Cu(OTf)₂-Catalyzed Selective Opening of Aryl and Vinyl Epoxides with Carbonyl Compounds to Give 1,3-Dioxolanes

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Abstract: Copper(II) triflate catalyzes the ring-opening of aryl- and vinyl-substituted epoxides with various carbonyl compounds to furnish 1,3-dioxolanes under mild conditions. Alkyl- and alkoxy-carbonyl-substituted epoxides remain unchanged under reaction conditions. This allows selective opening of aryl-substituted epoxides in the presence of alkyl-substituted ones.

Key words: epoxide-opening, dioxolanes, copper triflate, chemoselectivity

Epoxides are important and useful intermediates for the synthesis of organic structures due to their ease of preparation and their propensity for strain-induced ring-opening reactions. Transformation of epoxides to 1,2-diol moieties have been applied to synthesis of complex natural compounds.² 1,3-Dioxolanes are useful blocks in synthetic chemistry as synthetic equivalents of 1,2-diols.^{3,4} Lewis acid-catalyzed epoxide-opening with carbonyl compounds has attracted considerable attention as a convenient way of synthesizing 1,3-dioxolanes. A number of Lewis acids and transition metal complexes including BF₃·OEt₂,⁵ titanium salts,⁶ AlCl₃,⁷ iron(III) salts,⁸ BiCl₃,⁹ CuSO₄,¹⁰ RuCl₃,¹¹ tin(IV) salts,^{8b,12} iridium complexes¹³ and MeReO₃,¹⁴ have been used to catalyze this transformation. The most active catalysts (BF₃·OEt₂,⁵ TiCl₄^{6b} and SnCl₄^{8b}) catalyze the formation of 1,3-dioxolane at -78 °C. Iron(III) salts,⁸ [CpIr(NCMe)₃]^{2+,13} and MeReO₃¹⁴ catalyze epoxide-opening with carbonyl compounds at room temperature while BiCl₃⁹, CuSO₄,¹⁰ and RuCl₃¹¹ convert epoxides to 1,3-dioxolanes at reflux.¹⁵ Despite the substantial difference in activity of these catalysts reaction rates for epoxides having different substitution patterns are very similar.¹⁶ None of the catalysts described in the literature demonstrates any preference for opening of epoxides having substituents with specific steric or electronic requirements.

As a part of our research program aimed at developing synthetic methods for substituted dioxolanes, we attempted to identify catalysts and conditions that can be applied to differentiate epoxides with aryl and alkyl substitution in the dioxolene formation reaction.

SYNLETT 2005, No. 5, pp 0854–0856 Advanced online publication: 09.03.2005 DOI: 10.1055/s-2005-864795; Art ID: S06004ST © Georg Thieme Verlag Stuttgart · New York A series of experiments was carried out at various temperatures using conventional catalysts to determine, if the conditions for selective opening of aryl-substituted epoxides can be established. We found that BF₃·OEt₂ (2 mol%) converts both styrene oxide and 1,2-epoxybutane to the corresponding 1,3-dioxolanes (temperature range -20 to -78 °C). SnCl₄ is less reactive towards dioxolane formation then BF₃·OEt₂, however, both styrene oxide and 1,2-epoxybutane form 1,3-dioxolanes with comparable rates at -78 °C and at higher temperatures. TiCl₄ and AlCl₃ demonstrated comparable reactivity towards alkyland aryl-substituted epoxides at various temperatures.

Herein, we report the mild and selective opening of aryland vinyl-substituted epoxides catalyzed by $Cu(OTf)_2$. Alkyl-substituted epoxides are not reactive under the described conditions.

Copper(II) triflate acts as a catalyst to transform epoxides into the corresponding 1,3-dioxolanes. While this reaction is very fast in the case of aryl- and vinyl-substituted epoxides [styrene oxide-opening with acetone gives 100% conversion to 2,2-dimethyl-4-phenyl-1,3-dioxolane (1) after 1 h at -20 °C] alkyl-substituted epoxides do not react under these conditions. A competition experiment (equimolar mixture of styrene and butene oxides was used as a substrate) demonstrated the complete conversion of styrene oxide to the corresponding dioxolane. Butene oxide remained unchanged under the reaction conditions (1 h at -20 °C).¹⁷ Moreover, the Cu(OTf)₂-catalyzed reaction of alkyl-substituted epoxides with carbonyl compounds is quite sluggish at room temperature (Table 1).

Cu(OTf)₂

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R	Ö	R	
Entry	R	Temp (°C)	Conversion (%)
1	Phenyl	-20	100
2	CH ₂ OC ₆ H ₅	25	2
3	Et	25	Nr
4	CH ₂ Br	25	Nr

^a The reactions were carried out using 2 mol% of $Cu(OTf)_2$, reaction time: 1 h.



Scheme 1 Cu(OTf)₂-catalyzed styrene oxide-opening with acetone

Copper(II) triflate-catalyzed styrene oxide reaction with acetone produced a number of by-products resulting from the epoxide rearrangement and the subsequent reactions namely phenyl-acetaldehyde **2** and dioxolane **3** (Scheme 1).

When one equivalent of acetone was used for the reaction, 10-20% of both by-products were formed depending on the exact reaction conditions (temperature, the rate of the

 Table 2
 Cu(OTf)₂-Catalyzed Epoxide-Opening with Carbonyl Compounds^a



^a Reactions were carried out at -20 °C, 10 equiv of the carbonyl compound, 2 mol% of Cu (OTf)₂ unless noted otherwise. ^b All the products had physical data identical to that reported in the literature.

^c The product have been isolated as a *cis/trans* mixture.

^d The reaction was carried out at r.t., slow (0.08 mL/h) addition of styrene oxide.

^e The starting material was a 1:1 mixture of *cis*- and *trans*-isomers.

epoxide addition). Side reactions can be minimized using a large (10 equiv) excess of acetone to furnish dioxolane **1** in 95% isolated yield¹⁸ (Table 2). Phenyl-acetaldehyde **2** and dioxolane **3** were not detected in the reaction mixture under these conditions.

The same reaction conditions were applied to various carbonyl compounds and epoxides (Table 2) to afford good to high yields of 1,3-dioxolanes.¹⁹

The reaction of an enantiopure styrene oxide was tested. (*R*)-Styrene oxide reacts with acetone in the presence of $Cu(OTf)_2^{20}$ with inversion of configuration to give enantiomerically enriched (*S*)-2,2-dimethyl-4-phenyl-1,3-dioxolane (4:1 *S*:*R* ratio).

In summary, an efficient method to selectively convert aryl- and vinyl-substituted epoxides into 1,3-dioxolanes in the presence of alkyl- and alkoxycarbonyl-substituted epoxides is reported.

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- (15) Typical catalyst loadings are 2–20 mol%.
- (16) Data presented for K₅CoW₁₂O₄-catalyzed epoxide-opening with carbonyl compound suggest that aryl-substituted epoxides react with higher rates than alkyl-substituted ones. However, no specific comparisons of reactivity are made. See: Habibi, M. H.; Tangestaninejad, S.; Mirkhani, V.; Yadollahi, B. *Catal. Lett.* **2001**, *75*, 205.
- (17) The competition experiment was carried out as follows: $Cu(OTf)_2$ (2 mol%) was dissolved in CH_2Cl_2 (1 mL) and dry acetone (1.5 mL, 10 equiv). The reaction mixture was cooled to -20 °C, a mixture of styrene oxide (1 mmol) and 1-butene oxide (1 mmol) was added dropwise. The reaction mixture was stirred for 1 h at -20 °C, poured onto sat. aq NaHCO₃ solution (5 mL). CH_2Cl_2 (10 mL) was added and the organic

layer was separated. The reaction mixture was analyzed by ¹H NMR. Complete conversion to 1,3-dioxolane was detected for styrene oxide. 1-Butene oxide remains unchanged.

- (18) Typical procedure for epoxide-opening with carbonyl compounds is as follows: Cu(OTf)₂ (2 mol%) was dissolved in CH₂Cl₂ (1 mL) and dry acetone (1.5 mL, 10 equiv). The reaction mixture was cooled to -20 °C, styrene oxide (2 mmol) was added dropwise. The reaction mixture was stirred for 1 h at -20 °C, poured onto sat. aq NaHCO₃ solution (5 mL). CH₂Cl₂ (10 mL) was added and the organic layer was separated. The product was purified by flash chromatography (10% EtOAc in hexane) to give 2,2-dimethyl-4-phenyl-1,3-dioxolane in 95% yield. ¹H NMR (400 MHz, CDCl₃): $\delta = 1.52$ (s, 3 H), 1.58 (s, 3 H), 3.72 (dd, J = 8.2, 8.1 Hz, 1 H), 4.34 (dd, J = 8.1, 6.3 Hz, 1 H), 5.10 (dd, J = 7.9, 6.3 Hz, 1 H), 7.20–7.60 (m, 5 H). ¹³C NMR (400 MHz, CDCl₃): $\delta = 139.48, 128.99, 128.50, 126.68, 110.15, 78.40, 72.14, 27.06, 26.45.$
- (19) For all compounds the physical data corresponded to that published earlier.
- (20) Conditions: 5 mol% of Cu(OTf)₂, -80 °C, 178 h.