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

**Ronald Grigg,* Paul Stevenson, and Tanachat Worakun**

*Department of Chemistry, Queen's University, Belfast BT9 5AG, Northern Ireland*

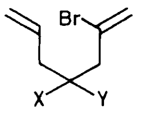
2-Bromo-1,6-dienes are catalytically cyclised to give conjugated 5-membered bis-exocyclic dienes and 6-membered mono-exocyclic dienes by rhodium and palladium catalysts, the specificity for a 5- or 6-membered ring being a function of substrate, catalyst, and added base; 2-bromo-1,7-dienes cyclise regiospecifically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

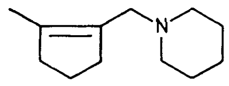
**Table 1.** Regioselectivity of catalytic cyclisations of 2-bromo-1,6-dienes in acetonitrile at 80 °C.[a]

| 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 |

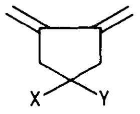
[a] Reactions in the presence of $K_2CO_3$ (2 mol. equiv.) as base except where otherwise indicated. [b] Isolated yield. [c] Estimated by n.m.r. (250 MHz). [d] In the presence of $NEt_3$ (2 mol. equiv.) as base. [e] Plus 50% starting material. [f] Estimated by g.l.c. (2 m, 5% SGR). [g] *Ca.* 15% of double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



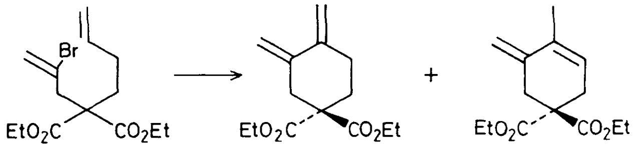
**(1)**



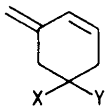
**(2)**



**(3)**

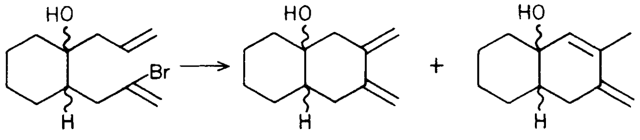


**(10)** **(11)** **(12)**

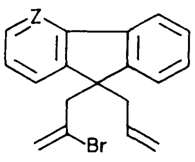


**(4)**

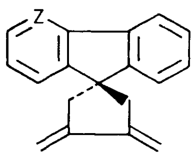
a; X = Y = H
b; X = Y = $CO_2Et$
c; X = Me, Y = COPh
d; X = Y = COMe



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

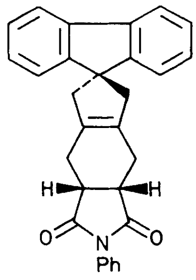


**(5)**

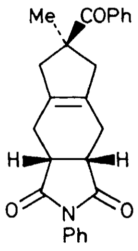


**(6)**

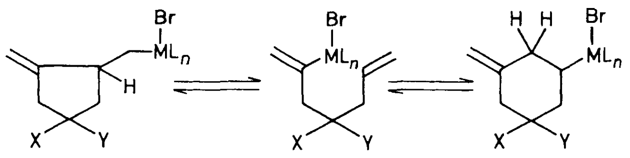
a; Z = CH
b; Z = N



**(16)**



**(17)**



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

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**)‡

---

† 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.

*Received, 8th May 1984; Com. 620*

## References

1 R. F. Heck, *Org. React.*, 1982, **27**, 345.

2 M. O. Terpko and R. F. Heck, *J. Am. Chem. Soc.*, 1979, **101**, 5281; M. Mori and Y. Ban, *Tetrahedron Lett.*, 1979, 1133; M. Mori, S. Kudo, and Y. Ban, *J. Chem. Soc., Perkin Trans. 1*, 1979, 771.

3 C. K. Narula, K. T. Mak, and R. F. Heck, *J. Org. Chem.*, 1983, **48**, 2792; L. Shi, C. K. Narula, K. T. Mak, L. Kao, Y. Xu, and R. F. Heck, *ibid.*, 1983, **48**, 3894.

4 S. H. Bertz, *J. Am. Chem. Soc.*, 1981, **103**, 3599; 1982, **104**, 5801.

5 B. M. Trost and M. Lautens, *J. Am. Chem. Soc.*, 1983, **105**, 3343.

6 Compounds (**1b**—**d**) were prepared by sequential allylation and 2-bromoallylation of the corresponding β-dicarbonyl compounds by the method of A. W. Johnson, E. Markham, and R. Price, *Org. Synth.*, Coll. Vol. 5, p. 785.

7 J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 734.

---

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