Organic &
Biomolecular Chemistry

ROYAL SOCIETY
OF CHEMISTRY

PAPER

View Article Online
View Journal | View Issue

Check for updates

Cite this: *Org. Biomol. Chem.*, 2020, **18**, 1760

Ruthenium-catalysed cyclisation reactions of 1,11-dien-6-ynes leading to biindenes†

Takanori Matsuda * and Naoto Yonekubo

Received 28th January 2020,
Accepted 15th February 2020

DOI: 10.1039/d0ob00179a

rsc.li/obc

1,2-Bis(2-allylphenyl)ethynes undergo cycloisomerisation reactions in the presence of Cp*Ru(II) catalysts to produce 2,2′-dimethyl-3*H*,3′*H*-1,1′-biindenes. On the other hand, tandem ring-closing metathesis of 1,2-bis(2-allylphenyl)ethynes using the Hoveyda–Grubbs 2nd generation catalyst led to the formation of 2,2′-unsubstituted biindenes. Various symmetrical and unsymmetrical bicyclic dienes were prepared by these ruthenium-based cyclisation methods.

Introduction

3*H*,3′*H*-1,1′-Biindenes have previously been prepared by the oxidative homocouplings of (1*H*-inden-1-yl)lithiums to yield diastereomeric mixtures of 1*H*,1′*H*-1,1′-biindenes, followed by base-promoted double bond isomerisation.[1] There are fewer than fifty known biindenes, and some of them have been used as ligands for transition metals,[2] while a biindene-derived diol has been used as a chiral ligand in the titanium(IV)-catalysed enantioselective additions of diethylzinc to aldehydes.[3]

Transition-metal-catalysed cycloisomerisation reactions of enynes are powerful tools for the synthesis of various carbo- and heterocyclic compounds.[4] This method allows for the rapid atom-economical construction of a complex cyclic structure from a linear substrate. The ring-closing metathesis (RCM) of dienes and enynes revolutionised the way in which cycloalkenes are assembled, and has been extremely useful in modern organic synthesis.[5] Herein, we report that 1,11-dien-6-ynes can undergo both cycloisomerisation and tandem RCM reactions catalysed by ruthenium complexes. Notably, these reactions are used to prepare 1,1′-biindenes from 1,2-bis(2-allylphenyl)ethynes.

Results and discussion

When 1,2-bis(2-allylphenyl)ethyne (**1a**)[6] was heated at 60 °C in EtOH in the presence of 5 mol% $CpRuCl(PPh_3)_2$ for 24 h, it cycloisomerised to afford 2,2′-dimethyl-3*H*,3′*H*-1,1′-biindene (**2a**) in 21% yield (Table 1, entry 1). The use of $Cp^*RuCl(PPh_3)_2$ improved the yield of **2a** to 45% (entry 2), while the reaction in the presence of Cp*RuCl(cod) afforded **2a** in 34% yield (entry 3). The use of a cationic ruthenium catalyst generated *in situ* from Cp*RuCl(cod) and $NaPF_6$ gave **2a** in 55% yield (entry 4); indeed, preformed cationic $[Cp^*Ru(MeCN)_3]PF_6$ exhibited comparable activity (entry 5). The effect of the phosphine ligand was next examined; **2a** was formed in 38% yield when the Cp*RuCl(cod)–BINAP catalyst system was used (entry 6); however, use of $P(C_6F_5)_3$ increased the yield of **2a** to 61%, together with a 24% yield of the [2 + 2 + 2] cycloadduct **3a** (entry 7).[7,8] The reaction performed in MeOH in the presence of Cp*RuCl(cod)–$P(C_6F_5)_3$ furnished **2a** in 85% isolated yield without any noticeable amount of **3a** (entry 8). A similar result was obtained when the reaction was performed at 40 °C (entry 9). Interestingly, the reaction delivered cycloadduct **3a** as the major product when performed in *i*-PrOH (entries 10 and 11).[9]

With the optimised reaction conditions in hand, various diallyl diphenylacetylenes **1b–l** bearing substituents on their benzene rings were subjected to the ruthenium-catalysed cycloisomerisation conditions (Table 2). The reaction of 1,2-bis(2-allyl-4-methylphenyl)ethyne (**1b**) afforded tetramethylbiindene **2b** in 67% yield (entry 1), whereas symmetrical dienynes **1c** and **1d** bearing methyl or methoxy groups the 5 positions of their benzene rings afforded **2c** and **2d**, respectively, in good yields (entries 2 and 3). In contrast, the reactions of chloro- and trifluoromethyl-substituted dienynes **1e** and **1f** formed the [2 + 2 + 2] cycloadducts **3** as major products under the standard conditions (**1e**: **2e** 24% + **3e** 41%; **1f**: **3f** 87%). The cycloisomerisation products from **1e** and **1f** were obtained as the major products in yields of 44% and 29%, respectively, when the reaction was performed with $[Cp^*Ru(MeCN)_3]PF_6$ (entries 4 and 5). The naphthalene derivative **1g** was also converted into the corresponding product **2g** (entry 6), while unsymmetrically substituted biindenes **2h–l** were similarly prepared by cycloisomerising dienynes **1h–l** (entries 7–11).

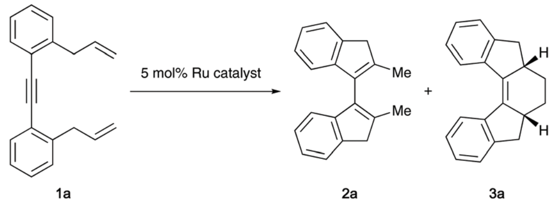
The cycloisomerisation conditions were successfully applied to dienyne **1m** devoid of *o*-phenylene tethers, which

---

Department of Applied Chemistry, Tokyo University of Science, 1-3 Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan. E-mail: mtd@rs.tus.ac.jp

† Electronic supplementary information (ESI) available: Experimental procedures and characterisation data for new compounds. See DOI: 10.1039/d0ob00179a

Table 1 Ruthenium-catalysed cycloisomerisation of 1,2-bis(2-allylphenyl)ethyne (**1a**)[a]



Entry	Ru catalyst	Ligand (mol%)	Additive	Solvent	Temp. (°C)	Time (h)	Yield[b] (%) of **2a**	Yield[b] (%) of **3a**
1	$CpRuCl(PPh_3)_2$	—	—	EtOH	60	24	21	
2	$Cp^*RuCl(PPh_3)_2$	—	—	EtOH	60	4	45	
3	Cp*RuCl(cod)	—	—	EtOH	60	24	34	
4	Cp*RuCl(cod)	—	$NaPF_6$	EtOH	60	24	55	
5	$[Cp^*Ru(MeCN)_3]PF_6$	—	—	EtOH	60	12	56	
6	Cp*RuCl(cod)	*rac*-BINAP (5)	—	EtOH	60	24	38	
7	Cp*RuCl(cod)	$P(C_6F_5)_3$ (10)	—	EtOH	60	24	61	24
8	Cp*RuCl(cod)	$P(C_6F_5)_3$ (10)	—	MeOH	60	24	85	
9	Cp*RuCl(cod)	$P(C_6F_5)_3$ (10)	—	MeOH	40	24	87	
10	Cp*RuCl(cod)	$P(C_6F_5)_3$ (10)	—	*i*-PrOH	60	24	11	55
11	Cp*RuCl(cod)	$P(C_6F_5)_3$ (10)		*i*-PrOH	40	24	14	75

[a] Reaction conditions: **1a** (0.050 mmol), ruthenium catalyst (2.5 μmol, 5 mol%), ligand (Ru : P = 1 : 2), solvent (0.5 mL, 0.1 M). [b] Isolated yield.

led to the formation of 1,1′-bicyclopentene **2m** in 82% yield in the presence of $[Cp^*Ru(MeCN)_3]PF_6$ (Scheme 1, (a)). The alternative cycloisomerisation product **4m** was obtained in 55% yield when **1m** was reacted at 0 °C (Scheme 1, (b)).[10,11] Heating **4m** in the presence of the ruthenium catalyst gave **2m** in 49% yield, but no isomerisation was observed in the absence of the ruthenium catalyst. Based on these results as well as previous studies, we conclude that 2-methylene-1,1′-bi(cyclopentylidene) **4m** is the initial cycloisomerisation product, and that **4m** is also catalytically isomerised to **2m** by the ruthenium catalyst.

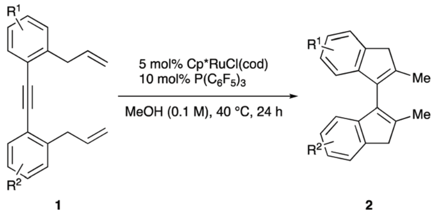
Two possible reaction pathways can be proposed for the ruthenium-catalysed cycloisomerisation of 1,11-dien-6-yne **1** (Scheme 2). Path (a) involves the formation of a hydroruthenium species from the catalyst and MeOH,[12] a Markovnikov hydroruthenation to the C═C bond of **1** to form **A**, consecutive carboruthenation (through **B** to **C**), β-hydride elimination that releases **4**, and the final double bond isomerisation of **4** to afford product **2**. On the other hand, in path (b), dienyne **1** first undergoes oxidative cyclisation on ruthenium to generate the ruthenacyclopentene species **D**. The unreacted alkene moiety in **D** then inserts into the Ru–C(sp^2) bond to give the ruthenacycloheptene intermediate **E**. Subsequent β-hydride elimination (to form **F**) followed by reductive elimination yields **4**, which then isomerises to **2** catalysed by a hydroruthenium species. Alternatively, β-hydride elimination from **D** generates alkenylruthenium hydride **G**, which also leads to **4** through intramolecular carboruthenation (to **F**) or hydroruthenation (to **H**). Reductive elimination from intermediate **E** is possible, which gives rise to the [2 + 2 + 2] cycloadduct **3**.

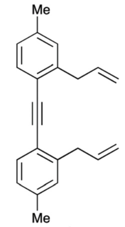
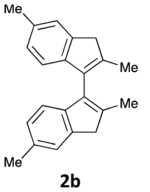
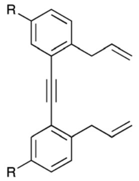
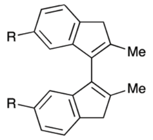
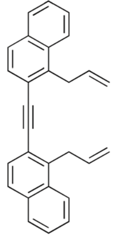
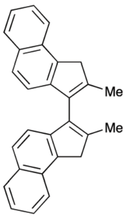
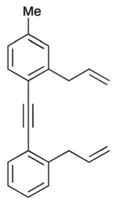
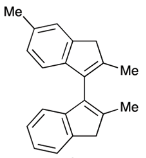
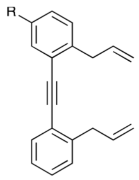
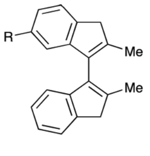
Dienyne **1n** or **1o**, in which one allyl group is replaced with a crotyl or a methallyl group, was found to be unreactive toward cycloisomerisation, which reveals that the reaction is limited to dienynes with unsubstituted C═C double bonds (Chart 1). Moreover, 1,2-bis[2-(vinyloxy)phenyl]ethyne (**1p**) also failed to react, and a complex mixture of products was obtained when unsymmetrical dienyne **1q**, bearing malonate and *o*-phenylene tethers, was reacted.[13]

We have been interested in the catalytic syntheses of silole derivatives[14] and the cycloisomerisation of bis-silicon-bridged **1r** was envisaged as a method for the synthesis of a bi(1-silaindene).[15] However, the reaction of **1r** under conditions similar to those described above led to a totally different outcome: 1,1′,2,2′-tetrahydro-4,4′-bi(1-silanaphthalene) **5** was obtained in 43% yield as the sole product after full conversion of **1r** (Scheme 3). The silanaphthalene **5** may have formed through a stitching reaction mediated by a hydroruthenium species in a manner analogous to the path (a) in Scheme 2, but with initial anti-Markovnikov hydroruthenation.

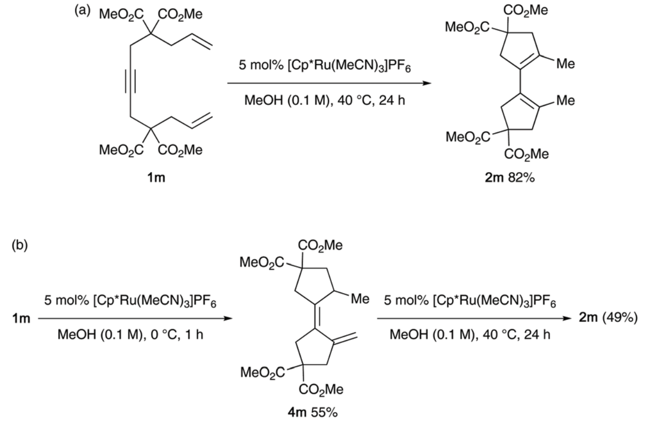
Tandem ring-closing metathesis (RCM) of 1,11-dien-6-ynes that form 1,1′-bicyclopentene derivatives has previously been studied,[16] but those of 1,2-bis(2-allylphenyl)ethynes have, to the best of our knowledge, never been examined. If allowed, this reaction provides a route to 3,3′*H*-1,1′-biindenes that lack substituents at their 2 and 2′ positions, which is complementary to the cycloisomerisation of **1**. Tandem RCM of **1a** in the presence of the Hoveyda–Grubbs 2nd generation catalyst at 100 °C in toluene (0.1 M) afforded the desired biindene **6a** in 60% yield (Table 3, entry 1). A lower concentration of **1a** resulted in an improved yield of **6a**, and 0.02 M was found to be optimal for the present reaction (entries 2 and 3). Other Grubbs catalysts were not suitable for this transformation (entries 4 and 5), while the reaction with 3 mol% catalyst gave a

Table 2 Cycloisomerisation of dienynes **1**

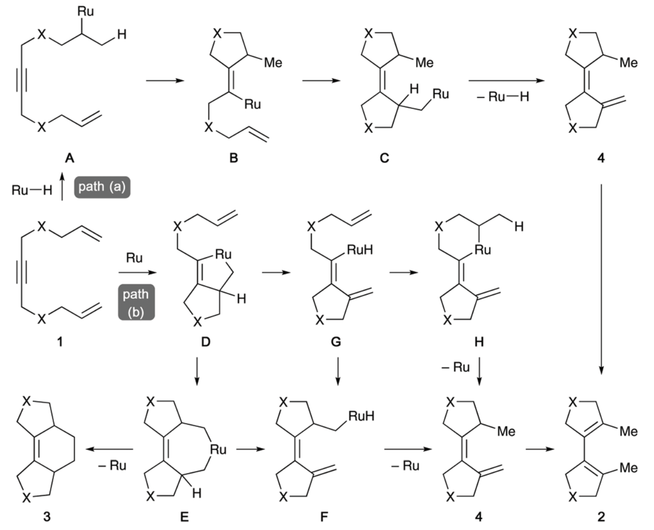


Entry	Dienyne **1**	Product **2**	Yield^a (%)
1	 **1b**	 **2b**	67
			
2	**1c** (R = Me)	**2c**	72
3	**1d** (R = OMe)	**2d**	63
4[b,c,d]	**1e** (R = Cl)	**2e**	44
5[b,d]	**1f** (R = CF_3)	**2f**	29
6[e]	 **1g**	 **2g**	39
7	 **1h**	 **2h**	90
			
8	**1i** (R = Me)	**2i**	86
9	**1j** (R = OMe)	**2j**	84
10[d]	**1k** (R = Cl)	**2k**	55
11[d]	**1l** (R = CF_3)	**2l**	45

[a] Isolated yield (average of two runs). [b] 5 mol% $[Cp^*Ru(MeCN)_3]PF_6$ was used as catalyst. [c] Reaction was performed at 60 °C. [d] The crude reaction mixtures contained byproducts such as **3**. [e] Reaction was performed at 80 °C in MeOH (0.05 M).



Scheme 1 Cycloisomerisation of **1m**.



Scheme 2 Possible reaction pathways for the cycloisomerisation of **1m** (X = $C(CO_2Me)_2$).

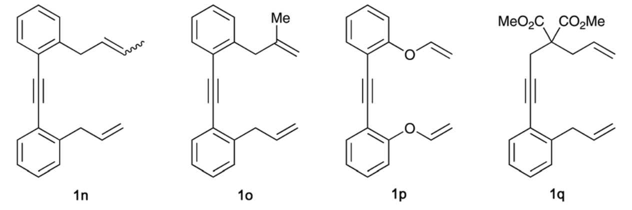
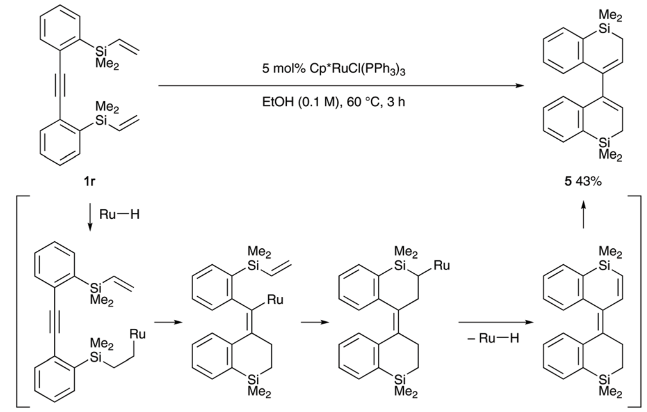


Chart 1 Dienynes that failed to undergo ruthenium-catalysed cycloisomerisation.

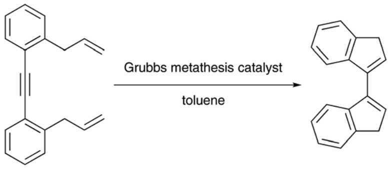
similar result (entry 6). As for the reaction temperature, 100 °C was found to be the best among those examined for the RCM of **1** (entries 6–8).

Various diallyl diphenylacetylenes **1b–l**, which were successfully cycloisomerised (*vide supra*), were examined under the RCM conditions (Table 4). Symmetrical (**1b–g**) and unsymme-



Scheme 3 Cycloisomerisation of **1r**.

Table 3 Tandem RCM of **1a**



Entry	Grubbs catalyst (mol%)	Conc. (M)	Temp. (°C)	Time (h)	Yield[a] (%)
1	Hoveyda–Grubbs 2nd cat. (5)	0.1	100	0.5	60
2	Hoveyda–Grubbs 2nd cat. (5)	0.04	100	1	67
3	Hoveyda–Grubbs 2nd cat. (5)	0.02	100	3	77
4	Grubbs 2nd cat. (5)	0.02	100	6	44
5	Stewart–Grubbs cat. (5)	0.02	100	6	26
6	Hoveyda–Grubbs cat. 2nd (3)	0.02	100	6	82
7	Hoveyda–Grubbs cat. 2nd (3)	0.02	90	6	67
8	Hoveyda–Grubbs cat. 2nd (3)	0.02	110	6	74

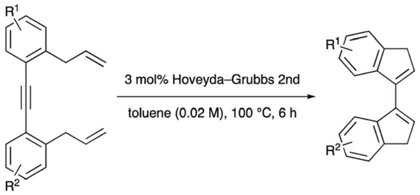
[a] Isolated yield.

trical (**1h–l**) dienynes were converted through tandem RCM into biindenes **6b–l** in yields ranging from 63% to 96%. Furthermore, dienynes **1o–q**, which failed to cycloisomerise, also reacted to afford the corresponding metathesis products **4o–q**, respectively, in good yields. However, the attempted tandem RCM of the bis-silicon-bridged **1r** resulted in no conversion under various metathesis conditions.

Conclusions

In conclusion, we developed ruthenium-catalysed cycloisomerisation and tandem-RCM methods for the synthesis of bicyclic conjugated dienes, in which two rings (cycloalkenes) are constructed. Cycloisomerisation of 1,11-dien-6-ynes afforded 2,2′-dimethyl-[1,1′-bi(cyclopentene)] derivatives catalysed by Cp*Ru. On the other hand, 2,2′-unsubsituted bicyclopentenes were prepared through the tandem RCM of 1,11-dien-6-ynes with the Hoveyda–Grubbs catalyst.[17]

Table 4 Tandem RCM of dienynes **1**



1 **6**

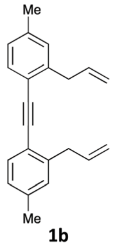
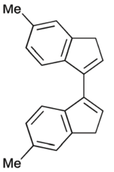
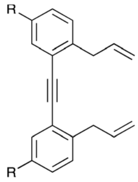
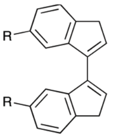
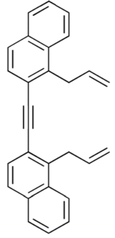
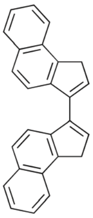
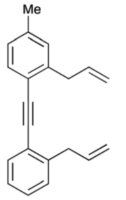
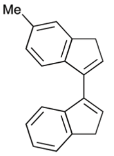
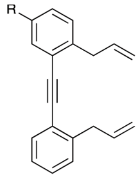
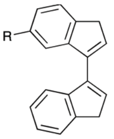
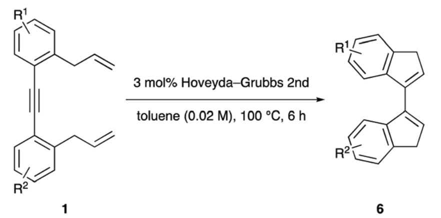
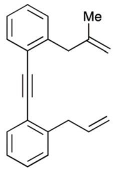
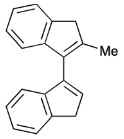
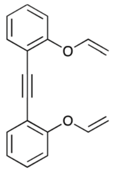
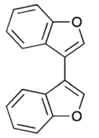
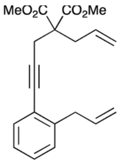
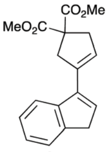
Entry	Dienyne **1**	Product **6**	Yield[a] (%)
1	 **1b**	 **6b**	74
			
2	**1c** (R = Me)	**6c**	86
3	**1d** (R = OMe)	**6d**	63
4	**1e** (R = Cl)	**6e**	96
5	**1f** (R = CF_3)	**6f**	83
6	 **1g**	 **6g**	68
7	 **1h**	 **6h**	90
			
8	**1i** (R = Me)	**6i**	77
9	**1j** (R = OMe)	**6j**	74
10	**1k** (R = Cl)	**6k**	80
11	**1l** (R = CF_3)	**6l**	85

Table 4 *(Contd.)*



Entry	Dienyne **1**	Product **6**	Yield[a] (%)
12	 **1o**	 **6o**	75
13	 **1p**	 **6p**	93
14	 **1q**	 **6q**	85

[a] Isolated yield (average of two runs).

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was supported by JSPS, Japan (Grant-in-Aid for Scientific Research (C) No. 16K05783).

Notes and references

1 P. Nicolet, J.-Y. Sanchez, A. Benaboura and M. J. M. Abadie, *Synthesis*, 1987, 202–203.

2 (*a*) T. R. Kelly and P. Meghani, *J. Org. Chem.*, 1990, **55**, 3684–3688; (*b*) R. C. Kerber and B. Waldbaum, *Organometallics*, 1995, **14**, 4742–4754; (*c*) B. R. Waldbaum and R. C. Kerber, *Inorg. Chim. Acta*, 1999, **291**, 109–126; (*d*) D. Tews and P. E. Gaede, *Organometallics*, 2001, **20**, 3869–3875.

3 X.-w. Yang, J.-h. Shen, C.-s. Da, H.-s. Wang, W. Su, D.-x. Liu, R. Wang, M. C. K. Choi and A. S. C. Chan, *Tetrahedron Lett.*, 2001, **42**, 6573–6575.

4 For recent reviews on transition-metal-catalysed cycloisomerisations, see: (*a*) C. Aubert, L. Fensterbank, P. Garcia, M. Malacria and A. Simonneau, *Chem. Rev.*, 2011, **111**, 1954–1993; (*b*) I. D. G. Watson and F. D. Toste, *Chem. Sci.*, 2012, **3**, 2899–2919; (*c*) Y. Yamamoto, *Chem. Rev.*, 2012, **112**, 4736–4769; (*d*) A. Marinetti, H. Jullien and A. Voituriez, *Chem. Soc. Rev.*, 2012, **41**, 4884–4908; (*e*) D.-H. Zhang, Z. Zhang and M. Shi, *Chem. Commun.*, 2012, **48**, 10271–10279; (*f*) D. P. Day and P. W. H. Chan, *Adv. Synth. Catal.*, 2016, **358**, 1368–1384; (*g*) C. I. Stathakizis and A. L. Zografos, *Nat. Prod. Rep.*, 2016, **33**, 1093–1117; (*h*) Y. Hu, M. Bai, Y. Yang and Q. Zhou, *Org. Chem. Front.*, 2017, **4**, 2256–2275.

5 *Handbook of Metathesis*, ed. R. H. Grubbs, Wiley-VCH, Weinheim, 2003, vol. 2.

6 Dienynes **1** were easily prepared by the Stille coupling of 1,2-bis(2-bromophenyl)ethynes with allyltributylstannane.

7 For ruthenium-catalysed [2 + 2 + 2] cycloaddition of 1,11-dien-6-ynes, see: (*a*) D. Tanaka, Y. Sato and M. Mori, *J. Am. Chem. Soc.*, 2007, **129**, 7730–7731. For the reaction catalysed by rhodium complexes, see: (*b*) H. Sagae, K. Noguchi, M. Hirano and K. Tanaka, *Chem. Commun.*, 2008, 3804–3806.

8 Results with other phosphine ligands (**2a**/**1a** + **3a**): PPh_3 (12%/30%); P(*c*-Hex)$_3$ (8%/38%); $P(OPh)_3$ (18%/69%); DPPE (6%/30%); DPPBZ (25%/62%).

9 The formation of a ruthenium hydride might be suppressed in *i*-PrOH in our case; hence the reaction is directed to proceed via the path (b) in Scheme 2. The results in other solvents are as follows: *t*-BuOH (**2a** not detected, **3a** 11%); no reaction in $(CF_3)_2CHOH$.

10 A similar cycloisomerisation catalysed by a rhodium(I) complex has been reported. D. S. Perekalin, N. V. Shvydkiy, Y. V. Nelyubina and A. R. Kudinov, *Chem. – Eur. J.*, 2015, **21**, 16344–16348. See alsoA. A. Suleymanov, D. V. Vasilyev, V. V. Novikov, Y. V. Nelyubina and D. S. Perekalin, *Beilstein J. Org. Chem.*, 2017, **13**, 639–643.

11 The corresponding double bond isomers were also detected when **1k** and **1l** were reacted in the presence of $[Cp^*Ru(MeCN)_3]PF_6$.

12 Y. Yamamoto, Y. Nakagai, N. Ohkoshi and K. Itoh, *J. Am. Chem. Soc.*, 2001, **123**, 6372–6380.

13 See the ESI† for other unsuccessful cycloisomerisation substrates.

14 (*a*) T. Matsuda, Y. Suda and Y. Fujisaki, *Synlett*, 2011, 813–816; (*b*) T. Matsuda, Y. Yamaguchi, M. Shigeno, S. Sato and M. Murakami, *Chem. Commun.*, 2011, **47**, 8697–8699; (*c*) T. Matsuda and Y. Ichioka, *Org. Biomol. Chem.*, 2012, **10**, 3175–3177.

15 S. Yamaguchi, C. Xu, H. Yamada and A. Wakamiya, *J. Organomet. Chem.*, 2005, **690**, 5365–5377.

16 (*a*) S.-H. Kim, W. J. Zuercher, N. B. Bowden and R. H. Grubbs, *J. Org. Chem.*, 1996, **61**, 1073–1081; (*b*) H. Clavier, A. Correa, E. C. Escudero-Adán, J. Benet-Buchholz, L. Cavallo and S. P. Nolan, *Chem. – Eur. J.*, 2009, **15**, 10244–10254.

17 For a related study that employs dienes, see: D. Sémeril, C. Bruneau and P. H. Dixneuf, *Helv. Chim. Acta*, 2001, **84**, 3335–3341.