Syntheses and UV/Vis Properties of Amino-Functionalized Fulgimides

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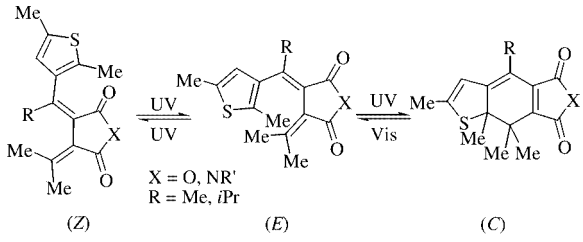
Functionalized fulgimides are regarded as a promising class of photochromic compounds for modulating the structure and function of biomolecules. A new synthetic route to fulgimides bearing amino-functionalized substituents at the imide nitrogen atom has been developed. The synthesis of the fulgimides has been achieved by base-catalyzed cyclization of phenacyl esters of the succinamic acids derived from fulgides and *N*-Boc-protected alkyl- and aryl-substituted diamines with triethylamine or *tert*-butyllithium. The UV/Vis spectroscopic data and the photochromic properties of these new compounds have been studied.

Introduction

Photochromic molecules have become important targets for optical data storage and as optical switches.[1,2] Fulgides display excellent fatigue resistance and thermal stability of their photochromic isomers.[3−6] In general, fulgides exist in three isomeric states as (*Z*), (*E*) and (*C*) forms. The (*Z*) and (*E*) forms can reversibly be converted into each other by irradiation with UV light and both have similar optical properties. Upon irradiation of the generally pale yellow (*E*) isomers with UV light an electrocyclic ring-closure reaction occurs and the thermally stable colored (*C*) forms of fulgides are formed. The (*C*) isomers are almost planar and their extended π-electron system causes a strong and broad absorption band in the Vis wavelength range. The reverse reaction to (*E*)-fulgides is achieved, for example, by exposure to white light (Scheme 1). The almost unique thermal stability of the photoisomeric states of fulgides is essential for their application in optical data storage as well as for biological applications.[1,7−10] In the latter case the severe structural change during photocyclization is of interest for modulating the structure and function of biomolecules by irradiation with light of different wavelengths.[7,8] For biological applications high solvolytic resistance is required. Therefore, the studies presented here focus on the imide derivatives of fulgides, which have been less intensively and systematically studied in the past.[9] In addition, the imide moiety allows the introduction of functional substituents at the imide nitrogen atom to allow attachment to biomolecules.[7,8] For instance, *N*-(4-carboxyphenyl)furyl-[9] and *N*-(carboxymethyl)thienylfulgimides[7,8] have been prepared and the latter, activated as *N*-hydroxysuccinimide active esters, have been employed for the modification of α-chymotrypsin and concavalin A and have been attached to lysine residues.



Scheme 1

Herein, we describe the synthesis of fulgimides (Schemes 2 and 3) bearing amino-functionalized substituents at the imide nitrogen atom, derived from thienylfulgides **1** with an isopropyl or methyl group as the substituent R (Scheme 1). A bulky isopropyl group instead of a methyl residue is known to increase the steric hindrance and constraints of the exocyclic double bond, thereby lowering the efficiencies for (*E*)-to-(*Z*) isomerization and increasing the (*E*)-to-(*C*) isomerization quantum yields.[10] In the past 3-furyl-, 3-thienyl- and 3-indolylfulgimides were synthesized by cyclization of succinamic acids and derivatives stemming from the reaction of the parent fulgide with a primary amine or ammonia.[11−16] Treatment with acetyl chloride or acetic anhydride at high temperature usually furnished the fulgimides in unsatisfactorily low yields. For example, Matsushima reported the synthesis of *N*-aryl-substituted furylfulgimides in 12−18% yield employing acetyl chloride.[9] Heller et al.[11,12] described the synthesis of furyl- and arylfulgimides by treatment of succinic hemi-esters with Grignard salts of primary amines and subsequent cyclization to the imide

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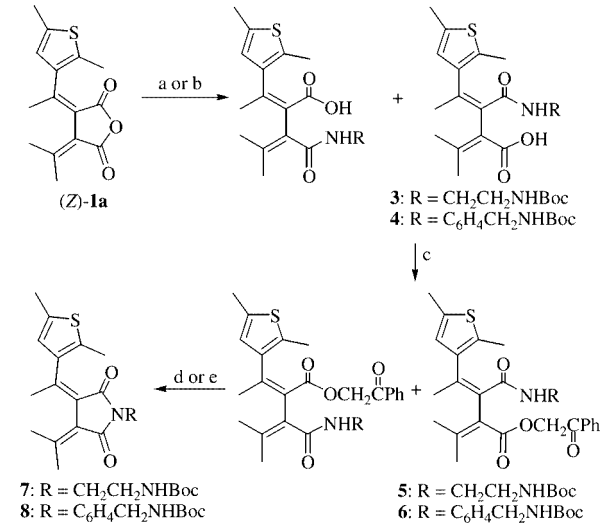
with acetyl chloride in 35% yield. Recently, Rentzepis[17] reported the synthesis of *N*-alkyl- and *N*-aryl-2-indolylfulgimides by $ZnCl_2$ or $ZnBr_2$ in the presence of HMDS (1,1,1,3,3,3-hexamethyldisilazane) in benzene at high temperature in 80−90% yield. Cyclization strategies in the absence of acidic reagents or Lewis acids have been less intensively studied. Ringsdorf et al.[15] reported on the treatment of a furylfulgimide with ammonia followed by esterification of the succinamic acid intermediate with diazomethane. Subsequent base-catalyzed cyclization applying sodium methoxide furnished the fulgimide in 15% yield. From the latter, *N*-substituted derivatives were prepared by the reaction with bromo- or hydroxy-substituted compounds.[15] Recently, Yokoyama et al. reported a similar route, which afforded a 3-indolylfulgimide in 95% yield by using sodium hydride in the cyclization step.[16] In this paper, we describe base-catalyzed cyclization strategies that were developed for the synthesis of *N*-Boc-protected thienylfulgimides. We also report on the deprotection of these fulgimides.

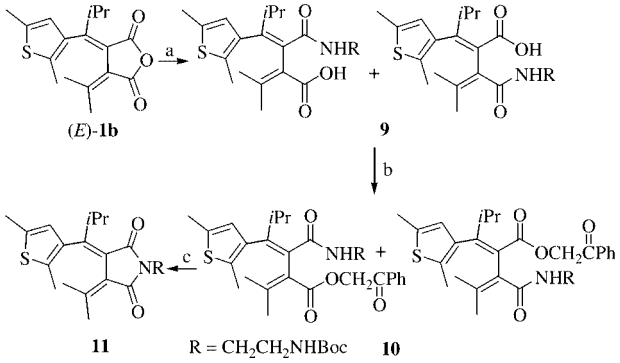


Scheme 2. a) $H_2NCH_2CH_2NHBoc$ (**2a**), CH_2Cl_2, reflux, 3 h, **3**: 99%; b) $H_2NC_6H_4CH_2NHBoc$ (**2b**), CH_2Cl_2, reflux, 3 d, **4**: 87%; c) phenacyl bromide, NEt_3, ethyl acetate, room temp., **5**: 86%; **6**: 96%; d) Method A: *t*BuLi (2.2 equiv.), THF, −78 °C, **7**: 48%; e) Method B: NEt_3 (10%), CH_2Cl_2, room temp., **8**: 51%

Results and Discussion

Synthesis

The fulgides (*Z*)-**1a**[18] (Scheme 2) and (*E*)-**1b**[19] (Scheme 3) were synthesized by Stobbe condensation[20] of diethyl or dimethyl isopropylidenesuccinate with (2,5-dimethyl-3-thienyl) methyl ketone and (2,5-dimethyl-3-thienyl) isopropyl ketone, respectively, followed by hydrolysis and subsequent cyclization of the resulting diacids with acetic anhydride or dicyclohexylcarbodiimide. Separation of the major isomers was achieved by chromatography or crystallization. Treatment of the fulgide (*Z*)-**1a** (Scheme 2) and (*E*)-**1b** (Scheme 3) with *tert*-butyl (2-aminoethyl)-carbamate (**2a**) in refluxing dichloromethane gave the regioisomeric succinamic acids in > 99% yield as inseparable mixtures. The reaction of the aniline compound **2b** with (*Z*)-**1a** (Scheme 2) similarly afforded a mixture of regioisomeric compounds **4** in 87% yield.



Scheme 3. a) $H_2NCH_2CH_2NHBoc$ (**2a**), CH_2Cl_2, reflux, 3 h, quant; b) phenacyl bromide, NEt_3, ethyl acetate, room temp., 94%; c) *t*BuLi (2.4 equiv.), THF, −78 °C, 40%

Various strategies and reaction conditions were examined to achieve cyclization to the corresponding imide. Starting from the succinamic acids **3** with dicyclohexylcarbodiimide in dichloromethane, fulgimide (*Z*)-**7** was isolated after 2 d at room temperature in only 13% yield, owing to slow and incomplete turnover.[21] Reactions of the regioisomeric succinamic acids **3** and **4** with either $ZnCl_2$ and $ZnBr_2$ (1 equiv.) in the presence of HMDS (1.5 equiv.) in refluxing benzene according to Rentzepis[17] generally led to inconsistent results. The formation of substantial amounts of by-products was observed due to deprotection and (*Z*)/(*E*) isomerization. Traces of hydrogen chloride were obviously difficult to avoid. However, compound (*Z*)-**7** was isolated in 11% yield from the isolated crude material by flash chromatography on silica gel.

We then prepared the regioisomeric phenacyl ester amides **5**, **6** (Scheme 2) and **10** (Scheme 3) from the succinamic acids, phenacyl bromide (1.1 equiv.) and triethylamine (2.1 equiv.) in ethyl acetate.[21] The products were purified by chromatography on silica gel and isolated in > 86% yield. Under these reaction conditions, subsequent cyclization to the fulgimides was not observed (TLC monitoring). However, separate treatment of the regioisomeric phenacyl ester arylamide **6** with triethylamine furnished the fulgimide (*Z*)-**8** upon increasing the amount to 10% triethylamine in dichloromethane. After 3 d at room temperature, ca. 70% turnover and the formation of by-products was determined by TLC monitoring and by ^1H NMR spectroscopy of the crude material isolated. Pure compound (*Z*)-**8** was isolated in 51% yield by flash chromatography. However, when applied to the phenacyl ester alkylamides **5** and **10**, this reaction protocol led to poor turnovers and unsatisfactory yields (Table 1). Whereas compound (*Z*)-**7** was isolated in 31% yield (ca. 35% turnover), for (*E*)-**11** less than 10% turnover was observed within 7 d according to ^1H NMR spectroscopy of the crude material isolated. Fortunately, treatment of **5** with *tert*-butyllithium (2.2 equiv.) in THF at −78 °C resulted in 80% turnover and gave product (*Z*)-**7** in 48%

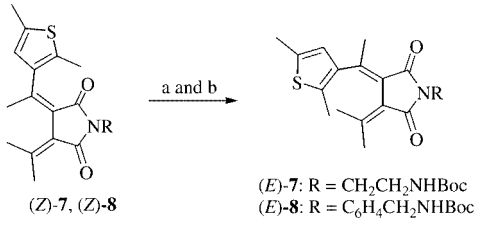
yield after flash chromatography on silica gel. Increasing the excess of *tert*-butyllithium and prolonged reaction times led only to formation of substantial amounts of by-products. The reaction of the sterically demanding phenacyl ester alkylamide **10** with *tert*-butyllithium (2.4 equiv.) gave 50% turnover in 6 h and fulgimide (*E*)-**11** was isolated in 40% yield (flash chromatography) in pure form. However, treatment of the phenacyl ester arylamide **6** with *tert*-butyllithium resulted in the formation of substantial amounts of by-products and incomplete turnover. Fulgimide (*Z*)-**8** was isolated in 14% yield.

Table 1. Synthesis of fulgimides according to Schemes 2 and 3

Entry	Starting material	Method	Reaction time [h]	Product	Yield[a] [%]
1	**5**	A	2[b]	**7**	48
2	**5**	B	144	**7**	31
3	**6**	A	6[c]	**8**	14
4	**6**	B	72	**8**	51
5	**10**	A	6[d]	**11**	40
6	**10**	B	188	**11**	10[e]

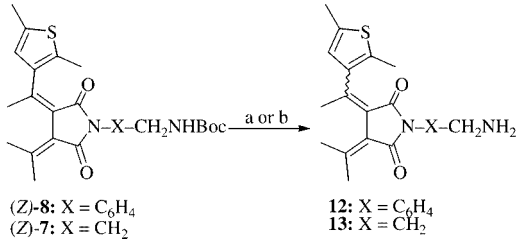
[a] Isolated yield. [b] 2.2 equiv. of *t*BuLi. [c] 3.0 equiv. of *t*BuLi. [d] 2.4 equiv. of *t*BuLi. [e] Turnover according to ^{1}H NMR spectroscopy of the crude material isolated.

The (*E*) isomers (*E*)-**7** and (*E*)-**8** (Scheme 4) were prepared by irradiation of a solution of the (*Z*) isomers at 365 nm (200 W mercury lamp) until the photostationary state was reached (14 h). The deep red solutions obtained, enriched in the (*C*) forms, were converted into the (*E*) isomers with 514-nm light (1000-W xenon lamp). The resulting crude product mixtures were then separated by column chromatography to yield 57% of (*E*)-**7** and 73% of (*E*)-**8**.



Scheme 4. a) (*E*)-**7**: toluene, room temp., 365 nm, 13.5 h; then daylight, 4 h, 57%; b) (*E*)-**8**: toluene, room temp., 365 nm, 12 h; then daylight, 4 h, 73%

HCl in dioxane was applied successfully for the deprotection of (*Z*)-**8** (Scheme 5).[22] However, (*E*)/(*Z*) isomerization was observed, yielding (*Z*)-**12** in a ratio (*Z*)/(*E*) = 91:9 (^{1}H NMR spectroscopy). Upon purification by reversed-phase HPLC, **12** was isolated in 89% yield [(*Z*)/(*E*) = 88:12]. Deprotection of the Boc-protected fulgimide (*Z*)-**7** with TFA in dichloromethane proved to be a challenge.[22] Reactions employing 5% TFA in dichloromethane at room temperature looked very promising but during concentration of the reaction mixture (*E*)/(*Z*) isomerization and the formation of by-products were again observed. Similar results were obtained upon treatment of (*Z*)-**7** with 50% TFA in dichloromethane. However, (*E*)/(*Z*) isomerization could be avoided employing 5% TFA followed by subsequent workup with diluted aqueous ammonia solution prior to concentration. Thus, fulgimide (*Z*)-**13** was isolated in 87% yield and 90−95% purity according to ^{1}H NMR spectroscopy and HPLC analysis of the crude product isolated. All attempts to increase the purity applying flash chromatography failed. Preparative reversed-phase HPLC with acetonitrile/water containing 1% TFA led to (*E*)/(*Z*) isomerization.



Scheme 5. a) (*Z*)-**8**: HCl in dioxane, 89%, ratio (*Z*)/(*E*) = 88:12; b) (*Z*)-**7**: 5% TFA in CH_2Cl_2, then aqueous NH_3 solution, 87%

X-ray Analysis

The structure of fulgimide (*Z*)-**7** was determined by X-ray structure analysis (Figure 1). The triene system of (*Z*)-**7** is twisted, owing to the steric hindrance caused by the atoms C(8) and C(15) and the atoms O(1) and C(6). The torsion angle C(7)−C(9)−C(10)−C(13) is −51.0°, which is slightly larger than for other (*Z*)-fulgides. For example, a phenyl-substituted (*Z*)-thienylfulgide[23] was reported to contain a corresponding torsion angle of −48° and for a (*Z*)-furylfulgide[24] a torsion angle of −47° was determined. In contrast to this, (*E*)-thienylfulgides[23] and (*E*)-furylfulgides[24] have a smaller torsion angle of 39 and −39.6°,

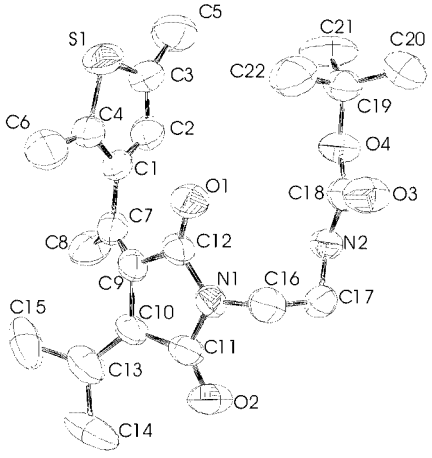


Figure 1. ORTEP plot of (*Z*)-**7**; selected bond lengths [pm], angles [°] and torsion angles [°]: N(1)−C(11) 139.4(6), N(1)−C(12) 139.0(6), C(1)−C(4) 136.7(7), C(1)−C(7) 149.6(6), C(7)−C(9) 133.6(8), C(9)−C(10) 147.0(6), C(10)−C(13) 135.7(7); C(7)−C(9)−C(10) 128.9(5), C(9)−C(10)−C(13) 127.6(5); C(7)−C(9)−C(10)−C(13) −51.0(9), C(12)−C(9)−C(10)−C(11) −17.4(5), C(1)−C(7)−C(9)−C(10) −179.0(5); for further details see Exp. Sect. and ref.[25]

respectively. The inner torsion angle of the imide ring system of (*Z*)-**7** [C(12)−C(9)−C(10)−C(11)] is −17.4°. This value is in good accord with those of other (*Z*)-fulgides (−18, −15.7°) as well as (*E*)-fulgides (15, −16.5°).[23,24] Between the two isomers the torsion angle C(1)−C(7)−C(9)−C(10) does differ significantly and this angle indicates whether the double bond is (*Z*)- or (*E*)-configured. For (*Z*)-furylfulgides this torsion angle is 173.2° in contrast to −8.5° for (*E*)-furylfulgides.[24] The torsion angle for (*Z*)-**7** is consistently −179.0°. Steric repulsion between the atoms C(8) and C(15) also widens the bond angles of (*Z*)-**7**. The bond angles C(7)−C(9)−C(10) and C(9)−C(10)−C(13) are 128.9 and 127.6°. These values are close to those of other (*Z*)-thienylfulgides[23] (130.3, 128.7°) and (*Z*)-furylfulgides[24] (128.4, 130.7°) whereas the bond angles for (*E*)-thienylfulgides[23] (132.1, 131.5°) and (*E*)-furylfulgides[24] (132.1, 131.2°) are slightly higher.

Photochromism and UV/Vis Spectroscopy

Figure 2 displays the photochromism of compound **8** in toluene solution at room temperature. Irradiation of the (*Z*) and the (*E*) form at 366 nm is shown, indicating ring closure to the (*C*) form by the increasing absorption around 526 nm. Because of the (*Z*)/(*E*) isomerization prior to cyclization isosbestic points for this electrocyclic ring-closure process are not observed. Ring opening of the (*C*) isomer was accomplished by irradiation at 514 or 520 nm of the solutions enriched in the (*C*) form obtained from either the (*Z*) or (*E*) isomer. For this reaction process the isosbestic points are listed in Table 2 as well as the absorption maxima of the fulgides and fulgimides measured in toluene.

The UV/Vis spectra of (*Z*)-**1a** and (*E*)-**1b** as well as of (*Z*)-**7**, (*E*)-**7** and (*Z*)-**8**, (*E*)-**8** show a typical maximum at ca. 311−339 nm, whereas for (*E*)-**11** (315 nm) and (*Z*)-**13** (321 nm) only absorption shoulders are detected in the corresponding wavelength range. The data are consistent with previously published work.[9] The spectral features reveal that selective excitation of the (*E*) forms at 365 nm is less effective because of significant absorption of the light by the (*C*) forms formed. The (*E*) configuration was found to shift the absorption maximum to shorter wavelengths compared to the (*Z*) configuration. For the (*C*) isomers a broad maximum at about 514−526 nm is observed. In the case of *N*-arylfulgimide **8** the absorption maxima of the (*Z*), (*E*) and (*C*) form are red-shifted by about 6−15 nm compared to the isomers of the *N*-alkylfulgimide **7**.

We have also determined the ratio of the isomers in the photostationary states at 365 and 514 nm by ^{1}H NMR spectroscopy in [D$_8$]toluene. The data published previously for (*E*)-**1b** by Effenberger et al.[19] were confirmed, whereas for (*Z*)-**1a** the data were found to deviate from the literature.[18] For adamantylidene-substituted *N*-methyl- and *N*-phenylfurylfulgimides Heller et al.[11] determined a 55:45 and a 30:70 mixture of the (*C*) and the (*E*) form in the photostationary state (pss) measured by ^{1}H NMR spectroscopy upon irradiation in CDCl$_3$ (366 nm). In contrast to these examples for fulgimides **7** and **8** in [D$_8$]toluene the influence of aryl or alkyl substituents on the imide nitrogen

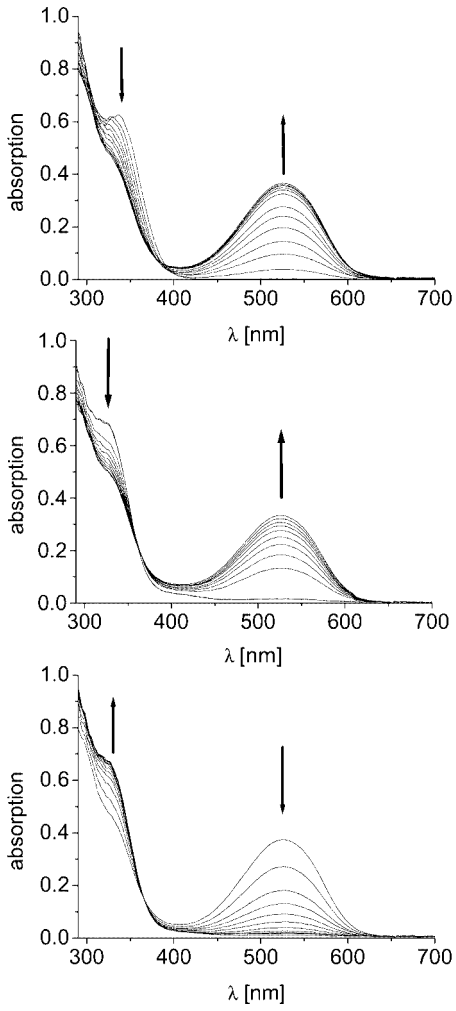


Figure 2. Change of UV/Vis spectra of fulgimide **8**: $c = 1.0 \times 10^{-4}$ mol/L in toluene, XBO 1000 W; top: (*Z*)-**8**, 365-nm filter, T_{max}: 50%, HW: 10 nm, Δt = 60 s, pss reached after 600 s; center: (*E*)-**8**, 365-nm filter, T_{max}: 50%, HW: 10 nm, Δt = 60 s, pss reached after 540 s; bottom: solution enriched in (*C*)-**8** (Entry 4, Table 2, pss$_{365}$) obtained by irradiation of (*Z*)-**8**, 514-nm filter, T_{max}: 50%, HW: 10 nm, Δt = 10 s, pss reached after 80 s

atom is found to be negligible. According to Rentzepis[17], substituents at the *N*-position of 2-indolylfulgimides were also found to have little effect on the photochromism and the absorption maxima. For compound (*Z*)-**7** a ratio of (*Z*)/(*E*)/(*C*) = 9:31:60 (Entry 3, Table 2) was determined and similar results were obtained for (*Z*)-**8** (Entry 4, Table 2). For compound (*Z*)-**13**, bearing the more polar amino group, the absorption maxima are lower in intensity and only 51% of (*C*)-**13** was determined in the pss by ^{1}H NMR spectroscopy. However, irradiation of (*E*)-**11** containing the bulky isopropyl group led to a photostationary equilibrium containing 67% of the (*C*) form. Similarly, in the literature for a 3-indolylfulgimide[16] possessing an isopropyl group, a 68% (*C*)-form content has been reported at the photostationary state of UV irradiation (405 nm) although the (*Z*) isomers of 3-indolylfulgides and -fulgimides are not involved in the photochromic reaction. However, Matsushima[9] reported not less than 80% conversion into the (*C*)

Table 2. UV/Vis data of fulgides and fulgimides in toluene

Entry	Compound	λ_Z [a]	ε_Z [b]	λ_E [a]	ε_E [b]	λ_C [a]	pss_{365} (*Z*)/(*E*)/(*C*)[c]	pss_{514} (*Z*)/(*E*)/C[c]	Isosbestic $point_{514}$
1	(*Z*)-**1**	339	7980	–	–	524	8:11:81	12:88:0	393
2	(*E*)-**2**	–	–	327	3920	524	0:8:92	0:100:0	382
3	(*E*)-**7***/*(*Z*)-**7**	328	5460	311	7410	516	9:31:60	10:90:0	368
4	(*E*)-**8***/*(*Z*)-**8**	334	6250	326	6850	526	9:34:57	9:91:0	362
5	(*E*)-**11**	–	–	315	5150	518	5:28:67	5:95:0	357
6	(*Z*)-**13**	321	4440	–	–	514	16:33:51	19:81:0	370

[a] [nm]. [b] [$dm^3 \cdot mol^{-1} \cdot cm^{-1}$]. [c] Ratios determined by ^1H NMR spectroscopy in [D_8]toluene in the pss upon illumination with 365 nm and 514 nm, respectively.

forms during measurements focusing on the photochemical reversibility and recyclizability of fulgimides in toluene solutions and solid PMMA films. Likewise, Rentzepis[17] observed more than 80% transformation of the (*E*) form to the (*C*) form for 2-indolylfulgimides in either CH_3CN or hexane. However, the data of these authors do not refer to NMR measurements and thus a comparison of the data seems to be inappropriate since the ratios determined in the photostationary states depend upon the concentration of the photochromic compounds.

Conclusion

Boc-protected amino-functionalized thienylfulgimides have been synthesized from phenacyl ester amides by a base-catalyzed cyclization strategy employing triethylamine for arylamides and *tert*-butyllithium for alkylamides. Deprotection of (*Z*)-**7**, furnishing (*Z*)-**13** and avoiding (*E*)/(*Z*) isomerization, was carried out with 5% TFA in dichloromethane and subsequent workup with aqueous ammonia solution. The UV/Vis data and photochromic properties of the synthesized fulgimides have been determined and the results obtained have been discussed in relation to their structure and in comparison to literature data. We are evaluating applications of the amino-functionalized fulgimides.

Experimental Section

General Remarks: Melting points were measured with a Büchi apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded with a Bruker AC 200, AM 400 or DRX 500 spectrometer, residual solvent protons were used as internal standard. All chemical shifts are given in ppm relative to TMS and coupling constants in Hz. FT IR spectra were recorded with a Nicolet Avatar 360 FT IR or a Perkin–Elmer FT IR spectrometer 1760X. Low- and high-resolution electron-impact mass spectra (EIMS, 70 eV) were recorded with a Finnigan MAT 95 SQ or a Varian MAT 711 spectrometer. Elemental analyses were carried out by the Microanalytical Division of the Institute of Organic Chemistry at the University of Mainz (Germany) or were measured with an Elementar Vario EI from Analytik Jena at the Institute of Chemistry, TU Berlin. For TLC, Merck silica-gel 60-F_{254} plates were used. Flash chromatography was performed on silica gel (ICN silica, 32–63 μm, 60 Å, ICN Biomedicals GmbH). Column chromatography was carried out using the technique developed by Helquist et al.[26] but without inert gas on silica gel (ICN silica, 63–200 μm, 60 Å, ICN Biomedicals GmbH). All reactions were performed under argon. Solvents were dried before use according to standard procedures.[27] The amines $H_2NCH_2CH_2NHBoc$ (**2a**)[28] and $H_2NC_6H_4CH_2NHBoc$ (**2b**)[29] and the fulgides **1a**[18] and **1b**[19] were prepared according to literature procedures. *tert*-Butyllithium (1.6 M in pentane) was purchased from Aldrich. Changes in the absorption spectra of fulgides and fulgimides in toluene ($c = 1 \times 10^{-4}$ mol/L) were investigated by light irradiation starting from the (*Z*) isomers at 365 nm (365-nm interference filter, Amko, Tornesch) and by light irradiation starting from the (*C*) isomers in the pss at 514 nm (514-nm interference filter, Amko, Tornesch) and were determined with an MCS 320/340 Diodenarray spectrometer from Zeiss with an irradiation beam of a xenon lamp 1000 XBO (Osram, München) vertical to the measuring cell. These measurements were carried out at the University of Mainz in the research group of Prof. Dr. H. Meier, Institut für Organische Chemie. The irradiation was carried out in 10- or 30-s intervals for 365 and 520 nm, respectively, in order to bring about the pss. Otherwise, photoirradiation was performed at the TU Berlin using a high-pressure mercury lamp 200 HBO (Osram, München) with a 365-nm interference filter (Amko, Tornesch) and a xenon lamp 1000 XBO (Osram, München) with a 514-nm interference filter (Amko, Tornesch) or by exposure to daylight. Samples were placed at the focus of the irradiation beam (suprasil lens, focus 10 cm) and 2 cm behind the corresponding filter. The isomeric ratio in the pss was determined by irradiation of the compounds in [D_8]toluene in a quartz NMR tube and by integration of the corresponding signals of the hydrogen atoms in the 4-position of the thiophene moiety ($\delta = 5.8–6.6$ ppm). The NMR spectroscopic data of the fulgimides in [D_8]toluene are listed in Table 3. Large-scale photoisomerization using the high-pressure mercury lamp 200 HBO at 365 nm were carried out in a round-bottom flask placed 4 cm behind the filter and about 12 cm behind the suprasil lens (focus 10 cm). All experiments were conducted with a 5-cm water filter between the lamp and the lens to cut off the IR irradiation of the lamp. All solutions were degassed and stirred during irradiation.

3: A solution of *tert*-butyl (2-aminoethyl)carbamate (**2a**) (0.96 g, 5.79 mmol) in CH_2Cl_2 (5 mL) was added to a solution of fulgide **1a** (1.50 g, 5.43 mmol) in CH_2Cl_2 (50 mL). The mixture was refluxed for 3 h and the solvent was evaporated under reduced pressure. The crude product was then purified by chromatography on silica gel using ethyl acetate/methanol (67:33, *v*/*v*) as eluent to give **3** as a yellow solid. Yield: 2.34 g (99%), mixture of isomers, ratio I/II = 55:45 (^1H NMR); m.p. 68–70 °C; $R_f = 0.59$ [ethyl acetate/methanol, 67:33, *v*/*v*). ^1H NMR (200 MHz, $CDCl_3$; 25 °C): isomer I: $\delta = 7.59$ (br. s, 1 H, NH), 6.41 (s, 1 H, 4-H thienyl), 5.20 (br. s, 1 H, NH), 3.35–3.48 (m, 2 H, CH_2), 3.25–3.35 (m, 2 H, CH_2), 2.32 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3), 1.93 (s, 3 H, CH_3), 1.85 (s,

Table 3. ^{1}H NMR spectroscopic data of fulgimides in [D$_8$]toluene

Compound	4-H	Me[a]	Me	Me	Me	Me	*t*Bu
(*Z*)-**7**	6.56	2.51	2.51	2.36	1.89	1.66	1.58
(*E*)-**7**	6.42	2.82	2.43	2.25	2.14	1.27	1.59
(*C*)-**7**	5.81	2.33	1.96	1.84	1.70	[b]	1.59
(*Z*)-**8**	6.54	2.55	2.52	2.36	1.93	1.75	1.65
(*E*)-**8**	6.44	2.89	2.47	2.28	2.18	1.33	1.68
(*C*)-**8**	5.83	2.39	1.97	1.85	1.60	[b]	1.67
(*E*)-**11**	6.62	2.39	2.11	1.33	[b] [c]	–	1.60
(*C*)-**11**	6.12	1.99	1.87	1.72	[b]	–	1.61
(*Z*)-**12**	6.53	2.53	2.49	2.35	1.88	1.65	–
(*E*)-**12**	6.40	2.84	2.44	2.24	2.17	1.26	–
(*C*)-**12**	5.80	2.34	1.94	1.83	1.66	1.57	–

[a] The signals of the methyl groups are listed according to their chemical shifts. [b] The signal is overlapped by adjacent signals of the other isomers. [c] The signal is overlapped by the signals of residual solvent protons of [D$_8$]toluene.

3 H, CH_3), 1.74 (s, 3 H, CH_3), 1.37 (s, 9 H, *t*Bu); isomer II: δ = 6.46 (s, 1 H, 4-H thienyl), 6.19 (br. s, 1 H, NH), 4.58 (br. s, 1 H, NH), 3.00−3.25 (m, 2 H, CH_2), 2.80−3.00 (m, 2 H, CH_2), 2.38 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3), 2.08 (s, 3 H, CH_3), 1.88 (s, 3 H, CH_3), 1.75 (s, 3 H, CH_3), 1.39 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, mixture of isomers, * minor component): δ = 171.8, 157.1, 156.3, 146.2*, 142.0, 141.0, 137.6, 137.2*, 135.7, 133.0, 132.0, 131.0*, 127.3, 125.3, 79.8, 41.1*, 40.8, 40.3, 28.3, 22.2, 21.8, 21.4, 21.0*, 15.1, 13.6, 13.5* ppm. IR (KBr): $\tilde{\nu}$ = 3358, 3063, 2978, 2921, 2864, 2734, 1696, 1646, 1577, 1523, 1448, 1393, 1367, 1273, 1250, 1171 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 436 (14) [M$^+$], 261 (45). HR MS (70 eV, EI): calcd. 436.2032, found 436.2031 (for $C_{22}H_{32}N_2O_5S$).

5: A solution of phenacyl bromide (1.25 g, 6.30 mmol) in ethyl acetate (10 mL) was added dropwise to a solution of **3** (2.50 g, 5.73 mmol) in ethyl acetate (50 mL), followed by dropwise addition of triethylamine (0.89 mL, 12.0 mmol). After a few minutes, a colorless precipitate was formed and the solution turned orange. The mixture was stirred for 4 d (TLC monitoring). Then water (50 mL) was added and the aqueous layer was separated and extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with water (50 mL), 0.5 M $KHCO_3$ solution (50 mL), and water (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by chromatography on silica gel using light petroleum ether/ethyl acetate (80:20 → 67:33 → 50:50, *v*/*v*) as eluent to give **5** as a colorless solid. Yield: 2.73 g (86%), mixture of isomers, ratio I/II = 60:40 (^{1}H NMR); m.p. 47−48 °C; R_f = 0.18 (light petroleum ether/ethyl acetate, 67:33, *v*/*v*). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): isomer I: δ = 7.41−7.95 (m, 5 H, Ar-H), 6.42 (s, 1 H, 4-H thienyl), 5.28 (br. s, 2 H, CH_2), 3.46−3.55 (m, 2 H, CH_2), 3.28−3.34 (m, 2 H, CH_2), 3.23 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3), 2.05 (s, 3 H, CH_3), 1.99 (s, 3 H, CH_3), 1.77 (s, 3 H, CH_3), 1.36 (s, 9 H, *t*Bu); isomer II: δ = 7.41−7.95 (m, 5 H, Ar-H), 6.75−6.82 (br. s, 1 H, NH), 6.51 (s, 1 H, 4-H thienyl), 5.28 (br. s, 2 H, CH_2), 3.14−3.22 (m, 2 H, CH_2), 2.95−3.01 (m, 2 H, CH_2), 2.39 (s, 3 H, CH_3), 2.29 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 2.09 (s, 3 H, CH_3), 1.83 (s, 3 H, CH_3), 1.40 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C, mixture of isomers, * minor component): δ = 193.3, 193.1*, 169.8, 169.5*, 166.0, 165.8*, 156.1, 156.0*, 155.4, 149.2, 141.1, 138.5, 138.3*, 137.2*, 136.4, 135.9*, 134.2, 134.1*, 134.0, 133.7*, 132.2, 131.0*, 129.0, 128.9*, 128.5, 127.9, 127.6*, 126.0, 125.2*, 79.0, 66.0, 65.8*, 41.4, 41.0*, 39.4, 28.4, 28.4*, 24.7*, 23.1, 22.5, 21.6, 21.6*, 21.0*, 15.1, 15.1*, 13.5, 13.4* ppm. IR (KBr): $\tilde{\nu}$ = 3369, 3055, 2980, 2922, 2864, 1703, 1655, 1599, 1582, 1511, 1451, 1392 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 554 (18) [M$^+$], 394 (42), 258 (100). HR MS (70 eV, EI): calcd. 554.2451, found 554.2451 (for $C_{30}H_{36}N_2O_6S$).

(*Z*)-7: A solution of *tert*-butyllithium (1.5 M in pentane, 1.87 mL, 3.17 mmol) was added to a solution of **5** (800 mg, 1.44 mmol) in THF (50 mL) at −78 °C. The mixture was stirred for 2.5 h and brine (100 mL) was added. The aqueous layer was extracted with diethyl ether (2 × 100 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel with light petroleum ether/ethyl acetate (80:20 → 67:33 → 50:50, *v*/*v*) as eluent to give **7** as a yellow solid. Yield: 290 mg (48%) [besides 177 mg (22%) **5**]; m.p. 49−50 °C; R_f = 0.51 (light petroleum ether/ethyl acetate, 67:33, *v*/*v*). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 6.50 (s, 1 H, 4-H thienyl), 4.85 (br. s, 1 H, NH), 3.55 (t, $^3J_{H,H}$ = 5 Hz, 2 H, CH_2), 3.35 (m, $^3J_{H,H}$ = 5 Hz, 2 H, CH_2), 2.38 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.89 (s, 3 H, CH_3), 1.42 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 168.4, 166.0, 155.8, 148.0, 141.5, 137.3, 136.3, 135.4, 125.3, 124.8, 123.9, 79.1, 39.8, 37.2, 28.3, 26.9, 26.1, 21.7, 15.2, 14.1 ppm. IR (KBr): $\tilde{\nu}$ = 3355, 2977, 2921, 1776, 1699, 1587, 1515, 1439, 1392, 1367 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 418 (28) [M$^+$], 347 (100). HR MS (70 eV, EI): calcd: 418.1926; found 418.1926 (for $C_{22}H_{30}N_2O_4S$).

4: Fulgide **1a** (478 mg, 1.73 mmol) and *tert*-butyl (4-aminobenzyl)-carbamate (**2b**) (500 mg, 2.25 mmol) were dissolved in CH_2Cl_2 (30 mL). The mixture was refluxed for 72 h and the solvent was evaporated in vacuo. The crude product was then purified by flash chromatography on silica gel with light petroleum ether/ethyl acetate (83:17 → 67:33 → 0:100, *v*/*v*) as eluent to give **4** as a yellow solid. Yield: 748 mg (87%), mixture of isomers, ratio I/II = 46:54 (^{1}H NMR); m.p. 167 °C; R_f = 0.13 (light petroleum ether/ethyl acetate, 67:33, *v*/*v*). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): isomer I: δ = 7.18 (d, $^3J_{H,H}$ = 7.9 Hz, 2 H, Ar-H), 7.17 (br. s, 1 H, NH), 7.04 (d, $^3J_{H,H}$ = 7.9 Hz, 2 H, Ar-H), 6.57 (s, 1 H, 4-H thienyl), 4.83 (br. s, 1 H, NH), 4.24 (s, 2 H, CH_2-Ar), 2.44 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3), 2.12 (s, 3 H, CH_3), 2.03 (s, 3 H, CH_3), 1.83 (s, 3 H, CH_3), 1.45 (s, 9 H, *t*Bu) ppm; isomer II: δ = 8.77 (br. s, 1 H, NH), 7.53 (d, $^3J_{H,H}$ = 7.9 Hz, 2 H, Ar-H), 7.25 (d, $^3J_{H,H}$ = 7.9 Hz, 2 H, Ar-H), 6.45 (s, 1 H, 4-H thienyl), 4.88 (br. s, 1 H, NH), 4.26 (s, 2 H, CH_2-Ar), 2.37 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3), 2.05 (s, 3 H, CH_3), 2.01 (s, 3 H, CH_3), 1.82 (s, 3 H, CH_3), 1.45 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): isomer I: δ = 169.0, 168.5, 155.7, 146.5, 142.4, 138.5, 136.3, 135.9, 135.5, 133.6, 130.8, 127.9, 125.8, 124.3, 120.6, 79.5, 44.0, 28.2, 22.1, 22.0, 21.8, 15.0, 13.3 ppm. IR (KBr): $\tilde{\nu}$ = 3338, 2977, 2920, 2862, 1696, 1594, 1516, 1447, 1413, 1367, 1249, 1169 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 498 (64) [M$^+$], 277 (70), 165 (100). HR MS (70 eV, EI): calcd. 498.2188, found 498.2191 (for $C_{27}H_{34}N_2O_5S$).

6: A solution of phenacyl bromide (439 mg, 2.21 mmol) in ethyl acetate (5 mL) was added to a solution of **4** (1.00 g, 2.01 mmol) in ethyl acetate (30 mL). Triethylamine (0.58 mL, 4.21 mmol) was added dropwise and the mixture was stirred at room temp. for 16 h. Water (30 mL) was added and the aqueous layer was separated and extracted with ethyl acetate (2 × 30 mL). The organic layers were washed with water (30 mL), saturated $NaHCO_3$ solution (30 mL), and water (30 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel with light petroleum ether/ethyl acetate (83:17 → 67:33 → 50:50 → 0:100, *v*/*v*) as eluent to give a colorless solid. Yield: 1.19 g (96%), mixture of isomers, ratio I/II = 90:10 (^{1}H NMR); m.p. 61−63 °C;

R_f = 0.40 (light petroleum ether/ethyl acetate, 67:33, *v*/*v*). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): isomer I: δ = 8.09 (br. s, 1 H, NH), 7.91−7.95 (m, 2 H, Ar-H), 7.57−7.63 (m, 1 H, Ar-H), 7.45−7.50 (m, 2 H, Ar-H), 7.30 (d, $^3J_{H,H}$ = 8.3 Hz, 2 H, Ar-H), 7.10 (d, $^3J_{H,H}$ = 8.1 Hz, 2 H, Ar-H), 6.56 (s, 1 H, 4-H thienyl), 5.43 (s, 2 H, CH_2), 4.72 (br. s, 1 H, NH), 4.18 (s, 2 H, CH_2-Ar), 2.37 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3), 2.29 (s, 3 H, CH_3), 2.07 (s, 3 H, CH_3), 1.93 (s, 3 H, CH_3), 1.42 (s, 9 H, *t*Bu) ppm; isomer II (signals are overlapped by adjacent signals of isomer I): δ = 7.86 (d, $^3J_{H,H}$ = 7.7 Hz, 2 H, Ar-H), 7.68 (d, $^3J_{H,H}$ = 8.3 Hz, 2 H, Ar-H), 6.42 (s, 1 H, 4-H thienyl), 4.24 (s, 2 H, CH_2-Ar), 2.35 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3), 2.06 (s, 3 H, CH_3), 1.83 (s, 3 H, CH_3), 1.43 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$, 25 °C): isomer I: δ = 193.9, 166.8, 165.8, 155.9, 155.5, 139.0, 137.9, 137.8, 137.0, 134.2, 134.1, 133.6, 132.6, 129.0, 128.0, 127.9, 125.5, 123.6, 120.2, 120.0, 79.5, 66.0, 44.4, 28.5, 24.8, 22.7, 21.9, 15.3, 13.7 ppm. IR (ATR): $\tilde{\nu}$ = 3345, 3060, 2976, 2919, 2861, 1246, 1205, 1170 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 616 (25) [M$^+$], 259 (93), 231 (100). HR MS (70 eV, EI): calcd. 616.2607, found 616.2605. $C_{35}H_{40}N_2O_6S$ (616.8): calcd. C 68.16, H 6.54, N 4.54; found C 67.78, H 6.83, N 4.77.

(*Z*)-8: Triethylamine (2 mL) was added dropwise to a solution of **6** (300 mg, 0.49 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred at room temp. for 72 h. Then water (15 mL) was added and the aqueous layer was separated and extracted with CH_2Cl_2 (2 × 20 mL). The organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel with light petroleum ether/ethyl acetate (83:17 → 67:33, *v*/*v*) as eluent to give **8** as a slightly yellow solid. Yield: 120 mg (51%) [by chromatography 71 mg of starting material **6** (24%) was isolated; yield of **8** based on isolated **6**: 68%]; m.p. 73 °C; R_f = 0.62 (light petroleum ether/ethyl acetate, 67:33, *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.25−7.33 (m, 4 H, Ar-H), 6.54 (s, 1 H, 4-H thienyl), 4.79 (br. s, 1 H, NH), 4.28 (d, $^3J_{H,H}$ = 5.5 Hz, 2 H, CH_2-Ar), 2.46 (s, 3 H, CH_3), 2.39 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3), 2.10 (s, 3 H, CH_3), 2.01 (s, 3 H, CH_3), 1.44 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 167.3, 164.6, 155.6, 148.7, 142.2, 138.5, 137.5, 135.1, 135.3, 131.0, 128.8, 127.7, 127.5, 127.0, 125.0, 124.7, 123.7, 79.4, 44.2, 28.2, 26.9, 15.2, 14.1 ppm. IR (ATR): $\tilde{\nu}$ = 3376, 2977, 2918, 1755, 1707, 1632, 1599, 1514, 1437, 1366, 1251, 1165 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 480 (18) [M$^+$], 424 (30), 409 (100). HR MS (70 eV, EI): calcd. 480.2083, found 480.2088. $C_{27}H_{32}N_2O_4S$ (480.2): calcd. C 67.47, H 6.71, N 5.83; found C 67.18, H 6.87, N 5.55.

(*E*)-7: A solution of (*Z*)-**7** (858 mg, 1.79 mmol) in degassed toluene (50 mL) was irradiated with 365-nm light [high-pressure mercury lamp 200 HBO (Osram, München), 365-nm interference filter (Amko, Tornesch)] for 13.5 h (TLC monitoring). The resulting red solution was exposed to daylight. After 4 h, the solution was light orange. The solvent was evaporated in vacuo and the resulting mixture of isomers was separated by flash chromatography on silica gel with light petroleum ether/ethyl acetate (80:20, *v*/*v*) as eluent to give (*E*)-**7**. Yield: 485 mg (57%), besides 243 mg (28%) of an (*E*)/(*Z*) mixture, ratio (*E*)/(*Z*) = 30:70; R_f = 0.60 (light petroleum ether/ethyl acetate, 67:33, *v*/*v*). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 6.49 (s, 1 H, 4-H thienyl), 4.93 (br. s, 1 H, NH), 3.71−3.77 (m, 2 H, CH_2), 3.35−3.38 (m, 2 H, CH_2), 2.58 (s, 3 H, CH_3), 2.38 (s, 3 H, CH_3), 2.26 (s, 3 H, CH_3), 2.10 (s, 3 H, CH_3), 1.40 (s, 9 H, *t*Bu), 1.21 (s, 3 H, CH_3) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 168.8, 168.2, 155.7, 149.0, 143.4, 140.2, 136.7, 133.5, 125.5, 123.9, 122.9, 79.0, 39.5, 37.3, 28.2, 25.2, 21.8 (2 C), 14.9, 14.5 ppm. IR (ATR): $\tilde{\nu}$ = 3388, 2978, 2936, 1745, 1693, 1516, 1433, 1391, 1366, 1174 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 418 (22) [M$^+$], 347 (100). HR MS (70 eV, EI): calcd. 418.1926, found 418.1927 (for $C_{22}H_{32}NO_5S$).

(*E*)-8: A solution of fulgimide (*Z*)-**8** (920 mg, 1.91 mmol) in degassed toluene (80 mL) was irradiated with 365-nm light [high-pressure mercury lamp 200 HBO (Osram, München), 365-nm interference filter (Amko, Tornesch)] for 12 h (TLC monitoring). The resulting red solution was exposed to daylight. After 4 h, the solution was light yellow. The solvent was evaporated in vacuo and the resulting mixture of isomers was separated by flash chromatography on silica gel with light petroleum ether/ethyl acetate (83:17, *v*/*v*) as eluent to give **(*E*)-8**. Yield: 668 mg (73%) [besides 212 mg (23%) of (*Z*)-**8**]; m.p. 68 °C; R_f = 0.70 (light petroleum ether/ethyl acetate, 67:33, *v*/*v*). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 7.31−7.43 (m, 4 H, Ar-H), 6.53 (s, 1 H, 4-H thienyl), 4.84 (br. s, 1 H, NH), 4.33 (d, $^3J_{H,H}$ = 6.3 Hz, 2 H, CH_2-Ar), 2.61 (s, 3 H, CH_3), 2.40 (s, 3 H, CH_3), 2.29 (s, 3 H, CH_3), 2.18 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.46 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 167.8, 167.3, 155.8, 150.1, 144.5, 140.4, 138.9, 137.0, 133.7, 131.2, 128.0, 127.1, 125.7, 124.0, 122.9, 79.5, 44.3, 28.4, 25.6, 22.2 (2 C), 15.1, 14.7 ppm. IR (ATR): $\tilde{\nu}$ = 3384, 2977, 2921, 1751, 1700, 1514, 1367, 1167, 1147 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 480 (17) [M$^+$], 424 (25), 409 (100). HR MS (70 eV, EI): calcd. 480.2083, found 480.2087. $C_{27}H_{32}N_2O_4S$ (480.2): calcd. C 67.47, H 6.71, N 5.83; found C 67.40, H 6.79, N 5.67.

9: A mixture of fulgide **2** (300 mg, 0.99 mmol) and *tert*-butyl (2-aminoethyl)carbamate **2a** (205 mg, 1.28 mmol) was dissolved in CH_2Cl_2 (30 mL) and refluxed for 3 h. Then CH_2Cl_2 (20 mL) was added and the organic layer was extracted with aqueous HCl (0.1 M, 2 × 20 mL), dried ($MgSO_4$), and the solvent was concentrated under reduced pressure. The resulting yellow product **9** was used without further purification. Yield: 456 mg (quant.), m.p. 76−77 °C; R_f = 0.67 (ethyl acetate/methanol, 67:33, *v*/*v*). ^{1}H NMR (200 MHz, $CDCl_3$; 25 °C): δ = 7.30 (br. s, 1 H, NH), 6.16 (s, 1 H, 4-H thienyl), 5.02 (br. s, 1 H, NH), 3.42−3.54 (m, 2 H, CH_2), 3.30−3.42 (m, 2 H, CH_2), 3.15 (sept, $^3J_{H,H}$ = 6.4 Hz, 1 H, C*H*Me$_2$), 2.33 (s, 3 H, CH_3), 2.16 (s, 3 H, CH_3), 1.89 (s, 3 H, CH_3), 1.84 (s, 3 H, CH_3), 1.44 (s, 9 H, *t*Bu), 1.00 (br. s, 6 H, CH(C*H*$_3$)$_2$] ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 170.9, 170.0, 156.8, 149.8, 148.8, 135.0, 133.3, 132.6, 131.2, 125.8, 124.7, 79.6, 40.5, 32.6, 28.2, 24.1, 22.8, 22.1, 21.4, 14.9, 14.1 ppm. IR (ATR): $\tilde{\nu}$ = 3344, 2972, 2931, 2871, 1697, 1640, 1586, 1521, 1449, 1365, 1251, 1172 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 464 (50) [M$^+$]. HR MS (70 eV, EI): calcd. 464.2345, found 464.2345 (for $C_{24}H_{36}N_2O_5S$).

10: A mixture of **9** (425 mg, 0.92 mmol) and phenacyl bromide (230 mg, 1.16 mmol) was dissolved in ethyl acetate (30 mL) and triethylamine (0.28 mL, 2.04 mmol) was added dropwise. After a few minutes, a colorless precipitate was formed and the solution turned orange. The mixture was stirred for 24 h and water (20 mL) was added. The aqueous layer was extracted with ethyl acetate (2 × 15 mL). The combined organic layers were washed with water (20 mL), 0.5 M $KHCO_3$ solution (20 mL), and water (20 mL), dried ($MgSO_4$), and concentrated in vacuo. The product **10** was used without further purification. Yield: 550 mg (94%); m.p. 54 °C; R_f = 0.21 (light petroleum ether/ethyl acetate, 67:33, *v*/*v*). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 7.92−8.02 (m, 2 H, Ar-H), 7.45−7.75 (m, 4 H, Ar-H, NH), 6.10 (s, 1 H, 4-H thienyl), 5.32 (br. s, 2 H, CH_2), 3.45−3.58 (m, 2 H, CH_2), 3.30−3.42 (m, 2 H, CH_2), 3.22 (m, $^3J_{H,H}$ = 6.8 Hz, 1 H, C*H*Me$_2$), 2.34 (s, 3 H, CH_3), 2.10 (s, 3 H, CH_3), 2.05 (s, 3 H, CH_3), 2.01 (s, 3 H, CH_3), 1.39 (s, 9 H, *t*Bu), 0.98 [br. s, 6 H, CH(C*H*$_3$)$_2$] ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 193.2, 170.2, 165.1, 155.9, 153.4, 147.1, 134.8, 134.3, 133.7, 133.2, 132.4, 128.9, 127.7, 125.8, 123.4, 78.8, 65.4, 41.3, 39.0,

32.5, 28.3, 24.9, 22.2, 21.2, 15.0, 14.0 (one quaternary carbon signal in the aromatic region is overlapped by adjacent signals) ppm. IR (ATR): $\tilde{\nu}$ = 3359, 2967, 2933, 1695, 1650, 1518, 1451, 1367, 1246, 1202, 1174 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 582 (10) [M^+], 463 (60), 329 (100). HR MS (70 eV, EI): calcd. 582.2764, found 582.2767. $C_{32}H_{42}N_2O_6S$ (582.8): calcd. C 65.95, H 7.26, N 4.81; found C 65.66, H 7.25, N 4.43.

(*E*)-11: A solution of *tert*-butyllithium (1.7 M in pentane, 0.32 mL, 0.548 mmol) was added to a solution of **10** (133 mg, 0.23 mmol) in THF (10 mL) at −78 °C. The mixture was stirred for 6.5 h and brine (15 mL) was added. The aqueous layer was extracted with diethyl ether (2 × 10 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel with light petroleum ether/ethyl acetate (83:17 → 75:25, *v*/*v*) as eluent to give **11** as an orange solid. Yield: 41 mg (40%); m.p. 41 °C; R_f = 0.80 (light petroleum ether/ethyl acetate, 67:33, *v*/*v*). ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 6.55 (s, 1 H, 4-H thienyl), 4.89 (br. s, 1 H, NH), 4.39 (sept, $^3J_{H,H}$ = 6.8 Hz, 1 H, C*H*Me$_2$), 3.60−3.85 (m, 2 H, CH_2), 3.33−3.45 (m, 2 H, CH_2), 2.41 (s, 3 H, CH_3), 2.34 (s, 3 H, CH_3), 1.96 (s, 3 H, CH_3), 1.40 (s, 9 H, *t*Bu), 1.33 [d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH(CH_3)$_2$], 1.24 (s, 3 H, CH_3), 0.76 [d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH(CH_3)$_2$] ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 168.4, 155.8, 154.3, 148.8, 136.1, 135.6, 133.3, 125.3, 124.7, 123.1, 79.2, 37.3, 30.2, 29.7, 28.3, 26.0, 23.2, 21.7, 20.4, 15.2, 14.1 ppm (one quaternary carbon signal in the aromatic region is overlapped by adjacent signals). IR (ATR): $\tilde{\nu}$ = 3385, 2917, 1745, 1693, 1513, 1434, 1390, 1365, 1248, 1174 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 446 (10) [M^+], 390 (20), 346 (70). HR MS (70 eV, EI): calcd. 446.2239, found 446.2241 (for $C_{24}H_{34}N_2O_4S$).

(*Z*)-12: HCl in dioxane (4 M, 5 mL) was added to fulgimide (*Z*)-**8** (32 mg, 0.067 mmol) at 0 °C. The mixture was stirred for 40 min and then the solution was allowed to warm to room temperature. After additional 50 min, the crude product was isolated by lyophilization to give a yellow solid (40 mg); (*E*)/(*Z*) isomerization of the crude product was observed by ^1H NMR spectroscopy [ratio (*Z*)/(*E*) = 91:9]. The crude product was purified by preparative HPLC (Luna C18, 50 cm × 4.6 cm, acetonitrile/water, 50:50, *v*/*v* + 0.1% TFA). The presence of TFA in the eluent proved to be necessary for chromatography of the free amine, and because of (*E*)/(*Z*) isomerization the product was isolated as a mixture of isomers. Yield: 25 mg [89%, ratio (*Z*)/(*E*) = 88:12]. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): (*Z*) isomer: δ = 7.14−8.10 (m, 7 H, Ar-H, NH_3), 6.54 (s, 1 H, 4-H thienyl), 3.82−4.00 (m, 2 H, CH_2), 2.44 (s, 3 H, CH_3), 2.34 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3), 2.13 (s, 3 H, CH_3), 2.05 (s, 3 H, CH_3) ppm; (*E*) isomer: δ = 7.14−8.10 (m, 7 H, Ar-H, NH_3), 6.54 (s, 1 H, 4-H thienyl), 3.82−4.00 (m, 2 H, CH_2), 2.59 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 2.18 (s, 3 H, CH_3), 2.02 (s, 3 H, CH_3) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 167.5, 165.5, 151.4, 144.5, 137.9, 136.1, 135.7, 132.5, 132.0, 130.1, 127.8, 124.7, 124.2, 122.8, 43.5, 27.1, 26.3, 21.8, 14.8, 13.9 ppm. IR (ATR): $\tilde{\nu}$ = 3420, 2960, 2923, 1751, 1700, 1518, 1437, 1374, 1207, 1135 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 380 (46) [M^+ − HCl], 365 (100) [M^+ − HCl − CH_3]. HR MS (70 eV, EI): calcd. 380.1559 [M^+ − HCl], found 380.1559.

(*Z*)-13: Trifluoroacetic acid (3 mL) was added dropwise to a solution of (*Z*)-**7** (307 mg, 0.73 mmol) in CH_2Cl_2 (57 mL). After 2 h, the reaction mixture was washed with aqueous ammonia (5%, 45 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL) and the organic layers were dried ($MgSO_4$) and concentrated in vacuo to give (*Z*)-**13** as a yellow solid. Yield: 204 mg (87%); R_f = 0.11 (ethyl acetate/methanol, 67:33, *v*/*v*). ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 6.50 (s, 1 H, 4-H thienyl), 3.56 (t, $^3J_{H,H}$ = 6.1 Hz, 2 H, CH_2), 2.85 (t, $^3J_{H,H}$ = 6.1 Hz, 2 H, CH_2), 2.41 (s, 3 H, CH_3), 2.39 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3), 2.03 (s, 3 H, CH_3), 1.94 (s, 3 H, CH_3) 1.76 (br. s, 2 H, NH_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 168.7, 166.1, 147.8, 141.3, 137.1, 136.4, 135.5, 125.5, 124.9, 124.0, 40.9, 40.6, 26.9, 26.2, 21.7, 15.2, 14.1 ppm. MS (70 eV, EI): *m*/*z* (%) = 318 (100) [M^+], 303 (40) [M^+ − CH_3]. HR MS (70 eV, EI): calcd. 318.1402, found 318.1410 (for $C_{17}H_{22}N_2O_2S$).

X-ray Crystallographic Analysis of (*Z*)-7:[25] Suitable single crystals of (*Z*)-**7** (yellow prisms) were obtained by careful addition of a layer of pentane to a concentrated solution (*Z*)-**7** of in dichloromethane. After the two-phase system had been allowed to stand unperturbed for some days in the dark at room temperature, suitable crystals had formed at the boundary between the two solvent layers. $C_{22}H_{30}N_2O_4S$ with M_r = 418.54 g/mol; crystal size: 0.60 × 0.32 × 0.18 mm; orthorhombic crystal system with space group $Pna2_1$ and Z = 4, a = 2139.16(6), b = 1185.47(4), c = 899.04(2) pm; V = 2.27988(11) nm^3, $\rho_{calcd.}$ = 1.219 $Mg{\cdot}m^{-3}$; $F(000)$ = 896; linear absorption coefficient μ = 0.171 mm^{-1}; type of diffractometer: Siemens SMART CCD; T = 293(2) K; Mo-K_α radiation; scan type: ω-scans; θ range 1.90−24.99°; index ranges −25 ≤ h ≤ 20, −14 ≤ k ≤ 14, −10 ≤ l ≤ 10; reflections collected 13546; independent reflections 3964 (R_{int} = 0.0946); observed reflections 2029 [$I > 2\sigma(I)$], reflection used for refinement 3964; Flack parameter (absolute structure) = 0.18(17); program system used: SHELXS-97, SHELXL-97 and SHELXTL; empirical absorption correction, direct methods, full-matrix refinement at F^2 with all independent reflection, weighting scheme SHELXL; goodness-of-fit parameter (based on F^2) S = 0.670; residual densities $\Delta\rho_{max}$ and $\Delta\rho_{min.}$ = 134 and −172 e × nm^{-3}. Hydrogen atoms: refined with riding model, refined with a temperature factor 1.5 times U_{eq} of the carbon atoms; non-hydrogen atoms: refined anisotropically. Data/restraints/parameters: 3964/1/275; R index (all data): wR_2 (based on F^2) = 0.1646; R index (conventional) [$I > 2\sigma(I)$]: R_1 (based on F) = 0.0518.

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