Tetrahedron xxx (2015) 1–12

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Investigation of cationic Claisen-type electrophilic rearrangements of amides

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ARTICLE INFO

Article history:
Received 3 May 2015
Received in revised form 4 June 2015
Accepted 8 June 2015
Available online xxx

Dedicated with respect and admiration to Professor Barry M. Trost on the occasion of the Tetrahedron Prize for Creativity in Organic Chemistry 2014

Keywords:
oxa and aza-Claisen
Amides
Rearrangement
Hydrocoumarin
Isoquinolinone

ABSTRACT

Herein we report an extension of the electrophilic rearrangement of amides to the preparation of α-prenyl-hydrocoumarins, indoles, isoquinolines and dihydro-isoquinolinones. An unusual competitive sulfonyl migration, uncovered upon attempted aza-Claisen rearrangement, is also described.

1. Introduction

The Claisen and related rearrangements are well-established tools in organic synthesis.[1] Our group has reported a 'Claisen-like' intramolecular rearrangement of keteniminium salts, opening a direct and stereoselective route towards challenging substituted lactones.[2] As depicted in Scheme 1a, this process converts simple ω-allyloxy, -propargyloxy and benzyloxyamides into α-substituted lactones in the presence of triflic anhydride (Tf_2O) and 2,4,6-collidine.[2a,3] The formation of the intermediate iminium ether **1a** (Scheme 1a) has been confirmed and lends support to the original mechanistic proposal, involving an intramolecular cyclization followed by a [3,3] sigmatropic rearrangement.[4] Furthermore, incorporation of a phenyl ring within the alkyl tether restricted the conformational freedom and facilitated the cyclization/rearrangement of amide **2** (Scheme 1b).[5]

These results encouraged us to explore these reactions further and, eventually, to develop an aza-Claisen variant, by replacing the oxygen tethering element with a nitrogen atom. In particular, we hoped that this might open a new platform to assemble heterocyclic compounds (Scheme 1c), a valuable endeavour for synthesis, medicinal chemistry and materials science.[6,7]

2. Results and discussion

The recently reported methodology for the preparation of α-substituted lactones via a [3,3] sigmatropic rearrangement, involving the formation of a keteniminium ion intermediate, presents several advantages: high accessibility of starting materials; relatively high yields; broad substrate scope and simple reaction conditions. This procedure was applied for the preparation of α-prenyl hydrocoumarin derivatives, useful as substrates in organocatalytic transformations.[8] Thus, in our initial studies, we attempted to prepare five-membered ring substrates by applying the rearrangement conditions (Tf_2O, collidine, 120 °C, 5 min) to the readily available *o*-allyl phenol **4**. Indeed, the rearrangement intermediate

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http://dx.doi.org/10.1016/j.tet.2015.06.027
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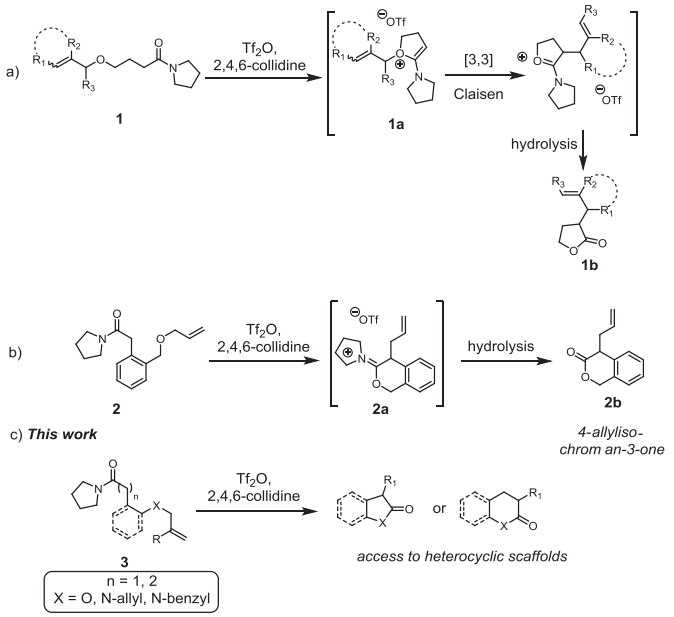
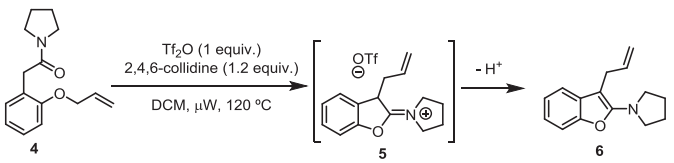


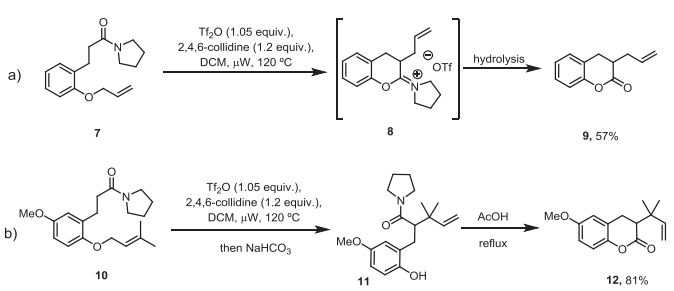
Scheme 1. Preparation of lactones and ring-fused heterocycles by a Claisen-like rearrangement via formation of iminium ether intermediates.

5 was detected by NMR of the reaction mixture (Scheme 2). However, efforts to hydrolyse the intermediate **5** proved fruitless, as the 2-aminobenzofuran **6** resulted as the only observable product.



Scheme 2. Rearrangement of **4** to a benzofuran derivative **6**.

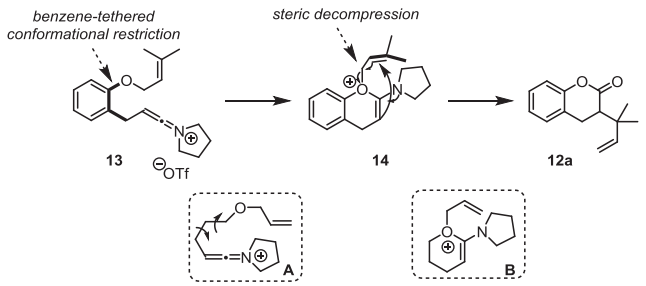
Acknowledging that the aromaticity of benzofuran **6** was behind our inability to hydrolise **6**, we turned towards substrate **7**, obtained from commercially available α,β-unsaturated coumarin. It is worth noting here that hydrocoumarins, also known as flavanoids, show vast biological activity.[9] Although a simple alkylation can provide derivatization on α-position, sterically hindered alkyl and aryl substituents cannot readily be introduced via alkylation. Recognizing the facile reactivity shown above, we presumed that hydrocoumarin-derived substrates would be capable candidates for the rearrangement reaction. After simple preparation of substrate **7**, subsequent rearrangement provided α-allylated compound **9** upon hydrolysis in moderate yield (Scheme 3a).



Scheme 3. Rearrangement of substrates **7** and **10**.

We thus decided to probe this methodology for the synthesis of α-reverse prenylated hydrocoumarin derivatives (Scheme 3b). Reverse prenylation is typically a challenging transformation and [3,3] sigmatropic rearrangement of a 'normal' prenyl substrate such as **10**, whenever possible, offers a straightforward alternative.[10] Under the standard rearrangement conditions, **10** was completely consumed to a new product after hydrolytic work-up. NMR analysis revealed that this was in fact the ring-opened amide **11** (in a mixture with collidine). After a survey of different conditions, we found that exposure to boiling acetic acid led to the hydrocoumarin **12** in 81% yield.

It should be noted that, in our original study of this transformation (Scheme 1a),[1a] reverse prenylation was not possible. Thus, the success observed in the transformations of Scheme 3 is worthy of note. As depicted in Scheme 4, it is likely that the presence of the aromatic ring in **13** facilitates the nucleophilic attack of the oxygen atom, placing it in closer proximity to the keteniminium ion when compared to the aliphatic chain **A** (represented in the box) (Scheme 4). Furthermore, steric decompression during the rearrangement event (compare **14** with **B**) might also account for the reaction outcome.



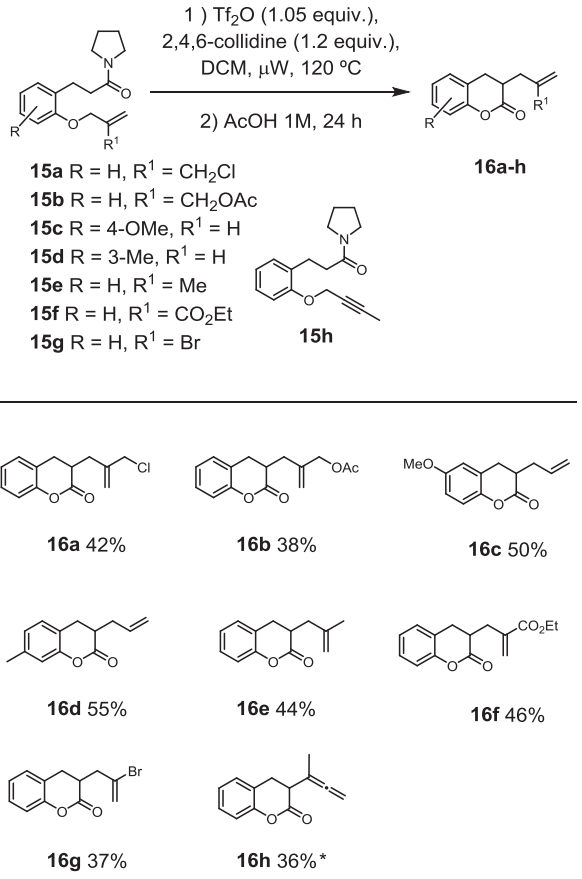
Scheme 4. Conformational and electronic comparison of rearrangements for acyclic and aromatic substrates.

We then proceeded to examine the reaction scope for the preparation of hydrocoumarins with a series of allyl and alkynyl substrates (Scheme 5).

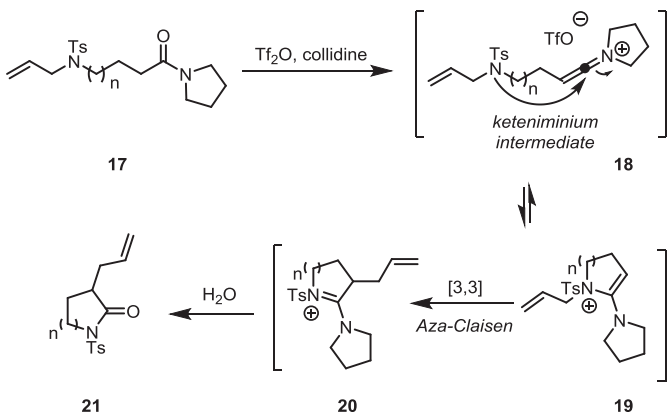
In spite of the generally moderate yields, all the substrates probed gave the corresponding hydrocoumarins. Substitution at the aromatic ring did not influence the reaction outcome, as well as substitution at the olefinic tether. Compound **16g** was isolated in a lower yield due to concomitant decomposition under the reaction conditions. A propargylated substrate furnished the corresponding hydrocoumarin **16h** possessing an allene group. However, the reaction did not proceed for substrates carrying a substituent at the terminal carbon of the double bond. The observed lower reactivity of these compounds might be due to the additional steric hindrance during the rearrangement step.

At this juncture, we became interested in investigating the aza-variant of this transformation. In this apparently simple replacement of oxygen for nitrogen, substrate design was a concern from the outset, as the reaction was expected to proceed according to the mechanism[2a,3] depicted in Scheme 6. In the aza-substrate an additional substituent is required at the nitrogen atom. Importantly, this substituent must be capable of reducing the nucleophilicity of the *N*-atom while at the same time not competing with the amide for the electrophilic Tf_2O activator (thus excluding amide, carbamate—and related—groups from consideration). The tosyl (Ts) group covers these requirements and it was therefore the substituent of choice.

Our preliminary studies focused on alicyclic amine substrates. The starting materials were prepared in two simple steps. Having



Scheme 5. Rearrangement of allyloxyamides **15a**–**g** and propargylamide **15h** to hydrocoumarins **16a**–**h**.



Scheme 6. Foreseen mechanism for the aza-Claisen rearrangement.

compounds **22a**–**c** in hands the rearrangement conditions were applied and, surprisingly, instead of the expected α-substituted lactams **21**, the amidinium derivatives **23a**–**c** were observed (Scheme 7).

The surprising formation of compounds **23** indicates that, for these substrates, the rearrangement conditions promote tosyl migration instead of the expected aza-Claisen rearrangement. The allyl and benzyl-substituted derivatives **22a** and **22b** afforded similar results. However, for the propargyl derivative **22c**, an additional cyclization event took place concurrently with tosyl migration. The unusual structure of **23b** was confirmed by X-ray analysis of a crystal obtained after anion exchange of triflate by the tetrafluoroborate ion (Fig. 1).

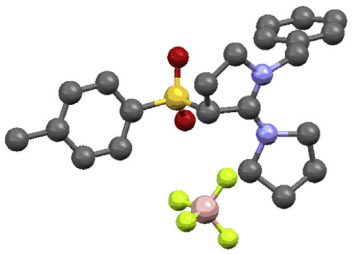
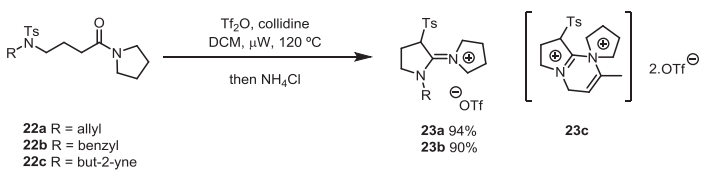


Fig. 1. X-ray structure of **23b** after anion exchange.

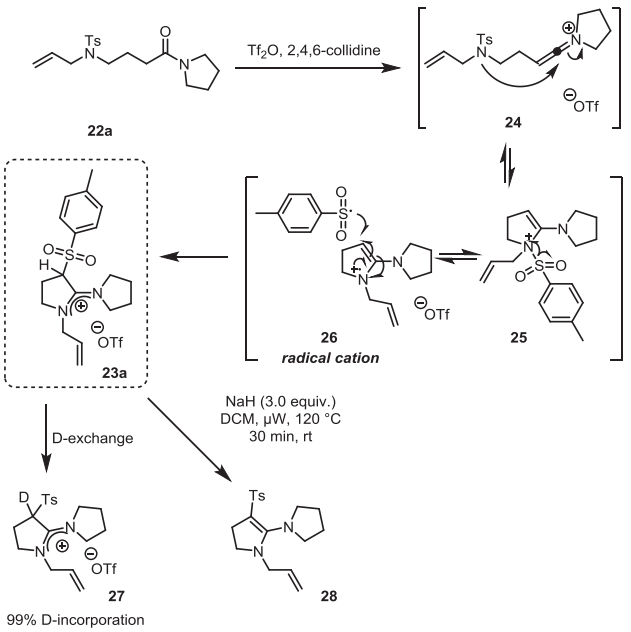
Sulfonamides typically rank amongst the most stable amine protecting groups.[11] Cleavage of the RO_2S–N bond has been documented to occur under relatively harsh conditions, including dissolving metal reduction.[12,13] It should be noted that a 1,2-*N*-to-*C* tosyl rearrangement has been reported in specifically substituted *N*-tosyl ynamides.[13] The observed tosyl migration in the rearrangement of **22a**,**b** to **23a**,**b** allows speculation about either a direct 1,3-rearrangement (which we believe is precluded by geometric reasons) or the involvement of free-radical species. The transient formation of sulfonyl radicals has been proposed under reductive and photoinduced desulfonylation of indoles.[14] As most sulfur-based radicals, sulfonyl radicals are very stable, and a tosyl migration may occur through homolytic dissociation of a key intermediate such as **23a** (Scheme 8). The recombination of the two species **26** may occur faster than their diffusion and it is possible that this process is energetically more favourable than allyl migration.

Hydrolysis of the amidinium **23a** turned out to be very difficult. A control experiment established the acidity of the methine proton of **23a**, as shown by the observed deuteration under mild basic conditions (such as either satd $NaHCO_3$ or satd Na_2CO_3 in D_2O, Scheme 8 and confirmed by NMR). Upon treatment of **23a** with NaH, the formation of dihydropyrrole **28** was observed.

Based on these preliminary results employing tosyl protection, we decided to explore the aza-Claisen rearrangement for the construction of heterocyclic compounds adopting a different strategy. The first experiments focused on the use of *N*-diallylated anilines as rearrangement substrates aiming to obtain fused five- or six-membered ring heterocycles. Thus, upon treatment of **29** with Tf_2O and 2,4,6-collidine, at room temperature or under microwave conditions, a mixture was observed, wherein intermediate **30** was detected (NMR analysis). After purification, **31** could be isolated in 45% yield (Scheme 9). The allyl chain in compound **31** is located at the indolic C-7 position. The aza-Claisen rearrangement of *N*-

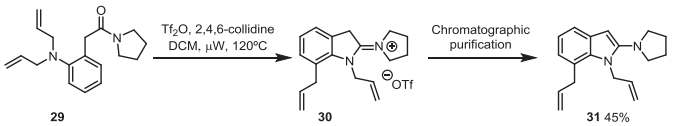


Scheme 7. Unexpected rearrangement of amides **22a**–**c**.



Scheme 8. Proposed mechanism for the observed tosyl migration upon rearrangement of **22a**.

allylanilines is a known transformation.[15,16] The [3,3]-sigmatropic rearrangement of *N*-allyl-*N*-arylamines usually requires high temperatures affording the corresponding anilines along with undesired by-products.[17] Due to the biological relevance of indole derivatives,[18] other substrates akin to **29** were then tested, including *N*-benzyl and *N*-propargyl derivatives. However, the corresponding indoles were obtained in low yield as mixtures of regioisomeric rearrangement products.[19] The difficulty in hydrolysing **31** might be attributed to the aromaticity of the indole nucleus, similarly to benzofuran **6** (Scheme 2).

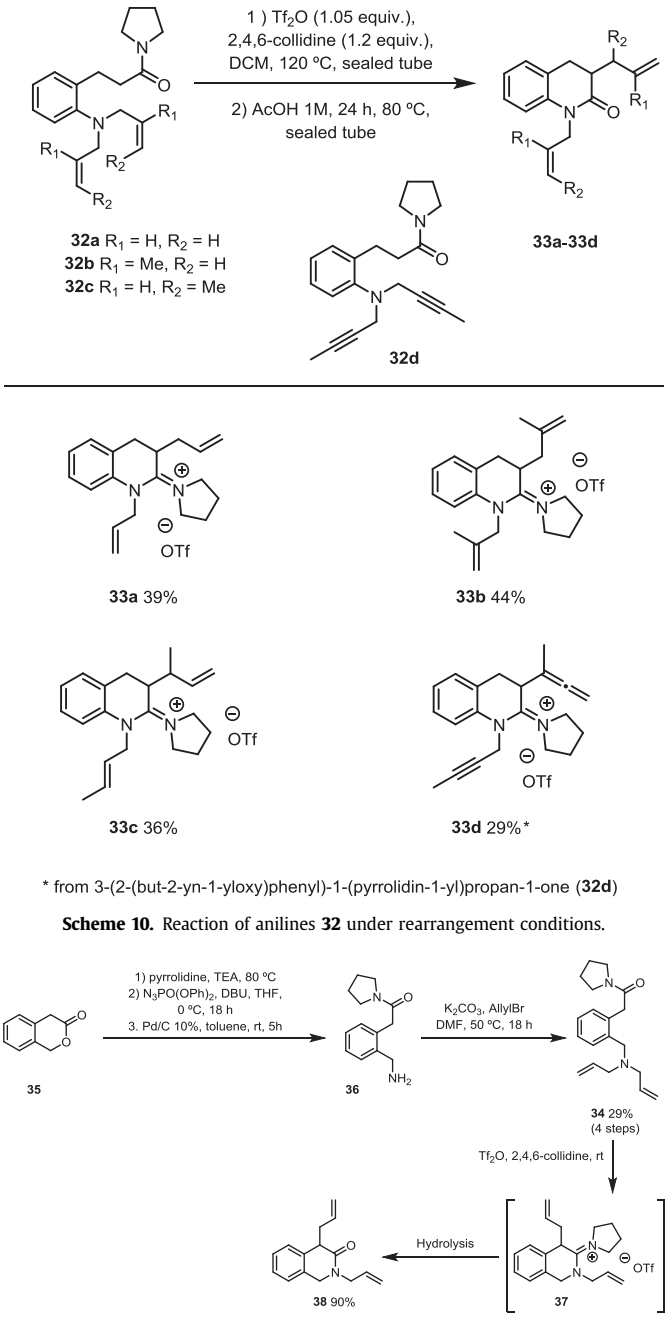


Scheme 9. Reaction of aniline **29** under rearrangement conditions with formation of indole **31**.

Despite the disappointing results obtained for the indoles, we decided to investigate whether the same strategy could be applied to the preparation of fused six-membered nitrogenated heterocycles, such as isoquinolinones and hydroquinolinones. Experiments carried with substrate **32a** under the standard conditions led to the formation of **33a** in 39% yield (Scheme 10).

Substrates **32b** and **32c** also afforded the corresponding dihydroquinolinium triflates **33b** and **33c** with moderate yields. The position of the substituents at the double bond, i.e., inner and outer carbons, had a slight effect on the yield of the rearrangement compounds **33b** and **33c**. The lower yield observed for **33c** might be due to a possible steric hindrance of the methyl substituent at the outer olefinic carbon. The same was observed for compound **33d** that contains the allene moiety.

Furthermore, we investigated the possibility of achieving dihydroisoquinolones, and substrate **34** was prepared from the isochromanone **35**, via benzylamine **36** (Scheme 11). Pleasingly, treatment of **34** under the rearrangement conditions afforded **37** that was successfully hydrolysed using a saturated $NaHCO_3$ solution into the corresponding isoquinolone **38** in 90% yield.



* from 3-(2-(but-2-yn-1-yloxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one (**32d**)

Scheme 10. Reaction of anilines **32** under rearrangement conditions.

Scheme 11. Preparation of 2,4-diallyl-1,4-dihydroisoquinolin-3(2*H*)-one **38**.

Similarly to the results obtained previously in the oxygenated series,[5] compound **34** underwent rearrangement under very mild conditions and a high conversion. Following hydrolysis, the dihydroisoquinoline **38** was obtained in very high yield.

3. Conclusions

We have expanded the scope of the electrophilic Claisen rearrangement of conformationally restricted amides incorporating an aromatic ring. This procedure was applied to oxygen-based substrates, including the preparation of α-reversed prenyl hydrocoumarin derivatives, useful substrates for organocatalytic reactions, in high yield. The strategy proved useful for the conversion of diverse alkyl and alkynyl substrates into the corresponding hydrocoumarins. We also investigated an aza-Claisen rearrangement applying the same protocol. Surprisingly, it was observed that the simplest nitrogen-containing derivatives do not undergo

Please cite this article in press as: Padmanaban, M.; et al., Tetrahedron (2015), http://dx.doi.org/10.1016/j.tet.2015.06.027

rearrangement but rather tosyl migration. Conversely, conformationally restricted aromatic substrates led to smooth rearrangement, enabling the preparation of a variety of rearranged quinolinones and isoquinolinones.

4. Experimental section

Unless otherwise stated, all glassware was flame-dried before use and all reactions were performed under an atmosphere of argon. All solvents were distilled from appropriate drying agents prior to use. All reagents were used as received from commercial suppliers unless otherwise stated. Reaction progress was monitored by thin layer chromatography (TLC) performed on aluminium plates coated with silica gel F254 with 0.2 mm thickness. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm or by staining using potassium permanganate. Flash column chromatography was performed using silica gel 60 (230–400 mesh, Merck and co.). Neat infra-red spectra were recorded using a Perkin–Elmer Spectrum 100 FTIR spectrometer. Wavenumbers ($\tilde{\nu}=1/\lambda$) are reported in cm^{-1}. Mass spectra were obtained using a Finnigan MAT 8200 or (70 eV) or an Agilent 5973 (70 eV) spectrometer, using electrospray ionization (ESI). All 1H NMR and 13C NMR spectra were recorded using a Bruker AV-400 or AV-600 spectrometer at 300 K. Chemical shifts were given in parts per million (ppm, δ), referenced to the solvent peak of CDCl3, defined at δ=7.26 ppm (1H NMR) and δ=77.16 (13C NMR). Coupling constants are quoted in Hz (*J*). 1H NMR splitting patterns were designated as singlet (s), doublet (d), triplet (t), quartet (q), pentet (p). Splitting patterns that could not be interpreted or easily visualized were designated as multiplet (m) or broad (br).

4.1. 3-(2-(Allyloxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one (7)

A mixture of dihydrocoumarin (0.37 g, 0.32 mL, 2.5 mmol, 1.0 equiv), pyrrolidine (0.36 g, 0.42 mL, 5 mmol, 2.0 equiv) and triethylamine (0.76 g, 1.0 mL, 7.5 mmol, 3.0 equiv) was heated to reflux at 90 °C for 16 h. The mixture was evaporated to dryness afforded the desired product as a yellow solid. The crude product used further without any purification. To a solution of the crude amide (0.548 g, 2.5 mmol, 1.0 equiv) in THF (5 mL) was added NaH (0.2 g, 60 percent suspension in mineral oil, 5.0 mmol, 2.0 equiv) portion wise at 0 °C and brought to rt for 2 h. Then 3-bromoprop-1-ene (0.60 g, 0.63 mL, 5.0 mmol, 2.0 equiv) was added drop wise through syringe in 10 min and let it stir 16 h. When the reaction was completed, water was added carefully (10 mL) and the resulting mixture was extracted with ethyl acetate (50 mL). The organic phase was washed with brine (3×25 mL) and dried over Na_2SO_4. The solvent was removed in vacuum. Column chromatography afforded *3-(2-(allyloxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**7**) as a colourless oil (0.52 g, 80%); R_f (EtOAc/heptane=40/60): 0.12; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.14 (m, 2H), 6.89–6.81 (m, 2H), 6.06–6.02 (m, 1H), 5.40 (dq, *J*=17.2, 1.6 Hz, 1H), 5.25 (dq, *J*=10.5, 1.6 Hz, 1H) 4.54 (dt, *J*=5.0, 1.5 Hz, 2H), 3.45 (t, *J*=6.7 Hz, 2H), 3.31 (t, *J*=6.7 Hz, 2H), 2.99 (t, *J*=8.2 Hz, 2H), 2.55 (t, *J*=8.2 Hz, 2H), 1.89–1.79 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.46, 156.56, 133.62, 130.44, 130.17, 127.42, 120.81, 117.21, 111.58, 68.80, 46.66, 45.65, 35.19, 26.56, 26.16, 24.50 ATR-FTIR (cm^{-1}): 3445, 3063, 2970, 2870, 1632, 1432, 1343, 1239, 1191, 1165, 1047, 1020, 997, 868, 752, 638; ESI-MS: calculated $[M+Na]^+$ for $C_{16}H_{21}O_2NNa$: 282.1465, found: 282.1460.

4.2. 3-(5-Methoxy-2-((3-methylbut-2-en-1-yl)oxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one (10)

Following the procedure described for **7**: ^{1}H NMR (500 MHz, $CDCl_3$), δ 7.09 (d, *J*=8.20 Hz, 1H), 6.44 (d, *J*=2.29 Hz, 1H), 6.40 (dd, *J*=8.20, 2.36 Hz, 1H), 5.47 (t, *J*=6.59 Hz, 1H), 4.49 (d, *J*=6.60 Hz, 2H), 3.78 (s, 3H), 3.46 (t, *J*=6.76 Hz, 2H), 3.35 (t, *J*=6.65 Hz, 2H), 2.89 (dd, *J*=9.15, 6.92 Hz, 2H), 2.45–2.64 (m, 2H), 1.80–1.93 (m, 4H), 1.78 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$), δ 171.7, 159.3, 157.6, 137.4, 130.4, 122.4, 120.0, 103.8, 99.5, 64.8, 55.4, 46.6, 45.5, 35.5, 26.1, 26.0, 25.8, 24.5, 18.2. ESI-MS: calculated $[M+Na]^+$ for $C_{19}H_{27}O_3NNa$: 340.1889, found: 340.1886.

4.3. 3-(2-((2-(Chloromethyl)allyl)oxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one (15a)

A mixture of dihydrocoumarin (0.74 g, 0.64 mL, 5.0 mmol, 1.0 equiv), pyrrolidine (0.72 g, 0.84 mL, 10 mmol, 2.0 equiv) and triethylamine (1.52 g, 2.0 mL, 15 mmol, 3.0 equiv) was heated to reflux at 90 °C for 16 h. The mixture was evaporated to dryness afforded the desired product as a yellow solid. The crude product used further without any purification. To a solution of the crude amide (1.1 g, 5.0 mmol, 1.0 equiv) in THF (10 mL) was added NaH (0.4 g, 60% suspension in mineral oil, 10 mmol, 2.0 equiv) portion wise at 0 °C and brought to rt for 2 h. Then, 3-chloro-2-(chloromethyl)prop-1-ene, (1.25 g, 1.2 mL, 10 mmol, 2.0 equiv) was added drop wise through syringe in 10 min and let it stir 16 h. When the reaction was done, water was added carefully (10 mL) and the resulting mixture was extracted with ethyl acetate (50 mL). The organic phase was washed with brine (3×25 mL) and dried over Na_2SO_4. The solvent was removed in vacuum. Column chromatography afforded *3-(2-((2-(chloromethyl)allyl)oxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**15a**) as a colourless oil (0.88 g, 57%); R_f (EtOAc/heptane=40/60): 0.11; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.15 (m, 2H), 6.91–6.85 (m, 2H), 5.38–5.37 (m, 2H), 4.64 (br s, 2H), 4.21 (br s, 2H), 3.45 (t, *J*=6.6 Hz, 2H), 3.29 (t, *J*=6.5 Hz, 2H), 3.00 (t, *J*=7.4 Hz, 2H), 2.55 (t, *J*=7.5 Hz, 2H), 1.89–1.79 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 156.3, 141.1, 130.5, 130.2, 127.5, 121.1, 117.3, 111.5, 68.0, 46.6, 45.7, 45.3, 35.2, 26.4, 26.2, 24.5; ATR-FTIR (cm^{-1}): 2973, 2872, 1636, 1493, 1444, 1342, 1275, 1260, 1239, 1191, 1110, 1150, 1050, 763, 750, 633; ESI-MS: calculated $[M+Na]^+$ for $C_{17}H_{22}ClO_2NNa$: 330.1231, found: 330.1227.

4.4. 2-((2-(3-oxo-3-(Pyrrolidin-1-yl)propyl)phenoxy)methyl) allyl acetate (15b)

To a solution of 3-(2-((2-(chloromethyl)allyl)oxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one (0.462 g, 1.5 mmol, 1.0 equiv) in DMF (4 mL), was added KOAc (0.162 g, 1.65 mmol, 1.10 equiv), and the solution was heated at 65 °C for 18 h. After 18 h, cooled to room temperature then H_2O (5 mL) and Et_2O (5 mL) were then added, and the layers were separated. The organic layer was then washed with H_2O (3×10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure, to give *2-((2-(3-Oxo-3-(pyrrolidin-1-yl) propyl)phenoxy)methyl)allyl acetate* (**15b**) as colourless oil (0.35 g, 70%); R_f (EtOAc/heptane=40/60): 0.08; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.14 (m, 2H), 6.91–6.82 (m, 2H), 5.39 (br s, 1H), 5.32 (br s, 1H), 4.69 (br s, 2H), 4.56 (br s, 2H), 3.45 (t, *J*=6.8 Hz, 2H), 3.29 (t, *J*=6.8 Hz, 2H), 2.99 (t, *J*=8.0 Hz, 2H), 2.54 (t, *J*=7.9 Hz, 2H), 2.08 (s, 3H), 1.89–1.78 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 170.7, 156.4, 139.8, 130.5, 130.2, 127.5, 121.1, 116.0, 111.4, 68.5, 64.8, 46.6, 45.7, 35.1, 26.4, 26.2, 24.5, 20.9; ATR-FTIR (cm^{-1}): 2977, 2874, 1740, 1639, 1493, 1451, 1372, 1343, 1276, 1260, 1239, 1191, 1110, 1027, 915, 764, 750, 633; ESI-MS: calculated $[M+Na]^+$ for $C_{19}H_{25}O_4NNa$: 354.1676, found: 354.1686.

4.5. 3-(2-(Allyloxy)-5-methoxyphenyl)-1-(pyrrolidin-1-yl) propan-1-one (15c)

5-methoxy-indan-1-one (1.62 g, 10.0 mmol, 1.0 equiv) in 100 mL of DCM cooled to 0 °C was added $NaHCO_3$ (1.7 g, 20 mmol,

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2.0 equiv). To this, 3-chloro-perbenzoic acid (4.5 g, 20 mmol, 2.0 equiv) was added portion wise, and the reaction mixture was stirred at 0 °C for 2 h and at room temperature for 16 h. The precipitate was filtered off and washed with DCM. The filtrate was washed with saturated solution of $NaHCO_3$ and dried over Na_2SO_4. After evaporation of the solvent under vacuum 6-methoxy-chroman-2-one was obtained as brown oil (1.5 g, 84%), which was used without further purification. To a mixture of crude dihydrocoumarin (1.5 g, 8.4 mmol, 1.0 equiv), pyrrolidine (1.2 g, 1.41 mL, 16.8 mmol, 2.0 equiv) and triethylamine (2.56 g, 3.5 mL, 25.3 mmol, 3.0 equiv) was heated to reflux at 90 °C for 16 h. The mixture was evaporated to dryness to afford the desired product as a pale brown sticky liquid. The crude product used further without any purification. To a solution of the crude amide (1 g, 4.0 mmol, 1.0 equiv) in THF (10 mL) was added NaH (0.32 g, 60% suspension in mineral oil, 8.0 mmol, 2.0 equiv) portion wise at 0 °C and brought to rt for 2 h. Then, 3-bromoprop-1-ene (1.0 g, 0.7 mL, 8.0 mmol, 2.0 equiv) was added drop wise through syringe in 10 min and let it stir 16 h at room temperature. When the reaction was done, water was added carefully (20 mL) and the resulting mixture was extracted with ethyl acetate (100 mL). The organic phase was washed with brine (3×50 mL) and dried over Na_2SO_4. The solvent was removed in vacuo. Several column chromatography afforded *3-(2-(allyloxy)-5-methoxyphenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**15c**) as a brown sticky liquid (0.30 g, 26%); R_f (EtOAc/heptane=40/60): 0.10; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79–6.75 (m, 2H), 6.67 (dd, J=8.8, 3.0 Hz, 1H), 6.08–6.01 (m, 1H), 5.38 (dq, J=17.2, 1.6 Hz, 1H), 5.24 (dq, J=10.5, 1.4 Hz, 1H), 4.49 (dt, J=5.1, 1.5 Hz, 2H), 3.75 (s, 3H), 3.46 (t, J=6.7 Hz, 2H), 3.32 (t, J=6.6 Hz, 2H), 2.96 (t, J=8.0 Hz, 2H), 2.54 (t, J=8.0 Hz, 2H), 1.90–1.80 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 153.8, 150.8, 133.9, 131.6, 117.2, 116.4, 112.9, 111.7, 69.7, 55.8, 46.7, 45.7, 35.3, 26.8, 26.2, 24.6; ATR-FTIR (cm^{-1}): 2971, 2872, 1638, 1499, 1432, 1276, 1260, 1042, 997, 930, 804, 764, 633; ESI-MS: calculated $[M+Na]^+$ for $C_{17}H_{23}O_3NNa$: 312.1570, found: 312.1566.

4.6. 3-(2-(Allyloxy)-4-methylphenyl)-1-(pyrrolidin-1-yl) propan-1-one (15d)

To 6-methyl-indan-1-one (0.585 g, 4.0 mmol, 1.0 equiv) in 40 mL of DCM cooled to 0 °C was added $NaHCO_3$ (0.67 g, 8 mmol, 2.0 equiv). 3-Chloro-perbenzoic acid (1.8 g, 8 mmol, 2.0 equiv) was added portion wise, and the reaction mixture was stirred at 0 °C for 2 h and at room temperature for 16 h. The precipitate was filtered off and washed with DCM. The filtrate was washed with $NaHCO_3$ and dried over Na_2SO_4. After evaporation of the solvent under vacuum, 7-methylchroman-2-one was obtained as brown oil, which was used without further purification. A mixture of crude dihydrocoumarin (0.4 g, 2.5 mmol, 1.0 equiv), pyrrolidine (0.35 g, 0.41 mL, 5.0 mmol, 2.0 equiv) and triethylamine (0.75 g, 1.0 mL, 7.5 mmol, 3.0 equiv) was heated to reflux at 90 °C for 16 h. The mixture was evaporated to dryness to afford the desired product as a pale brown oil. The crude product used further without any purification. To a solution of the crude amide (0.6 g, 2.5 mmol, 1.0 equiv) in THF (5 mL) was added NaH (0.2 g, 60% suspension in mineral oil, 5.0 mmol, 2.0 equiv) portion wise at 0 °C and brought to rt for 2 h. Then 3-bromoprop-1-ene (0.60 g, 0.63 mL, 5.0 mmol, 2.0 equiv) was added drop wise through syringe in 10 min and let it stir 16 h. When the reaction was done, water was added carefully (10 mL) and the resulting mixture was extracted with ethyl acetate (50 mL). The organic phase was washed with brine (3×25 mL) and dried over Na_2SO_4. Several column chromatography afforded *3-(2-(allyloxy)-4-methylphenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**15d**) as a brown oil (0.15 g, 22%); R_f (EtOAc/heptane=40/60): 0.11; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, J=7.5 Hz, 1H), 6.69 (d, J=7.5 Hz, 1H), 6.65 (s, 1H), 6.11–6.01 (m, 1H), 5.43–5.38 (m, 1H), 5.27–5.24 (m, 1H), 4.54–4.53 (m, 2H), 3.45 (t, J=6.6 Hz, 2H), 3.32 (t, J=6.5 Hz, 2H), 2.95 (t, J=8.0 Hz, 2H), 2.53 (t, J=8.0 Hz, 2H), 2.31 (s, 3H), 1.90–1.84 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 156.5, 137.3, 133.8, 130.2, 127.2, 121.4, 117.2, 112.6, 68.8, 46.7, 45.7, 35.5, 26.2, 26.2, 24.6, 21.6; ATR-FTIR (cm^{-1}): 2973, 2871, 1723, 1640, 1507, 1433, 1275, 1260, 1193, 1158, 1027, 930, 764, 750; ESI-MS: calculated $[M+Na]^+$ for $C_{17}H_{23}O_2NNa$: 296.1621, found: 296.1617.

4.7. 3-(2-((2-Methylallyl)oxy)phenyl)-1-(pyrrolidin-1-yl) propan-1-one (15e)

Mixture of dihydrocoumarin (see SI) (0.37 g, 0.32 mL, 2.5 mmol, 1.0 equiv), pyrrolidine (0.36 g, 0.42 mL, 5 mmol, 2.0 equiv) and triethylamine (0.76 g, 1.0 mL, 7.5 mmol, 3.0 equiv) was heated to reflux at 90 °C for 16 h. The mixture was evaporated to dryness to afford the desired product as a yellow solid. The crude product used further without any purification. To a solution of the crude amide (0.548 g, 2.5 mmol, 1.0 equiv) in THF (5 mL) was added NaH (0.2 g, 60% suspension in mineral oil, 5.0 mmol, 2.0 equiv) portion wise at 0 °C and brought to rt for 2 h. Then, 3-bromo-2-methylpropene, (0.68 g, 0.5 mL, 5.0 mmol, 2.0 equiv) was added drop wise through syringe in 10 min and let it stir 16 h. When the reaction was done, water was added carefully (10 mL) and the resulting mixture was extracted with ethyl acetate (50 mL). The organic phase was washed with brine (3×25 mL) and dried over Na_2SO_4. The solvent was removed in vacuum. Column chromatography afforded *3-(2-((2-methylallyl)oxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**15e**) as a colourless oil (0.6 g, 87%); R_f (EtOAc/heptane=40/60): 0.18; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.13 (m, 2H), 6.89–6.81 (m, 2H), 5.09 (br s, 1H), 4.98 (br s, 1H), 4.44 (s, 2H), 3.45 (t, J=6.8 Hz, 2H), 3.30 (t, J=6.7 Hz, 2H), 3.00 (t, J=6.4 Hz, 2H), 2.56 (t, J=6.4 Hz, 2H), 1.89–1.81 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 156.7, 141.2, 130.5, 130.1, 127.5, 120.8, 112.5, 111.5, 71.7, 46.7, 45.7, 35.2, 26.6, 26.2, 24.5, 19.7; ATR-FTIR (cm^{-1}): 2971, 2870, 1640, 1492, 1435, 1343, 1294, 1238, 1191, 1164, 1110, 1055, 1016, 899, 752, 632; ESI-MS: calculated $[M+H]^+$ for $C_{17}H_{24}O_2N$: 274.1802, found: 274.1801.

4.8. Ethyl 2-((2-(3-oxo-3-(pyrrolidin-1-yl)propyl)phenoxy) methyl)acrylate (15f)

A mixture of dihydrocoumarin (0.37 g, 0.32 mL, 2.5 mmol, 1.0 equiv), pyrrolidine (0.36 g, 0.42 mL, 5 mmol, 2.0 equiv) and triethylamine (0.76 g, 1.0 mL, 7.5 mmol, 3.0 equiv) was heated to reflux at 90 °C for 16 h. The mixture was evaporated to dryness afforded the desired product as a yellow solid. The crude product used further without any purification. To a solution of the crude amide (0.548 g, 2.5 mmol, 1.0 equiv) in THF (5 mL) was added NaH (0.2 g, 60% suspension in mineral oil, 5.0 mmol, 2.0 equiv) portion wise at 0 °C and brought to rt for 2 h. Then, ethyl 2-(bromomethyl) acrylate (1.0 g, 0.7 mL, 5.0 mmol, 2.0 equiv) was added drop wise through syringe in 10 min and let it stir 16 h. When the reaction was done, water was added carefully (10 mL) and the resulting mixture was extracted with ethyl acetate (50 mL). The organic phase was washed with brine (3×25 mL) and dried over Na_2SO_4. The solvent was removed in vacuum. Column chromatography afforded *ethyl 2-((2-(3-oxo-3-(pyrrolidin-1-yl)propyl)phenoxy)methyl)acrylate* (**15f**) as a yellow oil (0.64 g, 77%); R_f (EtOAc/heptane=40/60): 0.15; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.17 (m, 2H), 6.91–6.85 (m, 2H), 6.39 (q, J=1.3 Hz, 1H), 6.00 (q, J=1.3 Hz, 1H), 4.76 (t, J=1.6 Hz, 2H), 4.25 (t, J=7.1 Hz, 2H), 3.44 (t, J=6.7 Hz, 2H), 3.28 (t, J=6.7 Hz, 2H), 3.00 (t, J=8.0 Hz, 2H), 2.54 (t, J=8.0 Hz, 2H), 1.88–1.79 (m, 4H), 1.32 (t, J=7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 165.6, 156.3, 136.4, 130.5, 130.2, 127.5, 126.2, 121.2, 111.6, 66.2, 61.0, 46.6, 45.7, 35.1, 26.5, 26.2, 24.5, 14.3; ATR-FTIR (cm^{-1}): 3462, 2974, 2873, 1717, 1639, 1493, 1437, 1274, 1243, 1175, 1156, 1110, 1053, 953, 891, 631; ESI-MS: calculated $[M+Na]^+$ for $C_{19}H_{25}O_4NNa$: 354.1676, found: 354.1678.

Please cite this article in press as: Padmanaban, M.; et al., Tetrahedron (2015), http://dx.doi.org/10.1016/j.tet.2015.06.027

4.9. 3-(2-((2-Bromoallyl)oxy)phenyl)-1-(pyrrolidin-1-yl) propan-1-one (15g)

A mixture of dihydrocoumarin (0.37 g, 0.32 mL, 2.5 mmol, 1.0 equiv), pyrrolidine (0.36 g, 0.42 mL, 5 mmol, 2.0 equiv) and triethylamine (0.76 g, 1.0 mL, 7.5 mmol, 3.0 equiv) was heated to reflux at 90 °C for 16 h. The mixture was evaporated to dryness afforded the desired product as a yellow solid. The crude product used further without any purification. To a solution of the crude amide (0.548 g, 2.5 mmol, 1.0 equiv) in THF (5 mL) was added NaH (0.2 g, 60% suspension in mineral oil, 5.0 mmol, 2.0 equiv) portion wise at 0 °C and brought to rt for 2 h. Then, 2,3-dibromopropene, (1.0 g, 0.5 mL, 5.0 mmol, 2.0 equiv) was added drop wise through syringe in 10 min and let it stir 16 h. When the reaction was done, water was added carefully (10 mL) and the resulting mixture was extracted with ethyl acetate (50 mL). The organic phase was washed with brine (3×25 mL) and dried over Na_2SO_4. The solvent was removed in vacuum. Column chromatography afforded *3-(2-((2-bromoallyl)oxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**15g**) as yellow oil (0.46 g, 54%); R_f (EtOAc/heptane=40/60): 0.14; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.14 (m, 2H), 6.91 (td, J=7.4, 0.6 Hz, 1H), 6.78 (d, J=8.1 Hz, 1H), 6.01 (m, 1H), 5.68–5.67 (m, 1H), 4.64 (br s, 2H), 3.45 (t, J=6.7 Hz, 2H), 3.32 (t, J=6.7 Hz, 2H), 3.01 (t, J=7.6 Hz, 2H), 2.57 (t, J=7.6 Hz, 2H), 1.90–1.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 155.7, 130.7, 130.3, 127.5, 127.5, 121.6, 118.2, 111.6, 71.8, 46.7, 45.7, 35.2, 26.5, 26.2, 24.5; ATR-FTIR (cm^{-1}): 2971, 2871, 1636, 1492, 1438, 1343, 1275, 1260, 1190, 1164, 1109, 1035, 763, 750, 633; ESI-MS: calculated $[M+Na]^+$ for $C_{16}H_{20}BrO_2NNa$: 360.0570, found: 360.0566.

4.10. 3-(2-(But-2-yn-1-yloxy)phenyl)-1-(pyrrolidin-1-yl) propan-1-one (15h)

A mixture of dihydrocoumarin (0.37 g, 0.32 mL, 2.5 mmol, 1.0 equiv), pyrrolidine (0.36 g, 0.42 mL, 5 mmol, 2.0 equiv) and triethylamine (0.76 g, 1.0 mL, 7.5 mmol, 3.0 equiv) was heated to reflux at 90 °C for 16 h. The mixture was evaporated to dryness to afford the desired product as a yellow solid. The crude product used further without any purification. To a solution of the crude amide (0.548 g, 2.5 mmol, 1.0 equiv) in THF (5 mL) was added NaH (0.2 g, 60% suspension in mineral oil, 5.0 mmol, 2.0 equiv) portion wise at 0 °C and brought to rt for 2 h. Then, 1-bromo-2-butyne (0.67 g, 0.5 mL, 5.0 mmol, 2.0 equiv) was added drop wise through syringe in 10 min and let it stir 16 h. When the reaction was done, water was added carefully (10 mL) and the resulting mixture was extracted with ethyl acetate (50 mL). The organic phase was washed with brine (3×25 mL) and dried over Na_2SO_4. The solvent was removed in vacuum. Column chromatography afforded *3-(2-(but-2-yn-1-yloxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**15h**) as a colourless oil (0.5 g, 74%); R_f (EtOAc/heptane=40/60): 0.15; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.16 (m, 2H), 6.95–6.88 (m, 2H), 4.66 (q, J=2.3 Hz, 2H), 3.45 (t, J=6.8 Hz, 2H), 3.35 (t, J=6.7 Hz, 2H), 2.97 (t, J=6.4 Hz, 2H), 2.55 (t, J=6.4 Hz, 2H), 1.89–1.80 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 155.9, 130.6, 130.4, 127.4, 121.3, 111.9, 83.4, 74.5, 56.6, 46.7, 45.7, 35.3, 26.7, 26.3, 24.6, 3.8; ATR-FTIR (cm^{-1}): 2949, 2870, 1633, 1492, 1437, 1343, 1293, 1222, 1189, 1166, 1141, 1048, 1006, 868, 753, 632; ESI-MS: calculated $[M+Na]^+$ for $C_{17}H_{21}O_2NNa$: 294.1465, found: 294.1465.

4.11. General procedure for *N*-alkylated tosyl amides

NaH (60% suspension in mineral oil, 3.0 equiv) was suspended in DMF (0.5 M) and cooled to 0 °C. A DMF solution (0.08 M) of methyl-*N*-(4-oxo-4-(pyrrolidin-1-yl)butyl) benzenesulfonamide (1.0 equiv) was added slowly to the above mixture. The reaction mixture was stirred at room temperature for 35 min. The alkyl bromide (2.5 equiv) was added drop wise and the mixture was stirred at room temperature until consumption of the starting material. The mixture was washed consecutively with satd NH_4Cl, brine, water and extracted with EtOAc. The combined organic extracts were dried (Na_2SO_4), filtered and concentrated in vacuum. The crude mixtures were purified by silica gel column chromatography (Pentane/EtOAc, gradient from 40 to 100%) to afford the desired products.

4.12. *N*-allyl-4-methyl-*N*-(4-oxo-4-(pyrrolidin-1-yl)butyl)-benzenesulfonamide (22a)

The general procedure for the preparation of substrates was adapted using NaH (140.4 mg, 3.5 mmol, 3.0 equiv, 0.5 M in DMF), 4-methyl-*N*-(4-oxo-4-(pyrrolidin-1-yl)butyl)benzene-sulfonamide (362.9 mg, 1.2 mmol, 1.0 equiv, 0.08 M in DMF) and allyl bromide (0.25 mL, 2.93 mmol,2.5 equiv), to give *N-allyl-4-methyl-N-(4-oxo-4-(pyrrolidin-1-yl)butyl)-benzenesulfon amide* (**22a**) (331.6 mg, 81%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, J=8.0 Hz, 2H), 7.22 (d, J=8.0 Hz, 2H), 5.57–5.46 (m, 1H), 5.11 (dd, J=17.0 Hz, 1.0 Hz, 1H), 5.04 (dd, J=10.0 Hz, 1.0 Hz, 1H), 3.73 (d, J=6.5 Hz, 2H), 3.41–3.33 (m, 4H), 3.13 (t, J=7.0 Hz, 2H), 2.35 (s, 3H), 2.25 (t, J=7.0 Hz, 2H), 1.92–1.74 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): 170.6, 143.2, 136.9, 132.9, 129.7, 127.1, 119.1, 50.6, 46.8, 46.5, 45.7, 31.2, 26.1, 24.4, 22.9, 21.5. IR (neat, cm^{-1}): 2972, 1634, 1435, 1331, 1153, 1090, 917, 731, 659; HRMS: calculated $[M+Na]^+$ for $C_{18}H_{26}N_6NaO_3S$: 373.1555, found: 373.1556.

4.13. *N*-benzyl-4-methyl-*N*-(4-oxo-4-(pyrrolidin-1-yl)butyl)-benzenesulfonamide (22b)

The general procedure for the preparation of substrates was adapted using NaH (150.0 mg, 3.75 mmol, 3.0 equiv, 0.5 M in DMF), 4-methyl-*N*-(4-oxo-4-(pyrrolidin-1-yl)butyl)benzene-sulfonamide (388.01 mg, 1.25 mmol, 1.0 equiv, 0.08 M in DMF) and benzyl bromide (0.37 mL 3.10 mmol, 2.5 equiv), to give *N-benzyl-4-methyl-N-(4-oxo-4-(pyrrolidin-1-yl)butyl)-benzene-sulfonamide* (**22b**) (392.9 mg, 79%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, J=8.0 Hz, 2H), 7.34–7.23 (m, 7H), 4.29 (s, 2H), 3.38 (t, J=7.0 Hz, 2H), 3.24 (t, J=7.0 Hz, 2H), 3.18 (t, J=7.0 Hz, 2H), 2.43 (s, 3H), 2.08 (t, J=7.5 Hz, 2H), 1.89 (quint., J=7.0 Hz, 2H), 1.80 (quint., J=7.0 Hz, 2H), 1.69 (quint., J=7.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): 170.4, 143.2, 136.7, 136.5, 129.7, 128.6, 128.5, 127.7, 127.2, 52.4, 48.1, 46.4, 45.5, 31.2, 26.0, 24.3, 23.0, 21.5. IR (neat, cm^{-1}): 2873, 1633, 1437, 1333, 1154, 1001, 923, 815, 727, 697; HRMS: calculated $[M+Na]^+$ for $C_{22}H_{28}N_2NaO_3S$: 423.1716, found: 423.1713.

4.14. *N*-(but-2-yn-1-yl)-4-methyl-*N*-(4-oxo-4-(pyrrolidin-1-yl) butyl)benzene-sulfonamide (22c)

The general procedure for the preparation of substrates was adapted using NaH (186.0 mg, 4.65 mmol, 3.0 equiv, 0.5 M in DMF), 4-methyl-*N*-(4-oxo-4-(pyrrolidin-1-yl)butyl)benzene-sulfonamide (480.3 mg, 1.55 mmol, 1.0 equiv, 0.08 M in DMF) and propargyl bromide (0.34 mL, 3.90 mmol, 2.5 equiv), to give *N-(but-2-yn-1-yl)-4-methyl-N-(4-oxo-4-(pyrrolidin-1-yl)butyl)benzene-sulfonamide* (**22c**) (488.1 mg, 87%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, J=7.0 Hz, 2H), 7.29 (d, J=8.0 Hz, 2H), 4.06 (s, 2H), 3.51–3.43 (m, 4H), 3.24 (t, J=7.0 Hz, 2H), 2.42 (s, 3H), 2.38 (t, J=7.5 Hz, 2H), 2.00–1.90 (m, 4H), 1.87 (quint., J=7.0 Hz, 2H), 1.52 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 170.8, 143.2, 135.9, 129.2, 127.9, 81.6, 71.6, 46.7, 45.8, 36.6, 31.1, 26.1, 24.4, 22.2, 21.4, 3.3. IR (neat, cm^{-1}): 2874, 1631, 1438, 1329, 1156, 1088, 1004, 908, 814, 726, 653; HRMS: calculated $[M+Na]^+$ for $C_{19}H_{26}N_2NaO_3S$: 385.1555, found: 385.1556.

4.15. 2-(2-(Diallylamino)phenyl)-1-(pyrrolidin-1-yl)ethanone (29)

2-(2-Aminophenyl)-1-(pyrrolidin-1-yl)ethanone (see SI) (210 mg, 1.07 mmol) was dissolved in DMF (10 mL). Na_2CO_3 (171 mg, 3.2 mmol)

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and allyl bromide (0.37 mL, 3.2 mmol) were added and the mixture was stirred at 100 °C overnight. The reaction was quenched with water, extracted with EtOAc, washed with water and brine, dried over Na_2SO_4 and evaporated to dryness. Purification by flash column chromatography using a gradient system from hexane to hexane:ethyl acetate (2:3), afforded the product *2-(2-(Diallylamino) phenyl)-1-(pyrrolidin-1-yl)ethanone* (**29**) as colourless oil (170 mg, 65%); R_f (hexane/EtOAc=3/2): 0.3; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.23–7.10 (m, 2H), 7.08–7.03 (m, 2H), 5.75 (ddt, J=16.5, 10.2, 6.2 Hz, 2H), 5.17–5.08 (m, 4H), 3.75 (s, 2H), 3.60–3.43 (m, 6H), 3.29 (t, J=6.5 Hz, 2H), 1.81–1.79 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.6, 149.8, 135.1 (2C), 131.9, 130.1, 127.1, 124.2, 122.8, 117.5 (2C), 56.5 (2C), 46.8, 45.9, 37.8, 26.2, 24.5; IR (neat, cm^{-1}): 2974, 2876, 1623, 1420; HRMS: calculated for $C_{18}H_{24}N_2O$ $[M+Na]^+$: 307.1778, found: 307.1781.

4.16. 3-(2-(Diallylamino)phenyl)-1-(pyrrolidin-1-yl)propan-1-one (32a)

To a 3-(2-aminophenyl)-1-(pyrrolidin-1-yl)propan-1-one (see SI) (0.13 g, 0.6 mmol, 1.0 equiv) solution in DMF (2.5 mL) was added K_2CO_3 (0.33 g, 2.38 mmol, 4.0 equiv) and allyl bromide (0.21 mL, 2.38 mmol, 4.0 equiv) at 0 °C. The mixture was stirred at 50 °C for 16 h. The mixture was diluted with ethyl acetate (10 mL) and washed with water (3×25 mL). The organic phase was dried over Na_2SO_4 and evaporated to dryness. Column chromatography (EtOAc/hexane: 10/40 to 20/30) afforded *3-(2-(diallylamino)phenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**32a**) as a white oil (0.13 g, 73%); R_f (EtOAc): 0.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–6.99 (m, 4H), 5.79 (ddt, J=16.6, 10.2, 6.3 Hz, 2H), 5.16–5.06 (m, 4H), 3.55 (d, J=6.3 Hz, 4H), 3.48 (t, J=6.7 Hz, 2H), 3.31 (t, J=6.6 Hz, 2H), 3.07–3.05 (m, 2H), 2.60–2.55 (m, 2H), 1.91–1.81 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 149.9, 138.2 (2C), 135.3, 130.1, 126.6, 124.3, 123.3, 117.4 (2C), 56.9 (2C), 46.6, 45.7, 35.9, 27.0, 26.2, 24.5; FTIR (neat, cm^{-1}): 3376, 1643, 1432; ESI-MS: calculated $[M+Na]^+$ for $C_{19}H_{26}N_2ONa$: 321.1943, found: 321.1924.

4.17. 3-(2-((2-Methylallyl)oxy)phenyl)-1-(pyrrolidin-1-yl) propan-1-one (32b)

To a 3-(2-aminophenyl)-1-(pyrrolidin-1-yl)propan-1-one (see SI) (0.17 g, 0.78 mmol, 1.0 equiv) solution in DMF (3 mL) was added K_2CO_3 (0.32 g, 2.34 mmol, 3.0 equiv) and 3-bromo-2-methylpropene (0.24 mL, 2.34 mmol, 3.0 equiv) at 0 °C. The mixture was stirred at 50 °C for 16 h. The mixture was diluted with ethyl acetate (10 mL) and washed with water (3×25 mL). The organic phase was dried over Na_2SO_4 and evaporated to dryness. Column chromatography (EtOAc/hexane: 10/40 to 20/30) afforded *3-(2-(bis(2-methylallyl)amino)phenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**32b**) as a yellow oil (0.19 g, 75%); R_f (EtOAc): 0.75; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.19 (m, 1H), 7.14–7.07 (m, 2H), 7.05–6.96 (m, 1H), 4.91 (s, 2H), 4.82 (s, 2H), 3.50–3.44 (m, 6H), 3.34–3.31 (m, 2H), 3.16–3.12 (m, 2H), 2.60–2.56 (m, 2H), 1.92–1.82 (m, 4H), 1.71 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): 171.3, 150.2, 142.9, 137.32, 129.7, 126.3 (2C), 123.8, 122.3, 113.3 (2C), 60.7 (2C), 46.6, 45.7, 35.7, 26.2, 25.8, 24.5, 21.1 (2C); FTIR (neat, cm^{-1}): 3380, 2971, 1645, 1434; ESI-MS: calculated $[M+Na]^+$ for $C_{21}H_{30}N_2ONa$: 349,2256, found: 349,2246.

4.18. 3-(2-(Di(*E*)-but-2-enylamino)phenyl)-1-(pyrrolidin-1-yl) propan-1-one (32c)

To a 3-(2-aminophenyl)-1-(pyrrolidin-1-yl)propan-1-one (see SI) (0.2 g, 0.92 mmol, 1.0 equiv) solution in DMF (4 mL) was added K_2CO_3 (0.51 g, 3.66 mmol, 4.0 equiv) and crotyl bromide (0.38 mL, 3.66 mmol, 4.0 equiv) at 0 °C. The mixture was stirred at 50 °C for 16 h. The mixture was diluted with ethyl acetate (10 mL) and washed with water (3×25 mL). The organic phase was dried over Na_2SO_4 and evaporated to dryness. Column chromatography (EtOAc/hexane: 10/40 to 20/30) afforded *3-(2-(bis(2-methylallyl)amino)phenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**32c**) as a yellow oil (0.24 g, 84%); R_f (EtOAc): 0.7; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–6.99 (m, 4H), 5.54–5.38 (m, 4H), 3.49–3.44 (m, 6H), 3.30–3.28 (m, 2H), 3.04–3.02 (m, 2H), 2.58–2.54 (m, 2H), 1.89–1.81 (m, 4H), 1.62 (d, J=6.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 171.7, 150.4, 138.2, 130.0, 128.2, 128.1, 126.5, 123.9, 123.3, 55.9 (2C), 46.6, 45.7, 36.0, 27.3, 26.2, 24.5, 17.9 (2C); FTIR (cm^{-1}): 3380, 2933, 1645, 1434; ESI-MS: calculated $[M+Na]^+$ for $C_{21}H_{30}N_2ONa$: 349.2256, found: 349.2244.

4.19. 3-(2-(Dibut-2-ynylamino)phenyl)-1-(pyrrolidin-1-yl) propan-1-one (32d)

To a 3-(2-aminophenyl)-1-(pyrrolidin-1-yl)propan-1-one (0.2 g, 0.92 mmol, 1.0 equiv) solution in DMF (4 mL) was added K_2CO_3 (0.38 g, 2.75 mmol, 3.0 equiv) and 3-bromo-2-methylpropene (0.24 mL, 2.75 mmol, 3.0 equiv) at 0 °C. The mixture was stirred at 50 °C for 16 h. The mixture was diluted with ethyl acetate (10 mL) and washed with water (3×25 mL). The organic phase was dried over Na_2SO_4 and evaporated to dryness. Column chromatography (EtOAc/hexane: 10/40 to 20/30) afforded *3-(2-(bis(2-methylallyl)amino)phenyl)-1-(pyrrolidin-1-yl)propan-1-one* (**32d**) as a white solid (0.23 g, 78%); R_f: 0.7 (EtOAc); mp: 72–75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.15 (m, 3H), 7.08–7.05 (m, 1H), 3.77 (s, 4H), 3.49–3.45 (m, 2H), 3.41–3.37 (m, 2H), 3.41–3.37 (m, 2H), 3.00–2.94 (m, 2H), 1.91–1.79 (m, 10H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 149.1, 138.1, 130.1, 126.7, 125.2, 123.2, 80.3 (2C), 75.0 (2C), 46.7, 45.7, 43.2 (2C), 36.3, 27.5, 26.3, 24.6, 3.7 (2C); FTIR (neat, cm-1): 3376, 2923, 1643, 1436; ESI-MS: calculated $[M+Na]^+$ for $C_{21}H_{26}N_2ONa$: 345.1943, found: 345.1930.

4.20. 2-(2-((Diallylamino)methyl)phenyl)-1-(pyrrolidin-1-yl) ethanone (34)

3-Isochromanone (**35**) (0.50 g, 3.37 mmol) was refluxed in pyrrolidine (0.55 mL, 6.75 mmol) and triethylamine (1.4 mL, 10.1 mmol) until total consumption of starting material, R_f=0.3 EtOAc. The mixture was evaporated to dryness and the product was used without further purification; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (dd, J=7.1, 1.8 Hz, 1H), 7.27–7.24 (m, 2H), 7.15 (dd, J=7.2, 1.6 Hz, 1H), 4.60 (s, 2H), 3.77 (s, 2H), 3.65 (t, J=6.8 Hz, 2H), 3.47 (t, J=6.9 Hz, 2H), 2.04–1.98 (m, 2H), 1.91–1.85 (m, 2H) (OH fast exchange—not observed); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.4, 140.6, 133.9, 130.9, 130.6, 128.3, 127.8, 63.8, 47.5, 46.4, 39.0, 26.3, 24.4; IR (cm^{-1}): 3357, 2971, 2874, 1614, 1440, 1015, 747; HRMS: calculated for $C_{13}H_{17}NO_2$ $[M+Na]^+$: 242.1152, found: 242.1151.

2-(2-(Hydroxymethyl)phenyl)-1-(pyrrolidin-1-yl)ethanone (200 mg, 0.92 mmol) was dissolved in THF (6 mL) and the flask was placed in an ice bath. Diphenyl phosphoryl azide (0.25 mL, 1.19 mmol) was then added followed by DBU (0.18 mL, 1.19 mmol) and the mixture was allowed to reach room temperature and stirred overnight. The mixture was dissolved with EtOAc, washed with water and brine, dried over Na_2SO_4 and evaporated to dryness. The crude product was used without further purification (R_f=0.5 EtOAc). The crude product was dissolved in toluene (4.5 mL) and 10% Pd/C (97 mg, 10 mol%) was added. The mixture was stirred under H_2 atmosphere for 5 h until total consumption of starting material (R_f=0.1 EtOAc). The mixture was filtered through a Celite pad and evaporated to dryness. The crude product **36** was dissolved in THF (6 mL) and K_2CO_3 (633 mg, 4.58 mmol) and allyl bromide (0.2 mL, 2.29 mmol) were added and the mixture was stirred at 50 °C overnight. The reaction was filtrated through a Celite pad and evaporated to dryness. The crude product was purified by flash

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column chromatography using a gradient system from hexane to hexane: ethyl acetate (1:5). The product *2-(2-((diallylamino)methyl) phenyl)-1-(pyrrolidin-1-yl)ethanone* (**34**) was obtained as an yellow oil (80 mg, 29% over 4 steps); R_f=0.2, hexane:EtOAc (1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.21–7.16 (m, 4H), 5.83 (ddt, J=13.1, 10.1, 6.5 Hz, 2H), 5.18–5.11 (m, 4H), 3.85 (s, 2H), 3.55–3.49 (m, 4H), 3.38 (t, J=6.5 Hz, 2H), 3.03 (d, J=5.8 Hz, 4H), 1.93–1.83 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.2, 135.7 (2C), 135.1, 130.8, 129.4, 127.5, 126.5, 126.3, 117.7 (2C), 56.6, 46.9, 46.0, 39.3, 26.3 (2C), 24.6 (2C); IR (neat, cm^{-1}): 3372, 2974, 2874, 1639, 1417, 915, 748; HRMS: calculated for $C_{19}H_{26}N_2O$ $[M+Na]^+$: 321.1939 found: 321.1937.

4.21. Rearrangements–general procedure

To a flame-dried screw-capped microwave test tube equipped with a magnetic stir bar was added the allyloxyamide derivative (0.25 mmol, 1.0 equiv) followed by DCM (0.08 M) under Argon atmosphere. To this stirred solution, triflic anhydride (1.05 equiv) was added dropwise and stirred at ambient temperature for 15 min. After stirring for 15 min, 2,4,6-collidine (1.2 equiv) was added dropwise and the reaction mixture was heated in a microwave reactor at 120 °C for 5 min. After compressed air cooling to room temperature, 1 M AcOH (5 mL) was added and the biphasic mixture was stirred at room temperature for 24 h. The aqueous phase was separated and extracted with dichloromethane. The combined organic layers were washed with saturated brine and dried over Na_2SO_4, filtered, and concentrated in vacuum. Pre-adsorbed on silica gel and purified by flash column chromatography on silica gel to yield the corresponding 3-allyl dihydrocoumarin derivatives.

4.22. 3-Allylchroman-2-one (9)

Following the general procedure, treatment of 3-(2-(allyloxy) phenyl)-1-(pyrrolidin-1-yl)propan-1-one (**7**) (65 mg, 0.25 mmol, 1.0 equiv) and triflic anhydride (44 μL, 0.26 mmol, 1.05 equiv) with 2,4,6-collidine (40 μL, 0.3 mmol, 1.2 equiv) in DCM (3 mL) was heated at 120 °C for 5 min in a microwave reactor. After cooled to room temperature 1 M AcOH (5 mL) was added and stirred at room temperature for 24 h. Aqueous work followed by flash column chromatography afforded *3-allylchroman-2-one* (**9**) as a colourless liquid (27 mg, 57%); R_f (EtOAc/heptane=10/90): 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.23 (m, 1H), 7.18–7.16 (m, 1H), 7.11–7.03 (m, 2H), 5.86–5.81 (m, 1H), 5.16–5.11 (m, 2H), 2.98 (dd, J=14.6, 4.8 Hz, 1H), 2.85–2.68 (m, 3H), 2.36–2.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 151.8, 134.4, 128.4, 128.3, 124.5, 122.7, 118.3, 116.7, 38.9, 34.1, 28.8; ATR-FTIR (cm^{-1}): 3074, 2915, 1766, 1642, 1616, 1589, 1489, 1459, 1357, 1275, 1232, 1196, 1144, 998, 917, 753, 633; ESI-MS: calculated $[M+Na]^+$ for $C_{12}H_{12}O_2Na$: 211.0730, found: 211.0723.

4.23. 6-methoxy-3-(2-methylbut-3-en-2-yl)chroman-2-one (12)

Following the general procedure: ^{1}H NMR (500 MHz, CDCl3), δ 7.02 (d, J=8.34 Hz, 1H), 6.62 (dd, J=8.36, 2.54 Hz, 1H), 6.55 (d, J=2.50 Hz, 1H), 5.87 (dd, J=17.34, 10.85 Hz, 1H), 5.02 (dd, J=14.07, 6.11 Hz, 2H), 3.78 (s, 3H), 2.95 (dd, J=15.92, 6.33 Hz, 1H), 2.84 (dd, J=15.92, 9.51 Hz, 1H), 2.57 (dd, J=9.48, 6.35 Hz, 1H), 1.23 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$), δ 168.6, 159.6, 152.3, 145.2, 128.2, 114.9, 112.6, 110.1, 101.9, 55.5, 48.3, 29.7, 26.3, 25.5, 23.5; ESI-MS: calculated $[M+Na]^+$ for $C_{15}H_{18}O_3Na$: 269.1148, found: 269.1148.

4.24. 3-(2-(Chloromethyl)allyl)chroman-2-one (16a)

Following the general procedure, treatment of 3-(2-((2-(chloromethyl)allyl)oxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one (**15a**) (77 mg, 0.25 mmol, 1.0 equiv) and triflic anhydride (44 μL, 0.263 mmol, 1.05 equiv) with 2,4,6-collidine (40 μL, 0.30 mmol, 1.2 equiv) in DCM (3 mL) was heated at 120 °C for 5 min in a microwave reactor. After cooled to room temperature 1 M AcOH (5 mL) was added and stirred at room temperature for 24 h. Aqueous work followed by flash column chromatography afforded *3-(2-(chloromethyl)allyl)chroman-2-one* (**16a**) as a colourless liquid (25 mg, 42%); R_f (EtOAc/heptane=10/90): 0.33; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.17 (m, 2H), 7.12–7.04 (m, 2H), 5.31 (br s, 1H), 5.05 (br s, 1H), 4.09 (app d, J=2.2 Hz, 2H), 3.05 (dd, J=14.8, 5.4 Hz, 1H), 3.03–2.87 (m, 2H), 2.80 (dd, J=15.1, 4.9 Hz, 1H), 2.38 (dd, J=14.2, 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 151.7, 141.5, 128.5, 128.3, 124.6, 122.3, 117.8, 116.7, 47.9, 37.7, 33.8, 29.1; ATR-FTIR (cm^{-1}): 2917, 2849, 1767, 1589, 1489, 1459, 1360, 1260, 1231, 1131, 918, 764; ESI-MS calculated $[M+Na]^+$ for $C_{13}H_{13}ClO_2Na$: 259.0496, found: 259.0500.

4.25. 2-((2-Oxochroman-3-yl)methyl)allyl acetate (16b)

Following the general procedure, treatment of 2-((2-(3-oxo-3-(pyrrolidin-1-yl)propyl)phenoxy)methyl)allyl acetate (**15b**) (83 mg, 0.25 mmol, 1.0 equiv) and triflic anhydride (44 μL, 0.26 mmol, 1.05 equiv) with 2,4,6-collidine (40 μL, 0.3 mmol, 1.2 equiv) in DCM (3 mL) was heated at 120 °C for 5 min in a Microwave reactor. After cooled to room temperature 1 M AcOH (5 mL) was added and stirred at room temperature for 24 h. Aqueous work followed by flash column chromatography afforded 2-((2-oxochroman-3-yl) methyl)allyl acetate as a colourless liquid (25 mg, 38%); R_f (EtOAc/heptane=10/90): 0.13; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2H), 7.18–7.04 (m, 2H), 5.22 (br s, 1H), 5.03 (br s, 1H), 4.55 (br s, 2H), 3.03 (dd, J=15.2, 5.4 Hz, 1H), 2.94–2.74 (m, 3H), 2.26 (dd, J=14.5, 5.3 Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.5, 151.7, 140.1, 128.5, 128.3, 124.6, 122.4, 116.7, 116.3, 66.5, 37.6, 33.7, 28.8, 21.0; ATR-FTIR (cm^{-1}): 2163, 1767, 1741, 1655, 1616, 1589, 1489, 1459, 1372, 1232, 1162, 1132, 1030, 918, 764; ESI-MS: calculated $[M+Na]^+$ for $C_{15}H_{16}O_4Na$: 283.0941, found: 283.0945.

4.26. 3-Allyl-6-methoxychroman-2-one (16c)

Following the general procedure, treatment of 3-(2-(allyloxy)-5-methoxyphenyl)-1-(pyrrolidin-1-yl)propan-1-one (**15c**) (72 mg, 0.25 mmol, 1.0 equiv) and triflic anhydride (44 μL, 0.26 mmol, 1.05 equiv) with 2,4,6-collidine (40 μL, 0.3 mmol, 1.20 equiv) in DCM (3 mL) was heated at 120 °C for 5 min in a microwave reactor. After cooled to room temperature 1 M AcOH (5 mL) was added and stirred at room temperature for 24 h. Aqueous work followed by flash column chromatography afforded *3-allyl-6-methoxychroman-2-one* (**16c**) as a colourless liquid (27 mg, 50%); R_f (EtOAc/heptane=10/90): 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (d, J=8.8 Hz, 1H), 6.75 (dd, J=8.8, 2.8 Hz, 1H), 6.68 (d, J=2.8 Hz, 1H), 5.88–5.78 (m, 1H), 5.15–5–11 (m, 2H), 3.78 (s, 3H), 2.94 (dd, J=14.7, 4.7 Hz, 1H), 2.82–2.66 (m, 3H), 2.37–2.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 156.2, 145.67, 134.5, 123.6, 118.3, 117.4, 113.4, 113.3, 55.8, 38.8, 34.1, 29.0; ATR-FTIR (cm^{-1}): 2916, 2848, 1765, 1493, 1460, 1434, 1376, 1261, 1226, 1153, 1129, 1033, 750, 723, 617; ESI-MS: calculated $[M+Na]^+$ for $C_{13}H_{14}O_3Na$: 241.0835, found: 241.0839.

4.27. 3-Allyl-7-methylchroman-2-one (16d)

Following the general procedure, treatment of 3-(2-(allyloxy)-4-methylphenyl)-1-(pyrrolidin-1-yl)propan-1-one (**15d**) (68 mg, 0.25 mmol, 1.0 equiv) and triflic anhydride (44 μL, 0.26 mmol, 1.05 equiv) with 2,4,6-collidine (40 μL, 0.3 mmol, 1.2 equiv) in DCM (3 mL) was heated at 120 °C for 5 min in a microwave reactor. After cooled to room temperature 1 M AcOH (5 mL) was added and

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stirred at room temperature for 24 h. Aqueous work-up followed by flash column chromatography afforded *3-allyl-7-methylchroman-2-one* (**16d**) as a colourless liquid (28 mg, 55%); R_f (EtOAc/heptane=10/90): 0.43; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, J=7.6 Hz, 1H), 6.89 (app d, J=7.8 Hz, 1H), 6.85 (app s, 1H), 5.89–5.79 (m, 1H), 5.15–5.11 (m, 2H), 2.94 (dd, J=14.2, 3.2 Hz, 1H), 2.80–2.67 (m, 3H), 2.36–2.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 151.6, 138.6, 134.5, 127.9, 125.2, 119.5, 118.3, 117.1, 39.1, 34.1, 28.4, 21.2; ATR-FTIR (cm^{-1}): 2978, 2922, 1767, 1626, 1588, 1509, 1440, 1417, 1356, 1253, 1214, 1142, 1120, 918, 813, 765, 633; ESI-MS: calculated $[M+Na]^+$ for $C_{13}H_{14}O_2Na$: 225.0886, found: 225.0890.

4.28. 3-(2-Methylallyl)chroman-2-one (16e)

Following a general procedure, treatment of 3-(2-((2-methylallyl)oxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one (**15e**) (68 mg, 0.25 mmol, 1.0 equiv) and triflic anhydride (44 μL, 0.26 mmol, 1.05 equiv) with 2,4,6-collidine (40 μL, 0.3 mmol, 1.2 equiv) in DCM (3 mL) was heated at 120 °C for 5 min in a microwave reactor. After cooled to room temperature 1 M AcOH (5 mL) was added and stirred at room temperature for 24 h. Aqueous work followed by flash column chromatography afforded *3-(2-methylallyl)chroman-2-one* (**16e**) as a colourless liquid (22 mg, 44%). This product was obtained with 20% of the impurity, which cannot be removed by chromatography; R_f (EtOAc/heptane=10/90): 0.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.16 (m, 2H), 7.11–7.04 (m, 2H), 4.89 (br s, 1H), 4.74 (br s, 1H), 3.00 (dd, J=15.2, 5.5 Hz, 1H), 2.90–2.83 (m, 1H), 2.77–2.70 (m, 2H), 2.20 (dd, J=14.1, 4.8 Hz, 1H), 1.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 151.8, 141.5, 128.4, 127.7, 124.5, 122.5, 116.7, 113.8, 37.9, 37.2, 28.5, 21.9; ATR-FTIR (cm^{-1}): 3074, 2933, 1760, 1650, 1616, 1589, 1490, 1459, 1377, 1356, 1232, 1196, 1161, 1130, 1057, 998, 918, 755; ESI-MS: calculated $[M+Na]^+$ for $C_{13}H_{14}O_2Na$: 225.0886, found: 225.0881.

4.29. Ethyl 2-((2-oxochroman-3-yl)methyl)acrylate (16f)

Following the general procedure, treatment of *ethyl 2-((2-(3-oxo-3-(pyrrolidin-1-yl)propyl)phenoxy)methyl)acrylate* (**15f**) (83 mg, 0.25 mmol, 1.0 equiv) and triflic anhydride (44 μL, 0.26 mmol, 1.05 equiv) with 2,4,6-collidine (40 μL, 0.3 mmol, 1.2 equiv) in DCM (3 mL) was heated at 120 °C for 5 min in a microwave reactor. After cooled to room temperature 1 M AcOH (5 mL) was added and stirred at room temperature for 24 h. Aqueous work followed by flash column chromatography afforded *ethyl 2-((2-oxochroman-3-yl)methyl)acrylate* (**16f**) as a colourless liquid (30 mg, 46%); R_f (EtOAc/heptane=10/90): 0.19; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.23 (m, 1H), 7.15 (app d, J=7.2 Hz, 1H), 7.10–7.02 (m, 2H), 6.31 (s, 1H), 5.68 (s, 1H), 4.20 (q, J=7.2 Hz, 2H), 3.11–2.94 (m, 3H), 2.80–2.73 (m, 1H), 2.48–2.43 (m, 1H), 1.29 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 166.6, 151.7, 137.2, 128.4 (for 2 carbons), 128.3, 124.4, 122.5, 116.7, 61.1, 38.3, 32.8, 29.0, 14.3; ATR-FTIR (cm^{-1}): 2982, 1765, 1711, 1630, 1589, 1489, 1459, 1368, 1305, 1275, 1231, 1200, 1149, 1127, 1026, 955, 919, 756, 689, 633; ESI-MS: calculated $[M+Na]^+$ for $C_{15}H_{16}O_4Na$: 283.0941, found: 283.0936.

4.30. 3-(2-Bromoallyl)chroman-2-one (16g)

Following the general procedure, treatment of 3-(2-((2-bromoallyl)oxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one (**15g**) (85 mg, 0.25 mmol, 1.0 equiv) and triflic anhydride (44 μL, 0.263 mmol, 1.05 equiv) with 2,4,6-collidine (40 μL, 0.3 mmol, 1.2 equiv) in DCM (3 mL) was heated at 120 °C for 5 min in a microwave reactor. After cooled to room temperature 1 M AcOH (5 mL) was added and stirred at room temperature for 24 h. Aqueous work followed by flash column chromatography afforded *3-(2-bromoallyl)chroman-2-one* (**16g**) as a colourless liquid (25 mg, 37%); R_f (EtOAc/heptane=10/90): 0.36; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.19 (m, 2H), 7.13–7.05 (m, 2H), 5.73 (br s, 1H), 5.58 (br s, 1H), 3.20 (dd, J=14.3, 3.8 Hz, 1H), 3.13–3.00 (m, 2H), 2.74 (dd, J=15.1, 3.3 Hz, 1H), 2.59 (dd, J=14.5, 5.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 151.7, 130.2, 128.6, 128.4, 124.6, 122.3, 120.3, 116.8, 41.6, 37.6, 28.3; ATR-FTIR (cm^{-1}): 1765, 1631, 1458, 1358, 1275, 1232, 1148, 1037, 918, 754, 661; ESI-MS: calculated $[M+Na]^+$ for $C_{12}H_{11}BrO_2Na$: 290.9814, found: 290.9820.

4.31. 3-(Buta-2,3-dien-2-yl)chroman-2-one (16h)

Following the general procedure, treatment of 3-(2-(but-2-yn-1-yloxy)phenyl)-1-(pyrrolidin-1-yl)propan-1-one (**15h**) (68 mg, 0.25 mmol, 1.0 equiv) and triflic anhydride (44 μL, 0.26 mmol, 1.05 equiv) with 2,4,6-collidine (40 μL, 0.3 mmol, 1.2 equiv) in DCM (3 mL) was heated at 120 °C for 5 min in a Microwave reactor. After cooled to room temperature 1 M AcOH (5 mL) was added and stirred at room temperature for 24 h. Aqueous work followed by flash column chromatography afforded *3-(Buta-2,3-dien-2-yl)chroman-2-one* (**16h**) as a colourless liquid using pentane and Et_2O as a eluent mixture (18 mg, 36%); R_f (EtOAc/heptane=10/90): 0.33; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.21 (m, 1H), 7.16 (app d, J=7.1 Hz, 1H), 7.07 (td, J=7.6, 1.0 Hz, 1H), 7.01 (app d, J=8.1 Hz, 1H), 4.72–4.63 (m, 2H), 3.32–3.27 (m, 1H), 3.09–3.07 (m, 2H), 1.83 (t, J=3.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8, 168.5, 151.7, 128.5, 128.3, 124.5, 122.4, 116.6, 95.3, 77.4, 43.3, 28.8, 17.4; ATR-FTIR (cm^{-1}): 2953, 2916, 2848, 1770, 1489, 1459, 1375, 1263, 1230, 1186, 1128, 981, 915, 749, 633; ESI-MS: calculated $[M+Na]^+$ for $C_{13}H_{12}O_2Na$: 223.0730, found: 225.0722.

4.32. 1′-Allyl-3′-tosyl-1,2′-bipyrrolidine (23a)

Isolated in 94% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.80–7.76 (m, 2H), 7.45–7.41 (m, 2H), 5.95–5.87 (ddt, J=17.2, 10.6, 6.5 Hz, 1H), 5.52 (dt, J=17.0, 1.5, 1H), 5.43 (dt, J=10.5, 1.5 Hz, 1H), 4.88 (d, J=8.0 Hz, 1H), 4.51–4.44 (m, 1H), 4.42–4.36 (m, 1H), 4.29–4.23 (m, 1H), 4.18–4.04 (m, 3H), 4.18–4.13 (m, 1H), 4.12–4.04 (m, 2H), 3.87–3.81 (m, 1H), 3.65 (t, J=10 Hz, 1H), 2.99–2.89 (m, 1H), 2.48 (s, 3H), 2.24–2.17 (m, 1H), 2.16–2.08 (m, 2H), 2.06–2.00 (m, 1H), 1.99–1.92 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): 158.5, 146.9, 134.1, 130.6, 130.5, 128.6, 119.8, 70.4, 55.5, 55.0, 51.9, 51.5, 25.9, 24.3, 23.8, 21.8.

4.33. 1-(1-Benzyl-3-tosylpyrrolidin-2-ylidene)pyrrolidin-1-ium (23b)

Isolated 90% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.78 (d, J=8.0 Hz, 2H), 7.49–7.43 (m, 4H), 7.41–7.36 (m, 3H), 5.23 (d, J=17.0 Hz, 1H), 4.91 (d, J=8.5 Hz, 1H), 4.83 (d, J=17.0 Hz, 1H), 4.50–4.42 (m, 1H), 4.25–4.15 (m, 2H), 4.08–3.99 (m, 1H), 3.81–3.73 (m, 1H), 3.62 (t, J=9.0 Hz, 1H), 3.05–2.94 (m, 1H), 2.47 (s, 3H), 2.26–2.05 (m, 3H), 2.07–1.94 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): 158.7, 146.9, 133.5, 133.1, 130.6, 129.5, 128.6, 126.7, 70.5, 55.7, 55.1, 53.3, 51.7, 26.0, 24.2, 23.8, 21.8. Structure unambiguously determined by X-ray diffraction (see SI for details).

4.34. 2′-Methyl-8′-tosyl-4′,6′,7′,8′-tetrahydrospiro[pyrrolidine-1,1′-pyrro-lo[1,2-*a*]pyrimidine]-1,5′-diium (23c)

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (d, J=8.0 Hz, 2H), 7.59 (d, J=8.0 Hz, 2H), 5.93 (d, J=6.5 Hz, 1H), 5.24 (d, J=8.5 Hz, 1H), 4.79 (dd, J=17.0, 6.0 Hz, 1H), 4.29–4.23 (m, 3H), 4.11 (dt, J=11.4, 7.2 Hz, 1H), 4.03–4.01 (m, 1H), 3.72 (t, J=10.3 Hz, 1H), 3.59 (dt, J=10.3, 6.7 Hz, 1H), 2.72–2.70 (m, 1H), 2.50 (s, 3H), 2.42 (dd, J=14.7, 5.7 Hz, 1H), 2.19 (s, 3H), 2.15–2.11 (m, 2H), 2.03–2.00 (m, 2H); ^{13}C NMR

Please cite this article in press as: Padmanaban, M.; et al., Tetrahedron (2015), http://dx.doi.org/10.1016/j.tet.2015.06.027

(150 MHz, $CDCl_3$): 159.7, 149.3, 147.9, 134.3, 131.4, 130.1, 125.2, 123.1, 121.0, 118.8, 116.5, 70.5, 58.3, 54.9, 52.7, 45.5, 26.6, 24.9, 23.9, 21.6, 19.6. Note: the product was isolated as a mixture with the starting material. HRMS: exact mass calculated for $[M]^{2+}$ [OTf]-($[C_{19}H_{26}F_3N_2O_2S]_2^{+2}[OTf]^-$ Mw=644; 495=644- OTf): 495.1234, found: 495.1230.

4.35. 1,7-Diallyl-2-(pyrrolidin-1-yl)-1*H*-indole (31)

To a flame-dried screw-capped microwave test tube equipped with a magnetic stir bar was added the derivative **29** (20 mg, 0.07 mmol, 1.0 equiv) followed by DCM (0.1 M) under Argon atmosphere. To this stirred solution triflic anhydride (1.05 equiv) was added dropwise and stirred at ambient temperature for 15 min. After stirring for 15 min, 2,4,6-collidine (1.20 equiv) was added dropwise, the reaction mixture was heated in a microwave reactor at 120 °C for 5 min. After cooling to room temperature, water was added and the biphasic mixture was stirred at room temperature for 24 h. The aqueous phase was separated and extracted with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4, filtered, and concentrated in vacuum. Compound was purified by flash column chromatography (gradient hexane:EtOAc 1:1 to EtOAc:MeOH 10%) to yield the product **31** as a white solid (8 mg, 43%); R_f (EtOAc/hexane=1:1): 0.2; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.28–7.16 (m, 1H), 6.92 (dd, J=7.5, 0.8 Hz, 1H), 6.84 (d, J=8.2 Hz, 1H), 6.03 (ddt, J=17.2, 10.4, 5.2 Hz, 2H), 5.91 (s, 1H), 5.14–5.05 (m, 2H), 4.91–4.78 (m, 4H), 3.70–3.69 (m, 2H), 3.54–3.42 (m, 4H), 1.97–1.78 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 150.4, 138.8, 136.7, 133.7, 129.6, 122.6, 122.0, 119.8, 117.2, 115.6, 115.1, 86.4, 53.2 (2C), 46.5, 36.2, 24.8 (2C); ESI-MS: calculated for $C_{18}H_{22}N_2$ $[M+Na]^+$: 266.1782, found: 266.1783.

4.36. General procedure for 3,4-dihydro-2(1*H*)-quinolinone-like scaffolds

To a flame-dried screw-capped sealed tube equipped with a magnetic stir bar was added the derivative **32** (0.15 mmol, 1.0 equiv) followed by DCM (0.08 M) was added under the atmosphere of Argon. To this stirred solution triflic anhydride (1.05 equiv) was added dropwise and stirred at ambient temperature for 15 min. After stirring for 15 min, 2,4,6-collidine (1.20 equiv) was added dropwise, the reaction mixture was heated at 120 °C for 5 min. After cooling to room temperature, 1 M AcOH (5 mL) was added and the biphasic mixture was stirred at room temperature for 24 h. The aqueous phase was separated and extracted with dichloromethane. The combined organic layers were washed with water and brine, dried over Na_2SO_4, filtered, and concentrated in vacuum.

4.37. 1-(1,3-Diallyl-3,4-dihydroquinolin-2(1*H*)-ylidene)pyrrolidinium triflate (33a)

Purification by flash column chromatography (gradient DCM to DCM:MeOH 5%) afforded *1-(1,3-diallyl-3,4-dihydroquinolin-2(1H)-ylidene) pyrrolidinium triflate* (**32a**) (25 mg, 0.06 mmol, 39%); R_f (DCM/methanol 2%): 0.15; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.15 (m, 4H), 5.95 (ddd, J=15.5, 10.2, 4.6 Hz, 1H), 5.65 (ddd, J=16.5, 8.5, 6.2 Hz, 1H), 5.38–5.27 (m, 2H), 5.12 (d, J=10.0 Hz, 1H), 4.96–4.91 (m, 1H), 4.81–4.78 (m, 2H), 4.32–4.30 (m, 1H), 4.03–4.02 (m, 2H), 3.85–3.81 (m, 1H), 3.54–3.52 (m, 1H), 3.33 (dd, J=16.0, 4.6 Hz, 1H), 2.78 (d, J=15.0 Hz, 1H), 2.21–2.13 (m, 4H), 2.00–1.94 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 138.3, 133.1, 132.8, 129.1, 128.0, 126.6, 126.3, 119.7, 119.6, 118.9, 55.3, 54.6, 53.7, 38.4, 32.1, 27.3, 26.6, 24.0; IR (NaCl, cm^{-1}): 3380, 1662, 1574, 1434, 1263; ESI-MS: calculated for $C_{19}H_{25}N_2$ $[M]^+$: 281.2012, found: 281.2005.

4.38. 1-(1,3-bis(2-methylallyl)-3,4-dihydroquinolin-2(1*H*)-ylidene)pyrrolidinium triflate (33b)

Purification by flash column chromatography (gradient DCM to DCM:MeOH 5%) afforded *1-(1,3-bis(2-methylallyl)-3,4-dihydroquinolin-2(1H)-ylidene) pyrrolidinium triflate* (**32b**) (30 mg, 0.07 mmol, 44%); R_f (DCM/methanol 2%): 0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.10 (m, 4H), 4.89 (s, 2H), 4.51 (s, 2H), 4.39–4.34 (m, 1H), 4.18–4.15 (m, 2H), 3.81–3.78 (m, 1H), 3.61–3.58 (m, 1H), 3.37–3.30 (m, 2H), 2.75 (dd, J=16.1, 2.1 Hz, 1H), 2.16–1.90 (m, 6H), 1.80–1.74 (m, 7H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 141.9, 139.5, 138.8, 129.2, 127.9, 126.6, 125.7, 118.5, 115.5, 114.6, 57.9, 54.1, 53.5, 36.8, 35.5, 26.8, 26.5, 23.9, 21.7, 20.2; IR (NaCl, cm^{-1}) 1660, 1582; ESI-MS: calculated for $C_{21}H_{29}N_2$ $[M]^+$: 309.2325, found: 309.2320.

4.39. (*E*)-1-(1-(but-2-enyl)-3-(but-3-en-2-yl)-3,4-dihydroquinolin-2(1*H*)-ylidene)pyrrolidinium triflate (33c)

Purification by flash column chromatography (gradient DCM to DCM:MeOH 5%) afforded *(E)-1-(1-(but-2-enyl)-3-(but-3-en-2-yl)-3,4-dihydroquinolin-2(1H)-ylidene)pyrrolidinium triflate* (**33c**) (25 mg, 0.05 mmol, 36%); R_f (DCM/methanol 2%): 0.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.25 (m, 1H), 7.15–7.06 (m, 3H), 5.73 (dd, J=15.7, 6.9 Hz, 1H), 5.58–5.56 (m, 1H), 5.35 (ddd, J=16.9, 10.8, 8.3 Hz, 1H), 4.92 (d, J=10.1 Hz, 1H), 4.82–4.61 (m, 3H), 4.25–4.22 (m, 1H), 4.03–3.86 (m, 3H), 3.0–3.20 (m, 2H), 2.91 (dd, J=15.0, 4.7 Hz, 1H), 2.20–2.06 (m, 5H), 1.77–1.71 (m, 3H), 1.08–1.06 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 138.9, 138.6, 131.3, 129.2, 129.1, 127.9, 126.1, 125.8, 125.2, 124.9, 117.7, 117.1, 56.4, 56.2, 54.1, 53.9, 53.2, 49.9, 41.6, 41.5, 38.3, 38.2, 27.3, 26.4, 24.2, 18.9, 18.8, 18.0, 13.7; IR (NaCl, cm^{-1}) 1613, 1584; ESI-MS: calculated for $C_{21}H_{29}N_2$ $[M]^+$: 309.2325, found: 309.2320.

4.40. 1-(1-(but-2-ynyl)-3-(buta-2,3-dien-2-yl)-3,4-dihydroquinolin-2(1*H*)-ylidene)pyrrolidinium triflate (33d)

The compound was purified by flash chromatography (DCM to DCM:MeOH 5%) to yield the *1-(1,3-diallyl-3,4-dihydroquinolin-2(1H)-ylidene)pyrrolidinium triflate* (**33d**) (20 mg, 0.04 mmol, 29%); R_f (DCM/methanol 2%): 0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J=8.2 Hz, 1H), 7.30 (t, J=7.9 Hz, 1H), 7.20–7.13 (m, 2H), 5.15–5.11 (m, 1H), 4.58–4.27 (m, 5H), 4.16 (td, J=11.2, 5.9 Hz, 1H), 4.05 (d, J=4.9 Hz, 1H), 3.66–3.59 (m, 1H), 3.52 (dd, J=15.9, 5.2 Hz, 1H), 2.81 (dd, J=15.9, 2.0 Hz, 1H), 2.29–2.07 (m, 3H), 1.95 (s, 3H), 1.84–1.81 (m, 1H), 1.68 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.2, 167.9, 141.3, 128.4, 128.3, 126.8, 117.9, 93.6, 84.2, 76.5, 75.3, 55.1, 53.7, 45.3, 44.9, 27.3, 26.9, 24.0 (2C), 16.6, 3.9; IR (NaCl, cm^{-1}): 3383, 1662, 1560, 1431; ESI-MS: calculated for $C_{21}H_{25}N_2$ $[M]^+$: 305.2012, found: 305.2009.

4.41. 2,4-Diallyl-1,2-dihydroisoquinolin-3(4*H*)-one (38)

To a flame-dried screw-capped microwave test tube equipped with a magnetic stir bar was added the derivative **34** (25 mg, 0.083 mmol, 1.0 equiv) followed by DCM (0.1 M) was added under the atmosphere of Argon. To this stirred solution triflic anhydride (1.05 equiv) was added dropwise and stirred at ambient temperature for 15 min. After stirring for 15 min, 2,4,6-collidine (1.2 equiv) was added dropwise, the reaction mixture was heated in a microwave reactor at 120 °C for 5 min. After cooling to room temperature, the mixture was evaporated and dissolved in THF (0.5 mL). A saturated solution of $NaHCO_3$ (0.5 mL) was added and the mixture was heated in the microwave reactor at 120 °C for 5 min. The organic layer was evaporated to dryness. Purification by flash column chromatography afforded the corresponding derivative **38** as a light yellow oil (17 mg, 0.078 mmol, 90%); ^{1}H NMR (500 MHz, $CDCl_3$) δ:

7.34–7.20 (m, 2H), 7.15 (d, J=7.5 Hz, 2H), 5.81–5.67 (m, 2H), 5.22–5.19 (m, 2H), 5.03–4.99 (m, 2H), 4.59 (d, J=15.8 Hz, 1H), 4.28–4.08 (m, 3H), 3.65 (t, J=6.5 Hz, 1H), 2.64–2.61 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.1, 135.9, 134.4, 132.8, 131.2, 127.8, 127.6, 126.7, 125.3, 118.0, 117.9, 49.9, 49.5, 47.4, 38.6; IR (NaCl, cm^{-1}): 2972, 2921, 1638, 915, 751; ESI-MS: calculated for $C_{15}H_{17}NONa$ $[M+Na]^+$: 250.1203, found: 250.1202.

Acknowledgements

The authors thank Fundação para a Ciência e Tecnologia for a PhD fellowship to L.C. (SFRH/BD/63407/2009), the funding to LAQV, REQUIMTE:UID/QUI/50006/2013 and access to spectrometers from the National NMR Facility (RECI/BBB-BQB/0230/2012). Generous support by the Deutsche Forschungsgemeinschaft (Grants MA 4861/1-1 and 1-2), the Max-Planck-Institut für Kohlenforschung (where parts of this research were carried out) and the University of Vienna is gratefully acknowledged.

Supplementary data

Supplementary data (experimental procedures, characterization data for new compounds and X-ray crystallographic data) related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.06.027.

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