Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 46 (2005) 3395–3398

Tetrahedron Letters

# Photodecarboxylative cyclizations of ω-phthalimido-*ortho*-phenoxy carboxylates

Ae Rhan Kim,[a] Kyoung-Sub Lee,[b] Cheon-Woo Lee,[b] Dong Jin Yoo,[b,*]
Fadi Hatoum[c] and Michael Oelgemöller[c,*]

[a]*Chonbuk National University, Department of Chemistry, 664-14 Doegjin-Dong, Chonju, Chonbuk 561-756, Republic of Korea*
[b]*Seonam University, Department of Chemistry, 720 Gwangchi-Dong, Namwon, Chonbuk 590-711, Republic of Korea*
[c]*Dublin City University, School of Chemical Sciences, Dublin 9, Ireland*

Received 23 December 2004; revised 8 March 2005; accepted 15 March 2005
Available online 2 April 2005

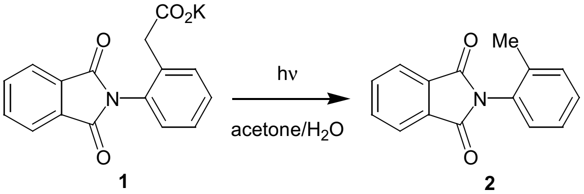
**Abstract**—ω-Phthalimido-*ortho*-phenoxy carboxylates efficiently undergo photodecarboxylative cyclizations in reasonable to good yields of 12–75%. Although the photocyclization efficiency decreases with increasing carbon chain lengths, target ring sizes up to 15 are successfully realized. Likewise, *intermolecular* photodecarboxylative additions of ω-phenoxy carboxylates to *N*-methyl phthalimide give hydroxyphthalimidines in yields of 45–73%.

The chemistry of electronically excited phthalimides is dominated by electron and hydrogen transfer reactions.[1] Among numerous synthetic applications, the photochemical decarboxylation (PDC) of ω-phthalimidoalkyl carboxylates has been developed by Griesbeck and co-workers as a versatile pathway to medium- and large-ring heterocycles.[2] We have recently reported the successful synthesis of macrocyclic alkynes following this PDC strategy.[3] As an extension of our work, we became interested in using *ortho*-substituted arenes as rigid linkers between the phthalimide chromophore and the terminal carboxylic acid chain. The U-shaped geometry of the central skeleton should favor a close contact geometry between the two active ends of the molecule preferably for medium size ring systems. In this paper, we describe the photochemistry of several ω-phthalimido-*ortho*-aryl carboxylates differing in the terminal carbon chain length and compare it with intermolecular addition reactions.

The first substrate we synthesized was 2-phthalimidophenyl acetic acid. Upon irradiation in aqueous acetone for 1 h its corresponding potassium salt **1** readily gave the simple decarboxylation ($CO_2H$/H-exchange) product **2** in a good yield of 62% (Scheme 1).[4] The *ortho*-$CH_3$-group of **2** showed a characteristic $^1H$ NMR singlet at 2.21 ppm.

Although compound **2** is known to undergo photocyclization to the corresponding five-membered ring via hydrogen abstraction,[5a,b] we were unable to detect any cyclization product under the given reaction conditions in the NMR spectrum or via TLC analysis of the crude reaction mixture.

For all other derivatives, we selected *N*-(2-hydroxyphenyl)-phthalimide as a useful and easily available building block. In contrast to compound **1**, the chain elongated ω-phthalimido-*ortho*-phenoxy acetate **3a** readily gave the six-membered product **4a** in 75% isolated yield after 1 h of irradiation.[6] In $CDCl_3$, the $^1H$ NMR spectrum



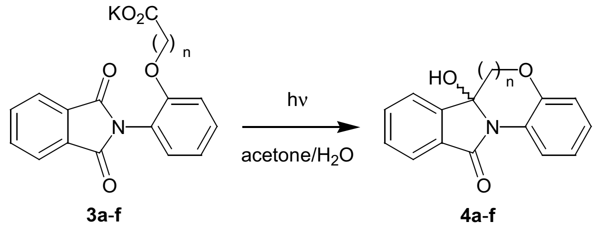
**Scheme 1.** Simple decarboxylation of **1**.

---

*Keywords*: Photodecarboxylation; Phthalimides; Cyclizations; Addition reactions; Photoinduced electron transfer.

* Corresponding authors. Tel.: +82 63 620 0137; fax: +82 63 620 0075 (D.J.Y.); tel.: +353 1 700 5312; fax: +353 1 700 5503 (M.O.); e-mail addresses: djyoo@seonam.ac.kr; michael.oelgemoeller@dcu.ie

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.03.090



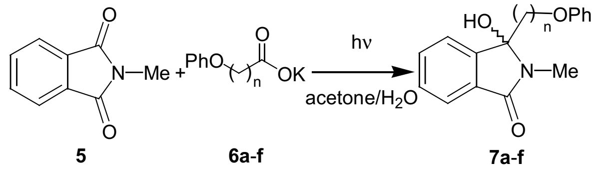
**Scheme 2.** Photodecarboxylative cyclization of **3**.

showed two clearly separated doublets for the O–CH$_2$ group at 3.82 and 4.74 ppm with a large $^2J$ coupling of 10.8 Hz. The hydroxy proton gave a broad singlet at 3.28 ppm, which was unambiguously assigned via H–D exchange with D$_2$O. Likewise, photolysis of compounds **3b–f** furnished the corresponding cyclization products **4b–f** (Scheme 2; Table 1). Noteworthy, the isolated yields decreased from 42% to 12% with increasing chain length. Furthermore, the irradiation time had to be extended (especially for the long chain derivatives **3e**, **f**) in order to reach high conversion rates. In all cases, the quaternary C–OH carbons showed characteristic $^{13}$C NMR resonances in CDCl$_3$ at 82.3 (**4a**), 92.3 (**4b**), 93.3 (**4c**), 93.0 (**4d**), 93.2 (**4e**) and 92.4 ppm (**4f**), respectively.

To account for the decrease in isolated yields during the *intramolecular* cyclization reaction, we have expanded our study to *intermolecular* addition reactions.[7] In all cases examined, *N*-methylphthalimide **5** was used as a model substrate and the phenoxy alkanoates **6** were varied. Irradiation of **5** in aqueous acetone for 1–3 h in the presence of 5 equiv of the potassium alkynoates **6a–f** gave the corresponding hydroxyphthalimidines **7a–f** in moderate to good yields between 45% and 73% (Scheme 3; Table 2).[8] Judged by isolated yields and irradiation times, the addition proceeded more efficiently than the corresponding cyclization.

**Table 1.** Product yields and irradiation times for the photodecarboxylative cyclizations of **1** and **3**

| Entry | *n* | Time | Yield **4** (%) | Ring-size |
|---|---|---|---|---|
| **1** | – | 1 h | 62 (**2**) | – |
| **3a** | 1 | 1 h | 75 | 6 |
| **3b** | 3 | 14 h | 42 | 8 |
| **3c** | 4 | 6 h | 36 | 9 |
| **3d** | 6 | 10 h | 24 | 11 |
| **3e** | 9 | 5 d | 12 | 14 |
| **3f** | 10 | 5 d | 19 | 15 |



**Scheme 3.** Photodecarboxylative addition to **5**.

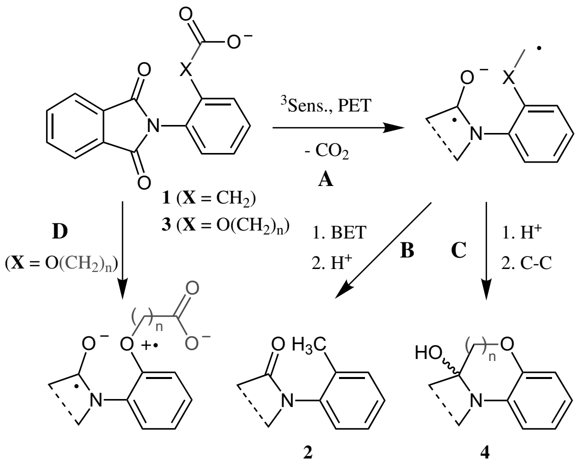
**Table 2.** Product yields and irradiation times for the photodecarboxylative additions to **5**

| Entry | *n* | Time (h) | Yield **7** (%) |
|---|---|---|---|
| **6a** | 1 | 1 | 73 |
| **6b** | 2 | 3 | 65 |
| **6c** | 3 | 1 | 55 |
| **6d** | 4 | 1 | 45 |
| **6e** | 9 | 1 | 47 |
| **6f** | 10 | 1 | 49 |

No simple decarboxylation (CO$_2^-$/H-exchange) products of **6a–f** were formed under the given conditions. In CDCl$_3$, the *N*-methyl group showed $^1$H NMR singlets at 2.86 (**7a**), 2.86 (**7b**), 2.77 (**7c**), 2.76 (**7d**), 2.91 (**7e**) and 2.88 ppm (**7f**), respectively.

The key step of the mechanistic scenario (Scheme 4; path **A**) is a rapid *intramolecular* electron transfer (PET) via the excited $^3\pi,\pi^*$ triplet state (**5**: $E_{00} = 3.1$ eV) or the higher $^3$n, π* state (**5**: $E_{00} \approx 3.6$ eV) of the phthalimide.[9] Subsequent decarboxylation of the carboxy radical gives the corresponding terminal carbon radical. In the case of substrate **1**, back electron transfer (BET) generates a carbanion,[10] which is protonated by water (path **B**). Although compound **2** is capable of undergoing a sequence of *intramolecular* H-abstraction and photocyclization, this reaction is highly sensitive to the irradiation conditions. Kanaoka and co-workers reported that best results were obtained with high-pressure mercury lamps, *tert*-butanol as solvent and quartz vessels,[5] and these conditions clearly differ from ours.

For all other derivatives, protonation and biradical combination gave the desired cyclization products **4** (path **C**). The latter process also occurred for the photodecarboxylative additions to the hydroxylphthalimidines **7**. For ω-phthalimidoalkoxy acetates, Yoon et al. have recently postulated an alternative electron transfer from the oxygen tether followed by α-decarboxylation (path **D**; n = 1).[11] This scenario would parallel PET reactions of related α-trimethylsilyl (TMS) methyl



**Scheme 4.** Mechanistic scenario.

ethers.[12] In contrast, the results from our present investigation suggest that electron transfer occurs from the carboxylate instead, independent from the position of the oxygen tether. This interpretation is in line with earlier studies on photoadditions of heteroatom-substituted carboxylates,[13] and is furthermore supported by the oxidation potentials of the competing donors ($E_{ox}$: $\mathrm{ROCH_2TMS} \ll \mathrm{RCO_2^-} \leqslant \mathrm{PhOR} < \mathrm{R_2O}$).[14,15]

As for related anthranilic acid-based analogues,[16] the success of the cyclization depended on the chain length and thus the ring-size of the corresponding product. In compound **3a**, the *ortho*-substitution pattern favors a close contact for electron transfer and consequently, the corresponding six-membered product was obtained in the best yield of 75%. Noteworthy, a slightly lower yield of 73% was reported for the corresponding ethylene-linked analogue.[2b] Further chain-elongation disturbed the necessary approach for the biradical combination due to steric overcrowding,[17] and consequently, the yields of **4** dropped below 20% and extended irradiation times were necessary to achieve high conversion rates. On the contrary, the chain length effected the photodecarboxylative addition less and yields were, in almost all cases, higher than for the *intramolecular* counterparts after 1–3 h.

## Acknowledgements

This work was supported by grant R05-2002-000-01419-0 from the Basic Research Program of the Korea Science and Engineering Foundation (KOSEF). D.J.Y. thanks KOSEF for a KOSEF-DFG fellowship during the summer of 2004 (F03-2004-000-10046-0) and Professor Axel G. Griesbeck (University of Cologne) for his support.

## References and notes

1. (a) Oelgemöller, M.; Griesbeck, A. G. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Lanci, F., Eds., 2nd ed.; CRC Press: Boca Raton, 2004, Chapter 88, pp 1–19; (b) Oelgemöller, M.; Griesbeck, A. G. *J. Photochem. Photobiol. C: Photochem. Rev.* **2002**, *3*, 109–127; (c) Coyle, J. D. In *Synthetic Organic Photochemistry*; Horspool, W. M., Ed.; Plenum Press: New York, 1984, pp 259–284; (d) Mazzocchi, P. H. *Org. Photochem.* **1981**, *5*, 421–471; (e) Kanaoka, Y. *Acc. Chem. Res.* **1978**, *11*, 407–413.
2. (a) Griesbeck, A. G.; Kramer, W.; Oelgemöller, M. *Synlett* **1999**, 1169–1178; (b) Griesbeck, A. G.; Henz, A.; Kramer, W.; Lex, J.; Nerowski, F.; Oelgemöller, M.; Peters, K.; Peters, E.-M. *Helv. Chim. Acta* **1997**, *80*, 912–933; (c) Griesbeck, A. G.; Henz, A.; Peters, K.; Peters, E.-M.; von Schnering, H. G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 474–476.
3. (a) Yoo, D. J.; Kim, E. Y.; Oelgemöller, M.; Shim, S. C. *Photochem. Photobiol. Sci.* **2004**, *3*, 311–316; (b) Yoo, D. J.; Kim, E. Y.; Oelgemöller, M.; Shim, S. C. *Heterocycles* **2001**, *54*, 1049–1055.
4. General procedure for irradiation: A mixture of $K_2CO_3$ (1 mmol) and the phthalimide (2 mmol) in $H_2O$ (ca. 2 mL) was heated to 60–70 °C for 1 min. Two-hundred milliliter of $H_2O$/acetone (1:1) was added and the mixture was irradiated (Rayonet Photochemical Reactor RPR-208; $\lambda = 300 \pm 20$ nm; ca. 800 W) at 15–20 °C in a Pyrex tube while purging with a constant stream of dry nitrogen. The progress of the reaction was followed by TLC analysis. After complete conversion (1 h to 5 d), most of the acetone was evaporated and the remaining mixture was extracted with $CH_2Cl_2$ ($2 \times 100$ mL). The combined organic layers were washed with 5% $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated to dryness. The products were obtained after column chromatography (eluent: *n*-hexane/EtOAc = 3/1).
   Selected physical and spectral data for the product *N*-(2-methylphenyl)-phthalimide **2**: colorless solid, mp 178–180 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 2.21$ (s, 3H), 7.20 (d, 1H, $J = 8.0$ Hz), 7.29–7.45 (m, 3H), 7.80 (dd, 2H, $J = 3.2$, 5.6 Hz), 7.96 ppm (dd, 2H, $J = 3.2$, 5.6 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 18.1$, 123.7, 126.8, 128.6, 129.4, 130.5, 131.1, 131.9, 134.2, 136.4, 167.2 ppm. IR (KBr): $\nu = 3485$, 3467, 3088, 3060, 2984, 2922, 1781, 1762, 1607, 1496, 1463, 1435, 1386, 1284, 1225, 1170, 1110, 1084, 1039, 942, 884, 856, 770, 720, 633, 527 cm$^{-1}$.
5. (a) Kanaoka, Y.; Nagasawa, C.; Nakai, H.; Sato, Y.; Ogiwara, H.; Mizoguchi, T. *Heterocycles* **1975**, *3*, 553–556; (b) Kanaoka, Y.; Koyama, K. *Tetrahedron* **1972**, 4517–4520; (c) Kanaoka, Y.; Koyama, K.; Hatanaka, Y. *J. Photochem.* **1985**, *28*, 575–576.
6. Selected physical and spectral data for the product 6*a*-hydroxy-6,6*a*-dihydro-5-oxa-aza-benzo[*a*]fluoren-11-one **4a**: colorless solid, mp 236–237 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 3.28$ (br s, 1H), 3.82 (d, 1H, $J = 10.8$ Hz), 4.74 (d, 1H, $J = 10.8$ Hz), 7.04–7.14 (m, 3H), 7.60 (m, 1H), 7.64–7.71 (m, 2H), 7.89 (d, 1H, $J = 7.2$ Hz), 8.19 ppm (d, 1H, $J = 7.2$ Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 70.6$, 82.3, 116.9, 121.5, 122.3, 122.6, 123.0, 124.5, 125.4, 131.0, 131.6, 133.3, 141.8, 153.1, 164.7 ppm. IR (KBr): $\nu = 3286$, 3063, 2993, 2860, 1676, 1612, 1500, 1466, 1381, 1306, 1277, 1221, 1132, 1082, 980, 881, 754, 694, 656 cm$^{-1}$.
7. (a) Oelgemöller, M.; Cygon, P.; Lex, J.; Griesbeck, A. G. *Heterocycles* **2003**, *59*, 669–684; (b) Griesbeck, A. G.; Oelgemöller, M. *Synlett* **1999**, 492–494.
8. General procedure for irradiation: *N*-Methylphthalimide (2 mmol) was dissolved in acetone (150 mL). A solution of the potassium phenoxy carboxylate (10 mmol) in water (150 mL) was added, and the mixture was irradiated (Rayonet Photochemical Reactor RPR-208; $\lambda = 300 \pm 20$ nm; ca. 800 W) at 15–20 °C in a Pyrex tube while purging with a slow stream of nitrogen. The progress of the reaction was followed by TLC analysis or by passing the departing gas stream through a saturated barium hydroxide solution. After 1–3 h of irradiation, most of the acetone was evaporated and the mixture was extracted with $CH_2Cl_2$ ($3 \times 100$ mL). The combined organic layers were washed with 5% $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated. The products were obtained after column chromatography (eluent: *n*-hexane/EtOAc = 1/3).
   Selected physical and spectral data for the product 3-hydroxy-2-methyl-3-phenoxymethyl-2,3-dihydro-isoindol-1-one **7a**: colorless solid, mp 140–142 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 2.86$ (s, 3H), 4.15 (bs, 1H), 4.25 (d, 1H, $J = 9.6$ Hz), 4.36 (d, 1H, $J = 9.6$ Hz), 6.78 (d, 2H, $J = 8.0$ Hz), 6.94 (t, 1H, $J = 8.0$ Hz), 7.22 (dd, 2H, $J = 8.0$, 8.0 Hz), 7.43 (t, 1H, $J = 7.6$ Hz), 7.49–7.69 ppm (m, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 24.0$, 69.0, 88.5, 114.7, 121.5, 122.1, 123.1, 129.4, 129.8, 131.4, 132.1, 144.9, 157.8, 167.7 ppm. IR (KBr): $\nu = 3307$, 3073, 2977, 2885, 1940, 1696, 1599, 1493, 1432, 1395, 1306, 1292, 1251, 1177, 1159, 1053, 1026, 963, 879, 809, 767, 705, 673, 509 cm$^{-1}$.

9. (a) Görner, H.; Griesbeck, A. G.; Heinrich, T.; Kramer, W.; Oelgemöller, M. *Chem. Eur. J.* **2001**, *7*, 1530–1538; (b) Görner, H.; Oelgemöller, M.; Griesbeck, A. G. *J. Phys. Chem. A* **2002**, *106*, 1458–1464.
10. Yokoi, H.; Nakano, T.; Fujita, W.; Ishiguro, K.; Sawaki, Y. *J. Am. Chem. Soc.* **1998**, *120*, 12453–12458.
11. Yoon, U. C.; Lee, C. W.; Oh, S. W.; Kim, H. J.; Lee, S. J. *J. Photo Sci.* **2000**, *7*, 143–148.
12. (a) Yoon, U. C.; Kim, H. J.; Mariano, P. S. *Heterocycles* **1989**, *29*, 1041–1064; (b) Yoon, U. C.; Oh, J. H.; Lee, S. J.; Kim, D. U.; Lee, J. G.; Kang, K.-T.; Mariano, P. S. *Bull. Korean Chem. Soc.* **1992**, *13*, 166–172.
13. Griesbeck, A. G.; Oelgemöller, M. *Synlett* **2000**, 71–72.
14. (a) Gutenberger, G.; Meggers, E.; Steckhan, E. In *Novel Trends in Electroorganic Synthesis*; Torii, S., Ed.; Springer: Tokyo, 1998, pp 367–369; (b) Yoshida, J. *Top. Curr. Chem.* **1994**, *170*, 39–81.
15. Eberson, L. In *Electron Transfer Reactions in Organic Chemistry*; Hafner, K., Ed.; Reactivity and Structure-Concepts in Organic Chemistry; Springer: Berlin, 1987; Vol. 25.
16. Griesbeck, A. G.; Kramer, W.; Heinrich, T.; Lex, J. *Photochem. Photobiol. Sci.* **2002**, *1*, 237–239.
17. (a) Griesbeck, A. G.; Heinrich, T.; Oelgemöller, M.; Molis, A.; Heidtmann, A. *Helv. Chim. Acta* **2002**, *85*, 4561–4578; (b) Wagner, P. *J. Acc. Chem. Res.* **1983**, *16*, 461–467.