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Single Electron Transfer Promoted Photocyclization Reactions of (ω-Phthalimidoalkylthio)acetic Acids

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Studies have been conducted to explore single electron transfer (SET) promoted photocyclization reactions of (ω-phthalimidoalkylthio)acetic acids (alkyl=ethyl, n-propyl, n-butyl, n-hexyl and n-nonyl). Photocyclizations occur in methanol in modest yields to produce cyclized products in which phthalimide carbonyl carbon is bonded to the carbon of side chain in place of the carboxylic group. The initially formed cyclized products undergo efficient water eliminations to produce enthiol ethers in secondary ground state reactions.

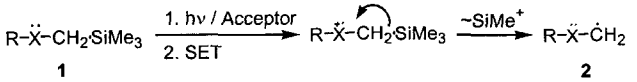
key words: photocyclizations, (ω-phthalimidoalkylthio)acetic acids, sequential single electron transfer-decarboxylation pathways

INTRODUCTION

There have been a number of reports on photocyclization reactions of N-substituted phthalimides leading to new heterocycles with either nitrogen and oxygen, nitrogen and sulfur or nitrogen and nitrogen atoms in the newly formed ring [2]. However the photocyclization reactions operated by a mechanistic route involving intramolecular hydrogen abstraction by excited phthalimide carbonyls or sequential single electron transfer(SET)-deprotonation and they suffered from both low regioselectivities and low product yields.

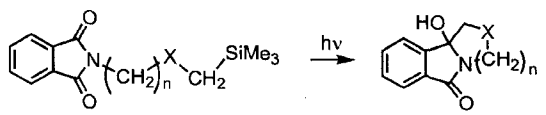
Our studies of SET photochemistry using α-silyl electron donors **1** have shown that photoinduced sequential SET-desilylation serves as an efficient and highly regioselective pathway for carbon centered radical **2** generation [3] (Scheme 1).

Phthalimides have been found to undergo smooth photoaddition reactions in methanol with α-silyl electron donors (**1**: X=O, S or NEt_2) to generate 3-substituted products *via* mechanistic routes which involve sequential SET-desilylation [4]. Similarly phthalimides tethered with α-silyl ether, thioether or amido groups(**3**: X=O, S or NAc) undergo efficient and high yielding photocyclization reactions to provide medium and large ring heterocycles **4** [5-8] (Scheme 2).



1 **2**

Scheme 1.

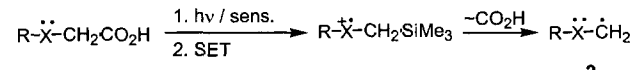


3 : X = O, S or NAc **4**

Scheme 2.

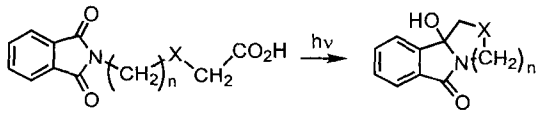
Early studies by Davidson have shown that sensitized photochemical reactions of α-heteroatom substituted carboxylic acids **5** with sensitizers such as biacetyl, aromatic ketones, quinones [9] and aromatic nitro compounds [10] lead efficient decarboxylation to generate carbon centered radical **2** *via* pathways involving SET from the carboxylic acids **5** to the excited states of sensitizers followed by decarboxylation (Scheme 3).

Results from our previous investigations of SET-promoted photocyclization reactions of phthalimides with α-silyl electron donors [5-8] and from Davidson's studies of sensitized photochemical reactions of carboxylic acids [9-10] suggest that SET-promoted photocyclization reactions of phthalimides tethered with α-heteroatom substituted carboxylic acids **6** will be efficient and might provide a regioselective route to various heteocycles (Scheme 4).



5: X = O, S or NH **2**

Scheme 3.



6: X = O, S or NAc

Scheme 4.

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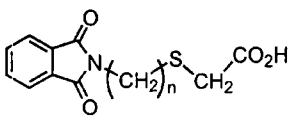


7a (n=2)
7b (n=3)
7c (n=4)
7d (n=6)
7e (n=10)

The studies for the photochemistry of (ω-phthalimidoalkoxy) acetic acids(**6**:X=O) have shown [11-12] that (ω-phthalimidoalkoxy) acetic acids(**6**:X=O, n=2~6) undergo efficient and regioselective photocyclization reactions to provide oxazaheterocycles via sequential SET-decarboxylation pathways.

In a continuation of our investigations aimed at developing new SET-promoted photochemical reactions of synthetic utility, we have explored photochemical reactions of (ω-phthalimidoalkylthio)acetic acids [**7a-e**].

The results of this effort, reported below, show that (ω-phthalimidoalkylthio)acetic acids (**7a-e**) also undergo efficient and regioselective photocyclization reactions exclusively *via* sequential SET-decarboxylation pathways.

MATERIALS AND METHODS

General Procedures

^{1}H nuclear magnetic resonance(NMR) and ^{13}C-NMR spectra were recorded using 200 MHz and 300 MHz spectrometers and chemical shifts are reported in parts per million downfield from tetramethylsilane employed as an internal standard; abbreviations used are s(singlet), d(doublet), t(triplet) and m(multiplet). Preparative photolyses were conducted with an apparatus consisting of a 450 W medium pressure mercury lamp surrounded by a Pyrex filter in a quartz immersion well under an inert atmosphere. Low and high resolution mass spectral analyses were performed by 70 eV on mass spectrometer.

*Preparations of ω-Phthalimidoalkyl Bromides (**8a-d**)*

ω-Phthalimidoalkyl bromides were propared by using reported method. Physical properties of prepared **8a**, **8c-d** are identical to those reported [13] and spectral data for **8b** are followings. Spectral data for **8b**; ^{1}H-NMR($CDCl_3$) δ 1.27-1.48(m, 10H, $NCH_2CH_2CH_2(C\underline{H}_2)_5$), 1.64-1.70(m, 2H, $NCH_2CH_2C\underline{H}_2$), 1.79-1.86(m, 2H, $NCH_2C\underline{H}_2$), 3.35-3.43(m, 2H, $C\underline{H}_2Br$), 3.66(t, 2H, J =7.2Hz, NCH_2), 7.69-7.84(m, 4H, aromatic); ^{13}C-NMR($CDCl_3$) δ 26.3(CH_2Br), 27.7, 28.1, 28.2, 28.6 and 28.8(CH_2), 32.4 ($NCH_2CH_2\underline{C}H_2$), 33.5($NCH_2\underline{C}H_2$), 37.5($NCH_2$), 122.6 and 133.4 (CH, aromatic), 131.7(C, aromatic), 167.7(C=O); IR(KBr) 1710 (C=O, stretching); MS(EI), m/z(rel. intensity) 351(M^+, 42), 272(6), 202(4), 174(13), 160(100), 133(14), 77(22); HRMS(EI), m/z 351.0812 ($C_{17}H_{22}BrNO_2$ requires 351.0834).

*Preparations of Ethyl (3-Bromopropylthio)acetate (**11**)*

To a solution of trimethylene sulfide (3.11 g, 41.9 mmol) in CH_3CN(20 mL) was added ethyl bromoacetate (7.00 g, 41.9 mmol) and the reaction mixture was heated for 24h at 80°C. After removal of CH_3CN under reduced pressure, the residue was subjected to column chromatography (silica, hexane) yielding ethyl (3-bromopropylthio)acetate (**11**, 5.06 g, 53%). Spectral data for **11**; ^{1}H-NMR($CDCl_3$) δ 1.12(t, 3H, J=7.1Hz, CH_3), 1.97(quint, 2H, J= 6.6Hz, $BrCH_2C\underline{H}_2$), 2.54-2.72(m, 2H, $CH_2C\underline{H}_2S$), 3.05(s, 2H, CH_2CO_2), 3.35(t, 2H, J=6.4Hz, $BrCH_2$), 4.02(q, 2H, J=7.1Hz, $C\underline{H}_2CH_3$); ^{13}C-NMR($CDCl_3$) δ 13.8(CH_3), 30.5($BrCH_2$), 31.4 ($BrCH_2\underline{C}H_2$), 31.5(CH_2S), 33.3($\underline{C}H_2CO_2$), 60.9($\underline{C}H_2CH_3$), 169.7 (C=O); IR(KBr) 1720(C=O stretching).

*Preparations of Ethyl (3-Phthalimidopropylthio)acetates (**9b**)*

To a solution of ethyl (3-bromopropylthio)acetate (**11**, 8.60 g, 37.7 mmol) in DMF (20 mL) was added potassium phthalimide (6.98 g, 37.7 mol) and the reaction mixture was heated for 4 h at 80°C. After removal of DMF *in vacuo*, the residue was dissolved in CH_2Cl_2 and filtered. Concentration of the filtrate and column chromatography (silica, chloroform) gave 9.03 g(78%) **9b**. Spectral data for **9b**; ^{1}H-NMR($CDCl_3$) δ 1.15(t, 3H, J=4.7Hz, CH_3), 1.57-1.92(m, 2H, $NCH_2C\underline{H}_2$), 2.59(t, 2H, J=4.7Hz, $NCH_2CH_2C\underline{H}_2$), 3.12(s, 2H, CH_2CO_2), 3.69(t, 2H, J=5.7Hz NCH_2), 4.06(q, 2H, J=4.8Hz, $C\underline{H}_2CH_3$), 7.60-7.65(m, 2H, aromatic), 7.71-7.74(m, 2H, aromatic); ^{13}C-NMR($CDCl_3$) δ 13.9(CH_3), 27.6($NCH_2\underline{C}H_2$), 29.6($NCH_2CH_2\underline{C}H_2$), 33.2($NCH_2$), 36.6($\underline{C}H_2CO_2$), 61.0($\underline{C}H_2CH_3$), 123.0 and 133.7(CH, aromatic), 131.9(C, aromatic), 168.0(C=O), 170.0(CO_2); IR(KBr) 1700(C=O, stretching); MS(EI), m/z(rel. intensity) 307(M^+, 9), 261(52), 188(36), 160(100), 104(27); HRMS (EI), m/z 307.0874($C_{15}H_{17}NO_4S$ requires 307.0878).

*Preparations of Ethyl (ω-Phthalimidoalkylthio)acetates (**9a, 9c-e**)*

A mixture of ethyl mercaptoacetate [14] (1.60 g, 13.3 mmol) and sodium hydride (0.32 g, 13.3 mmol) in DMF (20 mL) was stirred at 0°C under N_2 for 1 h. To the mixture ω-phthalimidoalkyl bromides(20.0 mmol, **8a**, 5.06 g; **8c**, 5.62 g; **8d**, 6.18 g; **8e**, 7.02 g) in DMF (10 mL) was added and heated for 8 h at 80°C. After removal of DMF *in vacuo*, the residue was dissolved in CH_2Cl_2 and filtered. Concentration of the filterate and column cromatography (silica, chloroform) gave ethyl (ω-phthalimidoalkylthio)acetates (**9a**, 2.49 g, 64%; **9c**, 3.12 g, 73%; **9d**, 3.03 g, 65%; **9e**, 3.90 g, 75%). Spectral data for **9a**; ^{1}H-NMR ($CDCl_3$) δ 1.27(t, 3H, J=7.6Hz, CH_3), 2.97(t, 2H, J=7.3Hz, $NCH_2C\underline{H}_2$), 3.32(s, 2H, CH_2CO_2), 3.75(t, 2H, J=4.5Hz, NCH_2), 4.20(q, 2H, J=4.8Hz, $C\underline{H}_2CH_3$), 7.72-7.75(m, 2H, aromatic), 7.83-7.88(m, 2H, aromatic); ^{13}C-NMR ($CDCl_3$) δ 14.0(CH_3), 30.3($NCH_2\underline{C}H_3$), 32.6(NCH_2), 36.0($\underline{C}H_2CO_2$), 61.2($\underline{C}H_2CH_3$), 123.2 and 133.9(CH, aromatic), 131.9(C, aromatic), 167.9(C=O), 170.0(CO_2); IR(KBr) 1710(C=O, stretching); MS(EI), m/z(rel. intensity) 293(M^+, 9), 247(41), 193(8), 160(79), 119(39), 105(14), 77(38), 59(100); HRMS(EI), m/z 293.0725($C_{14}H_{15}NO_4S$ requires 293.0722). Spectral data for **9c**; 1.05(t, 3H, J=7.4Hz, CH_3), 1.42-1.82(m, 4H, $NCH_2C\underline{H}_2C\underline{H}_2$), 2.49(t, 2H, J=5.4Hz, $CH_2C\underline{H}_2S$), 2.99(s, 2H, CH_2CO_2), 3.49(t, 2H, J=2.6Hz, NCH_2), 3.95(q, 2H, J=5.4Hz, $C\underline{H}_2CH_3$), 7.50-7.82(m, 4H, aromatic); ^{13}C-NMR($CDCl_3$) δ 13.1(CH_3), 25.8, 27.1, 31.5 and 33.1(CH_2), 37.0 ($\underline{C}H_2CO_2$), 60.6($\underline{C}H_2CH_3$), 122.6 and 136.4(CH, aromatic), 131.6

(C, aromatic), 167.7(C=O), 170.6(CO_2); IR(KBr) 1680(C=O, stretching); MS(EI), m/z(rel. intensity) 321(M^+, 36), 275(46), 234(9), 200(15), 160(100), 148(13), 130(18); HRMS(EI), m/z 321.1025 ($C_{16}H_{19}NO_4S$ requires 321.1035). Spectral data for **9d**; 1.29(t, 3H, J=7.2Hz, CH_3), 1.37-1.72(m, 8H, $NCH_2(CH_2)_4$), 2.63(t, 2H, J=7.2Hz, CH_2CH_2S), 3.20(s, 2H, CH_2CO_2), 3.68(t, 2H, J=7.2Hz, NCH_2), 4.18(q, 2H, J=7.1Hz, CH_2CH_3), 7.70-7.86(m, 4H, aromatic); ^{13}C-NMR($CDCl_3$) δ 14.0(CH_3), 26.1, 28.0, 28.2, 28.5, 32.2 and 33.4(CH_2), 37.6(CH_2CO_2), 60.9(CH_2CH_3), 122.9 and 133.6(CH, aromatic), 131.9(C, aromatic), 168.1(C=O), 170.2(CO_2); IR(KBr) 1720(C=O, stretching); MS(CI), m/z(rel. intensity) 350(M^++1, 36), 349(M^+, 31), 276(48), 228(55), 174(27), 160(100), 130(54), 115(75); HRMS(CI), m/z 350.1420($C_{18}H_{24}NO_4S$ requires 350.1426). Spectral data for **9e**; 1.20-1.61(m, 17H, $NCH_2(CH_2)_7CH_2SCH_2CO_2CH_2CH_3$), 2.57(t, 2H, J=7.3Hz, CH_2CH_2S), 3.15(s, 2H, CH_2CO_2), 3.62(t, 2H, J=7.2Hz, NCH_2), 4.06-4.22(m, 2H, CH_2CH_3), 7.64-7.81(m, 4H, aromatic); ^{13}C-NMR($CDCl_3$) δ 14.1(CH_3), 26.7, 28.4, 28.5, 28.6, 28.9, 29.0, 29.2, 32.6 and 33.6(CH_2), 37.9(CH_2CO_2), 61.6 (CH_2CH_3), 123.0 and 133.8(CH, aromatic), 132.1(C, aromatic), 168.4(C=O), 169.2(CO_2); IR(KBr) 1710(C=O, stretching); MS(EI), m/z(rel. intensity) 391(M^+, 4), 345(49), 304(17), 272(3), 174(28), 160(100), 130(14); HRMS(EI), m/z 391.1842($C_{21}H_{29}NO_4S$ requires 391.1817).

*Preparations of (ω-Phthalimidoalkylthio)acetic Acids (**7a-e**)*

To a solution of ethyl (ω-phthalimidoalkylthio)acetates (12.6 mmol, **9a**, 3.70 g; **9b**, 3.87 g; **9c**, 4.05 g; **9d**, 4.41 g; **9e**, 4.93 g) in 1,4-dioxane (10 mL) was added 35% HCl (2.5 mL) and the reaction mixture was heated for 7 h at 80°C. After removal of 1,4-dioxane under reduced pressure, the residue was subjected to column chromatography (silica, chloroform : ethyl acetate=4:1) yielding (ω-phthalimidoalky thio)acetic acids (**7a**, 1.88 g, 56%; **7b**, 1.87 g, 53%; **7c**, 2.11 g, 57%; **7d**, 2.15 g, 53%; **7e**, 2.11 g, 46%). Spectral data for **7a**; mp 108-112°C; ^{1}H-NMR ($CDCl_3$) δ 3.02(t, 2H, J=4.4Hz, NCH_2CH_2), 3.36(s, 2H, CH_2CO_2H), 3.96(t, 2H, J=5.3Hz, NCH_2), 7.71-7.87(m, 4H, aromatic), 9.3(s, 1H, CO_2H); ^{13}C-NMR($CDCl_3$) δ 30.5(NCH_2CH_2), 32.4(NCH_2), 36.0 (CH_2CO_2H), 123.4 and 134.0(CH, aromatic), 131.9(C, aromatic), 168.2(C=O), 175.6(CO_2H); IR(KBr) 3450-3100(br, OH stretching), 1770(C=O stretching); MS(CI), m/z(rel. intensity) 266(M^++1, 5), 265(M^+, 4), 247(70), 188(21), 160(100), 148(72), 117(7), 104(46); HRMS(CI), m/z 266.0487($C_{12}H_{12}NO_4S$ requires 266.0487). Spectral data for **7b**; mp 86-90°C; ^{1}H-NMR ($CDCl_3$) δ 1.93-2.03(m, 2H, NCH_2CH_2), 2.69(t, 2H, J=4.8Hz, $NCH_2CH_2CH_2$), 3.23(s, 2H, CH_2CO_2H), 3.77(t, 2H, J=4.6Hz, NCH_2), 7.66-7.81(m, 4H, aromatic), 9.4(s, 1H, CO_2H); ^{13}C-NMR($CDCl_3$) δ 27.6, 30.4 and 33.1(CH_2), 36.5(CH_2CO_2H), 123.2 and 133.9(CH, aromatic), 132.0 (C, aromatic), 169.0(C=O), 174.5(CO_2H); IR(KBr) 3380-3100 (br, OH stretching), 1700(C=O, stretching); MS(CI), m/z(rel. intensity) 280(M^++1, 0.2), 261(6), 221(9), 187(34), 160(100), 147 (15), 133(16); HRMS(CI), m/z 280.0661($C_{13}H_{14}NO_4S$ requires 280.0644). Spectral data for **7c**; mp 86-90°C; ^{1}H-NMR ($CDCl_3$) δ 1.67 -1.83(m, 4H, $NCH_2CH_2CH_2$), 2.72(t, 2H, J=4.8Hz, $CH_2SCH_2CO_2H$), 3.25(s, 2H, CH_2CO_2H), 3.70(t, 2H, J=4.6Hz, NCH_2), 7.70-7.85 (m, 4H, aromatic), 10.5(s, 1H, CO_2H); ^{13}C-NMR($CDCl_3$) δ 26.0, 27.4, 32.0 and 33.3(CH_2), 37.2(CH_2CO_2H), 123.1 and 133.8(CH, aromatic), 131.9(C, aromatic), 168.3(C=O), 175.8(CO_2H); IR(KBr) 3480-3100(br, OH stretching), 1720(C=O, stretching); MS(CI), m/z(rel. intensity) 294(M^++1, 1), 275(32), 202(65), 173(26), 160 (100), 148(44), 130(58); HRMS(CI), m/z 294.0802($C_{14}H_{16}NO_4S$ requires 294.0800). Spectral data for **7d**; mp 92-94°C; ^{1}H-NMR ($CDCl_3$) δ 1.36-1.72(m, 8H, $NCH_2(CH_2)_4$), 2.66(t, 2H, J=4.8Hz, $CH_2SCH_2CO_2H$), 3.24(s, 2H, CH_2CO_2H), 3.68(t, 2H, J=5.2Hz, NCH_2), 7.69-7.87(m, 4H, aromatic), 9.2(s, 1H, CO_2H); ^{13}C-NMR ($CDCl_3$) δ 26.1, 27.9, 28.2, 28.4, 32.4 and 33.2(CH_2), 37.7 (CH_2CO_2H), 123.0 and 133.7(CH, aromatic), 131.9(C, aromatic), 168.3(C=O), 175.6(CO_2H); IR(KBr) 3500-3100(br, OH stretching), 1720(C=O, stretching); MS(CI), m/z(rel. intensity) 322(M^++1, 0.6), 303(5), 263(5), 230(17), 186(9), 174(14), 160(100), 148(35), 130(32); HRMS(CI), m/z 322.1860($C_{16}H_{20}NO_4S$ requires 322.1068). Spectral data for **7e**; mp 78-81°C; ^{1}H-NMR ($CDCl_3$) δ 1.26-1.66(m, 14H, $NCH_2(CH_2)_7$), 2.61(t, 2H, J=7.3Hz, $CH_2SCH_2CO_2H$), 3.21 (s, 2H, CH_2CO_2H), 3.64(t, 2H, J=7.2Hz, NCH_2), 7.63-7.83(m, 4H, aromatic), 8.8(s, 1H, CO_2H); ^{13}C-NMR($CDCl_3$) δ 26.7, 28.1, 28.5, 28.9, 29.0, 29.1, 29.4, 32.5 and 33.1(CH_2), 37.5(CH_2CO_2H), 123.1 and 133.8(CH, aromatic), 131.2(C, aromatic), 168.2(C=O), 176.1(CO_2H); IR(KBr) 3400-3150(br, OH stretching), 1690(C=O, stretching).

*Irradiations of (ω-Phthalimidoalkylthio)acetic Acids (**7a-e**)*

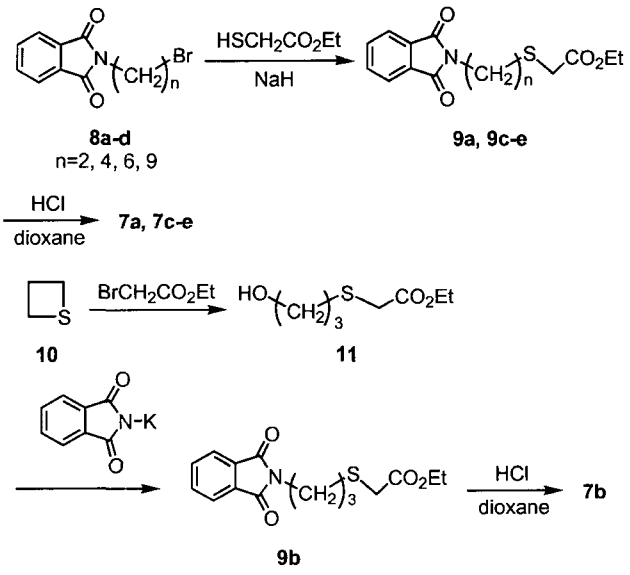
A solution of (ω-phthalimidoalkylthio)acetic acids (**7a**, 500 mg, 1.88 mmol; **7b**, 500 mg, 1.78 mmol; **7c**, 400 mg, 1.36 mmol; **7d**, 600 mg, 1.86 mmol; **7e**, 400 mg, 1.10 mmol) in 200 mL of methanol was irradiated with Pyrex-filtered light under N_2. Concentration of the photolyzate gave a residue which was subjected to column chromatography (silica, ethyl acetate:$CHCl_3$ =1:1) yielding photoproducts(**12a**, 36 mg, 19%; **15**, 20 mg, 13%; **12b**, 117 mg, 35%; **12c**, trace; **13a**, 70 mg, 33%; **13b**, 130 mg, 32%; **13c**, 191 mg, 72%; **14**, 50 mg, 19%). All physical properties of photoproducts **12a-c**, **13a-b** and **15** are identical to those of reported [5]. Spectral data for **13c**; ^{1}H-NMR ($CDCl_3$) δ 1.16-1.50(m, 10H, $SCH_2CH_2(CH_2)_5CH_2CH_2N$), 1.50-1.75(m, 4H, SCH_2CH_2 and NCH_2CH_2), 2.84(t, 2H, J=5.0Hz, SCH_2), 4.15(t, 2H, J=7.8Hz, NCH_2), 6.10(s, 1H, alkenic), 7.37-7.58(m, 3H, aromatic), 7.76(d, 1H, J=7.4Hz, aromatic); ^{13}C-NMR($CDCl_3$) δ 23.1, 24.0, 25.8, 26.1, 26.5 and 26.8(CH_2), 38.5(SCH_2), 40.5(NCH_2), 104.5(alkenic CH), 118.6, 122.9, 128.2 and 131.4(CH, aromatic), 127.6(alkenic C), 135.0 and 137.6(C, aromatic); MS(EI), m/z(rel. intensity) 301(M^+, 51), 268(10), 188(42), 160(100), 146(31), 130(28), 84(94); HRMS(EI), m/z 301.1500($C_{18}H_{28}NOS$ requires 301.1500). Spectral data for **14**; ^{1}H-NMR ($CDCl_3$) δ 1.10-1.50(m, 10H, $SCH_2CH_2(CH_2)_5CH_2CH_2N$), 1.69(quint, 2H, J=6.8Hz, SCH_2CH_2), 1.81(quint, 2H, J=6.8Hz, NCH_2CH_2), 2.85(t, 2H, J=6.8Hz, SCH_2), 3.73(t, 2H, J=6.8Hz, NCH_2), 5.97(s, 1H, alkenic), 7.43(t, 1H, J=7.4Hz, aromatic), 7.54(t, 1H, J=7.6Hz, aromatic), 7.80(d, 1H, J=7.4Hz, aromatic), 8.14(d, 1H, J=7.6Hz, aromatic); ^{13}C-NMR($CDCl_3$) δ 24.1, 24.9, 25.3, 25.5, 25.8 and 25.9(CH_2), 34.3(SCH_2), 38.8(NCH_2), 108.9(alkenic CH), 122.9, 124.0, 128.4 and 131.6(C, aromatic), 129.7(alkenic

C), 133.4 and 134.7(C, aromatic); MS(EI), m/z(rel. intensity) 301(M^+, 70), 268(14), 188(49), 160(100), 146(45), 130(30), 84(36); HRMS(EI), m/z 301.1503($C_{18}H_{28}NOS$ requires 301.1500).

RESULTS AND DICUSSION

Preparations of (ω-Phthalimidoalkylthio)acetic Acids

For these photochemical studies five (ω-phthalimidoalkylthio) acetic acids (**7a-e**) were selected and prepared in modest to good yields starting with ω-phthalimidoalkyl bromide **8a-d** or trimethylene sulfide **10** by use of the reaction sequences outlined in Scheme 5 (see Materials and Method section).



Scheme 5.

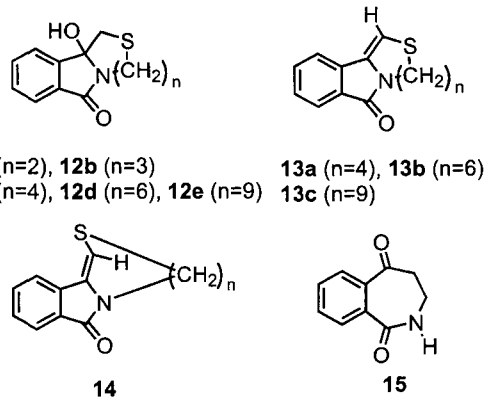
Photocyclizations of (ω-Phthalimidoalkythio)acetic Acids

Photocyclization reactions of (ω-phthalimidoalkylthio)acetic acies **7a-e** were explored. Preparative photocyclization reactions were performed by irradiation of methanol or acetone solutions of phthalimides (5.5-9.4 mM) by using Pyrex glass filtered-light (λ>290 nm) and products were separated by silica gel chromatography (see Materials and Methods section). Products distribution and yields along with reaction conditions employed were given in Table 1.

Table 1. Photochemical Reactions of (ω-Phthalimidoalkylthio) acetic Acids in Methanol

Phthalimide	Concentration (mM)	Reaction Time(h)	Conversion (%)	Product (yields)[a]
7a	9.4	9	46	**12a** (19) **15** (13)
7b	8.9	9	80	**12b** (35)
7c	6.9	9	68	**12c** (trace) **13a** (33)
7d	9.3	9	84	**13b** (32)
7e	5.5	9	80	**13c** (72) **14** (19)

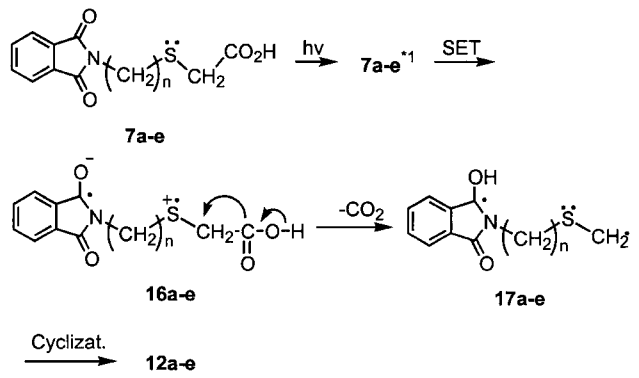
[a]Yields are based on consumed acetic acids **7a-e**.



Irradiation of (ω-phthalimidoalkylthio)acetic acids **7a-b** in methanol leads to modest yielding production of the cyclized products **12a-b** as the major products. Except in the case of (ω-phthalimidoalkylthio)acetic acids **7a-b** irradiations of phthalimides **7c-e** which contain longer alkyl units (n=4, 6, 9) in methanol lead to production of enthiol ethers **13b-c**, **14** as the major products. The yields of cyclized products and entiol ethers increased as ring size of the cyclized products. In photoreactions of **7d-e** (n=6, 9), the enthiol ether products **13a-c**, **14** become the exclusive products. In the case of (ω-phthalimidononylthio)acetic acids **7e,** two geoisomeric enthiol ether products **13c** and **14** are observed as a ratio of 7 to 2 (Z/E). The internal enthiol ethers are believed to be formed by dehydration of cyclized product **12b-e** which are formed by irradiation of phthalimides **7b-e**.

Strutural assignments to the photoadducts **12a-c**, **13a-b** were made on the basis of spectroscopic data which are identical to those reported earlier [5]. Structural assignments of two geoisomeric products **13e** and **14** were also made on the basis of spectroscopic data (see Materials and Methods Section). ^{13}C-NMR spectra of **13e** and **14** have resonace at 108.9 and 104.5 ppm (CH), and at 129.7 and 127.6 ppm (C) for their two olefinic carbons. Further their ^{1}H-NMR also show resonances at 6.10 and 5.97 ppm for the olefinic hydrogens respectively which indicate that product **13e** is (Z)-isomer while **14** has (E)-configuration around the double bonds. The resonance at 6.10 ppm for olefinic hydrogen of **13e** is more close to those of **13a-b** (6.31 and 6.20 ppm) [5] which contain all (Z)-configurations comparing with that of **14** (5.97 ppm).

The observations presented above show that (ω-phthalimidoalkylthio)acetic acids undergo photocyclization in methanol with high degree of chemoselectivity and regioselectivity to generate heterocycles with nitrogen and sulfur in the newly formed ring of various size (six to thirteen membered) in which the phthalimide carbonyl carbon is bonded to the α-sulfur atom in place of the carboxyl group. Except in the case of (ω-phthalimidoalkylthio)acetic acids **7a-b,** the initially formed photocyclization products **12c-e** undergo water elimination to yield olefinic products **13a-c** and **14** in secondary ground state reactions [4,6]. The generation of benzazepindione **15** in



Scheme 6.

photoreaction of (ω-phthalimidoethylthio)acetic acid (**7a**) has precedents in the photocyclizations of N-butylphthalimide and phthalimide-α-silyl-n-electron donor systems [5-7] and is believed to occur *via* triplet two-fold Norrish type II reactions. Results obtained in this study and those of our earlier investigations of photoinduced SET reactions of phthalimide-α-silyl-n-electron donor systems [4-7] and (ω-phthalimidoalkoxy) acetic acids [11] in methanol suggest that photocyclization in methanol leadings to **12a-e** occur *via* excited singlet state SET pathway (Scheme 6). Intramolecular SET in singlet excited phthalimides (**7a-e**^{*1}) results in generation of zwitterionic radical intermediates **16a-e** which undergo exculsive deproto-decarboxylation leading to biradicals **17a-e**. Biradical **17a-e** then undergo cyclization to produce cyclized products **12a-e**.

This study demonstrates that photoreactions of (ω-phthalimidoalkylthio)acetic acids lead to modest yielding production of cyclized products with high degree of chemoselectivity and regioselectivity.

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