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STUDIES ON THE CHEMISTRY OF DIOLS AND CYCLIC ETHERS-52.[1] MECHANISM AND STEREOCHEMISTRY OF DEHYDRATION OF OXOLANES TO DIENES

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Abstract - On γ-Al_2O_3, BPO_4 and NaX zeolite, the dehydration of (±)-2,2,3,4,5,5-hexamethyloxolane (2) in the vapour phase leads to the formation of 2,3,4,5-tetramethyl-1,5-hexadiene (8) in a slow process, while meso-2,2,3,4,5,5-hexamethyloxolane (3) is converted to 2,3,4,5-tetramethyl-2,4-hexadiene (7) with high selectivity in a fast reaction. These differences in reaction rate and selectivity indicate that the dehydration of 2 takes place by an E2 mechanism. In contrast, the steric strain in 3 results in ring opening by an E1 mechanism. These conclusions are supported by the nonselective transformations of 2,2,5,5-tetramethyloxolane (1) and 2,2,6,6-tetramethyloxane (4), and the dehydration of 1, 2 and 3 in the presence of formic acid in the liquid phase. The experimental observation prove that both the reactivity and the reaction directions in the dehydration of stereoisomeric oxolanes are determined by steric factors.

INTRODUCTION

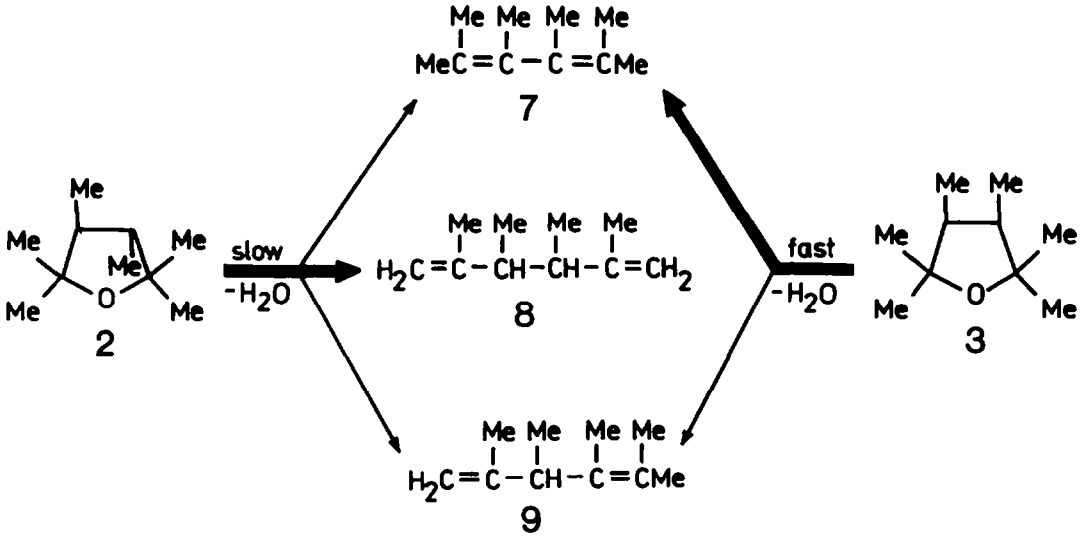
The dehydration of ethers to olefins, and that of cyclic ethers to unsaturated alcohols and dienes, are important reactions; they can be carried out in the liquid phase by the action of acids, or in the vapour phase in the presence of oxides, phosphates, zeolites and other heterogeneous catalyst.[2] Many studies have been made of the theoretical aspects of the dehydration of alcohols, and a number of reviews too have been published.[3] However, the literature does not appear to contain experimental data on the mechanisms and stereochemistry of dehydration of ethers and cyclic ethers. As Olah states, the cleavage of ethers has not been studied extensively.[4] This is rather surprising, for ether dehydration is one of the steps in the recently industrially important synthesis of gasoline from methanol in the presence of zeolites.[5]

We earlier studied the transformations of isomeric 2,2,3,4,5,5-hexamethyloxolanes (2 and 3) on γ-Al_2O_3.[6] It was observed that the dehydration proceeds at different rates and with different selectivities, depending on the steric structures of the starting compounds (Scheme 1).

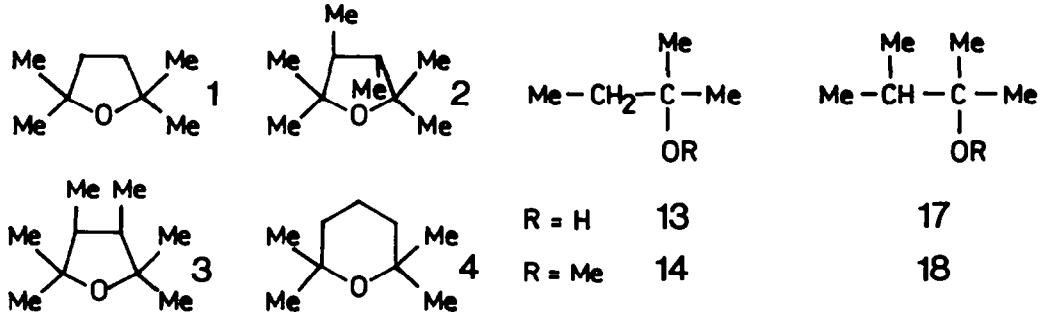
With a view to the interpretation and generalization of the mechanism and stereochemistry of the process, our investigations have been now extended to other dehydration catalysts (BPO_4 and NaX zeolite) and to homogeneous reaction (formic acid). For comparison, studies have also been made of the transformations of

other cyclic ethers (2,2,5,5-tetramethyloxolane (1) and 2,2,6,6-tetramethyloxane (4)) and some structurally related simply alcohols (2-methyl-2-butanol (13) and 2,3-dimethyl-2-butanol (17))and their methyl ethers (14 and 18).

An analysis of all the information collected permitted a comprehensive interpretation as regards the stereochemistry and the mechanistic aspects of the dehydration process.



Scheme 1



RESULTS AND DISCUSSION

The data on the dehydrations of 1, 2, 3 and 4 on γ-Al_2O_3, BPO_4 and NaX zeolite are to be found in Tables 1 and 2, the experimental observations relating to formic acid in Table 3, and the data on the further reactions of the product dienes under the given conditions in Table 4. The data demonstrate that

a. The transformation of 1 on BPO_4 and NaX zeolite proceeds with high selectivity to the corresponding 2,4-diene (5) (Scheme 2), but isomerization 6⟶5 is also involved under these conditions. Dehydration on γ-Al_2O_3 is not selective.
b. The transformations of 2 and 3 proceed selectively on γ-Al_2O_3. The selectivity is much lower on BPO_4 and NaX.
c. Under heterogeneous conditions, on all three catalysts 2 gives mainly 1,5-diene 8 with relatively low rate, while 3 reacts with higher rate and high selectivity to give the 2,4-diene 7.
d. The difference in reactivity of 2 and 3 is particularly marked in the homogeneous phase, when 2 undergoes practically no change; in fact, 2 can be

Table 1. Transformations of 1, 2, 3 and 4 on γ-Al_2O_3

Compound	Temp. °C	Conv. %	Selectivities, mol % 5	6		
1	250	6	57	43		
	275	20	55	45		
	300	40	30	70		
	325	66	30	70		
	350	82	29	71		
	375	96	23	77		
			7	8	9	U
2	250	2	25	50		25
	275	2	25	50		25
	300	18	8	50		42
	325	33	9	46		45
	350	78	5	55	13	27
	375	93	7	43	10	40
3	250	21	85		15	
	275	42	76		12	12
	300	64	80		12	8
	325	77	77		14	9
	350	89	70		15	15
	375	97	59		13	28
			10	11	12	C
4	200	37	39	32		29
	250	74	36	41	5	18
	300	94	37	45	5	13
	350	100	35	43	5	16

U = Unidentified, mainly decomposition products. C = Cyclogeraniolenes = isomeric trimethylcyclohexenes.

Table 2. Transformations of 1, 2 and 3 on BPO_4 and NaX zeolite

Compound	Temp. °C	BPO_4 Conv. %	Selectivities, mol % 5	6		U	NaX Conv. %	Selectivities, mol % 5	6		U
1	225	18	83	17							
	250	36	83	17							
	275	62	81	13		6	52	79	17		4
	300	82	80	13		7	60	78	15		7
	325	90	78	15		7	63	76	16		8
	350	93	75	10		6	66	76	15		9
			7	8	9	U		7	8		9
2	300	9	45	45		10	12	18	50		27
	350	31	42	52		6	34	21	55		24
	400	44	36	43		21					
3	250	8	49	20	14	17					
	300	30	47	13	7	33	30	54	33		13
	350	80	49	19	6	26	59	42	41		17
	400	93	40	21	7	33					

U = Unidentified, mainly decomposition products.

Table 3. Transformations of 1, 2 and 3 in formic acid at 120 °C

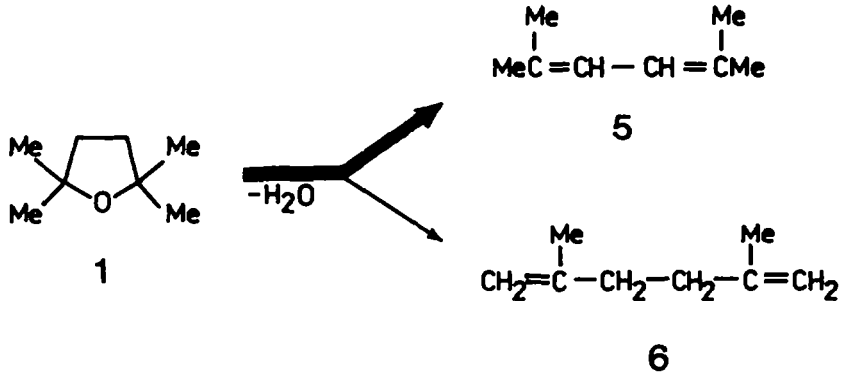
Compound	Reaction time, hr	Conv. %	Selectiv., mol. % 5	6	P	Compound	Reaction time, hr	Conv. %	Selectiv., mol % 7	8	other
1	2.5	53	28		72	2	24	1.5	67	33	
	7	83	20		80	3	3	14	83	17	
							12	41	56	12	32[a]

P = Polymeric material. [a]Racem cyclic ether 2.

Table 4. Transformations of the product dienes under different conditions

Compound	Catalyst	Temp. °C	Product composition, mol %			
			5	6	other	
5	Al_2O_3	375	100			
	BPO_4	300	100			
	NaX	300	80	20		
6	Al_2O_3	375	5	95		
	BPO_4	300	55	45		
	NaX	300	54	46		
5 + 6 (1:1)	formic acid[a]	120	23		55[b] + 22[c]	
			7	8	9	other
7	Al_2O_3	300	100			
	BPO_4	350	100			
	formic acid[d]	120	30	32		13[e] + 25[f]
8	Al_2O_3	300		100		
	BPO_4	350		100		
	formic acid[d]	120		80		20[f]
9	Al_2O_3	300			100	
	BPO_4	350			100	
			10	11	other[g]	
10 + 11 (1:2)	Al_2O_3	300	42	52	6	

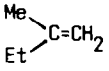
[a]Reaction time: 2 hr. [b]Polymeric material. [c]Cyclic ether 1. [d]Reaction time: 10 hr.
[e]Decomposition products. [f]Racem cyclic ether 2. [g]Cyclogeraniolenes.

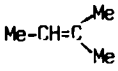


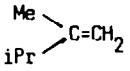
Scheme 2

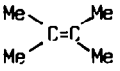
Table 5. Transformations of alcohols 13, 14 and their methyl ethers 17, 18 on γ-Al_2O_3 and NaX

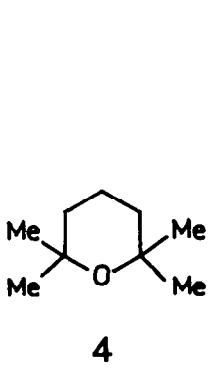
Catalyst	Temp. °C	Compound	Conv. %	Selectivities, mol % 15	16	Compound	Conv. %	Selectivities, mol % 19	20
Al_2O_3	275	13	68	47	53	17			
	300		74	52	48		77	86	14
	325		83	53	47		84	86	14
NaX	200		78	21	79		66	39	61
	250		85	18	82		71	46	54
	300		88	25	75		73	47	53
Al_2O_3	250	14	80	49	51	18	81	89	11
	275		89	47	53		93	87	13
	300		97	48	52		95	87	13
NaX	200		72	22	78		74	47	53
	250		83	27	73		84	44	56
	300		88	26	74		94	42	58

15 

16 

19 

20 



Scheme 3

Table 6. Transformations of the product olefins on γ-Al_2O_3 and NaX at 300 °C

Compound	Catalyst	Product composition, mol % 15	16
15 + 16 (1:1)	Al_2O_3	50	50
	NaX	31	69
		19	20
19	Al_2O_3	98	2
	NaX	41	59
20	Al_2O_3		100
	NaX	27	73

isolated during the transformations of dienes 7 and 8.

e. Selectivity cannot be observed in the transformation of 4 (Scheme 3).

f. During the dehydration under homogeneous conditions, in formic acid, a side-reaction (polymerization of the dienes) also occurs, mainly in the case of 1.

The studies of the structurally similar alcohols (13, 17) containing a tertiary C-O bond and similar substituents and their methyl ethers (14, 18) (Table 5) permit various findings.

g. The presence of the β-methyl group is an essential factor in the product distribution.

h. The product distributions on γ-Al_2O_3 and NaX zeolite differ considerably; the reason for this is that the olefins formed undergo isomerization on NaX zeolite (Table 6).

i. The product distribution and reactivity are practically not influenced by etherification of the OH group.

In the interpretation of the results, one of the starting points must be the final points above, i.e. the fact that the alcohols and their ethers react in the same way under the reaction conditions employed. This means that known observations relating to the dehydration of alcohols can also be applied in connection with the dehydration of ethers and cyclic ethers. Further, primarily in the interpretation of the stereochemistry, attention must be paid to the experimental data for 2 and 3 on γ-Al_2O_3, where the conditions are the most selective, and also the steric structures of the two compounds.

Examinations of molecular models of the two isomeric cyclic ethers shows that there is a substantial difference in stability between the two molecules. In one of the half-chair conformations of 2, only two steric repulsions need be considered: those between the 2 and 3 and the 4 and 5-methyl groups. However, in 3 both the half-chair conformations involve appreciable strain, because of the steric repulsions between the 2 and 3, the 3 and 4 the 4 and 5-methyl groups and, depending on the conformation, because of the 1,3-diaxial interaction between the 2 and 4 or the 3 and 5-methyl groups (Fig. 1).

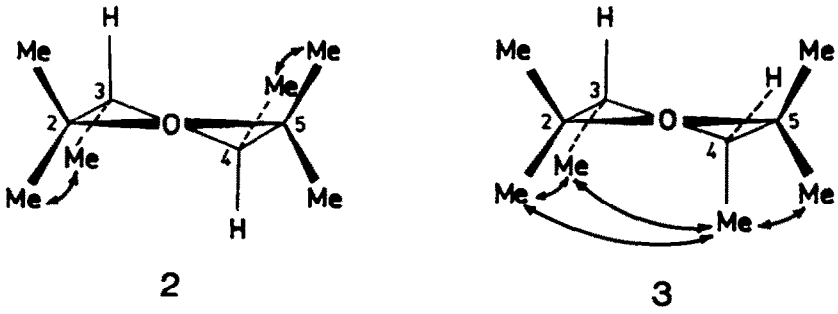
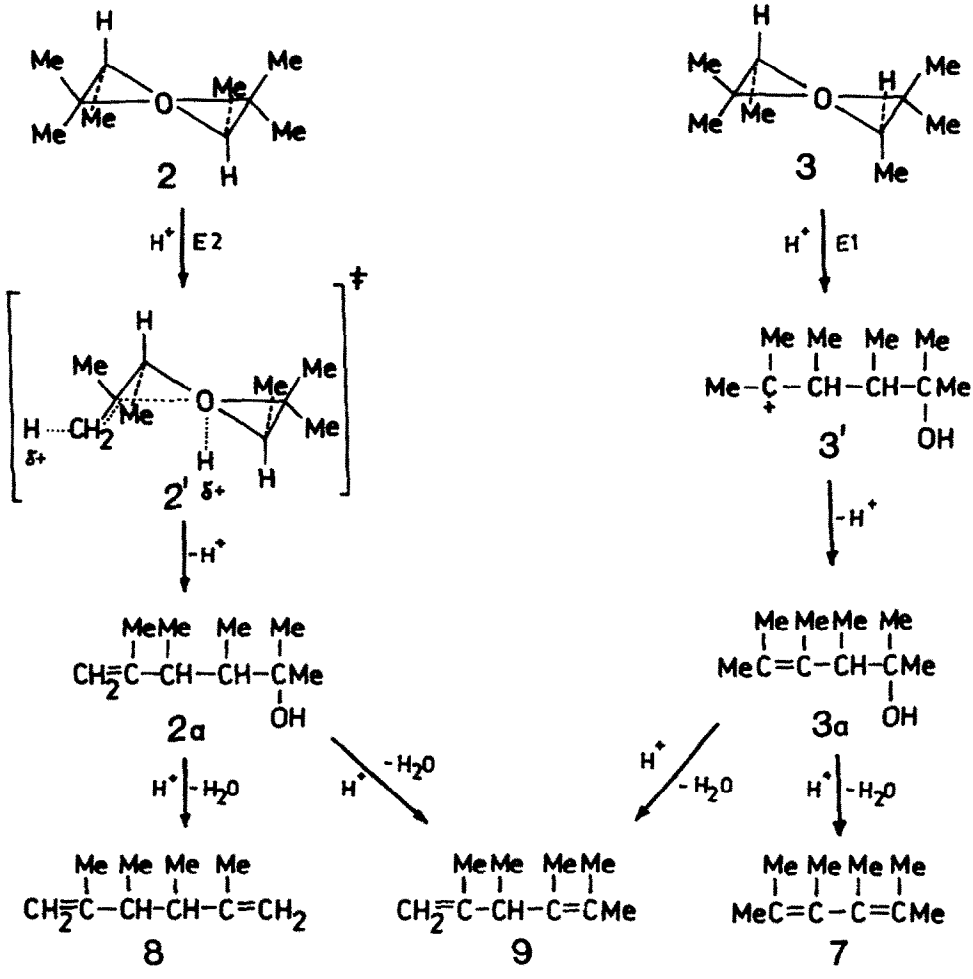


Fig. 1. Steric repulsions in stereoisomeric oxolanes 2 and 3

The above findings, together with the experimental results, in particular the essential difference between the reactivities and selectivities of 2 and 3, lead to the dehydration mechanism outlined in Scheme 4.

The fast transformation of 3 and the formation of the 2,4-diene 7 as main product suggest that the ring opening proceeds by an E1 mechanism. The rapid opening of the strained ring gives the carbenium ion 3'; known observations



Scheme 4

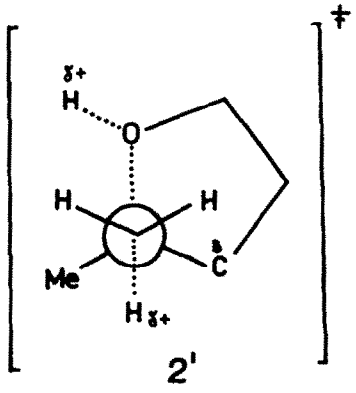
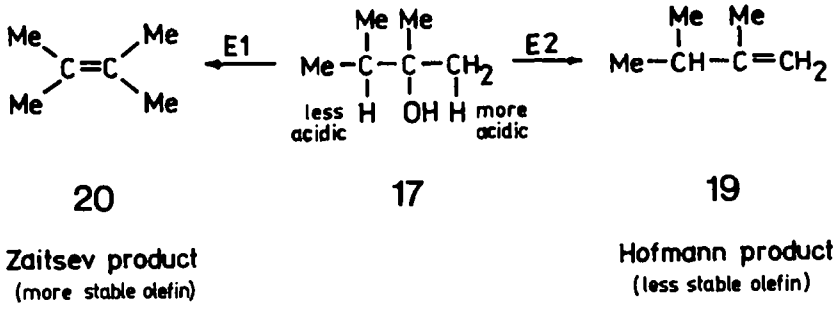


Fig. 2. Newman projection of transition state 2'
(the 3, 4 and 5-methyl groups are omitted for clarity)

relating to the E1 mechanism indicate that this will lead mainly to the formation of the Zaitsev product, i.e. the thermodynamically more stable product 3a, in which the olefin bond is more highly substituted. The much lower reactivity observed for the racemic compound 2 is in accord with the lower ring strain, and this suggests ring opening by an E2 mechanism, i.e. in a synchronous process. The free rotation of the methyl groups means that there is no obstacle to the development of the conformation necessary for concerted, anti-elimination cleavage of the C(2)-O bond and any of the hydrogens of one of the 2-methyl groups (transition state 2'), and hence the terminal olefin bond is formed (2a) (Fig. 2).

The selectivity of diene formation can be regarded as virtually decided when the first olefin bond is produced as a result of the ring opening. Although the unsaturated alcohols formed (2a, 3a) undergo loss of water by essentially the same mechanism, the development of the second C=C bond is influenced by the position of the olefin bond. The transformation of the corresponding tertiary alcohol (17) shows (Table 5) that water elimination on γ-Al_2O_3 gives terminal olefin (19); if it is borne in mind that the C(3) hydrogen is less acidic than the C(1) hydrogens as a result of the +I effect of the methyl groups, this is in accord with the E2 mechanism and the Hofmann rule (Scheme 5). Thus, 8 is formed as the main product of 2a. In the transformation of 3a, another factor predominates, i.e. the striving force for conjugation, and as a result the conjugated diene 7 is formed.



Scheme 5

It is very instructive to consider the minor products too. The fact that 2 gives a small amount of 9 only at higher temperatures underlines the importance of polarization of the different C-H bonds. The formation of 9 from 3 at all temperatures indicates a competition between the two factors governing water loss from 3a; the difference in acidity of the β-hydrogens and the driving force to conjugation, the latter predominating. The formation of a small amount of conjugated diene 7 from 2 indicates that ring opening by an E1 mechanism can occur here too, though to only a very low extent.

In agreement with the above, 1 similarly gives 1,5-diene (6) as main product on Al_2O_3 at higher temperatures, i.e. the absence of steric strain results here too in ring opening predominantly by an E2 mechanism, with the formation of a terminal olefin bond. The foregoing conclusions are confirmed by the non-selective dehydration of 4, though the observed product distribution is influenced by the conversion of the dienes to cyclogeraniolenes. During the ring opening of 4 by the E2 mechanism, cleavage of the C(2)-O bond may occur with the synchronous splitting-off of one of the hydrogens of a methyl group via a transition state similar to 2' (Fig. 2). At the same time, the necessary anti-periplanar conformation is given for the C(2)-O bond and the C(3) equatorial hydrogen (Fig. 3). Thus, there

are equal probabilities that a terminal or an internal olefin bond will result.

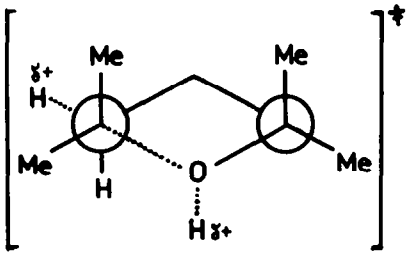


Fig. 3. Transition state of protonated 4 leading to the formation of an internal olefin bond.

The transformations of 2 and 3 under homogeneous conditions lend support to the above picture. In formic acid 2 is practically stable, i.e. the difference in reactivity between the two compounds is even more significant in this medium. The difference in reactivity of the isomers, manifested in the lack of ring opening of 2, is very strong evidence in favour of the E2 mechanism. This mechanism requires the participation of a suitable base in the synchronous proton loss, but such a base is obviously not present in the aqueous acidic mecium.[8] Here too, just as on the heterogeneous catalysts, the reaction of 3 leads to the conjugated diene 7 with high selectivity.

CONCLUDING REMARKS

On the basis of the above observations, the generalization may be drawn that the reaction conditions are not the deciding factor in the process of dehydration of the stereoisomeric oxolanes; the direction of the transformation and the reactivities of the isomers are rather governed by the steric structures of the starting cyclic ethers. Because of the diverse experimental procedures and dehydrating agents used and the structural varieties of the compounds studied, the conclusions arrived at can be considered to be generally valid for the mechanism and stereochemistry of the dehydration of ethers and cyclic ethers.

ACKNOWLEDGEMENTS

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EXPERIMENTAL

Methods.

The heterogeneous catalytic studies were carried out by a pulse method in a glass microreactor coupled to a Carlo Erba Mod GV gas-chromatograph, 1 μl pulses being used.[9] The temperature was controlled to an accuracy of ±0.1 °C with a PID (proportional-differential-integral) regulator. Measurements were made in a stream of hydrogen as carrier gas (40 ml/min), and analyses were performed with the use of columns 1.2 m in length, under the following conditions: 1: 20% 1,2,3-tris(2-cyanoethoxy)-propane, 65 °C; 2 and 3: 15% Apiezon M, 130 °C; 13 and 14: 15% Apiezon M, 60 °C; 17 and 18: 15% Apiezon M, 80 °C. In the product analysis of 4, a 4 m long 15% diphenylformamide column was used (100 °C; 40 ml/min hydrogen).

In studies in the solution phase, 1 mmol cyclic ether was mixed with 5 ml formic acid and refluxed at 120 °C.[10] After cooling, the reaction mixture was diluted with 10 ml water and extracted with 3 ml hexane, followed by chromatography.

Materials.

Catalysts. The γ-Al_2O_3 was a Strem product (No. 13-225, BET surface area: 100 m^2/g). Titrations with n-butylamine and benzoic acid in benzene solution[11] were used to determine the numbers of acidic and basic centres, respectively (acidic centres: 0.20 mequ./g; basic centres: 0.46 mequ./g). This method gives values for Broensted acidity and basicity. 50 mg of the 0.25-0.40 mm grain size fraction was used; pretreatment: 40 ml/min air, 60 min, 300 °C, then 40 ml/min hydrogen, 30 min,

300°C. The BPO_4 (Ventron product, 50 mg powder) was treated for 5 h at 400 °C in 40 ml/min hydrogen (acidic centres: 0.97 mequ./g; basic centres: 0.12 mequ./g). The NaX zeolite was a Strem product (011878-G; acidic centres: 0.30 mequ./g; basic centres: 0.54 mequ./g). 5 mg of the 0.25-0.40 mm grain size fraction was used after pretreatment at 300 °C for 60 min in 40 ml/min hydrogen.

Formic acid. This was a 98-100% product of Loba Chemie.

Compounds examined.

2,2,5,5-Tetramethyloxolane (1). Prepared from 2,5-dimethyl-2,5-hexanediol by dehydration [12] (61%, bp 112-114 °C). The dienes 2,5-dimethyl-2,4-hexadiene (5) and 2,5-dimethyl-1,5-hexadiene (6) were obtained from 1 by dehydration (4 g Al_2O_3, 350 °C)on a preparative scale in a flow reactor, followed by distillation.

(±)-2,2,3,4,5,5-Hexamethyloxolane (2) and meso-2,2,3,4,5,5-hexamethyloxolane (3). (±)- and meso-3,4-dimethyl-2,5-hexanedione were prepared from ethyl methyl ketone in the presence of PbO_2 [13] (33%; isomer ratio according to GC: 55:45). A mixture of the isomeric diols (79%, bp 85-100 °C/2.5 torr) was obtained from the mixture of diones through a Grignard reaction with MeI. During the ring closure, [12] a mixture of 17.4 g (0.1 mol) diol, 0.6 g (0.0034 mol) $PdCl_2$ and 0.6 g (0.0045 mol) $CuCl_2$ was kept at 140-150 °C in a vacuum produced by a water-pump. The product distilling as an aqueous azeotrope at 80-90 °C was separated and dried, and redistilled at 83-90 °C at 28 torr (11.2 g, 72%). The cyclic ethers were separated from the mixture by glc (2 m, 15% LAC 296 column, 100 °C, 120 ml/min hydrogen). ^1H NMR (60 MHz, CCl_4): 2: 1.14 and 0.94 (each s, 2 and 5 Me), 0.86 (d, 3 and 4 Me), $J_{H,H}$= 2 Hz, $J_{Me,H}$= 7 Hz; 3: 1.16 and 1.05 (each s, 2 and 5 Me), 0.9 (d, 3 and 4 Me); $J_{H,H}$=5 Hz; $J_{Me,H}$= 7.5 Hz.

In the synthesis of dienes 2,3,4,5-tetramethyl-2,4-hexadiene (7), 2,3,4,5-tetramethyl-1,5-hexadiene (8) and 2,3,4,5-tetramethyl-1,4-hexadiene (9), dehydration of the cyclic ether mixture on a preparative scale in a flow reactor (10 g NaX zeolite, 300 °C) was followed by preparative glc (2 m 15% Apiezon M, 130 °C, 200 ml/min hydrogen). ^1H NMR (60 MHz, CCl_4): 7: 1.62 (s), 1.48 (s); 8 2.15 (m), 1.6 (m), 1.6 (s), 0.98 (d); 9: 2.2 (m), 1.5 (s), 0.95 (d).

2,2,5,5-Tetramethyloxane (4). Prepared by the dehydration of 2,6-dimethyl-2,6-heptanediol with 10% sulphuric acid (55%, bp 140 °C).

A mixture of 2,6-dimethyl-2,5-heptadiene (10) and 2,6-dimethyl-1,5-heptadiene (11) was prepared by the dehydration of 2,6-dimethyl-5-hepten-2-ol with phosphoric acid.

2-Methyl-2-butanol (13) was a commercial product (Reanal, Budapest).

A 1:1 mixture of 2-methylbut-1-ene (15) and 2-methylbut-2-ene (16) was prepared by the dehydration of 13 on Al_2O_3 at 300 °C.

2,3-Dimethyl-2-butanol (17) was synthesized by the reaction of acetone and isoPrMgBr (41%, bp 114-116 °C).

2,3-Dimethylbut-1-ene (19) and 2,3-dimethylbut-2-ene (20) were Fluka products and were used without further purification.

2-Methoxy-2-methylbutane (14) and 2-methoxy-2,3-dimethylbutane (18). Prepared by the sulphuric-acid catalyzed intermolecular dehydration of 13 and 17, respectively, in the presence of methanol [14] (14: bp 80-82 °C; 18: bp 101-104 °C).

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