Selective Formation of Substituted Cyclopentane Derivatives from Hexa-1,5-dienes *via* Oxidative Cyclization in the Presence of Pd(OAc)$_2$–MnO$_2$–Benzoquinone as Catalyst

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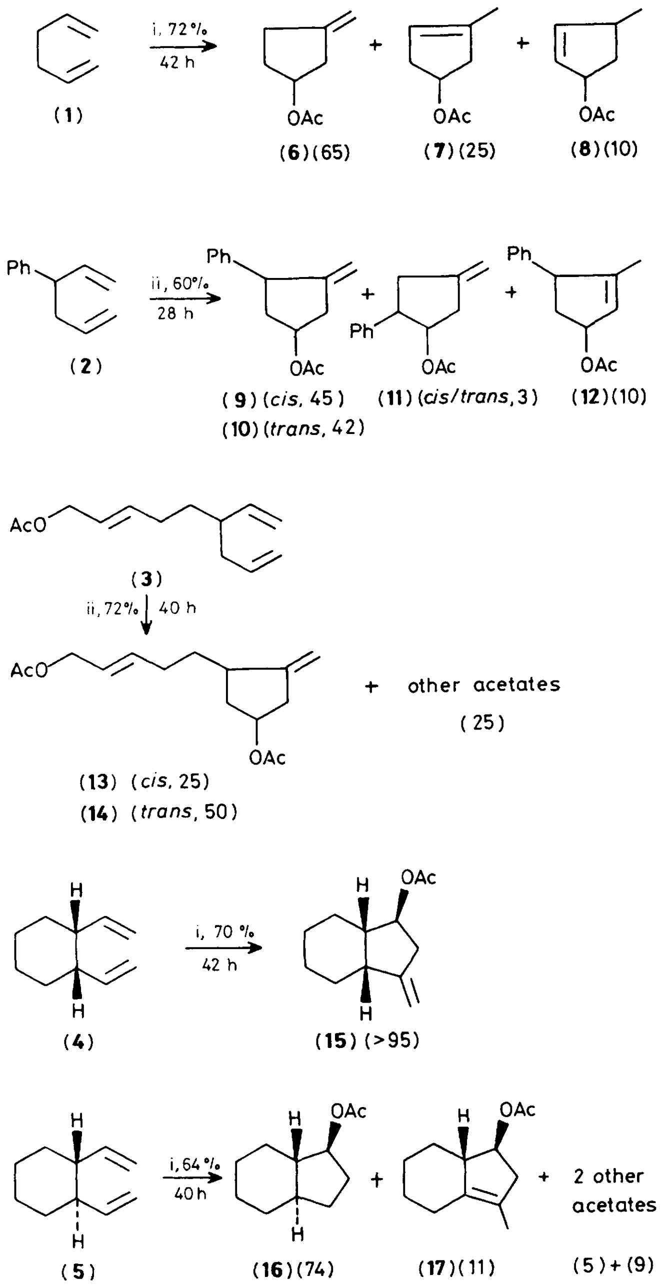
Hexa-1,5-dienes undergo oxidative ring closure catalysed by palladium acetate using *p*-benzoquinone–manganese dioxide as oxidant to give acetoxy-substituted methylene-cyclopentane derivatives.

There is a growing interest in synthetic methods for the construction of five-membered ring systems.[1] It has been shown that palladium-catalysed oxidative cyclization[2] of hexa-1,5-dienes can lead to functionalized cyclopentanes.[3] However, these reactions suffer from the disadvantages that they require stoicheiometric amounts of palladium(II) salts,[3a] or that the catalytic reactions are not general owing to the reoxidation system used: Pb(OAc)$_4$[3b] or CuCl$_2$.[3c]

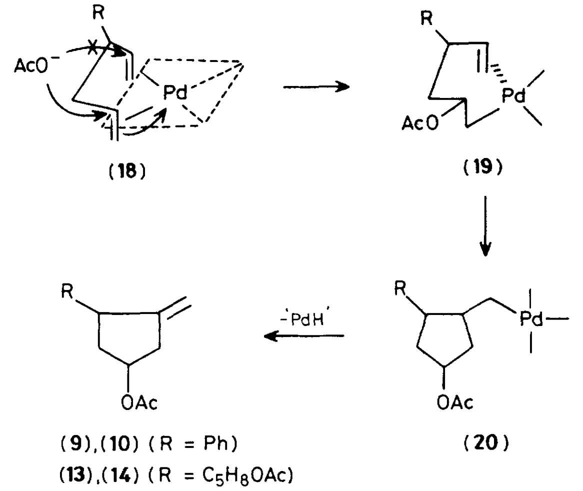
We report here that the use of a binary Pd^{II} regenerating oxidation system, composed of *p*-benzoquinone and MnO$_2$[4] in



Scheme 1. *Reagents.* i, $Pd(OAc)_2$ (0.05 equiv.), *p*-benzoquinone (0.2 equiv.), MnO_2 (1 equiv.), HOAc, room temp.; ii, $Pd(OAc)_2$ (0.05 equiv.), *p*-benzoquinone (0.25 equiv.), MnO_2 (0.75 equiv.), HOAc, room temp. Relative proportions of the isomeric products are shown in parentheses.

acetic acid, leads to a quite general cyclization of mono- and di-substituted hexa-1,5-dienes. Provided the 2- and 5-positions are unsubstituted, we observed the unique formation of cyclopentanes, substituted by an acetoxy group and, principally, by the thermodynamically non-favoured exomethylene group (Scheme 1).

In a typical experiment, a solution of the diene (1 mmol) in anhydrous acetic acid (5 ml) was stirred in the presence of $Pd(OAc)_2$ (0.05 mmol), *p*-benzoquinone (0.2 mmol), and MnO_2 (1 mmol), at room temperature for 24—72 h. After aqueous work-up and extraction with pentane the crude mixture was purified by flash chromatography and the products separated by h.p.l.c.



Scheme 2

Thus, hexa-1,5-diene (**1**) was transformed (72% yield) into a mixture of the unsaturated acetoxy-cyclopentanes (**6**) (65%), (**7**) (25%), and (**8**) (10%). Higher temperatures (50 °C) and greater than equimolar quantities of MnO_2 gave lower yields and, in the latter case, significant quantities of bisacetoxylated products. The 3-phenyl substituted hexa-1,5-diene (**2**)[†] gave rise to a higher chemoselectivity (90% of isomers with an exomethylene group). Furthermore, this reaction (60% yield) showed a high degree of regioselectivity (97%). The cyclization of the triene (**3**), which can be synthesized in a few steps *via* Pd-catalysed oligomerisation of butadiene with *N*,*N*-dimethylallylamine,[5] demonstrates that allylic acetoxy groups are not affected by the reaction conditions. Analogous reactions were observed with the *cis*- or *trans*-substituted 1,2-divinylcyclohexanes (**4**) and (**5**) respectively. The formation of (**15**) (70%) and (**16**) (64%) proceeded with remarkable diastereoselectivities, with >95% (1*R**,6*S**,7*S**) isomer being formed in the case of (**15**).[‡] Consequently, in contrast to the $PdCl_2$–$CuCl_2$ catalyst, which leads to rearranged products,[3c] our new method can be used efficiently for the preparation of either *cis*- or *trans*-fused hydrindane derivatives.[§]

The high degree of regioselectivity [cyclization of (**2**) and (**3**)] and diastereoselectivity [cyclization of (**4**) and (**5**)] is a consequence of the initial acetoxypalladation of the co-ordinated (chelated) non-conjugated 1,5-diene. Owing to the steric requirements during the carbon–palladium bond form-

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[†] Prepared by Wittig reaction of 2-phenylpent-4-enal.[10]

[‡] All new compounds gave satisfactory analytical [compounds (**9**), (**10**), (**13**), (**14**), (**15**), and (**16**)] and/or spectroscopic data. Selected ^1H n.m.r. data ($CDCl_3$), (**9**): δ 7.15—7.4 (m, 5H), 5.2 (quintet, *J* 7 Hz, 1H), 4.98—5.05 (m, 1H), 4.53—4.60 (m, 1H), 3.65 (br. t, *J* 10 Hz, 1H), 2.83—3.02 (m, J_{gem} 17 Hz, 1H), 2.45—2.67 (m, 2H), 2.04 (s, 3H), 1.86—2.05 (ddd, *J* 13, 10, and 7 Hz, 1H); (**13**): δ 5.73—5.82 (m, J_{trans} 16 Hz, 1H), 5.54—5.63 (m, J_{trans} 16 Hz, 1H), 5.07 (quintet, *J* 6.5 Hz, 1H), 4.83—4.94 (m, 2H), 4.51 (d, *J* 6.5 Hz, 1H) 2.72—2.80 (m, J_{gem} 17 Hz, 1H), 2.36—2.44 (m, J_{gem} 17 Hz, 1H), 2.25—2.34 (m, 1H), 2.07 (s, 3H), 2.03 (s, 3H), 2—2.2 (m, 3H), 1.72—1.81 (m, 1H), and 1.39—1.48 (m, 2H); (**15**): 4.90 (br., $w_{1/2}$ 6 Hz, 1H), 4.82 (br., $w_{1/2}$ 9.5 Hz, 2H), 2.83 (m, part of an AB, *J* 18, 7.5, 2.5, and 2.5 Hz, 1H), 2.67 (br., $w_{1/2}$ 15 Hz, 1H), 2.35 (d, part of an AB, *J* 18 Hz, 1H), 1.98 (s, 3H), 1.93—2.08 (m, 1H), 1.75 (br., $w_{1/2}$ 21 Hz, 1H), 1.57—1.7 (m, 3H), 1.27—1.36 (m, 2H), 1.13—1.27 (m, 1H), and 0.85—0.96 (m, 1H).

[§] Compounds (**15**) and (**16**) can also be rearranged to the thermodynamically more stable compound (**17**)[3c] in the presence of *p*-$MeC_6H_4SO_3H$ in hexane (room temp ; 2—3 days).

ation, compounds such as (**2**) and (**3**) are mainly attacked at the sterically less hindered C-5 atom. The predominant formation of the exomethylene group, after cyclization (C–C bond formation) and palladium hydride abstraction, seems to be a characteristic of this, chloride-free, oxidation system (Scheme 2). It is interesting that compounds with primary carbon–palladium bonds of the type (**20**) are known to be susceptible to different ionic transpositions[3c,6,7] when $PdCl_2$–$CuCl_2$ is the oxidation catalyst.

The transformation of easily accessible[5a,b,8] or commercially available hexa-1,5-dienes to functionalized cyclopentane derivatives is of synthetic value and may be complementary to Trost's trimethylenemethane cycloaddition method (Pd^0-catalysed methylenecyclopentane formation).[1a,9]

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