Ring-opening reaction of 4,4,5,8-tetramethyl-1-oxaspiro[2.5]octane to 2,2,3,6-tetramethylcyclohexanecarbaldehyde over heterogeneous catalysts

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The heterogeneously catalyzed ring-opening reaction of 4,4,5,8-tetramethyl-1-oxaspiro[2.5]octane (**1**) has been carried out in a fixed bed as well as in a batch reactor. In the presence of a silica catalyst yields up to 53% of the important fragrance intermediate 2,2,3,6-tetramethylcyclohexane carbaldehyde (**2**) could be achieved.

Keywords: zeolites, 4,4,5,8-tetramethyl-1-oxaspiro[2.5]octane, epoxide rearrangement

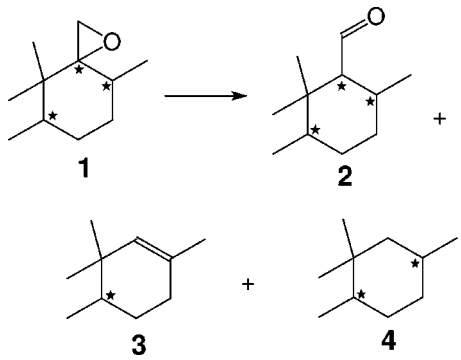
1. Introduction

In the field of industrial fragrance chemicals the catalytic and selective ring-opening reaction of epoxides serves as a valuable synthesis step. The conversions of various epoxides, like terpene oxides, styrene oxide or alkene oxides have been intensely studied [1–6,11].

Among those epoxide-rearrangement reactions there is the conversion of 4,4,5,8-tetramethyl-1-oxaspiro[2.5]octane **1**, which can be obtained in a multi-step synthesis from good available (−)-(*S*)-β-citronellol or (+)-(*R*)-pulegone [7]. With acidic catalysts **1** reacts, beside many other products, to the industrially desired 2,2,3,6-tetramethylcyclohexanecarbaldehyde **2** (scheme 1).

The aldehyde **2** is described as a key molecule for the synthesis of different highly active fragrances like the saturated alcohol 1-(2,2,3,6-tetramethyl-1-cyclohexyl)-3-hexanol **5** highly regarded by perfumers because of its woody-/ambra-like character [8]. The suitable stereochemistry, not focused on in this article, is described to play an important role [8]. As reported in patents of Firmenich S.A., the ring-opening reaction of **1** was preferably carried out with Lewis acidic homogeneous catalysts such as BF_3-etherate [4], MgI_2 [7] or $SnCl_4$ [7] with almost complete yield at room temperature in toluene as the solvent. These catalysts, however, imply a process limitation to discontinuous liquid-phase conditions. Major drawbacks are given by a relatively complicated separation procedure of products and catalyst in addition to corrosion, loss of catalyst and environmental problems such as high salt formation.

The heterogeneously catalyzed rearrangement of **1** has received no attention in literature so far, only the ring



Scheme 1. Main products of the ring-opening reaction of **1** under gas-phase conditions.

cleavage of the structurally related epoxide 1,6-dioxaspiro[2.5]octane was reported [4,9]. In this case, over B-MFI zeolite and SiO_2 as catalysts more than 95% yield of 4-formylpyrane could be achieved in a fixed-bed reactor under gas-phase conditions [4,9].

Therefore, the aim of this work was the evaluation of a simple heterogeneously catalyzed process. First, following the results of the 1,6-dioxaspiro[2.5]octane rearrangement [9], continuous gas-phase conditions were applied in a fixed-bed reactor and secondly under liquid-phase conditions in a slurry reactor.

2. Experimental

2.1. Catalysts

The silica D11-10, BPO_4 and H–B-ZSM-5 ($SiO_2/B_2O_3 = 34$) were kindly provided by BASF AG, H-ZSM-5 ($SiO_2/Al_2O_3 = 60$) zeolite by Uetikon AG and the H-US-Y

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(SiO_2/Al_2O_3 = 70) zeolite by Grace GmbH and Nb_2O_5 by Niobium Products Co. The preparation of H-US-Y(70) treated with HCl is described in the literature [11].

2.2. Reaction

Epoxide **1** (purity 92%, *trans/cis* ratio = 85% : 15% (GC)) was kindly provided by Firmenich S.A.

2.2.1. Gas-phase reaction in a fixed-bed reactor

The fixed-bed reactions were carried out in a coil-shaped steel reactor (6 mm i.d., 900 mm length) installed in a temperature-controlled oven. 2 g catalyst in the form of small particles (1.0–1.6 mm) were placed at the end of the reactor. The feed stock (20 wt% **1** in solvent) was injected into the reactor using a metering pump. N_2 was used as purge gas (5 l/h). The reaction course was periodically followed by GC (Siemens Sichromat 3 using a 25 m capillary column (Ultra-2), a heating rate of 5 K/min from 50 to 280 °C). Quantitative calibrations with standard samples showed that no reactant/products retained in the GC column. The weights of the catalyst before and after the catalytic reaction gave information about coked products on the catalyst surface. Only experiments with a mass balance of >95% are evaluated. The compounds were identified by GC-MS (Varian MAT 112s), GC-IR or NMR results.

2.2.2. Liquid-phase reaction in a slurry reactor

For the experimental standard procedure 15.0 g of 4,4,5,8-tetramethyl-1-oxaspiro[2.5]octane was stirred in 30.0 g of toluene, brought to reaction temperature in a flask equipped with a double-wall cooling system and mixed with 2.0 g of powdered catalyst under careful temperature control. Product samples were taken from reaction mixture by means of a syringe filter and analyzed by GC and GC-MS.

2.2.3. Characterization

The catalyst D11-10 was characterized by N_2 adsorption and NH_3-TPD (figure 1). A BET surface area of 177 m^2/g and a distinct hysteresis at high p/p_0 values indicating the presence of meso- and macro-pores have been found. These large pores reduce transport problems and help the products in easier desorption and easier migration out of the catalyst framework. NH_3-TPD was performed in the range 100–650 °C using a 300 mg sample in small particles (1–1.6 mm), He as the carrier gas (1.8 l/h) and a heating rate equal to 10 °C min^{-1}. After treatment at 550 °C for 5 h under He flow and then cooling down to 25 °C, the sample was saturated with NH_3 and afterwards it was flushed under the He carrier flow (1.8 l/h) for 3 h at 100 °C. The NH_3-TPD profile was recorded using an on-line GC (TCD) system. Thereby a composition of two overlapping peaks was found at 180 and 310 °C. These temperatures correspond to weak acidic sites like silanol groups (FTIR analysis) and to strong acidic sites caused by Al impurities (1.7 mg/g) identified by ICP analysis, respectively.

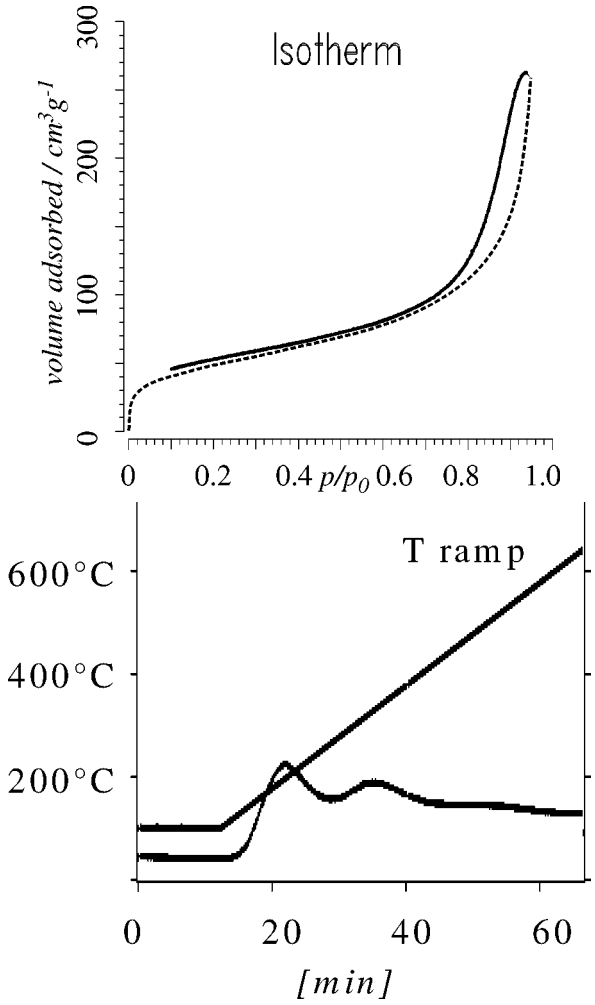

Figure 1. N_2 adsorption/desorption and NH_3-TPD profile of SiO_2 catalyst D11-10.

3. Results and discussion

The catalytic experiments carried out showed that two main reactions took place: rearrangement of **1** to the aldehyde **2** and a deoxygenation reaction to the olefin 1,3,3,4-tetramethylcyclohex-1-ene **3**, which is assumed to be caused by a formaldehyde elimination reaction. Also observed was a deoxygenation reaction to the saturated 1,1,2,5-tetramethylcyclohexane, explained by elimination of CO. The elimination of CO is caused by strong acidic sites [12] and high temperature. There are several other by-products such as 2,2,3,6-tetramethylcyclohex-1-enylmethanol, ring-contracted compounds and double-bond isomers of dimethylisopropylenecyclopentene. However, not all of them could be identified by GC-MS data.

3.1. Gas-phase reaction in a fixed-bed reactor

The first tests were carried out to evaluate the behavior of different catalysts under gas-phase conditions (table 1). It was observed that conversion of **1** decreased rapidly in the presence of various acidic zeolites H–B-ZSM-5, H-ZSM-5 and H-US-Y. This behavior was even more pronounced

with BPO_4 and Nb_2O_5. The low service times of the catalysts are assumed to be caused by strongly adsorbed compounds as well as coke precursors blocking the acidic sites. In this case the selectivity to **2** was very low, because the most of the starting material was converted to heavy products such as coke precursor. Surprisingly, a silica catalyst having gentle acidity showed the best performance. Maintaining a selectivity to **2** of about 40% there was no drop in conversion of **1** observed after 8 h time on stream (TOS), even at 230 °C.

On account of high activity and selectivity of this silica catalyst D11-10, the influence of temperature was studied in the range of 150–300 °C (figure 2).

It is advantageous to run the reaction at about 250–300 °C. In this range complete epoxide conversion is achieved within 6 h TOS in combination with the highest aldehyde selectivities of 45%. The higher selectivity at 300 °C can be explained by the facilitation of the desorption of the desired product. The formations of **2** and **4** are increased by increasing the temperature. Compound **3** passes a maximum around 200 °C. Likewise, complete epoxide conversion is achieved with even WHSV = 3 h^{-1}.

A further optimization step includes a change of the solvent THF to the more apolar solvent toluene (figure 3). Thereby, selectivity to **2** could be enhanced to 53% at complete conversion (figure 3) and no drop of deactivation could be observed within 8 h TOS. The positive effect of toluene in comparison to THF might be explained by a different adsorption behavior towards the active sites of the silica catalyst.

It is surprising that silica gel D11-10 shows better results than zeolites in the gas-phase rearrangement reaction. In the case of 1,6-dioxaspiro[2,5]octane excellent results were obtained in the presence of this silica gel as well as of pentasil zeolites [6]. In the present case the starting material seems to be too bulky and cannot enter the pores of the middle-sized weakly acid boron pentasil zeolite.

On example of using H-ZSM-5(60) the selectivity of **2** could be influenced by changing the nitrogen flow rate from 5 to 12 l/h (table 2). A shorter contact time at the same flow rate has a slightly positive effect on the formation of **2** due to the reduced formaldehyde elimination to **3**. Thereby the conversion is reduced.

Table 1
Conversion of 4,4,5,8-tetramethyl-1-oxaspiro[2.5]octane and selectivities of main products **2**, **3** with different catalysts in a fixed-bed reactor.[a]

Catalyst (modul)	Conversion (%)	Selectivities (%)		Drop of conversion (TOS 2/6 or 2/8 h (*))
		2	**3**	
H–B-ZSM-5(34)	88.9[b]	42.1	15.0	94/87
H-ZSM-5(60)	95.6[c]	39.8	22.5	99/83*
H-US-Y(70)	98.5[c]	29.2	25.2	100/96*
BPO_4	3.4[c]	29.4	<0.1	52/2*
Nb_2O_5	71.7[b]	25.2	17.4	81/65
SiO_2 D11-10[d]	100[b]	39.9	32.5	100/100

[a] Catalyst 2.0 g (1.0–1.6 mm); 20 wt% **1** in THF; WHSV = 1 h^{-1}; T = 180 °C; p = 1 bar; N_2 carrier gas = 5 l/h; TOS = time on stream.
[b] TOS = 4 h.
[c] TOS = 6 h.
[d] T = 230 °C.

3.2. Fluid-phase reaction in a slurry reactor

In contrast to the gas-phase reactions, zeolitic catalysts show a superior catalytic performance in the liquid phase in a slurry reactor. Good conversions and selectivities are obtained over H-US-Y(70) and H-US-Y(70) treated with HCl, whose catalytic features are described elsewhere (table 3) [11].

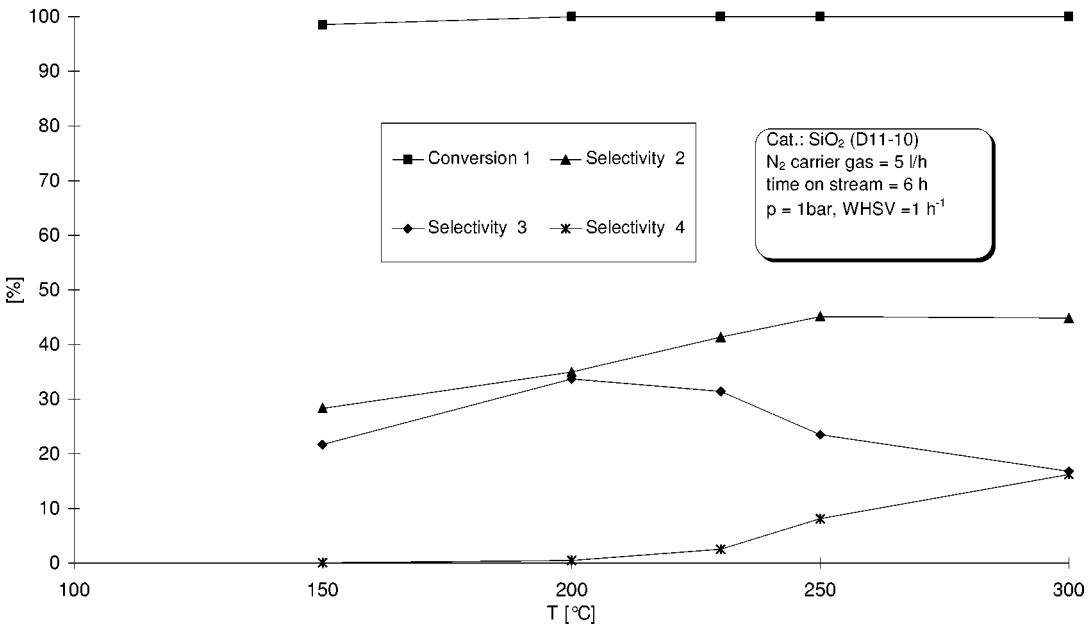

Figure 2. Influence of temperature on conversion of **1** (20 wt% in THF) and selectivity to **2**–**4** over silica catalyst in a fixed-bed reactor.

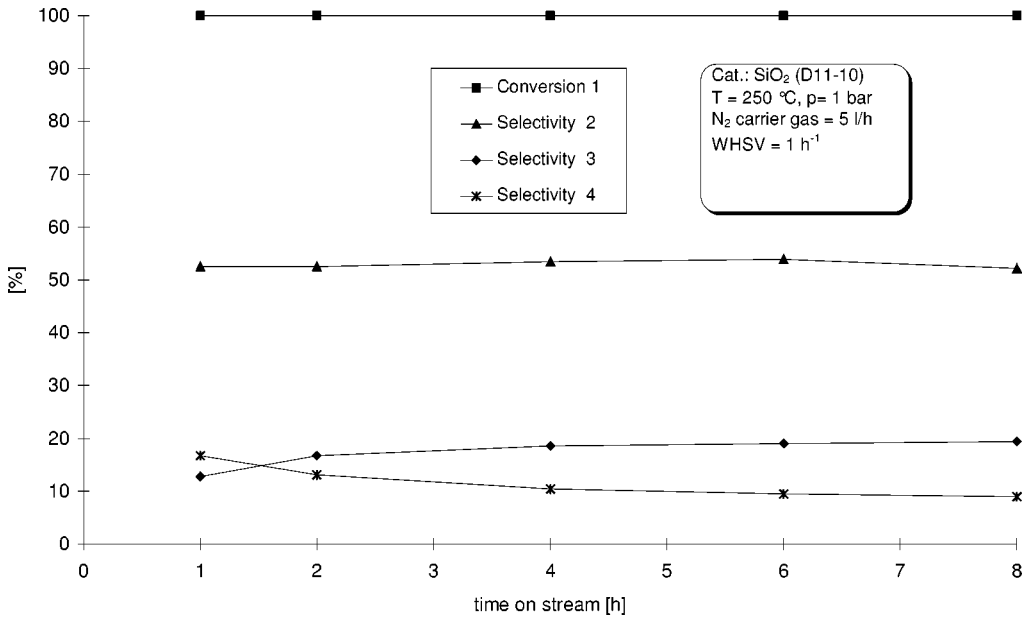

Figure 3. Conversion of **1** (20 wt% in toluene) and selectivity to **2**–**4** in a fixed-bed reactor.

Table 2
Influence of reduced contact time on rearrangement of SP in the gas phase using H-ZSM-5(60).[a]

WHSV (h^{-1})	Nitrogen flow (l/h)	Residence time (s)	Conversion (%)	Selectivities (%)	
				2	**3**
1	5	3.1	96	40	23
1	12	1.3	96	48	19
1	12[b]	0.7	74	49	18

[a] Catalyst 2.0 g H-ZSM-5(60) (1.0–1.6 mm); 20 wt% **1** in THF; $p = 1$ bar; TOS = 6 h; N_2 carrier gas; $T = 180\,^{\circ}C$, TOS = time on stream.
[b] Catalyst 1.0 g.

Table 3
Liquid-phase reactions for the rearrangement of **1** to **2** using catalyst A and acid-treated catalyst B in toluene.[a]

Catalyst	T (°C)	t (h)	Conversion **1** (%)	Selectivity **2** (%)
H-US-Y(70)	0	6	12.5	63.4
		24	22.0	59.8
		72	29.9	55.2
H-US-Y(70)/HCl	0	2	47.1	59.8
		24	79.2	58.6
		72	95.1	47.2
H-US-Y(70)/HCl	25[b]	6	99.7	41.0
		24	100.0	44.0

[a] Catalyst 2.0 g; feed: 4,4,5,8-tetramethyl-1-oxaspiro[2.5]octane (SP); load = 7.5; solvent: 30.0 g toluene; treatment: HCl (0.01 ml); $T = 24$ h; ratio: 10 ml acid/g catalyst; dried at 120 °C/24 h; calcined for 6 h/550 °C.
[b] Short heating to 50 °C because of exothermic reaction.

Highest selectivities are obtained at the very low temperature of about 0 °C. In order to achieve high conversion long residence times are necessary. That means the space time yield (STY) in the liquid phase at low temperatures is less than the STY in the gas phase. The HCl-treated H-US-Y zeolite shows a better catalytic performance than the untreated one. The reason for that is the high Lewis acidity in this particular material [11].

Table 4
Influence of temperature of the rearrangement of **1** to **2** using H-ZSM-5 (60) in the liquid phase.

Temperature (°C)	t (h)	Conversion SP (%)	Selectivity CC (%)
25	24	4.6	0.0
65	8	7.8	21.8
160[b]	8	91.1	31.0

[a] Catalyst 0.5 g; feed: 4,4,5,8-tetramethyl-1-oxaspiro[2.5]octane (SP) 20% in THF; load = 4; CC = 2,2,3,6-tetramethylcyclohexanecarbaldehyde.
[b] Solvent = anisole.

H–B-ZSM-5, H–Al-ZSM-5, Nb_2O_5, BPO_4 and SiO_2 are not suitable catalysts for the conversion in the liquid phase and H-ZSM-5(60) shows a good catalytic performance only at high temperature (table 4).

4. Conclusion

In summary, we have established a facile heterogeneous catalytic method for the synthesis of the aldehyde intermediate 2,2,3,6-tetramethylcyclohexanecarbaldehyde (**2**) with easy handling, lack of corrosion and ease of separation of the product from the catalyst. A silica catalyst is most suitable for the conversion in the gas phase, whereas a H-US-Y(70) treated with HCl shows the best performance in the liquid phase. Furthermore, it was realized that the introduction of an alkyl residue in position 5 of the ring system leads to a clear drop in the 5-alkyl-4-formylpyrane selectivity in comparison to the conversion of the compound without this alkyl group. The yield obtained in the

presence of heterogeneous catalysts is not as high as in the presence of the conventionally used homogeneous system. Improvement of the heterogeneous catalysts is still necessary.

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