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Photolytic Generation of Carbon Radicals from Barton Esters: Recent Developments

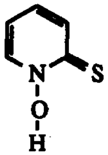
Derek H. R. Barton, Joseph Cs. Jaszberenyi* and Dagang Tang

Department of Chemistry, Texas A&M University, College Station, Texas 77843

Abstract: *O*-Acyl derivatives of *N*-hydroxy-2-thiopyridone can be photolysed with suitable commercial visible-light lamps to give reactions with very short half-lives (down to 20 s) at 0° C or room temperature.

O-Acyl derivatives of thiohydroxamic acids[1] and hydroxamic acids[2] are useful precursors of various carbon-centered (mostly alkyl or substituted alkyl), nitrogen-centered, oxygen-centered and other radicals.[3] The most often used and most versatile examples are various *O*-acyl derivatives **2** (Barton esters) of the thiohydroxamic acid *N*-hydroxy-2-thiopyridone **1**. The usefulness of these acyl derivatives has been demonstrated in several cases and often reviewed in the chemical literature.[4] Other thiocarbonyl compounds **3** have also been described, sometimes showing very short half-lives.[5]

The easy access to carbon radicals starting from these compounds is related to the fact, that radical cycles are readily initiated by attack of chalcophylic radicals on the thiocarbonyl group of the thiopyridone moiety, as well as by thermolytic or photolytic methods. Thus, Barton esters became key compounds in several functional group transformations,[6] often important in the chemistry of Natural Products. One occasional drawback is the somewhat long reaction time, required for the visible (tungsten) light photolysis at low temperatures. In order to overcome this problem and improve the usefulness of thiohydroxamates we initiated an investigation of various commercially available lamps as potential light sources for the photolysis of *O*-acyl thiohydroxamates and related compounds. We report herein that modestly priced lamps are available that can considerably shorten the time required for visible light photolysis of *O*-acyl-2-thiopyridone derivatives **2**.



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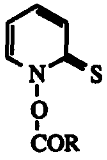

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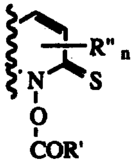


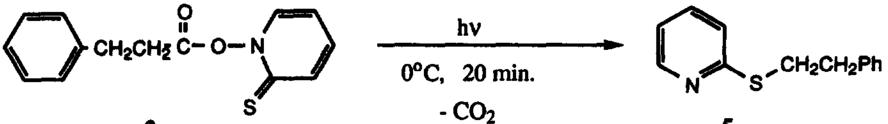
3

R-Br

4

In **2** and **4**: R = **a**: β-phenethyl- **b**: isopropyl- **c**: 1-adamantyl- **d**: pentadecyl-

Three Barton esters, a primary, a secondary and a tertiary radical precursor **2a-c**, respectively, were selected for these studies. After some preliminary experiments with **2b** and **2c**, respectively, the dihydrocinnamate **2a** was used for the comparative photolyses. The samples of **2a** were photolyzed for 5 or 20 min in about 0.1 M (0.0965 M) solutions in $CDCl_3$ at 0°C and analyzed by ^1H NMR (**Scheme 1, Table I**).



2a **5**

Scheme 1

Table I. Photolysis of thiohydroxamate **2a** with various light sources (without a radical trap).

Entry	light source (5 min. photolysis)	Photolysis (%)	Entry	light source (20 min. photolysis)	Photolysis (%)
1	Texan sunshine	100	11	Sunlux Super Ace[g] 360 W	93.5
2	Q-Beam[7] 100 W (Xe)[a]	88	12	ITS[h] 500 W (Q-H)	80
3	Crystal[e] 200 W (W)	71	13	300 W white[e] (W)	79
4	Baja[b] 100 W (Q-H)[8]	62	14	15 W Osram[i] (focused) (F)	70.5
5	Mercury vapor bulb[f] 175 W	57	15	White bulb[e] (W) 250 W	64
6	1.5 million candlepower quartz-halogen lamp	52	16	300 W white[j] (Q-H)	56
7	Halogen 150 W[c] (Q-H)	26	17	Mercury vapor[k] 175 W	55
8	Halogen 150 W[c] (w/o filter)	47	18	Blazer MM 55[l] (Q-H)	51
9	Halogen[d] 90 W (Q-H)	25	19	Daylux-50[TM,m]	42
10	Halogen[d] 90 W (w/o filter)	39	20	Osram[n] 20 W (F)	33

(Xe) = xenon (Q-H) = quartz-halogen (W) = tungsten (F) = fluorescent

[a] This lamp was operated with a 12 V power supply (FAW 12-8.3K). For longer photolyses we drilled holes on the lamp housing to allow air cooling of the reflector and the whole lamp. Compressed air was allowed to flow through the lamp house during photolysis. This increases the lifetime of the lamp and the 100 W bulb (Osram Xenophot).

[b] Baja C52C 6 1/4" diameter 12 V 'Desert Fox' round lamp equipped with a 100 W H3 quartz halogen bulb. This lamp was operated with a 12 V power supply (FAW 12-8.3K).

[c] 150 W replacement for 90 W. GE halogen floodlight 90PAR/FL/HAL (17451). Complete photolysis was observed in 20 min. with the original lamp and also with a modified version where the front glass was removed with a diamond saw. (We do not recommend this procedure.)

[d] Philips 90 W halogen spot MASTER Line™ lamp 90PAR38/H/SP (130V) (Product # 377838).[9]

[e] General Electric.[10] [f] Model 950-1175.[11]

[g] Sunlux Super Ace R57 lamp (NHR 360 LC), 360 W (Iwasaki Electric Co., Ltd.).[12]

[h] Yardglow 500 W portable halogen light (ITS Industries).[13]

[i] Osram, 15 W DULUX® EL fluorescent reflector lamp H7JDULUX-EL001 (DB 065).[14]

[j] Night Vigil™ quartz halogen lamp (Model 3030WH) (120 V, 60 Hz, 300 W AC).[15]

[k] Without the white glass bulb. (We do not recommend the removal of the glass bulb.)

[l] Blazer® MM55 quartz halogen spotlight. 250,000 candlepower at 15 V.[8] Operated with a 12 V power supply (FAW 12-8.3K).

[m] Daylux-50™ narrow spot lamp (C.E.W. Lighting, Inc., Dallas).[16]

[n] Osram DULUX® EL fluorescent lamp H7JDULUX-EL002.[14]

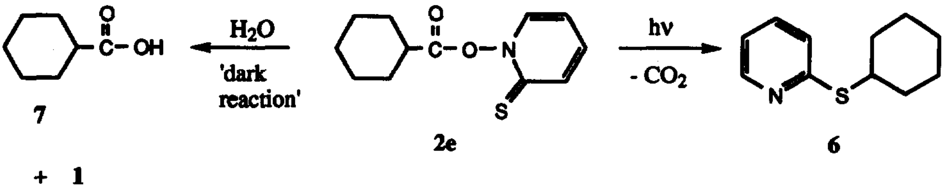
Based on these data we narrowed the range of lamps and shortened the photolysis reaction time. After some further experiments we have chosen the Brinkmann® Q-Beam® MAX MILLION™ 1,000,000 candlepower spotlight[7] for further visible light photolysis experiments. This lamp has a 12V, 100W xenon bulb, a computer-designed parabolic reflector and a well-focused beam. Photolysis of a $CDCl_3$ solution of **2a** in a highly reflecting Dewar flask (Aldrich) was complete within less than 1 min with an estimated half-life of about 20 s. There was no need for temperature or atmosphere control during this relatively fast photolysis. Photolysis experiments with **2a-c** and CBr_4 as a trap (5 equiv) gave the corresponding nor-alkyl bromides **4a-c** in 93, 85 and 93% yield (^{1}H NMR). The photolysis reaction times for **2a-c** with the xenon lamp were 1 min, 1 min and 3 min, respectively. A preparative-scale photolysis of the palmitoyl derivative **2d** gave the nor-bromide **4d** in a 79% isolated yield in a very clean reaction.

These findings show that *O*-acyl-*N*-hydroxy-2-thiopyridone derivatives have the built-in potential to be photolyzed very efficiently with well focused suitably powerful visible light sources. This can help to overcome the occasional problems associated with ionic side-reactions (hydrolysis). Competing hydrolysis can be eliminated in water containing solutions in the presence of Fe(III) or Cu(II) ions by the use of the Q-beam® xenon lamp. These experiments were designed for the study of the mechanism of the Gif-type oxidations of saturated hydrocarbons[17-20] (**Table II**, **Scheme 2**).

Table II. Photolysis of thiohydroxamate 2e with two different light sources in the presence of metal ions and water.

Entry	lamp[a]	Fe(III)[b]	Yield (%)[c]		Entry	lamp	Cu(II)[f]	Yield (%)	
		(mmol)	6	7			(mmol)	6	7
1[d]	A	0.01	88	trace	1[d]	A	0.01	79	10
2	B	0.01	trace	95	2	B	0.01	30	53
3	A	0.02	93	13	3[e]	A	0.1	90	trace
4	A	0.05	3	90	4	B	0.1	74	12
5[e]	A	0.1	92	trace	5	A	0.2	94	trace
6	B	0.1	44	48	6	B	0.2	52	28
7	A	0.2	88	trace	7	A	0.5	90	trace
8	B	0.2	6	76	8	B	0.5	32	56
9	A	0.5	50	36	9	A	1.0	70	20
10	B	0.5	trace	84	10	B	1.0	18	76

[a] Lamp A: 100 W xenon Q-Beam® 1 million candlepower lamp. Lamp B: 200 W clear tungsten lamp. [b] As $Fe(NO_3)_3 \cdot 9H_2O$. [c] Determined by capillary glc with naphthalene as internal standard. (Other products and/or remaining starting material not measured. Accuracy ± 3%.) [d] Entries 1-4 (with Fe(III)) and 1-2 (with Cu(II)): the reactions were carried out in a pyridine:water = 9:1 solution (1 mmole/10 ml). [e] Entries 5-10 (Fe(III)) and 3-10 (Cu(II)): reactions in a solution in dry pyridine. The water was introduced only as the hydrate of the given metal salts (0.5 mmole/15 ml dry pyridine). [f] As $Cu(OAc)_2 \cdot H_2O$. The reactions were carried out at 0°C. Lamp distance from reaction vessels: 20 cm.



Scheme 2

Further work on the technical improvement of the generation of carbon radicals by visible light photolysis is in progress in our laboratories.[21]

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9 Philips Lighting Company, 200 Franklin Square Drive, Somerset, NJ 08875-6800.
10 GE Lighting, General Electric Company, Nela Park, Cleveland, OH 44112.
11 Innovative Controls, Inc., 12164 Hempstead Highway, Houston, TX 77902.
12 Iwasaki Electric Co., Ltd., 12-4 Shiba 3-chome, Minato-ku, Tokyo, Japan.
13 ITS Industries, Carmel, Indiana 46032.
14 Osram Corporation, 110 Bracken Road, Montgomery, NY 12549.
15 Lights of America, Walnut, CA 91789.
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21 The use of Californian sunshine has also been advocated. See Dauben, W. G.; Kowalczyk, B. A.; Bridon, D. P. *Tetrahedron Lett.* **1989**, *30*, 2461. However, it would be difficult to beat free Texan sunshine (Table I, entry 1. The time of photolysis was 2.20 p.m. CST, 2-12-1993. Temperature: 20.2°C. In fact, the photolysis was complete in about 2 min. with a half-life of less than one min.). Those who live in more northern climes will note that we were using Texan February sunshine.

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