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PALLADIUM(0) CATALYZED 3-AZA-COPE REARRANGEMENT OF N-ALLYLENAMINES

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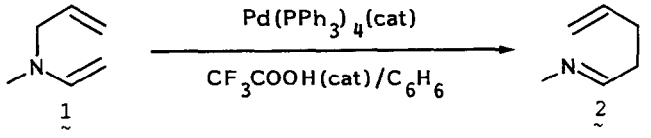
Summary: Pd(0) complexes catalyze the 3-Aza-Cope rearrangement of N-allylenamines to the corresponding δ,ε-unsaturated imines or γ,δ-unsaturated carbonyl compounds in the presence of trifluoroacetic acid as co-catalyst.

The Cope rearrangements are of considerable synthetic utility. There have been many reports on the attempts to improve the usefulness of aliphatic Claisen rearrangements as a tool for organic synthesis, either by lowering the activation energy of the reaction or by increasing the functionalization of the products.[1] As the former approach transition metal catalyzed rearrangements have been studied extensively,[2-4] and the mechanistic understanding is in progress.[5]

We wish to report that N-allylenamines (1) undergo Pd(0) catalyzed 3-Aza-Cope rearrangement to give the corresponding δ,ε-unsaturated imines (2) in the presence of trifluoroacetic acid as co-catalyst as depicted in eq 1. The 3-Aza-Cope rearrangement is highly useful, because the substrates of N-allyl-



1 2 (1)

enamines are readily prepared from N-allylamines and aldehydes,[6] and the carbon-carbon bond formation proceeds selectively to give various imines and the related compounds. Since the thermal rearrangement requires high reaction temperature (170-250°C),[7] lowering the activation energy seems to be required. The titanium induced 3-Aza-Cope rearrangements have been carried out using 0.25 mole of $TiCl_4$, but their yields are low (16-64 %), and the reaction cannot be applied to the enamines of simple ketones such as benzophenone and

cyclohexanone.[8]

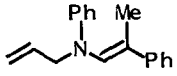
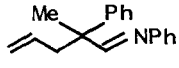
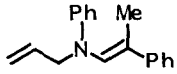
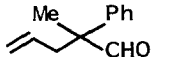
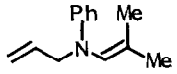
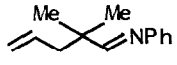
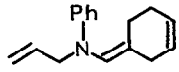
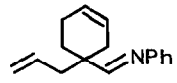
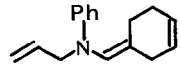
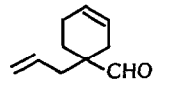
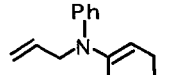
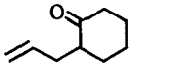
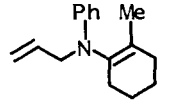
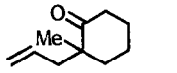
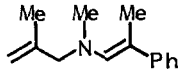
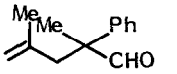
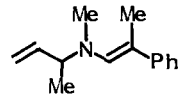
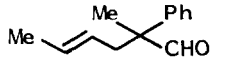
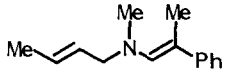
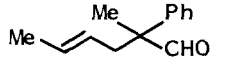
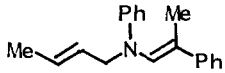
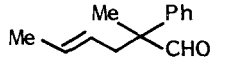
As a typical example, the palladium catalyzed reaction of N-allyl-N-phenyl-2-phenyl-1-propenylamine was examined precisely. The rearrangement does not proceed by using a transition metal catalyst alone. Addition of a catalytic amount of certain protic acid promotes the reaction dramatically. It was found that using $Pd(PPh_3)_4$ catalyst and trifluoroacetic acid co-catalyst the rearrangement proceeds quantitatively. Using other catalysts such as Pd(II), Ru(II), Rh(I), and Mo(0) complexes, the enamine does not undergo the rearrangement even in the presence of proton catalyst. Using benzene or toluene as a solvent the enamine was converted into the imine in excellent yield (100 %). THF is a poor solvent (24 %), and CH_3CN and CH_2Cl_2 retard the rearrangement completely. The catalytic effect of acids is also enormous. Beside CF_3COOH, CH_3SO_3H and p-TsOH can be used similarly as co-catalyst. Other acids such as acetic acid, HCl, and Lewis acids ($AlCl_3$, $BF_3 \cdot OEt_2$) retard the rearrangement completely.

A typical procedure is as follows: A mixture of N-allyl-N-phenyl-2-phenyl-1-propenylamine (1.0 mmol), $Pd(PPh_3)_4$ (0.05 mmol), and CF_3COOH (0.025 mmol) in dry benzene (6 mL) was stirred at 50°C under argon for 20 h. After removal of benzene in vacuo, the residue was subjected to column chromatography (Al_2O_3, ether-hexane). Kugelrohr distillation gave N-phenyl-2-methyl-2-phenyl-4-pentenylideneamine (82 %) (bp 150-152°C / 2 mmHg). For the preparation of the corresponding aldehyde, a solution of the imine in benzene was stirred with a 0.5 N HCl solution at room temperature for 4 h. After usual work-up, Kugelrohr distillation gave 2-methyl-2-phenyl-4-pentenal (78 %) (bp 136-140°C / 31 mmHg).

The representative results of the palladium catalyzed rearrangement of enamines are summarized in Table 1. Generally, δ,ε-unsaturated imines have been prepared in excellent yields. The rearranged products are highly useful precursor of spiro compounds (Entries 4,5). Further, the enamines of simple ketones undergo the rearrangement smoothly (Entries 6,7). The imines thus obtained are readily hydrolyzed upon treatment with a 0.5 N HCl solution giving γ,δ-unsaturated carbonyl compounds, which are versatile synthetic intermediates. Furthermore, the reduction of the imines thus obtained gives the corresponding δ,ε-unsaturated amines.

The reaction can be rationalized by assuming Scheme 1. The first step is the protonation of the enamine 1 to give ammonium ion 3. Insertion of Pd(0) species into the carbon-nitrogen bond of 3 gives π-allyl complex and enamine. We have shown that enamines undergo facile nucleophilic attack towards π-allylpalladium intermediates to give allyliminium salts.[9] The similar nucleophilic reaction of the enamine gives iminium ion 4 and Pd(0) catalyst. The deprotonation of 4 gives imine 2 along with proton which is again utilized for the protonation of the starting enamine. Importantly the protonation

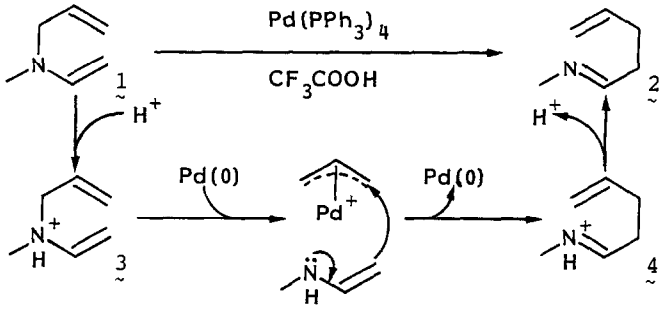
Table 1. $Pd(PPh_3)_4$/ CF_3COOH-Catalyzed 3-Aza-Cope Rearrangement of N-Allylenamines[a]

Entry	Substrate	Temp. (°C)	Product[b,c]	Yield (%)[d]
1		50		82
2		50		78
3		100		99[e]
4		100		98
5		50		85
6		50		77
7		100		69
8		100		78
9		100		79[e]
10		100		62
11		80		58

a) The reaction was carried out similar to the procedure described in the text except otherwise indicated. b) The products gave satisfactory IR, NMR, and mass spectral data. c) The carbonyl compounds were obtained by hydrolysis with HCl (0.5 N) after the rearrangement. d) Isolated yield by Kugelrohr distillation. e) Isolated yield by column chromatography.

gives ammonium ion 3, which is the good leaving group towards the oxidative addition of Pd(0) species.[10] The mechanism which involves the Pd(II) induced rearrangement seems to be eliminated by the following facts. (i) The rearrangement does not proceed with Pd(II) complexes. (ii) The rearrangement of N-(1-methylallyl)enamine gave [3,3]-rearranged trans-4-heptenal after

Scheme 1.



hydrolysis (Entry 9), while that of N-crotylenamine produced [1,3]-rearranged trans-4-heptenal, and the cis-isomer and 3-methyl-4-pentenal could not be detected among the product (Entries 10,11). Work is currently in progress on the extention of this reaction to other system and on the application to the synthesis of natural products.

References and Notes

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