

Supporting Information Part I

A Soluble, Halogen-free Oxalate from Methyl Salicylate for Chemiluminescence Demonstrations

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S Supporting Information

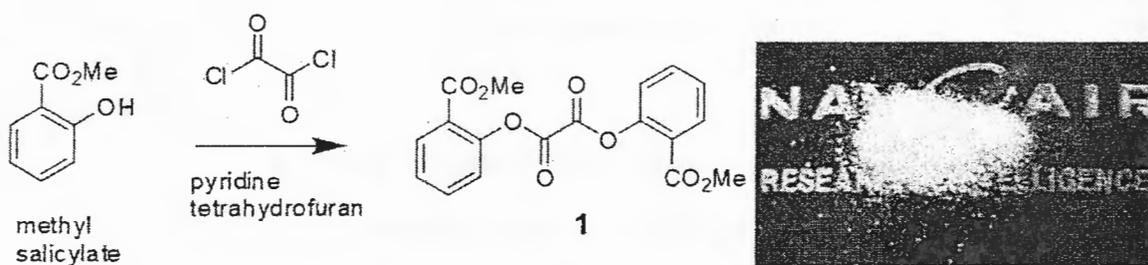
ABSTRACT: A new compound, bis[2-(methoxycarbonyl)phenyl]oxalate, made from methyl salicylate (oil of wintergreen) was found to be an excellent replacement for the typical halogen or nitro substituted oxalate esters used in peroxyoxalate chemiluminescence demonstrations. The compound is easily prepared and has good solubility in organic solvents such as ethyl acetate which is an environmentally friendly solvent to use in the demonstration.

KEYWORDS: K-12 School Science, Undergraduate Organic Chemistry, Demonstrations, Natural Products, Essential Oils, Fluorescence, Solubility, Sustainable Chemistry

Among a series of chemical demonstrations given at a local high school the chemiluminescence display was a hit even among the more uninterested students.¹⁻⁸ All the students were familiar with Cyalume® glowsticks as well as lightning bugs (beetle family Lampyridae) which facilitated making a learning connection between demonstration and the natural world. A new compound bis[2-(methoxycarbonyl)phenyl]oxalate (**1**)⁹ was prepared by esterification of the natural product methyl salicylate with oxalyl chloride in the presence of base as outlined in Figure 1.¹⁰ The molecule has good solubility in typical organic solvents including ethyl acetate (100 mg / 5 mL @ 23 °C) which is a 'green' solvent to employ in the demonstration, since it is naturally occurring, sustainable, rapidly biodegradable and non-toxic.^{11,12} Most importantly, compound **1** produced chemiluminescence in much the same way as bis(2,4,6-trichlorophenyl)oxalate (TCPO), which was used in early rehearsals of the demonstration.¹³

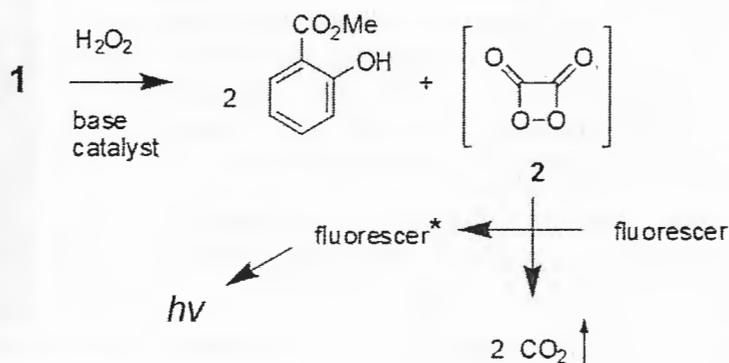
Figure 1. Preparation of bis[2-(methoxycarbonyl)phenyl]oxalate (**1**) from the natural product methyl salicylate





The putative reaction mechanism for light generation in the peroxyoxalate chemiluminescence system is shown in Figure 2.¹⁴⁻¹⁶ Hydrogen peroxide will react with 1 under base catalysis to regenerate methyl salicylate as well as produce 1,2-dioxetanedione (2). The latter, highly reactive molecule decomposes releasing energy that excites the fluorescer or dye present in the mixture.¹⁷ Subsequently, the excited fluorescer upon returning to ground state, releases energy in the form of the light observed.

Figure 2. Mechanism for peroxyoxalate chemiluminescence



DEMONSTRATION

Overview

The bis[2-(methoxycarbonyl)phenyl]oxalate (1) can be prepared by the instructor as shown in Figure 1.

Chemicals and Glassware

Oxalyl chloride; methyl salicylate; pyridine; tetrahydrofuran; ethyl acetate; perylene; 30% hydrogen peroxide; sodium salicylate; 4L polyethylene bottle and funnel for waste collection.

Synthesis of bis[2-(methoxycarbonyl)phenyl]oxalate (1)

A 250 mL round-bottomed flask equipped with magnetic stir bar was charged with methyl salicylate (3.85 g, 25.3 mmol, 2 equiv), pyridine (4.97 g, 63 mmol, 2.3 equiv) and tetrahydrofuran (50 mL). The mixture was cooled in an ice bath and oxalyl chloride (1.6 g, 12.7 mmol, 1 equiv) was added dropwise by pipette for 15 min. Copious solids precipitated during the addition (pyridine hydrochloride). The cooling bath was removed and the mixture was stirred at rt for 1 h. Afterwards, H₂O (50 mL from the tap) was added which dissolved the salt and precipitated the product. After stirring 15 min, the white precipitate was collected on a porcelain Büchner funnel with medium filter paper. The solid was air dried on the frit for 30 min (3.88 g, 86%). Although not necessary, the product can be recrystallized from isopropanol, EtOH, EtOAc, MeCN, toluene or tetrahydrofuran in the form of plates or rhombs. Mp 134-136 °C (MeCN, not corrected). ¹H NMR (300 MHz, CDCl₃): δ 8.17-8.09 (m, 2H), 7.70-7.60 (m, 2H), 7.47-7.38 (m, 2H), 7.37-7.27 (m, 2H), 3.92 (s, 6H); ¹³C (75 MHz, CDCl₃): δ 164.55, 155.58, 149.69, 134.36, 132.29, 127.23, 123.32, 122.79, 52.56. Elemental analysis calculated for C₁₈H₁₄O₈: C, 60.34; H, 3.94. Found: C, 60.20; H, 4.09.

Chemiluminescence Procedure

A 10 mL conical flask equipped with stir bar was charged with **1** (100 mg) and 5 mL EtOAc. All the solids are allowed to dissolve and then 20 mg perylene was added (which may not completely dissolve). Next, sodium salicylate (15 mg) was added, which acts as basic catalyst, and finally one drop of 30% H₂O₂ followed by a quick shake of the flask. A brilliant blue color will be generated by chemiluminescence and is best observed in a darkened room with shades drawn. Typical duration of light is about 30 minutes. If the flask is capped, make sure it is loosely closed to allow for the small amount of by-product CO₂ to escape. Other dyes can be substituted resulting in different colors of light.¹⁸ The scale can be increased for larger audiences [20 fluid ounce, polyethylene terephthalate soft drink bottle: 525 mL EtOAc, 525 mg **1**, 120 mg perylene, 100 mg sodium salicylate, 250 µL 30% H₂O₂]. By carefully wafting the fumes of the reaction mixture post-demonstration, the odor of methyl salicylate will noted.

HAZARDS

The preparation of **1** should be carried out in a fume cupboard and those conducting the operations should wear personal protective equipment: laboratory coat, safety glasses or goggles and chemical resistant gloves. Oxalyl chloride is a lachrymator so keep its bottle capped as much as possible. Pyridine is an irritant with a noxious odor so minimize contact. Tetrahydrofuran and ethyl acetate are flammable liquids and should be kept away from flame and hot surfaces which could cause ignition. Perylene is a polyaromatic hydrocarbon and possibly carcinogenic in chronic exposure and so anyone handling this compound, and especially solutions thereof, should be wearing gloves. Hydrogen peroxide (30%) is an irritant that can cause burns to skin and so thick, chemically resistant gloves should be worn when handling this material during the demonstration. Although it has an agreeable odor, methyl

salicylate is a severe eye irritant and so goggles, safety glasses or faceshield should be worn at all times when handling this substance. Although sodium salicylate is a mild base, it may be caustic to mucous membranes, so avoid forming dust when handling this material which could be inhaled or come in contact with eyes. It is unknown what the hazards of compound **1**, but it is assumed that it, in contact with water, will undergo hydrolysis to salicylic acid and or methyl salicylate, so MSDS sheets on these substances should be consulted.

DISCUSSION

A new molecule, bis[2-(methoxycarbonyl)phenyl]oxalate (**1**), was prepared that can be used to demonstrate the phenomena of chemiluminescence. Methyl salicylate, which serves the role of starting material as well as by-product, is a naturally occurring substance (e.g. birch family *Betulaceae*) found in consumer products that students are aware of such as Listerine® and Bengay® and so its release into the environment is not of critical concern. In contrast, the xenobiotics 2,4,6-trichlorophenol (TCP)¹⁹ and 2,4-dinitrophenol (DNP)²⁰ associated with the widely used chemiluminescence reagents TCPO and bis(2,4-dinitrophenyl)oxalate (DNPO) are priority pollutants,²¹ environmentally persistent and likely to bioaccumulate²² in aquatic organisms since mechanisms do not exist in nature for their rapid biodegradation. By adopting this new oxalate ester, these chemistry demonstrations will have a less toxic footprint.^{23,24} The synthesis procedure for **1** described here is quick and uncomplicated and could be adapted to the undergraduate laboratory, adding to the rich chemistry salicylic acid already offers.^{25,26} Besides the environmental concerns, compound **1** will cost less to prepare than either TCPO or DNPO (methyl salicylate \$55/6.6 mole; TCP \$98/5.1 mole; DNP \$90/5.4 mole), assuming an identical procedure and similar yield.²⁷ As oxalyl chloride is relatively inexpensive (\$375/7.9 mole) and the other solvents and reagents employed are cheap and available in bulk, it leaves one to wonder about the high price of DNPO (\$174/1g) and TCPO (\$635/5g), which are presumably used solely for chemical educational and outreach.

This demonstration is not time consuming and could be joined with other short demonstrations such as the triboluminescence of sucrose crystals in the presence of methyl salicylate (Wint-O-Green lifesavers™) and still allow for class discussion afterwards.²⁸⁻³⁰

ASSOCIATED CONTENT

Supporting Information

Further background information of structure-activity relationships in regard to chemiluminescence of bis(aryl)oxalates, along with ¹H, ¹³C NMR spectra of bis[2-(methoxycarbonyl)phenyl]oxalate (**1**) (Fig. 1 and Fig. 2) and X-ray crystal structure plot (Fig. 3) can be found in the Supporting Information Part II. This material is available via the Internet at <http://pubs.acs.org>.

Table 1. Emissions of Oxalate Esters in the Presence of Hydrogen Peroxide with Rubrene As a Fluorophore

Ester	Intensity of Emission	Duration/min
bis(4-nitrophenyl) oxalate	strong	15–20
bis(<i>p</i> -cresyl) oxalate	no emission	—
bis(2,4-dinitrophenyl) oxalate	very strong	10–15
bis(2,4,6-trichlorophenyl) oxalate	strong	15–20
bis(3,4,6-trifluorophenyl) oxalate	strong	< 5 ^a
bis(3,4,5-trimethoxyphenyl) oxalate	no emission	—

^aBis(2,3,6-trifluorophenyl) oxalate discolored solutions of acceptors (most likely oxidation of the acceptor by hydrogen peroxide). Emission of light did not last long. After addition of solution of acceptor to such a reaction mixture, emission of light resumed.

Chemiluminescence with Amides

A number of amides of oxalic acid are also chemiluminescent, but were not suitable for this experiment. Amides are more difficult to prepare compared to esters. Reaction between an amine and an acyl chloride may be very vigorous and as a result some students ended up with a black sludge. When students carefully followed the experimental procedure, the resulting amides worked very well in a chemiluminescent reaction. However, chemiluminescent amides are very reactive and, upon addition of hydrogen peroxide in the presence of an acceptor, there is only a brief intense flash of light. Oxalyl chloride is also chemiluminescent and gives off a flash of light under the same conditions (18). Thus, if the preparation of an amide does not go to completion, unreacted oxalyl chloride will give a false positive reaction. There was

no such problem with esters as the activity of oxalyl chloride (a brief flash of light) was easily distinguished from that of an ester (an emission of light that lasts for minutes).

Results

The success rate in a mix-and-split combinatorial synthesis experiment was only ~50%, compared to ~80% in parallel combinatorial synthesis. A success meant that a student observed a chemiluminescence reaction when there should have been one.

In a subsequent experiment, students examined the chemiluminescence reaction itself. When doing initial tests on oxalate esters, the students used rubrene as an acceptor (Table 1). In the final part of the exercise, students examined the effect of the acceptor on the efficiency of a chemiluminescence reaction (as determined by the intensity of emitted light) and the effect of the acceptor on the color of emitted light. We found that a number of inexpensive acceptors are suitable for this experiment (Table 2). Among them, freshly isolated chlorophyll gave the best results. However, not all oxalate esters gave a positive chemiluminescence reaction with all of the acceptors. Among the acceptors we used, rubrene gave a positive reaction with the largest number of esters (Figure 2). A reaction mixture can be heated in a water bath to increase the intensity of the emitted light (Figure 3).

It was interesting for the students to compare colors of light emitted by anthracene and 9,10-diphenylanthracene (Figure 4). Since colors of the emitted light depend on the degree of conjugation in the acceptors, by comparing the colors, or even better the emission spectra, students can make conclusions about the degree of conjugation between the two phenyl substituents and the anthracene ring in 9,10-diphenylanthracene.

Table 2. Behavior of Acceptors in a Reaction of Bis(2,4-dinitrophenyl) oxalate with Hydrogen Peroxide

Acceptor	Color of Emitted Light	Intensity ^a	Duration
anthracene	blue	medium	5 min
xanthone	yellow-white	weak	2 min
1,10-phenanthroline	pale yellow	very weak	few seconds
chlorophyll	red	strong	5 min
stilbene	pale yellow	weak	2–5 min
fluorescein	yellow	weak	5 min
9,10-diphenylanthracene	blue	strong	15 min
rubrene	yellow-orange	very strong	10–15 min
2-naphthol	pale blue	weak	2 min
2-nitro-1-naphthol	yellow	weak	1 min
2,4-dinitro-1-naphthol	yellow-green	medium	few seconds
naphthalene	pale yellow	very weak	few seconds
benzil	pale yellow	very weak	few seconds
dibenzalacetone	pale green	weak	few seconds
methyl salicylate	pale blue	weak	1 min
β -carotene	blue-green	weak	1 min

^aStrong—emission can be seen in a room with lights off (emergency light was on, external light coming in through windows was not blocked); medium—can be seen in a room, but best seen in a dark box; weak—can be seen in a dark box; very weak—can be seen in a dark box after eyes have adapted to darkness.