Rhodium- and Palladium-catalysed Formation of Conjugated Mono- and Bis-exocyclic Dienes. 5-*Exo-Trig versus* 6-*Endo-Trig* Cyclisations

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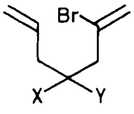
2-Bromo-1,6-dienes are catalytically cyclised to give conjugated 5-membered bis-exocyclic dienes and 6-membered mono-exocyclic dienes by rhodium and palladium catalysts, the specificity for a 5- or 6-membered ring being a function of substrate, catalyst, and added base; 2-bromo-1,7-dienes cyclise regiospecifically to give 6-membered rings.

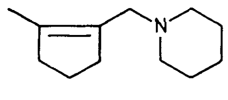
The palladium-catalysed vinylation of aryl, heteroaryl, vinyl, or benzyl halides (Heck reaction)[1] has proved to be a valuable method for carbon–carbon bond formation in the appropriate synthetic context. A few examples of the use of intramolecular Heck reactions for the preparation of 5—7-membered benzo-heterocycles have been reported[2] but, in general, little synthetic use has been made of the intramolecular version of the reaction. Two recent papers[3] on the palladium(II)-catalysed cyclisation of 1- or 2-bromo-1,ω-dienes in the presence of piperidine to give cyclic allylic amines [*e.g.* (**1a**) → (**2**)] prompts us to summarise our contrasting results with similar substrates.

Table 1. Regioselectivity of catalytic cyclisations of 2-bromo-1,6-dienes in acetonitrile at 80 °C.[a]

Substrate	Catalyst (mole %)	Time/h	% Yield[b]	Ratio (**3**) : (**4**)[c]
(**1b**)	$Pd(OAc)_2$ (2), PPh_3 (4)	1	67	5 : 4
(**1b**)	$Pd(PPh_3)_4$ (3)	4	74	1 : 10
(**1b**)	$RhCl(PPh_3)_3$ (5)	6	63	5 : 1
(**1c**)	$Pd(OAc)_2$ (5), PPh_3 (10)	35	73	2.5 : 1
(**1c**)[d]	$Pd(OAc)_2$ (10), PPh_3 (20)	48	81	1 : 2.5
(**1c**)	$Pd(PPh_3)_4$ (5)	6	81	1 : 1
(**1c**)	$RhCl(PPh_3)_3$ (5)	43	45[e]	6 : 1
(**1d**)	$RhCl(PPh_3)_3$ (5)	24	55[f]	10 : 1
(**1d**)	$Pd(OAc)_2$ (5), PPh_3 (10)	2.5	74[c,g]	2.8 : 1
(**1d**)	$Pd(PPh_3)_4$ (5), PPh_3 (10)	1.25	64[c,h]	1.5 : 1

[a] Reactions in the presence of K_2CO_3 (2 mol. equiv.) as base except where otherwise indicated. [b] Isolated yield. [c] Estimated by n.m.r. (250 MHz). [d] In the presence of NEt_3 (2 mol. equiv.) as base. [e] Plus 50% starting material. [f] Estimated by g.l.c. (2 m, 5% SGR). [g] *Ca.* 15% of double bond isomers of (**3d**) and (**4d**) also formed. [h] *Ca.* 34% of double bond isomers of (**3d**) and (**4d**) also formed.


(1)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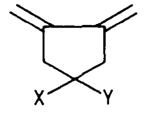
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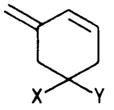
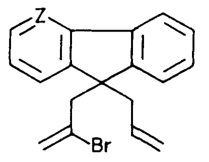
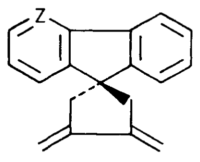

(4)

a; X = Y = H
b; X = Y = CO_2Et
c; X = Me, Y = COPh
d; X = Y = COMe


(5)

a; Z = CH
b; Z = N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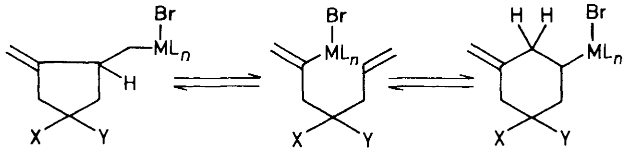
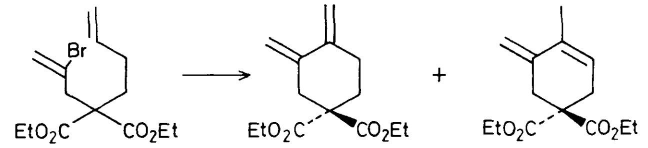
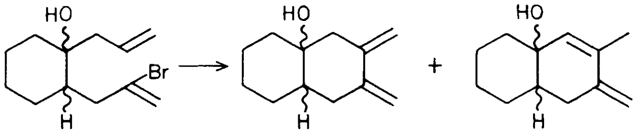
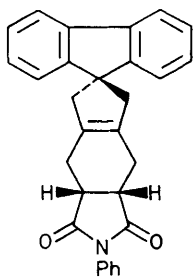

(7) **(8)** **(9)**


(10) **(11)** **(12)**


(13) **(14)** **(15)**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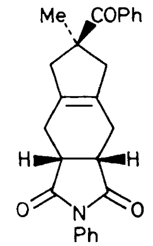
(17)

The Diels–Alder reaction is a process of wide ranging synthetic utility with the capacity for creating four chiral centres in a single step, *i.e.* a process in which there is a substantial increase in complexity.[4] Thus the combination of consecutive metal-catalysed creation of Diels–Alder precursors (diene and/or dienophile) with Diels–Alder cycloadditions is an attractive goal in synthetic methodology. One partial solution to this problem has been reported involving a molybdenum(0)-catalysed double bond isomerisation in a bis-allylic acetate.[5] We now report the successful catalytic creation of conjugated dienes and an interesting and potentially useful variation of product with catalyst.

Reaction of the 2-bromo-1,6-dienes (**1b**—**d**)[6] with $Pd(OAc)_2$, $Pd(PPh_3)_4$, or $RhCl(PPh_3)_3$ in boiling acetonitrile in the presence of 2 equivalents of base leads to the formation of mixtures of cyclic dienes (**3**) and (**4**) (Table 1).†

The diene (**3**) is the product of a 5-*exo-trig* cyclisation whilst (**4**) arises from a 6-*endo-trig* cyclisation.[7] For substrate (**1b**), $RhCl(PPh_3)_3$ favours the 5-*exo-trig* product (**3**) whilst Pd^0 favours the 6-*endo-trig* product (**4**) (Table 1). The results (Table 1) with (**1c**) and (**1d**) illustrate the sensitivity of the cyclisation to substrate structure, catalyst, and base. In contrast to (**1b**—**d**) the fluorene derivatives (**5a**) and (**5b**)‡

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† All new compounds reported have microanalytical and spectroscopic data in accord with their structures.

‡ Compounds (**5a**) and (**5b**) were prepared by sequential treatment of the parent fluorene and azafluorene with allyl bromide and 2,3-dibromopropene using t-butyl-lithium as base. Compound (**10**) was prepared from diethyl butenylmalonate, sodium ethoxide, and 2,3-dibromopropene in dry ethanol. Compound (**13**) was prepared by the addition of allylmagnesium bromide to 2-allylcyclohexanone.

undergo a regiospecific 5-*exo-trig* cyclisation (70—90%) to give (**6a**) and (**6b**) respectively with both palladium and rhodium catalysts; *e.g.* (**5a**) cyclises [5 mole % $RhCl(PPh_3)_3$, K_2CO_3 (2 equiv.), MeCN, 80 °C, 2.5 h] to give a (**6a**) (80%). The use of Rh^I complexes for Heck-type reactions has not been previously reported.

The varying ratio of 5-*exo-trig* (**3**) to 6-*endo-trig* product (**4**) (Table 1) could be accounted for by the equilibria (**7**) $\rightleftharpoons$ (**8**) $\rightleftharpoons$ (**9**). Irreversible β-hydride elimination (due to presence of base) from (**7**) and (**9**) then leads to (**3**) and/or (**4**). Experiments are in hand to test the hypothesis that (**3**) is the kinetically controlled product and (**4**) the thermodynamically controlled product.

Extension to 2-bromo-1,7-dienes has been briefly investigated. The bromo-1,7-diene (**10**)‡ cyclises [10 mole % $Pd(OAc)_2$, 20 mole % PPh_3, K_2CO_3 (2 equiv.), MeCN, 80 °C, 4 h] regiospecifically *via* a 6-*exo-trig* process to give a 4 : 1 mixture (86%) of (**11**) and (**12**). G.l.c. monitoring of the reaction clearly showed that (**12**) was derived from (**11**) by a regiospecific isomerisation. No 7-membered ring product could be detected. The bromo-1,7-diene (**13**) (isomer mixture)‡ undergoes an analogous cyclisation [5 mole % $Pd(OAc)_2$, 10 mole % PPh_3, 80 °C, 23 h] to give a 2 : 1 mixture (67%) of (**14**) and (**15**).

All the bis-exocyclic dienes (**3**), (**6**), (**11**), and (**14**) undergo Diels–Alder reactions under mild conditions (25—60 °C) with *N*-phenylmaleimide (NPM) to give the corresponding cycloadducts in high yield. Thus (**6a**) and NPM (C_6H_6, 25 °C, 6 h) give the adduct (**16**) (94%) whilst (**3c**) and NPM react ($CHCl_3$, 60 °C, 15 min) stereospecifically to give (**17**) (90%).§

Further studies of the scope of these reactions are in progress. We thank the Department of Education, Northern Ireland, the S.E.R.C., and Queen's University for support.

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§ Stereochemistry assigned on the basis of nuclear Overhauser enhancement difference spectroscopy.