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Synthesis of Polycyclic Ketones via Carbonylative Cyclization of Organopalladium Compounds Derived from Norbornene and Norbornadiene

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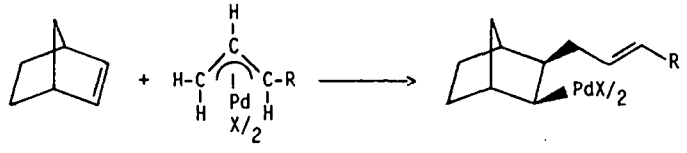
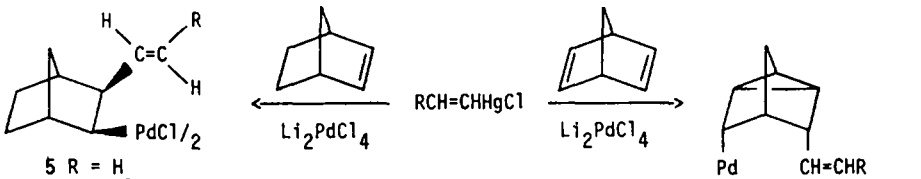
Abstract - The bicyclic and tricyclic organopalladium compounds prepared via π-allyl- and vinylpalladium additions to norbornene and norbornadiene respectively undergo cyclization upon reaction with carbon monoxide in methanol to afford an interesting variety of polycyclic ketones. The nature of the ligand on palladium (chloride versus hexafluoroacetylacetonate) and the presence or absence of triethylamine is observed to have a pronounced effect on the nature of the products formed in these carbonylation reactions.

π-Allyl-[2-7] and vinylpalladium[8-10] compounds have been reported to add to bicyclic alkenes, such as norbornene and norbornadiene, to afford stable organopalladium addition compounds (eqs. 1, 2). During the course of our work with organopalladium compounds, we had occasion to carbonylate



	R	X
1	H	Hfacac
2	H	Cl
3	CH_3	Hfacac
4	CH_3	Cl

(1)



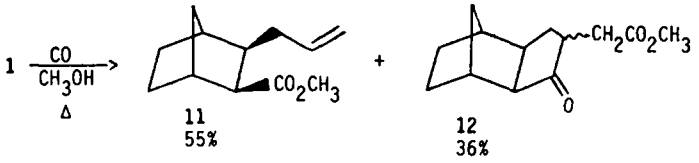
5 R = H
6 R = Cl
7 R = t-Bu

8 R = CH_3 (cis)
9 R = Cl (trans)
10 R = t-Bu (trans)

(2)

some of these compounds. We wish to report now that these compounds react with carbon monoxide in methanol to provide an interesting variety of polycyclic ketones.

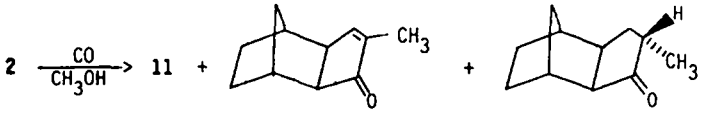
The addition of (π-allyl)palladium hexafluoroacetylacetonate to norbornene affords compound 1 in good yield.[6] This compound reacts with carbon monoxide in refluxing methanol to afford two major products 11 and 12 (eq. 3). Replacing the Hfacac ligand by chloride and subsequent



11 55%
12 36%

(3)

carbonylation affords only minor amounts of ester 11 and none of compound 12. Instead, ketones 13 and 14 are formed as the major products (eq. 4). The exo methyl stereochemistry of ketone 14 was

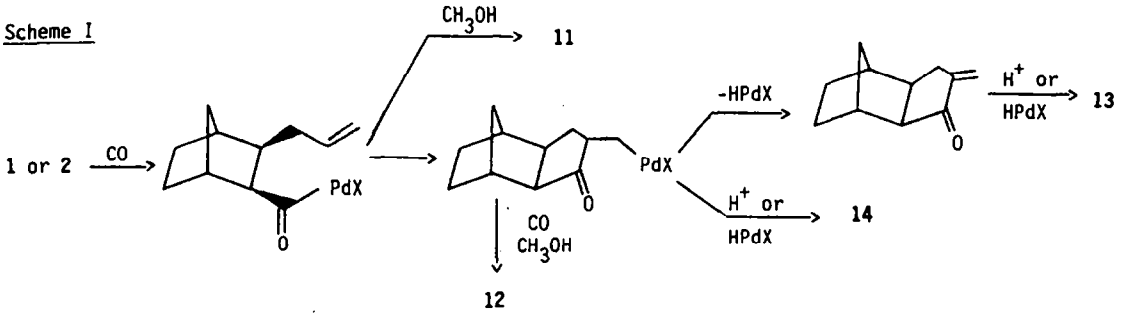


8% 13 75% 14 13%

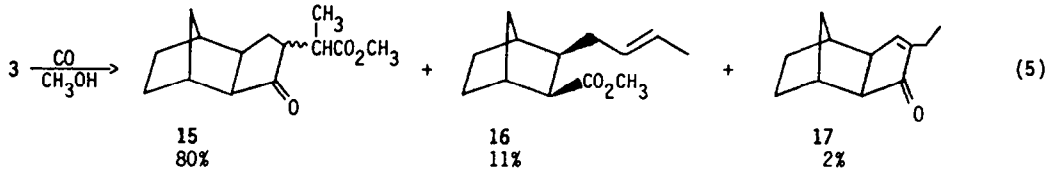
(4)

assigned based on the fact that the hydrogenation of enone 13 affords a saturated ketone which is isomeric to ketone 14. Since hydrogenation is expected to occur from the exo face of enone 13, the hydrogenation product must be the methyl epimer of enone 14. The carbonylation products apparently arise as shown in Scheme I.

Scheme I



Analogous carbonylation reactions have been carried out on compounds **3** and **4** with the following results (eqs. 5, 6). Now the γ-keto ester is the major product when Hfacac is the



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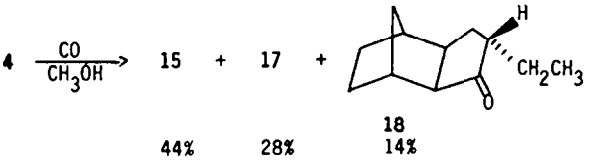
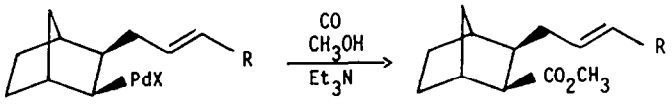


(6)

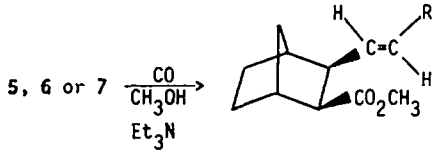
ligand. Only minor amounts of ester **16** or enone **17** are formed. With the chloride complex **4**, the γ-keto ester **15** still predominates, but enone **17** and saturated ketone **18** again become major products. The stereochemistry of ketone **18** was assigned as described above for ketone **14**.

The carbonylation of compounds **1-4** in the presence of Et_3N gave only the corresponding uncyclized methyl esters in high yield (eq. 7).



(7)

We have also examined the carbonylation of organopalladium complexes **5-7**. In the presence of triethylamine, carbonylation affords high yields of a single product, the uncyclized ester (eq. 8).[10] In the absence of triethylamine, these esters remained the major products, but their yields

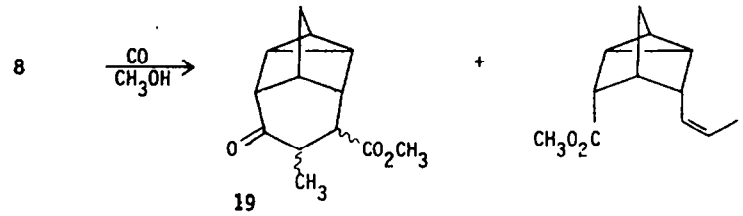


R = H 78%
R = Cl 94%
R = t-Bu 78% (93% by gas chromatographic analysis)

(8)

dropped significantly. There was no evidence for any cyclization products in any of these reactions.

The carbonylation of compounds **8-10** has provided some interesting results. Compound **8** and a compound prepared in a similar fashion and presumed to be compound **9** have previously been carbonylated to afford similar cyclization products (eqs. 9, 10).[11]



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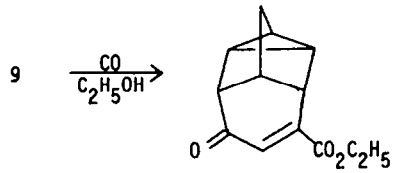
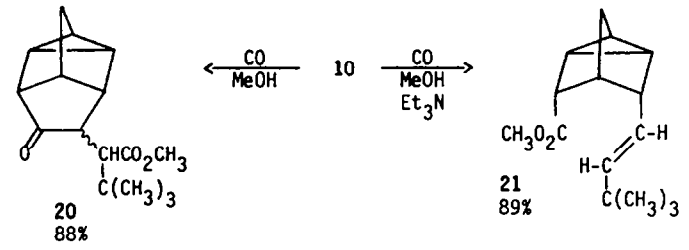


(10)

Unlike the above cyclizations, compound **10** underwent carbonylation in the absence of triethylamine with formation of a five-membered ring ketone (eq. 11). The product exhibited ketone absorption in the infrared spectrum at 1780 cm^{-1}, while Vedejs ketone **19** reportedly absorbs at



(11)

1727 cm^{-1}. The bulky t-butyl group completely reverses the direction of cyclization in this case. In the presence of triethylamine, the uncyclized ester **21** is obtained in high yield.[10]

In conclusion, by the appropriate choice of unsaturated organopalladium compound and palladium ligand, the carbonylation of these substrates can be directed so as to afford a variety of different polycyclic ketones and esters.

Experimental Section

Equipment. Melting points were determined on a Thomas Hoover Capillary Melting Point apparatus and are uncorrected. ^1H NMR spectra were obtained on a Varian Associates HA-100 NMR spectrometer, while the infrared spectra were recorded on a Beckman IR-4250 spectrophotometer. Exact masses were measured on an AEI MS-902 high resolution mass spectrometer. Gas chromatographic yields were determined using appropriate hydrocarbon internal standards on a Varian 2700 or 3700 gas chromatograph. Elemental analyses were performed by Galbraith Laboratories in Knoxville, Tennessee.

The (π-allyl)palladium adducts **1** and **2** were prepared according to the literature procedure.[6] The organopalladium hexafluoroacetylacetonate **3** was prepared as follows. The appropriate (π-allyl)palladium hexafluoroacetylacetonate (2.8 mmol) and norbornene (2.8 mmol) were stirred in benzene (3 ml) at room temperature for 24-48 h and then chromatographed on a florisil column using methylene chloride as the eluant. Removal of the solvent afforded compound **3** in 99% yield. This was recrystallized from hexane in 50% yield: mp 84.5-85.5°C; ^1H NMR ($CDCl_3$) δ 0.9-2.5 (11 H, m, norbornyl), 1.7 (3 H, d, J = 5.3 Hz, CH_3), 3.2 (1 H; dd; J = 1.8, 7.1 Hz; endo H next to Pd), 5.0-5.1 (2 H, m, vinyl), 5.9 (1 H, s, Hfacac); IR ($CHCl_3$) 3010, 2950, 2870, 1640, 1600, 1550, 1520, 1470, 1380, 1340, 1250, 1190, 1150, 1090, 1060, 1030, 990, 960, 940 and 670 cm^{-1}. Anal. Calcd for $C_{16}H_{18}F_6O_2Pd$: C, 41.53; H, 3.92. Found: C, 41.54; H, 3.90.

Organopalladium compound **4** was prepared as follows. Bis[chloro(1,2,3-trihaptobutene)-palladium(II)] (0.985 g, 2.5 mmol) and 1.27 g (5.75 mmol) of silver trifluoroacetate in 50 ml of dichloromethane were stirred at room temperature for 1 h. Norbornene (0.942 g, 10 mmol) was added and the resulting mixture was stirred overnight. The solution was then filtered through Celite to remove the silver salts, washed successively with aqueous ammonium chloride and aqueous sodium chloride, and dried over sodium sulfate. Removal of the solvent afforded 1.42 g (98% yield) of a yellow solid which was recrystallized from dichloromethane to give 0.70 g (48% yield): mp 164-167°C; ^1H NMR ($CDCl_3$) δ 0.9-2.7 (11 H, m, norbornyl), 1.8 (3 H, d, J = 3.6 Hz, CH_3), 3.2 (1H; dd; J = 1.5, 6.8 Hz; endo H next to Pd), 4.8-5.4 (2 H, m, vinyl); IR ($CHCl_3$) 3010, 2960, 2880, 1450, 1380, 1310, 1300, 1280, 1190, 1140, 1080, 1060, 1035, 980, 960 and 940 cm^{-1}. Anal. Calcd for $C_{11}H_{17}PdCl$: C, 45.39; H, 5.89. Found: C, 45.26; H, 5.99.

The vinylpalladium adducts **5-7** and **10** were prepared according to our general literature procedure.[9,10]

All carbonylation reactions were carried out using the following general procedure. The organopalladium compound (1 mmol) was weighed into a round bottom flask equipped with a septum inlet, magnetic stirring bar, and gas inlet tube. After flushing with nitrogen, 10 ml of methanol was added by syringe and the mixture was cooled to -78°C. Then, when used, 1.4 ml (10 mmol) of triethylamine was added by syringe. After flushing with carbon monoxide, a balloon containing carbon monoxide was attached to the gas inlet tube and the reaction mixture was slowly allowed to warm to room temperature while stirring. The stirring was continued overnight. The reaction mixture containing no triethylamine was refluxed an additional 3-24 h under one atm of carbon monoxide in order to complete the reaction. Ether and activated carbon were added to the reaction mixture which was then filtered. The reaction mixture containing triethylamine was washed with 2N hydrochloric acid and aqueous sodium chloride, and dried over sodium sulfate. Removal of the solvent and column chromatography, where necessary, gave essentially pure products. The following reactions were run in this fashion.

Carbonylation of compound **1**. Compound **11**: 55% yield; ^{1}H NMR ($CDCl_3$) δ 1.00-2.13 (12 H, m, norbornyl, allylic), 3.63 (3 H, s, OCH_3), 4.74-5.16 (2 H, m, $=CH_2$), 5.40-6.00 (1 H, m, CCH=C); IR (CCl_4) 3080 (C=CH), 2950, 2870, 2840, 1735 (C=O), 1640 (C=C), 1460, 1375, 1365, 1300, 1180, 1170, 1150, 1115, 1035 and 910 (vinyl) cm^{-1}; MS, m/z 194.13055 (calcd for $C_{12}H_{18}O_2$, 194.13068). Compound **12**: 36% yield; ^{1}H NMR ($CDCl_3$) 0.8-1.7 (7 H, m), 1.8-2.7 (8 H, m), 3.7 (3 H, s, OCH_3); IR (CCl_4) 2960, 2880, 1730 (C=O), 1465, 1440, 1420, 1365, 1325, 1300, 1250, 1200, 1170, 1120, 1060 and 860 cm^{-1}; MS, m/z 222.12636 (calcd for $C_{13}H_{18}O_3$, 222.12560).

Carbonylation of compound **2**. Compound **11**: 8% yield (see above). Compound **13**: 75% yield; ^{1}H NMR ($CDCl_3$) δ 0.88-1.65 (6 H, m), 1.78 (3 H, t, J = 1.5 Hz, CH_3), 2.08-2.70 (4 H, m), 7.18 (1 H, m, C=CH); IR (neat) 3020, 2940, 2920, 2860, 1740, 1700 (C=O), 1635 (C=C), 1450, 1375, 1325, 1290, 1250, 1180, 1125, 1070, 1050 and 840 cm^{-1}; MS, m/z 162.10429 (calcd for $C_{11}H_{14}O$, 162.10446). Compound **14**: 13% yield; ^{1}H NMR ($CDCl_3$) δ 0.90-2.50 (16 H, m); IR (CCl_4) 2950, 2880, 1730 (C=O), 1450, 1425, 1285, 1245 (C-O), 1165 and 830 cm^{-1}; MS, m/z 164 (parent), 149 (P-CH_3), 135, 121, 108, 94, 79, 66. Hydrogenation of compound **13** (5% Pd/C, EtOH, 1 atm, 25°C) gave a different isomer - MS, m/z 164.12044 (calcd for $C_{11}H_{16}O$, 164.12012).

Carbonylation of compound **3**. Compound **15**: 80% yield; mixture of 3 isomers in ratio 7:5:4; ^{1}H NMR ($CDCl_3$) 0.9-1.7 (7 H, m), 1.1 and 1.2 (3 H, d, J = 10 Hz, CH_3), 1.9-2.9 (7 H, m), 3.57 and 3.60 (3 H, s, OCH_3); IR (CCl_4) 2970, 2890, 1740 (C=O), 1470, 1440, 1250, 1205, 1160 and 1070 cm^{-1}; MS, m/z 236.14151 (calcd for $C_{14}H_{20}O_3$, 236.14125). Compound **16**: 11% yield; ^{1}H NMR δ 1.0-2.5 (15 H, m), 3.5 (3 H, s, OCH_3), 5.3 (2 H, m, CH=CH); IR (CCl_4) 3030 (=CH), 1740 (C=O), 1370, 1170, 1040 and 970 cm^{-1}; MS, m/z 208.14607 (calcd for $C_{13}H_{20}O_2$, 208.14633). Compound **17**: 2% yield; ^{1}H NMR ($CDCl_3$) δ 0.9-1.8 (6 H, m), 1.1 (3 H, t, J = 6.8 Hz, CH_3), 1.9-2.7 (6 H, m), 7.1 (1 H, m, CH=C); IR (CCl_4) 3040 (=CH), 2970, 2880, 1710 (C=O), 1630 (C=C), 1460, 1250, 1185, 1050 and 900 cm^{-1}; MS, m/z 176.12004 (calcd for $C_{12}H_{16}O$, 176.12012).

Carbonylation of compound **4**. Compound **15**: 44% yield (see above). Compound **17**: 28% yield (see above). Compound **18**: 14% yield; only characterized by GC-MS; hydrogenation of compound **17** gave a different isomer.

Carbonylation of compounds **1-4** in the presence of Et_3N afforded only the corresponding uncyclized esters in near quantitative yield (see eq. 7). The spectral data for compounds **11** and **16** are listed above.

The spectral data for the esters obtained upon carbonylation of compounds **5-7** in triethylamine are reported elsewhere (see eq. 8).[10]

Carbonylation of compound **10**. Compound **20**: 88% yield; ^{1}H NMR ($CDCl_3$) δ 0.9-1.25 (3 H, m, nortricyclyl), 1.0 (9 H, s, t-Bu), 1.55 (2 H, m, H adjacent to ketone and ester), 2.50 (1 H, m, H adjacent to ketone and cyclopropane), 3.33 (3 H, s, CH_3); IR (CCl_4) 3070, 2995, 2970, 2950, 2920, 2880, 2845, 1780, 1740, 1480, 1470, 1405, 1375, 1350, 1330, 1320, 1310, 1285, 1275, 1270, 1255, 1240, 1230, 1210, 1200, 1185, 1180, 1160, 1130, 1120, 1080, 1070, 1060, 1040, 1010, 980, 967, 960, 950, 940, 935, 910, 890 and 860 cm^{-1}; MS, m/z 262.15909 (calcd for $C_{16}H_{23}O_3$, 262.15689).

Spectral data for the ester **21** obtained upon carbonylation of compound **10** in the presence of triethylamine (eq. 11) are reported elsewhere.[10]

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References and Notes

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