 7.45–7.55 (br.

m, 4 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 24.2 (*t*, CH_2); 24.6 (*t*, CH_2); 25.0 (*t*, CH_2); 26.2 (*t*, CH_2); 26.3 (*t*, CH_2); 26.5 (*t*, CH_2); 28.6 (*t*, CH_2); 35.5 (*t*, CH_2); 36.8 (*t*, CH_2COH); 39.1 (*t*, $NHCH_2$); 43.5 (*t*, NCH_2); 91.7 (*s*, COH); 122.2 (*d*, arom. CH); 123.4 (*d*, arom. CH); 129.5 (*d*, arom. CH); 130.1 (*d*, arom. CH); 132.1 (*s*, arom. C_q); 147.2 (*s*, arom. C_q); 167.9 (*s*, CON); 170.0 (*s*, CH_2CO). ESI-MS: 367.3 (70, $[M+Na]^+$). Anal. calc. for $C_{20}H_{28}N_2O_3$ (344.2): C 69.74, H 8.19, N 8.13; found: C 69.89, H 8.04, N 7.78.

Data of **5e**: ^{1}H-NMR (300 MHz, $CDCl_3$): 1.06 (*t*, $^3J = 7.2$, Me); 1.11–1.39 (br. *m*, 8 CH_2); 2.06 (*t*, $^3J = 7.2$, $NHCH_2$); 4.12 (*s*, NCH_2); 7.64 (*m*, 2 arom. H); 7.70 (*m*, 2 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 14.7 (*q*, Me); 25.3 (*t*, CH_2); 27.2 (*t*, CH_2); 29.5 (*t*, CH_2); 29.6 (*t*, CH_2); 29.7 (*t*, CH_2); 29.8 (*t*, CH_2); 29.8 (*t*, CH_2); 34.6 (*t*, $NHCH_2CH_2$); 40.8 (*t*, NCH_2); 60.6 (*t*, $NHCH_2$); 123.8 (*d*, 2 arom. CH); 132.6 (*s*, 2 arom. C_q); 134.8 (*s*, 2 arom. CH); 168.3 (*s*, 2 CON); 175.9 (*s*, CH_2CO).

*4,5,6,7,8,9,10,11,12,13,14,14a-Dodecahydro-14a-hydroxy-[1,4]diazacyclohexadecino[16,1-*a*]isoindole-2,19(1*H*,3*H*)-dione* (**4f**) *and* N*-Undecyl-2,3-dihydro-1,3-dioxo-1*H*-isoindole-2-acetamide* (**5f**). For procedure and anal. data, see [2].

*4,5-Dihydro-11b-hydroxy-1*H*-[1,4]diazepino[2,1-*a*]isoindole-3,7(2*H*,11b*H*)-dione* (**7a**). Following the general photolysis procedure, a mixture of 113 mg (0.40 mmol) of **6a** and 28.0 mg (0.20 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 10:1 was irradiated for 5 h. After extraction with CH_2Cl_2, acidification of the aq. phase and extraction with AcOEt, 22.3 mg (24%) of **7a** was obtained as a yellow oil that could not be purified any further. $\Delta pH_{control} = +0.08$; $\Delta pH_{hv} = +1.40$. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 2.79 (*m*, CH_2CON); 3.79 (*m*, $NHCH_2$); 3.98 (*m*, NCH_2); 7.34 (*m*, arom. H); 7.46 (*m*, 2 arom. H); 7.60 (*m*, arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 36.0 (*t*, CH_2CON); 37.1 (*t*, $NHCH_2$); 40.0 (*t*, NCH_2); 104.5 (*s*, COH); 121.2 (*d*, arom. CH); 122.5 (*d*, arom. CH); 128.1 (*s*, arom. C_q); 130.2 (*d*, arom. CH); 131.3 (*d*, arom. CH); 140.0 (*s*, arom. C_q); 168.0 (*s*, CON); 169.1 (*s*, CONH).

*1,5,6,7,8,14b-Hexahydro-14b-hydroxy-[1,4]diazecino[2,1-*a*]isoindole-3,10(2*H*,4*H*)-dione* (**7b**). Following the general photolysis procedure, a mixture of 130 mg (0.40 mmol) of **6b** and 28.0 mg (0.20 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 9:1 was irradiated for 5 h. After extraction with CH_2Cl_2, acidification of the aq. phase, and extraction with AcOEt, 65.8 mg (60%) of **7b** was obtained after CC (MeOH/CH_2Cl_2 1:7) as a yellowish oil. $\Delta pH_{control} = -0.13$; $\Delta pH_{hv} = +2.20$. IR (CsI): 3288, 2933, 2256, 1770, 1703, 1699, 1694, 1661, 1652, 1634, 1563, 1557, 1470, 1398, 1301, 1153, 1055, 823, 764. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 0.94–1.62 (br. *m*, 3 CH_2); 2.00 (*m*, CH_2CON); 3.30 (*m*, NCH_2); 3.51 (*m*, 1 H, $NHCH_2$); 3.74 (*m*, 1 H, $NHCH_2$); 6.54 (*s*, OH); 7.42–7.63 (*m*, 4 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 24.4 (*t*, CH_2); 25.2 (*t*, CH_2); 25.8 (*t*, CH_2); 33.3 (*t*, CH_2CON); 36.2 (*t*, NCH_2); 46.6 (*t*, $NHCH_2$); 88.2 (*s*, COH); 121.6 (*d*, arom. CH); 122.2 (*d*, arom. CH); 129.1 (*d*, arom. CH); 131.0 (*d*, arom. CH); 131.5 (*s*, arom. C_q); 146.3 (*s*, C_q); 166.7 (*s*, CON); 174.7 (*s*, CONH). Anal. calc. for $C_{15}H_{18}N_2O_3 \cdot 1.5\ H_2O$ (301.1): C 59.79, H 7.02, N 9.30; found: C 60.24, H 6.84, N 8.94.

*4,5,6,7,8,9,10,11,12,13-Decahydro-19b-hydroxy-1*H*-[1,4]diazacyclopentadecino[2,1-*a*]isoindole-3,15(2*H*,19b*H*)-dione* (**7c**). Following the general photolysis procedure, a mixture of 155 mg (0.40 mmol) of **6c** and 28.0 mg (0.20 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 1:1 was irradiated for 3 h. After extraction with CH_2Cl_2, acidification of the aq. phase, and extraction with AcOEt, 41.3 mg (30%) of **7c** was obtained as a yellowish oil that could not be purified further. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.20–1.32 (*m*, 6 CH_2); 1.48–1.88 (*m*, 2 CH_2); 2.26 (*m*, CH_2); 3.34 (*m*, 3 H, NCH_2, $NHCH_2$); 4.10 (*dd*, $^3J = 13.8$, 4.9, 1 H, NCH_2); 6.02 (*s*, OH); 6.71 (br. *t*, NH); 7.38 (*dd*, $^3J = 7.2$, 1.9, arom. H); 7.52 (*m*, 3 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 24.5 (*t*, CH_2); 24.7 (*t*, CH_2); 25.7 (*t*, CH_2); 25.8 (*t*, CH_2); 26.2 (*t*, CH_2); 26.4 (*t*, CH_2); 26.6 (*t*, CH_2); 27.1 (*t*, CH_2); 35.3 (*t*, CH_2CON); 40.1 (*t*, NCH_2); 48.5 (*t*, $NHCH_2$); 89.8 (*s*, COH); 122.0 (*d*, arom. CH); 122.9 (*d*, arom. CH); 129.7 (*d*, arom. CH); 130.9 (*s*, arom. C_q); 132.5 (*d*, arom. CH); 146.2 (*s*, arom. C_q); 167.8 (*s*, CON); 176.3 (*s*, CONH).

*3,4,7,8,9,10,11,11a-Octahydro-11a-hydroxy-1*H*-[1,4,7]triazacyclotridecino[13,1-*a*]isoindole-2,5,16(6*H*)-trione* (**9a**). Following the general photolysis procedure, a mixture of 150 mg (0.40 mmol) of **8a** and 28.0 mg (0.20 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 10:1 was irradiated for 5 h. After extraction with CH_2Cl_2, acidification of the aq. phase, and extraction with AcOEt, 67.6 mg (51%) of **9a** was obtained after CC (MeOH/CH_2Cl_2 1:7) as a yellowish oil. $\Delta pH_{control} = -0.16$; $\Delta pH_{hv} = +1.30$. IR (CsI): 3680, 3509, 3482, 3245, 2946, 2851, 1746, 1703, 1699, 1422, 1048, 822, 771. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 1.02–1.23 (br. *m*, 3 CH_2); 1.85 (*m*, CH_2COH); 1.92 (*m*, CH_2COH); 2.96 (*m*, 1 H, $NHCH_2$); 3.12 (*m*, 1 H, $NHCH_2$); 3.61 (*m*, $NHCH_2CO$); 3.79 (*m*, 1 H, NCH_2); 4.25 (*s*, NCH_2); 7.21 (*t*, $^3J = 5.6$, NH); 7.47 (*m*, arom. H); 7.48 (*m*, arom. H); 7.59 (*m*, arom. H); 7.66 (*m*, arom. H); 8.27 (*t*, $^3J = 6.3$, NH). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 25.6 (*t*, CH_2); 27.4 (*t*, CH_2); 33.7 (*t*, $NHCH_2CH_2$); 37.1 (*t*, CH_2COH); 39.8 (*t*, $NHCH_2$); 41.6 (*t*, NCH_2); 44.5 (*t*, $NHCH_2CO$); 90.8 (*s*, COH); 122.2 (*d*, arom. CH); 123.0 (*d*, arom. CH); 129.5 (*d*, arom. CH); 130.7 (*s*, arom. C_q); 132.8 (*d*, arom. CH); 148.2 (*s*, arom. C_q); 167.9 (*s*, CON); 169.5 (*s*, NCH_2CO); 169.9 (*s*, $NHCH_2CO$). ESI-MS: 354.2 ([70, $[M+Na]^+$). ESI-

HR-MS (peak-matching, reference ion: PPG 367, resolution > 7000): 354.143 (calc.: 354.1430 (*M*) from the obs. signal for $C_{17}H_{21}N_3O_4Na^+$ ($[M+Na]^+$)).

*3,4,5,6,7,8,9,10,11,12,13,14,15,16,16a-Tetradecahydro-16a-hydroxy-[1,4,7]triazacyclooctadecino[18,1-*a*]isoindole-2,5,21(1*H*)-trione* (**9b**). Following the general photolysis procedure, a mixture of 183 mg (0.40 mmol) of **8b** and 28.0 mg (0.20 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 1:1 was irradiated for 3 h. After extraction with CH_2Cl_2, acidification of the aq. phase, and extraction with AcOEt, 111 mg (69%) of **9b** was obtained after CC ($MeOH/CH_2Cl_2$ 1:10) as a yellow oil. $\Delta pH_{control} = -0.03$; $\Delta pH_{hv} = +1.60$. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 0.80 (*m*, 1 H, CH_2); 1.13 (*m*, 1 H, CH_2); 0.95–1.25 (br. *m*, 6 CH_2); 1.34 (*m*, 1 H, CH_2); 1.37 (*m*, 1 H, CH_2); 1.86 (*m*, 1 H, C*H*$_2$COH); 1.96 (*m*, 1 H, C*H*$_2$COH); 2.90 (*m*, 1 H, NHC*H*$_2$); 3.41 (*m*, 1 H, NHC*H*$_2$); 3.68 (*d*, $^3J = 4.1$, 1 H, NHC*H*$_2$CO); 3.88 (*d*, $^3J = 6.0$, 1 H, NHC*H*$_2$CO); 3.94 (*m*, 1 H, NCH_2); 4.09 (*m*, 1 H, NCH_2); 6.13 (*s*, OH); 7.27 (*dd*, $^3J = 4.1$, 2.8, NH); 7.40 (*dd*, $^3J = 7.2$, 1.2, arom. H); 7.45 (*m*, arom. H); 7.51 (*m*, arom. H); 7.58 (*t* (partly obscured), NH); 7.66 (*d*, $^3J = 7.5$, arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 22.8 (*t*, C*H*$_2$CH$_2$COH); 23.4 (*t*, CH_2); 25.4 (*t*, CH_2); 25.8 (*t*, CH_2); 26.8 (*t*, CH_2); 26.9 (*t*, CH_2); 27.9 (*t*, NHCH$_2$*C*H$_2$); 28.5 (*t*, CH_2); 36.3 (*t*, *C*H$_2$COH); 36.9 (*t*, $NHCH_2$); 41.9 (*t*, NCH_2); 42.0 (*t*, NH*C*H$_2$CO); 90.4 (*s*, COH); 121.8 (*d*, arom. CH); 122.5 (*d*, arom. CH); 128.5 (*d*, arom. CH); 130.3 (*s*, arom. C_q); 131.8 (*d*, arom. CH); 147.6 (*s*, arom. C_q); 167.6 (*s*, CON); 167.7 (*s*, NCH$_2$*C*O); 168.5 (*s*, NHCH$_2$*C*O). ESI-MS: 424.3 (100, $[M+Na]^+$). ESI-HR-MS (peak-matching, reference ion: PPG 389, resolution > 8000): 424.222 ($[M+Na]^+$, $C_{22}H_{31}N_3O_4Na$; calc.: 424.221). Anal. calc. for $C_{22}H_{31}N_3O_4$ (401.2): C 65.81, H 7.78, N 10.47; found: C 64.97, H 7.08, N 10.11.

*4,5,8,9,10,11-Hexahydro-17b-hydroxy-1*H*-[1,4,7]triazacyclotridecino[2,1-*a*]isoindole-3,6,13(2*H*,7*H*,17b*H*)-trione* (**9c**). Following the general photolysis procedure, a mixture of 154 mg (0.40 mmol) of **8c** and 28.0 mg (0.20 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 10:1 was irradiated for 3 h. After extraction with CH_2Cl_2, acidification of the aq. phase, and extraction with AcOEt, 55.7 mg (42%) of **9c** resulted after CC ($MeOH/CH_2Cl_2$ 1:7) as a yellow oil. $\Delta pH_{control} = +0.17$; $\Delta pH_{hv} = +2.20$. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 1.49 (*m*, CH_2); 1.62 (*m*, CH_2); 1.75 (*m*, CH_2); 2.05 (*m*, 1 H, C*H*$_2$CON); 2.15 (*m*, 1 H, C*H*$_2$CON); 3.24 (*dd*, 1 H, NHC*H*$_2$CON); 3.37 (*m*, NCH_2); 3.42 (*dd*, 1 H, NHC*H*$_2$COH); 3.70 (*dd*, 1 H, NHC*H*$_2$COH); 3.85 (*dd*, 1 H, NHC*H*$_2$CON); 6.55 (*s*, OH); 6.79 (*d*, $^3J = 6.6$, NH); 7.44 (*m*, arom. H); 7.52 (*m*, arom. H); 7.52 (*m*, arom. H); 7.61 (*m*, arom. H); 8.51 (*t*, $^3J = 6.0$, NH). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 22.7 (*t*, CH_2); 24.5 (*t*, CH_2); 26.7 (*t*, CH_2); 35.8 (*t*, *C*H$_2$CON); 38.0 (*t*, NCH_2); 43.5 (*t*, NH*C*H$_2$CON); 45.4 (*t*, NH*C*H$_2$COH); 87.8 (*s*, COH); 121.1 (*d*, arom. CH); 122.1 (*d*, arom. CH); 129.1 (*d*, arom. CH); 131.0 (*s*, arom. C_q); 131.7 (*d*, arom. CH); 146.1 (*s*, arom. C_q); 167.5 (*s*, CON); 169.1 (*s*, NHCH$_2$*C*O); 174.0 (*s*, CH$_2$*C*ON). Anal. calc. for $C_{17}H_{21}N_3O_4$ (331.2): C 61.62, H 6.39, N 12.68; found: C 60.87, H 6.42, N 12.70.

*1,4,5,7,8,9,10,11,12,13,14,15,16,22b-Tetradecahydro-22b-hydroxy-1*H*-[1,4,7]triazacyclooctadecino[2,1-*a*]isoindole-3,6,18(2*H*)-trione* (**9d**). Following the general photolysis procedure, a mixture of 183 mg (0.40 mmol) of **8d** and 28.0 mg (0.20 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 5:1 was irradiated for 5 h. After extraction with CH_2Cl_2, acidification of the aq. phase, and extraction with AcOEt, 91.5 mg (57%) of **9d** resulted after CC ($MeOH/CH_2Cl_2$ 1:1) as a yellow oil. $\Delta pH_{control} = -0.12$; $\Delta pH_{hv} = +2.00$. IR (CsI): 3612, 3519, 3475, 3245, 2951, 2845, 1746, 1709, 1695, 1414, 1048, 822, 778. ^{1}H-NMR: (300 MHz, $CDCl_3$/(D_6)DMSO): 0.98–1.07 (*m*, CH_2); 1.17–1.25 (*m*, CH_2, C*H*$_2$CH$_2$CH$_2$CON); 1.49 (*m*, C*H*$_2$CH$_2$CON); 1.60 (*m*, CH_2); 1.78 (*m*, CH_2); 2.10 (*m*, C*H*$_2$CON); 3.18 (*m*, 1 H, NCH_2); 3.34 (*m*, 1 H, NCH_2); 3.42 (*m*, 1 H, NHC*H*$_2$CON); 3.59 (*m*, 1 H, NHC*H*$_2$CON); 3.71 (*m*, 1 H, NHC*H*$_2$COH); 3.74 (*m*, 1 H, NHC*H*$_2$COH); 6.42 (*s*, OH); 7.01 (*d*, $^3J = 5.6$, NH); 7.41 (*m*, arom. H); 7.49 (*m*, arom. H); 7.49 (*m*, arom. H); 7.54 (*t*, $^3J = 5.6$, NH); 7.60 (*m*, arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 24.2 (*t*, *C*H$_2$CH$_2$CH$_2$CON); 25.7 (*t*, CH_2); 26.0 (*t*, *C*H$_2$CH$_2$CON); 26.9 (*t*, CH_2); 27.3 (*t*, CH_2); 27.5 (*t*, CH_2); 32.2 (*t*, CH_2); 34.7 (*t*, *C*H$_2$CON); 38.2 (*t*, NCH_2); 42.4 (*t*, NH*C*H$_2$CON); 43.2 (*t*, NH*C*H$_2$COH); 88.4 (*s*, COH); 121.9 (*d*, arom. CH); 122.0 (*d*, arom. CH); 128.9 (*d*, arom. CH); 131.3 (*d*, arom. CH); 131.7 (*s*, arom. C_q); 145.6 (*s*, arom. C_q); 167.0 (*s*, CON); 168.9 (*s*, NHCH$_2$*C*O); 172.9 (*s*, CH$_2$*C*ON). ESI-MS: 424.3 (100, $[M+Na]^+$). ESI-HR-MS (peak matching, reference ion: PPG 389, resolution > 8000): 424.222 ($[M+Na]^+$, $C_{22}H_{31}N_3O_4Na$; calc.: 424.2213). Anal. calc. for $C_{22}H_{31}N_3O_4$ (401.2): C 65.81, H 7.78, N 10.47; found: C 65.01, H 7.00, N 10.24.

*4,5-Dihydro-13b-hydroxy-5-methyl-1*H*-[1,4,7]triazonino[2,1-*a*]isoindole-3,6,9(2*H*,7*H*,13b*H*)-trione* (**11**). Following the general photolysis procedure, a mixture of 133 mg (0.40 mmol) of **10** and 28.0 mg (0.20 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 4:1 was irradiated for 5 h. Extraction of the aq. phase gave 40.5 mg (35%) of **11** as a yellowish oil. $\Delta pH_{control} = +0.13$; $\Delta pH_{hv} = +2.03$. IR (CsI): 3315, 2951, 2257, 1648, 1561, 1538, 1391, 1295, 1152, 1055, 1014, 893, 724. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 2.85 (*s*, NMe); 3.62 (*m*, MeNC*H*$_2$); 3.85–4.28 (*m*, 4 H, NHCH$_2$COH, NCH_2); 7.34–7.69 (*m*, 4 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 37.2 (*q*, NMe); 42.7 (*t*, NCH_2); 51.4 (*t*, MeN*C*H$_2$); 56.3 (*t*, $NHCH_2$); 84.0 (*s*, COH); 122.8 (*d*, arom. CH); 124.0

(*d*, arom. CH); 129.6 (*d*, arom. CH); 130.2 (*s*, arom. C_q); 130.9 (*d*, arom. CH); 144.3 (*s*, arom. C_q); 165.1 (*s*, CON); 170.7 (*s*, *C*ONMe); 171.8 (*s*, CONH). ESI-MS: 289.3 (80, $[M+H]^+$). ESI-HR-MS (peak matching, reference ion: PPG 331, resolution >7000): 289.315 ($[M+H]^+$, $C_{14}H_{15}N_3O_4$; calc.: 289.3146). Anal. calc. for $C_{14}H_{15}N_3O_4$ (289.1): C 58.13, H 5.23, N 14.53; found: C 58.33, H 5.15, N 14.21.

*1,4,5,7,8,16b-Hexahydro-16b-hydroxy-8-methyl-[1,4,7,10]tetraazacyclododecino[2,1-*a*]isoindole-3,6,9,12(2*H*,10*H*)-tetraone* (**13**). Following the general photolysis procedure, a mixture of 156 mg (0.40 mmol) of **12** and 28.0 mg (0.20 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 4:1 was irradiated for 5 h. Extraction of the aq. phase and subsequent CC (MeOH:CH_2Cl_2 1:7) afforded 42.9 mg (31%) of **13** as a yellowish oil. $\Delta pH_{control} = -0.21$; $\Delta pH_{hv} = +1.85$. IR (CsI): 3448, 2951, 2845, 2256, 1655, 1395, 1131, 699. ^{1}H-NMR (300 MHz, $CDCl_3$/(D_6)DMSO): 2.79 (*s*, NMe); 3.68 (*s*, MeNCH_2); 3.86–4.24 (*m*, 2 NHCH_2COH, NCH_2); 7.4 (*t* (partly obscured), NH); 7.6 (*t* (partly obscured), NH); 7.36–7.71 (*m*, 4 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$/(D_6)DMSO): 37.1 (*q*, Me); 42.0 (*t*, NCH_2); 43.6 (*t*, $NHCH_2$); 51.6 (*t*, MeNCH_2); 56.3 (*t*, NHCH_2COH); 84.1 (*s*, COH); 122.8 (*d*, arom. CH); 123.9 (*d*, arom. CH); 128.3 (*d*, arom. CH); 129.4 (*s*, arom. C_q); 130.8 (*d*, arom. CH); 138.7 (*s*, C_q); 164.9 (*s*, CON); 170.6 (*s*, *C*ONMe); 171.3 (*s*, CONH); 172.8 (*s*, CONH). Anal. calc. for $C_{16}H_{18}N_4O_5 \cdot 1.5\ H_2O$ (346.3): C 55.49, H 5.24, N 16.18; found: C 55.73, H 5.11, N 15.89.

*1,2,3,3a,5,6,9,9a-Octahydro-9a-hydroxypyrrolo[2′,1′:9,10][1,4,7,10]tetraazacyclododecino[2,1-*a*]iso indole-4,7,14,17(8*H*,16*H*)-tetraone* (**15**). Following the general photolysis procedure, a mixture of 167 mg (0.40 mmol) of **14** and 28.0 mg (0.20 mmol) of K_2CO_3 in 20 ml of H_2O/acetone 4:1 was irradiated for 5 h. Extraction of the aq. phase and subsequent CC (MeOH:CH_2Cl_2 1:10) afforded 65.5 mg (44%) of **15** as a yellowish oil. $\Delta pH_{control} = +0.12$; $\Delta pH_{hv} = +2.90$. IR (CsI): 3468, 2934, 1652, 1399, 1312, 1088, 769, 703. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.76–1.93 (*m*, 2 CH_2); 3.65 (*m*, CH_2); 4.01–4.52 (*m*, 2 NHCH_2, NCH_2); 4.74 (*m*, CH); 7.4 (*t* (obscured), NH); 7.7 (*t* (obscured), NH); 7.38–7.78 (*m*, 4 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 26.0 (*t*, NCH_2CH_2); 32.2 (*t*, NCHCH_2); 41.0 (*t*, NCH_2); 42.1 (*t*, NCH_2CH_2); 44.3 (*t*, $NHCH_2$); 54.7 (*t*, NHCH_2COH); 58.2 (*d*, CH); 86.5 (*s*, COH); 123.4 (*d*, arom. CH); 123.7 (*d*, arom. CH); 130.0 (*d*, arom. CH); 132.1 (*s*, arom. C_q); 132.4 (*d*, arom. CH); 143.9 (*s*, arom. C_q); 168.9 (*s*, CON); 170.8 (*s*, CONMe); 171.9 (*s*, CONH); 172.6 (*s*, CONH). Anal. calc. for $C_{18}H_{20}N_4O_5$ (372.4): C 58.06, H 5.41, N 15.05: found: C 57.98, H 5.18, N 14.89.

*2,3,6,7,8a,9,10,11,21,22-Decahydro-20b-hydroxy-1*H*-dipyrrolo[2′,1′:12,13:2′,1′:6,7][1,4,7,10,13]pentazacyclopentadecino[2,1-*a*]isoindole-5,8,13,16,23(14*H*,20b*H*,23a*H*)-pentaone* (**17**). Following the general photolysis procedure, a mixture of 53 mg (0.10 mmol) of **16** and 7.2 mg (0.05 mmol) of K_2CO_3 in 1 ml of H_2O/acetone 1:1 was irradiated for 5 h. Extraction of the aq. phase and purification by CC (MeOH/CH_2Cl_2 1:5) afforded 25.6 mg (53%) of **17** as a colorless oil. ESI-MS: 492.2 (100, $[M+Na]^+$). ESI-HR-MS (peak-matching, reference ion: PPG 505, resolution >7000): 492.186 ($[M+Na]^+$, $C_{23}H_{27}N_5O_6Na$; calc. 492.1859).

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