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Highly selective isomerization of *N*-allylamides and *N*-allylamines

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Abstract—A highly selective rhodium and ruthenium catalyzed transformation of *N*-allylamines and *N*-allylamides to the corresponding 1-propenyl derivatives is described. Strong *E*-selectivity in the isomerization of allylamines was observed. The first catalytic system containing a transition metal complex for *Z*-selective isomerization of allylamides is presented. An application of siliceous mesoporous cellular foams for effective removal of the catalyst from the post-reaction mixture is described.

Enamides and enamines are interesting intermediates for various transformations. *N*-Propenyl amides are substrates for the synthesis of heterocyclic systems,[1] Diels–Alder cycloaddition,[2] reduction to enamines,[3] enamide–olefin ring-closing metathesis[4] and are thoroughly investigated monomers and co-monomers.[5] Several methods for the synthesis of enamides has been reported. The most general method is *N*-acylation of *N*-allylimines with an acyl halide or acid anhydride.[3,6] Some enamides can also be synthesized via vinylation of amides with vinyl halides in the presence of nickel complexes[7] or via titanium-mediated coupling of ynamides with aldehydes and ketones.[8] But the yield of enamides is often modest and conditions used are in many cases quite harsh. The most convenient method for the synthesis of *N*-propenyl amides consists in the isomerization of the appropriate *N*-allyl amides catalyzed by LDA,[9] *n*-BuLi[10] and, particularly, by transition metal complexes. Ruthenium,[11] iron,[11a,d,12] cobalt[13] and rhodium[11a,12a,14] complexes have been applied. Isomerization of *N*-allylamides to enamides is very attractive because *N*-allylamides are available via standard synthetic methods. Enamines occupy a prominent place as intermediates in organic synthesis,[15] in the biological world and as monomers for polymerization.[16] There are many methods for enamine formation such as: condensation of a secondary amine with a carbonyl compound,[17] hydroamination of alkynes,[18] methylenation of amides,[19] vinylamination.[20] An alternative method for the synthesis of enamines is the isomerization of allylamines using strong bases such as *t*-BuOK,[21] *n*-BuLi[22] or ruthenium,[23] rhodium[24] and iron[25] complexes. The stereospecific isomerization of prochiral allylamines using catalysts based on Rh, Ir and Ru having chiral ligands gives the corresponding chiral enamines, which can then be hydrolyzed to obtain chiral aldehydes.[26] Isomerization of *N*-allyl to *N*-propenyl amines is also the key step in the deprotection of amino groups[27] protected as their *N*-allyl derivatives.

In the present work, we describe a convenient and very selective (frequently *E* or *Z* selective) method of synthesis of *N*-(1-propenyl) enamines and enamides via isomerization of appropriate *N*-allyl compounds.

The results of the isomerization of some *N*-allylamides are summarized in Table 1. In all reactions the conversion and selectivity to 1-propenyl derivatives was mainly or exclusively quantitative. As expected, the isomerization of the *N*-allylamides shown in Table 1 led to the formation of a mixture of (*E*) and (*Z*) or (*E*,*E*) and (*E*,*Z*)-enamides.

In our earlier papers we demonstrated that only *N*-aryl-*N*-allyl-amides can be isomerized selectively to (*E*)-enamides in the presence of $[RuClH(CO(PPh_3)_3)]$,

Keywords: Selective isomerization; (*Z*)-Enamides; (*E*)-Enamines.
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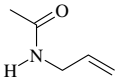
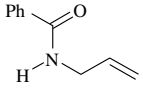
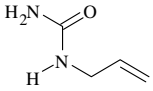
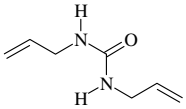
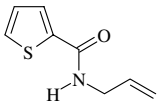
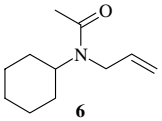
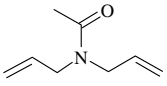
Table 1. Isomerization of *N*-allylamides ($QCH_2CH{=}CH_2$) to enamides ($QCH{=}CHCH_3$) catalyzed by $[RuClH(CO)(PPh_3)_3]$[a]

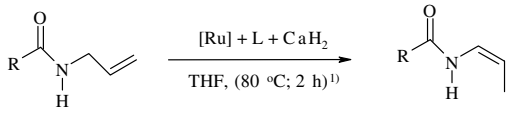
N-Allylamide	*T* (°C), τ (h)	S/C	So	Enamide	
				y[b] (%)	*E*/*Z*[c]
 **1**	80, 2	96	C_6H_6, 0.50	100, 85[d]	59/41
 **2**	80, 3	59	C_6H_6, 0.50	100, 84[d]	67/33
 **3**	80, 3	143	THF, 1.00	100	42/58
 **4**	80, 3	53	THF, 2.50	100	79/21[e]
 **5**	70, 3	57	C_6H_6, 0.84	100	77/23
 **6**	120, 2	200	—	100, 93[f]	85/15
 **7**	120, 2	98	—	100, 70[f]	44/66

[a] Experimental procedure as in our previous work;[11e] S/C—substrate/catalyst; So—solvent, cm^3 per 1 mmol of substrate; *y*—yield of the double bond migration product, determined by ^1H NMR.
[b] Conversion was always quantitative (determined by ^1H NMR and GC–MS).
[c] Determined by ^1H NMR and GC–MS.
[d] Isolated yield after reduced pressure distillation.
[e] *EZ*/*ZZ*.
[f] Isolated yield after column chromatography.

$[RuCl_2(PPh_3)_3]$ or $[RhH(CO(PPh_3)_3)]$.[11e,f] This (*E*)-selectivity is a result of a specific coordination of the metal atom by the aryl substituent.[11e,f] However, the application of a new catalytic system, containing a precursor—$\{[RuCl_2(1,5\text{-COD})]_x\}$, a phosphine ligand and a hydride ligand donor affords a quantitative (*Z*)-selective isomerization of some *N*-allylamides (see Fig. 1).

To the best of our knowledge, this is the first example of a selective isomerization of allyl systems exclusively to (*Z*)-1-propenyl derivatives in the presence of transition metal complexes. The formation of (*Z*) isomers in this reaction is, in our opinion, a result of steric interactions in the transition state (see Fig. 2A).

In the transition state, due to the aforementioned steric effects, the bulky phosphite ligand is on the other side of



R = CH_3, Ph, NH_2; [Ru] = $\{[RuCl_2(1,5\text{-COD})]_x\}$;
L = tris(2,4-di-*t*-butylphenyl) phosphite
amide : [Ru] : L : CaH_2 = 100 : 1 : 1 : 10
1) *N*-allylbenzamide: 90 °C/4 h, *N*-allylurea: 100° C/1 h

Figure 1. Stereoselective isomerization of *N*-allylamides to (*Z*)-enamides.[28]

the [Ru]–H elimination plane than groups Q and CH_3. In such a conformation, steric interactions between Q, CH_3 and other Ru ligands are minimized. We have observed a similar effect in the isomerization of R–S–$CH_2CH{=}CH_2$ ($R = Me_3C$ or Ph_3C).[29] It is noteworthy

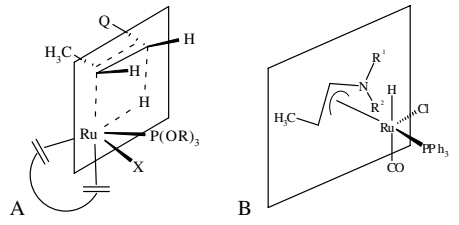


Figure 2. (A) The postulated transition structure for the (*Z*)-selective isomerization of *N*-allylamides (R = 2,4-di-*t*-butylphenyl; X = H or Cl). (B) Coordination of the ruthenium atom by *N*-(1-propenyl)amines (this suggestion is based on the results of quantum chemical calculations).

that the application of such phosphine ligands as triphenylphosphine, tris(*o*-tolyl)phosphine or triphenyl phosphite leads to a mixture of (*E*) and (*Z*)-enamides. In order to remove [Ru] from the post-reaction mixture, siliceous mesoporous cellular foams (MCFs) were used, which constitute a new class of materials with well-defined uniform ultralarge mesopores.[30] We have found that [Ru] separation efficiency using a column with MCFs[31,32] was significantly higher compared with a typical silica gel (200–400 mesh, ALDRICH) (Table 2).

Isomerization of *N*-allylamines, in turn, generally showed high (*E*) selectivity. In our opinion, it is a result of a specific coordination of the metal atom by the substrates and products of double bond migration. Quantum chemical calculations[33] suggest that the substrate and the product coordinate the ruthenium atom mostly through the double bond (from the allyl or propenyl fragment) and, in the case of amines, the nitrogen atom (Fig. 2B). In particular, the coordination of the product has, in our opinion, a profound impact on (*E*)-stereoselectivity. The decrease in (*E*)-selectivity of the reaction in the case of isomerization of amine **13** is due to a steric influence of Me_3Si groups, which hinder the participation of the nitrogen atom in the coordination of the metal atom. On the other hand, amine **12** can coordinate through both nitrogen atom and the double bond from the allyl (and 1-propenyl) fragments in so many various ways that it is difficult to predict stereoselectivity using this simple rationale.

Acknowledgements

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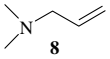
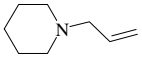
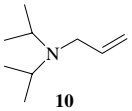
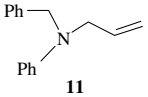
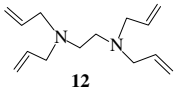
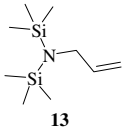
Table 2. Isomerization of *N*-allylamines ($QCH_2CH{=}CH_2$) to enamines ($QCH{=}CHCH_3$) catalyzed by [M]: $[RhH(CO)(PPh_3)_3]$ and $[RuClH(CO)(PPh_3)_3]$[a]

N-Allylamine	*T* (°C), τ (h)	S/C, [M]	So	Enamine	
				y[b] (%)	*E*/*Z*[c]
 **8**	60, 2	108, [Rh]	C_6D_6, 1.1	>98	100/0
 **9**	80, 2	73, [Rh]	C_6D_6, 0.63	>98	100/0
 **10**	80, 2 60, 2	65, [Rh] 67, [Ru]	C_6D_6, 0.71 C_6D_6, 0.71	>99 >99	100/0 100/0
 **11**	80, 2	41, [Rh]	C_6D_6, 1.1	>99	99/1
 **12**	60, 2	41, [Rh]	C_6D_6, 1.1	>98	83/10/7/0/0[d]
 **13**	100, 3	120, [Ru]	C_6H_6, 1.1	>98	89/11

[a] Experimental procedure as described earlier for *N*-allylamides;[11e] S/C—substrate/catalyst; So—solvent, cm^3 per 1 mmol of substrate; *y*—yield of the double bond migration product, determined by ^1H NMR.
[b] Conversion was always quantitative (determined by ^1H NMR and GC–MS).
[c] Determined by ^1H NMR and GC–MS.
[d] *EEEE*/*EEEZ*/*EEZZ*/*EZZZ*/*ZZZZ*.

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28. *Synthesis of (Z)-N-(1-propenyl) amides (general procedure)*: *N*-Allyl amide (0.01 mol), {[$RuCl_2$ (1,5-COD)]$_x$} (1 mol%), tri(2,4-di-*t*-butylphenyl) phosphite (1 mol%) and CaH_2 (10 mol%) in 5 cm^3 THF were heated at 80 °C for 2 h (*N*-allylbenzamide: 90 °C/4 h, *N*-allylurea: 100 °C/1 h) under argon. After cooling to room temperature, 10 cm^3 of a mixture of benzene–hexane (1:3) was added. Precipitated ruthenium compounds and phosphine were filtered off. The filtrate was purified by chromatography on a column containing 0.6 g of siliceous mesoporous cellular foams. After evaporating the solvent, the residue was distilled under reduced pressure. (*N*-(1-Propenyl)urea was recrystallized from methanol). (*Z*)-*N*-(1-Propenyl)ethanamide: (90 °C/10 mmHg). ^1H NMR ($CDCl_3$): $\delta = 8.37$ (d, $J = 6.9$ Hz, –N*H*–CH=CHCH$_3$), 6.66 (ddq, 1H, $J = 7.2$, 6.9, 1.5 Hz, –NH–C*H*=CHCH$_3$), 4.79 (dq, 1H, $J = 7.2$, 6.6 Hz, –NH–CH=C*H*CH$_3$), 2.10 (s, 3H, –C*H*$_3$), 1.62 (dd, 3H, $J = 6.6$, 1.5 Hz, –NH–CH=CHC*H*$_3$). ^{13}C NMR (300 MHz, $CDCl_3$): $\delta = 168.5$ (–*C*OCH$_3$); 122.0 (–*C*H=CHCH$_3$); 106.0 (–CH=*C*HCH$_3$); 23.0 (–CO*C*H$_3$); 11.1 (–CH=CH*C*H$_3$). MS (EI, 70 eV) *m*/*z*: $M^+ = 99$ (13), 84 (3), 56 (100), 52 (2).
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31. Siliceous mesoporous cellular foams (MCFs) are a new class of porous materials with spherical pores, which are obtained using oil in water microemulsion as a template. The preparation procedure has been described earlier.[30] The texture parameters (specific surface area, S_{BET}; pore volume, V_p; diameter of cells, d_s and diameter of interconnected windows, d_w) of calcined materials were obtained using the nitrogen adsorption method. Nitrogen isotherms were measured by Micromeritics ASAP 2000 instrument at 77 K. *Preparation of MCFs*: In a typical procedure, surfactant Pluronic PE 9600 (0.4 mmol) was dissolved in 1.6 M HCl (75 mL) at room temperature. 1,3,5-Trimethylbenzene (17 mmol) and NH_4F (0.6 mmol) were added under vigorous stirring and the mixture was heated to 333 K. Following 1 h of stirring, TEOS was added (4.4 g). The mixture was stirred for 2 h and subsequently stored at 333 K for 20 h and at 373 K for 24 h. After cooling to room temperature, the precipitate was isolated by filtration, dried at room temperature for 4 days and calcined at 773 K for 8 h. Texture parameters of the calcined MCFs were: $S_{BET} = 650\ m^2/g$, $V_p = 2.5\ cm^3/g$, $d_s = 30$ nm and $d_w = 15$ nm.

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33. Theoretical calculations: all calculations were performed using GAMESS: Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. J.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Su, S.; Windus, T. L.; Dupuis, M. J.; Montgomery, A. *J. Comput. Chem.* **1993**, *14*, 1347–1363; and its PC version: PC GAMESS: Granovsky, Alex A, http://classic.chem.msu.su/gran/gamess/index.html; MOLDEN: Schaftenaar, G.; Noordik, J. H. *J. Comput. Aided Mol. Des.* **2000**, *14*, 123–134, was used for Z-matrix construction and visualization of results. The geometries were optimized at MP2 RHF level, using 6-31G(d,p) basis set. In order to predict how the allyl compounds and their propenyl isomers are coordinated by the metal atom, we have analyzed the shapes of the RHF canonical orbitals. It was assumed that these regions of the molecule where HOMO − 1 and HOMO are significantly nonzero may participate in donor bonding with the metal, and those where LUMO and LUMO + 1 are localized are involved in back-bonding.