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Photoinduced SET phthalimidation of unactivated double bonds and its application to the synthesis of protected phenethylamines

Rafael Suau,* Rafael García-Segura, Cristobal Sánchez-Sánchez, Ezequiel Pérez-Inestrosa and Ana María Pedraza

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Málaga, E-29071 Málaga, Spain

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Abstract—Phthalimide, in equilibrium with its conjugate base, adds photochemically to cyclohexene and aryl-substituted alkenes (photophthalimidation). The efficient, predictable regioselective photophthalimidation of styrenes constitutes a synthetically useful process for the preparation of *N*-phenethyl-phthalimides. A possible mechanism for the photophthalimidation involves the nucleophilic attack of phthalimide anion on the alkene cation-radical generated by single electron transfer to excited phthalimide.

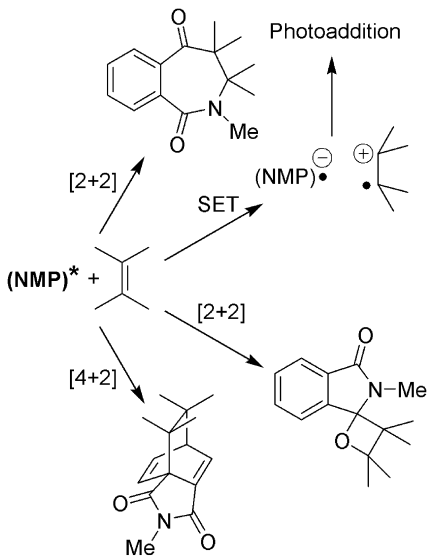
1. Introduction

The photochemical behavior of *N*-methylphthalimide (NMP) in the presence of alkenes is strongly dependent on the irradiation conditions and the oxidation potential of the C=C double bond, as found in a wide range of interesting reactions (Scheme 1).[1] The singlet excited state of NMP undergoes [2+2] photocycloaddition to the C–N bond to give [2]benzazepinediones for alkenes with an oxidation potential higher than 2.1 V.[2] With more readily oxidized alkenes, SET takes place and yields the radical-ion pair (back electron transfer regenerates the starting material); the radical-cation can be trapped by nucleophilic solvents or transfer a proton, and radical coupling leads to the photoaddition products.[3] Intermolecular Paterno-Buchi reaction and oxetane formation have been reported to occur from the triplet excited state of NMP.[4] Also, ^{3}(NMP)* is the excited state responsible for the [4+2] photocycloaddition to the aromatic ring,[5] which is assumed to be initiated by an allowed [2+2] cycloaddition and followed by a [1,3] sigmatropic rearrangement.[5c]

The photochemical reactivity of phthalimide (PHT-H) is rather slow and remains under explored.[3d] At low conversions (10–15%) in alcoholic solvents photoinduced SET from styrene or α-methyl styrene to the excited PHT-H is the major reaction pathway and the compound resulting from photoaddition with incorporation of solvent is the main reaction product (Scheme 2). [2+2] Photocycloaddition to benzazepinediones has also been observed, albeit in low yields in the presence of ethanol or isopropanol as solvent.

If SET could be avoided the photochemical [2+2] cycloaddition to ring-expanded [2]benzazepin-1,5-diones could be turned into a synthetically useful reaction (Scheme 2).

With this aim, the photocycloaddition of phthalimide anion to alkenes was investigated. The results showed that the singlet excited state of phthalimide anion efficiently adds to alkenes, in a regioselective manner, the reaction being



Scheme 1.

Keywords: electron transfer; imides; amination; alkenes; photochemistry; radicals and radical reactions.

* Corresponding author. Tel./fax: +34-952-13-19-34; e-mail: suau@uma.es

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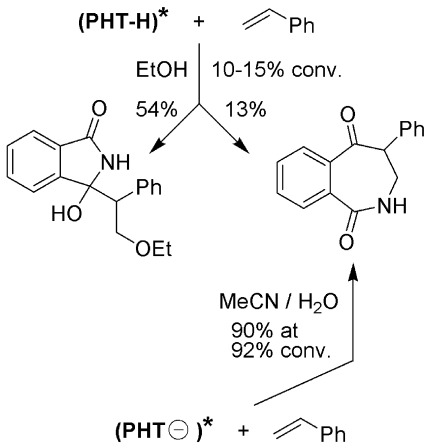


Scheme 2.

2. Results and discussion

The [2+2] photocycloaddition of cyclohexene to excited phthalimide anion (started by adding NaOH to an acetonitrile/water solution of PHT-H) is a stereospecific process that yields the ring expanded *cis*-**1** adduct.[6] However, epimerization to *trans*-**1** also occurs owing to the basicity of the reaction medium. Decreasing the concentration of NaOH reduced the overall photocycloaddition yield and resulted in the formation of *N*-cyclohexylphthalimide (**2**). In order to obtain insight into these competitive reactions, the effect of the concentration of NaOH used during the irradiation of phthalimide in the presence of cyclohexene and α-methylstyrene was investigated. The reactions were monitored by HPLC and the results are shown in Figure 1.

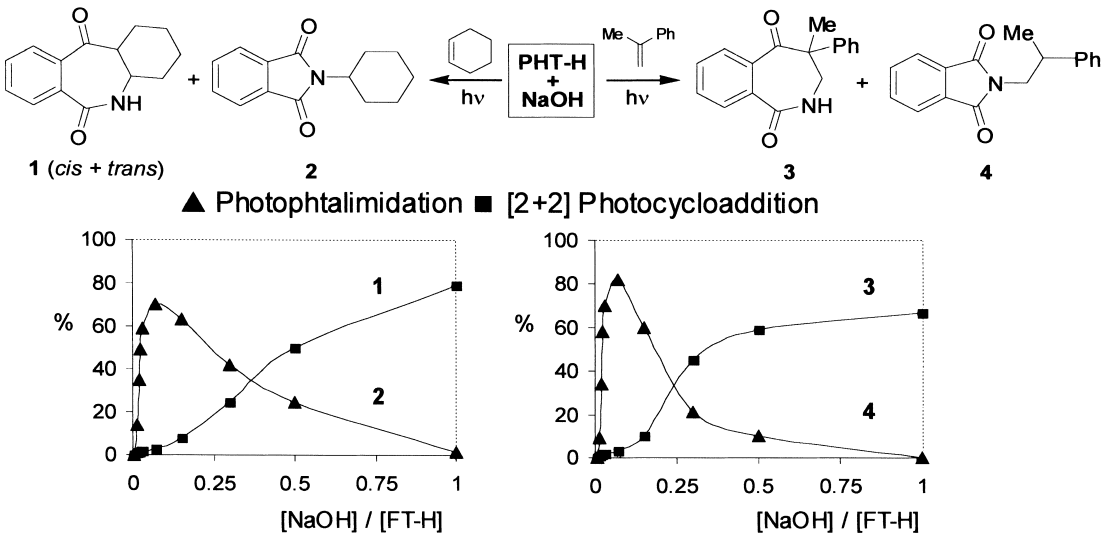
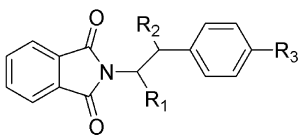
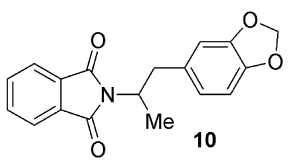


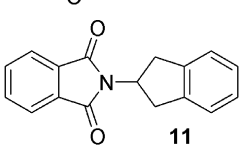
Figure 1.

independent of the ionization potential of the alkene.[6] Additional findings included a significant reduced photocycloaddition yield when the irradiation was done in MeOH, *t*-BuOH or THF,[7] and that the best irradiation conditions were those obtained by dissolving PHT-H in acetonitrile/water and adding NaOH followed by the alkene. Under such conditions, the reaction was found to be strongly dependent on the NaOH concentration. Thus, at concentrations of PHT-H exceeding that of NaOH, a new reaction occurred, viz. the addition of phthalimide to the alkene double bond (i.e. photophthalimidation).[8] This paper describes in detail the photochemistry of the PHT-H⇆PHT$^-$ equilibrium in the presence of alkenes and the role of excited phthalimide in a SET primary process. The results reveal efficient, regioselective photoaddition of phthalimide to unactivated double bonds. Of special interest is the photophthalimidation of styrene derivatives, which provides a direct, simple entry to phenethylphthalimides. These compounds are major intermediates in the synthesis of a structural variety of alkaloids and the preparation of many pharmaceuticals[9] or even as such [phenethylphthalimides exhibit varied biological activity[10] including thalidomide-like activity on the production of tumor necrosis factor α (TNF-α)].[11]



	R_1	R_2	R_3
5	H	H	H
6	Me	H	H
7	Ph	Ph	H
8	H	H	OMe
9	Me	H	OMe





Scheme 3.

Table 1. Effect of the NaOH concentration on the photoreaction of phthalimide with cyclohexene and α-methylstyrene in acetonitrile/water

Sample	[NaOH]/[PHT-H]	Alkene (equiv.)	Conversion (%)	[2+2] Photo-cycloaddition (%)	Photo-phthalimidation (%)
A	0.07	Cyclohexene (75)	76[a]	**1** (<3)	**2** (87)
B	0.5	Cyclohexene (75)	80[a]	**1** (40)	**2** (25)
C	1.5	Cyclohexene (75)	88[a]	**1** (84)	**2** (<5)
D	0.07	α-Methylstyrene (8.1)	54[b]	**3** (<4)	**4** (82)
E	0.5	α-Methylstyrene (8.1)	66[b]	**3** (53)	**4** (12)
F	1.5	α-Methylstyrene (8.1)	68[b]	**3** (70)	**4** (<3)

[a] Conversion and yields are given on consumed phthalimide.
[b] Conversion and yields are given on consumed olefin.

Table 2. Photophthalimidation of alkenes (0.5 equiv.) in the irradiation of phthalimide (6.8 equiv.)/NaOH (0.5 equiv.) in acetonitrile/water

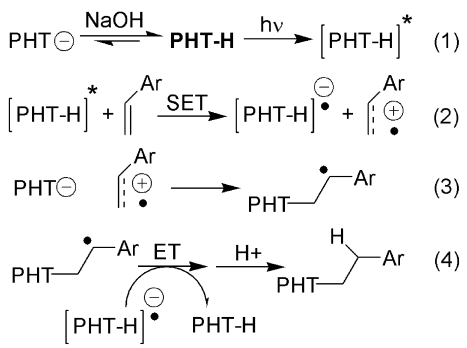
Entry	Alkene	Time (h)	Conversion (%)	Photo-phthalimidation product (% yield)[a]
1	α-Methylstyrene	4	80	**4** (90)
2	Styrene	11	81	**5** (72)
3	*trans*-β-Methyl-styrene	12	73	**6** (59)
4	*trans*-Stilbene	25	76	**7** (71)
5	4-Methoxy-styrene	6	92	**8** (75)
6	*trans*-Anethole	14	76	**9** (60)
7	Isosafrole	6	71	**10** (51)
8	Indene	6	75	**11** (90)

[a] Yields are referred to consumed olefin.

The reaction develops quite similarly for both alkenes. At very low base concentrations photophthalimidation prevails, the maximum being reached at an 0.06–0.08 NaOH/PHT-H ratio. The situation is reversed when the concentration of NaOH approaches that of phthalimide: phtotophthalimidation is suppressed and [2+2] photocycloaddition prevails. This result, obtained at low conversions (15–20%), was reproduced on a preparative scale (Table 1) by conducting the irradiations to a high conversion which provided evidence for the synthetic value of this reaction.

Preparative irradiation of the alkenylbenzenes was done using excess phthalimide in order to prevent absorption of light by the olefin or the phenethylphthalimide (Table 2 and Scheme 3). Otherwise, a secondary photochemistry was initiated by γ-hydrogen abstraction that was followed by Yang cyclization and ring expansion—a process that is well documented for these systems.[1,12]

In all cases, photophthalimidation took place in a regioselective manner. With β-methyl substituted styrenes, the reaction was found to be slower and yields to be moderate (entries 3, 6 and 7). ^{1}H NMR spectroscopy of the irradiation crude, following removal of excess phthalimide revealed the occurrence of [2+2] photocycloaddition; yields, however, never exceeded 10%. On the other hand, photophthalimidation of indene was very effective, still when the concentration of NaOH was increased.



Scheme 4.

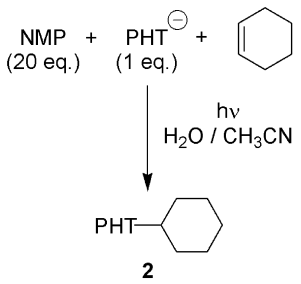
A tentative mechanism for the phthalimidation is proposed in Scheme 4.

Under the irradiation conditions used, the phthalimide anion concentration was too low for radiation to be absorbed, so the first step must involve light absorption by phthalimide. PHT-H is known to be non-fluorescent and its anion strongly fluorescent.[6,13] No fluorescence from phthalimide anion was detected at the low concentrations of base [NaOH] employed. The Weller equation predicts an exoergic electron transfer from styrenes (E_{red}<2 V) to excited phthalimide (E^{00} 80 Kcal/mol; E_{ox} −1.4 V). The cation-radical will be regioselectively trapped by phthalimide anion to render the aryl-stabilized radical (Eqs. (2) and (3)).

The reaction of styrene cation-radicals with good nucleophiles is known to occur at a roughly diffusion rate in acetonitrile/water, and no evidence for competing back electron transfer for nucleophiles such as azide or cyanide has been obtained.[14] Back electron transfer from the phthalimide anion-radical to the radical, followed by protonation of the resulting anion (Eq. (4)) would give the final photoaddition product.

Findings in support of this mechanistic proposal were derived from two additional experiments. As expected, the irradiation of a large excess of *N*-methylphthalimide (NMP) in the presence of phthalimide anion (20/1 ratio) and cyclohexene produced the *N*-cyclohexylphthalimide (**2**) (Scheme 5).

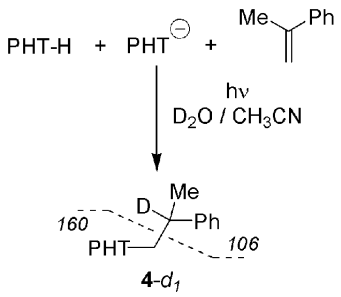
This confirms the role of neutral phthalimide as the photosensitizer for the reaction that induces the SET



Scheme 5.

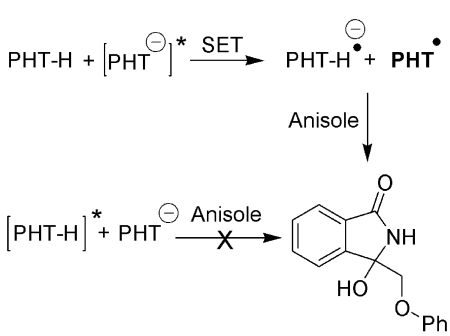
process, and that phthalimide anion must take part in it as a ground-state nucleophile. The final step, which electron transfer from the phthalimide anion-radical to the carbon-centered radical to the corresponding anion, must be followed by protonation.

Consistent with this proposal, the irradiation of PHT-H⇆PHT$^-$ and α-methylstyrene in D_2O yielded the photoaddition product (**4**-d_1), with quantitative incorporation of deuterium at the benzylic position (Scheme 6).



Scheme 6.

One alternative mechanism involving PHT$^-$ as electron donor instead of the alkene is conceivable. In such a case, the key step of the reaction would involve the formation of the electrophilic phthalimidyl radical and addition to the C=C double bond, a process previously demonstrated for the photoinduced addition of *N*-bromophthalimide to alkenes.[15] We recently found phthalimidyl radical, generated by SET from excited phthalimide anion to ground state phthalimide, to exhibit exceptional H-atom abstraction reactivity and in the presence of anisole the photoaddition product being the only product isolated (Scheme 7).[7]



Scheme 7.

However, under the photophthalimidation conditions (PHT-H≫PHT$^-$) used no photoadduct with anisole was detected. In the absence of further information, it is difficult to ascertain whether this alternative mechanism can be competitive, so we consider more reliable the previous one.

Intra and intermolecular photoamination of alkenes and arenes, mediated by photoinduced SET, has shown a high synthetic potential.[16–18] In most cases, the excited arene or alkene transfers one electron to an acceptor and the resulting radical-cation is then trapped by ammonia or amines. For styrene derivatives and *p*-dicyanobenzene as ground state electron acceptor, photoamination by ammonia at the double bond takes place in moderate yields.[19] The reaction is significantly improved by the use of *m*-dicyanobenzene and the addition of polyphenylbenzenes as π-donor stabilizers of the styrene radical-cation. Work-up of the photolysate requires acetylation to protect the phenethylamine in order to enable the extensive chromatography required to separate the components. The photophthalimidation reaction of aryl-substituted olefins outlined above is advantageous in that the sensitizer and nucleophile are the same compound, that they can be used in a large excess to avoid preventing secondary photochemistry and that excess phthalimide can be readily separated from the protected phenethylamine simply by extraction with NaOH solution.

3. Experimental

Melting points were determined on a Gallenkamp instrument and are given uncorrected. IR spectra were recorded on a Bruker FT-IR Equinox 55 spectrometer equipped with a Specac Golden Gate ATR accessory. Absorption spectra were recorded on an HP 8452A Diode Array Spectrophotometer. Low-resolution MS (EI) spectra were recorded on an HP-MS 5988A spectrometer operating at 70 eV and HRMS were recorded on a VG Autospec spectrometer. NMR spectra were recorded on 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. Coupling constants are given in hertz. 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 $MgSO_4$. HPLC analyses were carried out on a Hewlett–Packard 1050 chromatograph equipped with an ODS Hypersil column, (5 μm, 200×4.6 mm); a column temperature of 32°C was used and UV detection performed at 220 and 254 nm. Photochemical reactions were performed at 20°C in a 250 mL immersion well photoreactor (Pyrex) equipped with a 125 W medium pressure mercury lamp. A stream of nitrogen was passed through the solution during irradiation. Yields are given on consumed phthalimide.

3.1. Irradiation of phthalimide with cyclohexene. Effect of the NaOH concentration

Phthalimide (1 g, 6.8 mmol) was dissolved in acetonitrile (200 mL) and water (22 mL), and supplied with cyclohexene (5 mL, 75 mmol). The solution was distributed into 10 test tubes. To each tube, a gradient of 1 M NaOH solution (0.01, 0.02, 0.04, 0.06, 0.08, 0.10, 0.30, 0.50, 0.70, 1.00 mL) was added. The tubes were degassed, fitted around the lamp and refrigerated by water. Samples were irradiated for

15 min. From each tube, 2 mL was taken, neutralized with 0.1 M HCl, diluted with 2 mL of methanol and analyzed by HPLC (eluted with methanol/water, 40:60; flow rate 0.8 mL/min). At low base concentration the chromatograms exhibited three signals corresponding to phthalimide (rt=2.9 min), *cis*-benzazepindione (**1**, rt=3.4 min) and *N*-cyclohexylphthalimide (**2**, rt=8.7 min). At high concentrations of NaOH, a forth peak appeared, the isomerized *trans*-benzazepinedione (rt=3.7 min). The results are shown in Figure 1.

Preparative irradiation: three samples (A, B, C) containing phthalimide (1 g, 6.8 mmol), cyclohexene (5 mL, 75 mmol) in acetonitrile (140 mL) and water (20 mL) were prepared and supplied with 1 M NaOH (0.48, 3.40 and 10.20 mL for A, B and C, respectively) followed by irradiation for 1.5 h. Each sample was neutralized, most of the solvent removed under vacuum, and the crude reaction mixture taken up by water (40 mL) and extracted with $CHCl_3$. The organic layer was dried, the solvent removed and the residue column-chromatographed (silica gel, hexane/EtOAc from 2:1 to 1:1) to afford *N*-cylohexylphthalimide (**2**) [mp 169–171°C (MeOH) (lit.,[21] 168.5–171°C)], unchanged phthalimide and benzazepinedione **1**. The conversion and yield for each sample are given in Table 1.

3.2. Irradiation of phthalimide with α-methylstyrene. Effect of NaOH concentration

Phthalimide (1 g, 6.8 mmol) was dissolved in acetonitrile (180 mL) and water (20 mL), and supplied with α-methylstyrene (4.4 mL, 34 mmol). The solution was distributed into 10 test tubes. To each tube, a gradient of 1 M NaOH solution (0.01, 0.02, 0.04, 0.06, 0.08, 0.10, 0.30, 0.50, 0.70, 1.00 mL) was added. The samples were irradiated as described above. After 80 min, conversions close to 15% were obtained. Samples were neutralized, diluted with methanol and analyzed by HPLC (elution with methanol/-water 48:52, flow rate 1 mL/min). The chromatogram exhibited four peaks corresponding to phthalimide (rt=0.5 min), benzazepinedione (rt=1.4 min), α-methylstyrene (rt=5.2 min) and the *N*-substituted phthalimide (**4**, rt=8.8 min). The results are shown in Figure 1.

Preparative irradiation: three samples (C, D, E) containing phthalimide (1 g, 6.8 mmol), α-methylstyrene (1.05 mL, 8.1 mmol) in acetonitrile (130 mL) and water (15 mL) were prepared and supplied with 1 M NaOH (0.48, 3.4 and 10.2 mL for D, E and F, respectively), followed by irradiation for 2 h. Each sample was neutralized, most of the acetonitrile removed under vacuum, water was added (50 mL) and the mixture extracted with $CHCl_3$. The organic layer was dried, the solvent removed and the residue column-chromatographed (silica gel, hexane/EtOAc from 2:1 to 1:1) to afford unchanged α-methylstyrene, alkylated phthalimide (**4**) (see below), unchanged phthalimide and benzazepinedione **3**. The conversion and yield for each sample are given in Table 1.

3.3. General procedure for the preparative irradiation of phthalimide and styrene derivatives

The homogeneous solution consisting of phthalimide (1 g, 6.8 mmol), NaOH (0.5 mL of a 1 M solution), 133 mL of acetonitrile, 17 mL of water and the alkene (2.1 mmol) was irradiated for the stated time. The disappearance of the alkene was monitored by HPLC. Most of the acetonitrile was removed under vacuum and dichloromethane (100 mL) was added to the residue. The organic layer was washed twice with a 5% aqueous NaOH solution to remove excess phthalimide. The dried organic solution was concentrated under vacuum and, in most cases, the residue was induced to crystallize. In some experiments the unchanged alkene prevented crystallization, so it was removed by filtration through a small pack of silica gel.

3.4. With cyclohexene

3.4.1. 2-Cyclohexyl-1*H*-isoindole-1,3(2*H*)-dione (2). White crystals; mp 169–171°C (MeOH) [lit.,[20] 168.5–171°C].

3.5. With α-methylstyrene

3.5.1. 2-(2-Phenylpropyl)-1*H*-isoindole-1,3(2*H*)-dione (4). White solid; mp 68–70°C (EtOAc); [lit.,[11a] 84.5°C (EtOAc/hexane)]; [Found: C 76.84, H 5.81, N 5.25. $C_{17}H_{15}NO_2$ requires C 76.96, H 5.70, N 5.28]; ν_{max} (neat) cm^{-1} 1770, 1702; δ_H ($CDCl_3$) 7.89–7.65 (m, 4H, ArH), 7.35–7.16 (m, 5H, ArH), 3.92 (dd, 1H, J=13.4, 7.0 Hz, NCH), 3.82 (dd, 1H, J=13.4, 7.0 Hz, NCH), 3.39 (m, 1H, ArCH), 1.35 (d, 3H, J=7.4 Hz, CH_3); δ_C ($CDCl_3$) 168.2 (C1, C3), 143.2 (C3′), 133.7 (C5, C6), 131.9 (C3a, C7a), 128.4 (C5′, C7′), 127.2 (C4′, C8′), 123.1 (C4, C7), 126.7 (C6′), 44.8 (CH_2), 38.4 (CH), 18.9 (CH_3); *m/z* (EI) 265 (M^+, 37), 160 (100), 118 (55).

3.6. With styrene

3.6.1. 2-(Phenylethyl)-1*H*-isoindole-1,3(2*H*)-dione (5). White crystals; mp 127–129°C (EtOH) [lit.,[21] 131–132°C]; [Found: C 76.34, H 5.31, N 5.55. $C_{16}H_{13}NO_2$ requires C 76.48, H 5.21, N 5.57]; ν_{max} (neat) cm^{-1} 1770, 1704; δ_C ($CDCl_3$) 168.1 (C1, C3), 137.9 (C3′), 133.8 (C4, C7), 132.0 (C3a, C7a), 128.8 128.5 (C4′, C5′, C7′, C8′), 126.6 (C6′), 123.1 (C5, C6), 39.21 (CH), 34.5 (CH_2); *m/z* (EI) 251 (M^+, 37), 160 (100).

3.7. With *trans*-β-methyl-styrene

3.7.1. 2-[1-Methyl(phenyl)ethyl]-1*H*-isoindole-1,3(2*H*)-dione (6). White crystals; mp 75–77°C (MeOH) [lit., 48°C (EtOAc/hexane)[11a] and 78–79°C (ether/hexane)[22] for the (*S*)-enantiomer]; [Found: C 77.08, H 5.60, N 5.44. $C_{17}H_{15}NO_2$ requires C 76.96, H 5.70, N 5.28]; ν_{max} (neat) cm^{-1} 1765, 1698; δ_C ($CDCl_3$) 168.3 (C1, C3), 138.3 (C3′), 131.8 (C3a, C7a), 133.7, 128.8, 128.3, 126.4, 122.9 (C4–C7, C4′–C8′), 48.6 (CH), 39.8 (CH_2), 18.2 (CH_3); *m/z* (EI) 265 (M^+, 9), 174 (100).

3.8. With *trans*-stilbene

3.8.1. 2-(1-Diphenylethyl)-1*H*-isoindole-1,3(2*H*)-dione (7). White amorphous powder; mp 147–148°C (EtOAc/hexane); [Found: C 80.36, H 5.36, N 4.28. $C_{22}H_{17}NO_2$ requires C 80.71, H 5.23, N 4.28]; ν_{max} (neat) cm^{-1} 1770,

1711; δ_H ($CDCl_3$) 7.75–7.60 (m, 4H, ArH), 7.59–7.09 (m, 10H, ArH), 5.65 (dd, 1H, *J*=11.1, 5.7 Hz, H1′), 4.00 (dd, 1H, *J*=13.9, 11.1 Hz, H2′), 3.50 (dd, 1H, *J*=13.9, 11.1 Hz, H2′); δ_C ($CDCl_3$) 168.2 (C1, C3), 139.3, 137.9 (C1″, C2″), 131.7 (C3a, C7a), 133.8, 128.9, 128.7, 128.6, 128.5, 128.1, 127.9, 126.6, 123.1 (ArCH), 56.0 (NCH), 37.1 (CH_2); *m/z* (EI) 327 (M^+, 11), 180 (100).

3.9. With 4-methoxy-styrene

3.9.1. 2-[(4-Methoxyphenyl)ethyl]-1*H*-isoindole-1,3(2*H*)-dione (8). White crystals; mp 135–136°C (MeOH) [lit.,[23] 139–140°C]; [Found: C 72.40, H 5.41, N 4.90. $C_{17}H_{15}NO_3$ requires C 72.58, H 5.37, N 4.98]; ν_{max} (neat) cm^{-1} 1767, 1703; δ_C ($CDCl_3$) 168.0 (C1, C3), 158.2 (C6′), 133.7, 129.7, 123.0, 113.8 (C4–C7, C4′, C5′, C7′, C8′), 131.9, 129.9 (C3a, C7a, C3′), 55.0 (OCH_3), 39.3 (CH), 33.5 (CH_2); *m/z* (EI) 281 (M^+, 1), 134 (100).

3.10. With *trans*-anethole

3.10.1. 2-[(4-Methoxyphenyl)-1-methylethyl]-1*H*-isoindole-1,3(2*H*)-dione (9). White crystals; mp 61–62°C ($CHCl_3$); [Found: C 72.77, H 5.88, N 4.82. $C_{18}H_{17}NO_3$ requires C 73.20, H 5.80, N 4.74]; ν_{max} (neat) cm^{-1} 1769, 1690; δ_H ($CDCl_3$) 7.80–7.60 (m, 4H, ArH), 7.09 (d, 2H, *J*=8.6 Hz, H4′, H8′) 6.72 (d, 2H, *J*=8.6 Hz, H5′, H7′), 4.59 (m, 1H, NCH), 3.72(s, 1H, OCH_3), 3.26 (dd, 1H, *J*=13.5, 9.4 Hz, H2′), 3.02 (dd, 1H, *J*=13.5, 6.8 Hz, H2′), 1.51 (d, 3H, *J*=6.8 Hz, CH_3); δ_C ($CDCl_3$) 168.3 (C1, C3), 158.1 (C6′), 131.8, 130.4 (C3′, C3a, C7a), 133.7, 129.8, 122.9, 113.7 (C4–C7, C4′, C8′, C5′, C7′), 55.1 (OCH_3), 48.7 (NCH), 38.9 (CH_2), 18.2 (CH_3); *m/z* (EI) 295 (M^+, 6), 174 (100), 148 (84), 121 (48).

3.11. With isosafrole

3.11.1. 2-(1,3-Benzodioxol-5-yl-1-methylethyl)-1*H*-isoindole-1,3(2*H*)-dione (10). Syrup; ν_{max} (neat) cm^{-1} 1765, 1688; δ_H ($CDCl_3$) 7.80–7.60 (m, 4H, ArH), 6.65 (m, 3H, ArH), 5.85 (s, 2H, OCH_2O), 4.57 (m, 1H, H1′), 3.24 (dd, 1H, *J*=13.8, 9.3 Hz, H2′), 2.98 (dd, 1H, *J*=13.8, 6.7 Hz, H2′), 1.50 (d, 3H, *J*=7.0 Hz, CH_3); δ_C ($CDCl_3$) 168.4 (C1, C3), 147.6, 146.1 (C5′, C6′), 132.1, 131.9 (C3′, C3a, C7a), 133.7 (C5, C6), 123.0 (C4, C7), 121.9, 109.3, 108 (C4′, C8′, C7′), 100.8 (OCH_2O), 48.8 (NCH), 38.6 (CH_2), 18.2 (CH_3); *m/z* (EI) 309 (M^+, 12), 174 (100), 162 (5), 147 (15); EI-HRMS calcd for $C_{18}H_{15}NO_4$ 309.1001, found 309.1008.

3.12. With indene

3.12.1. 2-(2,3-Dihydro-1*H*-inden-2-yl)-1*H*-isoindole-1,3(2*H*)-dione (11). White needles; mp 196–197°C (EtOH) [lit.,[24] 194–195°C (CH_2Cl_2/hexane)]; [Found: C 77.20, H 4.94, N 5.30. $C_{17}H_{13}NO_2$ requires C 77.55, H 4.98, N 5.32]; ν_{max} (neat) cm^{-1} 1767, 1698; *m/z* (EI) 263 (M^+, 20), 116 (100).

3.13. Irradiation in CH_3CN/D_2O

The homogeneous solution consisting of phthalimide (100 mg, 0.68 mmol), NaOH (0.05 mL of a 1 M solution), 13 mL of acetonitrile, 2 mL of 99% D_2O and α-methylstyrene (0.5 mL) was irradiated for 45 min. The reaction mixture was worked up as above and the crude product chromatographed, compound **4**-d_1 (32 mg) was isolated.

3.13.1. 2-(2-Deutero-2-phenylpropyl)-1*H*-isoindole-1,3(2*H*)-dione (4-d_1). δ_H ($CDCl_3$) 7.8–7.6 (m, 4H, ArH), 7.25 (m, 5H, ArH), 3.90 (d, 1H, *J*=13.4 Hz, NCH), 3.80 (d, 1H, *J*=13.4 Hz, NCH), 1.35 (s, 3H, CH_3); δ_C ($CDCl_3$) 168.2 (C1, C3), 143.3 (C3′), 133.8 (C5, C6), 131.8 (C3a, C7a), 128.4 (C5′, C7′), 127.2 (C4′, C8′), 123.1 (C4, C7), 126.7 (C6′), 44.7 (CH_2), 18.9 (CH_3); *m/z* (EI) 266 (M^+, 36), 160 (100), 119 (24).

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