Nucleophile assisted hydrolysis of carbon–oxygen bonds in ethers

Catherine Polydore [a], D. Max Roundhill [a,*], Heng-Qian Liu [b]

[a] *Department of Chemistry, Texas Tech University, Lubbock, TX 79409-1061, USA*
[b] *Department of Chemistry, Nankai University, Tianjin 300071, PR China*

Abstract

The hydrolysis of ether bonds is a potentially green method for using plants as a source of chemicals. Although the arylalkyl ether anisole can be hydrolyzed to phenol and methanol in the presence of aluminum chloride, the method has the disadvantage that it produces large amounts of alumina as by product. Since the carbon atoms of ethers that are directly bound to the oxygen have carbonium ion character, nucleophilic attack is a possible route to inducing cleavage of these carbon–oxygen bonds. The hydrolysis of the carbon–oxygen bond in ethers is induced by molybdate as nucleophile, or by aluminum phosphate in combination with ultrasound. High yields are obtained with epoxides, and significantly lower yields with trimethylene oxide and tetrahydrofuran. The molybdate or phosphate oxoanion acts as the nucleophile. Calculations have been carried out to determine patterns affecting the enthalpy of the hydrolysis of ethers to alcohols. These show that the reaction is close to being thermoneutral, but that both ether hydrolysis and ether ammonolysis are enthalpically favored, especially for ethers that have sterically bulky or fluorinated substituents. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Ether; Molybdate; Hydrolysis; Computational; Epoxide

1. Introduction

Many of the fuels and commodity chemicals developed and used during the 20th century were derived from oil. Although this has led to strong economic growth, there is a need to consider alternate feedstock in order to guarantee that this growth continues. One such feedstock is biomass, which is a renewable resource that represents a useful involvement of solar energy in the production of chemicals. A significant difference between oil and biomass is that the former is assembled with carbon–carbon bonds, but the latter has both carbon–carbon and carbon–oxygen bonds. If biomass is to be used as a source for both commodity

and speciality chemicals, selective reactions for the cleavage of carbon–oxygen bonds will be required. In this paper we report our results aimed at catalyzing the hydrolysis of carbon–oxygen ether bonds.

Biomass, humus materials, and lignin contain carbon–oxygen ether bonds where the carbon bonded to the oxygen is part of either an aliphatic or aromatic functionality. Hydrolysis of an ether results in the formation of alcohols (Eq. (1)).

$$\text{R} \overset{\text{O}}{\diagdown \diagup} \text{R}_1 + \text{H}_2\text{O} \longrightarrow \text{R}{-}\text{OH} + \text{R}_1{-}\text{OH} \quad (1)$$
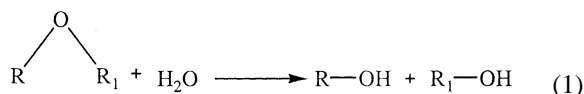
This reaction has however received little study, and for simple aliphatic and aromatic ethers the reaction is close to being thermoneutral. For aliphatic ethers the electronegativity of the oxygen center results in the carbon directly bonded to it having carbonium

* Corresponding author. Tel.: +1-806-742-3067;
fax: +1-806-742-1289.
E-mail address: uldmr@ttacs.ttu.edu (D.M. Roundhill).

ion character. A strategy to effecting ether hydrolysis therefore is to target nucleophilic attack at this carbon center in conjunction with increasing the electrophilicity at this carbon by coordinating a metal cation to the ether oxygen [1–6]. Since there is precedent for ether hydrolysis in the conversion of ethylene oxide into ethylene glycol in the presence of molybdate as a nucleophile, this gives a point where to begin [7]. An advantage of a nucleophile such as molybdate is that the intermediate molybdenum alkoxide that is formed undergoes subsequent hydrolysis to the alcohol and molybdic acid, thereby allowing for the molybdate to act as a catalyst. The molybdate ion is introduced as its bis-(triphenylphosphine)iminium (PPN$^+$) salt in order to make it more compatible with the organic ether phase.

2. Results and discussion

As an initial survey of catalyzed hydration reactions of ethers we have chosen examples of cyclic ethers of different ring sizes, a sterically hindered aliphatic ether, an aromatic ether, and an ether with both an aliphatic and aromatic substituent. Initially we investigated whether Friedel Crafts type reaction conditions could lead to the hydrolysis of an ether bond. This reaction was carried out using anisole as the ether. We find that refluxing a solution of anisole in benzene with aluminum chloride for 6 h, followed by cooling to 0 °C and transfer into water results in two layers. Extraction of the organic materials into diethyl ether followed by TLC analysis shows that there has been a 20% conversion to phenol. Although this reaction results in the hydrolysis of anisole, it is environmentally unacceptable because it results in the formation of large amounts of aluminum salts, and is of little potential value. We have therefore sought more environmentally benign methods of carrying out the hydrolysis of carbon–oxygen ether bonds using molybdate as a nucleophile, or aluminum phosphate as an electrophile–nucleophile combination.

For molybdate as the nucleophile we have investigated 3-, 4-, 5-, and 6-membered ring epoxides, as well as an aromatic and a sterically bulky aliphatic acyclic ether. Refluxing 1,2-epoxybutane and water in the presence of (PPN)$_2$MoO$_4$ results in a 90% conversion to 1,2-butanediol. By contrast the 4-membered

ring ether, trimethylene oxide, gives only a 3–5% conversion to 1,2-propanediol under the same conditions. The cyclic ethers tetrahydrofuran and 1,4-dioxane that have even less strained rings do not undergo hydrolysis. Similarly, the acyclic ethers anisole and phenyl ether are not hydrolyzed to alcohols. Based on the concept that catalyzed hydrolysis may be observed with a nucleophilic anion and an electron poor cation, we have studied these reactions in the presence of a suspension of aluminum phosphate as a heterogeneous catalyst. The concept is that the aluminum(III) cation is a strong Lewis acid, and that the phosphate anion is a potential nucleophile for an ether molecule that is bound to the aluminum phosphate surface [8]. No alcohols are observed under thermal conditions, but under ultrasound conditions a 3–5% conversion of an ether into the corresponding diol is observed with 1,2-epoxybutane, trimethylene oxide, tetrahydrofuran, and anisole. [1] The effect of the ultrasound is at present unknown, but a possibility is that its function is to facilitate desorption from the aluminum phosphate surface, thereby making it available for further reaction. No reaction is found with either 1,4-dioxane or anisole. These experimental results are collected in Table 1. These data show diols can be obtained under thermal conditions in the presence of (PPN)$_2$MoO$_4$, or under sonication conditions with aluminum phosphate. For the highly strained 3-membered ring epoxide the yield of diol is high, but the yield decreases with the 4-membered ring trimethylene oxide, and the 5- and 6-membered ring analogs, tetrahydrofuran and dioxane. Although these conversions to alcohols with both molybdate ion and aluminum phosphate are low, these are still two of the very few examples for the hydrolysis of a carbon–oxygen ether bond to give an alcohol.

From thermodynamic considerations, the hydrolysis of an ether molecule to a pair of alcohols is a conversion that is close to being thermoneutral. An alternate strategy to addressing which ethers may undergo hydrolysis is to take a computational approach. Using the SPARTAN package of programs we have computationally estimated the enthalpic change in the hydrolysis of a series of ethers [9]. The

---

[1] The ultrasound experiments were carried out using a Branson 1200 ultrasonic bath. Diols were analyzed both by thin layer chromatography against authentic samples, and spot tests.

Table 1
Hydrolysis of ethers in the presence of $(PPN)_2MoO_4$ or $AlPO_4$

Compound	Product	Hydrolysis	
		$(PPN)_2MoO_4$	$AlPO_4$ (ultrasound)
1,2-Epoxybutane	1,2-Butanediol	Yes (~90%)	Yes (~3–5%)
Trimethylene oxide	1,3-Propanediol	Yes (3–5%)	Yes (~3–5%)
Tetrahydrofuran	1,4-Butanediol	No	Yes (~3–5%)
1,4-Dioxane	Ethylene glycol	No	No
tert-Butyl methyl ether	*tert*-Butanol and methanol	No	No
Diphenyl ether	Phenol	No	No
Anisole	Phenol and methanol	No	Yes (~3–5%)

ethers have been chosen so that there are examples of aliphatic, aromatic, and sterically hindered ethers, in addition to ones with strongly electron withdrawing fluorine substituents. These calculated enthalpy data for ether hydrolysis that have been obtained by both semi-empirical methods and density functional theory are collected in Table 2. These calculations have been carried out by calculating the enthalpy of each compound in the reaction to obtain the enthalpy change in the reaction. The calculations using density functional theory have been carried out using geometry optimization at the DN** level, which is the highest level of density functional theory calculation available in the SPARTAN package. Although differences between the lower level semi-empirical PM3 and the higher level density functional theory methods are apparent, some general features emerge. These data show that for simple ethers the hydrolysis is close to being thermoneutral, with the higher level density functional theory calculations being closer in value to this premise. The introduction of either fluorine or sterically bulk substituents causes the reaction to be

enthalpically more favorable. Because of the unavailability of these fluoroethers we have not tested this prediction by experiment. For the sterically hindered *tert*-butyl methyl ether we observe no products of hydrolysis (Table 1), but we cannot discount the possibility that steric factors inhibit nucleophilic attack at the carbon atom of the *tert*-butyl group that is bound to the ether oxygen.

An alternate approach to achieve the cleavage of the carbon–oxygen ether bond is to carry out an ammonolysis reaction. Since there are close similarities between the chemistries of water and ammonia [10], such a comparison is a useful one. Nevertheless, differences are to be expected since the ammonolysis reaction involves the cleavage of an N–H bond rather than an O–H bond, and it results in the formation of an alcohol and an amine rather than a pair of alcohol molecules. The computational data on such ammonolysis reactions are shown in Table 3. Again, the PM3 method gives somewhat more negative values

Table 2
Computational enthalpies (kcal mol^{-1}) for the hydrolysis of ethers[a]

Ether	ΔH_1	ΔH_2
EtOEt	−5.5	+1
Tetrahydrofuran	−3	−1
Me_3COCMe_3	−12	−13
$PhCH_2OMe$	−3	+1
$PhOCF_3$	−9	−2
$C_6F_5OC_6F_5$	−10	−11

[a] ΔH_1, semi-empirical (PM3) methods; ΔH_2, density functional theory.

Table 3
Computational enthalpies (kcal mol^{-1}) for the ammonolysis of ethers[a]

Ether	ΔH_1	ΔH_2
EtOEt	−10	−3
Me_3COCMe_3	−17	+3
PhOMe	−8[b], −14[c]	1[b], −3[c]
$(CF_3)_3COC(CF_3)_3$	–	−40
PhOPh	–	−4
$C_6F_5OC_6F_5$	−22	−23

[a] ΔH_1, semi-empirical (PM3) methods; ΔH_2, density functional theory.
[b] Ammonolysis to PhOH and $MeNH_2$.
[c] Ammonolysis to $PhNH_2$ and MeOH.

than does the density functional theory, and again introducing fluorine substituents onto the ether leads to more negative ammonolysis enthalpies. Nevertheless the differences in the values obtained by the PM3 and density functional theory methods are more pronounced for the ammonolysis than are found for the hydrolysis reaction.

3. Conclusions

We conclude that although the molybdate induced hydrolysis of aliphatic ethers gives high yields for the highly strained 3-membered ring epoxides, low yields are observed for other ethers. In addition we observe low yield conversions of ethers into alcohols in the presence of aluminum phosphate under ultrasound conditions. By using semi-empirical (PM3) and density functional methods to calculate the enthalpies, the hydrolysis of ethers is found to be close to thermoneutral. The most favored reactions occur with sterically hindered ethers and those with fluorine substituents on the alkyl or aryl groups.

References

[1] T.B. Rauchfuss, F.T. Patino, D.M. Roundhill, Inorg. Chem. 14 (1975) 652.
[2] D.M. Roundhill, W.B. Beaulieu, U. Bagchi, J. Am. Chem. Soc. 101 (1979) 5428.
[3] A. Benefiel, D.M. Roundhill, Inorg. Chem. 25 (1986) 4027.
[4] L. Djakovitch, F. Moulines, D. Astruc, New J. Chem. 20 (1996) 1071.
[5] J.S. Kim, J.H. Reibenspies, M.Y. Darensbourg, J. Am. Chem. Soc. 118 (1996) 4115.
[6] J.R. Briggs, A.M. Harrison, J.H. Robson, Polyhedron 5 (1986) 281.
[7] J.P. Nilsson, C.-M. Andersson, Tetrahedron Lett. 38 (1997) 4635.
[8] Y. Izumi, M. Onaka, Adv. Catal. 38 (1992) 245.
[9] SPARTAN, Vers. 5.0, Wavefunction, Inc., Irvine, CA.
[10] T.W.J. Taylor, W. Baker, Sidgwick's Organic Chemistry of Nitrogen, Oxford University Press, Oxford, 1942.