

Photochemically Catalyzed Diels-Alder Reaction of Azadienes with 2,3-Dihydrofuran by 2, 4, 6-Triphenylpyrylium Salt: Synthesis of Styrylfuroquinoline Derivatives

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Abstract: Photochemically promoted Diels-Alder reactions of 1, 4-diaryl-1-azabutadienes with 2,3-dihydrofuran were achieved by using 2, 4, 6-triphenylpyrylium tetrafluoroborate as catalyst to produce corresponding styrylfuroquinolines in high yield.

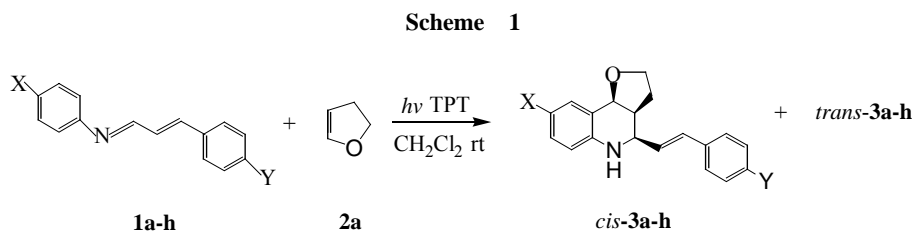
Keywords: Photocatalysis, cycloaddition, 1, 4-diaryl-1-azabutadienes, styrylfuroquinolines.

Photoinduced electron transfer (PET) method has attracted great attention in past two decades in the Diels-Alder reaction, especially when the reaction is not successful under thermal condition¹. The synthetical potential of these PET-catalyzed reactions has been investigated intensely². The Diels-Alder reaction of 1-azadiene is a mainstay of heterocycles and natural product synthesis³. A limitation to the application of azadienes is that azadienes generally require some form of activation to achieve synthetical utility. With appropriate substitution on the 1-aza-1, 3-diene are reactive as either electron-rich or electron-deficient Diels-Alder dienes to electron-deficient or electron-rich dienophiles. However, 1,4-diphenyl-1-azabutadiene is less reactive to either electron-rich or electron-deficient dienophiles. The successful [4+2] reaction for 1, 4-diphenyl-1-azabutadiene was few³.

We recently found that PET or ET could activate the catalyzation of the imino Diels-Alder reaction of arylimines and styrenes⁴. We now reported the photocatalyzed Diels-Alder reaction of 1, 4-diphenyl-1-azabutadiene with 2, 3-dihydrofuran using 2, 4, 6-triphenylpyrylium tetrafluoroborate (TPT) as a photocatalyst which has been proven to be efficient electron transfer catalyst to induce Diels-Alder reactions¹⁻².

Irradiation at $\lambda \geq 345$ nm of a deaerated anhydrous CH_2Cl_2 solution of the azadienes **1** with 2, 3-dihydrofuran **2a** and a catalytic amount of 2, 4, 6-triphenylpyrylium tetrafluoroborate (TPT) at ambient temperature for 8-12 hours afforded corresponding 4-styrylfuro[3, 2-c]quinolines **3** in high yields as shown in **Table 1**. The products were obtained as mixtures of *cis* and *trans* isomers, which were separated by column chromatography and further purified by preparative TLC and fully identified by ¹H, ¹³C and 2D NMR spectroscopy⁵.

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**Table 1** Reactions of azadiene **1** with dihydrofuran **2a**

Azadienes	X		t (h)	Conv. (%)	Yields (%) ^a	<i>cis-3</i> : <i>trans-3</i> ^b
	X	Y				
1a	H	H	12	96	85	66:34
1b	CH ₃	H	12	95	90	72:28
1c	Cl	H	8	97	90	62:38
1e	H	NO ₂	8	93	87	60:40
1f	CH ₃	NO ₂	8	95	84	65:35
1g	Cl	NO ₂	8	93	88	68:32
1h	CH ₃ O	NO ₂	12	90	85	62:38

^a Yields of isolated products based on conversion of **1**; ^b Ratio determined by ¹H NMR.

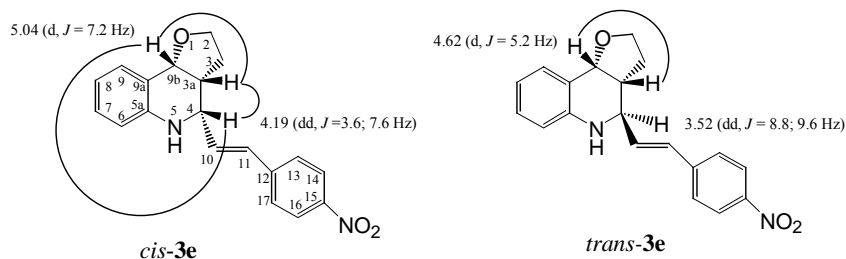
The products obtained in the reaction of azadienes **1** with 2, 3-dihydrofuran **2a** are furoquinolines as depicted in **Scheme 1**, instead of furopyridines as predicted. This result shows that the reaction is an imino Diels-Alder reaction of 2-azadienes, but not of 1-azadienes. The reason is probably due to the 2-azadienes usually has higher electron density than 1-azadiene³. Another reason for this regioselectivity should be attributed to the steric effects of the large phenyl group that inhibit the [4+2] cycloaddition of 1-azadienes and directs the reaction toward the [4+2] cycloaddition of 2-azadiene.

It is seen from **Table 1** that the photocatalyzed imino Diels-Alder reactions of **1** with 2, 3-dihydrofuran **2a** was completely regioselective giving high yield of furo[3,2-*c*]quinoline derivatives. However, when **1** reacted with 3, 4-dihydro-2*H*-pyran **2b**, the conversion of **1** and the yield of pyrano[3, 2-*c*]quinolines was very low under the same experimental conditions even after prolonged irradiation.

The stereochemistry of *cis-3* and *trans-3* was determined by chemical shift consideration and NOESY experimental as shown in **Figure 1**: a reciprocal interaction was observed among H-4, H-3a, and H-9b in *cis-3e*. On the other hand, in the case of *trans-3e*, only a strong reciprocal interaction is found between H-3a and H-9b, but none between H-4 and H-9b.

Since no reaction took place in the absence of TPT or in the dark at ambient temperature, hence the reaction might be reasonable as a PET catalyzed reaction. The lower oxidation potential of **2a** ($E^{\text{ox}} = 1.40 \text{ V vs SCE}^{4a}$) than those of **1** (e.g., $E^{\text{ox}} = 1.58 \text{ V vs SCE}$ for **1a**^{2e}) favors the prior electron transfer from **2a** to excited TPT to produce 2, 4, 6-triphenylpyranil radical and cation radical of **2a** which added to the C=N bond of azadienes to produce the dihydrofuran oxonium ion and aniliny radical. The intramolecular addition of oxonium ion to the phenyl of aniliny radical to give quinoline cation radicals and the next electron transfer from 2, 4, 6-triphenylpyranil radical to the quinoline cation radicals yield the products and TPT.

Figure 1 Selected chemical shifts and NOESY correlations of the *cis*-**3e** and *trans*-**3e**



General Procedure

The anhydrous CH_2Cl_2 solution (50 mL) of the azadiene **1** (2 mmol), 2, 3-dihydrofuran **2a** (2.5 mmol) and 2, 4, 6-triphenylpyrylium tetrafluoroborate TPT (0.01 mmol) was bubbled with argon for half an hour and irradiated with a 250 W high-pressure Hg lamp in a Pyrex bottle under stirring at ambient temperature. After completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure and the residual was separated on column chromatography eluted with hexane/acetone (10:1 v/v) to give furoquinoline derivatives **3**. The *cis* and *trans* isomers were separated and purified on preparative thin layer chromatography eluted with hexane/acetone (12:1 v/v). The crude products were recrystallized from ethanol.

Acknowledgment

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References and Notes

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- Selected data for the products *cis*-**3e**: Yellow needles, mp: 215-216 °C (uncor.). HR-ESI-MS: 323.1395 (calcd. for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_3 + \text{H}^+$, 323.1390). MS (EI), m/z (%): 322 (M^+ , 32), 277 (23), 252 (22), 231 (15). ^1H NMR (400 MHz, CDCl_3 , δ ppm): 2.04-2.10 (m, 2H, H-3), 2.77 (m, 1H, H-3a), 3.84-3.90 (m, 2H, H-2), 4.19 (dd, 1H, $J = 3.6$ Hz; 7.6 Hz, H-4), 5.04 (d, 1H, $J = 7.2$, H-9b), 6.51 (dd, 1H, $J = 7.6$ Hz; 15.6 Hz, H-10), 6.62 (d, 1H, $J = 8.0$, H-6), 6.69 (d, 1H, $J = 15.6$, H-11), 6.80 (dd, 1H, $J = 7.6$, 8.0, H-6), 7.11 (dd, 1H, $J = 7.6$, 8.0, H-7), 7.36 (d, 1H, $J = 8.4$, C-9), 7.51 (d, 1H, $J = 8.8$, H-13), 8.18 (d, 1H, $J = 8.8$, H-14). ^{13}C NMR (100.08 MHz, CDCl_3 , δ ppm): 23.4 (C-3), 42.0 (C-3a), 55.7 (C-4), 66.2 (C-2), 75.2 (C-9b), 115.0 (C-6), 119.2 (C-8), 123.5 (C-9a), 124.0 (C-14), 126.8 (C-13), 127.3 (C-10), 128.7 (C-9), 131.2 (C-11), 130.4 (C-7), 142.8 (C-12), 143.9 (C-5a), 147.3 (C-15). *Trans*-**3e**: Yellow needles, mp: 171-172 °C (uncor.). HR-ESI-MS: 323.1397 (calcd. for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_3 + \text{H}^+$, 323.1390). MS (EI),

m/z (%): 322 (M^+ , 38), 291(18), 277 (29), 252 (20), 231(10), 1H NMR (400 MHz, $CDCl_3$, δ ppm): 1.91 (m, 1H, H-3), 2.21 (m, 1H, H-3), 2.30 (m, 1H, H-3a), 3.52 (dd, 1H, $J = 8.8$ Hz; 9.6 Hz, H-4), 3.78 (m, 1H, H-2), 4.02 (m, 1H, H-2), 4.62 (d, 1H, $J = 5.2$, H-9b), 6.42 (dd, 1H, $J = 8.4$ Hz; 15.6 Hz, 1H, H-10), 6.67 (d, 1H, $J = 8.0$, H-6), 6.74 (d, 1H, $J = 15.6$, H-11), 6.83 (dd, 1H, $J = 7.2$, 8.0, H-6), 7.13 (dd, 1H, $J = 7.6$, 8.0, H-7), 7.38 (d, 1H, $J = 8.0$, C-9), 7.56 (d, 1H, $J = 8.8$, H-13), 8.21 (d, 1H, $J = 8.8$, H-14). ^{13}C NMR (100.08 MHz, $CDCl_3$, δ ppm): 28.8 (C-3), 41.4 (C-3a), 55.8 (C-4), 65.2 (C-2), 75.5 (C-9b), 115.2 (C-6), 118.7 (C-8), 120.1 (C-9a), 123.9 (C-14), 127.0 (C-13), 128.9 (C-9), 129.0 (C-10), 131.1 (C-7), 134.8 (C-11), 142.6 (C-12), 144.2 (C-5a), 147.5 (C-15).

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