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THE REACTION OF 1-ALKOXYCARBONYL-1H-AZEPINE WITH PALLADIUM ACETATE IN BENZENE

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Abstract— Heating of 1-alkoxycarbonyl-1H-azepines in benzene in the presence of palladium acetate followed by addition of water afforded 2-alkoxycarbonyl-7-phenyl-2-azabicyclo[4.1.0]hept-4-en-3-ols via reaction of the azepines with palladium salt coordinated by phenyl group, which is derived from palladium acetate and benzene.

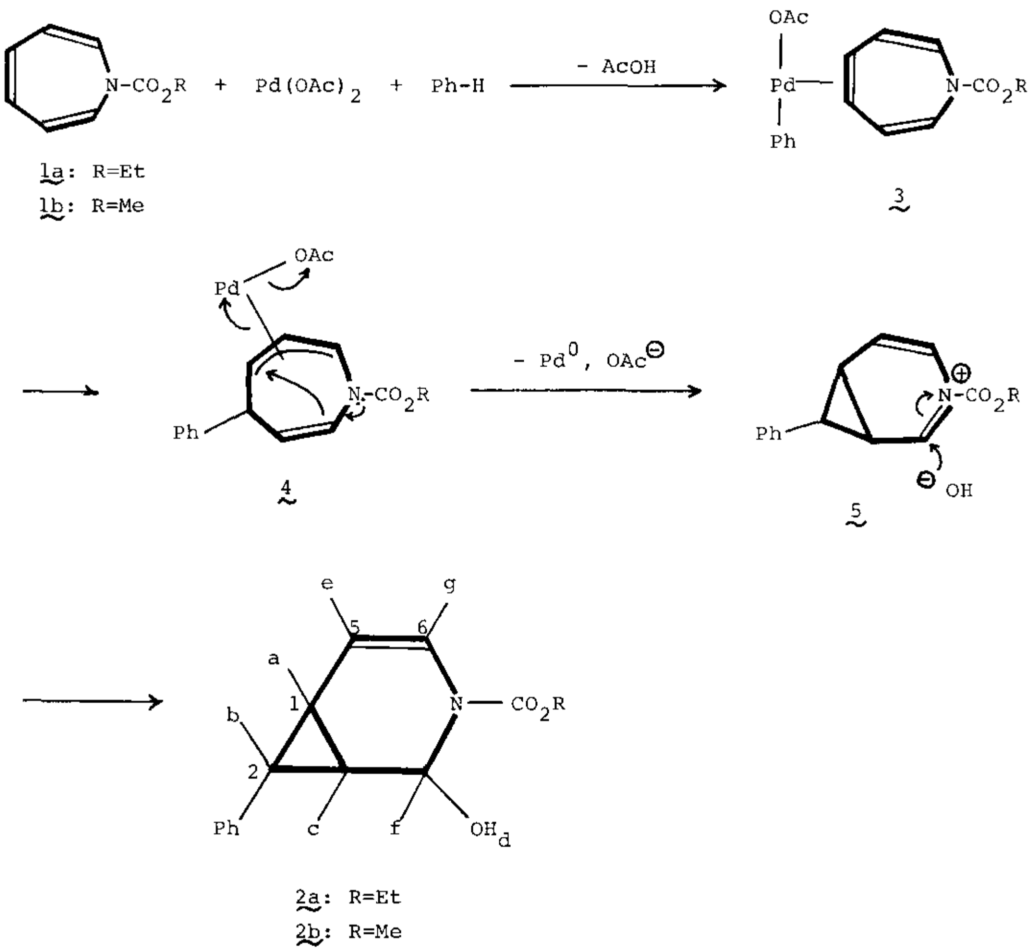
A lot of papers have been published concerning addition, substitution, and molecular rearrangement reactions of olefins in the presence of transition metal complexes. Heck et al.[1] and Moritani et al.[2] have documented a seriese of reports on aromatic substitution of olefins in the presence of palladium salts. Recently, Horino et al. reported vinylic substitution of troponoid compounds, seven-membered ring unsaturated compounds, catalized by palladium (0) complex.[3] Reactions of heterocyclic compounds with palladium complexes have also been investigated actively. Fujiwara et al.[4] and Itahara[5] have documented alkenylation and arylation reactions of five-membered unsaturated heterocyclic compounds such as furans and pyrroles in the presence of palladium salts. However, reaction of seven-membered unsaturated heterocyclic compounds with transition metal complexes are scarecely known. Reaction of azepines with transition metal complexes have never been reported, while a lot of detailed papers concerning addition or rearrangement reactions of azepines have been published.[6] The author has researched reaction of 1-alkoxycarbonyl-1H-azepines with palladium acetate in benzene followed by addition of water leading to bicyclic compounds. Here the result will be discussed.

1-Ethoxycarbonyl-1H-azepine (1a) was heated at 80°C for 6 h in anhydrous benzene in the presence of one molar equivalent of palladium acetate and five molar equivalents of sodium acetate. Addition of water to the reaction mixture followed by separation and purification on thin-layer chromatography on silica gel afforded *2a in a 15% yield as an oily material. The same* reaction but using 1-methoxycarbonyl-1H-azepine (1b) gave an oil of 2b in a 12% yield. The spectral properties of the products are as follows.

2a: Found: m/z 259.1226. Calcd for $C_{15}H_{17}NO_3$: m/z 259.1204. Mass m/z (rel intensity): 259 (M^+, 31), 242 (100), 230 (16), 198 (15). IR (oil): 3410, 3030, 2980, 1715, 1410, 1320 cm^{-1}. UV (EtOH): 240 nm (log ε, 3.60). ^1H NMR ($CDCl_3$) δ: 1.28 (t, 3H, J=7.0 Hz), 1.70 (m, 1H, H_a), 2.10 (m, 1H, H_b), 2.28 (m, 1H, H_c), 4.21 (q, 2H, J=7.0 Hz), 4.98 (s, 1H, H_d), 5.50 (m, 1H, H_e), 6.11 (s, 1H, H_f), 6.40 (m, 1H, H_g), 6.9-7.4 (m, 5H, Ph). Coupling constants in Hz: J_{ab}=8.0, J_{ac}=2.0, J_{ae}= 5.0, J_{bc}=4.0, J_{cf}=1.0, J_{eg}=8.0, (J_{df}=6.0, measured in acetone-d_6). ^{13}C NMR ($CDCl_3$) δ: 20.067 (C_1), 29.692 (C_2), 33.651 (C_3), 71.866 (C_4), 110.246 (C_5), 119.511 (C_6).

2b: Found: m/z 245.1064. Calcd for $C_{14}H_{15}NO_3$: m/z 245.1051. Mass m/z (rel intensity): 245 (M^+, 23), 228 (100), 194 (25), 180 (23), 142 (45). IR (oil): 3410, 3030, 2970, 1715, 1445, 1340 cm^{-1}. UV (EtOH): 242 nm (log ε, 3.69). ^1H NMR ($CDCl_3$) δ: 1.68 (m, 1H, H_a), 2.12 (m, 1H, H_b), 2.28 (m, 1H, H_c), 3.75 (s, 3H), 4.90 (s, 1H, H_d), 5.50 (m, 1H, H_e), 6.10 (s, 1H, H_f), 6.35 (m, 1H, H_g), 6.9-7.4 (m, 5H, Ph). Coupling constants in Hz: J_{ab}=8.0, J_{ac}=2.0, J_{ae}=5.0, J_{bc}=4.0, J_{cf}= 1.0, J_{eg}=8.0, (J_{df}=6.0, measured in acetone-d_6). ^{13}C NMR ($CDCl_3$) δ: 19.965 (C_1), 29.728 (C_2), 33.691 (C_3), 71.926 (C_4), 110.673 (C_5), 119.328 (C_6).

The structures of the products were deduced as shown in the figure on the basis of their spectral properties especially those of the NMR spectral data employing the double resonance technique using 200 MHz NMR spectrometer as follows. The molecular ion peaks in the mass spectra indicate that 2a, b are adducts of the azepines (1a, b) with phenyl and hydroxy groups. The chemical shifts of the signals in the ^1H NMR and ^{13}C NMR spectra show that 2 contains only one olefinic bond except those of the phenyl group. The chemical shifts and the coupling constants of H_a, H_b, H_c, H_e, and H_g suggest the existence of a vinylcyclopropane moiety. The existence of the cyclopropane unit is also supported by the chemical shifts of C_1, C_2, and C_3 in the ^{13}C NMR spectra.[7] The fact that the signals of H_d dissapears in the ^1H NMR spectra measured in the presence of deuterium oxide demonstrates that the proton H_d belongs to a hydroxy group. The coupling constant between H_d and H_f, which is observed in the ^1H NMR spectra measured in acetone-d_6, clearly shows that H_f and the hydroxy group are attached to the same carbon atom. These facts indicate the structures of the products to be as shown in the figure.[8] The reaction is explained to proceed as follows. Reaction of the azepine (1) with palladium acetate in the presence of benzene gives the complex (3). The *subsequent insertion of the azepine moiety to the palladium-phenyl bond forms the* phenylated π-allyl-type complex (4),[9] which then gives the cationic intermediate of a norcaradiene-type (5) leaving free palladium metal and acetoxy anion.[2] Addition of hydroxy anion to 5 affords the bicyclic product 2.



1a: R=Et
1b: R=Me

3

4

5

2a: R=Et
2b: R=Me

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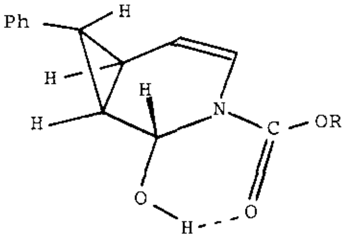
8) The value of the coupling constant J_{ac} is reasonable for the coupling constant between cis-protons of three-membered rings. The coupling constants J_{ab} and J_{bc}, which are larger than J_{ac} seem to suggest that H_b are in trans-configuration to H_a and H_c. The small value of the coupling constant J_{cf} is considered to show that the diheadral angle between H_c and H_f is close to 90°. The flapping of the six-membered ring moiety is hindered by a hydrogen bond between the hydroxy group and the ester group. These facts suggest the stereochemistry of 2 to be as shown bellow.



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