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ONE-POT PALLADIUM-CATALYZED SYNTHESIS OF 2,3-DISUBSTITUTED BICYCLO[2.2.1]HEPTANES AND BICYCLO[2.2.1]HEPT-5-ENES

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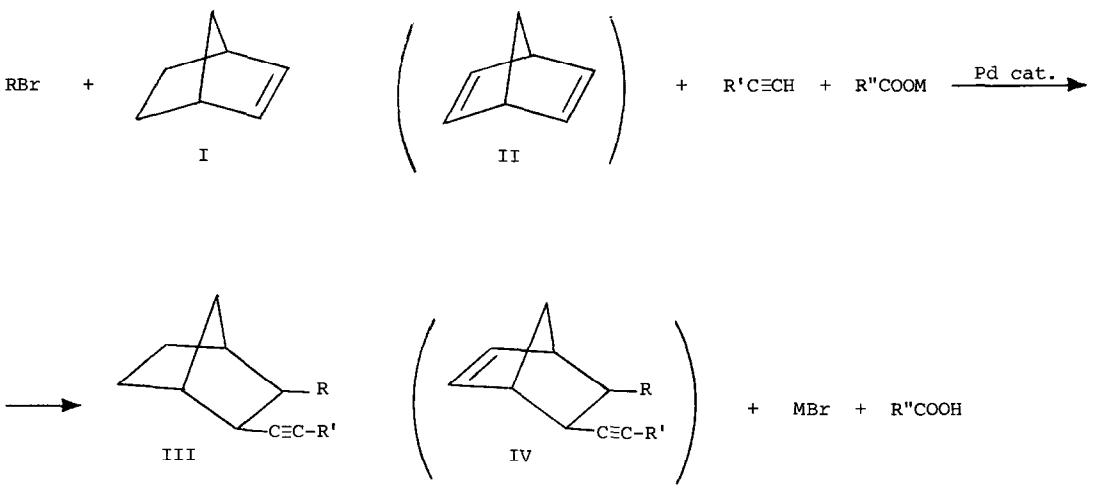
Summary: A new and highly stereoselective palladium-catalyzed synthesis is reported, based on two subsequent insertions of the bicyclo[2.2.1]heptene system into an aryl or vinylpalladium bond, formed in situ from aryl or vinyl bromides.

Recent papers on the synthesis of prostaglandin endoperoxide analogs[1] prompt us to report a new catalytic synthesis resulting from our studies on palladium-catalyzed insertion processes.[2-4] The new synthesis directly gives 2,3-disubstituted bicyclo[2.2.1]heptanes and bicyclo[2.2.1]hept-5-enes starting from aryl or vinyl bromides RBr, bicyclo[2.2.1]hept-2-(or 2,5-di)ene, alkyl or aryl-acetylenes R'C≡CH and an alkali carboxylate R"COOM (R" = organic chain; M = Na, K) in presence of Pd(0) complexes with triarylphosphines as catalysts, according to the following equation:



The reaction takes place simply by heating the reactants at about 80° for some hours under nitrogen. The products correspond to a *cis, exo* addition of R- and R'C≡C- to the double bond. It is worth noting that *cis, exo* addition to norbornadiene has also been achieved by this technique.[4] The mercury acetate technique leads to *endo* addition of aryl and vinyl groups (see ref.1 for

literature). Double bonds in R were found in the E form even starting from Z compounds.

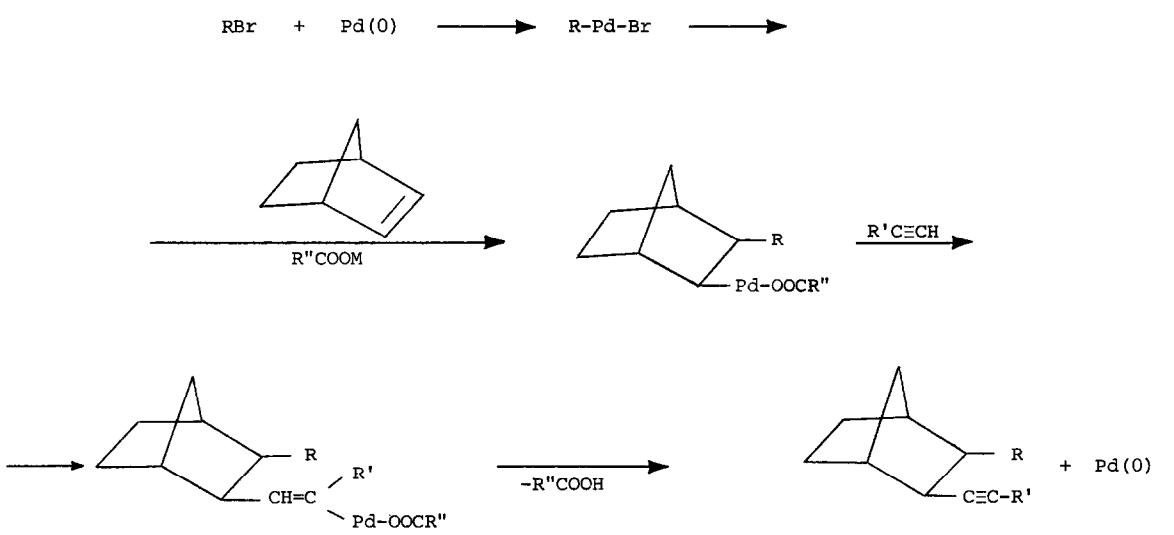
The results obtained with different aryl and vinyl halides (1 mol) on one side and with alkyl or arylacetylenes (1 mol) on the other in anisole at 80° for 8 h, in presence of MeCOOK (1 mol) and $Pd(PPh_3)_4$ (0.03 mol) as catalyst, are reported in the following Table.

Bicyclic system	R in RBr	R' in R'C≡CH	Products III, IV Isolated yield %
I	Ph	Ph	42
I	PhCH=CH	Ph	68[a]
I	PhCH=CH	$CH_3(CH_2)_5$	52
I	PhCH=CH	$(CH_3)_2C$-OH	72
I	PhCH=CH	$(CH_3)_2C$-NH_2	86
I	CH_3CH=CH	Ph	61
I	CH_2=CH	Ph	69
II	PhCH=CH	Ph	59

[a] 0.015 mol of catalyst.

It is interesting to note that under similar conditions the reaction of allyl bromide does not give significant amounts of product III (R = allyl, R' = phenyl).

We postulate a stepwise course (oxidative addition of RBr to Pd, double bond insertion, triple bond insertion, H-elimination) as shown in the following Scheme.



Competition of the alkyne with the strained olefin for coordination with palladium leads, in some cases, to the formation of substantial amounts of product resulting from direct reaction of RBr with the alkyne[5] without insertion of the double bond (21% of PhC≡CPh in the first experiment reported in the Table).

The products, which are colourless oils or solids, are easily isolated by conventional techniques. Satisfactory spectral data were obtained for all compounds. Significant ^1H (60, 100 and 270 MHz) and ^{13}C (25.2 MHz) NMR data ($CDCl_3$, TMS) are given below:

III (R = Ph, R' = Ph), m.p. 56-58°, ^1H NMR (60 MHz): δ 7.4-6.7 (m, 10H), 2.99 (AB system, 2H, HC(2), HC(3)), 2.53 (m, 2H, HC(1), HC(4)), 2.08 (br d, J = 10 Hz, 1H, HC(7 *syn* to the substituents), 1.8-1.1 (m, 5H); ^{13}C NMR: δ 143.3, 131.1, 128.3, 127.6, 126.9, 125.5, 124.1 (aromatic carbons), 91.9, 84.6 (s, alkyne carbons), 52.1 (d, C(3)), 44.3 (d, C(2)), 43.0, 41.3 (d, C(4), C(1)), 36.5 (t, C(7)), 31.0, 28.2 (t, C(5), C(6)).

III (R = PhCH=CH, R' = Ph), m.p. 52-54°, ^1H NMR (270 MHz): δ 7.5-7.1 (m, 10H, aromatic protons), 6.5-6.3 (m, ABX system, 2H, vinyl protons), 2.82 (dd, J = 2 Hz, J = 8.5 Hz, 1H, HC(2)), 2.53-2.44 (m, 2H, HC(3), HC(1)), 2.18 (m, 1H, HC(4)), 1.92 (d quintets, J = 2 Hz, J = 10 Hz, 1H, HC(7 *syn*)), 1.60-1.51 (m, 2H, HC(5 *exo*), HC(6 *exo*)), 1.31-1.19 (m, 3H, HC(5 *endo*), HC(6 *endo*), HC(7 *anti*) centered at 1.23); ^{13}C NMR: δ 137.7, 132.9, 131.2, 128.7, 128.2, 127.8, 127.1, 126.5, 125.9, 123.9, 91.5, 83.7, 49.6, 44.2, 42.8, 40.6, 34.8, 29.3, 28.5.

III (R = PhCH=CH, R' = $CH_3(CH_2)_5$), ^1H NMR (100 MHz): δ 7.4-7.1 (m, 5H), 6.40-6.25 (m, 2H), 2.60 (br d, J = 8 Hz, 1H, HC(2)), 2.50-2.24 (m, 2H, HC(1), HC(3)), 2.24-1.98 (m, 3H, HC(4), $-CH_2-C\equiv$), 1.88 (br d, J = 9 Hz, 1H, HC(7 *syn*)), 1.7-0.7 (m, 16H); ^{13}C NMR: δ 137.9, 133.4, 128.3, 128.1, 126.4, 125.8, 83.3, 81.4, 49.4, 44.4, 43.0, 40.0, 34.5, 31.3, 29.4, 29.2, 28.5, 22.5, 18.9, 14.0.

III (R = PhCH=CH, R' = $(CH_3)_2C-OH$), ^1H NMR (100 MHz): δ 7.4-7.1 (m, 5H), 6.4-6.2 (m,2H), 2.61 (br d, J = 8 Hz, 1H, HC(2)), 2.50-2.24 (m, 2H, HC(1), HC(3)), 2.15 (m, 2H, HC(4), -OH), 1.84 (br d, J = 10 Hz, 1H, HC(7 *syn*)), 1.8-1.1 (m, 11H); ^{13}C NMR: δ 137.5, 132.7, 128.6, 128.2, 126.6, 125.7, 88.5, 83.5, 65.0, 49.3, 44.0, 42.7, 39.7, 34.6, 31.7, 29.2, 28.4.

III (R = PhCH=CH, R' = $(CH_3)_2C-NH_2$), ^1H NMR (60 MHz): δ 7.5-7.0 (m, 5H), 6.4-6.2 (m, 2H), 2.58 (br d, J = 8 Hz, 1H, HC(2)), 2.4-2.0 (m, 3H, HC(1), HC(3), HC(4)), 1.9 (s, 2H, $-NH_2$), 1.8 (br d, J = 9 Hz, 1H, HC(7 *syn*)), 1.6-1.0 (m, 11H).

III (R = $CH_3CH=CH$, R' = Ph), m.p. 44-46°, ^1H NMR (100 MHz): δ 7.5-7.1 (m, 5H), 5.8-5.2 (m, 2H), 2.7 (br d, J = 8 Hz, 1H, HC(2)), 2.50-2.14 (m, 2H, HC(1), HC(3)), 2.06 (m, 1H, HC(4)), 1.94-1.05 (m, including a doublet at 1.70, J = 6 Hz, 9H).

III (R = $CH_2=CH$, R' = Ph), ^1H NMR (100 MHz): δ 7.5-7.1 (m, 5H), 6.2-5.8 (m, 1H), 5.1-4.8 (m, 2H), 2.76 (br d, J = 8.5 Hz, 1H, HC(2)), 2.54-2.20 (m, 2H, HC(1), HC(3)), 2.14 (m, 1H, HC(4)), 1.86 (br d, J = 10 Hz, 1H, HC(7 *syn*)), 1.7-1.1 (m, 5H); ^{13}C NMR: δ 143.5, 134.2, 130.8, 130.0, 127.2, 116.1, 94.5, 86.5, 53.4, 47.4, 45.6, 43.1, 37.6, 32.3, 31.5.

IV (R = PhCH=CH, R' = Ph), m.p. 63-65°, ^{1}H NMR (100 MHz): δ 7.5-7.0 (m, 10 H), 6.6-6.3 (m, 2H), 6.16 (AB system, 2H), 3.07 (m, 1H, HC(1))), 2.86-2.60 (m, 2H, HC(2), HC(4)), 2.60-2.34 (m, 1H, HC(3)), 2.00(br d, J = 9 Hz, 1H, HC(7 *anti*)), 1.52 (br d, J = 9 Hz, 1H, HC(7 *syn* to the double bond); ^{13}C NMR: δ 137.8, 137.7, 136.4, 133.0, 131.3, 129.8, 128.2, 127.9, 127.2, 126.6, 125.9, 123.8, 91.7, 83.5, 49.8, 48.7, 45.6, 44.4, 36.0.

IR spectra are in accord with the proposed structures. In particular the acetylenic function present in the 2-substituent revealed (with the exception of the 1-octynyl chain) its characteristic absorption at 2220 cm^{-1}. The CH=CH group, contained in some substituents, absorbed at 960-965 cm^{-1} (E-double bond).

The mass spectra showed the typical fragmentation of the norbornane ring. The loss of *m/e* 66 was especially evident in IV, which had a parent peak of very low intensity.

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References

1. (a) R. C. Larock, J. P. Burkhart and K. Oertle, *Tetrahedron Lett.* 23, 1071 (1982); (b) R. C. Larock, D. R. Leach and S. M. Bjorge, *Tetrahedron Lett.* 23, 715 (1982).
2. M. Catellani, G. P. Chiusoli, W. Giroldini and G. Salerno, *J. Organomet. Chem.* 199, C21 (1980).
3. M. Catellani and G. P. Chiusoli, *J. Organomet. Chem.* 233, C21 (1982).
4. M. Catellani, G. P. Chiusoli and P. Sgarabotto, *J. Organomet. Chem.*, in press.
5. L. Cassar, *J. Organomet. Chem.* 93, 253 (1975).

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