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Intermolecular Formyloxy-Arylation of Alkenes by Photoredox Meerwein Reaction

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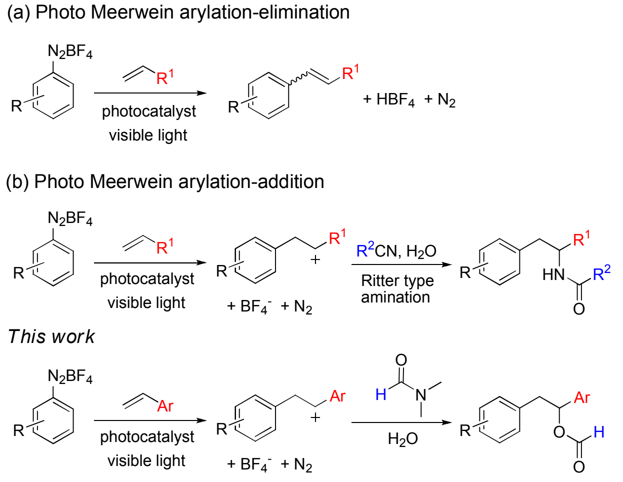
ABSTRACT: The intermolecular formyloxylation-arylation of stilbenes occurs in the presence of diazonium salts, a photocatalysts, visible light and DMF. The photo-Meerwein addition products are obtained in good yields up to 76 %. We propose the formation of an iminium ion intermediate, which is hydrolyzed 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, e.g. Eosin Y or Ru(bipy)$_3$Cl$_2$, 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.

Scheme 1. Types of photo Meerwein arylation reactions: (a) photo Meerwein arylation-elimination, (b) photo Meerwein arylation-addition with nitriles and with dimethylformamide

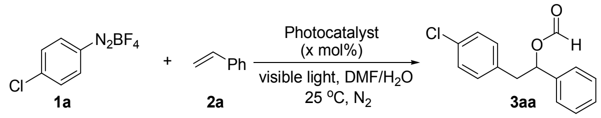


2. RESULTS AND DISCUSSION

Diazonium salts are labile towards base. The selection of a non-basic 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-Dimethylformamide (DMF) is widely used as a dipolar aprotic solvent. DMF can act as 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 ambiguously confirmed by X-ray single crystal analysis (Figure 1). No significant product formation is observed in the absence of the photocatalyst or the light source.

Table 1. Optimizing Reaction Conditions.[a]



Entry	Conditions	Yield % [b]
1	$Ru(bpy)_3Cl_2(H_2O)_6$ (0.7 mol%)	59
2	$Ru(bpy)_3Cl_2(H_2O)_6$ (1.3 mol%)	71
3	$Ru(bpy)_3Cl_2(H_2O)_6$ (2.0 mol%)	**76**
4	$Ru(bpy)_3Cl_2(H_2O)_6$ (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)	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 H_2O	64
18	H_2O (2.0 equiv.)	71
19	H_2O (5.0 equiv.)	65
20	H_2O (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 ESI for the detailed structures of the photocatalysts. [c]Isolated yields given. [d]No light.

Furthermore, 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 $[Ru(bpy)_3]Cl_2(H_2O)_6$ and 1 equiv. of water in 0.5 mL of DMF at room temperature.

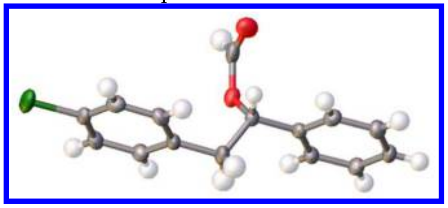
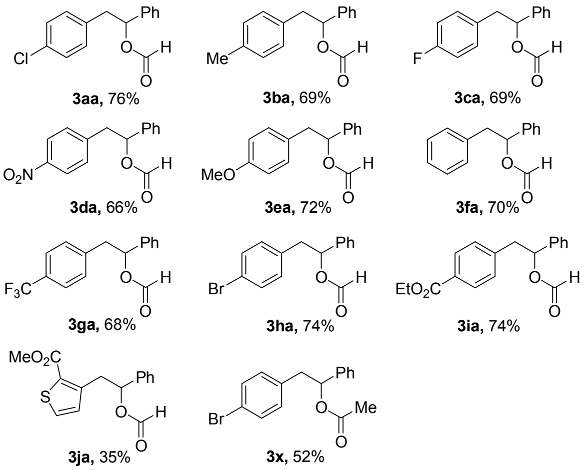


Figure 1. Molecular structure of compound **3aa** in the solid state

Next, we explored the scope of the diazonium salts and 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** only in 35% yield along with the photo-Meerwein arylation-elimination product in 15% yield.

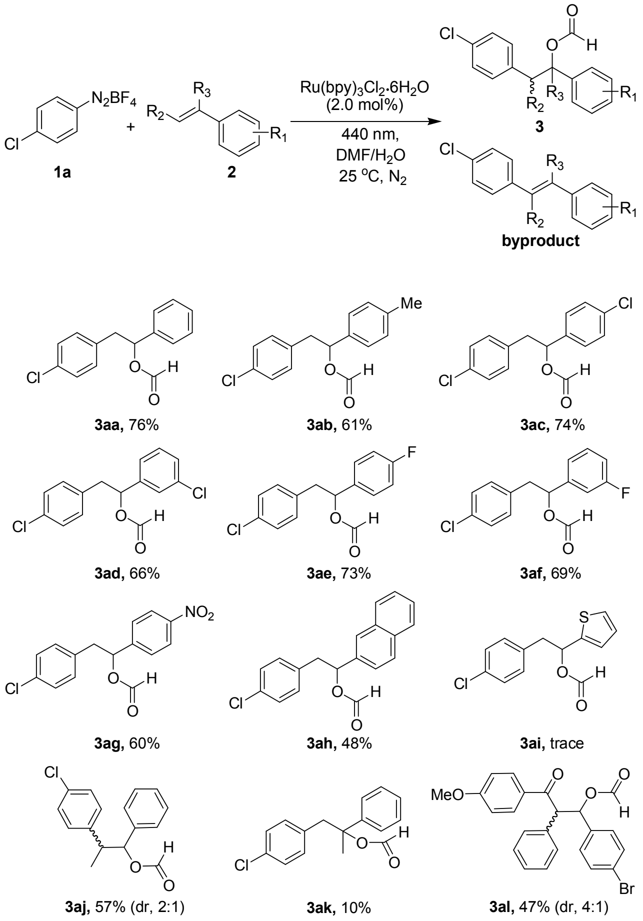
Table 2. Scope of the aryl diazonium salts.[a]



[a]The reaction was carried out with **1** (0.2 mmol), styrene **2** (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.

Different aryl alkenes were used in the reaction and the results are summarized in Table 3. Styrenes with electron-withdrawing, -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-beta-methylstyrene and benzalacetone provide the addition products in 57% or 47% yield, resp., but with only low diastereoselectivity (d.r. 2:1). The X-ray crystal structure analysis of compound **3al** (see supporting information) shows the configuration of its major diastereoisomer. Alpha-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.

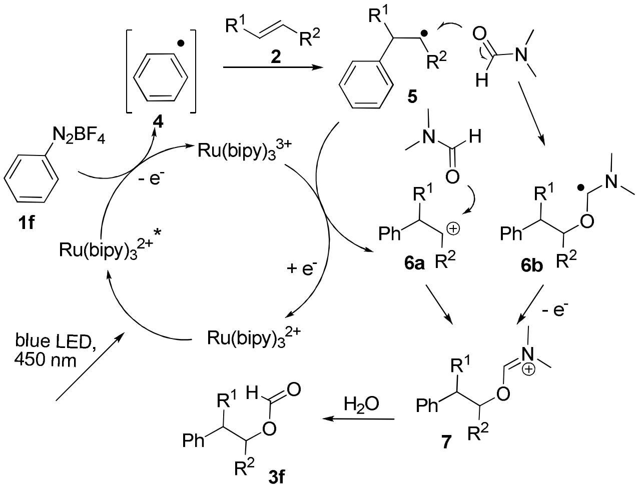
Table 3. Scope of alkenes.



[a]The reaction was carried out with **1a** (0.2 mmol), styrene **2** (0.8 mmol), [Ru(bpy)3]Cl2(H2O)$_6$ (0.02 eqiv), 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.

If N,N-dimethylacetamide is used instead of DMF the corresponding product **3X** is obtained in 52%. A plausible mechanism of the photoreaction is proposed in Scheme 2 based on previous work, the trapping of radical intermediates and experiments using labelled 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 either oxidized by Ru(III) to give an carbenium-ion intermediate **6a** and reacts with the carbonyl oxygen of N,N-dimethylformylamide 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 to trap the aryl radical addition intermediate, which supports this being an intermediate during the photoreaction. The use of DMF-d7 gave the product with deuterium label at the formyl position (see supporting information for data), while in reactions with added D2O instead of water no deuterium incorporation was observed.

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 Advance 300 MHz spectrometer in CDCl3 solution with internal solvent signal peak at 7.26 ppm. ^{13}C NMR were recorded at 75 MHz spectrometer in CDCl3 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) was added drop wise. The resulting reaction mixture was stirred for 40 min at 0-5°C and the obtained precipitate was collected by filtration, dried and re-dissolved in a minimum amount of acetone. Diethyl ether was added until precipitation of diazonium tetrafluoroborate, which is 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 magnetic stirring bar was charged with the photocatalyst $[Ru(bpy)_2]Cl_2\,(H_2O)_6$ (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 cooling device maintaining a temperature around 25 °C. After 1.5 h of irradiation, 10 mL of water were added to the reaction mixture, which was then extracted with dichloromethane (3 x 30 mL). The combined organic phases was dried over Na_2SO_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. NMR and MS spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

[1] a) R. Pschorr, *Ber. Dtsch. Chem. Ges.* **1896**, *29*, 496-501; b) H. Meerwein, E. Büchner, K. van Emster, *J. Prakt. Chem.* **1939**, *152*, 237-266.

[2] a) C. S. Rondestvedt, in *Organic Reactions,* John Wiley & Sons, Inc., **2011**, 225–259. b) M. R. Heinrich, *Chem. Eur. J.* **2009**, *15*, 820-833.

[3] a) M. R. Heinrich, A. Wetzel, M. Kirschstein, *Org. Lett.* **2007**, *9*, 3833-3835. b) G. Pratsch, C. A. Anger, K. Ritter, M. R. Heinrich, *Chem. Eur. J.* **2011**, *17*, 4104-4108. c) G. Pratsch, M. R. Heinrich, in *Top. Curr. Chem.*, Springer-Verlag Berlin Heidelberg, **2012**, 33-60. d) A. Wetzel, V. Ehrhardt, M. R. Heinrich, *Angew. Chem., Int. Ed.* **2008**, *47*, 9130-9133. e) A. Wetzel, G. Pratsch, R. Kolb, M. R. Heinrich, *Chem. Eur. J.* **2010**, *16*, 2547-2556. f) M. R. Heinrich, O. Blank, D. Ullrich, M. Kirschstein, *J. Org. Chem.* **2007**, *72*, 9609-9616. g) M. R. Heinrich, O. Blank, S. Wölfel, *Org. Lett.* **2006**, *8*, 3323-3325. h) M. R. Heinrich, A. Wetzel, M. Kirschstein, *Org. Lett.* **2007**, *9*, 3833-3835. i) S. B. Höfling, A. L. Bartuschat, M. R. Heinrich, *Angew. Chem., Int. Ed.* **2010**, *49*, 9769-9772. i) M. K. Staples, R. L. Grange, J. A. Angus, J. Ziogas, N. P. H. Tan, M. K. Taylor, C. H. Schiesser, *Org. Biomol. Chem.* **2011**, *9*, 473-479. j) F. W. Wassmundt, W. F. Kiesman, *J. Org. Chem.,* **1995**, *60*, 196-201. k) F. Y. Mo, G. B. Dong, Y. Zhang, J. B. Wang, *Org. Biomol. Chem.* **2012**, *11*, 1582-1593. l) C. Gall, *Chem. Rev.* **1988,** *88*, 756-792. m) M. R. Heinrich, *Chem. Eur. J.* **2009**, *15*, 820-833. n) J. Xuan, W. J. Xiao *Angew. Chem. Int. Ed.* **2012,** *51*, 6828-6838.

[4] a) D. P. Hari, B. König, *Angew. Chem. Int. Ed.* **2013**, *52*, 4734-4743. b) D. P. Hari, P. Schroll, B. König, *J. Am. Chem. Soc.* **2012**, *134*, 2958 – 2961. c) P. Schroll, D. P. Hari, B. König, *ChemistryOpen* **2012**, *1*, 130 -133. d) D. P. Hari, T. Hering, B. König, *Org. Lett*. **2012**, *14*, 5334 – 5337.

[5] a) D. P. Hari, T. Hering, B. König, *Angew. Chem. Int. Ed.* **2014**, *53*, 725-728. b) G. Fumagalli, S. Boyd, M. F. Greaney, *Org. Lett.* **2013,** *15*, 4398-4401.

[6] a) M. Hartmann, Y. Li, A. Studer, *J. Am. Chem. Soc.* **2012,** *134*, 16516–16519.

[7] a) J. Muzart, Tetrahedron. **2009**, *65*, 8313-8323. b) S. T. Ding, N. Jiao, *Angew. Chem. Int. Ed.* **2014**, *53*, 725-728. c) M. Suchý, A. A. H. Elmehriki, R. H. E. Hudson, *Org. Lett.* **2011,** *13*, 3952-3955. d) S. P. Khanapure, S. Manna, J. Rokach, R. C. Murphy, P. Wheelan, W. S. Powell, *J. Org. Chem.* **1995,** *60*, 1806-1813. e) M. B. Pizzuti, A. J. Minnaard, B. L. Feringa, *Org. Biomol. Chem.* **2008,** *6*, 3464-3466. f) M. J. Johansson, K. H. O. Andersson, N. Kann, *J. Org. Chem.* **2008**, *73*, 4458-4463. g) G. Zoppellaro, V. Enkelmann, A. Geies, M. Baumgarten, *Org. Lett.* **2004**, *6*, 4929-4932. h) G. S. Kumar, C. U. Maheswari, R. A. Kumar, M. L. Kantam, K. R. Reddy, *Angew. Chem. Int. Ed.* **2011**, *50*, 11748-11751. i) S. Ushijima, H. Togo, *Synlett.* **2010,** 1067-1070. j) T. Schareina, A. Zapf, M. Beller, *Chem. Commun.* **2004**, 1388-1389.

[8] a) S. Kobayashi, M. Sugiura, C. Ogawa, *Adv. Synth. Catal.* **2004**, *346*, 1023-1034. b) A. Jutand, *Chem. Rev.* **2008**, *108*, 2300-2347; c) S. Yamaguchi, H. Shinokubo, A. Osuka, *Inorg. Chem.* **2009**, *48*, 795-797. d) T. Cottineau, M. Richard-Plouet, J.-Y. Mevellec, L. Brohan, *J. Phys. Chem. C* **2011**, *115*, 12269-12274; e) M. C. Das, H. Xu, Z. Wang, G. Srinivas, W. Zhou, Y.-F. Yue, V. N. Nesterov, G. Qian, B. Chen, *Chem. Commun.* **2011**, *47*, 11715-11717. f) C. Femoni, M. C. Iapalucci, G. Longoni, S. Zacchini, *Dalton Trans.* **2011**, *40*, 8685-8694. g) H. Arora, J. Cano, F. Lloret, R. Mukherjee, *Dalton Trans.* **2011**, *40*, 10055-10062. h) E. A. Mikhalyova, S. V. Kolotilov, M. Zeller, L. K. Thompson, A. W. Addison, V. V. Pavlishchuk, A. D. Hunter, *Dalton Trans.* **2011**, *40*, 10989-10996. i) Y. Nakao, H. Idei, K. S. Kanyiva, T. Hiyama, *J. Am. Chem. Soc.* **2009**, *131*, 5070-5071. j) Y. Li, Y. Xie, R. Zhang, K. Jin, X.Wang, C. Duan, *J. Org. Chem.* **2011**, *76*, 5444-5449. k) Á lvarez, R.; Pérez, M.; Faza, O. N.; de Lera, A. R. *Organometallics* **2008**, *27*, 3378-3389.

[9] M. D. Konieczynska, C. Dai, C. R. J. Stephenson *Org. Biomol. Chem.,* **2012**, *10*, 4509-4511. b) C. H. Dai, J. M. R. Narayanam, C. R. J. Stephenson, *Nat. Chem.* **2011**, *3*, 140-145.

[10] Y. Q. Zou, W. Guo. F. L. Liu, L. Q. Lu, J. R. Chen, W. J. Xiao. *Green Chem*. **2014**, *16*, 3787–3795.

[11] P. Hanson, J. R. Jones, A. B. Taylor, P. H. Walton, A. W. Timms, *J. Chem. Soc.,Perkin Trans. 2* **2002**, 1135-1150.

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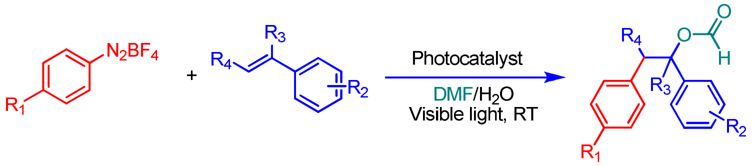

22 examples, yield up to 76%