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Rhodium(I)-catalysed skeletal reorganisation of benzofused spiro[3.3]heptanes *via* consecutive carbon–carbon bond cleavage†‡

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Skeletal reorganisation of benzofused spiro[3.3]heptanes has been achieved using rhodium(I) catalysts. The reaction of benzofused 2-(2-pyridylmethylene)spiro[3.3]heptanes proceeds *via* sequential C–C bond oxidative addition and β-carbon elimination. On the other hand, benzofused spiro[3.3]heptan-2-ols undergo two consecutive β-carbon elimination processes. In both cases, substituted naphthalenes are obtained.

Introduction

Transition-metal-catalysed C–C bond cleavage reactions have seen increasingly active development, showcasing the feasibility of unique transformations that are difficult to achieve by conventional methods.[1] In particular, ring opening of benzocyclobutenones[2] and benzocyclobutenols[3] has recently attracted much attention as it enables facile access to benzofused cyclic structures *via* coupling and rearrangement reactions.[4,5] Several research groups have performed computational studies on the site selectivity of the catalytic ring opening of benzocyclobutenes possessing oxygen functionalities.[2b,c,3f,i] However, more experiments on benzocyclobutenes without heteroatom substituents as well as the factors governing the selectivity of the bond cleavage are required (Fig. 1(a)).

Two consecutive C–C bond cleavages of spiro[3.3]heptan-2-ones and spiropentanes, catalysed by rhodium(I) have been reported,[6,7] whereas the reaction of benzofused spirocycles has not yet been investigated. We recently reported rhodium(I)-catalysed skeletal reorganisation of (2-pyridylmethylene)cyclobutanes to form indane skeletons.[8] Our continuing interest in discovering and developing C–C bond cleavage reactions of strained carbocycles[9] led to the conception of catalytic ring opening of benzofused spiro[3.3]heptane derivatives involving two C–C bond cleavages (Fig. 1(b)). Herein, we report the first experimental study of the rhodium(I)-catalysed skeletal reorganisation of benzofused 2-(2-pyridylmethylene)spiro[3.3]heptanes and spiro[3.3]heptan-2-ols. In both cases, the reactions afford substituted naphthalenes *via* two C–C bond cleavages.

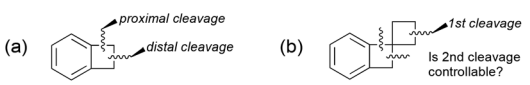

Fig. 1 C–C bond cleavage of benzocyclobutene and benzospiro[3.3]heptane.

Results and discussion

The benzofused 2-(2-pyridylmethylene)spiro[3.3]heptanes **1** used in this study were prepared *via* the Wittig olefination or McMurry coupling of the corresponding ketones, which were obtained from benzocyclobutenones in three steps.[10] Heating **1a** at 150 °C in *p*-xylene in the presence of 5 mol% $RhCl(PPh_3)_3$, which was the best catalyst identified in our previous study,[8] led to the formation of 1-methyl-3-(2-pyridylmethyl)naphthalene (**2a**) in 90% yield *via* skeletal reorganisation involving two consecutive C–C bond cleavages (Scheme 1). From our recent studies and the structure of the product, the skeletal reorganisation of **1a** would proceed as follows. The pyridine nitrogen directs the first C–C bond cleavage by oxidative addition of the C–C bond to rhodium(I) to afford spirocyclic rhodacycle **A**, which contains a (cyclobutylmethyl)rhodium(III) moiety. The second C–C bond cleavage by β-carbon elimination from this intermediate can proceed *via* two pathways. However, cleavage occurs site-selectively at the distal C–C bond to give the seven-membered rhodacycle **B**. The interaction between rhodium and benzene would be insufficient to cleave the proximal C–C bond, probably because of the restrained flexibility of the spirocyclic intermediate. Instead, the more accessible C(sp^3) in the four-membered ring interacts with

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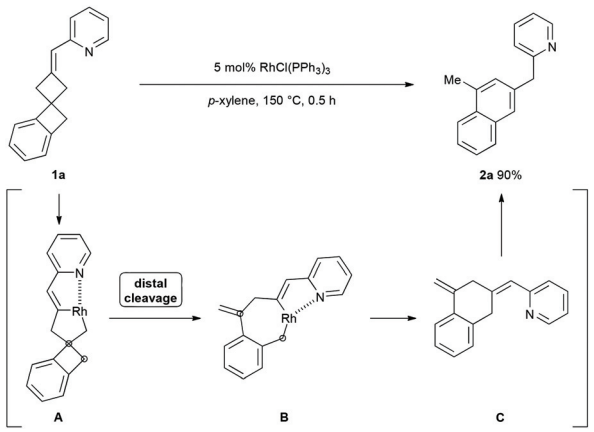
‡ Electronic supplementary information (ESI) available: Experimental procedures and characterisation data for new compounds. See DOI: 10.1039/c6ob01344a



Scheme 1 Rhodium(I)-catalysed reaction of benzofused 2-(2-pyridylmethylene)spiro[3.3]heptane **1a**.

rhodium to induce distal C–C bond cleavage. Subsequent reductive elimination yields tetralin **C**, which aromatises to naphthalene **2a** under the reaction conditions.

The scope of the rhodium(I)-catalysed skeletal reorganisation was explored, and the results are shown in Chart 1 and Scheme 2. The reaction of 3-methyl-2-pyridyl derivative **1b** afforded **2b** in 86% yield. Mono- and dialkoxynaphthalenes **2c–f** were obtained in 51–82% yields by the reaction of the corresponding substrates **1c–f** possessing alkoxy groups on the benzene ring. Naphthalene products **2g** and **2h** were obtained in high yields when using substrates **1g** and **1h** possessing substituents at the vinylic position. Naphthalene-fused spiroheptane **1i** also participated in the reaction to afford 2,4-disubstituted phenanthrene **2i**.

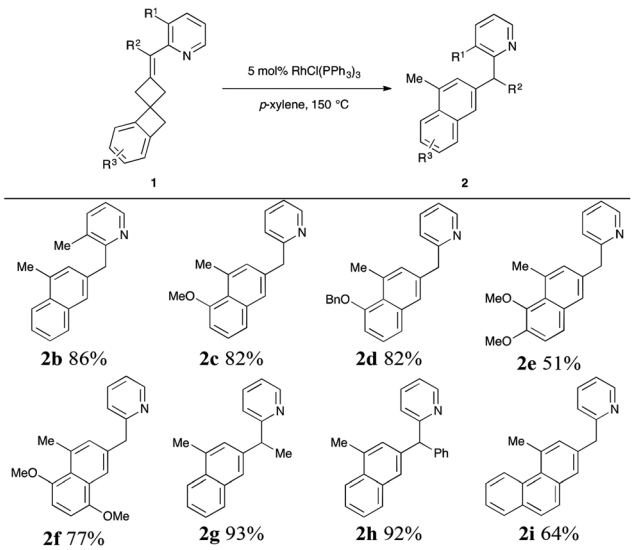
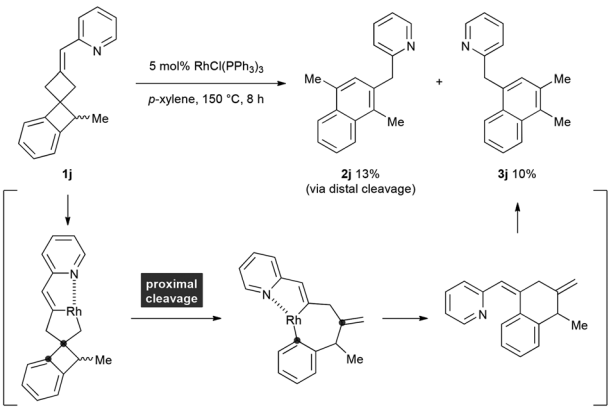


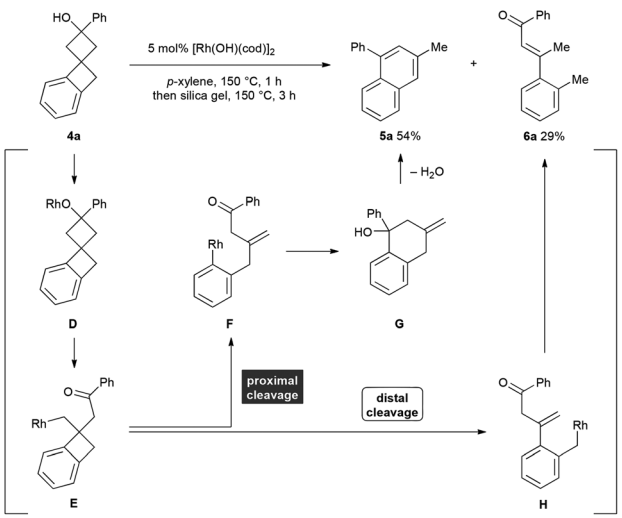
Chart 1 Rhodium(I)-catalysed skeletal reorganisation of **1b–i**. Reaction conditions: **1** (0.081–0.150 mmol), $RhCl(PPh_3)_3$ (4.0–7.5 μmol, 5 mol% Rh), *p*-xylene (1.0–1.5 mL), 150 °C, 0.5–1.0 h.



Scheme 2 Proximal C–C bond cleavage in reaction of **1j**.

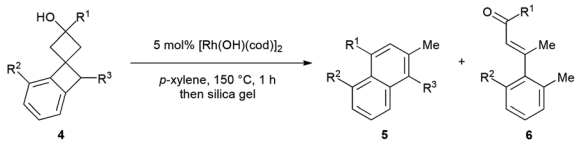
When **1j** having a methyl substituent at the spiro[3.3]heptane skeleton[11] was used in the reaction, a mixture of two isomeric naphthalenes (**2j** : **3j** = 57 : 43) was obtained in 23% combined yield after 8 h, indicating that the substituent influences the site selectivity as well as reaction efficiency (Scheme 2).[12] In this case, the expected second distal C–C bond cleavage would be sterically obstructed by the methyl group, allowing partial cleavage of the proximal C–C bond.

We anticipated that benzofused spiro[3.3]heptan-2-ols would also be amenable to an analogous skeletal reorganisation, because four-membered *tert*-alcohols have often been employed in rhodium(I)-catalysed C–C bond cleavage reactions.[13] The reaction of benzofused spiro[3.3]heptan-2-ol **4a**[14] at 150 °C in *p*-xylene, in the presence of a catalytic amount of $[Rh(OH)(cod)]_2$ (10 mol% Rh; cod = cycloocta-1,5-diene), gave two products: naphthalene **5a** and α,β-unsaturated ketone **6a** in 54% and 29% yields, respectively (Scheme 3). Both products were formed *via* two consecutive β-carbon elimination processes; after the first C–C bond cleavage of rhodium(I) cyclobu-



Scheme 3 Rhodium(I)-catalysed reaction of benzofused spiro[3.3]heptan-2-ol **4a**.

Table 1 Skeletal reorganisation–dehydration of **4b–g** [a]



Entry	4	R^1	R^2	R^3	5 (% yield)[b]	6 (% yield)[b]
1	**4b**	2-Thienyl	H	H	**5b** (28)	**6b** (25)
2	**4c**	Bu	H	H	**5c** (46)	**6c** (16)
3	**4d**	Me	OMe	H	**5d** (80)	**6d** (8)
4	**4e**	Et	H	Me	**5e** (64)	—
5	**4f**	2-Thienyl	H	Me	**5f** (56)	—
6	**4g**	Me	OMe	Et	**5g** (62)	—

[a] Reaction conditions: **4** (0.100–0.150 mmol), $[Rh(OH)(cod)]_2$ (5.0–7.5 μmol, 10 mol% Rh), *p*-xylene (1.0–1.5 mL), 150 °C, 1.0–2.5 h; then silica gel, 1.0–5.5 h. [b] Isolated yield.

tanolate **D**, the reaction followed two different pathways at (cyclobutylmethyl)rhodium(I) intermediate **E** and eventually led to the products. Proximal C–C bond cleavage by β-carbon elimination was dominant in the reaction of hydroxy-substituted **4**, unlike in the case of 2-pyridylmethylene derivatives **1**, wherein distal C–C bond cleavage is preferred. The resulting arylrhodium(I) **F** adds intramolecularly to the ketonic carbonyl group to give tetralinol **G** after protonation. Subsequent aromatisation involving dehydration is facilitated upon the addition of silica gel,[15] resulting in the formation of naphthalene **5a**. On the other hand, distal C–C bond cleavage of (cyclobutylmethyl)rhodium(I) **E** generates benzylrhodium(I) **H**, which furnishes ketone **6a** through protonation and double bond isomerisation.

Table 1 summarises the results obtained for other benzofused spiro[3.3]heptanols **4b–g**.[14] Similar results were obtained with spiroheptanols having 2-thienyl and butyl groups (**4b** and **4c**); naphthalenes **5** and ketones **6** were obtained, with the former being the predominating product (Table 1, entries 1 and 2). Installation of a methoxy group into the benzene ring of substrate improved the yield of naphthalene **5d** to 80%, with an excellent **5d**/**6d** ratio (10 : 1) (entry 3). This result could be explained as follows: increasing the electron density of the benzene ring strengthens the η^2-coordination of benzene to rhodium(I), thus making the proximal C–C bond cleavage more probable so that arylrhodium(I) is generated. Methyl substitution into the spiro[3.3]heptane skeleton again impeded distal C–C bond cleavage in the reaction of benzofused spiro[3.3]heptanols **4e–g**; the second C–C bond cleavage occurred exclusively at the proximal bond, affording naphthalenes **5e–g** as the sole products.

Conclusions

In summary, we have developed the rhodium(I)-catalysed skeletal reorganisation of benzofused spiro[3.3]heptanes **1** and **4**, which furnished substituted naphthalenes *via* two consecutive C–C bond cleavages. In the reaction of 2-pyridylmethylene-substituted derivatives **1**, the first C–C bond cleavage proceeded *via* oxidative addition and the second β-carbon elimination occurred *via* preferential distal bond cleavage. In contrast, the reaction of hydroxyl-substituted derivatives **4** involved two β-carbon elimination processes, and the second cleavage occurred predominantly at the proximal bond. Particularly in this case, selective proximal C–C bond cleavage during the second β-carbon elimination was feasible by substitution at the appropriate positions of substrate **4**.

Experimental section

General procedure for rhodium(I)-catalysed rearrangement of 1

A Schlenk tube was charged with **1** (0.100 mmol) and RhCl$(PPh_3)_3$ (5.0 μmol, 5 mol% Rh), and the tube was evacuated and backfilled with nitrogen. *p*-Xylene (1.0 mL) was added *via* a syringe through the septum, and the mixture was heated at 150 °C with stirring for the indicated period of time. The reaction mixture was cooled to room temperature and then filtered through a plug of Florisil® washing with hexane–AcOEt (1 : 1), and the filtrate was concentrated. The residue was purified by preparative TLC on silica gel to afford naphthalene **2**.

General procedure for rhodium(I)-catalysed rearrangement of 4

A Schlenk tube was charged with **4** (0.100 mmol) and $[Rh(OH)(cod)]_2$ (5.0 μmol, 10 mol% Rh), and the tube was evacuated and backfilled with nitrogen. *p*-Xylene (1.0 mL) was added *via* a syringe through the septum, and the mixture was heated at 150 °C with stirring. Silica gel (50–100 mg) was added, and the mixture was further heated at 150 °C. The reaction mixture was cooled to room temperature and then filtered through a plug of Florisil® washing with hexane–AcOEt (1 : 1), and the filtrate was concentrated. The residue was purified by preparative TLC on silica gel to afford naphthalene **5**.

Acknowledgements

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10 See the ESI.‡

11 Used as unknown mixtures of two diastereomers.

12 A 57 : 43 mixture of **2j** and **3j** was obtained in 36% combined yield when the reaction of **1j** was catalysed by $[RhCl(cod)]_2$ (5 mol% Rh) and $(4\text{-}MeC_6H_4)_3P$ (10 mol%) for 16 h.

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14 **4a**, **4b** and **4g** are single diastereomers, and the rest are mixtures of two diastereomers: **4c** (*ca.* 1 : 1), **4d** (17 : 1), **4e** (*ca.* 1 : 1) and **4f** (1.3 : 1).

15 When the reaction of **4a** was performed without silica gel treatment, **5a** and **6a** were obtained in 20% and 28% yields, respectively.

