Tetrahedron Letters, Vol.22, No.26, pp 2479 - 2482, 1981
Printed in Great Britain

0040-4039/81/262479-04 \$02.00/0

CHIRALITY TRANSFER. A STEREOSPECIFIC PALLADIUM SALT CATALYZED PHENYLATION OF CHIRAL BUTENOLS.

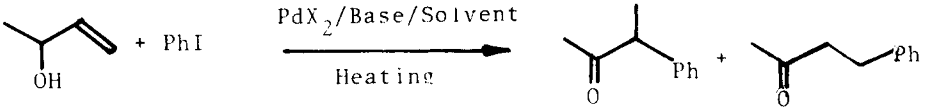
William SMADJA, Stanislas CZERNECKI, Guy VILLE and Constantin GEORGOULIS*

Laboratoire de Cinétique et Mécanismes de Réactions Organiques, CNRS ER 84 associée à
l'Université Pierre et Marie Curie, Paris VI; 4, place Jussieu, 75230 Paris Cedex 05.

(R)-(-) and (S)-(+)-3-phenyl butanones have been obtained by a 20% stereospecific palladium catalyzed β-phenylation of the corresponding chiral butenols, the catalyst acting preferentially, through an alkoxide complex, by one face of the alcohol double bond, e.g. the *si* face of (R)-(-)3-butene-2-ol(I).

The palladium catalyzed arylation of olefins, a C-C bond formation (1), proceeds by a mechanism not completely known, although a *cis*-addition of "ArPdX" followed by a *cis*-elimination of "HPdX" is generally accepted (2).

This reaction has been extended to the arylation of allylic alcohols (3) leading to arylated ketones.



(I) (II) (III) 10% (IV) 90%

In a previous study of the stereochemistry of the isomerization of allylic alcohols to ketones (4a), we have shown that a $RuCl_3$-NaOH catalyst is able to differentiate the two diastereofaces of the starting double bond and this stereoselective interaction has been attributed to the existence of a *ruthenium alkoxide complex*.

In this context and because of the preparative interest of palladium catalyzed arylation (4b) we undertook the phenylation of (R)-(-) and (S)-(+)-3-butene-2-ols (I), in which the β-prochiral carbon atom can serve as a convenient probe for detection of an eventual stereoselective β-phenylation yielding the branched ketone (III). 3-Butene-2-ol was chosen for this study because of the known structure (5), specific rotation (5,6) and C.D. curve (7) of the minor reaction product, namely (S)-(+)-3-phenyl-butanone (III).

First attempts, using the Melpolder-Heck procedure (3a)(PhI, $Pd(OAc)_2$, Et_3N, DMF) were unsuccessful whereas the Chalk-Magennis technique (3b, 8)(PhI, $PdCl_2$, $HNaCO_3$, DMF) affords the optically active branched ketone (III)(9).

TABLE : STEREOSPECIFIC β-PHENYLATION OF CHIRAL BUTENOL(I)

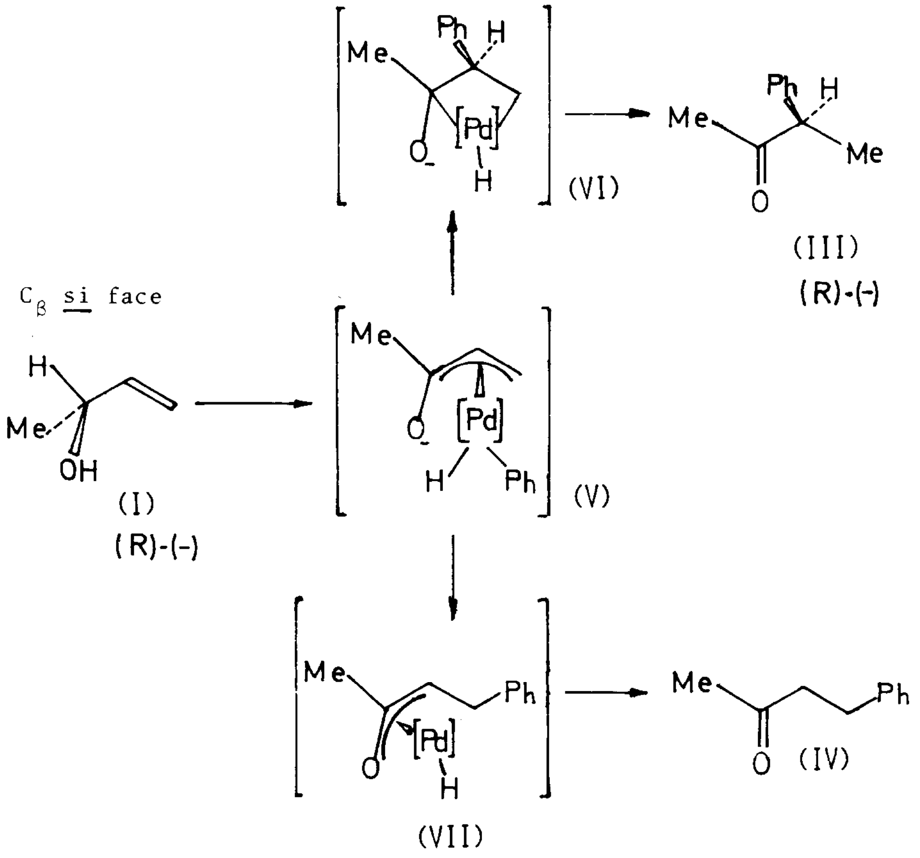
Starting butenol	Chemical(a) yield %	Ketone(III)	Optical yield %
(S)-(+)(I) $[\alpha]_D$ 25.1°(neat) o.p.(h) 74%(e)	70(b)	(S)-(+)(b) $[\alpha]_D$ 33.9°(C 4.8 ether) o.p.(h) 9.2%(f)	12.5
	70(c)	(S)-(+)(c) $[\alpha]_D$ 63.3°(C 4.5 ether) o.p.(h) 17.2%(f)	23
(R)-(-)-(I) $[\alpha]_D$ 19.5°(neat) o.p.(h) 57.5%(e)	61(d)	(R)-(-)(d) $[\alpha]_D$ 38.5°(C 4.8 ether) o.p.(h) 10.5%(f)(g)	18

(a) The chemical yield of isolated products includes the linear ketone. (b) 3.5 h at 130°C and work-up by steam distillation. (c) 1 hour at 130°C and work-up by extraction. (d) 1 hour at 130°C and steam distillation. (e) calculated from the value $[\alpha]_D$ 33.8° (neat)(13). (f) calculated from the value 368° (benzene)(5). (g) C.D. curve θ_{295}-3,980. (h) o.p.: optical purity = $[\alpha]$ obs./$[\alpha]$ max.x 100.

Each enantiomer of chiral butenol leads to optically active 3-phenyl-butanone (III) having preferentially the same configuration (Table). The optical purity has been calculated from the value 368°(benzene)(5) for the specific rotation of (S)-(+)-(III)(10). The C.D. curves of the two enantiomeric ketones obtained are mirror images; the one corresponding to (S)-(+)-3-phenyl-butanone is identical to that already described by Djerassi (7). In order to exclude a possible racemization during H.P.L.C. we submitted repeatedly the branched ketone (S)-(+)-(III) with $[\alpha]_D$ 70°(C 4.8 ether) to the isolation procedure and did not observe any loss of optical rotation. Nevertheless, the actual asymmetric induction ocurring in this reaction should be higher than the one observed because of racemization due to the experimental conditions as shown by the decrease of the rotation observed with increasing periods of heating (footnotes b and d in the table).

The stereochemistry observed in this paper debars the exclusive formation of a decomplexed enol, as an intermediate, in the multistep-1,2 addition-elimination mechanism which has been proposed (3a, b) to explain the phenylation in β-position. It is in agreement with a palladium alkoxide complex leading to a Π-allyl complex (V) from which the transfer of the phenyl group in β or γ position and of the hydrogen atom in γ or β position affords the ketones (III) and (IV) *via* the palladacyclobutane (VI)(12) and the complex (VII) respectively. The asymmetric induction observed in this study allows us to

Scheme : Pathway followed by the stereospecific β-phenylation of 3-butene-2-ol (I).



conclude that the catalyst interacts preferentially with the *si* face of allylic alcohol (R) and that the phenyl group is transferred with retention from the Π-allyl complex (V)(11).

The existence of such a complex derives from our previous data with the RuCl$_3$-NaOH system (4a) and is supported by the negative results obtained with the Melpolder-Heck procedure in this work. The failure in this last case may be attributed to the presence of the triethylamine, which strongly coordinates the palladium intermediate, preventing its interaction with the hydroxyl group

We wish to thank Dr. Bollard for the c.d.measurements and Dr. C. Agami for helpful discussion. We are indebted to Mrs. Fusey for her technical assistance and to M. Vijayakumaran for a sample of the semicarbazone of (S)-(+)-(III) ketone.

References and Notes

1) R.F. HECK, Acc.Chem.Res., 12, 146, (1979).

2) J. MARCH, "Advanced Organic Chemistry", 2nd ed.Mc.GRAW HILL, New-York, p. 656, (1977).

3) a) J.B. MELPOLDER and R.F. HECK, J.Org.Chem., 41, 265, (1976).
b) A.J. CHALK and S.A. MAGENNIS, J.Org.Chem., 41, 273 and 1206, (1976).
c) Y. TAMARU, Y. YAMADA and Z.I. YOSHIDA, Tetrahedron Lett., 329, (1979).

4) a) W. SMADJA, G. VILLE and C. GEORGOULIS, J.Chem.Soc.,Chem.Comm.,584, (1980).
b) S. CZERNECKI and F. GRUY, Tetrahedron Lett., 437, (1981).

5) R.D. CLARK and H.S. MOSHER, J.Org.Chem., 35, 1114, (1970).

6) a) K. MISLOW and J. BRENNER, J.Amer.Chem.Soc., 75, 2318, (1953).
b) K. MISLOW and Ch.L. HAMMERMESH, *ibid.*, 77, 1590, (1955).

7) G. BARTH, W. VOELTER, H.S. MOSHER, E. BUNNENBERG and C. DJERASSI, J.Amer.Chem.Soc., 92, 875, (1970).

8) The typical procedure for phenylation of allylic alcohol was the following : a solution of 3-butene-2-ol (720 mg, 10 mmol) in dry DMF (8 ml) in the presence of NaHCO$_3$(1 g, 12 mmol), PdCl$_2$(17 mg, 0,1 mmol), PhI(1,1 ml 10 mmol) is heated 1 to 3.5 hours at 100°C. The reaction is followed by G.L.C.(SE 30,10% chromosorb Q 80-100 mesh 4 m 125°C 1.25 bar). After work-up, the separation of the branched ketone from the mixture has been made by H.P.L.C. on Chromatospac 100 (Jobin-Yvon), column packed with silicagel H type 60 (Merck), the elution using an ether-pentane(1-4) mixture monitored by refractive index.

9) The branched ketone (S)-(+)-(III) is pure by G.L.C. analysis and has been fully characterized by N.M.R.(^{1}H, ^{13}C), I.R. and mass spectroscopy.

10) The calculated maximum value in the literature concerning the specific rotation of chiral 3-phenyl butanone is $[\alpha]_D$ 866° (cyclohexane)(6) although the value 368°(benzene) has been mesured (5) and used in this work to calculate the optical purity of (III). Our choice for the latter value is in agreement with the optical purity (17.7%) of a sample (S)-(+)-(III) ketone semicarbazone mp 169-170°C(litt.(5): 180-181°C for optically pure material) which has been prepared from the ketone with $[\alpha]_D$ 75° (C 2.2 benzene) and which is 20.4% optically pure.

11) J.E. BACKWALL, R.E. NORDBERG, E.E. BJORMAN and C. MOBERG, J.Chem.Soc., Chem.Comm., 943, (1980).

12) M. EPHRITIKHINE, M.L.H. GREEN and R.E. MACKENZIE, J.Chem.Soc., Chem.Comm., 619, (1976).

13) R.H. PICKARD and J. KENYON, J.Chem.Soc., 1938, (1913).

(Received in France 13 March 1981)