Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 47 (2006) 1145–1151
Tetrahedron Letters

Catalyst economy. Part 2: Sequential metathesis—Kharasch sequences using the Grubbs metathesis catalysts☆

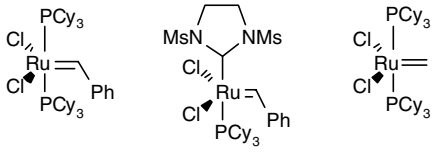
Chris D. Edlin,[a] James Faulkner[b] and Peter Quayle[b,*]

[a]Medicinal Chemistry 1, GlaxoSmithKline Medicines Research Centre, Gunnels Wood Road, Stevenage, Herts. SG1 2NY, UK
[b]School of Chemistry, The University of Manchester, Manchester M13 9PL, UK

Received 14 November 2005; revised 1 December 2005; accepted 5 December 2005

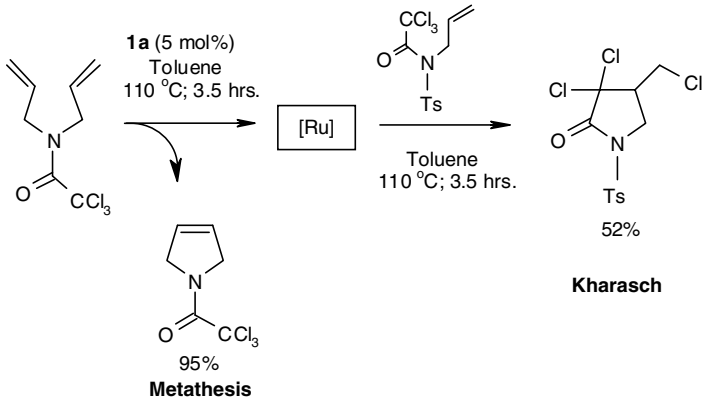
Abstract—Sequential ring-closing metathesis (RCM)–Kharasch cyclizations are promoted by the Grubbs metathesis catalysts and provide rapid access to bicyclic lactones and lactams.
© 2005 Elsevier Ltd. All rights reserved.

Recently, we demonstrated[1] that the Grubbs carbene complex **1a**, more usually associated with metathesis chemistry,[2] also proves to be an efficient catalyst for the promotion of intramolecular Kharasch reactions.



1a **1b** **1c**

Circumstantial evidence[3] suggests that this non-metathetical activity[4] is associated with the in situ decomposition of the initial carbene complex to an as of yet uncharacterized ruthenium complex(es).[5] Such species not only promote ATRC reactions but are also responsible[3] for alkene isomerization, redox isomerization of allylic alcohols and transfer hydrogenation reactions. Furthermore, we have also shown, in competition experiments,[6] that the relative rates of these reactions may be quite different, as in the case of RCM reactions leading to five-membered heterocycles, which are much more rapid than the alternative ATRC reactions leading to butyrolactones or butyrolactams (Scheme 1). Indeed



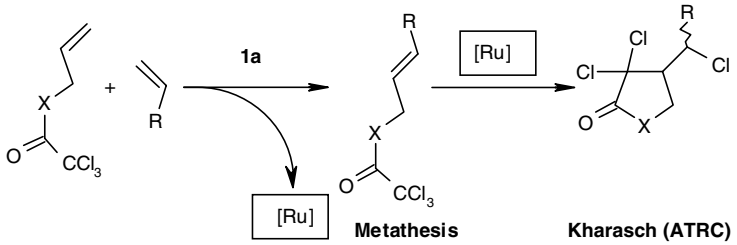
Scheme 1. Sequential metathesis–Kharasch reactions: initial investigations.[6]

Keywords: Grubbs; Metathesis; Kharasch; Cyclization; Tandem; ATRC; RCM; Metathesis; Radical.

☆ For part 1 of this series, see Ref. 6.

* Corresponding author. Tel.: +44 161 275 4619; fax: +44 161 275 4598; e-mail: peter.quayle@manchester.ac.uk

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.12.018



Scheme 2. Proposed tandem metathesis–Kharasch sequence.

the ATRC component is usually only observed when the reaction mixture is heated in excess of 80 °C whereas RCM reactions are frequently observed to proceed at or near ambient temperatures. This dual reactivity raises the possibility that different carbon–carbon bond-forming reactions may be incorporated into a synthetic sequence where the outcome is pre-determined by the relative rates of the potential bond-forming reactions.

With this thought in mind, we decided to test whether it would be possible to engineer reaction sequences, which involve sequential metathesis–Kharasch cascades in which the initial metathesis reaction proceeds rapidly but necessarily generates a thermally unstable methylidene complex **1c**. Decomposition of **1c** under the reaction conditions would then generate a metathetically inactive catalyst, '[Ru]', which is however still capable of promoting ATRC reactions (Scheme 2). The use of the ruthenium catalyst (or precatalyst) to promote different carbon–carbon bond-forming reactions in this manner is a concept we have coined[6] as 'catalyst economy', a sequence which falls into the broader category of 'concurrent catalysis' as adumbrated by Ajamian and Gleason.[7] These multiple catalytic cycles have great potential in organic synthesis[8] and the report by Snapper[9] prompts us to communicate some of our most recent findings in this area.

Our first attempt to validate such a hypothesis centred on possibly the worst case scenario, that of cross metathesis[10] (CM)-ATRC reaction sequences. Initial blank reactions confirmed that trichloroacetamide **2** underwent ATRC reaction reasonably rapidly at 80 °C (CuCl/dHbipy[†], 5 mol %; $ClCH_2CH_2Cl$; 80 °C; 3.5 h), affording the γ-lactam **4** in 89% isolated yield.

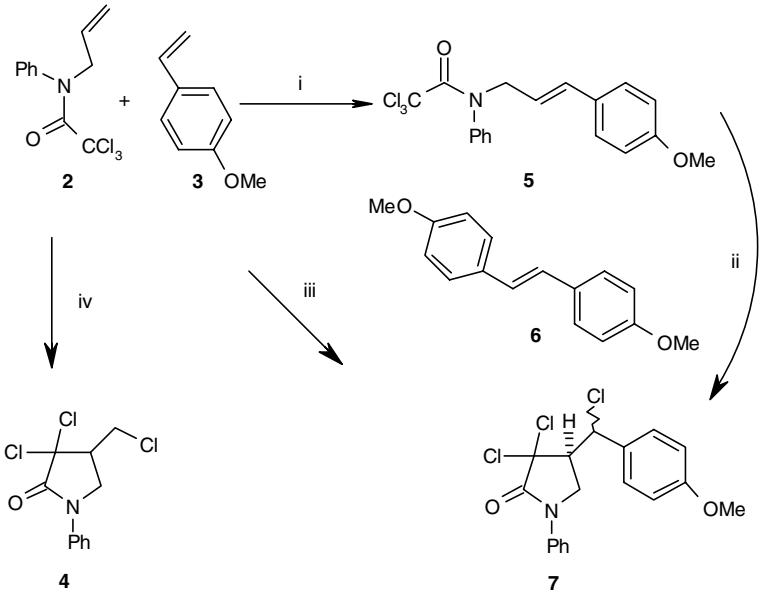
Encouragingly, we also observed that exposure of a mixture of **2** and **3** (**2**:**3** = 1:5) in toluene to catalyst **1a** (5 mol %; 40 °C; 2 h) afforded the cross-metathesis product **5** in 69% yield (E:Z > 95:5) together with the stilbene derivative **6**. We were unable to detect any of the co-metathesis product derived from **2** or γ-lactam **4**, which would be the result of a competing ATRC reaction. We also verified, in a separate experiment, that a purified sample of the cross metathesis product **5** was amenable to radical cyclization, as its exposure to an ATRC catalyst (CuCl/dHbipy, 5 mol %; $ClCH_2CH_2Cl$; 80 °C; 3.5 h) afforded the γ-lactam **7** in 60% yield (as a 1:1 mixture of diastereoisomers). That these two different carbon–carbon bond-forming reactions (i.e., metathesis followed by Kharasch) could be telescoped into a single sequence[11] was realized when we observed that cross metathesis of **2** with **3**, at 40 °C, as above, followed by thermolysis at 110 °C led to the isolation of γ-lactams **7** in 29% overall yield, as a 3:2 mixture of diastereoisomers (Scheme 3). We also note, in this case, that the stereochemical course of the cyclization reaction leading to **7** is dependent upon the nature of the catalyst system utilized in the ATRC reaction.[12] Similarly, cross metathesis of **2** with the styrenes **9**, **10** and **11** proceeded smoothly at 40 °C (12 h) which, followed by thermolysis at 110 °C (3 days), resulted in the isolation of the γ-lactams **12a**–**c** in moderate overall yields (26%, 32% and 23%, respectively) as a single diastereoisomer in each case (Scheme 4).

From our preliminary studies, we also conclude that the nature of the *N*-substituent may play a critical role in determining the outcome of these tandem reactions.

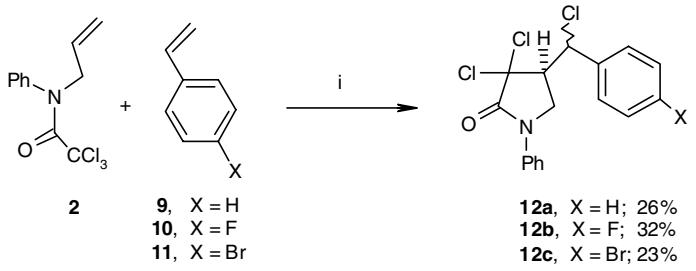
For example, co-metathesis of **2** becomes the dominant reaction pathway, leading to the isolation of **8** as the major product (78% isolated yield; E:Z > 95:5), when **3** was exchanged for the more hindered alkene partners in the initial cross metathesis reaction. Alternatively, in the case where the *N*-substituent is simply hydrogen, as in the case of **13**, attempted cross metathesis with 3,3-dimethylbut-1-ene resulted in the isomerization[13] of the substrate to enamide **14**, whereas an *N*-tosyl-substituent (as in the case **15**) appeared to shut down[14] the initial metathesis reaction completely (Scheme 5).

Notwithstanding these complications, we were encouraged enough to investigate these reactions further and thought it best to attempt RCM-ATRC reactions with the expectation that the initial metathesis reaction would become more favourable. To this end, trichloroacetate **18**, which is readily prepared in a three-step sequence from commercially available allyl vinyl ether in 93% overall yield, was chosen as our initial test substrate. In passing it is worth mentioning that the Claisen rearrangement of allyl vinyl ether into aldehyde **16** is best accomplished using the now ubiquitous application of microwave technology.[15] Aldehyde **16** can be prepared in quantitative yield on a 20 g scale in this manner. Reaction of **16** with vinyl magnesium bromide and subsequent trichloroacetylation of **17** afforded the key substrate **18** in near quantitative yield. After some experimentation, we observed that exposure of **18** to the Grubbs catalyst **1a** in the presence of a Cu(I) co-catalyst[16] led directly to the isolation of the bicyclic lactone

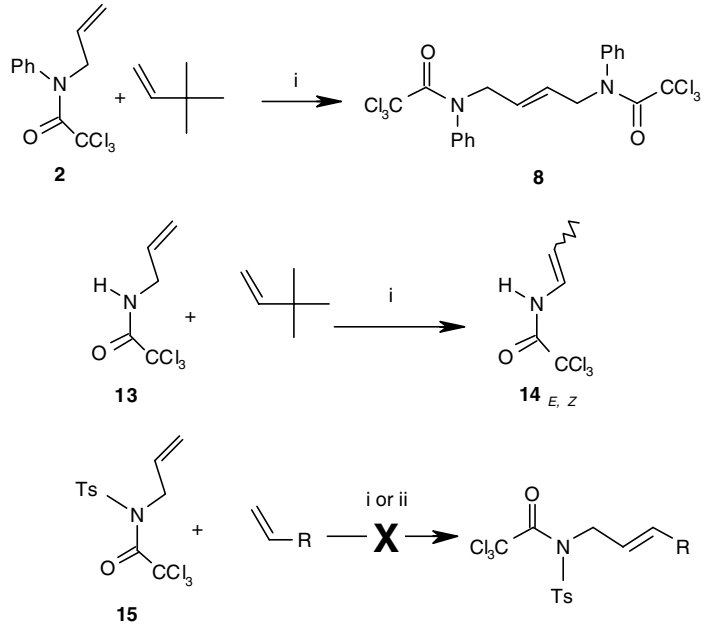
[†] dHbipy = 4,4′-di-*n*-heptyl-2,2′-bipyridine.



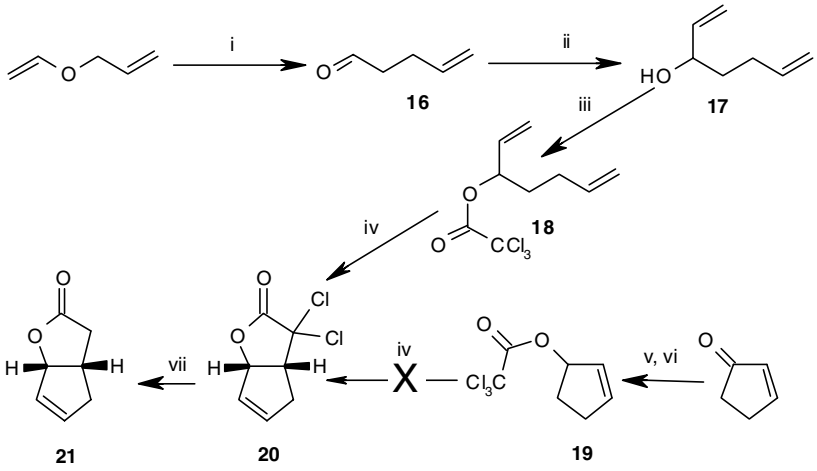
Scheme 3. Reagents and conditions: (i) **1b**, 5 mol%; toluene; 40 °C; 12 h; 69%; (ii) CuCl, 5 mol %; dHbipy, 5 mol %; toluene; 110 °C; 3 days; 60%; (iii) (a) **1b**, 5 mol %; toluene; 40 °C; 12 h; (b) 110 °C; 3 days; 29% overall yield; (iv) CuCl, 5 mol %; dHbipy, 5 mol %; toluene; 110 °C; 3.5 h; 89%.



Scheme 4. Reagents and conditions: (i) **1b**, 5 mol %; toluene, 40 °C; 12 h; (ii) 110 °C; 3 days.



Scheme 5. Reagents and conditions: (i) **1b**, 5 mol %; CH_2Cl_2; 40 °C; 16 h; (ii) **1b**, 5 mol %; toluene, 12 h; 40 °C.



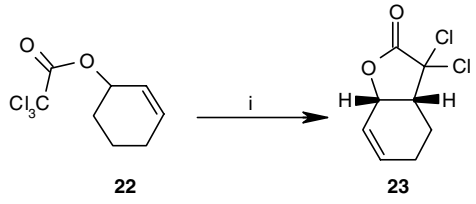
Scheme 6. Reagents and conditions: (i) microwave irradiation, neat, 1 h; 100%; (ii) vinyl magnesium bromide, 1.5 equiv; Et_2O, −78 °C; 98%; (iii) trichloroacetyl chloride, 1.2 equiv; triethylamine 1.2 equiv; Et_2O; 0 °C; 95%; (iv) **1b**, 5 mol %; CuCl, 5 mol %; dHbipy, 5 mol %; $CDCl_3$, 2 h at 20 °C and then 3 h at reflux; 95%; (v) (a) $CeCl_3$, 1.1 equiv; EtOH; 0 °C; (b) $NaBH_4$, 0.5 equiv; 0 °C; 50%; (vi) trichloroacetyl chloride, 1.2 equiv; triethylamine, 1.2 equiv; Et_2O; 0 °C; unstable oil; (vii) Zn, 10 equiv; 1:3 AcOH–H_2O; 100 °C; 69%.

20 in 95% isolated yield. Dechlorination of **20** was readily achieved (Zn, $AcOH_{(aq)}$) in good yield affording the unsaturated lactone **21**,[17] a potentially useful intermediate in the synthesis of prostaglandins and related natural products (Scheme 6).

Further experimentation (vide infra) indicated that trichloroacetate **19**, the product of the initial RCM reaction, is formed rapidly (<2 h at 20 °C) but is extremely labile, and readily suffers decomposition at the temperature normally employed in the ATRC reaction. In fact, the unstable ester **19** could not be converted into lactone **20** using either copper or ruthenium (Grubbs **1a** or **1b**) catalysts alone using our standard set of reaction conditions. This observation leads us to suggest therefore that the Ru–Cu catalyst combination may increase both the rate of the RCM and ATRC reactions and leads us to speculate that a bi-metallic catalyst[18] may be responsible for promoting this particular reaction sequence.

Superficially, the overall transformation of **18** into **20** could be described as a tandem RCM–ATRC–elimination–isomerization reaction, the later stages of which bore close resemblance to the Grubbs-promoted ATRC conversion of the related substrate **22** into lactone **23**[1,3] (Scheme 7).

A closer examination of the reaction depicted in Scheme 6 suggests that this mechanistic description may not be the case as monitoring the conversion of **18** into **20** in $CDCl_3$ by ^1H NMR spectroscopy proved to be quite revealing. From these investigations, it appeared that the initial RCM reaction proceeds rapidly, generating trichloroacetate **19**. However, this product is thermally unstable and fragments leading to the generation of cyclopentadiene is then converted into the final product **20**.

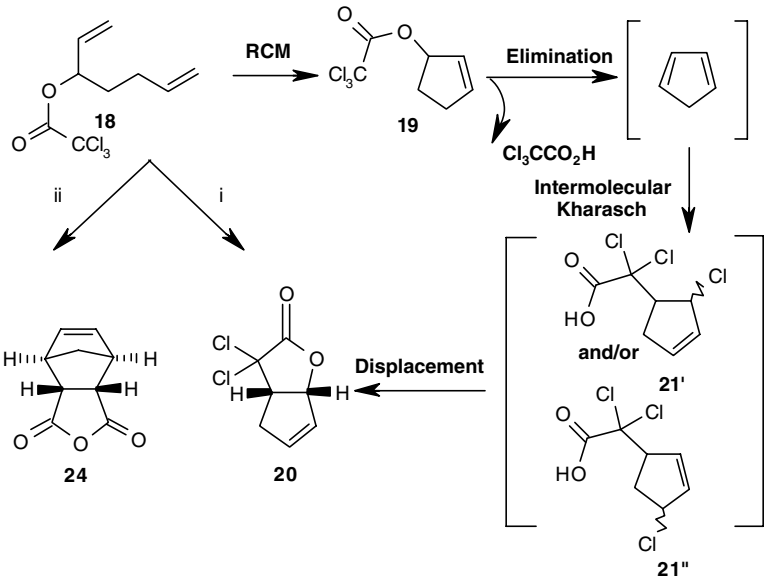


Scheme 7. Reagents and conditions: **1a**, 5 mol %; toluene; 110 °C; 12 h; 80%.

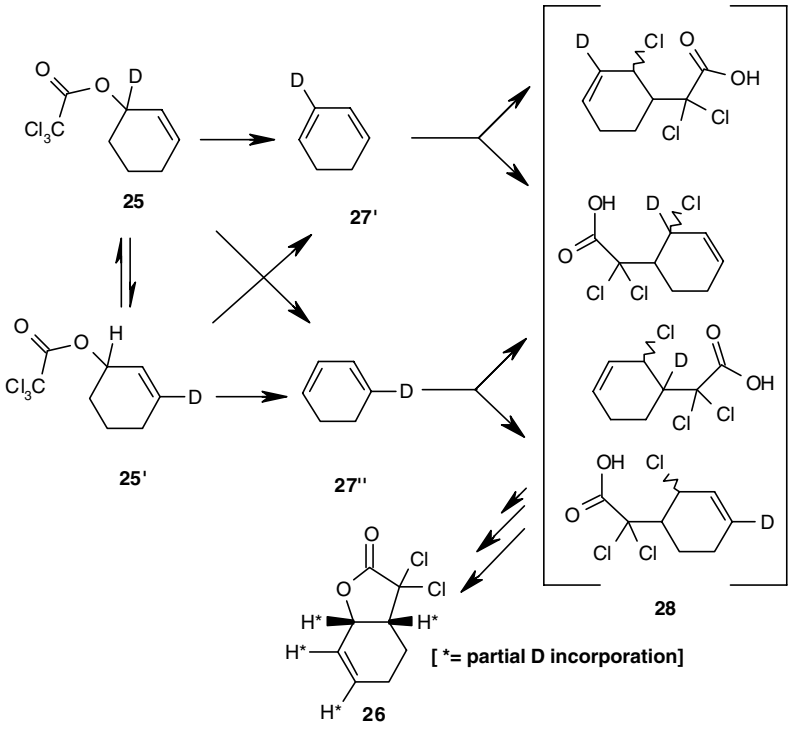
The fact that cyclopentadiene is also generated during the course of the preparative sequence was inferred by its interception with maleic anhydride, affording the Diels–Alder adduct **24** in 92% isolated yield when carried out under our standard operating conditions. This set of observations suggests that the overall process, **18** to **20**, is the best described as cascade of reactions involving an RCM–elimination–intermolecular Kharasch addition[19a]–displacement pathway, as depicted in Scheme 8.

We suggest therefore that this transformation proceeds via the intermediacy of **21′** and/or **21″**, the products of an intermolecular Kharasch reaction. Once formed, these intermediates can undergo cyclization, by either S_N2 or S_N2' pathways,[19b] to the observed bicyclic lactone **20**. This result also sheds light onto the highly regioselective deuterium scrambling, which we previously observed in the Grubbs-mediated ATRC reaction of the mono-deuterated substrate **25**.

We now invoke a similar elimination–*intermolecular*–Kharasch addition–displacement pathway for the conversion of **22** into **23**, which in this case proceeds via the intermediacy of cyclohexa-1,3-diene. In the case of the deuterated substrate **25**, intermolecular capture (products of 1,2-addition shown for clarity) of dienes **27′** and **27″** followed by intramolecular displacement of the allylic chlorides **28** now accounts for the observed regiochemistry of the deuterium scrambling in the final product **26** (Scheme 9). Furthermore, ^2H NMR experiments revealed that the scrambling of the deuterium label in **25** is rapid at or near ambient temperature and takes place more rapidly than the Kharasch reaction.



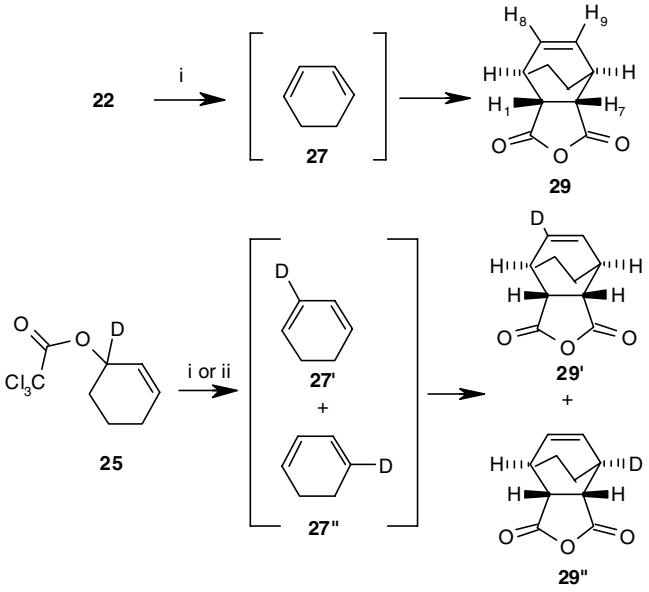
Scheme 8. Reagents and conditions: (i) (a) **1b**, 5 mol %; CuCl 5 mol %; dHbipy 5 mol %; $CDCl_3$; 2 h; 20 °C; (b) reflux; 3 h; 95%; (ii) as in (i) but with the addition of maleic anhydride (1 equiv) as co-reactant; 92%.



Scheme 9. Proposed pathway for the conversion of **25** into **26**.

In consonance with this proposal, we also note that exposure of **22** to the Grubbs catalyst **1b** in the presence of maleic anhydride (1 equiv) results in the isolation of the Diels–Alder adduct, **29** in excellent yield, suggesting that the [4+2]-cycloaddition reaction of cyclohexa-1,3-diene again competes favourably with the intermolecular Kharasch reaction (Scheme 10). Moreover, exposure of the deuterated substrate, **25**, to the same set of reaction conditions, with *or* without the ruthenium catalyst, but in the presence of maleic anhydride (1 equiv) results in the isolation of the Diels–Alder adducts **29′** and **29″** in good isolated yields (79–94%). The ^2H NMR spectrum of the mixture **29′/29″** confirms that the deuterium label is equally scrambled between C1/C7 and C8/C9 (Scheme 10) and also established the intermediacy of the deuterated dienes **27′/27″** during the course of the cyclization sequence leading from **25** to **26**.

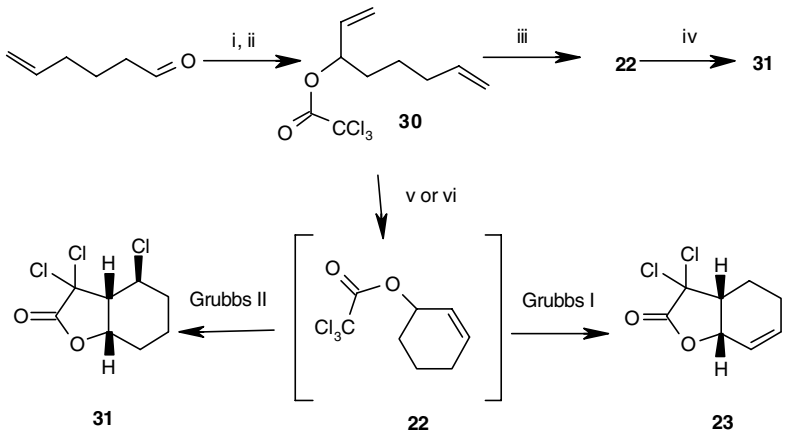
We have also established separately, in a preliminary set of investigations, that cyclization of the readily available trichloroacetate **30** to ester **22** could be effected using **1b** in $ClCH_2CH_2Cl$ (98% yield) and that **22** could be cyclized to trichlorolactone **31** under copper catalysis in 79% isolated yield.



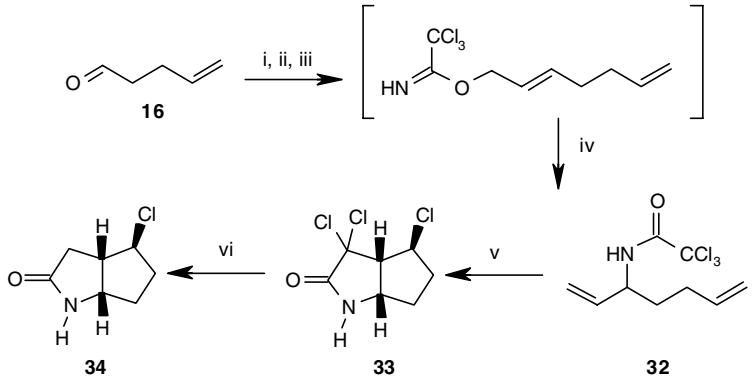
Scheme 10. Reagents and conditions. For **22** to **29**: (i) **1a**, 5 mol %; maleic anhydride, 1.0 equiv; $CDCl_3$; reflux; 92%. For **25** to **29′/29″**: (i) **1a**, 5 mol %; maleic anhydride, 1.0 equiv; toluene; reflux; 3.5 h; 94%; (ii) maleic anhydride, 1.0 equiv; toluene; reflux; 3.5 h; 79%.

In an attempt to combine these two processes, we now report that exposure of **30** to the first Grubbs catalyst **1a** (5 mol % in degassed toluene) first at ambient temperature for 3 h then under conditions of mild thermolysis (110 °C; 16 h) afforded, directly, the unsaturated lactone **23** in 64% isolated yield together with trace quantities (<5%) of trichlorolactone **31**. Alternatively, repeating this reaction, this time with the second generation catalyst **1b**, resulted in the isolation of trichlorolactone **31** as the major product (in 62% yield) together with a minor amount of the unsaturated lactone **23** (ca. 5% by ^1H NMR analysis of the crude reaction mixture), Scheme 11. In both instances, the sequential RCM–Kharasch sequences proceeded without the requirement of a copper co-catalyst whilst the product distribution is obviously dependent upon the catalyst system employed. The factors affecting the partitioning of the substrate by the different starter complexes in this reaction are not, as yet, apparent although this empirical observation has obvious synthetic implications.

Finally, we have also found that these sequential RCM–Kharasch reactions can also be applied to the synthesis of bicyclic lactams. For example, Wittig homologation



Scheme 11. Reagents and conditions: (i) $CH_2{=}CHMgBr$, 1.5 equiv; Et_2O; −78 °C; 82%; (ii) trichloroacetyl chloride, 1.2 equiv; triethylamine, 1.2 equiv; Et_2O; 0 °C; 85%; (iii) **1b**, 5 mol %; $ClCH_2CH_2Cl$; 3 h; 20 °C; 98%; (iv) CuCl, 5 mol %; dHbipy, 5 mol %; $ClCH_2CH_2Cl$; 80 °C; 79%. (v) (a) **1a**, 5 mol %; toluene; 3 h; 20 °C; (b) 110 °C; 16 h; 64%; (vi) (a) **1b**, 5 mol %; toluene; 3 h; 20 °C; b. 110 °C; 16 h; 62%.



Scheme 12. Reagents and conditions: (i) $Ph_3P{=}CHCO_2Et$, 1.3 equiv; CH_2Cl_2; 20 °C; 94%; (ii) Dibal-H, 2.0 equiv; THF; −78 °C; 97%; (iii) (a) NaH, 1.5 equiv; THF; 0 °C; (b) Cl_3CCN, 1.5 equiv; 0 °C; (iv) xylenes; Δ; 12 h; 85% over two steps; (v) **1b**, 5 mol %; xylenes; 20 °C, 3 h then 2 days at 120 °C; 82–91%; (vi) Zn, 10 equiv; 1:3 AcOH–H_2O; 100 °C; 73%.

of pent-4-enal **16**, reduction (Dibal-H), imidate formation followed by Overman rearrangement led directly to trichloroacetamide **32** in 87% overall yield. Gratifyingly, thermolysis of a solution of **32** in xylenes containing catalyst **1b** (5 mol %) afforded lactam **33** as a single diastereoisomer in 91% isolated yield. Dechlorination ($Zn–HOAc_{(aq)}$) of **33** proved to be highly selective affording the mono-chlorolactam **34**[20] in 73% yield (Scheme 12). In contrast to Snapper's report,[9] we find that although the second generation catalyst **1b** converts **32** slowly to lactam **33** it does so in a more reproducible manner than with the first generation catalyst **1a**.

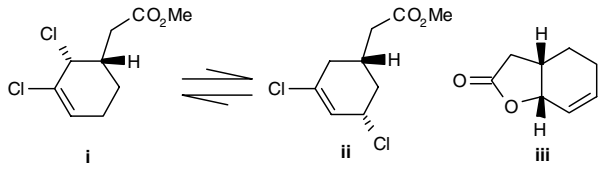
In conclusion, we have demonstrated that the Grubbs metathesis catalysts can not only promote metathesis and ATRC reactions,[1,6] but that the two separate reactions can be telescoped together providing rapid access to bicyclic lactones and lactams. We anticipate that the use of organometallic catalysts in this manner may have substantial applications in organic synthesis and is an area which we are now actively pursuing.

Acknowledgements

We thank the EPSRC and GSK for support of this research.

References and notes

1. Quayle, P.; Fengas, D.; Richards, S. *Synlett* **2003**, 1797–1800.
2. Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117–7140; Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4490–4527.
3. Edlin, C. D.; Faulkner, J.; Fengas, D.; Knight, C. K.; Parker, J.; Preece, I.; Quayle, P.; Richards, S. N. *Synlett* **2005**, 572–576.
4. For representative examples see: Maifeld, S. V.; Tran, M. N.; Lee, D. *Tetrahedron Lett.* **2005**, *46*, 105–108; Hahn, D.-W.; Byun, D.-M.; Tae, J. *Eur. J. Org. Chem.* **2005**, 63–67; Lopez, F.; Delgado, A.; Rodriguez, J. R.; Castedo, L.; Mascarenas, J. L. *J. Am. Chem. Soc.* **2004**, *126*, 10262–10263.
5. For seminal investigations in this area see: Dinger, M. B.; Mol, J. C. *Eur. J. Inorg. Chem.* **2003**, 2827–2833; Banti, D.; Mol, J. *J. Organomet. Chem.* **2004**, *689*, 3113–3116; Hong, S. H.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2004**, *126*, 7414–7415; Trnka, T. M.; Morgan, J. P.; Sanford, M. S.; Wilhelm, T. E.; Scholl, M.; Choi, T.-L.; Ding, S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 2546–2558; For a theoretical treatment see: van Rensburg, W. J.; Steynberg, P. J.; Meyer, W. H.; Kirk, M. M.; Forman, G. S. *J. Am. Chem. Soc.* **2004**, *126*, 14332–14333.
6. Faulkner, J.; Edlin, C. D.; Fengas, D.; Preece, I.; Quayle, P.; Richards, S. N. *Tetrahedron Lett.* **2005**, *46*, 2381–2385.
7. Ajamian, A.; Gleason, J. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 3754–3760.
8. Fogg, D. E.; dos Santos, E. N. *Coord. Chem. Rev.* **2004**, *248*, 2365–2679; Schmidt, B. *Eur. J. Org. Chem.* **2004**, 1865–1880; Wasilke, J.; Obrey, S. J.; Baker, R. T.; Bazan, G. C. *Chem. Rev.* **2005**, *105*, 1001–1020.
9. Seigal, B. A.; Fajardo, C.; Snapper, M. L. *J. Am. Chem. Soc.* **2005**, *127*, 16329–16332.
10. For CM approaches to styrenes see: Chatterjee, A. K.; Toste, D. F.; Choi, T.-L.; Grubbs, R. H. *Adv. Synth. Catal.* **2002**, *344*, 634–637; Ferré-Filmon, K.; Delaude, L.; Demonceau, A.; Noels, A. F. *Eur. J. Org. Chem.* **2005**, 3319–3325; For guiding principles see: Chatterjee, A. K.; Choi, T.-L.; Sanders, W. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370.
11. Concurrent catalysis has precedent in the polymer literature: Bielawski, C. W.; Louie, J.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 12872–12973; For dual reactivity (ATRP and metathesis) see: Delaude, L.; Delfosse, S.; Richel, A.; Demonceau, A.; Noels, A. F. *Chem. Commun.* **2003**, 1526–1527, and references cited therein.
12. The copper(I)-dHbipy system affords **7** as a 1:1 mixture of diastereoisomers.
13. c.f. Formentín, P.; Gimeno, N.; Steinke, J. H. G.; Vilar, R. *J. Org. Chem.* **2005**, *70*, 8235–8238; Fürstner, A.; Thiel, O. R.; Ackermann, L.; Schanz, H.-J.; Nolan, S. P. *J. Org. Chem.* **2000**, *65*, 2204–2207; For a timely review see: Escoubet, S.; Gastaldi, S.; Bertrand, M. *Eur. J. Org. Chem.* **2005**, 3855–3873.
14. This may be due to the formation of stable, metathetically inactive, chelated complexes. For discussion see: Zaja, M.; Connon, S. J.; Dunne, A. M.; Rivand, M.; Buschmann, N.; Jiricek, J.; Blechert, S. *Tetrahedron* **2003**, *59*, 6545–6558.
15. See: Davis, C. J.; Hurst, T. E.; Jacob, A. M.; Moody, C. J. *J. Org. Chem.* **2005**, *70*, 4414–4422; Castro, A. M. M. *Chem. Rev.* **2004**, *104*, 2939–3002, and references cited therein.
16. See: Rivard, M.; Blechert, S. *Eur. J. Org. Chem.* **2003**, 2225–2228, for an example of the activating effect of Cu(I) salts in CM reactions.
17. Zanoni, G.; Castronovo, F.; Perani, E.; Vidari, G. *J. Org. Chem.* **2003**, *68*, 6803–6805; Lactone **20** has also been prepared previously: Fleming, I.; Au-Yeung, B.-W. *Tetrahedron* **1981**, *37*, 13–24.
18. Quebatte, L.; Solari, E.; Scopelliti, R.; Severin, K. *Organometallics* **2005**, *24*, 1404–1406; Quebatte, L.; Scopelliti, R.; Severin, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1520–1524.
19. Intermolecular Kharasch reactions with buta-1,3-dienes has precedent: (a) Startsev, V. V.; Zubbritskii, L. M.; Petrov, A. A. *Zh. Obsch. Khim.* **1985**, *55*, 702–703; For the preparation of γ-butyrolactones via intermolecular Kharasch reactions see: Nakano, T.; Oh-Hashi, N.; Ino, Y.; Nagai, Y. *Main Group Met. Chem.* **2000**, *23*, 259–264; Matsumoto, H.; Nakano, T.; Ohkawa, K.; Nagai, Y. *Chem. Lett.* **1978**, 363–366; For related S_N2 and S_N2' cyclization reactions see: (b) Schomburg, D.; Landrey, D. N. *J. Org. Chem.* **1981**, *46*, 170–172; Bolster, M. G.; Lagnel, B. M. F.; Jansen, B. J. M.; Morin, C.; de Groot, A. *Tetrahedron* **2001**, *57*, 8369–8379; Ammann, W.; Pfund, R. A.; Ganter, C. *Helv. Chim. Acta* **1982**, *65*, 986–1020; Känel, H.-R.; Ganter, C. *Helv. Chim. Acta* **1985**, *68*, 1226–1234; The suprafacial 1,3-allylic interconversion of **i** and **ii** has been desrcibed (Chiche, L.; Christol, H.; Coste, J.; Pietrasanta, F.; Plénat, F. *Can. J. Chem.* **1981**, *59*, 164–174), as has their conversion into the lactone **iii**.



20. All new compounds were fully characterized by high field ^1H and ^{13}C NMR, IR, mass spectrometry (low and high resolution) and/or combustion microanalysis.