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Development of a convenient synthetic route to aminochromenes via Buchwald C–N coupling

Ekaterina A. Shilova,[a,b,*] Valery P. Perevalov,[b] André Samat[a] and Corinne Moustrou[a]

[a]*Université de la Méditerranée, UMR CNRS 6114, Faculté des Sciences de Luminy, Case 901, 13288 Marseille Cedex 09, France*
[b]*Department of Technology of Organic Intermediates and Dyestuffs, Mendeleev University of Chemical Technology, Moscow, Russia*

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Abstract—A convenient new synthetic route to *p*-aminophenylaminobenzo- and naphthopyrans was developed via palladium-catalyzed C–N coupling. It was demonstrated that novel targeted aminoderivatives reveal photochromic properties. The structure of intermediate *p*-nitrophenylaminochromenes was confirmed by X-ray crystallographic analysis.

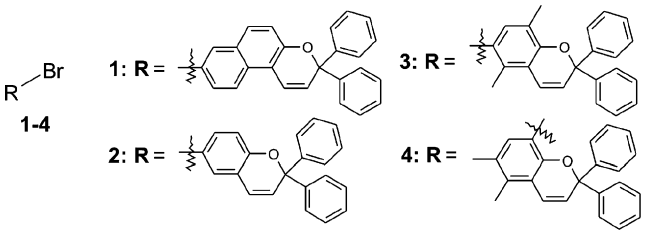
Diarylbenzo- and naphthopyrans are of special interest as photochromic compounds and thus have been the subject of investigation aiming to develop novel materials widely adopted in ophthalmic glasses, electronic display systems, optical switches, and temporary or permanent memories.[1] Functionalization of chromenes with amino group greatly enlarges their field of applications: aromatic amines are integral part of pharmaceuticals, dyes, polymers, organic materials with important electronic properties.[2] Because of its particular reactive properties, presence of the aminogroup significantly enables the synthesis of a wide range of modified chromenes. The inclusion of various substitutents into the chromene molecules allows us to control their photochromic properties. Aminogroup also plays a critical role for joining another photochromic system to existing chromene to obtain two-wavelength fluorescent selectable markers.[3] However, any synthetic route to aminochromenes has not been described. The above context prompted us to develop a convenient approach to introduce the aminogroup into chromene molecules.

In our previous paper[4] we showed that the functionalization of naphthopyran unit could be made by Buchwald–Hartwig C–N coupling.[5] Here we evaluate the applicability of palladium-catalyzed protocols for the creation of novel *p*-substituted phenylaminochromenes.

Bromochromenes **1**–**4** (Scheme 1) were used as convenient starting material for the synthesis. These compounds are very stable and easily obtained in one step through condensation of commercially available 1,1-diphenylpropyn-1-ol with bromonaphthalenes or bromophenols.[6]

Our studies began using palladium-catalyzed C–N coupling of bromochromenes **1**–**4** with 4-aminoacetanilide followed by hydrolysis of obtained acetamides **1a**–**4a** leading to the targeted aminochromenes **1b**–**4b** (Scheme 2).

The coupling was carried out in the presence of tris(dibenzylideneacetone)dipalladium(0) (2 mol %), 2-(di-*t*-butylphosphino)biphenyl (4 mol %), aryl halide (0,9 mmol), amine (1 mmol), sodium *tert*-butoxide (1.4 mmol) in refluxing toluene (1 mL/mmol) under argon.[7] By this synthetic way, a significant amount of starting material **1**–**4** remained after 2 or 3 days of



Scheme 1. Starting bromochromenes.

Keywords: Aminochromene; Nitrochromene; Buchwald palladium-catalyzed C–N coupling.
* Corresponding author. Tel.: +33 4 91 82 91 54; fax: +33 4 91 82 93 01; e-mail: shilova@discoverylab.eu

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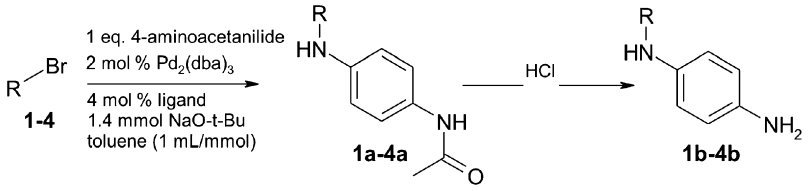


Scheme 2. Synthesis of aminochromenes via 4-aminoacelanilide.

Table 1. Pd-Catalyzed amination of bromochromenes via Scheme 1

Aryl halide	Product	Time (h)	Yield (%)
1	**1a**	72	31
2	**2a**	48	37
3	**3a**	48	42
4	**4a**	48	44

Table 2. Pd-Catalyzed amination of bromochromenes via Scheme 3

Aryl halide	Product	Time (h)	Yield (%)
1	**1c**	12	80
2	**2c**	6	89
3	**3c**	6	98
4	**4c**	6	86

heating causing low yields for the preparation of **1a**–**4a**[8] (Table 1).

Aminochromenes **1b**–**4b**[9] were then obtained in 85–90% yields by hydrolysis[10] of the corresponding acetamides. In order to increase the yields and to diminish the time of the amination step we decided to change 4-aminoacetanilide for 4-nitroaniline (Scheme 3) expecting that a better result in this case could be reached due to the influence of electron-accepting ability of nitrogroup. Compounds **1c**–**4c** were obtained during 6–12 h in 80–98% yields[11] (Table 2).

The structure of intermediate nitroderivative **3c** was determined by the X-ray crystallographic analysis of Figure 1.

Following reduction[12] of nitroderivatives **1c**–**4c** gave the resulting aminochromenes **1b**–**4b** in 85–95% yields.

The compared overall yields of compounds **1b**–**4b** obtained by two different synthetic strategies are collected in Table 3.

Thus the use of aromatic amine with electron-accepting unit is effective for palladium-catalyzed amination.

Photochemical properties[13] of novel targeted compounds were studied. Investigated aminochromenes **1b**–**4b** show absorbances in the UV spectra region but they were transparent in the visible spectra region. After the irradiation of UV light during 10 s the absorbance of closed form of chromenes decreased while a new absorption peak was found at 550–580 nm region indicating that the pyran moiety isomerizes to its merocyanine

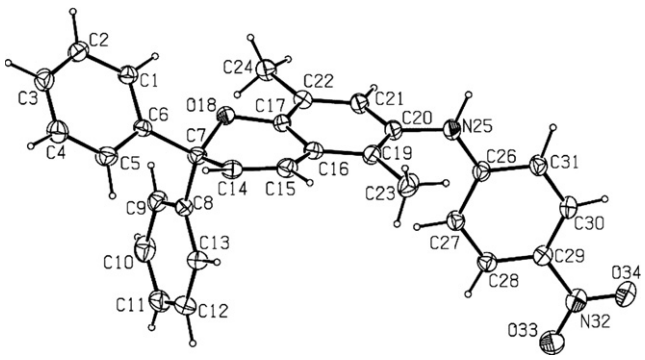


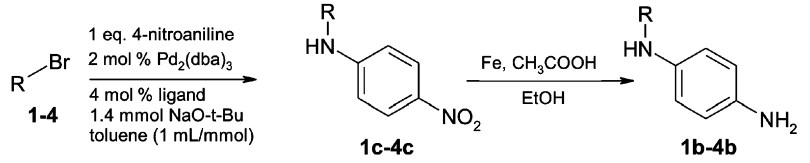
Figure 1. The molecular structure of the crystalline compound **3c**.

Table 3. Compared overall yields of **1b**–**4b** via Schemes 1 and 3

Product	Yield (%) (via 4-aminoacetanilide)	Yield (%) (via 4-nitroaniline)
1b	15	78
2b	26	85
3b	35	95
4b	38	80

forms. Figure 2 displays the absorption pattern of the closed and open forms of **1b** and **3b** in the visible range.

In summary, we developed a new simple and efficient synthetic way for obtaining *p*-aminophenylaminobenzo- and naphthopyrans. Two possible routes of synthesis were compared. It was shown that the better results of palladium-catalyzed C–N coupling could be obtained when the starting arylamine includes an electron-accepting unit. Novel *p*-aminophenylaminochromenes reveal



Scheme 3. Synthesis of aminochromenes via 4-nitroaniline.

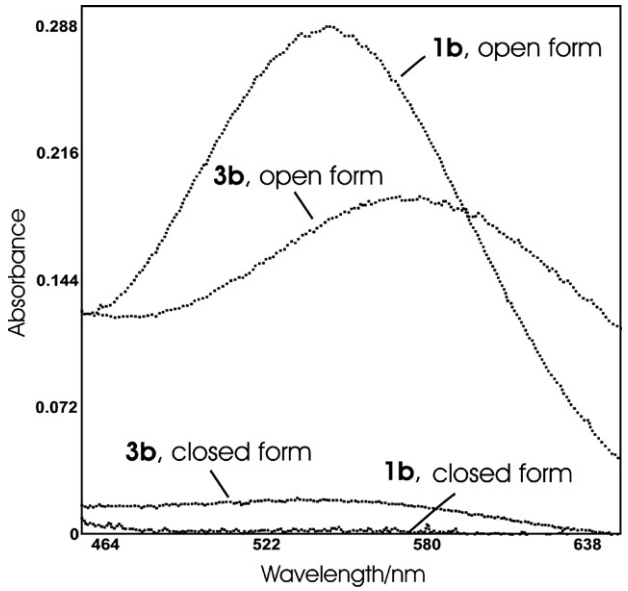


Figure 2. Absorption spectra of **1b** and **3b** (acetonitrile solutions, $C = 0.84 \times 10^5$ M) under dark condition (closed forms) and under UV-irradiation (open forms).

photochromic properties. The structure of intermediate nitrophenylaminochromenes was investigated by X-ray crystallographic analysis. Since the easy approach to synthesize aminochromenes was found, it opens interesting perspectives regarding an application in variable optical transmission materials.

Acknowledgments

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References and notes

1. (a) *Photochromism: Molecules and Systems*; Dürr, H., Bouas-Laurent, H., Eds.; Elsevier: Amsterdam, 1990; (b) Gemert, B. V. *Organic Photochromic and Thermochromic Compounds*; Plenum Press: New York, 1999; (c) *Organic Photochromic and Thermochromic Compounds*; Crano, J. C., Guglielmetti, R. J., Eds.; Kluwer Academic/Plenum Publishers: New York, 1999; Vols. 1 and 2, (d) McArdle, C. B. *Applied Photochromic Systems*; Blackie: London, 1992.
2. (a) Ivaki, T.; Yasuhara, A.; Sakamoto, T. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1505–1510; (b) Negwer, M. *Organic Chemical Drugs and their Synonyms (International Survey)*, 7th ed.; Akademie Verlag Gmbh: Berlin, 1994; (c) D'Aroano, G.; Schavion, G.; Leclerc, M. *Chem. Mater.* **1995**, *7*, 33–35; (d) Greco, G. E.; Popa, A. I.; Schrock, R. R. *Organometallics* **1998**, *17*, 5591–5593.
3. Ortica, F.; Moustrou, C.; Berthet, J.; Favaro, G.; Mazzucato, U.; Samat, A.; Gugliemetti, R.; Vermeerch, G.; Mazzucato, U. *Photochem. Photobiol.* **2003**, *78*, 558–566.
4. Shilova, E. A.; Moustrou, C.; Samat, A. *Tetrahedron Lett.* **2005**, *46*, 8857–8859.
5. (a) Queiroz, M.-J. R. P.; Abreu, A.; Ferreira, P. M. T.; Oliveira, M.; Dubest, R.; Aubard, J.; Samat, A. *Org. Lett.* **2005**, *7*, 4811–4814; (b) Muchi, A.; Buchwald, S. *Top. Cur. Chem.* **2002**, *219*, 131–209; (c) Wolfe, J. P.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6359–6362; (d) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805–818; (e) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125–146; (f) Wolf, J. P.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1144–1157.
6. (a) Bougdid, L. Ph.D. Thesis, Université de la Méditerranée, **2006**; (b) Frigoli, M.; Moustrou, C.; Samat, A.; Gugliemetti, R. *Eur. J. Org. Chem.* **2003**, 2799–2812.
7. *General procedure for the amination reactions:* A Schlenk flask was charged with aryl halide (0,9 mmol), amine (1 mmol), sodium *tert*-butoxide (1.4 mmol), tris(dibenzylideneacetone)dipalladium(0) (2 mol %), 2-(di-*t*-butylphosphino)biphenyl (4 mol %) in toluene (1 mL/mmol) under argon. The flask was immersed in an 80 °C oil bath with stirring until the starting material had been completely consumed as judged by GC analysis. The solution was then allowed to cool to room temperature, taken up in either and filtered. The solution was concentrated to dryness under reduced pressure. The crude material was purified by column chromatography with cyclohexane–acetone (90:10).
8. (a) *N*-[4-(3,3-Diphenyl-3*H*-benzo[*f*]chromen-8-ylamino)-phenyl]-acetamide **1a**. ^{1}H NMR (acetone, ppm): $\delta = 1.42$ (s, 3H), 6.47 (d, $J = 9.9$, 1H), 7.11 (s, 1H), 7.15 (s, 1H), 7.18 (s, 1H), 7.20–7.41 (m, 10H), 7.51–7.64 (m, 6H), 7.96 (d, $J = 9.9$, 1H). ^{13}C NMR (acetone, ppm): $\delta = 149.4$ (1C), 146.2 (1C), 141.4 (1C), 133.9 (1C), 133.3 (1C), 131.7 (1C), 132.6 (1C), 129.3 (1C), 129.1 (1C), 128.9 (4C), 128.2 (2C), 127.6 (4C), 125.5 (1C), 123.4 (1C); 121.5 (1C), 121.2 (1C), 121.1 (1C), 120.7 (2C), 119.3 (2C), 119.2 (2C), 115.5 (1C), 111.3 (1C), 82.7 (1C), 27.5 (1C); (b) *N*-[4-(2,2-Diphenyl-2*H*-chromen-6-ylamino)-phenyl]-acetamide **2a**. ^{1}H NMR (acetone, ppm): $\delta = 2.25$ (s, 3H), 6.48 (d, $J = 9.9$, 1H), 6.50 (d, $J = 8.7$, 2H), 6.62 (d, $J = 8.7$, 2H), 6.90 (s, 1H), 6.94 (d, $J = 9.9$, 1H), 7.17–7.34 (m, 10H), 7.46–7.52 (m, 4H). ^{13}C NMR (acetone, ppm): $\delta = 150.2$ (1C), 147.9 (1C), 146.6 (2C), 144.1 (1C), 143.1 (1C), 136.1 (1C), 129.7 (1C), 129.3 (1C), 128.9 (4C), 128.2 (2C), 127.4 (4C), 127.0 (1C), 123.8 (1C), 122.4 (1C), 121.5 (2C); 120.2 (1C), 116.4 (2C), 81.7 (1C), 23.7 (1C). MS (FAB+) exact mass for $C_{29}H_{25}N_2O_2$ $[M+H]^+$ 433, found 433; (c) *N*-[4-(5,8-Dimethyl-2,2-diphenyl-2*H*-chromen-6-ylamino)-phenyl]-acetamide **3a**. ^{1}H NMR (acetone, ppm): $\delta = 2.12$ (s, 3H), 2.17 (s, 3H), 2.26 (s, 3H), 6.49 (d, $J = 9.9$, 1H), 6.51 (d, $J = 8.7$, 2H), 6.62 (d, $J = 8.7$, 2H), 6.91 (s, 1H), 6.95 (d, $J = 9.9$, 1H), 7.17–7.38 (m, 9H), 7.49–7.53 (m, 4H). ^{13}C NMR (acetone, ppm): $\delta = 150.1$ (1C), 147.8 (1C), 146.7 (2C), 144.1 (1C), 143.2 (1C), 136.1 (1C), 129.8 (1C), 129.3 (1C), 128.9 (4C), 128.2 (2C), 127.5 (4C), 127.0 (1C), 126.4 (1C), 123.9 (1C), 122.3 (1C), 121.4 (2C); 120.3 (1C), 116.5 (2C), 81.8 (1C), 27.4 (1C), 15.9 (1C), 13.4 (1C); (d) *N*-[4-(5,6-Dimethyl-2,2-dipheny-2*H*-chromen-8-yl)-phenyl]-acetamide **4a**. ^{1}H NMR (acetone, ppm): $\delta = 2.15$ (s, 3H), 2.18 (s, 3H), 2.26 (s, 3H), 6.47 (d, $J = 10.11$, 2H), 6.70 (d, $J = 9.10$, 2H), 7.48–7.26 (m, 9H), 7.68 (d, $J = 7.10$, 4H), 8.01 (d, $J = 9.10$, 2H). ^{13}C NMR (acetone, ppm): $\delta = 153.9$ (1C), 145.9 (2C), 145.7 (1C), 139.7 (1C), 132.3 (1C), 130.6 (1C), 129.4 (4C), 128.7 (2C), 127.9 (4C), 127.8 (1C), 127.6 (1C), 126.7 (1C), 123.9 (1C), 122.7 (1C), 121.9 (2C), 119.6 (1C), 114.9 (2C), 82.7 (1C), 23.6 (1C), 20.9 (1C), 14.7 (1C). MS (FAB+) exact mass for $C_{31}H_{29}N_2O_2$ $[M+H]^+$ 461, found 461.

9. (a) (3,3-Diphenyl-3*H*-benzo[*f*]chromen-8-yl)-(4-amino-phenyl)-amine **1b**. ^{1}H NMR (acetonitrile, ppm): $\delta = 4.31$ (s, 2H), 5.51 (s, 1H), 6.32 (d, $J = 9.9$, 1H), 6.53 (d, $J = 8.7$, 2H), 6.83 (d, $J = 8.7$, 2H), 6.96–7.34 (m, 10H), 7.38–7.42 (m, 4H), 7.76 (d, $J = 9.0$, 1H). ^{13}C NMR (acetonitrile, ppm): $\delta = 148.8$ (1C), 146.3 (2C), 144.9 (1C), 144.2 (1C), 133.6 (1C), 131.9 (1C), 129.2 (1C), 128.8 (4C), 128.7 (1C), 128.2 (2C), 127.6 (4C); 124.6 (1C), 123.8 (2C), 120.2 (1C), 120.8 (1C), 120.5 (1C), 119.1 (1C), 116.0 (2C), 115.5 (1C), 108.5 (1C), 82.6 (2C); (b) *N*-(2,2-Diphenyl-2*H*-chromen-6-yl)-benzyl-1,4-diamine **2b**. ^{1}H NMR (acetone, ppm): $\delta = 2.92$ (s, 2H), 6.40 (d, $J = 10.0$, 1H), 6.47 (d, $J = 8.7$, 2H), 6.63 (d, $J = 8.7$, 2H), 6.87 (s, 1H), 6.95 (d, $J = 10.1$, 1H), 7.19–7.35 (m, 9H), 7.50–7.55 (m, 4H). ^{13}C NMR (acetone, ppm): $\delta = 147.6$ (1C), 146.5 (2C), 144.0 (1C), 143.4 (1C), 135.7 (1C), 129.8 (1C), 128.9 (4C), 128.0 (2C), 127.3 (4C), 126.9 (1C), 126.7 (1C), 123.8 (1C), 122.5 (1C), 121.3 (2C), 120.2 (1C), 116.2 (2C), 81.9 (1C); (c) (5,8-Dimethyl-2,2-diphenyl-2*H*-chromen-6-yl)-(4-amino-phenyl)–amine **3b**. ^{1}H NMR (acetone, ppm): $\delta = 2.12$ (s, 3H), 2.25 (s, 3H), 2.92 (s, 2H), 6.40 (d, $J = 10.0$, 1H), 6.47 (d, $J = 8.7$, 2H), 6.63 (d, $J = 8.7$, 2H), 6.87 (s, 1H), 6.95 (d, $J = 10.1$, 1H), 7.19–7.35 (m, 7H), 7.50–7.55 (m, 4H). ^{13}C NMR (acetone, ppm): $\delta = 147.6$ (1C), 146.5 (2C), 144.0 (1C), 143.4 (1C), 135.7 (1C), 129.8 (1C), 128.9 (4C), 128.0 (2C), 127.3 (4C), 126.9 (1C), 126.7 (1C), 123.8 (1C), 122.5 (1C), 121.3 (2C); 120.2 (1C), 116.2 (2C), 81.9 (1C), 15.8 (1C), 13.0 (1C); (d) *N*-(5,6-Dimethyl-2,2-diphenyl-2*H*-chromen-8-yl)-benzyl-1,4-diamine **4b**. ^{1}H NMR (acetone, ppm): $\delta = 2.17$ (s, 3H), 2.27 (s, 3H), 3.05 (s, 2H), 6.43 (d, $J = 10.0$, 1H), 6.67 (d, $J = 8.9$, 2H), 6.73 (d, $J = 8.9$, 2H), 6.89 (s, 1H), 7.19 (d, $J = 10.1$, 1H), 7.26–7.35 (m, 7H), 7.50–7.58 (m, 4H). ^{13}C NMR (acetone, ppm): $\delta = 145.8$ (1C), 145.0 (2C), 138.0 (1C), 135.4 (1C), 130.1 (1C), 128.8 (1C), 127.9 (4C), 126.7 (2C), 124.3 (4C), 121.9 (1C), 126.7 (1C), 123.8 (1C), 122.5 (1C), 121.3 (2C), 120.2 (1C), 111.2 (2C), 80.0 (1C), 19.8 (1C), 15.6 (1C).
10. *Hydrolysis procedure*: Acetanilide (1 mmol) in 10% HCl (30 mL) was stirred at reflux during 30 min, The solution was then allowed to cool to room temperature, 20% NaOH (aqueous) was added until pH 7–8, then the mixture was extracted five times with EtOAc and purified by column chromatography with cyclohexane–acetone (90:10).
11. (a) (3,3-Diphenyl-3*H*-benzo[*f*]chromen-8-yl)-(4-nitro-phenyl)-amine **1c**. ^{1}H NMR (acetone, ppm): $\delta = 6.37$ (d, $J = 9.9$, 1H), 7.04 (d, $J = 9.2$, 2H), 7.12–7.24 (m, 7H), 7.30–7.34 (m, 2H), 7.42–7.44 (m, 4H), 7.54–7.58 (d, $J = 9.5$, 2H), 7.93 (s, 1H), 8.00 (d, $J = 9.3$, 2H), 8.45 (s, 1H). ^{13}C NMR (acetone, ppm): $\delta = 151.8$ (1C), 150.7 (1C), 145.9 (2C), 139.8 (1C), 136.9 (1C), 130.9 (1C), 129.8 (1C), 129.5 (1C), 128.8 (4C), 128.2 (2C), 127.5 (4C); 126.7 (2C), 123.9 (1C), 123.6 (1C), 120.3 (1C), 119.8 (1C), 119.1 (1C), 115.4 (1C), 114.3 (2C), 83.8 (1C); (b) (2,2-Diphenyl-2*H*-chromen-6-yl)-(4-nitrophenyl)-amine **2c**. ^{1}H NMR (acetone, ppm): $\delta = 3.42$ (s, 1H), 6.46 (d, $J = 10.11$, 2H), 6.66 (d, $J = 9.16$, 1H), 6.84–7.00 (m, 2H), 7.04 (s, 1H), 7.24–7.50 (m, 6H), 7.50 (d, $J = 7.10$, 4H), 7.84 (m, 1H), 8.03 (d, $J = 9.17$, 2H). ^{13}C NMR (acetone, ppm): $\delta = 149.7$ (1C), 146.3 (1C), 145.5 (2C), 139.0 (1C), 137.9 (1C), 130.3 (1C), 128.2 (1C), 127.7 (1C), 129.6 (4C), 128.5 (2C), 127.6 (4C), 127.1 (2C), 120.7 (1C), 116.4 (1C), 113.6 (1C), 109.4 (2C), 82.1 (1C); (5,8-Dimethyl-2,2-diphenyl-2*H*-chromen-6-yl)-(4-nitrophenyl)-amine **3c**: (c) Shilova, E. A.; Moustrou, C.; Samat, A. *Tetrahedron Lett.* **2005**, *46*, 8857; (d) (5,6-Dimethyl-2,2-diphenyl-2*H*-chromen-8-yl)-(4-nitrophenyl)-amine **4c**. ^{1}H NMR (acetone, ppm): $\delta = 2.15$ (s, 3H), 2.18 (s, 3H), 3.04 (s, 1H), 6.45 (d, $J = 10.11$, 2H), 6.68 (d, $J = 9.10$, 1H), 7.19 (s, 1H), 7.48–7.26 (m, 7H), 7.65 (d, $J = 7.10$, 4H), 8.05 (d, $J = 9.10$, 2H).^{13}C NMR (acetone, ppm): $\delta = 153.8$ (1C), 145.9 (2C), 145.5 (1C), 139.6 (1C), 131.3 (1C), 130.1 (1C), 129.1 (4C), 128.4 (2C), 127.6 (4C), 127.5 (1C), 127.1 (1C), 126.8 (2C), 126.5 (1C), 122.6 (1C), 122.5 (1C), 114.5 (2C); 82.7 (1C), 20.9 (1C), 14.7 (1C).
12. *Reduction procedure*: A mixture of nitroderivative (1 mmol), iron powder (1 mmol), glacial acetic acid (10 mmol), and absolute EtOH (20 mL) was stirred at reflux for 3 h. The reaction was allowed to cool to room temperature and was poured into H_2O (45 mL), 20% NaOH (aqueous) was added until pH 7–8 and the resulting emulsion was extracted twice with EtOAc. The combined organic extracts were washed with H_2O, dried (Na_2SO_4), and purified by column chromatography with cyclohexane–acetone (90:10).
13. Photochemical measures were performed in acetonitrile solutions ($C = 0.84 \times 10^{-5}$ M) of spectrometric grade at 20°. The analysis cell was placed in a sample chamber in *Cary 50 Scan* spectrophotometer. The solutions were stirred continuously during experiments. An *Oriel-150-W-high-pressure* Xe lamp was used for irradiation, 520 mW/cm^2.