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Isomerizations on Silica Gel: Synthesis of Allenyl Ketones and the First Nazarov Cyclizations of Vinyl Allenyl Ketones

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Abstract

Dess-Martin oxidation followed by the chromatographic workup of crude, terminal propargyl ketones **5** on silica gel directly leads to terminal allenyl ketones **6**. When the other substituent on **5** was electron-rich, **7** was observed as side-product. If the other substituent on **5** was electron-poor, the isomeric 1-propynyl ketone **8** was the side-product. Chromatography of the crude propargyl vinyl ketones **10** on silica gel delivers the products of a Nazarov cyclization. © 1998 Elsevier Science Ltd. All rights reserved.

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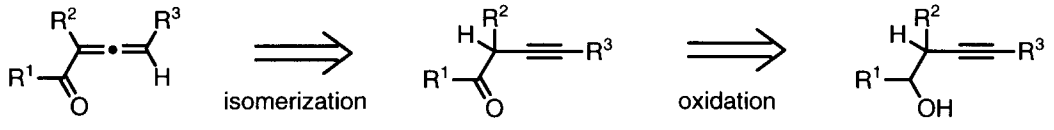
A frequently applied method for the synthesis of allenyl ketones **1** is the oxidation of the easily available homopropargylic alcohols **3** to propargyl ketones **2** followed by a base-catalyzed isomerization of **2** to **1**[1].



1 **2** **3**

These oxidations were performed either with the Dess-Martin periodinane (DMP)[1,2], Cr^{VI}-reagents[3,4] or by the Swern procedure[1]. For the isomerization usually aqueous sodium hydrogen carbonate[5] or triethylamine[1] was used[6]. During chromatography on aluminium oxide as stationary phase comparable isomerizations have been observed[7,8]. As far as propargyl ketones are concerned, there exist only sporadic reports on such isomerizations initiated by silica gel: one of a

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non-terminal[9] and one of terminal propargyl ketones[8]. But these isomerizations seemed not to be general, otherwise the base-induced isomerizations mentioned above would not be necessary.

In the case of terminal propargyl ketones **4**, we have now observed the direct and clean formation of **6** during the chromatographic workup of **5** on silica gel. As a control experiment we conducted a Dess-Martin-oxidation of **4g** in $CDCl_3$. The NMR spectra of the crude reaction mixture showed only the signals of **5g**, no **6g** was detectable[10] (the same is true for **9c**, see below). The mixture remained unchanged for one week. This probably originates from the acetic acid set free during the Dess-Martin oxidation, in a weakly acidic medium **5** did not isomerize to **6**[4,5] (in the presence of strong acids it does)[11].

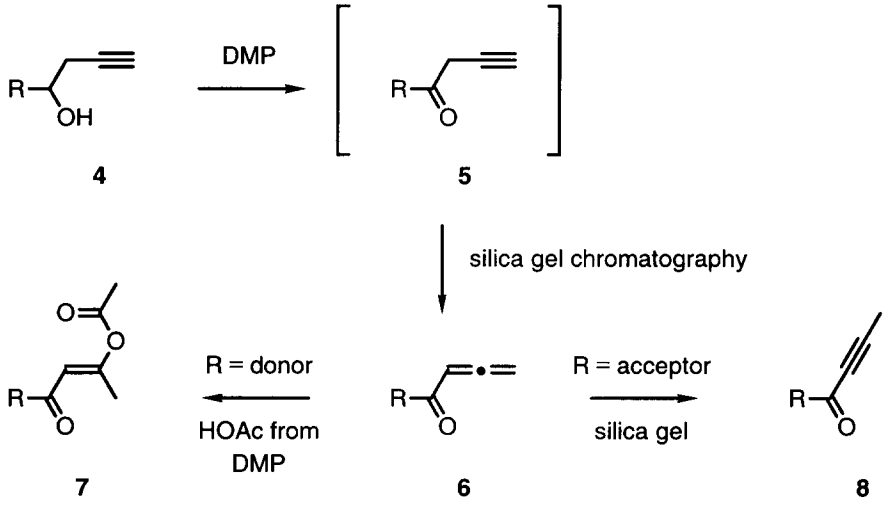


Table 1
Dess-Martin oxidation of **4** and subsequent chromatographic workup on silica gel

4	R	7 (%)	6 (%)	8 (%)
a	3,4-[OCH_2O]C_6H_3	21	60	--
b	3,4-$(MeO)_2C_6H_3$	15	73	--
c	2,4,6-$(MeO)_3C_6H_2$	12	54	--
d	3-[$CH(OH)CH_2C{\equiv}CH$]C_6H_4	8	45[a]	--
e	4-[$CH(OH)CH{=}C{=}CH_2$]C_6H_4	7	40[a]	--
f	4-(MeS)C_6H_4	10	60	5
g	3-(MeO)C_6H_4	5	67	12
h	4-(CHO)C_6H_4	--	77	4
i	4-(CO_2Me)C_6H_4	--	59	5
j	4-(NO_2)C_6H_4	--	45	22
k	2-(NO_2)C_6H_4	--	41	23
l	4-(MeO)$C_6H_4CH_2$[b]			

[a] yield reduced due to oxidation of the second hydroxyl group
[b] prepared by a different route

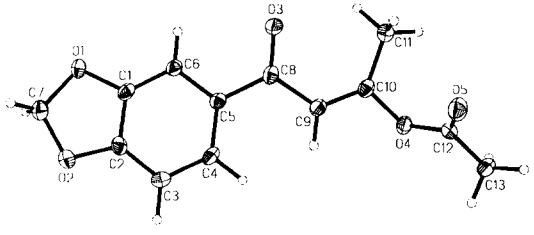
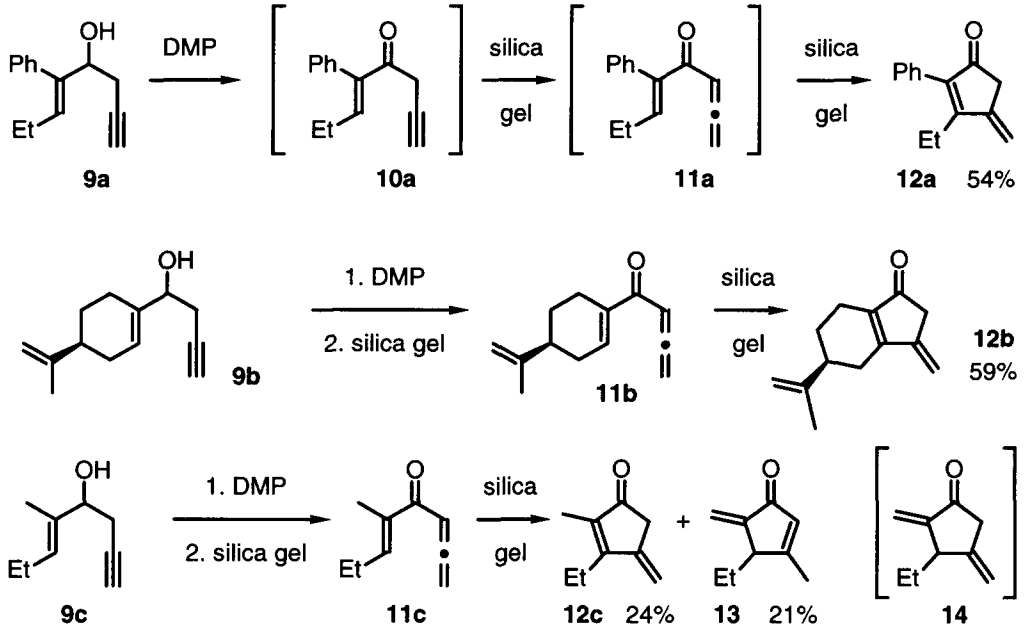


Figure 1. ORTEP-plot of **7a**

When this reaction mixture was directly placed on the chromatography column (without aqueous workup, this possibility is described in the literature)[12], the acetic acid and **5** separate and then **5** isomerizes to **6**. This separation before isomerization is necessary, when only some silica gel was added to the reaction mixture of the Dess-Martin oxidation mentioned above, no isomerization was observed.

While in most Dess-Martin oxidations followed by chromatographic workup exclusively **6** was formed, in the case of substrates with electron-rich or electron-poor aryl-substituents side products were observed (see table 1). The oxidation of **4a-4e** delivered some (*E*)-β-acetoxy-β-methyl-enone **7a-7e**. The (*E*)-configuration of the trisubstituted double bond in **7** was proven by two X-ray structure determinations (**7c**[2] and **7a**, the latter is depicted in Figure 1)[13]. When in a control experiment acetic acid was added to **6l**, a similar addition was observed. Two minor side products formed, which did not survive the chromatographic workup. So the formation of **7** is best explained by **5** just starting to isomerize on the column while not being completely separated from the acetic acid. On the other hand, with electron-poor substituents **4h-4k** the isomerization did not stop at **6**, the tautomeric 1-propynyl ketones **8h-8k** were formed as side-products! Unexpected was the reaction of the two substrates **4f** and **4g** in which both side products **7** and **8** were formed.



Then we investigated the synthesis of allenyl vinyl ketones **11** from the corresponding propargyl vinyl carbinols **9**. We were unable to isolate **11** in the case of substrates having a donor substituent α to the ketone as in **9a-9c**. Instead **12**, the product of a Nazarov cyclization[14] was obtained. Allenyl vinyl ketones have never been applied as substrates in Nazarov cyclizations before. Usually a strong Brønsted acid like H_2SO_4 or a strong Lewis acid like Fe^{III} is necessary to

induce the Nazarov cyclization of divinyl ketones, donors α to the ketone accelerate the reaction. In our case obviously the combination of such donors and the enhanced reactivity of the allene allows silica gel to catalyze the Nazarov cyclization. Interestingly in ref. [8] the isomerization to allenyl vinyl ketones bearing α-donors on aluminium oxide is described to occur without subsequent Nazarov cyclization.

If a short column was used for the chromatography, from the reaction mixtures that were obtained from **9b** or **9c**, small amounts of **11b** or **11c** could be isolated. When **11b** or **11c** were placed on a silica gel column again, they cyclized to **12b** respectively **12c/13**. Thus the intermediacy of **11** in the formation of **12** was proven. On the other hand with the strong donor in **9a** it was impossible to stop the reaction at the stage of **11a**.

In the case of α-substituents bearing hydrogen atoms in β-position to the carbonyl-group as in **9c**, besides **12c** an isomeric divinyl ketone **13** was formed (probably via tautomerization of **14**).

The 3-alkylidene-2-cyclopentenones **12** obtained that way are interesting building blocks, which recently have been described in the literature for the very first time[15].

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