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# A mild method for eliminating alkyl ethers to alkenes<sup>†</sup>

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A method for the conversion of methyl ethers into alkenes is described. In a one-step and mild procedure, both conjugated and isolated cyclic alkenes are accessible in mostly good yields using triflic anhydride in combination with triethylamine. This elimination procedure can also be applied to ethyl and benzyl ethers.

The creation of double bonds is a chemical transformation which is often required in organic syntheses. Due to the fact that alkyl ethers and especially methyl ethers are easily accessible and therefore frequently used as protecting groups in these syntheses, their elimination is an attractive method for the formation of alkenes.

In general, conversion of alkyl ethers to alkenes is accomplished in two steps – ether cleavage to the corresponding alcohol<sup>1</sup> or bromide<sup>2</sup> followed by elimination. To date, many procedures have been described for the dehydration of alcohols, most of which include *in situ* transformations into suitable leaving groups. Among them ester pyrolysis,<sup>3</sup> the Chugaev elimination,<sup>4</sup> Monson's method,<sup>5</sup> and the use of methyl *N*-(triethylammoniumsulfonyl)carbamate, also known as Burgess reagent.<sup>6,7</sup> However, only a few individual examples for the direct elimination of alkyl ethers have been described so far. For instance, the elimination of steroid methyl ethers by using BF<sub>3</sub>etherate or chlorotrimethylsilane in combination with acetic anhydride.<sup>8,9</sup> Besides, elimination products are frequently observed (mostly as side products) when alkyl ethers are treated with strong Lewis acids.<sup>10</sup>

Nevertheless, to the best of our knowledge, there is no general method available for the mild elimination of alkyl ethers, yet.<sup>11</sup> Herein we present a mild and effective one-step procedure for the direct conversion of aliphatic alkyl and particularly methyl ethers into alkenes.

In the initial experiment we intended to convert the hydroxyl function of phenol  $1^{12}$  into the triflate using triflic anhydride (1.5 equiv.) along with triethylamine (1.5 equiv.) in dichloromethane at 0 °C. Surprisingly, we also observed the elimination of the methoxy group yielding xanthene 2 in 82% (Scheme 1).

While the conversion of alcohols into the corresponding triflates followed by an elimination step is already known under the applied conditions,<sup>13</sup> it has never been used for the *in situ* 



Scheme 1 Initial experiment: conversion of alcohol 1 into triflate 2 accompanied by the elimination of the methyl ether.

Table 1 Optimisation of the reaction conditions



Entry	Reagents (1.50 equiv.)	Temperature/ reaction time	Yield
1	NEt <sub>2</sub> , Tf <sub>2</sub> O	0 °C. 1.5 h	84
2	DIPEA, $Tf_2O$	0 °C, 1.5 h	79
3	<i>N,N</i> -Dimethyl-1- phenylethylamine, Tf <sub>2</sub> O	0 °C, 1.5 h	38
4	NEt <sub>3</sub> , MsCl	Reflux, 5 h, then r.t., 7 days	49

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synthesis of alkenes from methyl ethers before. Therefore we started further investigations towards a general one-step elimination protocol allowing the synthesis of different alkenes. Surprisingly, the elimination reaction did not occur using *N*-phenyl-bis(trifluoromethanesulfonimide) as triflating reagent instead of triflic anhydride and the application of triflic acid resulted in an unidentifiable fluorescing mixture. Besides, when only one reagent, either NEt<sub>3</sub> or Tf<sub>2</sub>O, was used, no reaction occurred or decomposition was observed, respectively. Furthermore, changing the solvent from dichloromethane to tetrahydrofuran led to poorer yield (61%). Further

investigations were implemented on the related substrate **3**-**OMe**, in which only the elimination can take place (Table 1).

If  $Tf_2O$  and  $NEt_3$  were used as reagents, xanthene 4 could also be isolated in excellent yield (84%). We also explored the replacement of  $NEt_3$  by other tertiary amine bases like DIPEA (entry 2) or *N*,*N*-dimethyl-1-phenylethylamine (entry 3). However, in both cases the yields decreased to 79% and 38%, respectively. Moreover, using mesyl chloride instead of triflic anhydride greatly decelerated the elimination. Thus, a reaction could neither be detected after stirring the mixture at 0 °C for 2 h nor after refluxing for 5 h. Further stirring the reaction

Table 2       Scope of the alkyl ether elimination reaction							
Entry	Substrate	Product	Equiv. of the reagents $(Tf_2O \text{ and } NEt_3)$	Temperature/reaction time	Yield <sup>a</sup> [%]		
1	OMe Sa		1.5	0 °C, 1.5 h	73		
2	OMe 5b		1.5	0 °C, 1.5 h to r.t., 4 h	29		
3a 3b 3c	MeO Ta-OMe	$ \begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $	1.5 3.0 1.5	0 °C, 1.5 h 0 °C, 1.5 h r.t., 1.5 h	$ \begin{array}{r} 61 (1)^{b} \\ 71 (2)^{b} \\ 71 (3)^{b} \end{array} $		
4a 4b	MeO 7b Ph	Ph + Ph 8a 8b	1.5 3.0	0 °C, 1.5 h 0 °C, 1.5 h to r.t., 1 day	Only traces 78 $(3/1)^c$		
5	Br	Br	1.5	0 °C, 2 h	58		
6	Eto Ta-OEt	Ph + Ph 8a 8b	1.5	0 °C, 1.5 h to r.t., 3 days	47 (1.5/1) <sup>c</sup>		
7	Br H 3-OBn	Br O 4	1.5	0 °C, 1.5 h	27		
8	BnO 7a-OBn	Ph + Ph 8a 8b	1.5	0 °C, 1.5 h to r.t., 3 days	15 (1.9/1) <sup>c</sup>		
9	MeO 9	OBn 10	1.5 3.0	0 °C, 1.5 h 0 °C, 1.5 h	20 35 (73 brsm) <sup>d</sup>		

<sup>*a*</sup> Isolated yields. <sup>*b*</sup> Yield of the side product **8b** in parenthesis. <sup>*c*</sup> Ratio of **8a** : **8b** (determined by <sup>1</sup>H NMR) in parenthesis. <sup>*d*</sup> Starting material **9** was used as a mixture of isomers (*cis/trans* = 1 : 2.5); ratio of reisolated starting material (*cis/trans* = 1 : 1) showed, that only the *trans*-isomer had reacted.

mixture for 7 days at room temperature led to the desired xanthene 4 in poorer yield (entry 4). Therefore  $Tf_2O$  and  $NEt_3$  proved to be the best combination for the elimination of methyl ethers.

With our reaction conditions in hand, we first tested the elimination reaction on the methoxy tetrahydronaphthalenes **5a** and **5b** (Table 2, entry 1 and 2), both resulting in the same binaphthalene **6**.

Due to the fact that the two substrates, **5a** and **5b**, led to exactly the same product, the reactions proceed in all likelihood *via* intermediary occurring 1,2-dihydronaphthalene, which subsequently dimerises under the reaction conditions to the binaphthalene **6**, as already reported.<sup>14–16</sup> Thus, the elimination reaction primarily gave the desired elimination product in acceptable yields.

Knowing that the method is efficient in eliminating methoxy groups, resulting in a conjugated  $\pi$ -system, we proceeded to investigate systems leading to isolated double bonds (entry 3 and 4). The conversion of trans-(4-methoxycyclohexyl)benzene (7a-OMe) afforded the alkene 8a in good yield, which could be improved by increasing the equivalents of both reagents (entry 3b) or applying higher reaction temperatures (entry 3c). In addition, isomer 8b was obtained as a side product (<3%), giving indications on the mechanism. Unexpectedly almost no reaction occurred in case of the cis-isomer 7b under the same conditions (entry 4a), but the products 8a and 8b could still be obtained by increasing the amount of the reagents, higher temperature and longer reaction time (entry 4b). In addition, the described method could be successfully used for the elimination of the open-chain substrate (3-methoxybutyl)benzene, but resulted in an inseparable mixture of probably five isomers (according to GC-MS) in moderate yield (37%, see ESI<sup>†</sup>).

In order to determine whether this reaction is capable of eliminating ethyl and benzyl ethers, we tested the reaction conditions starting from ethyl ethers **3-OEt** and **7a-OEt** as well as from benzyl ethers **3-OBn** and **7a-OBn**, respectively (entry 5–8). To our delight both substrates could be converted into the corresponding alkenes. However, full conversion required longer reaction times and sometimes higher temperatures and resulted in poorer yields. Thus, we tested whether methyl ethers can be eliminated selectively in presence of benzyl ethers using test substrate **9** (entry 9). The methyl ether could be converted into the alkene **10** without affecting the benzyl ether function, proofing that under mild conditions the elimination of methyl ethers is selective.

Based on the fact that only the *trans*-isomer **7a-OMe** reacted, as well as the occurrence of the migrated double bond (**8b**), we propose an E1 mechanism, which is depicted in Scheme 2, using the example of the conversion of methyl ether **7a-OMe**. According to this mechanism, initially the methoxy group is triflated leading to the oxonium species **11**. We assume that due to steric reasons the generation of the intermediate **11** is preferred when the methoxy group is in equatorial position of the cyclohexane chair. As a consequence of the phenyl substituent acting as an anchor group, the cyclohexane conformation with the phenyl substituent being in equatorial position is favored. Thus the 4-methoxy group is in the equatorial position



Scheme 2 Proposed mechanism for the elimination reaction using the example of methyl ether **7a-OMe**.

only in case of the *trans*-isomer **7a-OMe**. Elimination of methyl trifluoromethanesulfonate<sup>17</sup> results in the carbocation **12a** which is able to react *via* a Wagner–Meerwein rearrangement yielding carbenium ion **12b**. Ensuing base-induced deprotonation gives the final elimination products **8a** and **8b**, respectively.

#### Conclusions

In summary, we report that methyl ethers can be easily converted into alkenes by using triflic anhydride in combination with a tertiary amine base. The described method can also be applied for the synthesis of alkenes starting from ethyl and benzyl ethers.

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