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Synthesis of benzo-fused medium ring cyclic ethers via a Michael addition–ring closing metathesis strategy involving nitroaliphatic compounds

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Abstract—Nitroalkenes derived from *O*-protected salicylaldehyde undergo facile Michael-type addition of nucleophiles possessing unsaturated tether. Ring closing metathesis of the Michael adducts provides benzo-fused medium ring cyclic ethers possessing a nitroalkyl functionality.

1. Introduction

A large number of bioactive natural products possess functionalized medium-sized rings.[1] Medium-sized oxacycles,[2] in particular, constitute a common skeleton in many macrocycles,[3] marine toxins,[4] allelopathic agents,[5] anticancer compounds[6] and other bioactive natural products.[7] Although various coupling,[8] ring expansion/fragmentation,[9] rearrangement[10] and other miscellaneous methods[11] are available in the literature, ring closing metathesis (RCM)[12] is obviously the method of choice to access medium-sized oxacycles.[13] However, synthesis of RCM precursors often involves cumbersome multi-step reaction sequences.

Benzo-fused medium ring oxacycles, in particular, are seen in allelopathic natural products such as helianane,[14] heliannuol A,[15] heliannuol H, heliannuol K, etc. (Fig. 1).[5] We report here a facile and efficient synthesis of such oxacycles based on the excellent Michael acceptor ability of conjugated nitroalkenes. In fact, Michael addition to nitroalkenes[16] has emerged as a very useful and convenient initiating step for the synthesis of more complex molecules via enolate trapping and other inter- and intramolecular reactions of the Michael adducts often involving the nitroalkyl moiety.[17–21] Our strategy relies on the ring closing metathesis (RCM) of the Michael adducts arising from addition of carbon and heteroatom centred nucleophiles possessing an unsaturated tether to nitroalkenes. Such a Michael addition–RCM strategy has not been employed for the synthesis of medium-sized rings until recently.[22] Furthermore, although Grubbs catalysts are well-known for their functional group tolerance,[23] there is only one report, to our knowledge, which describes RCM of a substrate possessing a nitroaliphatic moiety.[22]

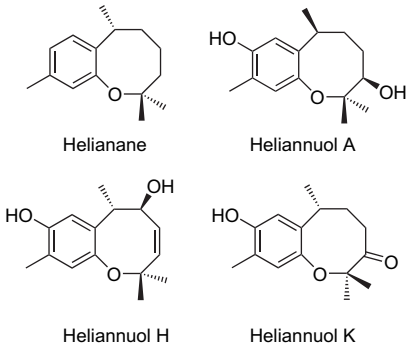

Figure 1.

2. Results and discussion

It was envisioned that cyclic ethers of type **1** possessing a nitroalkyl moiety would arise via ring closing metathesis of α,ω-diene **2** (Scheme 1). Diene **2**, the key RCM precursor, would be accessible via Michael-type addition of various nucleophiles of type **3** possessing an unsaturated tether to *O*-protected nitroarene **4**. Aldehyde **5** would be a suitable precursor to nitroarene **4** as the former can be subjected to condensation with nitromethane (Henry reaction).[17,24]

Keywords: Medium ring ethers; Michael addition; Ring closing metathesis; Nitro compounds.
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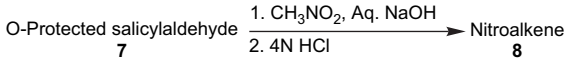
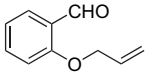
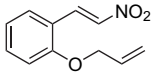
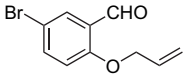
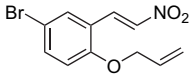
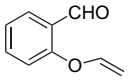
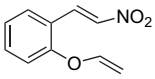
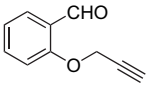
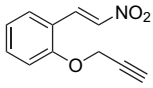
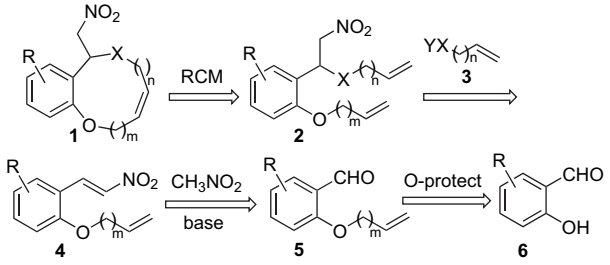
Table 1. Preparation of nitroalkenes **8** from *O*-protected salicylaldehydes



Entry	*O*-Protected salicylaldehyde **7**	Nitroalkene **8**, yield[a] (%)
1	**7a** 	**8a**  77
2	**7b** 	**8b**  78
3	**7c** 	**8c**  84
4	**7d** 	**8d**  82

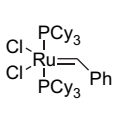
[a] Isolated yield after purification by silica gel column chromatography.

Thus, the nitroalkenes **8a–d** were prepared in high yields from their corresponding *O*-protected salicylaldehydes **7a–d** via Henry reaction with nitromethane (Table 1, see also Section 4).

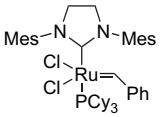


Scheme 1.

Our initial experiment using *o*-allyloxynitrostyrene **8a** with allyl magnesium bromide **9a** provided Michael adduct **10a** in 78% yield (Table 2, entry 1). Subsequently, a dilute solution of **10a** (~0.002 M) was heated in toluene at 80 °C in the presence of 5 mol % of Grubbs catalyst **G1** in anticipation of obtaining the cyclic ether **11a**. Indeed, we were pleased to isolate the benzo-fused eight-membered cyclic ether **11a** possessing a nitromethyl moiety in good yield (60%) after 8 h. These results encouraged us to subject all the nitrostyrenes **8a–d** to the Michael addition of various Grignard reagents **9a–c** possessing an unsaturated tether. These experiments provided adducts **10b–h** in high yield (63–75%, Table 2, entries 2–8). The diverse Michael adducts **10b–h** possessing a unique α,ω-unsaturation were then subjected to RCM as in the case of **10a**. As expected, **10b** provided the desired eight-membered ether **11b** in high yield (70%, Table 2, entry 2). Formation of nine-membered cyclic ether was also facile as the RCM products **11c** and **11d** were isolated in 65 and 69% yields, respectively (Table 2, entries 3 and 4).



G1



G2

Our attempts to construct a 10-membered ring via RCM of Michael adduct **10e** using Grubbs catalyst **G1** or **G2** provided only traces of the desired product **11e** (Table 2, entry 5). The RCM of vinyl ether **10f** was also not facile under a variety of conditions using **G1** and **G2** (Table 2, entry 6).[25]

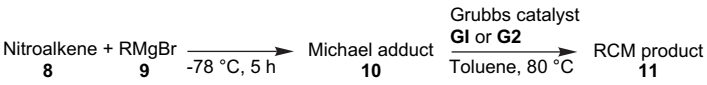
The benzo-fused medium ring cyclic ethers could be constructed via enyne metathesis as well. For instance, the propargyl ethers **10g** and **10h** underwent RCM in the presence of 10 mol % of **G1** to afford the dienes **11g** and **11h**, respectively, in moderate yield (Table 2, entries 7 and 8).

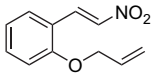
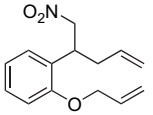
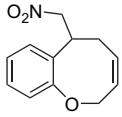
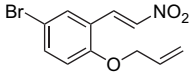
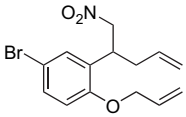
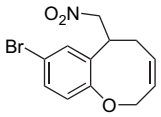
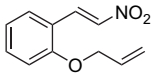
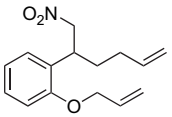
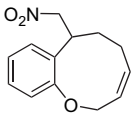
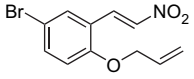
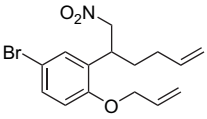
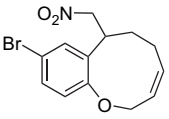
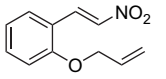
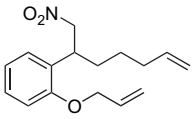
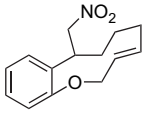
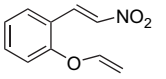
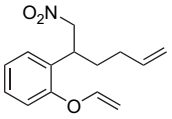
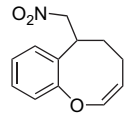
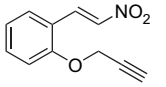
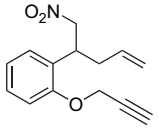
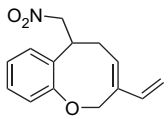
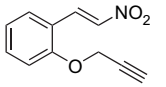
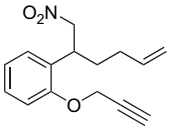
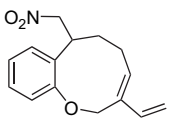
Having constructed eight- and nine-membered benzo-fused cyclic ethers **11** via RCM of Michael adducts **10** arising from addition of Grignard reagents **9** to nitroalkenes **8**, we turned our attention to generate novel functionalized medium rings, including those possessing additional heteroatoms, via a similar strategy. The key RCM precursors, e.g. **13**, in this scheme could be prepared via conjugate addition of other nucleophiles possessing an unsaturated tether, e.g. **12**, to nitroalkenes **8** (Table 3). For instance, conjugate addition of allyl malonate **12a** to nitroalkene **8a** provided the adduct **13a** in 70% yield (Table 3, entry 1). The Michael adduct **13a** underwent smooth RCM in the presence of 7 mol % of **G1** providing the nine-membered cyclic ether **14a** in 62% yield.

Our Michael addition–RCM strategy has been employed to construct benzo-fused medium ring ethers possessing an additional heteroatom in the ring besides the nitroalkyl side chain. Thus, conjugate addition of allyl alcohol **12b** and allyl mercaptan **12c** provided the Michael adducts **13b–e** in high yield (68–78%, Table 3, entries 2–5). Even though Michael adduct **10f**, derived from nitroalkene **8c** (Table 2, entry 6), was unreactive, we generated RCM precursors **13c** and **13e** from **8c** (Table 3, entries 3 and 5) to examine whether additional heteroatom in the chain would facilitate ring closure. However, attempted RCM of Michael adducts **13c** and **13e** did not proceed (Table 3, entries 3 and 5).[25] On the other hand, while Michael adduct **13b** provided only complex mixture (Table 3, entry 2), **13d** could be successfully cyclized to the nine-membered ring containing both oxygen and sulfur **14d** in 40% yield (Table 3, entry 4).

Application of the above Michael–RCM sequence for the synthesis of allelopathic natural products such as helianane, heliannuol A, etc., which possess a benzo-fused medium ring (eight-membered) cyclic ether skeleton will be reported in due course. The nitroalkyl moiety is expected to be the latent functionality for the benzylic methyl group in these natural products. Expanding the scope of the above strategy by employing other Michael acceptors such as α,β-unsaturated ketones, esters, etc. is also an attractive prospect.

Table 2. Michael addition of Grignard reagents **9** to nitrostyrenes **8** and subsequent ring closing metathesis of the Michael adducts **10** to medium ring ethers **11**



Entry	Nitroalkene **8**	RMgBr **9** R=	Michael adduct **10**	Yield[a] (%)	RCM cat and conditions	RCM product **11**	Yield[a] (%)
1	**8a** 	**9a** Allyl	**10a** 	78	**G1**,[b] 8 h	**11a** 	60
2	**8b** 	**9a** Allyl	**10b** 	73	**G1**,[b] 8 h	**11b** 	70
3	**8a** 	**9b** Homo-allyl	**10c** 	75	**G1**,[b] 8 h	**11c** 	65
4	**8b** 	**9b** Homo-allyl	**10d** 	75	**G1**,[b] 8 h	**11d** 	69
5	**8a** 	**9c** *n*-Pentenyl	**10e** 	69	**G1** or **G2**[c]	**11e** 	<5[d]
6	**8c** 	**9b** Homo-allyl	**10f** 	63	**G1** or **G2**[c]	**11f** 	—
7	**8d** 	**9a** Allyl	**10g** 	68	**G1**,[e] 15 h	**11g** 	20
8	**8d** 	**9b** Homo-allyl	**10h** 	70	**G1**,[e] 12 h	**11h** 	43

[a] Isolated yield after purification by silica gel column chromatography.
[b] 5 mol %.
[c] Variety of conditions.
[d] Considerable amounts of dimers were isolated in these cases.
[e] 10 mol %.

3. Conclusions

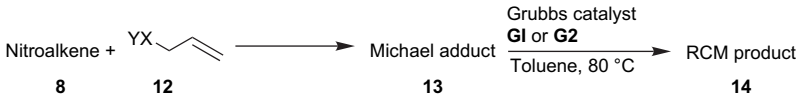
β-Nitrostyrenes possessing *o*-allyloxy, *o*-vinyloxy and *o*-propargyloxy groups undergo facile Michael addition of a variety of carbon and heteroatom centred nucleophiles containing an unsaturated tether to afford novel substrates suitable for ring closing metathesis. The RCM of majority of these substrates, except those containing the vinyl ether moiety, to eight- and nine-membered rings takes place satisfactorily. The novel benzo-fused medium ring cyclic ethers possess nitroalkyl and olefinic/dienic moieties, which can be easily transformed to other functionalities.

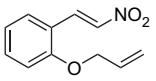
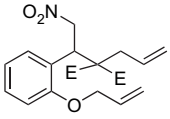
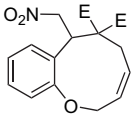
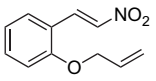
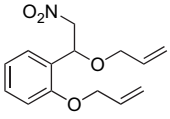
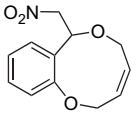
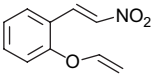
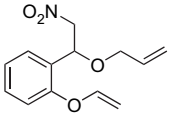
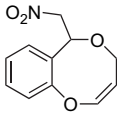
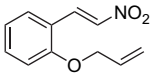
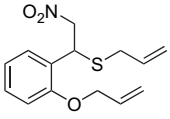
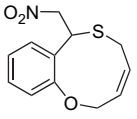
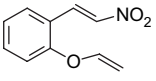
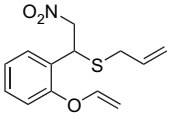
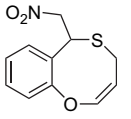
4. Experimental section

4.1. General

Melting points are uncorrected. IR spectra were recorded on a Perkin Elmer Spectrum One FT spectrometer. NMR spectra (^{1}H and ^{13}C) were recorded on an AMX-400 or VXR-300S spectrometer. ^{1}H–^{1}H COSY spectra were recorded on an AMX-400 spectrometer using gDQCOSY pulse sequence. Coupling constants (*J* values) are given in hertz. High resolution mass spectra were recorded at 60–70 eV on a Waters Micromass Q-TOF spectrometer (ESI, Ar) or

Table 3. Michael addition of C and heteroatom centred nucleophiles **12** to nitrostyrenes **8** and subsequent ring closing metathesis of the Michael adducts **13** to medium ring ethers **14**



Entry	8	12 XY=	Reagents and conditions	Michael adduct 13	Yield[a] (%)	RCM cat and conditions	RCM product 14	Yield[a] (%)
1	**8a** 	**12a** $CH\text{-}E_2$[b]	^{t}BuOK, THF, −20 °C	**13a** 	70	**G1**,[c] 20 h	**14a** 	62
2	**8a** 	**12b** OH	^{t}BuOK, THF, −60 °C, 20 min	**13b** 	78	**G1** or **G2**	**14b** 	—[d]
3	**8c** 	**12b** OH	^{t}BuOK, THF, −60 °C, 20 min	**13c** 	70	**G1** or **G2**	**14c** 	—[e]
4	**8a** 	**12c** SH	Et_3N, THF, rt, 12 h	**13d** 	68	**G1**,[c] 10 h	**14d** 	40
5	**8c** 	**12c** SH	Et_3N, THF, rt, 12 h	**13e** 	70	**G1** or **G2**	**14e** 	—[e]

[a] Isolated yield after purification by silica gel column chromatography.
[b] E=CO_2Et.
[c] 7 mol %.
[d] Complex mixture.
[e] Vinyl ethers **13c** and **13e** remained unreactive under a variety of conditions using **G1** and **G2**, see Ref. 25.

on a JEOL MSRoute spectrometer (EI). *O*-Protected salicylaldehydes **7a–d**[26] and nitroalkenes **8a**[27] and **8d**[28] are known compounds.

4.2. General procedure for the preparation of nitrostyrenes 8

To an ice-cold mixture of *O*-protected salicylaldehyde **7** (0.05 mol), nitromethane (3.4 mL, 0.05 mol) in methanol (10 mL) was added dropwise. Cold aqueous NaOH (42%, 10 mL) was then added over 10 min, maintaining the temperature at 5 °C and the reaction mixture was stirred for 15 min at the same temperature. The reaction mixture containing a white precipitate was diluted with ice-cold water (20 mL) and the resulting solution was added dropwise to cold aqueous 4 N HCl (25 mL). The yellow precipitate was filtered under suction, washed thoroughly with water and recrystallized from hot ethanol.

4.2.1. Representative data: 1-(2-nitrovinyl)-2-(vinyloxy)-benzene (8c). Yield 84%; bright yellow solid; mp 71 °C; IR (film) cm^{-1} 1634 (s), 1508 (m), 1348 (m), 1241 (s) and 1147 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.65 (dd, J=6.0, 2.0 Hz, 1H), 4.94 (dd, J=13.5, 2.0 Hz, 1H), 6.64 (dd, J=13.5, 6.0 Hz, 1H), 7.06–7.18 (m, 2H), 7.44–7.54 (m, 2H), 7.80 (d, J=14.0 Hz, 1H) and 8.16 (d, J=14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.0, 116.5, 120.2, 123.5, 131.4, 133.2, 134.3, 138.6, 146.7 and 156.3; MS (ESI) *m/z* (rel intensity) 192 (M^+, 20%), 144 (100) and 121 (50); HRMS calcd for $C_{10}H_{10}NO_3$ (M^+) 192.0661, found 192.0659.

4.3. General procedure for the addition of Grignard reagents 9 to nitroalkenes 8

To activated Mg turnings (38 mg, 1.6 mmol) in dry ether (2 mL), at room temperature, was added alkyl halide (0.5 mmol) under N_2. After the reaction had begun, the remaining alkyl halide (1.0 mmol) in ether (2 mL) was added dropwise. Stirring was continued at room temperature for 2 h. The reagent **9** was diluted with dry THF (2 mL) and the resulting mixture was cooled to −78 °C. A solution of nitroalkene **8** (1.0 mmol) in dry THF (1.5 mL) was then added dropwise to the reaction mixture and the reaction mixture

was stirred for 2 h at −78 °C. The reaction mixture was then brought to room temperature and stirring continued for another 8 h. The reaction mixture was then poured into saturated aqueous ammonium chloride (5 mL) and was extracted with ether (3×20 mL). The combined organic layers were washed with brine (10 mL), dried (anhyd Na_2SO_4) and concentrated in vacuo to afford a yellowish oil. Purification of this residue by silica gel column chromatography using ethyl acetate/petroleum ether (1:9) as eluent provided pure Michael adducts **10**.

4.3.1. Representative data: 1-(allyloxy)-2-(1-nitropent-4-en-2-yl)benzene (10a). Yield 78%; pale yellow liquid; IR (film) cm^{-1} 3080 (w), 2919 (w), 2866 (w), 1552 (s), 1493 (m), 1453 (m), 1379 (m), 1240 (m), 1132 (m), 1020 (m), 997 (m), 922 (s) and 754 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 2.47–2.66 (m, 2H), 3.89 (quintet, J=7.3 Hz, 1H), 4.56 (dt, J=5.1, 1.4 Hz, 2H), 4.68 (ABqd, J=12.4, 7.2 Hz, 2H), 5.00–5.11 (m, 2H), 5.31 (dABq, J=10.5, 1.5 Hz, 1H), 5.45 (dABq, J=17.1, 1.5 Hz, 1H), 5.61–5.70 (m, 1H), 6.10 (m, 1H), 6.90 (dd, J=17.0, 7.6 Hz, 2H), 7.06 (dd, J=7.6, 1.6 Hz, 1H) and 7.20 (dt, J=6.5, 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.8, 39.3, 68.8, 78.4, 112.1, 117.4, 117.5, 120.9, 127.2, 128.5, 128.9, 133.0, 134.9 and 156.2; MS (ESI) *m/z* (rel intensity) 270 (MNa^+, 20%), 201 (28), 187 (90), 147 (100) and 99 (90); HRMS calcd for $C_{14}H_{17}NO_3Na$ (MNa^+) 270.1106, found 270.1110.

4.4. Procedure for the addition of malonate 12a to nitroalkene 8a

To a solution of allyl diethylmalonate **12a** (0.307 g, 1.5 mmol) in THF (3 mL), cooled to −20 °C under N_2, was added ^{t}BuOK (0.168 g, 1.5 mmol) in portions over 10 min and the reaction mixture was stirred at room temperature for 30 min. The reaction mixture was then cooled to −20 °C and a solution of nitroalkene **8a** (0.205 g, 1.0 mmol) in THF (3 mL) was added dropwise at −20 °C during 5 min. The reaction mixture was stirred at 0 °C for 30 min, quenched with saturated aqueous NH_4Cl (2 mL) and extracted with ether (3×10 mL). The combined organic layers were washed with water (3 mL) and brine (10 mL), dried (anhyd Na_2SO_4) and concentrated in vacuo. The crude product was purified by silica gel column chromatography using EtOAc/*n*-hexane (1:4) as eluent to afford pure Michael adduct **13a**.

4.4.1. Diethyl 2-allyl-2-(1-(2-(allyloxy)phenyl)-2-nitroethyl)malonate (13a). Yield 70%; white solid; mp 38 °C; IR (film) cm^{-1} 2985 (w), 1729 (s), 1552 (m), 1399 (s), 1384 (m), 1305 (m), 1216 (m), 1008 (m), 934 (m) and 759 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 1.25–1.31 (m, 7H), 2.25–2.40 (m, 1H), 2.45–2.55 (m, 1H), 4.16–4.32 (m, 4H), 4.56 (dt, J=5.1, 1.6 Hz, 2H), 4.87–5.10 (m, 4H), 5.29 (dd, J=10.5, 1.2 Hz, 1H), 5.43 (d, J=1.2 Hz, 1H), 5.85 (m, 1H), 6.06–6.08 (m, 1H), 6.87 (dd, J=15.7, 7.4 Hz, 2H), 7.04 (d, J=7.4 Hz, 1H) and 7.22 (dd, J=15.7, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.0, 38.5, 60.9, 61.6, 61.7, 69.2, 78.1, 112.7, 117.4, 118.7, 120.9, 123.8, 129.4, 133.0, 157.1, 169.6 and 169.9; MS (ESI) *m/z* (rel intensity) 428 (MNa^+, 55%), 360 (20), 233 (100), 159 (55) and 99 (40); HRMS calcd for $C_{21}H_{27}NO_7Na$ (MNa^+) 428.1685, found 428.1686.

4.5. General procedure for the addition of allyl alcohol 12b to nitroalkenes 8

A solution of allyl alcohol **12b** (1.74 g, 30 mmol) in THF (25 mL) was stirred at −20 to −60 °C, while ^{t}BuOK (3.38 g, 30 mmol) was added in small portions. After the entire base had dissolved, a solution of nitroalkene **8** (8 mmol) in THF (15 mL) was added dropwise over 15 min. After continued stirring for another 15 min, the reaction mixture was cooled to 0 °C and AcOH (2.5 mL) was added, followed by water (20 mL). The reaction mixture was extracted with EtOAc (2×40 mL) and the combined organic layers were washed with water (25 mL), dried (anhyd Na_2SO_4) and concentrated in vacuo. The crude residue was purified by silica gel column chromatography using EtOAc/*n*-hexane (1:9) as eluent to afford pure Michael adducts **13b–c**.

4.5.1. Representative data: 1-(allyloxy)-2-(1-(allyloxy)-2-nitroethyl)benzene (13b). Yield 78%; pale yellow liquid; IR (film) cm^{-1} 3081 (w), 2923 (w), 2862 (w), 1556 (s), 1489 (m), 1454 (m), 1380 (m), 1239 (m), 1103 (m), 929 (m) and 758 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 3.89 (ddt, J=12.6, 5.9, 1.3 Hz, 1H), 4.05 (ddt, J=12.6, 5.3, 1.4 Hz, 1H), 4.45 (dd, J=12.8, 9.9 Hz, 1H), 4.57 (dd, J=12.7, 2.9 Hz, 3H), 5.18 (tABq, J=10.6, 1.2 Hz, 1H), 5.28 (tABq, J=15.9, 1.6 Hz, 2H), 5.45 (dABq, J=17.2, 1.4 Hz, 1H), 5.58 (dd, J=9.9, 2.7 Hz, 1H), 5.81–5.92 (m, 1H), 6.00–6.11 (m, 1H), 6.90 (d, J=7.7 Hz, 1H), 7.02 (td, J=7.7, 0.8 Hz, 1H), 7.30 (td, J=7.7, 1.6 Hz, 1H) and 7.44 (dd, J=7.4, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 68.6, 70.5, 72.6, 78.9, 111.7, 117.3 (×2), 121.1, 124.6, 126.9, 129.6, 132.6, 133.8 and 155.5; MS (ESI) *m/z* (rel intensity) 286 (MNa^+, 28%), 203 (57), 145 (53), 119 (38) and 99 (100); HRMS calcd for $C_{14}H_{17}NO_4Na$ (MNa^+) 286.1055, found 286.1055.

4.6. General procedure for the addition of allyl mercaptan 12c to nitroalkenes 8

To a stirred solution of allyl mercaptan **12c** (0.16 g, 2.2 mmol) and Et_3N (0.06 mL, 0.2 equiv) in THF (2.5 mL) at 0 °C was added a solution of nitroalkene **8** (2 mmol) in THF (1.5 mL) over 15 min and the reaction mixture was stirred at room temperature overnight (12 h). The reaction mixture was then diluted with water (5 mL) and extracted with EtOAc (2×10 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), dried (anhyd Na_2SO_4) and concentrated in vacuo. The crude residue was purified by silica gel column chromatography using EtOAc/*n*-hexane (1:9) as eluent to afford pure Michael adducts **13d–e**.

4.6.1. Representative data: allyl(1-(2-(allyloxy)phenyl)-2-nitroethyl)sulfane (13d). Yield 68%; pale yellow liquid; IR (film) cm^{-1} 3020 (s), 2920 (w), 1600 (m), 1555 (s), 1492 (m), 1425 (m), 1376 (m), 1216 (m), 926 (m) and 759 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 3.15–3.21 (m, 2H), 4.60 (d, J=4.8 Hz, 2H), 4.75 (dd, J=10.9, 6.1 Hz, 1H), 4.85 (dd, J=12.8, 7.3 Hz, 1H), 4.90 (dd, J=10.9, 7.3 Hz, 1H), 5.17 (td, J=9.1, 1.1 Hz, 2H), 5.32 (dt, J=9.7, 0.6 Hz, 1H), 5.47 (dt, J=17.1, 1.5 Hz, 1H), 5.74–5.82 (m, 1H), 6.02–6.12 (m, 1H), 6.88 (d, J=8.2 Hz, 1H), 6.94 (t, J=7.5 Hz, 1H), 7.25 (td, J=7.5, 1.2 Hz, 1H) and 7.31 (dd, J=7.6, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.4,

41.2, 69.0, 78.5, 112.4, 117.5, 117.9, 121.0, 125.9, 128.8, 129.3, 132.8, 133.7 and 155.9; MS (ESI) *m/z* (rel intensity) 302 (MNa^+, 40%), 206 (100) and 160 (90); HRMS calcd for $C_{14}H_{17}NO_3NaS$ (MNa^+) 302.0827, found 302.0824.

4.7. General procedure for ring closing metathesis (RCM)

To a solution of Michael adduct **10** or **13** (0.25 mmol) in degassed toluene (60 mL) was added dropwise a solution of bis(tricyclohexylphosphine)-benzylideneruthenium dichloride (Grubbs catalyst **G1**, 5–10 mol %) in degassed toluene (100 mL). The resulting solution was allowed to stir at 80 °C for several hours. Toluene was removed in vacuo and the residue was purified by silica gel column chromatography using EtOAc/*n*-hexane (1:9) as eluent to afford the cyclized product **11** or **14**.

4.7.1. Representative data: 5,6-dihydro-6-(nitromethyl)-2*H*-benzo[*b*]oxocine (11a). Yield 60%; pale yellow liquid; IR (film) cm^{-1} 3079 (w), 2926 (w), 1551 (s), 1493 (m), 1452 (m), 1423 (m), 1379 (m), 1241 (m), 1019 (m), 997 (m), 917 (m) and 755 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 2.35–2.39 (m, 1H), 3.12 (ABq, J=11.6 Hz, 1H), 3.65–3.75 (m, 1H), 4.39 (dd, J=15.4, 5.0 Hz, 1H), 4.41–4.51 (m, 2H), 4.92 (dt, J=15.4, 2.9 Hz, 1H), 5.41 (ddABq, J=10.6, 4.9, 1.4 Hz, 1H), 5.73–5.83 (m, 1H), 7.03–7.11 (m, 3H) and 7.28 (dd, J=3.4, 1.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.5, 43.8, 72.8, 81.4, 123.3, 125.0, 127.7, 129.4, 130.0, 130.6, 132.2 and 157.0; MS (ESI) *m/z* (rel intensity) 242 (MNa^+, 100%), 159 (80); HRMS calcd for $C_{12}H_{13}NO_3Na$ (MNa^+) 242.0793, found 242.0798.

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Supplementary data

Complete characterization data for all the new compounds and known compounds for which data are not available in the literature as well as copies of ^1H, ^{13}C NMR and relevant ^1H–^1H COSY spectra are provided as Supplementary data. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.09.009.

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