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Original Scientific Article

Photodecarboxylation of *N*-Adamantyl- and *N*-Phenylphthalimide Dipeptide Derivatives†

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Abstract. New dipeptide derivatives **1** and **3** were synthesized and their reactivity in the photochemical reaction of decarboxylation was investigated. The photodecarboxylation of *N*-adamantyl derivatives **1a** and **1b** and *N*-phenylphthalimide derivatives **3a** and **3b** probably takes place from the triplet excited state. The triplet excited state of **1a**, **3a** and **3b** was characterized by laser flash photolysis. *N*-phenylphthalimides **3a** and **3b** undergo 2−5 times more efficient photodecarboxylation than *N*-adamantylphthalimides **1a** and **1b**. The aminoacid residue (Phe or Gly) at the C-terminus of the dipeptide does not influence the photodecarboxylation efficiency. Product selectivity in the photoreactions is determined by the conformation of the molecules. *N*-phenylphthalimides with the separated electron donor (carboxylate) and acceptor moiety (phthalimide) give only simple decarboxylation products, whereas *N*-adamantyl derivatives also give cyclization products.

Keywords: photodecarboxylation, dipeptides, phthalimides

INTRODUCTION

Photodecarboxylation is an important photochemical reaction with many applications in organic synthesis.[1] For example, photodecarboxylation of Barton esters can induce radical chain reactions,[2] whereas degradation of some classes of organic compounds can be carried out by photo-Colbe reaction.[3] Photodecarboxylation is also important for the chromophores that compose nonsteroidal non-inflammatory drugs such as ketoprofen, and naproxen. Since these drugs are known to induce photoalergy, their photochemistry has been thoroughly investigated.[4] Generally, the mechanism of photodecarboxylation can take place *via* homolytic cleavage giving radicals.[5] The other suggested mechanism includes photoejection of an electron from the carboxylates and formation of radicals.[6] A special interest was directed to the photodecarboxylation of ketoprofene and similar derivatives.[7] Although some controversy was encountered regarding the reactive excited state of ketoprofen,[8] it is generally accepted that the decarboxylation gives carbanionic species.[9]

Synthesis of phthalimide derivatives attracts organic chemists due to their application in the amine protection,[10] as well as their biological activity.[11] Furthermore, phthalimide has shown a potential as a useful chromophore that can initiate many synthetically applicable photochemical reactions giving rise to complex heteropolycyclic derivatives.[12] These reactions include photocycloadditions,[13] cyclizations initiated by H-abstraction,[14] or photoinduced electron transfer (PET).[15] In the PET reactions, the phthalimide is an electron acceptor, whereas a donor of an electron can be carboxylate[16] or silyl derivative.[17] Using photoinduced decarboxylation initiated by the phthalimide chromophore, Griesbeck *et al*. developed synthetic methods for the preparation of medium and large-cyclic ethers[18] and cyclic peptides,[19] and developed novel chiral photocages.[20] Later, Oelgemöller *et al*. used photoinduced decarboxylation for the acetate,[21] benzyl,[22] or α-amino acid addition to the phthalimide,[23] or for the formation of cyclic aryl ethers,[24] which was also conducted in the microflow reactors.[25] We have recently demonstrated that photoinduced decarboxylation of 3-(*N*-phthalimi-do)-1-adamantane carboxylic acid initiate addition of the photogenerated radical to electron deficient alkenes.[26] The latter photoaddition is feasible only in the systems wherein the phthalimide is separated by a rigid spacer from the electron donor to prevent the cyclization reaction. In the flexible systems, cyclization takes place, and we have recently shown that it takes place with high enantioselectivity due to memory of chirality. Thus, cyclization of dipeptide **1a** containing L-phenylalanine gives **2a** as the major product in 65 % yield with the ee > 99 % (Eq. 1).[27]

† Dedicated to Dr. Mirjana Eckert-Maksić on the occasion of her 70th birthday.

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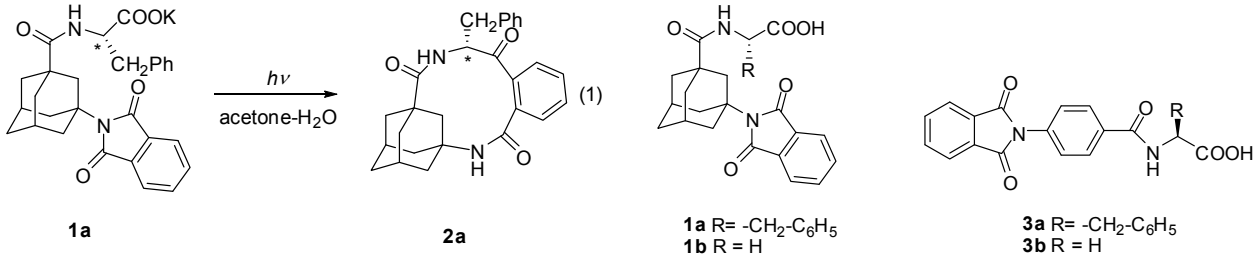


Chart 1.

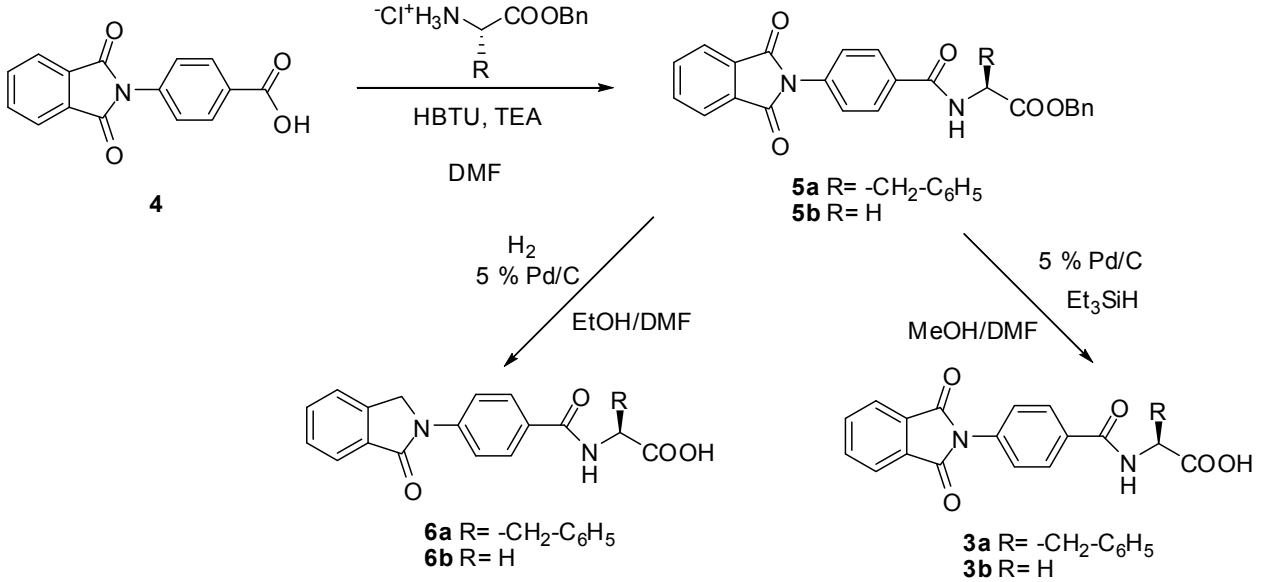
Herein we investigate further the scope of the photodecarboxylation in a series of dipeptide derivatives wherein the N-terminus is activated by phthalimide. The investigated molecules comprise of *N*-adamantylphthalimide derivatives **1a**, **1b**, and *N*-phenylphthalimide derivatives **3a**, **3b** (Chart 1). The molecules are designed to probe for the efficiency of photodecarboxylation depending on the spacer between the electron donor (carboxylate) and the acceptor (phthalimide). Although photochemistry of *N*-alkylphthalimides has been well documented, reports on photochemistry of *N*-phenylphthalimides are scarce.[28] The C-terminus of the dipeptides bears two distinctly different amino acids, glycine and phenylalanine. The anticipated photodecarboxylation should give rise to two different radical species, and therefore, it is anticipated to proceed with different efficiency. We performed preparative photolyses and isolated or characterized primary photoproducts and determined quantum efficiency of their formation. In addition, to get more information about the mechanism of the photochemical reactions and to characterize the excited states involved, we carried out laser flash photolysis (LFP).

RESULTS AND DISCUSSION

Synthesis

Adamantyl dipeptide derivatives **1a** and **1b** were synthesized from the *N*-phthalimide derivative of 3-aminoadamantane-1-carboxylic acid, prepared as previously described.[26,27] The acid was activated with *N,N'*-Dicyclohexylcarbodiimide (DCC) and treated with *N*-hydroxysuccinimide (NHS) to give iminoester derivative[27] which was treated with unprotected L-phenylalanine or glycine in the presence of a base to afford the desired peptides **1a** and **1b** in good yields, that were purified by column chromatography.

N-phenylphthalimide dipeptides **3a** and **3b** were prepared from acid **4**.[26] Attempts to activate acid **4** by DCC and NHS failed. Therefore, we used a stronger activation reagent, *N,N,N',N'*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (HBTU).[29] The acid was activated *in situ* and reacted with ethyl or benzyl ester L-phenylalanine or glycine (Scheme 1). The esters **5a** and **5b**, as well as the corresponding ethyl



Scheme 1.

Table 1. Photolysis of phthalimides **1a**, **1b, 3a**, and **3b** under different conditions[a]

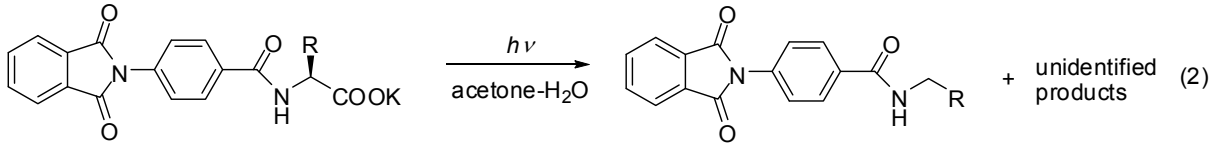
Comp.	Solvent	Conc. (mg/mL)	Time (min)	Reactant (%)[d]	Products[c] Decarboxylation Product	Cyclization Product	Unidentified Products
1a	acetone-H_2O (3:1)	10/20	30	15 (**1a**)	≈ 10 (**8a**)	40 (**2a**)	35
	acetone-H_2O (3:1)	100/100	20	70 (**1a**)	Traces (**8a**)	13 (**2a**)	17
	CH_3CN-H_2O (3:1)	10/20	30	90 (**1a**)	Traces (**8a**)	10 (**2a**)	-
1b	acetone-H_2O (3:1)[b]	78/185	21	70 (**1b**)	Traces (**8b**)	15 (**9b**) 8 (**2b**)	7
	acetone-H_2O (3:1)	20/20	20	21 (**1b**)	10 (**8b**)	Traces (**9b**+**2b**)	69
	acetone-H_2O (3:1)	200/100	15	65 (**1b**)	5 (**8b**)	Traces (**9b**+**2b**)	30
	CH_3CN-H_2O (3:1)	20/20	20	>90 (**1b**)	Traces (**8b**)	Traces (**9b**+**2b**)	<10
3a	acetone-H_2O (3:1)	20/20	3	60 (**3a**)	20 (**7a**)	0	20
	CH_3CN-H_2O (3:1)	20/20	3	85 (**3a**)	10 (**7a**)	0	5
3b	acetone-H_2O (3:1)	20/20	10	40 (**3b**)	15 (**7b**)	0	45
	acetone-H_2O (3:1)	100/100	10	10 (**3b**)	5 (**7b**)	0	85
	CH_3CN-H_2O (3:1)	20/20	10	60 (**3b**)	15 (**7b**)	0	25

[a] Irradiations were carried out in N_2-purged solutions in the presence of 0.5 equivalents of K_2CO_3. Luzchem or Rayonet reactor was equipped with 8 or 16 lamps, respectively, with the irradiation maximum at 300 nm.
[b] Irradiation was carried out in Luzchem reactor equipped with 3 lamps (300 nm).
[c] The ratio of products determined from the NMR spectra of crude mixture. The number in parenthesis corresponds to the obtained cyclization product.
[d] The conversion was obtained by the weight of the photoproducts after separation from the unreacted acids **1a,b** and **3a,b**.

ester **5bEt**, were prepared in good to moderate yields. Using the same activation protocol we also prepared the corresponding ethyl and benzyl gylcine esters of the adamantane derivative (**1bEt**, **1bBz**). However, all attempts to perform basic or acidic hydrolysis of these esters failed, mostly due to the competitive ring-opening of the phthalimide moiety. Therefore, the benzyl protection of the esters was inferred to be more rewarding, enabling the selective deprotection by hydrogenolysis. However, the usual protocol by use of Pd/C, in addition to the cleavage of the esters, gave phthalides **6a** and **6b**. A successful benzyl ester deprotection was achieved in a reaction of triethylsilane and Pd/C (5 %) with *in situ* formed H-radicals.[30] The deprotection was carried out in methanol-DMF and furnished desired products **3a** and **3b** in good yields (Scheme 1).

Photochemistry

To isolate and characterize photoproducts, preparative irradiations of **1b**, **3a**, and **3b** were carried out. Irradiations were carried out in acetone-H_2O (3:1) in the presence of 0.5 equivalents of K_2CO_3 as a base, according to the previously documented conditions for efficient intra- or intermolecular electron transfer and photodecarboxylation.[18–26] However, under these conditions, irradiation of the phenyl derivatives **3a** and **3b** gave complex mixtures of many products. Chromatographic isolation of the photoproducts was problematic due to their poor solubility in most of the commonly used solvents. However, photolyses (10 min, 16 lamps) taken to lower conversion gave photodecarboxylation products **7a** and **7b** (formed as major products in small amounts, < 20 %) which were detected by NMR and HPLC (Eq. 2, Table 1). To fully characterize **7a** and **7b**, they were prepared by an independent synthetic method, by applying the above-described protocol (HBTU activation, Scheme 1), from acid **4** phenylethylamine and methylamine, respectively (see the experimental). Irradiation of the isolated derivatives **7a** and **7b**, under the same conditions as used in the photolysis of **3a** and **3b**, lead to a fast formation of numerous products and high-weight material. All attempts to isolate some of the secondary photoproducts failed due to the problems of solubility, the material was lost on the column chromatography on silica or alumina.



3a R= -CH_2-C_6H_5
3b R= H

7a R= -CH_2-C_6H_5
7b R= H

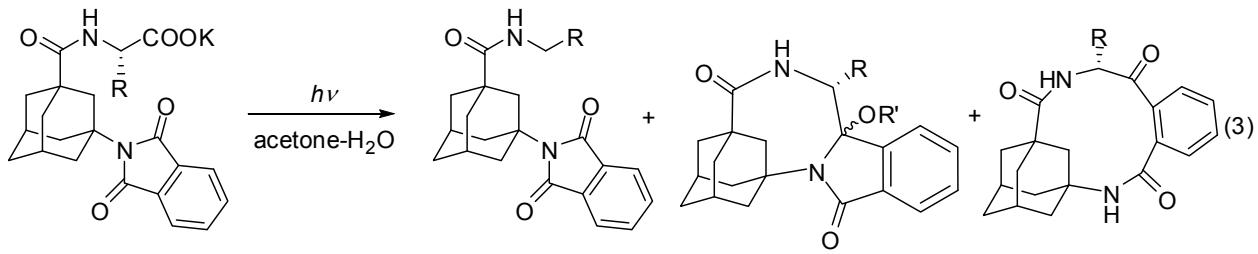
Irradiation of the adamantane derivatives **1a** and **1b** under the same conditions as used for the phenyl derivatives, taken to low conversion, gave cleaner photochemical reactions and furnished two types of products, decarboxylation **8**, and cyclization products **9** and **2** (Eq. 3). The photolysis of the glycine derivative **1b** taken to a low conversion (30 %) gave the cyclization products (8 % of **2b** and 15 % of **9b**), and traces of **8b**. Irradiation to the conversion of 80 % gave **8b** (10 %), along with numerous unidentified products. Attempts to isolate these products failed due to high adsorptivity on silica and alumina. To characterize the decarboxylation product **8b** which was formed in low yield, it was prepared in the independent synthetic method. The succinimide ester[27] was treated with methylamine to afford **8b** in good yield. Irradiation of **8b** under the same conditions as **1b** gave numerous products. Furthermore, the photodecomposition of **8b** proceeded ten times slower than the decarboxylation of **1b**. Attempts to isolate some of the secondary products from **8b** failed.

Irradiation of the isolated **8a** and **8b**, similar to the photolysis of **7a** and **7b**, gave many products. However, photodecomposition was much slower with the adamantyl derivatives (conversion 5−10 % after 15 minutes), than with the phenyl derivatives (conversion ≈ 30 % after 10 minutes). The secondary photochemical reaction of adamantyl derivatives **8a** and **8b** are anticipated, probably involving intramolecular H-abstractions from the adamantyl moiety, as previously reported.[14] However, it is not yet clear which photochemical transformations are involved in the photodecomposition of the phenyl derivatives **7a** and **7b**.

The structures of the cyclization photoproducts **9b** and **2b** were determined by use of 1D and 2D NMR techniques (COSY, NOESY, HSQC and HMBC). In the ^{1}H NMR spectrum of the glycine product **9b**, a characteristic singlet corresponding to the methoxy group was observed at δ 3.88 ppm, whereas in the ^{13}C NMR, the corresponding quartet was observed at 52.80 ppm. Further, in the aliphatic part of the ^{13}C NMR spectrum, in addition to 7 signals of the adamantane C-atoms, a doublet at 44.8 ppm can be seen corresponding to the glycine CH_2 after the loss of the carboxylate. In the ^{1}H NMR the glycine CH_2 appears as a singlet at 3.73 ppm. In the aromatic part of the spectrum four different C-H signals were observed, indicating a loss of the symmetry of the phthalimide moiety. Interactions seen in 2D NMR were fully in agreement with the assigned structure. The methoxy group was probably introduced in the molecule during the chromatographic separation on a thin layer of silica using CH_2Cl_2/CH_3OH/TFA as eluent.

The assignation of the structure to the cyclization product **2b** was straightforward from its ^{1}H and ^{13}C NMR spectra. In the ^{13}C NMR spectra three characteristic singlets in low magnetic field can be seen corresponding to three carbonyl groups; they appear at δ 187.7, 179.1 and 171.7 ppm. In addition, a characteristic singlet at 3.74 ppm in ^{1}H, and a triplet at 43.77 ppm in the ^{13}C NMR correspond to the glycine CH_2. All interactions seen in the 2D NMR fully corroborate the assigned structures.

To further investigate the photochemical reactivity of phthalimides **1a**, **1b**, **3a** and **3b** irradiations were carried out in different solvents: acetone, CH_3CN, acetone-H_2O (3:1) and CH_3CN-H_2O (3:1). In all aqueous solvents the irradiation experiments were conducted in the presence of 0.5 equivalents of base (K_2CO_3) to assure deprotonation of the acid moiety. After irradiations, a composition of the photolysates was analyzed by



1a R= CH_2-C_6H_5
1b R= H

8a R= -CH_2-C_6H_5
8b R= H

9a R= CH_2-C_6H_5, R' = CH_3
9b R= H, R' = CH_3

2a R= CH_2-C_6H_5
2b R= H

HPLC, NMR, and in some cases a chromatographic separation was carried out. Due to the solubility problems, irradiations in the presence of the base could be conducted only in the presence of H_2O, since K-salts were not soluble in neat CH_3CN or acetone. Nevertheless, NMR and HPLC analysis after irradiations of the colloidal solutions of the K-salts in CH_3CN or acetone indicated formation of the same products as in the aqueous solvents, but with significantly lower efficiency (100 times). The highest photoreactivity for all derivatives was observed in acetone-H_2O (3:1) in the presence of K_2CO_3 which is in agreement with the sensitization mechanism of photoexcitation and anticipated electron transfer from carboxylate to phthalimide.[26,27] In addition, for **1a** and **1b** a difference in the product distribution was observed when the irradiation was performed in acetone-H_2O (3:1) and CH_3CN-H_2O (3:1). In acetone-H_2O the cyclization products were predominantly formed, whereas in CH_3CN-H_2O cyclization and simple decarboxylation products were formed in comparable yields. For **3a** and **3b** we could not observe a difference in the product distribution, but the process was more efficient in acetone. The findings clearly indicate that acetone acts as a triplet sensitizer and induce photochemical reactions of **1a**, **1b**, **3a**, and **3b**. Moreover, a different ratio between the cyclization and the simple decarboxylation photoproducts obtained from **1a** and **1b** in CH_3CN-H_2O and acetone-H_2O (Table 1) suggests involvement of singlet and triplet excited states, with the cyclization taking place *via* the triplet.

It is known that phthalimides are unstable under basic conditions and undergo ring opening. Therefore, the stability of phthalimides **1b** and **3b** (c = 2.0 ×10^{-3} M) in CH_3CN-H_2O was tested in the presence of different concentrations of K_2CO_3 (c = 1.0 ×10^{-3} and 1.0 ×10^{-2} M). The progress of the reaction was monitored by UV-vis spectroscopy (see the supporting info.) Whereas decomposition of **1b** at $c(K_2CO_3)$ = 1.0 ×10^{-3} M after 20 h did not take place, a slow decomposition at 10^{-2} M was observed (pseudounimolecular $k \approx 8\times10^{-5}$ s^{-1}). On the contrary, a slow decomposition of **3b** was observed already at $c(K_2CO_3)$ = 1.0 ×10^{-3} M (pseudounimolecular $k \approx 1\times10^{-5}$ s^{-1}). These results indicate that under the irradiation conditions adamantyl derivatives **1a** and **1b** probably did not undergo ring opening, whereas for the phenyl derivatives **3a** and **3b** competitive base promoted ring opening could take place.

To investigate which excited state is involved in the formation of the photoproducts, irradiation of **1b** (c = 7 ×10^{-4} M) was performed in CH_3CN-H_2O in the presence of K_2CO_3 and potassium sorbate, an ubiquitous quencher of the triplet excited state (E_T = 246 kJ mol^{-1}).[31] The quenching of the photoreaction of **1b** was accomplished with potassium sorbate in the concentrations 0.1−0.4 M, indicating involvement of the triplet excited state in the photoproducts formation.

Irradiation of 3-(*N*-phthalimido)-1-adamantane carboxylic acid in the presence of a base and electron deficient alkenes gave rise to photodecarboxylation and radical addition of the adamantane to the alkene double bond.[26] We attempted to perform the analogous addition to acrylonitrile with the photogenerated radicals from **1a**, **1b**, **3a**, and **3b**. Irradiations were performed in the presence of 100 equivalents of acrylonitrile, but no addition products were detected. Since the adamantyl derivatives **1a** and **1b** after the initial decarboxylation give the cyclization products, the finding is logical. We have already reported that the separation of the electron donor and the acceptor is essential to enable the addition.[26] However it is yet not clear why radical addition cannot take place from the phenyl derivatives **3a** and **3b**. Probably, the anticipated radicals from **3a** and **3b** (vide infra), are stabilized by the amino substituent, and therefore, less reactive. Hence, only photodecarboxylation products **7a** and **7b** can be detected, and the addition does not take place.

On attempts to perform photoaddition to acrylonitrile we observed quenching of the photoreaction of **1a** and **1b** with acrylonitrile. With the phenyl derivatives **3a** and **3b**, no quenching was observed. This observation can be rationalized by the quenching of the triplet excited state of *N*-alkylphthalimides by acrylonitrile. The triplet energy of acrylonitrile is 297 kJ mol^{-1},[32] which is similar to the triplet energy of *N*-methylphthalimide, 293 kJ mol^{-1}.[33] Furthermore, this finding suggests that *N*-phenylphthalimides have lower triplet energy than the analogous *N*-alkylphthalimides. The energy transfer to acrylonitrile induces polymerization consuming the alkene, and therefore, the addition to the double bond does not take place. It is interesting to note that quenching of the triplet state of 3-(*N*-phthalimido)-1-adamantane carboxylic acid by acrylonitrile was not observed.[26]

Quantum efficiency for the photodecomposition (Φ_d) of **1a**, **1b**, **3a**, and **3b** was determined in CH_3CN-H_2O (3:1) and acetone-H_2O (3:1) in the presence of K_2CO_3 as a base. For the determination of Φ_d in CH_3CN-H_2O (3:1), a primary actinometer was used, photolysis of valerophenone in aqueous solvent giving acetophenone.[34] For the photoreaction in acetone-H_2O (3:1) we used a secondary actinometer, photocyclization of 6-[(*N*-phthalimido)methyl]cyclohexane carboxylic acid.[35] The photosensitized reaction (irradiation in acetone-H_2O) gave mostly the cyclization products in case of **1**, or photodecarboxylation products in case of **3**. Direct excitation (irradiation in CH_3CN-H_2O) gave photodecarboxylation products in case of **1** and **3**. From the values compiled in Table 2 it is evident that phototransformation is more efficient in acetone-H_2O than in

Table 2. Quantum yields for the decomposition (Φ_d) of **1a**, **1b**, **3a** and **3b** in CH_3CN-H_2O (3:1) and acetone-H_2O (3:1)

Compound	acetone-H_2O[a]	CH_3CN-H_2O[b]
1a	0.06±0.002 [c]	0.011±0.001 [d]
1b	0.3±0.02 [c]	0.0135±0.0005 [d]
3a	0.28±0.02 [d]	0.015±0.003 [d]
3b	0.38±0.06 [d]	0.005±0.003 [d]

[a] Photocyclization of 6-[(*N*-phthalimido)methyl]cyclohexane carboxylic acid was used as a secondary actinometer (Φ_R = 0.3).[35] Photoconversion was determined from ^{1}H NMR spectra of the crude photolysis mixture.
[b] Photolysis of valerophenone in aqueous CH_3CN was used as an actinometer (formation of acetophenone, Φ = 0.65±0.03).[34] Photoconversion was determined by HPLC.
[c] Quantum yield for the formation of cyclization products.
[d] Quantum yield for the formation of decarboxylation products.

CH_3CN-H_2O. Lower efficiency of the reaction in CH_3CN-H_2O is probably due to a low efficiency of intersystem crossing (ISC). Furthermore, it is interesting to note a higher efficiency for the aceton-sensitized reaction for the phenyl, than for the adamantyl derivatives. This observation could be rationalized with significantly different photophysical properties of *N*-phenylphthalimide derivatives[36] compared to *N*-alkyl derivatives.[35] The difference in the reactivity of **1a** *vs* **1b**, may be explained by an energy transfer from the triplet excited state of phthalimide to phenylalanine, giving rise to non-productive deactivation from the excited state. Such an energy transfer is not feasible with the glycine derivative **1b**.

Laser Flash Photolysis (LFP)

To get a better insight into the mechanism of the photochemical transformations of **1** and **3** and characterize the triplet excited states we carried out LFP measurements. The measurements were conducted in N_2- and O_2-purged CH_3CN and CH_3CN-H_2O solutions. For the excitation of samples, a frequency quadrupled Nd:YAG laser with the output at 266 nm was used. LFP for **3b** in CH_3CN gave transient absorption spectra characterized by two bands, a stronger absorption with a maximum at 330−340 nm, and a weaker broad band at 530 nm, both decaying with the rate constant $k = 4.4 \times 10^5$ s^{-1} (Figure 1 right). The observed transient was quenched by O_2 with the rate constant $k_q = 2.8 \times 10^9$ M^{-1} s^{-1}. According to the precedent spectra[36] and quenching with O_2, the transient was assigned to the triplet state of *N*-phenylphthalimide. Similarly, L-phenylalanine derivative **3a** showed transient spectra with a maximum at 330−340 nm, and a weaker band at 530 nm, both assigned to the triplet-triplet absorption of *N*-phenylphthalimide. In N_2-purged CH_3CN solution the triplet of **3a** decayed slower (compared to **3b**) with the rate constant $k = 1.1 \times 10^5$ s^{-1}.

The adamantyl derivative **1a** gave rise to distinctly different transient absorption spectra in CH_3CN then the phenyl derivatives, with only one maximum at 340 nm. The transient decayed in N_2-purged solution with the rate $k = 1.5 \times 10^6$ s^{-1}, and was quenched by O_2 ($k_q = 1.4 \times 10^9$ M^{-1} s^{-1}). Based on the quenching with O_2 and precedent spectra,[14f] it was assigned to the triplet state of phthalimide. The lifetime of the triplet of **1a** is significantly shorter than for 3-(*N*-phthalimido)-1-adamantane carboxylic acid (Table 3). This observation could be explained by intramolecular energy transfer from the triplet state of phthalimide to the phenylalanine. However, due to the overlapping of the absorption of the phthalimide and phenylalanine triplet,[37] we could not resolve the signals. The quenching of the triplet by phenylalanine is also in agreement with the observed lower quantum efficiency of decomposition for **1a** compared to **1b** (vide supra, Table 2).

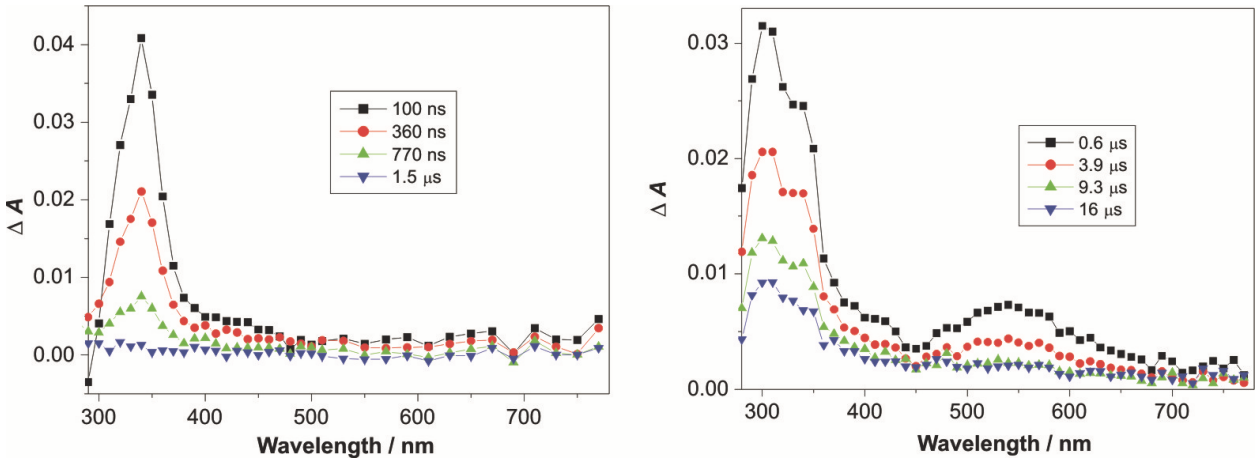


Figure 1. Transient absorption spectra of **1a** (left) and **3a** (right) in N_2-purged CH_3CN.

Table 3. Properties of triplet excited state of **1a**, **3a** and **3b** obtained by LFP

Compound	τ / μs [a]	Φ_{ISC} [b]	k_q / $M^{-1}s^{-1}$ [c]
1a	0.66±0.01	0.11±0.02	1.4×10^9
3a	8.5±0.3	0.07±0.01	2.1×10^9
3b	2.27±0.02	0.10±0.01	2.8×10^9
3-(*N*-phthalimido)adamantane-1-carboxylic acid [d]	13	0.22	2.0×10^9
N-PhePhth [e]	11.5	0.03	-

[a] Lifetime of the triplet excited state in N_2-purged solution.
[b] Φ_{ISC} in CH_3CN, determined by comparing intensity of the signal with the optically matched solution of *N*-methylphthalimide in CH_3CN ($\Phi_{ISC} = 0.8$)[35]
[c] Rate constant for the quenching of the triplet with O_2 in CH_3CN.
[d] Taken from the Ref. 26.
[e] *N*-phenylphthalimide, the values taken from the Ref. 36.

The addition of K_2CO_3 to the aqueous solution leads to a change of the observed transient absorption spectrum of **1a** (Figure 2) and increase of the lifetime (τ > ms, due to low intensity of the signal and long lifetime we could not determine its decay precisely). The new species is assigned to the radical-anion formed by PET, in accordance with the precedent literature.[14f] LFP experiments for **3a** and **3b** in the presence of K_2CO_3 (c = 0.01 M) gave no transient absorption signal, suggesting that triplet and subsequent transient species have very short lifetimes under these conditions. Short lifetime of the *N*-phenylphthalimide triplets can be rationalized by a fast electron transfer from carboxylate, which is also demonstrated by efficient photodecarboxylation quantum yield (vide supra). However, it should be noted that *N*-phenylphthalimides are very sensitive to basic conditions, undergoing ring opening. Thus, absence of signal in the transient absorption is due to competative fast decomposition of the sample.

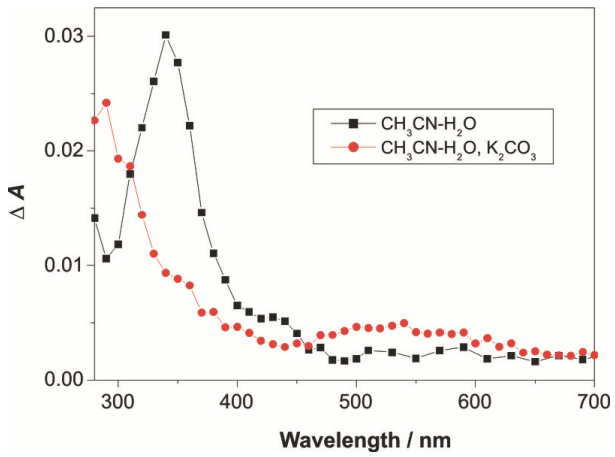
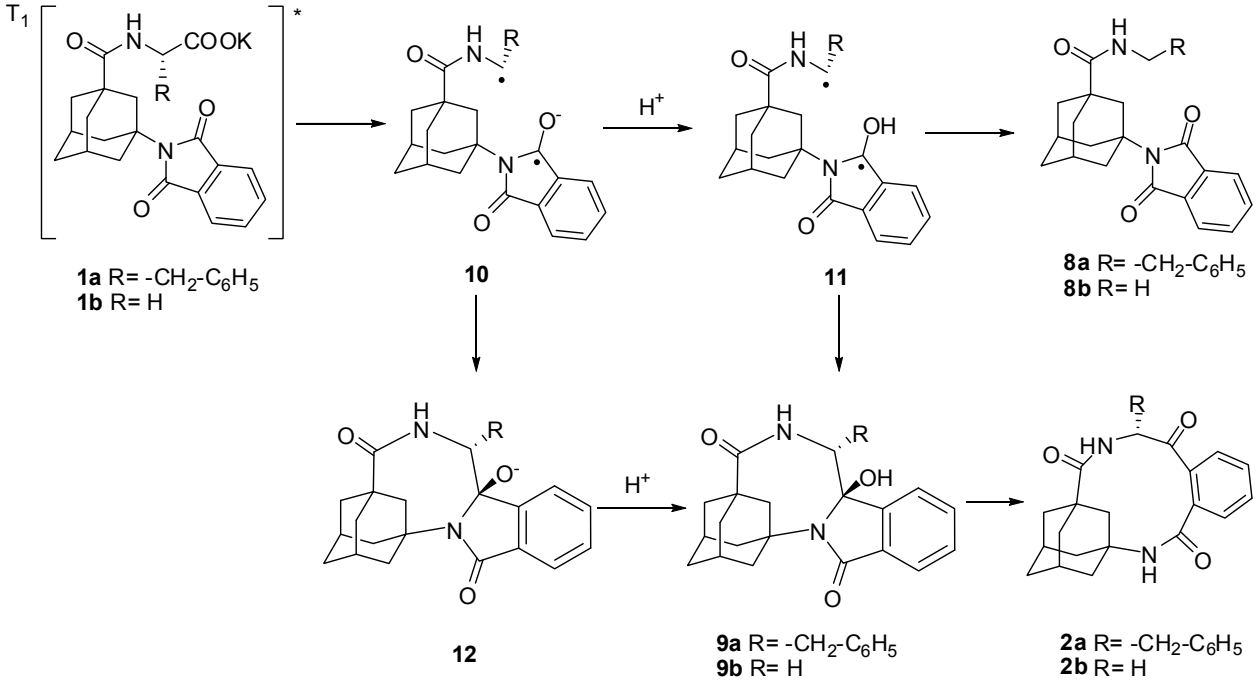


Figure 2. Transient absorption spectra of **3a** in N_2-purged CH_3CN-H_2O (1:1) at pH 7 and in the presence of K_2CO_3, c = 0.01 M.

Photochemical Reaction Mechanism

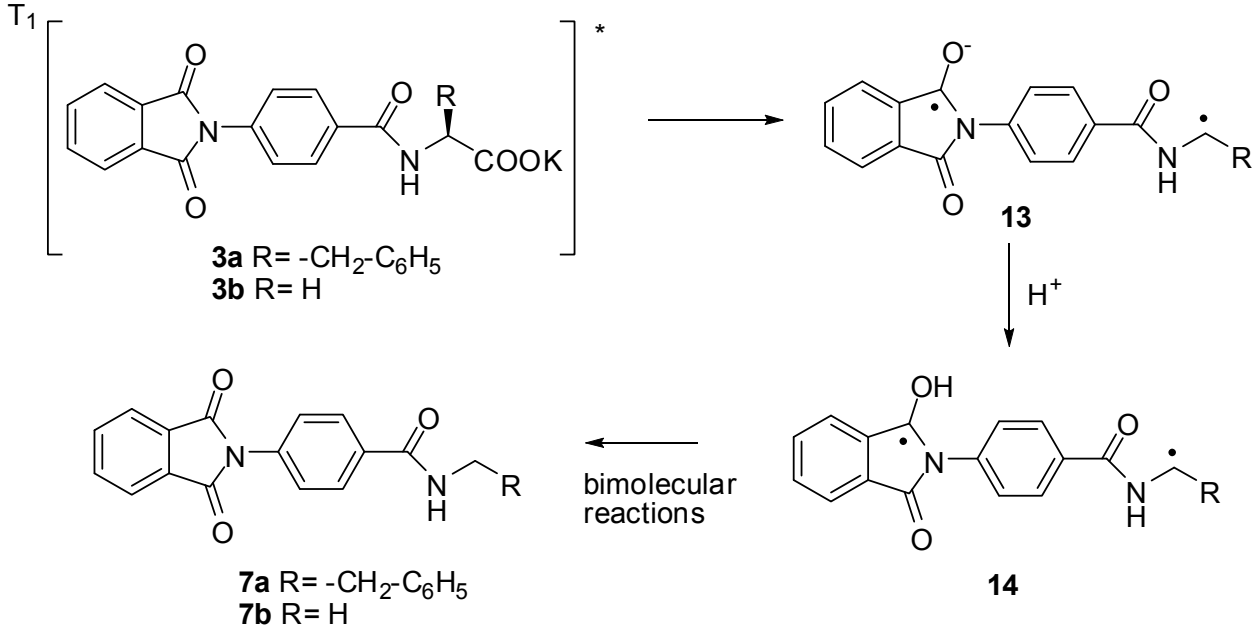
Based on the preparative photolyses and LFP measurements the photochemical reaction mechanisms for the transformations of **1** and **3** can be proposed. On direct excitation, *N*-alkyl and *N*-phenylphthalimides undergo ISC with a low quantum efficiency of 10 % and populate triplet excited states. Photodecarboxylation and formation of photoproducts from **1** and **3** probably takes place from the triplet excited state, as suggested by the quenching with potassium sorbate and acrylonitile. One of the deactivation channels from the triplet excited state is PET, followed by a rapid irreversible decarboxylation. LFP measurement in the presence of K_2CO_3 strongly indicated presence of the phthalimide radical-anion. The biradical anion **10** can be protonated to biradical **11**, or undergo ring closure to anion **12** (Scheme 2). Nevertheless, the ring closure to **12** or **9** is enantioselective (in case of **1a**) due to the memory of chirality.[27] Biradical **11** probably undergoes unimolecular or bimolecular H-transfer and give simple decarboxylation products **8a** or **8b**. Although these products are formed in higher yields in CH_3CN-H_2O than in acetone-H_2O, they are probably formed from the triplet excited state *via* some other low efficient mechanism known in the photochemistry of carboxylic acids.[2–8] In addition to PET, the other channel for the deactivation from the triplet excited state is probably energy transfer from the phthalimide to the phenylalanine, not leading to any stable product.

Photophysical properties of *N*-phenylphthalimides are different from the adamantyl analogues. ISC and population of the triplet excited state takes place with the similar efficiency. However, the deactivation from the triplet by electron transfer probably takes place more efficiently, as suggested by higher quantum efficiency of decarboxylation. It gives biradical-anion **13**. Contrary to the adamantane derivatives, **13** cannot undergo intramolecular cyclization. Most probably it decays by



Scheme 2.

protonation giving biradical **14** (Scheme 3). Since intramolecular H-transfer in **14** is not possible, only bimolecular reactions give rise to the decarboxylation product. Furthermore, biradical probably undergo many competitive intermolecular H-abstractions giving rise to a number of unidentified products. As discussed above, nonreactivity of **13** or **14** in the radical additions to double bonds could possibly be attributed to lower reactivity of the radical due to the presence of N-substituent. The other option for the decay of biradical-anion **13** would be back electron transfer giving carbanion. However the latter pathway is less likely due to poor electron accepting properties and low reduction potential of the acetamido group.



Scheme 3.

CONCLUSION

We have prepared new dipeptide derivatives activated by the phthalimide chromphore. On irradiation of these dipeptides photoinduced decarboxylation takes place. The efficiency of the process depends on the spacer between the electron donor (carboxylate) and the electron acceptor (phthalimide in the triplet excited state). *N*-phenylphthalimides undergo 2−5 times more efficient photodecarboxylation than *N*-adamantylphthalimides. The photodecarboxylation and cyclization of *N*-adamantyl derivatives **1a** and **1b** and photodecarboxylation of *N*-phenylphthalimide **3a** and **3b** probably proceeds from triplet excited state. The amino acid residue (Phe or Gly) at the C-terminus of the dipeptide does not influence the photodecarboxylation efficiency. Product selectivity in the photoreactions is mostly determined by the molecular conformation. Due to the rigid geometry *N*-phenylphthalimide derivatives with the separated donor and acceptor moiety gave only simple decarboxylation products. On the contrary, *N*-adamantyl derivatives wherein the donor and acceptor can get in close contact gave cyclization products. Formation of cyclic products with adamantylphenylalanine takes place with the memory of chirality and ee > 99 %. Therefore, it is anticipated that this cyclization will have an important impact to the future photochemical synthetic methods for the formation of cyclic peptidomimetics.

EXPERIMENTAL

General

^{1}H and ^{13}C NMR spectra were recorded on a on a Bruker Avance Spectrometer at 300 or 600 MHz. All NMR spectra were measured in $CDCl_3$, DMSO-d_6 or CD_3OD using tetramethylsilane as a reference. High-resolution mass spectra (HRMS) were measured on an Applied Biosystems 4800 Plus MALDI TOF/TOF instrument. IR spectra were recorded on FT-IR ABB Bonem MB 102 spectrophotometer. Melting points were obtained using an Original Kofler Mikroheitztisch apparatus (Reichert, Wien) and are uncorrected. Silica gel or alumina was used for the chromatographic purifications. Solvents were purified by distillation. The chemicals for the synthesis were obtained from the usual commercial sources. Photochemical reactions were carried in a Rayonet or a Luzchem reactor in quartz cuvettes. CH_3CN used in the irradiation experiments was of HPLC purity, whereas acetone was of p.a. purity. They were used as received, and were not further purified. Synthesis and characterization of **1a**, **2a**, and **9a** has been reported.[27]

*2-{[3-(*N*-phthalimido)-1-adamantyl]carboxamido}acetic acid (**1b**)*

A round bottom flask was charged with of glycine (5 mmol) and TEA (triethylamine, 0.697 mL, 5 mmol), and dissolved in a mixture of THF-H_2O (1:1, 20 mL). To the reaction mixture, a solution of *N*-succimidyl[3-(*N*-phthalimido)-1-adamantyl]formiate[27] (1.990 g, 4.5 mmol) in THF (15 mL) was added dropvise, and the reaction was stirred at rt for 3 days. When the reaction was finished, 1M HCl (20 mL) was added, and the product was extracted with ethyl acetate (3×20 mL). The extracts were dried over anhydrous $MgSO_4$, the solution was filtered and the solvent removed on a rotary evaporator to afford crude products. The product was purified by column chromatography on silica gel with 5−10 % MeOH/CH_2Cl_2 and 10 % MeOH/EtOAc. The pure product was obtained in the yield of 60−80 %.

Colourless oil; IR (KBr) ν_{max}/cm^{-1}: 3412 (m), 2917 (m), 2852 (w), 2360 (w), 1707 (s), 1654 (m), 1540 (m), 1458 (w), 1369 (m), 1316 (m), 1078 (w), 875 (w), 720 (m), 668 (w); ^{1}H NMR (300 MHz, CD_3OD) δ/ppm: 7.78 (s, 4H), 3.87 (d, J = 4.0 Hz, 2H), 2.62−2.56 (m, 4H), 2.50 (d, J = 12.3 Hz, 2H), 2.31 (s, 2H), 2.05−1.80 (m, 5H), 1.74 (d, J = 12.4 Hz, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ/ppm: 170.9 (s, 1C), 135.2 (d, 2C), 133.1 (s, 1C), 123.5 (d, 2C), 61.4 (s, 1C), 44.1 (s, 1C), 42.7 (t, 1C), 42.3 (t, 1C), 40.4 (t, 2C), 38.9 (t, 2C), 36.3 (t, 1C), 31.1 (d, 2C); HRMS calcd. for $C_{21}H_{22}N_2O_5$ 421.1160, obsd. 421.1161.

p-*(N-phthalimido)benzoic Acid (**4**)*[38]

A round bottom flask was charged with phthalic anhydride (6.0 g, 0.041 mol) and melted. To the melt *p*-aminobenzoic acid (4.40 g, 0.032 mol), suspended in DMF (10 mL) was added in several portions. The reaction mixture was heated and stirred for 20 minutes without stopper with occasional addition of DMF (~2×2 mL). When the reaction was finished and when all DMF evaporated, the mixture was cooled and suspended in EtOAc (100 mL). The suspension was washed with 10 % HOAc (70 mL), and then with 10 % $NaHCO_3$ (70 mL). During this washing, the product was suspended between the organic and the aqueous layer in a form of colourless solid. The suspended product in EtOAc was filtered through a sinter (D-4) and dried in vacuum oven at 60 °C and 10 mbar. The pure product **7** was obtained (7.1 g, 83 %) in a form of colourless crystals.

General Procedure for the Synthesis of Benzyl Esters 5a and 5b

A round bottom flask was charged with **4** (534 mg, 2 mmol), dry DMF (10 mL), TEA (0.557 mL, 4 mmol), and HBTU (796 mg, 2.1 mmol). After stirring at rt for 10 min., 2.1 mmol of benzyl ester of glycine or L-

phenylalanine hydrochloride were added, and the reaction mixture was stirred for 1 day in the case of **5a** and 4 days in the case of glycine derivative **5b**. To the reaction mixture brine (50 mL) was added and extraction with diethyl ether was carried out (1×50 mL). The product in a form of colourless solid was suspended between the organic and aqueous layers. After removal of the aqueous layer, the suspension of solid in ether was washed with 1M HCl (50 mL), H_2O (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and again with H_2O (50 mL). The suspension was filtered through a sinter (D-4) and the solid product was dried in a vacuum oven at 60 °C and 10 mbar to afford the pure products.

*N-{4-[N-(benzyloxycarbonyl-2-phenylethan-1-yl)carbamoyl]phenyl}phthalimide (**5a**)*

707 mg (75 %); colourless solid; mp, 204−206 °C; IR (KBr) ν_{max}/cm^{-1}: 3326 (m), 3062 (w), 3029 (w), 1707 (s), 1637 (m), 1506 (m), 1389 (m), 1084 (w), 849 (w), 718 (m), 528 (w); ^{1}H NMR (300 MHz, d_6-DMSO) δ/ppm: 8.96 (d, J = 7.7 Hz, 1H, NH), 8.08−7.86 (m, 6H), 7.54 (d, J = 8.6 Hz, 2H), 7.40−7.15 (m, 10H), 5.30−5.00 (m, 2H), 4.76−4.68 (m, 1H), 3.27−3.01 (m, 2H); ^{13}C NMR (75 MHz, d_6-DMSO) δ/ppm: 171.5 (s, 1C), 166.7 (s, 1C), 166.0 (s, 2C), 137.6 (s, 1C), 135.9 (s, 1C), 134.8 (d, 2C), 134.6 (s, 1C), 133.1 (s, 1C), 131.5 (s, 2C), 129.1 (d, 2C), 128.4 (d, 2C), 128.3 (d, 2C), 128.0 (d, 1C), 127.9 (d, 2C), 127.7 (d, 2C), 126.9 (d, 2C), 126.5 (d, 1C), 123.5 (d, 2C), 66.0 (t, 1C), 54.5 (d, 1C), 36.2 (t, 1C); HRMS calcd. for $C_{31}H_{24}N_2O_5$ 527.1577, obsd. 527.1569.

*N-{4-[N-((benzyloxycarboyl)methyl)carbamoyl]phenyl}phthalimide (**5b**)*

503 mg (65 %); colourless solid; mp, 245−247 °C; IR (KBr) ν_{max}/cm^{-1}: 3337 (w), 1759 (m), 1701 (s), 1647 (m), 1506 (m), 1391 (m), 1312 (w), 1207 (m), 1119 (w), 887 (w), 719 (m), 530 (w); ^{1}H NMR (300 MHz, d_6-DMSO) δ/ppm: 9.11 (t, J = 5.7 Hz, 1H, NH), 8.14−7.89 (m, 6H), 7.60 (d, J = 8.5 Hz, 2H), 7.40−7.25 (m, 5H), 5.18 (s, 2H), 4.12 (d, J = 5.7 Hz, 2H); ^{13}C NMR (75 MHz, d_6-DMSO) δ/ppm: 169.7 (s, 1C), 166.7 (s, 1C), 166.1 (s, 2C), 134.8 (d, 2C), 134.6 (s, 1/2C), 133.0 (s, 1/2C), 131.5 (s, 2C), 128.4 (d, 2C), 128.1 (d, 1C), 127.9 (d, 2C), 127.8 (d, 2C), 127.0 (d, 2C), 123.5 (d, 2C), 65.9 (t, 1C), 41.4 (t, 1C); HRMS calcd. for $C_{24}H_{18}N_2O_5$ 437.1108, obsd. 437.1099.

*N-{4-[N-((ethyloxycarbonyl)methyl)carbamoyl]phenyl}phthalimide (**5bEt**)*

The compound was prepared according to the general procedure for the preparation of benzyl esters **5a** and **5b**, but the ethyl ester of glycine was used instead of the benzyl. The reaction furnished pure product (332 mg, 36 %).

Colourless solid; mp, 202−204 °C; IR (KBr) ν_{max}/cm^{-1}: 3421 (s), 3315 (s), 2916 (m), 1709 (s), 1639 (m), 1508 (m), 1389 (m), 1097 (w), 856 (w), 719 (m); ^{1}H NMR (300 MHz, CD_3OD) δ/ppm: 8.05−7.96 (m, 4H), 7.94−7.88 (m, 2H), 7.65 (d, J = 8.8 Hz, 2H), 4.25 (q, J = 7.1 Hz, 2H), 4.16 (s, 2H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ/ppm: 169.8 (s, 1C), 166.7 (s, 1/2C), 166.4 (s, 1/2C), 134.9 (s, 1C), 134.5 (d, 2C), 133.0 (s, 1C), 131.6 (s, 2C), 127.8 (d, 2C), 126.2 (d, 2C), 123.8 (d, 2C), 61.6 (t, 1C), 41.9 (t, 1C), 14.1 (q, 1C); HRMS calcd. for $C_{19}H_{16}N_2O_5$ 375.0951, obsd. 375.0948.

*Benzyl-2-{[3-(*N*-phthalimido)-1-adamantyl]carboxamido}acetate (**1bBz**)*

A round bottom flask was charged with 3-(*N*-phthalimido)-1-adamantane carboxylic acid (400 mg, 1.23 mmol), HBTU (490 mg, 1.29 mmol), TEA (351 μL, 2.52 mmol) and CH_2Cl_2 (3 mL), and stirred at rt for 10 min. Then, benzyl ester of glycine hydrochloride (231 mg, 1.29 mmol) was added and stirring was continued for 3 days. When the reaction was completed, brine (50 mL) was added, resulting in a white suspension which was extracted with diethyl ether (1×50 mL). The organic layer was washed with 1M HCl (50 mL), H_2O (50 mL), saturated $NaHCO_3$ (50 mL), and again with H_2O (50 mL), and dried over anhydrous $MgSO_4$. The solution was filtered and the solvent was removed on a rotary evaporator to afford the crude product that was purified by column chromatography on silica gel with 10 % EtOAc/CH_2Cl_2.

552 mg (95 %); colorless solid; mp, 136−138 °C; IR (KBr) ν_{max}/cm^{-1}: 3437 (m), 2941 (m), 2854 (m), 1709 (s), 1639 (m), 1522 (m), 1369 (m), 1318 (m), 1221 (m), 1080 (w), 974 (m), 839 (s), 756 (m), 723 (m), 642 (w); ^{1}H NMR (600 MHz, $CDCl_3$) δ/ppm: 7.73−7.70 (m, 2H), 7.66−7.62 (m, 2H), 7.36−7.24 (m, 5H), 6.35 (t, J = 5.0 Hz, 1H), 5.15 (s, 2H), 4.05 (d, J = 5.2 Hz, 2H), 2.60 (s, 2H), 2.54 (d, J = 12.0 Hz, 2H), 2.44 (d, J = 12.0 Hz, 2H), 2.28 (s, 2H), 1.92 (d, J = 12.2 Hz, 2H), 1.85 (d, J = 12.2 Hz, 2H), 1.75 (d, J = 12.6 Hz, 1H), 1.64 (d, J = 12.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ/ppm: 176.4 (s, 1C), 169.8 (s, 1/2C), 169.3 (s, 1/2C), 135.1 (s, 1C), 133.6 (d, 2C), 131.7 (s, 2C), 128.4 (d, 2C), 128.3 (d, 1C), 128.1 (d, 2C), 122.4 (d, 2C), 66.9 (t, 1C), 60.1 (s, 1C), 42.6 (s, 1C), 41.2 (t, 1C), 41.1 (t, 1C), 39.1 (t, 2C), 37.8 (t, 2C), 34.9 (t, 1C), 29.3 (d, 2C); HRMS calcd. for $C_{28}H_{28}N_2O_5$ 495.1890, obsd. 495.1885.

General Procedure for the Hydrogenolysis on Pd/C

In a vessel for hydrogenation was placed **5a** (500 mg, 1 mmol) or **5b** (500 mg, 1.2 mmol) and dissolved in a mixture of dry DMF (75 mL) and aps. EtOH (40 mL), and 10 % Pd/C (300 mg) was added. The hydrogenation was carried out, for 1 day at 55 psi. The crude reaction mixture was filtered, and the solvent was evaporated on a rotary evaporator. The residue was dissolved in EtOAc (20 mL) and extracted with 10 % $NaHCO_3$

(3×15 mL). Combined aqueous layers were acidified to pH 3 with 1M HCl, and then extracted with EtOAC (3×15 mL). The organic layers were dried over anhydrous $MgSO_4$, filtered and the solvent was removed. The pure product was obtained after crystallization from EtOAc/MeOH in a form of colourless crystals in ≈ 30 % yield.

*2-[4-(1-Oxoisoindolin-2-yl)benzamido]-3-phenylpro-panoic Acid (**6a**)*[40]
Colourless solid; ^{1}H NMR (300 MHz, d_6-DMSO) δ/ppm: 12.74 (br s, 1H), 8.66 (d, J = 7.5 Hz, 1H), 8.01 (d, J = 8.7 Hz, 2H), 7.89 (d, J = 8.7 Hz, 2H), 7.81 (d, J = 7.4 Hz, 1H), 7.72−7.67 (m, 2H), 7.57 (t, J = 7.0 Hz, 1H), 7.32−7.09 (m, 5H), 5.07 (s, 2H), 4.64−4.60 (m, 1H), 3.23−3.02 (m, 2H); ^{13}C NMR (75 MHz, d_6-DMSO) δ/ppm: 173.2 (s, 1C), 167.0 (s, 1C), 165.6 (s, 1C), 142.1 (s, 1C), 141.1 (s, 1C), 138.2 (s, 1C), 132.6 (d, 1C), 132.2 (s, 1C), 129.1 (d, 2C), 128.3 (d, 3C), 128.2 (d, 2C), 126.3 (d, 1C), 123.4 (d, 2C), 118.1 (d, 2C), 54.2 (d, 2C), 50.4 (t, 1C), 36.3 (t, 1C).

*2-[4-(1-Oxoisoindolin-2-yl)benzamido] acetic Acid (**6b**)*[39]
Colourless solid; ^{1}H NMR (300 MHz, d_6-DMSO) δ/ppm: 12.59 (s, 1H), 8.86 (t, J = 5.8 Hz, 1H), 8.07−7.95 (m, 4H), 7.85−7.52 (m, 4H), 3.94 (d, J = 5.8 Hz, 2H); ^{13}C NMR (75 MHz, d_6-DMSO) δ/ppm: 171.3 (s, 1C), 166.9 (s, 1C), 165.7 (s, 1C), 142.0 (s, 1C), 141.0 (s, 1C), 132.5 (d, 1C), 132.1 (s, 1C), 128.9 (s, 1C), 128.2 (d, 3/2C), 123.3 (d, 2/3C), 118.2 (d, 2C), 50.4 (t, 1C), 41.2 (t, 1C).

General Procedure for the Synthesis of Acids 3a and 3b

A two neck round bottom flask was charged with benzyl ester **5a** (500 mg, 1 mmol) or **5b** (500 mg, 1.2 mmol), 10 % Pd/C (100 mg) and abs MeOH (30 mL). The flask was closed with a septum and purged with nitrogen in order to remove air. The the suspension 10 equivalents of Et_3SiH were added during one hour. The reaction was monitored on TLC. After the reaction was finished, the reaction mixture was filtered, and the solvent was removed on a rotary evaporator. To the residue cold MeOH (25 mL) was added to precipitate the product. The product was filtered off through a Hirsch funnel and dried in a vacuum oven at 60 °C and 10 mbar.

N-*{4-[*N-*(1-carboxy-2-phenylethan-1-yl)carbamoyl]phenyl}phthalimide (**3a**)*[40]
267 mg (65 %); colourless solid; ^{1}H-NMR (600 MHz, d_6-DMSO) δ/ppm: 8.36 (d, J = 7.2 Hz, 1H, NH), 7.99−7.96 (m, 2H), 7.93−7.89 (m, 4H), 7.54 (d, J = 8.5 Hz, 2H), 7.32−7.29 (d, J = 7.3 Hz, 2H), 7.25 (t, J = 7.4 Hz, 2H), 7.16 (t, J = 7.3 Hz, 1H), 4.60−4.55 (m, 1H), 3.23 (dd, J = 4.2, 13.3 Hz, 1H), 3.07 (dd, J = 10.3, 13.3 Hz, 1H); ^{13}C NMR (75 MHz, d_6-DMSO) δ/ppm: 166.8 (s, 1C), 165.3 (s, 2C), 138.8 (s, 1C), 134.8 (d, 2C), 134.3 (s, 1C), 133.9 (s, 1C), 131.5 (s, 2C), 129.1 (d, 2C), 128.0 (d, 2C), 127.7 (d, 2C), 126.9 (d, 2C), 126.1 (d, 1C), 123.5 (d, 2C), 55.1 (d, 1C), 36.8 (t, 1C).

N-*{4-[*N-*(carboxymethyl)carbamoyl]phenyl}phthalimide (**3b**)*[41]
301 mg (77 %); colourless solid; ^{1}H NMR (600 MHz, CD_3OD) δ/ppm: 8.00 (d, 2H, J = 8.5 Hz), 7.99−7.96 (m, 2H), 7.91−7.87 (m, 2H), 7.62 (d, 2H, J = 8.5 Hz), 4,12 (s, 2H); ^{1}H NMR (600 MHz, d_6-DMSO) δ/ppm: 12.59 (br. s, 1H), 8.92 (t, J = 5.7 Hz, 1H), 8.06−7.90 (m, 6H), 7.59 (d, J = 8.4 Hz, 2H), 3.96 (d, J = 5.8 Hz, 2H); ^{13}C NMR (150 MHz, d_6-DMSO) δ/ppm: 171.1 (s, 1C), 166.7 (s, 2C), 165.5 (s, 1C), 134.8 (d, 2C), 134.5 (s, 1C), 133.2 (s, 1C), 131.5 (s, 2C), 127.8 (d, 2C), 126.9 (d, 2C), 123.5 (d, 2C), 41.3 (t, 1C).

General Procedure for the Synthesis of Decarboxylation Products 7a and 7b

A round bottom flask was charged with acid **4** (200 mg, 0.748 mmol), HBTU (298 mg, 0.786 mmol), TEA (for **7a** 0.104 mL, 0.748 mmol, 1 equivalent, and for **7b** 0.208 mL, 1.496 mmol, 2 equivalents) and DMF (10 mL), and stirred for 10 min. After activation of the acid, $HCl{\times}NH_2CH_3$ (50 mg, 0.748 mmol) or 2-phenylethylamine (94 μL, 0.748 mmol) was added. The reaction mixture was stirred at rt for 4 days. After the reaction was completed, DMF was removed on a rotary evaporator. To the crude reaction mixture brine (30 mL) and EtOAc (50 mL) were added. The product was suspended in a form of white solid between the aqueous and organic layer. After filtration of this mixture through a sinter, the precipitate was three times washed with ethyl acetate (3×15 mL) and dried over P_2O_5.

N-*{4-[*N-*(2-phenylethan-1-yl)carbamoyl]phenyl}phthalimide (**7a**)*[40]
275 mg (100 %); colourless solid; mp, 322−324°C, sublimation at 268−270 °C; ^{1}H NMR (600 MHz, d_6-DMSO) δ/ppm: 8.71 (s, 1H, NH), 8.01−7.91 (m, 6H), 7.55 (d, J = 8.2 Hz, 2H), 7.33−7.25 (m, 4H), 7.21 (t, J = 6.9 Hz, 1H), 3.53−3.51 (m, 2H), 2.88 (t, J = 7.4 Hz, 2H); ^{13}C NMR (150 MHz, d_6-DMSO) δ/ppm: 166.8 (s, 1C), 165.5 (s, 2C), 139.5 (s, 1C), 134.8 (d, 2C), 134.2 (s, 1C), 134.0 (s, 1C), 131.5 (s, 2C), 128.6 (d, 2C), 128.3 (d, 2C), 127.7 (d, 2C), 126.9 (d, 2C), 126.1 (d, 1C), 123.5 (d, 2C), 40.9 (t, 1C), 35.0 (t, 1C); HRMS calcd. for $C_{23}H_{18}N_2O_3$ 393.1209, obsd. 393.1206.

N-*{4-[(*N-*methyl)carbamoyl]phenyl}phthalimide (**7b**)*[40]
182 mg (87 %); colourless solid; mp, 303−305 °C, sublimation at 238−240°C; ^{1}H NMR (300 MHz, d_6-DMSO) δ/ppm: 8.56 (d, J = 4.5 Hz, 1H), 8.04−7.87 (m, 6H), 7.55 (d, J = 8.6 Hz, 2H), 2.81 (d, J = 6.4 Hz, 3H); ^{1}H

NMR (300 MHz, MeOD) δ/ppm: 8.01−7.95 (m, 4H), 7.93−7.90 (m, 2H), 7.64−7.60 (m, 2H), 2.94 (s, 3H); ^{13}C NMR (150 MHz, MeOD) δ/ppm: 170.1 (s, 1C), 168.4 (s, 2C), 137.8 (s, 1C), 135.9 (d, 2C), 133.1 (s, 2C), 128.8 (d, 2C), 127.7 (d, 2C), 124.7 (d, 2C), 27.0 (q, 1C), one singlet (1C) is not detected; HRMS calcd. for $C_{16}H_{12}N_2O_3$ 303.0740, obsd. 303.0744.

N-*[3-(*N-*methyl)carbamoyl-1-adamantyl]phthalimide* ***(8b)***

A round bottom flask was charged with a solution of methylamine hydrochloride (62 mg, 0.922 mmol), TEA (257 μL, 1.844 mmol) and THF (5 mL). To the solution succinimide (428 mg, 1.014 mmol) was added during 30 minutes. The reaction was conducted at rt for 2 days. The solvent was removed on a rotary evaporator and 0.5M HCl (10 mL) was added. The extraction with ethyl acetate (3×10 mL) was carried out, and the extracts were dried over $MgSO_4$. After filtration and removal of the solvent the crude product was obtained that was purified by column chromatography on silicagel with CH_2Cl_2 and 2−5 % MeOH/CH_2Cl_2 as eluent, and cristallization from hexane/CH_2Cl_2/MeOH mixture. The pure product was isolated in a form of colourless crystals.

73 mg (23 %); colourless crystals; mp, 205−207 °C; IR (KBr) ν_{max}/cm^{-1}: 3348 (m), 2914 (m), 2850 (m), 1707 (s), 1635 (m), 1541 (m), 1466 (w), 1364 (m), 1313 (m), 1078 (m), 974 (w), 872 (w), 719 (m), 640 (w), 534 (w); ^{1}H NMR (600 MHz, CD_3OD) δ/ppm: 7.73 (s, 4H), 2.85−2.68 (m, 3H), 2.58−2.53 (m, 4H), 2.47 (d, J = 12.2 Hz, 2H), 2.27 (br. s, 2H), 1.91 (d, J = 12.4 Hz, 2H), 1.87−1.78 (m, 3H), 1.70 (d, J = 1.8 Hz, 1H); ^{13}C NMR (75 MHz, d_6-DMSO) δ/ppm: 176.1 (s, 1C), 169.0 (s, 2C), 134.3 (d, 2C), 131.2 (s, 2C), 122.5 (d, 2C), 59.8 (s, 1C), 42.0 (s, 1C), 41.2 (t, 1C), 38.8 (t, 2C), 37.6 (t, 2C), 34.8 (t, 1C), 29.0 (q, 1C), 25.9 (d, 2C); HRMS, calcd. for $C_{20}H_{22}N_2O_3$ 339.1703, obsd. 339.1707.

Stability of Phthalimides in the Presence of K_2CO_3

To the solutions of **1b** and **3b** in CH_3CN-H_2O (3:1, c = 1×10^{-3} M) were added aqueos solutions of K_2CO_3 to reach the final concentration of K_2CO_3 $c = 1\times10^{-3}$ M or 1×10^{-2} M. The UV-vis spectra were recorded prior to the addition of base, and afterwards in the intervals of 1 hour (see the supporting info.).

Irradiation Experiments, General

In a quartz vessel a solutions of acids **1a**, **1b**, **3a**, or **3b** (c ≈ 5−7 × 10^{-3} M) and 0.5 equivalents of K_2CO_3 in acetone-H_2O (3:1) or CH_3CN-H_2O (3:1) were prepared. After purging with N_2 for 20 minutes, the solutions were irradiated at 300 nm in a Luzchem reactor with 8 lamps. During the irradiation the solution was cooled with a fan equipped in the reactor. After irradiation, solvent was removed by evaporation, and crude reaction mixture was chromatographed on column and/or thin layer of silica gel.

Decarboxylation product **8b** (5 mg, 5 %) was isolated from the crude photoreaction mixture after several column chromatographies on silicagel EtOAc/CH_2Cl_2 and MeOH/EtOAc as eluent, and rechromatography on TLC with EtOAc/MeOH/CH_2Cl_2 (5:10:85).

Glycine derivatives **12a** and **13a** were isolated after preparative thin layer chromatography of the crude photoreaction mixture on silica gel with CH_2Cl_2/TFA/MeOH (30:0.07:69.93).

*2,12-Diaza-10-methoxy-hexacyclo[12.5.1.1^{1,16}.1^{14,18}.0^{4,9}]doeicosa-4,6,8-trien-3,13-dion (**9b**)*

Colourless oil; IR (KBr) ν_{max}/cm^{-1}: 3421 (s), 2917 (m), 2852 (m), 2361 (m), 1718 (m), 1654 (m), 1399 (w), 1314 (w), 1090 (w), 668 (w); ^{1}H NMR (600 MHz, CD_3OD) δ/ppm: 7.89 (dd, J = 0.6, 7.7 Hz, 1H), 7.59 (td, J = 7.6, 1.2 Hz, 1H), 7.50 (td, J = 7.7, 1.2 Hz, 1H), 7.42 (dd, J = 0.6, 7.6 Hz, 1H), 3.88 (s, 3H), 3.73 (s, 2H), 2.26−2.20 (m, 7H), 2.11 (d, J = 11.2 Hz, 2H), 1.91 (d, J = 12.1 Hz, 2H), 1.88 (d, J = 12.1 Hz, 2H), 1.76 (d, J = 12.5 Hz, 1H), 1.71 (d, J = 12.5 Hz, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ/ppm: 178.9 (s, 1C), 171.9 (s, 1C), 168.5 (s, 1C), 140.8 (s, 1C), 133.2 (d, 1C), 131.0 (d, 1C), 130.2 (d, 1C), 129.9 (s, 1C), 128.9 (d, 1C), 54.0 (s, 1C), 52.8 (q, 1C), 44.8 (t, 1C), 43.8 (s, 1C), 43.6 (t, 1C), 41.2 (t, 2C), 39.2 (t, 2C), 36.5 (t, 1C), 30.9 (d, 2C).

*2,12-Diaza-pentacyclo[12.5.1.1^{1,16}.1^{14,18}.0^{4,9}]doeicosa-4,6,8-trien-3,10,13-trion (**2b**)*

Colourless oil; IR (KBr) ν_{max}/cm^{-1}: 3394 (s), 2916 (s), 2850 (m), 1617 (s), 1593 (s), 1566 (s), 1388 (m), 1321 (w), 718 (w), 608 (w); ^{1}H NMR (300 MHz, CD_3OD) δ/ppm: 7.61−7.50 (m, 2H), 7.46−7.33 (m, 2H), 3.74 (s, 2H), 2.32 (s, 2H), 2.27−2.06 (m, 6H), 1.93−1.88 (m, 4H), 1.81−1.68 (m, 2H); ^{13}C NMR (75 MHz, CD_3OD) δ/ppm: 187.7 (s, 1C), 179.1 (s, 1C), 171.7 (s, 1C), 140.8 (s, 1C), 136.1 (s, 1C), 130.6 (d, 1C), 129.1 (d, 1C), 129.0 (d, 1C), 128.9 (d, 1C), 53.8 (s, 1C), 44.7 (s, 1C), 43.8 (t, 1C), 43.1 (t, 1C), 41.3 (t, 2C), 39.2 (t, 2C), 36.6 (t, 1C), 30.8 (d, 2C).

Irradiation in the Presence of Acrylonitrile

A quartz vessel was charged with a solution of **1a**, **1b**, **3a** or **3b** (10 mg/20 mL) in acetone-water (3:1), and 0.5 equivalents of K_2CO_3 were added. The solution was purged with N_2 for 15 minutes. After the purging, acrylonitrile (100 μL) was added and the solution was irradiated at 300 nm in Luzchem reactor (8 lamps) for 10−30 min. After the irradiation, the solvent was removed on a rotary evaporator and ^{1}H NMR spectrum was recorded.

Irradiation in the Presence of Potassium Sorbate

A solution of **1b** in CH_3CN-water (3:1, 10 mg/20 mL) was placed to three quartz cuvettes (5 mL to the each cuvette. To the cuvettes an aqueous solution of K_2CO_3 (0.5 equivalents) and potassium sorbate were added, and the solutions were diluted with CH_3CN-water (3:1) to reach the final concentrations of **1b**, $c = 7 \times 10^{-4}$ M, and the sorbate in the concetrations 0, 0.010 M and 0.035 M. The solutions were purged with N_2 for 15 minutes and irradiated at 300 nm in Luzchem reactor (6 lamps) for 30 min. After the irradiation, the solvent was removed on a rotary evaporator and ^{1}H NMR spectra were recorded.

Determination of the Decarboxylation Quantum Yields in CH_3CN-H_2O

In four quartz cuvettes (25 mL) was placed a solution of **1a**, **1b**, **3a**, and **3b** in CH_3CN-H_2O (3:1), and K_2CO_3 (0.5 equivalents) was added. To the fifth cuvette was placed a solution of actinometer, valerophenone in CH_3CN-H_2O (formation of acetophenone in aqueous solution $\Phi = 0.65 \pm 0.03$).[33] Concentrations of the solutions were adjusted to have absorbance at 254 nm in the range 0.6−0.8. The solutions were purged with nitrogen for 15 min, and irradiated at the same time in a Luzchem reactor (1 or 2 lamps, 254 nm) for 30 s, 1 min, or 20−60 min in the case of **4a,b**, and **5a,b**. During the irradiations small aliquots of the photoreaction mixture were taken by use of a syringe and analysed by HPLC.

Determination of Photoreaction Quantum Yields in Acetone-H_2O

In four quartz cuvettes (25 mL) was placed a solution of **1a**, **1b** (5×10^{-3} mol/L), **3a**, and **3b** (2.5×10^{-3} mol/L) in acetone-H_2O (3:1), 0.5 equivalents of K_2CO_3 was added. To the fifth cuvette was placed a solution of actiometer 6-[(*N*-phthalimido)methyl]cyclohexane carboxylic acid (5×10^{-3} mol/L, formation of cyclic product, $\Phi_R = 0.3$).[34] After 20 minutes of purging with nitrogen, the solutions were irradiated at 300 nm in a Luzchem photoreactor (3 lamps) for 3, 6 and 21 min. After each irradiation, a small aliquot of the photolysis mixture was taken, solvent was removed on a rotary evaporator and the residue analyzed by HPLC and ^{1}H NMR.

Laser Flash Photolysis (LFP)

LFP facility employing a YAG laser, with a pulse width of 10 ns and excitation wavelength 266 nm. Static cells (0.7 cm) were used and solutions were purged with nitrogen or oxygen for 20 min prior to measurements. Absorbances at 266 nm were ≈ 0.4−0.6.

Supplementary Materials. – Supporting informations to the paper are enclosed to the electronic version of the article. These data can be found on the website of *Croatica Chemica Acta* (http://public.carnet.hr/ccacaa).

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REFERENCES

1. M. Lukeman, Photodecarboxylation of arylacetic acids, in: *CRC Handbook of Organic Photochemistry and Photobiology*, 3rd ed. Eds.: A. G. Griesbeck, M. Oelgemöller, F. Ghetti, CRC Press, Boca Raton 2012, pp. 715−726.
2. a) D. H. R. Barton, P. Blundell, J. C. Jaszberenyi, *J. Am. Chem. Soc*., **113** (1991) 6937−6942; b) P. I. Dalko, The photochemistry of Barton esters In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed. Eds. W. Horspool, F. Lenci, CRC Press, Boca Raton, Fl 2004, chapter 67.
3. a) T. Minabe, D. A. Tryk, P. Sawunyama, Y. Kikuchi, K. Hashimoto, and A. Fujishima, *J. Photochem. Photobiol A: Chem*. **137** (2000) 53−62; b) M. Tamimi, S. Qourzal, A. Assabbane, J. M. Chovelon, C. Ferronato, and Y. Ait-Ichou, *Photochem. Photobiol. Sci*. **5** (2006) 477−482.
4. F. Boscá, M. L. Marín, and M. A. Miranda, *Photochem. Photobiol*. **74** (2001) 637−655.
5. a) T. O. Meiggs and S. I. Miller, *J. Am. Chem. Soc*. **94** (1972) 1989−1996; G. A. Epling and A. Lopes, *J. Am. Chem. Soc*. **99** (1977) 2700−2704.
6. F. Boscá, M. A. Miranda, G. Carganico, and D. Mauleón, *Photochem. Photobiol*. **60** (1994) 96−101.
7. G. Cosa, M. Lukeman, and J. C. Scaiano, *Acc. Chem. Res*. **42** (2009) 599−607.
8. a) S. Monti, S. Sortino, G. De Guidi, and G. Marconi, *J. Chem. Soc. Faraday Trans*. **93** (1997) 2269−2275; b) G. Cosa, L. J. Martínez, and J. C. Scaiano, *Phys. Chem. Chem. Phys*. **1** (1999) 3533−3537; c) M.-D. Li, C. S. Yeung, X. Guan, J. Ma, W. Li, C. Ma, and D. L. Phillips, *Chem Eur. J*. **17** (2011) 10935−10950.
9. M. Laferrière, C. N. Sanramé, and J. C. Scaiano, *Org. Lett*. **6** (2004) 873−875.
10. a) Z.-G. Le, Z.-C. Chen, Y. Hu, and Q.-G. Zheng, *Synthesis* (2004) 208−202; b) S. E. Sen and S. L. Roach, *Synthesis* (1995) 756−758; c) J. O. Osby, M. G. Martin, and B. Ganem, *Tetrahedron Lett*. **25** (1984) 2093−2096.
11. a) Y. Shibata, K. Sasaki, Y. Hashimoto, and S. I. Iwasaki, *Chem. Pharm. Bull*. **44** (1996) 156-162. b) S. H. L. Kok, R. Gambari, C. H. Chui, M. C. W. Yuen, E. Lin, R. S. M. Wong, F. Y. Lau, G. Y. M. Cheng, W. S. Lam, S. H. Chan, K. H. Lam, C. H. Cheng, P. B. S. Lai, M. W. Y. Yu, F. Cheung, J. C. O. Tang, and A. S. C. Chan, *Bioorg. Med. Chem*. **16** (2008) 3626−3631; c) Y. Shibata, M. Shichita, K. Sasaki, K. Nishimura, Y. Hashimoto, and S. Iwasaki, *Chem. Pharm. Bull*. **43** (1995) 177−179; d) K. Sasaki, Y. Shibata, K. Nishimura, Y. Hashimoto, and S. Iwasaki, *Biol. Pharm. Bull*. **17** (1994) 1313−1315; e) A. Orzesko, R. Gralewska, B. J. Starosciak, and Z. Kazimierczuk, *Acta Biochimica Polonica* **47** (2000) 87-94; f) A. Orzeszko, B. Kaminska, G. Orzeszko, and B. J. Starosciak, *Il Farmaco* **55** (2000) 619-623; g) J. Vamecq, K. Van Derpoorten, J. H. Poupaert, J. Balzarini, E. De Clercq, and J. P. Stables, *Life Sciences* **63** (1998) 267-274; h) V. L. M. Sena, R. M. Srivastava, R. O. Silva, and V. L. M. Lima, *Il*

Farmaco **58** (2003) 1283–1288; i) J. M. Chapman Jr., G. H. Cocolas, and I. H. Hall, *J. Med. Chem.* **22** (1979) 1399–1402; j) J. M. Chapman Jr., G. H. Cocolas, and I. H. Hall, *J. Pharm. Sci.* **72** (1983) 1344–1347.

12. a) A. G. Griesbeck, W. Kramer, and M. Oelgemöller, *Synlett* (1999) 1169–1178; b) A. G. Griesbeck, N. Hoffmann, and K.-D. Warzecha, *Acc. Chem. Res.* **40** (2007) 128–140; c) M. Horvat, K. Mlinarić-Majerski, and N. Basarić, *Croatica Chem Acta*, **83** (2010) 179–188.
13. a) P. H. Mazzocchi, F. Khachik, and P. Wilson, *J. Am. Chem. Soc.* **103** (1981) 6498–6499; b) P. H. Mazzocchi, and L. Klinger, *J. Am. Chem. Soc.* **106** (1984) 7567–7572; c) P. H. Mazzocchi, S. Minamikawa, and P. Wilson, *J. Org. Chem.* **50** (1985) 2681–2684; d) G. McDermott, D. J. Yoo, and M. Oelgemöller, *Heterocycles* **65** (2005) 2221–2257.
14. a) Y. Kanaoka, Y. Migita, and K. Koyama, *Tetrahedron Lett* (1973) 1193–1196; b) Y. Kanaoka and C. Nagasawa, *Heterocycles* **3** (1975) 553–556; c) Y. Kanaoka, *Acc. Chem. Res.* **11** (1978) 407–413; d) A. G. Griesbeck and H. Mauder, *Angew. Chem. Int. Ed. Engl.* **31** (1992) 73–75; e) A. G. Griesbeck, *Liebigs Ann.* (1996) 1951–1955; f) N. Basarić, M. Horvat, K. Mlinarić-Majerski, E. Zimmernann, J. Neudörfl, and A. G. Griesbeck, *Org. Lett.* **10** (2008) 18, 3965–3968; g) M. Horvat, H. Görner, K.-D. Warzecha, J. Neudorfl, A. G. Griesbeck, K. Mlinarić Majerski, and N. Basarić; *J. Org. Chem.* **74** (2009) 8219–8231; h) N. Basarić, M. Horvat, O. Franković, K. Mlinarić-Majerski, J. Neudörfl, and A. G. Griesbeck, *Tetrahedron* **65** (2009) 1438–1444; j) N. Cindro, M. Horvat, K. Mlinarić-Majerski, A. G. Griesbeck, and N. Basarić, *Beilstein J. Org. Chem.* **7** (2011) 270–277; k) N. Cindro, I. Halasz, K. Mlinarić-Majerski, and N. Basarić, *Eur. J. Org. Chem.* (2013) 929–938.
15. a) U. C. Yoon and P. S. Mariano, *Acc. Chem. Res.* **34** (2001) 523–533; b) M. Oelgemöller and A. G. Griesbeck, *J. Photochem. Photobiol. C: Photochem. Rev.* **3** (2002) 109–127.
16. a) A. G. Griesbeck and M. Oelgemöller, *Synlett* (1999) 492–494; b) M. Oelgemöller and A. G. Griesbeck, *Single-Electron-Transfer Processes in Phthalimide Systems*, in: *CRC Handbook of Organic Photochemistry and Photobiology*, W. M. Horspool and F. Lenci (Eds.), CRC Press, Boca Raton, FL, 2004; p. 1–19; c) K.-D. Warzecha, H. Görner, and A. G. Griesbeck; *J. Phys. Chem. A* **110** (2006) 3356–3363.
17. a) U. C. Yoon, S. W. Oh, J. H. Lee, J. H. Park, K. T. Kang, and P. S. Mariano, *J. Org. Chem.* **66** (2001) 939–943; b) U. C. Yoon, Y. X. Jin, S. W. Oh, C. H. Park, J. H. Park, C. F. Campana, X. Cai, E. N. Duesler, and P. S.Mariano, *J. Am. Chem. Soc.* **125** (2003) 10664–10671; c) U. C. Yoon, H. C. Kwon, T. G. Hyung, K. H. Choi, S. W. Oh, S. Yang, Z. Zhao, and P. S. Mariano, *J. Am. Chem. Soc.* **126** (2004) 1110–1124; d) U. C. Yoon, P. S. Mariano, *The Photochemistry of Silicon Substituted Phthalimides*, In *CRC Handbook of Organic Photochemistry and Photobiology*, W. M. Horspool and F. Lenci (Eds.), CRC Press, Boca Raton, FL, 2004; 85, p.–15; e) U. C. Yoon and P. S. Mariano, *Mechanistic and Synthetic Aspects of SET-Promoted Photocyclization Reactions of Silicon Substituted Phthalimides*, In *Organic Photochemistry and Photophysics*, V. Ramamurthy, K. Schanze (Eds.), CRC Press, Taylor & Francis Group, Boca Raton, FL, 2006; p. 179–206; f) D. W. Cho, J. H. Choi, S. W. Oh, C. Quan, U. C. Yoon, R. Wang, S. Yang, and P. S. Mariano, *J. Am. Chem. Soc.* **130** (2008) 2276–2284.
18. a) A. G. Griesbeck, A. Henz, K. Peters, E.-M. Peters, and H. G. von Schnering, *Angew. Chem. Int. Ed.* **34** (1995) 474–476; b) A. G. Griesbeck, A. Henz, W. Kramer, J. Lex, F. Nerowski, M. Oelgemöller, K. Peters, and E.-M. Peters, *Helv. Chim. Acta* **80** (1997) 912–933; c) A. G. Griesbeck, F. Nerowski, and J. Lex, *J. Org. Chem.* **64** (1999) 5213–5216; d) A. G. Griesbeck, M. Oelgemöller, J. Lex, A. Haeusler, and M. Schmittel, *Eur. J. Org. Chem.* (2001) 1831–1843; e) A. G. Griesbeck, W. Kramer, T. Heinrich, and J. Lex, *Photochem. Photobiol. Sci.* **1** (2002) 237–239.
19. a) A. G Griesbeck, T. Heinrich, M. Oelgemöller, J. Lex, and A. Molis, *J. Am. Chem. Soc.* **124** (2002) 10972–10973; b) A. G. Griesbeck, T. Heinrich, M. Oelgemoller, A. Molis, and A. Heidtmann, *Helv. Chim. Acta* **85** (2002) 4561–4578.
20. a) A. Soldevilla and A. G. Griesbeck, *J. Am. Chem. Soc.* **128** (2006) 16472–16473; b) A. Soldevilla, R. Pérez-Ruiz, Y. Díaz Miara, and A. G. Griesbeck, *Chem. Commun.* **46** (2010) 3747–3749.
21. a) F. Hatoum, S. Gallager, and M. Oelgemöller, *Tetrahedron Lett.* **50** (2009) 6593–6596; b) F. Hatoum, J. Engler, C. Zelmer, J. Wißen, C. A. Motti, J. Lex, and M. Oelgemöller, *Tetrahedron Lett.* **53** (2012) 5573–5577.
22. a) F. Hatoum, S. Gallagher, L. Baragwanath, J. Lex, and M. Oelgemöller, *Tetrahedron Lett.* **50** (2009) 6335–6338; b) V. Belluau, P. Noeureuil, E. Ratzke, A. Skvortsov, S. Gallagher, C. A. Motti, and M. Oelgemöller, *Tetrahedron Lett.* **51** (2010) 4738–4741.
23. S. Gallagher, F. Hatoum, N. Zientek, and M. Oelgemöller, *Tetrahedron Lett.* **51** (2010) 3639–3641.
24. Y.-J. Lee, D.-H. Ahn, K. S. Lee, A. R. Kim, D. J. Yoo, and M. Oelgemöller, *Tetrahedron Lett.* **52** (2011) 5029–5031.
25. O. Shvydkiv, S. Gallagher, K. Nolan, and M. Oelgemöller, *Org. Lett.* **12** (2010) 5170–5173.
26. M. Horvat, K. Mlinarić-Majerski, A. G. Griesbeck, and N. Basarić, *Photochem. Photobiol. Sci.* **10** (2011) 610–617.
27. T. Šumanovac Ramljak, M. Sohora, I. Antol, D. Kontrec, N. Basarić, and K. Mlinarić-Majerski, *Tetrahedron Lett.* **55** (2014) 4078–4081.
28. a) M. Terashima, K. Koyama, and Y. Kanaoka, *Chem. Pharm. Bull.* **26** (1978) 630–632; b) Y. Kanaoka, C. Nagasawa, H. Nakai, Y. Sato, H. Ogiwara, and T. Mizoguchi, *Heterocycles* **3** (1975) 553–556.
29. V. Dourtoglov and B. Gross, *Synthesis* (1984) 572–575.
30. P. K. Mandal and J. S. McMurray, *J. Org. Chem.* **72** (2007) 6599–6601.
31. a) M. Montalti, A. Credi, L. Prodi, and M. Teresa Gandolfi, *Handbook of Photochemistry*, 3rd ed. Taylor & Francis, Boca Raton, 2006; b) A. C. Velosa, W. J. Baader, C. V. Stevani, C. M. Mano, and E. J. H. Bechara, *Chem. Res. Toxicol.* **20** (2007) 1162–1169; c) B. P. Ngoy, P. Šebej, T. Šolomek, B. H. Lim, T. Pastierik, B. S. Park, R. S. Givens, D. Heger, and P. Klán, *Photochem. Photobiol. Sci.* **11** (2012) 1465–1475.
32. Y. Ren, Z. Wang, H. Zhu, S. J. Weininger, and W. G. McGimpsey, *J. Am. Chem. Soc.* **117** (1995) 4367–4373.
33. a) V. Wintgens, P. Valat, J. Kossanyi, L. Biczok, A. Demeter, and T. Bérces, *J. Chem. Soc. Faraday Trans.* **90** (1994) 411–421; b) A. G. Griesbeck and H. Görner, *J. Photochem. Photobiol. A: Chem.* **129** (1999) 111–119.
34. a) P. J. Wagner, *J. Am. Chem. Soc.* **89** (1967) 5898–5901; b) H. J. Kuhn, S. E. Braslavsky, and R. Schmidt, *Pure Appl. Chem.* **76** (2004) 2105–2146; c) R. G. Zepp, M. M. Gumz, W. L. Miller, and H. Gao, *J. Phys. Chem. A* **102** (1998) 5716–5723.
35. a) H. Görner, A. G. Griesbeck, T. Heinrich, W. Kramer, and M. Oelgemöller, *Chem. Eur. J.* **7** (2001) 1530–1538; b) H. Görner, M. Oelgemöller, and A. G. Griesbeck, *J. Phys. Chem. A* **106** (2002) 1458–1464.
36. C. E. Hoyle, E. T. Anzures, P. Subramanian, R. Nagarajan, and D. Creed, *Macromolecules* **25** (1992) 6651–6657.
37. D. V. Bent and E. Hayon, *J. Am. Chem. Soc.* **97** (1975) 2606–2612.
38. G. Vanags and A. Veinbergs, *Ber. Dtsch. Chem. Ges.* B **75B** (1942) 1558–1569.
39. Y. Tsuruta and K. Kobashi, *Jpn. Kokai Tokkyo Koho* (1987), JP 62198658 A 19870902

40. a) N. S. Khalaf, A. Ragab El-Sayed, H. A. Eyada, and H. M. Hassan, *Al-Azhar Bull. Sci.* **7** (1996) 1251−1259; b) A. Ragab El-Sayed, N. S. Khalaf, and H. M. Hassan, *Proc. Indian Nat. Sci. Acad., A: Phys. Sci.* **63** (1997) 337−344.
41. A. H. Bedair, R. Q. Lamphon, and S. S. Ghazal*; J. Serbian Chem. Soc*. **52** (1987) 477−486.

Supporting information

for

Photodecarboxylation of *N*-Adamantyl- and *N*-Phenylphthalimide Dipeptide Derivatives

By

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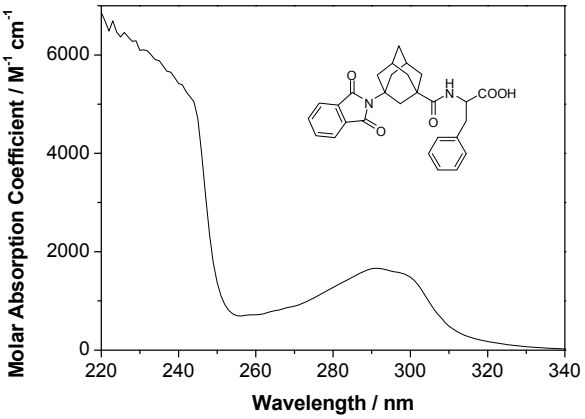
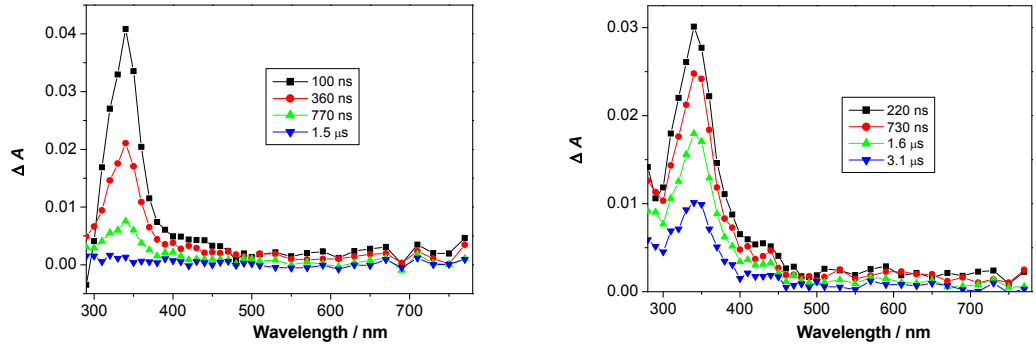
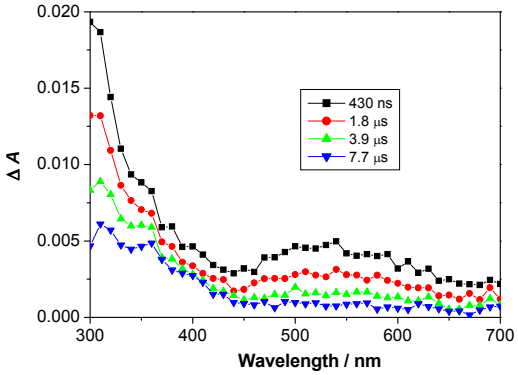
1. UV-vis Spectra and Laser Flash Photolysis



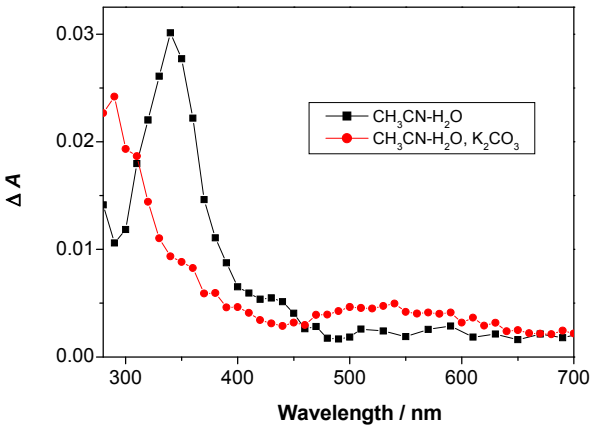
Absorption spectrum of **1a** in CH_3CN.



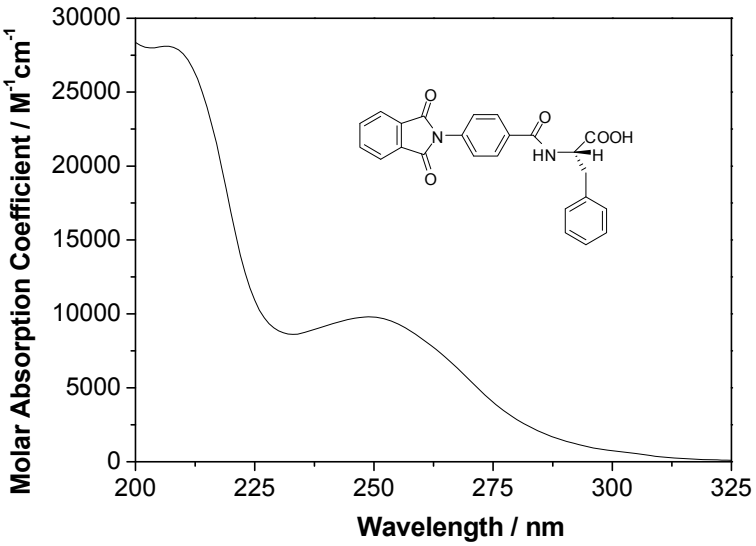
Transient absorption spectra of **1a** in N_2-purged CH_3CN (left) and CH_3CN-H_2O (1:1) (right).



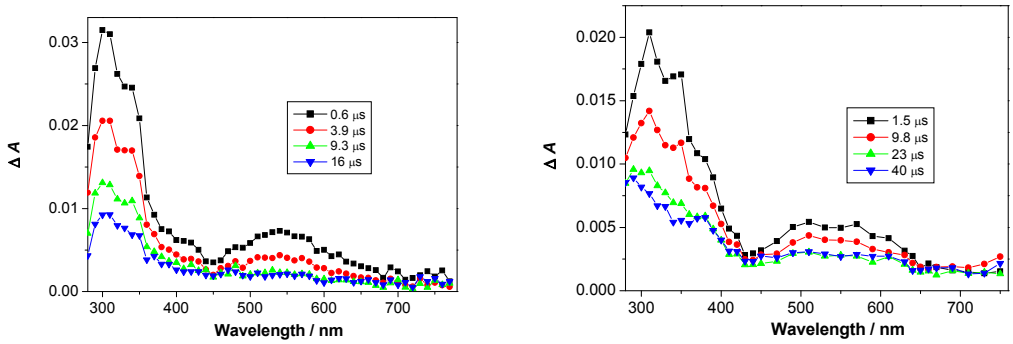
Transient absorption spectra of **1a** in N_2-purged CH_3CN-H_2O (1:1) in the presence of K_2CO_3 c = 0.01 M.



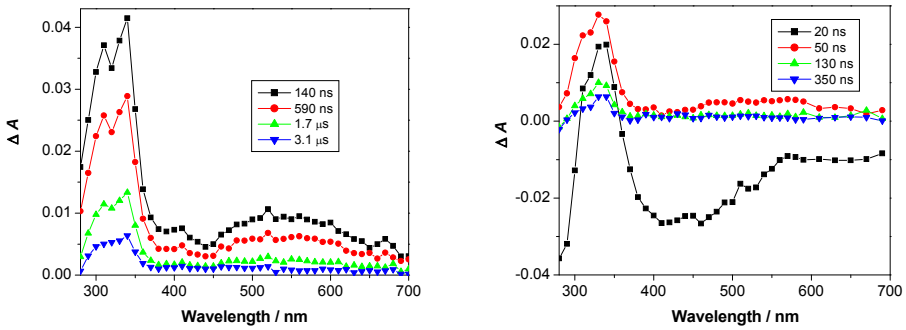
Transient absorption spectra of **1a** in N_2-purged CH_3CN-H_2O (1:1) at pH 7 and in the presence of K_2CO_3 c = 0.01 M.



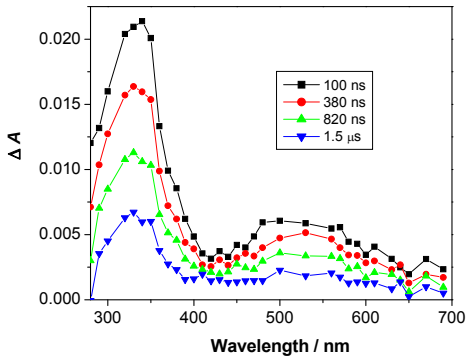
Absorption spectrum of **3a** in CH_3CN.



Transient absorption spectra of **3a** in N_2-purged CH_3CN (left) and CH_3CN-H_2O (1:1) (right).



Transient absorption spectra of the **3a** in N_2-purged CH_3CN (left) and O_2-purged CH_3CN (right).



Transient absorption spectra of **3a** derivative in N_2-purged CH_3CN-H_2O (1:1).

2. Stability of phthalimides in basic conditions

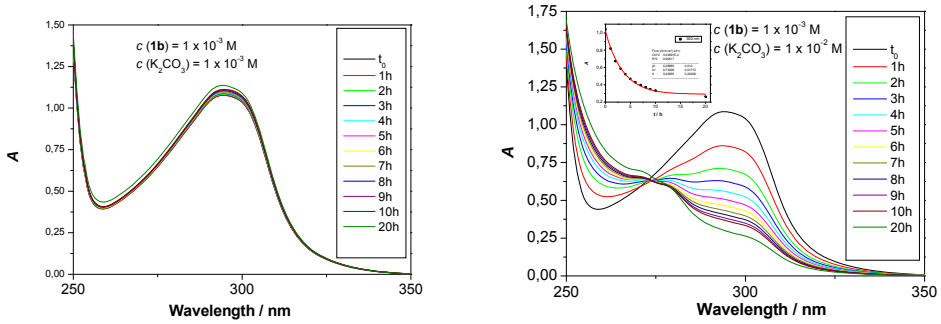


Fig. Absorption spectra of **1b** in CH_3CN-H_2O ($c = 1\times10^{-3}$ M) in the presence of K_2CO_3 (left, $c = 1\times10^{-3}$ M; right $c = 1\times10^{-2}$, inset: dependence of the absorbance at 300 nm)

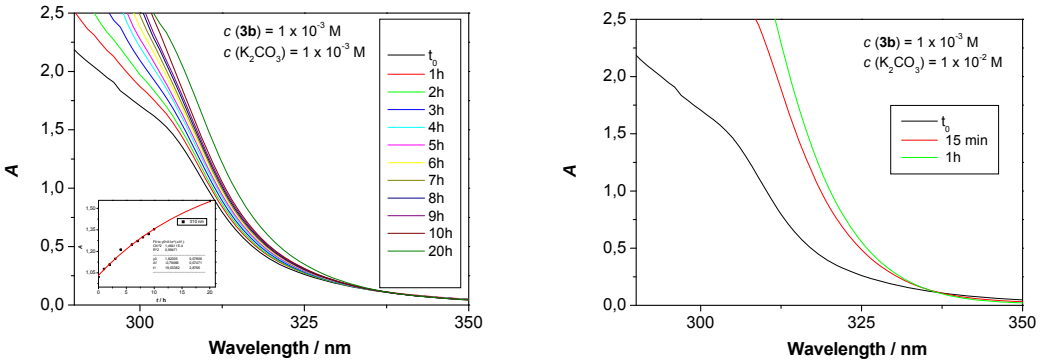
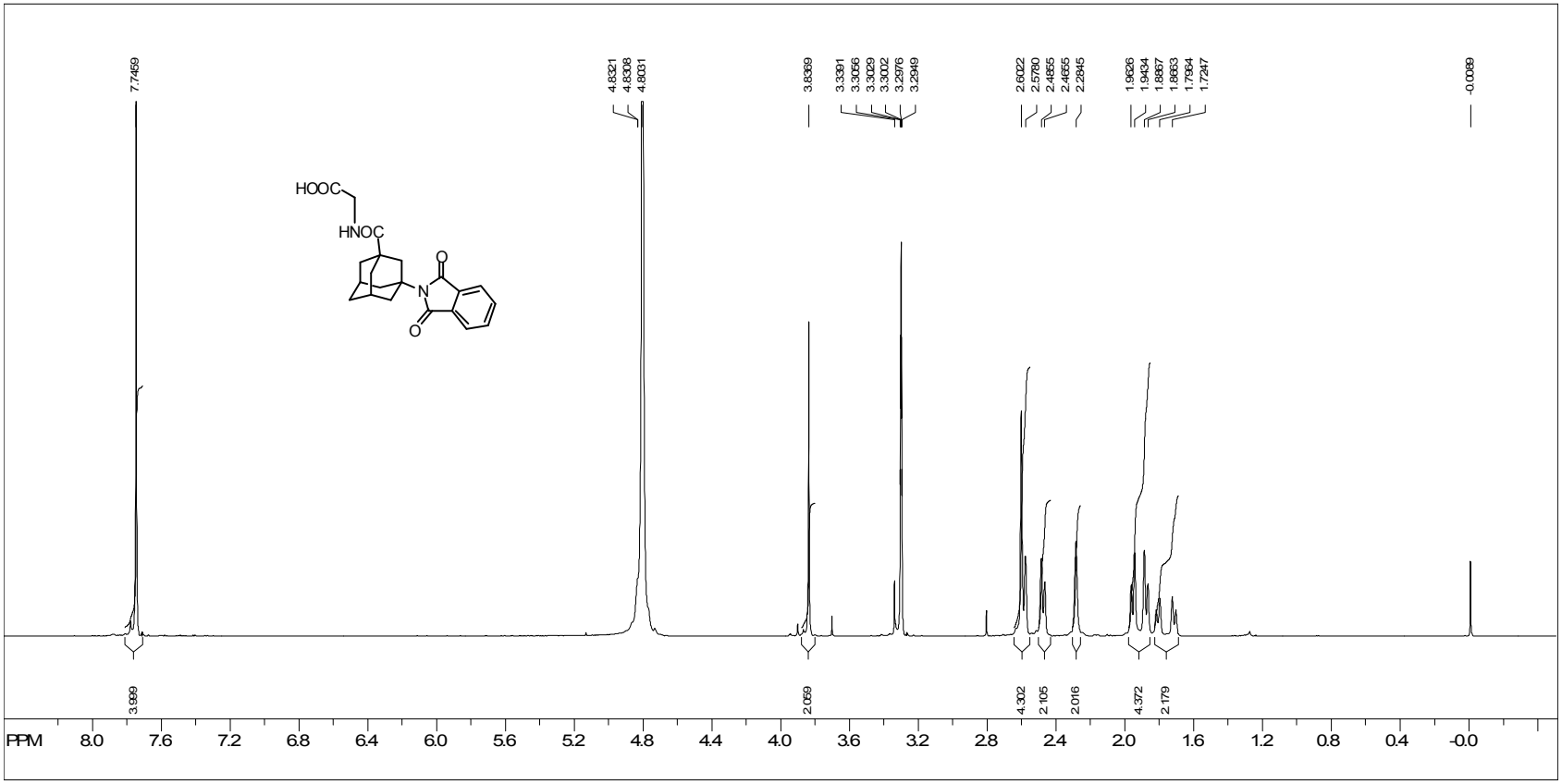
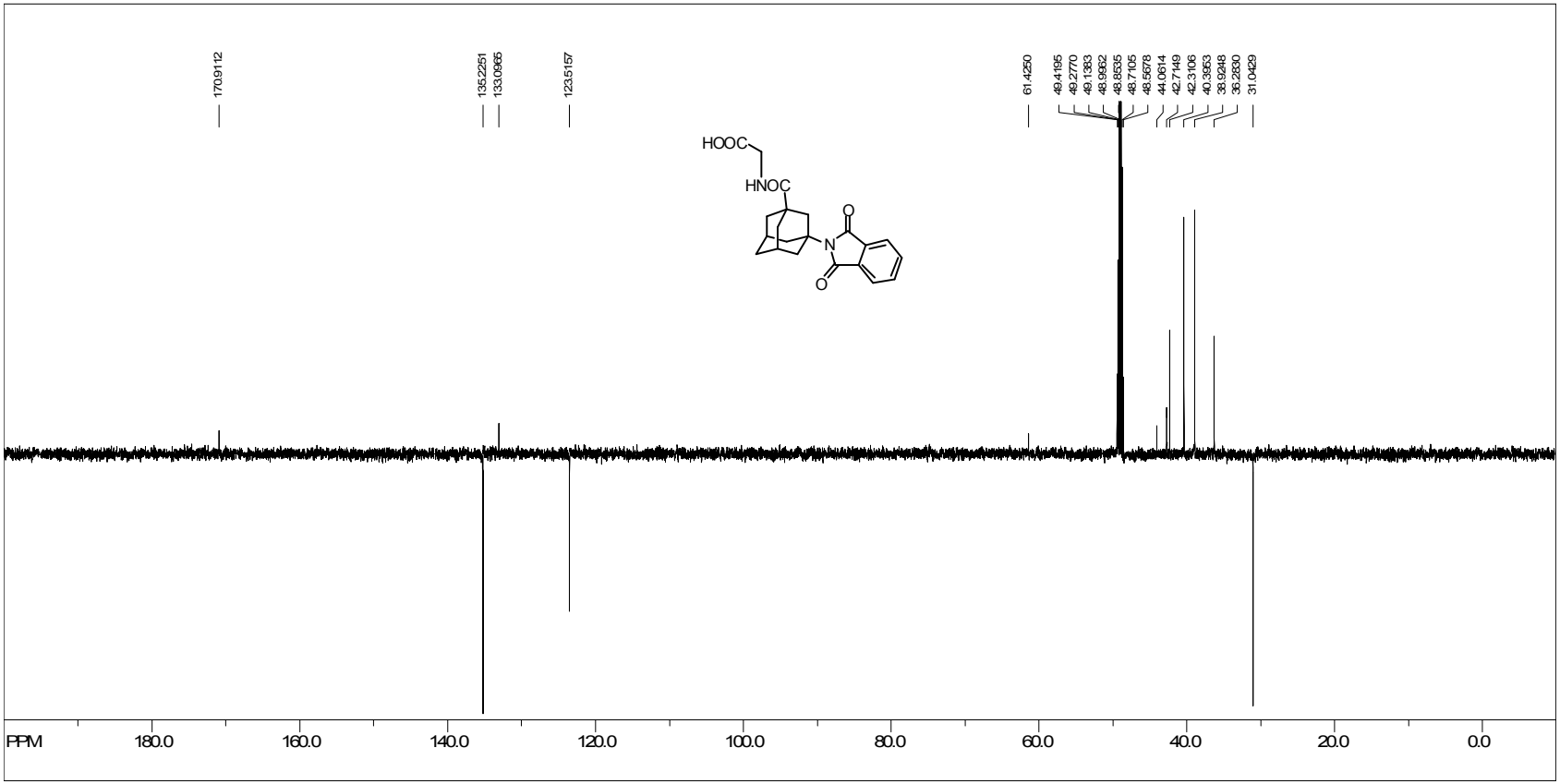


Fig. Absorption spectra of **3b** in CH_3CN-H_2O ($c = 1\times10^{-3}$ M) in the presence of K_2CO_3 (left, $c = 1\times10^{-3}$ M, inset: dependence of the absorbance at 310 nm; right $c = 1\times10^{-2}$)

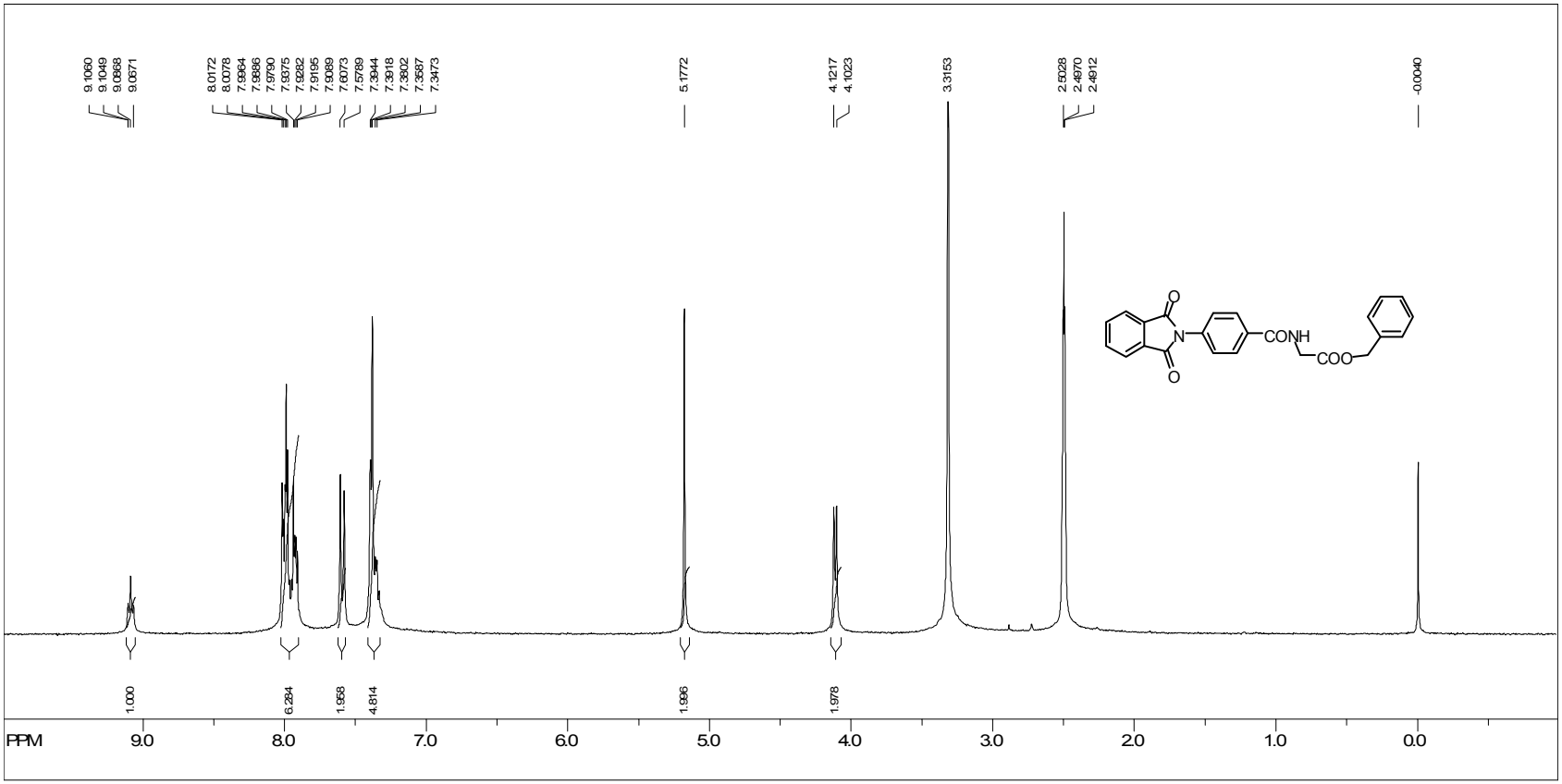
^{1}H NMR (300 MHz, CD_3OD) of **1b**



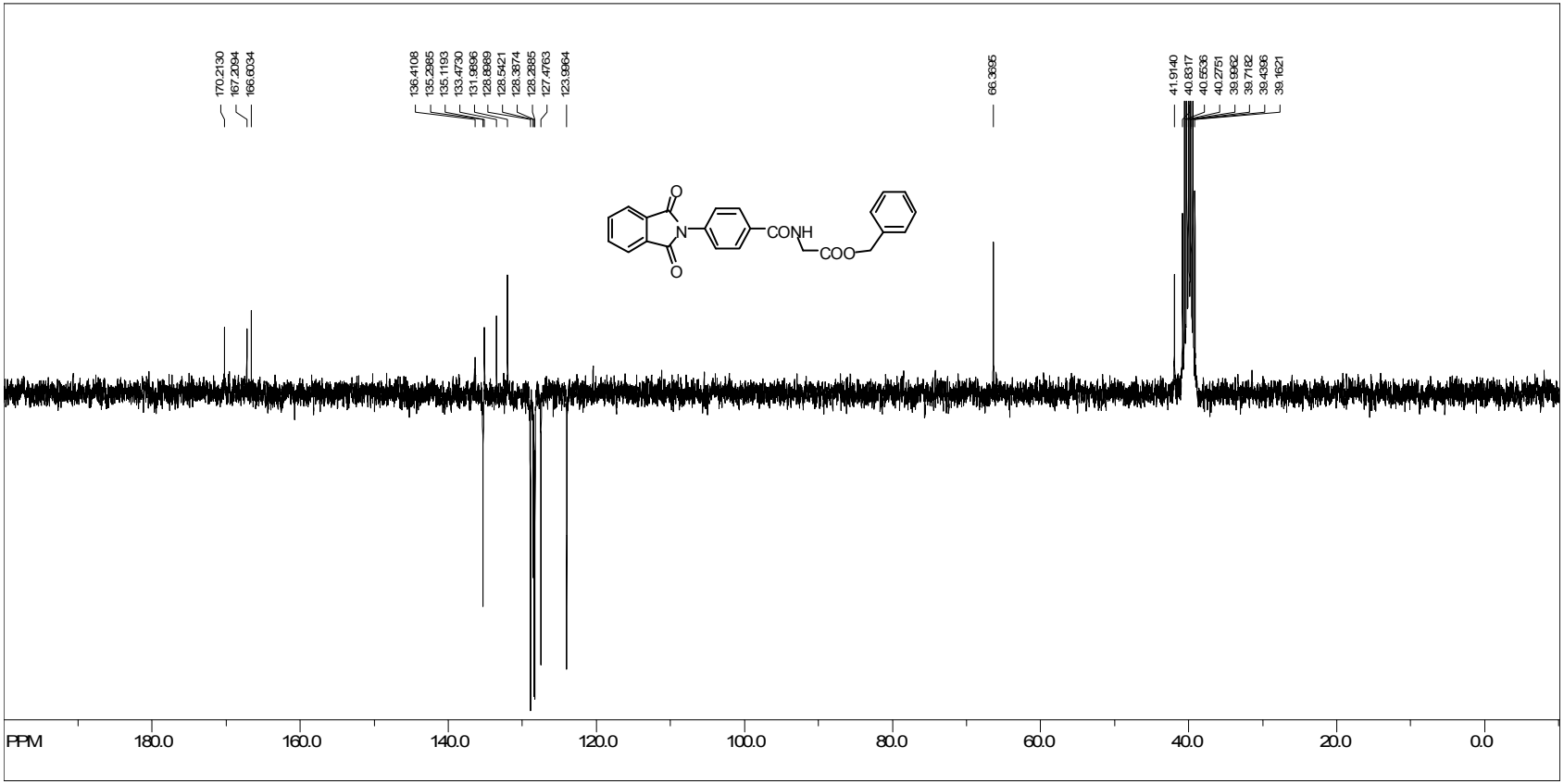
^{13}C NMR (150 MHz, CD_3OD) of **1b**



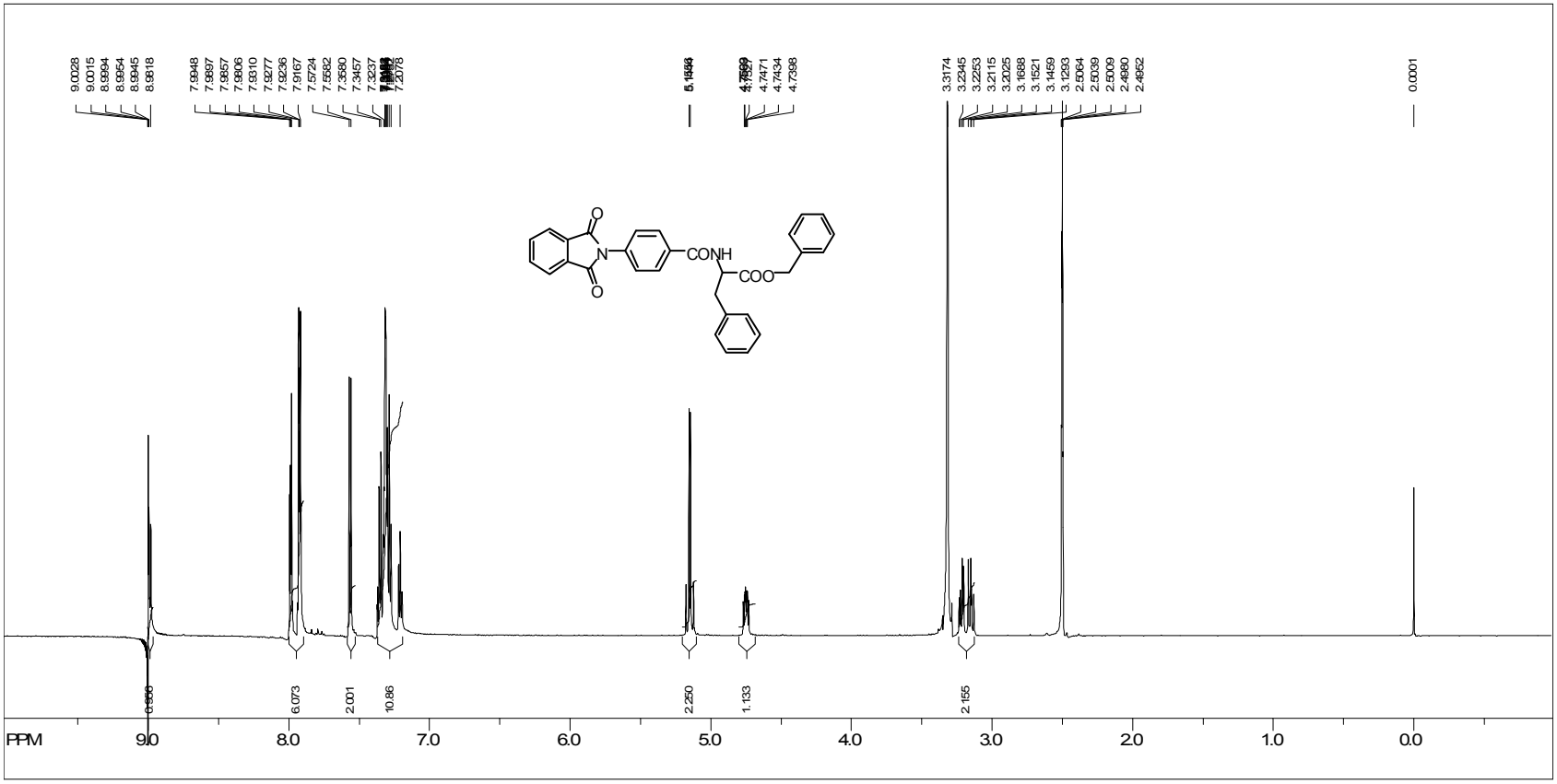
^{1}H NMR (300 MHz, d_6-DMSO) of **5b**



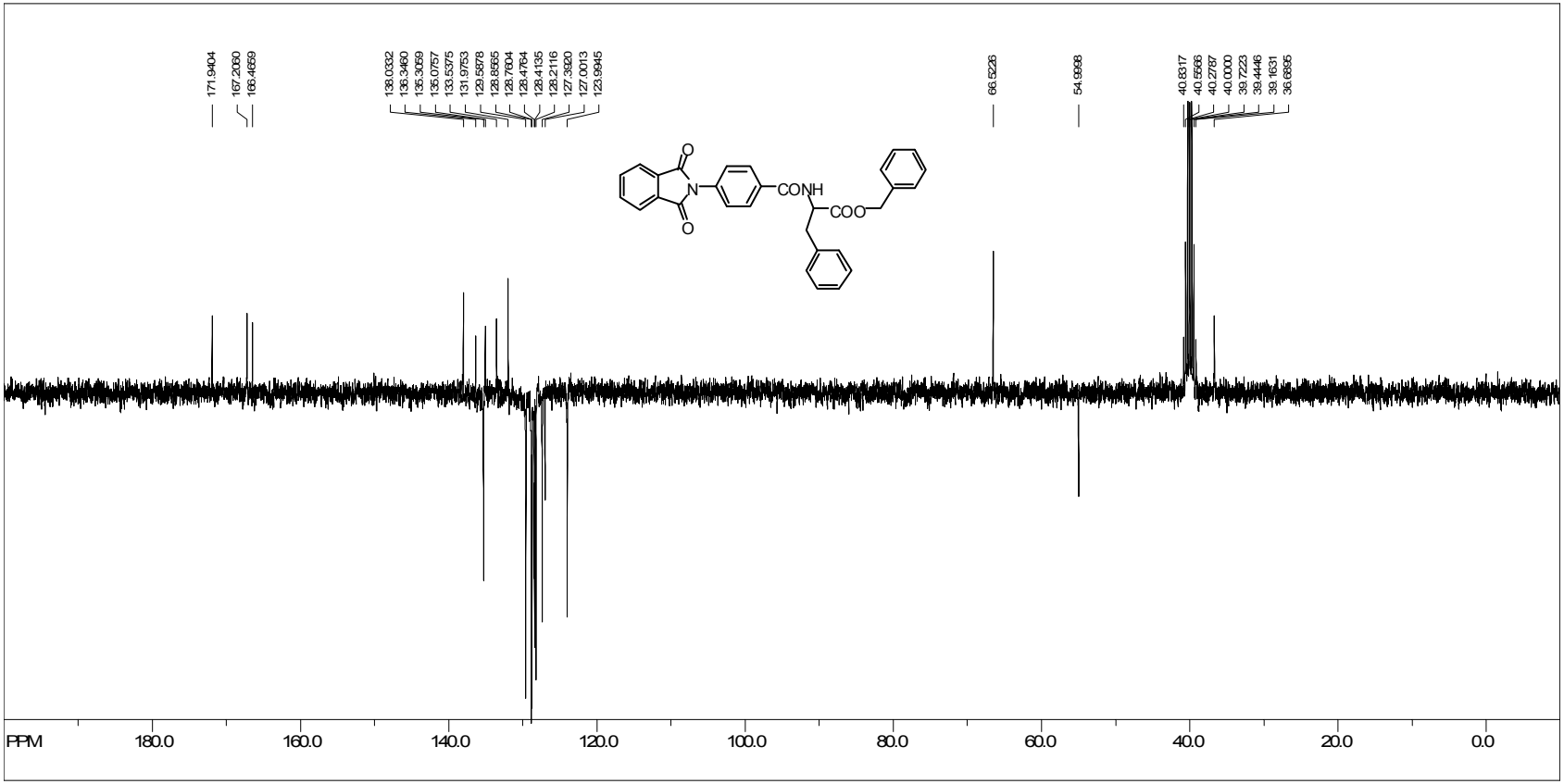
^{13}C NMR (75 MHz, d_6-DMSO) of **5b**



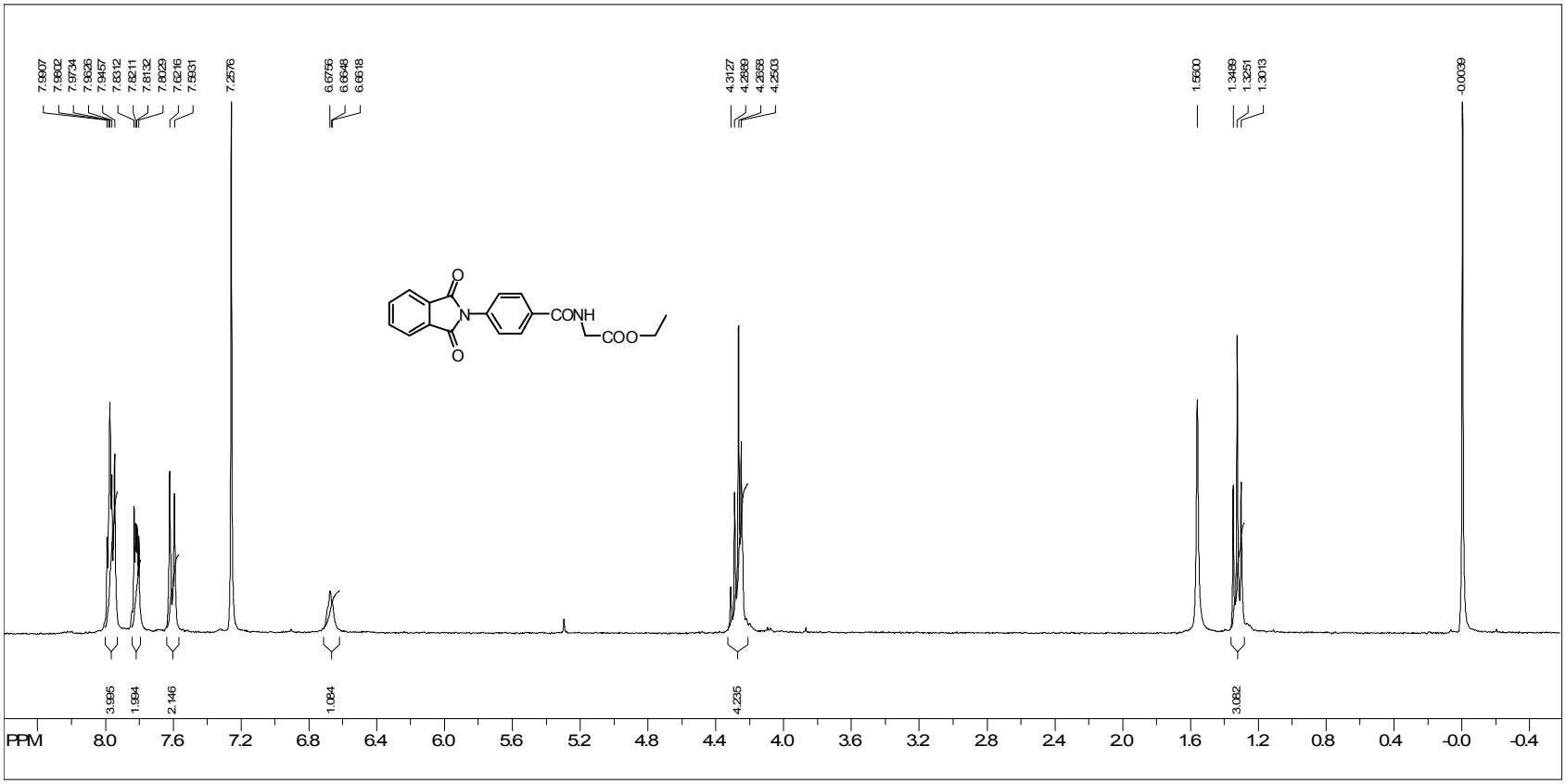
^{1}H NMR (300 MHz, *d*$_6$-DMSO) of **5a**



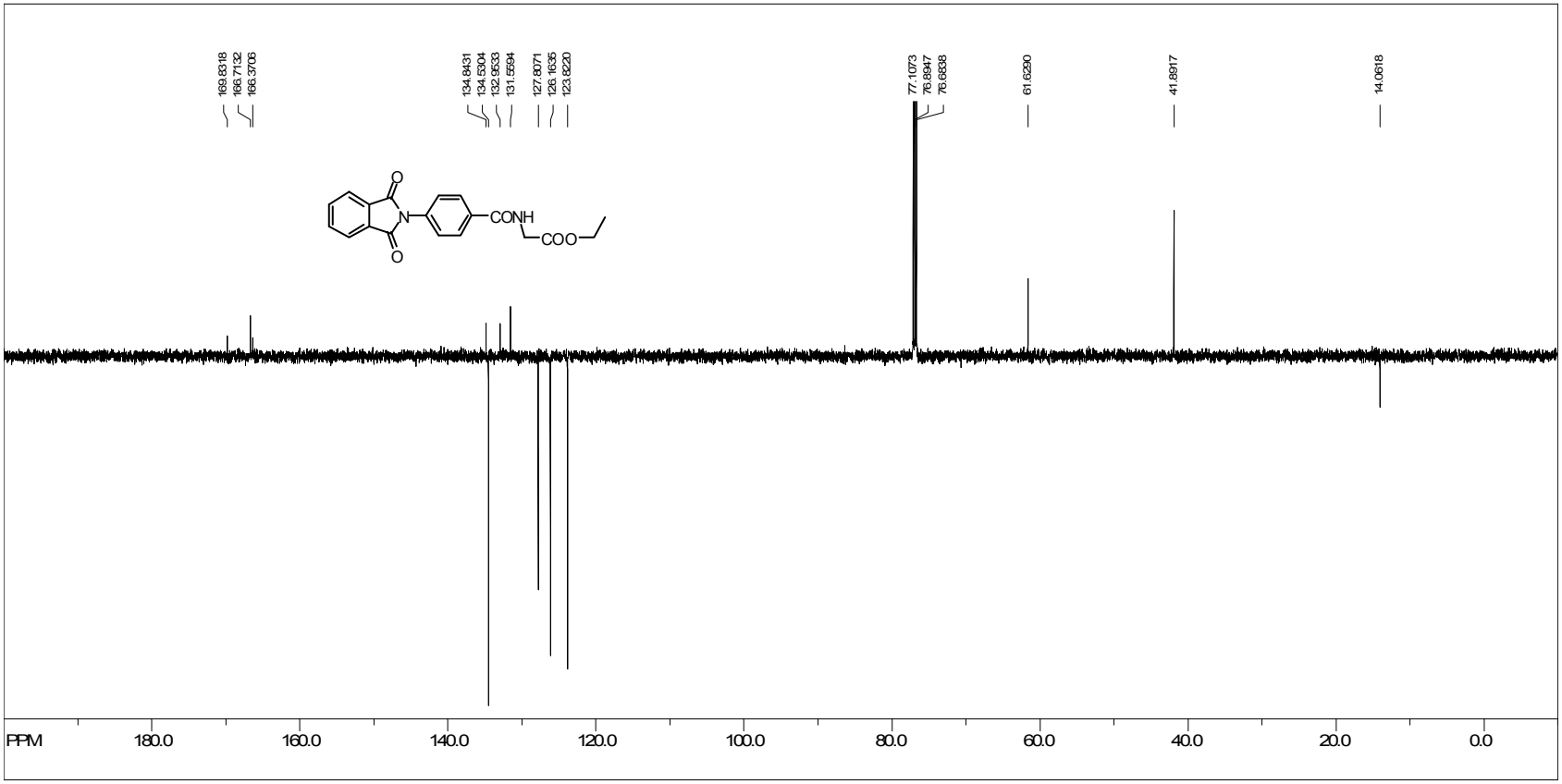
^{13}C NMR (75MHz, *d*$_6$-DMSO) of **5a**



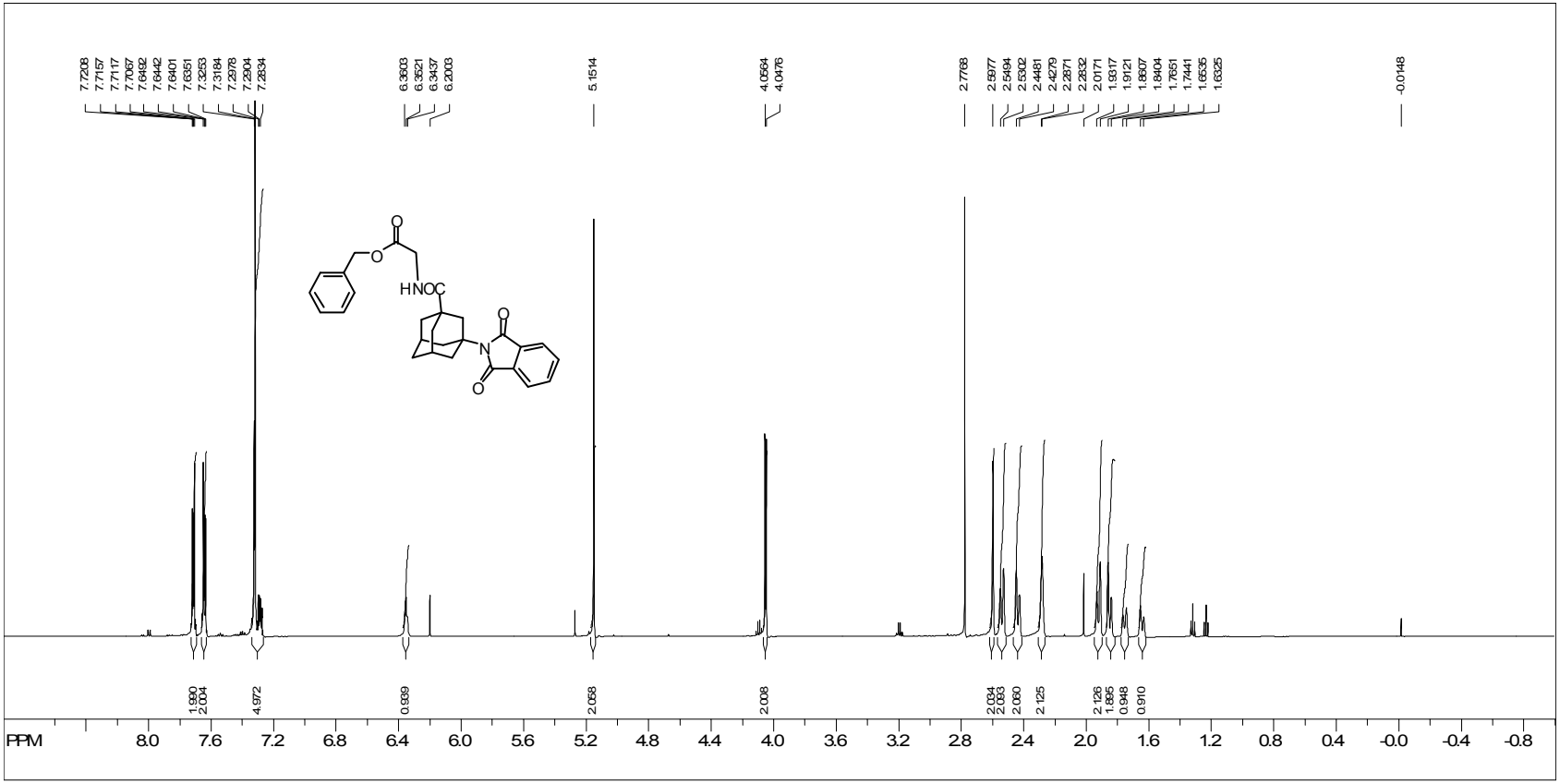
^{1}H NMR (300 MHz, $CDCl_3$) of **5bEt**



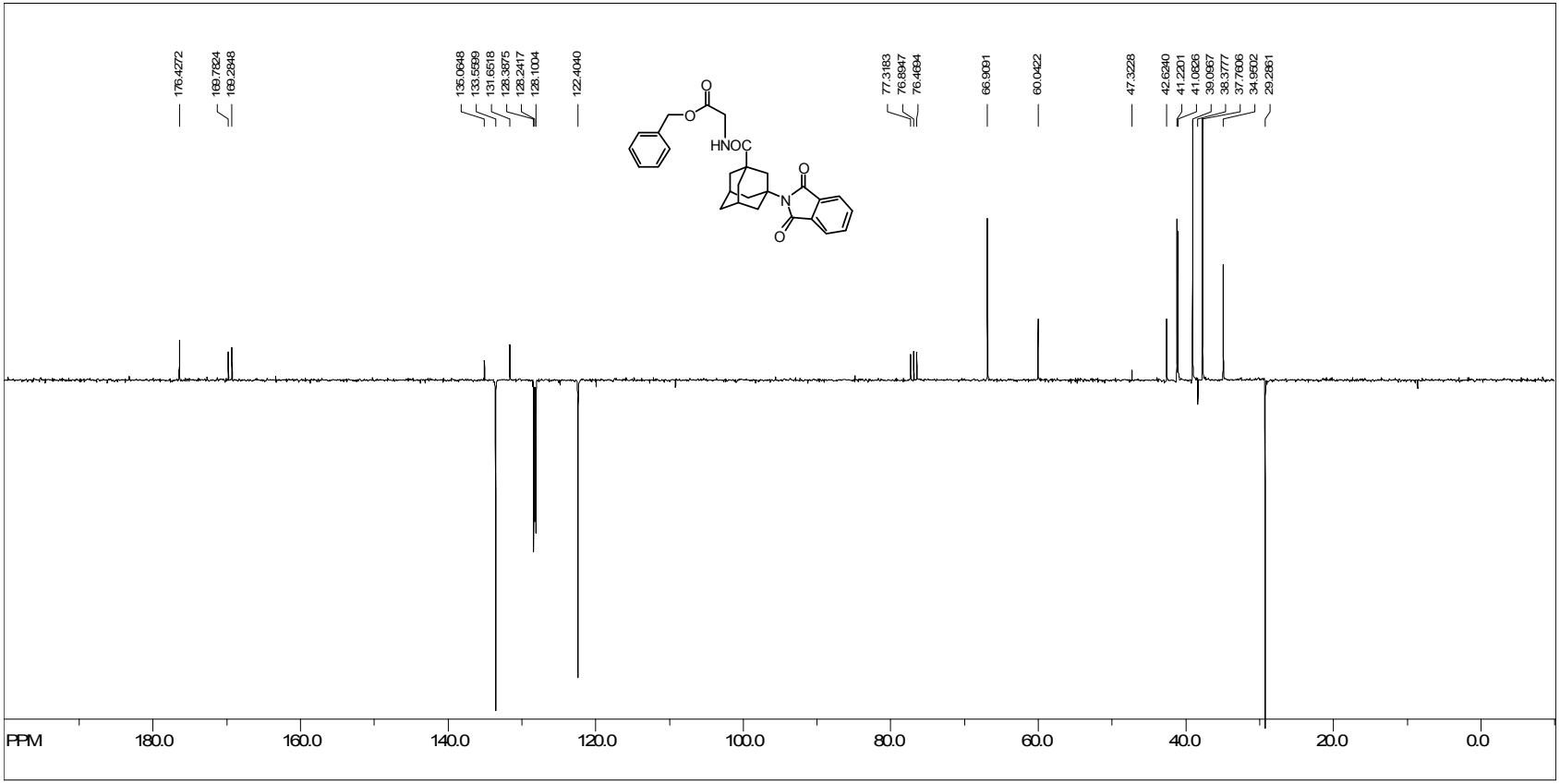
^{13}C NMR (150 MHz, $CDCl_3$) of **5bEt**



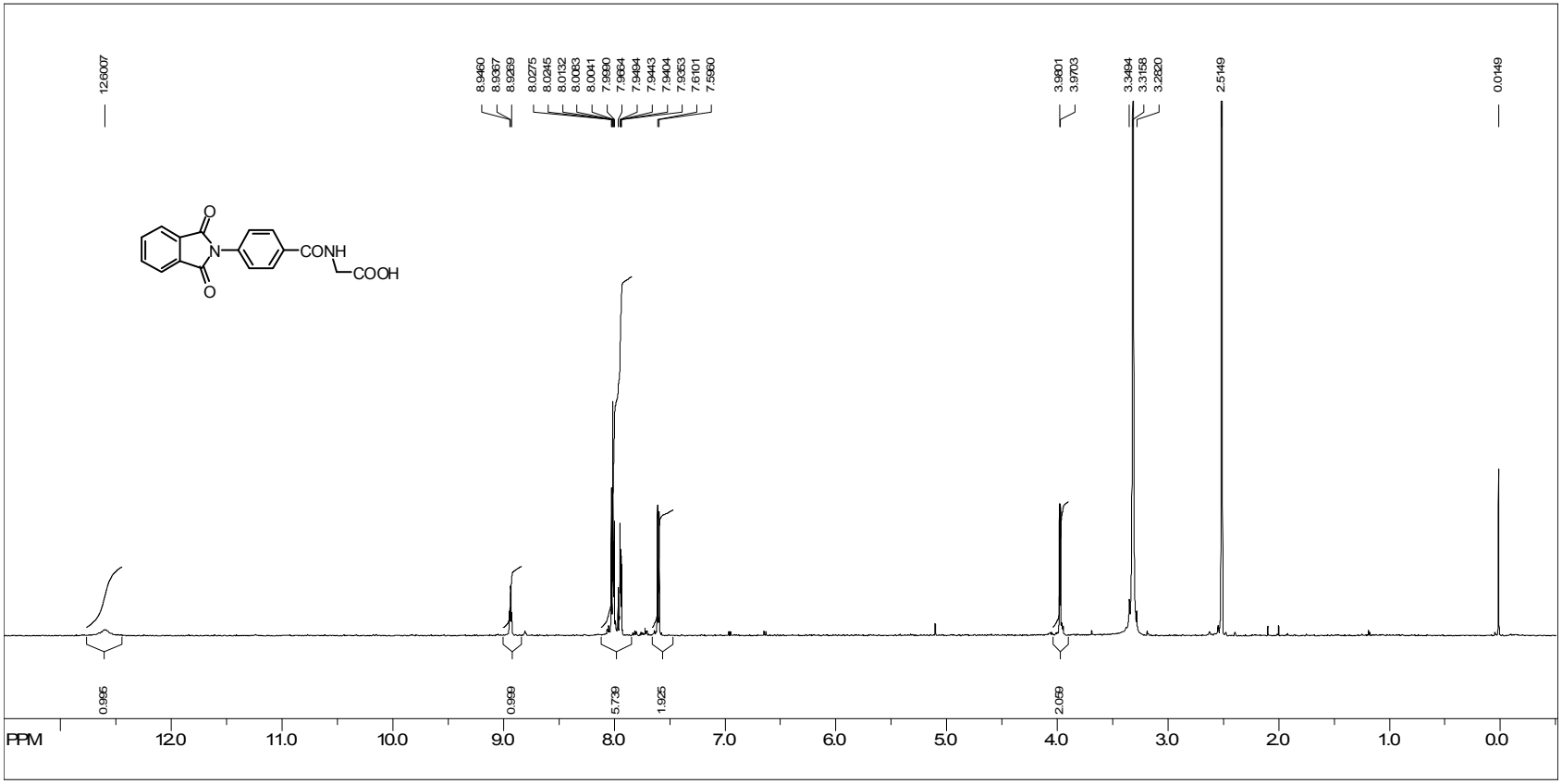
^{1}H NMR (600 MHz, $CDCl_3$) of **5aBz**



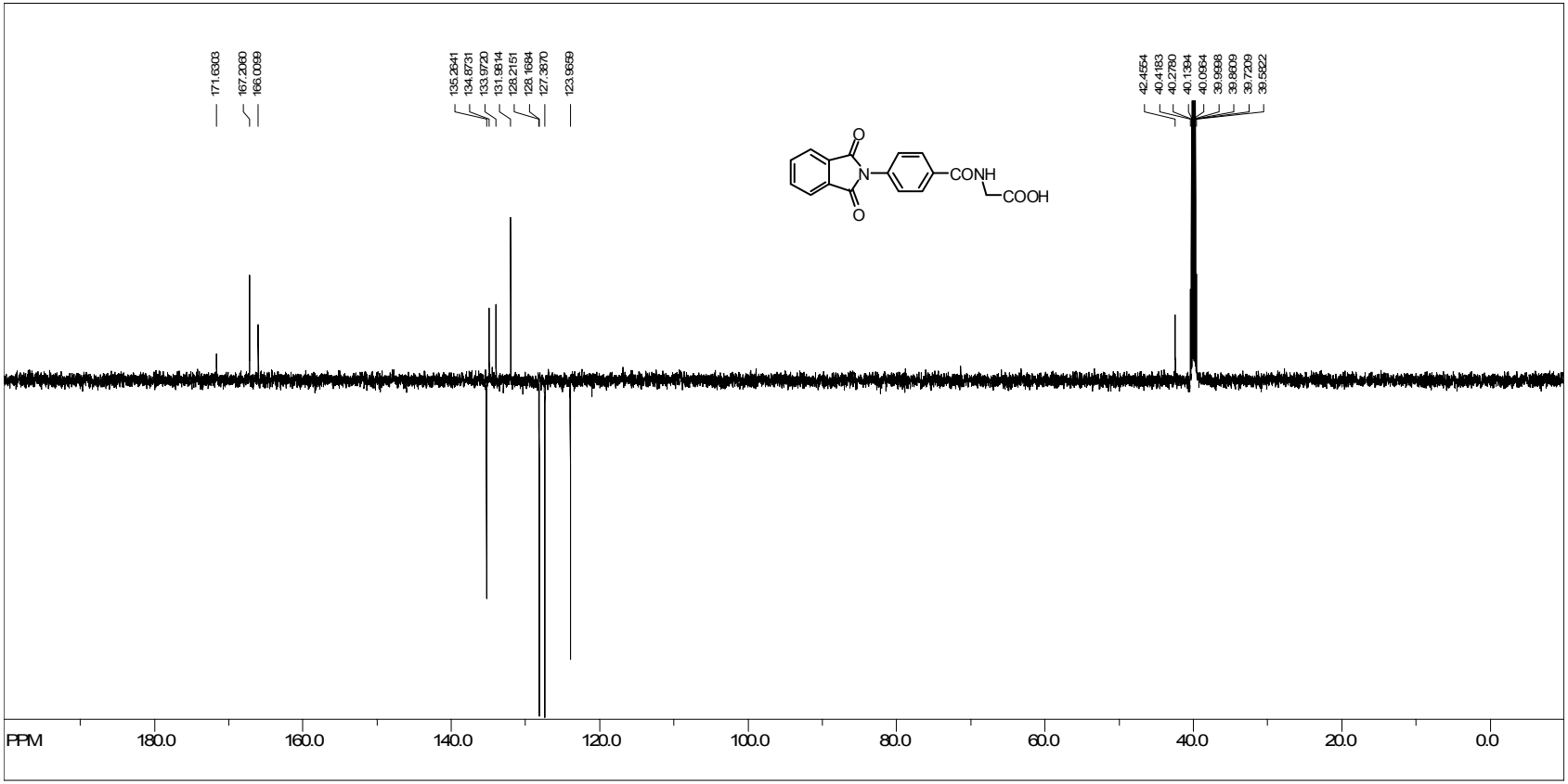
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **5aBz**



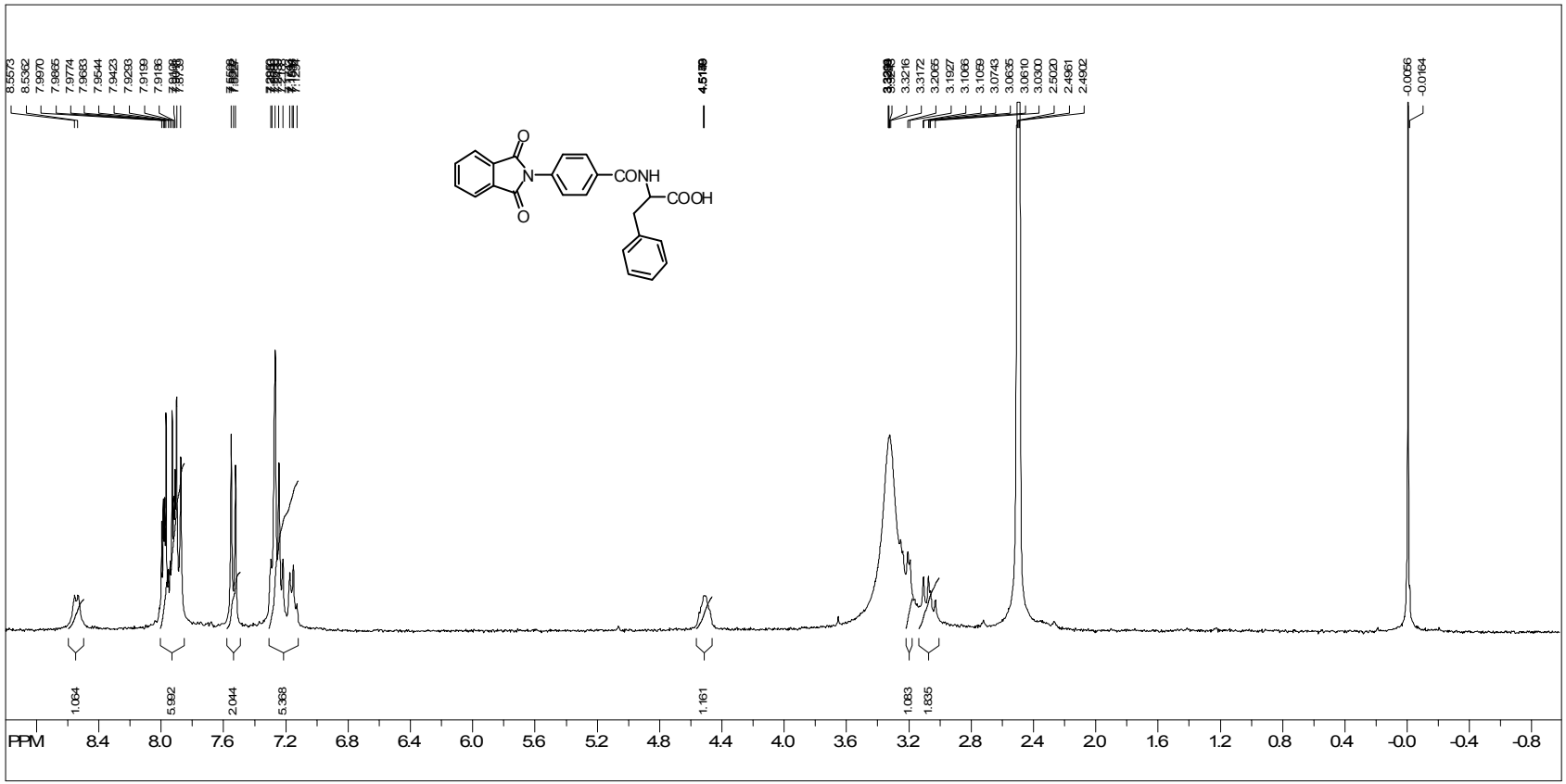
^{1}H NMR (600 MHz, *d*$_{6}$-DMSO) of **3b**



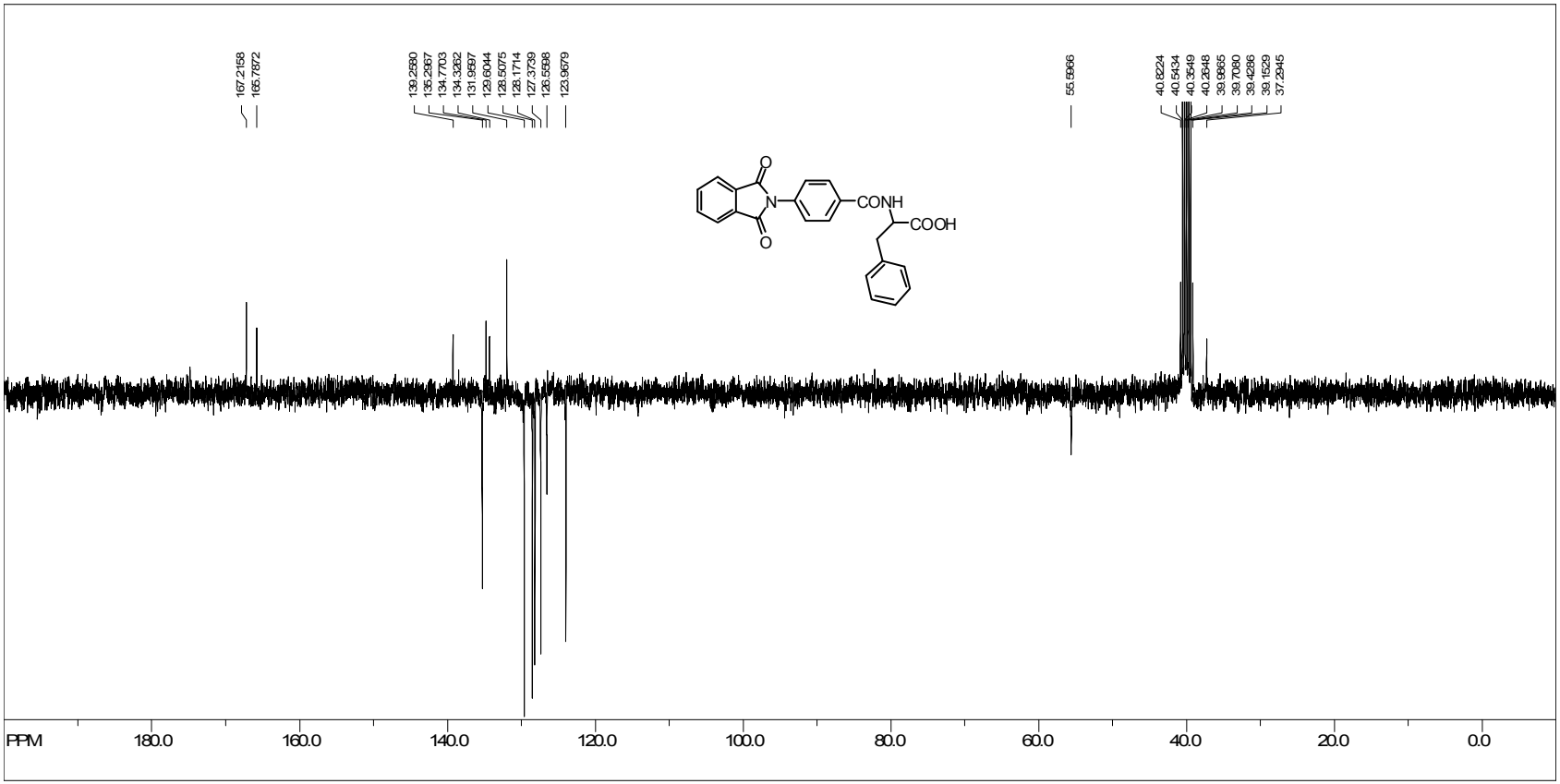
^{13}C NMR (150 MHz, *d*$_6$-DMSO) of **3b**



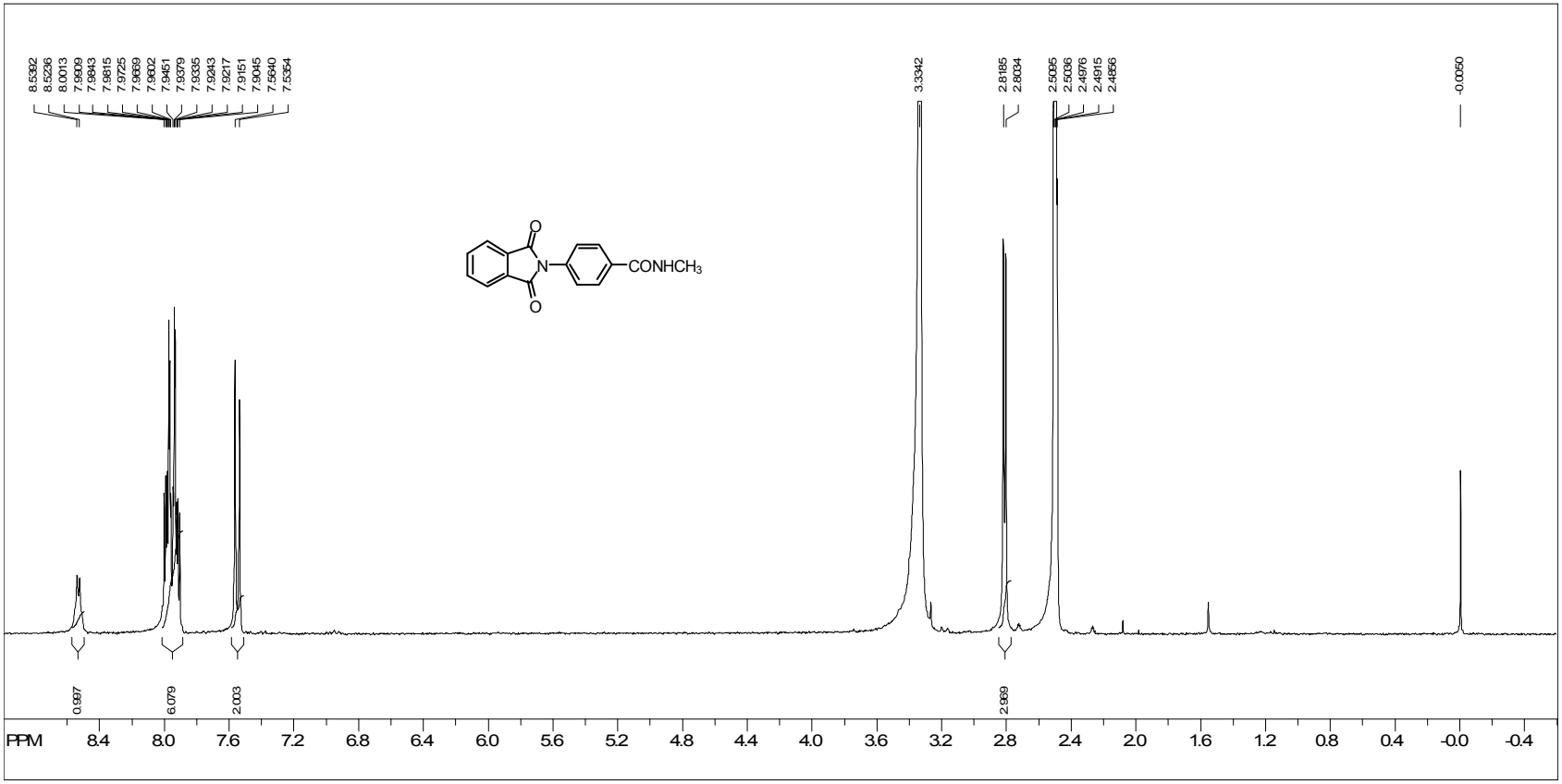
^{1}H NMR (600 MHz, *d*$_6$-DMSO) of **3a**



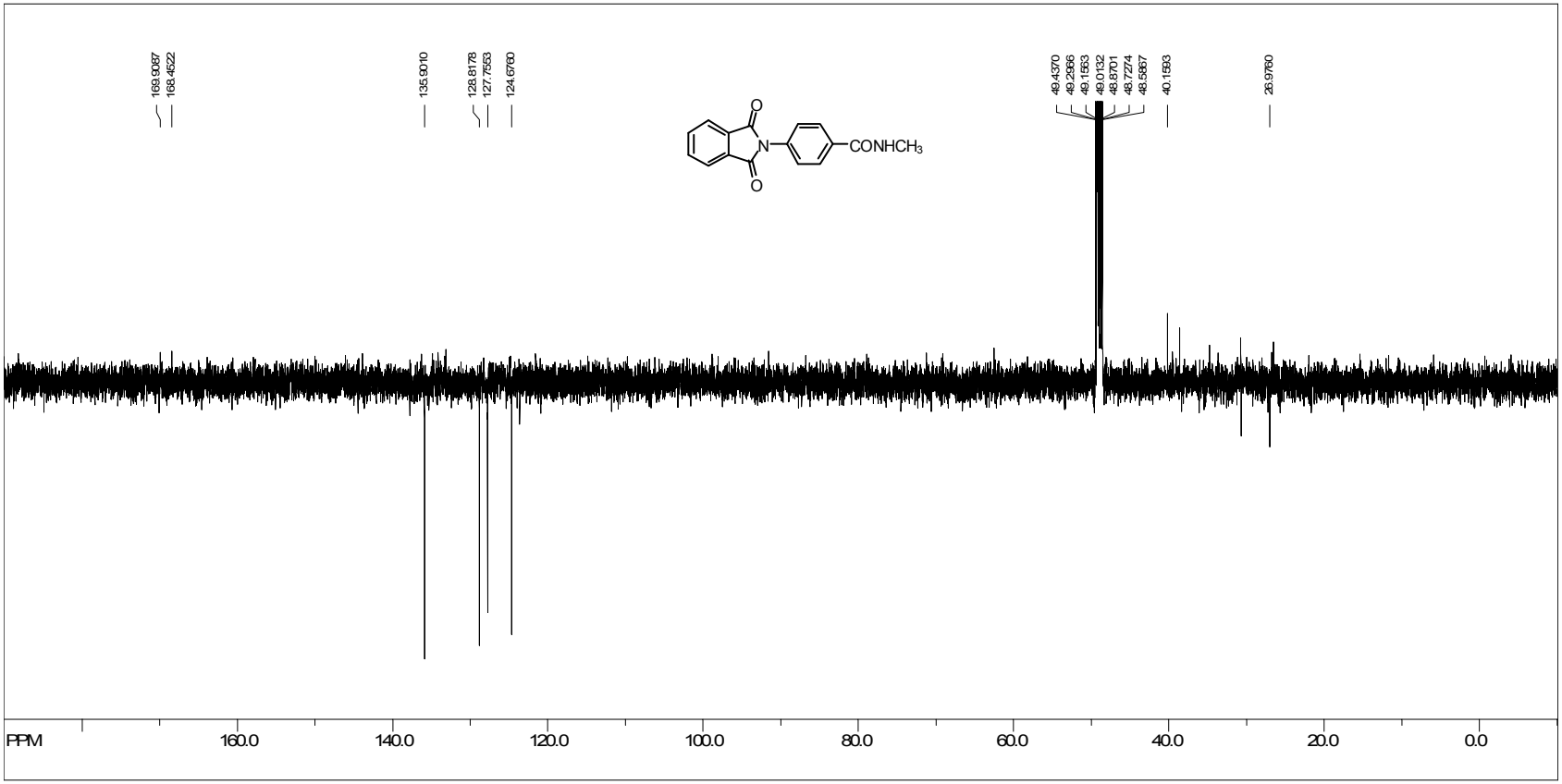
^{13}C NMR (75 MHz, d_6-DMSO) of **3a**



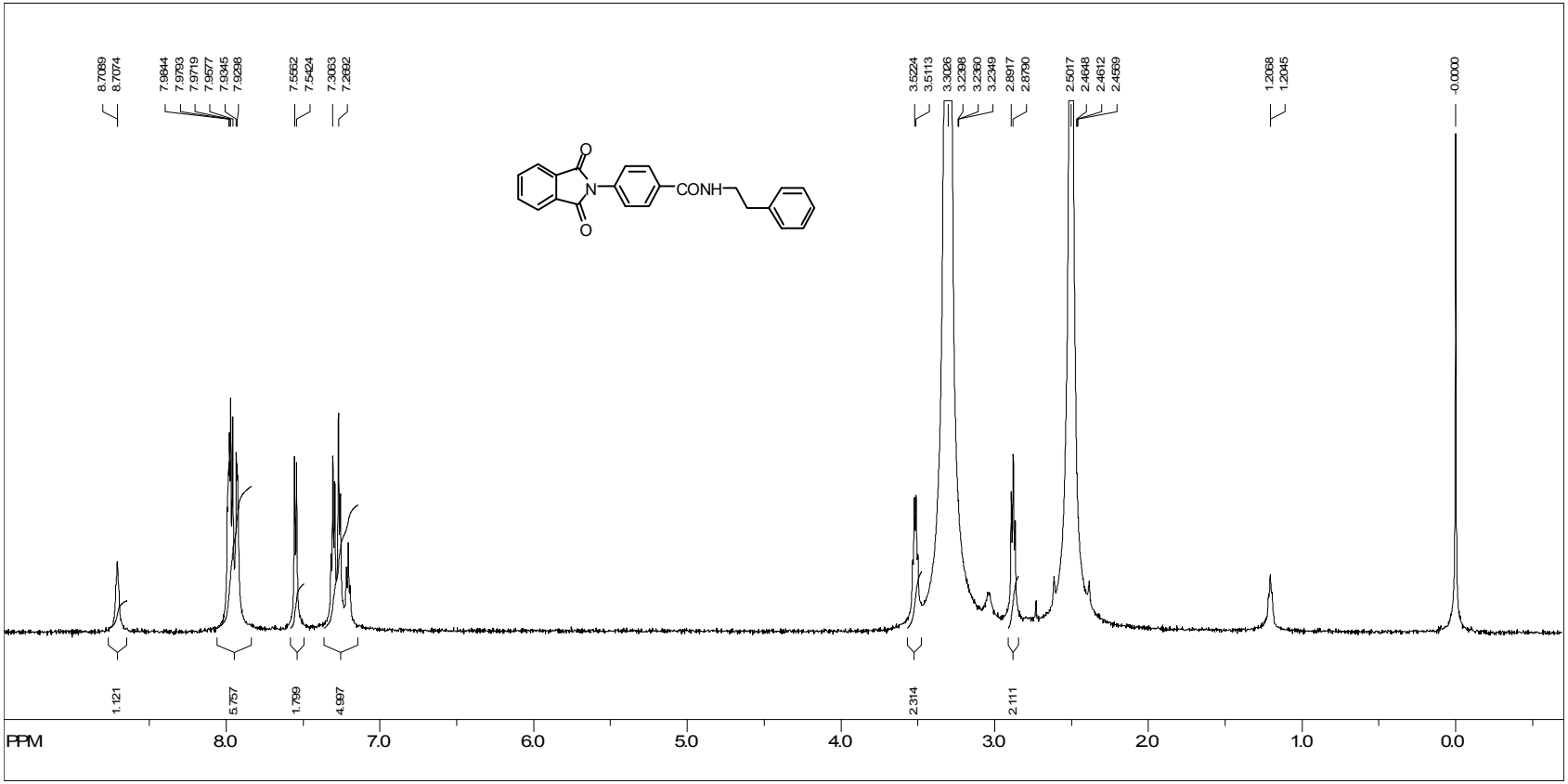
^{1}H NMR (300 MHz, d_6-DMSO) of **7b**



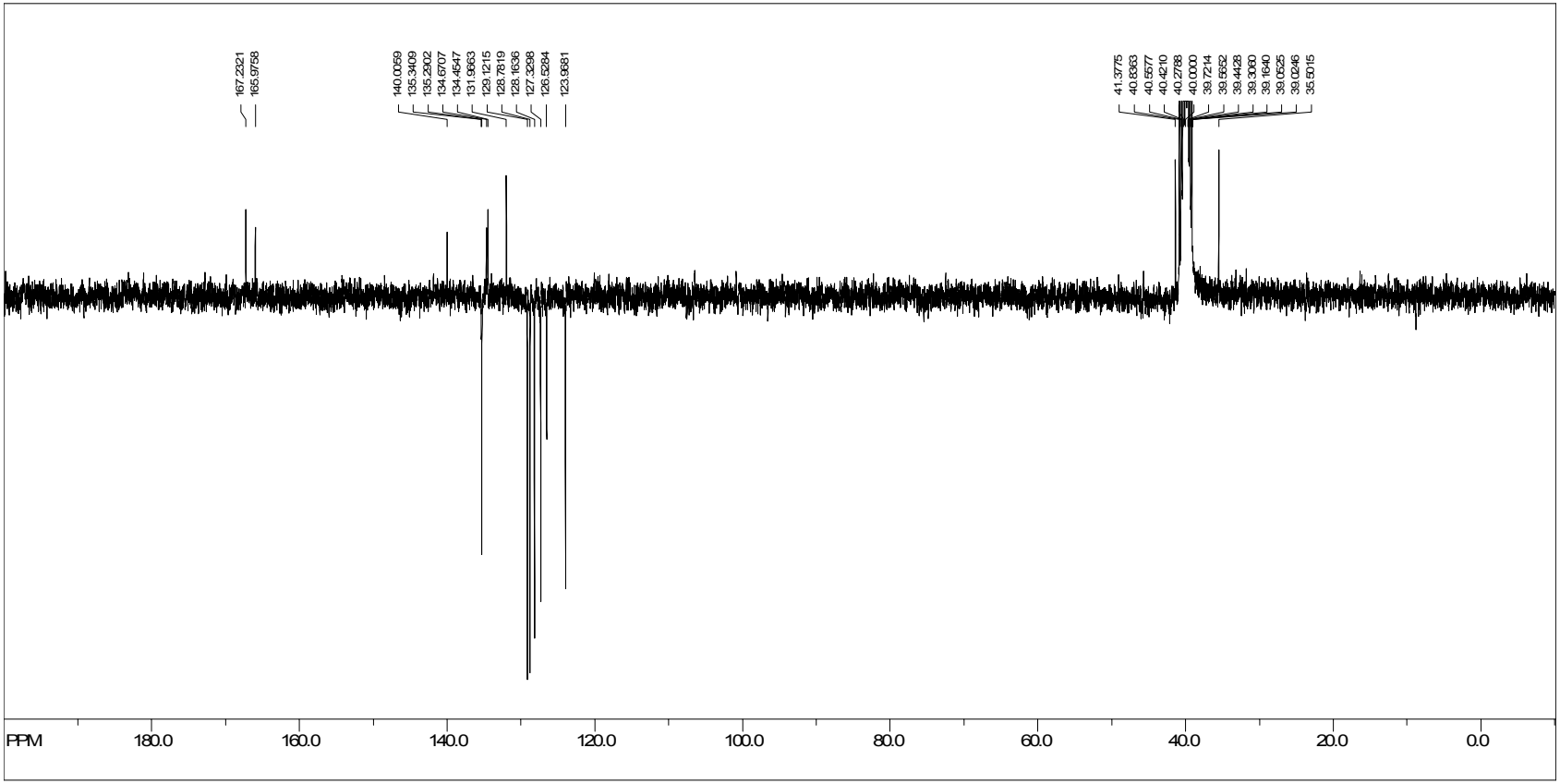
^{13}C NMR (150 MHz, CD_3OD) of **7b**



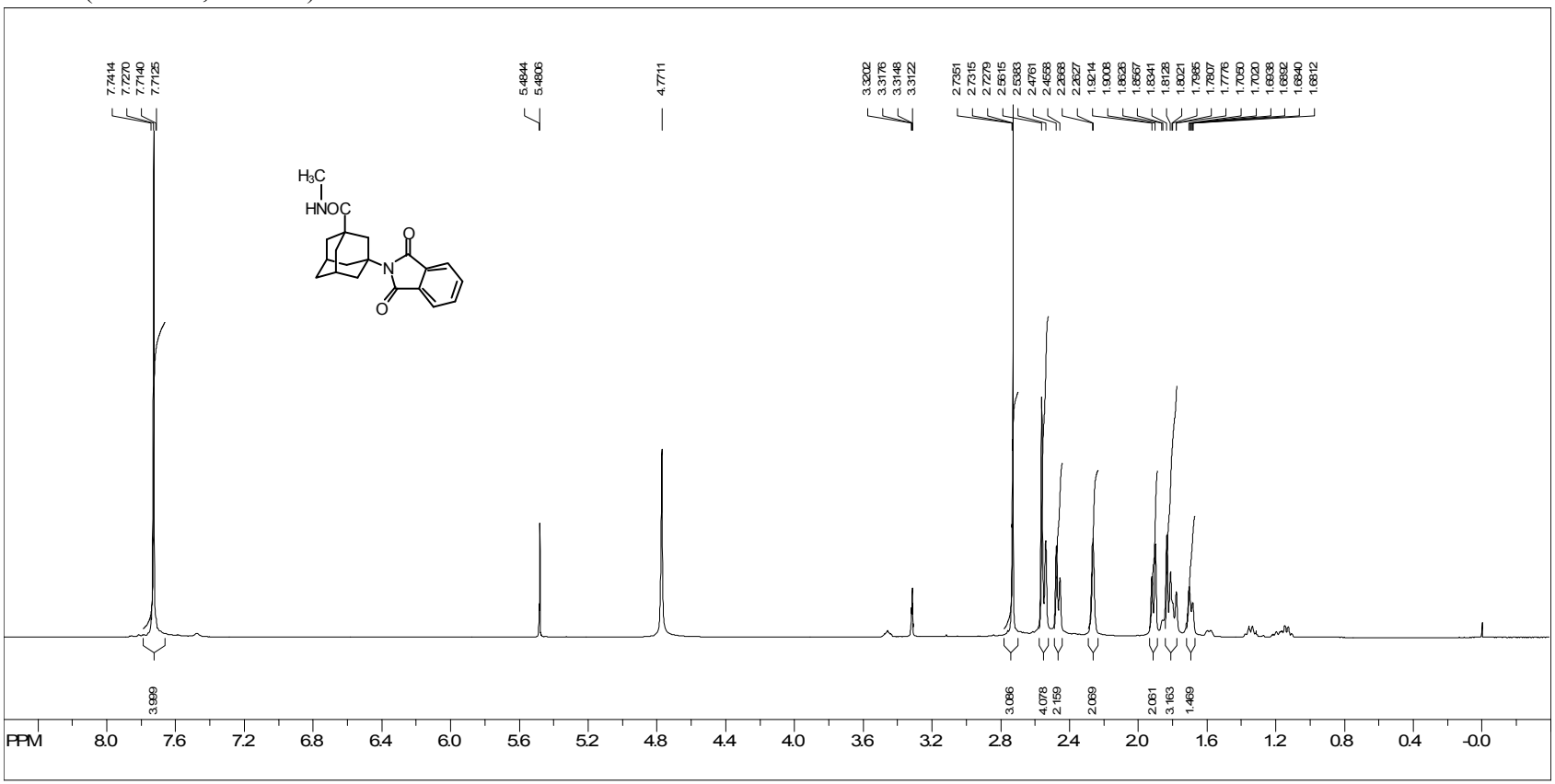
^{1}H NMR (600 MHz, *d*$_{6}$-DMSO) of **7a**



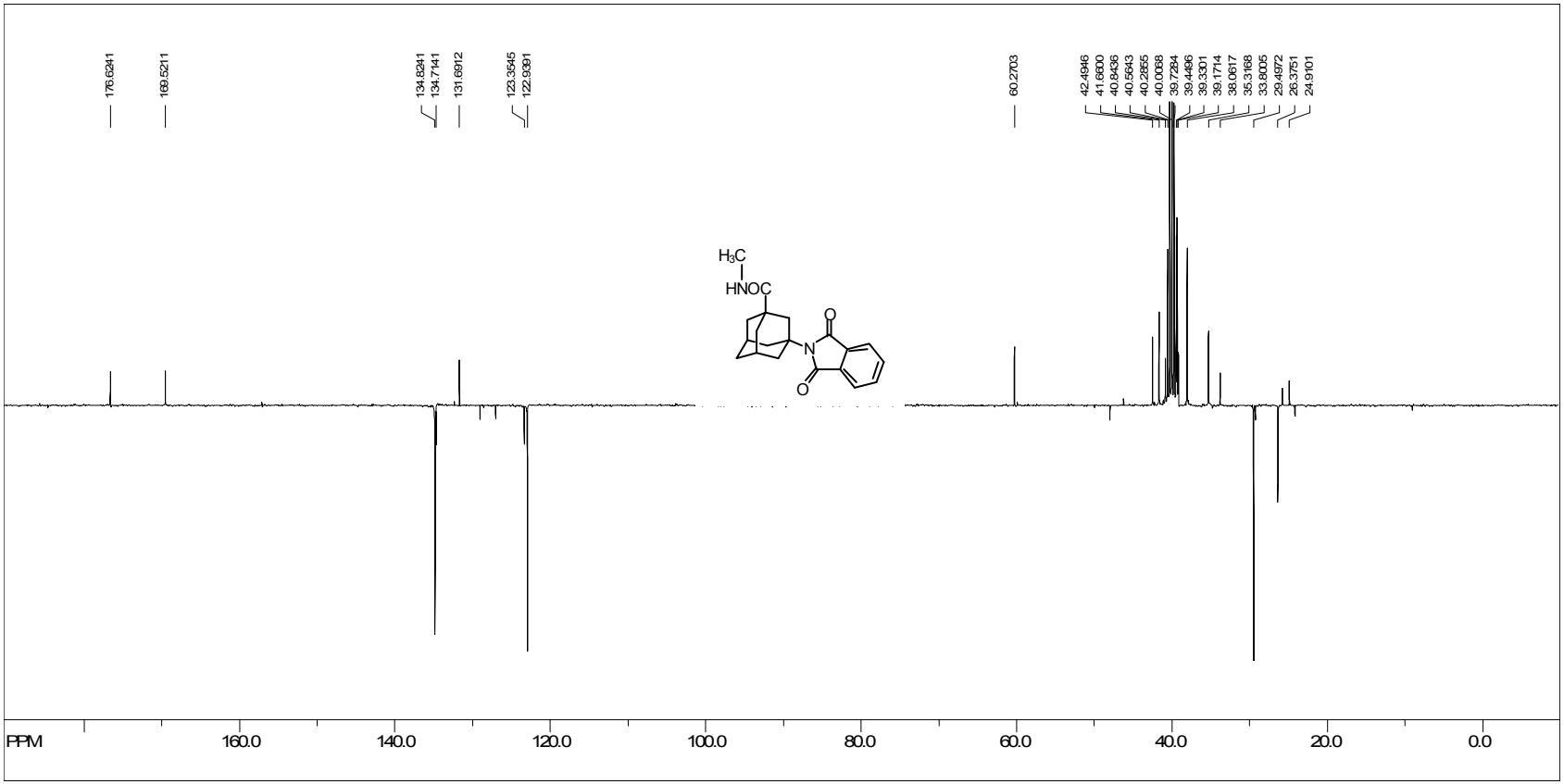
^{3}C NMR (150 MHz, *d*$_{6}$-DMSO) of **7a**



NMR (600 MHz, CD_3OD) of **8b**



^{13}C NMR (75 MHz, *d*$_6$-DMSO) of **8b**



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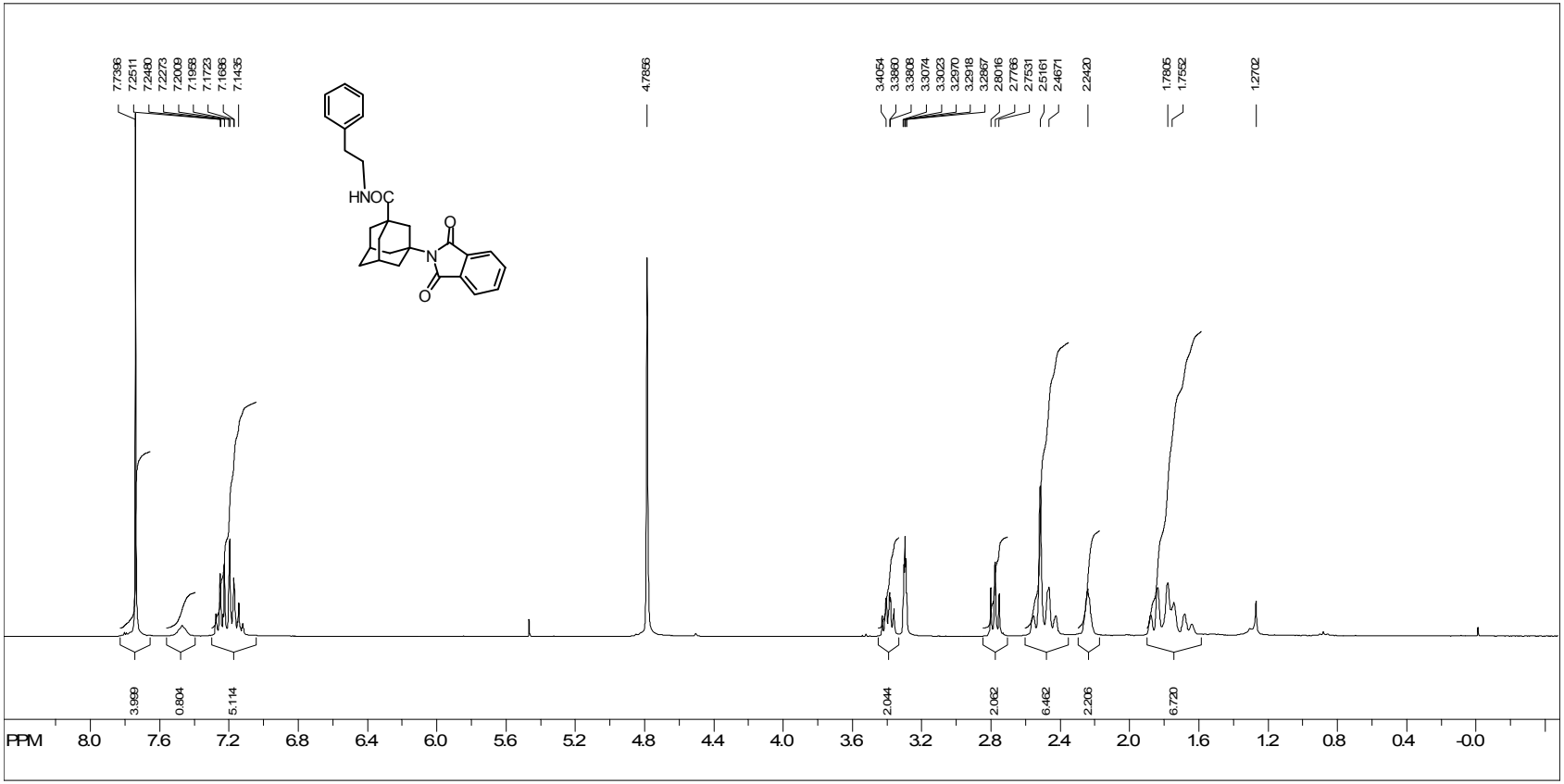
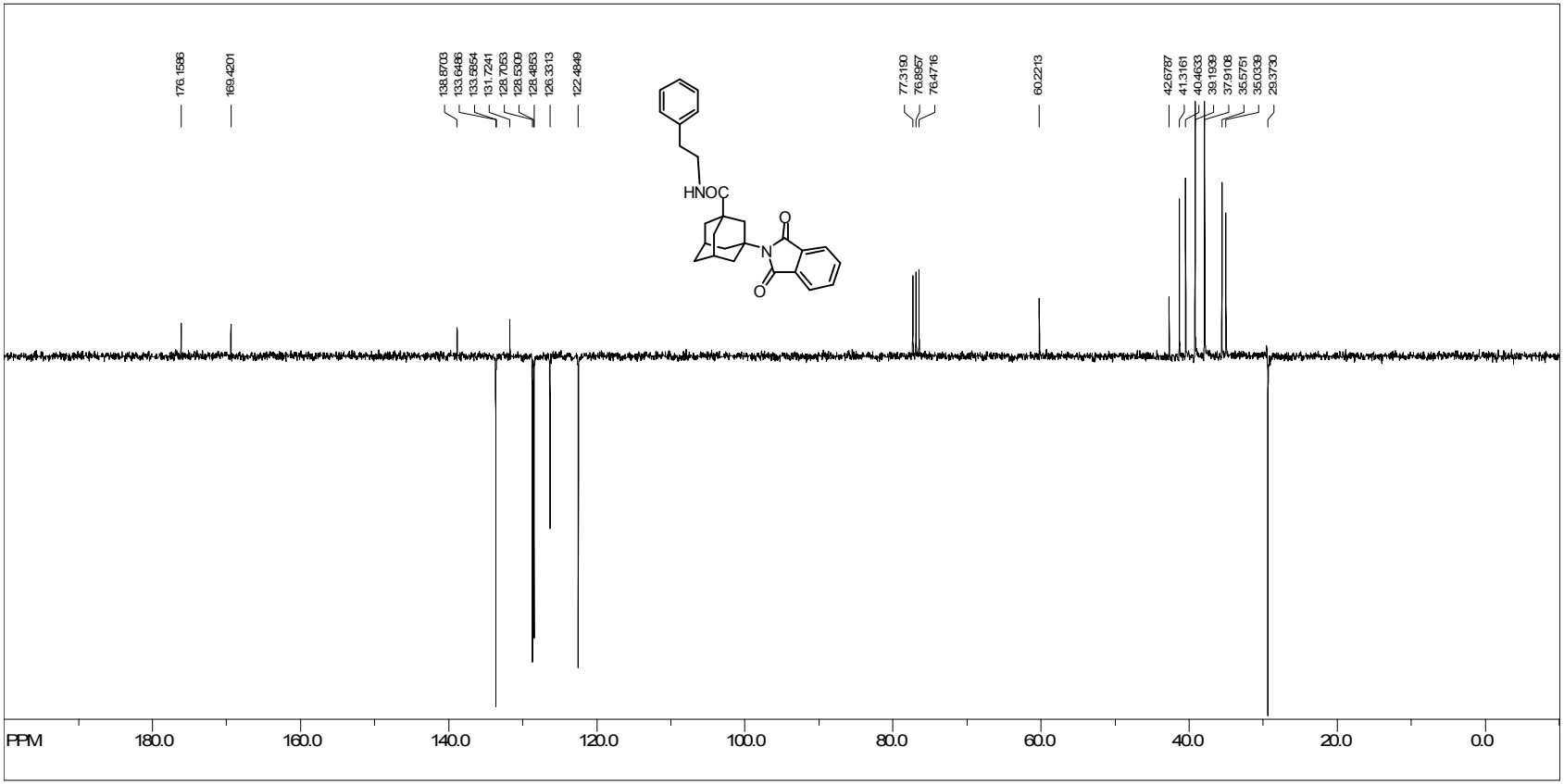
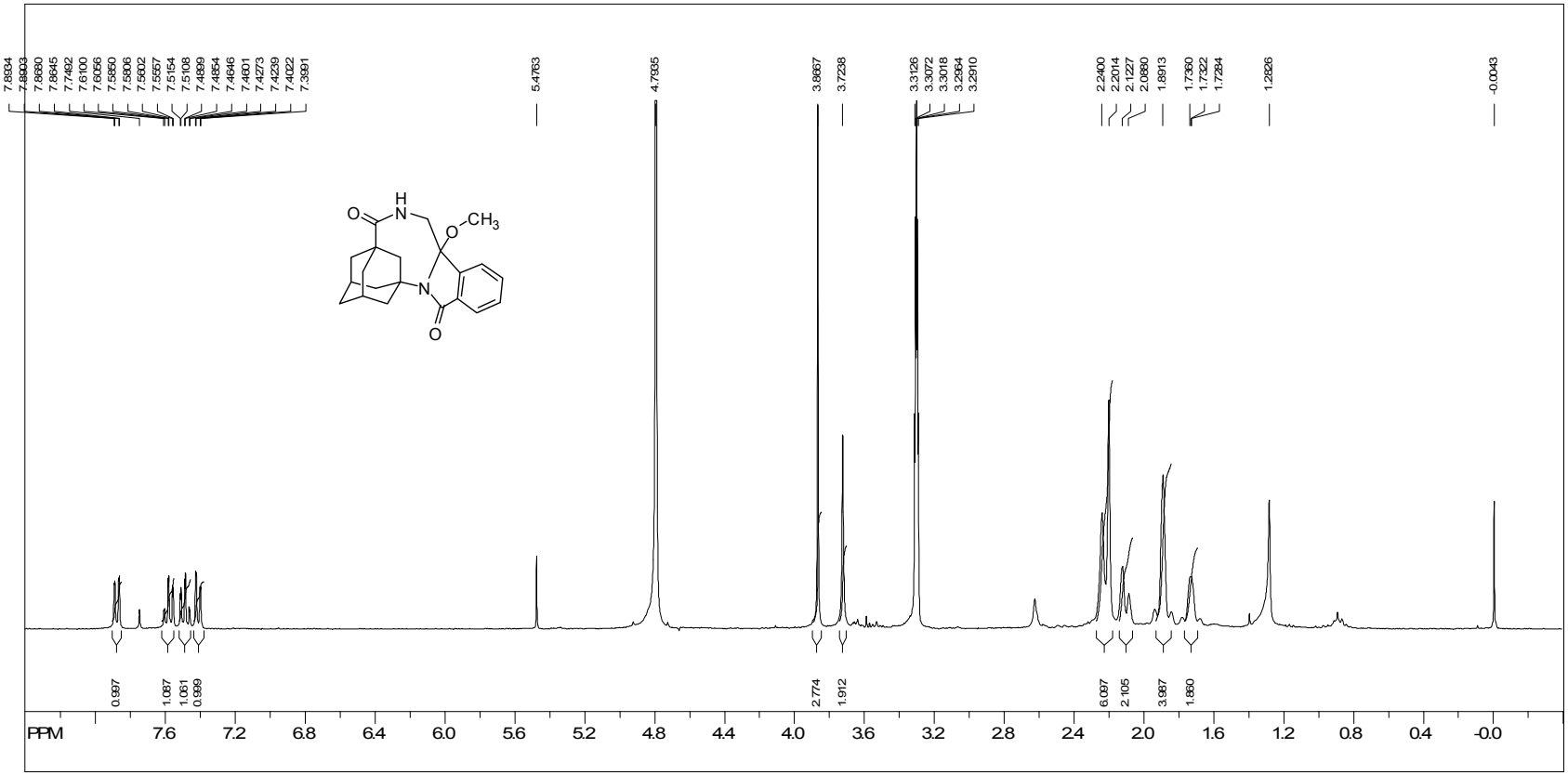


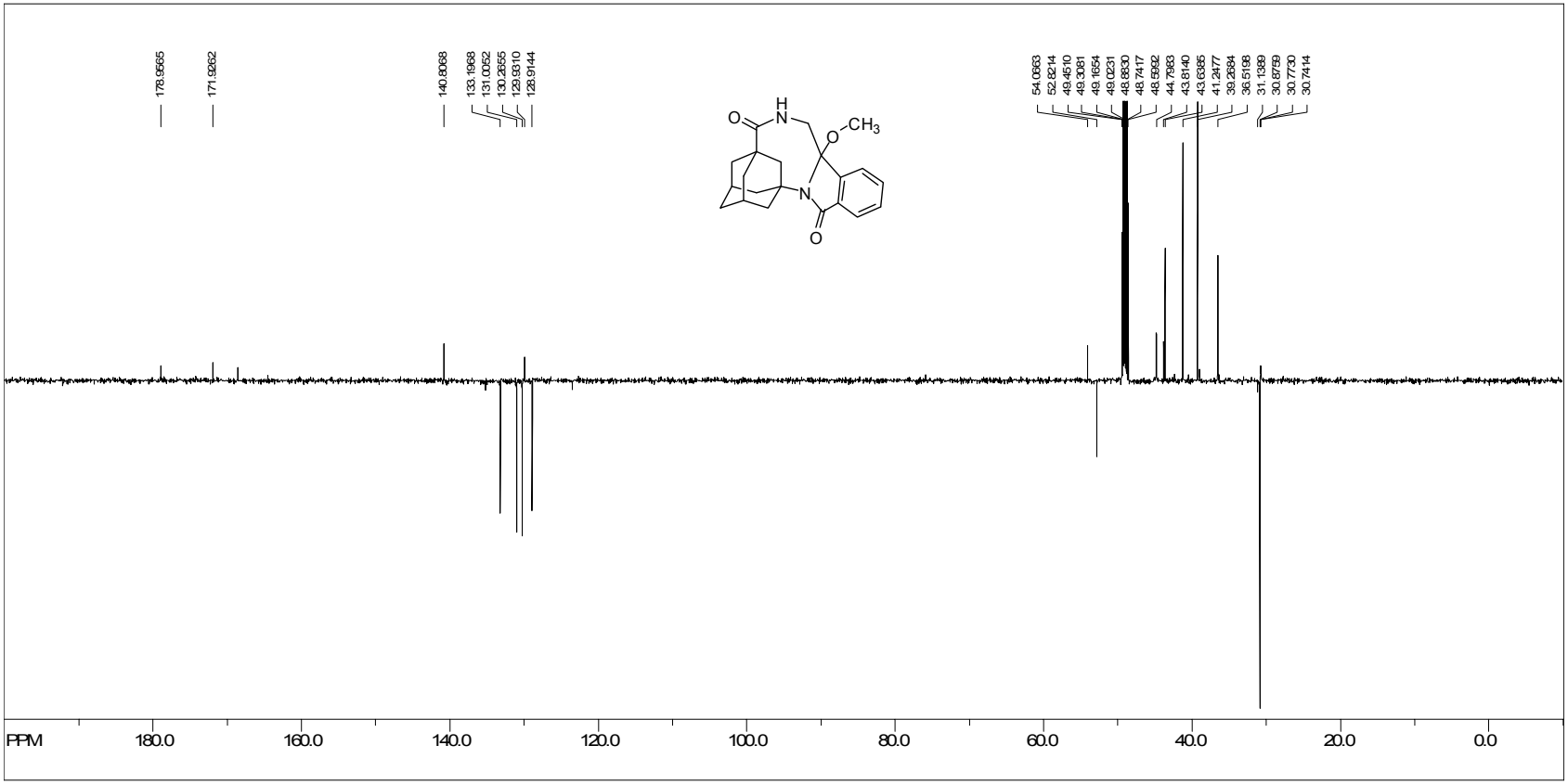
^{13}C NMR (75 MHz, $CDCl_3$) of **8a**



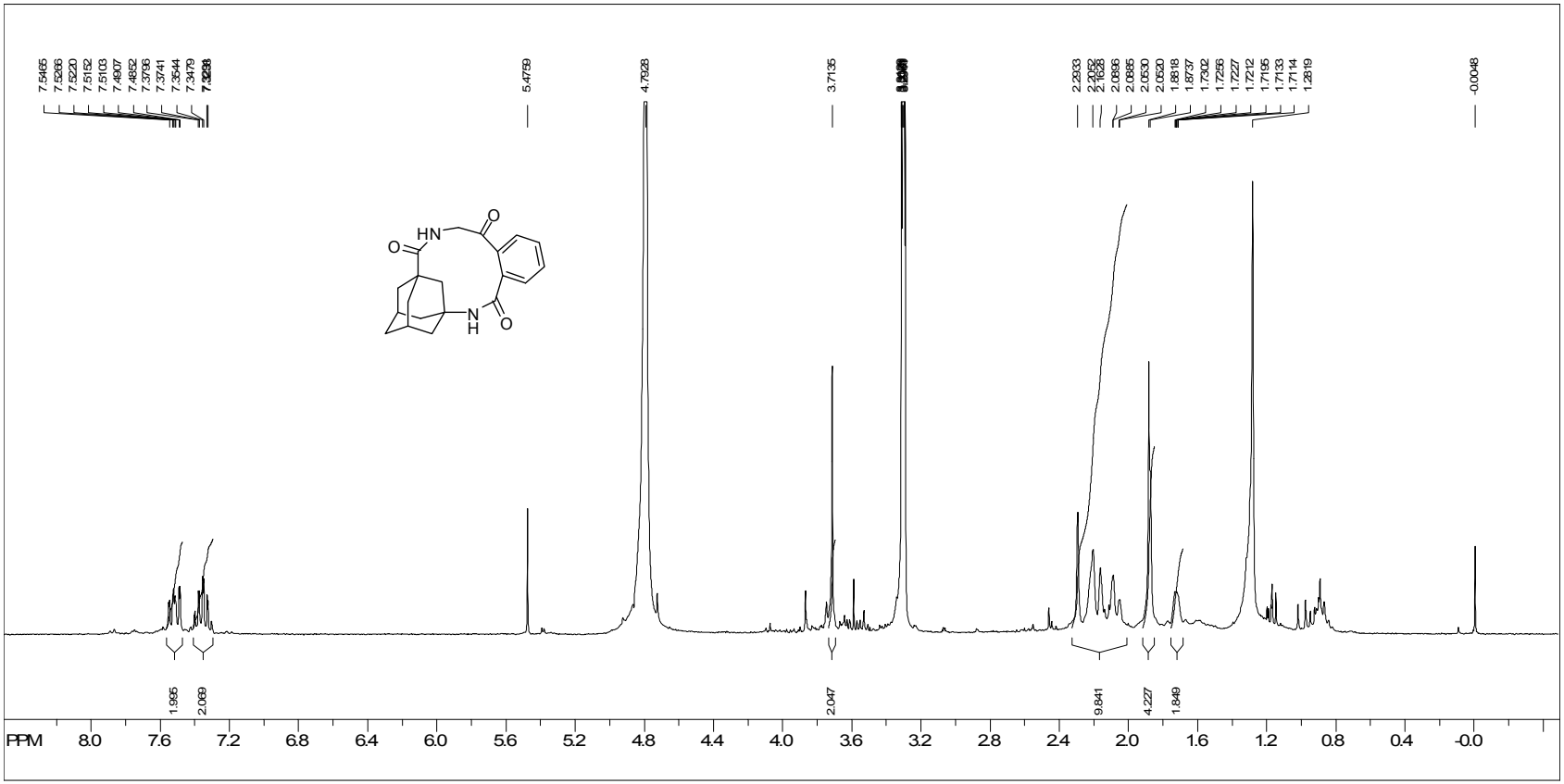
^{1}H NMR (600 MHz, CD_3OD) spectrum of **9b**



^{13}C NMR (150 MHz, CD_3OD) of **9b**



^{1}H NMR (300 MHz, CD_3OD) of **2b**



^{13}C NMR (75 MHz, CD_3OD) of **2b**