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One-Pot Synthesis of Novel Photochromic Oxazine Compounds

Weili Zhao*,†,‡ and Erick M. Carreira*,§

Key Laboratory for Special Functional Materials of the Ministry of Education, Henan University, Kaifeng, 475004, China, School of Pharmacy, Fudan University, Shanghai, 201203, China, and Laboratorium für Organische Chemie, ETH-Zürich, CH-8093, Zürich, Switzerland

zhaow@henu.edu.cn; carreira@org.chem.ethz.ch

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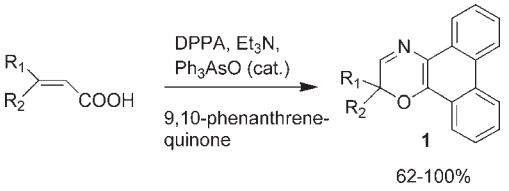
ABSTRACT



A one-pot domino synthesis of photochromic 2,2-diarylphenanthro-(9,10)-[2*H*]-[1,4]-oxazines in excellent yield is described starting with acrylic acid derivatives. The reaction mechanism was studied by ReactIR and UV−vis. The cascade sequence of the reactions involves five transformations, namely, acyl azide formation, Curtius rearrangement, arsonium ylide formation, aza-Wittig, and final cyclization to the title compounds.

Photochromic molecules which undergo reversible color change upon absorption of light (i.e., sunlight) have led over the last number of decades to intense investigations in a wide range of potential applications such as optical switches, memory storage, imaging devices, as well as ophthalmic lenses.[1] Currently, the largest commercial use of organic photochromic dyes is in the ophthalmic lens industry in the design and synthesis of photochromic compounds with improved properties; these include spiropyrans,[2] diaryl naphthopyrans,[3] and spirooxazines.[4] It is generally accepted that diaryl naphthopyrans are more fatigue-resistant than spiroindolinonaphthopyrans.[3,5] Spiroindolinophenanthroxazines were reported to have extraordinary stability against thermal and photochemical degradation.[6] In contrast to the well studied spirooxazine, non-spirooxazine photochormic compounds have been neglected.[7,8] 2,2-Diaryl naphtho-[2*H*]-[1,4]-oxazine compounds were claimed to have better fatigue resistance than the structurally closely related naphthopyrans.[7a] We have been interested in novel 2,2-

† Henan University.
‡ Fudan University.
§ ETH-Zürich.

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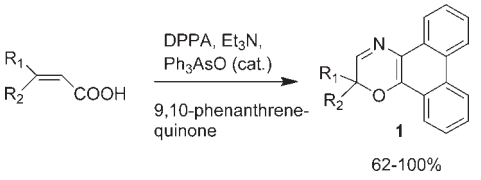
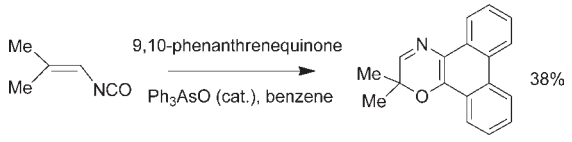
disubstituted phenanthroxazine (**1**) with the expectation that novel oxazines may derive benefits from both spiroindolinophenanthroxazines and 2,2-diaryl-[2*H*]-naphtho-[1,4]-oxazine.[9] However, the known 2,2-disubstituted [2*H*]-[1,4]-oxazine compounds and the methodologies for their preparation are extremely limited. Herein we report an efficient one-pot synthesis of 2,2-disubstituted phenanthro-(9,10)-[2*H*]-[1,4]-oxazine **1**.



The reported method for preparation of 2,2-[bis(*p*-dimethylamino)phenyl]phenanthro-(9,10)-[2*H*]-[1,4]-oxazine is limited to the use of functionalized, activated ethyl amines to undergo reaction with phenanthrene-(9,10)-dione monooxime.[8] α-Halo or hydroxy aromatic acetaldehyde reacting with *o*-aminohydroxyaromatic compounds was also reported to generate 2,2-disubstituted [2*H*]-[1,4]-naphthoxazine.[7] The yield has been reported to be modest, and the product is difficult to purify, based on our experience. 2,2-Disubstituted phenanthro-(9,10)-[2*H*]-[1,4]-oxazines were previously prepared from isocyanates in relatively low yields (Scheme 1).[10] For example, 2,2-dimethyl phenanthro-(9,10)-[2*H*]-[1,4]-oxazine and 2-phenyl phenanthro-(9,10)-[2*H*]-[1,4]-oxazine were reported to be isolated in yields of 38 and 40%, respectively.[10]

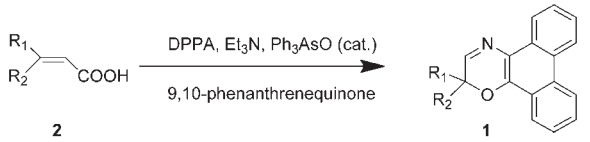
Scheme 1. Previously Reported Synthetic Method for the Preparation of 2-Substituted [2*H*]-[1,4]-Oxazine[10]



The method of Frøyen describes the use of alkenyl isocyanates;[10] however, the fact that these are not readily available sets a limit to the approach.[11] There are various problems associated with the preparation and isolation of vinyl isocyanates as well as their precursors, namely, acryloyl azides. Preparation of acryloyl azides from the corresponding hydrazides and nitrous acid is frequently hampered due to competitive cyclization of the unsaturated hydrazides.[12] To generate acryloyl azides from vinyl acid chlorides and sodium azide, the acid chlorides must be carefully purified to avoid the generation of very explosive hydrazoic acid. Such reactions may not be entirely reliable and may be difficult to control. Acryloyl azides could also be prepared directly by Yamada's protocol from acrylic acids and diphenylphosphoryl azide (DPPA) in a nonpolar solvent in the presence of a base such as triethylamine or 1,8-bis(dimethylamino)naphthalene (proton sponge);[13,14] however, low yields of isocyanates were obtained following heating.[13] It is known that the vinylisocyanates polymerize easily even at room temperature.[12,15] Additionally, isocyanates are generally extremely sensitive to acid (polymerization)[15] and to Et_3N under heating (isomerization to isocyanurates).[13] In the reported attempts at preparation of styryl isocyanate with modified Yamada conditions, no desired product could be isolated.[13]

Despite difficulties outlined above, Frøyen's method is distinct in that it provides a method for the introduction of an imine onto a quinone which is sensitive to strongly basic and nucleophilic conditions.[10] An iminoarsenane is believed to be the key intermediate, which was observed to have low reactivity toward isocyanates but high reactivity toward ketones.[10] In line with our interest in photoactive compounds, we have explored the development of mild, efficient methods for the synthesis of oxazines by taking advantage of the iminoarsenane intermediate. It is known that the sensitivity of iminoarsenanes toward moisture and electrophiles is attenuated by the presence of electron-withdrawing groups attached to the nitrogen atom. We speculated that styryl-conjugated iminoarsenane may provide enough reactivity toward quinones and decrease sensitivity to moisture, thus leading to reaction conditions potentially compatible with isocyanates prepared in situ by Yamada's protocol. As discussed below, we have reduced these hypotheses to reality in the form of a convenient, one-pot procedure to synthesize photochromic 2,2-diarylphenanthro-(9,10)-[2*H*]-[1,4]-oxazine (Scheme 2).

Scheme 2. One-Pot Synthesis of 2,2-Substituted Phenanthro-(9,10)-[2*H*]-[1,4]-oxazine (**1**)[a]



a: $R_1 = R_2$ = Ph, 100%
b: R_1 = Ph, R_2 = *p*-MeOPh, 100%
c: R_1 = Ph, R_2 = *p*-FPh, 100%
d: $R_1 = R_2$ = *p*-MeOPh, 94%
e: R_1 = *p*-MeOPh, R_2 = *p*-MorpholinoPh, 100%
f: R_1 = *p*-MeOPh, R_2 = *p*-PiperidinoPh, 96%
g: R_1 = Ph, R_2 = Cyclopropyl, 80%
h: R_1 = Ph, R_2 = Methyl, 62%

[a] Regents and conditions: DPPA (1.2 equiv), Et_3N (5.0 equiv), triphenylarsine oxide (0.05 equiv), 9,10-phenanthrenequinone (0.7–0.8 equiv), toluene, 60 °C, over 3 h. The yield reported was based on 9,10-phenanthrenequinone, and the reaction temperature was 80 °C for compound **1h**.

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Our procedure commences with 3,3-diaryl acrylic acids **2**, which are easily obtained by Horner–Wadsworth–Emmons reaction of aldehydes followed by saponification of the isolated esters. We have developed a one-pot reaction for the conversion of the acrylic acids to vinyl isocyanates. In the experiment, diphenylphosphoryl azide (DPPA) was used as an azide source and a catalytic amount of triphenylarsine oxide (5 mol %) was generally required to generate aza-ylide. The optimum ratio was found to be acrylic acid/DPPA/TEA/quinone/Ph_3AsO = 1:1.2:5:0.7:0.05. At least 1 equiv of triethylamine (Et_3N) was required; the use of excess Et_3N was found to be beneficial in the overall formation of oxazine. The best solvent for the reaction was identified as toluene or benzene. Excellent yields of phenanthroxazine were obtained for diaryl-substituted species, and the yield is essentially unchanged within the reaction temperature range from 60 to 100 °C for 2,2-diaryl-substituted oxazines. The best yield for 2-cyclopropyl-2-phenylphenanthro-(9,10)-[2*H*]-[1,4]-oxazine (**1g**) was 80% when the reaction was performed at 60 °C. However, 2-methyl-2-phenylphenanthro-(9,10)-[2*H*]-[1,4]-oxazine (**1h**) was obtained in lower yield (39%) when the reaction was performed at 60 °C. The yield was improved to 62% when the reaction was conducted at 80–100 °C. Under reflux conditions, 54% yield of **1h** was isolated.

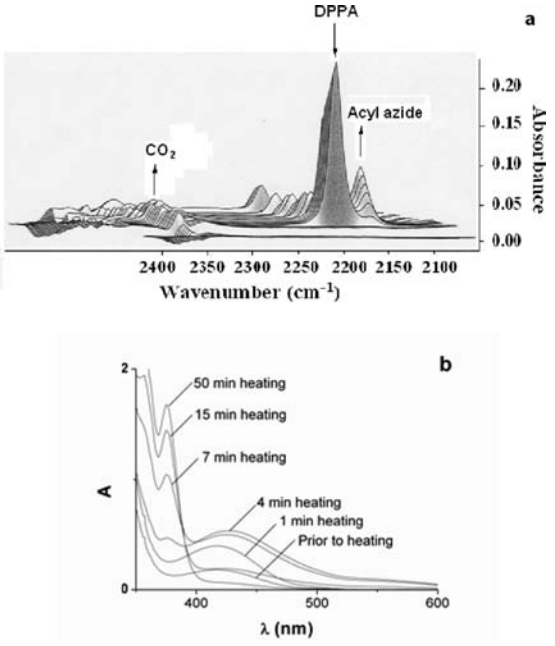


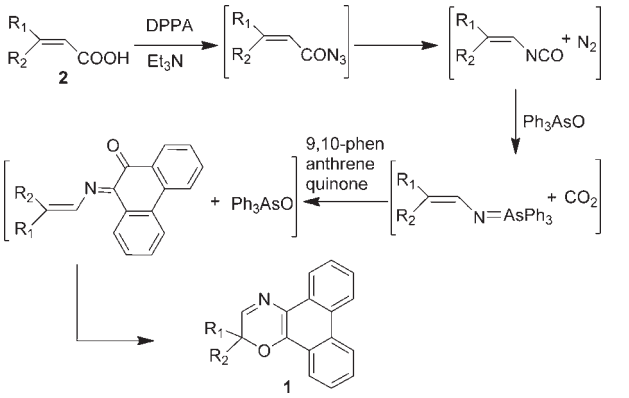
Figure 1. Reaction that results from monitoring the formation of 2,2-diphenylphenanthro-(9,10)-[2*H*]-[1,4]-oxazine in toluene: (a) in situ ReactIR spectra; (b) UV–vis spectra.

The success of the method piqued our interest in the reaction mechanism. We employed in situ ReactIR spectroscopic techniques and UV–vis spectrometric methods to monitor the formation of **1a** (see Supporting Information for details). The results are shown in Figure 1.

The consumption of DPPA and formation of acyl azide intermediate can be clearly observed by in situ ReactIR spectroscopy, and the generation of CO_2 is also captured. The formation of the iminoquinone intermediate and the generation of compound **1a** could be observed by UV–vis. On the basis of our observation, we believed the reaction involves five transformations shown in Scheme 3.

The fast reaction of DPPA and acid in the presence of base leads to an acyl azide. The acyl azide undergoes Curtius rearrangement to form an isocyanate. This isocyanate is trapped by Ph_3AsO to form the corresponding arsonium ylide, which undergoes the Staudinger–Meyer–Hauser (aza-Wittig) reaction with 9,10-phenanthrenequinone to generate a quinone imine intermediate that then cyclizes to the targeted oxazines (**1**).

Scheme 3. Mechanism of Formation of Oxazine **1**



We believe the success of the one-pot reaction is due to a sequence of efficient transformations in a domino fashion. Excess triethylamine ensures fast formation of acryloyl azide. The unstable vinyl isocyanate generated by Curtius rearrangement is rapidly trapped by triphenylarsine oxide to generate iminoarsenane, which is in turn stabilized by virtue of the styryl substitution and consequently has low sensitivity to moisture. The arsonium ylide has low reactivity toward isocyanates (several orders less reactive than its phosphonium analogue) and high reactivity toward ketones (more reactive than the corresponding phosphonium analogue).[10] It is noteworthy that reaction commences with an acid, and the arsonium ylide formed and reacted uneventfully in the presence of a large excess of phosphoric acid diphenyl ester byproduct.

The current one-pot strategy provides a number of advantages. It provides much higher yield and avoids use of unstable vinyl isocyanate generated from acrylic acid. The one-pot method is sensitive neither to moisture nor to air. The solvent may be employed directly from commercially available sources without further purification. The one-pot method we developed is also not sensitive to the order of addition of reagents, and the product is amenable to convenient purification procedures. Finally, it should

also be noted that all experimental attempts involving separate steps were significantly inferior to the one-pot procedure described herein and led to product formation in lower yield.

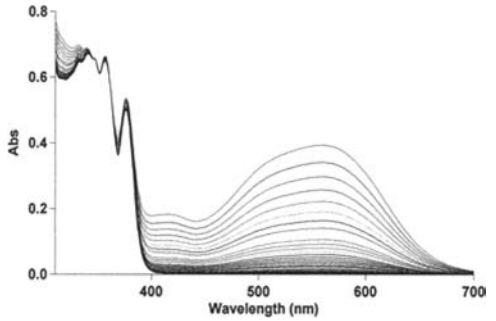


Figure 2. Fading of the colored form of 2-(*p*-methoxyphenyl)-2-(*p*-piperidinophenyl)-phenanthro-(9,10)-[2*H*]-[1,4]-oxazine in hexane with 6.57 s/scan.

All of the synthesized oxazine compounds are photochromic, displaying rather interesting features. The colored forms of the 2,2-diarylphenanthro-(9,10)-[2*H*]-[1,4]-oxazine compounds exhibit two or three absorption bands. For example, the colored forms of 2-(*p*-methoxyphenyl)-2-(*p*-piperidinophenyl)phenanthro-(9,10)-[2*H*]-[1,4]-oxazine **1f** are shown in Figure 2. Upon irradiation with UV (366 nm) light, the colorless solution of **1f** turned blue-gray, which has a very broad of absorption and relatively fast fading ($t_{1/2}$ = 31.5 s in hexane, 16.0 s in dioxane, and 4.9 s in acetonitrile). This is very unusual for photochromic oxazine compounds which cover the entire visible region. Further detailed study on the photochromism of these compounds is currently under investigation and will be reported in due course.

In conclusion, we have developed a one-pot methodology for efficient synthesis of novel 2,2-diarylphenanthro-(9,10)-[2*H*]-[1,4]-oxazine compounds using triphenylarsine oxide catalyzed domino reactions starting from an acrylic acid. The one-pot synthesis procedure is marked by high efficiency and high yield, involving five reagents and accompanying transformations.

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Supporting Information Available. Characterization data for oxazines as well as the detailed reaction mechanistic studies using ReactIR and UV−vis spectrometers. This material is available free of charge via the Internet at http://pubs.acs.org.