69. Copper(II) Triflate, a New Reagent for Mild Dehydration of Alcohols: Synthetic Usefulness and Mechanistic Insight

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Dedicated to Professor *H. Zollinger* on the occasion of his retirement

(8.I.87)

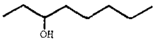
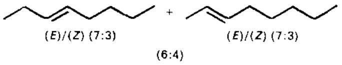
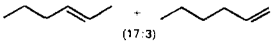
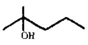
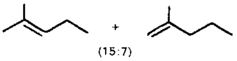
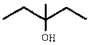
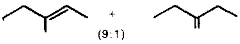
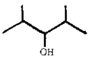
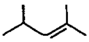
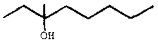
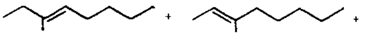
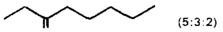
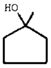
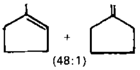
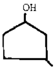
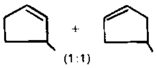
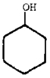
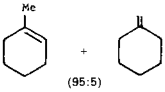
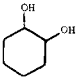
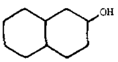
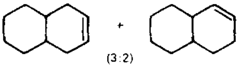
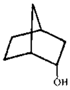
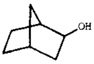
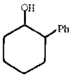
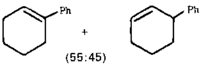
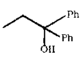
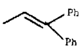
The effectiveness of copper(II) triflate (copper(II) trifluoromethanesulfonate) as a new dehydrating reagent for a variety of alcohols has been demonstrated. Based on several control experiments, a possible mechanism is suggested.

Introduction. – Olefin synthesis *via* alcohols is a fundamental organic transformation for which a large number of catalysts and reagents have been developed. The conventional dehydration catalysts include protic acids and metallic oxides, sulfides, zeolites, anhydrous $CuSO_4$, as well as HMPA [1–3]. While a major drawback in the acid-catalysed (H_2SO_4, H_3PO_4) dehydration reactions is the formation of rearranged products and ether by-products, other methods require elevated temperatures and/or a fairly large amount of catalyst or reagent. More recently, dialkoxydiaryl sulfuranes have been introduced by *Martin* and *Arhart* [4]. These intriguing reagents dehydrate alcohols by a dissociative mechanism which is quite different from the usual acid-catalysed elimination process. *Corey et al.* [5], and *Knochel* and *Seebach* [6] introduced $CuCl_2$/dicyclohexylcarbodiimide as an efficient dehydrating agent for β-hydroxycarbonyl compounds and nitrated alcohols.

Lately, metallic triflates (trifluoromethanesulfonates) have found increased application, however, the full potential of these reagents remains to be explored. *Kochi* and co-workers [7] [8] used copper(II) triflate ($Cu(OTf)_2$) in their electron-transfer studies and in cyclopropanation of olefins with CH_2N_2. $Cu(OTf)_2$ has also been used as a catalyst in 1,3-dipolar addition [9] and in oxidation reactions [10]. *Corey* and *Shimoji* showed that $Mg(OTf)_2$ and $Zn(OTf)_2$ are efficient catalysts for thioketalizations [11].

Results and Discussion. – In the course of some of our current studies concerned with the development and chemistry of new reagents based on metal triflates and fluorosulfates, we have found that $Cu(OTf)_2$ is an efficient dehydrating agent for a variety of tertiary, secondary, and primary alcohols, as well as diols, and, therefore, should find a wider synthetic application. *Table 1* summarizes our experiments. The reactions were carried out using only 0.1 mol-equiv. of $Cu(OTf)_2$ in decalin or heptane, or with no solvent. The olefin products and H_2O by-product were removed from the reaction mixture by distillation. The isolated yields varied from 30 to 92% depending on the substrate. Increasing the molar ratio of $Cu(OTf)_2$ to alcohol led to only a modest increase

Table 1. *Dehydration of Alcohols with* $Cu(OTf)_2$ (0.1 mol-equiv.)

Alcohol	Olefin products[a])	Yield [%][b])
	 (E)/(Z) (7:3) + (E)/(Z) (7:3) (6:4)	85
	 (17:3)	38
	 (15:7)	88
	 (9:1)	92
		73
	 +	65
	 (5:3:2)	73
	 (48:1)	45
	 (1:1)	74
		71
	 (95:5)	58
		35
	 (3:2)	68
		32[c])
		30[c])
	 (55:45)	66
		72[c])

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[a]) The olefinic products were characterized by capillary GC coinjection with pure authentic samples as well as by IR and ^{1}H-NMR.

[b]) Isolated yield.

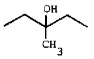
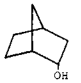
[c]) Pot residue was polymeric.

in isolated yields and did not warrant the use of more $Cu(OTf)_2$. Overheating of the reaction mixtures should be avoided, as polymerization of the olefins becomes a major process above 150°, even though the olefin is continuously being removed. High-boiling olefins should thus be isolated under reduced pressure.

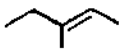
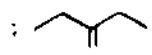
Preferred formation of *Zaitsev* orientation products and (*E*)-olefins is strongly indicative of a carbocationic mechanism. Furthermore, dehydration of *exo*- and *endo*-norbornanol gave, apart from norbornylene, also norbornane (GC/MS, 30%) indicative of competing hydride abstraction by norbornyl cation.

Table 2 summarizes a comparison of $Cu(OTf)_2$ dehydration with those of 95% H_2SO_4 [12] and $POCl_3$/pyridine [13] methods for 3-methyl-3-pentanol, 1-hexanol, and *endo*-norbornanol. The $Cu(OTf)_2$ method is overall superior both in terms of yield and simpleness of the dehydration procedure.

Table 2. *Comparison of* $Cu(OTf)_2$ *Dehydration* (Method A) *with* H_2SO_4 (Method B), *and Phosphorous Oxychloride/Pyridine* (Method C) *for Selected Alcohols*

Alcohol	*Method*	Yield of olefin(s) [%]
 OH CH3	*A*	92
	B[a])	48
	C[c])	55
 CH2OH	*A*	38
	B	trace
	C	trace
 OH	*A*	32
	B[c])	23
	C	55

[a]) Substrate/H_2SO_4 molar ratio 18:1; product isolated by direct distillation.

[b]) Reported yield is based on ^1H-NMR after workup:  :  85:15.

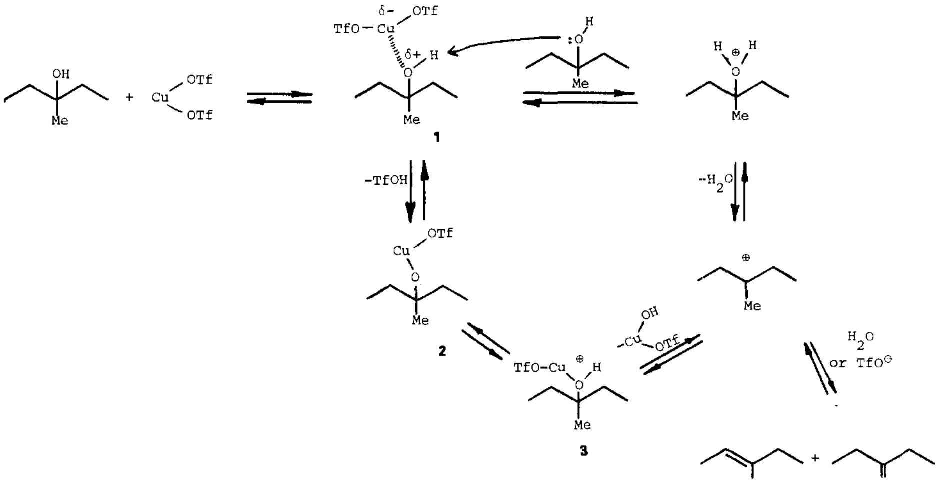
[c]) Whereas norbornylene could not be isolated by distillation, quenching of the reaction mixture and workup showed norbornylene, norborane, and unreacted alcohol (cap. GC). The reported yield is based on GC after response factor correction.

Considering the role of the reagent, we reasoned that, if the reactions are catalysed by traces of triflic acid (trifluoromethanesulfonic acid) impurity, which might be present in $Cu(OTf)_2$, then, other metal triflates should be equally suitable as dehydrating agents, since the common preparative method for the synthesis of metal triflates is *via* triflic acid and metal carbonates or metal oxides. However, in control experiments, we found that neither $Zn(OTf)_2$ nor $Mg(OTf)_2$ can promote dehydration of cyclohexanol to cyclohexene, suggesting an initial '*Lewis*-acid'-type interaction between the alcohol and the more electron-deficient copper. Moreover, contrary to anhydrous $CuSO_4$-catalysed dehydration reactions [2], which are completely suppressed on addition of a drop of pyridine, in a control experiment $Cu(OTf)_2$ dehydration of 3-methyl-3-pentanol was not suppressed by addition of 0.05 equiv. of 2,6-di(*tert*-butyl)-4-methylpyridine as a proton trap. We also found that the distillation residue contained 2,6-di(*tert*-butyl)-4-methylpyridinium triflate (IR, NMR), confirming that, although triflic acid is not present at the start of the reaction, it has been generated during the dehydration.

In a ^{13}C-NMR control experiment, 0.2 mol-equiv. of $Cu(OTf)_2$ was added to 3-methyl-3-pentanol in (D_6)acetone *(Vortex)*. The ^{13}C-NMR spectrum of the resulting homogeneous green solution showed that the signals of C(3), CH_3–C(3), and the methylene-C-atoms were all broadened and were shifted downfield ($\Delta\delta$(^{13}C) 3.1, 2.2, and 0.5 ppm, respectively), but the C(1), C(5) signal remained sharp and shifted slightly upfield ($\Delta\delta$(^{13}C) −0.9 ppm). Attempts to carry out a complete variable-temperature DNMR study of this solution were unsuccessful, as the triflate precipitated from (D_6)acetone below room temperature. $Cu(OTf)_2$ was also not sufficiently soluble in SO_2.

The following mechanism *(Scheme)* appears to be compatible with our data.

Scheme



The alcohol interacts with the electron-deficient $Cu(OTf)_2$ to form a labile intermediate **1**, which can either transfer proton to another alcohol or eliminate triflic acid to form an alkoxycopper triflate intermediate **2**. *O*-Protonation of **2** and loss of Cu(OH)(OTf) leads to the carbocation. Proton removal from the carbocation can be accomplished either by H_2O by-product or by TfO^-. Absence of any detectable skeletal rearrangement products in these reactions suggests that there must not be any significant build up of 'free' triflic acid in solution during dehydration, emphasizing the equilibrium nature of the process.

In conclusion, we believe that facile dehydration of alcohols with $Cu(OTf)_2$, which is demonstrated here, is just one of possible future applications of this interesting reagent, and studies in other directions are warranted.

We thank Prof. *Edwin Gould* of Kent State for a helpful discussion and a critical review of the manuscript. Financial assistance by Kent State University through a start-up fund is gratefully acknowledged.

Experimental Part

General. The alcohol starting materials and the authentic olefins were commercially available samples *(Aldrich)* of highest purity and used without further purification. $Cu(OTf)_2$ was prepared from $CuCO_3$ and triflic acid, according to *Jenkins* and *Kochi* [7], or purchased from *Fluka.* $Mg(OTf)_2$ and $Zn(OTf)_2$ were prepared according to *Corey* and *Shimoji* [11]. GC anal. were performed on a *Hewlett-Packard 5890* gas chromatograph equipped with a fused silica capillary column and an on-line automatic integrator. IR spectra were recorded on a *Perkin-Elmer* model *283* instrument. ^{13}C- and ^{1}H-NMR spectra were run on a *Varian FT-80* and *Varian EM360* instruments, respectively.

General Procedure for Dehydration Reactions. To the alcohol (10 mmol), dissolved or suspended in decalin (5 ml) or heptane (5 ml), was added 1 mmol of $Cu(OTf)_2$ at room temperature. The heterogeneous mixture was slowly heated in an oil bath with magnetic stirring inside a microdistillation unit equipped with a short *Vigreux* column, and the olefin products distilled out, either at atmospheric pressure or at reduced pressure, depending on the b.p. of the olefins. The reaction mixtures were not usually heated above 160°. In cases where the b.p. of the olefin products was higher than heptane or decalin, either no solvent was used or the solvent and the olefin were both distilled out of the mixture, and the olefin was further purified by fractional distillation.

REFERENCES

[1] J. March, 'Advanced Organic Chemistry', 3rd edn., Wiley Interscience, New York, 1985, p. 901–902 and ref. given therein.
[2] R.V. Hoffman, R.D. Bishop, P.M. Fitch, R. Hardenstein, *J. Org. Chem.* **1980,** *45,* 917.
[3] R.S. Manson, D.N. Priest, *J. Org. Chem.* **1971,** *36,* 3826.
[4] J.C. Martin, R.J. Arhart, *J. Am. Chem. Soc.* **1971,** *93,* 2339; b) J.C. Martin, R.J. Arhart, *ibid.* **1971,** *93,* 2342; c) R.J. Arhart, J.C. Martin, *ibid.* **1971,** *94,* 5003.
[5] E.J. Corey, N.H. Anderson, R.M. Carlson, J. Paust, E. Vedejs, J. Vlattas, R.E.K. Winter, *J. Am. Chem. Soc.* **1968,** *90,* 3246.
[6] P. Knochel, D. Seebach, *Synthesis* **1982,** 1017.
[7] C.L. Jenkins, J.K. Kochi, *J. Am. Chem. Soc.* **1972,** *94,* 856.
[8] R.G. Salomon, J.K. Kochi, *J. Am. Chem. Soc.* **1973,** *95,* 3300.
[9] Ph.G. Moniotte, A.J. Hubert, Ph.Teyssie, *J. Organomet. Chem.* **1975,** *88,* 115.
[10] Y. Kobayaski, T. Taguchi, E. Tokuno, *Tetrahedron Lett.* **1977,** 3741.
[11] E.J. Corey, K. Shimoji, *Tetrahedron Lett.* **1983,** *24,* 169.
[12] F.C. Whitmore, A.H. Homeyer, *J. Am. Chem. Soc.* **1933,** *35,* 4195; D.G. Botteron, G.P. Shulman, *J. Org. Chem.* **1962,** *27,* 785.
[13] R.R. Sauers, *J. Am. Chem. Soc.* **1959,** *81,* 4873.