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Photoinduced Addition of Phthalimide to Unactivated Alkynes†

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ABSTRACT

Photoexcited phthalimide in equilibrium with its conjugated base produces the regioselective hydrophthalimidation of conjugated alkynes. The vinylphthalimide thus obtained is hydrolyzed to the corresponding carbonyl compound. With unconjugated alkynes, the outcome is a double addition of phthalimide to the triple bond. The reaction is assumed to take place via single electron transfer from either the alkyne or the phthalimide anion to the excited phthalimide as the primary photoprocess.

INTRODUCTION

The photochemistry of the phthalimide system (particularly that of *N*-Me and *N*-alkyl phthalimides) has aroused widespread interest after pioneering work by Kanaoka (1). Intramolecular photocyclization (2), intermolecular photocycloaddition (3) and photoaddition (4–6) are the major processes that have been observed so far. Most of these reactions are initiated by single electron transfer (SET) from a donor to the excited phthalimide acceptor (7,8). The intermolecular photochemistry of phthalimide (PHT-H) has been much less extensively investigated. Maruyama and Kubo (9) showed the irradiation of phthalimide with styrenes as donors in alcoholic solvents to give photoaddition products (**1**) (Fig. 1). The reaction involves SET from the styrene to phthalimide to give the corresponding radical-ion pair, followed by trapping of the styrene radical-cation by the solvent and radical recombination.

Recently, we found that irradiation of phthalimide in equilibrium with its conjugate base (PHT-H $\rightleftarrows$ PHT$^-$) triggered various types of processes. Thus, selective excitation of the anion, [PHT$^-$] >> [PHT-H], in the presence of hydrogen donors yielded isoindanones (**2**), which formed via the electrophilic phthalimidyl radical. With alkenes and styrenes, however, the main reaction was the regioselective, stereospecific [2+2] cycloaddition that generated [2]benzazepinedione (**3**) (10, 11) (Fig. 2). In contrast with related reactions in *N*-methylphthalimides (12), this process is independent of the ionization potential of the alkene.

On the other hand, when phthalimide is the excited species (Fig. 3), [PHT-H] >> [PHT$^-$] in the presence of alkenes or styrenes, regioselective (anti-Markovnikov) addition to the C=C double bond (**4**) occurs with a high efficiency (13). In the reaction, phthalimide acts as an SET photosensitizer and its anion as a nucleophile by adding to the cation-radical of the alkene. As predicted by the Weller equation (14), an exoergic electron transfer to excited phthalimide ($E_{red} = -1.45$ V and $E^{00} = 3.8$ eV for S_1) from alkenes with oxidation potentials below 2.0 V takes place.

On the basis of the foregoing, alkynes with an appropriate oxidation potential can be expected to undergo photochemical addition to PHT-H to give the corresponding vinyl-phthalimides; such enimides must be easily hydrolyzed to the corresponding aldehydes or ketones, thus facilitating the hydration of alkynes with light and water as consumable reagents. This paper reports our results for the photochemical addition reaction of phthalimide in equilibrium with its anion and alkynes. The reaction was found to be dependent on the oxidation potentials of the alkyne. Thus, conjugated phenyl-alkynes (with oxidation potentials below 2.0 V) undergo regioselective hydrophthalimidation to the corresponding vinylphthalimides, whereas unconjugated alkynes (with oxidation potentials above 2.4 V) undergo 1,2-double addition to phthalimide. Both reactions proceed with good yields, but low conversions, which reduces their synthetic relevance.

MATERIALS AND METHODS

Chemicals. Phthalimide and sodium hydroxide were purchased from Panreac (Barcelona, Spain). Phenylethyne, 1-phenyl-1-propyne, 1,2-diphenylethyne, 1-hexyne and 3-hexyne were supplied in the highest available grade by Aldrich (Madrid, Spain) and used as received. Acetonitrile was obtained in high-performance liquid chromatography (HPLC) grade from Merck (Barcelona, Spain).

General remarks. Melting points were determined by using a Gallenkamp apparatus from Sanyo Gallenkamp (Loughborough, UK) and are given uncorrected. Absorption spectra were recorded on a Hewlett-Packard 8452A Diode Array Spectrophotometer; low-resolution mass spectrometry (MS) (electron impact; EI) on a Hewlett-Packard 5988A mass spectrometer operating at 70 eV; and high-resolution MS on a Kratos MS 50 TC mass spectrometer from Mass Spectrometry International, Ltd. (Manchester, UK). Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker WP-200 SY instrument from Bruker BioSpin GmbH (Rheinstetten, Germany) at 200 MHz for ^{1}H and 50.3 MHz for ^{13}C. Chemical shifts are given relative to the residual signal for the solvent, $\delta_H = 7.24$ ppm, and $\delta_C = 77.0$ ppm for deuteriochloroform (SdS, Peypin, France). Thin-layer chromatographic analyses were performed on silica gel 60 F 256 plates, and column chromatography was carried out on silica gel 60 (70–230 mesh) from Merck. Organic solutions were dried with $MgSO_4$. Unless otherwise stated, solutions were irradiated at room temperature in a 250 mL

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Abbreviations: EI, electron impact; HPLC, high-performance liquid chromatography; HRMS, high-resolution mass spectrometry; MP, melting point; MS, mass spectrometry; NMR, nuclear magnetic resonance; SET, single electron transfer.

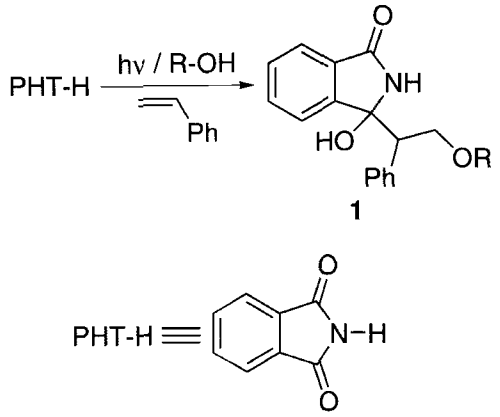

Figure 1. Intermolecular photochemistry of phthalimide with styrenes.

immersion well photoreactor (Pyrex) equipped with a 125 W medium-pressure mercury lamp. A nitrogen stream was passed through the medium during irradiation. The solvent and excess alkyne from the irradiated solutions were removed under vacuum, the residue being taken up in dichloromethane and the solution washed with 1 *M* NaOH solution. Finally, the organic layer was dried and concentrated to dryness, the residue being column chromatographed. Reaction progress was monitored by HPLC. The yields given are based on the alkyne uptake.

Irradiation of PHT-H/NaOH/phenylethyne. A solution of phthalimide (1.0 g, 6.8 mmol), NaOH (2.0 mL of a 1 *M* solution) and phenylethyne (0.75 mL, 6.8 mmol) in 130 mL of acetonitrile and 20 mL of water was irradiated for 4 h to obtain 300 mg of **5**, which was a 1:1 mixture of isomers *E* and *Z* (89% at 20% conversion).

*2-[(E)-2-phenylvinyl]-1H-isoindole-1,3(2H)-dione (**E-5**).* Yellow crystals; melting point (mp) 187–188°C; UV/vis (CH_3CN) λ_{max} (ε): 282 (24 658); ^1H NMR (200 MHz, $CDCl_3$) δ 8.00–7.73 (m, 4H, ArH), 7.66 (d, 1H, J = 15.3 Hz, H-2′), 7.55–7.20 (m, 6H, H-1′ and ArH); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 166.4, 135.9, 134.5, 131.7, 128.7, 127.6, 126.2, 123.6, 120.2, 117.6; EI MS (*m/z*) 249 (M^+, 100), 220 (19), 204 (25); EI high-resolution mass spectrometry (HRMS) (calculated for $C_{16}H_{11}NO_2$) 249.0790, found 249.0785.

*2-[(Z)-2-phenylvinyl]-1H-isoindole-1,3(2H)-dione (**Z-5**).* Yellow crystals; mp 125–126°C; UV/vis (CH_3CN) λ_{max} (ε): 282 (14 450); ^1H NMR (200 MHz, $CDCl_3$) δ 7.95–7.70 (m, 4H, ArH), 7.25 (m, 5H, ArH), 6.61 (d, 1H, J = 9.2 Hz, H-2′), 6.30 (d, 1H, J = 9.2 Hz, H-1′); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 166.2, 134.8, 134.2, 131.9, 129.8, 128.3, 128.1, 127.9, 123.6, 116.1; EI MS (*m/z*) 249 (M^+, 100), 220 (20), 204 (28); EI HRMS (calculated for $C_{16}H_{11}NO_2$) 249.0790, found 249.0789.

Irradiation of PHT-H/NaOH/D_2O/phenylethyne. A solution of phthalimide (0.2 g, 1.4 mmol), NaOH (0.5 mL of a 1 *M* solution) and phenylethyne (0.26 mL, 2.4 mmol) in 30 mL of acetonitrile and 5 mL of D_2O was irradiated for 4 h to obtain 126 mg of **5**-[^{2}H], which was a 1:1 mixture of isomers *E* and *Z* (84% at 25% conversion).

*2-[(E)-[2-^{2}H]-2-phenylvinyl]-1H-isoindole-1,3(2H)-dione (**E-5**-[^{2}H]).* Yellow crystals; mp 174–175°C; UV/vis (CH_3CN) λ_{max} (ε): 282

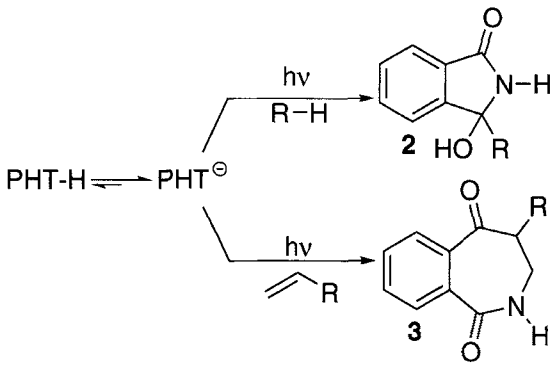

Figure 2. Photochemistry of phthalimide at [PHT⁻] >> [PHT-H] with hydrogen donors and alkenes or styrenes.

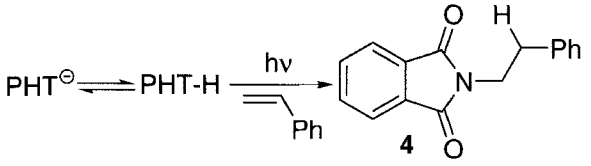

Figure 3. Photochemistry of phthalimide at [PHT⁻] << [PHT-H] with alkenes or styrenes.

(20 575); ^1H NMR (200 MHz, $CDCl_3$) δ 8.00–7.73 (m, 4H, ArH), 7.55–7.20 (m, 6H, H-1′ and ArH); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 166.3, 135.8, 134.5, 131.6, 128.7, 127.6, 126.2, 123.6, 117.4; EI MS (*m/z*) 250 (M^+, 80), 222 (14), 205 (23), 104 (100); EI HRMS (calculated for $C_{16}H_{10}DNO_2$) 250.0853, found 250.0843.

*2-[(Z)-[2-^{2}H]-2-phenylvinyl]-1H-isoindole-1,3(2H)-dione (**Z-5**-[^{2}H]).* Colorless crystals; mp 109–110°C; UV/vis (CH_3CN) λ_{max} (ε): 262 (8325); ^1H NMR (200 MHz, $CDCl_3$) δ 7.95–7.70 (m, 4H, ArH), 7.25 (m, 5H, ArH), 6.30 (s, 1H, H-1′); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 166.3, 134.9, 134.3, 132.0, 129.8, 128.3, 128.1, 123.6, 116.1; EI MS (*m/z*) 250 (M^+, 80), 222 (13), 205 (24), 104 (100).

Irradiation of PHT-H/NaOH/1-phenyl-1-propyne. A solution of phthalimide (1.0 g, 6.8 mmol), NaOH (2.0 mL of a 1 *M* solution) and 1-phenyl-1-propyne (0.85 mL, 6.8 mmol) in 130 mL of acetonitrile and 20 mL of water was irradiated for 4 h to obtain 380 mg of **4**, which was a 2:1 mixture of isomers *E* and *Z* (85% at 25% conversion).

*2-[(E)-1-methyl-2-phenylvinyl]-1H-isoindole-1,3(2H)-dione (**E-6**).* Colorless syrup; UV/vis (CH_3CN) λ_{max} (ε): 252 (1446); ^1H NMR (200 MHz, $CDCl_3$) δ 7.77–7.68 (m, 4H, ArH), 7.20–7.10 (m, 5H, ArH), 6.75 (s, 1H, H-2′), 2.17 (s, 3H, Me); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 167.5, 136.2, 134.5, 131.7, 130.0, 129.1, 128.6, 126.2, 123.6, 18.5; EI MS (*m/z*) 263 (M^+, 45), 130 (22), 116 (100); EI HRMS (calculated for $C_{17}H_{13}NO_2$) 263.0946, found 263.0945.

*2-[(Z)-1-methyl-2-phenylvinyl]-1H-isoindole-1,3(2H)-dione (**Z-6**).* Colorless crystals; mp 111–112°C; UV/vis (CH_3CN) λ_{max} (ε): 252 (1246); ^1H NMR (200 MHz, $CDCl_3$) δ 8.00–7.71 (m, 4H, ArH), 7.41–7.22 (m, 5H, ArH), 6.60 (s, 1H, H-2′), 2.25 (s, 3H, Me); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 167.3, 135.1, 134.2, 131.9, 131.1, 129.1, 128.3, 127.4, 123.5, 17.6; EI MS (*m/z*) 263 (M^+, 46), 130 (23), 116 (100); EI HRMS (calculated for $C_{17}H_{13}NO_2$) 263.0946, found 263.0944.

Irradiation of PHT-H/NaOH/1,2-diphenylethyne. A solution of phthalimide (1.0 g, 6.8 mmol), NaOH (2.0 mL of a 1 *M* solution) and 1,2-diphenylethyne (1.8 g, 10.0 mmol) in 130 mL of acetonitrile and 20 mL of water was irradiated for 4 h to obtain 315 mg of **7** (89% at 11% conversion).

*2-[(E)-1,2-diphenylvinyl]-1H-isoindole-1,3(2H)-dione (**7**).* Colorless crystals; mp 170–171°C; UV/vis (CH_3CN) λ_{max} (ε): 286 (13 118); ^1H NMR (200 MHz, $CDCl_3$) δ 7.99–7.70 (m, 4H, ArH), 7.40–7.10 (m, 10H, ArH), 6.78 (s, 1H, H-vinyl); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 167.3, 135.7, 135.0, 134.4, 134.2, 132.1, 131.9, 130.5, 129.9, 129.5, 129.0, 128.8, 128.7, 128.6, 128.1, 127.9, 127.8, 125.3, 123.9, 123.7; EI MS (*m/z*) 325 (M^+, 48), 178 (100), 165 (25); EI HRMS (calculated for $C_{22}H_{15}NO_2$) 325.1103, found 274.1106.

Irradiation of PHT-H/NaOH/1-hexyne. A solution of phthalimide (2.0 g, 13.60 mmol), NaOH (4.0 mL of a 1 *M* solution) and 1-hexyne (0.3 mL, 2.64 mmol) in 200 mL of acetonitrile and 70 mL of water was irradiated with a 400 W lamp from Photochemical Reactors, Ltd. (Berkshire, UK) for 1 h to obtain 230 mg of **8** (80% at 29% conversion).

*2-[2-(1,3-Dioxo-1,3-dihydro-2H-isoindol-2-yl)hexyl]-1H-isoindole-1,3(2H)-dione (**8**).* Colorless crystals; mp 129–130°C; UV/vis (CH_3CN) λ_{max} (ε): 294 (3325); ^1H NMR (200 MHz, $CDCl_3$) δ 7.80–7.60 (m, 8H, ArH), 4.55–4.25 (m, 2H, H-1′, H-2′), 3.84 (d, 1H, J = 10.8 Hz, H-2′), 2.22 (m, 1H, H-3′), 1.92 (m, 1H, H-2′), 1.27 (m, 4H, 2 × CH_2), 0.91 (t, 3H, J = 7.0 Hz, Me); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 168.6, 167.9, 133.6, 131.4, 123.2, 51.1, 39.3, 28.6, 27.9, 22.1, 13.2; EI MS (*m/z*) 229 (16), 216 (42), 160 (100), 148 (33), 130 (32); EI HRMS (calculated for $C_{22}H_{20}N_2O_4$) 376.1423, found 376.1420.

Irradiation of PHT-H/NaOH/3-hexyne. A solution of phthalimide (2.0 g, 13.60 mmol), NaOH (4.0 mL of a 1 *M* solution) and 1-hexyne (0.3 mL, 2.64 mmol) in 200 mL of acetonitrile and 70 mL of water was irradiated with a 400 W lamp for 1 h to obtain 256 mg of **9** (86% at 30% conversion).

*2-[2-(1,3-Dioxo-1,3-dihydro-2H-isoindol-2-yl)-1-ethylbutyl]-1H-isoindole-1,3(2H)-dione (**9**).* Colorless crystals; mp 175–180°C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.820–7.50 (m, 8H, ArH), 4.43 (q, 1H,

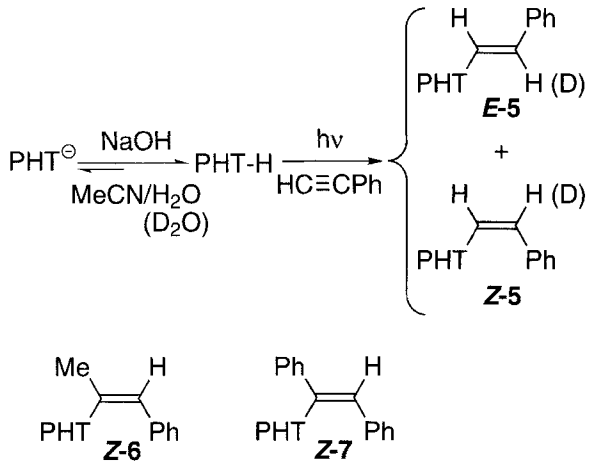

Figure 4. Irradiation of the system [PHT⁻] << [PHT-H] with unactivated alkynes.

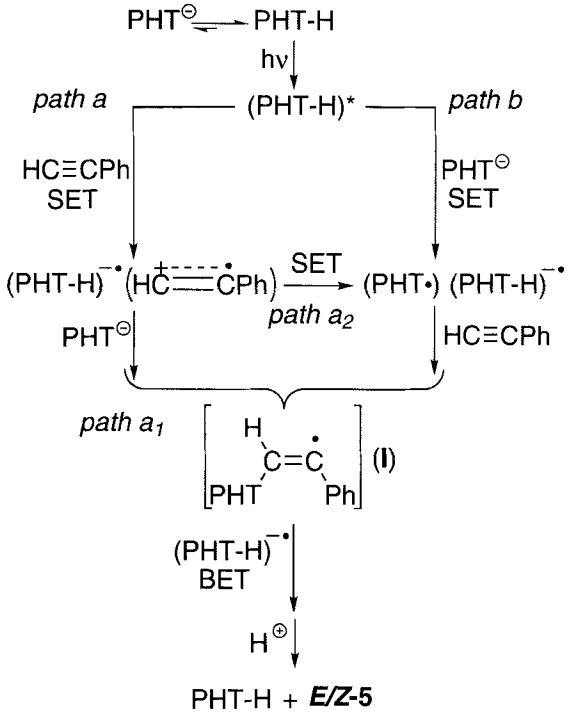

Figure 5. Proposed mechanism for the irradiation at [PHT⁻] << [PHT-H] with unactivated alkynes.

J = 7.0 Hz, H-3), 3.78 (q, 1H, J = 7.0 Hz, H-4), 1.79–45 (m, 4H, 2 × CH_2), 1.04 (t, 3H, J = 7.0 Hz, Me), 0.95 (t, 3H, J = 7.0 Hz, Me); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 171.3, 166.6, 142.9, 134.4, 134.3, 133.4, 132.2, 131.8, 131.0, 124.2, 123.6, 123.5, 123.4, 122.0, 91.7, 61.3, 27.9, 27.2, 11.3, 9.4; EI MS (*m/z*) 229 (15), 200 (100), 130 (42), 104 (45), 78 (71); EI HRMS (calculated for $C_{22}H_{20}N_2O_4$) 376.1423, found 376.1417.

Irradiation of 4NPHT-H/NaOH/1-hexyne. A solution of 4-nitrophthalimide (1.0 g, 5.2 mmol), NaOH (2.0 mL of a 1 *M* solution) and 1-hexyne (0.6 mL, 5.2 mmol) in 130 mL of acetonitrile and 20 mL of water was irradiated for 2 h to obtain **10a** (200 mg, 28%) and **10b** (120 mg, 47%) (75% at 30% conversion).

*2-[(E)-hex-1-enyl]-5-nitro-1H-isoindole-1,3(2H)-dione (**10a**).* Yellow syrup; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.67 (d, 1H, J = 2.0 Hz, H-4), 8.60 (dd, 1H, J = 8.0, 2.0 Hz, H-6), 8.04 (d, 1H, J = 8.0 Hz, H-7), 6.07 (ddd, 1H, J = 8.5, 7.1, 1.3 Hz, H-1′), 5.80 (m, 1H, H-2′), 2.05 (m, 2H, CH_2), 1.44 (m, 4H, 2 × CH_2), 0.85 (t, 3H, J = 7.1 Hz, Me); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 164.8, 164.5, 151.9, 136.4, 133.5, 129.4, 124.7, 119.0, 134.6, 115.6, 30.8, 28.0, 22.3, 13.6; EI MS (*m/z*) 274 (M^+, 5), 231 (68), 185 (46), 103 (33), 82 (100) ; EI HRMS (calculated for $C_{14}H_{14}N_2O_4$) 274.0954, found 274.0945.

*2-(1-Butylvinyl)-5-nitro-1H-isoindole-1,3(2H)-dione (**10b**).* Yellow syrup; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.63 (d, 1H, J = 2.0 Hz, H-4), 8.55 (dd, 1H, J = 7.9, 2.0 Hz, H-6), 8.02 (d, 1H, J = 7.9 Hz, H-7), 6.59 (m, 2H, H-vinyl), 2.16 (m, 2H, CH_2), 1.40 (m, 4H, 2 × CH_2), 0.90 (t, 3H, J = 7.0 Hz, Me); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 164.5, 164.3, 151.9, 136.1, 133.1, 129.5, 124.6, 118.8, 130.6, 117.1, 31.3, 30.7, 22.1, 13.9; EI MS (*m/z*) 274 (M^+, 10), 231 (100), 185 (52), 103 (43); EI HRMS (calculated for $C_{14}H_{14}N_2O_4$) 274.0954, found 274.0954.

Irradiation of 4-NPHT-H/NaOH/3-hexyne. A solution of 4-nitrophthalimide (1.0 g, 5.2 mmol), NaOH (2.0 mL of a 1 *M* solution) and 3-hexyne (0.6 mL, 5.0 mmol) in 130 mL of acetonitrile and 20 mL of water was irradiated for 45 min to obtain 217 mg of **11**, which was a 1:1 mixture of isomers *E* and *Z* (72% at 22% conversion).

*2-[(E)-1-ethylbut-1-enyl]-5-nitro-1H-isoindole-1,3(2H)-dione (**E-11**).* Yellow syrup; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.66 (d, 1H, J = 1.6 Hz, H-4), 8.59 (dd, 1H, J = 8.0, 1.6 Hz, H-6), 8.08 (d, 1H, J = 8.0 Hz, H-7), 5.50 (t, 1H, J = 7.4 Hz, H-2′), 2.43 (m, 2H, CH_2), 2.25 (m, 2H, CH_2), 1.08 (t, 3H, J = 7.4 Hz, Me), 0.93 (t, 3H, J = 7.6 Hz, Me); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 165.8, 165.5, 151.8, 136.3, 133.3, 129.3, 124.6, 118.8, 130.9, 134.3, 22.3, 20.8, 13.8, 11.7; EI MS (*m/z*) 274 (M^+, 12), 245 (100), 103 (28); EI HRMS (calculated for $C_{14}H_{14}N_2O_4$) 274.0954, found 274.0963.

*2-[(Z)-1-ethylbut-1-enyl]-5-nitro-1H-isoindole-1,3(2H)-dione (**Z-11**).* Yellow syrup; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.67 (d, 1H, J = 1.6 Hz, H-4), 8.60 (dd, 1H, J = 7.9, 1.6 Hz, H-6), 8.08 (d, 1H, J = 7.9 Hz, H-7), 5.73 (tt, 1H, J = 6.2, 6.2, 1.1, 1.1 Hz, H-2′), 2.32 (m, 2H, CH_2), 1.87 (m, 2H, CH_2), 1.03 (t, 3H, J = 7.4 Hz, Me), 0.96 (t, 3H, J = 7.6 Hz, Me); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 165.2, 164.9, 151.8, 136.3, 133.4, 129.3, 124.7, 118.9, 130.6, 131.9, 27.5, 21.3, 13.3, 11.4; EI MS (*m/z*) 274 (M^+, 12), 245 (100), 103 (43); EI HRMS (calculated for $C_{14}H_{14}N_2O_4$) 274.0954, found 274.0956.

Hydrolysis of 2-[2-phenylvinyl]-1H-isoindole-1,3(2H)-dione. A solution of ***E/Z-5*** (*viz.* a mixture of isomers *E/Z*, 50 mg, 0.2 mmol) in 10 mL of 1:1 THF-H_2O containing 50 μL of 98% H_2SO_4 was refluxed for 10 h, after which the solvent was removed under vacuum, the residue taken up in dichloromethane and the solution washed with 1 *M* NaOH. The organic layer was then concentrated to dryness to obtain 23 mg (96%) of phenylacetaldehyde. ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.79 (bs, 1H, CHO), 7.25 (m, 5H, ArH), 3.69 (m, 2H, CH_2).

Hydrolysis of 2-[(Z)-1-methyl-2-phenylvinyl]-1H-isoindole-1,3(2H)-dione. A solution of ***E/Z-6*** (50 mg, 0.2 mmol) was treated as above to obtain 24 mg (90%) of phenylacetone. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.40–7.10 (m, 5H, ArH), 3.70 (s, 2H, CH_2), 2.15 (s, 3H, Me).

RESULTS AND DISCUSSION

The longest wavelength absorption maximum of phthalimide in acetonitrile/water mixtures lies at 290 nm; the addition of NaOH results in a redshift in the absorption spectrum to λ_{max} 330 nm (5,13). Interestingly, although phthalimide and its *N*-alkyl derivatives are weakly fluorescent species (14,15), phthalimide anion (PHT-H/NaOH, ratio 2:3) exhibits maximum fluorescence emission at 440 nm ($\phi_F = 2.10^{-2}$), and its excitation spectrum agrees with the absorption spectrum.

Thus, at [NaOH] >> [PHT-H], phthalimide anion absorbs light (Pyrex filter) and undergoes regioselective [2+2] photocycloaddition to unactivated alkenes to give [2]benzazepinediones (11). Under these conditions, no reaction or quenching of the fluorescence is observed upon excitation of phthalimide anion in the presence of phenylethyne or 1-hexyne. In fact, neither reaction was found to occur on irradiating phthalimide in the presence of alkynes, whether conjugated or unconjugated, in the absence of NaOH.

However, keeping the concentration of base at a low enough level ensures that phthalimide will absorb light—no fluorescence from phthalimide anion will be detected. Thus, irradiation of a degassed (1:1:0.2) solution of phthalimide, phenylethyne and

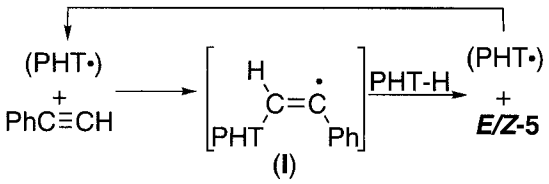

Figure 6. Alternative radical-chain mechanism for the irradiation at [PHT⁻] << [PHT-H] with unactivated alkynes.

NaOH in acetonitrile/water for 4 h resulted in the development of a deep yellow color. The reaction exhibited a low conversion (20%) and yielded an *E*/*Z* mixture of the hydrophthalimidation product (**5**) (89% based on the alkyne uptake) (Fig. 4). Prolonged irradiation times failed to increase the conversion.

At 300 nm, the UV/vis spectrum of **5** exhibits a strong absorption band (ε 24 685 for ***E*-5**, and 14 450 for ***Z*-5**) relative to phthalimide (ε 1565); therefore, as the reaction develops, light is absorbed by the enimide, which halts the process and leads to a photostationary mixture of the addition products. Under identical conditions, 1-phenylpropyne afforded a mixture of **E-6** and ***Z*-6**. Finally, irradiation in the presence of 1,2-diphenylethyne gave ***Z*-7** as the main product.

Various mechanisms are theoretically possible for this reaction (Fig. 5). SET to the excited phthalimide from either the alkyne or phthalimide anion might be the primary photoprocess. In the former case (path a), the cation-radical of the alkyne might react with phthalimide anion either through regioselective nucleophilic addition to give the vinyl radical (**I**) (path a_1) or electron transfer (path a_2) to produce the electrophilic phthalimidyl radical (reaction of the cation radical of the alkyne with other nucleophiles in the medium, water or hydroxide anion, was rejected because neither aldehydes or ketones were detected) (18,19).

Based on the oxidation potentials for the three alkynes (*viz.* 1.89 V for phenylethyne, 1.42 V for 1-phenylpropyne and 0.86 V for 1,2-diphenylethyne) as compared with the oxidation potential of phthalimide anion (1.46 V), SET from the phthalimide anion and the alkyne radical cation is expected to be more favorable than nucleophilic addition (path a_2).

The formation of this radical might also take place via SET from the phthalimide anion to exicted phthalimide (path b). The formation of the vinyl radical (**I**) would result from the regioselective radical addition of the phthalimidyl radical to the alkyne. The regioselectivity of this last pathway is well documented for the photochemical addition of halo-phthalimide to alkynes involving a radical chain reaction (20,21).

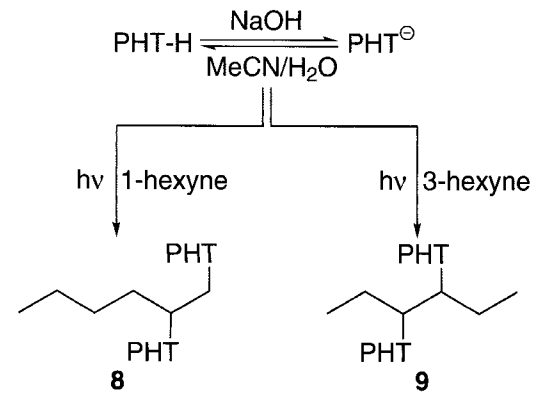

Figure 7. Irradiation of the system at [PHT⁻] << [PHT-H] with unconjugated alkynes.

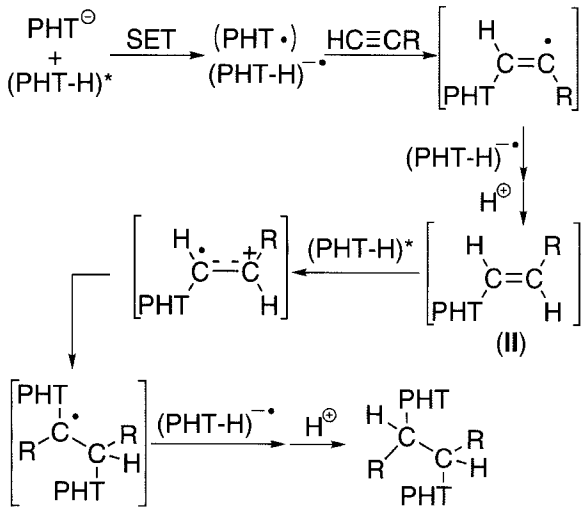

Figure 8. Proposed mechanism for the irradiation at [PHT⁻] << [PHT-H] with unactivated alkynes.

Back electron transfer from the anion-radical of phthalimide to **I** gave a vinyl anion, which was protonated. Consistent with this last step, the reaction in acetonitrile/D_2O involved the quantitative incorporation of deuterium at the benzylic position.

Also, the possibility of the vinyl-radical (**I**) capturing hydrogen from PHT-H (or PHT-D), an exoergic process by more than 30 kcal/mol, to regenerate the phthalimidyl radical and to undergo a radical chain reaction cannot be excluded (Fig. 6). However, we detected no products resulting from homocoupling or a reduction of the phthalimide anion-radical in the reaction (22).

With unconjugated alkynes such as 1-hexyne and 3-hexyne, irradiation under identical conditions as with the conjugated ones resulted in the double addition of phthalimide to the triple bond instead of the process leading to the hydrophthalimidation product (Fig. 7). Compound **8** was isolated in an 80% yield (29% conversion) and compound **9** in an 86% yield (30% conversion).

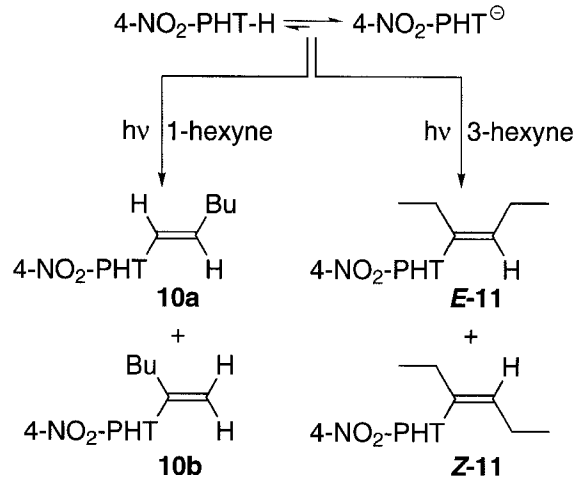

Figure 9. Irradiation of the system at [4-NO_2-PHT⁻] << [4-NO_2-PHT-H] with unactivated alkynes.

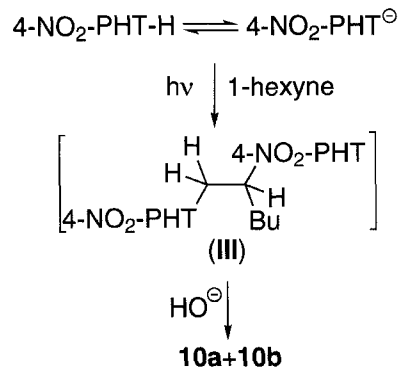

Figure 10. Phthalimide elimination.

With 1- and 3-hexyne, which possess a high oxidation potential (3.32 V and 2.48 V, respectively), the Weller equation predicts a highly unfavorable electron transfer ($\Delta G >> 0$) to the singlet excited state of the phthalimide; therefore, SET can take place only from the phthalimide anion and path b must operate in the process leading to the unconjugated vinyl-phthalimide (Fig. 8).

Addition of the electrophilic phthalimidyl radical to the alkyne gave the vinyl radical, which afforded the enimide (**II**) after back electron transfer and protonation. This vinyl phthalimide behaves as an electron-rich alkene with an oxidation potential low enough to ensure an SET to excited phthalimide. A second regioselective addition of the phthalimide anion to the cation-radical, followed by BET (back electron transfer) and protonation, gave the end product. However, the possibility of a second addition of phthalimidyl radical to **II** cannot be excluded.

The insertion of a nitro group at position 4 in the phthalimide was expected to lower the reduction potential more markedly than should the energy of the excited state of the imide, thus facilitating the primary electron transfer from unconjugated alkynes. In fact, irradiation of 4-nitrophthalimide and 1-hexyne (Fig. 9) gave a mixture of the vinylphthalimides **10a** (28%) and **10b** (47%) (at 30% conversion).

Although the formation of **10a** exhibits the same regioselectivity observed with the other conjugated alkynes, the reverse regioselective addition to **10b** is unlikely to follow the same mechanism. More probably, both compounds are formed through phthalimide elimination of the double addition product (**III**) by the hydroxyl anion (Fig. 10).

The same result was obtained by irradiating with 3-hexyne; a 72% mixture of isomers ***E*-11** and ***Z*-11**, at 22% conversion, was isolated.

The photochemical hydrophthalimidation of alkynes is of doubtless interest regarding the synthetic applications of vinylphthalimides; in addition, the enimides can be hydrolyzed to the corresponding carbonyl compounds. Treatment of the mixture of ***E*/*Z*-5** and ***E*/*Z*-6** in THF/H_2O with an acid catalyst (Cat. H_2SO_4) afforded phenylacetaldehyde and phenylacetone, respectively, in quantitative yield, so it must involve the regioselective anti-Markovnikov hydration of alkynes with light and water as the reagents (Fig. 11).

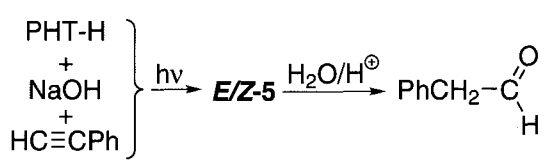

Figure 11. Regioselective anti-Markovnikov hydration of alkynes.

Unfortunately, the reaction is quenched by photophthalimidation products that reduce conversion to levels precluding synthetic application of this novel process. The use of the phthalimide anion and of other SET photosensitizers absorbing at longer wavelengths than phthalimide is currently being examined with a view to making this reaction synthetically competitive with the base or metal catalyzed thermal hydroamination of alkynes (23).

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