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NEW PALLADIUM MEDIATED CYCLOPENTANATION OF ALKENES BEARING A δ NUCLEOPHILIC SUBSTITUENT

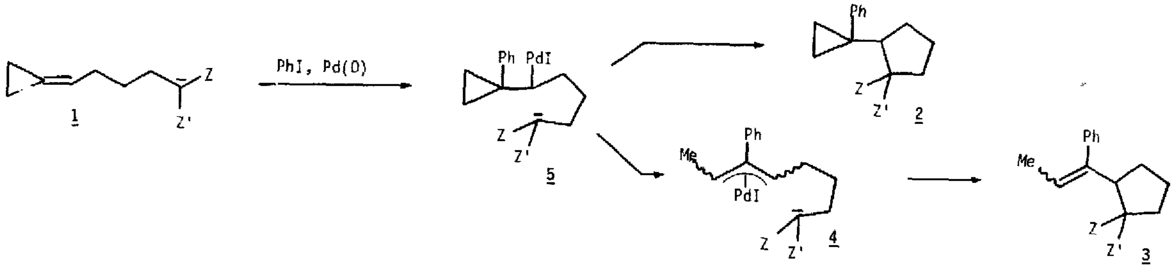
Guy FOURNET, Geneviève BALME and Jacques GORE,

Laboratoire de Chimie Organique I , U.A. 467 du CNRS , Université Claude Bernard
ESCIL - 43 Bd du 11 Novembre 1918, 69622 VILLEURBANNE, France.

Summary. A σ-alkylpalladium intermediate generated by carbopalladation of a double bond can be intramolecularly trapped by a β-diester or a β-keto ester enolate if a cyclopentane ring is formed. Otherwise, normal β-elimination is observed.

Recent studies have been concerned with the intramolecular HECK reaction forming bicyclic or polycyclic systems with five or six membered rings (1)(2). More particularly, OVERMAN et al have shown that a σ-alkyl palladium intermediate produced by an intramolecular HECK reaction can be trapped by neighboring double bonds to give bis-cyclisation products. However, for the success of these cyclizations, the alkyl palladium intermediate must not be capable of a β-elimination.

Recently, we have shown that the carbopalladation of alkylidenecyclopropanes of type 1 leads mainly to cyclized products 2 besides small quantities of 3 (3) (scheme 1).

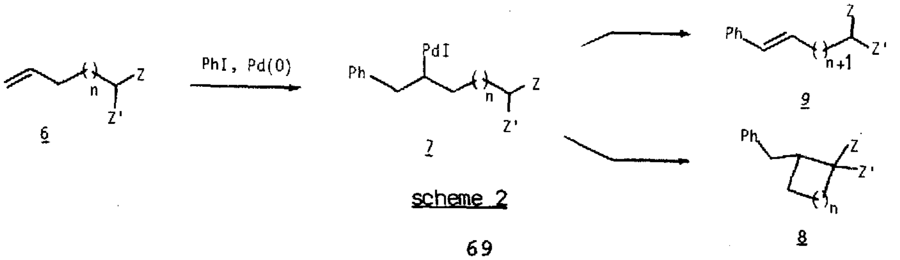


Z,Z' = electron withdrawing groups

scheme 1

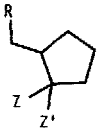
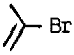
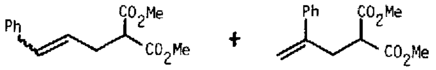
It was then assumed that 3 was formed from the cyclization of the π-allyl-palladium species 4 resulting from the rearrangement of the initially formed σ-alkyl α-cyclopropyl-palladium intermediate 5 while 2 came from the direct cyclization of this intermediate.

Consequently, we became interested in the study of the Heck-reaction of alkenes of type 6 in order to see if the σ-alkyl palladium intermediate 7 can be intramolecularly attacked by the internal nucleophile leading to 8 before giving rise to a β-elimination process producing the normal Heck compound 9 (scheme 2).



scheme 2

Effectively for n=2, three examples (table) show clearly that the trapping of the σ-alkyl palladium intermediate 7 by the internal nucleophile is considerably faster than the β-elimination reaction, since 8a, 8b and 8c are respectively the only isolated products (4) when 6a and 6b are submitted to the conditions described below (Table). Unfortunately neither the anion of 6c nor that of 6d could be transformed into cyclohexanic or cyclopropanic compound. Only the β-elimination products are then obtained as in the case of the slow reaction of the γ-ethylenic benzylamine 10 leading only to 11 with exclusively the E configuration.

	Starting material	RX	Reaction time	Product		isolated yield
6a	n=2 Z=Z'=CO_2Me	PhI	75mn		8a R=Ph Z=Z'=CO_2Me	75%
6a	n=2 Z=Z'=CO_2Me		105mn		8b R= Z=Z'=CO_2Me	57%
6b	n=2 Z=CO_2Me Z'=COMe	PhI	4h	8	8c R=Ph Z=CO_2Me Z'=COMe (2 diastereoisomers 70/30)	75%
6c	n=3 Z=Z'=CO_2Me=Z'	PhI	20h	mixture of β-elimination products**		
6d	n=0 Z=Z'=CO_2Me=Z'	PhI	16h	 Z+E - mixture 1:1:1		65%
10		PhI	16h			60%

* Complete disparition of the starting material.

** this mixture could have arisen from a non-regiospecific addition of phenylpalladium iodide on the double-bond, a non-stereoselective β-elimination and a migration of the double-bond along the chain.

typical procedure : the anion of 6a, prepared in DMSO (5) with 1,1 molar eq. of NaH, is heated at 85°C over a period of 75 mn with 4% molar eq. of palladium bis(dibenzylidene acetone), 4% molar eq. of bis(diphenylphosphino)-1,2 ethane and 1,1 mol eq. of PhI. Classical work up followed by chromatography on silicagel gives 8a.

TABLE

We are currently trying to apply the new annulation process to the stereoselective synthesis of polycyclic compounds.

References and notes

1. For leading references, see :
   a) E.I.NEGISHI, Y.ZHANG and B.O'CONNOR, Tetrahedron Lett., 1988, 29, 2915.
   b) R.C.LAROCK, H.SONG, B.E.BAKER and W.H.GONG, Tetrahedron Lett., 1988, 29, 2919.
2. M.M.ABELMAN and L.E.OVERMAN, J.Amer.Chem.Soc., 1988, 110, 2328.
3. G.FOURNET, G.BALME and J.GORE, Tetrahedron Lett., 1987, 28, 4533 ; Tetrahedron, in press.
4. All new compounds were fully characterized by microanalysis, MS, ^1H and ^{13}C NMR spectroscopy.
5. The same reactions were unsatisfactory when run in boiling THF : after 24 hours, 6a is only partially transformed in small amounts of 8a (<10%) accompanied by several unidentified products.

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