

317. The Formation of Cyclic Ethers by Intramolecular Addition and Substitution Processes in the Reaction of Olefinic Alcohols with Lead Tetraacetate¹). Part I

Preliminary Communication

by Mihailo Lj. Mihailović²), Živorad Čeković, Jezdimir Stanković, Nebojša Pavlović, Stanimir Konstantinović and Silvija Djokić-Mazinjanin

Department of Chemistry, Faculty of Sciences, University of Belgrade, and Institute for Chemistry, Technology and Metallurgy, Belgrade, Yugoslavia

(9. XI. 73)

The lead tetraacetate (LTA) oxidation of saturated alcohols in non-polar solvents affords usually as major products unsubstituted tetrahydrofuran-type ethers, the formation of which involves intramolecular 1,5-hydrogen abstraction by the initially produced alkoxy radicals, followed by internal attack of the hydroxylic oxygen on the electron-deficient δ -carbon atom [2]. On the other hand, when treated with LTA in benzene, unsaturated alcohols containing a spatially accessible Δ^4 - or Δ^5 -olefinic linkage undergo intramolecular addition of the hydroxylic oxygen to the double bond, resulting in the formation of acetoxyated or unsaturated five-membered cyclic ethers (from Δ^4 -alkenols) and six-membered cyclic ethers (from Δ^4 - and Δ^5 -alkenols) [2–4]. The mechanistic course of this internal cyclization is not as yet quite clear; several possibilities have been envisaged, such as initial attack of LTA on the hydroxyl group or on the ethylenic grouping, followed by a free-radical or ionic reaction sequence, or a successive combination of homolytic and heterolytic steps [2–4]³).

In this paper we present results of the LTA oxidation of some simple, conformationally mobile unsaturated open-chain alcohols containing an unsubstituted terminal Δ^3 -, Δ^4 -, Δ^5 -, Δ^6 - and Δ^7 -double bond. Products and yields of these reactions are summarized in the *Scheme*⁴).

The following comments about the results obtained can be made.

1) The absence of cyclic ethers among the reaction products indicates that in Δ^3 -alkenols, such as 1-octen-4-ol (**1**), the hydroxyl oxygen does not undergo intramolecular addition to the double bond or intramolecular substitution at the saturated δ -carbon

¹) Commun. 29 on 'Reactions with lead tetraacetate'. For paper 28 see [1].

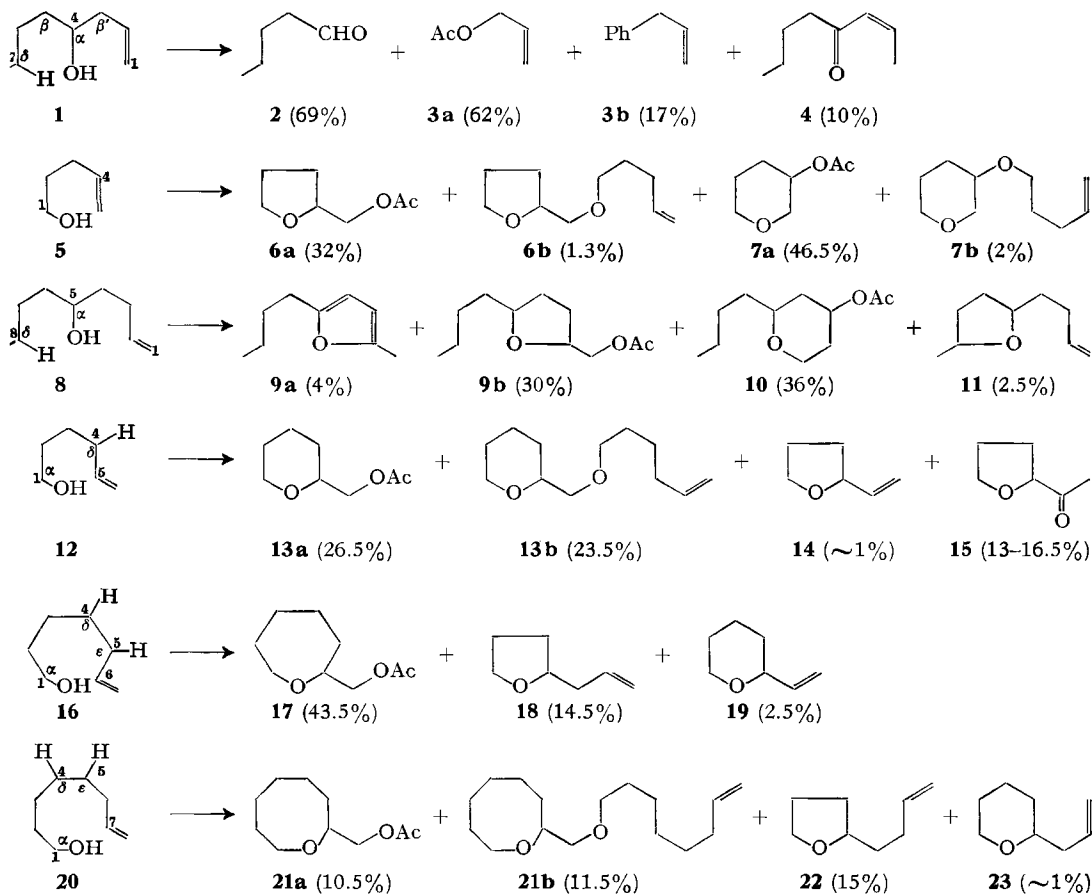
²) Address for correspondence: Department of Chemistry, Faculty of Sciences, Studentski trg 16, P.O.B. 550, 11001 Belgrade, Yugoslavia.

³) The formation of acetoxyated ethers (from 4-penten-1-ol and LTA) has alternatively been formulated as proceeding by a more or less simultaneous decomposition-addition process involving the intermediate alkenyloxy-lead^{IV}-acetate complex [5].

⁴) The structures of the products given in the *Scheme* were established on the basis of elemental microanalysis and spectral data (IR., NMR., mass), and/or by comparison with authentic compounds synthesized independently. Yields were determined planimetrically from analytical GL.-chromatograms. In addition to the products shown, starting alcohols (5–10%), their acetates (5–15%) and small amounts (1–5%) of the corresponding carbonyl compounds (aldehydes or ketones) were usually also found in the reaction mixtures.

Scheme⁴⁾

(solvent: benzene; temp.: 80°; ROH:LTA = 1:1)



atom. The preferred process here is β -fragmentation (which occurs to the extent of about 80%) with the formation of a carbonyl fragment **2** and products (**3a** and **3b**) derived from the relatively stable allyl radical (and/or the corresponding allyl cation) counter-fragment. As described previously [5], 3-buten-1-ol behaves in a similar way.

2) When primary and secondary Δ^4 -alkenols, such as 4-penten-1-ol (**5**) and 1-nonen-5-ol (**8**), are oxidized thermally by LTA in benzene, internal 1,6-addition leading to tetrahydropyran-type ethers (**7** and **10**, respectively) is preferred (particularly in the case of **5**) to 1,5-addition resulting in the formation of five-membered cyclic ethers (**6** and **9**, respectively)⁵⁾. This is in marked contrast to other cyclizations of **5** (and **8**), involving either homolytic processes via intermediate alkenyloxy radicals

⁵⁾ The thermal LTA oxidation of **5** in benzene has been previously reported to give the cyclic ethers **6a** + **7a** in an overall yield of 40% [5] and 71–90% [4] [6], the **6a**:**7a** ratio being 35:65 [5] and 18:82 [4]. (The latter relative proportion, according to our results, does not seem to be correct.)

[6–7] or heterolytic reactions initiated by attack of external reagents on the ethylenic linkage with formation of ionic intermediates [8–9], which all afford exclusively five-membered tetrahydrofuran-type derivatives.

3) A rather dramatic difference in the distribution of cyclization products was observed by changing reaction conditions in the LTA oxidation of 4-penten-1-ol (**5**). Thus, as shown in the Table, whereas the thermal LTA reactions of **5** in benzene alone (runs **a** and **b**) or in starting alcohol as solvent (run **c**) favour closure to a tetrahydropyran ring (**7**), whereby the five-membered and six-membered cyclic ethers are produced in a **6:7** ratio of about 40:60⁵⁾, the UV.-photolytic LTA reaction in benzene (run **d**) and the thermal LTA reaction in benzene/pyridine (run **e**) afford the tetrahydrofuran derivative **6a** in large excess, *i.e.* **6:7** = 97.5:2.5 and 98.8:1.2, respectively. These results indicate that in the LTA oxidation of **5**, reaction conditions can seriously affect the nature and/or reactivity of the intermediate species generated by homolytic and heterolytic pathways [1].

Table⁵⁾

5	LTA	6a	+	6b	+	7a	+	7b	Ratio 6:7
	Reaction conditions								
	(solvent, temp., ROH:LTA)								
(a)	benzene, 80°, 1:1	32		1.3		46.5		2	40 :60
(b)	benzene, 80°, 1:4	30		0.5		58.5		1	34 :66
(c)	5 as solvent, 20°, 10:1	6.5		26		9		37	41.5:58.5
(d)	benzene, UV.-hv, 20°, 1:1.5	75		–		2		–	97.5: 2.5
(e)	benzene, 80°, 1:1 + pyridine (8 mol-equiv.)	79		–		1		–	98.8: 1.2
		(+ 4-pentenal, 12%)							

4) In the thermal LTA oxidations (in benzene) of 5-hexen-1-ol (**12**)⁶⁾, 6-hepten-1-ol (**16**) and 7-octen-1-ol (**20**), as shown in the Scheme, internal addition of the hydroxyl oxygen takes place exclusively on the nearer olefinic carbon, thus furnishing the cyclic ether with the smaller ring, *i.e.* a six-membered ring (**13**) is formed from **12**, a seven-membered ring (**17**) from **16**, and an eight-membered ring (**21**) from **20**. The latter two results are, to our knowledge, the first examples of intramolecular 1,7- and 1,8-addition in Δ^6 - and Δ^7 -ethylenic alcohols, respectively⁷⁾.

5) The LTA oxidation of **5**, **12** and **20** affords not only acetoxyated cyclic ethers (**6a**, **7a**, **13a**, **21a**) but also, in varying amounts, the corresponding alkenyloxy-cyclic ethers (**6b**, **7b**, **13b**; **21b**); the ratio of ethers **a** and **b** appears to be dependent on the relative proportion of starting alcohol and LTA (see Table, runs **a**, **b** and **c**).

6) Intramolecular addition of the hydroxyl oxygen to the olefinic double bond to give cyclic ethers proceeds more easily than ether ring closure by way of intramolecular substitution involving either non-activated δ -carbon atoms, as shown in the LTA reactions of **8** (compare yields of (**9** + **10**) and **11**), **16** (compare yields of **17** and **18**) and **20**

⁶⁾ The LTA oxidation of **12** in refluxing benzene was previously reported to afford the cyclic ether **13a** as sole cyclization product (in 37% yield) [10].

⁷⁾ In the oxymercuration-demercuration of 6-hepten-1-ol (**16**), the intermediately generated 6-carbonium ion does not undergo ring closure to a seven-membered cyclic ether (whereas the same reaction with 5-hexen-1-ol (**12**) produces, *via* a 5-carbon cation, tetrahydropyran in quantitative yield) [9].

(compare yields of **21** and **22**), or even allylic (δ - or ϵ -) C–H bonds which, therefore, do not appear to be particularly activated (by the adjacent ethylenic linkage) for internal H-abstraction, as illustrated by the LTA oxidations of **12** (compare yields of **13** and (**14** + **15**)) and **16** (compare yields of **17** and **19**)⁸).

The authors are grateful to the *Serbian Republic Research Fund* and to the *Serbian Academy of Sciences and Arts* for financial support.

REFERENCES

- [1] *M. Lj. Mihailović, J. Bošnjak & Ž. Čeković*, *Helv.*, in the press.
 [2] a) *K. Heusler & J. Kalvoda*, *Angew. Chem.* **76**, 518 (1964); *Angew. Chem. internat. Edit.* **3**, 525 (1964); b) *M. Lj. Mihailović & Ž. Čeković*, *Synthesis* **1970**, 209, and references cited therein; c) *M. Lj. Mihailović & R. E. Pavtch*, in 'Selective Organic Transformations', Vol. **2**, pp. 97–182; ed. by B. S. Thyagarajan, Wiley-Interscience, New York–London 1972, and references cited therein.
 [3] *R. M. Moriarty*, in 'Selective Organic Transformations', Vol. **2**, pp. 183–237; ed. by B. S. Thyagarajan, Wiley-Interscience, New York–London 1972, and references cited therein.
 [4] *J.-M. Surzur & M.-P. Bertrand*, *Bull. Soc. chim. France* **1973**, 1861, and references cited therein.
 [5] *S. Moon & J. M. Lodge*, *J. org. Chemistry* **29**, 3453 (1964).
 [6] *J.-M. Surzur, P. Cozzone & M.-P. Bertrand*, *C. r. hebd. Séances Acad. Sci. (C)* **1968**, 908.
 [7] a) *J.-M. Surzur, M.-P. Bertrand & R. Nouguier*, *Tetrahedron Letters* **1969**, 4197; b) *M.-P. Bertrand & J.-M. Surzur*, *Bull. Soc. chim. France* **1973**, 2393; c) *R. D. Rieke & N. A. Moore*, *Tetrahedron Letters* **1969**, 2035; d) *R. D. Rieke & N. A. Moore*, *J. org. Chemistry* **37**, 413 (1972).
 [8] a) *D. L. H. Williams*, *Tetrahedron Letters* **1967**, 2001; b) *D. L. H. Williams, E. Bienvenue-Goetz & J. E. Dubois*, *J. chem. Soc. (B)* **1969**, 517; c) *A. Bresson, G. Dauphin, J.-M. Geneste, A. Kergomard & A. Lacourt*, *Bull. Soc. chim. France* **1971**, 1080.
 [9] *H. C. Brown, P. J. Geoghegan, Jr., J. T. Kurek & G. J. Lynch*, *Organometal. Chem. Syn.* **1**, 7 (1970/1971).
 [10] *S. Moon & L. Haynes*, *J. org. Chemistry* **31**, 3067 (1966).

- ⁸) However, with increasing distance between the double bond and the hydroxyl group (in the olefinic alcohol) the case of internal addition relative to intramolecular substitution slowly decreases, as evident from the ratios of 'addition' cyclic ethers to 'substitution' cyclic ethers, *i.e.* for **8**, (**9** + **10**):**11** = 96.5:3.5; for **12**, **13**:(**14** + **15**) = 78:22–74.5:25.5; for **16**, **17**:(**18** + **19**) = 72.5:27.5; for **20**, **21**:(**22** + **23**) = 58:42.

318. Kinetische Untersuchung der durch Imidazol katalysierten Acylübertragung von Thioestern auf Cyanessigeste, einer Modellreaktion zur enzymatischen Knüpfung von C, C-Bindungen von Helmut Wenck¹⁾ und Michael Schallies

aus dem Physiologisch-chemischen Institut der Universität Tübingen

(4. IX. 73)

Zusammenfassung. – Die durch Imidazol katalysierte Acylübertragung von Thioestern auf Cyanessigsäureäthylester in wässrigem Medium als Modellreaktion zur enzymatischen Knüpfung von C, C-Bindungen besteht aus zwei Teilreaktionen: Bildung von N-Acetylimidazol und

¹⁾ Neue Postanschrift: Prof. Dr. H. Wenck, Lehrstuhl für Chemie und Didaktik der Chemie, Pädagogische Hochschule Westfalen-Lippe, Lampingstrasse 3, D-48 Bielefeld, Deutschland.