

# Photochemically catalysed Diels–Alder reaction of *N*-arylimines by 2,4,6-triphenylpyrylium salt : synthesis of furo- and pyranoquinoline derivatives

Wei Zhang\*, Yanping Guo, Li Yang and Zhong-Li Liu

National Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China

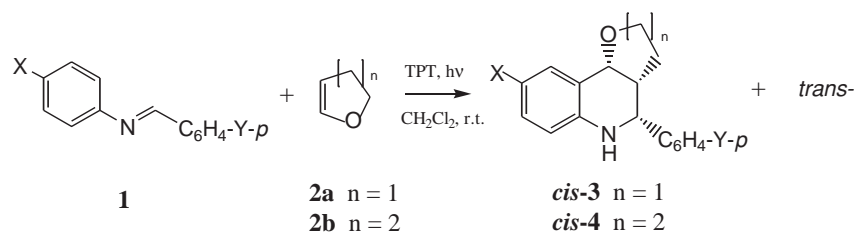
Photochemically promoted Diels–Alder reactions of *N*-arylimines with 2,3-dihydrofuran and 3,4-dihydro-2*H*-pyran were achieved by using 2,4,6-triphenylpyrylium tetrafluoroborate as a catalyst to produce the corresponding furo- and pyranoquinolines in high yield.

**Keywords:** Diels–Alder reaction, *N*-arylimines, 2,4,6-triphenylpyrylium tetrafluoroborate

The furoquinoline and pyranoquinoline subunits are present in many alkaloids<sup>1</sup> and derivatives of these alkaloids possess a wide range of biological activities.<sup>2</sup> A variety of approaches have been developed for the synthesis of these skeletons. The Imino Diels–Alder reactions of *N*-arylimines with electron-rich dienophiles provide an easy entry into quinoline derivatives. This imino Diels–Alder reaction has been reported to be catalysed by BF<sub>3</sub>·Et<sub>2</sub>O and other Lewis acids,<sup>3a–d</sup> lanthanide triflate,<sup>3e–f</sup> triphenylphosphonium perchlorate,<sup>3g</sup> 2,3-dichloro-5,6-dicyano-*p*-benzoquinone,<sup>3h</sup> and protic acids.<sup>3i–j</sup> As a part of our ongoing research program into the synthetic potential of photocatalysed

reactions, we found recently that 2,4,6-triphenylpyrylium tetrafluoroborate (TPT) which has been widely used as a photosensitiser to induce Diels–Alder reactions,<sup>4</sup> can act as an efficient photocatalyst for the imino Diels–Alder reaction between *N*-arylimines and styrenes.<sup>5</sup> We now report the synthesis of furo and pyranoquinolines by photocatalysed imino Diels–Alder reaction of *N*-arylimines with 2,3-dihydrofuran (**2a**) and 3,4-dihydro-2*H*-pyran (**2b**).

Irradiation at  $\lambda \geq 345$  nm of a deaerated anhydrous CH<sub>2</sub>Cl<sub>2</sub> solution of the *N*-arylimine (**1**) with 2,3-dihydrofuran (**2a**) and a catalytic amount of 2,4,6-triphenylpyrylium tetrafluoroborate



**Scheme 1**

**Table 1** Preparation of furo[3,2-*c*]quinolines (**3**)

|           | Arylimines        |                   | <i>t</i> /h | Conversion <sup>a</sup> /% | Yield/% <sup>b</sup><br><b>3</b> ( <i>cis/trans</i> ) <sup>c</sup> | M.p./ <i>T</i> / °C<br><i>cis/trans</i> Found (Lit) |
|-----------|-------------------|-------------------|-------------|----------------------------|--|---|
|           | X                 | Y                 |             |                            |  |   |
| <b>1a</b> | H                 | H                 | 8           | 95                         | 84 <sup>d</sup>  | 115–116 <sup>d</sup> (117–118 <sup>3e</sup> )       |
| <b>1b</b> | CH <sub>3</sub>   | H                 | 8           | 98                         | 85 <sup>d</sup>  | 102–103 <sup>d</sup> (101–102 <sup>3c</sup> )       |
| <b>1c</b> | CH <sub>3</sub> O | H                 | 8           | 90                         | 78 <sup>d</sup>  | 130–131 <sup>d</sup> (132–133 <sup>3e</sup> )       |
| <b>1d</b> | CH <sub>3</sub> O | CH <sub>3</sub> O | 8           | 87                         | 75 <sup>d</sup>  | 175–176 <sup>d</sup>                                |
| <b>1e</b> | CH <sub>3</sub>   | CH <sub>3</sub> O | 8           | 92                         | 83 <sup>d</sup>  | 158–159 <sup>d</sup>                                |
| <b>1g</b> | CH <sub>3</sub>   | NO <sub>2</sub>   | 12          | 97                         | 88 (58:42) <sup>e</sup>  |   |
| <b>1h</b> | Cl                | NO <sub>2</sub>   | 12          | 98                         | 91 (63:37)   | 262–263/206–207                                     |
| <b>1i</b> | CH <sub>3</sub> O | NO <sub>2</sub>   | 18          | 95                         | 80 (66:33) <sup>e</sup>  |   |

<sup>a</sup>Conversion based on **1**; <sup>b</sup>Isolated yield based on **1**; <sup>c</sup>Ratio determined by <sup>1</sup>H NMR spectra.

<sup>d</sup>*cis* isomer; <sup>e</sup>Yield of mixture of *cis* and *trans* isomers.

**Table 2** Preparation of pyrano[3,2-*c*]quinolines (**4**)

|           | Arylimines        |                   | <i>t</i> /h | Conversion <sup>a</sup> /% | Yield/% <sup>b</sup><br><b>3</b> ( <i>cis/trans</i> ) <sup>c</sup> | M.p./ <i>T</i> / °C<br><i>cis/trans</i> Found (Lit) |
|-----------|-------------------|-------------------|-------------|----------------------------|--|---|
|           | X                 | Y                 |             |                            |  |   |
| <b>1a</b> | H                 | H                 | 24          | 88                         | 78 <sup>d</sup>  | 129–130 <sup>d</sup> (lit. 130–132 <sup>3e</sup> )  |
| <b>1b</b> | CH <sub>3</sub>   | H                 | 24          | 92                         | 83 (82:18)   | 135–136/109–110                                     |
| <b>1c</b> | Cl                | H                 | 24          | 95                         | 83 <sup>d</sup>  | 169–170 <sup>d</sup> (lit. 170–172 <sup>3e</sup> )  |
| <b>1d</b> | CH <sub>3</sub> O | H                 | 36          | 55                         | 72 <sup>d</sup>  | 144–145 <sup>d</sup> (lit. 144–146 <sup>3e</sup> )  |
| <b>1e</b> | CH <sub>3</sub>   | CH <sub>3</sub> O | 36          | 75                         | 70 (85:15)   | 151–152/126–127                                     |
| <b>1g</b> | CH <sub>3</sub>   | NO <sub>2</sub>   | 24          | 94                         | 85 (65:38) <sup>e</sup>  |   |
| <b>1h</b> | Cl                | NO <sub>2</sub>   | 24          | 90                         | 86 (70:30) <sup>e</sup>  |   |
| <b>1i</b> | CH <sub>3</sub> O | NO <sub>2</sub>   | 36          | 35                         | 65 (64:36)   | 247–248/193–194                                     |

<sup>a</sup>Conversion based on **1**; <sup>b</sup>Isolated yield based on **1**; <sup>c</sup>Ratio determined by <sup>1</sup>H NMR spectra.

<sup>d</sup>*cis* isomer; <sup>e</sup>Yield of mixture of *cis* and *trans* isomers.

\* Correspondence. E-mail: zhangwei6275@sina.com

(**TPT**) at room temperature for 8–18 hours afforded the corresponding furo[3,2-*c*]quinolines (**3**) in high yields as shown in Table 1. The products were obtained a mixtures of *cis*- and *trans*-isomers, which were separated by recrystallisation or by column chromatography and fully identified by  $^1\text{H}$ ,  $^{13}\text{C}$  and 2D NMR spectroscopy. Similarly, *N*-arylimine (**1**) reacted with 3,4-dihydro-2*H*-pyran (**2b**) under the same experimental conditions to yield the pyrano[3,2-*c*]quinolines (**4**) in high yield. A longer irradiation time was required to complete the reaction (Table 2).

It is seen from Table 1 and 2 that the photocatalysed imino Diels–Alder reactions of *N*-arylimines (**1**) with 2,3-dihydrofuran (**2a**) or 3,4-dihydro-2*H*-pyran (**2b**) was not only completely regioselective giving high yields of furo[3,2-*c*]quinoline or pyrano[3,2-*c*]quinoline derivatives, but also highly diastereoselective. The stereochemistry of **3** and **4** was determined by chemical shift consideration and NOESY experiments. For example, in the NMR spectra of *cis*-**3h** and *trans*-**3h**, the proton of 9*b*-position was assigned at 5.23 ppm as doublet and 4.55 ppm as doublet, respectively. The stereochemistry at the ring junction was readily assigned as *cis* from the axial-equatorial coupling constants of  $J_{9b-3a}$  of 7.6 Hz in *cis*-**3h** and 5.6 Hz in *trans*-**3h**. The configuration between H-4 and H-3*a* in *cis*-**3h** was also assigned as *cis* from the equatorial–equatorial coupling constants  $J_{4-3a}$  of 2.2 Hz. This was further confirmed by NOESY experiments as shown in Fig. 1. Reciprocal interactions were observed between H-4, H-3*a*, and H-9*b*. On the other hand, in the case of *trans*-**3h**, the proton of 4-position was assigned at 3.90 ppm as doublet. The relevant coupling constant 10.8 Hz between H-4 and H-3*a* was indicative of the *anti* axial-axial orientation of protons H-4 and H-3*a*. This orientation is only possible when the pyran ring and phenyl group are on the opposite sides of the quinoline ring of *trans*-**3h**. The NOESY experiment confirmed the orientation of H-4 and H-3*a* as shown in Fig. 1. A strong reciprocal interaction was found between H-3*a* and H-9*b*, a weak one between H-3*a* and H-4, and none between H-4 and H-9*b*, all in accord with a *trans* configuration.

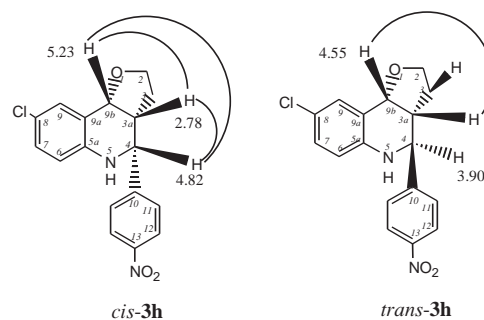
Since no reaction took place in the dark or in the absence of **TPT** at room temperature, the reaction might be rationalised as a photoinduced electron transfer catalysed reaction as shown in Scheme 2. The higher reactivity of 2,3-dihydrofuran (**2a**) towards the aryylimines than that of 3,4-dihydro-2*H*-pyran (**2b**) may arise from the lower oxidation potential of 2,3-dihydrofuran ( $E^{\text{ox}} = 1.28 \text{ V vs SCE}$ )<sup>6</sup> compared to that of 3,4-dihydro-2*H*-pyran ( $E^{\text{ox}} = 1.47 \text{ V vs SCE}$ )<sup>7</sup>.

## Experimental

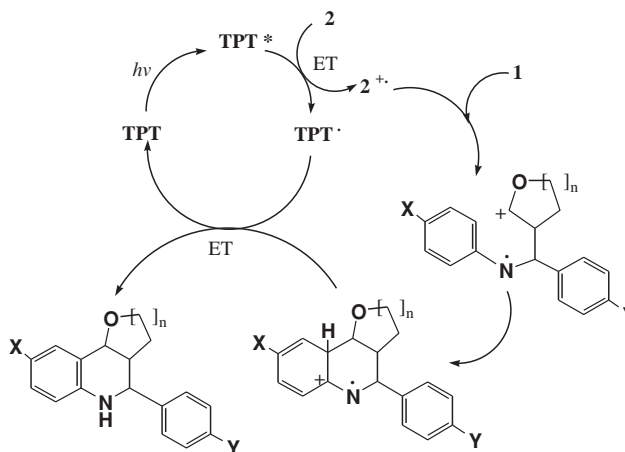
Melting points were recorded on a Yanagimoto melting point apparatus and are uncorrected. Analyses were carried out on a PERKIN-ELMER 2400 II analyzer.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker AM-400 NMR or a Bruker DRX-200 NMR spectrometers in  $\text{CDCl}_3$  with TMS as an internal standard. HR-ESI-MS and EI-MS were recorded with a Bruker APEX II FT-MS and a HP 5988 A mass spectrometers, respectively.

### General procedure for the photochemical reactions

To a anhydrous  $\text{CH}_2\text{Cl}_2$  solution (50 ml) containing the *N*-arylimine (**1**, 2.0 mmol) and 2,3-dihydrofuran (**2a**, 2.5 mmol), or 3,4-dihydro-2*H*-pyran (**2b**, 2.5 mmol) was added catalytic amounts of 2,4,6-triphenylpyrylium tetrafluoroborate (**TPT**, 8 mg, 0.02 mmol). Argon was bubbled through the mixture for half an hour and irradiated with a 250 W high-pressure Hg lamp in a Pyrex vessel with stirring at room temperature. After completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure and the products were separated by silica gel column chromatography eluted with hexane/acetone (v/v 10:1) to afford mixtures of *cis*- and *trans*-isomers of **3** or **4**. The solid was further purified by recrystallisation from ethanol to give pure *cis*-isomer of **3a–e** or **4a** and **4c–d**. In the case of mixture of *cis*- and *trans*-isomers of **3h** or **4i**, further separation and purification were performed by preparative thin layer chromatography



**Fig. 1** Selected chemical shifts and NOESY correlations of the *cis*-**3h** and *trans*-**3h**.



**Scheme 2**

to give the pure *cis*- and *trans*-isomers. The separation of mixtures of *cis*- and *trans*-isomer of **3g** and **3i**, or **4g** and **4h** were difficult even by preparative thin layer chromatography. All the *cis*-**3** or *cis*-**4** products showed similar  $^1\text{H}$  NMR spectra; the *trans*-**3** or *trans*-**4** also showed similarities in their  $^1\text{H}$  NMR spectra. Typical examples were as follows:

*Cis*-2,3,3*a*,4,5,9*b*-hexahydro-4-*p*-nitrophenyl-8-chlorofuro[3,2-*c*]quinoline (*cis*-**3h**): Yellow needles, m.p.: 262–263 °C; HR-ESI-MS: 331.0848 (calcd. for  $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_3\text{Cl}+\text{H}^+$ , 331.0846) (Found: C, 61.58; H, 4.65; N, 8.38 %.  $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_3\text{Cl}$  requires C, 61.72; H, 4.58; N, 8.37 %);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ): 1.47 (m, 1H, H-3), 2.11 (m, 1H, H-3), 2.78 (m, 1H, H-3*a*), 3.71–3.86 (m, 2H, H-2), 4.82 (d, 1H,  $J = 2.8$ , H-4), 5.23 (d, 1H,  $J = 7.6$ , H-9*b*), 6.59 (d, 1H,  $J = 8.6$ , H-6), 7.10 (dd, 1H,  $J = 8.6$ , 2.8, H-7), 7.39 (d, 1H,  $J = 2.8$ , H-9), 7.65 (d,  $J = 8.8$ , H-11), 8.26 (d,  $J = 8.8$ , H-12);  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ): 24.23 (C-3), 44.89 (C-3*a*), 56.84 (C-4), 66.62 (C-2), 75.19 (C-9*b*), 116.37 (C-6), 123.96 (C-12), 124.39 (C-9*a*), 127.26 (C-11), 128.53 (C-9), 129.03 (C-8), 129.66 (C-7), 142.43 (C-5*a*), 147.49 (C-10), 149.13 (C-13);  $m/z$ : 332 ( $\text{M}+2^+$ ), 330 ( $\text{M}^+$ ).

*Trans*-2,3,3*a*,4,5,9*b*-hexahydro-4-*p*-nitrophenyl-8-chlorofuro[3,2-*c*]quinoline (*trans*-**3h**): Yellow needles, m.p.: 202–203 °C; HR-ESI-MS: 331.0844 (calcd. for  $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_3\text{Cl}+\text{H}^+$ , 331.0846) (Found: C, 61.63; H, 4.47; N, 8.52 %.  $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_3\text{Cl}$  requires C, 61.72; H, 4.58; N, 8.47 %);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ): 1.67 (m, 1H, H-3), 2.04 (m, 1H, H-3), 2.44 (m, 1H, H-3*a*), 3.82–3.87 (m, 1H, H-2), 3.90 (d, 1H,  $J = 10.8$ , H-9*b*), 4.01–4.07 (m, 1H, H-2), 4.55 (d, 1H,  $J = 5.0$ , H-4), 6.61 (d, 1H,  $J = 8.6$ , H-6), 7.10 (dd, 1H,  $J = 8.6$ , 2.8, H-7), 7.38 (d, 1H,  $J = 2.8$ , H-9), 7.64 (2H, d,  $J = 8.8$ , H-11), 8.26 (2H, d,  $J = 8.8$ , H-12).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ): 28.5 (C-3), 43.4 (C-3*a*), 57.4 (C-4), 65.2 (C-2), 75.3 (C-9*b*), 116.1 (C-6), 121.5 (C-9*a*), 123.6 (C-8), 124.0 (C-12), 128.9 (C-9), 129.0 (C-11), 130.7 (C-7), 143.2 (C-5*a*), 147.8 (C-10), 148.7 (C-13).  $m/z$ : 332 ( $\text{M}+2^+$ ), 330 ( $\text{M}^+$ ).

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