Journal of Photoscience (2000), Vol. 7(4), pp. 143 - 148

Photocyclization Reactions of (ω-Phthalimidoalkoxy)acetic Acids *via* Sequential Single Electron Transfer-Decarboxylation Pathways

Ung Chan Yoon*, Chan Woo Lee[1], Sun Wha Oh, Hyun Jin Kim and Sang Jin Lee
Department of Chemistry and the Chemistry Institute for Functional Materials, Pusan National University, Pusan 609-735, Korea

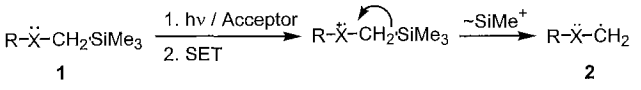
Studies have been conducted to explore single electron transfer (SET) promoted photocyclization reactions of (ω-phthalimidoalkoxy)acetic acids(alkoxy=ethoxy, n-propoxy and n-butyloxy). Photocyclizations occur in methanol or acetone in high yields to produce cyclized products in which phthalimide carbonyl carbon is bonded to the carbon of side chain in place of the carboxylic group. These photocyclizations are thought to proceed through pathways involving intramolecular SET from oxygen in the α-carboxymethoxy groups to the singlet excited state phthalimide moieties followed by decarboxylation of the intermediate α-carboxymethoxy cation radicals and cyclizations by radical coupling. The photocyclizations occur *ca.* three times faster in both methanol or acetone with one equivalent of sodium hydroxide added to the reactions and occur slower in acetone than in methanol. The efficient and regioselective cyclization reactions observed for photolyses in methanol represent synthetically useful processes for construction of heterocyclic compounds.

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

INTRODUCTION

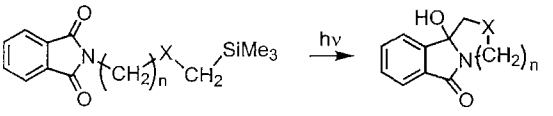
There have been a number of reports on photocyclization reactions of N-substituted phthalimides leading to new heterocycles with either nitrogen and oxygen, nitrogen and sulfur or nitrogen and nitrogen atoms in the newly formed ring [2]. However the photocyclization reactions operated by a mechanistic 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] (Scheme1).



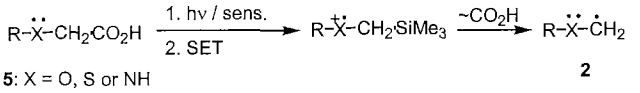
Scheme 1.

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 ?-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** [5-7] (Scheme 2).



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, quinines [8] and aromatic nitro compounds [9] 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).

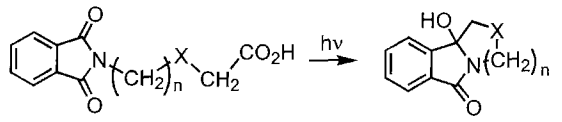


Scheme 3.

Results from our previous investigations of SET-promoted photocyclization reactions of phthalimides with α-silyl electron donors [5-7] and from Davidson's studies of sen-

*To whom correspondence should be addressed.
E-mail : ucyoon@hyowon.cc.pusan.ac.kr
Received 30 October 2000; accepted 5 December 2000

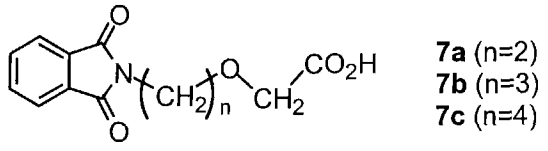
sitized photochemical reactions of carboxylic acids [8] suggest that SET-promoted photocyclization reactions of phthalimides tethered with α-heteroatom substituted carboxylic acids **6** will be efficient and might provide a regioselective route to various heteocycles (Scheme 4).



6: X = O, S or NAc

Scheme 4.

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



7a (n=2)
7b (n=3)
7c (n=4)

The results of this effort, reported below, show that (ω-phthalimidoalkoxy)acetic acids (**7a-c**) 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 Ethyl (ω-Hydroxyalkoxy)acetates (9a-c)

To excess amount of ethylene glycol (**8a**, 14.9 g, 0.24 mol), 1,3-propandiol (**8b**, 18.3 g, 0.24 mol) or 1,4-butandiol (**8c**, 16.2 g, 0.18 mol) was added Na metal (1.38 g, 0.06 mol) portionwise over a 24 h period with stirring. To this solution was added ethyl bromoacetate (10.0 g, 0.06 mol) dropwise and the resulting mixture was heated for 5 h at room temperature. The mixture was extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried and concentrated in reduced pressure to a residue. The residue was subjected to column chromatography (hexane:CHCl3=3:1) to give ethyl(ω-hydroxyalkoxy)acetates (**9a**, 8.17 g, 92%; **9b**, 7.39 g, 76%; **9c**, 8.88 g, 84%). Spectral data for **9a**; ^{1}H-NMR($CDCl_3$) δ 1.24(t, 3H, J=7.2Hz, $CO_2CH_2C\underline{H}_3$), 2.90(br, 1H, OH), 3.61-3.75(m, 4H, $HOCH_2C\underline{H}_2O$), 4.09(s, 2H, $OC\underline{H}_2CO_2$), 4.18(q, 2H, J=7.2Hz, $CO_2C\underline{H}_2CH_3$); ^{13}C-NMR($CDCl_3$) δ 13.8($CO_2CH_2\underline{C}H_3$), 60.7($CO_2\underline{C}H_2CH_3$), 61.2($HOCH_2\underline{C}H_2O$), 68.2($HO\underline{C}H_2CH_2O$), 73.1($O\underline{C}H_2CO_2$), 170.7(ester C=O); IR(KBr), 3250-3500(br, OH stretching), 1750 cm^{-1}(C=O, stretching); MS(EI), m/z(rel. intensity) 148(M^+, 2), 130(3), 117(34), 103(7), 102(14), 87(100), 74(74); HRMS(EI), m/z 148.0737($C_6H_{12}O_4$ requires 148.0736). Spectral data for **9b**; ^{1}H-NMR($CDCl_3$) δ 1.24(t, 3H, J=7.2Hz, $CO_2CH_2C\underline{H}_3$), 1.72-1.88(m, 2H, $HOCH_2C\underline{H}_2CH_2O$), 2.50(br.s, 1H, OH), 3.60-3.68(m, 2H, $HOCH_2CH_2C\underline{H}_2O$), 3.69-3.80(m, 2H, $HOC\underline{H}_2CH_2CH_2O$), 4.03(s, 2H, $OC\underline{H}_2CO_2$), 4.15(q, 2H, J=7.2Hz, $CO_2C\underline{H}_2CH_3$); ^{13}C-NMR($CDCl_3$) δ 14.0($CO_2CH_2\underline{C}H_3$), 31.9($CO_2\underline{C}H_2CH_3$), 60.1($HOCH_2\underline{C}H_2CH_2O$), 61.6($HOCH_2CH_2\underline{C}H_2O$), 68.3($HO\underline{C}H_2CH_2CH_2O$), 69.6($O\underline{C}H_2CO_2$), 170.8 (ester C=O); IR(KBr) 3250-3500(br, OH stretching), 1750cm^{-1} (C=O, stretching); MS(CI), m/z(rel. intensity) 163(M^++1, 62), 145(100), 117(18), 100(14), 89(44), 59(42); HRMS(CI), m/z 163.0979($C_7H_{15}O_4$ requires 163.0970). Spectral data for **9c**; ^{1}H-NMR($CDCl_3$) δ 1.15(t, 3H, J=7.2Hz, $CO_2CH_2C\underline{H}_3$), 1.42-1.66(m, 4H, $HOCH_2C\underline{H}_2CH_2CH_2O$), 3.13(br.s, 1H, OH), 3.40-3.53(m, 4H, $HOC\underline{H}_2CH_2CH_2C\underline{H}_2O$), 3.94(s, 2H, $OC\underline{H}_2CO_2$), 4.73(q, 2H, J=7.2Hz, $CO_2C\underline{H}_2CH_3$); ^{13}C-NMR($CDCl_3$) δ 14.1 ($CO_2CH_2\underline{C}H_3$), 26.3($HOCH_2CH_2\underline{C}H_2CH_2O$), 29.6($HOCH_2\underline{C}H_2CH_2CH_2O$), 62.5($CO_2\underline{C}H_2CH_3$), 64.6($HOCH_2CH_2CH_2\underline{C}H_2O$), 68.3($HO\underline{C}H_2CH_2CH_2CH_2O$), 71.7($O\underline{C}H_2CO_2$), 170.4(ester C=O); IR(KBr), 3250-3500(br, OH stretching), 1750cm^{-1} (C=O, stretching); MS(EI), m/z(rel. intensity) 176(M+, 2), 175(M^+-1, 32), 162(53), 149(77), 117(19); HRMS(EI), m/z 176.1065($C_8H_{16}O_4$ requires 176.1049).

Preparations of Ethyl (ω-Iodoalkoxy)acetates (10a-c)

To a solution of ethyl (ω-hydroxyalkoxy)acetates (27.0 mmol, **9a**, 4.00 g; **9b**, 4.38 g; **9c**, 4.75 g) and triethylamine (4.10 g, 27 mmol) in 100 mL of ether was added methane sulfonyl chloride (4.64 g, 40.5 mmol) dropwise in 20 mL of ether for 1 h at 0℃. The solution was stirred for 5 h at room temperature, extracted with water, dried, and concentrated to afford a residue. Continuouesly, to a solution of sodium iodide (13.0 g, 87.0 mol) in 100 mL of acetone was added the mesylates residue and the resulting mixture was stirred for 20 h at 60℃. The mixture was cooled to the room temperature and extracted with n-pentane. The pentane solution was washed with water, dried, and concentrated to a residue which was subjected to column chromatography (hexane:ethyl acetate=10:1) to give ethyl(ω-Iodoalkoxy)acetates (**10a**, 5.66 g, 81%; **10b**, 6.04 g, 82%; **10c**, 5.40 g, 70%). Spectral data for **10a**; ^{1}H-NMR($CDCl_3$) δ 1.26(t, 3H, J=7.1Hz, $CO_2CH_2C\underline{H}_3$), 3.26(t, 2H, J=7.0Hz, $IC\underline{H}_2CH_2O$), 3.80(t, 2H, J=7.0Hz, $ICH_2C\underline{H}_2O$), 4.11(s, 2H, $OC\underline{H}_2CO_2$), 4.19(q, 2H, J=7.2Hz, $CO_2C\underline{H}_2CH_3$); ^{13}C-NMR δ ($CDCl_3$)

13.7($CO_2CH_2\underline{C}H_3$), 60.1($I\underline{C}H_2CH_2O$), 67.4($CO_2\underline{C}H_2CH_3$), 67.7($ICH_2\underline{C}H_2O$), 71.4($O\underline{C}H_2CO_2$), 169.3(ester C=O); IR(KBr) 1750(C=O stretching), 1350(asymmetric C-O-C stretching), 1100cm^{-1}(symmetric C-O-C stretching); MS(CI), m/z(rel. intensity) 259(M^++1, 100), 155(32), 132(85), 131(98), 117(44); HRMS(CI), m/z 259.9819 ($C_6H_{12}O_3I$ requires 259.9831). Spectral data for **10b**; ^{1}H-NMR(CDCl3) δ 1.21(t, 3H, J=7.0Hz, $CO_2CH_2C\underline{H}_3$), 2.10-2.17(m, 2H, $ICH_2C\underline{H}_2CH_2O$), 3.18(t, 2H, J=7.2Hz, $IC\underline{H}_2CH_2CH_2O$), 3.57(t, 2H, J=5.8Hz, $ICH_2CH_2C\underline{H}_2O$), 4.06(s, 2H, $OC\underline{H}_2CO_2$), 4.20(q, 2H, J=7.0Hz, $CO_2C\underline{H}_2CH_3$); ^{13}C-NMR($CDCl_3$) δ 14.9($CO_2CH_2\underline{C}H_3$), 32.1($I\underline{C}H_2CH_2CH_2O$), 33.3($I\underline{C}H_2CH_2CH_2O$), 64.4($CO_2\underline{C}H_2CH_3$), 68.3($ICH_2CH_2\underline{C}H_2O$), 71.1($O\underline{C}H_2CO_2$), 170.1(ester C=O); IR(KBr), 1760(C=O stretching), 1350(asymmetric C-O-C stretching), 1100 cm^{-1}(symmetric C-O-C stretching). Spectral data for **10c**; ^{1}H-NMR($CDCl_3$) δ 1.27(t, 3H, J=7.2Hz, $CO_2CH_2C\underline{H}_3$), 1.70(quintet, 2H, J=6.8Hz, $ICH_2C\underline{H}_2CH_2CH_2O$), 1.93(quintet, 2H, J=6.8Hz, ICH_2CH_2 $CH_2C\underline{H}_2CH_2O$), 3.22(t, 2H, J=6.8Hz, $IC\underline{H}_2CH_2CH_2CH_2O$), 3.53(t, 2H, J=6.8Hz, $ICH_2CH_2CH_2C\underline{H}_2O$), 4.03(s, 2H, $OC\underline{H}_2CO_2$), 4.20(q, 2H, J=7.2Hz, $CO_2C\underline{H}_2CH_3$); ^{13}C-NMR($CDCl_3$) δ 6.6($I\underline{C}H_2CH_2CH_2CH_2O$), 14.2($CO_2CH_2\underline{C}H_3$), 30.1($ICH_2\underline{C}H_2$ CH_2CH_2O), 30.4($ICH_2\underline{C}H_2CH_2CH_2O$), 60.8 ($CO_2\underline{C}H_2CH_3$), 68.3($ICH_2CH_2CH_2\underline{C}H_2O$), 70.5($OCH_2CO_2$), 170.4(ester C=O); IR(KBr) 2900(aliphatic CH stretching), 1750(C=O stretching), 1350(asymmetric C-O-C stretching), 1100 cm-1(symmetric C-O-C stretching); MS(EI), m/z(rel. intensity) 286 (M^+, 1), 241(3), 213(8), 183(73), 159(100) ; HRMS(EI), m/z 286.0042($C_8H_{15}O_3I$ requires 286.0066).

Preparations of Ethyl (ω-Phthalimidoalkoxy)acetates (11a-c)

To a solution of ethyl (ω-iodoalkoxy)acetates (30.0 mmol, **10a**, 7.77 g; **10b**, 8.19 g; **10c**, 8.58 g) in DMF (50 mL) was added potassium phthalimide (5.56 g, 30.0 mol) and the reaction mixture was stirred for 3 h at 90°C. After removal of DMF in vacuo, the residue was dissolved in CH_2Cl_2 and filtered. The filtered solution was subjected to column chromatography (hexane:ethyl acetate=3:1) to give ethyl(ω-phthalimidoalkoxy)acetates (**11a**, 6.98 g, 84%; **11b**, 7.16 g, 82%; **11c**, 6.50 g, 71%). Spectral data for **11a**; ^{1}H-NMR($CDCl_3$) δ 1.09(t, 3H, J=7.2Hz, $CO_2CH_2C\underline{H}_3$), 3.74(t, 2H, J=4.8Hz, $NC\underline{H}_2CH_2O$), 3.82(t, 2H, J=4.8Hz, $NCH_2C\underline{H}_2O$), 3.99(s, 2H, $OC\underline{H}_2CO_2$), 4.02 (q, 2H, J=7.2Hz, $CO_2C\underline{H}_2CH_3$), 7.58-7.74(m, 4H, aromatic); ^{13}C-NMR($CDCl_3$) δ 13.9($CO_2CH_2\underline{C}H_3$), 37.0($N\underline{C}H_2CH_2O$), 60.5($CO_2\underline{C}H_2CH_3$), 67.7($NCH_2\underline{C}H_2O$), 68.0 ($O\underline{C}H_2CO_2$), 123.1(CH, aromatic), 131.9(C, aromatic), 133.7(CH, aromatic), 167.9 (imide C=O), 169.8(ester C=O); MS(EI), m/z(rel. intensity) 277(M^+, 19), 204(21), 190 (96), 174(100), 160(92) 130(48); HRMS(EI), m/z 277.0940($C_{14}H_{15}O_5N$ requires 277.0950). Spectral data for **11b**; ^{1}H-NMR($CDCl_3$) δ 1.22(t, 3H, J=7.1Hz, $CO_2CH_2C\underline{H}_3$), 1.95-2.05(m, 2H, $NCH_2C\underline{H}_2CH_2O$), 3.55(t, 2H, J=7.1 Hz, $NC\underline{H}_2CH_2C\underline{H}_2O$), 3.79(t, 2H, J=7.1Hz $NCH_2CH_2C\underline{H}_2O$), 4.02(s, 2H, $OC\underline{H}_2CO_2$), 4.14(q, 2H, J=7.1Hz, $CO_2C\underline{H}_2CH_3$), 7.66-7.82(m, 4H, aromatic); ^{13}C-NMR($CDCl_3$) δ 14.1($CO_2CH_2\underline{C}H_3$), 28.6($NCH_2\underline{C}H_2CH_2O$), 35.2($N\underline{C}H_2CH_2CH_2O$), 60.6($CO_2\underline{C}H_2$ CH_3), 68.4($NCH_2CH_2\underline{C}H_2O$), 69.1($O\underline{C}H_2CO_2$), 123.0(CH, aromatic), 132.1(C, aromatic), 133.8(CH, aromatic), 168.2(imide C=O), 170.2(ester C=O); MS(EI), m/z(rel. intensity) 291(M^+, 1), 218(M^+-$CO_2CH_2CH_3$, 2), 204(M^+-$CH_2CO_2CH_2CH_3$, 48), 188(96), 160(100), 148(16), 130(22); HRMS(EI), m/z 291.1095(C15H17NO5 requires 291.1107). Spectral data for **11c**; ^{1}H-NMR($CDCl_3$) δ 1.25(t, 3H, J=7.2Hz, $CO_2CH_2C\underline{H}_3$), 1.63-1.76(m, 4H, $NCH_2C\underline{H}_2CH_2CH_2O$), 3.54(t, 2H, J=6.3Hz, $NC\underline{H}_2CH_2CH_2CH_2O$), 3.70(t, 2H, J=7.1Hz, $NCH_2CH_2CH_2C\underline{H}_2O$), 4.02(s, 2H, $OC\underline{H}_2CO_2$), 4.18(q, 2H, J=7.2Hz, $CO_2C\underline{H}_2CH_3$), 7.67-7.81(m, 4H, aromatic); ^{13}C-NMR($CDCl_3$) δ 14.2($CO_2CH_2\underline{C}H_3$), 25.2($NCH_2\underline{C}H_2CH_2CH_2O$), 26.0($NCH_2CH_2$ $\underline{C}H_2CH_2O$), 37.6($N\underline{C}H_2CH_2CH_2CH_2O$), 60.8($\underline{C}O_2CH_2CH_3$), 68.3($NCH_2CH_2$ $CH_2\underline{C}H_2O$), 71.0($O\underline{C}H_2CO_2$), 123.1(CH, aromatic), 132.1(C, aromatic), 133.8(CH, aromatic), 168.4(imide C=O), 170.5(ester C=O); MS(EI), m/z(rel. intensity) 305(M^+, 23), 218(23), 202(18), 160(100), 133(10); HRMS(EI), 305.1279 ($C_{16}H_{19}NO_5$ requires 305.1263).

Preparations of (ω-Phthalimidoalkoxy)acetic Acids (7a-c)

To a solution of ethyl (ω-phthalimidoalkoxy)acetates (18.0 mmol, **11a**, 5.00 g; **11b**, 5.24 g; **11c**, 5.49 g) in 1,4-dioxane (30 mL) was added HCl (36%, 20.0 mmol) dropwise for 1 h at 25 °C. The solution was stirred for 3 h at room temperature and was concentrated to afford a residue. The residues were subjected to column chromatography (hexane:ethyl acetate=1:10) to give (ω-phthalimidoalkoxy)acetic acids (**7a**, 3.09 g, 69%; **7b**, 2.27 g, 48%; **7c**, 1.80 g, 36%). Spectral data for **7a**; ^{1}H-NMR ($CDCl_3$) δ 3.79(t, 2H, J=5.0Hz, $NC\underline{H}_2CH_2O$), 3.92(t, 2H, J=5.0Hz, $NCH_2C\underline{H}_2O$), 4.10(s, 2H, $OC\underline{H}_2CO_2$), 7.68-7.85(m, 4H, aromatic), 7.80-8.20(br, 1H, $CO_2\underline{H}$); ^{13}C-NMR($CDCl_3$) δ 37.4($N\underline{C}H_2CH_2O$), 67.6($NCH_2\underline{C}H_2O$), 68.8($O\underline{C}H_2CO_2$), 123.4(CH, aromatic), 132.0(C, aromatic), 134.1(CH, aromatic), 168.4(imide C=O), 173.5(acid C=O) ; IR(KBr) 1750(acid C=O stretching), 1720 cm-1(imide C=O stretching); MS(CI), m/z(rel. intensity) 250(M^++1, 80), 204(34), 174(50), 160(100); HRMS(CI), m/z 250.0713($C_{12}H_{11}O_5N$ requires 250.0715). Spectral data for **7b**; ^{1}H-NMR($CDCl_3$) δ 1.25-2.00(m, 2H, $NCH_2C\underline{H}_2CH_2O$), 3.50-3.75(m, 4H, $NC\underline{H}_2CH_2C\underline{H}_2O$), 3.92(s, 2H, $OC\underline{H}_2CO_2$), 7.52-7.75(m, 4H, aromatic); ^{13}C-NMR($CDCl_3$) δ 27.7 ($NCH_2\underline{C}H_2CH_2O$), 34.7($N\underline{C}H_2CH_2CH_2O$), 68.0($NCH_2CH_2\underline{C}H_2O$), 70.2($O\underline{C}H_2CO_2$), 123.1(CH, aromatic), 131.9(C, aromatic), 134.0(CH, aromatic), 168.4(imide C=O), 173.5(acid C=O); MS(CI), m/z(rel. intensity) 264(M^++1, 17), 204(M^+-CH_2CO_2H, 22), 188(71), 160(100), 148(39), 130(23); HRMS(CI), m/z 264.0868(C13H14NO5 requires 264.0872). Spectral data for **7c**; 1H-NMR(DMSO-d6) δ 1.48-1.69(m, 4H, $NCH_2C\underline{H}_2C\underline{H}_2CH_2O$), 3.40-3.62(m, 4H, $NC\underline{H}_2CH_2CH_2C\underline{H}_2O$), 3.67(s, 2H, $OC\underline{H}_2CO_2$), 7.82(s, 4H, aromatic); ^{13}C-NMR (DMSO-d6) δ 24.8 and 26.3($NCH_2\underline{C}H_2CH_2CH_2O$), 37.3($N\underline{C}H_2CH_2CH_2CH_2O$), 69.2 ($NCH_2$ $CH_2CH_2\underline{C}H_2O$), 70.0($O\underline{C}H_2CO_2$), 122.9(CH, aromatic), 131.5(C, aromatic), 134.3(CH, aromatic), 167.8(imide C=O),

175.2(ester C=O); IR(KBr) 1750(acid C=O stretching), 1720cm-1(imide C=O stretching); MS(EI), m/z(rel. intensity) 277(M^+, 2), 232 (M^+-CO_2H, 2), 218(M^+-CH_2CO_2H, 11), 202(28), 188(10), 173(26), 160(100), 149(47), 130(27), 105(35), 77(40); HRMS(EI), m/z 277.0925($C_{14}H_{15}NO_5$ requires 277.0950).

Irradiations of (ω-Phthalimidoalkoxy)acetic Acids (7a-c) in CH_3OH

The methanol solutions (100mL) containing (ω-phthalimidoalkoxy)acetic acids (**7a**, 100 mg, 0.40 mmol; **7b**, 100 mg, 0.38 mmol; **7c**, 100 mg, 0.36 mmol) with 1 eq NaOH, without NaOH were irradiated through Pyrex-filtered light under N_2. Concentration of the photolyzate gave a residue which was subjected to column chromatography (silica, ethyl acetate:CH_2Cl_2=1:2) yielding cyclized product **12a-c** [10]. The reaction conditions and products yields are given in Table 1.

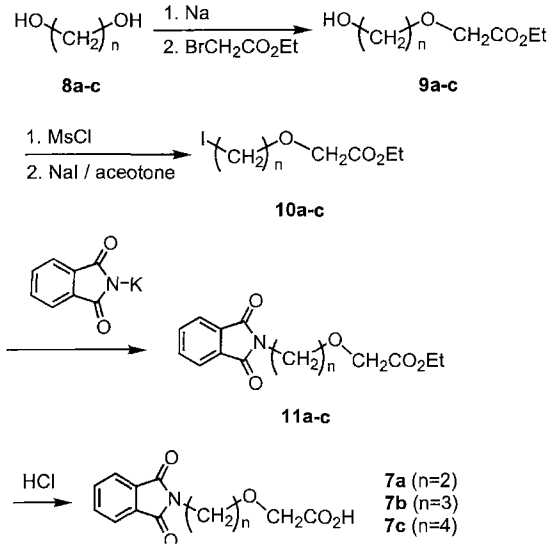
Irradiations of (ω-Phthalimidoethoxy)acetic Acids (7a) in Acetone

The acetone solution(100mL) containing (ω-phthalimidoethoxy)acetic Acids (**7a**, 100 mg, 0.40 mmol) with 1 eq NaOH, without NaOH was irradiated through Pyrex-filtered light under N_2. Concentration of the photolyzate gave a residue which was subjected to column chromatography(silica, ethyl acetate:CH_2Cl_2=1:2) yielding cyclized product 12a. The reaction conditions and products yields are given in Table 1.

RESULTS

Preparations of (ω-Phthalimidoalkoxy)acetic Acids

For these photochemical studies three (ω-phthalimidoalkoxy)acetic acids (**7a-c**) were selected and prepared in modest to good yields starting with the corresponding alkanediols **8a-c** by use of the reaction sequences outlined in Scheme 5 (see Materials and Method section).



Scheme 5.

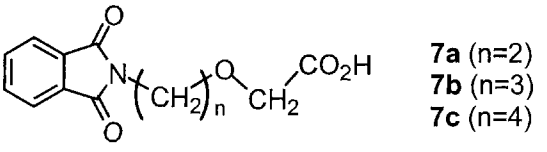
Photocyclizations of (ω-Phthalimidoalkoxy)acetic Acids

Photocyclization reactions of (ω-phthalimidoalkoxy)acetic acids **7a-c** were explored. Preparative photocyclization reactions were performed by irradiation of methanol or acetone solutions of phthalimides (3.6-4.0 mM) with or without one equivalent of sodium hydroxide by using Pyrex glass filtered-light (λ>290 nm) and products **12a-c** were separated by silica gel chromatography (see Materials and Methods section). Products and yields along with reaction conditions employed were given in Table 1.

Table 1. Photochemical Reactions of (ω-Phthalimidoalkoxy)acetic Acids.

Acetic Acid	Concentration (mM)	Solvent	Reaction Time(h)	conversion (%)	Product (yields)[a]
7a	4.01	CH_3OH	3	100	**12a** (85%)
7a	4.01	CH3OH/1eq NaOH	1	100	**12a** (95%)
7a	4.01	acetone	10	100	**12a** (85%)
7a	4.01	acetone/1eq NaOH	3	100	**12a** (90%)
7b	3.80	CH_3OH	3	100	**12b** (74%)
7b	3.80	CH_3OH/1eq NaOH	1	100	**12b** (92%)
7c	3.61	CH_3OH	3	100	**12c** (79%)
7c	3.61	CH_3OH/1eq NaOH	1	100	**12c** (90%)

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

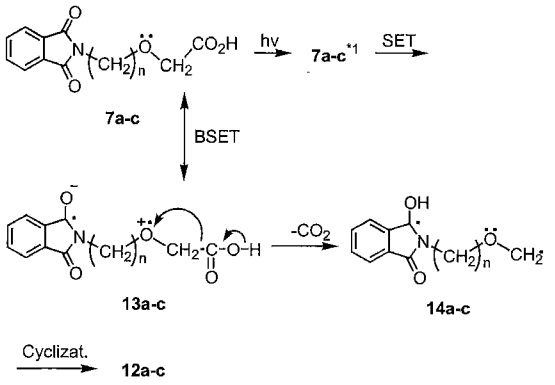


Irradiation of (ω-phthalimidoalkoxy)acetic acids (**7a-c**) in methanol leads to rapid and high yielding production of the cyclized products **12a-c** exclusively [10]. The presence of one equivalent of sodium hydroxide in methanol solutions of acids **7a-c** enhances their conversion rate ca. three times and improves product yields compared with those without sodium hydroxide. Photoreaction of **7a** in acetone occurs ca. three times more slowly in spite that product yield is not significantly changed [11]. The presence of sodium hydroxide in acetone solution of **7a** increases conversion rate of **7a** in the approximately same extent with that in methanol.

Discussion

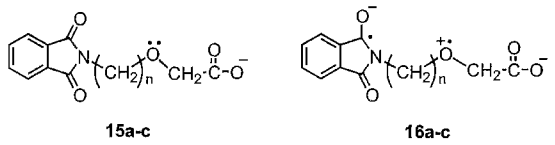
The observations presented above show that (ω-phthalimidoalkoxy)acetic acids undergo photocyclization in methanol or acetone with high degrees of chemoselectivity and regioselectivity to generate cyclized products of six to eight membered ring. The process formally involves bond formation between the phthalimide carbonyl and α-oxygen carbon in

place of the carboxyl group. Results obtained in this study that reactions in methanol are faster than in acetone and those of our earlier investigations [4-7] of photoinduced SET reactions of phthalimide-α-silyl-n-electron donor systems in methanol suggest that photocyclization in methanol leadings to **12a-c** occur via excited singlet state SET pathways [14] (Scheme 6). Intramolecualr SET in singlet excited phthalimides (**7a-c**^{*1}) results in generation of zwitterionic radical intermediates **13a-c** which undergo exculsive deproto-decarboxylation leading to biradicals **14a-c**. Biradical **14a-c** then undergo cyclization to produce cyclized products **12a-c**.



Scheme 6.

Addition of base such as sodium hydroxide in the photoreactions of **7a-c** results deprotonation of carboxylic group to generate carboxylate anions **15a-c**. The generated α-alkoxycarboxylate anion group of 15a-c is expected to be better electron donor than α-alkoxycarboxylic acid group of **13a-c** and more efficient SET from α-alkoxycarboxylate group of **15a-c** in their excited states is expected.



Furthermore decarboxylation of intermediates **16a-c** formed by intramolecular SET from excited state carboxylates **15a-c** is also thought to be occur faster than deproto-decarboxylation of **13a-c** [15] and thus forward decarboxylation process to biradicals 14a-c becomes more competitive than back electron transfer BSET) towards to ground state **7a-c**. More efficient SET in the excited state of **15a-c** and more competitive forward decarboxylation both might account for faster photocyclizations of **7a-c** in the presence of sodium hydroxide in methanol or acetone.

Acknowledgement-This research was supported by the Pusan National University Research Grant.

REFERENCES

1. Studies reported in this paper was mainly conducted as part of the master work of C. W. L. at the Pusan National University (1992) and a preliminary result reported at the 71th Korean Chemical Society Meeting in 1993 (Abstract p.200).
2. (a) Kanaoka, Y. (1978) Photoreactions of Cyclic Imides. Examples of Synthetic Organic Photochemistry. *Acc. Chem. Res.* **11**, 407-413. (b) Colye, J. D. (1984) Phthalimide and Its Derivatives. *Synthetic Organic Photochemistry*, p.258-284, Horsepool, W. M. ed. Plenum, New York. (c) Mazzocchi, P. H. (1981) The Photochemistry of Imides. *Organic Photochemistry*, vol.5, p.421-471, Padwa, A. ed. Marcel Dekker, New York.
3. (a) Brumfield, M. A., Quillen, S. L., Yoon, U. C. and Mariano, P. S. (1984) A Novel Method for Heteroatom-Substituted Free Radical Generation by Photochemical Electron-Transfer-Induced Desilylation of $RXCH_2SiMe_3$ Systems. *J. Am. Chem. Soc.*, **104**, 6855-6865. (b) Ohga, K., Yoon, U. C. and Mariano, P. S. (1984) Exploratory and Mechanistic Studies of the Electron-Transfer-Initiated Photoaddition Reactions of Allylsilane-Iminium Salt System. *J. Org. Chem.*, **49**(2), 213. (c) Hasegawa, E., Brumfield, M. A., Mariano, P. S. and Yoon, U. C. (1988) Photoadditions of Ethers, Thioethers, and Amines to 9,10-Dicyanoanthracene by Electron Transfer Pathways. J. Org. Chem., 53(23), 5435-5442. (d) Yoon, U. C., Kim, J. U., Hasegawa, E. and Mariano, P. S. (1987) Electron-Transfer Photochemistry of α-Silylamine-Cyclohexenone Systems. Medium Effects on Reaction Pathways Followed. *J. Am. Chem. Soc.*, **109**, 4421-4423. (e) Hasegawa, E., Xu, W., Mariano, P. S., Yoon, U. C. and Kim, J. U.(1988) Electron Transfer-Induced Photoadditions of the Silylamine, Et_2NCH_2TMS to α, β-unsaturated Cyclohexenones. Dual Reaction Pathways Based on Ion-Pair-Selective Cation Radical Chemistry. *J. Am. Chem. Soc.*, **110**, 8099-8111. (f) Yoon, U. C., Kim, Y. C., Choi, J. J., Kim, D. U., Mariano, P. S., Cho, I. S. and Jeon, Y. T. (1992) Photoaddition Reactions of Acenaphthylenedione with α-Silyl-n-Electron Donors via Triplet Single Electron Transfer-Desilylation and Triplet Hydrogen Atom Abstraction Pathways. *J. Org. Chem.*, **57**, 1422-1428. (g) Yoon, U. C. and Mariano, P. S. (1992) Mechanistic and Synthetic Aspects of Amine-Enone Single Electron Transfer Photochemistry. *Acc. Chem. Res.*, **25**, 233-240. (h) Yoon, U. C., Mariano, P. S., Givens, R. S. and Atwater, B. W. (1994) Photoinduced Electron Transfer Chemistry of Amine and Related Electron Donors. Advances *in Electron Transfer chemistry*, vol. 4, p.117-205, ed. By Mariano, P. S., JAI Press.
4. Yoon, U. C., Oh, J. H., Lee, S. J., Kim, D. U., Lee, J. G., Kang, K. T. and Mariano, P. S. (1992) Photocyclization Reactions of N-(Trimethylsilylmethoxy)phthalimides. Efficient and Regioselective Route to Heterocycles. *Bull. Korean Chem. Soc.*, **13**(2), 166-172.

5. Yoon, U. C., Lee, S. J., Lee, K. J., Lee, C. W., Cho, S. J. and Mariano, P. S. (1994) Exploratory Studies of Photocyclization Reactions of N-(Trimethylsilylmethylthioalkyl)phthalimides. *Bull. Korean Chem. Soc.*, **15**(2), 154-161.
6. Yoon, U. C., Kim, J. W., Ryu. J. Y., Cho, S. J., Oh, S. W. and Mariano, P. S. (1997) Single Electron Transfer Induced Photocyclization Reactions of N-[(N-Trimethylsilylmethyl)aminoalkyl]phthalimides. *J. Photochem. Photobiol. A.*, 145-154.
7. Davidson, R. S. and Steiner, P. R. (1972) Mechanism of the Phtoinduced Decarboxylation of Carboxylic Acids Sensitized by Aromatic Ketones and Quinones. *J. Chem. Soc. Perkin* II, 1357-1362.
8. Davidson. R. S., Korkut, S. and Steiner, P. R. (1971) The Photoinduced Decarboxylation of N-(2-Chlorophenyl)glycine and (Phenylthio)acetic acid Sensitized by Aromatic Nitro Compounds. Chem. Comm., 1052.
9. Physical properties of products **12a-c** were identical to those of reported [5].
10. Photodecarboxylation reactions of compound **7a** [12] and ω-phthalimidoalkynoic acids[13] in acetone in the presence of K_2CO_3 were reported.
11. Griesbeck, A. G., Henz, A., Kramer, W., Lex, J., Nerowski, F. and OelgemOller, M. (1997) Synthesis of Medium and Large Ring Compounds Initiated by Photochemical Decarboxylation of ?-Phthalimidoalkanoates. *Helv. Chim. Acta.*, **80**, 912-933.
12. Yoo, D. J., Kim, E. Y. and Shim, S. C. (2000) Synthesis of Heterocyclic Ring Compounds Initiated by Photochemical Decarboxylation of ω-Phthalimidoalkyne Caboxylic Acids. *Annaul Meeting of the Korean Society of Photoscience*, Taejon, Korea, Abstract p.48.
13. Because photoreaction of **7a** in acetone produce the same cyclized product **12a** exclusively even through in slower rate, less efficient triplet state SET is thought to occur in acetone.
14. (a) Su, Z., Falvey, D. E., Yoon, U. C. and Mariano, P. S. (1997) The Dynamics of α-Anilino Carboxylate and Related Cation Radical α-Heterolytic Fragmentations. *J. Am. Chem. Soc.*, **119**(22), 5261-5262. (b) Su, Z., Mariano, P. S., Falvey, D. E., Yoon, U. C. and Oh, S. W. (1998) Dynamics of Anilinium Radical α-Heterolytic Fragmentation Processes. Electrofugal Group, Substituent, and Medium Effects on Desilylation, Decarboxylation, and Retro-Aldol Cleavage Pathways. *J. Am. Chem. Soc.*, **120**(41), 10676-10686.