# Intermolecular Formyloxyarylation of Alkenes by Photoredox Meerwein Reaction

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S *Supporting Information*

ABSTRACT: The intermolecular formyloxylation−arylation of stilbenes occurs in the presence of diazonium salts, a photocatalyst, visible light, and DMF. The photo-Meerwein addition products are obtained in good yields up to 76%. We propose the formation of an iminium ion intermediate, which is hydrolyzed to the product.

KEYWORDS: *formyloxylation-arylation, Meerwein reaction, photocatalysis, diazonium salts, N,N-dimethylformamide*
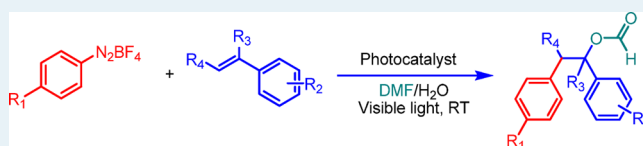
1. INTRODUCTION

The arylation of alkenes is an important transformation in organic synthesis. First reports of the reaction using aryl radicals generated from diazonium salts by the Meerwein protocol date back more than 100 years;[1] however, the classic reaction conditions of the Meerwein arylation require metal salts, such as copper oxides, and aqueous media, leading to side reactions and only moderate product yields.[2] Therefore, many improved protocols for arylations with diazonium salts have been reported over the years.[3] The recently introduced photo-Meerwein arylation uses visible-light-induced electron transfer from a photoredox catalyst, for example, eosin Y or $Ru(bpy)_3Cl_2$, to reduce the diazonium salt to aryl radicals, providing a clean conversion under mild conditions.[4] Most of the reported applications of the photo-Meerwein arylation apply an arylation−elimination sequence, regenerating the alkene double bond. The equally important Meerwein arylation addition reaction, in which a nucleophile adds to the carbenium ion intermediate obtained from aryl radical addition and oxidation of the benzyl radical, is less explored in its photocatalytic variant. We recently reported the intermolecular amino arylation of alkenes by photoredox Meerwein addition using nitriles as nucleophile and subsequent Ritter reaction,[5] but there are still few reports about photoredox oxy arylations employing diaryliodonium.[6] Here, we describe the related formyloxy arylation of alkenes by photo-Meerwein addition in the presence of dimethylformamide (Scheme 1). The three-component reaction allows the facile functionalization of styrene derivatives.

2. RESULTS AND DISCUSSION

Diazonium salts are labile toward base. The selection of a nonbasic nucleophile to trap the carbenium ion intermediate arising from aryl radical addition to the alkene and oxidation by back electron transfer to the photocatalysts (see below for the mechanistic proposal) is therefore essential. *N,N*-Dimethylfor-

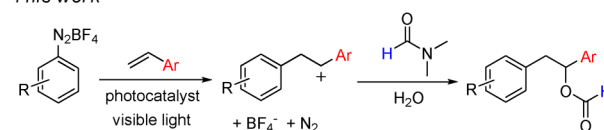## Scheme 1. Types of Photo-Meerwein Arylation Reactions[a]

(a) Photo Meerwein arylation-elimination
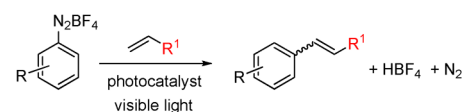
(b) Photo Meerwein arylation-addition
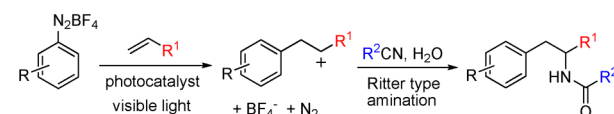
This work

[a](a) Photo-Meerwein arylation−elimination, (b) photo-Meerwein arylation−addition with nitriles and with dimethylformamide.

mamide (DMF) is widely used as a dipolar aprotic solvent. DMF can act as an electrophile[7] in reactions with organometallic reagents and as a nucleophile or ligand in coordination chemistry.[8] In visible light photoredox catalysis, DMF was recently employed to generate the Vilsmeier reagent.[9]

Irradiating 4-chlorophenyl diazonium tetrafluoroborate (**1a**) and styrene (**2a**) in the presence of eosin Y (2 mol %) in 0.5 mL of DMF with 530 nm green light gave the alkene formyloxylation arylation product **3aa** in 41% yield (Table 1, entry 10). The molecular structure of the compound was unambiguously confirmed by X-ray single crystal analysis

Table 1. Optimizing Reaction Conditions[a]

entry	conditions	yield %[c]
1	Ru(bpy)₃Cl₂(H₂O)₆ (0.7 mol %)[b]	59
2	Ru(bpy)₃Cl₂(H₂O)₆ (1.3 mol %)	71
3	Ru(bpy)₃Cl₂(H₂O)₆ (2.0 mol %)	**76**
4	Ru(bpy)₃Cl₂(H₂O)₆ (2.7 mol %)	71
5	2a (2.0 equiv)	64
6	2a (3.0 equiv)	66
7	2a (6.0 equiv)	75
8	1.0 h	59
9	2.0 h	60
10	eosin Y (2.0 mol %)	41
11	sulforhodamine B (2.0 mol %)	44
12	Rose Bengal (2.0 mol %)	43
13	Rhodamine B acid (2.0 mol %)	47
14	1a (0.8 M)	48
15	1a (0.6 M)	70
16	1a (0.2 M)	56
17	no H₂O	64
18	H₂O (2.0 equiv)	71
19	H₂O (5.0 equiv)	65
20	H₂O (10.0 equiv)	58
21	no photocatalyst	0
22	no light	trace

[a]All reactions were carried out on a scale of 0.2 mmol of the diazonium salt at 25 °C. [b]See the Supporting Information for the detailed structures of the photocatalysts. [c]Isolated yields given.

(Figure 1). No significant product formation is observed in the absence of the photocatalyst or the light source. Furthermore,
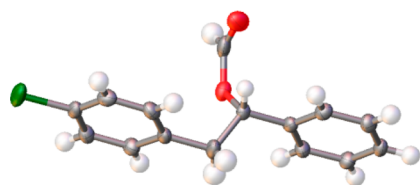

Figure 1. Molecular structure of compound **3aa** in the solid state.

we examined the influence of the water content, the type and amount of the photocatalyst, and the number of equivalents of styrene on the reaction yield. Product **3aa** was obtained in 76% yield (Table 1, entry 3) when the diazonium salt **1a** (0.2 mmol) was reacted with 4 equiv of styrene (**2a**) in the presence of 2 mol % of [Ru(bpy)₃]Cl₂(H₂O)₆ and 1 equiv of water in 0.5 mL of DMF at room temperature.

Next, we explored the scope of the diazonium salts; the results are summarized in Table 2. Aryl diazonium salts bearing electron-withdrawing, -neutral, and -donating substituents react smoothly, affording the corresponding products in good yields. Several functional groups, including ester, nitro, halide, ether, and alkyl groups, are tolerated in the photoreaction. Heteroaryl diazonium salt **1j** gave product **3ja** in only 35% yield along with the photo-Meerwein arylation−elimination product in 15% yield.

Different aryl alkenes were used in the reaction; the results are summarized in Table 3. Styrenes with electron-withdrawing,
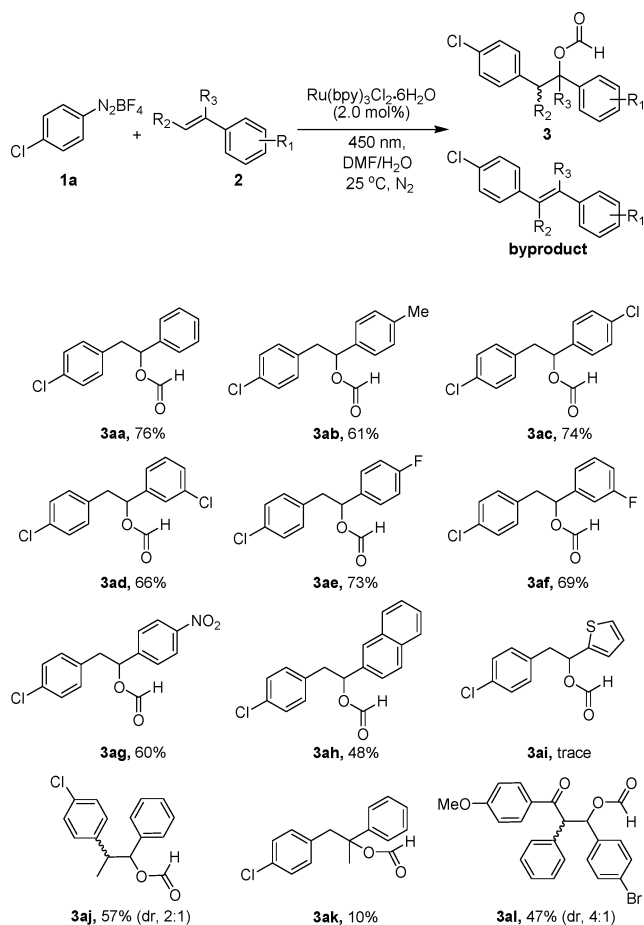
Table 2. Scope of the Aryl Diazonium Salts[a]

3aa, 76%   **3ba**, 69%   **3ca**, 69%

3da, 66%   **3ea**, 72%   **3fa**, 70%

3ga, 68%   **3ha**, 74%   **3ia**, 74%

3ja, 35%   **3x**, 52%

[a]The reaction was carried out with **1** (0.2 mmol), styrene **2a** (0.8 mmol), [Ru(bpy)₃]Cl₂(H₂O)₆ (0.004 mmol), and 1.0 equiv of water in 0.5 mL of DMF. Yields of isolated products are given.

-neutral, and -donating substituents at the para position yield the corresponding products in moderate to good yields under standard reaction conditions. The internal alkenes trans-β-methylstyrene and benzalacetone provide the addition products in 57% and 47% yield, respectively, but with only low diastereoselectivity (d.r. 2:1 and 4:1, respectively). The X-ray crystal structure analysis of compound **3al** (see Supporting Information) shows the configuration of its major diastereoisomer. α-Methylstyrene yields the corresponding addition product in only 10%, with elimination product dominating. The scope of alkenes is limited to alkenyl arenes. Double bonds with rigid cyclic structure, such as indene, or alkenes bearing no aryl substituent, such as p-benzoquinone and methyl acrylate, do not convert to the corresponding product in significant yields.

If N,N-dimethylacetamide is used instead of DMF, the corresponding product **3x** is obtained in 52% yield. A plausible mechanism of the photoreaction based on previous work is proposed in Scheme 2, the trapping of radical intermediates and experiments using labeled compounds. The aryl radical **4** is produced by a single-electron transfer from the excited state of the photocatalyst [Ru(bpy)₃]²⁺* to the diazonium salt **1f**. Addition of the aryl radical to alkene **2** generates the corresponding benzyl radical intermediate **5**, which is oxidized by Ru(III) to give a carbenium ion intermediate **6a** and reacts with the carbonyl oxygen of N,N-dimethylformamide to generate the iminium ion intermediate **7**. Hydrolysis of the iminium ion yields the formyloxylation product **3f**. Alternatively, benzyl radical **5** reacts first with DMF, giving **6b**, which is oxidized by Ru(III), yielding iminium ion **7**. The addition of a radical intermediate to DMF has been proposed previously.[9,10] The addition of TEMPO to the reaction mixture allows trapping of the aryl radical addition intermediate, which supports its being an intermediate during the photoreaction. The use of DMF-d₇ gave the product with deuterium label at the formyl position (see the Supporting Information for data), whereas in reactions with added D₂O instead of water, no deuterium incorporation was observed.

Table 3. Scope of Alkenes[a]

3aa, 76%   3ab, 61%   3ac, 74%

3ad, 66%   3ae, 73%   3af, 69%

3ag, 60%   3ah, 48%   3ai, trace

3aj, 57% (dr, 2:1)   3ak, 10%   3al, 47% (dr, 4:1)

[a]The reaction was carried out with **1a** (0.2 mmol), styrene **2** (0.8 mmol), [Ru(bpy)$_3$]Cl$_2$(H$_2$O)$_6$ (0.02 equiv), and 1 equiv of water in 0.5 mL of DMF. Yields of isolated products. In the case of compound **3ak**, the elimination product is the major product. In the case of compound **3al** phenyldiazonium tetrafluoroborate was used instead of **1a**.

Scheme 2. Proposed Mechanism of the Photo-Meerwein Addition Reaction with DMF
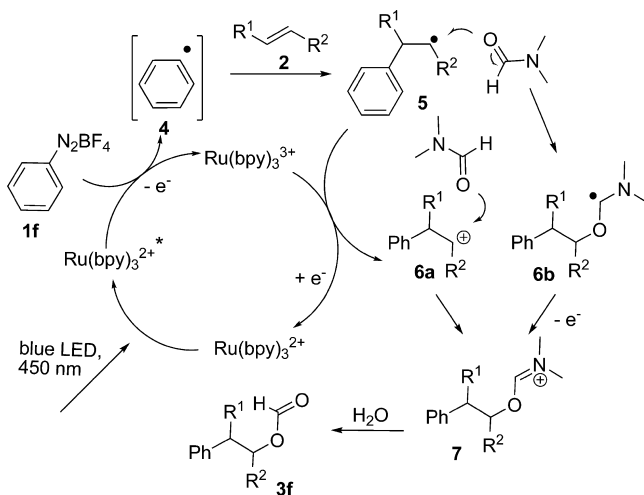
3. CONCLUSION

The intermolecular formyloxylation–arylation of stilbenes is possible by photoredox Meerwein addition reaction in the presence of diazonium salts and DMF. The addition products are obtained in good yields up to 76%. We propose the formation of an iminium ion intermediate, which is hydrolyzed to the target product.

4. EXPERIMENTAL SECTION

General Information. Unless otherwise noted, commercial reagents and starting materials were used either as p.a. grade or treated according to literature known procedures. Proton NMR spectra were recorded on a Bruker Avance 300 MHz spectrometer in CDCl$_3$ solution with internal solvent signal peak at 7.26 ppm. ^{13}C NMR were recorded using a 75 MHz spectrometer and in CDCl$_3$ solution and referenced to the internal solvent signal at 77.00 ppm. Proton NMR data are reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet), and coupling constants (Hz). All reactions were monitored by thin-layer chromatography using Merck silica gel plates 60 F254; visualization was accomplished with short wave UV light (254 nm).

Procedure for the Preparation of Aryl Diazonium Tetrafluoroborates.[11] The appropriate aniline (10 mmol) was dissolved in a mixture of 3.4 mL of hydrofluoroboric acid (50%) and 4 mL of distilled water. The reaction mixture was cooled to 0 °C using an ice–water bath, and then sodium nitrite (NaNO$_2$) solution (0.69 g in 1.5 mL of water) was added dropwise. The resulting reaction mixture was stirred for 40 min at 0–5 °C, and the obtained precipitate was collected by filtration, dried, and redissolved in a minimum amount of acetone. Diethyl ether was added until precipitation of diazonium tetrafluoroborate, which was filtered, washed several times with small portions of diethyl ether, and dried under vacuum.

General Procedure for the Reaction of Arenediazonium Tetrafluoroborates with Alkenes. A 5 mL snap vial equipped with a magnetic stirring bar was charged with the photocatalyst [Ru(bpy)$_3$]Cl$_2$ (H$_2$O)$_6$ (0.004 mmol, 0.02 equiv), arenediazonium tetrafluoroborate (0.2 mmol, 1 equiv), alkene (0.8 mmol, 4.0 equiv), water (0.2 mmol, 1 equiv), and DMF (0.5 mL). The reaction mixture was degassed by three "pump–freeze–thaw" cycles via a syringe needle. The vial was irradiated through the vial's plane bottom side using 450 nm blue LEDs with a cooling device maintaining a temperature around 25 °C. After 1.5 h of irradiation, 10 mL of water was added to the reaction mixture, which was then extracted with dichloromethane (3 × 30 mL). The combined organic phases were dried over Na$_2$SO$_4$ and concentrated in vacuum. The residue was purified by flash column chromatography using petrol ether/ethyl acetate (30:1) as eluent.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

The following file is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b00314.

NMR and MS spectra of all new compounds (PDF)

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Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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