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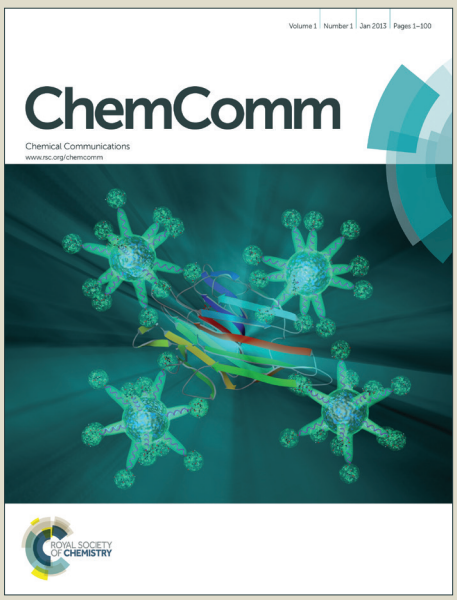

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A rhodium(I)-catalysed formal intramolecular C–C/C–H bond metathesis

Cite this: DOI: 10.1039/x0xx00000x

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Received 00th January 2012,
Accepted 00th January 2012

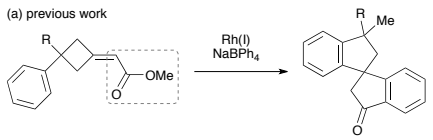
DOI: 10.1039/x0xx00000x

www.rsc.org/

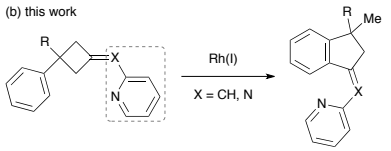
Phenylcyclobutanes underwent skeletal reorganisation in the presence of Wilkinson's catalyst to afford indanes through a cascade process of chelation-assisted C–C bond cleavage and intramolecular C–H bond cleavage.

Transition-metal-catalysed cleavage of unreactive bonds, such as C–H and C–C bonds, offers conceptually novel and strategically innovative methods for synthesizing organic molecules. Catalytic functionalisations of C−H bonds have emerged as useful tools in organic synthesis.[1] Catalytic cleavage of C–C bonds and its synthetic utilisation have also gained considerable attention in recent years.[2]

We recently reported rhodium(I)-catalysed arylation of 2-(3-arylcyclobutylidene)acetates with tetraarylborates (eqn (1)).[3] The reaction includes one β-carbon elimination[4] and two 1,4-rhodium migration[5] events in the catalytic cycle as the C–C bond and C–H bond cleavage processes, respectively, to furnish spirobiindanones. In our continuing effort to discover catalytic molecular transformations involving multiple cleavages of unreactive bonds, we envisaged that a new reaction might occur with the structurally relevant (2-pyridylmethylene)cyclobutanes, possibly triggered by the pyridine-directed cleavage of the cyclobutane C–C bond. It was found that a rhodium(I) complex catalyses a new skeletal reorganisation of (2-pyridylmethylene)cyclobutanes to ring-expanded products, as reported herein (eqn (2)). In addition, the reaction was successfully applied to the chelation-assisted rearrangement of cyclobutanones, affording 1-indanones via imines formed from cyclobutanones with 2-aminopyridines.

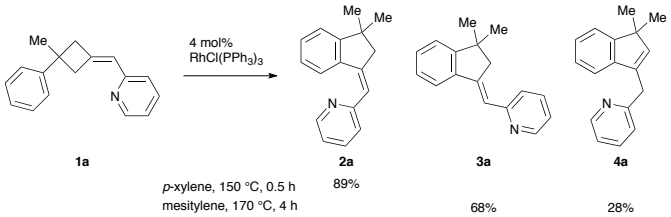


(1)



(2)

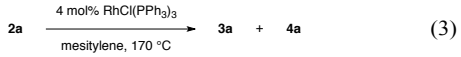
(2-Pyridylmethylene)cyclobutanes **1** used in this study were prepared by Wittig olefination or McMurry coupling of the corresponding cyclobutanones. 1-Methyl-1-phenyl-3-(2-pyridylmethylene)cyclobutane (**1a**) was heated in *p*-xylene at 150 °C in the presence of 4 mol% of Wilkinson complex ($RhCl(PPh_3)_3$) (Scheme 1). The starting material was converted into a single product within 30 min. The product obtained after purification was (*Z*)-1,1-dimethyl-3-(2-pyridylmethylene)indane (**2a**, 89% yield).[6] The reaction of phenylcyclobutane **1a** involved cleavage of the cyclobutane C–C and aromatic C–H bonds, resulting in ring expansion to indane **2a**. This can be viewed as a formal intramolecular C–C/C–H bond metathesis reaction. On the other hand, when the reaction was performed in mesitylene at 170 °C for 4 h, a different result was obtained: indane with *E* geometry **3a** and indene **4a** were formed in 96% yield, at a ratio of 7:3.



Scheme 1 Reaction of **1a** in the presence of $RhCl(PPh_3)_3$

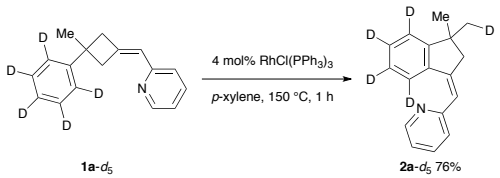
Subjecting **2a** to more severe reactions conditions (170 °C) resulted in double bond isomerisation of the (*Z*)-isomer **2a** to **3a** and **4a**, indicating that **2a** was the initial product and it underwent isomerisation at higher temperature (eqn (3)). No

isomerisation was observed in the absence of the rhodium catalyst under otherwise identical conditions.



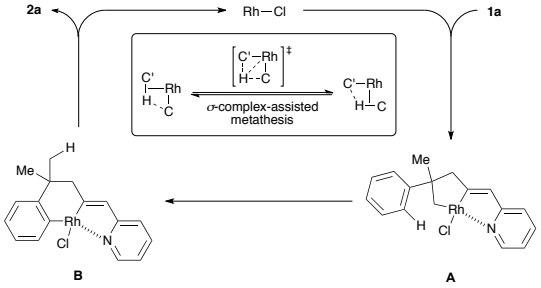
(3)

To gain mechanistic insights into the skeletal reorganisation, a deuterium-labelling experiment was conducted with cyclobutane **1a**-d_5 having a C_6D_5 group (Scheme 2). In this experiment, one deuterium atom was transferred to the indane methyl group of **2a**-d_5.



Scheme 2 Deuterium-labelling experiment with **1a**-d_5

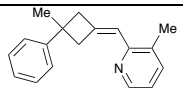
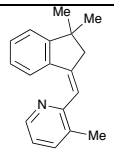
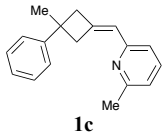
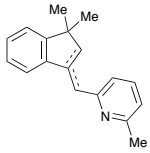
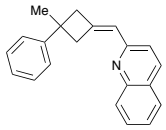
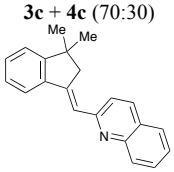
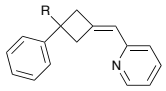
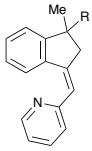
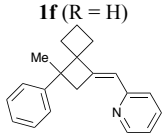
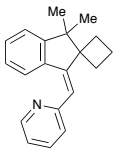
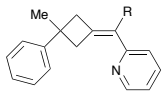
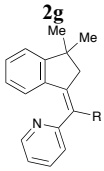
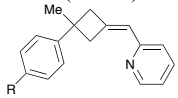
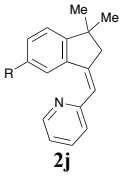
We propose a possible mechanism for the rhodium(I)-catalysed skeletal reorganisation of **1a** in Scheme 3, albeit we have no conclusive data to support it. First, the C–C activation is assisted by the pyridine directing group[7] to form five-membered rhodacycle **A**. The resulting alkylrhodium moiety of **A** then undergoes σ-complex-assisted metathesis with the pendant arene C–H bond to generate six-membered rhodacycle **B**.[8,9] This intramolecular C–H activation step can be viewed as a variant of 1,4-rhodium migration.[10] Finally, reductive elimination provides **2a** and the active rhodium(I) catalyst.

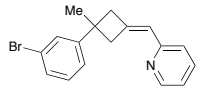
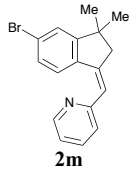
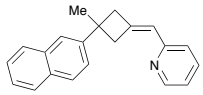
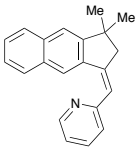
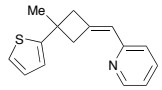
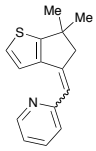


Scheme 3 Proposed mechanism for the skeletal reorganisation of **1a** to **2a**

We next investigated the rhodium-catalysed skeletal reorganisation of a variety of alkylidenecyclobutanes **1** (Table 1). First, the effect of the pyridine moieties was briefly evaluated (entries 1–3). The reaction of [(3-methyl-2-pyridyl)methylene]cyclobutane **1b** afforded the corresponding indane **2b** as the sole product in good yield (entry 1). On the other hand, the reaction efficiency was reduced with 6-methyl-2-pyridyl and 2-quinolyl groups (**1c** and **1d**, respectively); in these cases, the isomerised products were obtained (entries 2 and 3). The reaction of 2-pyrazyl and 8-quinolyl derivatives was unsuccessful (not shown in the table). Thus, the original 2-pyridyl group was critical to the success of the reaction. Then, the effects of substituents on the cyclobutane ring were examined. While 1,1-diphenylcyclobutane **1e** was successfully converted into indane **2e** in 80% yield (entry 4), no reaction was observed with the monosubstituted **1f** (entry 5).[11] Substrate **1g**, containing a spiro[3.3]heptane moiety, also underwent skeletal reorganisation to furnish spiro[cyclobutane-1,2′-indane] **2g** in 69% yield (entry 6). We also explored substitution at the vinylic position and established that methyl (**1h**) and phenyl (**1i**) groups participate in this reaction to afford indanes (**2h** and **2i**) possessing tetrasubstituted alkene moieties (entries 7 and 8). Cyclobutane **1j**–**l** having 4-substituted phenyl groups at the 1 position afforded the corresponding 5-substituted indanes **2j**–**l** in excellent yields (entries 9–11).[12] The reaction of 3-bromophenyl and 2-naphthyl derivatives (**1m** and **1n**) provided single isomers (**2m** and **2n**), which were derived from the cleavage of the more accessible C–H bonds of the aromatic rings (entries 12 and 13). A heteroaromatic substituent, a 2-thienyl group, was tolerated under the reaction condition, but the product was obtained as a mixture of *Z*- and *E*-isomers (entry 14).

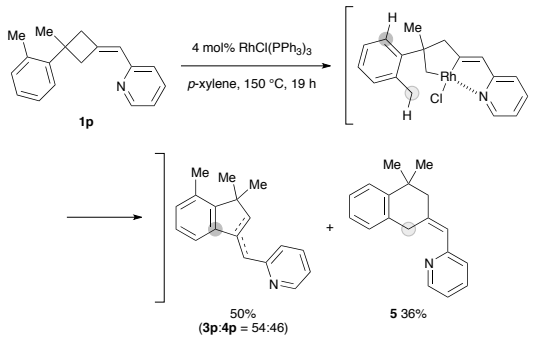
Table 1 Rhodium(I)-catalysed skeletal reorganisation of **1**[a]

Entry	1	Time (h)	2	Yield[b] (%)
1	 **1b**	1	 **2b**	74
2[c]	 **1c**	24	 **3c** + **4c** (70:30)	90
3	 **1d**	35	 **3d**	37
				
4	**1e** (R = Ph)	2	**2e**	80
5	**1f** (R = H)		**2f**	NR[d]
6[e]	 **1g**	23	 **2g**	69
				
7[e]	**1h** (R = Me)	24	**2h**	46
8[e]	**1i** (R = Ph)	18	**2i**	58
				
9	**1j** (R = Me)	0.7	**2j**	84
10	**1k** (R = Cl)	0.8	**2k**	87
11	**1l** (R = CF_3)	1.3	**2l**	82

12[e]	 **1m**	9.5	 **2m**	45
13	 **1n**	7.5	 **2n**	63
14[e]	 **1o**	24	 **2o** + **3o** (54:46)	54

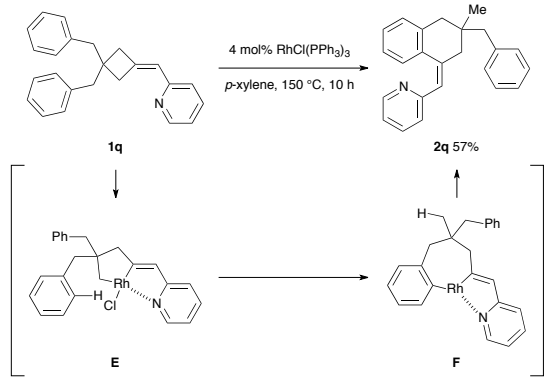
[a] Unless otherwise noted, cyclobutane **1** was heated in *p*-xylene (0.10 M) at 150 °C in the presence of 4 mol% $RhCl(PPh_3)_3$. [b] Isolated yield. [c] The reaction was performed in mesitylene at 170 °C. [d] No reaction. [e] The reaction was performed with 10 mol% $RhCl(PPh_3)_3$.

In the case of the sterically demanding 2-methylphenyl derivative **1p**, tetraline **5** was obtained in addition to the expected products **3** and **4**, indicating that 1,5-migration[13] is also possible with an appropriate substrate (Scheme 4).



Scheme 4 Skeletal reorganisation of **1p**

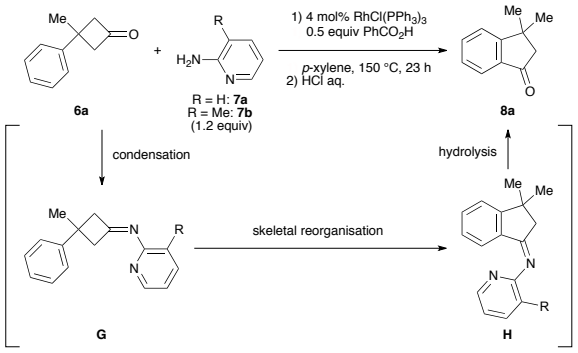
Indeed, dibenzylcyclobutane derivative **1q** reacted under identical conditions to provide tetraline **2q** through a mechanism involving the formation of five-membered rhodacycle **E**, σ-bond metathesis with the arene C–H bond to form seven-membered rhodacycle **F**, and subsequent reductive elimination (Scheme 5).

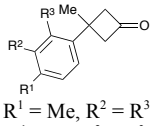
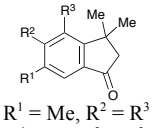
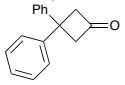
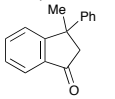
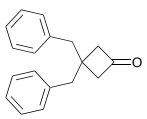
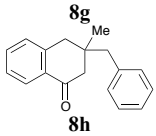


Scheme 5 Skeletal reorganisation of **1q**

Considering the structural similarity between the 2-pyridylmethylene and 2-pyridylimino groups, we anticipated that ketimines derived from cyclobutanones and 2-aminopyridines are also amenable to the skeletal reorganisation. Thus, cyclobutanone **6a**, 2-aminopyridines (**7**, 1.2 equiv), and benzoic acid (0.5 equiv) were reacted in *p*-xylene at 150 °C in the presence of the rhodium(I) catalyst (Table 2).[14] Cyclobutanone ketimine **G**, formed *in situ* from the condensation of **6a** and 2-aminopyridine **7a**, analogously underwent skeletal reorganisation to afford indanone ketimine **H**. Subsequent acid hydrolysis of **H** afforded 1-indanone **8a** in 84% yield (entry 1).[15] The reaction of 2-amino-3-picoline **7b** provided the product **8a** in 79% yield. Other 3-aryl-3-methylcyclobutanones **6b**–**f** were also converted to indanones **8b**–**f** under the same reaction conditions,[16] and 3,3-diphenylcyclobutanone **6g** yielded 3-methyl-3-phenyl-1-indanone **8g** (entries 2–7). In the case of 3,3-dibenzylcyclobutanone **6h**, 1,5-rhodium migration occurred to afford 1-tetralone **8h** (entry 8).

Table 2 Skeletal reorganisation of **6** to **8**[a]



Entry	Cyclobutanone **6**	Product **8**	Yield[b] (%) with **7a**;**7b**
1	**6a** 	**8a** 	84;79
2	**6b**: R^1 = Me, R^2 = R^3 = H	**8b**: R^1 = Me, R^2 = R^3 = H	65;72
3	**6c**: R^1 = Cl, R^2 = R^3 = H	**8c**: R^1 = Cl, R^2 = R^3 = H	73;76
4	**6d**: R^2 = Me, R^1 = R^3 = H	**8d**: R^2 = Me, R^1 = R^3 = H	51;77
5	**6e**: R^2 = Br, R^1 = R^3 = H	**8e**: R^2 = Br, R^1 = R^3 = H	71;61
6	**6f**: R^3 = Me, R^1 = R^2 = H	**8f**: R^3 = Me, R^1 = R^2 = H	28;40
7	 **6g**	 **8g**	52;66
8	 **6h**	 **8h**	41;77

[a] Reaction conditions: Cyclobutanone **6** (0.200 mmol), aminopyridine **7** (0.240 mmol), benzoic acid (0.100 mmol), and $RhCl(PPh_3)_3$ (0.010 mmol, 5 mol%) were heated in *p*-xylene (2.0 mL) for 11–24 h. [b] Isolated yield.

In summary, we elaborated a novel ring expansion reaction of 1-aryl-3-(2-pyridylmethylene)cyclobutanes in the presence

of Wilkinson's catalyst, producing 3-(2-pyridylmethylene)indanes. Overall, the reaction involves intramolecular C–C/C–H bond metathesis, which is achieved by successive pyridine-directed cleavage of the C–C bond of cyclobutane and C–H bond cleavage through intramolecular σ-bond metathesis. Apart from the one-carbon ring expansion, two-carbon ring expansion triggered by 1,5-migration occurring in the reaction of dibenzylcyclobutane derivatives was exploited to obtain tetraline derivatives. This work demonstrates that transition-metal-catalysed successive cleavage of unreactive bonds has incredible potential for use in unique and original bond manipulation of organic compounds. We plan to explore this strategy further, in a future study.

This work was supported by JSPS, Japan (Grant-in-Aid for Scientific Research (C) No. 25410054) and the Sumitomo Foundation.

Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental procedures and characterisation data for new compounds. See DOI: 10.1039/c000000x/

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