Tetrahedron Letters,Vol.23,No.50,pp 5279-5282,1982 0040-4039/82/505279-04$03.00/0
Printed in Great Britain

STEREOCHEMISTRY IN THE PALLADIUM-CATALYZED REARRANGEMENT OF SOME CYCLOHEX-2-ENYL ACETOACETATES

J.C.Fiaud and L.Aribi-Zouioueche

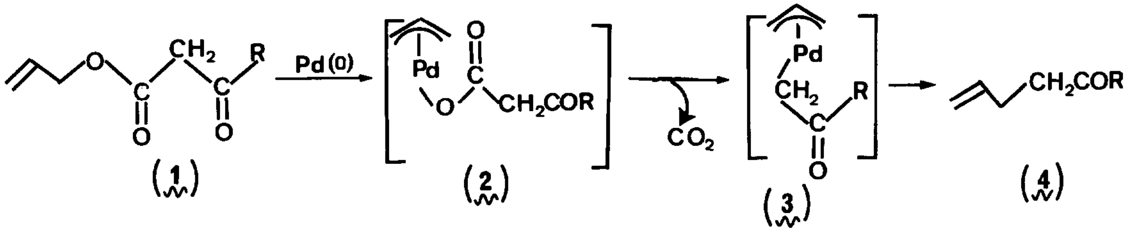
Laboratoire de Synthèse Asymétrique, associé au CNRS LA 255
Université Paris-Sud, 91405-Orsay, France.

Summary

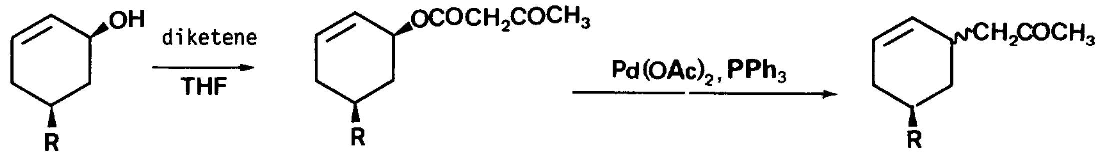
The palladium-catalyzed decarboxylation and rearrangement of cis-5-substituted-cyclohex-2-enyl acetoacetates to give the corresponding methyl ketone proceed mostly with retention of configuration, indicative of an enolate addition to the π-allylic ligand trans to the palladium. The reaction from the trans-isomer is not stereoselective.

We have recently reported that the palladium-catalyzed substitution of cyclohex-2-enyl acetates by the pre-formed lithium enolate of acetone occurred with overall retention of configuration[1].

The palladium-catalyzed rearrangement of allylic β-ketocarboxylates (1) has been shown to proceed under mild conditions, via a π-allyl palladium (II) enolate intermediate (3), produced in situ from decarboxylation of the π-allyl palladium (II) β-ketocarboxylate (2), to give the ketone (4) in moderate to good yields[2,3].



To compare the stereoselectivity of attack of the in situ produced enolate with the externally added one, we looked at the stereochemical out come of the palladium-catalyzed rearrangement of the 5-substituted-cyclohex-2-enyl acetoacetates (6) prepared by reaction of diketene[4] with cis-5-phenylcyclohex-2-enol (5a)[5] and cis-5-isopropylcyclohex-2-enol (5b)[6] (Scheme 1). (6) (4 mmol) in THF (20 ml) in the presence of 0.2 mmol $Pd(OAc)_2$ and 0.8 mmol PPh_3 were heated for 12 h at 55°C. After aqueous work up, the elimination product (1,3-diene) and ketone (7) were collected by Kugelrhor distillation. The results are shown in Table 1.



(5) (6) (7)

a : R = Ph
b : R = iPr

Scheme 1 (Only one enantiomer is shown)

Table 1 : Stereochemical results in the palladium-catalyzed rearrangement of acetoacetates made up from allylic alcohols (7).

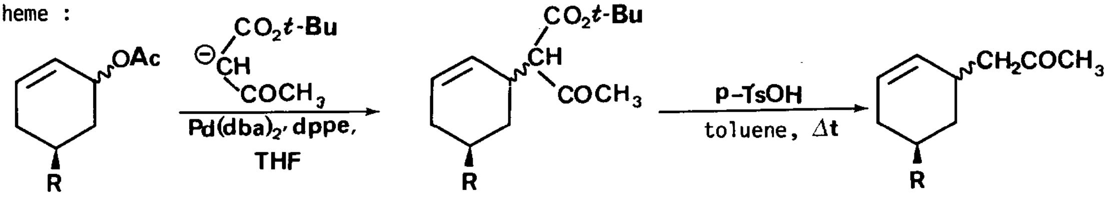
Alcohol (5)		Ketone (7)		
	cis/*trans* purity [a]		(*cis*/*trans* ratio) [a]	Yields (%) [b]
cis-(5a)	95:5	(7a)	80:20	53
cis-(5b)	91:9	(7b)	86:14	45
cis(-)-carveol	91:9	carveylacetone[c]	85:15	42
trans-(5a)	24:76	(7a)	66:34	45

a) Determined by g.l.c. (capillary column, OV1, 15 m).

b) Isolated material with satisfactory elemental analysis.

c) Racemic.

Cis and *trans* (7a) were prepared for comparison by the palladium-catalyzed reaction of the sodium salt of t-butyl acetoacetate with the corresponding acetate (8)[7], according to the Scheme :



(8) (9) (7)

The reaction was assumed to proceed with overall retention of configuration as it has been shown for the palladium-catalyzed reaction of stabilized enolates on cyclohexenyl acetates[9]. The Table indicates that the palladium-catalyzed rearrangement of *cis*-(6) proceeds with major retention of configuration. Provided that the displacement of the acetoacetate group (in analogy to the acetate group) by the Pd(0) complex occurs with inversion[10], these results suggest that the enolate ion rather the π-allylic ligand trans to the palladium attacks than undergoing intramolecular transfer delivery from the metal center. This is the agreement with the previously described stereochemistry of attack of ketone enolates to π-allyl palladium complexes[11] and to allylic acetates in the palladium-catalyzed reaction[1].

Moreover, the palladium-catalyzed rearrangement of the acetoacetate of (-)*cis*-carveol led to racemic *cis*-carveylacetone, confirming the intermediacy of a π-allyl palladium (II) complex. Nevertheless, the rearrangement of *trans*-(7a) was not stereoselective. As it was checked that both *cis*- and *trans*-(7a) were stereochemically stable in the conditions of the reaction, the loss of selectivity can be attributed to a competing process, that could likely be a palladium-assisted epimerization of the starting acetoacetate, in analogy to the process described with allylic acetates[12].

ACKNOWLEDGEMENTS

The authors thank Professor H.B.Kagan for fruitful discussions and "La Compagnie des Métaux Précieux" for a loan of palladium chloride. Financial support by the C.N.R.S. is acknowledged On of us (L.A.Z.) is indebted to the Ministère Algérien de l'Enseignement et de la Recherche for a fellowship.

REFERENCES

1. J.C.Fiaud and J.L.Malleron, J.C.S.Chem.Comm., 1981, 1159.
2. I.Shimizu, T.Yamada and J.Tsuji, Tetrahedron Lett., 21, 3199 (1980).
3. T.Tsuda, Y.Chujo, S.Nishi, K.Tawara and T.Saegusa, J.Am.Chem.Soc., 102, 6381, (1980).
4. W.Kimel and A.C.Cope, J.Am.Chem.Soc., 65, 1992 (1943).
5. E.Dunkelblum, R.Levene and J.Klein, Tetrahedron, 28, 1009 (1972).

6. R.L.Frank and H.K.Hall,Jr., J.Am.Chem.Soc., *72*, 1645 (1950).

7. *Trans*-5-phenyl cyclohex-2-enyl acetate (**8a**) was produced from *cis*-(**5a**) according to a described procedure (O.Mitsunobu, Synthesis, *1981*, 1) and gave through saponification the corresponding alcohol *trans*-(**5a**).

8. Treatment of (**8**) with 2 mol % of $Pd(dba)_2$ and 2 mol % of diphenylphosphinoethane (dppe) in THF with the sodium salt of t-butyl acetoacetate led to the alkylation product (**9**) (60 % yield) which afforded the ketones (**7**) upon refluxing in toluene with *p*-TsOH. *Cis*- and *trans*- ketones (**7**) showed different chromatographic (g.l.c., capillary column OV1, 15 m) and spectroscopic characteristics *cis*-(**7a**) : ^{13}C n.m.r. ($CDCl_3$; Me_4Si) 30.74 ; 33.41 ; 33.77 ; 37.05 ; 40.57 ; 50.28 ; 126.37 ; 127.04 ; 127.65 ; 128.98 ; 130.25 ; 130.62 ; 146.88 ; 208.11.
trans-(**7a**) : ^{13}C n.m.r. ($CDCl_3$; Me_4Si) 30.43 ; 30.61 ; 34.86 ; 36.02 ; 49.61 ; 126.31 ; 127.16 ; 127.58 ; 128.62 ; 130.25 ; 130.62 ; 146.64 ; 207.99.

9. B.M.Trost and T.R.Verhoeven, J.Org.Chem., *41*, 3215 (1976).

10. B.M.Trost and T.R.Verhoeven, J.Am.Chem.Soc., *102*, 4730 (1980).

11. B.Akermark and A.Jutand, J.Organometal.Chem., *217*, C 41 (1981).

12. B.M.Trost, T.R.Verhoeven and J.M.Fortunak, Tetrahedron Lett., *1979*, 2301.

(Received in France 2 August 1982)