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# Acyloxyetherifications mediated by lead tetracarboxylates

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ABSTRACT

Lead(IV) tetracarboxylates are capable of reacting with unsaturated alcohols to give the products of cyclic acyloxyetherification, usually as a mixture of tetrahydro-2*H*-pyranyl and tetrahydrofuranyl compounds.

Ligand coupling processes[1] mediated by lead(IV) have recently been demonstrated to enable synthetically useful carbon-carbon bond forming reactions,[2–7] and cyclisation reactions are beginning to emerge which are driven by this reagent.[8,9] We have reported that the reaction of lead(IV) tetracarboxylates with carboxylic acids containing unsaturated side chains gives acyloxylactone products in a diastereoselective process, in which one of the carboxylate ligands becomes incorporated into the lactone product;[10] the reaction can be extended to lead(IV) tetrazolates to give the analogous outcome. Mechanistically, it is thought that these cyclisations occur by initial carboxylate metathesis followed by π-complexation prior to lactone formation driven by reductive elimination from lead(IV).[11] It was of interest to establish whether this process might be extendable to other substrates, and obvious candidates were unsaturated alcohols. Electrophilic halogen-mediated etherifications are known,[12] and similar processes with thallium(III),[13,14] mercury(II)[15] and palladium(II)[16,17] have been reported. The reaction of lead(IV) tetraacetate with 3-butenol has been thoroughly investigated by Moon[18–23] who identified several fragmentation pathways that proceed through either radical or cationic intermediates, initiated by the formation of an alkoxytriacetate lead(IV) intermediate.[24–26] However, when the chain length is long enough (e.g., with 4-pentenol as the substrate), tetrahydrofuranyl and tetrahydropyranyl products are observed.[23,27] Mihailovic took this further and demonstrated for a range of unsaturated alcohols that products of cyclisation could be readily formed,[28] and similar cycloetherifications were identified in bicyclic templates.[29] However, it was found that the distribution of products depended strongly on the nature of the solvent and on the application of thermal or photochemical conditions. Of interest was an examination of this process with lead tetrathiophene carboxylate, which has been shown to be an effective reagent for alcohol oxidations[30] and plumbolactonisations.[10]

4-Penten-1-ols with alkyl substituents at positions 2–4 were reacted with lead(IV) tetra(2-thiophenecarboxylate), readily prepared by metathesis of lead tetraacetate with 4 equiv of 2-thiophenecarboxylic acid, in α,α,α-trifluorotoluene at 90 °C under argon.[10] The reactions were monitored visually and once the colour had changed from bright yellow to white, the reactions were stopped, and the solvent was removed. Purification by column chromatography gave the tetrahydropyrans **2a**–**e** and tetrahydrofurans **3a**–**e**, as shown in Scheme 1 and Table 1. The best yield was obtained for 4-methylpent-4-en-1-ol **1d** which gave predominantly the tetrahydropyranyl product **2d**; all other substrates gave a mixture of tetrahydropyranyl and tetrahydrofuranyl products **2a**–**c**,**e** and **3a**–**c**,**e**, in which the former generally predominated, in moderate combined yields. The ring assignment was made using a combination of techniques: HMBC experiments confirmed the pyran ring as a result of three-bond coupling between the carbonyl carbon and H3, C6 and H2 and of C2 with H6; for the tetrahydrofuran-type products, correlation of the carbonyl carbon to both methylene hydrogens and of C2 to H5 confirmed the proposed structure (Fig. 1). Of interest is that the presence of a double bond substituent did not hinder the closure of 4-hexenol, leading to ethers **2e** and **3e**, and that products arising from 5-*exo* and 6-*endo* cyclisation were obtained; this is in marked contrast to plumbolactonisations[31] using lead(IV) tetra(2-thiophenecarboxylate), for which double bond substituents are not tolerated, and only 5-*exo* cyclisations are observed. No products arising from direct 1,2-dicarboxylation of the double bond were isolated.

The stereochemistry of the tetrahydropyran products was established by n.O.e. analysis (Fig. 2); ether **2b** was found to be the *cis*-diastereomer, but **2c** and **2e** were found to be the *trans*-diastereomers. The stereochemistry of the minor tetrahydrofuran derivatives was not examined. These cyclisations appear to be analogous to palladium chloride and mercury(II) trifluoroacetate-mediated processes, and the observed regiochemistry is in agreement with electrophile-induced cyclisations to tetrahydropyrans and tetrahydrofurans as reported by Cardillo and Orena,[32] for which the formation of 6-membered rings proceeds under high

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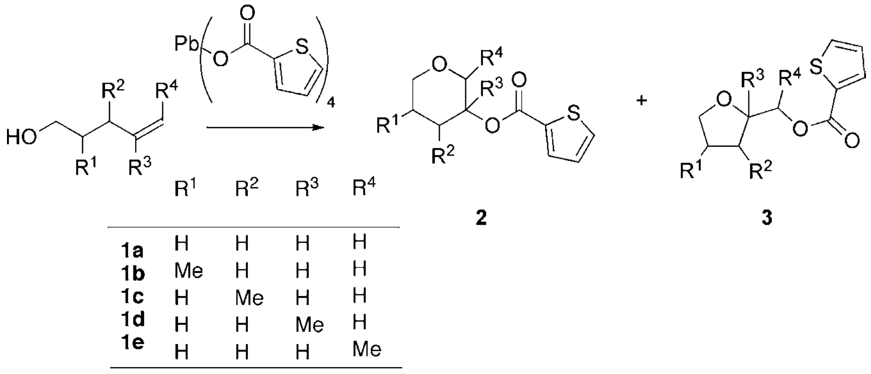

| | R1 | R2 | R3 | R4 |
|---|---|---|---|---|
| **1a** | H | H | H | H |
| **1b** | Me | H | H | H |
| **1c** | H | Me | H | H |
| **1d** | H | H | Me | H |
| **1e** | H | H | H | Me |

**Scheme 1.**

**Table 1**
Results of plumboetherification of substituted pent-4-en-1-ols according to Scheme 1

| Entry | $R^1$ | $R^2$ | $R^3$ | $R^4$ | Reaction time | Yield **2a**–**e** (%) | Yield **3a**–**e** (%) |
|---|---|---|---|---|---|---|---|
| **a** | H | H | H | H | 30 min | 26 | 10 |
| **b** | Me | H | H | H | 2 h | 15 | 8 |
| **c** | H | Me | H | H | 1 h | 20 | 17 |
| **d** | H | H | Me | H | 45 min | 68 | – |
| **e** | H | H | H | Me | 25 min | 15 | 14 |

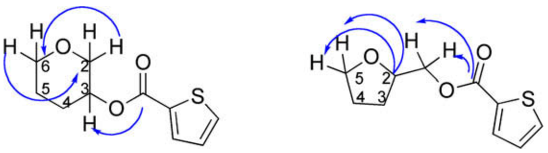

**Figure 1.** Assingment of ring structures by HMBC cross peaks analysis.

**Table 2**
Temperature/time studies of the reaction of 4-penten-1-ol with lead(IV) tetra(2-thiophenecarboxylate)

| Entry | Temperature (°C) | Time | Yield **2a** (%) | Yield **3a** (%) |
|---|---|---|---|---|
| 1 | 90 | 15 min | 34 | 18 |
| 2 | 60 | 2 h | 30 | 22 |
| 3 | 30 | 22 h | 37 | 24 |

1,2- or 1,3-stereocontrol and the equatorially substituted compounds are formed preferentially. Yields of cyclisation products could be dramatically improved by conducting the reactions at elevated temperature or for longer reaction times as shown in Table 2, although the ratio of tetrahydropyranyl and tetrahydrofuranyl products remained almost constant.

To investigate the possibility of a radical pathway for the reaction, 4-penten-1-ol was treated with lead(IV) tetra(2-thiophenecarboxylate) in the presence of 1,1-diphenylethylene; this approach has in the past been applied successfully to demonstrate the presence of radical intermediates by trapping.[33,34] Under these conditions, however, both the 5- and 6-membered ring ether products were isolated in 24% and 40% yields, respectively, and 1,1-diphenylethylene was recovered quantitatively, implying that radical intermediates are not involved in the reaction. It seems most probable that initial carboxylate/alcohol exchange at the lead(IV) centre gives a lead-alkoxide type intermediate, and that this is followed by cyclisation in a manner analogous to that which we had proposed previously,[11] possibly by ligand coupling with the intermediacy of a σ-lead(IV) intermediate.

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## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.12.071.

## References and notes

1. Oae, S.; Uchida, Y. *Acc. Chem. Res.* **1991**, *24*, 202–208.
2. Abramovitch, R. A.; Barton, D. H. R.; Finet, J.-P. *Tetrahedron* **1988**, *44*, 3039–3071.
3. Barton, D. H. R. In *Heteroatom Chemistry*; Block, E., Ed.; VCH Publishers: New York, 1990; p Chapter 5.

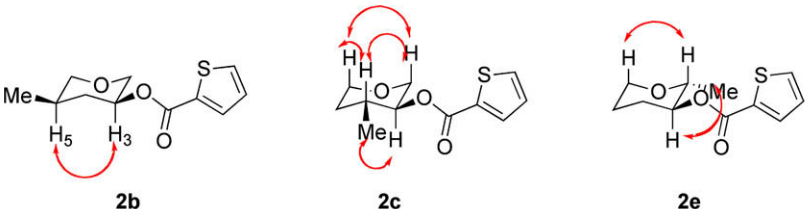

**Figure 2.** Stereochemical assignment by NOE analysis.

4. Barton, D. H. R.; Parekh, S. I. *Pure Appl. Chem.* **1993**, *65*, 603–608.
5. Pinhey, J. T. *Aust. J. Chem.* **1991**, *44*, 1353–1382.
6. Pinhey, J. T. In *Comprehensive Organometallic Chemistry II*; McKillop, A., Ed.; Pergamon: Oxford, 1995. pp. Vol. 11, Chapter 11.
7. Elliott, G. I.; Konopelski, J. P. *Tetrahedron* **2001**, *57*, 5683–5705.
8. Elkhayat, Z.; Safir, I.; Dakir, M.; Arseniyadis, S. *Tetrahedron: Asymmetry* **2007**, *18*, 1589–1602.
9. Khan, F. A.; Sudheer, C.; Soma, L. *Chem. Commun.* **2007**, 4239–4241.
10. Moloney, M. G.; Nettleton, E.; Smithies, K. *Tetrahedron Lett.* **2002**, *43*, 907–909.
11. Moloney, M. G. *Main Group Met. Chem.* **2001**, *24*, 653–660.
12. Semmelhack, M. F. *Comprehensive Organic Synthesis: Selectivity, Strategy and Efficiency in Modern Organic Chemistry: Additions to and substitution at C–C π bonds*, 1992, Vol. 4.
13. Ferraz, H. M. C.; Brocksom, T. J.; Pinto, A. C.; Abla, M. A.; Zocher, D. H. T. *Tetrahedron Lett.* **1986**, *27*, 811–814.
14. Michael, J. P.; Ting, P. C.; Bartlett, P. A. *J. Org. Chem.* **1985**, *50*, 2416–2423.
15. Holmes, C. P.; Bartlett, P. A. *J. Org. Chem.* **1989**, *54*, 98–108.
16. Semmelhack, M. F.; Zhang, N. *J. Org. Chem.* **1989**, *54*, 4483–4485.
17. McCormick, M.; Monahan, R.; Soria, J.; Goldsmith, D.; Liotta, D. *J. Org. Chem.* **1989**, *54*, 4485–4487.
18. Moon, S.; Campbell, W. *Chem. Commun.* **1966**, 470.
19. Moon, S.; Haynes, L. *J. Org. Chem.* **1966**, *31*, 3067–3069.
20. Moon, S.; Clifford, P. R. *J. Org. Chem.* **1967**, *32*, 4017–4020.
21. Moon, S.; Waxman, B. H. *J. Org. Chem.* **1969**, *34*, 288–292.
22. Moon, S.; Bohm, H. *J. Org. Chem.* **1972**, *37*, 4338–4340.
23. Moon, S. *J. Org. Chem.* **1964**, *29*, 3456–3458.
24. Mosher, W. A.; Kehr, C. L.; Wright, L. W. *J. Org. Chem.* **1961**, *26*, 1044–1046.
25. Cainelli, G.; Kamber, B.; Keller, J.; Mihailovic, M. L.; Arigoni, D.; Jeger, O. *Helv. Chim. Acta* **1961**, *44*, 518–528.
26. Partch, R. E. *J. Org. Chem.* **1963**, 276–277.
27. Moon, S.; Lodge, J. M. *J. Org. Chem.* **1964**, *29*, 3453–3456.
28. Mihailovic, M. L.; Cekovic, Z.; Stankovic, J.; Pavlovic, N.; Konstantinovic, S.; Djokic-Mazinjanin, S. *Helv. Chim. Acta* **1973**, *56*, 3056–3059.
29. Moriarty, R. M.; Kapadia, K. *Tetrahedron Lett.* **1964**, 1165–1170.
30. Buston, J. E. H.; Howell, H. J.; Moloney, M. G.; Poster, V. *Main Group Met. Chem.* **1998**, *21*, 51–54.
31. Cottrell, I.F.; Cowley, A.R.; Croft, L.; Hymns, L.; Moloney, M.G.; Nettleton, E.J.; Smithies, K.; Thompson, A.L. *Tetrahedron*, **2009**, in press.
32. Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321–3408.
33. Norman, R. O. C.; Thomas, C. B. *J. Chem. Soc. B* **1967**, 771–779.
34. Kochi, J. K. *J. Am. Chem. Soc.* **1965**, *87*, 1811–1812.