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Palladium catalysed [2 + 2 + 1] intramolecular cycloaddition for the preparation of bicyclo[3.3.0]octa-1.5-dien-3-ones from 1,6-diynes†

Ronald Grigg,*[a] Lixin Zhang,[a] Simon Collard[b] and Ann Keep[b]
[a] Molecular Innovation, Diversity and Automated Synthesis (MIDAS) Centre, School of Chemistry, Leeds University, Leeds, UK LS2 9JT. E-mail: R.Grigg@chem.leeds.ac.uk
[b] Johnson Matthey, Orchard Road, Royston, Herts, UK SG8 5HE

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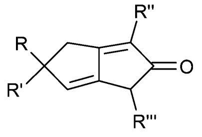
Palladium catalysed [2 + 2 + 1] cycloaddition of 1,6-heptadiynes with CO (1 atm) furnishes bicyclo[3.3.0]octa-1,5-dien-3-ones in 30–74% yield.

The stoichiometric reaction of an alkene, an alkyne and dicobalt hexacarbonyl, the Pauson–Khand (PK) reaction, involves a formal [2 + 2 + 1] cycloaddition of an alkyne, an alkene and carbon monoxide.[1] The intramolecular version of this cycloaddition has been widely used for the synthesis of polycyclic compounds and further development of the Pauson–Khand reaction continues to attract attention.[2–4]

In contrast, the transition metal-catalysed [2 + 2 + 1] cycloaddition of 1,6-heptadiynes with CO to form **1** has been little investigated and the parent skeleton **2** is unknown.



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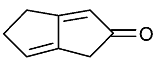

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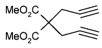
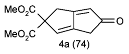
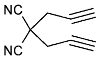
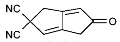
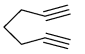
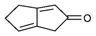
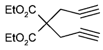
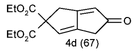
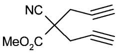
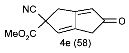
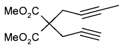
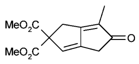
The first reported synthesis of the bicyclo[3.3.0]octa-1,5-dien-3-one skeleton involved stoichiometric $Fe(CO)_5$ mediated [2 + 2 + 1] cycloaddition of 1,7-TMS-diynes (TMS = trimethylsilyl) and carbon monoxide, followed by oxidative demetalation of the resulting (η^4-cyclopentadienone) iron tricarbonyl complexes using Me_3NO.[5] The same stoichiometric two step process was applied for the syntheses of 2-[4-pentenyl]bicyclo[3.3.0]octa-1,5-dien-3-one from 12-substituted dodec-1-ene-6,11-diynes.[6]

The first catalytic synthesis of bicyclo[3.3.0]octa-1.5-dien-3-ones involving a rhodium complex-catalyzed silylcarbodicyclisation of 4,4-disubstituted 1,6-heptadiyne with *tert*-butyldimethylsilane under 50 atm of carbon monoxide was reported in 1996.[7]

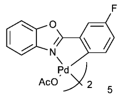
Palladium on carbon catalysed cyclocarbonylation of 1,6-dialkynes in alcohol gave bicyclo[3.3.0]octa-1,4-dien-3-ones as non-isolated intermediates. The reactive cyclopentadienone moiety rendered these species prone to Diels–Alder dimerisation or trapping by alkoxide conjugate addition.[8] Dicobalt octacarbonyl-catalyzed [2 + 2 + 1] cyclization of 1,6-diynes in the presence of 2 equivalents of phenylacetylene and under CO (30 atm) generates bicyclo[3.3.0]octa-1,4-dien-3-ones which react further in a [2 + 2 + 2] cycloaddition with the phenylacetylene to give tricyclic products.[9] Iridium complexes and methylidynetricobalt nonacarbonyl are both reported to catalyze the [2 + 2 + 1] cycloaddition of 1,6-disubstituted-1,6-diynes, with aryl or Ar_3Si substituents, with CO producing bicyclo[3.3.0]cyclopenta-1,4-dien-3-ones.[10] In these cases the 2,4-diaryl or di-Ar_3Si moieties stabilize the cyclopentadienone moiety.

We now report the cyclisation–carbonylation of **3** occurs on treatment with a catalyst system comprising 5 mol% $Pd(OAc)_2$/10 mol% PPh_3 (Table 1, entries 1, 2, 3, 6) or 2 mol% PdCy **5** (entries 4, 5)[11] and K_2CO_3 (2 eq) in DMF or THF (Scheme 1) under CO (1 atm) to afford **4**. The structure of **4a** was established from its ^1H and ^{13}C NMR spectra, microanalysis and mass spectroscopy and confirmed by an X-ray crystal structure (Fig. 1).‡

Table 1 Palladium catalysed [2 + 2 + 1] cycloaddition reaction

Entry	Diyne	Solvent	Time/h	Product (%)
1		DMF	16	 4a (74)
2		THF	8	 4b (64)
3		DMF	16	 4c (33)
4[a]		DMF	8	 4d (67)
5[a]		DMF	8	 4e (58)
6		DMF	48	 4f (30)

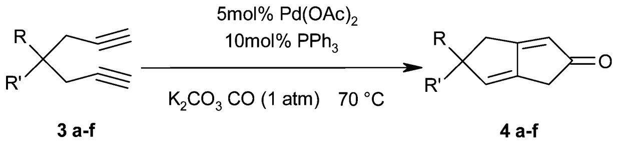
[a] Entries 4 and 5: 2 mol% **5**.



5

Low yields were observed for 1,6-heptadiyne (Table 1, entry 3) and 1,6-octadiyne (Table 1, entry 6). In the latter case the reaction was also substantially slower and diyne **6** did not afford any **7** but was partially degraded to **8** (Scheme 2).

Our proposed mechanism is shown in Scheme 3. The diynes undergo cycloisomerisation to **9** with palladium(0), followed by



Scheme 1

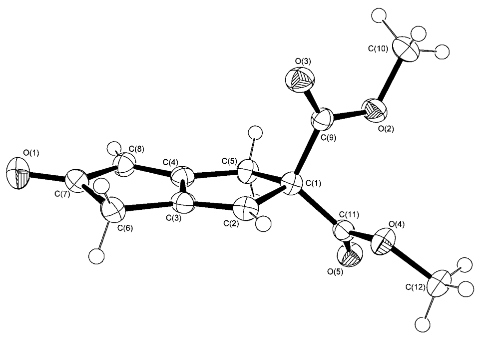


Fig. 1 X-Ray crystal structure of **4a**.

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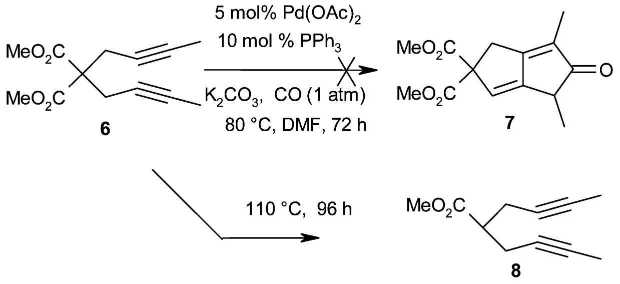
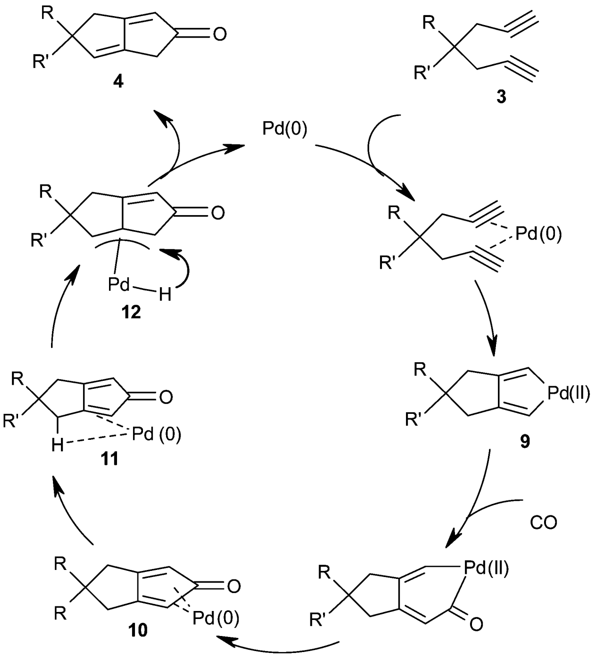
† Electronic supplementary information (ESI) available: experimental. See http://www.rsc.org/suppdata/cc/b3/b302841k/

DOI: 10.1039/b302841k



Scheme 2

CO insertion and reductive elimination to form the bicyclic intermediate **10**. Subsequent palladium catalysed double bond migration *via* π-allyl formation gives the more stable final product **4**. Although no role is assigned to the K_2CO_3 base in Scheme 3 it is an important part of the catalytic system. Its omission results in a complex mixture. It would seem most likely that it plays a role in the proton transfer process **11** → **12** → **4**.



Scheme 3

We thank Tetley and Lupton and Johnson Matthey for scholarships (to L. Z.) and Leeds University for support.

Notes and references

‡ *Crystallographic data* for **4a**: $C_{12}H_{12}O_5$, M = 236.22, triclinic, a = 5.70010(10), b = 9.0939(3), c = 11.3003(4) Å, V = 552.52(3) Å^3, T = 150(2) K, space group $P1$, Z = 2, absorption coefficient = 0.111 mm^{-1}, 8959 reflections collected, 2146 independent (R_{int} = 0.0531) which were used in all calculations. The final R indices were 0.0429 (R_1) and 0.1133 (wR_2). CCDC 206592. See http://www.rsc.org/suppdata/cc/b3/b302841k/ for crystallographic data in CIF or other electronic format.

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