Synthesis of Sulfur-Containing Tricyclic Ring Systems by Means of Photoinduced Decarboxylative Cyclizations

Axel G. Griesbeck,*[a] Michael Oelgemöller,[a] Johann Lex,[a] Andreas Haeuseler,[c] and Michael Schmittel[c]

Dedicated to Professor Siegfried Hünig on occasion of his 80th birthday

Keywords: Cyclic voltammetry / Cyclizations / Decarboxylations / Electron transfer / Photochemistry / Phthalimides / Thioethers

The intramolecular and intermolecular photoinduced electron transfer reactions of a series of mercaptoacetic acid and mercaptopropionic acid derivatives were investigated. In the intermolecular series, the phthalimidoalkylsulfanylalkylcarboxylates **1a–j** and **2** were transformed into the tricyclic ring systems **3a–j** and **4**, respectively, with high regioselectivities. The mercaptoacetic acid and 2-mercaptopropionic acid derived substrates **1a–g** and **2** readily cyclized in good to excellent yields (60–98%) but with low diastereoselectivities (except for **1d**), whereas the corresponding 3-mercaptopropionic acid derived substrates **1h–j** gave the corresponding tricyclic products **3h–j** after prolonged irradiation, but with poor yields (11–20%). The intermolecular version – i.e., photodecarboxylative addition to *N*-methylphthalimide (**5**) as electron acceptor – was successful with mercaptoacetic acid, and 2-mercaptopropionic acid substrates **6a–c** and the addition products **7a–c** were obtained in high yields (57–90%). No addition, however, was observed with 3-(methylsulfanyl)propionic acid (**6d**). The regioselectivity of decarboxylation proceeded in a controlled manner for the mercaptosuccinic acid derivatives in both the intramolecular (with **8a–c**) and the intermolecular (with **9**) versions. Comparison between sulfur-activated and nonactivated species (**13**, **15**) or irradiation of **1a** under nonactivating conditions showed that the carboxylate anion in the position α to the electron-donating sulfur atom acts as a superior leaving group. This efficiency is drastically reduced for carboxylate anions in the β position. With the former substrates, the photochemical cyclization proceeds with high product yields. Quantum yield measurements for decomposition (Φ_d as a measure for cyclization) supported these observations. CV measurements indicated preorientation prior to electron transfer in the intramolecular pathway.

Introduction

The photoinduced electron transfer (PET) reactivity of phthalimides has been intensively studied during the last decade.[1,2] In the photochemical cyclization of ω-imidocarboxylates, the carboxylate anion acts as the electron-donating part and the electronically excited imido group as electron acceptor. The scope and limitations of this method have been investigated intensively, and a large number of macrocyclic ring systems bearing a variety of functional groups has been synthesized.[3] A similar reactivity pattern has been reported for alkyl (ω-imidoalkyl) sulfides – i.e., thioethers also show excellent donor activity for electron transfer reactions yielding sulfur-containing macrocycles.[4] Unlike that of the decarboxylative cyclization, the regioselectivity of the heterocyclic ring formation depends critically on the spacer chain separating the phthalimide chromophore from the thioether group. Furthermore, the cyclization sometimes proceeds only with low quantum and chemical yields, presumably due to efficient competing back-electron processes.[4,5] To overcome these disadvantages, we looked for a powerful method by which the regioselectivity of ring formation could be controlled and chemical yields optimized. This method combines thioether and carboxylate functionalities in acceptor-donor-donor triads. Because of the low oxidation potentials of the thioether fragment (for Me_2S: $E_{Ox.}$ = 1.23 V in MeCN vs. SCE)[6] in comparison with the carboxylate anion (for $MeCO_2^-$: $E_{Ox.}$ = 1.54 V in MeCN, 2.65 V in H_2O vs. SCE)[7] it was expected that sulfur oxidation should dominate the photoinduced electron transfer.

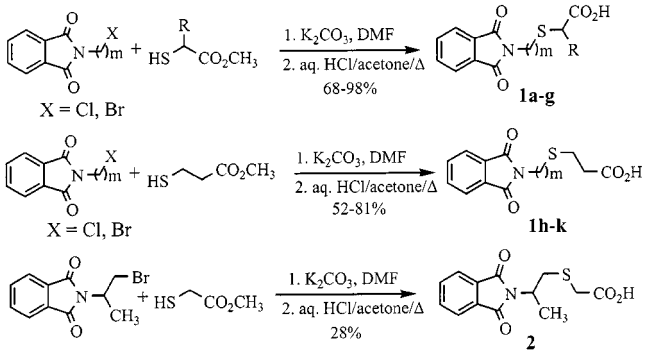
[a] Institut für Organische Chemie, Universität zu Köln, Greinstr. 4, 50939 Köln, Germany
Fax: (internat.) + 49-(0)221/470-5057
E-mail: griesbeck@uni-koeln.de
[b] Inoue Photochirogenesis Project, ERATO, JST, 4-6-3 Kamishinden, Toyonaka-shi, Osaka, 560-0085, Japan
[c] FB 8 – OC I (Chemie-Biologie) der Universität–GH Siegen, Adolf-Reichwein-Str. 2, 57068 Siegen, Germany

Results and Discussion

Intramolecular Reactions

The phthalimidoalkylsulfanylcarboxylic acids **1a–k** and **2** were easily available from the corresponding *N*-(hydroxyalkyl)phthalimides and mercaptocarboxylic acids. The *N*-

  1434–193X/01/0510–1831 $ 17.50+.50/0



Scheme 1. Synthesis of starting materials **1a**−**1k** and **2**

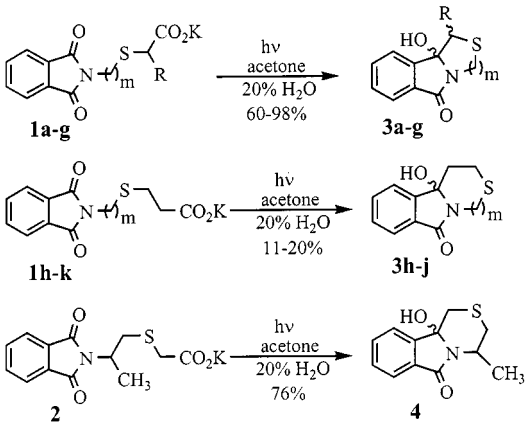
Table 1. Starting materials **1a**−**k**

	1a	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**
m =	1	1	2	2	3	3	4
R =	H	CH_3	H	CH_3	H	CH_3	H
yield (%)	68	98	79	82	82	78	77
	1h	**1i**	**1j**	**1k**			
m =	1	2	3	4			
yield (%)	59	72	52	81			

(hydroxyalkyl)phthalimides were prepared from phthalic anhydride and the corresponding amino alcohols[8] or phthalimide and formaldehyde,[9] respectively. Compounds **1a**, **1b**, and **1h** were synthesized by an alternative method based on the work of Gong and Iwasawa,[10] by condensation of *N*-(hydroxymethyl)phthalimide and the mercaptocarboxylic acid in a mixture of trifluoromethaneacetic acid and trifluorosulfonic acid. All other compounds were obtained after transformation of the hydroxy derivatives into the halogenated phthalimides using PBr_3 (for $m \geq 2$)[8] or thionyl chloride (for $m = 1$),[11] coupling[5] with the methyl mercaptocarboxylates (prepared according to ref.[12]), and hydrolysis to give the free acids **1** and **2**.[13] (Scheme 1, Table 1).

Under standard irradiation conditions at 300 nm in acetone/water mixtures, the potassium salts of substrates **1** and **2** cyclized with concomitant extrusion of CO_2 to give the medium-sized or macrocyclic products **3** and **4**. The efficiency of this reaction was strongly dependent on the nature of the carbon chain separating the thioether sulfur atom and the carboxylate group (Scheme 2, Table 2, Figure 1). The structures of the medium-sized heterocycles **3h**, **3i**, and **4** were established by X-ray structure analyses.

The shift in efficiency noticeable in Table 2 corresponds to the change in the hydrocarbon linker from methylene to ethylene. The mercaptoacetic acid and 2-mercaptopropionic acid derivatives **1a**−**g** and **2** gave the corresponding cyclization products **3a**−**g** and **4** in high yields and with high regioselectivities. In all cases, the activation of the electron donor terminus involved decarboxylation and thus generation of a primary radical at the terminal carbon atom. This phenomenon thus already demonstrated that these reactions were initiated by means of one-electron oxidation (PET) of the sulfur atom. The strongest evidence came from



Scheme 2. Photolysis of **1a**−**1k** and **2**: macrocyclic products **3a**−**3j** and **4**

Table 2. Photolysis of **1a**−**k** and **2**: macrocyclic products **3a**−**3j** and **4**

	3a	**3b**	**3c**	**3d**	**3e**	**3f**	**3g**	**3h**	**3i**	**3j**	**3k**	**4**
m =	1	1	2	2	3	3	4	1	2	3	4	–
R =	H	CH_3	H	CH_3	H	CH_3	H	–	–	–	–	–
yield (%)	95	98	61	60	62	93	66	20	11	15	–[a]	76
de (%)[b]	–	36	–	> 95	–	4	–	–	–	–	–	10

[a] Decomposition. – [b] Determined by ^1H NMR (±5%). –

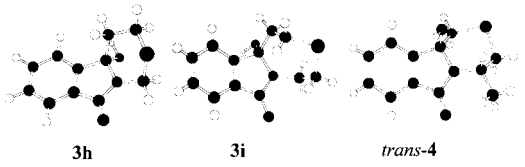


Figure 1. X-ray structures of **3h**, **3i**, and *trans*-**4** (Chem3D drawings)

the position of C−H activation: The homolytic carbon−hydrogen (Norrish) bond cleavage should involve either adjacent (γ or δ) hydrogen atoms or the weaker secondary α-thio C−H bonds. Ring closure at the internal methylene group in the position α to the sulfur atom (as described by Sato and Kanaoka for the methyl thioethers)[5] was not observed, indicating that the number of carbon atoms between the phthalimide chromophore and the sulfur atom (*m*) does not influence the cyclization efficiency at all. Relative to the mercaptoacetic acid and 2-mercaptopropionic acid derivatives, the conversions and yields dropped drastically for the 3-mercaptopropionic acid derivatives **1h**−**k**, and the photoreactions became more sluggish. Although the cyclization was still an important pathway for product formation, several photochemical cleavage products were detected by GC-MS analysis. Obviously, side reactions were competing successfully with ring formation for the mercaptopropionic acid derivatives. In the case of substrate **1k**, only decomposition was observed, indicating that an increase in the primary spacer length (*m*) between chromophore and sulfur atom resulted in further reduction of the efficiency of cyclization.

The photolyses of the methyl-branched starting materials **1b**, **1d**, **1f**, and **2** resulted in the formation of diastereoisomeric products **3b**, **3d**, **3f**, and **4**, with the methyl groups *cis* or *trans* to the hydroxy groups. The relative configuration of **4** was established by X-ray structure analysis. In all other cases, the chemical shifts in the ^{1}H NMR spectra were assigned to the corresponding diastereoisomers on the basis of the PM3-optimized geometries,[14] as shown for **3b** in Figure 2.

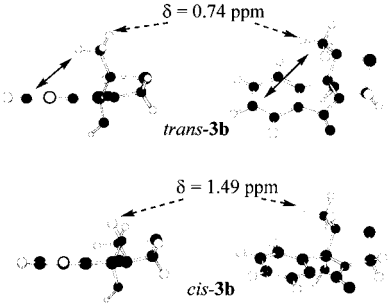


Figure 2. Diastereoisomer assignment for **3b**

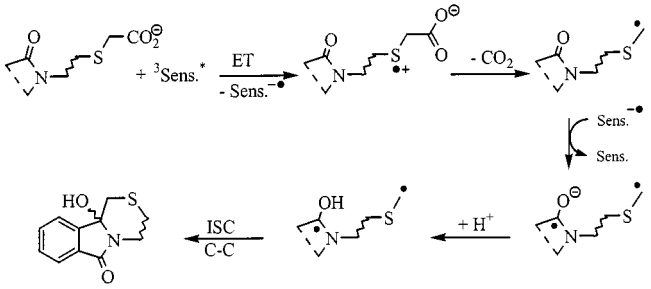
The methyl group in the *trans* diastereoisomer is strongly influenced by the shielding effect of the aromatic ring (represented by the arrow), whereas no such effect was observed in the case of the *cis* isomer.[5] This effect − which was also observed for the corresponding methine proton − falls off with increasing ring size (Table 3), and for **3f** the differences were negligible. From the NMR analysis, the major diastereoisomers could be assigned for **3b** and **3d** as *trans* and for **3f** and **4** as *cis*.

Table 3. ^{1}H-NMR chemical shifts of ring methyl groups in **3b**, **3d**, and **3f**

	Ring size	*de* (%)	δ (CH_3) *trans*	δ (CH_3) *cis*
3b	5	36	0.78	1.49
3d	6	> 95	0.88	–
3f	7	7	1.43	1.47

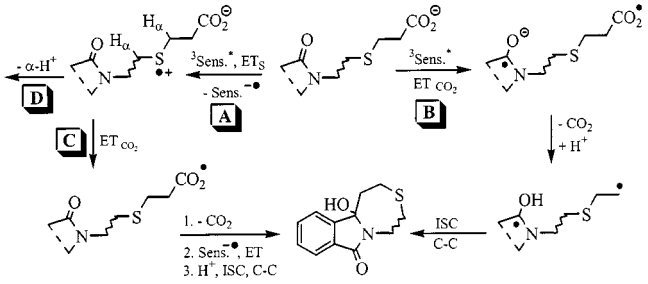
The excellent cyclization efficiency of the mercaptoacetic acid and 2-mercaptopropionic acid derived starting materials can be explained mechanistically by a sulfur-assisted α-decarboxylation reaction (Scheme 3). The recently postulated intramolecular photoinduced electron transfer (PET) mechanism involving the thioether as the electron-donating species and the triplet excited phthalimide as the electron-accepting one[5] has been established for direct excitation of the chromophore.[15]

Under the sensitization conditions used in the experiments described here, an intermolecular photoinduced electron transfer (PET) involving triplet excited acetone was confirmed.[15] The thioether is thus oxidized by PET to a sulfur-centered radical cation. Unlike the case of the simple dialkyl sulfide substrates,[5] no deprotonation from the respective α-CH position occurred, but regioselective extrusion of CO_2 took place, with formation of an α-thio C radical. A secondary electron transfer from the acetone radical anion simultaneously generates the phthalimide radical anion, which combines with the terminal carbon radical to give the tricyclic products **3** and **4**. This mechanism convincingly mirrors the photocyclization of α-(silylthiomethoxy)[16] or α-(stannylthiomethoxy)[17] derivatives in which trialkylsilyl and trialkylstannyl cations serve as leaving groups. Mariano, Yoon, and co-workers have also demonstrated that quantum efficiencies for cyclization increase for analogous *N*-(aminoethyl)phthalimides bearing H, TMS, or CO_2^- as the terminal α groups.[18] The presence of the appropriate α leaving group CO_2 obviously enhances the chemical reactivity of the radical ion pair and suppresses the unproductive back electron transfer (BET) reaction.[19]



Scheme 3. Mechanistic scenario for α-(alkylthio)carboxylates

For the 3-mercaptopropionic acid derivatives, product formation can no longer be explained by a sequence of PETs involving sulfur atom oxidation and subsequent extrusion of CO_2. These cases might alternatively proceed by direct electron transfer involving the carboxylate anion (path **B**, Scheme 4).



Scheme 4. Mechanistic scenario for β-(alkylthio)carboxylates

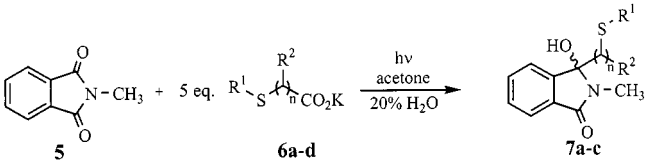
For the corresponding phthalimido-ω-carboxylic acids, this electron transfer is assumed to proceed in an intramolecular fashion involving the $^3\pi,\pi^*$ state.[15] The remarkable drop in efficiency can be interpreted in terms of the weaker donor properties of the carboxylate anion in comparison to the thioether group. Thus, the low yields for cyclization, and also the low degrees of conversion (52−71% reisolated starting material), indicate that the primary electron transfer still occurs from the thioether function (path **A**), but is mainly followed by rapid nonproductive BET.[20] Alternatively, the sulfur radical cation might act as a *mediator* for a second intramolecular electron transfer from the carboxylate (path **C**), followed by decarboxylative cyclization similar to path **B**.

This sequential process, however, can most probably be ruled out, because no reactivity was observed in the corres-

ponding intermolecular experiments (vide infra). Methylene hydrogen atoms in positions α to a sulfur-centered radical cation are known to be highly acidic and deprotonation consequently generates a corresponding α-carbon radical. This may give rise to the observed unselective fragmentation reactions (path **D**). In the case of the extremely unselective decomposition of **1k**, the analogous thiomethyl derivative undergoes deprotonation and subsequent cyclization exclusively at the internal CH_2 group,[5] and therefore compound **1k** might largely be the product of path **D**.

Intermolecular Reactions

Decarboxylative addition reactions of carboxylates and α-oxocarboxylates to phthalimides have been reported recently.[21] We have also shown that heteroatoms in close proximity to the carboxylic group greatly influence the efficiency of addition.[22] In order to examine the possible interaction between thioether and the carboxylate donor groups, intermolecular reactions in which these donors were separated by methylene or ethylene spacers were investigated. As a model substrate, *N*-methylphthalimide (**5**) was irradiated in aqueous acetone in the presence of 5 equiv. of the (alkylsulfanyl)carboxylates **6a**−**d** (Scheme 5).



Scheme 5. Intermolecular reactions with *N*-methylphthalimde

The potassium salts of the mercaptoacetic acid and 2-mercaptopropionic acid derivatives **6a**−**c** ($n = 1$) readily added to the carbonyl group of the phthalimide with concomitant decarboxylation to give the addition products **7a**−**c** in good to excellent yields. The product **7b**, from the addition of the 2-(methylsulfanyl)propionic derivative, was formed as a 1:1 mixture of diastereoisomers, of which the *u* isomer was suitable for X-ray structure analysis. Compound **7a** was likewise appropriate for X-ray structure analysis (Figure 3).

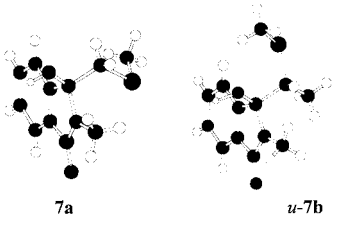


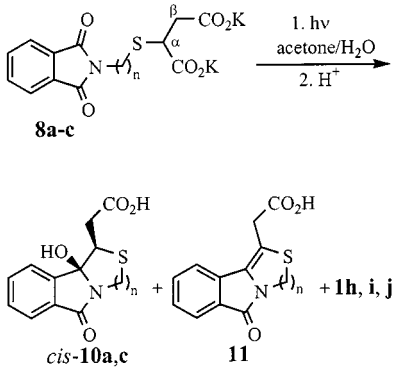
Figure 3. X-ray structures of **7a** and *u*-**7b** (Chem3D drawings)

In contrast with these results, potassium 2-(methylsulfanyl)propionate (**6d**) ($n = 2$) gave no trace of addition product, even after prolonged irradiation (Table 4). This behavior differs from the intramolecular reactions with substrates **1h**−**1j**, and consequently the thioether moiety must serve as a hole trap in intermolecular PET whereas oxidation of the carboxylate group is still possible in the intramolecular version. The latter oxidation seemingly is not mediated by a sulfur-centered radical cation for substrates with ethylene spacers ($n = 2$).

Table 4. Photolysis of **6a**−**d** with **5**: addition products **7a**−**c**

	6a	**6b**	**6c**	**6d**
R^1	Me	Me	Ph	Me
R^2	H	Me	H	H
n	1	1	1	2
yield of **7** (%)	90	78	57	–

In order to evaluate the mechanistic scenario further, especially the efficiency of α-decarboxylation, the mercaptosuccinic acid derivatives **8a**−**c** and **9** were applied in intramolecular and intermolecular reactions (Scheme 6).

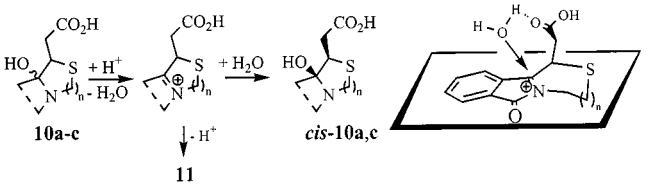


Scheme 6. Photocyclization of (thioalkyl)succinic acid derivatives **8a**−**c**

With these model compounds, it was possible to study the intramolecular competition between α- and β-decarboxylation. The electron transfer step also generates different species: anion biradicals or solvent-separated radical/radical anion pairs. Irradiation of **8a**−**c** in aqueous acetone resulted in α-decarboxylation irrespective of the spacer chain lengths. Together with the expected cyclization products **10**, additional products from the noncyclization path (CO_2/H exchange) **1h**−**j** were also obtained (Table 5). Compound **11** was isolated as the dehydration product from **8b**, as a result of the acidic workup conditions. Interestingly, the γ-hydroxy acids **10a** and **10c** were also formed in diastereomerically pure (*cis*) form (within the detection limit of ^{1}H NMR integration). This unusual result can be explained by an acid-catalyzed epimerization through the corresponding acyliminium cation,[23] which is hydrated in a stereoselective manner controlled by the carboxylate group (Scheme 7). We have recently reported an analogous acid-catalyzed *trans*/*cis* isomerization during the synthesis of benzopyrrolizidines.[24]

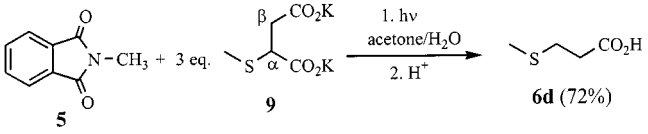
Table 5. Photolysis of **8a**−**c**: product yields (%)

Substrate	*n*	**10**	**11**	**1**
8a	1	76	–	traces
8b	2	–	39	41
8c	3	57	–	28



Scheme 7. Mechanistic scenario for the formation of *cis*-γ-hydroxy acids **10**

A striking result was obtained when *N*-methylphthalimide was irradiated in the presence of 3 equiv. of the dipotassium salt of (methylsulfanyl)succinic acid **9**: The "simple" decarboxylation product **6d** was isolated in 72% yield (Scheme 8). Small quantities of addition products (< 5%) were detected in the NMR spectrum of the crude photolysis mixture. This reaction also revealed the specific role of acetone as a solvent *and* sensitizer: The radical combination product **12** was isolated (and characterized by X-ray structure analysis) in 10% yield (Figure 4). This product also demonstrated the reluctant behavior of **9** with respect to photoaddition with *N*-methylphthalimide.



Scheme 8. Intermolecular photoreaction between **9** and *N*-methylphthalimide

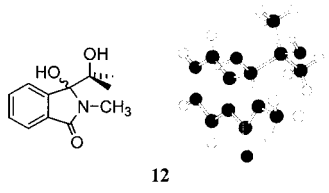
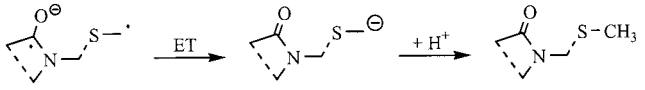


Figure 4. X-ray structure of **12** (Chem3D drawing)

The formation of the free acids **1h**−**j**, as well as **6d**, can be explained by assuming a second (thermal) electron transfer from the imide radical anion back to the carbon radical. This process generates a carbanion which is immediately protonated by water (Scheme 9).[25] This process is energetically feasible either for the intramolecular or for the intermolecular version (indicated by the dashed line in Scheme 9). Analogous decarboxylation products were also formed as side products in the photolysis of phthalimido-ω-carboxylates.[3,26] In special cases, such as the photolysis of 1-adamantanecarboxylate in the presence of **5**, the corresponding hydrocarbon became the sole product.[21]



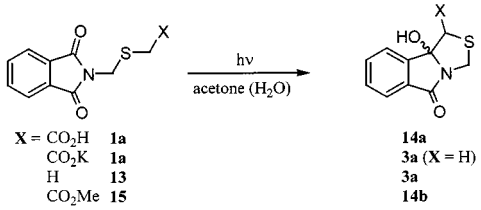
Scheme 9. Formation of "simple" decarboxylation products

Further Mechanistic Implications

In the intermolecular version, the radical cation of **9** can easily escape from the solvent cage and is deactivated in secondary processes.[6] These processes are especially favored in the presence of free ions and may therefore be likely under the reaction conditions used. The radical (or, prior to protonation, the radical anion) of *N*-methylphthalimide (**5**) can combine with the acetone radical anion to give **12**. Similar acetone trapping products have also been found by other groups.[27]

In order to compare the cyclization efficiencies of *carboxy-activated* versus *nonactivated* ω-phthalimidoalkyl thioether, the substrates **1a** and **13** were irradiated in pure acetone *in the absence* of potassium carbonate. In the case of **1a**, prolonged irradiation was necessary to drive the reaction towards near complete conversion, whereas with **13** no product formation was observed at all (within the detection limit of ^{1}H NMR). Compound **1a** gave (beside the diastereoisomers **14a**) large amounts of the decarboxylation/cyclization product **2a**, an observation supported by the results reported by Davidson and co-workers.[19] In order to establish whether carboxylic esters also activate the PET cyclization, the corresponding methyl ester **15** was investigated; it in fact cyclized after prolonged irradiation (80% conversion), yielding a mixture of diastereoisomers **14b**.

For compound **14**, the *trans* diastereoisomer was found to be the major product, in analogy to the diastereoselectivity pattern described for the branched substrate **1b**. Beside cyclization products, small amounts of several bond cleavage products (ca. 10−15%) were detected by GC-MS analyses of the crude reaction mixtures. In contrast to this, the potassium salt of **1a** gave the desired photoproduct **3a** after relatively short irradiation, in 90% yield and in high purity (Scheme 10, Table 6). This difference clearly demonstrates that a carboxylate group in a position α to the sulfur radical cation readily increases the cyclization efficiency, which fits



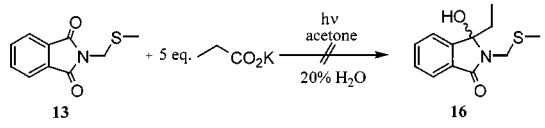
Scheme 10. Comparison of cyclization efficiencies: activation by carboxylate

with the results reported by Mariano and co-workers.[18] In addition, aqueous solvents also influence the efficiency of photoreactions, and may therefore play an important role in the reactions described here.[28]

Table 6. Photolysis of **1a**, **13**, and **15** − product composition (normalized to 100%)

	X	conv. [%]	**3a** [%]	**14** [%] (*de*)
1a-H	COOH	80	45	55 (76)
1a-K	COOK	100	100	–
13	H	< 5	–	–
15	COOMe	80	–	100 (34)

When the substrate **13** was irradiated under intermolecular photoalkylation conditions (5 equiv. of potassium propionate),[21] no addition product (**16**) was observed (Scheme 11). This result again strongly supports the supposition that the electron transfer occurs primarily from the sulfur atom and not from the carboxylate. In **13**, the sulfur acts as a "hole trap", as in the inverse intermolecular reaction of *N*-methylphthalimide (**5**) with the potassium salt of (methylsulfanyl)propionic acid **6d** (Scheme 5).



Scheme 11. Unproductive photoaddition: **13** acts as hole trap

Quantum Yield Studies

Further evidence for the proposed reaction mechanism was provided by measurements of quantum yields of decomposition (Φ_d), which can be taken as a measure of cyclization efficiency under *direct* excitation conditions. The quantum yields of selected substrates were measured upon excitation at 308 nm in argon-saturated aqueous solutions at pH = 9 or in acetonitrile (Table 7).[29] In pure acetonitrile, in which the acids are present in their nondissociated forms, the quantum yields are low, and in the same range as the thioalkyl derivatives.[4,5]

Table 7. Quantum yields for decomposition (Φ_d)

	1a	**1b**	**1h**	**8a**	**13**
H_2O, pH = 9	0.12	0.10	< 0.05	0.13	0.01
MeCN	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03

Obviously, the carboxylate group is unreactive under these conditions and electron transfer is followed by rapid *non*productive BET. Under basic conditions at pH = 9, the quantum yields for decomposition increase for the α-carboxy derivatives **1a**, **1b**, and **8a**. Activation therefore proceeds solely for the α-carboxylates and not for the corresponding β-carboxylates or acids (α and β with respect to the sulfur position).

Electrochemical Measurements

The differences in reactivity between the intermolecular and intramolecular reactions (addition versus cyclization) of the β-(mercaptoalkyl)propionate substrates (i.e., **6d** versus **1h−j**) was striking and can be rationalized by assuming preorientation phenomena in the ground and/or excited states.[30] We have already postulated these interactions as a reason for the high efficiency and selectivity of the decarboxylative cyclization reaction. In a simple description of this phenomenon, the templating metal ion (such as potassium, which emerged as the optimal metal) acts as an anchor and stabilizes an optimal geometry of the donor-acceptor couple for PET and consequently also for combination of the subsequently formed biradical (Figure 5).

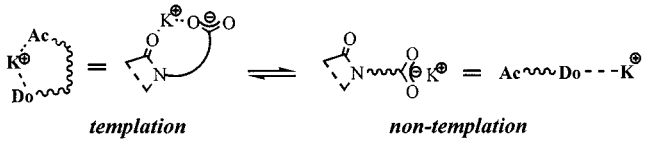


Figure 5. Preorientation induced by templating potassium cations

Detailed studies concerning the nature of the base supported this assumption: Only group I and II metal cations favored cyclization or decarboxylation products, whereas organic bases were less activating.[3] Under the aqueous irradiation conditions, the nontemplated form might be favored (as a solvent-separated ion pair, for example) but should nevertheless exist in equilibrium with the templated form. Mariano and co-workers postulate analogous free zwitterionic or solvent-separated ionic structures, respectively, to explain the solvent and base effects in the photochemistry of anilinium carboxylates.[18]

Attempts to detect these potassium salt preorientation phenomena by NMR failed, but we were finally able to observe a comparable hydrogen bond activity for the free acids **1a** and **1h** by cyclic voltammetric (CV).[31] Strong hydrogen bonding is also assumed to be responsible for the effective α-decarboxylation of *N*-phthaloyl α-amino acids,[32] and might also explain the formation of the decarboxylative cyclization product **3a** under nonactivating conditions (vide supra). Even at low scan rates (50 mV s^{-1}), the compounds **1a** and **1h** showed reversible[33] reduction waves (**III**), at $E_{1/2} = -1.87$ and -1.77 V, respectively (in MeCN, vs. ferrocene), to the corresponding radical anions. Additionally, two broad anodically shifted pre-waves were detected (**I** and **II**, Figure 6, Table 8); these can be explained by hydrogen bonding between the carbonyl function of the phthalimide and the carboxylic proton.

Because of the partial protonation of the carbonyl group, its acceptor strength is increased and therefore an anodic shift of the corresponding waves is observed. The origin of the pre-waves can be either intramolecular (**II**) or a combination of intramolecular and intermolecular hydrogen bonding (**I**) (Figure 7). The latter assignment can be explained by considering that additional hydrogen bonding with the second carbonyl group should lead to an even more pronounced anodic shift.[31c]

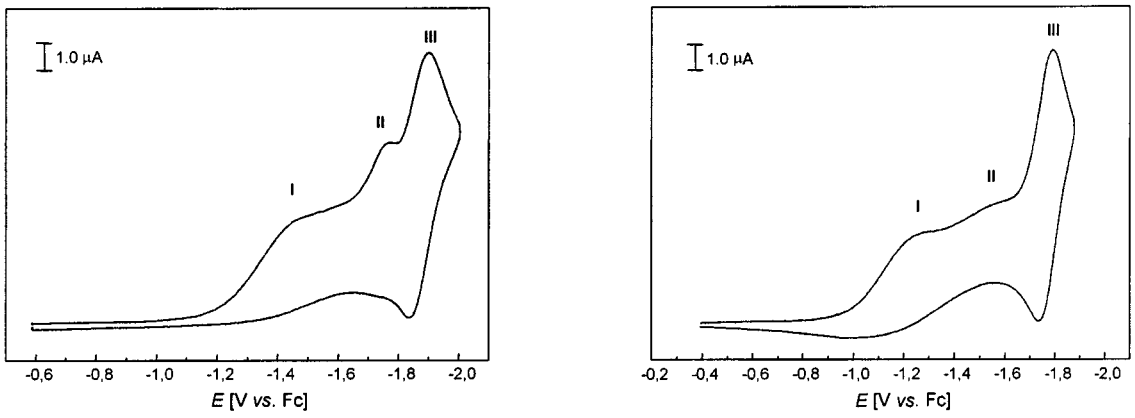


Figure 6. Cyclic voltammogram (in MeCN vs. ferrocene) of **1a** (left) and **1h** (right)

Table 8. Reduction potentials (V; in MeCN vs. ferrocene) for **1a** and **1h**

	$E_{1/2}$ (**III**)	E_{pc}(**II**)	E_{pc}(**I**)
1a	−1.87	−1.74	−1.50
1h	−1.77	−1.50	−1.20

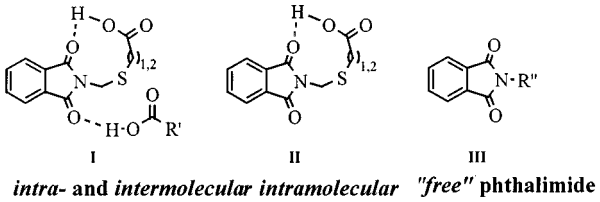


Figure 7. Intramolecular and intermolecular hydrogen bonding in **1a** and **1h**

A confirmation of the depicted model is suggested from CV experiments in the presence of external base or acid. Both pre-waves (**I** and **II**) disappeared completely when 1 equiv. of the nontemplating base DBU[34] (Figure 8) was added, whereas the addition of trifluoromethanesulfonic acid (CF_3SO_3H) resulted in an increase in current amplitude for the waves **I** and **II**. In both cases, only the first pre-wave (**I**) could be detected after the addition of more than 2 equiv. of acid.[35]

A definite assignment of the intermolecular and intramolecular nature of the pre-waves was obtained by varying the substrate concentration and the scan rate in the CV measurements.[36] Only the first pre-wave depends on these two parameters, thus indicating that intermolecular hydrogen bonds are clearly involved in wave **I**. For example, at lower concentrations and higher scan rates, a cathodic shift of **I** is observed, whereas the potential of **II** does not change. A qualitative assessment of the magnitude of the intramolecular hydrogen bonding (cf. waves **II**) of substrates **1a** and **1h** is equally possible. As wave **II** is more pronounced for **1a** than for **1h** (judged by height and area), intramolecular hydrogen bonding should be more prominent in **1a**. Adopting these results for the corresponding potassium salts as well, the template effects might actually be responsible (at least in part) for the efficiency of the PET cyclization for **1h**. The weaker donor property of the carboxylate is partly compensated by a close carboxylate−acceptor contact.

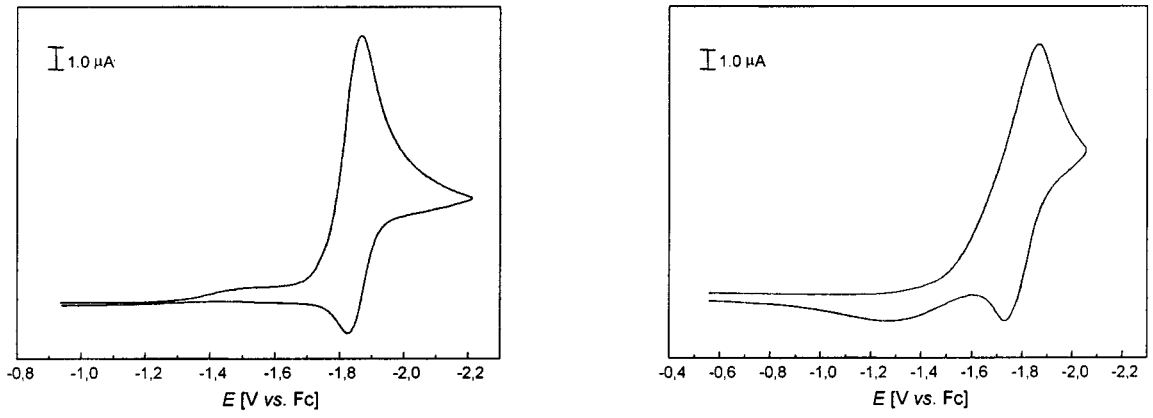


Figure 8. Cyclic voltammogram (in MeCN vs. ferrocene) of **1a** (left) and **1h** (right) after addition of 1 equiv. of DBU

Conclusion

Photodecarboxylative cyclization and addition reactions of mercaptoacetates and 2-mercaptopropionates proceeds regioselectively and in high yields, whereas the corresponding 3-mercaptopropionates show reduced activity and product formation only in the intramolecular pathway. The α-carboxylate group can be used as a powerful directing and activating group to synthesize sulfur-containing macrocycles or addition products. Although the β-carboxylate derivatives undergo cyclization less efficiently, this route is still attractive because the corresponding products are not available through the thioalkyl,[5] α-(silylthiomethoxy),[16] or α-(stannylthiomethoxy)[17] approaches. Preorientation is a useful explanation, supported by the efficiency of product formation, quantum yields of decomposition, and electrochemical measurements.

Experimental Section

1. General: For special procedures for the synthesis of starting materials, see below. For standard procedures for the synthesis of *N*-(hydroxyalkyl)phthalimides, see ref.[8] and ref.[9] For standard procedures for the synthesis of *N*-(halogenoalkyl)phthalimides, see ref.[8] and ref.[11] For a standard procedure for the synthesis of methyl (mercaptoalkyl)carboxylates, see ref.[12] For a standard procedure for the synthesis of (methylsulfanyl)carboxylic acids (**6** and **9**), see ref.[37] Compound **13** was prepared from potassium phthalimide and methylthiomethyl chloride according to ref.[5] Compound **5** was synthesized by a method described by Schindlbauer.[38] − Rayonet® RPR-208 chamber photoreactors (8 × 3000Å lamps, ca. 800 W, λ = 300 ± 10 nm) and immersion wall reactors (λ > 280 nm) were used for irradiation experiments. − Column chromatography: Silica gel (Macherey & Nagel) 230−240 mesh; *n*-hexane, ethyl acetate. − M.p.: Büchi melting point apparatus, type no. B-535; uncorrected values. − IR: Perkin−Elmer 1600, FT-IR spectrometer; $\tilde{\nu}$ in cm^{-1}. − NMR: ^1H: Bruker AC 300 F (300 MHz), Bruker DPX 300 (300 MHz); ^{13}C: Bruker AC 300 F (75.5 MHz), Bruker DPX 300 (75.5 MHz), C multiplicities were determined by DEPT; δ in ppm, *J* in Hz. − Mass spectrometry (EI or CI): Finnigan Incos 500; *m*/*z* (%). − For GC-MS studies the products were transformed into their corresponding TMS ethers and esters using *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide (MSTFA).[39] − UV/Vis: Perkin−Elmer Lambda 7, UV/Vis spectrophotometer; λ in nm (ε). − HR mass spectrometry (FAB): Finnigan MAT H-SQ 30. − Combustion analyses: Elementar Vario EL. − Cyclic voltammetry:[40] Princeton Applied Research Model 362 potentiostat with a Philips model PM 8271 XYt-recorder for scan rates < 1 V s^{-1}. For fast scan cyclic voltammetry, a Hewlett Packard Model 331A4 Function Generator was used, connected to a three-electrode potentiostat developed by Amatore.[41] Data were recorded with an HP 54510A digitizing oscilloscope linked to a 486DX33 computer using HP data transfer program Scopelink. The I_{pc}/I_{pa} ratios were determined according to Nicholson's equation.[42] − X-ray data for **3i** and *u*-**7b**, see ref.[43] and ref.[44], respectively.

2. Phthalimidoalkylsulfanyl Carboxylic Acids. − General Procedure:[5,13] A suspension of the *N*-(halogenoalkyl)phthalimide (10 mmol), the methyl mercaptocarboxylate (12 mmol), and K_2CO_3 (24 mmol) in 50 mL of DMF was stirred at room temp. overnight. The reaction mixture was diluted with H_2O (100 mL) and extracted with AcOEt (3 × 100 mL). The organic solution was dried ($MgSO_4$) and concentrated. The methyl ester was redissolved in a mixture of acetone, H_2O, and conc. HCl soln. (40:28:12, v/v/v), and heated under reflux for 2 h. After cooling to room temp., the volume of the solution was reduced by 50% under vacuum; it was then diluted with H_2O (100 mL) and extracted with AcOEt (3 × 100 mL). The organic layer was dried ($MgSO_4$) and concentrated to dryness. Alternatively, the acids **1a**, **1b**, and **1h** were obtained according to Gong and Iwasawa's method,[10] by condensation of the *N*-(hydroxymethyl)phthalimide and the mercaptocarboxylic acid in a mixture of TFA and trifluoromethanesulfonic anhydride (19:1, v/v). The thiosuccinic acids **8a**−**c** were synthesized by hydrolysis of the corresponding dimethyl esters in a mixture of acetic acid and HCl (5:1, v/v), according to ref.[5] All starting materials gave satisfactory elemental analyses or molecular masses from high resolution MS spectra (HR-MS).

(Phthalimidomethylsulfanyl)acetic Acid (1a): M.p. 100−102°C. − IR (KBr): $\tilde{\nu}$ = 3064, 1717, 1635, 1094, 935, 722. − ^1H NMR (300 MHz, $CDCl_3$): δ = 3.52 (s, 2 H), 4.88 (s, 2 H), 7.73 (dd, *J* = 5.3, 3.1, 2 H), 7.86 (dd, *J* = 5.3, 3.1, 2 H), 9.26 (br. s, 1 H, OH). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 33.9 (CH_2), 39.6 (CH_2), 123.7 (CH), 131.9 (C), 134.4 (CH), 167.6 (C), 175.8 (C). − MS (70 eV, TMS derivative); *m*/*z* (%): 323 (4) [M^+], 234 (8), 192 (33), 160 (100), 104 (18), 89 (56), 76 (23), 73 (56). − UV/Vis (CH_3CN): λ = 219 (37700), 291 (1950).

2-(Phthalimidomethylsulfanyl)propionic Acid (1b): M.p. 120−123°C. − IR (CsI): $\tilde{\nu}$ = 1776, 1727, 1716, 1409, 1380, 1284, 1032, 914, 725. − ^1H NMR [300 MHz, $CDCl_3$/[D_6]DMSO (ca. 10%)]: δ = 1.34 (d, *J* = 7.2 Hz, 3 H), 3.65 (q, *J* = 7.2 Hz, 1 H), 4.74 (d, *J* = 14.4 Hz, 1 H), 4.88 (d, *J* = 14.4 Hz, 1 H), 7.63 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2 H). − ^{13}C NMR [75.5 MHz, $CDCl_3$/[D_6]DMSO (ca. 10%)]: δ = 17.3 (CH_3), 38.6 (CH), 41.8 (CH_2), 123.2 (CH), 131.7 (C), 134.0 (CH), 167.1 (C), 174.6 (C). − MS (70 eV, TMS derivative); *m*/*z* (%): 337 (9) [M^+], 322 (2), 248 (1), 192 (27), 160 (100), 146 (23), 104 (12), 76 (12), 73 (56). − UV/Vis (CH_3CN): λ = 218 (27600), 292 (1200).

(2-Phthalimidopropylsulfanyl)acetic Acid (2): M.p. 105−110°C. − IR (CsI): $\tilde{\nu}$ = 3395, 1775, 1727, 1716, 1409, 1380, 1283, 1032, 914, 725, 532. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.46 (d, *J* = 6.9 Hz, 3 H), 3.01 (dd, *J* = 14.0, 5.0 Hz, 1 H), 3.07 (d, *J* = 15.1 Hz, 1 H), 3.20 (dd, *J* = 14.0, 10.5 Hz, 1 H), 3.25 (d, *J* = 15.1 Hz, 1 H), 4.46 (qdd, *J* = 10.5, 6.9, 5.0 Hz, 1 H), 7.62 (dd, *J* = 5.2, 3.0 Hz, 2 H), 7.73 (dd, *J* = 5.2, 3.0 Hz, 2 H), 8.13 (br. s, 1 H, OH). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 17.8 (CH_3), 32.3 (CH_2), 35.1 (CH_2), 45.1 (CH), 123.1 (CH), 131.5 (C), 133.8 (CH), 168.2 (C), 174.4 (C). − UV/Vis (CH_3CN): λ = 218 (29100), 292 (1300).

(2-Phthalimidoethylsulfanyl)acetic Acid (1c): M.p. 103−105°C. − IR (CsI): $\tilde{\nu}$ = 3243, 1767, 1718, 1700, 1430, 1400, 1383, 1259, 1129, 1096, 938, 721, 535. − ^1H NMR (300 MHz, $CDCl_3$): δ = 2.97 (t, *J* = 6.6 Hz, 2 H), 3.32 (s, 2 H), 3.92 (t, *J* = 6.6 Hz, 2 H), 7.69 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.81 (dd, *J* = 5.5 Hz, 3.0, 2 H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 30.4 (CH_2), 32.3 (CH_2), 35.9 (CH_2), 123.4 (CH), 131.8 (C), 134.0 (C), 168.2 (C), 175.5 (s, C). − UV/Vis (CH_3CN): λ = 207 (8900), 220 (35700), 292 (1800).

2-(2-Phthalimidoethylsulfanyl)propionic Acid (1d): M.p. 93−95°C. − IR (CsI): $\tilde{\nu}$ = 1773, 1718, 1439, 1425, 1399, 1108, 1071, 935, 717. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.41 (d, *J* = 7.1 Hz, 3 H), 3.00 (m, 2 H), 3.57 (q, *J* = 7.1 Hz, 1 H), 4.01 (m, 2 H), 7.70 (dd, *J* = 5.6, 3.1 Hz, 2 H), 7.83 (dd, *J* = 5.6, 3.1 Hz, 2 H), 8.82 (br. s, 1 H, OH). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 16.9 (CH_3), 30.4 (CH_2), 36.9 (CH_2), 40.3 (CH), 123.8 (CH), 132.3 (C), 134.5

(CH), 168.6 (C), 178.7 (C). − UV/Vis (CH_3CN): λ = 207 (7400), 221 (30700), 239 (10400), 292 (1900).

(3-Phthalimidopropylsulfanyl)acetic Acid (1e): M.p. 94−95°C. − IR (CsI): ṽ = 1767, 1718, 1684, 1409, 1258, 869, 727, 531. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.98 (quin., *J* = 7.1 Hz, 2 H), 2.70 (t, *J* = 7.1 Hz, 2 H), 3.24 (s, 2 H), 3.78 (t, *J* = 7.1 Hz, 2 H), 7.69 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.82 (dd, *J* = 5.5, 3.0 Hz, 2 H), 10.10 (br. s, 1 H, OH). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 27.6 (CH_2), 29.9 (CH_2), 33.2 (CH_2), 36.8 (CH_2), 123.3 (CH), 132.0 (C), 134.0 (CH), 168.4 (C), 175.5 (C). − UV/Vis (CH_3CN): λ = 220 (35600), 240 (11000), 292 (2000).

2-(3-Phthalimidopropylsulfanyl)propionic Acid (1f): Oil. − IR (CsI): ṽ = 1771, 1713, 1438, 1398, 1368, 1188, 721. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39 (d, *J* = 7.2 Hz, 3 H), 1.94 (m, 2 H), 2.66 (m, 2 H), 3.37 (q, *J* = 7.2 Hz, 1 H), 3.74 (m, 2 H), 7.67 (dd, *J* = 5.6, 3.1 Hz, 2 H), 7.79 (dd, *J* = 5.6, 3.1 Hz, 2 H), 7.75 (br. s, 1 H, OH). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 16.7 (CH_3), 27.9 (CH_2), 28.8 (CH_2), 36.9 (CH_2), 40.9 (CH), 123.2 (CH), 131.9 (C), 133.9 (CH), 168.3 (C), 178.0 (C). − UV/Vis (CH_3CN): λ = 231 (15900), 239 (10500), 291 (1400).

(4-Phthalimidobutylsulfanyl)acetic Acid (1g): M.p. 80−83°C. − IR (CsI): ṽ = 1769, 1701, 1440, 1399, 1314, 1021, 717, 530. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.62 (m, 2 H), 1.76 (m, 2 H), 2.67 (t, *J* = 7.2 Hz, 2 H), 3.20 (s, 2 H), 3.66 (t, *J* = 6.9 Hz, 2 H), 7.67 (dd, *J* = 5.6, 3.1 Hz, 2 H), 7.80 (dd, *J* = 5.6, 3.1 Hz, 2 H), 8.18 (br. s, 1 H, OH). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.1 (CH_2), 27.5 (CH_2), 32.0 (CH_2), 33.3 (CH_2), 37.3 (CH_2), 123.2 (CH), 131.9 (C), 133.9 (C), 168.4 (C), 175.6 (C). − UV/Vis (CH_3CN): λ = 218 (40300), 232 (14800), 240 (10800), 291 (1800).

3-(Phthalimidomethylsulfanyl)propionic Acid (1h): M.p. 156−160°C. − IR (CsI): ṽ = 1768, 1714, 1710, 1698, 1427, 1385, 733, 532. − ^{1}H NMR [300 MHz, $CDCl_3$/CF_3CO_2H (ca. 10%)]: δ = 2.49 (t, *J* = 7.0 Hz, 2 H), 2.71 (t, *J* = 7.0 Hz, 2 H), 5.09 (s, 2 H), 7.59 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.69 (dd, *J* = 5.5, 3.0 Hz, 2 H). − ^{13}C NMR [75.5 MHz, $CDCl_3$/CF_3CO_2H (ca. 10%)]: δ = 26.5 (CH_2), 34.3 (CH_2), 39.1 (CH_2), 124.1 (CH), 131.4 (C), 134.9 (CH), 168.7 (C), 179.1 (C). − UV/Vis (CH_3CN): λ = 207 (7200), 222 (29800), 292 (1800).

3-(2-Phthalimidoethylsulfanyl)propionic Acid (1i): M.p. 110−112°C. − IR (CsI): ṽ = 1767, 1714, 1442, 1394, 1202, 719, 527. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.66 (t, *J* = 7.1 Hz, 2 H), 2.83 (t, *J* = 6.9 Hz, 2 H), 2.84 (t, *J* = 7.1 Hz, 2 H), 3.88 (t, *J* = 6.9 Hz, 2 H), 7.70 (dd, *J* = 5.4, 3.1 Hz, 2 H), 7.83 (dd, *J* = 5.4, 3.1 Hz, 2 H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.1 (CH_2), 30.0 (CH_2), 34.3 (CH_2), 36.8 (CH_2), 123.4 (CH), 131.9 (C), 134.0 (C), 168.1 (C), 177.3 (C). − MS (70 eV, TMS derivative); *m*/*z* (%): 351 (7) [M^+], 336 (10), 308 (2), 278 (2), 262 (2), 192 (27), 160 (100), 146 (23), 104 (12), 76 (12), 73 (56). − UV/Vis (CH_3CN): λ = 209 (7800), 221 (31500), 239 (10900), 292 (1900).

3-(3-Phthalimidopropylsulfanyl)propionic Acid (1j): M.p. 76−77°C. − IR (CsI): ṽ = 1775, 1713, 1415, 1399, 1015, 723. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.94 (quin., *J* = 7.1 Hz, 2 H), 2.54−2.2.65 (m, 4 H), 2.76 (t, *J* = 7.1 Hz, 2 H), 3.76 (t, *J* = 7.0 Hz, 2 H), 7.69 (dd, *J* = 5.5, 3.1 Hz, 2 H), 7.82 (dd, *J* = 5.5, 3.1 Hz, 2 H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.6 (CH_2), 28.3 (CH_2), 29.5 (CH_2), 34.5 (CH_2), 37.0 (CH_2), 123.3 (CH), 132.0 (C), 134.0 (CH), 168.4 (C), 177.3 (C). − UV/Vis (CH_3CN): λ = 220 (34000), 240 (10400), 291 (1800).

3-(4-Phthalimidobutylsulfanyl)propionic Acid (1k): M.p. 79−81°C. − IR (CsI): ṽ = 1775, 1713, 1699, 1695, 1442, 1398, 1031, 722, 530. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.61 (m, 2 H), 1.77 (m, 2 H), 2.59 (m, 4 H), 2.74 (dt, *J* = 7.4, 1.8 Hz, 2 H), 3.68 (t, *J* = 7.0 Hz, 2 H), 7.69 (dd, *J* = 5.6, 3.1 Hz, 2 H), 7.82 (dd, *J* = 5.6, 3.1 Hz, 2 H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.6 (CH_2), 26.8 (CH_2), 27.7 (CH_2), 31.5 (CH_2), 34.5 (CH_2), 37.4 (CH_2), 123.2 (CH), 132.0 (C), 133.9 (C), 168.4 (C), 177.2 (C). − UV/Vis (CH_3CN): λ = 218 (38000), 232 (14800), 240 (10700), 292 (1800).

2-(Phthalimidomethylsulfanyl)succinic Acid (8a): M.p. 213−215°C. − ^{1}H NMR [300 MHz, $CDCl_3$/CF_3CO_2H (ca. 10%)]: δ = 2.54 (dd, *J* = 17.3, 6.6 Hz, 1 H), 2.81 (dd, *J* = 17.3, 8.5 Hz, 1 H), 3.88 (dd, *J* = 6.6, 8.5 Hz, 1 H), 4.78 (d, *J* = 14.3 Hz, 1 H), 5.93 (d, *J* = 14.3 Hz, 1 H), 7.63 (dd, *J* = 5.4, 3.0 Hz, 2 H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2 H). − ^{13}C NMR [75.5 MHz, $CDCl_3$/CF_3CO_2H (ca. 10%)]: δ = 36.2 (CH_2), 39.1 (CH_2), 42.3 (CH), 123.2 (CH), 131.8 (C), 134.0 (CH), 167.1 (C), 172.1 (C), 173.4 (C).

2-(2-Phthalimidoethylsulfanyl)succinic Acid (8b): M.p. 157−160°C (decomp.). − ^{1}H NMR [300 MHz, $CDCl_3$/CF_3CO_2H (ca. 10%)]: δ = 2.83 (dd, *J* = 17.8, 4.9 Hz, 1 H), 3.03 (m, 2 H), 3.19 (m, 1 H), 3.85 (dd, *J* = 4.9, 9.9 Hz, 1 H), 4.01 (m, 2 H), 7.80 (dd, *J* = 5.4, 3.4 Hz, 2 H), 7.89 (dd, *J* = 5.4, 3.4 Hz, 2 H). − ^{13}C NMR [75.5 MHz, $CDCl_3$/CF_3CO_2H (ca. 10%)]: δ = 30.3 (CH_2), 35.4 (CH_2), 36.7 (CH_2), 40.2 (CH), 124.3 (CH), 131.1 (C), 135.3 (CH), 170.2 (C), 177.5 (C), 178.3 (C).

2-(3-Phthalimidopropylsulfanyl)succinic Acid (8c): M.p. 168−171°C (decomp.). − ^{1}H NMR [300 MHz, $CDCl_3$/CF_3CO_2H (ca. 10%)]: δ = 2.03 (m, 2 H), 2.79 (m, 3 H), 3.08 (dd, *J* = 17.8, 9.7 Hz, 1 H), 3.67 (dd, *J* = 5.6, 9.7 Hz, 1 H), 3.83 (m, 2 H), 7.77 (dd, *J* = 5.6, 3.2 Hz, 2 H), 7.86 (dd, *J* = 5.6, 3.2 Hz, 2 H). − ^{13}C NMR [75.5 MHz, $CDCl_3$/CF_3CO_2H (ca. 10%)]: δ = 27.5 (CH_2), 29.5 (CH_2), 35.6 (CH_2), 37.2 (CH_2), 40.8 (CH), 123.9 (CH), 131.3 (C), 135.0 (CH), 169.8 (C), 170.7 (C), 177.4 (C).

3. Photoreactions: General Procedure. − 3.1: A mixture of K_2CO_3 (1 mmol, 2 mmol for **8**) and the substrate (2 mmol) in water (10 mL) and acetone (10 mL) was heated gently until extrusion of CO_2 had stopped. Additional water (50 mL) and acetone (130 mL) were added. A homogeneous solution resulted, and this was irradiated (λ = 300 nm ± 10 nm) in a Pyrex tube for 12−24 h while purging with a slow stream of nitrogen, and cooling to ca. 15°C. The residual solution was extracted with CH_2Cl_2 (3 × 100 mL), washed with 5% $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated to dryness. The products were obtained after column chromatography or recrystallization from acetone or acetone/*n*-hexane.

9b-Hydroxy-1,9b-dihydrothiazolo[4,3-*a*]isoindol-5-one (3a): M.p. 121−122°C (124−125°C).[5] − IR (CsI): ṽ = 3345, 1700, 1683, 1402, 1381, 1062, 769, 709, 694. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.83 (d, *J* = 11.3 Hz, 1 H, SCH_2C), 3.29 (d, *J* = 11.3 Hz, 1 H, SCH_2C), 3.98 (br. s, 1 H, OH), 4.23 (d, *J* = 8.8 Hz, 1 H, NCH_2S), 4.77 (d, *J* = 8.8 Hz, 1 H, NCH_2S), 7.46 (m, 1 H, Ar-H), 7.57 (m, 3 H, Ar-H). − ^{13}C NMR [75.5 MHz, $CDCl_3$/[D_6]DMSO (ca. 10%)]: δ = 38.3 (CH_2), 40.7 (CH_2), 96.2 (C), 121.3 (CH), 122.0 (CH), 128.7 (CH), 129.1 (C), 132.1 (C), 145.5 (C), 166.1 (C). − MS (70 eV, TMS-derivative); *m*/*z*: 279 (7) [M^+], 264 (5), 232 (100), 218 (10), 204 (10), 190 (15), 160 (5), 134 (5), 89 (7), 73 (40), 59 (8), 51 (5). − MS (FAB); *m*/*z* (%): 208 (17) [M^+], 190 (12), 161 (2), 147 (2). − UV/Vis (CH_3CN): λ = 220 (10200), 229 (7400), 231 (4400). − HR-MS (PI-FAB): 208.044 ± 0.002 (calcd. 208.043).

9b-Hydroxy-1-methyl-1,9b-dihydrothiazolo[4,3-*a*]isoindol-5-one (*cis*-3b): M.p. 131−135°C. − IR (CsI): ṽ = 3319, 1699, 1695, 1683, 1468, 1380, 1050, 764, 696. − ^{1}H NMR (300 MHz, $CDCl_3$ in mixture with *trans*-**3b**): δ = 1.49 (d, *J* = 6.7 Hz, 3 H, CH_3), 3.20 (q,

J = 6.7 Hz, 1 H, SC*H*), 4.14 (br. s, 1 H, OH), 4.19 (d, *J* = 8.8 Hz, 1 H, NCH_2S), 4.69 (d, *J* = 8.8 Hz, 1 H, NCH_2S), 7.41−7.59 (m, 4 H, Ar-H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.4 (CH_3), 41.4 (CH), 48.4 (CH_2), 96.2 (C), 122.0 (C), 124.0 (CH), 130.4 (CH), 130.7 (C), 133.2 (CH), 144.1 (C), 167.9 (C). − MS (70 eV, TMS derivative); *m*/*z*: 293 (5) [M$^+$], 278 (6), 249 (5), 232 (100), 218 (8), 204 (12), 160 (8), 89 (7), 73 (48), 59 (22), 51 (2). − MS (FAB); *m*/*z* (%): 222 (39) [M$^+$], 204 (100), 188 (9), 160 (23), 131 (14), 105 (13). − UV/Vis (CH_3CN): λ = 240 (3900). − HR-MS (PI-FAB): 222.059 ± 0.002 (calcd. 222.059).

***trans*-3b:** ^{1}H NMR (300 MHz, $CDCl_3$ in mixture with *cis*-**3b**): δ = 0.74 (d, *J* = 7.0 Hz, 3 H, CH_3), 3.58 (q, *J* = 7.0 Hz, 1 H, SC*H*), 4.19 (d, *J* = 8.8 Hz, 1 H, NCH_2S), 4.26 (br. s, 1 H, OH), 4.78 (d, *J* = 8.8 Hz, 1 H, NCH_2S), 7.41−7.59 (m, 4 H, Ar-H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.1 (CH_3), 40.9 (CH), 47.8 (CH_2), 100.6 (C), 122.6 (CH), 123.8 (CH), 130.2 (CH), 132.1 (C), 133.1 (CH), 143.2 (C), 167.6 (C).

10b-Hydroxy-4-methyl-1,3,4,10b-tetrahydro[1,4]thiazino[3,4-*a*]isoindol-6-one (*cis*-4): M.p. 153−155°C. − ^{1}H NMR {300 MHz, $CDCl_3$/[D$_6$]DMSO (ca. 10%) in mixture with *trans*-**4**}: δ = 1.49 (d, *J* = 7.1 Hz, 3 H, CH_3), 2.42 (ddd, *J* = 13.5, 2.0 Hz, 1 H, SCH_2CN), 2.62 (d, *J* = 13.5 Hz, 1 H, SCH_2CN), 2.81 (dd, *J* = 13.6, 4.3 Hz, 1 H, SCH_2CO), 3.05 (dd, *J* = 13.5, 2.0 Hz, 1 H, SCH_2CO), 4.81 (qdd, *J* = 7.1, 4.3, 2.0, 1 H, NC*H*), 5.29 (br. s, 1 H, OH), 7.35−7.50 (m, 3 H, Ar-H), 7.68 (ddd, *J* = 7.4, 1.0 Hz, 1 H, Ar-H). − ^{13}C NMR {75.5 MHz, $CDCl_3$/[D$_6$]DMSO (ca. 10%)}: δ = 18.5 (CH_3), 33.3 (CH_2), 38.2 (CH_2), 43.2 (CH), 84.0 (C), 121.2 (CH), 123.2 (CH), 129.4 (CH), 130.4 (C), 132.0 (CH), 147.2 (C), 165.2 (C).

***trans*-4:** ^{1}H NMR {300 MHz, $CDCl_3$/[D$_6$]DMSO (ca. 10%) in mixture with *cis*-**4**}: δ = 1.72 (d, *J* = 6.9 Hz, 3 H, CH_3), 2.54 (d, *J* = 14.5 Hz, 1 H, SCH_2CN), 2.55 (d, *J* = 5.2 Hz, 1 H, SCH_2CN), 2.57 (d, *J* = 13.2 Hz, 1 H, SCH_2CO), 3.03 (d, *J* = 13.2 Hz, 1 H, SCH_2CO), 4.00 (qdd, *J* = 6.9, 5.2, 14.5 Hz, 1 H, NC*H*), 5.54 (br. s, 1 H, OH), 7.35−7.50 (m, 3 H, Ar-H), 7.63 (ddd, *J* = 7.4, 0.9 Hz, 1 H, Ar-H). − ^{13}C NMR {75.5 MHz, $CDCl_3$/[D$_6$]DMSO (ca. 10%)}: δ = 18.6 (CH_3), 33.6 (CH_2), 37.2 (CH_2), 50.4 (CH), 85.0 (C), 121.2 (CH), 123.1 (CH), 129.4 (CH), 131.8 (CH), 131.9 (C), 146.1 (C), 165.6 (C).

10b-Hydroxy-1,3,4,10b-tetrahydro[1,4]thiazino[3,4-*a*]isoindol-6-one (3c): M.p. 160−162°C (162−164°C).[5] − IR (CsI): ṽ = 3389, 3057, 1716, 1699, 1694, 1683, 1403, 1357, 1088, 958, 754, 693. − ^{1}H NMR {300 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%)}: δ = 2.40−2.55 (m, 2 H, SCH_2CN), 2.58 (d, *J* = 13.3 Hz, 1 H, SCH_2CO), 3.08 (d, *J* = 13.3 Hz, 1 H, SCH_2CO), 3.26 (ddd, *J* = 13.2 Hz, 4.7, 10.7, 1 H, NCH_2), 4.29 (ddd, *J* = 13.2, 2.6 Hz, 1 H, NCH_2), 6.04 (br. s, 1 H, OH), 7.42 (m, 1 H, Ar-H), 7.49−7.61 (m, 3 H, Ar-H). − ^{13}C NMR {75.5 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%)}: δ = 27.6 (CH_2), 37.6 (CH_2), 37.9 (CH_2), 83.7 (C), 122.5 (CH), 123.5 (CH), 130.0 (CH), 131.8 (C), 132.6 (CH), 149.3 (C), 164.7 (C). − MS (FAB); *m*/*z* (%): 222 (61) [M$^+$], 204 (100), 177 (10), 174 (12), 105 (8). − UV/Vis (CH_3CN): λ = 263 (3600), 345 (9400). − HR-MS (PI-FAB): 222.060 ± 0.002 (calcd. 222.059).

10b-Hydroxy-1-methyl-1,3,4,10b-tetrahydro[1,4]thiazino[3,4-*a*]isoindol-6-one (*trans*-3d): M.p. 122−125°C. − IR (CsI): ṽ = 3252, 1690, 1664, 1476, 1439, 1303, 1023, 773, 700. − ^{1}H NMR {300 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%)}: δ = 0.88 (d, *J* = 7.0 Hz, 3 H, CH_3), 2.45 (ddd, *J* = 13.0, 3.0, 13.0 Hz, 1 H, SCH_2CN), 2.87 (ddd, *J* = 13.0, 3.6, 13.0 Hz, 1 H, SCH_2CN), 3.38 (m, 2 H, SCH_2CO, NCH_2), 4.35 (ddd, *J* = 13.0, 3.0, 3.0 Hz, 1 H, NCH_2), 4.35 (d, *J* = 4.2 Hz, 1 H, OH), 7.53 (ddd, *J* = 5.9, 2.5 Hz, 1 H, Ar-H), 7.62 (m, 2 H, Ar-H), 7.70 (d, *J* = 7.5 Hz, 1 H, Ar-H). − ^{13}C NMR {75.5 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%)}: δ = 16.8 (CH_3), 21.7 (CH_2), 37.2 (CH), 41.1 (CH_2), 87.2 (C), 122.4 (CH), 123.3 (CH), 129.7 (CH), 132.0 (C), 132.5 (CH), 148.5 (C), 165.3 (C). − MS (FAB); *m*/*z* (%): 236 (67) [M$^+$], 218 (28), 174 (6), 160 (7). − UV/Vis (CH_3CN): λ = 229 (7700), 262 (3600). − HR-MS (PI-FAB): 236.074 ± 0.002 (calcd. 236.075).

11b-Hydroxy-1,3,4,11b-tetrahydro[1,4]thiazepino[3,4-*a*]isoindol-7-one (3e): M.p. 183−186°C (187−189°C).[5] − IR (CsI): ṽ = 3433, 1672, 1472, 1420, 1071, 1027, 764, 704, 693. − ^{1}H NMR {300 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%)}: δ = 1.75−2.00 (m, 2 H, C−CH_2−C), 2.58 (dd, *J* = 3.9, 8.6 Hz, 2 H, SCH_2CC), 3.05 (d, *J* = 15.1 Hz, 1 H, SCH_2CO), 3.19 (ddd, *J* = 14.6, 2.9, 11.9 Hz, 1 H, NCH_2), 3.42 (d, *J* = 15.1 Hz, 1 H, SCH_2CO), 3.80 (ddd, *J* = 14.6, 3.4 Hz, 1 H, NCH_2), 6.23 (br. s, 1 H, OH), 7.39 (m, 1 H, Ar-H), 7.48−7.58 (m, 3 H, Ar-H). − ^{13}C NMR {75.5 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%)}: δ = 29.4 (CH_2), 34.7 (CH_2), 38.6 (CH_2), 43.6 (CH_2), 92.4 (C), 122.6 (CH), 122.8 (CH), 129.7 (CH), 132.5 (CH), 133.3 (C), 148.0 (C), 167.6 (C). − MS (FAB); *m*/*z* (%): 236 (21) [M$^+$], 119 (18), 115 (15), 105 (29). − UV/Vis (CH_3CN): λ = 227 (5900), 240 (1200). − HR-MS (PI-FAB): 236.074 ± 0.002 (calcd. 236.075).

11b-Hydroxy-1-methyl-1,3,4,11b-tetrahydro[1,4]thiazepino[3,4-*a*]-isoindol-7-one (*cis*-3f): M.p. 200−203°C. − ^{1}H NMR {300 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%) in mixture with *trans*-**3f**}: 1.47 (d, *J* = 7.2, 3 H, CH_3), 1.56−1.78 (m, 1 H, CCH_2C), 1.92−2.20 (m, 1 H, CCH_2C), 2.40−2.59 (m, 1 H, SCH_2CC), 2.68 (ddd, *J* = 14.3 Hz, 12.5, 3.7, 1 H, SCH_2CC), 2.81 (q, *J* = 7.2 Hz, 1 H, SCH_2CO), 3.22 (ddd, *J* = 14.5, 12.5, 2.0 Hz, 1 H, NCH_2), 3.65−3.78 (m, 1 H, NCH_2), 6.32 (br. s, 1 H, OH), 7.38−7.61 (m, 4 H, Ar-H). − ^{13}C NMR {75.5 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%)}: δ = 18.7 (CH_3), 27.9 (CH_2), 30.9 (CH_2), 38.7 (CH), 53.5 (CH_2), 91.6 (C), 122.6 (CH), 125.0 (CH), 129.6 (CH), 132.1 (CH), 132.3 (C), 145.4 (C), 167.4 (C).

***trans*-3f:** ^{1}H NMR {300 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%) in mixture with *cis*-**3f**}: δ = 1.43 (d, *J* = 7.5 Hz, 3 H, CH_3), 1.56−1.78 (m, 1 H, CCH_2C), 1.92−2.20 (m, 1 H, CCH_2C), 2.40−2.59 (m, 1 H, SCH_2CCN), 2.77−2.85 (m, 1 H, SCH_2CCN), 3.25 (q, *J* = 7.5 Hz, 1 H, SC*H*CO), 3.59 (ddd, *J* = 14.1, 5.7, 1.3 Hz, 1 H, NCH_2), 3.65−3.78 (m, 1 H, NCH_2), 6.29 (br. s, 1 H, OH), 7.38−7.61 (m, 4 H, Ar-H). − ^{13}C NMR {75.5 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%)}: δ = 16.6 (CH_3), 27.6 (CH_2), 33.8 (CH_2), 36.9 (CH), 51.5 (CH_2), 94.3 (C), 123.0 (CH), 123.5 (CH), 129.7 (CH), 131.6 (CH), 134.1 (C), 149.3 (C), 166.4 (C).

12b-Hydroxy-1,3,4,5,6,11b-hexahydro[1,4]thiazocino[3,4-*a*]isoindol-8-one (3g): Oil. − IR (film): ṽ = 3256, 2927, 1703, 1698, 1668, 1470, 1417, 1073, 1024, 1004, 763, 700. − ^{1}H NMR {300 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%)}: δ = 1.65 (m, 2 H, SCCH_2CCN), 1.85 (m, 1 H, NCCH_2), 1.98 (m, 1 H, NCCH_2), 2.45 (dd, *J* = 6.9, 5.3 Hz, 2 H, SCH_2CC), 3.10 (d, *J* = 15.2 Hz, 1 H, SCH_2CO), 3.20 (d, *J* = 15.2 Hz, 1 H, SCH_2CO), 3.52 (ddd, *J* = 14.4, 8.1, 5.0 Hz, 1 H, NCCH_2), 3.73 (ddd, *J* = 14.4, 6.2 Hz, 1 H, NCCH_2), 6.16 (s, 1 H, OH), 7.42 (ddd, *J* = 7.5, 2.2 Hz, 1 H, Ar-H), 7.49 (d, *J* = 7.5 Hz, 1 H, Ar-H), 7.53 (ddd, *J* = 7.5, 1.0 Hz, 1 H, Ar-H), 7.58 (d, *J* = 7.5 Hz, 1 H, Ar-H). − ^{13}C NMR {75.5 MHz, [D$_6$]acetone/[D$_6$]DMSO (ca. 10%)}: δ = 27.0 (CH_2), 27.1 (CH_2), 32.8 (CH_2), 37.3 (CH_2), 39.1 (CH_2), 89.7 (C), 122.5 (CH), 122.7 (CH), 129.7 (CH), 132.5 (CH), 133.0 (C), 148.5 (C), 168.0 (C). − MS (FAB); *m*/*z* (%): 250 (70) [M$^+$], 232 (100), 218 (5), 186 (12), 160 (26), 115 (6), 104 (38). − UV/Vis (CH_3CN): λ = 226 (6700), 246 (3000). − HR-MS (PI-FAB): 250.093 ± 0.003 (calcd. 250.090).

10b-Hydroxy-1,10b-dihydro[1,4]thiazino[3,4-*a*]isoindol-6-one (3h): M.p. 103−106°C. − ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 1.57 (ddd, *J* = 14.9, 2.2, 4.6 Hz, 1 H, C*H*$_2$COH), 2.70 (m, 2 H, C*H*$_2$CCOH), 3.43 (ddd, *J* = 11.0, 2.2 Hz, 1 H, C*H*$_2$COH), 4.50 (d, *J* = 13.0 Hz, 1 H, SC*H*$_2$N), 4.91 (d, *J* = 13.0 Hz, 1 H, SC*H*$_2$N), 5.37 (d, *J* = 2.2 Hz, 1 H, OH), 7.55 (m, 1 H, Ar-H), 7.65 (m, 1 H, Ar-H), 7.71 (dd, *J* = 7.5, 0.9 Hz, 1 H, Ar-H), 7.87 (m, 1 H, Ar-H). − ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 24.2 (CH$_2$), 37.0 (CH$_2$), 38.5 (CH$_2$), 85.5 (C), 122.5 (CH), 123.9 (CH), 130.3 (CH), 133.1 (CH), 135.3 (C), 149.9 (C), 163.8 (C).

11b-Hydroxy-1,4,5,11b-tetrahydro[1,4]thiazepino[4,5-*a*]isoindol-7-one (3i): M.p. 94−98°C. − IR (CsI): ṽ = 3251, 1773, 1718, 1678, 1665, 1469, 1399, 1086, 766, 720. − ^{1}H NMR {300 MHz, CDCl$_3$/[D$_6$]DMSO (ca. 10%)}: δ = 2.02 (ddd, *J* = 19.2 Hz, 12.1, 10.5, 1 H, C*H*$_2$COH), 2.49−2.68 (m, 4 H, 2 × SC*H*$_2$), 3.02 (ddd, *J* = 13.9, 10.8, 3.1 Hz, 1 H, C*H*$_2$COH), 3.51 (ddd, *J* = 14.4 Hz, 10.8, 2.4, 1 H, NC*H*$_2$), 4.21 (ddd, *J* = 14.4, 11.6, 4.6 Hz, 1 H, NC*H*$_2$), 6.05 (br. s, 1 H, OH), 7.40 (ddd, *J* = 7.3 Hz, 1.2 Hz, 1 H, Ar-H), 7.46 (d, *J* = 7.3 Hz, 1 H, Ar-H), 7.52 (ddd, *J* = 7.3, 1.2 Hz, 1 H, Ar-H), 7.65 (d, *J* = 7.3 Hz, 1 H, Ar-H). − ^{13}C NMR {75.5 MHz, CDCl$_3$/[D$_6$]DMSO (ca. 10%)}: δ = 24.4 (CH$_2$), 28.5 (CH$_2$), 40.9 (CH$_2$), 43.0 (CH$_2$), 89.4 (C), 121.3 (CH), 122.0 (CH), 128.6 (CH), 130.6 (C), 131.7 (CH), 147.5 (C), 166.5 (C). − MS (FAB); *m*/*z* (%): 236 (10) [M$^+$], 218 (5), 176 (6). − UV/Vis (CH$_3$CN): λ = 216 (22000). − HR-MS (PI-FAB): 236.073 ± 0.003 (calcd. 236.075).

12b-Hydroxy-1,4,5,12b-tetrahydro[1,5]thiazocino[4,5-*a*]isoindol-8-one (3j): Oil. − ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 1.66 (m, 2 H, NCC*H*$_2$), 2.42 (m, 1 H, C*H*$_2$COH), 2.47 (m, 2 H, SC*H*$_2$CCN), 2.67−2.83 (m, 3 H, C*H*$_2$COH, SC*H*$_2$CCC), 3.52 (ddd, *J* = 16.7 Hz, 11.4, 5.2, 1 H, NC*H*$_2$), 3.63 (ddd, *J* = 14.5, 6.1, 2.2 Hz, 1 H, NC*H*$_2$), 5.19 (br. s, 1 H, OH), 7.47−7.91 (m, 4 H, Ar-H). − ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 27.7 (CH$_2$), 27.8 (CH$_2$), 30.4 (CH$_2$), 37.5 (CH$_2$), 38.3 (CH$_2$), 90.0 (C), 122.9 (CH), 123.1 (CH), 130.1 (CH), 132.8 (CH), 133.1 (C), 147.9 (C), 168.0 (C).

(9b-Hydroxy-5-oxo-5,9b-dihydro-1*H*-thiazolo[4,3-*a*]isoindol-1-yl)-acetic Acid (*cis*-10a): Oil. − ^{1}H NMR (300 MHz, CDCl$_3$ in mixture with **1h**): δ = 3.11 (dd, *J* = 19.0, 1.9 Hz, 1 H, C*H*$_2$COOH), 3.46 (dd, *J* = 19.0, 8.1 Hz, 1 H, C*H*$_2$COOH), 4.18 (dd, *J* = 8.1, 1.9 Hz, 1 H, SC*H*), 4.54 (d, *J* = 9.7 Hz, 1 H, SC*H*$_2$N), 5.08 (d, *J* = 9.7 Hz, 1 H, SC*H*$_2$N), 7.50−7.80 (m, 4 H, Ar-H). − MS (70 eV, TMS derivative); *m*/*z* (%): 423 (8) [M$^+$], 408 (4), 350 (1), 289 (3), 246 (82), 160 (4), 73 (100), 59 (10).

(6-Oxo-3,4-dihydro[1,4]thiazino[3,4-*a*]isoindol-1-yl)acetic Acid (11): Oil. − ^{1}H NMR {300 MHz, CDCl$_3$/[D$_6$]acetone (ca. 10%) in mixture with **1i**}: δ = 3.15 (m, 2 H, SC*H*$_2$), 3.66 (s, 2 H, C*H*$_2$COOH), 4.11 (m, 2 H, NC*H*$_2$), 7.41 (dd, *J* = 7.5 Hz, 1 H, Ar-H), 7.55 (dd, *J* = 7.5 Hz, 1 H, Ar-H), 7.72 (m, 1 H, Ar-H), 7.80 (m, 1 H, Ar-H). − ^{13}C NMR (75.5 MHz, [D$_6$]DMSO): δ = 25.7 (CH$_2$), 38.2 (CH$_2$), 38.4 (CH$_2$), 112.0 (C), 121.5 (CH), 122.4 (CH), 127.1 (CH), 127.6 (C), 127.8 (C), 131.3 (CH), 133.3 (C), 164.5 (C), 170.3 (C). − MS (70 eV, TMS-derivative); *m*/*z* (%): 333 (23) [M$^+$], 318 (4), 289 (20), 216 (23), 160 (3), 89 (3), 73 (100), 58 (7).

(11b-Hydroxy-7-oxo-3,4,7,11b-tetrahydro-1*H*-[1,4]thiazepino[3,4-*a*]isoindol-1-yl)acetic Acid (*cis*-10c): Oil. − ^{1}H NMR (300 MHz, [D$_6$]DMSO in mixture with **1j**): δ = 1.84 (m, 1 H, NCC*H*$_2$), 2.03 (m, 1 H, NCC*H*$_2$), 2.19 (dd, *J* = 15.7, 12.5, 1 H, C*H*$_2$COOH), 2.67 (m, 2 H, C*H*$_2$COOH, SC*H*$_2$), 3.20−3.40 (m, 2 H, NC*H*$_2$, SC*H*$_2$), 3.56 (dd, *J* = 10.4 Hz, 12.5, 1 H, SC*H*), 3.81 (d, *J* = 14.7 Hz, 1 H, NC*H*$_2$), 6.79 (br. s, 1 H, OH), 7.52−7.66 (m, 4 H, Ar-H), 12.40 (br. s, 1 H, COO*H*). − ^{13}C NMR (75.5 MHz, [D$_6$]DMSO): δ = 27.2 (CH$_2$), 34.0 (CH$_2$), 37.7 (CH$_2$), 38.3 (CH$_2$), 52.9 (CH), 92.9 (C), 122.2 (CH), 124.2 (CH), 129.6 (CH), 131.7 (CH), 133.1 (C), 144.5 (C), 166.9 (C), 172.3 (C).

9b-Hydroxy-5-oxo-5,9b-dihydro-1*H*-thiazolo[4,3-*a*]isoindole-1-carboxylic Acid (*cis*-14a): Oil. − ^{1}H NMR (300 MHz, CDCl$_3$ in mixture with *trans*-**14a** and **3a**): δ = 3.95 (s, 1 H, SC*H*), 4.46 (d, *J* = 8.3, 1 H, SC*H*$_2$N), 4.90 (d, *J* = 8.3, 1 H, SC*H*$_2$N), 7.30−7.80 (m, 4 H, Ar-H). − GC-MS (70 eV, TMS derivative); *m*/*z* (%): 395 (4) [M$^+$], 380 (1), 307 (1), 278 (1), 232 (78), 160 (75), 89 (6), 73 (100), 59 (4).

***trans*-14a:** ^{1}H NMR (300 MHz, CDCl$_3$ in mixture with *cis*-**14a** and **3a**): δ = 4.00 (s, 1 H, SC*H*), 4.36 (d, *J* = 8.0 Hz, 1 H, SC*H*$_2$N), 4.98 (d, *J* = 8.0 Hz, 1 H, SC*H*$_2$N), 7.30−7.80 (m, 4 H, Ar-H). − GC-MS (70 eV, TMS derivative); *m*/*z* (%): 395 (6) [M$^+$], 380 (2), 307 (2), 278 (1), 232 (100), 160 (8), 89 (7), 73 (93), 59 (5).

Methyl 9b-Hydroxy-5-oxo-5,9b-dihydro-1*H*-thiazolo[4,3-*a*]isoindole-1-carboxylate (*cis*-14b): Oil. − ^{1}H NMR (300 MHz, CDCl$_3$ in mixture with *trans*-**14b**): δ = 3.86 (s, 3 H, CH$_3$), 4.20 (s, 1 H, SC*H*), 4.48 (d, *J* = 8.8 Hz, 1 H, SC*H*$_2$N), 4.93 (d, *J* = 8.8 Hz, 1 H, SC*H*$_2$N), 7.44−7.68 (m, 4 H, Ar-H). − GC-MS (70 eV, TMS-derivative); *m*/*z* (%): 337 (1) [M$^+$], 322 (1), 233 (12), 160 (100), 89 (2), 77 (18), 59 (3).

***trans*-14b:** ^{1}H NMR (300 MHz, CDCl$_3$ in mixture with *cis*-**14b**): δ = 3.20 (s, 3 H, CH$_3$), 4.13 (s, 1 H, SC*H*), 4.37 (d, *J* = 8.4 Hz, 1 H, SC*H*$_2$N), 4.98 (d, *J* = 8.4 Hz, 1 H, SC*H*$_2$N), 7.44−7.68 (m, 4 H, Ar-H). − MS (70 eV, TMS derivative); *m*/*z* (%): 337 (4) [M$^+$], 322 (2), 248 (2), 232 (100), 175 (5), 160 (6), 89 (6), 73 (38), 59 (6).

3. Photoreactions: General Procedure. − 3.2: *N*-Methylphthalimide (2 mmol) was dissolved in acetone (240 mL). A solution of potassium carboxylate (10 mmol) in water (60 mL) was added, and the mixture was irradiated (λ = 300 nm ± 10 nm) at 15°C in a Pyrex tube for 12−24 h, while purging with a slow stream of N$_2$. The solution was extracted with CH$_2$Cl$_2$ (3 × 100 mL), washed with 5% NaHCO$_3$ and brine, dried (MgSO$_4$), and concentrated to dryness. The products were obtained after column chromatography or recrystallization from toluene/petroleum ether or acetone/*n*-hexane.

3-Hydroxy-2-methyl-3-methylsulfanylmethyl-2,3-dihydroisoindol-1-one (7a): M.p. 110−114°C (114−116°C).[5] − IR (CsI, alkene[45]): ṽ = 3019, 1615, 1473, 1430, 1335, 1029, 1015, 822, 751, 693. − ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 1.75 (s, 3 H, SC*H*$_3$), 2.90 (s, 3 H, NC*H*$_3$), 3.21 (d, *J* = 14.1 Hz, 1 H, SC*H*$_2$), 3.29 (d, *J* = 14.1 Hz, 1 H, SC*H*$_2$), 5.50 (s, 1 H, OH), 7.50 (ddd, *J* = 7.5, 1.1, 1 H, Ar-H), 7.59 (ddd, *J* = 7.5 Hz, 1.1, 1 H, Ar-H), 7.63 (ddd, *J* = 7.5, 1.1, 0.9 Hz, 1 H, Ar-H), 7.71 (ddd, *J* = 7.5, 1.1, 0.9 Hz, 1 H, Ar-H). − ^{13}C NMR (75.5 MHz, [D$_6$]acetone): δ = 15.7 (CH$_3$), 22.5 (CH$_3$), 39.8 (CH$_2$), 89.9 (C), 122.1 (CH), 122.3 (CH), 129.2 (CH), 131.5 (CH), 132.5 (C), 146.8 (C), 166.2 (C). − MS (70 eV); *m*/*z* (%): 205 (100) [M$^+$ − H$_2$O], 190 (63), 162 (47), 146 (45), 130 (24), 77 (51), 50 (18). − UV/Vis (CH$_3$CN, alkene[45]): λ = 344 (17200), 266 (4700), 218 (16900), 210 (6400). − C$_{11}$H$_{11}$NOS (205.27, alkene[45]): C 64.36, H 5.40, N 6.82; found C 63.37, H 5.45, N 6.66.

3-Hydroxy-2-methyl-3-(1-methylsulfanylethyl)-2,3-dihydroisoindol-1-one (*l*-7b): M.p. 132−134°C. − IR (CsI): ṽ = 3265, 1686, 1681, 1670, 1478, 1428, 1012, 769, 705. − ^{1}H NMR (300 MHz, CDCl$_3$ in mixture with *u*-**7b**): δ = 1.25 (d, *J* = 7.0 Hz, 3 H, SCC*H*$_3$), 1.97 (s, 3 H, SC*H*$_3$), 2.80 (s, 3 H, NC*H*$_3$), 3.26 (q, *J* = 7.0 Hz, 1 H, SC*H*), 4.44 (s, 1 H, OH), 7.38 (m, 1 H, Ar-H), 7.47 (m, 2 H, Ar-H), 7.57 (d, *J* = 7.5 Hz, 1 H, Ar-H). − ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 15.6 (CH$_3$), 16.2 (CH$_3$), 24.5 (CH$_3$), 49.1 (CH), 91.7

Table 9. X-ray data for *trans*-**4**, **3h**, **7a**, and **12**[46]

No.	*trans*-**4**	**3h**	**7a**	**12**
emp. formula	$C_{12}H_{13}NO_2S$	$C_{11}H_{11}NO_2S$	$C_{11}H_{13}NO_2S$	$C_{12}H_{15}NO_3$
molecular mass	235.29	221.27	223.28	221.25
cryst. dim. [mm]	0.3 × 0.2 × 0.15	0.2 × 0.15 × 0.2	0.3 × 0.3 × 0.2	0.2 × 0.2 × 0.15
a [pm]	1076.0(1)	860.2(1)	1010.4(1)	799.0(1)
b [pm]	1349.1(1)	1588.8(2)	1080.4(1)	914.3(1)
c [pm]	823.3(1)	848.5(1)	1103.9(1)	919.4(1)
α [°]			77.41(1)	68.31(1)
β [°]	107.88(1)	116.41(1)	75.42(1)	84.12(1)
γ [°]			77.28(1)	65.94(1)
V [10^6pm^3]	1137.4(2)	1038.6(2)	1120.6(2)	568.9(1)
Z	4	4	4	2
$\rho_{calcd.}$	1.374	1.415	1.323	1.291
crystal system	monoclinic	monoclinic	triclinic	triclinic
space group	$P2_1/c$	$P2_1/n$	$P\bar{1}$	$P\bar{1}$
no. refl. meas.	4864	2480	4344	4101
no. uni. refl.	2488	2247	4344	2125
no. obs. refl.[a]	1578	1682	3324	1344
R	0.050	0.047	0.044	0.055
R_w[b]	0.089	0.103	0.110	0.105
largest diff. peak/hole [eÅ^{-3}]	0.25/−0.20	0.27/−0.30	0.31/−0.34	0.15/−0.16

[a] For $F > 2\sigma(F)$. − [b] Weight: $R_w = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]1/2$.

(C), 122.1 (CH), 123.1 (CH), 129.8 (CH), 131.8 (CH), 131.9 (C), 145.1 (C), 170.0 (C). − GC-MS (70 eV); *m/z* (%): 219 (24) [$M^+ - H_2O$], 204 (18), 189 (4), 173 (96), 162 (100), 144 (25), 91 (10), 76 (32), 51 (5). − UV/Vis (CH_3CN): λ = 226 (7900), 238 (3800), 256 (2800). − $C_{12}H_{15}NO_2S$ (237.31): C 60.73, H 6.37, N 5.90; found C 60.29, H 6.39, N 5.77.

***u*-7b:** ^{1}H NMR (300 MHz, $CDCl_3$ in mixture with *l*-**7b**): 0.75 (d, *J* = 7.0 Hz, 3 H, SCC*H*$_3$), 2.31 (s, 3 H, SC*H*$_3$), 2.76 (s, 3 H, NC*H*$_3$), 3.25 (q, *J* = 7.0 Hz, 1 H, SC*H*), 4.09 (s, 1 H, OH), 7.38 (ddd, *J* = 7.5 Hz, 1 H, Ar-H), 7.51 (m, 2 H, Ar-H), 7.98 (d, *J* = 7.5 Hz, 1 H, Ar-H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 16.1 (CH_3), 17.4 (CH_3), 23.3 (CH_3), 47.6 (CH), 92.8 (C), 122.9 (CH), 123.8 (CH), 129.7 (CH), 131.6 (C), 131.8 (CH), 144.6 (C), 167.3 (C). − GC-MS (70 eV); *m/z* (%): 219 (16) [$M^+ - H_2O$], 204 (10), 189 (3), 173 (56), 162 (100), 144 (23), 91 (6), 76 (34), 51 (9).

3-Hydroxy-2-methyl-3-phenylsulfanylmethyl-2,3-dihydroisoindol-1-one (7c): M.p. 94−96°C. − IR (CsI): ṽ = 3288, 1686, 1480, 1423, 1078, 745, 701. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.61 (s, 3 H, NCH_3), 3.46 (d, *J* = 14.1 Hz, 1 H, SC*H*$_2$), 3.60 (d, *J* = 14.1 Hz, 1 H, SC*H*$_2$), 3.64 (br. s, 1 H, OH), 7.11 (br. m, 5 H, Ar-H), 7.37 (br. m, 3 H, Ar-H), 7.57 (m, 1 H, Ar-H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 23.3 (CH_3), 41.1 (CH_2), 90.2 (C), 122.0 (CH), 122.8 (CH), 127.0 (CH), 128.8 (CH), 129.7 (CH), 131.3 (CH), 131.4 (C), 132.0 (CH), 135.0 (C), 145.4 (C), 167.6 (C). − MS (70 eV); *m/z* (%): 285 (1) [M^+], 267 (1), 176 (1), 162 (100), 133 (22), 130 (9), 77 (30), 51 (11). − UV/Vis (CH_3CN): λ = 253 (10300), 252 (10300). − $C_{16}H_{15}NO_2S$ (285.36): C 67.34, H 5.29, N 4.90; found C 67.02, H 5.30, N 4.76.

3-Hydroxy-3-(1-hydroxy-1-methylethyl)-2-methyl-2,3-dihydroisoindol-1-one (12): M.p. 164−166°C. − IR (CsI): ṽ = 3506, 3226, 1674, 1473, 1426, 1185, 1069, 767. − ^{1}H NMR {300 MHz, $CDCl_3$/[D$_6$]DMSO (ca. 10%)}: δ = 0.88 (s, 3 H, C*H*$_3$C), 1.21 (s, 3 H, C*H*$_3$C), 2.99 (s, 3 H, NC*H*$_3$), 3.39 (s, 1 H, OH), 5.89 (s, 1 H, OH), 7.32 (ddd, *J* = 7.4, 1.2, 1.0, 1 H, Ar-H), 7.38 (ddd, *J* = 7.4, 1.1 Hz, 1 H, Ar-H), 7.54 (dd, *J* = 6.8, 1.2 Hz, 1 H, Ar-H), 7.63 (dd, *J* = 6.8, 1.1 Hz, 1 H, Ar-H). − ^{13}C NMR {75.5 MHz, $CDCl_3$/[D$_6$]DMSO (ca. 10%)}: δ = 23.7 (CH_3), 25.9 (CH_3), 26.3 (CH_3), 75.7 (C), 92.9 (C), 122.4 (CH), 123.8 (CH), 128.9 (CH), 130.9 (CH), 132.4 (C), 146.0 (C), 167.6 (C). − MS (70 eV); *m/z*: 204 (1) [M^+ − OH], 188 (3), 175 (1), 162 (100), 148 (2), 133 (21), 105 (22), 77 (35), 52 (8). − $C_{12}H_{15}NO_3$ (221.26): C 65.14, H 6.83, N 6.33; found C 65.39, H 6.85, N 5.98.

Acknowledgments

This research project was financially supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the Volkswagenstiftung, Degussa-Hüls AG, Bayer AG, and Merck KGaA.

[1] [1a] A. G. Griesbeck, *Chimia* **1998**, *52*, 272. − [1b] A. G. Griesbeck, *Liebigs Ann.* **1996**, 1951.
[2] [2a] Y. Kanaoka, *Acc. Chem. Res.* **1978**, *87*, 407. − [2b] Y. Kanaoka, *J. Soc. Org. Synth. Chem. (Tokyo)* **1975**, *33*, 949. − [2c] J. D. Coyle in *Synthetic Organic Photochemistry* (Ed.: W. M. Horspool), Plenum Press, New York, **1984**, p. 259. − [2d] P. H. Mazzocchi, *Org. Photochem.* **1981**, *5*, 421. − [2e]A. G. Griesbeck, H. Mauder in *CRC Handbook of Organic Photochemistry and Photobiology* (Eds.: W. M. Horspool, P.-S. Song), CRC Press, Boca Raton, **1995**, p. 513.
[3] [3a] A. G. Griesbeck, W. Kramer, M. Oelgemöller, *Synlett* **1999**, 1169. − [3b] A. G. Griesbeck, A. Henz, W. Kramer, J. Lex, F. Nerowski, M. Oelgemöller, K. Peters, E.-M. Peters, *Helv. Chim. Acta* **1997**, *80*, 912.
[4] [4a] A. G. Griesbeck, J. Hirt, W. Kramer, P. Dallakian, *Tetrahedron* **1998**, *54*, 3169. − [4b] A. G. Griesbeck, J. Hirt, K. Peters, E.-M. Peters, H. G. von Schnering, *Chem. Eur. J.* **1996**, *2*, 1388.
[5] [5a] Y. Hatanaka, Y. Sato, H. Nakai, M. Wada, T. Mizoguchi, Y. Kanaoka, *Liebigs Ann. Chem.* **1992**, 1113. − [5b] Y. Sato, H. Nakai, M. Wada, T. Mizoguchi, Y. Hatanaka, Y. Migita, Y. Kanaoka, *Liebigs Ann. Chem.* **1985**, 1099.
[6] N. J. Pienta in *Photoinduced Electron Transfer* (Ed.: M. A. Fox, M. Chanon), Elsevier, Amsterdam, **1988**, p. 421.
[7] L. Eberson in *Electron Transfer Reactions in Organic Chemistry* ("Reactivity and Structure − Concepts in Organic Chemistry", V. 25) (Ed.: K. Hafner), Springer-Verlag, Berlin, **1987**.
[8] T. O. Soine, M. R. Buchdahl, *Org. Synth.* **1967**, 106.
[9] M. B. Winstead, H. W. Heine, *J. Am. Chem. Soc.* **1955**, *77*, 1913.
[10] Y.-D. Gong, N. Iwasawa, *Chem. Lett.* **1994**, 2139.
[11] G. H. L. Nefkens, *Nature (London)* **1962**, *193*, 974.
[12] J. Loccufier, E. Schacht, *Bull. Soc. Chim. Belg.* **1988**, *97*, 535.
[13] [13a] J. C. Sheehan, M. Goodman, G. P. Hess, *J. Am. Chem. Soc.* **1956**, *78*, 1367. − [13b] J. C. Sheehan, D. W. Chapman, R. W. Roth, *J. Am. Chem. Soc.* **1952**, *74*, 3822.

[14] The geometries were pre-optimized using a MM+ force field. PM3, as implemented in the Hyperchem software package, was used for further optimizations. Hyperchem Molecular Modeling System, Version 4 for Windows, Hypercube Inc. **1994**.
[15] H. Görner, A. G. Griesbeck, T. Heinrich, W. Kramer, M. Oelgemöller, *Chem. Eur J.*, in print.
[16] [16a] U. C. Yoon, S. J. Lee, K. J. Lee, S. J. Cho, C. W. Lee, P. S. Mariano, *Bull. Korean Chem. Soc.* **1994**, *15*, 154. – [16b] U. C. Yoon, H. J. Kim, P. S. Mariano, *Heterocycles* **1989**, *29*, 1041.
[17] T. Ikeno, M. Harada, N. Arai, K. Narasaka, *Chem. Lett.* **1997**, 169.
[18] [18a] Z. Su, P. S. Mariano, D. E. Falvey, U. C. Yoon, S. W. Oh, *J. Am. Chem. Soc.* **1998**, *120*, 10676. – [18b] Z. Su, D. E. Falvey, U. C. Yoon, P. S. Mariano, *J. Am. Chem. Soc.* **1997**, *119*, 5261.
[19] [19a] D. R. G. Brimage, R. S. Davidson, P. R. Steiner, *J. Chem. Soc., Perkin 1* **1973**, 526. – [19b] R. S. Davidson, P. R. Steiner, *J. Chem. Soc., Perkin 2* **1972**, 1357. – [19c] R. S. Davidson, P. R. Steiner, *J. Chem. Soc. C* **1971**, 1682.
[20] I. R. Gould, S. Farid, *Acc. Chem. Res.* **1996**, *29*, 522.
[21] [21a] A. G. Griesbeck, M. Oelgemöller, *Synlett* **1999**, 492. – [21b] A. G. Griesbeck, M. Oelgemöller, J. Lex, *Synlett* **2000**, 1454.
[22] A. G. Griesbeck, M. Oelgemöller, *Synlett* **2000**, 71.
[23] [23a] H. De Koning, W. N. Speckamp, *Methods of Organic Chemistry (Houben-Weyl)* **1995**, *21b*, 1953. – [23b] H. Hiemstra, W. N. Speckamp in *Comprehensive Organic Synthesis*, vol. 2 (Ed.: C. H. Heathcock), Pergamon Press, Oxford, **1991**, p. 1047.
[24] A. G. Griesbeck, F. Nerowski, J. Lex, *J. Org. Chem.* **1999**, *64*, 5213.
[25] H. Yokoi, T. Nakano, W. Fujita, K. Ishiguro, Y. Sawaki, *J. Am. Chem. Soc.* **1998**, *120*, 12453.
[26] A. G. Griesbeck, W. Kramer, M. Oelgemöller, *Green Chem.* **1999**, *1*, 205.
[27] [27a] H. J. Roth, G. Hundeshagen, *Arch. Pharm.* **1976**, *309*, 58. – [27b] M. Machida, H. Takechi, Y. Shishido, Y. Kanaoka, *Synthesis* **1982**, 1078.
[28] U. C. Yoon, S. W. Oh, S. M. Lee, S. J. Cho, J. Gamlin, P. S. Mariano, *J. Org. Chem.* **1999**, *64*, 4411.
[29] H. Görner, A. G. Griesbeck, M. Oelgemöller, unpublished results.
[30] [30a] P. J. Wagner, *Acc. Chem. Res.* **1983**, *16*, 461. – [30b] H. Jiang, H. Xu, J. Ye, *J. Chem. Soc., Perkin Trans. 2* **2000**, 925.
[31] [31a] Y. Ge, T. Ouimet, D. K. Smith, *J. Org. Chem.* **2000**, *65*, 8831. – [31b] N. Gupta, H. Linschitz, *J. Am. Chem. Soc.* **1997**, *119*, 6384. – [31c] J. Carr, L. Lambert, D. E. Hibbs, M. B. Hursthouse, K. M. Abdul Malik, J. H. R. Tucker, *Chem. Commun.* **1997**, 1649.
[32] [32a] Y. Sato, H. Nakai, T. Mizoguchi, M. Kawanishi, Y. Hatanaka, Y. Kanaoka, *Chem. Pharm. Bull.* **1982**, *30*, 1263. – [32b] Y. Sato, H. Nakai, T. Mizoguchi, M. Kawanishi, Y. Hatanaka, Y. Kanaoka, *Chem. Pharm. Bull.* **1973**, *21*, 1164.
[33] While wave **III** in Figure 6 appears only partly reversible, the reversibility is further increased in multisweep experiments.
[34] K. Soai, A. Ookawa, *J. Chem. Soc., Perkin Trans. 1* **1986**, 759.
[35] A. Haeuseler, M. Schmittel, A. G. Griesbeck, M. Oelgemöller, unpublished results.
[36] J. M. Savéant, E. Vianello, *Electrochim. Acta* **1967**, *12*, 1545.
[37] E. Larsson, *Ber. Dtsch. Chem. Ges.* **1930**, *63*, 1347.
[38] H. Schindlbauer, *Monatsh. Chem.* **1973**, *104*, 848.
[39] [39a] M. Donike, *Chromatographia* **1976**, *9*, 440. – [39b] M. Donike, *J. Chromatogr.* **1975**, *115*, 591. – [39c] M. Donike, R. Gola, L. Jaenicke, *J. Chromatogr.* **1977**, *134*, 385.
[40] M. Schmittel, A. Burghart, H. Werner, M. Laubender, R. Söllner, *J. Org. Chem.* **1999**, *64*, 3077.
[41] C. Amatore, C. Lefrou, F. Pflügler, *J. Electroanal. Chem. Interfacial* **1989**, *270*, 43.
[42] R. S. Nicholson, *Anal. Chem.* **1966**, 1406.
[43] K. Peters, E.-M. Peters, A. G. Griesbeck, M. Oelgemöller, *Z. Kristall. NCS* **1998**, *213*, 757.
[44] K. Peters, E.-M. Peters, M. Oelgemöller, J.-M. Cho, A. G. Griesbeck, *Z. Kristall. NCS* **2000**, *215*, 37.
[45] The alkene is formed by acid-catalyzed dehydration, a process known to proceed in the presence of catalytic amounts of acids.[24]
[46] X-ray structure analyses of *trans*-**4**, **3h**, **7a**, and **12**: *Data collection*: Nonius-Kappa-CCD diffractometer, room temperature, Mo-K_α radiation (λ = 0.71073 Å), graphite monochromator, $-\omega$ scans, 2 Θ limits [°]: 2−54. *Structure analysis and refinement*: solved by direct methods; full-matrix, least-squares refinement with anisotropic thermal parameters for C, N, and O and isotropic parameters for H. *Programs used:* SHELXS-97 for structure determination and SHELXL-97for refinement. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-156985 (*trans*-**4**), -156984 (**3h**), -156986 (**7a**), and -156987 (**12**),. Copies of the data can be obtained free of charge from CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033, E-mail: deposit@ccdc.cam.ac.uk].

Received November 8, 2000
[O00560]