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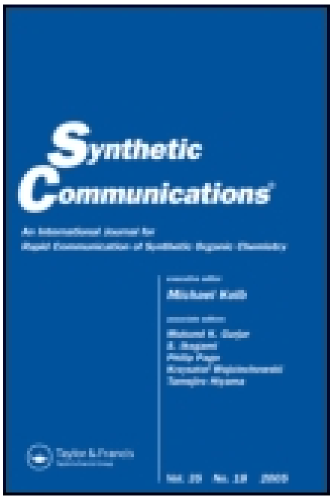

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

AN EFFICIENT METHOD FOR SELECTIVE DEPROTECTION OF TRIMETHYLSILYL ETHERS, TETRAHYDROPYRANYL ETHERS, ETHYLENE ACETALS, AND KETALS UNDER MICROWAVE IRRADIATION

A. R. Hajipour [a] , S. E. Mallakpour [b] , I. Mohammadpoor-Baltork [c] & S. Khoee [a]
[a] Pharmaceutical Research Laboratory , College of Chemistry , Isfahan University of Technology , Isfahan, 84156, I.R. Iran
[b] Pharmaceutical Research Laboratory , College of Chemistry , Isfahan University of Technology , Isfahan, 84156, I.R. Iran
[c] Department of Chemistry , Isfahan University , Isfahan, 81744, I.R. Iran
Published online: 16 Aug 2006.

To cite this article: A. R. Hajipour , S. E. Mallakpour , I. Mohammadpoor-Baltork & S. Khoee (2002) AN EFFICIENT METHOD FOR SELECTIVE DEPROTECTION OF TRIMETHYLSILYL ETHERS, TETRAHYDROPYRANYL ETHERS, ETHYLENE ACETALS, AND KETALS UNDER MICROWAVE IRRADIATION, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 32:4, 611-620, DOI: 10.1081/SCC-120002408

To link to this article: http://dx.doi.org/10.1081/SCC-120002408

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SYNTHETIC COMMUNICATIONS, 32(4), 611–620 (2002)

AN EFFICIENT METHOD FOR SELECTIVE DEPROTECTION OF TRIMETHYLSILYL ETHERS, TETRAHYDROPYRANYL ETHERS, ETHYLENE ACETALS, AND KETALS UNDER MICROWAVE IRRADIATION

A. R. Hajipour,[1,]* S. E. Mallakpour,[1,]*
I. Mohammadpoor-Baltork,[2] and S. Khoee[1]

[1]Pharmaceutical Research Laboratory,
College of Chemistry, Isfahan University of
Technology, Isfahan, 84156, I.R. Iran
[2]Department of Chemistry, Isfahan University,
Isfahan, 81744, I.R. Iran

ABSTRACT

1-Benzyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate (BAABOD) is a useful reagent for the selective cleavage of trimethylsilyl ethers, tetrahydropyranyl ethers, ethylene acetals and ketals to their corresponding alcohols, aldehydes and ketones. This method is very simple and efficient and the reaction has been carried out under microwave irradiation.

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*Corresponding authors.

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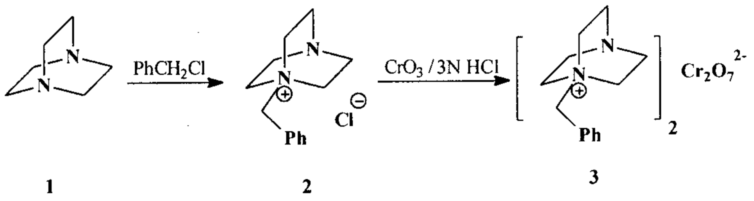
Trimethylsilyl ether, tetrahydropyranyl ether, ethylene acetals and ketals are widely used as protective groups during the synthesis of natural compounds.[1–3] A wide variety of methods are available for the conversion of alcohols to their trimethylsilyl ethers and tetrahydropyranyl ethers and much attention has been paid to the deprotection of these derivatives to give the parent alcohol or to give their corresponding carbonyl compounds via oxidative cleavage of the protected groups.[4–18] Deprotection of ethylene acetals and ketals to their carbonyl compounds under non aqueous and aprotic conditions is also very important in organic synthesis.[19–21] In the course of studies on the synthesis of biologically interesting natural products, a mild, fast and efficient method was required for the selective removal of the carbonyl or alcohol groups without any change in the other functional groups in polyfunctional molecules.

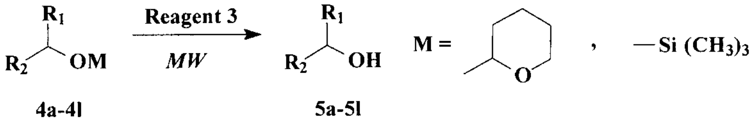
In recent years, there has been a growing interest in the application of microwave irradiation in chemical reaction enhancement,[22–25] because of its cleaner reactions, decreased reaction time and easier work-up. In a continuation of our ongoing efforts in this area,[26] herein we wish to report a facile method for the conversion of trimethylsilyl ether and tetrahydropyranyl ether and deprotection of ethylene acetals and ketals to their alcohol compounds under microwave irradiation.

Recently we have introduced 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]-octane dichromate (BAABOD) **3** for the oxidation of alcohols to their corresponding carbonyl compounds under microwave irradiation.[27] This new reagent has been readily prepared by reaction of an aqueous solution of 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane chloride **2** with CrO_3 in 3 N solution of HCl at room temperature as shown in Scheme 1. The resulting orange powder, which can be stored for months without loss of activity, is soluble in acetonitrile, acetone and *N*,*N*-dimethylformamide and slightly soluble in chloroform, ethylacetate and dichloromethane, but is not soluble in carbon tetrachloride, *n*-hexane and diethylether.



Scheme 1.

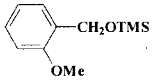
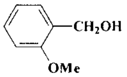
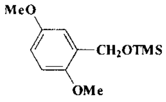
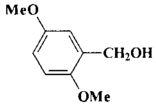
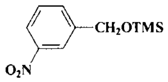
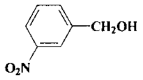
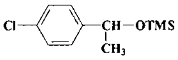
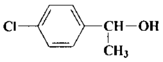
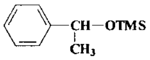
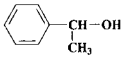
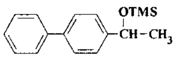
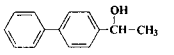
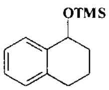
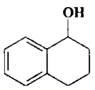
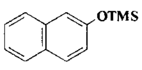
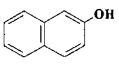
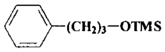
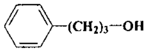
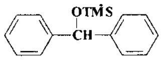
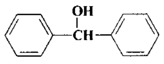
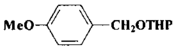
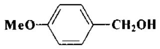
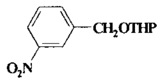
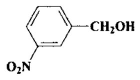
In this article we use this reagent for the deprotection of TMS- and THP-protected molecules to their corresponding alcohols under microwave irradiation. One equimolar of TMS- or THP-protected alcohols **4a**–**4l** was mixed with **3** in a mortar and ground with a pestle until the formation of a homogeneous mixture. Then the reaction mixture was transferred to an Erlenmeyer flask and was irradiated by microwave oven, until TLC showed complete disappearance of starting material. But during the solid phase irradiation, the reagent was destroyed gradually and the starting material remained intact. So, we decided to use a solvent, which can play three important roles: 1) as a primary absorber, 2) as a solvent for both the reagent and the product 3) as a factor for increasing the dielectric constant of the medium. By increasing the dielectric constant, the coupling with microwave increased. We tested several solvents such as CCl_4, *n*-hexane, toluene, *o*-cresol, acetonitrile and dichloromethane. The reaction failed to proceed in hexane and toluene, since they do not couple and therefore do not heat with microwave irradiation. So they are microwave inactive solvents. *o*-Cresol and acetonitrile are microwave active solvents, but during the reaction the starting material and the solvent were both degraded by reagent and produced several by products. Finally we choose dichloromethane, as a solvent which is microwave active and also does not interfere during the reaction processing. Therefore 1.5 mL of dichloromethane was added to one equimolar amount of TMS- or THP- protected alcohols **4a**–**4l** and reagent **3**. The mixture was irradiated with microwave oven, until TLC showed complete disappearance of starting materials (Scheme 2). Following the reaction by TLC shows that by disappearing of starting material spot, the corresponding alcohols appeared as the only product and no by-product was observed. The reaction was completed within 3–4 min and the pure alcohols were obtained by a simple work-up without further purification. The results illustrated in Table 1 indicate that the reaction can be used for a variety of TMS- and THP-protected primary and secondary benzylic alcohols.



Scheme 2.

In order to evaluate the effect of the microwave irradiation in this reaction, we tried the reaction of 2-nitrobenzyl alcohol TMS ether with

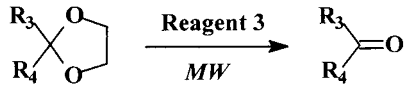
Table 1. Deprotection of Tetrahydropyranyl (THP) and Trimethylsilyl (TMS) Ethers **4a**–**4l** with Reagent **3** Under Microwave Irradiation[a]

Substrate		Product		Time (min)	Yield (%)	M.P(°C) or B.P(°C)/Torr Found	Reported[28]
4a		**5a**		3:00	84	248–250 /760	248–251 /760
4b		**5b**		3:00	93	122–125/1	381–383/10
4c		**5c**		3:30	95	30–32	29–31
4d		**5d**		3:00	96	119/10	118–119/10
4e		**5e**		3:20	91	20	18–20
4f		**5f**		3:30	89	–	94–96
4g		**5g**		3:00	92	102–104 /2	161–163 /10
4h		**5h**		3:00	85	122–123	120–121
4i		**5i**		3:00	90	235/760	231/760
4j		**5j**		3:50	87	65–67	63–65
4k		**5k**		3:20	94	23–25	22–24
4l		**5c**		3:25	93	30–32	29–31

[a] All of the compound were characterized by comparing with known compounds and their IR and ^{1}H NMR spectra.

reagent **3** without using any microwave irradiation. The reaction did not proceed at all after 60 min, grinding of the reaction mixture. The mechanism of the reaction is reported by us for the oxidation of alcohol by this reagent.[27]

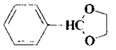
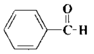
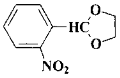
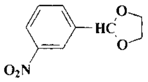
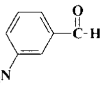
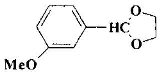
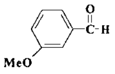
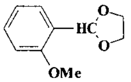
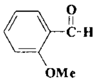
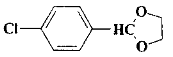
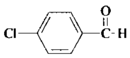
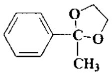
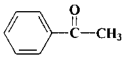
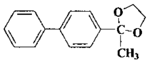
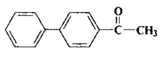
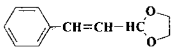
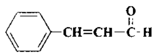
Deprotection of ethylene acetals and ketals to their carbonyl compounds were also performed under same conditions. The reactions were completed within 3–4 min and the pure aldehydes and ketones were obtained by a simple work-up (Scheme 3 and Table 2).



6a-6i **7a-7i**

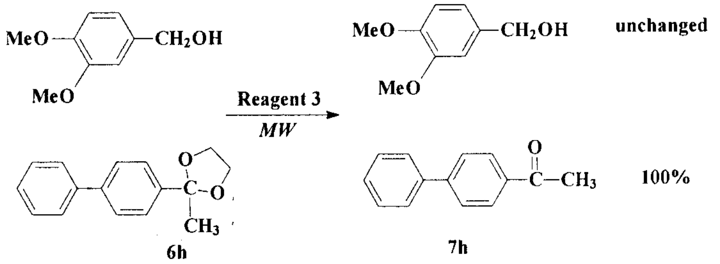
Scheme 3.

Table 2. Deprotection of Ethylene Acetals and Ketals **6a**–**6i** with Reagent **3** Under Microwave Irradiation[a]

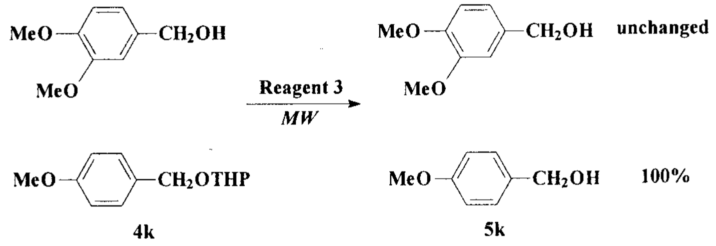
Substrate		Product		Time (min)	Yield (%)	M.P.(°C) or B.P.(°C)/Torr Found	Reported[29]
6a		7a		3:00	83	178–179/760	177–178/760
6b		7b		3:10	89	43–46	42–46
6c		7c		3:00	91	57–59	56–58
6d		7d		3:00	96	143/5	141/5
6e		7e		3:00	90	37–39	36–39
6f		7f		3:00	93	47–50	46–48
6g		7g		3:20	95	19–20	19
6h		7h		3:00	92	116–118	115–118
6i		7i		3:10	88	248/760	246/760

[a] All of the compound were characterized by comparing with known compounds and their IR and 1H NMR spectra.

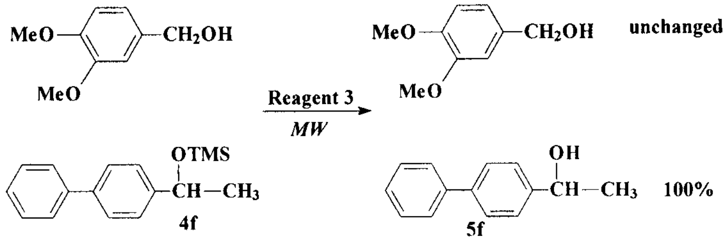
As we have reported in our previous work, microwave irradiation is very effective to convert aliphatic and benzylic alcohols to their corresponding aldehydes and ketones,[26b] herein our new findings show that under the same condition TMS-, THP-ether, ethylene acetals and ketals were deprotected to their corresponding alcohols and carbonyl compounds respectively. So, it is interesting to investigate the competitive reaction of alcohols and the mentioned protected compounds with this reagent under microwave irradiation. When we treated an equimolar amount of ethylene ketal **6h** with **3** in the 3,4-dimethoxybenzyl alcohol, the ketal **6h** was selectively deprotected and 3,4-dimethoxybenzyl alcohol was unchanged (Equation 1). When an equimolar amount of THP ether **4k** in presence of 3,4-dimethoxybenzyl alcohol was treated with reagent **3**, only the THP ether **4k** was selectively deprotected to its corresponding alcohol (Equation 2). Treatment of TMS ether **4f** in the presence of 3,4-dimethoxybenzyl alcohol, led to exclusive deprotection of TMS ether **4f** to the corresponding alcohol in 100% yield (Equation 3).



(Eq. 1)



(Eq. 2)



(Eq. 3)

In conclusion, we have developed a mild, fast and efficient method for the cleavage of TMS-, THP-ether, ethylene acetals and ketals under microwave irradiation, which is superior to previously reported methods in terms of selectivity, high yield, purity of the products, simple and rapid work-up. This method does not require a large excess of reagent and long reaction time. Notably ether, nitro, halogen and double bond functional groups present in the molecules were found to be resistant under the employed conditions.

EXPERIMENTAL SECTION

General

Trimethylsilyl ethers, tetrahydropyranyl ethers, ethylene acetals were prepared according to described procedures,[15,16] All of the products were characterized by comparison of their spectral (IR, ^{1}H-NMR), TLC and physical data (melting and boiling point) with those of authentic samples.[5,12,20,27–29] The reagent 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate (3) was prepared according to described procedures.[27] All ^{1}H-NMR spectra were recorded at 90 MHz in $CDCl_3$ and CCl_4 relative to TMS(0.00 ppm). All of the reactions were carried out in a hood with strong ventilation. IR spectra were recorded on Shimadzu 435 IR spectrophotometer. Spectra of solids were carried out using KBr pellets. Irradiation was carried out in a domestic microwave oven (Samsung 2450 MHz Watts), for an optimized time.

Deprotection of TMS-, THP-Ether

General Procedure

The deprotection of 2-nitrobenzyl alcohol TMS ether is representative of the general procedure employed. In a mortar, a mixture of the protected derivative **4c** (0.39 g, 1.6 mmol), 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octanedichromate (1.00 g, 1.6 mmol) was ground with a pestle in a mortar to form a homogeneous mixture. After transferring the mixture to an Erlenmeyer flask and adding 1.5 ml dichloromethane, it was irradiated with microwave oven, until TLC (eluent: CCl_4) showed complete disappearance of starting materials (Table 1). Then CCl_4 (15 ml) was added to the reaction mixture and after vigorous stirring the mixture was filtered off and the solvent was evaporated by rotary evaporator. The pure 2-nitrobenzyl alcohol was obtained and does not need further purification.

Deprotection of Ethylene Acetals and Ketals

General Procedure

The deprotection of 3-nitrobenzyl ethylene acetal **6c** is representative of the general procedure employed. The protected derivative **6c** (0.28 g, 1.61 mmol), 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octanedichromate (1.00 g, 1.61 mmol) was crushed with a pestle in a mortar to form a homogeneous mixture. After transferring the mixture to an Erlenmeyer flask and adding 1.5 ml dichloromethane, it was irradiated with microwave oven, until TLC (eluent: CCl_4) showed complete disappearance of starting materials (Table 2). CCl_4 (15 ml) was added to the reaction mixture and after vigorous stirring, the mixture was filtered off and the solvent was evaporated by rotary evaporator. The pure 3-nitrobenzaldehyde was obtained and does not need further purification.

ACKNOWLEDGMENT

We are thankful to Research Council of the Isfahan University of Technology (IUT) for the partial support of this work.

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Received in Japan December 20, 2000

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