

Brønsted acid catalyzed formation of 1,3-dioxolanes from oxiranes and ketones

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Abstract

The catalytic effect of various acid catalysts (heteropoly acids, Nafion-H, K10 montmorillonite, trifluoroacetic acid, methanesulfonic acid) and the effect of the structure of the reactants were investigated on the formation of 1,3-dioxolanes from oxiranes and ketones. The yield of 1,3-dioxolanes strongly depends on competing reactions, mainly on the ratio of polymerization. K10 montmorillonite was found to be the best catalyst resulting in the formation of 1,3-dioxolanes in 50–80% yield under optimal reaction conditions. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Heteropoly acids; Nafion-H; K10 montmorillonite; 1,3-Dioxolanes; Ketones

1. Introduction

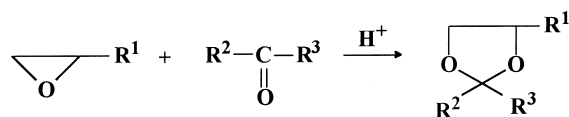
Great efforts of catalysis research have been devoted in recent years on the development and application of effective and safe heterogeneous catalysts. This is an important tendency in industry but also in the laboratory practice. These studies have been especially successful in the development of solid acids to replace aggressive and dangerous homogeneous acid catalysts.

Solid Brønsted acids with super acidic character, such as Nafion-H [1], K10-montmorillonite [2], and Keggin-type heteropoly acids [3–5], are of great interest in the synthesis of fine chemicals. Among numerous applications solid acids were found to be quite effective catalysts in the synthesis of 1,3-dioxolanes. 1,3-Dioxolanes are widely used as the protective group of the carbonyl and 1,2-diol functions in the

synthetic chemistry of carbohydrates, steroids, etc. [6]. In addition, compounds with 1,3-dioxolane structure or moiety are of interest in the manufacture of pharmaceuticals and fragrances. 1,3-Dioxolanes can easily be prepared from oxiranes with carbonyl compounds, mostly with ketones, in the presence of Brønsted or Lewis acid catalysts (Scheme 1). Among the solid acids, zeolites (ZSM-5, Y and ultrastabilized HUSY) gave moderate yields (11–56%) in the reaction of styrene oxide with acetone or 2-butanone [7]. Bentonite type clay was also used in the reaction of oxirane and methyloxirane with various carbonyl compounds (acetone, 2-butanone, 2-methylpropanal, etc.) [8,9]. It was shown, that the yields fundamentally depend on the structure of reactants and decreased with increasing molecular weight of both the oxirane and the carbonyl compound.

Torok et al. investigated the catalytic effect of various Lewis acids, for instance SnCl₄, TiCl₄, and BF₃–OEt₂ [10]. BF₃ was found to be the most effective catalyst (the yield of acetals varied between 40 and 95%), whereas SnCl₄ and TiCl₄ gave little or

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Scheme 1.

no acetal. Anhydrous CuSO_4 was also shown to be a suitable catalyst: in reacting with acetone oxiranes were converted to acetonides at a convenient rate and in good yields [11]. Recently, it was reported that methylrhenium trioxide (MTO) [12], RuCl_3 [13], and titanium derivatives of trifluoroacetic acid (TFA) and trifluoromethanesulfonic acid (TfOH), namely $\text{TiO}(\text{TFA})_2$ or $\text{TiCl}_3(\text{OTf})$ [14] were also very effective catalysts of this reaction. The achieved yields, 60–96% with MTO, 92–98% with $\text{TiCl}_3(\text{OTf})$ and 78–90% with $\text{TiO}(\text{TFA})_2$, are comparable to those observed with BF_3 .

Our work was initiated by the unique catalytic properties of heteropoly acids observed in various electrophilic catalytic processes [3–5,15], and later was extended to other acids including the solid acid Nafion-H and K10 montmorillonite. In this paper, we wish to report the results of our detailed investigations with respect to the synthesis of 1,3-dioxolanes carried out using various oxiranes, ketones and Brønsted acid catalysts.

2. Experimental

2.1. Materials

The oxiranes, ketones and aldehydes were Fluka and Aldrich products. They were dried on A4 molecular sieve and purified by distillation. Nafion-H was a DuPont product with an equivalent weight of 980 g/eq and an acid capacity of approximately 0.18 meq/g. Heteropoly acids ($\text{H}_4[\text{SiMo}_{12}\text{O}_{40}]$, $\text{H}_3[\text{PMo}_{12}\text{O}_{40}]$, $\text{H}_4[\text{SiW}_{12}\text{O}_{40}]$, $\text{H}_3[\text{PW}_{12}\text{O}_{40}]$), K10 montmorillonite, *p*-toluenesulfonic acid, methanesulfonic acid and trifluoroacetic acid were purchased from Aldrich.

2.2. Methods

Experiments were carried out in a magnetically stirred flask equipped with a dropping funnel and a

condenser. The oxirane was added to the mixture of the catalyst and the ketone through a dropping funnel. The heteropoly acids 1 wt.%, K10 montmorillonite 5 wt.% or Nafion-H 10 wt.% based on the oxirane were used. The ketone/oxirane ratio was changed between 1 and 10, and the adding time of oxirane was varied from 0 to 3 h. In experiments in the preparative scale the ketone/oxirane ratio was 4/1 and the adding time was 1 h. After the oxirane was added, the reaction mixture was stirred for 3 h (heteropoly acids), 8 h (K10) or 24 h (Nafion-H) at room temperature or for 2 h at 80°C. After removing the catalyst by filtration or neutralizing it by stirring with solid NaHCO_3 , the reaction products were distilled under atmospheric or reduced pressure depending on the boiling point of the products.

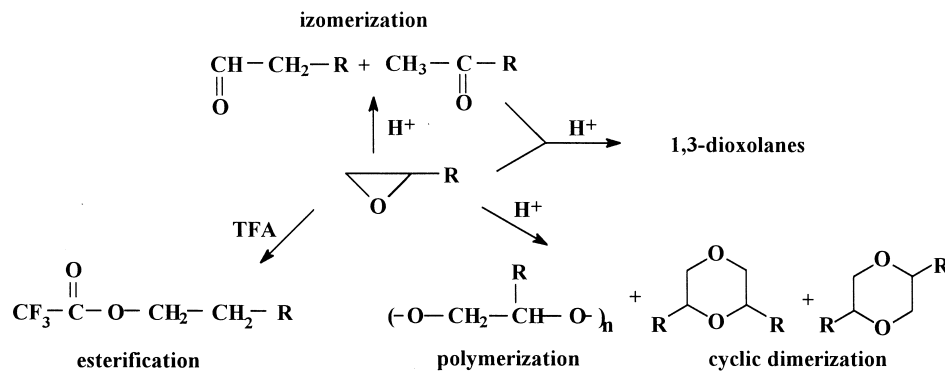
2.3. Analysis

The product distribution was determined with a Hewlett-Packard GC equipped with a 25 m DBWAX capillary column and a flame ionization detector. The GC/MS investigations were performed on an HP-5890 GC instrument equipped with a 50 m HP-1 capillary column and an HP-5970 mass selective detector. Individual compounds were identified on the basis of their retention times (in comparison with authentic samples) or by using the MS library search method.

3. Results and discussion

3.1. Brønsted acid catalyzed transformation of oxiranes

Oxiranes, when treated with Brønsted acids, undergo isomerization to carbonyl compounds, then the latter may further react with unreacted oxiranes to yield 1,3-dioxolane derivatives. In addition, oligomerization and polymerization to yield polyethers and cyclotrimerization to form substituted 1,3,5-trioxanes may occur [16]. Furthermore, ester formation may also take place (Scheme 2). Naturally, all these reactions affect the yield of 1,3-dioxolanes: polymerization and cyclodimerization lower the yield, isomerization decreases the selectivity, and ester formation can stop the catalytic processes. A careful selection of reaction



Scheme 2.

variables, therefore, is required to attain optimal yield of 1,3-dioxolanes.

We started our work by investigating the behavior of methyloxirane in the presence of selected Brønsted acid catalysts. The acid-catalyzed transformation of neat oxiranes are highly exothermic: without intensive cooling the reaction mixture boils up after the addition of the catalyst. The product compositions determined in reactions carried out at ambient temperature are shown in Table 1. Nafion-H, heteropoly acids and K10 montmorillonite catalyze polymerization as the main reaction route accompanied by isomerization (5–15%). Methanesulfonic acid, trifluoroacetic acid (TFA) and *p*-toluenesulfonic acid, in turn, bring about ester formation in a non-catalytic (stoichiometric) process. When larger than catalytic amounts of *p*-toluenesulfonic acid were used some polymerization and isomerization were also observed.

Table 1
Product compositions in the transformation of methyloxirane catalyzed by Brønsted acids

| Catalyst | Reaction time | Primary products |
|---|---------------|---------------------------------------|
| Nafion-H | 24 h | Isomers/polymers ^a : 10/90 |
| H ₄ [SiW ₁₂ O ₄₀] | 5 min | Isomers/polymers ^a : 6/94 |
| K10 montmorillonite | 5 min | Isomers/polymers ^a : 16/84 |
| <i>p</i> -Toluenesulfonic acid | 5 min | Ester |
| Methanesulfonic acid | 5 min | Ester |
| Trifluoroacetic acid | 5 min | Ester |

^a Linear polymers and cyclic dimers.

3.2. Polymerization of oxiranes in ketone–oxirane mixtures

Our preliminary experiments showed that side-reactions markedly affect the yield of the desired reaction, i.e. the formation of 1,3-dioxolanes. A synthetically viable process, therefore, requires to hinder these reactions, primarily polymerization.

The rate of polymerization can be affected by the ratio of the starting materials, the nature of catalysts, and the reaction conditions (temperature, rate of the addition of the reactants). The work-up of the reaction mixture can also play an important role. To clarify the importance of all these factors, a systematic study was carried out using methyloxirane and acetone as the reactants.

3.3. Effect of the reactant ratios

As it is well demonstrated by data in Table 2, the ratio of polymerization decreases with decreasing concentration of the oxirane. In spite of the observable further decrease, lowering the oxirane/ketone ratio below 1/4 is not practical, because of separation problems occurring in the work-up step. Besides the overall oxirane/acetone ratio, the actual concentration of oxirane in the reaction mixture is of importance which depends on the rate of its addition. Because the ratio of the oligomerization decreases only slightly with the increase in the addition time from 1 to 3 h (Table 2), the optimal addition time of 0.2 mol oxirane (methyloxirane/acetone ratio 1/4) seems to be 1 h.

Table 2
Effect of reactant ratio and rate of addition on the ratio of polymerization

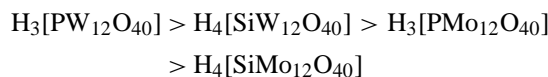
| Methyloxirane/ acetone ^a | Time of addition of 0.2 mol of methyloxirane | Polymer (%) |
|--|---|-------------|
| 1:1 | 1 h | 65 |
| 1:2 | 1 h | 45 |
| 1:3 | 1 h | 36 |
| 1:4 | 0 min ^b | 61 |
| 1:4 | 5 min | 47 |
| 1:4 | 1 h | 32 |
| 1:4 | 3 h | 31 |
| 1:10 | 1 h | 30 |

^a Catalyst: H₄[SiW₁₂O₄₀], after the addition of oxirane the reaction mixtures were stirred for 1 h at 20°C.

^b The oxirane was added at one portion.

3.4. Effect of the catalysts

Heteropoly acids are soluble in acetone and their acidity [17] in this media follows the sequence



The data in Table 3 reveal that the ratio of polymerization decreases somewhat with the increasing acid strength of heteropoly acids but this effect is not significant. The characteristics of Cs_{2.5}H_{0.5}[PW₁₂O₄₀] a widely studied, high surface area derivative are inferior to those found for the parent acid H₃[PW₁₂O₄₀]. A similar high activity to polymer formation was observed in the case of Nafion-H. Moreover, its activity is even lower, which is due to its especially low surface area. Methanesulfonic acid, trifluoroacetic acid and *p*-toluenesulfonic acid cannot be used as catalyst, because of ester formation mentioned above. On the

Table 3
Effect of the catalysts on the ratio of polymerization^a

| Catalyst | Time (h) | Polymer (%) |
|--|----------|-------------|
| H ₄ [SiMo ₁₂ O ₄₀] | 3 | 37 |
| H ₃ [PMo ₁₂ O ₄₀] | 3 | 38 |
| H ₄ [SiW ₁₂ O ₄₀] | 3 | 32 |
| H ₃ [PW ₁₂ O ₄₀] | 3 | 32 |
| Cs _{2.5} H _{0.5} [PW ₁₂ O ₄₀] | 6 | 57 |
| Nafion-H | 24 | 54 |
| K10 montmorillonite | 8 | 22 |

^a Methyloxirane/acetone: 1/4, temperature: 20°C.

basis of data in Table 3, K10 montmorillonite seems to be the most promising catalyst in terms of selectivity.

It is worth mentioning that the removal of the catalyst at the beginning of the work-up process of the reaction mixture is essential. In the presence of the catalyst, the 1,3-dioxolanes decompose during the distillation step. In contrast to the solid acids (Nafion-H, K10), that can be removed by a simple filtration, heteropoly acids require neutralization. We attempted to neutralize the reaction mixture by stirring with solid NaHCO₃ for 1 h, washing with 10% NaHCO₃ solution, or adding an equimolar amount of triethylamine. The use of solid NaHCO₃ proved to be the best and most convenient method, although, in the case of 1,3-dioxolanes with low water solubility, the washing with dilute NaHCO₃ also gave satisfactory results.

3.5. Effect of the structure of oxiranes and ketones

On the basis of the results summarized above, detailed studies with respect to the effect of the structure of the reactants were carried out using the following reaction conditions: 0.2 mol oxirane was added to the ice-cooled mixture of ketone and catalyst in 1 h (final ratio of oxirane/ketone is 1/4) followed by stirring the reaction mixture at room temperature for a given time depending on the catalyst.

As it is seen in Table 4, BF₃ used as the control catalyst, gave the best yields. The data also show that yields decrease with increasing molecular weight of the ketones. This unfavorable effect is a general phenomenon and is accounted for by the increasing steric hindrance of the carbonyl carbon exerted by the substituents. K10 gave the same yield as BF₃ in the case of acetone, but the decrease in yields with increasing molecular weight is more pronounced. Heteropoly acids, the catalysts initiating our work in this field, gave the lowest yields (only the results for H₄[SiW₁₂O₄₀] are shown), although the difference between the yields of different catalysts diminishes with increasing molecular weight of the ketones.

The data found for cyclohexene oxide (Table 5) reveal that, besides polymerization, another side-reaction, the formation of 1,2-cyclohexanediol also lowers the yield of 1,3-dioxolanes. 1,2-Cyclohexanediol may be formed during the hydrolysis of either cyclohexene oxide or the primary product 1,3-dioxolanes. This happened despite the use of dry acetone. The

Table 4
Yield of 1,3-dioxolanes in the reaction of methyloxirane with ketones^a

| Carbonyl compound | Catalyst | Time (h) | Yield (%) |
|----------------------|------------------|----------|-------------------------|
| Acetone | SiW ^b | 3 | 45 |
| | K10 | 8 | 78 |
| | BF ₃ | 2 | 78 |
| Cyclohexanone | SiW | 3 | 41 |
| | K10 | 8 | 75 |
| | BF ₃ | 2 | 86 |
| 4-Methyl-2-pentanone | SiW | 3 | 33 |
| | K10 | 8 | 38 (53/47) ^c |
| | BF ₃ | 2 | 66 |
| 3-Heptanone | SiW | 3 | 22 |
| | K10 | 8 | 24 (52/48) ^c |
| | BF ₃ | 2 | 39 |
| 2-Methyl propanal | K10 | 8 | 38 (71/29) ^c |

^a Temperature: 20°C.

^b SiW: H₄[SiW₁₂O₄₀].

^c Isomer ratio of *trans/cis*.

most important observation is that, in contrast with methyloxirane, the yield achieved with K10 is considerably higher than that of BF₃. Moreover, the higher boiling point of cyclohexene oxide allowed to increase the reaction temperature after the 1 h addition period. The higher reaction temperature (56°C for acetone and about 80°C for the other ketones) decreases substantially the reaction time and slightly increases selectivities (Table 5).

On the basis of the above results, K10 montmorillonite proved to be the best catalyst to form 1,3-dioxolanes from oxiranes and ketones. Table 6 gives the summary of the results including the reac-

Table 6
Yields of 1,3-dioxolanes using K10 montmorillonite as the catalyst

| Ketones | Oxiranes | | |
|----------------------|----------------------------|--------------------------------|----------------------------|
| | Methyloxirane ^a | Cyclohexene oxide ^b | Phenyloxirane ^c |
| Acetone | 78 | 75 | 79 |
| Cyclohexanone | 75 | 62 | 68 |
| 4-Methyl-2-pentanone | 38 | 60 | 59 |
| 3-Heptanone | 24 | 40 | 51 |

^a Reaction conditions: 8 h at 20°C.

^b Reaction conditions: 2 h at 56°C for acetone and 80°C for the other ketones.

^c Reaction conditions: 2 h at 80°C.

tion of phenyloxirane (last column). The yield of 2,2-dimethyl-4-phenyl-1,3-dioxolane formed with acetone is much higher than that reported for zeolites (11%) [7], and only somewhat lower than those found for TiCl₃(OTf) (95%) and TiO(TFA)₂ (85%) [14].

It is worth mentioning that the yield of 1,3-dioxolane decreases with the increase of the carbon number of ketones. This is a general phenomenon of the 1,3-dioxolane formation from oxiranes and ketones which is independent of the catalyst used.

4. Conclusions

Neither heteropoly acids and Nafion-H nor methanesulfonic acid, trifluoroacetic acid and *p*-toluenesulfonic acid are suitable catalysts for the synthesis of 1,3-dioxolane in the reaction between oxiranes and ketones, due to their high ability to catalyze side-reactions (polymerization of oxiranes and

Table 5
Product composition in the reaction of cyclohexene oxide with ketones^a

| Ketone | Catalyst | Time (h) | Polymer (%) | 1,3-Dioxolane (%) | 1,2-Cyclohexanediol (%) |
|----------------------|------------------|----------|-------------|-------------------|-------------------------|
| Acetone | SiW | 3 | 37 | 58 | 5 |
| | K10 | 18 | 20 | 69 | 12 |
| | K10 ^b | 2 | 20 | 75 | 5 |
| | BF ₃ | 2 | 54 | 40 | 5 |
| Cyclohexanone | K10 | 2 | 33 | 62 | 5 |
| 4-Methyl-2-pentanone | K10 | 2 | 37 | 60 | 3 |
| 3-Heptanone | K10 | 2 | 49 | 40 | 10 |

^a Temperature: 20°C.

^b One hour reflux after adding cyclohexene oxide to the reaction mixture.

ester formation). K10 montmorillonite, in turn, was found to be a good catalyst, although the yields are somewhat lower than those reported in the literature for MTO, RuCl_3 , $\text{TiCl}_3(\text{OTf})$ and $\text{TiO}(\text{TFA})_2$. However, due to its simple handling and advantageous low price, K10 montmorillonite can be considered a catalyst of synthetic significance for the reaction studied.

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