Photocycloaddition of Phthalimide Anion to Alkenes − A Highly Efficient, Convergent Method for [2]Benzazepine Synthesis

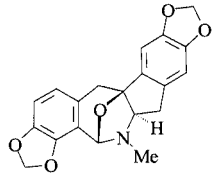
Rafael Suau,*[a] Cristóbal Sánchez-Sánchez,[a] Rafael García-Segura,[a] and Ezequiel Pérez-Inestrosa[a]

Keywords: Alkaloids / Nitrogen heterocycles / Photochemistry / Photocycloaddition / Ring-expansion

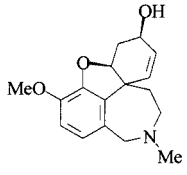
The excited state of phthalimide anion adds to cyclic, acyclic and aryl-conjugated alkenes in an efficient and regioselective manner to form [2]benzazepine-1,5-diones, substituted at positions 3 and/or 4. The reaction is independent of the ionization potential of the alkene. This process contrasts with the related reactions of *N*-methylphthalimide or phthalimide, which are limited by the requirement that the participating alkenes have oxidation potentials > ca. 2 V. Photocycloaddition of the phthalimide anion with indene serves as a concise method to prepare the basic skeleton found in members of the ribasine alkaloid family.

Introduction

The [2]benzazepine skeleton is a common structural feature found in a variety of naturally occurring and synthetic bioactive compounds. Examples are found in the ribasine-type alkaloids, which possess an indanobenzazepine structure,[1] and the galanthamine class of *Amarillidaceae* alkaloids, which have a spiro-linked benzazepine structure.[2] Galanthamine, the parent compound in the latter family, and its synthetic analogues are cholinesterase inhibitors and are currently undergoing testing in Alzheimer's disease therapy.[3] Other biologically prominent examples include fused pyrimido[5,4-*d*][2]benzazepines, which exhibit promising antitumor activity,[4] the conformationally restricted amino acids derived from 4-amino-1,3,4,5-tetrahydro[2]benzazepine-3-one, used in the synthesis of peptides,[5] and 1-aryl[2]benzazepinones, which are active on the central nervous system.[6,7]



Ribasine



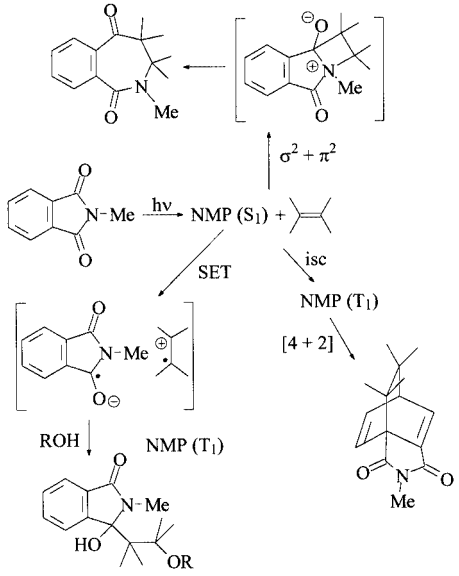
Galanthamine

Two major approaches to the synthesis of [2]benzazepine heterocycles have been employed.[8,9] One involves the intramolecular cyclization of appropriately substituted aromatic substrates, and the other the expansion of smaller rings.[10−17] A combination of both approaches has been used for the photochemical synthesis of [2]benzazepine-1,5-diones. Several photochemical approaches starting with suitably substituted *N*-alkylphthalimides and silylalkyl analogues, involving a hydroxyazetidine intermediate that opens to give the expanded benzazepinedione ring, have been developed.[18−23] These photoprocesses follow various pathways that include Norrish type II or sequential SET desilylation reactions followed by Yang cyclization,[24−27] ω-hydrogen abstraction/elimination,[28,29] single-electron transfer (SET) together with proton transfer[30,31] and SET followed by decarboxylative photocyclization.[32]

A more convergent approach is provided by the intermolecular photocycloaddition of alkenes to the C(O)−N bond of *N*-methylphthalimide (NMP). The reaction has been extensively investigated over the last two decades and is known to occur in a regio- and stereoselective manner, from the singlet excited state of the phthalimide and through an oriented exciplex[33] (Scheme 1). However, S_1 in NMP is competitively deactivated by SET from alkenes. The ion-radical pair, produced in this way, can undergo back-electron-transfer, thus quenching the excited state, or give reductive photoaddition to the carbonyl group. In the presence of nucleophilic solvents (alcohols), radical-cation trapping precedes radical coupling.[34,35] In some cases, intersystem crossing (isc) competes and alkenes add to the NMP triplet at the aromatic ring to give the [4+2] photocycloaddition products,[36−38] provided that the triplet energy of the alkene is higher than that of the imide.

A major drawback of the intermolecular $\sigma^2+\pi^2$ photocycloaddition approach for the synthesis of [2]benzazepines is its lack of universality, owing to competitive electron-transfer quenching by alkenes. For phthalimide and its *N*-

[a] Dpto. Química Orgánica, Facultad de Ciencias, Universidad de Málaga,
Campus Teatinos s/n, 29071 Málaga, Spain
Fax: (internat.) + 34-95/213-1941
E-mail: suau@uma.es



Scheme 1

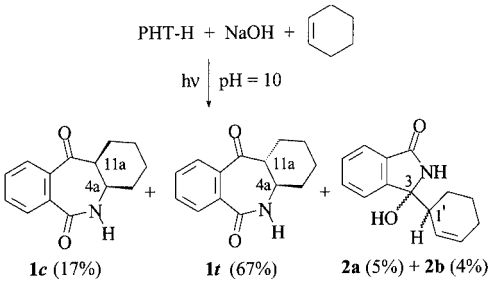
alkyl derivatives, with a singlet excited state energy of 80 kcal/mol and a reduction potential of −1.46 V,[39] thermodynamically allowed SET occurs when the oxidation potential of the alkene is less than ca. 2.1 V. Kubo[35] and Mazzocchi[34] showed that, while 1-substituted, and 1,1- and 1,2-disubstituted alkenes photoreacted with NMP to give the corresponding [2]benzazepine-1,5-diones, reactions of this type did not take place with cyclic (cyclopentene, cyclohexene), trisubstituted (2-methyl-2-butene) or tetrasubstituted (2,3-dimethyl-2-butene) alkenes.

The electron transfer process can be made endergonic by lowering the reduction potential of the phthalimide. Accordingly, we predicted that the phthalimide anion, while retaining [2+2] photocycloaddition reactivity, would not participate in photoinduced SET with alkenes. In this paper, we describe an investigation focussing on the photochemical behaviour of the phthalimide anion in the presence of alkenes. The results of this study demonstrated that the phthalimide anion underwent efficient, regiocontrolled [2+2] photocycloaddition to a wide variety of alkenes, independently of the ionization potential, and that the process served as a concise method for the synthesis of [2]benzazepines substituted at positions 3 and/or 4.

Results and Discussion

In an earlier effort,[40] photochemical reactions were performed by irradiation (1 h) of solutions of sodium phthalimide in methanol or *tert*-butyl alcohol, containing a ca. tenfold excess of cyclohexene. The [2+2] photocycloaddition products **1*c*** and **1*t*** were formed under these conditions in low yields (20 and 35% yield, respectively). In fact, the major photoreactions occurring under these conditions involved the solvents.[41]

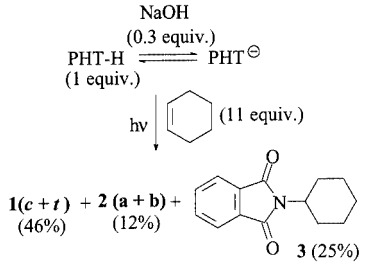
We have found that participation of the solvent in these photochemical reactions can be avoided by use of solutions of phthalimide (PHT-H) and cyclohexene in a 7:1 acetonitrile/water mixture, containing sufficient quantities of NaOH to maintain a pH of ca. 10. Irradiation of this solution (> 90% conversion) afforded an 84% yield of a mixture of *cis* (**1*c***) and *trans* (**1*t***) cycloadducts, in addition to 9% of a diastereomeric mixture of the allylic adducts **2a** and **2b** (Scheme 2).[42]



Scheme 2

The reduced value of the coupling constant ($J_{4a,11a}$ = 2.7 Hz) substantiated the *cis* stereochemistry of adduct **1*c***, while that in **1*t*** ($J_{4a,11a}$ = 11.8 Hz) was consistent with a *trans* configuration. From previous results from studies of the photocycloaddition of alkenes to phthalimides, it was assumed that the configuration of the alkene was retained in this reaction. As a result, formation of the *trans* isomer had to be due to base-catalysed isomerization of the initially formed *cis* isomer **1*c***. In fact, a methanol solution of **1*c*** was almost quantitatively converted into **1*t*** upon treatment with NaOH.

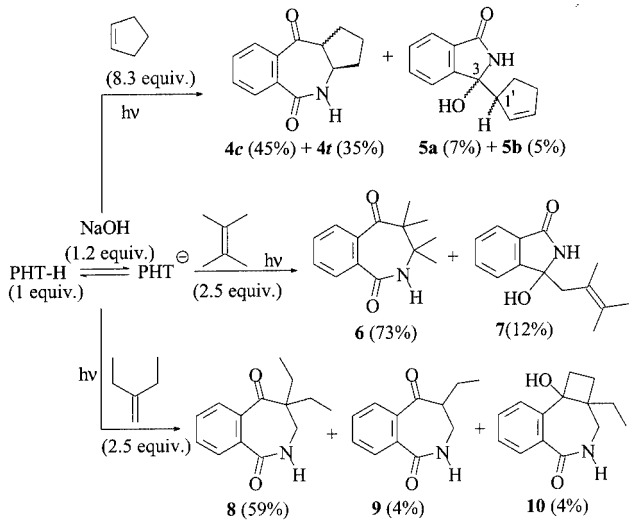
In order to prevent the secondary epimerization reaction, the base concentration used in the photoreaction was reduced by making [PHT-H] > [HO⁻]. Remarkable differences were observed as a result of this change. Namely, the overall yield of **1** (**1*c*** + **1*t***) was reduced to 46%, that of the allylic photoadducts **2a** and **2b** was slightly increased, and a new compound, *N*-cyclohexylphthalimide (**3**), was obtained. The formation of **3** is formally the result of photoaddition of phthalimide to the alkene double bond, a process previously described as the photophthalimidation of cyclohexene (Scheme 3).[43]



Scheme 3

The dependence of the nature of the photoreaction on base concentration is interesting. We found that photoreactions of phthalimide, at [PHT-H] ≈ [HO⁻], with cyclopentene, tetramethylethylene and 2-ethyl-1-butene, *three alkenes that are known not to give benzazepinediones with phthalimide or N-methylphthalimide*,[34,35] gave the respective photo-

cycloaddition products **4**, **6** and **8** in good yields. The reactions were all fast (30 min irradiation resulted in conversions of > 80%), and the yields in the photocycloaddition products ranged from 67 to 80% (Scheme 4).[44] For cyclopentene and tetramethylethylene, the allylic adducts **5a**, **5b** and **7** were also generated. However, the reaction behaviour of the asymmetric 2-ethyl-1-butene, although highly regioselective, was more complex since the benzazepinedione product **8** experienced secondary photochemistry by a rather efficient γ-hydrogen abstraction pathway to form a 1,4-biradical, which underwent β-cleavage (**9**) or Yang cyclization (**10**).[45]

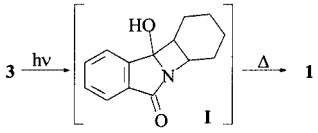


Scheme 4

The electronic absorption spectra of phthalimide in polar solvents, such as methanol or an acetonitrile/water mixture, are very similar. The longest-wavelength absorption maxima occur at λ_{max} = 290 nm and are ascribed to a π-π* transition.[46] The addition of NaOH to an acetonitrile/water solution of phthalimide resulted in a red shift in the electronic absorption spectrum to λ_{max} = 330 nm. This bathochromic shift is related to a new absorption band ascribed to the phthalimide anion (in equilibrium with its protonated form). Phthalimide[39,47] and *N*-alkylphthalimides[48,49] are poorly fluorescent species. In contrast, the phthalimide anion exhibits a significant fluorescence emission at 440 nm,[50] the maximum emission intensity being reached at a phthalimide/NaOH ratio of 2:3 in an acetonitrile/water solution ($\Phi_f = 2.10^{-2}$). This emission decays mono-exponentially with a lifetime of 4 ns, and its excitation spectrum reproduces the absorption spectrum. Interestingly, the fluorescence of the phthalimide anion was effectively quenched by addition of cyclohexene (the fluorescence intensity was halved upon addition of 12 equiv. of cyclohexene). This result suggests the involvement of the first singlet excited state of phthalimide anion in the photocycloaddition processes described above.

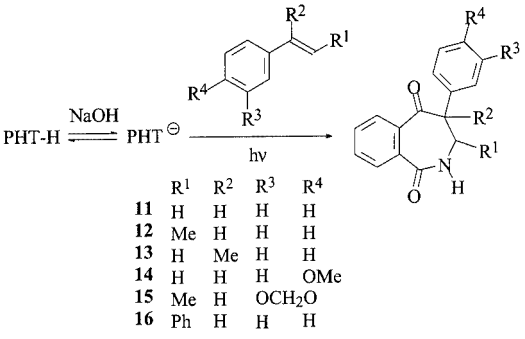
These findings resulted in the design of optimal photoaddition reaction conditions, involving irradiation of a solution of phthalimide (6.8 mmol), NaOH (10.2 mmol) and cyclohexene (78 mmol) in acetonitrile/water (3:1) for 25 min. This gave a 89% yield of adduct **1** (**1*c*** + **1*t***) at 90% conversion. Under identical conditions and with similar irradiation times, photoadducts **4** and **6** were obtained in 86% and 84% yields (at 80% and 85% conversions), respectively.

The observed formation of **3** (Scheme 3) suggests that an alternate mechanism might be responsible for the photocycloaddition process. Specifically, the excited state of *N*-cyclohexylphthalimide is known to undergo the Norrish type II reaction followed by Yang cyclization to produce the azetidine (**I**), which opens to yield the benzazepinedione **1** (Scheme 5).[25] However, this possibility can be discarded since no fluorescence was detected at NaOH concentrations < 1:10 relative to that of phthalimide. Also, the [2+2] photocycloaddition was nearly completely suppressed, while formation of **3** became dominant under these conditions. Moreover, cyclization of *N*-cyclohexylphthalimide was found to be roughly 40 times slower than the [2+2] photocycloaddition of phthalimide anion.



Scheme 5

Photoreactions with alkenylbenzenes (styrene and styrene derivatives) were more complicated (Scheme 6 and Table 1). These processes were much slower, since the alkene concentration had to be kept low to prevent competitive absorption of light. Owing to the need for long irradiation times, photoreactions were initially performed at low NaOH concentration to exclude thermal reaction with phthalimide. In all cases, the reactions were found to be regioselective, favouring products with the aromatic substituent at position 4 of the benzodiazepine ring system. Photoaddition of *trans*-β-methylstyrene yielded a mixture of *cis* (**12*c***) and *trans* (**12*t***) isomers in a ca. 1:1 ratio. The *trans* adduct **16*t*** was the major product formed in the photoreaction of *trans*-stilbene, while isosafrole yielded only the *trans* adduct **15**.[51]



Scheme 6

As would be expected, use of a higher PHT-H/NaOH ratio (1:1.5) and a 400-W medium-pressure mercury lamp resulted in increased photocycloaddition yields (90% for

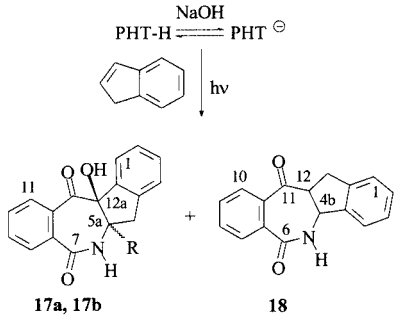
Table 1. Irradiation of PHT-H/NaOH in the presence of alkenylbenzenes

Alkenylbenzene	Alkene/PHT-H [mmol]	Irradiation time [h][a]	Conversion [%]	[2+2] Cycloadduct (yield [%])
Styrene	2.6	2	78	**11** (58)
trans-β-Methylstyrene	2	5	40	**12** (47)
α-Methylstyrene	5	1	91	**13** (41)
p-Methoxystyrene	2.2	2	74	**14** (41)
Isosafrole	2	5	28	**15** (51)
trans-Stilbene	1	4	20	**16** (78)

[a] All irradiations were carried out at a 3.4:1 PHT-H/NaOH ratio.

styrene, 72% for *trans*-β-methylstyrene and 68% for α-methylstyrene at 92%, 88% and 93% conversion, respectively).

An example of particular interest was the photocycloaddition of PHT-H to indene, a reaction that might provide a direct entry to the indeno[2,1-*c*][2]benzazepine skeleton present in members of the ribasine-type alkaloid family. Their synthesis by photocyclization of *N*-(2-indanyl)phthalimide or photocycloaddition of phthalimide and substituted phthalimides and indenes proved unsuccessful. However, irradiation of a solution of PHT-H/NaOH and indene (1:1.5:1.3 equiv. ratio) for 4 h (62% conversion) followed by chromatographic separation gave adduct **17a** as the major product, in 43% yield (Scheme 7).



Scheme 7

The spectroscopic properties of **17a** were consistent with those expected for a [2+2] photoadduct. However, its molecular composition of $C_{17}H_{13}NO_3$, consistent with a molecular ion peak at $m/z = 279$, suggested that it contained an additional oxygen atom. A lowfield quaternary carbon signal at $\delta = 93.8$ ppm and the ^{1}H NMR pattern (dd upon addition of D_2O) for the hydrogen atom α to the nitrogen atom suggested that the isolated product had a quaternary benzylic position vicinal to the ketone carbonyl group. Thus, the hydroxylated product **17a** was fully consistent with this data. A second product, diastereoisomer **17b** (10%), was also isolated. We believe that hydroxylation of the initial adduct took place during chromatographic separation. It should be noted that this position also contains hydroxy functionality in the ribasine alkaloids. A third adduct, **18** (7%), was also isolated, its regiochemistry inferred from the ^{1}H NMR splitting exhibited by 4b-H, which was coupled to the NH proton and to the bridged 11a-H atom. The value of the coupling constant $J_{4b,11a}$ indicated that **18** had a *trans* ring fusion stereochemistry. This is the first instance in which both regioisomeric adducts have been produced in the phthalimide anion photocycloaddition reactions.

Conclusion

The results presented above demonstrate that the phthalimide anion undergoes high-yielding photoaddition reactions with a wide variety of alkenes and that this process serves as a concise method for the synthesis of [2]benzazepine-1,5-diones. The efficiency of the reaction is independent of the ionization potential of the alkene, a likely result of the low reduction potential of the reactive PHT^- singlet excited state. The results of quenching of the fluorescence of the phthalimide anion by alkene can be used to design reaction conditions that optimize the photocycloaddition yields.

Experimental Section

General Remarks: Melting points were determined with a Gallenkamp instrument and are given uncorrected. IR spectra were recorded with a Perkin−Elmer 883 spectrophotometer and a Bruker FT-IR Equinox 55 spectrometer equipped with a Specac Golden Gate ATR accessory. Absorption spectra were recorded with an HP 8452A Diode Array Spectrophotometer. Emission spectra were obtained with a JASCO FP-750 Spectrofluorimeter interfaced to a Spectra Manager (v. 1.30.00) data station. Fluorescence quantum yields were determined by comparison with 0.1 M quinine sulfate in 0.05 M sulfuric acid as reference, by using the Demas method.[52] Fluorescence decay measurements were performed with an Aminco SLM 48000S spectrofluorimeter equipped with a 450-W xenon lamp, a Hamamatsu R928 photomultiplier tube detector and a Pockel cell electro-optic modulator. Fluorescence lifetime determinations were performed by use of multifrequency modulated excitation beams and a glycogen scattering solution as reference. Phase and modulation measurements used the "100-average" mode, in which each measurement was the average of 100 samplings, automatically conducted by the instrument circuitry over a period of approximately 25 s. Low-resolution MS (EI and CI) was recorded with an HP-MS 5988A spectrometer operating at 70 eV, and high-resolution MS was performed with a Kratos MS 50 TC mass spectrometer. NMR spectra were recorded with a Bruker WP-200 SY instrument, at 200 MHz for ^{1}H and 50.3 MHz for ^{13}C.

Chemical shifts are given relative to the residual signal of solvent, δ_H = 7.24 ppm and δ_C = 77.0 ppm for deuteriochloroform. TLC analyses were performed on silica gel 60 F 256 plates, and column chromatography was carried out on silica gel 60 (70−230 mesh). Organic solutions were dried with $MgSO_4$. Solutions were irradiated at room temperature in a 250-mL immersion well photoreactor (Pyrex) equipped with a 125-W medium-pressure mercury lamp (unless otherwise stated). A stream of nitrogen was passed through the medium during irradiation. Yields given are based on consumed phthalimide.

Irradiation of Sodium Phthalimide/Cyclohexene in Methanol: Sodium phthalimide (2 g, 11.8 mmol) was dissolved in MeOH (200 mL), a large excess of cyclohexene (12 mL) was added, and the clear solution was irradiated for 1 h. Most of the solvent was removed, and the crude reaction mixture was taken up in water (50 mL) and extracted with $CHCl_3$. The organic layer was dried, the solvent was removed, and the residue was column-chromatographed (silica gel; hexane/EtOAc from 2:1 to 1:1) to afford unchanged phthalimide (810 mg) and adduct **1*c*** (289 mg, 20%).

***cis*-3,4,4a,11a-Tetrahydro-1*H*-dibenzo[*b,e*]azepine-6,11(2*H*,5*H*)-dione (1*c*):** White crystals. M.p. 210−212 °C (EtOAc). IR (KBr): $\tilde{\nu}$ = 3188, 1656 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.92 (dd, *J* = 5.8, 2.8 Hz, 1 H, 10-H), 7.88−7.54 (m, 3 H, 7-H, 8-H, 9-H), 6.83 (br. d, *J* = 3.8 Hz, 1 H, NH), 4.25 (m, 1 H, 4a-H), 2.56 (ddd, *J* = 11.8, 4.0, 2.7 Hz, 1 H, 11a-H), 2.36−1.33 (m, 8 H, 4 × CH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 204.0 (C-11), 169.9 (C-6), 137.4 (C-10a), 131.8 (C-6a), 132.1, 131.9, 129.5, 128.0 (C-7, C-8, C-9, C-10), 55.8 (C-4a), 47.9 (C-11a), 29.4, 25.1, 22.6, 20.1 (CH_2) ppm. EIMS: *m*/*z* = 229 (27) $[M]^+$, 201 (19), 186 (11), 148 (100). $C_{14}H_{15}NO_2$ (229.28): calcd. C 73.34, H 6.59, N 6.11; found C 73.48, H 6.57, N 5.93.

Irradiation of Sodium Phthalimide/Cyclohexene in *tert*-Butyl Alcohol: The irradiation (1 h) and the workup were carried out as in methanol. On column chromatography of the reaction mixture, unchanged phthalimide was recovered (650 mg) together with the adduct **1*c*** (593 mg, 35%).

Irradiation of PHT-H/NaOH/Cyclohexene

At pH ≈ 10: An NaOH solution (1 M) was added to a solution of phthalimide (1 g, 6.8 mmol) and cyclohexene (5 mL, 75 mmol) in acetonitrile/water (7:1) until pH ≈ 10 was reached. The resulting homogeneous solution was irradiated for 30 min and neutralized with dilute HCl, and the solvent was removed. On column chromatography of the reaction mixture, unchanged phthalimide (92 mg, 9%) and the following four compounds were isolated: **1*c*** (228 mg, 17%), **1*t*** (924 mg, 67%), **2a** (69 mg, 5%) and **2b** (58 mg, 4%).

***trans*-3,4,4a,11a-Tetrahydro-1*H*-dibenzo[*b,e*]azepine-6,11(2*H*,5*H*)-dione (1*t*):** White crystals. M.p. 203−205 °C (EtOAc). IR (KBr): $\tilde{\nu}$ = 3189, 1655 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.91 (dd, *J* = 6.5, 2.1 Hz, 1 H, 10-H), 7.69−7.50 (m, 3 H, 7-H, 8-H, 9-H), 6.98 (br. d, *J* = 4.7 Hz, 1 H, NH), 3.48 (m, 1 H, 4a-H), 2.65 (dt, *J* = 11.8, 4.0 Hz, 1 H, 11a-H), 2.2−1.1 (m, 8 H, 4 × CH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 206.6 (C-11), 169.9 (C-6), 137.4 (C-10a), 131.8 (C-6a), 132.3, 131.1, 131.8, 128.1 (C-7, C-8, C-9, C-10), 60.2 (C-4a), 52.1 (C-11a), 30.6, 29.5, 24.8, 24.5 (CH_2) ppm. EIMS: *m*/*z* = 229 (52) $[M]^+$, 201 (23), 186 (16), 148 (100). $C_{14}H_{15}NO_2$ (229.28): calcd. C 73.34, H 6.59, N 6.11; found C 73.79, H 6.54, N 6.11.

3-(2-Cyclohexenyl)-2,3-dihydro-3-hydroxy-1*H*-isoindol-1-one (2a): White crystals. M.p.158−159 °C ($CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3380, 3191, 1680 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.80−7.45 (m, 4 H, Ar-H), 6.15 (s, 1 H, NH), 6.01 (m, 2 H, 2′-H, 3′-H), 3.00 (m, 1 H, 1′-H), 2.60 (s, 1 H, OH), 2.00−0.80 (m, 6 H, 3 × CH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 170.0 (C-1), 148.5 (C-3a), 131.0 (C-7a), 133.0, 131.9, 129.5, 125.0 (C-5, C-6, C-7, C-4), 123.5, 122.1 (C-2′, C-3′), 89.6 (C-3), 42.5 (C-1′), 24.5, 23.9, 21.0 (CH_2) ppm. EIMS: *m*/*z* = 229 (4) $[M]^+$, 212 (7), 148 (100). CIMS (CH_4): *m*/*z* = 230 (100) $[M + H]^+$, 213 (31), 212 (33). $C_{14}H_{15}NO_2$ (229.28): calcd. C 73.34, H 6.59, N 6.11; found C 73.25, H 6.83, N 5.95.

3-(2-Cyclohexenyl)-2,3-dihydro-3-hydroxy-1*H*-isoindol-1-one (2b): White crystals. M.p. 154−156 °C ($CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3376, 3198, 1678 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.75−7.40 (m, 4 H, Ar-H), 6.50 (s, 1 H, NH), 5.59−5.40 (m, 2 H, 2′-H, 3′-H), 2.90 (m, 1 H, 1′-H), 3.19 (s, 1H, OH), 2.10−0.90 (m, 6 H, 3 × CH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 169.3 (C-1), 147.9 (C-3a), 131.3 (C-7a), 132.1, 130.1, 129.0, 125.2 (C-5, C-6, C-7, C-4), 123.0, 122.5 (C-2′, C-3′), 89.5 (C-3), 43.5 (C-1′), 24.5, 23.5, 21.3 (CH_2) ppm. EIMS: *m*/*z* = 212 (3) $[M^+ - 17]$, 148 (100). CIMS (CH_4): *m*/*z* = 230 (100) $[M + H]^+$, 100], 213 (26), 212 (42). $C_{14}H_{15}NO_2$ (229.28): calcd. C 73.34, H 6.59, N 6.11; found C 73.28, H 6.31, N 5.96.

At [PHT-H]/[NaOH] = 1:0.3: A solution of phthalimide (1 g, 6.8 mmol), NaOH (2 mL of a 1 M solution) and cyclohexene (1 mL, 8.6 mmol) in 140 mL of acetonitrile and 20 mL of water was irradiated for 1/2 h. Workup of the reaction mixture was carried out as above and provided unchanged phthalimide (220 mg, 22%), **1*c*** (549 mg, 46%), **2a** + **2b** (137 mg, 12%) and **3** (297 mg, 25%).

***N*-Cyclohexylphthalimide (3):** White crystals. M.p. 169−171 °C (CH_3OH) (ref.[53] 168.5−171 °C).

Irradiation of PHT-H/NaOH with Other Alkenes: The homogeneous solution consisting of phthalimide (1 g, 6.8 mmol), NaOH (8 mL of a 1 M solution), 140 mL of acetonitrile, 20 mL of water and the alkene was irradiated for 30 min. Workup was as above, and chromatography gave the following results.

With Cyclopentene (56 mmol): Unchanged phthalimide (255 mg, 25%), **4*c*** (494 mg, 45%), **4*t*** (384 mg, 35%), **5a** (61 mg, 6%), **5b** (58 mg, 5%).

***cis*-1,2,3,3a,4,10a-Hexahydrocyclopenta[*c*][2]benzazepine-5,10-dione (4*c*):** White crystals. M.p. 210−211 °C (EtOAc) (ref.[25] 210−212 °C). IR (KBr): $\tilde{\nu}$ = 3248, 1697, 1650 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.90 (m, 1 H, 9-H), 7.69−7.35 (m, 3 H, 6-H, 7-H, 8-H), 6.65 (br. d, *J* = 2.6 Hz, 1 H, NH), 4.25 (m, 1 H, 3a-H), 3.12 (dt, *J* = 4.8, 9.3 Hz, 1 H, 10a-H), 2.40−1.70 (m, 6 H, 3 × CH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 204.0 (C-10), 171.1 (C-5), 139.7 (C-9a), 131.3 (C-5a), 131.9, 131.5, 129.6, 126.6 (C-6, C-7, C-8, C-9), 62.1 (C-3a), 53.6 (C-10a), 32.7, 24.1, 22.5 (CH_2) ppm. EIMS: *m*/*z* = 215 (7) $[M]^+$, 172 (35), 148 (100). CIMS (CH_4): *m*/*z* = 216 (100) $[M + H]^+$, 199 (50), 198 (46). $C_{13}H_{13}NO_2$ (215.25): calcd. C 72.53, H 6.09, N 6.51; found C 72.51, H 6.07, N 6.31.

***trans*-1,2,3,3a,4,10a-Hexahydrocyclopenta[*c*][2]benzazepine-5,10-dione (4*t*):** White crystals. M.p. 202−203 °C (EtOAc). IR (KBr): $\tilde{\nu}$ = 3250, 1696, 1650 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.10 (m, 2 H, 6-H, 9-H), 7.65 (m, 2 H, 7-H, 8-H), 6.89 (br. d, 1 H, NH), 3.90 (m, 1 H, 3a-H), 3.12 (m, 1 H, 10a-H-), 2.40−1.65 (m, 6 H, 3 × CH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 200.7 (C-10), 169.5 (C-5), 134.4 (C-9a), 131.5 (C-5a), 133.2, 131.6, 131.6, 129.3 (C-6 to C-9), 61.0 (C-3a), 53.9 (C-10a), 31.9, 26.6, 22.1 (CH_2) ppm. EIMS: *m*/*z* = 215 (10) $[M]^+$, 172 (47), 148 (100). *m*/*z* (CI, CH_4) 216 (100) $[M + H]^+$. $C_{13}H_{13}NO_2$ (215.25): calcd. C 72.53, H 6.09, N 6.51; found C 72.22, H 6.10, N 6.53.

3-(2-Cyclopentenyl)-2,3-dihydro-3-hydroxy-1*H*-isoindol-1-one (5a): White crystals. M.p. 158−159 °C ($CHCl_3$). IR (neat): $\tilde{\nu}$ = 3392,

3189, 1677 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.70−7.40 (m, 4 H, Ar-H), 6.35 (br. d, 1 H, NH), 6.05 (m, 2 H, 2′-H, 3′-H), 3.75 (s, 1H, OH), 3.55 (m, 1H, 1′-H), 2.40−1.00 (m, 4H, 2 × CH2) ppm. ^{13}C NMR ($CDCl_3$): δ = 169.4 (C-1), 148.1 (C-3a), 130.7 (C-7a), 135.5, 132.9, 129.5, 129.2 (C-4 to C-7), 123.4, 121.9 (C-2′, C-3′), 89.9 (C-3), 52.8 (C-1′), 32.3, 24.4 (CH_2) ppm. EIMS: *m/z* = 197 (1) [M^+ − 18], 151 (24), 130 (89), 148 (100). CIMS (CH_4): *m/z* = 216 (100) [M + H]$^+$, 199 (50), 198 (46). $C_{13}H_{13}NO_2$ (215.25): calcd. C 72.53, H 6.09, N 6.51; found C 72.24, H 6.04, N 6.31.

3-(2-Cyclopentenyl)-2,3-dihydro-3-hydroxy-1*H*-isoindol-1-one (5b): White crystals. M.p. 156−158 °C ($CHCl_3$). IR (neat): ṽ = 3396, 3191, 1676 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.60 (m, 4 H, Ar-H), 5.85 (m, 1 H, 2′-H), 5.50 (m, 1 H, 3′-H), 4.35 (s, 1 H, OH), 3.50 (m, 1 H, 1′-H), 2.35−1.50 (m, 4 H, 2 × CH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 169.3 (C-1), 147.3 (C-3a), 131.1 (C-7a), 134.8, 132.5, 129.5, 129.2 (C-4 to C-7), 123.3, 122.9 (C-2′, C-3′), 89.7 (C-3), 54.1 (C-1′), 32.1, 24.4 (CH_2) ppm. EIMS: *m/z* = 197 (2) [M^+ − 18], 151 (19), 130 (89), 148 (100). CIMS (CH_4): *m/z* = 216 (100) [M + H]$^+$, 199 (44), 198 (48). $C_{13}H_{13}NO_2$ (215.25): calcd. C 72.53, H 6.09, N 6.51; found C 72.25, H 6.01, N 6.32.

With Tetramethylethylene (17 mmol): Unchanged phthalimide (90 mg, 9%), **6** (1.10 g, 73%), **7** (195 mg, 12%).

3,4-Dihydro-3,3,4,4-tetramethyl-1*H*-2-benzazepine-1,5(2*H*)-dione (6): White crystals. M.p. 157−158 °C (EtOH) (ref.[44] 165 °C). IR (KBr): ṽ = 3216, 1648 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.12 (m, 1 H, 6-H), 7.90 (m, 1 H, 9-H), 7.60 (m, 2 H, 7-H, 8-H), 6.80 (br. d, 1 H, NH), 1.28 (s, 6 H, 2 × CH_3), 1.30 (s, 6 H, 2 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 204.8 (C-5), 168.5 (C-1), 135.5 (C-5a), 131.5 (C-9a), 132.4, 132.0, 130.8, 129.6 (C-6, C-7, C-8, C-9), 55.8 (C-3), 54.7 (C-4), 26.1, 22.2 (CH_3) ppm. EIMS: *m/z* = 174 (60), 159 (100). CIMS (CH_4): *m/z* = 232 (100) [M + H]$^+$. $C_{14}H_{17}NO_2$ (231.29): calcd. C 72.70, H 7.41, N 6.06; found C 72.69, H 7.41, N 6.15.

2,3-Dihydro-3-(2,3-dimethyl-2-butenyl)-3-hydroxy-1*H*-isoindol-1-one (7): White crystals. M.p. 155−156 °C (CH_2Cl_2). IR (KBr): ṽ = 3339, 3224, 1677 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.60−7.30 (m, 4 H, Ar-H), 6.95 (br. d, 1 H, NH), 3.90 (s, 1 H, OH), 2.90 (d, *J* = 13.9 Hz, 1 H, 1′-H), 2.65 (d, *J* = 13.9 Hz, 1 H, 1′-H), 1.70 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 168.8 (C-1), 149.1 (C-3a), 130.4 (C-7a), 132.5, 129.4, 123.3 122.2 (C-4 to C-7), 130.2, 122.5 (C-2′, C-3′), 88.6 (C-3), 43.1 (C-1′), 21.2, 20.8, 20.6 (CH_3) ppm. EIMS: *m/z* = 213 (7) [M^+ − 18], 185 (15), 148 (100). CIMS (CH_4): *m/z* = 232 (100) [M + H]$^+$, 214 (38). $C_{14}H_{17}NO_2$ (231.29): calcd. C 72.70, H 7.41, N 6.06; found C 72.94, H 7.35, N 5.98.

With 2-Ethyl-1-butene (16.4 mmol): Unchanged phthalimide (151 mg, 15%), **8** (790 mg, 59%), **9** (50 mg, 4%), **10** (a 1:1 mixture of the *cis* and *trans* isomers; 100 mg, 8%).

4,4-Diethyl-3,4-dihydro-1*H*-2-benzazepine-1,5(2*H*)-dione (8): White crystals. M.p. 135−136 °C (EtOAc/hexane, 1:1). IR (KBr): ṽ = 3280, 1658, 1632 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.38 (br. t, *J* = 6.0 Hz, 1 H, NH), 7.87 (m, 1 H, 6-H), 7.55 (m, 3 H, Ar-H), 3.37 (d, *J* = 6.0 Hz, 2 H, 3-H), 1.67 (m, 4 H, 2 × CH_2), 0.89 (t, *J* = 7.5 Hz, 6 H, 2 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 208.2 (C-5), 171.3 (C-1), 138.4 (C-5a), 131.0 (C-9a), 131.8, 131.6, 129.0, 127.7 (C-6, C-7, C-8, C-9), 58.3 (C-4), 45.1 (C-3), 25.6 (CH_2), 7.8 (CH_3) ppm. EIMS: *m/z* = 231 (2) [M]$^+$, 202 (27), 173 (43), 148 (100). CIMS (CH_4): *m/z* = 232 (100) [M + H]$^+$, 214 (31), 203 (24). $C_{14}H_{17}NO_2$ (231.29): calcd. C 72.70, H 7.41, N 6.06; found C 72.84, H 7.81, N 6.11.

4-Ethyl-3,4-dihydro-1*H*-2-benzazepine-1,5(2*H*)-dione (9): White crystals. M.p. 109−110 °C (EtOAc). IR (KBr): ṽ = 3208, 1686, 1657 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.15 (br. t, *J* = 5.6 Hz, 1 H, NH), 7.90 (m, 1 H, 6-H), 7.60 (m, 3 H, Ar-H), 3.45 (m, 2 H, 3-H), 2.81 (m, 1 H, 4-H), 1.75 (m, 2 H, CH_2), 1.00 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 206.0 (C-5), 171.5 (C-1), 137.1 (C-5a), 131.5 (C-9a), 132.2, 131.9, 129.5, 128.0 (C-6, C-7, C-8, C-9), 56.8 (C-4), 41.2 (C-3), 23.1 (CH_2), 11.3 (CH_3) ppm. EIMS: *m/z* = 203 (1) [M]$^+$, 174 (3), 148 (100). CIMS (CH_4): *m/z* = 204 (100) [M + H]$^+$, 175 (21). $C_{12}H_{13}NO_2$ (213.24): calcd. C 70.92, H 6.45, N 6.89; found C 71.18, H 6.10, N 6.36.

***cis*- and *trans*-2a-Ethyl-1,2,2a,3,4,9b-hexahydro-9b-hydroxy-5*H*-cyclobuta[*d*][2]benzazepin-5-one (10):** White crystals. M.p. 180−184 °C (EtOAc). IR (KBr): ṽ = 3311, 1636 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.85−7.36 (m, 8 H, Ar-H), 7.25 (br. t, *J* = 5.7 Hz, 1 H, NH), 6.84 (br. t, *J* = 5.7 Hz, 1 H, NH), 3.10−1.20 (m, 16 H, 8 × CH_2), 0.94 (t, *J* = 7.5 Hz, 3 H, CH_3), 0.73 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 173.8, 172.8 (C-5), 142.9, 142.2 (C-9a), 132.8, 131.2 (C-5a), 131.1, 130.7, 130.4, 129.6, 128.2, 127.1, 126.2, 124.2 (C-6, C-7, C-8, C-9), 78.6, 78.3 (C-9b), 56.6, 53.5 (C-2a), 45.9, 45.6 (C-3), 35.5, 30.7, 25.6, 25.5, 21.5, 20.9 (CH_2), 7.9, 7.4 (CH_3) ppm. EIMS: *m/z* = 231 (5) [M]$^+$, 203 (15), 174 (100), 160 (25), 130 (29). $C_{14}H_{17}NO_2$ (231.29): calcd. C 72.70, H 7.41, N 6.06; found C 72.38, H 7.41, N 6.04.

Improved Formation of Benzazepinediones 1, 4 and 6: Reactions were conducted with phthalimide (1 g, 6.8 mmol), NaOH (10.2 mL of a 1 M solution) [phthalimide/sodium hydroxide in 1:1.5 ratio], 140 mL of acetonitrile, 20 mL of water and excess alkene. After 25 min of irradiation, most of the phthalimide had reacted (TLC). The solvent and excess alkenes were removed under vacuum (the reaction mixtures with cyclohexene and cyclopentene were stirred in the dark for 30 min to allow equilibration of the benzazepinedione isomers before solvent removal). The residues were taken up in chloroform, the solutions were washed with water, and the organic layer was concentrated to dryness to give solids that were crystallized directly. With cyclohexene (11 equiv. excess): 1.25 g of **1*t*** (89% at 90% conversion).With cyclopentene (8 equiv. excess): 1.01 g of **4*t*** (86% at 80% conversion).With tetramethylethylene (2.5 equiv. excess): 1.12 g of **6** (84% at 85% conversion).

Irradiation of PHT-H/NaOH/Alkenylbenzenes: The homogeneous solution consisting of phthalimide (1 g, 6.8 mmol), NaOH (2 mL of a 1 M solution), 140 mL of acetonitrile, 25 mL of water and the alkenylbenzene was irradiated for the stated time. The reaction medium was neutralised (dilute HCl) and most of the acetonitrile was removed under vacuum. The residue was supplemented with 20 mL of a 1 M NaOH solution and H_2O (20 mL), and extracted with CH_2Cl_2. The organic layer was dried and concentrated in vacuo. The residue was applied to a column chromatography (silica gel) rinsing with hexane to remove excess of alkenylbenzene, adducts being eluted with hexane/EtOAc (from 2:1 to 1:1). The aqueous phase was acidified and extracted with Et_2O, removal of the solvent leaving a fraction consisting of unchanged phthalimide.

With Styrene (17.4 mmol, 2 h): Unchanged phthalimide (230 mg, 23%), **11** (770 mg, 58%).

3,4-Dihydro-4-phenyl-1*H*-2-benzazepine-1,5(2*H*)-dione (11): White crystals. M.p. 140−142°C ($CHCl_3$/hexane) [ref.[35] 127−130 °C (hexane)]. IR (neat): ṽ = 3187, 1658, 1597 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.97 (dd, *J* = 2.0, 6.6 Hz, 1 H, 6-H), 7.75−7.12 (m, 8 H, Ar-H), 4.18 (dd, *J* = 4.1, 9.9 Hz, 1 H, 4-H), 3.85 (ddd, *J* = 6.0, 9.9, 15.0 Hz, 1 H, 3ax-H), 3.65 (ddd, *J* = 6.0, 4.1, 15.0 Hz, 1 H, 3eq-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 204.2 (C-5), 171.2 (C-1),

137.4 (C-1′), 137.2 (C-5a), 132.5, 132.2, 129.8, 128.5 (C-6, C-7, C-8, C-9), 131.6 (C-9a), 129.1 (C-3′, C-5′), 128.0 (C-2′, C-6′), 127.8 (C-4′), 61.9 (C-3), 44.2 (C-4) ppm. EIMS: *m*/*z* = 251 (1) $[M]^+$, 222 (15), 165 (11), 104 (100). CIMS (CH_4): *m*/*z* = 252 (100) $[M + H]^+$, 223 (25). $C_{16}H_{13}NO_2$ (251.28): calcd. C 76.48, H 5.21, N 5.57; found C 76.70, H 5.17, N 5.50.

With *trans*-β-Methylstyrene (13.6 mmol, 5 h): Unchanged phthalimide (600 mg, 40%), **12*c*** (175 mg, 24%), **12*t*** (164 mg, 23%).

***cis*-3,4-Dihydro-3-methyl-4-phenyl-1*H*-2-benzazepine-1,5(2*H*)-dione (12*c*):** White crystals. M.p. 152−154 °C (EtOAc). IR (neat): $\tilde{\nu}$ = 3178, 1657, 1599 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.02 (m, 1 H, 6-H), 7.80−7.10 (m, 8 H, Ar-H), 5.75 (br. d, *J* = 6.0 Hz, 1 H, NH), 4.52 (dq, *J* = 6.0, 6.8, 2.6 Hz, 1 H, 3-H), 3.86 (d, *J* = 2.6 Hz, 1 H, 4-H), 1.12 (d, *J* = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 203.9 (C-5), 169.1 (C-1), 136.5 (C-5a), 135.1 (C-1′), 132.5, 131.7, 129.6, 128.4 (C-6, C-7, C-8,C-9), 127.5 (C-4′), 131.9 (C-9a), 130.3, 128.3 (C-2′, C-6′, C-3′, C-5′), 66.4 (C-3), 48.0 (C-4), 17.9 (CH_3) ppm. EIMS: *m*/*z* = 265 (1) $[M]^+$, 222 (100), 165 (25), 118 (42). CIMS (CH_4): *m*/*z* = 266 (100) $[M + H]^+$, 223 (20). $C_{17}H_{15}NO_2$ (265.31): calcd. C 76.96, H 5.70, N 5.28; found C 76.76, H 5.76, N 5.19.

***trans*-3,4-Dihydro-3-methyl-4-phenyl-1*H*-2-benzazepine-1,5(2*H*)-dione (12*t*):** White crystals. M.p. 207−208 °C (EtOAc). IR (neat): $\tilde{\nu}$ = 3180, 1665, 1596 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.00 (m, 1 H, 6-H), 7.80−7.05 (m, 8 H, Ar-H), 6.11 (br. d, *J* = 4.3 Hz, 1 H, NH), 4.22 (ddd, *J* = 4.3, 6.5, 11.4 Hz, 1 H, 3-H), 3.85 (d, *J* = 11.4 Hz, 1 H, 4-H), 1.15 (d, *J* = 6.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 204.5 (C-5), 170.4 (C-1), 137.8 (C-1′), 137.2 (C-5a), 132.2, 131.9, 129.3, 128.1 (C-6, C-7, C-8,C-9), 127.9 (C-4′), 131.6 (C-9a), 129.2, 127.8 (C-2′, C-6′, C-3′, C-5′), 69.5 (C-3), 50.2 (C-4), 17.7 (CH_3) ppm. EIMS: *m*/*z* = 265 (1) $[M]^+$, 222 (64), 165 (20), 118 (100). CIMS (CH_4): *m*/*z* = 266 (100) $[M + H]^+$, 223 (9). $C_{17}H_{15}NO_2$ (265.31): calcd. C 76.96, H 5.70, N 5.28; found C 76.65, H 5.74, N 5.18.

With α-Methylstyrene (34 mmol, 1 h): Unchanged phthalimide (90 mg, 9%), **13** (668 mg, 41%).

3,4-Dihydro-4-methyl-4-phenyl-1*H*-2-benzazepine-1,5(2*H*)-dione (13): White crystals. M.p. 149−150 °C (EtOAc); [ref.[35], 137.5−138 °C (hexane)]. IR (KBr): $\tilde{\nu}$ = 3205, 1683, 1669 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.88 (dd, *J* = 7.4, 2.0 Hz, 1 H, 6-H), 7.73 (br. t, 1 H, NH), 7.63 (dt, *J* = 7.4, 2.0 Hz, 1 H, 7-H), 7.56 (dt, *J* = 7.4, 2.0 Hz, 1 H, 8-H), 7.45 (dd, *J* = 7.4, 2.0 Hz, 1 H, 9-H), 7.36−7.17 (m, 5 H, Ar-H), 3.89 (dd, *J* = 16.0, 6.0 Hz, 1 H, 3-H), 3.48 (dd, *J* = 16.0, 6.0 Hz, 1 H, 3-H), 1.70 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 207.1 (C-5), 171.2 (C-1), 140.8 (C-1′), 137.9 (C-5a), 132.1, 132.0 129.3 128.6 (C-6, C-7, C-8, C-9), 131.0 (C-9a), 128.8 (C-3′, C-5′), 127.5 (C-4′), 126.3 (C-2′, C-6′), 59.4 (C-3), 49.9 (C-4), 21.8 (CH_3) ppm. EIMS: *m*/*z* = 265 (1) $[M]^+$, 236 (10), 118 (100). CIMS (CH_4): *m*/*z* = 266 (100) $[M + H]^+$, 237 (31). $C_{17}H_{15}NO_2$ (265.31): calcd. C 76.96, H 5.70, N 5.28; found C 76.87, H 5.69, N 5.19.

With *p*-Methoxystyrene (14.9 mmol, 2 h): Unchanged phthalimide (260 mg, 26%), **14** (585 mg, 41%).

3,4-Dihydro-4-(4-methoxyphenyl)-1*H*-2-benzazepine-1,5(2*H*)-dione (14): White crystals. M.p. 106−107 °C (EtOAc). IR (neat): $\tilde{\nu}$ = 3191, 1656, 1596 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.95 (d, *J* = 7.3 Hz, 1 H, 6-H), 7.73−7.52 (m, 3 H, Ar-H), 7.05 (d, *J* = 8.7 Hz, 2 H, 2′-H, 6′-H), 6.86 (d, *J* = 8.7 Hz, 2 H, 5′-H, 3′-H), 4.11 (dd, *J* = 4.0, 9.9 Hz, 1 H, 4-H), 3.78 (s, 3 H, OCH_3), 3.89−3.59 (m, 2 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 204.7 (C-5), 171.3 (C-1), 158.9 (C-4′), 137.1 (C-5a), 132.4, 132.1, 129.6, 128.3 (C-6, C-7, C-8, C-9), 131.5 (C-9a), 129.4 (C-1′), 128.9 (C-2′, C-6′), 114.3 (C-3′, C-5′), 61.0 (C-3), 55.1 (OCH_3), 44.1 (C-4) ppm. EIMS: *m*/*z* = 281 (1) $[M]^+$, 252 (32), 237 (9), 134 (100). CIMS (CH_4): *m*/*z* = 282 (100) $[M + H]^+$, 253 (13). $C_{17}H_{15}NO_3$ (281.31): calcd. C 72.58, H 5.37, N 4.98; found C 72.23, H 5.40, N 4.82.

With Isosafrole (13.6 mmol, 5 h): Unchanged phthalimide (720 mg, 72%), **15** (300 mg, 51%).

***trans*-4-(1,3-Benzodioxol-5-yl)-3,4-dihydro-1*H*-2-benzazepine-1,5(2*H*)-dione (15):** White crystals. M.p. 208−209 °C (EtOAc). IR (neat): $\tilde{\nu}$ = 3189, 1661, 1597 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.94 (dd, *J* = 1.8, 7.1 Hz, 1 H, 6-H), 7.72−7.58 (m, 2 H, 7-H, 8-H), 7.35 (dd, *J* = 1.8, 7.1 Hz, 1 H, 9-H), 6.77−6.54 (m, 3 H, Ar-H), 6.66 (br. s, 1 H, NH), 5.95 (s, 2 H, OCH_2O), 4.08 (m, 1 H, 3-H), 3.75 (d, *J* = 11.4 Hz, 1 H, 4-H), 1.17 (d, *J* = 6.7 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 204.4 (C-5), 170.5 (C-1), 148.2, 147.3 (C-3a′, C-7a′), 137.8 (C-5a), 131.4 (C-9a), 130.9 (C-5′), 132.4, 132.1, 130.8, 129.4 (C-6, C-7, C-8, C-9), 121.3 (C-6′), 108.9, 107.9 (C-4′, C-7′), 101.2 (C-2′), 68.9 (C-3), 50.3 (C-4), 17.8 (CH_3) ppm. EIMS: *m*/*z* = 309 (2) $[M]^+$, 266 (100), 162 (29), 152 (17). CIMS (CH_4): *m*/*z* = 310 (100) $[M + H]^+$, 267 (10). $C_{18}H_{15}NO_4$ (309.32): calcd. C 69.88, H 4.89, N 4.48; found C 69.47, H 4.93, N 4.44.

With *trans*-Stilbene (6.8 mmol, 4 h): Unchanged phthalimide (800 mg, 80%), **16*c*** (44 mg, 10%), **16*t*** (288 mg, 68%).

***cis*-3,4-Dihydro-3,4-diphenyl-1*H*-2-benzazepine-1,5(2*H*)-dione (16*c*):** Syrup. IR (KBr): $\tilde{\nu}$ = 3207, 1657, 1596 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.10−6.60 (m, 14 H, Ar-H), 6.40 (br. d, *J* = 6.5 Hz, 1 H, NH), 5.56 (dd, *J* = 6.5, 2.5 Hz, 1 H, H-3), 4.09 (d, *J* = 2.5 Hz, 1 H, H-4) ppm. ^{13}C NMR ($CDCl_3$): δ = 203.0 (C-5), 168.8 (C-1), 136.5, 136.4, 134.6, 133.2, 132.4, 131.0, 130.4, 129.2, 128.7, 128.4, 128.3, 127.6, 126.6, (aromatics), 67.8 (C-3), 57.6 (C-4) ppm. EIMS: *m*/*z* = 222 (100), 179 (25), 165 (25). CIMS (CH_4): *m*/*z* = 328 (100) $[M + H]^+$, 222 (11). $C_{22}H_{17}NO_2$ (327.38): calcd. C 80.70, H 5.24, N 4.28; found C 80.37, H 5.09, N 4.32.

***trans*-3,4-Dihydro-3,4-diphenyl-1*H*-2-benzazepine-1,5(2*H*)-dione (16t):** White crystals. M.p. 203−204 °C (EtOAc). IR (neat): $\tilde{\nu}$ = 3185, 1663, 1595 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.10−6.90 (m, 14 H, Ar-H), 6.30 (br. d, *J* = 4.6 Hz, 1 H, NH), 5.56 (dd, *J* = 11.7, 4.6 Hz, 1 H, 3-H), 4.09 (d, *J* = 11.7 Hz, 1 H, 4-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 204.0 (C-5), 169.5 (C-1), 137.8, 136.6, 136.3, 132.4, 132.1, 131.2, 129.7, 128.8, 128.7, 128.5, 128.2, 127.8, 127.6, 127.2 (aromatics), 68.7 (C-3), 59.5 (C-4) ppm. EIMS: *m*/*z* = 222 (100), 179 (10), 165 (21). CIMS (CH_4): *m*/*z* = 328 (100) $[M + H]^+$, 222 (14). $C_{22}H_{17}NO_2$ (327.38): calcd. C 80.70, H 5.24, N 4.28; found C 80.32, H 5.07, N 4.23.

Improved Formation of Benzazepinediones 14, 15 and 16: A homogeneous solution of phthalimide (1 g, 6.8 mmol), NaOH (10.2 mL of a 1 M solution) [phthalimide/sodium hydroxide in a 1:1.5 ratio], 140 mL of acetonitrile, 20 mL of water and excess alkenylbenzene, was irradiated (for the stated time) with a 400-W medium-pressure mercury lamp with Pyrex-filtered light until most of the phthalimide had reacted (TLC). The solvent and excess alkene were removed under vacuum, the residue was taken up in chloroform, the solution was washed with water, and the organic layer was concentrated to dryness to give a solid that was crystallized directly. With styrene (2.5 equiv. excess): 1.37 g of **11** (89% at 90% conversion). With *trans*-β-methylstyrene (2 equiv. excess): 1.24 g of **12** (86% at 80% conversion). With α-methylstyrene (2.5 equiv. excess): 1.29 g of **13** (84% at 85% conversion).

Irradiation of PHT-H/NaOH/Indene: A solution of phthalimide (1 g, 6.8 mmol), NaOH (10 mL of a 1 M solution) and indene (1 mL, 8.6 mmol) was irradiated for 4 h under a nitrogen stream. The reaction medium was neutralized (HCl), the solvent was removed, and the residue was column-chromatographed (silica gel; hexane/EtAcO, 2:1). Three main fractions were collected; the first one was unchanged PHT-H (400 mg, 2.6 mmol), followed by the diastereomeric adducts **17a** (480 mg, 43%) and **17b** (113 mg, 10%), and **18** (71 mg, 7%).

5,5a,6,12a-Tetrahydro-12a-hydroxyindeno[2,1-*c*][2]benzazepine-7,12-dione (17a): White crystals. M.p. 240−242 °C (EtOAc). IR (neat): $\tilde{\nu}$ = 3315, 3283, 1664, 1600 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.23 (m, 2 H, 8-H, 11-H), 7.60−7.00 (m, 6 H, Ar-H), 6.90 (br. d, *J* = 5.0 Hz, 1 H, NH), 4.49 (s, 1 H, OH), 4.20 (ddd, *J* = 5.0, 5.3, 11.4 Hz, 1 H, 5a-H), 3.35 (dd, *J* = 17.0, 5.3 Hz, 1 H, 5eq-H), 2.90 (dd, *J* = 17.0, 11.4 Hz, 1 H, 5ax-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 196.3 (C-12), 164.8 (C-7), 140.4, 135.8 130.1 (C-5a, C-9a, C-4a, C-11b), 134.8, 132.9, 129.4, 128.7, 128.3, 128.0, 127.5, 125.6 (C-1, C-2, C-3, C-4, C-8, C-9, C-10, C-11), 74.7 (C-12a), 55.8 (C-5a), 34.7 (C-5) ppm. EIMS: *m*/*z* = 279 (18) $[M]^+$, 262 (19), 234 (9), 118 (100). CIMS (CH_4): *m*/*z* = 280 (100) $[M + H]^+$, 262 (74). $C_{17}H_{13}NO_3$ (279.30): calcd. C 73.11, H 4.69, N 5.02; found C 73.20, H 4.61, N 5.12.

5,5a,6,12a-Tetrahydro-12a-hydroxyindeno[2,1-*c*][2]benzazepine-7,12-dione (17b): White crystals. M.p. 239−240 °C (EtOAc). IR (neat): $\tilde{\nu}$ = 3299, 3262, 1633, 1594 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 7.94 (dd, *J* = 7.0, 1.0 Hz, 1 H, 11-H), 7.60−6.90 (m, 7 H, Ar-H), 6.64 (br. d, *J* = 7.4 Hz, 1 H, NH), 4.90 (s, 1 H, OH), 4.38 (ddd, *J* = 7.4, 9.5, 9.8 Hz, 1 H, 5a-H), 3.37 (dd, *J* = 16.4, 9.8 Hz, 1 H, 5eq-H), 2.70 (dd, *J* = 16.4, 9.5 Hz, 1 H, 5ax-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 202.7 (C-12), 170.1 (C-7), 140.6 (C-4a, C-12b), 140.1 (C-11a), 136.2 (C-7a), 132.1 (C-9), 131.8 (C-10), 129.7, 129.2, 128.3, 127.6, 125.0, 123.9 (C-1, C-2, C-3, C-4, C-8, C-11), 93.8 (C-12a), 61.3 (C-5a), 38.3 (C-5) ppm. EIMS: *m*/*z* = 279 (3) $[M]^+$, 262 (6), 234 (3), 132 (100), 118 (74). CIMS (CH_4): *m*/*z* = 280 (100) $[M + H]^+$, 262 (69). $C_{17}H_{13}NO_3$ (279.30): calcd. C 73.11, H 4.69, N 5.02; found C 73.28, H 4.58, N 5.14.

4b,5,11a,12-Tetrahydroindeno[1,2-*c*][2]benzazepine-6,11-dione (18): White crystals. M.p. 237−239 °C (EtOAc). IR (neat): $\tilde{\nu}$ = 3161, 1648, 1591 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 8.25 (dd, *J* = 2.0, 7.4 Hz, 1 H, 10-H), 8.18 (dd, *J* = 1.8, 7.4 Hz, 1 H, 7-H), 7.4 (m, 6 H, Ar-H), 6.78 (br. d, *J* = 5.0 Hz, 1 H, NH), 5.20 (dd, *J* = 10.0, 5.0 Hz, 1 H, 4b-H), 3.65 (ddd, *J* = 10.2, 10.0, 8.6 Hz, 1 H, 11a-H), 3.45 (dd, *J* = 16.2, 8.6 Hz, 1 H, 12-H), 3.25 (dd, *J* = 16.2, 10.2 Hz, 1 H, 12-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 198.6 (C-11), 169.7 (C-6), 140.9 (C-12a, C-4a), 138.6 (C-10a), 134.0 (C-6a), 133.7 (C-8), 132.3 (C-9), 131.8, 129.3, 129.1, 127.6, 125.5, 122.6 (C-1, C-2, C-3, C-4, C-7, C-10), 62.8 (C-4b), 57.2 (C-11a), 32.3 (C-12) ppm. EIMS: *m*/*z* = 263 (13) $[M]^+$, 246 (100), 148 (13). CIMS (CH_4): *m*/*z* = 264 (100) $[M + H]^+$, 247 (10). HRMS for $C_{17}H_{13}NO_2$ $[M^+]$: calcd. 263.0946; found 263.0941; for $C_{17}H_{12}NO$ $[M^+ - 17]$: calcd. 246.0919; found 246.0920. $C_{17}H_{13}NO_2$ (263.31): calcd. C 77.54, H 4.98, N 5.32; found C 77.08, H 5.06, N 5.34.

Acknowledgments

The authors wish to acknowledge financial support from the Spanish DGES (project PB97-1077). Thanks are also due to Prof. Domingo Domínguez (Universidad de Santiago de Compostela, Spain) for the NOE experiments and helpful discussions, and to Prof. Francisco García Sánchez (Dept. Analytical Chemistry, Universidad de Málaga) for access to the equipment used to measure the fluorescence lifetimes.

[1] L. Ollero, L. Castedo, D. Domínguez, *Tetrahedron* **1999**, *55*, 4445−4456.
[2] S. F. Martin, in *The Alkaloids, Chemistry and Pharmacology* (Ed.: A. Brossi), Pergamon Press, New York, **1988**, vol. 30, pp. 251−376.
[3] L. J. Scott, K. L. Goa, *Drugs* **2000**, *60*, 1095−1122.
[4] W. Xia, S. Spector, L. Hardy, S. Zhao, A. Saluk, L. Alemane, N. Spector, *Proc. Natl. Acad. Sci. USA* **2000**, *97*, 7494−7499.
[5] J. R. Casimir, D. Tourwé, K. Iterbeke, G. Guichard, J-P. Briand, *J. Org. Chem.* **2000**, *65*, 6487−6492.
[6] E. J. Trybulski, R. I. Fryer, E. Reeder, S. Vitone, L. Todaro, *J. Org. Chem.* **1986**, *51*, 2191−2202.
[7] C. A. Busacca, R. E. Johnson, *Tetrahedron Lett.* **1992**, *33*, 165−168.
[8] S. Kasparek, *Adv. Heterocycl. Chem.* **1974**, *17*, 45−98.
[9] R. K. Smalley, in *Comprehensive Heterocyclic Chemistry* (Eds.: A. R. Katritzky, C. W. Rees), Pergamon Press, Oxford, **1984**, vol. 5, chapter 5.16, pp. 491−546.
[10] J. C. Martins, K. Van Rompaey, G. Wittmann, C. Tömböly, G. Tóth, N. De Kimpe, D. Tourwé, *J. Org. Chem.* **2001**, *66*, 2884−2886.
[11] A. García, S. Paz, D. Domínguez, *Tetrahedron Lett.* **2001**, *42*, 665−667.
[12] G. H. Merriman, D. M. Fink, B. S. Fred, B. E. Kurys, S. Pavlek, J. Varriano, E. F. Paulus, *Synlett* **2000**, 137−139.
[13] V. V. Kouznetsov, A. Palma, A. E. Aliev, *An. Quím. Int. Ed.* **1998**, *94*, 132−135.
[14] A. Arany, P. W. Groundwater, M. Nyerges, *Tetrahedron Lett.* **1998**, *39*, 3267−3268.
[15] C. Andrés, J. P. Duque-Soladana, J. M. Iglesias, R. Pedrosa, *Synlett* **1997**, 1391−1392.
[16] Y. Nagao, I-Y. Jeong, W. S. Lee, *Tetrahedron Lett.* **1996**, *37*, 393−396.
[17] [17a] F. D. Lewis, G. D. Reddy, B. E. Cohen, *Tetrahedron Lett.* **1994**, *35*, 535−538. [17b] F. D. Lewis, G. D. Reddy, *Tetrahedron Lett.* **1990**, *31*, 5293−5296.
[18] Y. Kanaoka, *Acc. Chem. Res.* **1978**, *11*, 407−413.
[19] P. H. Mazzocchi, in *Organic Photochemistry* (Ed.: A. Padwa), Marcel Dekker, New York, **1981**, vol. 5, pp. 421−471.
[20] J. D. Coyle, in *Synthetic Organic Photochemistry* (Ed.: W. M. Horspool), Plenum Press, New York, **1984**, pp. 259−283.
[21] H. Mauder, A. G. Griesbeck, in *CRC Handbook of Organic Photochemistry and Photobiology* (Eds: W. M. Horspool, P-S. Song), CRC Press, Boca Raton, **1995**, pp. 513−521.
[22] [22a] A. G. Griesbeck, *Chimia* **1998**, *52*, 272−283. [22b] A. G. Griesbeck, W. Kramer, M. Oelgenmoller, *Synlett* **1999**, 1169−1178.
[23] U. C. Yoon, P. S. Mariano, *Acc. Chem. Res.* **2001**, *34*, 523−533.
[24] Y. Kanaoka, Y. Migita, K. Koyama, Y. Sato, H. Nakai, T. Mizoguchi, *Tetrahedron Lett.* **1973**, *14*, 1193−1196.
[25] Y. Kanaoka, K. Koyama, J. L. Flippen, I. L. Karle, B. Witkop, *J. Am. Chem. Soc.* **1974**, *96*, 4719−4721.
[26] Y. J. Lee, R. Ling, P. S. Mariano, U. C. Yoon, D. U. Kim, S. W. Oh, *J. Org. Chem.* **1996**, *61*, 3304−3314.
[27] A. G. Griesbeck, J. Hirt, W. Kramer, P. Dallakian, *Tetrahedron* **1998**, *54*, 3169−3180.
[28] A. G. Griesbeck, H. Mauder, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 73−75.
[29] A. G. Griesbeck, A. Henz, W. Kramer, P. Wamser, K. Peters, E-M. Peters, *Tetrahedron Lett.* **1998**, *39*, 1549−1552.
[30] A. G. Griesbeck, A. Henz, J. Hirt, V. Ptatschek, T. Engel, D. Löffler, F. W. Schneider, *Tetrahedron* **1994**, *50*, 701−714.
[31] M. R. Paleo, D. Domínguez, L. Castedo, *Tetrahedron* **1994**, *50*, 3627−3638.
[32] A. G. Griesbeck, A. Henz, W. Kramer, J. Lex, F. Nerowski, M. Oelgemoller, K. Peters, E-M. Peters, *Helv. Chim. Acta* **1997**, *80*, 912−933.

[33] [33a] P. H. Mazzocchi, M. J. Bowen, N. K. Narain, *J. Am. Chem. Soc.* **1977**, *99*, 7063−7064. [33b] P. H. Mazzocchi, S. Minamikawa, M. Bowen, *J. Org. Chem.* **1978**, *43*, 3079−3080. [33c] P. H. Mazzocchi, S. Minamikawa, P. Wilson, *J. Org. Chem.* **1979**, *44*, 1186−1188. [33d] P. H. Mazzocchi, F. Khachik, P. Wilson, *J. Am. Chem. Soc.* **1981**, *103*, 6498−6499. [33e] P. H. Mazzocchi, S. Minamikawa, P. Wilson, M. J. Bowen, N. K Narian, *J. Org. Chem.* **1981**, *46*, 4846−4851. [33f] P. H. Mazzocchi, P. Wilson, F. Khachick, L. Klingler, S. Minamikawa, *J. Org. Chem.* **1983**, *48*, 2981−2989.

[34] [34a] P. H. Mazzocchi, S. Minamikawa, P. Wilson, *J. Org. Chem.* **1985**, *50*, 2681−2684. [34b] P. H. Mazzocchi, S. Minamikawa, P. Wilson, *Tetrahedron Lett.* **1978**, *19*, 4361−4364. [34c] P. H. Mazzocchi, L. Klingler, *J. Am. Chem. Soc.* **1984**, *106*, 7567−7572.

[35] [35a] K. Maruyama, Y. Kubo, *J. Org. Chem.* **1985**, *50*, 1426−1435. [35b] K. Maruyama, Y. Kubo, *Chem. Lett.* **1978**, 851−854. [35c] H. Hayashi, S. Nagakura, Y. Kubo, K. Maruyama, *Chem. Phys. Lett.* **1980**, *72*, 291−294.

[36] W. Schwack, *Tetrahedron Lett.* **1987**, *28*, 1869−1872.

[37] R. Suau, R. García-Segura, F. Sosa-Olaya, *Tetrahedron Lett.* **1989**, *30*, 3225−3228.

[38] Y. Kubo, E. Taniguchi, T. Araki, *Heterocycles* **1989**, *29*, 1857−1860.

[39] M. Frecero, E. Fasani, A. Albini, *J. Org. Chem.* **1993**, *58*, 1740−1745.

[40] R. Suau, R. García-Segura, *Tetrahedron Lett.* **1988**, *29*, 1071−1074.

[41] The photochemistry of phthalimide anion with alcohols and other hydrogen donors will be reported elsewhere.

[42] This type of allylic adducts is the only product formed upon irradiation of *N*-methylphthalimide and cyclohexene in acetonitrile: Y. Kanaoka, Y. Hatanaka, *Chem. Pharm. Bull.* **1974**, *22*, 2205−2206.

[43] R. Suau, R. García-Segura, C. Sánchez, A. M. Pedraza, *Tetrahedron Lett.* **1999**, *40*, 2007−2010.

[44] Compounds **1*c*** and **9** were obtained by [2+2] photocycloaddition of 3-ethoxyisoindolone to cyclohexene and tetramethylethylene, respectively, followed by acid hydrolysis: K. A. Howard, T. H. Koch, *J. Am. Chem. Soc.* **1975**, *97*, 7288−7305.

[45] Under these irradiation conditions, the photophthalimidation process (see ref.[43]) was also observed, but yields were low (< 5%).

[46] J. D. Coyle, G. L. Newport, A. Harriman, *J. Chem. Soc., Perkin Trans.* **1978**, 133−137.

[47] V. Wintgens, P. Valat, J. Kossanyi, L. Biczok, A. Demeter, T. Bérces, *J. Chem. Soc., Faraday Trans.* **1994**, *90*, 411−421.

[48] H. Hayashi, S. Nagakura, Y. Kubo, K. Maruyama, *Chem. Phys. Lett.* **1980**, *72*, 291−294.

[49] A. G. Griesbeck, H. Görner, *J. Photochem. Photobiol. A: Chem.* **1999**, *129*, 111−119, and references therein.

[50] P. Berci-Filho, F. H. Quina, M. H. Gehlen, M. J. Politi, M. G. Neumann, T. C. Barros, *J. Photochem. Photobiol. A: Chem.* **1995**, *92*, 155−161.

[51] Under these irradiation conditions, the photophthalimidation process was also observed, but yields were low (< 5%).

[52] J. N. Demas, G. A. Crosby, *J. Phys. Chem.* **1971**, *71*, 991−1024.

[53] R. Knorr, *Chem. Ber.* **1965**, *98*, 4038−4039.

Received January 16, 2002
[O02022]