Stereochemistry of the Reaction of an Optically Active π-Allylpalladium Complex with Nucleophiles

Tamio Hayashi,* Mitsuo Konishi, and Makoto Kumada

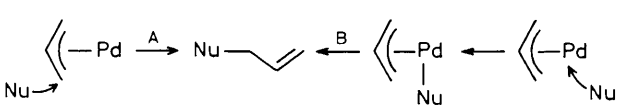
Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Kyoto 606, Japan

The stereochemistry of the reaction of π-allylpalladium complexes with nucleophiles has been elucidated using optically active (−)-(1*S*,2*R*,3*R*)-di-μ-chloro-bis(1-methyl-3-phenyl-π-allyl)dipalladium(II); dimethyl sodiomalonate and dimethylamine attack a carbon atom of the π-allyl ligand from the side opposite to the palladium (inversion), and phenyl and allyl Grignard reagents attack the π-allyl carbon atom from the same side as the palladium (retention).

The reactions of π-allylpalladium complexes with nucleophiles have found extensive application in organic synthesis[1] and considerable effort has been expended in determining the reaction mechanisms.[2—5] Studies on the stereochemistry of the nucleophilic reactions have shown that the reaction proceeds by one of two paths (Scheme 1), depending on the nature of the nucleophile, *i.e.*, path A where the nucleophile directly attacks a carbon atom of the π-allyl ligand from the side opposite to palladium (inversion) and path B where the nucleophile attacks palladium and reductive elimination gives the product (retention). The determination of the stereochemistry has made use of diastereoisomeric π-allylpalladium complexes[2—5] which give only one of the possible diastereoisomers on reaction with nucleophiles. One can argue, however, that the stereochemistry (inversion or retention) might be controlled by stereochemical factors in the diastereoisomeric systems, independent of the inherent nature of the nucleophilic reactions. Use of an enantiomeric π-allylpalladium complex, free from such complications, would provide the unequivocal stereochemistry of the nucleophilic reactions. We now report the first stereochemical results obtained from the reaction of an optically active π-allylpalladium complex with nucleophiles.

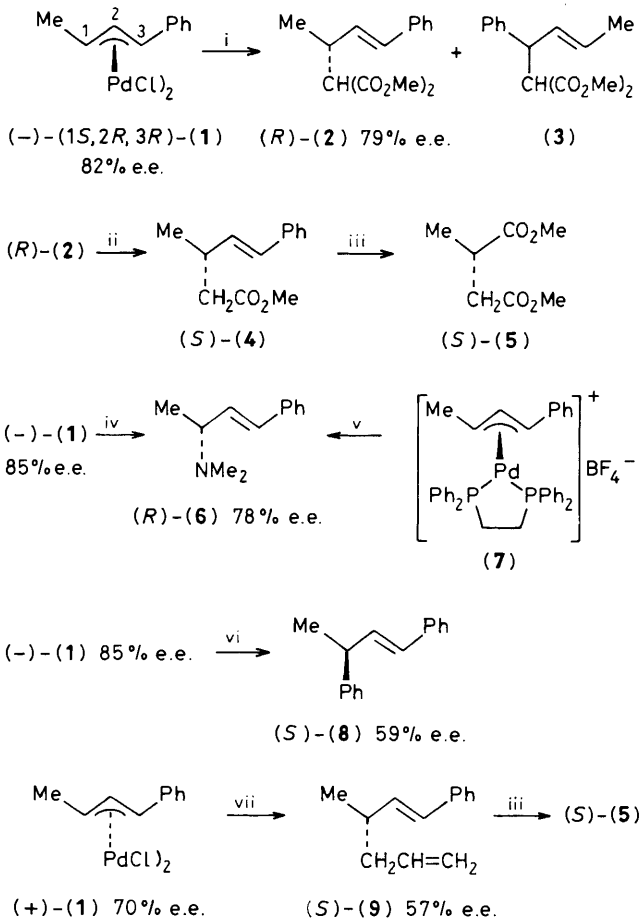
The optically active complex, di-μ-chloro-bis(1-methyl-3-phenyl-π-allyl)dipalladium (**1**),[6] was allowed to react with dimethyl sodiomalonate, dimethylamine, or phenyl and allyl Grignard reagents. The results obtained are summarized in Scheme 2.

Reaction of (−)-(1*S*,2*R*,3*R*)-(**1**) (82% e.e.) with the sodium salt of dimethyl malonate in the presence of 2 equiv. (with respect to Pd) of triphenylphosphine in benzene (room temp., 1 h) gave the allylated product, dimethyl [1-(*E*)-styrylethyl]malonate (**2**) (86% yield),† $[\alpha]_D^{20}$ +54.4° (*c* 1.2, $CHCl_3$), and its regioisomer (**3**) (5% yield). Decarbomethoxylation [LiI, NaCN, *N*,*N*-dimethylformamide (DMF)][2] of (**2**) gave the methyl ester (**4**), $[\alpha]_D^{20}$ +49.2° (*c* 1.3, CCl_4), whose enantiomeric purity was determined to be *ca.* 79% by ^1H n.m.r. spectroscopy using tris[di-(+)-campholylmethanato]-europium(III).[7] The methyl ester (**4**) was converted into (−)-(*S*)-dimethyl methylsuccinate (**5**)[8] by oxidative cleavage of the double bond (O_3/H_2O_2) followed by esterification (CH_2N_2). These results indicate that the allylated product (**2**) is the (*R*) isomer of *ca.* 79% e.e. and hence the nucleophilic reaction proceeds stereoselectively with inversion at C-1 (the numbering is shown in Scheme 2). It follows that the reaction of the dimethyl sodiomalonate takes path A, which confirms the mechanism proposed by Trost.[2]



Scheme 1

Dimethylamine was also found to attack the π-allyl ligand from the side opposite to palladium (inversion at C-1).[4,9] Thus, the reaction of (−)-(**1**) (85% e.e.) with dimethylamine (5 equiv.) and triphenylphosphine (2 equiv.) in tetrahydrofuran (THF) at room temperature for 10 min gave (*E*)-1-phenyl-3-dimethylaminobutene (**6**) (80% yield),†‡ which has $[\alpha]_D^{20}$ +32.9° (*c* 1.7, benzene) and is calculated to be 78% enantiomerically pure with (*R*) configuration.[10] The amine (**6**) of the same optical purity and configuration [(*R*), 78% e.e.]



Scheme 2. i, $NaCH(CO_2Me)_2$ (2 equiv.), PPh_3 (2 equiv.), C_6H_6, room temp., 1 h, 91%; ii, LiI, NaCN, DMF, reflux; iii, (1) O_3, EtOAc, (2) H_2O_2, (3) CH_2N_2, Et_2O; iv, $HNMe_2$ (5 equiv.), PPh_3 (2 equiv.), THF, room temp., 10 min, 80%; v, $HNMe_2$ (5 equiv.), THF, room temp., 2 min, 69%; vi, PhMgBr (4 equiv.), PPh_3 (2 equiv.), Et_2O, room temp., 21 h, 94%; vii, CH_2=$CHCH_2MgCl$ (5 equiv.), PPh_3 (2 equiv.), Et_2O, room temp., 26 h, 60%.

† All the allylated products shown [compounds (**2**), (**6**), (**8**), and (**9**)] have an (*E*)-styryl group, uncontaminated with the (*Z*)-isomer (within the limits of detection by g.l.c. or ^1H n.m.r. spectroscopy).

‡ No regioisomer was detected.

was also produced by the amination (room temp., 2 min, 69% yield) of a cationic π-allylpalladium complex (**7**)§ containing the 1,2-bis(diphenylphosphino)ethane ligand.

Carbon–carbon bond formation on the same face of the π-allyl ligand as palladium (retention at C-1) was observed in the reaction with Grignard reagents. Thus, (*S*)-(*E*)-1,3-diphenylbut-1-ene (**8**),†¶ 59% e.e. {$[\alpha]_D^{20}$ −31.3° (*c* 1.2, benzene)},[11] was obtained in 94% yield by the reaction of (−)-(**1**) (85% e.e) with phenylmagnesium bromide (4 equiv.) and triphenylphosphine (2 equiv.) in diethyl ether (room temp., 21 h). The reaction of (+)-(**1**) (70% e.e.) with allylmagnesium chloride in a similar manner gave the 1,5-diene (**9**)†¶ {$[\alpha]_D^{20}$ +26.6° (*c* 2.0, benzene)} (60% yield) which was shown to be the (*S*) isomer of 57% e.e. by degradation into (*S*)-(**5**).[8] The retention of stereochemistry may demonstrate that the attack of the Grignard reagents on palladium precedes carbon–carbon bond formation (path B).[5,12]

Received, 28th October 1983; Com. 1416

§ Prepared by the reaction of (−)-(**1**) (85% e.e.) with 1,2-bis(diphenylphosphino)ethane and sodium tetrafluoroborate in chloroform (98% yield).

¶ A small amount (<2%) of the regioisomer (attack at C-3) was also formed.

References

1 J. Tsuji, 'Organic Synthesis with Palladium Compounds,' Springer Verlag, New York, 1980; B. M. Trost, *Acc. Chem. Res.*, 1980, **13**, 385.
2 B. M. Trost, L. Weber, P. E. Strege, T. J. Fullerton, and T. J. Dietsche, *J. Am. Chem. Soc.*, 1978, **100**, 3416; B. M. Trost and T. R. Verhoeven, *J. Am. Chem. Soc.*, 1978, **100**, 3435.
3 D. J. Collins, W. R. Jackson, and R. N. Timms, *Aust. J. Chem.*, 1977, **30**, 2167; B. Akermark and A. Jutand, *J. Organomet. Chem.*, 1981, **217**, C41; J.-E. Backvall, R. E. Nordberg, E. E. Bjorkman, and C. Moberg, *J. Chem. Soc., Chem. Commun.*, 1980, 943; J.-E. Backvall and R. E. Nordberg, *J. Am. Chem. Soc.*, 1981, **103**, 4959; D. N. Jones and S. D. Knox, *J. Chem. Soc., Chem. Commun.*, 1975, 165.
4 B. Akermark, J.-E. Backvall, A. Lowenborg, and K. Zetterberg, *J. Organomet. Chem.*, 1979, **166**, C33.
5 J. S. Temple, M. Riediker, and J. Schwartz, *J. Am. Chem. Soc.*, 1982, **104**, 1310; Y. Castanet and F. Petit, *Tetrahedron Lett.*, 1979, 3221.
6 T. Hayashi, M. Konishi, and M. Kumada, *J. Chem. Soc., Chem. Commun.*, 1983, 736.
7 M. D. McCreary, D. W. Lewis, D. L. Wernick, and G. M. Whitesides, *J. Am. Chem. Soc.*, 1974, **96**, 1038.
8 S. G. Cohen and A. Milovanovic, *J. Am. Chem. Soc.*, 1968, **90**, 3495.
9 On the mechanism of amination: B. Akermark, G. Akermark, L. S. Hegedus, and K. Zetterberg, *J. Am. Chem. Soc.*, 1981, **103**, 3037.
10 Y. Yamamoto, J. Oda, and Y. Inoue, *J. Org. Chem.*, 1976, **41**, 303.
11 T. Hayashi, M. Konishi, M. Fukushima, T. Mise, M. Kagotani, M. Tajika, and M. Kumada, *J. Am. Chem. Soc.*, 1982, **104**, 180.
12 See also: S. Numata and H. Kurosawa, *J. Organomet. Chem.*, 1977, **131**, 301.