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Photochemistry

Photodecarboxylation of Adamantane Amino Acids Activated by Phthalimide

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Abstract: Adamantane α-, β-, and δ-amino acids activated by phthalimide (i.e., **3**–**6**) were synthesized, and their photochemical reactivities were investigated. Amino acid derivatives **3**–**6** underwent a photoinduced electron transfer (PET) and decarboxylation reaction sequence, most probably through a triplet excited state. The decarboxylations of the β-amino acid derivatives were succeeded by cyclization reactions that afforded complex polycyclic molecules with potential biological interest. The adamantyl radical that is produced by the photoinduced decarboxylation could be trapped by alkenes or oxygen to deliver adducts or alcohols, respectively. The photodecarboxylation process was shown to be more efficient under acetone sensitization conditions (with quantum yields, Φ = 0.02–0.5) than upon direct excitation, and the reactivity was dependent on the chain length (intramolecular distance) between the electron donor (carboxylate) and acceptor (phthalimide in the triplet excited state) of the derivative. The formation of different radicals, that is, the 1- or 2-adamantyl intermediate, probably does not affect the overall rate of the decarboxylation This current report provides a better understanding of photodecarboxylation and the rational design of molecular systems to undergo photoinduced decarboxylation and cyclization reactions.

Introduction

Photochemically induced decarboxylation reactions have been extensively investigated[1–3] because of their importance in organic synthesis,[4,5] the development of photocages,[6,7] and materials science[8] as well as the fact that some nonsteroidal anti-inflamatory drugs can induce a photoallergic response as a result of undergoing a photodecarboxylation process.[9–12] Photocatalytic decarboxylation reactions have recently experienced a revival in organic synthesis,[13–18] and significant progress has been made to elucidate the photodecarboxylation reaction mechanism that leads to anionic species.[19–28]

Photodecarboxylation can be initiated by the phthalimide chromophore in the triplet excited state, which acts as the electron acceptor in the photoinduced electron transfer (PET) reaction.[29,30] The PET-promoted decarboxylation by phthalimides has been used in macrocyclizations,[31] the cyclization of peptides,[32,33] photodecaging strategies,[34] and the enantioselective synthesis of benzodiazepines.[35] Moreover, photoinduced decarboxylation has been applied to the addition of acetates,[36,37] benzyl groups,[38–40] and α-amino acids to phthalimide[41] as well as to the formation of cyclic aryl ethers,[42] the process which was conducted in microflow reactors.[43] Phthalimide in the triplet excited state can also promote the elimination of silyl groups,[44] and – from a thermodynamic point of view – initiate all PET reactions in which the donor oxidation potential is <1.6 V versus saturated calomel electrode (SCE).[30,45]

We have recently discovered an efficient approach for the phthalimide-promoted photodecarboxylative radical addition to alkenes.[46] First, an unnatural adamantane γ-amino acid is activated by phthalimide. In its triplet excited state, the phthalimide of **1** is reduced to give a radical anion, whereupon the carboxylate group underwent an oxidation and the irreversible elimination of CO_2 (Scheme 1). The resulting radical could then be trapped by an electron-deficient alkene to deliver adduct **2**.[46]

Herein, we describe a more general investigation of the PET-promoted photodecarboxylation of a series of unnatural amino acids that are activated by phthalimides (i.e., **3**–**6**). All of the unnatural amino acids under investigation are adamantane derivatives, which are characterized by a rigid geometry and fixed length between the electron-donor (i.e., the carboxylate) and electron-acceptor groups (i.e., phthalimide). Specifically, phthalimide **3** is an α-amino acid derivative, where as **4** and **5** are derivatives of a β-amino acid. Phthalimides **6-E** and **6-Z** are δ-amino acid derivatives. The investigation was conducted to determine how the length between the electron donor and acceptor influences the decarboxylation efficiency. Moreover, derivatives **4** and **5** were strategically designed to investigate whether the rate of CO_2 elimination affects the overall reaction efficiency. The elimination of CO_2, in these two examples, should deliver two different adamantyl radicals. However, there

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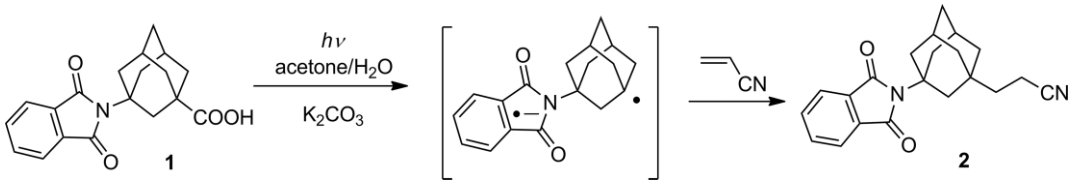
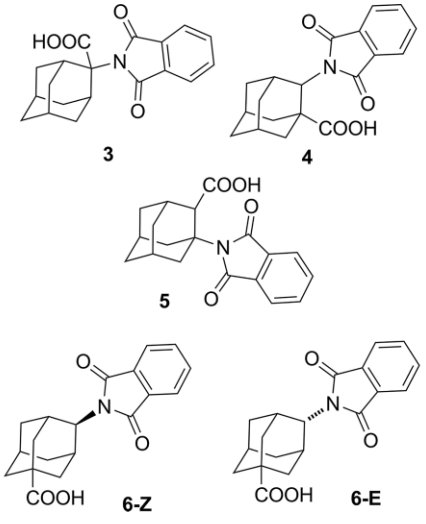


Scheme 1. Photochemical reaction of **1** in the presence of acrylonitrile.

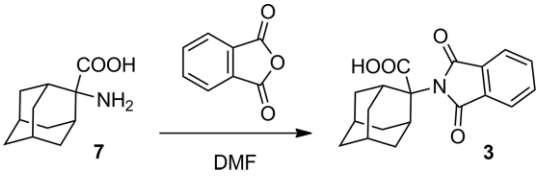
is no difference in the distances between the electron donor and acceptor. Preparative irradiations were also carried out under different conditions along with the isolation of the photoproducts. The photoreactions either delivered simple decarboxylation products or more complex polycyclic molecules, which are particularly interesting because of their anticipated biological activity.[47–51]



Results and Discussion

Synthesis

Phthalimide derivatives **3**–**6** were prepared in moderate to good yields by a condensation reaction between the corresponding amino acid and phthalic anhydride and using a modification[46] of a published procedure.[52,53] α-Amino acid **7**,[54] which was synthesized according to a known procedure[55] by starting from 2-adamantanone through a hydantoin derivative,[54] was transformed into the corresponding phthalimide **3** in moderate yield (Scheme 2).

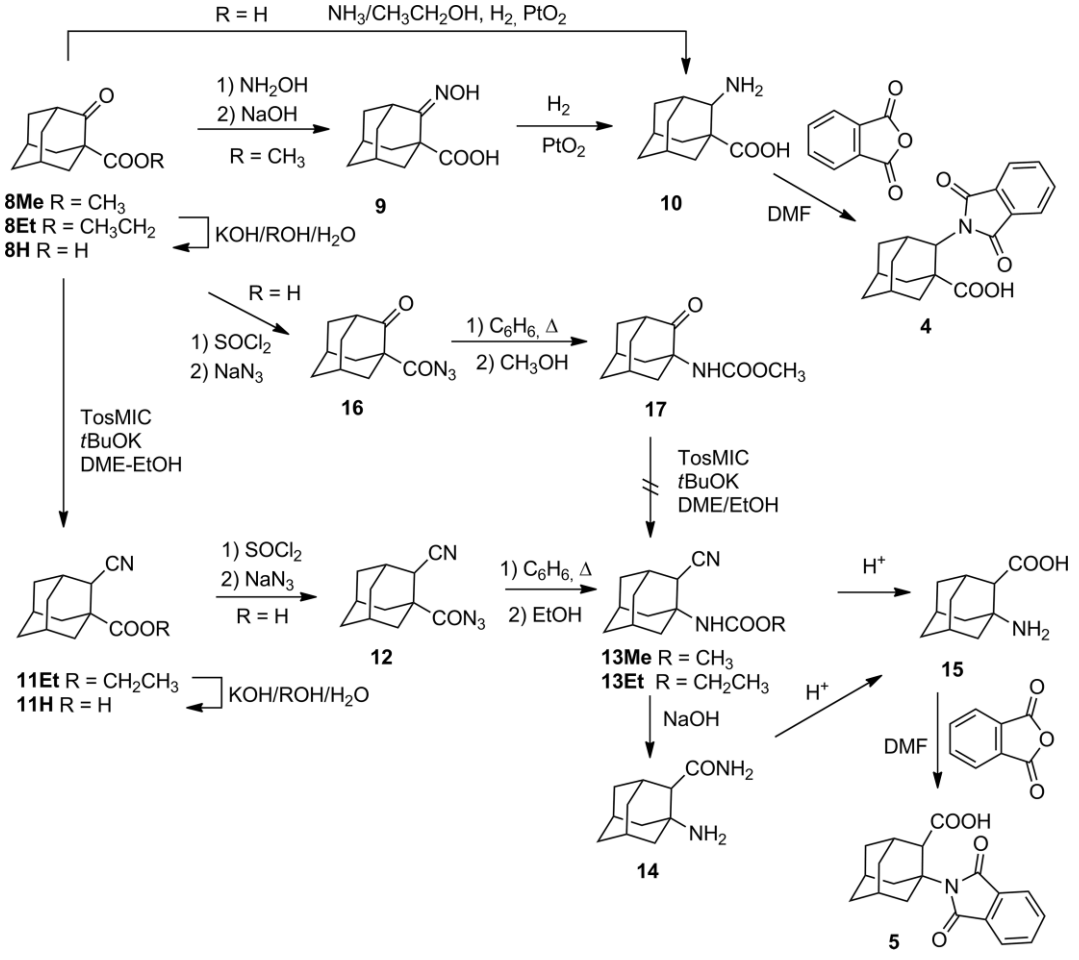


Scheme 2. Synthesis of phthalimide derivative of α-adamantane amino acid (DMF = *N*,*N*-dimethylformamide).

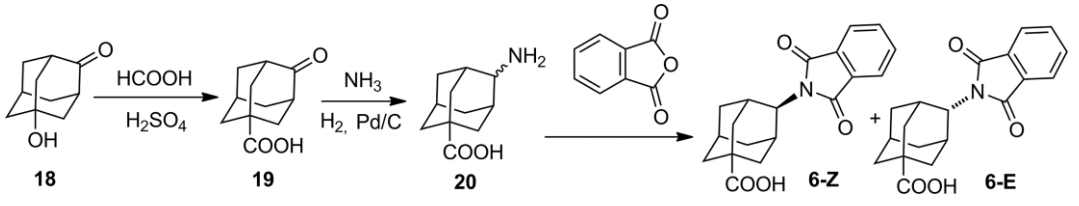
The syntheses of the adamantane β-amino acids activated by phthalimide (i.e., **4** and **5**) are shown in Scheme 3. β-Amino acids **10**[56] and **15**[57] were synthesized from known keto esters or ketoacid **8**[58–60] according to a modification[61] of a known procedure that took place in three steps[62] from homoadamantanone. Keto ester **8Me** was converted into an oxime that was hydrolyzed into oxime acid **9**.[59] The hydrogenation of **9** over PtO_2 afforded amino acid **10** in high yield. Alternatively, amino acid **10** was obtained by a reductive amination of ketoacid **8H** (Scheme 3).

The first step in the preparation of β-amino acid **15** from keto ester **8** involved a reaction with *p*-toluenesulfonylmethyl isocyanide (TosMIC), according to a modification of the known procedure,[63] to afford cyanide ester **11Et**[59] (Scheme 3). The hydrolysis into acid **11H**[60] followed by a reaction with $SOCl_2$ and NaN_3 afforded carbonyl azide **12**. The rearrangement of **12** by following a modification of a known procedure[64] gave an isocyanate, which was not isolated but instead treated with EtOH to afford carbamate **13Et** (87 % yield in four steps, starting from **11H**). We also attempted to prepare carbamate **13Me** by using another strategy, in which acid **8H** was first converted into carbonyl azide **16**. This azide then underwent the rearrangement into its corresponding isocyanate, and a further reaction with CH_3OH afforded carbamate **17** in good yields. However, the treatment of ketone **17** with TosMIC gave a poor yield of the desired carbamate **13Me**. Nevertheless, base hydrolysis of either carbamate **13Et** or **13Me** afforded amidoamine **14**, and subsequent acid hydrolysis gave the desired amino acid **15** in good yield along with a small amount of the hydroxy acid. Amino acids **10** and **15** were then treated with phthalic anhydride to yield the corresponding phthalimide derivatives **4** and **5**, respectively.

The synthesis of the diastereomeric phthalimide derivatives **6** started from hydroxy ketone **18**, which was obtained from the oxidation of adamantanone by chromic acid.[65] Alcohol **18** was converted into ketoacid **19**[66] by using a Koch–Haaf reaction, and ketone **19** was then transformed through a reductive amination into a diastereomeric mixture of amino acids **20**,[66] which were not separated. A condensation reaction with phthalic anhydride gave a mixture of diastereomers **6**, which were then separated and characterized (Scheme 4).



Scheme 3. Synthesis of phthalimide derivatives of β-adamantane amino acids (i.e., **4** and **5**; DME = 1,2-dimethoxyethane).



Scheme 4. Synthesis of phthalimide derivatives of δ-adamantane amino acid (i.e., **6-Z** and **6-E**).

Photochemical Reactivity

On the basis of literature precedent,[46,72] the excitation of phthalimides **3**–**6** in the presence of a base to deprotonate the carboxylic group is anticipated to lead to an irreversible PET decarboxylation and deliver simple decarboxylation or cyclization products. To probe the reactivity of phthalimides **3**–**6** towards decarboxylation, these compounds were irradiated at 300 nm in the presence of 0.5 equiv. K_2CO_3 in either CH_3CN/H_2O (2:1) or acetone/H_2O (2:1), where acetone acts as a triplet sensitizer. The irradiation of **3** and **4** was performed in both the presence and absence of base. The results of these experiments are summarized in Table 1. Regardless of the solvent in which the irradiation was conducted, the addition of base increased the efficiency of the photoreaction, as observed by the conversions reached over the same irradiation times. This finding is in line with the better electron-donating ability of carboxylates (10-undecenoic acid in CH_3CN in the presence of 0.5 equiv. of benzyltrimethylammonium hydroxide, irreversible process $E_{ox} \approx$ 1.38 V vs. Ag/AgCl[67]) versus carboxylic acids (10-undecenoic acid in CH_3CN, $E_{ox} \approx$ 1.85 V vs. Ag/AgCl[67]).[68,69] Moreover, the similar reaction efficiency upon sensitized excitation in acetone versus CH_3CN indicates that the decarboxylation takes place through the triplet excited state. Namely, the triplet energy of acetone (E_T = 332 kJ mol^{-1})[70] is higher than that of the *N*-alkylphthalimides (E_T = 297 kJ mol^{-1})[70] to allow for an exergonic energy transfer.

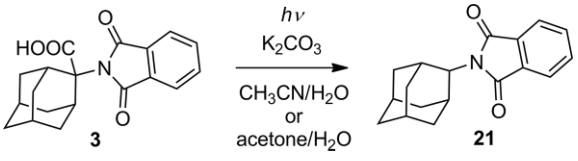
To isolate the photoproducts, preparative irradiation reactions of **3**–**6** were conducted in CH_3CN/H_2O (2:1) in the pres-

Table 1. Irradiation conditions, conversions, and product yields upon photolysis of phthalimides **3**–**6**.[a]

	Solvent, conditions	Time of irradiation	Conv. [%][b]	Products [% yield]
3	CH_3CN/H_2O, 2:1;	5 min	16	**21** (100)[b]
3	CH_3CN/H_2O, 2:1; no K_2CO_3	5 min	4	**21** (100)[b]
3	acetone/H_2O, 2:1	5 min	33	**21** (100)[b]
3	acetone/H_2O, 2:1; no K_2CO_3	5 min	7	**21** (100)[b]
4	CH_3CN/H_2O, 2:1;	5 min	82	**21** (20), **22** (80)[b]
4	CH_3CN/H_2O, 2:1; no K_2CO_3	5 min	17	**21** (76), **22** (24)[b]
4	acetone/H_2O, 2:1;	5 min	68	**21** (25), **22** (75)[b]
4	acetone/H_2O, 2:1; no K_2CO_3	5 min	8	**21** (38), **22** (62)[b]
5	CH_3CN/H_2O, 2:1	5 min	71	**23** (67), **24** (17), **25** (16)[b]
5	acetone/H_2O, 2:1	5 min	65	**23** (71), **24** (14), **25** (15)[b]
6-E	CH_3CN/H_2O, 2:1	1.5 min	2	**21** (100)[b,c]
6-E	acetone/H_2O, 2:1	3 min	2	**21** (100)[b,c]
6-Z	CH_3CN/H_2O, 2:1	1.5 min	18	**21** (100)[c]
6-Z	acetone/H_2O, 2:1	3 min	10	**21** (100)[c]

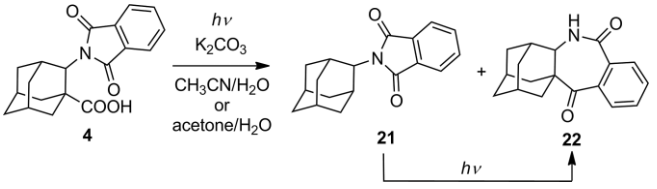
[a] The irradiation reactions were conducted by using a lamp with a 300 nm output. The concentration of the phthalimide solution was 1 mM (5 mg/15 mL), whereas that of the K_2CO_3 solution was 0.5 mM. The solutions were purged with N_2 prior to irradiation. [b] The percent conversion was determined by ^1H NMR spectroscopic analysis of the crude irradiation mixture. [c] The product ratio was determined by HPLC analysis.

ence of 0.5 equiv. K_2CO_3. Phthalimide **3** was irradiated until a high conversion was reached to cleanly afford phthalimide **21** (Scheme 5). Product **21**, which contains the phthalimide chromophore, can then undergo secondary photochemical reactions. However, intramolecular H-abstractions by the phthalimide group generally proceed with very low quantum efficiency as a result of inefficient formation of the reactive triplet state by intersystem crossing (ISC).[71] Therefore, in CH_3CN/H_2O, a much longer irradiation time is needed to transform **21** into its photochemical products.



Scheme 5. Photochemical reaction of **3**.

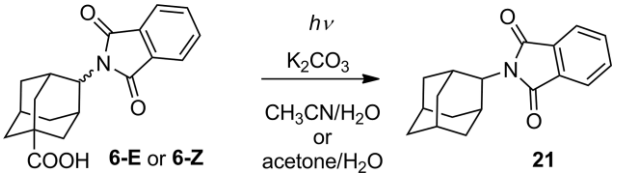
The irradiation of phthalimide **4** gave the simple decarboxylation product **21** and cyclic product **22** in a ratio of 1:3. However, the cyclic product could, in principle, be formed from **21** by a photochemical reaction (Scheme 6).[72] To investigate if **22** is a product of the decarboxylative cyclization of **4** or an H-abstraction of **21**, the composition of the irradiation mixture was analyzed during the process (see Supporting Information, Figure S1). Because **22** is formed as the major product after a short irradiation time (1 min) and the relative ratio of **22** to **21** does not change over the first few minutes of irradiation, we concluded that **22** is formed directly from **4**.



Scheme 6. Photochemical reaction of **4**.

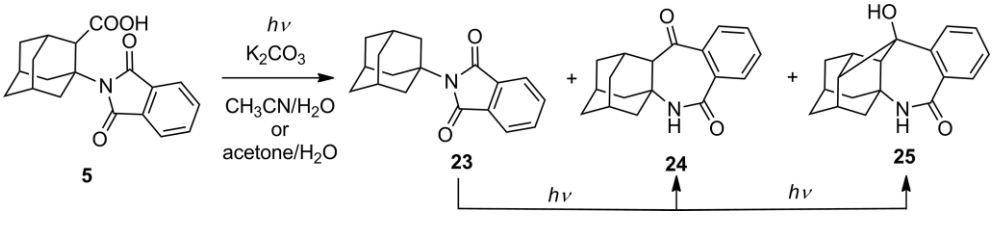
The irradiation of phthalimide **5** afforded the three products **23**–**25** (Scheme 7), the ratio of which depended on the irradiation time. Because **23** could undergo a photochemical intramolecular H-abstraction to give **24** and **25**,[73,74] it was important to investigate whether **24** was formed from the decarboxylative cyclization of **5** or from **23** (Scheme 7). Thus, the composition of the irradiation mixture was analyzed during the process (see Supporting Information, Figure S2). Although **24** is not the major product, its formation at an early irradiation time suggests that it is formed directly from **5**. Moreover, after longer irradiation times when the conversion of **5** was almost complete, the concentration of **23** increased but the content of **24** decreased as a result of a secondary photochemical reaction, that is, the transformation of **24** into **25**. This observed dependence of the distribution of photoproducts on the irradiation time can be explained by a more efficient photodecarboxylation process followed by H-abstraction, which is in line with literature precedent[71] and our quantum yield measurements (see below).

Similar to the photochemistry of **3**, the photolysis of either **6-E** or **6-Z** proceeded cleanly to give only one product, phthalimide **21** (Scheme 8). The reaction of **6-E**, however, was less efficient than that of **6-Z** (see below).



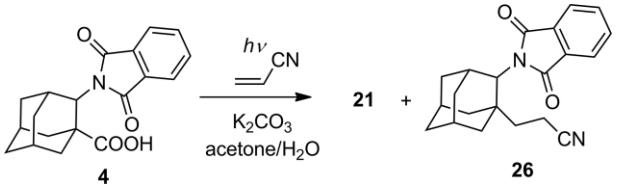
Scheme 8. Photochemical reaction of **6**.

The irradiation of **1** in the presence of an electron-deficient alkene gave adduct **2** as a result of trapping the radical formed during the decarboxylation. Similarly, the irradiation of **3** and **4**



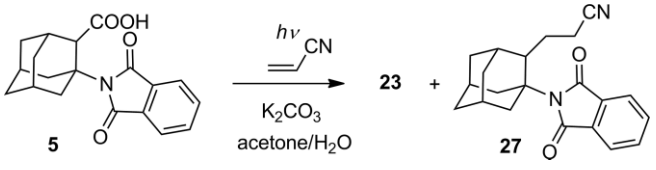
Scheme 7. Photochemical reaction of **5**.

in the presence of acrylonitrile was anticipated to form the radical-trapping products. Indeed, the irradiation of **4** gave adduct **26** as the major product (41 %) along with a small amount of the simple decarboxylation derivative **21** (Scheme 9). Product **22**, the result of a cyclization reaction, was not isolated.



Scheme 9. Photochemical reaction of **4** in the presence of acrylonitrile.

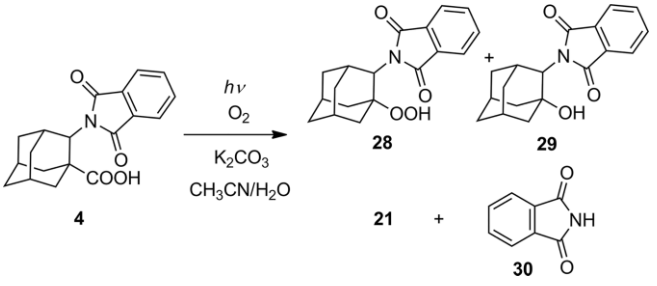
The photochemical reaction of **5** with acrylonitrile gave decarboxylation product **23** and adduct **27** in a ratio of 1:1 (Scheme 10). Similar to the photolysis of **4** in the presence of acrylonitrile, the cyclization products **24** and **25** were not isolated. It is interesting, however, that the photolysis of **5** (compared with **4**) gives a higher amount of the decarboxylation product than the acrylonitrile adduct. With theoretical[75] and experimental data[76] supporting the higher stability of the 1-adamantyl compared with the 2-adamantyl radical, the difference in the product distributions from the reactions of **4** and **5** can be explained by the lower selectivity of the more reactive 2-adamantyl radical.



Scheme 10. Photochemical reaction of **5** in the presence of acrylonitrile.

The similar efficiencies of the photochemical reactions of **3**–**6** upon irradiation in acetone/H_2O or CH_3CN/H_2O suggests that the photoreactions take place through the triplet excited state. To verify if the formation of the products stems from a triplet pathway, the irradiation of **4** was conducted in the presence of O_2, a ubiquitous triplet quencher. The preparative irradiation in the presence of O_2 gave the simple decarboxylation product **21**, oxidation products – peroxide **28** and alcohol **29**, and the cleavage product – phthalimide **30**, which were isolated and characterized (Scheme 11). Because of the instability of the peroxide, it decomposed upon chromatographic separation to give alcohol **29**. Oxidation products **28** and **29** were formed by the O_2 trapping of the radical that was produced during the decarboxylation process, analogous to the formation of radical-trapping products **26** and **27**.

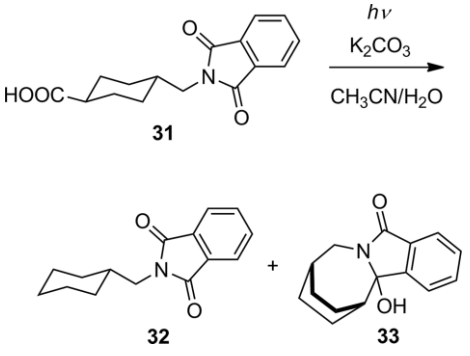
The irradiation of **4** was performed in N_2-purged, air-saturated, and O_2-purged solutions. Contrary to a previous report regarding phthalimide **1**,[46] the presence of O_2 quenched the decarboxylation reaction of **4**. This dependence of the photoconversion on O_2 concentration, which was demonstrated by experiments conducted in N_2-purged, air-saturated, and O_2-purged solutions, allowed for an estimation of the Stern–Volmer quenching constant, $K_{SV} = 774 \pm 2\ M^{-1}$ (see Supporting Information, Figure S3). Assuming that the quenching takes place at a



Scheme 11. Photochemical reaction of **4** in the presence of oxygen.

rate of $k_q = 2 \times 10^9\ M^{-1}\ s^{-1}$,[77] this experiment suggests that the reactive excited triplet state has a lifetime $\tau \approx 400$ ns. Transient absorption measurements should reveal the properties and reactivity of the triplet state involved (not within the scope of this manuscript).

To compare photochemical reactivities of **3**–**6** and investigate the influence of the molecular structure on the efficiency of the photodecarboxylation, quantum yield measurements of the photochemical reactions in CH_3CN/H_2O and acetone/H_2O were conducted. The measurements were performed in the presence of a secondary actinometer (i.e., not one of the standardized actinometers listed in ref.[78]), the photolysis of phthalimide **31** (Scheme 12) gave **32** and **33** ($\Phi_R = 0.3$).[79] The results are compiled in Table 2.



Scheme 12. Photochemical reaction used as a secondary actinometer.

Several general trends can be seen from the measured quantum yields of the photoreactions. Phthalimides undergo more efficient reactions upon sensitized excitation by acetone than upon direct excitation of the phthalimide chromophore at 254 or 300 nm. The difference in the efficiency is most pronounced for α-amino acid phthalimide derivative **3** (a 15 to 35 times more efficient reaction under sensitization conditions). For the β- and δ-amino acid phthalimide derivatives, the sensitized reactions are approximately two times more efficient or have a similar efficiency as those that undergo direct excitation of the phthalimide. These results suggest that the structure of the adamantane skeleton (although not a chromophore) affects the efficiency of intersystem crossing (ISC) by making it less efficient for the α-amino acid compared with that of the β- and δ-derivatives. Moreover, a different efficiency was observed for phthalimide derivatives **3** and **4** upon direct irradiation at 254 or 300 nm, which may be the result of the reaction taking place from a higher triplet excited state, the population of which de-

Table 2. Quantum efficiency for photoreaction (Φ_R) of **1** and **3**–**6**.

	Φ_R (acetone/H_2O)[a]	Φ_R (CH_3CN/H_2O)[b]	Φ_R (CH_3CN/H_2O)[c]
1	0.50[d]	0.11[d]	–
	0.47 ± 0.02[e]		
3	0.35 ± 0.03[e]	0.026 ± 0.002[f]	0.010 ± 0.002[f]
	0.35 ± 0.02[f]		
4	0.51 ± 0.05[e]	0.41 ± 0.03[f]	0.25 ± 0.01[f]
	0.44 ± 0.02[f]		
5	0.50 ± 0.04[e]	0.21 ± 0.02[f]	0.21 ± 0.03[f]
	0.44 ± 0.02[f]		
6-E	0.023 ± 0.002[e]	0.09 ± 0.01[e]	0.015 ± 0.001[e]
6-Z	0.15 ± 0.01[e]	0.19 ± 0.01[e]	0.11 ± 0.01[e]

[a] Quantum efficiency was measured in acetone/H_2O (2:1) in the presence of K_2CO_3 (0.5 equiv.) after irradiation at 300 nm by averaging the values obtained from three measurements. A secondary actinometer was used, namely, the photolysis of **31** in CH_3CN/H_2O (3:1) to give **32** and **33** (Φ_R = 0.30 ± 0.03).[79] [b] Quantum efficiency was measured in CH_3CN/H_2O (2:1) in the presence of K_2CO_3 (0.5 equiv.) upon irradiation at 254 nm by using a secondary actinometer, namely, the photolysis of **31** in CH_3CN/H_2O (3:1; Φ_R = 0.30). The errors correspond to the values obtained from three independent measurements. The quantum yield for the decomposition of **31** was taken from the literature and measured by using three primary actinometers, namely, potassium ferrioxalate (Φ_R = 1.25),[70,80] KI/KIO_3 (Φ_R = 0.74),[70,81] and valerophenone (Φ_R = 0.65 ± 0.03).[70,78] [c] Quantum efficiency was measured in CH_3CN/H_2O (2:1) in the presence of K_2CO_3 (0.5 equiv.) after irradiation at 300 nm by averaging the values obtained from three measurements and using a secondary actinometer, namely, the photolysis of **31** in CH_3CN/H_2O (3:1; Φ_R = 0.30). [d] Value was taken from the literature. See ref.[46]. [e] The analysis of the irradiated solution was performed by NMR spectroscopy. [f] The analysis of the irradiated solution was performed by HPLC.

pends on the excitation wavelength. Photochemical reactions of phthalimides from higher excited triplet states have been demonstrated.[74,77,82] However, it is unusual that upon excitation to S_2, the internal conversion into S_1 competes with the ISC. Such a pathway is plausible if the rate of the ISC is very fast ($k_{ISC} > 10^{11}$ s^{-1}), which is known to be the case for examples that obey El Sayed's rules and possible with carbonyl chromophores that have n,π* and π,π* excited states.[83]

A comparison of the efficiency of decarboxylation upon sensitization for phthalimides **4** and **5** (both β-amino acid derivatives), in which the distances between the electron donor (carboxylate) and the electron acceptor (phthalimide) are the same, does not reveal significant differences. The reaction of **4**, however, proceeds through 1-adamantyl radical **34**, whereas **5** progresses through 2-adamantyl radical **35** as an intermediate (Figure 1). The formation of these anticipated intermediates indicates that that irreversible decarboxylation step that affords the corresponding radical is not the slowest step in the process and suggests that the intramolecular PET process is the slowest step.

The most interesting feature of this investigated series of compounds is how the reaction efficiency is influenced by the distance between the electron donor and acceptor (for the plots of the efficiency dependence on the molecular distances, see Figures S4 and S5 in the Supporting Information). Thus, upon sensitization, δ-derivatives undergo a less efficent reaction than α-, β-, or γ-derivatives. Moreover, diastereomer **6-Z** undergoes approximately a 10 times more efficent reaction than that of the **6-E** isomer. Because both diastereomers give the same product and proceed through 1-adamantyl radical intermediate **36-Z** or **36-E**, the observed differences in the efficiency of the reactions are most likely from the different rates of the PET between the carboxylate and the phthalimide rather than the different rates of CO_2 elimination. Furthermore, the difference in the rates of the PET step for **6-E** and **6-Z** indicates that the electron transfer does not take place through the adamantane sigma bonds but instead through space, being faster for the Z isomer in which the phthalimide and carboxylate are closer. The result may also be related to the previous report by Griesbeck et al.,[84] in which a templating effect of K^+ between the carboxylate and the phthalimide was suggested. Namely, K^+ acts as an anchor and stabilizes the optimal geometry between the donor and acceptor.[84,85] Such a structure is not possible for the **6-E** isomer.

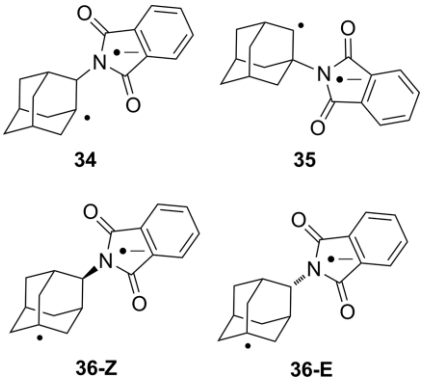


Figure 1. Anticipated radical intermediates in the photodecarboxylation of β-amino acid derivatives.

Conclusions

Unnatural adamantane α-, β-, and δ-amino acids activated by phthalimide (i.e., **3**–**6**) were synthesized. All derivatives **3**–**6** underwent a PET and decarboxylation, which was accompanied by a cyclization reaction in the case of the β-amino acid derivatives. The adamantyl radical that is formed by decarboxylation can be trapped by acrylonitrile or oxygen to give adducts or peroxides, respectively. The efficiency of the photodecarboxylation reaction is generally higher under acetone-sensitized conditions than upon direct excitation, which suggests that the photoreaction takes place through a triplet excited state. The efficiency of the photodecarboxylation is higher for α- and β- than for δ-derivatives, which indicates that the rate-determining step is probably the PET between the carboxylate and phthalimide moieties. This observation has important implications in the design of molecular systems for the synthesis of polycyclic and macrocyclic molecules by using a photodecarboxylative cyclization strategy.

Experimental Section

General Methods: The ^1H and ^{13}C NMR spectroscopic data were recorded at room temperature at either 300 or 600 MHz. TMS was used as an internal reference, and the chemical shifts were reported in ppm. Melting points were measured with a Mikroheiztisch apparatus. IR spectra were recorded with a spectrophotometer by using

KBr pellets for the samples. The frequencies of the characteristic band are reported in cm^{-1}. HRMS data were obtained on a MALDI TOF/TOF instrument. Irradiation experiments were performed in a reactor that was equipped with 11 lamps and provided a 300 nm output or a reactor that was equipped with 8 lamps at 254 or 300 nm (one lamp: 8 W). During the irradiation process, the irradiated solutions were continuously purged with Ar and cooled by a tap water finger condenser. Solvents for the irradiation processes were of HPLC purity. Chemicals were purchased from the usual commercial sources and used as received. Solvents for chromatographic separations were used as is from the supplier (p.a. or HPLC grade) or purified by distillation (CH_2Cl_2). Experimental procedures for the preparation of known intermediates are given in the Supporting Information.

2-Cyanoadamantane-1-carboxazide (12): A round-bottomed flask (250 mL) was charged with **11H** (3.05 g, 14.9 mmol) and $SOCl_2$ (50 mL), and the resulting mixture was heated at reflux for 1 h. The $SOCl_2$ was removed under reduced pressure, and the residue was dissolved in acetone (30 mL) and then cooled to 0 °C. A solution of NaN_3 (1.49 g, 22.9 mmol) in acetone (25 mL) and H_2O (15 mL) was added dropwise to the reaction mixture, as the temperature was kept at 0 °C. After the addition was complete, the mixture continued to stir at 0 °C for 30 min. H_2O (50 mL) was added, and the mixture was extracted with Et_2O (4 × 75 mL). The combine organic extracts were washed with a saturated aqueous $NaHCO_3$ solution (50 mL) and brine (25 mL), dried with anhydrous $MgSO_4$, and then filtered. The solvent was removed on a rotary evaporator to afford pure **12** (3.33 g, 97 %) as colorless crystals; m.p. 70–76 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.16 (br. s, 1 H), 2.32 (br. s, 1 H), 2.15 (ddd, *J* = 13.3, 2.5, 2.1 Hz, 1 H), 2.05–2.13 (m, 3 H), 2.02 (ddd, *J* = 13.3, 2.5, 2.1 Hz, 1 H), 1.93 (ddd, *J* = 12.6, 2.8, 2.1 Hz, 1 H), 1.88 (ddd, *J* = 13.3, 2.8, 2.1 Hz, 1 H), 1.79 (ddd, *J* = 12.6, 2.8, 2.1 Hz, 1 H), 1.69–1.77 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 182.3 (s), 120.3 (s), 44.8 (s), 39.5 (t), 38.5 (d), 35.7 (t), 35.6 (t), 34.1 (t), 32.2 (t), 31.1 (d), 27.0 (d), 26.8 (d) ppm. IR (KBr): $\tilde{\nu}$ = 2934, 2862, 2253, 2142, 1699, 1629, 1452, 1199, 988, 703 cm^{-1}. MS (ESI+): *m*/*z* = 203.

Ethyl 2-Cyanoadamantane-1-carbamate (13Et): A round-bottomed flask (100 mL) was charged with **12** (3.33 g, 14.5 mmol) and anhydrous benzene (50 mL), and the resulting mixture was heated at reflux for 2 h. Anhydrous EtOH (50 mL) was added, and the heating was continued over 1 d. The solvent was removed on a rotary evaporator, and the residue was purified by chromatography on a silica gel column (Et_2O/hexane, 3:7) to afford pure **13Et** (3.23 g, 88 % over two steps from **11H**) as a colorless solid; m.p. 113–116 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.73 (br. s, 1 H), 4.08 (q, *J* = 7.1 Hz, 2 H), 3.90 (br. s, 1 H), 2.64 (d, *J* = 12.2 Hz, 1 H), 2.36 (br. s, 1 H), 2.04–2.20 (m, 3 H), 2.01 (ddd, *J* = 12.2, 1.5, 2.7 Hz, 1 H), 1.59–1.82 (m, 7 H), 1.24 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.7 (s), 120.5 (s), 60.8 (t), 51.0 (s), 40.6 (d), 40.5 (t), 39.3 (t), 36.0 (t), 35.3 (t), 32.4 (t), 32.2 (d), 28.7 (d), 28.5 (d), 14.6 (q) ppm. IR (KBr): $\tilde{\nu}$ = 3347, 2997, 2983, 2932, 2919, 2859, 2241, 1705, 1524, 1455, 1281, 1234, 1061, 782, 600 cm^{-1}. MS (ESI+): *m*/*z* = 249.

1-Aminoadamantane-2-carboxamide (14): A round-bottomed flask (250 mL) was charged with **13** (720 mg, 2.90 mmol), a saturated solution of NaOH (75 mL), and EtOH (25 mL), and the resulting mixture was heated at 110–115 °C (oil bath) for 72 h. After cooling, H_2O (50 mL) was added, and the mixture was extracted with Et_2O (4 × 100 mL) and then CH_2Cl_2 (4 × 100 mL). The combined extracts were dried with anhydrous $MgSO_4$ and filtered, and the solvent was removed on a rotary evaporator to afford pure **14** (238 mg, 42 %) as a colorless solid; m.p. 186–190 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.06 (br. s, 1 H), 5.56 (br. s, 1 H), 2.66 (br. s, 1 H), 2.26 (br. s, 1 H), 2.18 (dd, *J* = 12.2, 1.8 Hz, 1 H), 2.05 (dd, *J* = 2.6, 3.0 Hz, 2 H), 1.56–1.86 (m, 7 H), 1.52 (ddd, *J* = 13.0, 1.6, 1.3 Hz, 1 H), 1.39 (br. s, 2 H), 1.32 (ddd, *J* = 12.2, 2.6, 1.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.2 (s), 54.2 (d), 51.2 (t), 49.6 (s), 40.6 (t), 37.4 (t), 36.3 (t), 32.4 (t), 31.3 (d), 30.2 (d), 29.0 (d) ppm. IR (KBr): $\tilde{\nu}$ = 3344, 3249, 2931, 2909, 2849, 1649, 1588, 1561, 1451, 1391, 1099, 926, 743 cm^{-1}. MS (ESI+): *m*/*z* = 195.

Methyl 2-Oxoadamantane-1-carbamate (17): Azide **16** (1.49 g, 6.80 mmol) was dissolved in benzene (35 mL), and the resulting mixture was heated at reflux for 3.5 h. Anhydrous CH_3OH (15 mL) was added, and the heating was continued overnight. The solvent was removed on a rotary evaporator, and the residue was purified by chromatography on a silica gel column (EtOAc/hexane, 1:1) to afford pure **17** (1.09 g, 70 %) as a colorless solid; m.p. 107–110 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.22 (br. s, 1 H), 3.62 (s, 3 H), 2.99 (d, *J* = 11.0 Hz, 1 H), 2.75 (br. s, 1 H), 2.21 (br. s, 2 H), 2.05 (ddd, *J* = 12.9, 2.9, 2.8 Hz, 2 H), 1.98 (d, *J* = 12.9 Hz, 2 H), 1.91 (d, *J* = 12.8 Hz, 1 H), 1.85 (dd, *J* = 12.8, 1.6 Hz, 1 H), 1.79 (d, *J* = 12.9 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 211.8 (s), 155.2 (s), 61.7 (s), 51.6 (q), 46.0 (d), 43.2 (t), 39.3 (t, 2 C), 34.7 (t, 2 C), 29.0 (d, 2 C) ppm. IR (KBr): $\tilde{\nu}$ = 3398, 2930, 2858, 1722, 1502, 1216, 1055, 777, 530 cm^{-1}. MS (ESI+): *m*/*z* = 246.

Methyl 2-Cyanoadamantane-1-carbamate (13Me): A round-bottomed flask (100 mL) under N_2 was charged with **17** (225 mg, 1.01 mmol), TosMIC (253 mg, 1.30 mmol), DME (6 mL), and anhydrous EtOH (0.11 mL, 1.88 mmol). The reaction mixture was cooled to 0 °C by using an ice bath, and *t*BuOK (350 mg, 3.12 mmol) was added in two portions over 10 min. The reaction mixture was stirred for 1 h, whereupon it was allowed to warm to room temp. The stirring was continued overnight, as the mixture was heated to 45 °C. After cooling to room temp., Et_2O (20 mL) was added, and the reaction mixture was filtered through a sintered glass funnel. The filter cake was washed with Et_2O (80 mL), and the solvent of the combined filtrates was removed on a rotary evaporator. The residue was purified by chromatography on a silica gel column (Et_2O/hexane, 1:1) to afford pure **13Me** (6 mg, 3 %) as colorless crystals; m.p. 155–158 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.88 (br. s, 1 H), 3.89 (br. s, 1 H), 3.64 (s, 3 H), 2.63 (d, *J* = 11.7 Hz, 1 H), 2.36 (dd, *J* = 2.6, 2.8 Hz, 1 H), 2.15 (dd, *J* = 2.6, 2.8 Hz, 1 H), 2.11 (dd, *J* = 2.6, 2.8 Hz, 1 H), 2.09 (ddd, *J* = 13.0, 2.3, 2.1 Hz, 1 H), 2.02 (ddd, *J* = 12.2, 2.8, 1.6 Hz, 1 H), 1.77 (ddd, *J* = 13.0, 2.8, 2.1 Hz, 1 H), 1.67–1.75 (m, 5 H), 1.65 (ddd, *J* = 12.2, 2.1, 1.6 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 155.0 (s), 120.4 (s), 51.8 (q), 51.0 (s), 40.5 (d), 40.4 (t), 39.2 (t), 35.9 (t), 35.2 (t), 32.3 (t), 32.1 (d), 28.7 (d), 28.4 (d) ppm. IR (KBr): $\tilde{\nu}$ = 3342, 3043, 2916, 2859, 2243, 1715, 1529, 1277, 1269, 1236, 1070, 613 cm^{-1}. MS (ESI+): *m*/*z* = 257.

General Procedure for the Syntheses of the Phthalimide Derivatives: A round-bottomed flask (50 mL) was charged with the amino acid derivative (10 mmol), phthalic anhydride (20 mmol), and DMF (4 mL), and the reaction mixture was heated at reflux for 2 d. The solvent was removed on a rotary evaporator. The resulting residue was suspended in CH_3CN (50 mL), and the unreacted amino acid was removed by filtration through a sintered glass funnel. The filter cake was washed with CH_3CN (100 mL) and acetone (100 mL), and the combined organic filtrates were concentrated on a rotary evaporator. The product was purified by chromatography on a silica gel column (10 % EtOAc in CH_2Cl_2).

2-Phthalimidoadamantane-2-carboxylic Acid (3): The reaction of 2-aminoadamantane-2-carboxylic acid (1.49 g, 7.63 mmol) and phthalic anhydride (2.24 g, 15.12 mmol) followed by purification gave **3** (780 mg, 31 %) as colorless crystals; m.p. 297–299 °C. ^{1}H NMR [300 MHz, dimethyl sulfoxide-d_6 ([D$_6$]DMSO)]: δ = 12.87 (br. s,

1 H), 7.80–7.89 (m, 4 H), 3.63 (br. s, 2 H), 2.10 (d, J = 12.2 Hz, 2 H), 1.60–1.92 (m, 10 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 171.8 (s), 169.0 (s, 2 C), 134.7 (d, 2 C), 131.1 (s, 2 C), 122.8 (d, 2 C), 71.2 (s), 36.9 (t), 33.8 (t, 2 C), 33.5 (t, 2 C), 29.6 (d, 2 C), 25.7 (d), 25.6 (d) ppm. IR (KBr): $\tilde{\nu}$ = 3437, 2923, 2857, 1774, 1723, 1706, 1624, 1365, 1303, 723 cm^{-1}. MS (ESI–): m/z = 324. HRMS (MALDI-TOF): calcd. for $C_{19}H_{19}NO_4Na$ [M + Na]$^+$ 348.1206; found 348.1206.

2-Phthalimidoadamantane-1-carboxylic Acid (4): By following the general procedure for the synthesis of the phthalimides, the reaction of amino acid **10** (1.75 g, 8.96 mmol) and phthalic anhydride (1.72 g, 11.61 mmol) following by purification on a silica gel column (25 % EtOAc in CH_2Cl_2) gave **4** (1.18 g, 41 %) as colorless crystals; m.p. 203–206 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73–7.81 (m, 2 H), 7.63–7.71 (m, 2 H), 4.66 (s, 1 H), 3.06 (d, J = 11.0 Hz, 1 H), 2.31 (br. s, 1 H), 1.74–2.14 (m, 10 H), 1.59 (d, J = 12.9 Hz, 1 H) ppm. The H atom of the carboxylic acid was not observed. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.8 (s), 169.2 (s, 2 C), 133.9 (d, 2 C), 132.1 (s, 2 C), 123.2 (d, 2 C), 59.4 (d), 43.7 (t), 43.6 (s), 37.7 (t), 37.1 (t), 34.9 (t), 33.3 (d), 30.7 (t), 28.1 (d), 26.9 (d) ppm. IR (KBr): $\tilde{\nu}$ = 3438, 2922, 2856, 1772, 1713, 1625, 1372, 1316, 1061, 720 cm^{-1}. MS (ESI+): m/z = 326. MS (ESI–): m/z = 324. HRMS (MALDI-TOF): calcd. for $C_{19}H_{19}NO_4Na$ [M + Na]$^+$ 348.1206; found 348.1201.

1-Phthalimidoadamantane-2-carboxylic Acid (5): By following the general procedure for the synthesis of the phthalimides, the reaction of amino acid **15** (480 mg, 2.46 mmol) and phthalic anhydride (1.00 g, 6.75 mmol) followed by purification on a silica gel column (10 % EtOAc in CH_2Cl_2) gave **5** (250 mg, 31 %) as colorless crystals; m.p. 271–274 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 12.12 (br. s, 1 H), 7.74–7.84 (m, 4 H), 3.89 (br. s, 1 H), 2.95 (d, J = 12.4 Hz, 1 H), 2.69 (d, J = 12.8 Hz, 1 H), 2.65 (d, J = 12.1 Hz, 1 H), 2.45 (br. s, 1 H), 2.10 (d, J = 12.1 Hz, 2 H), 1.99 (dd, J = 12.1, 2.4 Hz, 1 H), 1.77–1.83 (m, 3 H), 1.73 (d, J = 12.3 Hz, 1 H), 1.66 (d, J = 12.3 Hz, 1 H), 1.54 (d, J = 12.8 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 173.7 (s), 169.1 (s, 2 C), 134.4 (d, 2 C), 131.2 (s, 2 C), 122.5 (d, 2 C), 59.6 (s), 49.0 (d), 41.0 (t), 36.6 (t), 35.6 (t), 35.5 (t), 32.0 (d), 31.8 (t), 28.7 (d), 28.5 (d) ppm. IR (KBr): $\tilde{\nu}$ = 3448, 2927, 2911, 2852, 1765, 1702, 1374, 1300, 1080, 717 cm^{-1}. MS (ESI–): m/z = 324. MS (ESI+): m/z = 308, 280. HRMS (MALDI-TOF): calcd. for $C_{19}H_{19}NO_4Na$ [M + Na]$^+$ 348.1206; found 348.1194.

4-Phthalimidoadamantane-1-carboxylic Acid (6): By following the general procedure for the synthesis of the phthalimides, the reaction of amino acid **10** (320 mg, 1.64 mmol) and phthalic anhydride (1.36 g, 9.18 mmol) following by purification on a silica gel column (15 % EtOAc in CH_2Cl_2) gave a diastereomeric mixture of **6-E** and **6-Z** (270 mg, 50 %; according to the integration of the signals in the ^{1}H NMR, *E*/*Z*, 4:1) as colorless crystals. The pure diastereomers were isolated by MPLC (Licroprep 40–63 µm, RP-8, 310–35) using CH_3OH/H_2O [55:45 + 0.1 % trifluoroacetic acid (TFA), V ≈ 1.5 L) as the eluent. The samples were analysed by HPLC analysis [C18 column, CH_3OH/H_2O (57.5:42.5 + 0.1 % TFA)].

(*E*)-4-Phthalimidoadamantane-1-carboxylic Acid (6-E): Colorless crystals (80 mg, 15 %); m.p. 207–208 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 12.12 (br. s, 1 H), 7.82 (br. s, 4 H), 4.19 (br. s, 1 H), 2.68 (br. s, 2 H), 2.18 (d, J = 12.9 Hz, 2 H), 1.88–2.04 (m, 5 H), 1.84 (br. s, 2 H), 1.56 (d, J = 12.9 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 177.9 (s), 169.0 (s, 2 C), 134.3 (d, 2 C), 131.5 (s, 2 C), 122.7 (d, 2 C), 59.7 (d), 39.2 (t), 38.7 (t, 2 C), 31.4 (t, 2 C), 29.6 (d, 2 C), 26.1 (d) ppm. The signal of one quarternary C atom overlapped with that of DMSO. IR (KBr): $\tilde{\nu}$ = 3449, 2933, 2863, 1775, 1723, 1708, 1695, 1365, 1315, 1083, 714 cm^{-1}. MS (ESI–): m/z = 324. MS (ESI+): m/z = 348. HRMS (MALDI-TOF, mixture of **6-E** and **6-Z**): calcd. for $C_{19}H_{19}NO_4Na$ [M + Na]$^+$ 348.1206; found 348.1222.

(*Z*)-4-Phthalimidoadamantane-1-carboxylic Acid (6-Z): Colorless crystals (30 mg, 6 %); m.p. 210–212 °C. ^{1}H NMR (300 MHz, [D$_6$]-acetone): δ = 7.82 (br. s, 4 H), 4.29 (br. s, 1 H), 2.77 (br. s, 2 H), 2.51 (d, J = 13.3 Hz, 2 H), 1.88–2.10 (m, 7 H), 1.84 (d, J = 13.3 Hz, 2 H) ppm. The signal from the H atom of COOH was not observed because of the presence of H_2O in acetone. ^{13}C NMR (75 MHz, [D$_6$]acetone): δ = 178.6 (s), 170.0 (s, 2 C), 134.9 (d, 2 C), 133.0 (s, 2 C), 123.4 (d, 2 C), 60.6 (d), 39.9 (t), 38.0 (t, 2 C), 35.2 (t, 2 C), 31.7 (d, 2 C), 28.4 (d) ppm. One quarternary C atom was not observed. IR (KBr): $\tilde{\nu}$ = 3449, 2919, 2856, 1702, 1686, 1379, 1115, 714 cm^{-1}.

General Procedure for Analytical Irradiation Reactions: A quartz test tube was filled with a solution of phthalimide **3**–**6** (5 mg, 0.015 mmol) and K_2CO_3 (1.1 mg, 0.008 mmol) in either CH_3CN/H_2O (2:1) or acetone/H_2O (2:1; 15 mL). The resulting solution was purged with N_2 for 30 min, sealed, and irradiated in a reactor at 300 nm with 8 lamps (1 lamp, 8 W) over 1–5 min. The samples of the irradiated solutions were analyzed by HPLC at different time intervals. At the end of the irradiation process, the solvent was removed on a rotary evaporator, and the residue was analyzed by NMR spectroscopy.

General Procedure for Preparative Irradiation Reactions: A quartz vessel was filled with a solution of phthalimide **3** or **4** (100 mg, 0.31 mmol) and K_2CO_3 (21.2 mg, 0.15 mmol) in CH_3CN (150 mL) and H_2O (50 mL). The resulting solution was purged with Ar (30 min) and then irradiated in a reactor at 300 nm with 11 lamps (1 lamp, 8 W) over 0.5–2 h. The irradiated solution was continuously purged with Ar and cooled by a tap water finger condenser. The solvent from a sample of the irradiated solution (approximately 10 mL) was evaporated on a rotary evaporator, and the residue was analyzed by NMR spectroscopy. To the remaining irradiated mixture was added H_2O (150 mL), and the mixture was extracted with CH_2Cl_2 (5 × 100 mL). The combined extracts were dried with anhydrous $MgSO_4$ and filtered, and the solvent was removed on a rotary evaporator. The residue was purified by chromatography on a silica gel column (CH_2Cl_2 and CH_2Cl_2/EtOAc/CH_3OH, 17:2:1) followed by preparative TLC on silica gel (EtOAc/CH_2Cl_2, 1:5).

Irradiation of Phthalimide 3: Phthalimide **3** (100 mg, 0.31 mmol) was dissolved in CH_3CN/H_2O (3:1, 200 mL) in the presence of K_2CO_3 (21.2 mg, 0.15 mmol), and the mixture was irradiated in a reactor by using 11 lamps for 30 min. After workup, the evaporation of the solvent and purification by chromatography afforded **21** (50 mg, 58 %). The NMR spectroscopic data of *N*-(2-adamantyl)phthalimide (**21**) are in accord with those in the literature.[72]

Irradiation of Phthalimide 4: Phthalimide **4** (100 mg, 0.31 mmol) was dissolved in CH_3CN/H_2O (2:1, 150 mL) in the presence of K_2CO_3 (21.2 mg, 0.15 mmol), and the mixture was irradiated in a reactor by using 11 lamps for 30 h. After workup, the evaporation of the solvent and purification by chromatography afforded **21** (11 mg, 13 %) and **22** (51 mg, 59 %). The NMR spectroscopic data of products **21** and **22** are in accord with those in the literature.[72]

Irradiation of Phthalimide 5: Phthalimide **5** (5 mg, 0.015 mmol) in CH_3CN/H_2O (2:1, 15 mL) in the presence of K_2CO_3 (1.1 mg, 0.008 mmol) was irradiated in a reactor by using 8 lamps for 5 min. After the evaporation of the solvent, compounds **23**–**25** were identified in the crude mixture by comparison with authentic samples. The NMR spectroscopic data of the products are in accord with those in the literature.[72]

Irradiation of Phthalimide 6-E and 6-Z: Phthalimide **6-E** or **6-Z** (5 mg, 0.015 mmol) in CH_3CN/H_2O (2:1, 15 mL) in the presence of K_2CO_3 (1.1 mg, 0.008 mmol) was irradiated in a reactor by using 8 lamps for 3 min. After the evaporation of the solvent, compound

21 was identified in the crude mixture by comparison with an authentic sample. The NMR spectroscopic data of product **21** are in accord with those in the literature.[72]

Irradiation of Phthalimide 4 or 5 in the Presence of Acrylonitrile: A solution of **4** or **5** (20 mg, 0.06 mmol) in acetone/H_2O (2:1, 15 mL) and K_2CO_3 (4.4 mg, 0.031 mmol) was divided into 4 quartz test tubes. To each test tube, acrylonitrile (1 mL) was added. The solutions were purged with N_2 for 30 min, sealed, and then irradiated by using 8 lamps for 1 h. After irradiation, the solvent was removed on a rotary evaporator, and the residue was purified by chromatography on a preparatory TLC plate (EtOAc/Et_2O/hexane, 1:1:8). The irradiation of **4** afforded products **21** (0.3 mg, 2 %) and **26** (8.5 mg, 41 %). The irradiation of **5** afforded products **23** (4.0 mg, 23 %) and **27** (4.7 mg, 23 %).

***N*-{2-[1-(2-Cyanoethyl)]adamantyl}phthalimide (26):** Colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.82–7.87 (m, 2 H), 7.72–7.77 (m, 2 H), 4.43 (br. s, 1 H), 2.88 (ddd, *J* = 12.6, 3.0, 2.7 Hz, 1 H), 2.38 (d, *J* = 12.6 Hz, 1 H), 2.28 (ddd, *J* = 10.2, 7.0, 6.3 Hz, 1 H), 2.20 (ddd, *J* = 10.2, 6.3, 6.1 Hz, 1 H), 2.15 (br. s, 1 H), 2.11 (br. s, 1 H), 2.00 (br. s, 1 H), 1.96 [ddd (dt), *J* = 12.6, 2.6 Hz, 1 H], 1.88 [ddd (dt), *J* = 12.6, 2.6 Hz, 1 H], 1.79 (d, *J* = 12.1 Hz, 1 H), 1.75 (d, *J* = 12.1 Hz, 1 H), 1.68–1.73 (m, 2 H), 1.50–1.64 (m, 3 H), 1.64 (d, *J* = 12.3 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.8 (s, 2 C), 134.3 (d, 2 C), 132.1 (s, 2 C), 123.5 (d, 2 C), 120.5 (s), 60.4 (d), 43.4 (t), 39.4 (t), 37.9 (t), 37.3 (t), 36.1 (s), 35.5 (d), 35.1 (t), 31.5 (t), 28.9 (d), 27.8 (d), 11.0 (t) ppm. HRMS (MALDI-TOF): calcd. for $C_{21}H_{22}N_2O_2Na$ $[M + Na]^+$ 357.1573; found 357.1560.

***N*-{1-[2-(2-Cyanoethyl)]adamantyl}phthalimide (27):** Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.74–7.80 (m, 2 H), 7.67–7.73 (m, 2 H), 3.03 (d, *J* = 10.6 Hz, 1 H), 2.94 (d, *J* = 11.6 Hz, 1 H), 2.73 (d, *J* = 13.3 Hz, 1 H), 2.61 (d, *J* = 13.3 Hz, 1 H), 2.32 (ddd, *J* = 10.6, 7.1, 6.1 Hz, 1 H), 2.21 (ddd, *J* = 10.6, 7.1, 6.1 Hz, 1 H), 2.11–2.20 (m, 2 H), 1.78–2.05 (m, 6 H), 1.61–1.77 (m, 3 H), 1.48–1.54 (m, 1 H) ppm. ^{13}C NMR (75 MHz $CDCl_3$): δ = 170.1 (s, 2 C), 134.1 (d, 2 C), 122.9 (d, 2 C), 120.0 (s), 63.5 (s), 43.9 (d), 41.6 (t), 37.6 (t), 36.9 (t), 35.3 (t), 30.7 (d), 30.1 (t), 29.8 (d), 29.4 (d), 24.3 (t), 15.6 (t) ppm. The signal of the phthalimide quarternary C atom was not observed. HRMS (MALDI-TOF): calcd. for $C_{21}H_{22}N_2O_2Na$ $[M + Na]^+$ 357.1573; found 357.1574.

Irradiation of Phthalimide 4 in the Presence of Oxygen: A glass vessel was filled with a solution of phthalimide **4** (100 mg, 0.31 mmol) and K_2CO_3 (23 mg, 0.16 mmol) in CH_3CN/H_2O (3:1, 200 mL). The solution was purged with O_2 for 30 min and then irradiated in a reactor at 300 nm by using 10 lamps. The irradiated solution was continuously purged with O_2 and cooled by a tap water finger condenser. The solvent from a sample of the irradiated solution (approximately 10 mL) was removed on a rotary evaporator, and the residue was analyzed by NMR spectroscopy. To the remaining irradiated mixture was added H_2O (150 mL), and the mixture was extracted with CH_2Cl_2 (5 × 100 mL). The combined extracts were dried with anhydrous Na_2SO_4 and filtered, and the solvent was removed on a rotary evaporator. The residue was purified by chromatography on a silica gel column (CH_2Cl_2 and CH_2Cl_2/EtOAc/CH_3OH, 17:2:1) followed by preparative TLC on silica gel (EtOAc/CH_2Cl_2, 1:5) to afford **21** (4 mg, 4 %), **28** (13 mg, 14 %), **29** (9 mg, 10 %), and **30** (45 mg, 62 %).

2-Phthalimidoadamantane 1-Hydroperoxide (28): Oily crystals. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.02 (br. s, 1 H), 7.82–7.86 (m, 2 H), 7.70–7.74 (m, 2 H), 4.79 (br. s, 1 H), 2.87 (d, *J* = 13.0 Hz, 1 H), 2.57 (d, *J* = 12.0 Hz, 1 H), 2.44 (ddd, *J* = 12.0, 3.0, 2.7 Hz, 1 H), 2.35 (br. s, 2 H), 2.30 (br. s, 1 H), 1.85–1.95 (m, 3 H), 1.79 (d, *J* = 12.3 Hz, 1 H), 1.73 (d, *J* = 12.3 Hz, 1 H), 1.58 (d, *J* = 13.0 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4 (s, 2 C), 134.2 (d, 2 C), 132.0 (s, 2 C), 123.4 (d, 2 C), 81.3 (s), 59.4 (d), 42.2 (t), 39.1 (t), 37.7 (t), 36.0 (d), 35.3 (t), 32.2 (t), 30.8 (d), 30.2 (d) ppm. HRMS (MALDI-TOF): calcd. for $C_{18}H_{18}NO_4Na$ $[M - H + Na]^+$ 335.1134; found 335.1131.

***N*-[2-(1-Hydroxyadamantyl)]phthalimide (29):** Colorless crystals, m.p. 162–164 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78–7.86 (m, 2 H), 7.67–7.76 (m, 2 H), 4.28 (br. s, 1 H), 3.15 (br. s, 1 H), 2.76 (dd, *J* = 12.5, 3.0 Hz, 1 H), 2.51 (br. s, 1 H), 2.20 [ddd (dt), *J* = 11.3, 3.0 Hz, 2 H], 1.87–2.04 (m, 4 H), 1.80 (d, *J* = 12.5 Hz, 1 H), 1.67–1.76 (m, 3 H), 1.52 (d, *J* = 11.3 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3 (s, 2 C), 134.2 (d, 2 C), 132.0 (s, 2 C), 123.3 (d, 2 C), 69.0 (s), 66.3 (d), 46.9 (t), 41.1 (t), 37.4 (t), 36.6 (t), 35.0 (d), 31.0 (t), 30.6 (d), 29.7 (d) ppm. IR (KBr): $\tilde{\nu}$ = 3497, 2919, 2852, 1764, 1701, 1454, 1377, 1318, 1131, 1095, 1060, 893, 714 cm^{-1}. HRMS (MALDI-TOF): calcd. for $C_{18}H_{18}NO_2$ $[M - OH]^+$ 280.1343; found 280.1337.

Quantum Yield of Photodecarboxylation: The quantum yield of photodecomposition was determined by using a secondary actinometer, that is, the photolysis of **31** in CH_3CN/H_2O (3:1) to give **32** and **33** (Φ_R = 0.30 ± 0.03).[79] Quartz test tubes were filled with a solution (CH_3CN/H_2O, 2:1 or acetone/H_2O, 2:1) of phthalimide **2**–**6** (1 mM) that contained K_2CO_3 (0.5 mM). The solutions were purged with N_2 for 30 min and then irradiated at the same time in a reactor with 8 lamps at 254 or 300 nm for 90 s (for the acetone solutions, the irradiation was performed at 300 nm for 90 s). The compositions of the irradiated solutions were analyzed by HPLC. After the irradiation was complete, the solvent was removed on a rotary evaporator, and the residue was analyzed by NMR spectroscopy. Measurements were done in triplicate, and the mean value was reported. The quantum yield of the secondary actinometer upon irradiation at 254 nm was additionally verified by using three actinometers during the same experiment: ferrioxalate (Φ_{254} = 1.25),[70,80] KI/KIO_3 (Φ_{254} = 0.74),[70,81] and valerophenone (Φ_{254} = 0.65 ± 0.03),[70,78] as described previously.[86] Results are compiled in the Supporting Information.

Supporting Information (see footnote on the first page of this article): Experimental procedures of known reaction intermediates, details of irradiation experiments, determination of photodecarboxylation quantum yield, and ^{1}H and ^{13}C NMR spectra of all prepared compounds.

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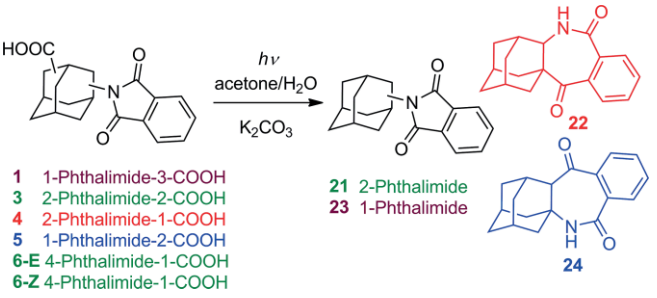

Adamantane α-, β-, and δ-amino acids activated by phthalimide were synthesized, and their photochemical reactivities were investigated. Derivatives **3**–**6** underwent a photoinduced electron transfer and decarboxylation reaction sequence, which was shown to proceed more efficiently under acetone sensitization (quantum yields, Φ = 0.02–0.5) than upon direct excitation.

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