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Transition metal halide promoted hydride transfer in *N,N*-diisoalkyl-*N*-propargylamines

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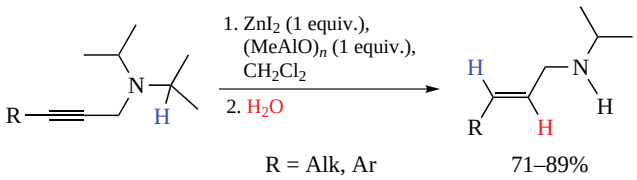
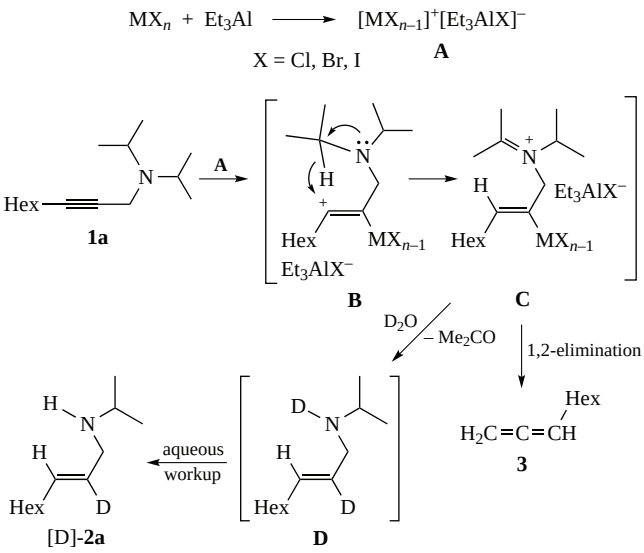
The reaction of *N,N*-diisopropyl-*N*-propargylamines with Et_3Al/MX_n system (MX_n = CuCl, CuBr, $ZnCl_2$, ZnI_2, CdI_2, $TiCl_4$, $ZrCl_4$, VCl_5, $TaCl_5$) in CH_2Cl_2 proceeds as an intramolecular red-ox hydride transfer affording N-dealkylated *N*-isopropyl-*N*-allylamines, allenes being formed as side products. The highest chemoselectivities and yields (71–89%) were attained by the application of new $ZnI_2/(MeAlO)_n$ system.



Keywords: allylic amines, hydride transfer, propargylic amines, methylalumoxane, zinc iodide, N-dealkylation.

We have previously found that the reaction of *N*-isoalkyl- and *N*-alkyl-*N*-*tert*-alkyl substituted propargylic amines with trialkylalanes in the presence of Cp_2ZrCl_2 gave (2*E*)-alkenylamines as a result of hydride transfer from the alkyl or isoalkyl group to the triple carbon–carbon bond and subsequent hydrolysis of thus formed iminium salts.[1,2] These salts were considered as intermediates in the processes of C(sp^3)–H and C(sp^3)–C(sp) activation in propargylic amines under the action of Zn,[3–6] Cd,[7] Cu[8,9] halides. It should be noted that all these processes required heating to 100 °C or higher. Therefore, we assumed that the use of these metal halides in the reaction of *N*-isoalkyl substituted propargylic amines with trialkylalanes could also promote the hydride transfer reaction leading to the formation of alkenyl-containing iminium salts and substituted allenes at room temperature. Additionally, it was interesting to examine activity of halides of the early transition metals (Ti, Zr, Nb, Ta) in this reaction. Such studies could promote the development of new reagents for activation of C(sp^3)–H and C(sp^3)–C(sp) bonds in propargylic amines and respond to the actual problem of allene synthesis from propargylic amines. To the best of our knowledge, transformation of *N*-isoalkyl substituted propargylic amines into allenes or N-dealkylated *N*-isopropyl-*N*-allylamines under the action of Zn, Cd or Cu halides at room temperature were never documented. Therefore, we planned to study the reaction of *N*-isoalkyl substituted propargylic amines with the MX_n–MOC reagent system in a molar ratio of 1 : 2, whereas MX_n stood for $ZnCl_2$, ZnI_2, CdI_2, CuCl, CuBr, $TiCl_4$, $ZrCl_4$, $NbCl_5$, $TaCl_5$, and MOC stood for Et_3Al, Et_2Zn, BuLi. These ratios of the organometallic compounds to the metal halides (2 : 1) proved to be optimal in the reaction of *N*-isoalkyl substituted propargylic amines with Me_3Al or $EtAlCl_2$ in the presence of Cp_2ZrCl_2.[1]

Herein, we found that the reaction of *N,N*-diisopropylnon-2-yn-1-amine **1a** with 1 equiv. of ZnI_2 and 2 equiv. of Et_3Al in dichloromethane at room temperature for 5 h after deuterolysis afforded (*E*)-2-deutero-*N*-isopropylnon-2-en-1-amine [D]-**2a** in high yield (89%) (Scheme 1, Table 1). After 18 h, the content of compound [D]-**2a** dropped to 57% while nona-1,2-diene **3** was detected in an amount of 36% (GC yield). When hexane was



Scheme 1 *Reagents and conditions*: MX_n (1 equiv.), Et_3Al (2 equiv.), CH_2Cl_2, room temperature, 1–18 h, then D_2O.

used instead of CH_2Cl_2, the yield of the reduction product [D]-**2a** dropped to 25% due to the poor solubility of ZnI_2. In ethereal solvents (diethyl ether, THF, 1,4-dioxane) the reaction did not occur. The reaction with CdI_2 proceeded in a similar way. However, when using $ZnCl_2$ instead of ZnI_2 it was not possible to achieve selective formation of the compound [D]-**2a**, namely, after 1 h both compounds [D]-**2a** and **3** in a ratio of 3 : 1 were formed with a total yield of 45%. Salt $TaCl_5$ showed lower activity towards substrate **1a** compared to zinc and cadmium halides. The use of CuCl, CuBr, $NbCl_5$, $TiCl_4$ or $ZrCl_4$ did not result in the formation of compound [D]-**2a**. As can be seen from Table 1, zinc and cadmium iodides showed the greatest activity and selectivity in the reaction under study when CH_2Cl_2 was used as a solvent.

The position of the deuterium atom and the configuration of the double bond in compound [D]-**2a** were determined using

Table 1 The reaction of *N*,*N*-diisopropylnon-2-yn-1-amine **1a** with Et_3Al (2 equiv.) and transition-metal halides MX_n (1 equiv.) in CH_2Cl_2 at room temperature.

Entry	MX_n	Time/h	Yield of [D]-**2a** (%)	Yield of **3** (%)
1	ZnI_2	5	89	–[a]
2	ZnI_2	18	57	36
3[b]	ZnI_2	18	25	–[a]
4	CdI_2	5	85	–[a]
5	CdI_2	18	61	29
6	$ZnCl_2$	1	34	11
7	$TaCl_5$	18	70	0

[a] Not detected. [b] Hexane was used instead of CH_2Cl_2.

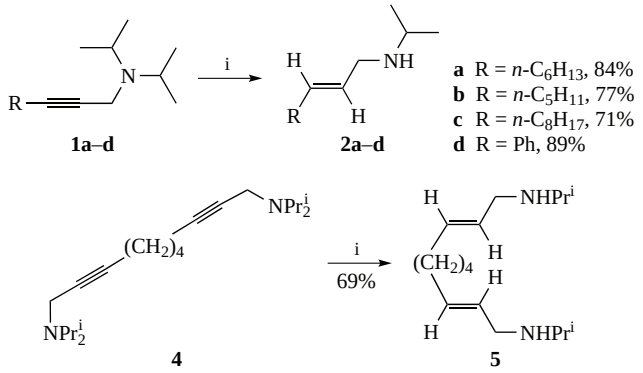
1D and 2D NMR spectroscopy. The NOESY experiment revealed a cross-peak between the NCH_2 protons and olefinic proton which indicated the *E*-configuration of the double bond. In addition, NCH_2 resonated in the ^1H NMR spectrum as a singlet while the sp^2-hybridized carbon atom at the deuterium atom resonates in the ^{13}C NMR spectrum as a characteristic triplet with $^1J_{CD}$ = 19 Hz.

According to the proposed plausible mechanism of the reaction (see Scheme 1), initial reagent complex **A** adds at substrate **1a** to form adduct **B** which would undergo intramolecular hydride transfer to afford metal-containing iminium salt **C**. Subsequent deuterolysis of the latter leads to deuterated reduction product **D**. A parallel reaction pathway involves the conversion of intermediate **C** into substituted allene **3** due to splitting of the C–N bond.

Apparently, one of the main factors to consider in the reaction is the ability of the organometallic compound (Et_3Al) to promote the ionization of the transition metal halide (see Scheme 1) forming active ionic complex. Therefore, we decided to study the interaction of propargylamine **1a** with Et_2Zn and BuLi in the presence of ZnI_2. In fact, the reaction of the compound **1a** with 2 equiv. of Et_2Zn in the presence of 1 equiv. of ZnI_2 in dichloromethane at room temperature for 5 h gave, after deuterolysis, substituted allylamine [D]-**2a** in 45% yield. When using BuLi instead of Et_3Al, the yield of compound [D]-**2a** dropped to 17%. The important role of using a two-component reagent system which promotes N-dealkylation of *N*,*N*-diisoalkyl-*N*-propargylamines under mild conditions should be noted. We have previously observed a similar activation of $Co(acac)_2$ with ZnI_2 in the reaction of [6π + 2π]-cycloaddition of 1,3-diynes to azepines.[10]

Methylalumoxane (MAO), $(AlMeO)_n$, is well known to be a catalyst activator for olefin polymerizations to form an ion pair between a cationic catalyst and a weakly basic MAO-derived anion. We assumed that mixing ZnI_2 with MAO could lead to a ionic complex capable of interacting with *N*-isoalkyl substituted propargylic amines. Indeed, the reaction of compound **1a** with 1 equiv. of each ZnI_2 and MAO in CH_2Cl_2 at room temperature for 5 h gave allylic amine **2a** in 84% yield (Scheme 2). The thus developed reagent system (ZnI_2–MAO) was successfully used to obtain other *E*-allylic amines **2b**–**d** in high yields. *N*-Isoalkyl substituted bis-propargylic diamine **4** derived from 1,7-octadyine was analogously converted into the corresponding bis-allylic diamine **5** in 69% yield.

To conclude, the presented study demonstrates the promise of using organoaluminum compounds to create new metal complex systems for activation of C(sp^3)–H, C(sp^3)–C(sp) and C–N



Scheme 2 *Reagents and conditions*: ZnI_2 (1 equiv.), $(MeAlO)_n$ (1 equiv.), CH_2Cl_2, room temperature, 5 h, then H_2O.

bonds in propargylic amines. The transformation of *N*,*N*-diisoalkyl substituted propargylic amines into the relative N-monodealkylated allylic amines under the action of Et_3Al and halides of transition metals of group IB (CuCl, CuBr), IIB ($ZnCl_2$, ZnI_2, CdI_2), IVB ($TiCl_4$, $ZrCl_4$), VB (VCl_5, $TaCl_5$) was examined, with ZnI_2 and CdI_2 showing the greatest activity and selectivity in the reaction carried out in CH_2Cl_2. New reagent system, ZnI_2–MAO, provides conversion of *N*,*N*-diisoalkyl substituted propargylic amines into *E*-allylic amines in high yield.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.01.013.

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