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A Photocatalytic Meerwein Approach for the Synthesis of Isochromanones and Isochromenones

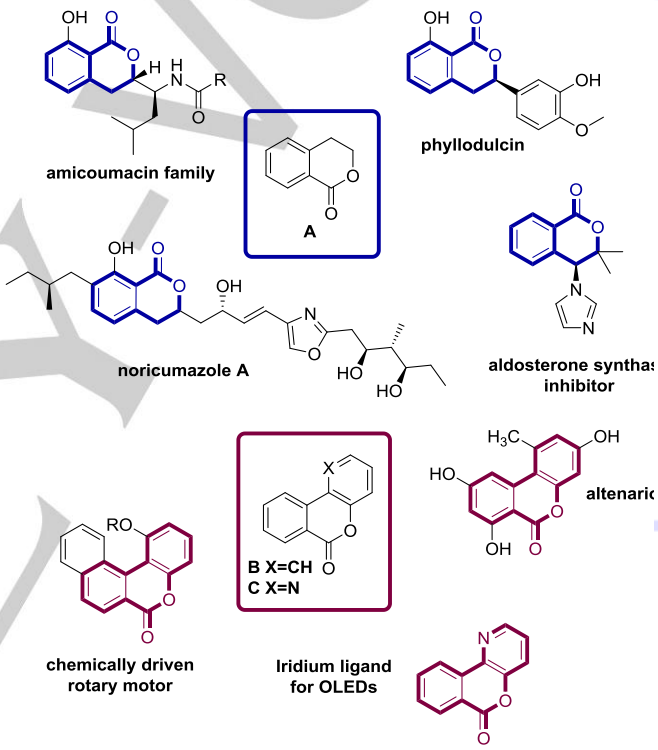
Stefano Crespi,[a] Stefanie Jäger,[b] Burkhard König*[b] and Maurizio Fagnoni*[a]

Abstract: A visible light Ru(II) photoredox Meerwein synthesis of isochromanones and isochromenones is described starting from diazonium salts of different substituted anthranilic acids. This approach allows the reliable and efficient preparation of structures found in many biologically active molecules or used in material chemistry.

Introduction

The isochromanone moiety (**A**, Scheme 1) is a recurrent structure in a huge number of molecules recognized to have biological and pharmacological activity.[1] 3,4–Dihydroisocoumarins are commonly isolated from a wide variety of natural sources such as plants, insects and microbes and their activity spans from antifungal to cytotoxic, antimalarial and antiallergical properties.[2] The interest on these molecules is clearly witnessed by the recent isolation of icumazole A and by the total synthesis of noricumazole A (Scheme 1), two molecules characterised by a marked activity against various fungi and yeasts.[2a] Moreover, (*S*)–4–(1H-imidazol–1–yl)–3,3–dimethylisochroman–1–one was discovered as a significant aldosterone inhibitor.[3] Noteworthy, amicoumacins (Scheme 1) belong to an interesting family of antibiotics bearing the isochromanone core that are currently under study for their antibacterial antinflammatory, antiulcer and antineoplastic action.[4] An interesting case is phyllodulcin (Scheme 1), a principal constituent of *Hydrangeae Dulcis Folium*, a natural medicine belonging to the Japanese heritage and its traditional pharmacopoeia. Phyllodulcin not only possesses antimicrobial activity, but has a well-known sweetening effect, 600–800 times as sweet as sucrose.[2b,5]

A structurally related class of compounds is represented by molecules possessing the isochromenone moiety (**B**, Scheme 1) that, as the isochromanones, belongs to the bigger isocoumarin–like product family.[6] Molecules bearing an isochromenone functionality possess various biological activities.[6] and they have found application in material chemistry, in liquid crystals and the construction of molecular machines.[7] In particular, heterosubstitued derivatives **C**, (Scheme 1) emerged as a class of iridium ligands in strongly emitting organometallic complexes, that could find application in the development of tunable OLEDs.[8]



Scheme 1. Examples of molecules possessing the isochromanone and isochromenone core.

The large number of applications triggered the development of various synthetic routes to compounds **A–C**. The synthesis of dihydroisocoumarins comprises ortho–lithiation of aromatic compounds,[9a] oxidation of the isochromane moiety,[9b,c] NHC,[9d] rhodium[9e–g] or palladium[9h] catalysed reactions, or procedures based either on rearrangements of isobenzofurans,[9i] or Passerini–aldol sequence.[3] Besides, isochromenone tricyclics are synthesized by metal–catalysed and metal free classic oxidative lactonization.[10] On the other hand, derivatives **C** can be prepared following a free radical pathway starting from ortho–bromobenzoic acids,[11] through a rearrangement of isoindolones[12] or by treating the diazonium salt of the anthranilic acid in the presence of $TiCl_3$ and 3–hydroxypyridines in aqueous hydrochloric acid.[13]

Herein we report the preparation of isochromanones and isochromenones by the photo–Meerwein reaction using the

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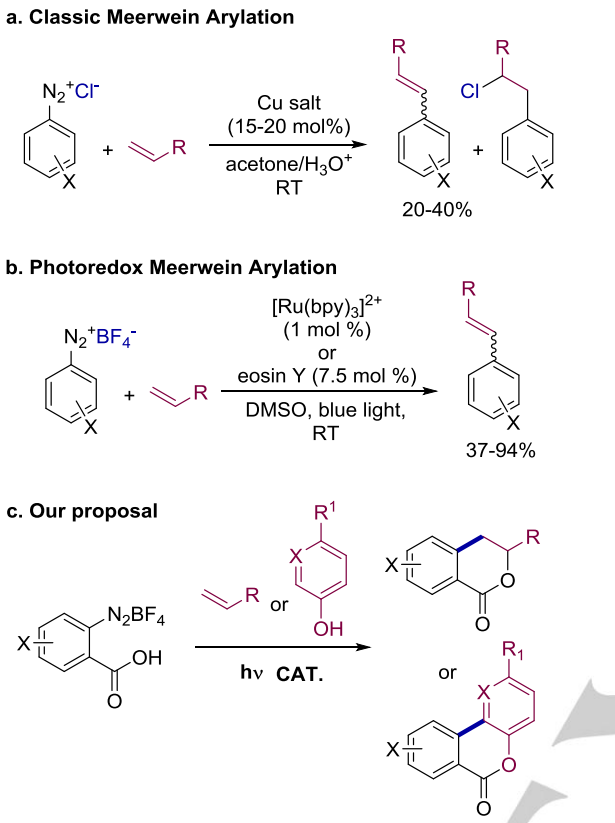
diazonium salts of different substituted anthranilic acids as the source of aryl radicals.[14]



Scheme 2. a) Classic Meerwein reaction, b) the photoredox catalytic variation of the Meerwein reaction and c) our reaction proposal.

The classic Meerwein arylation scheme reported by Hans Meerwein in 1939 involves the copper catalysed addition of an aryl diazonium salt to an electron–poor alkene,[15] but the yields are rather poor (only around 20–40%) with high catalyst loadings (Scheme 2a).[16] The use of an organometallic ($[Ru(bpy)_3]^{2+}$) or an organic (Eosin Y) photocatalyst allows the generation of aryl radicals from aryl diazonium salts under visible light irradiation by loss of molecular nitrogen. The radicals thus generated can be trapped by a suitable unsaturated compound forming a styrene in good yields (37–94%) by an addition–elimination reaction making use of low catalyst loadings (Scheme 2b).[16] We reasoned that the presence of an acidic moiety in the starting diazonium salt may drive a cyclization step to form the desired bi(tri)cyclic compound (Scheme 2c).[17]

Results and Discussion

In order to develop a photo–Meerwein arylation for isochoma(e)none synthesis, we first investigated a series of different reaction conditions. The model reaction chosen for the optimization was the one between diazonium salt **1a**, thoroughly studied in the past as aryne source,[18] and styrene **2**. First, a set of different solvents was tested using $Ru(bpy)_3Cl_2{\bullet}6H_2O$ (2 mol%, entries 1–5 Table 1) as the photocatalyst, and a ratio of **2**/**1a** of 5. Solvents spanning from MeCN and MeCN/water (9:1, volume ratio), to the protic (EtOH), polar aprotic (dry dimethylsulfoxide, DMSO) and non–polar (dichloromethane, DCM) were tested.

Table 1. Optimization of the reaction between diazonium salt **1a** and styrene **2**.[a]

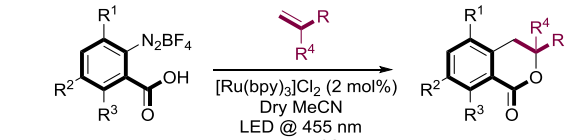
Entry	Solvent	Catalyst (mol%)	**1a**[b]	**2**[b]	**3** [%][c]
1	Dry MeCN	$[Ru(bpy)_3]^{2+}$ (2)	1 equiv.	5 equiv.	40 (37)[d]
2	MeCN/water 9:1	$[Ru(bpy)_3]^{2+}$ (2)	1 equiv.	5 equiv.	17
3	Dry DMSO	$[Ru(bpy)_3]^{2+}$ (2)	1 equiv.	5 equiv.	35
4	DCM	$[Ru(bpy)_3]^{2+}$ (2)	1 equiv.	5 equiv.	10
5	EtOH	$[Ru(bpy)_3]^{2+}$ (2)	1 equiv.	5 equiv.	21
6	Dry MeCN	Eosin Y (5)	1 equiv.	5 equiv.	34
7	Dry MeCN	$[Ru(bpy)_3]^{2}$ (2)$^{+}$	1 equiv.	1 equiv.	54
8	Dry MeCN	$[Ru(bpy)_3]^{2+}$ (2)	5 equiv.	1 equiv.	30
9	Dry MeCN	$[Ru(bpy)_3]^{2+}$ (2)	2 equiv.	1 equiv.	61
10	Dry MeCN	$[Ru(bpy)_3]^{2+}$ (2)	1 equiv.	3 equiv.	90 (86)[d]
11	Dry MeCN	$[Ru(bpy)_3]^{2+}$ (1)	1 equiv.	3 equiv.	78
12	Dry MeCN	$[Ru(bpy)_3]^{2+}$ (3)	1 equiv.	3 equiv.	87
13	Dry MeCN	–	1 equiv.	3 equiv.	6
14[e]	Dry MeCN	$[Ru(bpy)_3]^{2+}$ (2)	1 equiv.	3 equiv.	55

[a] Reactions are carried out under inert atmosphere (N_2) for 2 h at 23°C. [b] The limiting reagent concentration is 0.25M. [c] GC yields. [d] Isolated yields. [e] Reaction performed under aerated conditions.

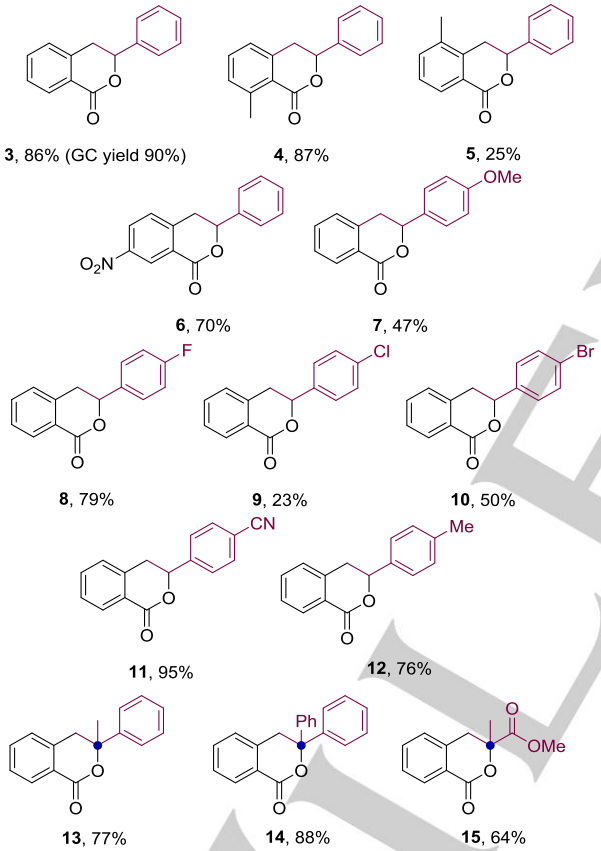
Irradiations were carried out by using 455 nm blue LEDs under inert atmosphere at 23 °C for 2 h. Dry MeCN (entry 1) was identified as the best reaction medium and isochomanone **3** was obtained in 40% GC yield (37% isolated yield). The same reaction in dry MeCN when replacing the metal complex photocatalyst by Eosin Y (7.5 mol%, Entry 6) gave a lower yield of **3**. Next, the reaction was further optimized using dry MeCN as the solvent and $Ru(bpy)_3Cl_2{\bullet}6H_2O$ as the catalyst, varying the proportion of the diazonium salt and the olefin. We observed that a combination of **1a** and **2** in a 1:3 ratio gave a significant increase in the yield of the reaction (Entry 10, Table 1), giving up to 90% of compound **3** (GC yield). Interestingly, higher amounts of **2** were found to be detrimental for the overall yield, probably due to polymerization reactions as indicated by the presence of a thick insoluble precipitate. The catalyst loading was tested and further experiments confirmed that the maximum conversion is

obtained with 2 mol% of $Ru(bpy)_3Cl_2 \cdot 6\ H_2O$ (Entries 10–12, Table 1). Two control experiments were also carried out in order to assess the role of the catalyst and the effect of air on the reaction. Thus, irradiating the diazonium salt and the olefin under uncatalyzed conditions led only to a small amount of **3** (6% yield, entry 13, Table 1).

Table 2. Photo-Meerwein synthesis of isochromanones **3-15**.



1a R^1=R^2=R^3=H
1b R^1=R^2=H, R^3=Me
1c R^1=Me; R^2=R^3=H
1d R^1=R^3=H, R^2=NO_2

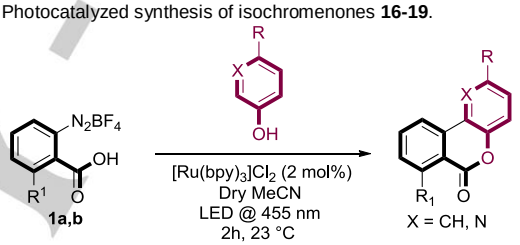


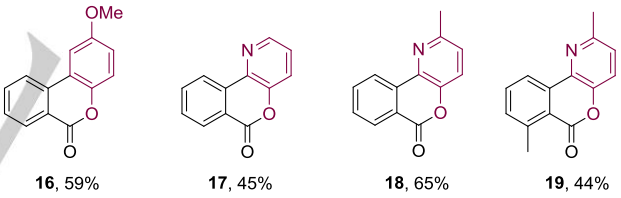
Furthermore, degassing was proven to be necessary for the outcome of the reaction since the irradiation in the presence of air leads to a significant yield drop (55% yield, entry 14). The reaction time was optmized and 2 h are sufficient to obtain a complete conversion of the diazonium salt (see Supporting Information, Table S1). Therefore, after the evaluation of various reaction parameters, the optimum conditions were those reported in Table 1, entry 10.

Having optimized the reaction conditions, we decided to investigate the reaction scope by using a series of diazonium salts of different benzoic acids and different substituted styrenes (Table 2). The photo–Meerwein reaction was found to occur in moderate to good yields (23–95%) affording a small library of 3,4–dihydroisocoumarins. Both the presence of different substituents on the ring of the diazonium salt and modifications of the electron demanding nature of the substituents on styrenes do not affect the reaction outcome. Both electron withdrawing and electron donating groups on the aromatic ring give acceptable yields of compounds **3-14**. To extend the scope of the reaction methyl methacrylate was used as olefin giving product **15** in 64% yield. The formation of quaternary carbons is possible by the transformation and illustrated by the synthesis of compounds **13**–**15** that were obtained in good yields.

In order to broaden the scope of the reaction, (hetero)aromatic compounds were tested as trapping agents of the aryl radicals extending our protocol to isochromenones (Table 3).

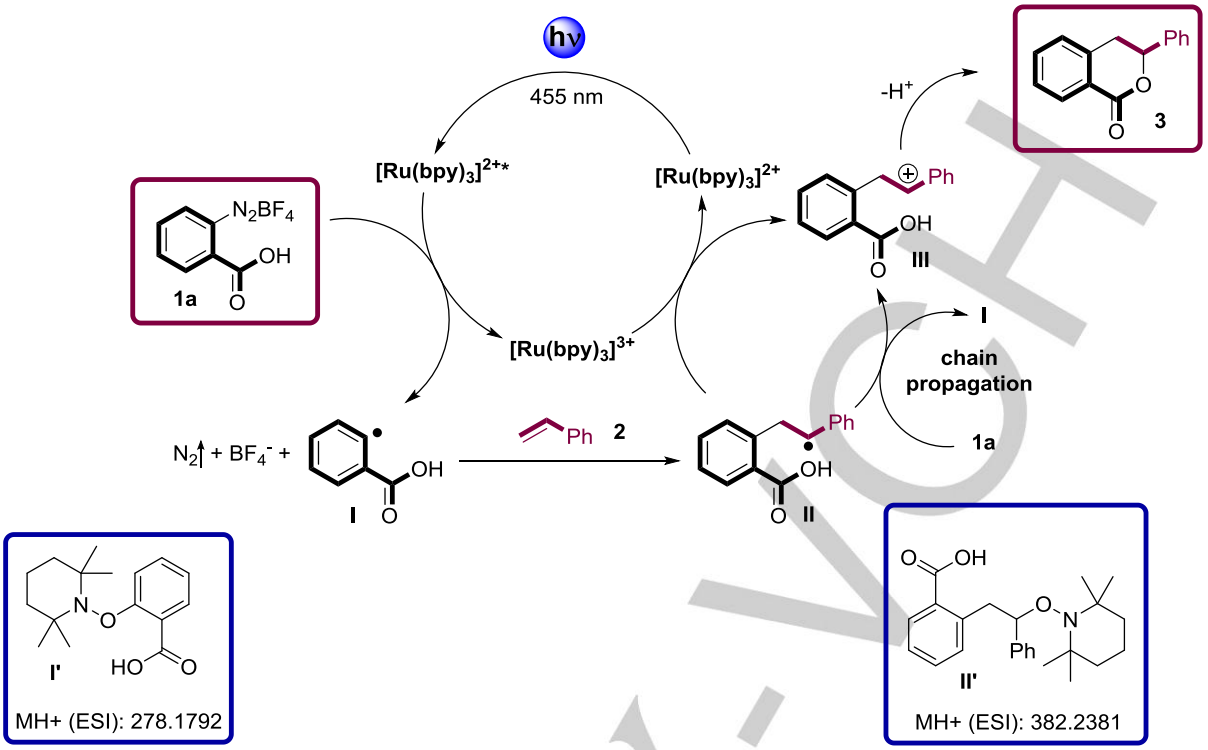
Table 3 Photocatalyzed synthesis of isochromenones **16-19**.





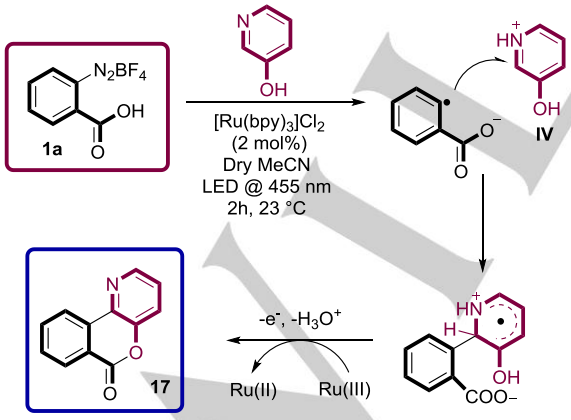
Hydroxy-substituted (hetero)aromatics were chosen due to the known ortho directing effect of the hydroxyl group on the regioselectivity of the radical attack.[13,19] Moreover, the presence of the hydroxy group allows the one–pot condensation of the carboxy group with the alcohol, affording the tricyclic compounds **16**–**19** in yields comparable with those achievable with thermal methods.[13]

A plausible mechanism of the reaction is shown in Scheme 3 for the reaction of **1a** and styrene. Experiments in the presence of TEMPO support a photo–Meerwein radical reaction pathway (see Supporting Information).[20] Oxidative quenching of the photoexcited Ru catalyst by the diazonium salt **1** followed by loss of N_2 leads to the aryl radical **I** that in the presence of styrene gives radical **II**. The catalytic cycle is closed by the electron transfer from **II** to the oxidized form of the catalyst generating the benzyl cation **III**.



Scheme 3. Proposed mechanism for the reaction of **1a** with styrenes. The intermediates trapped by TEMPO are highlighted.

A radical chain process can also be envisaged, in which intermediate **II** reduces the diazonium salt **1** directly. Such smart initiations of radical reactions have been reported for other photo-Meerwein reactions.[20] Branched π-nucleophiles like diphenylethylene or methyl methacrylate promote a better stabilization of the cationic intermediate allowing the formation of quaternary carbon centres in high yield, as demonstrated by products **13-15**. The final product **3** is obtained from ring closure and subsequent proton loss of the cation **III** (Scheme 3). Both radical intermediates **I** and **II** were trapped by TEMPO to give **I'** (MH^+ (ESI–MS): 278.1792) and **II'** (MH^+ (ESI–MS): 382.2381), respectively.



Scheme 4. Proposed mechanism for the reaction of **1a** with hydroxypyridines.

On the other hand, the selectivity of the attack in position 2 of the pyridine and phenolic ring can be explained on the basis of cases previously reported in the literature.[13,19] In particular for the hydroxypyridine reaction we propose the intermediacy of the 3–hydroxypyridinium cation **IV**, generated *in situ* from the interaction of the heterocyclic nitrogen and the carboxylic acid proton (Scheme 4).[13,19, 22]

Conclusions

In conclusion, we optimized and developed a photo-Meerwein procedure giving access to structurally diverse isochromanone derivatives bearing the dihydroisocoumarin core and to the (hetero)biaryl tricyclic isochromenones. The reported method is reliable and affords the desired products in good yields with high selectivity under mild conditions.

Experimental Section

Preparation of Aryldiazonium Tetrafluoroborates 1a-1d: Compounds **1a-1d** were prepared according to a modification of a literature procedure.[22] In a mixture of 2 mL of EtOH and 5 mL of 50% hydrofluoroboric acid, 15 mmol of the appropriate aniline were dissolved, assisting at the precipitation of a thick salt. The reaction mixture was then cooled to 0 °C using an ice bath, consequently a solution of 20 mmol of sodium nitrite in distilled water (1.35 g in 2 mL, 1.5 equiv.) was added dropwise in 5 minutes. The suspension was stirred for an additional 20 min at 0 °C and then the temperature was allowed to raise to RT, while the reaction was stirred for 30 min. The mixture was filtered and the recovered solid was washed with cold methanol, rinsed several times with diethyl ether and dried under vacuum.

Photocatalytic Synthesis of Isochromanones and Isochromenones: In a 5 mL snap vial 0.25 mmol of the appropriate aryl diazonium tetrafluoroborate, 0.75 mmol (3 equiv.) of the olefin or aromatic, and 3.7 mg (0.02 equiv.) $[Ru(bpy)_3]Cl_2•6H_2O$ were dissolved in 1 mL of dry MeCN. The vial was sealed with a septum and degassed via the "freeze-pump-method" (3×). The reaction mixture was stirred at 23 °C and irradiated from the bottom side of the vial for 2 h using blue LEDs (455 nm). After the irradiation time the mixture was diluted with water and washed three times with diethyl ether. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuum. The resulting crude product was further purified by column chromatography using a petrol ether/ethyl acetate as eluent. For GC analysis, the samples were taken directly after irradiation, 20 μL of isochroman were added as internal standard, and the mixture submitted to GC without further purification.

3-Phenylisochroman-1-one (3): Colourless solid (48.2 mg, yield 86%), m.p. 89–90°C (lit. 90–91°C[23]). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.57 (td, *J* = 7.5, 1.5 Hz, 1H), 7.52–7.36 (m, 6H), 7.29 (d, *J* = 7.5 Hz, 1H), 5.56 (dd, *J* = 12.0, 3.3 Hz, 1H), 3.34 (dd, *J* = 16.5, 12.0 Hz, 1H), 3.13 (dd, *J* = 16.5, 3.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.4, 139.0, 138.6, 134.0, 130.4, 128.7, 128.7, 127.9, 127.4, 126.1, 125.1, 80.0, 35.6. IR (neat, cm^{-1}) 3071, 2922, 2855, 1715, 1603, 1457, 1267, 1222, 991, 909, 764, 693. HRMS (EI) calcd. m/z for $C_{15}H_{12}O_2$ [$M^{•+}$] 224.08318; found 224.08275. The spectroscopic data of **3** are in accordance with previous data reported in the literature.[23]

8-Methyl-3-phenylisochroman-1-one (4): Colourless solid (51.8 mg, yield 87%), m.p. 147–148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53–7.33 (m, 6H), 7.26–7.21 (m, 1H), 7.11 (d, *J* = 7.4 Hz, 1H), 5.46 (dd, *J* = 12.0, 2.9 Hz, 1H), 3.32 (dd, *J* = 16.2, 12.0 Hz, 1H), 3.08 (dd, *J* = 16.2, 2.9 Hz, 1H), 2.72 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 143.1, 140.0, 138.6, 132.8, 131.3, 128.7, 128.6, 126.2, 125.2, 123.7, 79.3, 36.8, 22.3. IR (neat, cm^{-1}) 3075, 3019, 2952, 2922, 2855, 1707, 1595, 1461, 1282, 1126, 1066, 753, 704. HRMS (EI) calcd. m/z for $C_{16}H_{14}O_2$ [$M^{•+}$] 238.09883; found 238.09805.

5-Methyl-3-phenylisochroman-1-one (5): Colourless solid (15.0 mg, yield 25%), m.p. 90–91 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.08–7.96 (m, 1H), 7.56–7.30 (m, 8H), 5.52 (dd, *J* = 10.0, 5.4 Hz, 1H), 3.25–3.04 (m, 2H), 2.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.8, 138.8, 137.6, 135.3, 135.2, 128.7, 128.7, 128.3, 127.3, 126.2, 125.1, 79.4, 32.9, 18.9. IR (neat, cm^{-1}) 3067, 2963, 2922, 1707, 1595, 1469, 1245, 1107, 999, 741, 697. HRMS (EI) calcd. m/z for $C_{16}H_{14}O_2$ [$M^{•+}$] 238.09883; found 238.09821.

7-Nitro-3-phenylisochroman-1-one (6): Pale yellow solid (47.1 mg, yield 70%), m.p. 172–173 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.62–7.51 (m, 3H), 7.44 (tt, *J* = 7.7, 1.1 Hz, 1H), 7.39–7.33 (m, 2H), 7.28 (d, *J* = 7.7 Hz, 1H), 5.52 (dd, *J* = 11.9, 3.3 Hz, 1H), 3.29 (dd, *J* = 16.4, 11.9 Hz, 1H), 3.12 (dd, *J* = 16.4, 3.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.1, 138.6, 137.6, 134.1, 131.9, 130.5, 128.0, 127.8, 127.4, 125.0, 122.6, 79.2, 35.5. IR (neat, cm^{-1}) 3082, 3037, 2926, 2855, 1726, 1614, 152, 1424, 1346, 1260, 1137, 1066, 998, 760, 693. HRMS (EI) calcd. m/z for $C_{15}H_{11}NO_4$ [$M^{•+}$] 269.06826; found 269.06724.

3-(4-Methoxyphenyl)isochroman-1-one (7): White solid (29.9 mg, yield 47%), m.p. 109–110°C. (lit. 108-109 °C[24]). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.56 (td, *J* = 7.5, 1.5 Hz, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 8.6 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 2H), 5.50 (dd, *J* = 12.0, 3.1 Hz, 1H), 3.82 (s, 3H), 3.34 (dd, *J* = 16.5, 12.1 Hz, 1H), 3.09 (dd, *J* = 16.5, 3.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.5, 159.8, 139.1, 133.9, 130.6, 130.4, 127.8, 127.7, 127.4, 125.1, 114.0, 79.9, 55.4, 35.5. IR (neat, cm^{-1}) 3071, 2959, 2926, 2855, 1707, 1606, 1513, 1457, 1245, 1025, 831, 734. HRMS (EI) calcd. m/z for $C_{16}H_{14}O_3$ [$M^{•+}$] 254.09375; found 254.09331. The spectroscopic data of **7** are in accordance with previous data reported in the literature.[25]

3-(4-Fluorophenyl)isochroman-1-one (8): Pale yellow solid (47.8 mg, yield 79%), m.p. 84–85 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.58 (td, *J* = 7.5, 1.4 Hz, 1H), 7.52–7.39 (m, 3H), 7.29 (d *J* = 7.6 Hz, 1H), 7.18–7.05 (m, 2H), 5.54 (dd, *J* = 12.1, 3.2 Hz, 1H), 3.32 (dd, *J* = 16.5, 12.1 Hz, 1H), 3.11 (dd, *J* = 16.4, 3.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2, 162.8 (d, *J* = 247.4 Hz), 138.7, 134.4 , 134.0 , 130.5 , 128.1 , 128.0 , 127.4 , 125.0 , 115.7 (d, *J* = 21.6 Hz), 79.3 , 35.6. IR (neat, cm^{-1}) 3067, 3019, 2922, 2855, 1718, 1603, 1510, 1271, 1222, 1061, 831, 738 HRMS (EI) calcd. m/z for $C_{15}H_{11}FO_2$ [$M^{•+}$] 242.07376; found 242.07305 The spectroscopic data of **8** are in accordance with previous data reported in the literature.[26]

3-(4-Chlorophenyl)isochroman-1-one (9): White solid (14.9 mg, yield 23%), m.p. 82–83 °C (lit. 81–83 °C[25]). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.58 (td, *J* = 7.5, 1.5 Hz, 1H), 7.49–7.36 (m 5H), 7.28 (d, *J* = 7.6 Hz, 1H), 5.54 (dd, *J* = 11.9, 3.3 Hz, 1H), 3.30 (dd, *J* = 16.4, 11.9 Hz, 1H), 3.12 (dd, *J* = 16.4, 3.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.1, 138.6, 137.1, 134.5, 134.1, 130.5, 128.9, 128.0, 127.5, 127.4, 125.0, 79.2, 35.6. IR (neat, cm^{-1}) 3067, 2918, 1722, 1603, 1413, 1271, 1114, 831, 746, 705. HRMS (EI) calcd. m/z for $C_{15}H_{11}FO_2$ [$M^{•+}$] 258.04421; found 258.04377. The spectroscopic data of **9** are in accordance with previous data reported in the literature.[25]

3-(4-Bromophenyl)isochroman-1-one (10): White solid (37.9 mg, yield 50%), m.p. 106–107 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.62–7.51 (m, 3H), 7.49–7.40 (m, 1H), 7.39–7.33 (m, 2H), 7.28 (d, *J* = 7.5 Hz, 1H), 5.52 (dd, *J* = 11.8, 3.3 Hz, 1H), 3.28 (dd, *J* = 16.4, 11.9 Hz, 1H), 3.11 (dd, *J* = 16.5, 3.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.1, 138.6, 137.6, 134.1, 131.9, 130.5, 128.0, 127.8, 127.4, 125.0, 122.6, 79.2, 35.5. IR (neat, cm^{-1}) 3067, 2915, 1722, 1599, 1487, 1271, 1066, 1006, 839, 738, 693. HRMS (EI) calcd. m/z for $C_{15}H_{11}BrO_2$ [$M^{•+}$] 301.99220; found 301.99270.

3-(4-Cyanophenyl)isochroman-1-one (11): White solid (59.2 mg, yield 95%), m.p. 152–153 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.74–7.58 (AA'BB', 4H), 7.57 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.43 (tt, *J* = 7.6, 1.0 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 5.61 (dd, *J* = 11.4, 3.8 Hz, 1H), 3.27 (dd, *J* = 16.4, 11.5 Hz, 1H), 3.16 (dd, *J* = 16.4, 3.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 143.7, 138.2, 134.3, 132.6, 130.5, 128.2, 127.4, 126.7, 124.7, 118.4, 112.5, 78.8, 35.4. IR (neat, cm^{-1}) 3056 2930, 2229, 1707, 1607, 1458, 1274, 1062, 839, 749, 690. HRMS (EI) calcd. m/z for $C_{16}H_{11}NO_2$ [$M^{•+}$] 249.07843; found 249.07729.

3-(4-Methylphenyl)isochroman-1-one (12): White solid (45.3 mg, yield 76%), m.p. 96–97 °C (lit. 92–94 °C[25]). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.57 (td, *J* = 7.5, 1.5 Hz, 1H), 7.42 (tt, *J* = 7.6, 1.1 Hz, 1H), 7.39–7.19 (AA'BB', 4H), 7.28 (d, *J* = 7.8 Hz, 1H), 5.51

(dd, *J* = 12.0, 3.3 Hz, 1H), 3.33 (dd, *J* = 16.5, 12.0 Hz, 1H), 3.10 (dd, *J* = 16.5, 3.3 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.5, 139.1, 138.5, 135.6, 133.9, 130.4, 129.3, 127.8, 127.4, 126.1, 125.2, 80.0, 35.6, 21.2. IR (neat, cm^{-1}) 3034, 2918, 1718, 1606, 1461, 1267, 1118, 812, 738, 689. HRMS (EI) calcd. m/z for $C_{16}H_{14}O_2$ [$M^{\bullet+}$] 238.09883; found 238.09868.

3-Methyl-3-phenylisochroman-1-one (13): White solid (45.9 mg, yield 77%), m.p. 50–52 °C ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.50–7.39 (m, 3H), 7.32–7.15 (m, 5H), 3.52 (d, *J* = 16.4 Hz, 1H), 3.40 (d, *J* = 16.3 Hz, 1H), 1.75 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.3, 143.6, 137.9, 133.9, 130.0, 128.5, 127.7, 127.6, 127.5, 125.2, 124.7, 83.7, 39.1, 30.2. IR (neat, cm^{-1}) 3064, 2982, 2930, 1707, 1603, 1286, 1114, 760, 697. HRMS (EI) calcd. m/z for $C_{16}H_{14}O_2$ [$M^{\bullet+}$] 238.09883 found 238.09827. The spectroscopic data of **13** are in accordance with previous data reported in the literature.[27]

3,3-Diphenylisochroman-1-one (14): White solid (66.1 mg, yield 88%), m.p. 148–149 °C (lit. 148–149 °C[28]). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.50 (td, *J* = 7.5, 1.4 Hz, 1H), 7.47–7.39 (m, 4H), 7.36–7.16 (m, 9H), 3.82 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.1, 143.0, 138.2, 134.1, 130.2, 128.5, 127.7, 127.6, 127.5, 126.2, 125.7, 86.6, 39.1. IR (neat, cm^{-1}) 3030, 3067, 2922, 2855, 1718, 1603, 1446, 1282, 1237, 760, 701. HRMS (EI) calcd. m/z for $C_{21}H_{16}O_2$ [$M^{\bullet+}$] 300.11448; found 300.11383. The ^{1}H NMR and IR data of **14** are in accordance with previous data reported in the literature.[29]

Methyl 3-methyl-1-oxoisochromane-3-carboxylate (15): White solid (35.2 mg, yield 64%), m.p. 105–107 °C (lit. 104–105 °C[30]). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.51 (td, *J* = 7.5, 1.5 Hz, 1H), 7.42–7.33 (m, 1H), 7.20 (dt, *J* = 7.6, 0.6 Hz, 1H), 3.59 (s, 3H), 3.39 (d, *J* = 16.3 Hz, 1H), 3.29–3.14 (m, 1H), 1.75 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.2, 164.3, 136.3, 134.0, 130.1, 128.1, 127.5, 124.5, 82.0, 53.1, 37.0, 25.0. IR (neat, cm^{-1}) 3030, 2967, 2922, 2855, 1750, 1722, 1606, 1454, 1208, 1081, 738, 685. HRMS (ESI) calcd. m/z for $C_{21}H_{16}O_2H^+$ [(M + H)]$^+$ 221.0814; found 221.0818.

2-Methoxy-6H-benzo[c]chromen-6-one (16): White solid (33.4 mg, yield 59%), m.p. 123–124 °C (lit. 122–124 °C[31]). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.45–8.32 (m, 1H), 8.11–7.98 (m, 1H), 7.81 (dddd, *J* = 8.0, 7.3, 1.5, 0.6 Hz, 1H), 7.57 (ddt, *J* = 8.0, 7.3, 0.8 Hz, 1H), 7.48–7.43 (m, 1H), 7.33–7.23 (m, 1H), 7.03 (ddd, *J* = 9.0, 2.9, 0.6 Hz, 1H), 3.89 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.3, 156.3, 145.6, 134.7, 134.6, 130.6, 128.9, 121.7, 121.3, 118.7, 118.5, 117.1, 106.3, 55.8. IR (neat, cm^{-1}) 3071, 2963, 2922, 2833, 1707, 1599, 1573, 1494, 1412, 1204, 1036, 801, 764, 682. HRMS (EI) calcd. m/z for $C_{14}H_{10}O_3$ [$M^{\bullet+}$] 226.06245; found 226.06179.

6H-Isochromeno[4,3-b]pyridin-6-one (17): White solid (22.2 mg, yield 45%), m.p. 134–136 °C (lit. 134-136 °C[32]). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.72–8.65 (m, 1H), 8.61 (dd, *J* = 4.5, 1.5 Hz, 1H), 8.38 (ddd, *J* = 7.9, 1.4, 0.6 Hz, 1H), 7.91 (ddd, *J* = 8.1, 7.3, 1.4 Hz, 1H), 7.74–7.61 (m, 2H), 7.43 (dd, *J* = 8.3, 4.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.2, 147.7, 146.0, 136.8, 135.6, 135.2, 130.6, 130.1, 124.9, 124.8, 123.4, 122.4. IR (neat, cm^{-1}) 3056, 2922, 285, 1737, 1588, 1070, 723, 682. HRMS (ESI) calcd. m/z for $C_{13}H_9NO_2H^+$ [(M + H)]$^+$ 198.0550; found 198.0558. The spectroscopic data of **17** are in accordance with previous data reported in the literature.[33]

2-Methyl-6H-isochromeno[4,3-b]pyridin-6-one (18): White solid (29.0 mg, yield 55%), m.p. 139–140 °C (lit. 138–139 °C [32]). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.71–8.67 (m, 1H), 8.36 (dt, *J* = 7.8, 0.9 Hz, 1H), 7.93–7.84 (m, 1H), 7.67 (ddd, *J* = 8.0, 7.3, 1.3 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.26 (d, *J* = 8.5 Hz, 1H), 2.66 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.5, 155.0, 145.9, 135.7, 135.5, 135.0, 135.0, 130.3, 130.0, 125.1, 124.8, 123.4, 122.4, 24.2. IR (neat, cm^{-1}) 3078, 2952, 2855, 1730, 1573, 1435, 1267, 824, 743 HRMS (ESI) calcd. m/z for $C_{13}H_9NO_2H^+$ [(M + H)]$^+$ 212.0712; found 212.0719.

2,7-Dimethyl-6H-isochromeno[4,3-b]pyridin-6-one (19): White solid (24.8 mg, yield 44%) m.p. 150–152 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.68–8.56 (m, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.54–7.40 (m, 2H), 7.22 (d, *J* = 8.4 Hz, 1H), 2.85 (s, 3H), 2.64 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.8, 154.6, 145.7, 143.7, 137.0, 135.7, 134.2, 133.5, 124.6, 124.5, 121.5, 120.6, 24.2, 23.5. IR (neat, cm^{-1}) 3086, 2922, 2851, 1730, 1584, 1469, 1245, 1211, 1036, 828, 753. HRMS (ESI) calcd. m/z for $C_{14}H_{11}NO_2H^+$ [(M + H)]$^+$ 226.0870; found 226.0885.

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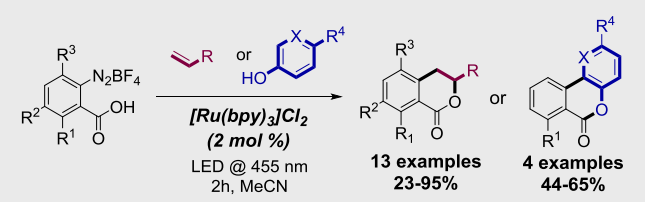

A mild and facile photoredox approach towards synthetically interesting isochromanones and isochromenones is presented. Diazonium salts of various functionalized anthranilic acids are converted to the desired bi– and tricyclic compounds in good to excellent yields.

Photoredox Catalysis

Stefano Crespi, Stefanie Jäger,

Burkhard König and Maurizio Fagnoni**

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A Photocatalytic Meerwein Approach for the Synthesis of Isochromanones and Isochromenones