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Synthesis of Cyclopentadienyl Enaminonitriles from α-Chlorovinyl *p*-Tolyl Sulfoxides and Acetonitrile with Three Consecutive Carbon-Carbon Bond-Formations

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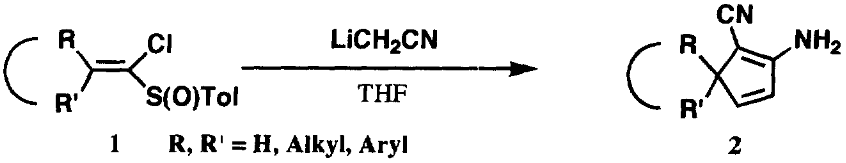
Abstract: Treatment of α-chlorovinyl *p*-tolyl sulfoxides with 5-equivalents of lithium carbanion of acetonitrile at -78 °C to room temperature afforded cyclopentadienyl enaminonitriles in high yields with three consecutive carbon-carbon bond-formations. The mechanism of this reaction and some reactions of the enaminonitriles are reported. © 1999 Elsevier Science Ltd. All rights reserved.

The formation of several carbon-carbon bonds in a one-flask multistep reaction is of high value in the synthesis of complex organic molecules. These reactions are sometimes called tandem or cascade reactions and they have received much attention these days.[1]

Recently, we have been investigating the use of α-halovinyl sulfoxides **1** in organic synthesis.[2] In continuation of our studies on developing new synthetic methods by using α-haloalkyl aryl sulfoxides, herein we report a novel synthesis of cyclopentadienyl enaminonitriles **2**, including the spiro-type, from **1** and acetonitrile with consecutive three carbon-carbon bond-formation.



α-Chlorovinyl *p*-tolyl sulfoxide **3**[2c] was reacted with 5-equivalents of lithium carbanion of acetonitrile (prepared from acetonitrile and *n*-butyllithium) at -78 °C to room temperature for 2 h (Scheme 1). The reaction gave a clean reaction mixture, and crystalline product **8** was obtained as colorless crystals in 92% yield. The IR spectra of the product **8** showed NH absorption at 3434 and 3346 cm^{-1}. The absorption at 2171 cm^{-1} was considered to be a nitrile; however, the value was abnormally low compared to the usual nitriles (2285-2200 cm^{-1}).[3] From other spectral data and X-ray crystallographic analysis,[4] the structure of the product was established as cyclopentadienyl enaminonitrile **8**.

We propose the mechanism of this very interesting reaction as follows (Scheme 1). Michael-type addition of the lithium carbanion of acetonitrile to the double bond of **3** gave α-sulfinyl carbanion having a chlorine atom **4**. This intermediate **4** was confirmed as follows: when this reaction was quenched after 2 min at -78 °C, the adduct **5** was obtained in 90% yield. Elimination of lithium chloride from **4** afford α-sulfinyl carbene **6** (or carbenoid),

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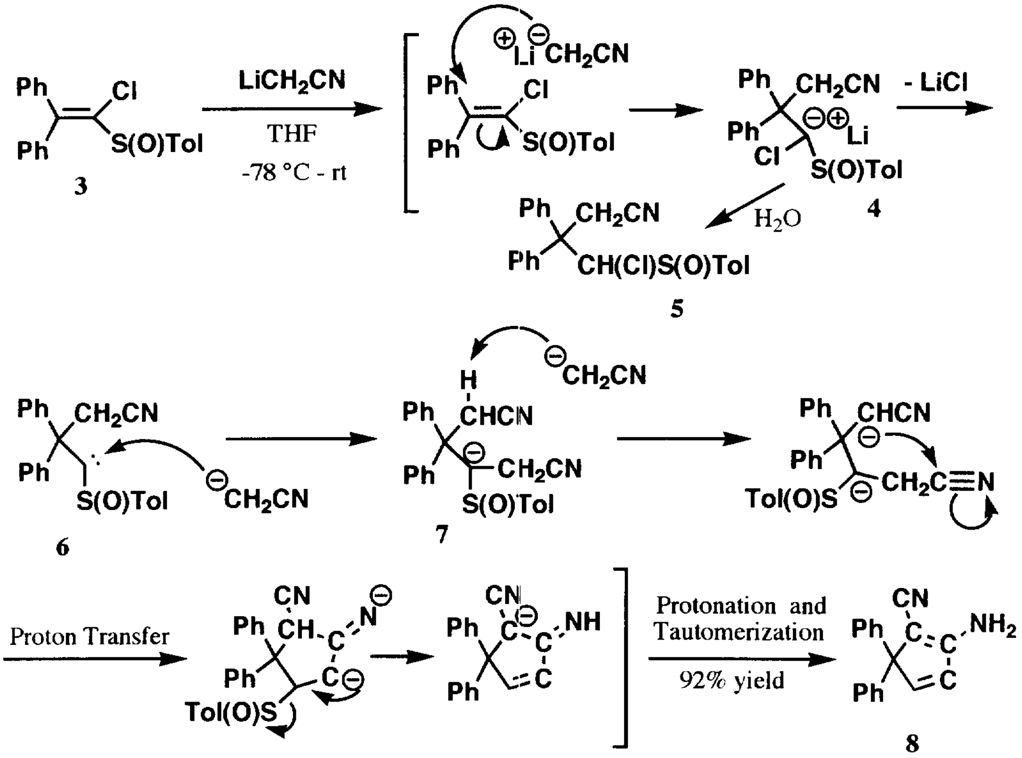
which was attacked by a second lithium carbanion of acetonitrile to give α-sulfinyl carbanion of dinitrile compound **7**. The Thorpe-Ziegler reaction[5] of the dinitrile **7** with the elimination of the sulfinyl group took place to give the cyclopentadienyl enaminonitrile **8** in high yield.

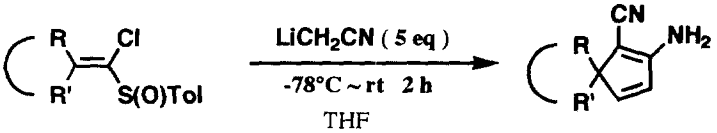
Scheme 1. Synthesis of Cyclopentadienyl Enaminonitriles **8** from α-Chlorovinyl *p*-Tolyl Sulfoxide **3** and the Proposed Mechanism

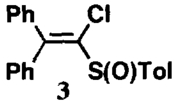
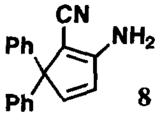
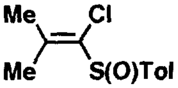
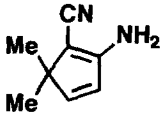
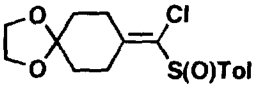
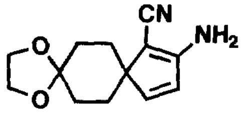
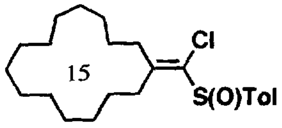
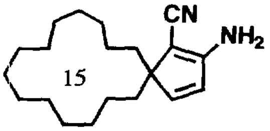
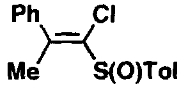
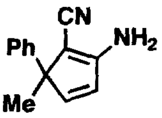
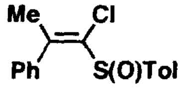
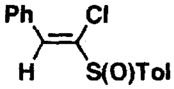
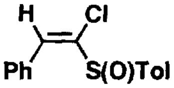
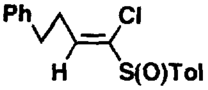
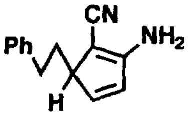
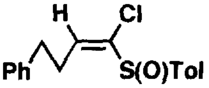


The results for the reaction of several α-chlorovinyl *p*-tolyl sulfoxides with lithium carbanion of acetonitrile are summarized in Table 1. Entries 1-6 show that, when both R and R' in the α-chlorovinyl sulfoxides are an alkyl or aryl group, the reaction gives high yields of the products. Entries 3 and 4 show that spiro-type pentadienyl enaminonitriles are obtained without any problem. Entries 5 and 6 indicate that both geometrical isomers react similarly with the carbanion of acetonitrile.

In contrast to the good results described above, the α-chlorovinyl sulfoxides having a hydrogen on their β-position showed very different results. Entries 7 and 8 show that the α-chlorovinyl sulfoxides derived from benzaldehyde gave only a tarry complex mixture. The α-chlorovinyl sulfoxides derived from dihydrocinnamaldehyde gave the desired product; however, the reaction mixture was rather complex and the yield of the enaminonitrile was low (entries 9 and 10). The reason for these results was attributed to the fact that the α-chlorovinyl sulfoxides have an acidic hydrogen on their β-position.

Table 1. Reactions of α-Chlorovinyl *p*-Tolyl Sulfoxides with $LiCH_2CN$



Entry	α-Chlorovinyl Sulfoxide	Enaminonitrile[a]	Yield / %[b]
1	 3	 8	92
2			87
3			97
4			77
5			96
6			93
7		Complex Mixture	
8			
9			28
10			23

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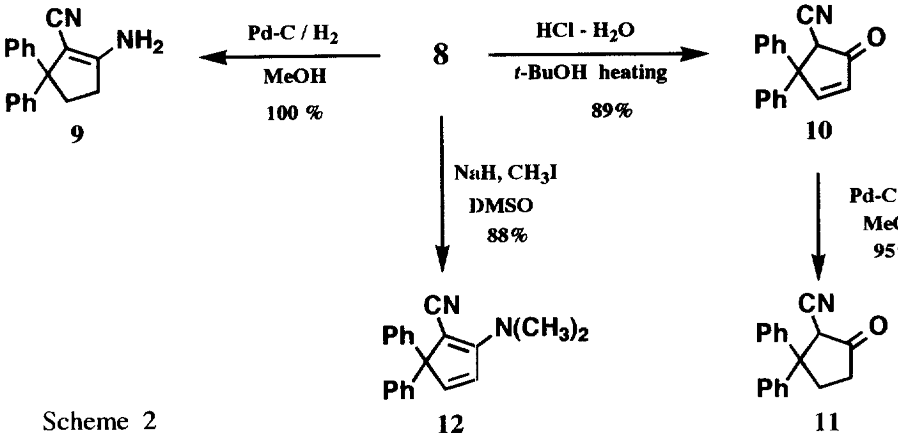
a) All the enaminonitriles were fully characterized by IR, NMR (^1H and ^{13}C), MS, and elemental analysis. b) Isolated yield after silica gel column chromatography.

In order to convert **8** into the compounds useful in organic synthesis, we tried some reactions to **8**. Preliminary results are shown in Scheme 2. Catalytic hydrogenation of **8** gave enaminonitrile **9** in quantitative yield. Hydrolysis of **8** with aq. HCl in *t*-BuOH gave ketonitrile **10** in good yield.[6] Catalytic hydrogenation of **10** reduced not the cyano group but only the carbon-carbon double bond to give **11**. Treatment of **8** with excess CH_3I in the presence of NaH gave *N*,*N*-dimethyl compound **12** in good yield.



Scheme 2

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4. We thank Dr. Takashi Watanabe and Dr. Yasuo Ohtsuka of Pharmaceutical Research Center, Meiji Seika Kaisha Ltd., for X-ray crystallographic analysis of **8**.

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