Tetrahedron: *Asymmetry* 26 (2015) 981–1035

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Tetrahedron: Asymmetry Report Number 157

Stimulating excursions into organolead chemistry: modular domino sequences triggered by oxidative cleavage

Valentina Abet, Rafael R. Castillo, Maurizio Aquino, Zoila Gandara, Siméon Arseniyadis *

Centre de Recherche de Gif, Institut de Chimie des Substances Naturelles, CNRS, F-91198 Gif-sur-Yvette Cedex, France

ARTICLE INFO

Article history:
Received 6 July 2015
Accepted 5 August 2015
Available online 21 September 2015

ABSTRACT

The present report intends to highlight the main lines of our investigation on a series of modular domino reactions focusing on a multi-task reagent, namely $Pb(OAc)_4$ in conjunction with an olefin as a source of complexity. It covers the design, development, and mechanistic aspects of a domino methodology discovered in our laboratory, which presents numerous challenges, including issues of chemo-, regio-, and diastereoselectivities. The principal characteristic of the chemistry presented is the potential of creating cyclic arrays that can be suitably functionalized for subsequent conversion into various complex systems. The effects of systematic variation of domino promoter, substitution pattern, solvent, temperature, and microwave activation on the outcome of the domino reaction are presented. In general terms, the domino chemistry reported here could be conveniently divided into two categories, dealing with first and second generation domino probes based on the nature of the angular substituent, each of which will be addressed in turn. This review is not intended to give an extensive coverage of the various uses of $Pb(OAc)_4$ in synthesis reported in the literature, but will expose relevant reactions where appropriate focusing exclusively on multi-stage transformations initiated by the reagent.

Contents

---

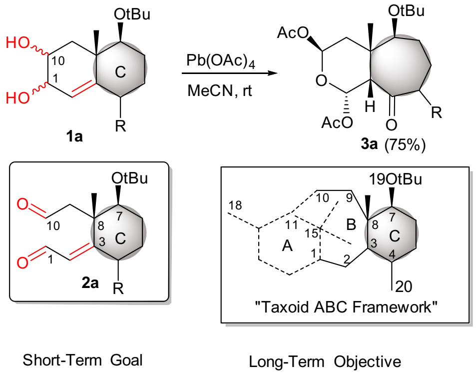
* Corresponding author.
E-mail address: simeon.arseniyadis@cnrs.fr (S. Arseniyadis).

http://dx.doi.org/10.1016/j.tetasy.2015.08.001
0957-4166/© 2015 Elsevier Ltd. All rights reserved.

1. Introduction and historical background

To assist understanding of the processes taking place, we adopt an overview of the mechanistic approach from the outset while the presentation of the results is organized according to the path followed after the oxidative cleavage step of the domino process. First-generation domino probes will be discussed in Part I. The second-generation modular domino reactions and the subsequent opening of the domino products to a variety of polycyclic systems will be presented in Part II. Special emphasis will be given to substrate–reagent–solvent scope with emphasis on mechanistic aspects and the feasibility of selective multi-directional domino transformations to form complex, stereodefined heterocyclic systems. The reviews already reported in the literature gave major importance to the uses of $Pb(OAc)_4$ in synthesis and methodology but were not much concerned with the reagent as a domino promoter. The present review deals with this.

Lead tetraacetate, a multipurpose oxidizing agent widely used in organic chemistry, is capable of reacting with a variety of functional groups in various solvents; its use in organic chemistry has been reviewed.[1] The basis of this review is the unsuspected course of the oxidative cleavage of type-**1** unsaturated *vic*-diols allowing the production of a significantly more complex molecule in a single synthetic operation.[2] During our synthetic program aimed at the total synthesis of taxoids, we needed a convenient source for suitably substituted, optically homogeneous, type-**2** cyclohexane derivatives to be used as right-half building blocks. In the course of attempting to reach this objective we serendipitously discovered the $Pb(OAc)_4$-mediated domino transformations, a process wherein several bond making/breakings are performed in a row. Thus, back in 1993 Dr Dmitry Yashunsky was the first to isolate a cycloheptanone-fused bis-acetoxyacetal **3a** while attempting to prepare a taxoid right-half building block **2a** from a Wieland–Miescher ketone derived octalin-diol **1a** (Scheme 1).[3] The $Pb(OAc)_4$-mediated oxidative cleavage of the latter gave rise unexpectedly to a ring expansion/rearrangement process in a single synthetic operation. Completion required 50 h of stirring in MeCN at rt. We designed this reaction for a totally different purpose, and albeit not appropriate for taxoid construction this serendipitous discovery turned out to be the key to the work presented in this review.[4] Even though a vast array of ring-expansion reactions exists in the literature, the mechanism of this domino process is unique while it offers numerous advantages over traditional variants. The reaction is trivial to set up and run and can be carried out on multigram scale.



Scheme 1. Look for something, find something else; the practice of total synthesis can often yield unexpected results.

Looking for further examples to confirm the generality, we elected to test the reduced **4b** as well as the lower homologs of **1a**, the Hajos–Parrish ketone derived unsaturated diols **4a** and **6a**, respectively.[5] Saturated bicyclic diols of type-**4** upon treatment with $Pb(OAc)_4$ led to the expected type-**5** dialdehydes resulting from a standard glycol fission. Insertion of an olefin into the bicyclic ring system completely modified the reaction outcome. When treated with 2 equiv of $Pb(OAc)_4$, **6a** suffered glycol fission to give **7a**, which initiated again an unprecedented sequence of events affording high molecular complexity and ring expansion under very mild conditions (compound **8a**, Scheme 2). These series required less than 12 h rt stirring in MeCN for completion. Thus, the credit goes to the olefin[6] as this is exemplified in Scheme 2. The unexpected course of this domino reaction was not without interest. What attracted us to this transformation was the