Chemical Science

Dynamic Article Links ►

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

EDGE ARTICLE

Diastereoselective Ring-Rearrangement Metathesis to Set the Stereochemistry of All-Carbon Quaternary Centres

Jingwei Li and Daesung Lee*

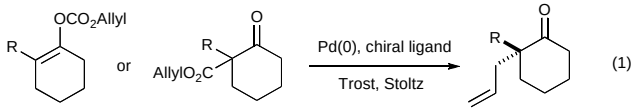
Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

A highly diastereoselective ring-rearrangement metathesis of cyclopentene derivatives containing all-carbon quaternary centres is reported. This tandem metathesis process provides cyclohexenes derivatives with two contiguous stereogenic centres, one of which is an all-carbon quaternary stereogenic centre, in high yields and excellent diastereoselecitivity. The efficacy of this methodology is showcased in the total synthesis of spiropiperidine alkaloid nitramine. In the meantime, it has been found that metathesis of the corresponding acyclic triene derivatives affords the same products with the same level of efficiency and diastereoselectivity.

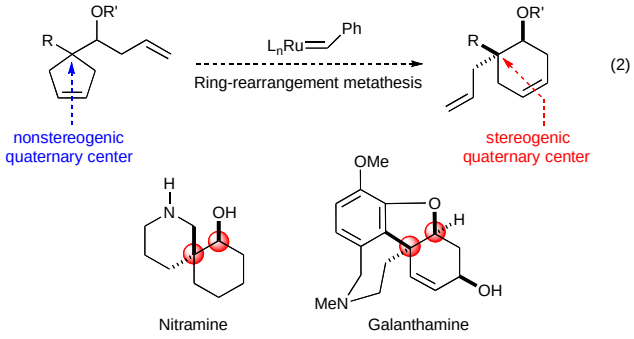
Introduction

Construction of all-carbon quaternary carbon centres is a significant challenge in organic chemistry. To address this issue, various methods have been developed, yet truly effective and general as well as readily executable user-friendly methods are still in demand. The *de novo* construction of quaternary centres with reagent-controlled stereo-induction under catalytic conditions is considered to be one of the most desirable strategies.[1] The palladium-catalyzed allylation reaction, developed independently by Trost[2] and Stoltz[3], is the state of the art technology of this approach (Eq 1).



(1)

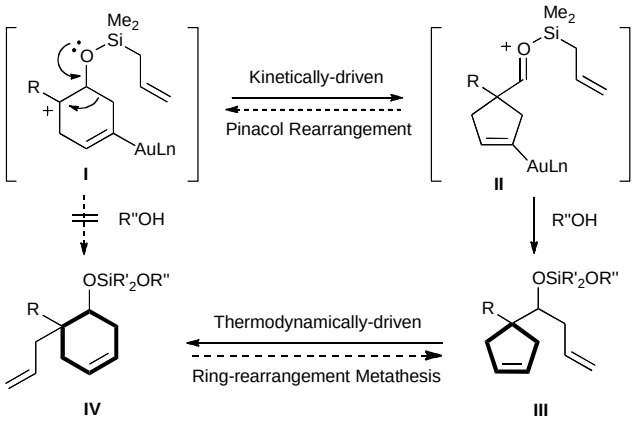
On the other hand, substrate-controlled relative stereo-induction utilizing an easily controllable and accessible stereogenic centre to create another stereogenic centre that is more difficult to establish by conventional methods, is another equally attractive strategy.[4] We envision that the merits of this approach could be readily explored utilizing a metathesis-based rearrangement of symmetric cyclopentene moiety to the corresponding cyclohexene derivatives, whereby setting the all-carbon quaternary stereogenic centre can be realized by the configuration of the secondary hydroxyl group (Eq 2). Conceptually, this approach not only complements the reagent-controlled stereo-induction but also has a significant merit in terms of installing two consecutive stereogenic centres and the extra unsaturation compared to that in Eq 1. The prowess of this approach would readily allow the synthesis of natural products such as nitramine and galanthamine.



(2)

While olefin metathesis has evolved to be a versatile and reliable tool for carbon-carbon bond formation in modern organic synthesis, a subset of olefin metathesis called ring-rearrangement metathesis (RRM) has been developed by Blechert and co-workers.[5a] This is a useful technology that involves one or more ring-closing and ring-opening steps, usually converting one strained cyclic structure to a new cyclic product.[5] Many variants of RRM have been reported in the literature, and in some occasions, stereogenic all-carbon quaternary centres were created by RRM. In their insightful application of RRM, Koreeda and coworkers converted functionalized norbornene derivatives to a tricyclic system containing a quaternary carbon center.[6a] Phillips and Pfeiffer also nicely accommodated a RRM strategy in their total synthesis of cyanthiwigin U.[6b] An excellent example of RRM to form cyclohexene derivatives containing a silyloxy-substituted quaternary center has been reported by Hoveyda using a chiral Mo-alkylidene complex, however, the corresponding RRM to establish an all-carbon quaternary center is not reported.[6c]

RRM reaction is unique in its capacity to make connectivity change in carbon-based molecular frameworks, which is not possible by any other bond-breaking and bond-forming processes. Therefore the RRM of **III** to generate **IV** is a formal reversion of



Scheme 1. Ring-rearrangement metathesis–based connectivity change

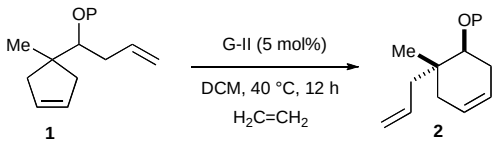
the connectivity change ensued in the ring contraction of cyclohexenyl cation **I** to the corresponding cyclopentenyl oxonium species **II** (Scheme 1).[7] As such, this RRM process indirectly overrides the kinetically-driven connectivity change of **I** to **II** by the counteraction of a thermodynamically-driven metathesis process. Given the characteristics of metathesis reaction, we envision that the higher reactivity of cyclopentene **III** than that of cyclohexene **IV** in their ring openings by Grubbs-type ruthenium alkylidenes would in theory result in depletion of **III** and accumulation of **IV**. More importantly, the stereochemistry of the all-carbon quaternary centre may be established diastereoselectively during the metathesis process by the influence of the stereogenic centre at the next carbon. Herein we describe an unprecedented diastereoselective RRM (*d*RRM) that effectively accomplish desymmetrization of cyclopentene moiety containing a nonstereogenic all-carbon quaternary centre. The utility and effectiveness of this RRM strategy was illustrated by the conversion of the resultant cyclohexene derivatives containing a stereogenic quaternary carbon centre to spiropiperidine alkaloid nitramine.

Results and Discussion

A. Diastereoselective ring-rearrangement metathesis (*d*RRM)

To explore the *d*RRM as a means to transform a cyclopentene derivative to the corresponding allyl-containing cyclohexene, phenoxydimethylsilyl protected cyclopentene **1f** was chosen as an initial test substrate because this compound could be easily prepared via gold-catalyzed isomerisation of the corresponding dimethylallylsilyl ether of 2-methyl-1-hexen-5-yn-3-ol followed by an intramolecular allyl trapping event.[7b] When **1f** was treated with a catalytic amount (5 mol%) of Grubbs second-generation catalyst in dichloromethane under ethylene gas,[8] a smooth transformation of **1f** to cyclohexene derivative **2f** occurred with a marginal level of diastereocontrol and conversion (Table 1, entry 6). We suspected that a right choice of hydroxy-protecting group would be important to achieve optimal conversion and diastereoselectivity. To establish a general trend, the protecting groups on cyclopentene derivatives **1** were systematically varied. Firstly, the parent compound **1a** without protecting group was examined but only low conversion to **2a**

Table 1. Diastereoselectivity in ring-rearrangement metathesis

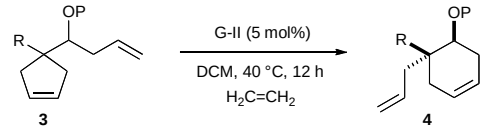


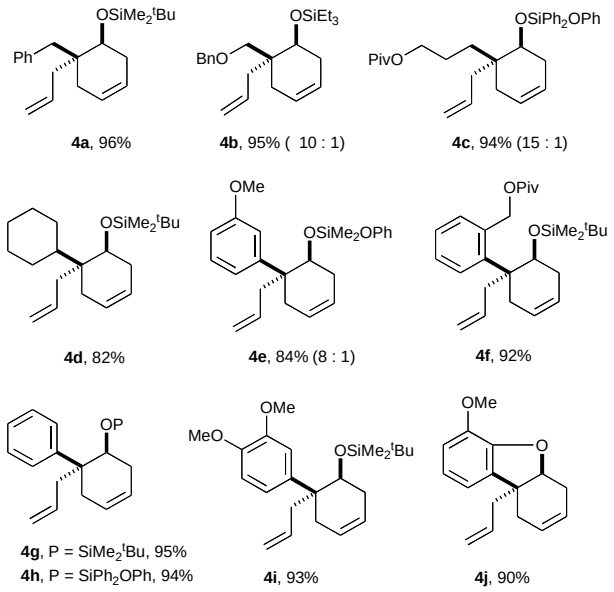
Entry	Substrate	P	Product	Selectivity	Conversion
1	**1a**	H	**2a**	1 : 1	low
2	**1b**	Ac	**2b**	1.3 : 1	low
3	**1c**	Et	**2c**	5 : 1	low
4	**1d**	^{i}Pr	**2d**	8 : 1	complete[a]
5	**1e**	$SiMe_3$	**2e**	2.5 : 1	complete
6	**1f**	$SiMe_2OPh$	**2f**	2.7 : 1	low
7	**1g**	$SiEt_3$	**2g**	8 : 1	complete
8	**1h**	$SiMe_2{}^{t}Bu$	**2h**	10 : 1	complete[b]

[a]65% isolated yield. [b]89% isolated yield.

with low selectivity was observed (entry 1). Acetate derivative **1b** behaved similarly but with a slightly increased selectivity of **2b** (entry 2). Considering that the strong chelation of the hydroxyl (**1a**), acetoxy (**1b**) and phenoxy (**1f**) group to the propagating ruthenium alkylidene species might be the cause of the low conversion, simpler alkyl and silyl group-containing substrates were explored (**1c**–**e**, **1g**, **1h**). Gratifyingly, complete conversion

Table 2. Scope of diastereoselective ring-rearrangement metathesis

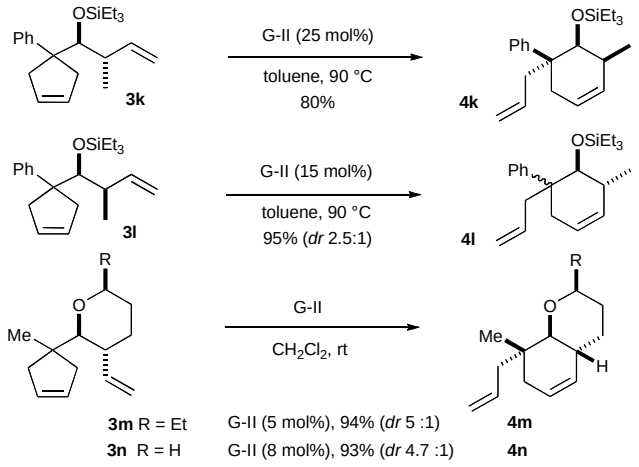




was achieved with these substrates except **1c** (entries 3–5, 7 and 8). The conversion and diastereoselectivity seem to depend on the size of the protecting groups on the oxygen such that the higher conversion and selectivity was achieved with sterically larger alkyl and silyl group. Among the tried, *tert*-butyldimethylsilyl group was found to be the optimal protecting group that yielded cyclohexene product **2h** in ≥10:1 diastereomeric ratio with complete conversion (entry 8).[9]

Next, we examined the substrate scope of this diastereoselective ring-rearrangement metathesis (*d*RRM) with different substituents at the quaternary carbon center (Table 2). The substrates were prepared by allylation/protection of the corresponding cyclopentene carboxaldehydes, which were obtained from either 2-aryl/alkyl substituted acrolein in 2 steps[7] or 2-arylacetic acid in 4 steps (see supporting information for details). With substrates **3a–j** containing more functionalized alkyl and aryl substituents compared to methyl in **1a–h**, good to excellent yields and diastereoselectivities for various cyclohexene derivatives **4a–j** were realized. Notably, higher diastereoselectivity was observed from substrates that contain an aryl group at the quaternary carbon (**4f–i**). In case of spirocyclic substrate **3j** with a fused aromatic moiety, only the *cis*-ring junction isomer **4j** was obtained in an excellent yield, which is the carbon backbone of many natural products including galanthamine. One salient feature of these processes is the lack of metathetic dimer formation once the products are generated.

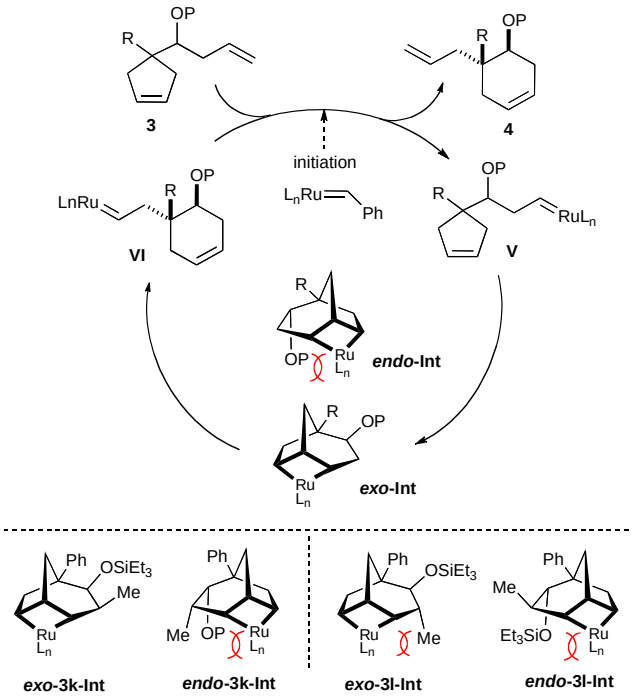
The RRM behavior of substrates containing multiple stereogenic centers was also examined (Scheme 2). For the diastereomeic substrates **3k** and **3l**, the RRM of the former provided a sole product **4k** in 80% yield whereas that of **3l** afforded **4l** in quantitative yield but with only 2.5:1 diastereoselectivity. Bicyclic substrates **3m** and **3n**[7b] with the relative 1,2-stereochemistry similar to that of **3l** underwent a smooth metathesis at room temperature to yield **4m** and **4n** in high yields with moderate diastereoselectivities. It is worthy of mentioning the reactivity difference of **3k**/**3l** versus **3m**/**3n**, where the former requires much harsher conditions (90 °C in toluene) than the latter (room temperature in CH_2Cl_2).



Scheme 2. *d*RRM of substrates with multiple stereogenic centers

B. Mechanism and diastereoselectivity

We propose that the current RRM catalytic cycle commences with the formation of a propagating ruthenium alkylidene intermediate **V** (Scheme 3). A ring-closing and ring-opening metathesis of the alkylidene moiety of **V** with the symmetrical endocyclic double bond would generate a structurally reorganized new ruthenium alkylidene **VI**. The diastereotopic facial differentiation of the double bond is made via the formation of metallacyclobutane intermediates ***exo*-Int** and ***endo*-Int**.



Scheme 3. Proposed catalytic cycle for *d*RRM

The main difference between these two intermediates is the orientation of the alkoxy substituent, which would suffer from a greater steric strain in the ***endo*-Int** intermediate relative to that in the ***exo*-Int**. This rationale corroborates the observed selectivity trend where the sterically larger alkoxy group provided higher diastereoselectivity. Once formed, intermediate **VI** undergoes an alkylidene exchange with another substrate, delivering the final product **4**, and the catalyst reinitiates a new catalytic cycle.

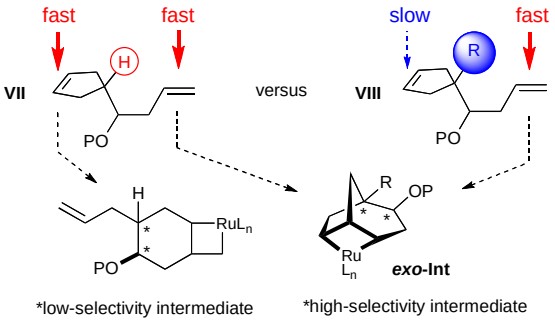
In case when there are two substituents in the alkenyl tether such as in substrates **3k–n**, the relative 1,2-stereochemistry could be reinforcing or interfering. For example, substrate **3k** leads to intermediates ***exo*-3k-Int** more favorably than ***endo*-3k-Int**, because the former has both the alkoxy and methyl substituents in sterically less congested *exo*-face as opposed to both in more congested *endo*-face in the latter. Therefore, the final product **4k** should be engendered via only the energetically more favorable intermediate ***exo*-3k-Int**. On the other hand, substrate **3l** will lead to both ***exo*-3l-Int** and ***endo*-3l-Int**, where one of the substituents is in *exo*-face and the other is in *endo*-face. The energy difference between these two intermediates would not be so substantial that product **4l** formed only in 2.5:1 ratio of diastereomers. Although the 1,2-stereochemical relationships in **3m** and **3n** are identical to

that of **3l**, the cyclic nature of the 1,2-vicinal substituents could make more pronounced differentiation between the energy of the *endo*- and *exo*-intermediates, leading to increased selectivity in **4m** and **4n**.

In 2006, Blechert and cowokers reported a related RRM process of cyclopentene derivative **VII** with a tertiary carbon centre at the branch point of the alkenyl group (Figure 1). Although the RRM product was obtained from this substrate (P = TBDMS) in excellent yield, the diastereoselectivity was low (2:1).[5a] To justify these outcomes, the authors proposed that the metathesis was initiated both at the pendant alkene and endocyclic double bond in **VII**.[5b]

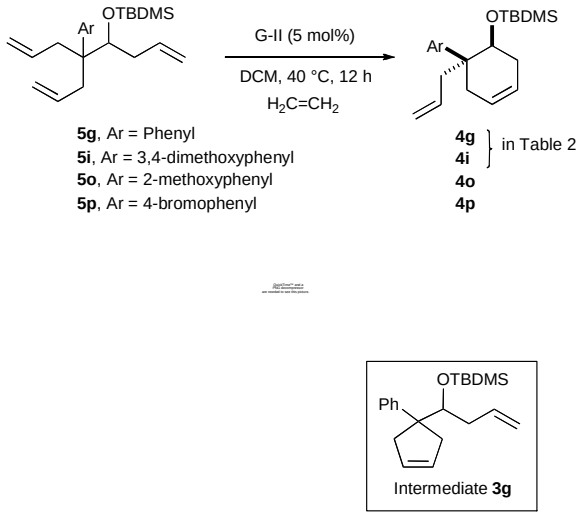
It is quite surprising that the RRM of **VII** and **VIII** shows such a stark difference in its diastereoselectivity despite their structural similarity. To reconcile these perplexing behaviours, we hypothesized that R group at the quaternary carbon center in **VIII** should play a crucial role for the observed high diastereoselectivity. As opposed to the two possible initiation events with Blechert substrate **VII**, leading to both the low and high-selectivity intermediates, the sterically demanding R group in substrate **VIII** prevents the initiation at the endocyclic double bond, rendering only the initiation at the pendant alkene possible, which ultimately lead to the high-selectivity intermediate (***exo*-Int**). It is obvious that the energy difference between the two bicyclic diastereomeric intermediates derived from the initiation at the endocyclic double bond will be smaller compared to that between the two intermediates ***exo*-Int** and ***endo*-Int** originated from the initiation at the pendant alkene. Currently, we don't have any evidence to completely rule out the possibility of initiation from the endocyclic double. However, even with this initiation event, the final outcome will not be altered because the incipient alkylidene species would undergo ring-closing metathesis to regenerate the cyclopentene much faster than to form cyclohexene product.[10]

Figure 1. Possible role of the quaternary R group in metathesis



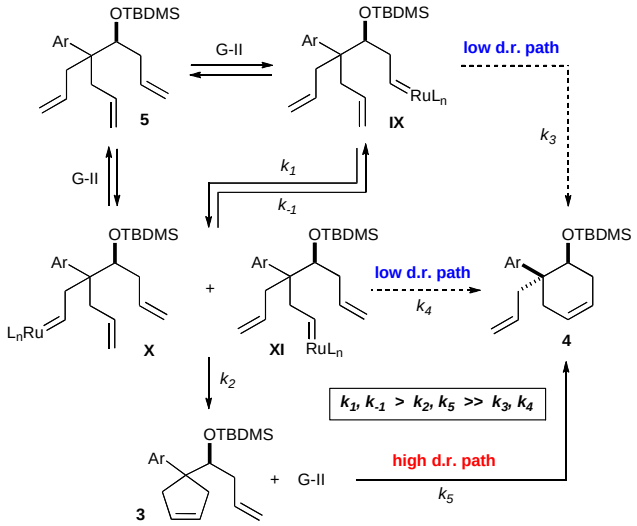
C. Metathesis of acyclic substrates containing three terminal alkenes

To further elucidate the origin of the observed diastereoselecitivity with substrate **3**, ring-closing metathesis (RCM) of the corresponding acyclic counterpart **5** was investigated (Scheme 4). Not surprisingly, when **5g**, **5i**, **5o**, and **5p** were subjected to the typical metathesis conditions product **4g**, **4i**, **4o**, and **4p** were obtained with the same level of efficiency and selectivity as the corresponding RRM of substrate **3**. A careful monitoring of the metathesis process of **5g** by ^{1}H NMR revealed the accumulation of an intermediate at the early stage, which then slowly disappeared while the product steadily increased. The characteristic ^{1}H NMR signature of the intermediate could be assigned to that of **3g**.



Scheme 4. Ring-closing metathesis of acyclic triene substrates

On the basis of this observation, we formulated an overall mechanistic picture as depicted in Scheme 5. We surmise that the initiation of ring-closing metathesis starts with any one of the three terminal alkenes in **5** with equal probability to form **IX** as well as two diastereomeric intermediates **X**, and **XI**. While these initially formed intermediates are in an equilibrium of rapid alkylidene exchanges (k_1 k_{-1} > k_2, k_5 >> k_3, k_4), the kinetically favourable ring-closure to form 5-membered ring occurs much faster than that of the 6-membered counterpart (k_2 >> k_3, k_4), draining the equilibrium down to the observed intermediate **3**. Once the concentration of **3** reached to a certain level, the highly diastereoselective RRM manifold starts to operate via a kinetically favorable initiation from only the terminal double bond, delivering the final product **4** with the observed selectivity.



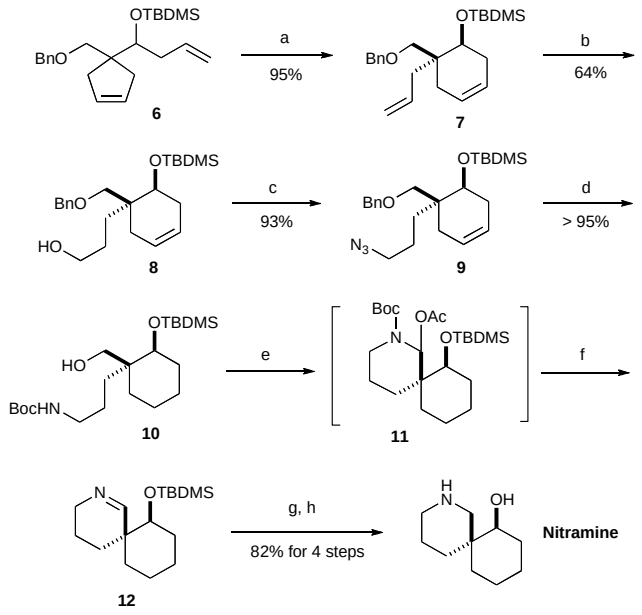
Scheme 5. Mechanistic rationale for the metathesis of acyclic substrates

D. Application of *d*RRM to a total synthesis of (±)-nitramine

Nitramine, a naturally occurring spiropiperidine alkaloid isolated from plants of the *Nitraria* genus, has a 2-azaspiro-[5,5]-undecanol structure.[11,12] Its structure closely resembles the molecular framework of the neurophysiologically important histrionicotoxin alkaloids.[13]

To illustrate the prowess of the newly developed highly diastereoselective *d*RRM reaction, a concise strategy for a total synthesis of nitramine was developed (Scheme 6). One of the main challenges in the synthesis of nitramine is the installation of quaternary carbon center with a correct stereochemistry relative to the secondary hydroxyl group at the next carbon.

The synthesis commenced with LAH reduction of commercially available dimethyl cyclopent-3-ene-1,1-dicarboxylate followed by monoprotection and a sequential Swern oxidation,[14] allylation and TBDMS protection, providing the RRM substrate **6**.[15] As expected, metathesis of diene **6** smoothly afforded the desired diastereomer **7** in 95% yield and high diastereoselectivity (>20:1). Subsequent hydroboration-oxidation[16] afforded advanced intermediate **8**. Several ring-closure strategies including S_N2, double S_N2 and double reductive amination, were not fruitful. Alternatively, **8** was transformed to the corresponding azide **9** under Mitsunobu reaction condition,[17] which was then subjected to hydrogenation conditions to delivered **10** in almost quantitative yield after Boc protection. Oxidation of the primary hydroxyl group of **10** with Dess-Martin periodinane[18] induced a spontaneous cyclization with concomitant incorporation of acetoxy group, providing bicyclic intermediate **11**. Treatment of **11** with TFA resulted in a cyclic imine **12**, which was reduced and desilylated to deliver the target natural product nitramine.



Scheme 6. Total synthesis of (±)-nitramine. *Reagents and conditions*: (a) Grubbs second-generation catalyst (4 mol%), CH_2Cl_2, $H_2C{=}CH_2$, rt, 95%; (b) 9-BBN, then $NaOH/H_2O_2$, 64%; (c) DEAD, PPh_3, DPPA, THF, 93%; (d) 10% Pd/C, H_2, $(Boc)_2O$, EtOAc, >95%; (e) Dess-Martin periodinane, $NaHCO_3$, CH_2Cl_2; (f) TFA, CH_2Cl_2; (g) $NaBH_4$, MeOH; (h) NH_4F, MeOH, 82% over four steps.

Conclusions

In summary, we have developed a highly diastereoselective ring-rearrangement metathesis of cyclopentene derivatives. This metathesis-based strategy to set up the stereochemistry at a non-stereogenic quaternary carboncenter provides an efficient entry to the synthesis of cyclohexene skeleton containing an all carbon quaternary stereogenic center. We also found that the same cyclohexene skeleton could be constructed through an alternative metathesis process starting from acyclic trienes. The effectiveness of *d*RRM reaction was illustrated in a concise stereocontrolled total synthesis of (±)-nitramine. The scope and utility of this diastereoselective metathesis will be further explored for the synthesis of other natural product targets.

Acknowledgements

The authors thank Xiaoguang Liu for preparation and characterization of compounds **3f** and **4f**. Mass Spectrometry Laboratory at the University of Illinois, Urbana-Champaign, is greatly acknowledged for acquisition of high resolution mass spectrometry data.

Notes and references

Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, IL60607, USA. E-mail: dsunglee@uic.edu, Homepage: http://www.chem.uic.edu/leegroup/index.html

† Electronic Supplementary Information (ESI) available: Experimental procedures and characterization data for new compounds are provided. See DOI: 10.1039/b000000x/

1 For reviews on the catalytic formation of quaternary stereocenters, see: (a) P. G. Cozzi, R. Hilgraf, N. Zimmermann, *Eur. J. Org. Chem.*, 2007, 5969; (b) B. M. Trost, C. Jiang, *Synthesis*, 2006, 369; (c)

Quaternary Stereocenters: Challenges and Solutions for Organic Synthesis Eds. J. Christoffers and A. Baro, Wiley-VCH, Weinheim, 2005; (d) J. Christoffers, A. Baro, *Adv. Synth. Catal.*, 2005, **347**, 1473; (e) C. J. Douglas, L. E. Overman, *Proc. Natl. Acad. Sci. USA,* 2004, **101**, 5363; (f) I. Denissova, L. Barriault, *Tetrahedron,* 2003, **59**, 10105; (g) J. Christoffers, A. Mann, *Angew. Chem., Int. Ed.*, 2001, **40**, 4591; (h) M. Sannigrahi, *Tetrahedron,* 1999, **55**, 9007; (i) E. J. Corey, A. Guzman-Perez, *Angew. Chem., Int. Ed.*, 1998, **37**, 388; (j) K. Fuji, *Chem. Rev.*, 1993, **93**, 2037; (k) S. F. Martin, *Tetrahedron,* 1980, **36**, 419.

2 (a) B. M. Trost, B. Schäffner, M. Osipov, D. A. A. Wilton, *Angew. Chem., Int. Ed.*, 2011, **50**, 3548; (b) B. M. Trost, R. N. Bream, J. Xu, *Angew. Chem., Int. Ed.*, 2006, **45**, 3109.

3 (a) D. C. Behenna, Y. Liu, T. Yurino, J. Kim, D. E. White, S. C. Virgil, B. M. Stoltz, *Nature Chem.*, 2012, **4**, 130; (b) D. C. Behenna, J. T. Mohr, N. H. Sherden, S. C. Marinescu, A. M. Harned, K. Tani, M. Seto, S. Ma, Z. Novák, M. R. Krout, R. M. McFadden, J. L. Roizen, J. A. Enquist Jr., D. E. White, S. R. Levine, K. V. Petrova, A. Iwashita, S. C. Virgil, B. M. Stoltz, *Chem.–Eur. J.*, 2011, **17**, 14199; (c) J. T. Mohr, M. R. Krout, B. M. Stoltz. *Org. Synth.,* 2009, **86**, 194; (d) J. T. Mohr, B. M. Stoltz. *Chem.–Asian J.,* 2007, **2**, 1476; (e) J. T. Mohr, D. C. Behenna, A. M. Harned, B. M. Stoltz. *Angew. Chem., Int. Ed.,* 2005, **44**, 6924; (f) D. C. Behenna, B. M. Stoltz. *J. Am. Chem. Soc.,* 2004, **126**, 15044.

4 Selected examples: (a) D. A. Evans, M. J. Dart, J. L. Duffy, M. G. Yang, *J. Am. Chem. Soc*., 1996, **118**, 4322; (b) J. S. Panek, P. F. Cirillo, *J. Am. Chem. Soc*., 1990, **112**, 4873; (c) E. Vedejs, W. H. Dent III, *J. Am. Chem. Soc*., 1989, **111**, 6861; (d) K. N. Houk, M. N. Paddon-Row, N. G. Rondan, Y.-D. Wu, F. K. Brwon, D. C. Spellmeyer, J. T. Metz, Y. Li, R. J. Loncharich, *Science,* 1986, **231**, 1108; (e) M. T. Reetz, K. Kesseler, A. Jung, *Tetrahedron Lett.,* 1984, **25**, 729; (f) N. T. Anh, *Top. Curr. Chem*., 1980, **88**, 146; (g) J. Huet, Y. Maroni-Barnaud, N. T. Anh, J. Seyden-Penne, *Tetrahedron Lett*., 1976, **155**, 159; (h) V. Prelog, *Helv. Chim. Acta*., 1953, **36**, 308; (i) D. J. Cram, F. A. Elhafez, *J. Am. Chem. Soc*., 1952, **74**, 5828.

5 (a) V. Bçhrsch, J. Neidhçfer, S. Blechert, *Angew. Chem., Int. Ed.,* 2006, **45**, 1302; (b) N. Holub, S. Blechert, *Chem.–Asian J.,* 2007, **2**, 1064; Recent RRM examples: (c) F. Gao, C. T. M. Stamp, P. D. Thornton, T. S. Cameron, L. E. Doyle, D. O. Miller, D. J. Burnell, *Chem. Commun*., 2012, **48**, 233; (d) J. Mandel, N. Dubois, M. Neuburger, N. Blanchard, *Chem. Commun*., 2011, **47**, 10284; (e) G. Vincent, C. Kouklovsky, *Chem.–Eur. J*., 2011, **17**, 2972; (f) J. Carreras, A. Avenoza, J. H. Busto, J. M. Peregrina, *J. Org. Chem*., 2011, **76**, 3381; (g) M. Donnard, T. Tschamber, D. Le Nouën, S. Desrat, ,K. Hinsinger, J. Eustache, *Tetrahedron*, 2011, **67**, 339.

6 (a) J. Holtsclaw, M. Koreeda, *Org. Lett*., 2004, **6**, 3719; (b) M. W. B. Pfeiffer, A. J. Phillips, *J. Am. Chem. Soc*., 2005, **127**, 5334; (c) X. Teng, D. R. Cefalo, R. R. Schrock, A. H. Hoveyda, *J. Am. Chem. Soc*., 2002, **124**, 10779.

7 (a) S. F. Kirsch, J. T. Binder, A. Duschek, T. T. Haug, C. Liébert, H. Menz, *Angew. Chem., Int. Ed.*, 2007 **46**, 2310; (b) J. Li, X. Liu, D. Lee, *Org. Lett.*, 2012, **14**, 410.

8 The effect of ethylene in ring size-selective RCM, see: K. Yoshida, Y. Kano, H. Takahashi, A. Yanagisawa, *Adv. Synth. Catal*., 2011, **353**, 1229.

9 The relative configurations were assigned by NOESY experiment and further confirmed by total synthesis of (±)-nitramine.

10 (a) Y. J. Kim, J. B. Grimm, D. Lee, *Tetrahedron Lett.*, 2007, **48**, 7961; A recent review on the Thorpe-Ingold effect, see: (b) M. E. Jung, G. Piizzi, *Chem. Rev.*, 2005, **105**, 1735.

11 N. Y. Novgorodova, S. K. Maekh, S. Y. Yunusov, *Chem. Nat. Prod*., 1973, **9**, 191.

12 Total syntheses of nitramine: (a) L. H. Hellberg, C. Beeson, R. Somanathan, C. de Graduados, *Tetrahedron Lett*., 1986, **27**, 3955; (b) P. J. McCloskey, A. G. Schultz, *Heterocycles,* 1987, **25**, 437; (c) D. Tanner, H. M. He, *Tetrahedron*, 1989, **45**, 4309; (d) T. Imanishi, T. Kurumada, N. Maezaki, K. Sugiyama, C. Iwata, *J. Chem. Soc., Chem. Commun*., 1991, 1409; (e) M. J. Wanner, G.-J. Koomen, *Tetrahedron Lett*., 1992, **48**, 3935; (f) B. Westermann, H. G. Scharmann, I. Kortmann, *Tetrahedron: Asymmetry,* 1993, **4**, 2119; (g) M. Keppens, N. De Kimpe, *J. Org. Chem*., 1995, **60**, 3916; (h) T. Yamane, K. Ogasawara, *Synlett,* 1996, 925; (i) B. M. Trost, R. Radinov, E. M. Grenzer, *J. Am. Chem. Soc*., 1997, **119**, 7879; (j) A. Deyine, J.-M. Poirier, L. Duhamel, P. Duhamel, *Tetrahedron Lett*., 2005, **46**, 2491. (k) E. R. Alonso, K. A. Tehrani, M. Boelens, N. de Kimpe, *Synlett,* 2005, 1726; (l) G. Pandey, P. Kumara C, S. K. Burugu, V. G. Puranik, *Eur. J. Org. Chem*., 2011, 7372.

13 J. W. Daly, *Proc. Natl. Acad. Sci. USA*, 1995, **92**, 9.

14 A. J. Mancuso, D. S. Brownfain, D. Swern, *J. Org. Chem*., 1978, **43**, 2480.

15 See the supporting information for details on the preparation of RRM substrate **6**.

16 H. C. Brown, G. Zweifel, *J. Am. Chem. Soc*., 1959, **81**, 247; (b) E. F. Knights, H. C. Brown, *J. Am. Chem. Soc*., 1968, **90**, 5281.

17 Y. Yoshimura, K. Kitano, K. Yamada, H. Satoh, M. Watanabe, S. Miura, S. Sakata, T. Sasaki, A. Matsuda, *J. Org. Chem.*, 1997, **62**, 3140.

18 (a) D. B. Dess, J. C. Martin, *J. Am. Chem. Soc*., 1991, **113**, 7277; (b) R. K. Boeckman, Jr., P. Shao, J. J. Mullins, *Org. Syn*., 2000, **77**, 141.

A highly diastereoselective ring-rearrangement metathesis of cyclopentene derivatives to set an all-carbon quaternary centre is developed.