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FIRM EVIDNCE FOR CIS-AMINOPALLADATION IN THE REACTION OF 1-AMINOHEXATRIENES WITH PALLADIUM DICHLORIDE

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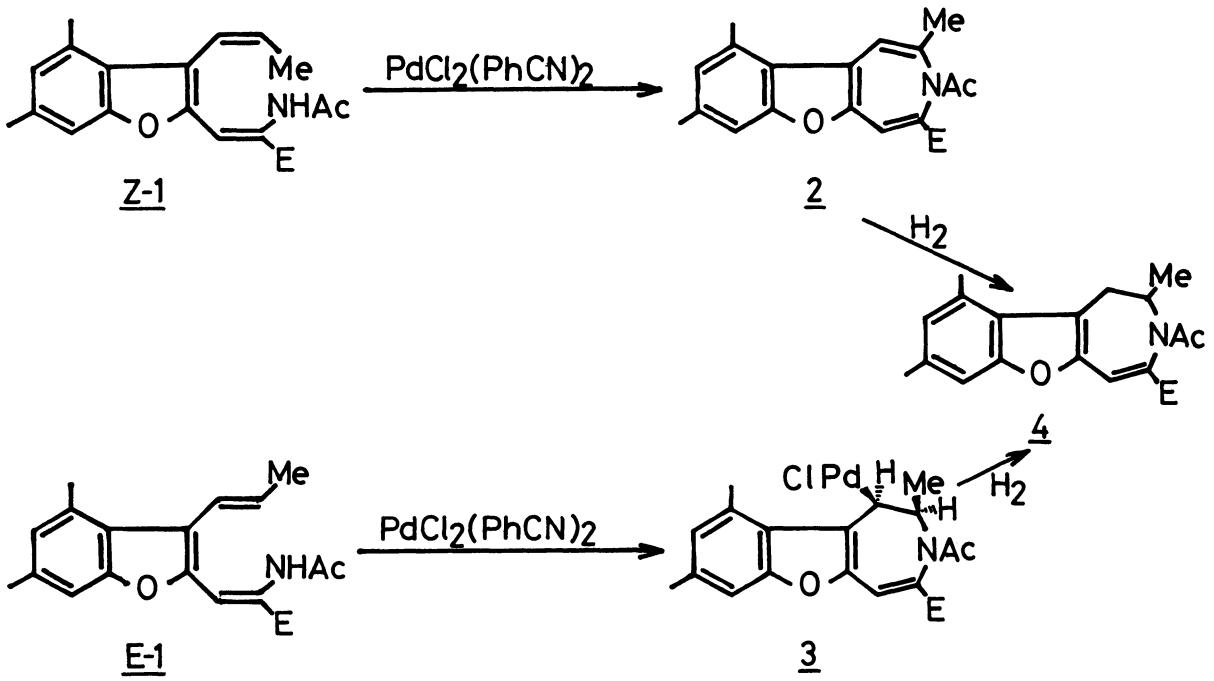
The reaction of $PdCl_2(PhCN)_2$ with ethyl α-N-acetyl-β-(4,6-dimethylbenzofuran-2-yl)acrylate, having a Z-propenyl group at 2-position of benzofuran ring, gave an azepine derivative, whereas its E-isomer afforded a Pd-σ-complex having azepine skeleton. Configurational assignment of the σ-complex, accomplished by methoxycarbonylation, clearly demonstrates that this intramolecular aminopalladation proceeds via cis-aminopalladation.

Intramolecular aminopalladation of allylaniline and related amines has been shown to be a useful method for the synthesis of N-containing 5- and 6-membered heterocycles.[1] This reaction is considered to proceed by trans-aminopalladation followed by cis-elimination of "PdH"[1a] in analogy with the well established intermolecular aminopalladation.[2] Our recent study revealed that palladium induced reaction of 1-aminohexatrienyl derivatives gave 7-membered ring compounds, azepines.[3] This type of endo-cyclization[4] is rare in intramolecular aminopalladation[1] but ideal for investigation of the stereochemistry in the course of the reaction, as stereochemically different Pd-σ-complexes are expected to be produced depending on E- and Z-configuration of the terminal olefinic linkage to which cyclization takes place. In this paper, we describe firm evedence for cis-addition of Pd and N in azepine formation from 1-aminohexatrienes.

In the presence of Na_2CO_3 the Z-isomer of ethyl α-N-acetylamino-β-(4,6-dimethyl-3-propenylbenzofuran-2-yl)acrylate Z-1 was stirred with 1.1 mol equiv. of $PdCl_2(PhCN)_2$ in acetonitrile at 40 °C under argon. The reaction mixture gradually

turned dark grey, which indicated the precipitation of Pd-black. After 43 h, filtration and usual work-up followed by separation on silica gel afforded yellow needles, mp 179.0-180.5 °C, in 65% yield. On the basis of elemental analysis and spectral data, this compound was identified as 3-acetyl-2-ethoxycarbonyl-4,6,8-trimethyl-3H-benzofuro[2,3-d]azepine 2.[5)]



Scheme 1.

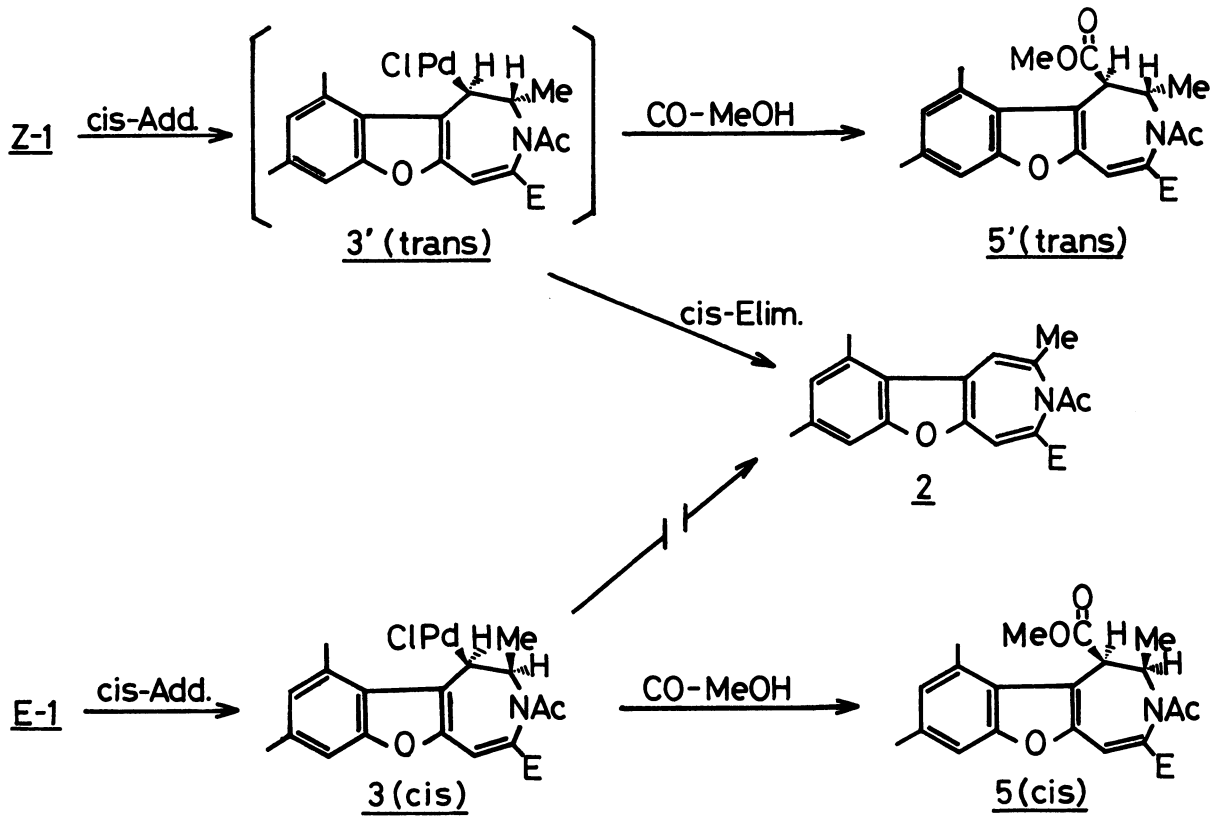
On the other hand, in the reaction of the E-isomer E-1 under the same conditions Pd-black was not formed, but the formation of yellow precipitate was observed. After 47 h, water was added, and the mixture was extracted with ether and dried over Na_2SO_4. Filtration of the precipitate, which is formed by addition of CCl_4, gave yellow powder 3, mp 170 °C (decomp.). Separation of the filtrate on analysis of this compound 3 shows empirical formula of $C_{21}H_{22}NO_4PdCl$. The IR spectrum shows no N-H stretching band and its NMR spectrum is as follows, (δ in $CDCl_3$); 1.32 (3H, t J=7.0 Hz), 1.67 (3H, s), 2.38 (3H, s), 2.43 (3H, s), 4.27 (2H, bq J=7.0 Hz), 4.61-5.17 (1H, m), 5.48 (1H, d J=6.0 Hz), 6.79 (1H, s), 6.97 (1H, s). These spectral data indicate that 3 is the σ-complex, which is formed by intramolecular attack of Pd and N towards the propenyl group. The structure was further confirmed by its hydrogenolysis to form Pd-black and 3-acetyl-2-ethoxy-carbonyl-4,6,8-trimethyl-4,5-dihydro-3H-benzofuro[2,3-d]azepine 4, identical with the com-

pound obtained by hydrogenation of 2.

The marked difference between the reaction of E-1 and Z-1, would be rationalized by the mechanism, as shown in Scheme 2.

Considering elimination of "PdH" generally proceeds with cis-stereochemistry,[6] the Pd-σ-complex 3' formed from Z-1 must have a trans-configuration, which can be attained be cis-addition of Pd and N to the propenyl group. In the case of E-1, cis-addition would result in the formation of Pd-σ-complex 3, having a cis-configuration. Absence of hydrogen, cis to Pd in 3, would make cis-elimination of "PdH" imppossible and allow 3 to be isolated as a stable compound. This result provides first example of the isolation of Pd-σ-complex in intramolecular aminopalladation.

In order to substantiate above consideration by elucidating the stereochemistry of the Pd-σ-complexes, we further attempted trapping 3 and 3' by carbonylation which is beleived to proceed with retention of configuration.[7] When 3 was stirred in acetonitrile in the presence of methanol under carbon monoxide, the expected methoxycarbonylated compound 5[5] was obtained. Addition of methanol and bubbling carbon monoxide into the reaction mixture of E-1 and Pd(II) also gave 5. However,



Scheme 2.

the same procedure in the case of the reaction of Z-1 and Pd(II), performed at 40 °C, did not give the desired methoxycarbonylated azepine 5'. Then, after the reaction was conducted at 0 °C for 66 h, methanol was added and the atmosphere was changed from argon to carbon monoxide. Although 5' was obtined by this method, the yield was only 7% and 2 was also accompanied.

Inspection of the NMR spectra of dihydroazepines 5 and 5', obtained, revealed that these were stereo-isomers and no contamination with each other. This result supports that aminopalladation proceeds stereospecifically. The coupling constants between the vicinal protons of dihydroazepine ring in 3, 5, and 5' were 6.0, 7.9, and 1.9 Hz, respectively. Larger coupling constants in 3 and 5 mean that 3 and 5 have cis-configuration and 5' trans-configuration.[8)]

The results clearly demonstrate that azepine ring formatin by the intramolecular aminopalladation of 1-aminohexatrienes proceeds by cis-addition of Pd and N followed by cis-elimination of "PdH".

References

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