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INTERCEPTION OF TETRAHEDRAL INTERMEDIATES IN Pd(II)-MEDIATED CYCLOALKENYLATIONS OF OLEFINIC ENOL ETHERS

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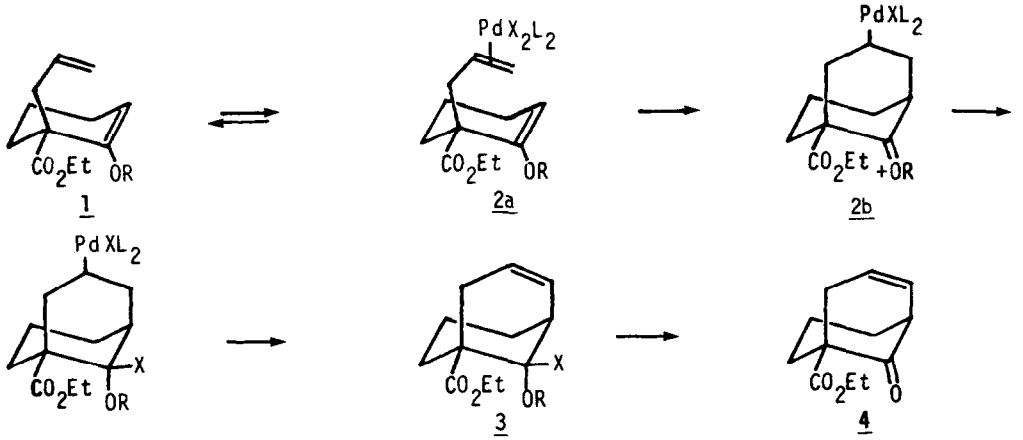
Summary: The tetrahedral intermediate 3 has been intercepted during Pd(II)-cycloalkenylation of olefinic enolsilane 1 (R=$SiMe_2$t-Bu). In a related manner, the allyl and crotyl enol ethers 5-8 give with $Pd(OAc)_2$ acetoxy tetrahydrofurans (9, 12, 14, 16,), convertible to butyrolactones or furans; competing Pd(II)-mediated Claisen rearrangement was not observed. The intramolecular Pd(II)-cycloalkenylation of the ketene acetal 17 leads to δ-lactones 18 and 19.

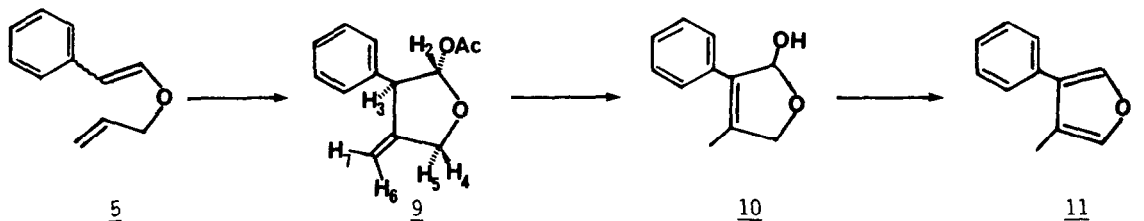
The palladium(II)-mediated intramolecular cycloalkenylation reaction between enol ethers and alkenes has become a general method[1] of strategic significance in alicyclic synthesis.[2] We have recently proposed[3] a mechanism for this reaction in which the rate-determining step is the attack by the enol ether double bond on the Pd-complexed pendant alkene (e.g. 2a→2b) with subsequent formation of a tetrahedral intermediate (e.g. 3) followed by its decomposition to yield the observed product (e.g. 4). We now describe the first isolation from such a reaction of a substance corresponding to 3 as well as the synthetic implications of the overall mechanism for the synthesis of certain oxaheterocycles.



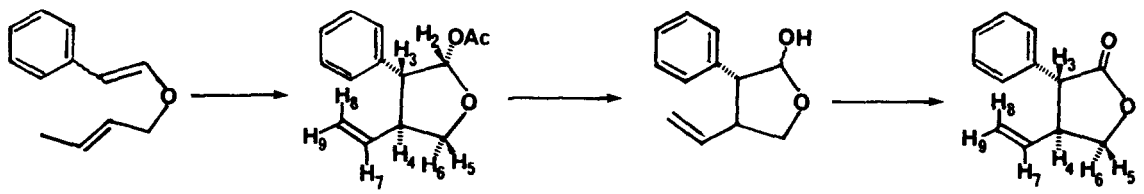
Reaction of the t-butyldimethylsilyl enol ether 1 (R=$SiMe_2$t-Bu) with $Pd(OAc)_2$ (1.0 eq., CH_3CN, 25°C, 24 h) gave on chromatography (Si gel, 20:1 hexane-EtOAc) a 31% yield of the known bicyclic ketoester 4 and 15% of an oil showing only ester IR absorption (1740 cm^{-1}) and ^{1}H-NMR as well as ^{13}C-NMR and mass spectra[4] consistent with the tetrahedral intermediate 3 (R=$SiMe_2$t-Bu, X=OAc, stereochemistry undefined). Upon brief standing in 0.2 M HCl this substance was quantitatively converted to the major cyclization product, ketoester 4.

For systems in which the tetrahedral intermediate would have enhanced stability it should be possible to isolate it in synthetically useful yields. We have therefore examined the novel Pd(II)-mediated chemistry of allyl enol ether derivatives 5-8. These substrates are of special interest because they are structurally capable of undergoing Pd-catalyzed Claisen rearrangement, as discussed in recent reviews by Overman[5] and Lutz.[6] Thus the present work offers a test of Claisen vs. cycloalkenylation pathways for substrates 5-8 under Pd(II) catalysis.

When 5 (1:1E/Z)[7] was reacted with $Pd(OAc)_2$ under the previously described conditions and the reaction worked up by filtration through successive layers of Florisil and Celite, followed by kugelrohr distillation at 0.2 mm, a 73% yield of the acetoxy tetrahydrofuran 9 was obtained.[8] The stereochemistry shown was assigned on the basis of coupling constants.[9] Mild methanolysis (Na_2CO_3, MeOH, 25°C, 1 h) converted 9 to 10 which with p-toluenesulfonic acid (C_6H_6, reflux, 2 h) gave in 73% overall yield the crystalline furan 11, mp 28-29°C.[10]



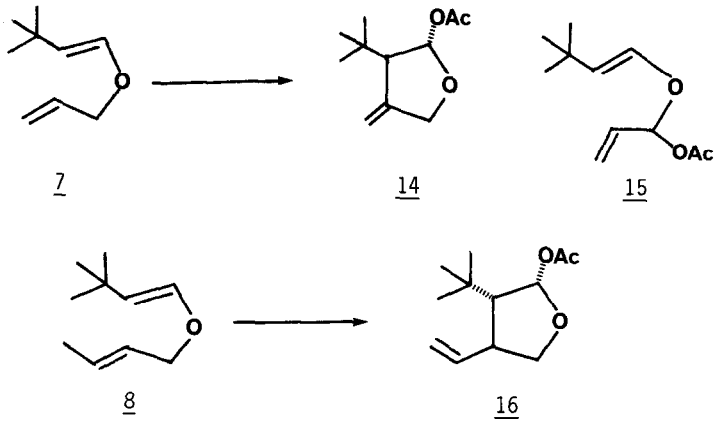
5 9 10 11



6 12 13

Enol ether 6 cyclized with $Pd(OAc)_2$ as above to yield 81% of the tetrahydrofuran 12, mp 69-71.5°C,[9,11] which on methanolysis and subsequent oxidation (PDC, CH_2Cl_2, 25°C, 2 h) gave the crystalline lactone 13,[12,16] mp 70-71°C, in 69% yield from 12.

The E-enol ether 7 cyclized in 51% yield to the tetrahydrofuran 14, accompanied by 15% of the allylic oxidation product 15.[13] The cyclization of 8 gave in 55% yield the tetrahydrofuran 16. The IR, MS and NMR spectra of 14 and 16 were appropriately parallel to those of 9 and 12.

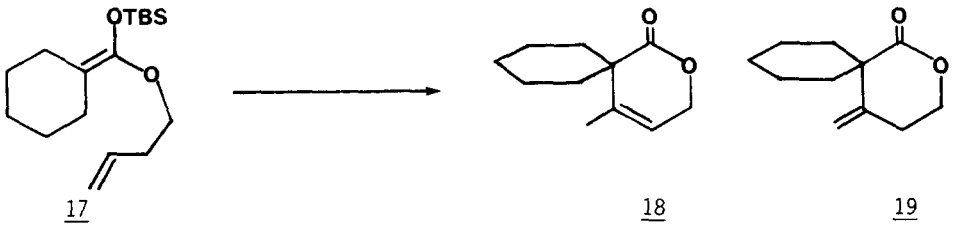


7 14 15

8 16

Heating of enol ethers 5-8 to 130-150°C for 3 h gave the expected Claisen rearrangement aldehydes. None of these aldehydes could be observed in the crude 300 MHz ^{1}H-NMR spectra of the Pd(II)-mediated reactions.

In addition to synthesis of tetrahydrofurans this method can be applied to the formation of lactones. Many ketene acetals derived from allylic esters undergo thermal Claisen rearrangement rapidly at room temperature, making them unattractive substrates for the Pd(II)-cycloalkenylation reaction. On the other hand, the t-butyldimethylsilyl ketene acetal 17 prepared from the butenyl ester (LDA, HMPA, TBSCl, THF, -78°→25°C, 4 h) could be cyclized with $Pd(OAc)_2$ to a 53% yield of lactones 18 and 19 (1.3:1). Warming these lactones with p-toluenesulfonic acid (0.1 eq., CH_2Cl_2, reflux, 10 h) converted them quantitatively to the endocyclic isomer 18.[14]



17 18 19

We conclude that the Pd(II)-cycloalkenylation predominates over Claisen rearrangement for systems such as 5-8 and provides access to simple oxaheterocycles from appropriate precursors.[17]

References

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2. Kende, A.S.; Sanfilippo, P. J. Syn. Comm., 1983, 13, 715; Kende, A. S.; Battista, R. A.; Sandoval, S. B. Tetrahedron Lett., 1984, 1341.
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4. 3: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.80(dt, J=10, 3 Hz, 1H), 5.41(m, 1H), 4.17(dq, J=10, 7Hz 1H), 4.03(dq, J=10, 7Hz, 1H), 3.72(dt, J=6, 3Hz, 1H), 2.97(brd, J=12Hz, 1H), 2.25(td, J=15, 5Hz, 1H), 2.11 (dd, J=12, 3Hz, 1H), 1.93(s, 3H), 1.89(dt J=15, 4Hz, 1H), 1.63(m, 2H), 1.40(m, 2H), 0.91(s, 9H), 0.27(s, 3H) 0.04(s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.63, 167.01, 127.95, 125.47, 104.23, 60.30, 51.26, 49.57, 38.89, 36.04, 33.85, 25.91, 22.39, 18.81, 14.13, 0.06, -3.28, -3.76; MS 325(M-tBu).
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6. Lutz, R. P. Chem. Rev., 1984, 84, 205.
7. Compounds 5-8 were prepared according to the method of Miller and McKean[15] from the corresponding diallyl or dicrotyl acetals in 50-60% yields after column chromatography (pentane-ether eluant). Compd. 5: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.65(d, J=6Hz, 2H), 7.30(m, 4H), 7.02(d, J=12Hz, 1/2H), 6.24(d, J=8Hz, 1/2H), 6.02(m, 1H), 5.94(d, J=12Hz, 1/2H), 5.32(m, 2H), 4.48(d, J=6Hz, 1H), 4.41(d, J=6Hz, 1H).
8. 9: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.30(t, J=6Hz, 2H-Ar), 7.23(m, 3H-Ar), 6.26(s, H-2), 5.16(dd, J=2, 1Hz, H-7), 5.04(dd, J=2, 1 Hz, H-6), 4.78(abq, J=2Hz, H-4 and H-5), 3.90(brs, H-3), 2.07(s, H_3CCO_2); IR 1749 cm^{-1}; MS 158(M-HOAc).
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10. 11: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.49(d, J=2Hz, 1H) 7.37(m, 4H), 7.30(m, 1H), 7.27(d, J=2Hz, 1H), 2.12(s, 3H); MS 158(M+); Anal. Calc.: C, 83.51; H, 6.37. Found: C, 83.30; H, 6.38.
11. 12: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33(t, J=6Hz, 2H-Ar), 7.24(m, 3H-Ar), 6.25(d, J=3.5Hz, H-2), 5.80(m, H-7), 5.04(d, J=9Hz, H-9), 5.01(d, J=19Hz, H-8), 4.28(t, J=9Hz, H-5), 3.92(t, J=9Hz, H-6), 3.22(dd, J=9, 3.5Hz, H-3), 3.01(p, J=9Hz, H-4), 2.08(s, H_3CCO_2); IR 1745 cm^{-1}; MS 172(M-HOAc).
12. 13: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.30(m, 5Ar-H), 5.80(m, H-7), 5.19(d, J=10Hz, H-9), 5.12(d, J=16Hz, H-8), 4.55(t, J=9Hz, H-5), 4.11(t, J=9Hz, H-6), 3.58(d, J=11Hz, H-3), 3.32(m, H-4); IR 1775 cm^{-1}; Exact Mass: obs. 188.0845, calc. for $C_{12}H_{12}O_2$ 188.0837.
13. 15: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.36(d, J=6Hz, 1H), 6.21(d, J=14Hz, 1H), 5.91(m, 1H), 5.54(d, J=18Hz, 1H), 5.38 (d, J=9Hz, 1H), 5.22 (d, J=14Hz, 1H) , 2.14(s, 3H), 1.04(s, 9H); IR 1738, 1655 cm^{-1}; MS 197(M-1), 155(M-$COCH_3$).
14. 18: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.61 (m, 1H), 4.74(m, 2H), 1.90(dd, J=12, 2Hz, 2H), 1.84(dt, J=13, 3Hz, 2H), 1.79(s, 3H), 1.71(brd, J=13Hz, 2H), 1.62(dt, J=13, 3Hz, 2H), 1.49(td, J=12, 2Hz, 2H); MS 180, 165, 152; Exact Mass: obs. 180.1166, calc. $C_{11}H_{16}O_2$, 180.1150.
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