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REACTION OF CYCLOALKANONE ENAMINES WITH ALLYLIC COMPOUNDS IN THE PRESENCE OF PALLADIUM COMPLEXES

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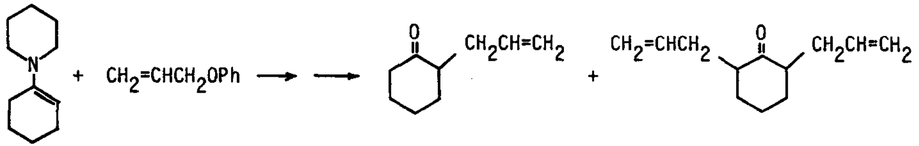
Although enamines have been well known as an active and important reagent of organic syntheses (1), their reactions with transition metal complexes have received little attention (2-6). Allylation of active-hydrogen compounds with allylic esters or phenoxides using palladium catalysts was reported to proceed *via* π-allylpalladium complexes (7,8). Tsuji et al. reported briefly the reaction of enamines with π-allylpalladium chloride (5).

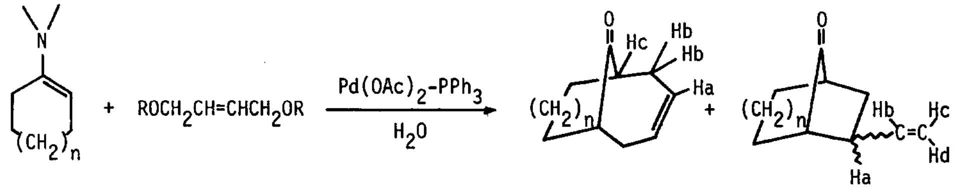
Hence, allylation of enamines with allylic esters or phenoxides is expected to be carried out catalytically. Further, bicycloketones are prepared by the reaction of enamines of cycloalkanones with 1,4-diacetoxy or 1,4-diphenoxy-2-butene.

A typical procedure is as follows: A mixture of 1-piperidinocyclohexene (0.1 mole), allyl phenoxide (0.11 mole), $Pd(OAc)_2$ (0.5 mmole) and PPh_3 (2 mmoles) in abs. benzene (50 ml) was heated at reflux under argon atmosphere (6 hr). After removal of benzene *in vacuo*, the residue was hydrolyzed by treatment with water (100 ml) at 100°(0.5 hr)and extracted with ether. The ether extract was washed with aqueous NaOH to remove phenol, concentrated and distilled to give a colorless liquid (79-122°/19 mm, 12 g), a mixture of 2-allylcyclohexanone (70 %) and 2,6-diallylcyclohexanone (13 %).



Reaction of 1-piperidinocyclopentene with allyl phenoxide gave similarly a mixture of 2-allylcyclopentanone (64 %) and 2,6-diallylcyclopentanone (21 %). Other allylic compounds such as allyl acetate, 1,2 or 3-methylallyl acetate or phenoxide, etc., were tested successfully to give the corresponding substituted allyl cycloalkanones. The effective palladium catalysts used were $Pd(OAc)_2$-PPh_3, $Pd(AcAc)_2$-PPh_3 and $Pd(PPh_3)_4$. Complexes of other transition metals such as $RhCl(PPh_3)_3$, $Pt(AcAc)_2$-PPh_3 and $RuCl_2(PPh_3)_3$ also showed catalytic activity in the order Pd->Rh->Pt->Ru-complex. The fact that the reaction of both crotyl acetate and 3-acetoxy-1-butene with 1-piperidinocyclohexene gave the same products, 2-(2-butenyl)cyclohexanone (trans/cis= 4.5), would suggest that these reactions proceed via a common intermediate, a π-1-methylallylpalladium complex.

If 1,4-diacetoxy or 1,4-diphenoxy-2-butene is used, 4-acetoxy (or phenoxy)-2-butenyl substituted enamine initially formed will again form a π-allylpalladium complex in which the β'-carbon may attack the π-allyl group intramolecularly to afford bicycloketones. In anticipation of this hypothesis, synthesis of bicycloketones from enamines of cycloalkanones by single step was carried out.



(I) (II) (III) (IV)

A mixture of 1,4-diphenoxy-trans-2-butene (12.0 g) (II, R=Ph), $Pd(OAc)_2$ (1 mmole), PPh_3 (4 mmoles) and 1-piperidinocyclopentene (7.7 g) (I, n=0) in abs. benzene was heated under argon atmosphere (3 hr). After the usual work-up, the products were submitted to silica gel chromatography. Distillation of the eluate gave bicyclo[4.2.1]non-3-en-9-one (III, n=0) (1.9 g, 28 %, bp 72-73°/4 mm, mp 49-50°), m/e= 136, ir; 3025 cm^{-1}(=CH), 1740 (C=O), nmr; δ 5.58 (Ha), 2.93 (Hc), 2.15 (Hb), 2.1-1.5 (other ring protons). 2,4-Dinitrophenylhydrazone, mp 182-183°. Hydrogenation over palladium sponge gave bicyclo[4.2.1]nonan-9-one, mp 109-110° (9). The results using other catalysts such as $Pd(AcAc)_2$-PPh_3 and $PdCl_2(PPh_3)_2$-PhONa were virtually identical with that described above.

Reaction of 1-pyrrolidinocyclohexene with 1,4-diacetoxy-2-butene (II, R= OAc) afforded a mixture of three products, bicyclo[4.3.1]dec-3-en-10-one (III, n=1), 6-exo-vinyl-bicyclo[3.2.1]-octan-8-one (IV, n=1) and 6-endo-vinyl-bicyclo[3.2.1]octan-8-one (IV, n=1). Each compound was separated by preparative vpc, and the structure was assigned on the basis of the following data.

Bicyclo[4.3.1]dec-3-en-10-one, mp 58-61°, m/e= 150, ir; 3015 cm^{-1}(=CH), 1700 (C=O), nmr; δ 5.75 (Ha), 2.63 (Hc), 2.28 (Hb), 2.1-1.3 (other ring protons). 2,4-Dinitrophenylhydrazone, mp 174-175°.

The configurational assignment (exo- or endo-vinyl) of compounds (IV) was based on the chemical shift of the Ha proton. In 2- substituted norbornanes, the absorption of the endo proton usually appears upfield than that of the corresponding exo proton (10, 11).

6-exo-Vinyl-bicyclo[3.2.1]octan-8-one, ir; 1745 cm^{-1}(C=O), 994 and 915 (terminal vinyl), nmr; δ 5.18 (Hb), 4.89 (Hc), 4.83 (Hd), 2.62 (Ha), 2.3-1.5 (other ring protons). The seven lines (Hb) collapsed to four lines on irradiation at δ 2.62 (Ha). 2,4-Dinitrophenylhydrazone, mp 127-130°. 6-endo-Vinyl-bicyclo[3.2.1]octan-8-one, ir; 1750 cm^{-1}(C=O), 993 and 915 (terminal vinyl), nmr; δ 6.02 (Hb), 5.15 (Hd), 5.13 (Hc), 2.84 (Ha), 2.4-1.4 (other ring protons). The seven lines (Hb) collapsed to four lines on irradiation at δ 2.84 (Ha). 2,4-Dinitrophenylhydrazone, mp 113-115°.

Similar reactions were performed on 1-pyrrolidinocycloheptene and 1-pyrrolidinocyclooctene, and the results are summarized in Table 1.

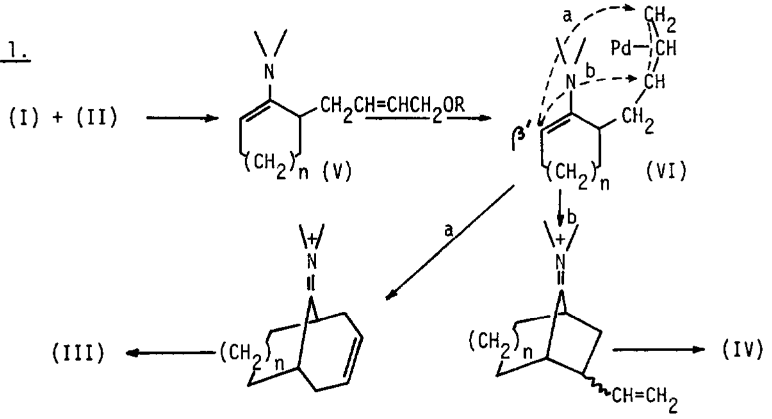
Table 1. Bicycloketones from Cycloalkanone Enamines

(I)	R of (II)	n	(III) (%)	(IV) (endo/exo) (%)
1-Piperidinocyclopentene	$COCH_3$	0	17	—
	C_6H_5	0	28	—
1-Pyrrolidinocyclohexene	$COCH_3$	1	30	34 (0.41)
1-Pyrrolidinocycloheptene	C_6H_5	2	28	39 (2.21)
1-Pyrrolidinocyclooctene	C_6H_5	3	12	28 (0.31)

A mixture of (I) (0.05 mole), (II) (0.05 mole), $Pd(OAc)_2$ (1 mmole) and PPh_3 (4 mmoles) in abs. benzene (100 ml) was refluxed for 3 hr under argon.

These reactions would be rationalized as shown in Scheme 1. Enamines (I) react with the π-allylpalladium complexe derived from (II) to give 4-phenoxy(or acetoxy)-2-butenyl substituted enamines (V). The enamines (V) also form π-allylpalladium complexes (VI), in which the β'-carbon attacks the π-allyl group intramolecularly either path a or b followed by hydrolysis to give bicycloketones (III) or (IV). In fact, when reaction of 1-piperidinocyclopentene with 1,4-diacetoxy-2-butene was stopped in the early stage, formation of (III, n=0) was negligible, and was obtained a hydrolysis product of an intermediate (V) (n=0, R=$COCH_3$), 2-(4-acetoxy-trans-2-butenyl)cyclopentanone. Ir; 1720 and 1740 sh (C=O). 2,4-Dinitrophenylhydrazone, mp 98-100°, ir; 1730 cm^{-1}(C=O).

Scheme 1.



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