A Facile *trans*-Reduction of Inactivated Alkynes with Lithium Aluminum Hydride and Lithium Iodide

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Triple bonds of organic compounds without active groups in their molecules such as hydrocarbon or protected alkynes were stereoselectively reduced to trans-alkenes with lithium aluminum hydride and lithium iodide in diglyme at 160-170^{0}C with good yields.

Keywords: Inactivated alkynes, Stereoselective reduction, Alkenes synthesis, Lithium Aluminum Hydride, Lithium Iodide

The stereoselective hydrogenation of alkynes to *cis (Z)*- or *trans (E)*-alkenes is an old but also new subject for chemists that make organic synthesis. *Cis*-alkenes are obtained in very good yields with superior ratio Z:E by reduction of alkynes with H_2 in the presence of Nickel or Palladium catalysts [1], other alkynes precursors of *cis*-retinoids were semi-hydrogenated with Cu/Ag-activated zinc dust [2] or completely reduced with decaboranes/Pd/C [3]. *Trans*-reduction of inactivated alkynes works in hard conditions with Na in NH_3 liq. [4] or hydroxyl activated alkynes with $LiAlH_4$ in diglyme at 120^0 C [5].

Experimental part

The products of the reactions were GC-MS and NMR analyzed. Electron impact (70 eV) mass spectra were obtained on Hewlett-Packard MD 5972 GC-MS instrument. GC analyses were performed on a Hewlett-Packard HP 5890 gas chromatograph. A HP-5MS capillary column (30 m x 0.25 mm x 0.33 μm) and helium gas were used for separations. Also we use a GC-MS Schimadzu QP 2010 Plus. ^{1}H-NMR (400 MHz or 600MHz) and ^{13}C-NMR (75 MHz) spectra were recorded at room temperature in $CDCl_3$ on a Bruker Advanced 400MHz/600MHz spectrometer, using the solvent line as reference. Thin layer chromatography (TLC) was conducted on silica gel 60 F254 TLC plates purchased from Merck. Chemicals were purchased from Aldrich, Merck and Alfa Aesar and were used without further purification. All crude products were purified by column chromatography on silica gel (Merck). All chemical reactions occurred in argon stream.

General procedure

As a practical procedure a solution of $LiAlH_4$ (16.7 mmol, 4.1eq.) and 20 mL of diglyme (diethylene glycol dimethyl ether) was used, under argon, and then LiI (4.48 mmol, 1.1 eq.) and alkyne, 4.08 mmol was added at room temperature. The mixture of the reaction was heated at reflux 160-170^{0}C for about 30-40 h and then a solution of 10 mL HCl 15% was added . The control of the reaction was made on TLC. The reaction mixture was extracted with 3X50 mL n-hexane. The combined organic extracts were successively washed with water, $NaHCO_3$ sat. solution and brine to neutral PH, dried over $MgSO_4$ anh. and concentrated under reduced pressure. The residue was purified over silica gel (n-Hexan: Et_2O=10:0.25) to obtain (*E*)-alkenes (ee. more that 95%) with 76-87% yields.

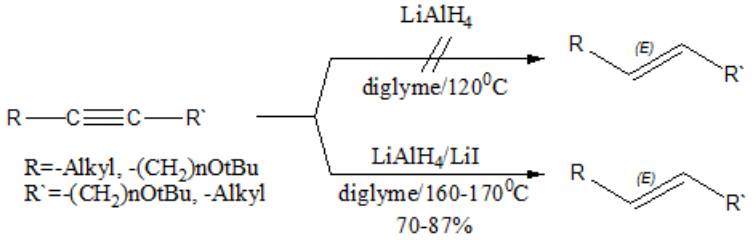
Results and discussions

We manage to hydrogenate inactivated alkynes to *trans*-alkenes (*E*-alkenes) using a modified older method described by A. Paretny [5] but in that case alkynes were activated with hydroxyl group, our method uses lithium aluminum hydride and lithium iodide in diglyme at 160-170^{0}C (scheme 1).

The lithium aluminum hydride and lithium iodide system is used also with success in Suzuki's reduction (chelation-controlled reduction of ketones to obtain *syn*-1,3-diols [6]). In our case we supposed that LiI has the ability to polarize the triple bond and thus to facilitate the hydride anion attack (H^-) from $LiAlH_4$ (fig. 1). Without lithium iodide the reaction does not occur.

We reduced alkynes in different conditions and solvents, the best result was obtained in diglyme at high temperature with 4.1 equivalents of $LiAlH_4$ and 1.1 equivalents of LiI. We observed that if less than 1.1 eq. of LiI is used the reaction is not complete. With 1 eq. LiI 10% of the substrate remains unreacted because lithium iodide is decomposed easily. The best solvent for this type of reaction is diglyme because it interacts very well with $LiAlH_4$ and the reaction mixture can be heated to high temperatures, at lesser temperatures the reaction works hardly.

The reduction of different inactivated alkynes, the time of the reaction, and yields are presented in table 1. In the



Scheme 1. Stereoselective reduction of inactivated alkynes

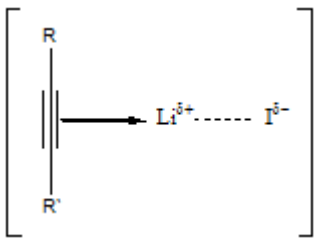


Fig. 1. Supposed interaction of LiI with triple bond

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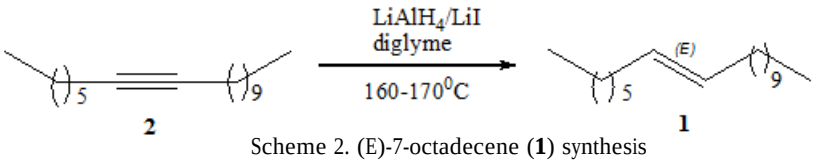
Table 1

PRODUCED VIA SCHEME 1

Entry	Substrate	Products *E*-isomer	Reaction Time (h)	Yield %
1	tBuO-$(CH_2)_4$-C≡C-$(CH_2)_5$-CH_3	tBuO-$(CH_2)_4$-HC=CH-$(CH_2)_5$-CH_3	32	76
2	tBuO-$(CH_2)_9$-C≡C-CH_3	tBuO-$(CH_2)_9$-HC=CH-CH_3	30	87
3	CH_3-$(CH_2)_5$-C≡C-$(CH_2)_9$-CH_3	CH_3-$(CH_2)_5$-HC=CH-$(CH_2)_9$-CH_3	40	80
4	$(CH_3)_2$CH-$(CH_2)_4$-C≡C-$(CH_2)_9$-CH_3	$(CH_3)_2$CH-$(CH_2)_4$-HC=CH-$(CH_2)_9$-CH_3	40	80
5	tBuO-$(CH_2)_6$-C≡C-$(CH_2)_3$-CH_3	tBuO-$(CH_2)_6$-HC=CH-$(CH_2)_3$-CH_3	32	80
6	tBuO-$(CH_2)_6$-C≡C-CH_3	tBuO-$(CH_2)_6$-HC=CH-CH_3	30	87
7	tBuO-$(CH_2)_5$-C≡C-$(CH_2)_4$-CH_3	tBuO-$(CH_2)_5$-HC=CH-$(CH_2)_4$-CH_3	32	76
8	tBuO-$(CH_2)_{10}$-C≡C-CH_2-CH_3	tBuO-$(CH_2)_{10}$-HC=CH-CH_2-CH_3	30	82



2 **1**

Scheme 2. (E)-7-octadecene (**1**) synthesis

case of alcohols protected with *tert*-Butyl there is no need to unprotect molecules as the reduction works directly on protected compounds. We observed that the reaction takes place in less time and with higher yields if the triple bond is marginal, if the triple bond is inside of the molecules the reaction takes place in a longer time and at lesser yields possibly because of steric hindrance (table 1).

Isomeric rapport E/Z was more that 95% E and it was determined by epoxidation of double bond of (*E*)-alkenes with MPPA (monoperoxyphtalic acid) by GC-MS analysis.

It is presented a particular example of *trans*-reduction with $LiAlH_4$ and LiI for the most inactivated alkyne 7-octadecyne (**2**) to **(***E*)-7-octadecene (**1**) (scheme 2).

Fig.2. Controlled on TLC after 12 h of the reaction (table 1, Entry 3)

The control of the reaction was made on TLC, eluent n-Hexane or n-Hexane:Et_2O=10:0.25 (fig. 2).

The product of the reaction was analyzed ^{1}H–NMR and ^{13}C-NMR (fig. 3, 5) and it was observed at δ 5.37–5.39

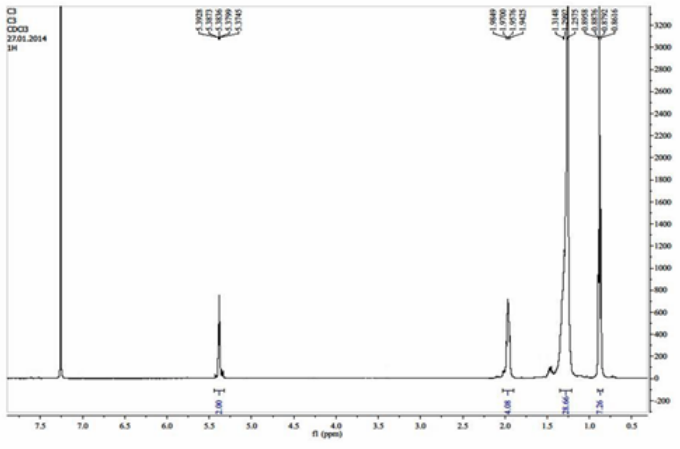


Fig. 3. ^{1}H-NMR Spectrum of (*E*)-7-octadecene (**1**): ^{1}H NMR δ 5.37–5.39 (m, 2H, -**H**C=C**H-**), 1.94-1.98 (m, 4H, -C**H**$_2$-HC=), 1.25–1.31 (m, 22H, -CH_2-), 0.86-0.89 (t, 6H, *J* = 6.5 Hz, -C**H**$_3$)

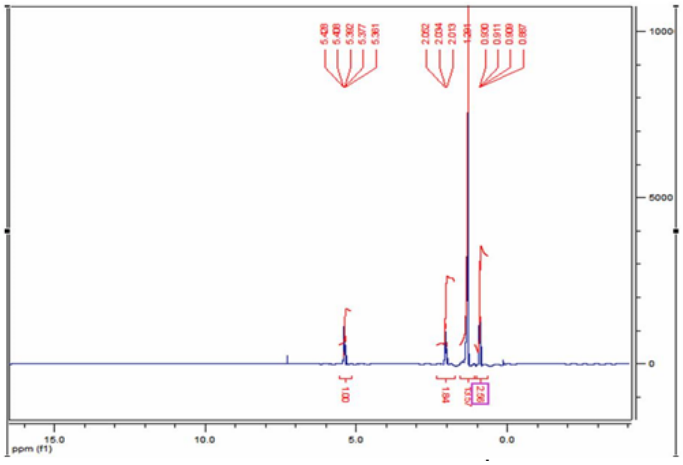


Fig. 4. ^{1}H-NMR Spectrum of (*Z*)-7-octadecene (monachalure): ^{1}H NMR: δ 5.36–5.42 (m, 2H, -**H**C=C**H-**), 2.01-1.06 (m, 4H, -C**H**$_2$-HC=), 1.29 (m, 22H, -CH_2-), 0.88-0.93 (t, 6H, *J* = 6.5 Hz, -C**H**$_3$)

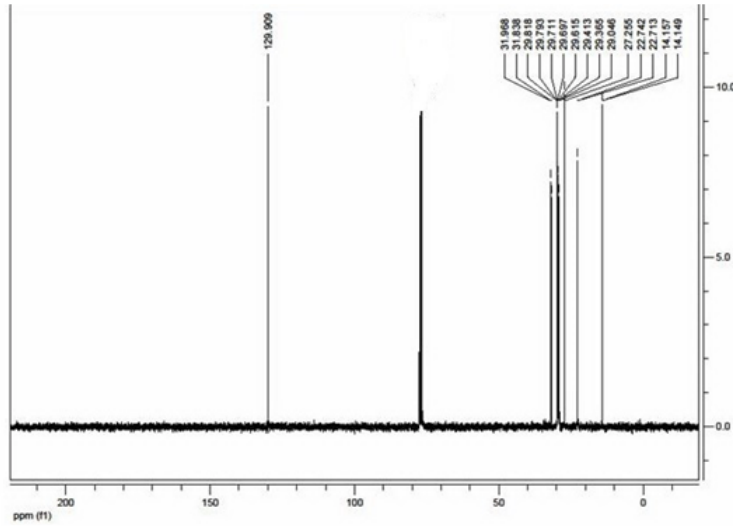


Fig. 5. C^{13}-NMR Spectrum of (*E*)-7-octadecene: ^{13}C NMR δ 129.90(2C=), 31.96(2C), 31.83(2C), 29.81(2C), 29.79, 29.71, 29.69, 29.61, 29.41, 29.36, 29.04, 27.25, 22.74, 22.71, 14.27, 14.19

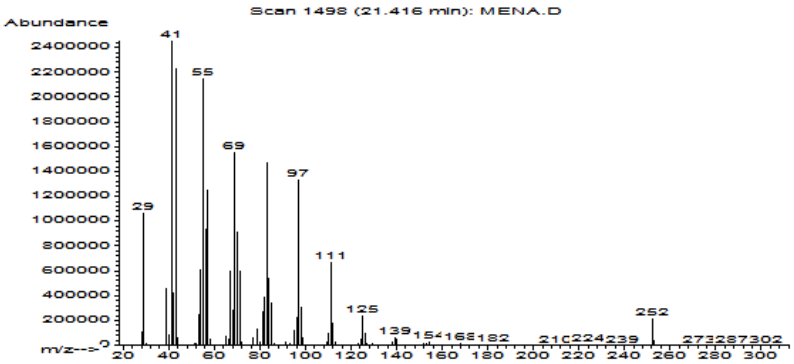


Fig. 6. Mass Spectrum of (*E*)-7-octadecene (**1**) M^+ = 252(10), 239(<1) 224(1), 196(<1), 182(<1), 168(1), 154(1.9),139(4), 125(11), 111(31.2), 97(59.8), 83(65.5), 69(73.4), 55(90), 41(100), 29(44.9)

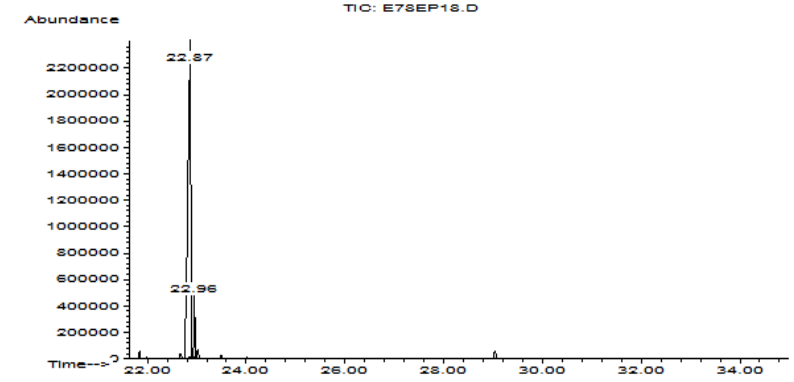
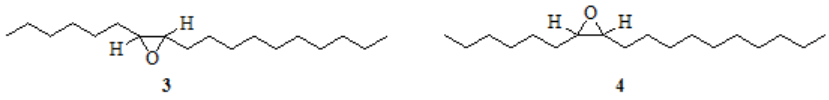


Fig. 7. Gas chromatogram of (*E*)-7,8-epoxyoctadecane (**3**)



3 **4**

Fig. 8. Structures of (*E*)-7,8-epoxyoctadecane (**3**) and (Z)-7,8-epoxyoctadecane (**4**)

specific protons to the double bond in *trans* (m, 2H, -**H**C=C**H**-) (fig. 3). We also made comparison with Z-isomer by NMR spectroscopy and we observed a difference of δ-ppm for ene-protons (fig. 4).

Isomeric rapport was determined approximately by epoxidation of (*E*)-7-octadecene (table 1, Entry 3, MS-spectrum fig. 6) with monoperoxyphtalic acid at 0^0C in diethyl ether and analyzed by GC-MS **(**fig. 7). It was observed that less by 5% (*Z*)-isomer (**2**) is formed (fig. 8). It is also presented MS spectrum of *E*- ***1*** and *Z*- ***2*** isomers (fig. 9, fig. 10).

This method is very important because we don't need to unprotect alkynes to hydroxyl alkynes and then make the reduction with $LiAlH_4$ in diglyme at 130^0C [8] reduction works directly on protected compounds. The method has applicability in semiochemical synthesis as synthesis of *(E)*-5-dodecenyl acetate (table 1, Entry 1) (**5**) the pheromonal component of *Agrotis segetum* and *Euxoa ochrogaster* or attractant for *Gnorimoschemini sp.*.

For example to obtain acetates from derivates of protected alkynes **5** there are two possibilities:

The first way is our method of reduction that occurred with 68% overall yields in only two steps and the second way is the classical method and in this case unprotection is needed first and then reduction of triple bond, so, the second method has three steps and occurred with 56% overall yield (scheme 3).

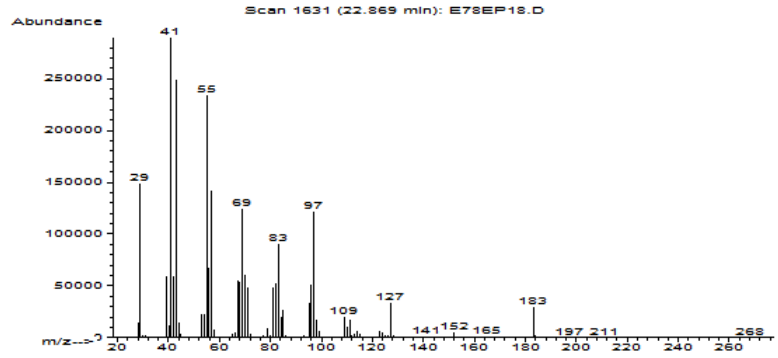


Fig .9. Mass spectrum of (*E*)-7,8-epoxyoctadecane (**3**)
M^+ = 268(<1), 211(<1), 197(<1), 183(12), 152(2.5), 141(<1), 127(15), 109(9), 97(55.9), 83(46), 69(59), 55(84), 41(100), 29(45.5).

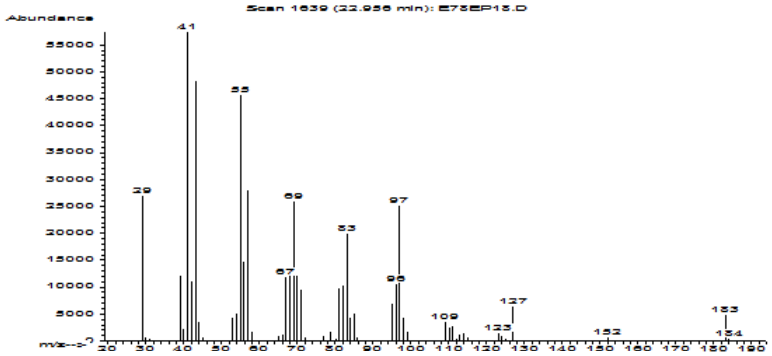
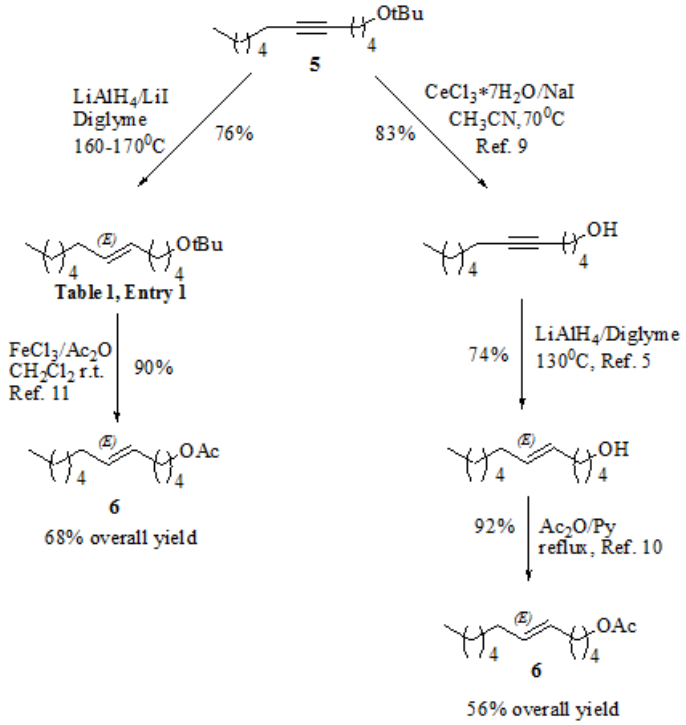


Fig. 10. Mass spectrum of (*Z*)-7,8-epoxyoctadecane (monachalure) (**4**)M^+-84 = 184(<1), 183(12), 152(<1), 141(<1), 127(15), 123(<1), 109(9), 97(55.9), 96(20), 83(47.9), 69(59), 67(21), 55(84), 41(100), 29(57)



Scheme 3. The two ways for (E)-5-dodecenyl acetate (**6**) synthesis

Conclusions

The reduction of inactivated alkynes with lithium aluminum hydride and lithium iodide in diglyme can be a general method of reduction to obtained *trans*-alkenes and can be very utile for chemists that make organic synthesis.

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