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Studies on the Chemistry of Diols and Cyclic Ethers-53.[x] Dehydration of 1,1-Bishydroxymethylcycloalkanes: a Quest for a 1,3-Hydride Shift

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Dedicated to Professor Gábor Fodor on the occasion of his 75th birthday.

Abstract - A study of the sulphuric acid-catalysed dehydrations of 1,1-bishydroxymethylcyclopropane, -cyclobutane, -cyclopentane and -cyclohexane (**1a-1d**) revealed that the product distributions are determined by the relative stabilities of carbenium ions and cycloalkane rings. The transformation of 1,1-bis[dideuteriohydroxymethyl]cyclohexane under kinetic control furnished evidence of a 1,3-hydride shift.

INTRODUCTION

In the 1950's a number of organic transformations were demonstrated to involve a 1,3-rearrangement. Despite this, books and monographs published in the 1960's which treated 1,2-rearrangements in detail either neglected or only superficially mentioned 1,3-rearrangements.[1-8] Later, however, the increasing number of new examples led to the recognition of 1,3-rearrangements as a subclass of molecular rearrangements.[9-15]

Among 1,3-migrations, 1,3-hydride shifts formally involving two electrons and three centres seem to play a minor role in organic chemistry. This is due to the high energy barrier as compared to those for 1,2- and 1,5-hydride shifts.[15, 16] As a result, at least in open-chain systems, 1,3-hydride shifts do not compete favourably with 1,2-shifts under thermodynamic control.[12, 14] Instead, two successive 1,2-shifts occur.

We encountered the problem of the 1,3-hydride shift in connection with our studies of the dehydration of 1,3-diols. It was recognised that 1,3-diols transform to carbonyl compounds on metal catalysts[17] and acidic catalysts.[18] On analogy with the well-known pinacol rearrangement characteristic of vicinal diols, we suggested the 1,3-hydride shift as one possible way of interpreting this reaction of 1,3-diols (Scheme I).

The results of kinetic investigations[19] and mechanistic studies with labelled compounds[20] later proved that the metal-catalysed dehydration follows a more complicated, multistep pathway (Scheme II), but the problem of the 1,3-hydride shift has intrigued us ever since.

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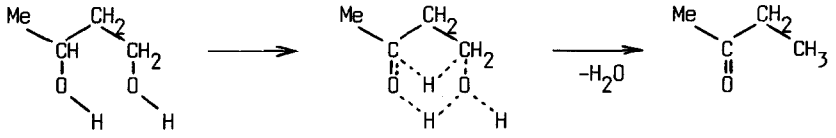
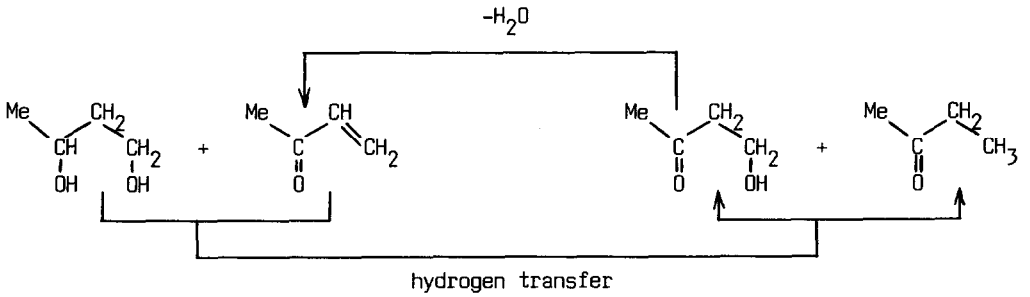
[x]Part 52: Molnár, Á.; Bartók, M. Tetrahedron **1987**, 43, 131-141.



Scheme I



Scheme II

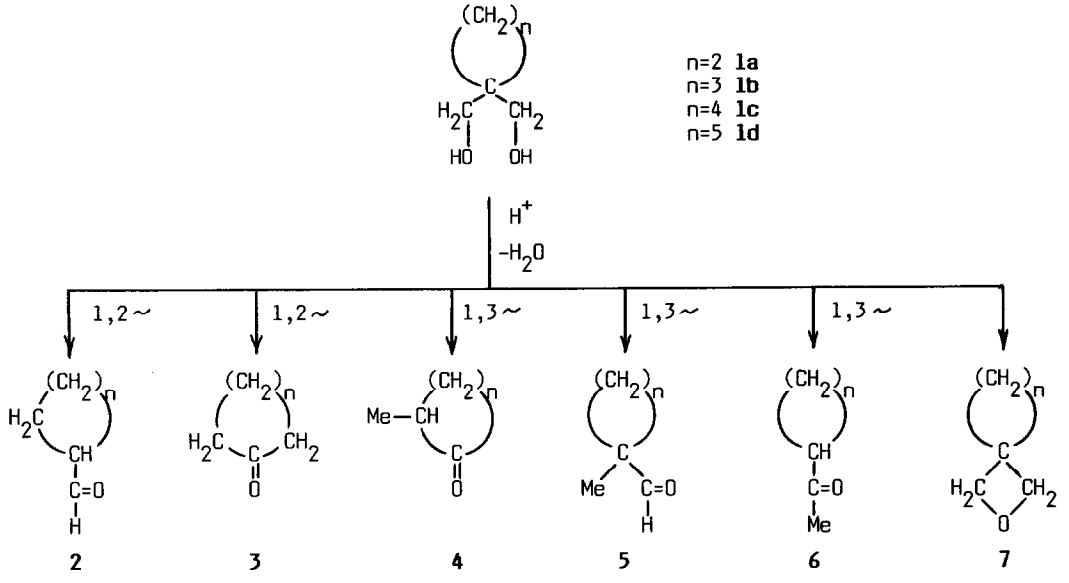
The problem of successive 1,2-shifts interfering with the 1,3-hydride shift can be overcome by using appropriately selected compounds. The thoroughly-studied bi- and tricyclic systems (norbornyl and adamantyl cations) are the best examples.[12, 14] Besides these systems, compounds in which the carbenium ion carbon is attached to a quaternary carbon atom might also be suitable for participation in a 1,3-shift.[15] 2,2-Disubstituted 1,3-propanediols satisfy this requirement. Earlier studies revealed, however, that under acidic conditions fragmentation and a 1,2-alkyl shift prevail and no evidence of a 1,3-hydride shift was found.[21-23] Similar compounds in which the quaternary carbon is part of a cycloalkane ring (1,1-bishydroxymethylcycloalkanes) are also promising models for such studies. It can reasonably be assumed that the structural change imposed by the ring system might favourably affect the conditions for the 1,3-shift during the dehydration of these compounds. Surprisingly, with the exception of one unsuccessful attempt to prepare the oxetane derivative from 1,1-bishydroxymethylcyclohexane,[24] no data are available on the dehydration of these compounds.[25, 26]

Systematic studies of four 1,1-bishydroxymethylcycloalkanes (**1a-1d**) have been undertaken with the aim of acquiring information about their ability to undergo the 1,3-hydride shift and about the effect of ring strain on the competing 1,2-alkyl and 1,3-hydride shifts.

RESULTS AND DISCUSSION

The characteristic transformations of 1,3-diols are well known.[26] When the possible reaction directions, the relative stabilities of small ring cycloalkanes and the different carbenium ions formed, and the ability of carbonyl compounds to undergo further re-

arrangement[27] are taken into account, the formation of the products depicted in Scheme III may be expected during the acid-catalysed dehydration of model compounds **1a-1d** (1,2 and 1,3 denote a 1,2-shift and a 1,3-shift, respectively).



Scheme III

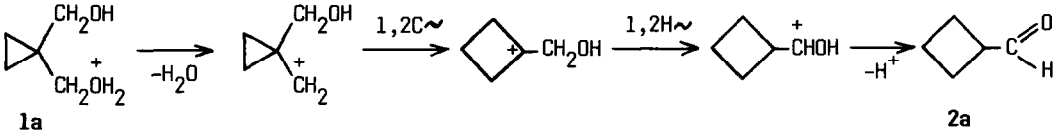
Table 1. Distribution of Liquid Products of Dehydration of 1,1-Bishydroxymethylcycloalkanes (mole %)[+]

Compound	Reaction conditions		Product distribution						n+1/n
	concentration of H_2SO_4	time	2	3	4	5	6	X	
1a	10%	24 h	100						100/0
1b	20%	24 h	83		11			6	94/0
	30%		66		25			9	91/0
1c	30%	48 h	51		35	4		10	86/4
1d	30%	48 h[x]	55	2	10	7	5	21	67/12
	45%		28	3	32	11	4	22	63/15
	70%	12 h[+]	4	3	33	4	26	30	40/30

[+]Yield of liquid products about 80%. X = Unidentified compounds. [x]Incomplete reaction. **n+1/n** = Ratio of compounds formed as a result of ring enlargement to compounds with original ring size (**2+3+4/5+6**).
[+]Extensive resinification took place possibly due to the polymerization of alkenes formed from carbenium ions in a competing proton loss.

The transformations of compounds **1a-1d** were carried out in sulphuric acid of different concentrations. The data in Table 1 reveal that all the expected carbonyl compounds are formed. It is evident that the most important factors determining the product distribution are the driving force towards the formation of a more stable carbenium ion (rearrangement of a primary to a tertiary ion) and the tendency of smaller rings to relieve themselves of ring strain by undergoing ring enlargement. This results in the predominance of products formed via ring enlargement in every case (last column in Table 1).

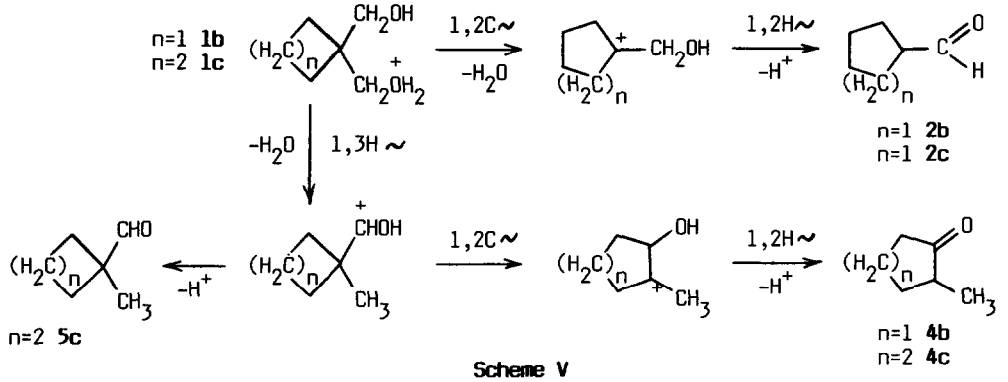
For the most strained cyclopropanediol (**1a**) the major driving force is ring enlargement. As a result, an immediate 1,2-alkyl shift (1,2C~) after protonation and loss of water leads to the formation of cyclobutanecarbaldehyde **2a** as the sole product (Scheme IV). Naturally, direct formation of the cyclobutyl cation with the synchronous loss of water and an alkyl shift can also be supposed.



1a **2a**

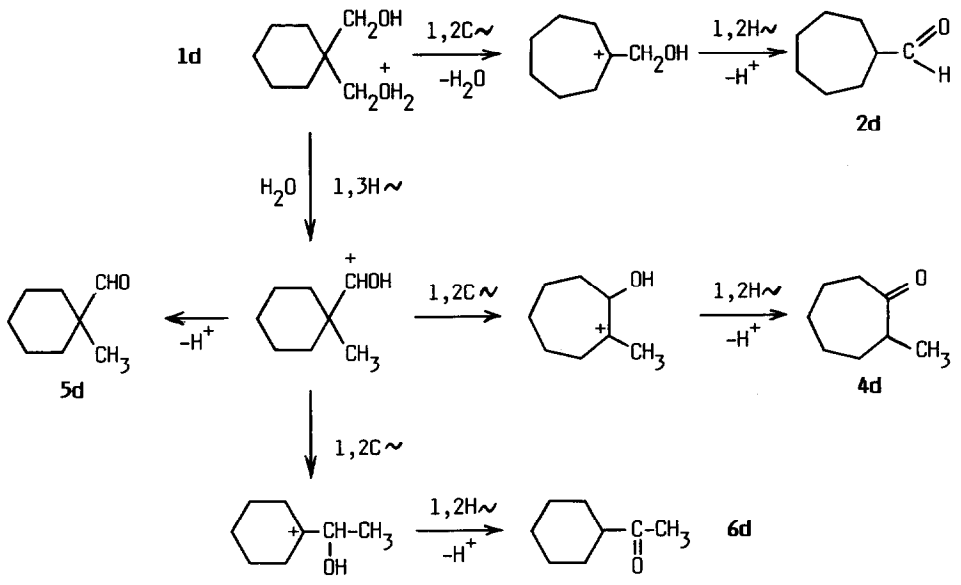
Scheme IV

On progressing from cyclopropane towards larger rings, the ring strain decreases and there is a corresponding slight decrease in the ratio **n+1/n**. As a result of this tendency, during the transformation of the cyclobutanediol (**1b**) and the cyclopentanediol (**1c**) a 1,3-hydride shift (1,3H~) can precede the 1,2-alkyl shift, permitting the formation of methylcycloalkanones **4b** and **4c**, respectively (Scheme V). Although **1b** produces only compounds with a larger (cyclopentane) ring, **1c** is the first compound in the homologous series to yield a product without ring enlargement (**5c**).



Scheme V

The most significant changes are observed with cyclohexanediol **1d**. Since cyclohexane is considered to be free of ring strain, this means that the stability of the different carbenium ions is the only factor affecting the product distribution (Scheme VI).



Scheme VI

Increase of the acid concentration results in a decreasing ratio **n+1/n**, which reaches a value of almost 1 (Table 1). This indicates a change-over from thermodynamic control to kinetic control. From the point of view of a 1,2- vs. a 1,3-shift, at higher acid concentrations the latter shift is of increasing significance. For example, the proportion of the products involving a 1,3-hydride shift (**4d**, **5d** and **6d**) increases dramatically with increasing acid concentration (Table 1, combined yield of **4d**, **5d** and **6d** = 22%, 47% and 63% on increase of the concentration of H_2SO_4 from 30% to 45% and then to 70%).

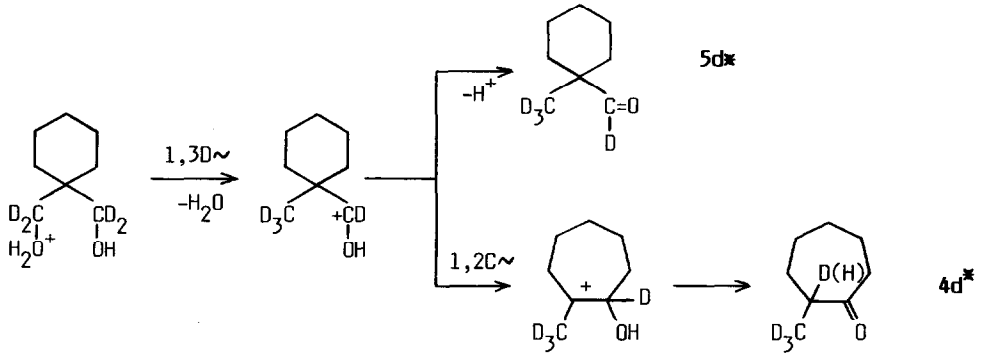
To obtain direct evidence of the 1,3-hydride shift, we examined the dehydration of the labelled compound 1,1-bis[dideuteriohydroxymethyl]cyclohexane. It follows from the above discussion that the use of concentrated sulphuric acid migth be expected to give the best results for a 1,3-shift. However, the low yield of liquid products and the very extensive deuterium loss led us to apply less forcing conditions. The results are given in Table 2.

Of the three compounds formed via a 1,3-hydride shift, **6d*** (an asterisk denotes a labelled compound) suffers extensive deuterium loss. This is due to the hydrogen-deuterium exchange taking place through the enol form under the given reaction conditions. A certain, but less severe deuterium loss also occurs in the formation of **4d*** and **5d***. Besides enolisation, this is probably due to the complicated interconversions (aldehyde-ketone and ketone-ketone rearrangements[27]) of different carbonyl compounds. Nevertheless, the high percentages of d_3 and d_4 products among the isotopomers of **4d*** and **5d*** unequivocally testify to a direct 1,3-hydride shift (Scheme VII).

Table 2. Results of Tracer Studies with 1,1-Bis[dideuteriohydroxymethyl]cyclohexane[+]

Product	D content, atom per molecule	D distribution	D atom loss /% loss	Labelled positions
2d* cycloheptanecarbaldehyde	2.86	d_1 0.06 d_2 0.04 d_3 2.76	1.06/27	formyl, C(2)
3d* cyclooctanone	0.56	d_1 0.22 d_2 0.34	3.36/86	C(2)
4d* 2-methylcycloheptanone	2.93	d_1 0.08 d_2 0.46 d_3 0.75 d_4 1.64	0.99/25	C(2), Me
5d* 1-methylcyclohexanecarbaldehyde	2.89	d_1 0.04 d_2 0.46 d_3 1.47 d_4 0.92	1.03/26	formyl, Me
6d* 1-cyclohexylethanone	1.80	d_1 0.06 d_2 1.68 d_3 0.06	2.12/54	C(1), Me

[+]Reaction conditions: 45% H_2SO_4, 24 h. Asterisks denote labelled compounds. D content of starting compound = 3.92 atoms per molecule.



Scheme VII

CONCLUSION

1,1-Bishydroxymethylcycloalkanes (**1a-1d**) proved to undergo a 1,3-hydride shift in their acid-catalysed dehydration to certain carbonyl compounds. In the transformation of the protonated diol into the more stable tertiary cation, there is a competition between a 1,2-alkyl and a 1,3-hydride shift. Increasing ring size is accompanied by an increasing significance of the 1,3-hydride shift. In the dehydration of 1,1- bishydroxymethylcyclohexane, the predominance of products formed via a 1,3-hydride shift was observed.

EXPERIMENTAL

Materials. The four 1,1-bishydroxymethylcycloalkanes **1a-1d** studied were synthesized by known methods. α,ω-Dibromoethane, -dibromopropane, -dibromobutane and -dibromopentane were reacted with diethyl malonate.[28] The diethyl cyloalkane-1,1-dicarboxylic acids thus prepared were converted to the corresponding diols **1a-1d** by $LiAlH_4$ reduction.[29] All compounds gave satisfactory elemental analyses, boiling and melting points, and IR and NMR spectra. 1,1-bis[dideuteriohydroxymethyl]cyclohexane was prepared by reducing diethyl cylohexane-1,1-dicarboxylic acid with $LiAlD_4$ (m.p. 96.5-97.5 ^{o}C, deuterium content = 3.92 atoms as determined by NMR). Reagent grade sulphuric acid (Farmitalia Carlo Erba, 96%) was used to carry out the acid-catalysed transformation of diols.

Method. A round-bottomed flask connected to a reflux condenser through a trap designed to return the heavier water layer was charged with 1 g of diol. After the addition of 40 ml of dilute sulphuric acid, the reaction mixture was stirred magnetically and heated at 150-155 ^{o}C. Acid concentrations and reaction times are indicated in Table 1. The organic phase separated in the trap was dried and subjected to analysis (in the case of **1a**, saturation with NaCl was necessary to achieve separation of the organic layer). **1d** and its labelled form were also transformed on a larger scale (5 g of diol) for identification.

Analyses. Product compositions were determined by means of GC (Carlo Erba Fractovap Mod. G, column: 1.2 m 15% SE 52 or CWAX 20M on Merck Kieselguhr, 100-140 ^{o}C, hydrogen carrier gas flow rate: 40-50 ml min^{-1}). The compounds formed were identified via the GC retentions of independently synthesised authentic compounds and GC+MS spectroscopy. After separation by preparative GC, compounds were also analysed by IR (UNICAM SP 1000) and NMR spectroscopy. Deuterium-labelled compounds were analysed by ^{1}H NMR spectroscopy (JEOL C 60-HL) and mass spectrometry (a Hewlett-Packard 5890A GC instrument coupled with a 5970 MSD quadrupole mass spectrometer; conditions: 50-m HP-1 column, 40-250 ^{o}C; EI source, 70 eV, 1-s scans, HP 59970 MS ChemStation data system). In the calculation of deuterium distributions (Table 2, column 3) in the product molecules formed from labelled **1d**, Beynon's method was used.[30, 31]

REFERENCES

1. Bartlett, P.D. in Organic Chemistry, Vol. III; Gilman, H., Ed.; Wiley: New York, 1953; pp. 1-121.
2. Ingold, C.K. Structure and Mechanism in Organic Chemistry; G. Bell: London, 1953.
3. Cram, D.J. in Steric Effects in Organic Chemistry; Newman, M.S., Ed.; Wiley: New York, 1956, pp. 304-348.
4. Wheland, G.W. Advanced Organic Chemistry; Wiley: New York, 1960.
5. Mathieu, J.; Allais, A. Cahiers de synthèse organique, Vol. VI; Masson et Cie: Paris, 1960.

6. Hine, J. Physical Organic Chemistry; McGraw-Hill: New York, 1962.
7. Mayo, P., Ed.; Molecular Rearrangements; Wiley: New York, 1963.
8. Rees, C.W. in Organic Reaction Mechanisms, 1966; Capon, B.; Rees, C.W., Eds.; Wiley: London, 1967, pp. 221-261.
9. Fodor, G. Magy. Kém. Lapja **1963**, 18, 593-597.
10. Bartók, M. Acta Phys. et Chem. Szeged **1963**, 9, 131-133.
11. Landis, P.S. in Mechanisms of Molecular Migrations, Vol. 2; Thyagarajan, B.S., Ed.; Wiley: New York, 1969; pp. 43-63.
12. Fry, J.L.; Karabatsos, G.J. in Carbonium Ions, Vol. II; Olah, G.A.; Schleyer, P.R., Eds.; Wiley: New York, 1970; pp. 521-571.
13. Stoodley, R.J. in Organic Reaction Mechanisms, 1970; Capon, B.; Rees, C.W., Eds.; Wiley: London, 1971, pp. 241-303.
14. Saunders, M.; Chandrasekhar, J.; Schleyer, P.R. in Rearrangements in Ground and Excited States, Vol. I; Mayo, P., Ed.; Academic Press: New York, 1980; pp. 1-53.
15. Ahlberg, P.; Jonsall, G.; Engdahl, C. Adv. Phys. Org. Chem. **1983**, 19, 223-379.
16. Watt, C.I.F. Adv. Phys. Org. Chem. **1988**, 24, 57-112.
17. Bartók, M.; Molnár, Á. Kém. Közl. **1976**, 45, 335-357.
18. Bartók, M. Kém. Közl. **1977**, 48, 155-166.
19. Molnár, Á.; Bartók, M. Acta Chim. Acad. Sci. Hung. **1976**, 89, 393-404.
20. Molnár, Á.; Bartók, M. J. Catal. **1981**, 72, 322-327.
21. Yvernault, T.; Mazet, M. Bull. Soc. Chim. Fr. **1967**, 2755-2763.
22. Yvernault, T.; Mazet, M. Bull. Soc. Chim. Fr. **1969**, 638-650.
23. Freidlin, L. Kh.; Sharf, V.Z.; Bartók, M.; Nazaryan, A.A. Izv. Akad. Nauk SSSR **1970**, 310-314.
24. Wittbecker, E.L.; Hall, H.K., Jr.; Campbell, T.W. J. Amer. Chem. Soc. **1960**, 82, 1218-1222.
25. Bartók, M.; Molnár, Á. in The Chemistry of Functional Groups, Supplement E, Part 2; Patai, S., Ed.; Wiley: Chichester, 1980; pp. 721-760.
26. Molnár, Á. in The Chemistry of Functional Groups, Supplement E2, Patai, S., Ed.; Wiley; in preparation.
27. Fry, A. in Mechanisms of Molecular Migrations, Vol. 4; Thyagarajan, B.S., Ed.; Wiley: New York, 1971; pp. 113-196.
28. Cason, F; Allen, C.F. J. Org. Chem. **1949**, 14, 1036-1038.
29. Searles, S., Jr.; Nickerson, R.G.; Witsiepe, W.K. J. Org. Chem. **1959**, 24, 1839-1844.
30. Beynon, J.H. Mass Spectrometry and its Applications to Organic Chemistry; Elsevier: Amsterdam, 1960; p. 296.
31. Silverstein, R.M.; Bassler, G.C.; Morrill, T.C. Spectrometric Identification of Organic Compounds; Wiley: New York, 1981; p.10.