Available online at www.sciencedirect.com

ScienceDirect

Mendeleev Commun., 2021, **31**, 696–697

Mendeleev Communications

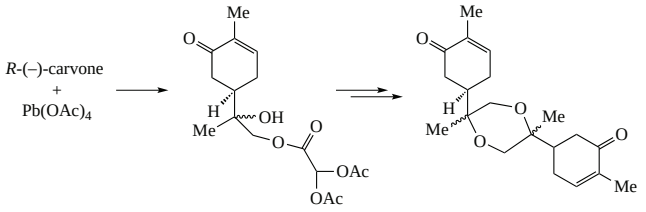
Lead tetraacetate assisted formation of bis(acetoxy)acetic acid derivative from carvone

Gul'naz R. Sunagatullina,* Alexander N. Lobov and Mansur S. Miftakhov

Ufa Institute of Chemistry, Ufa Federal Research Centre of the Russian Academy of Sciences, 450054 Ufa, Russian Federation. Fax: +7 347 235 6066; e-mail: tsynth@anrb.ru

DOI: 10.1016/j.mencom.2021.09.034

***R*-Carvone on heating with $Pb(OAc)_4$ in benzene gives (2*RS*)-2-hydroxy-2-[(1*S*)-4-methyl-5-oxocyclohex-3-en-1-yl)]-prop-1-yl bis(acetoxy)acetate. Alkaline hydrolysis of this compound affords the corresponding diol which under acidic catalysis is transformed into bis-hydroxy ether and 1,4-dioxane derivatives.**

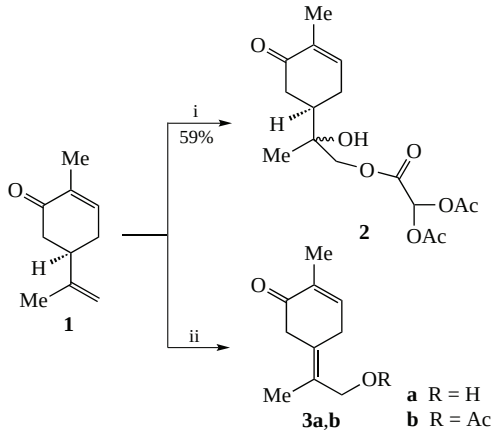


Keywords: carvone, lead tetraacetate, *gem*-acetoxylation reactions, diols, dimers, 1,4-dioxanes.

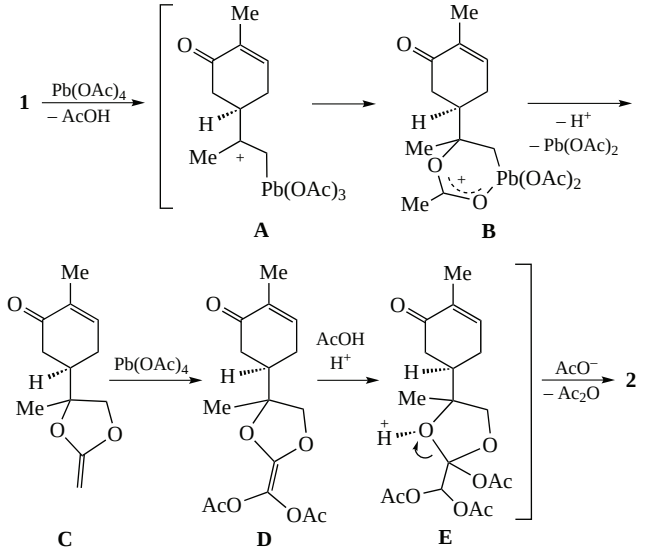
The availability, low cost, and obvious synthetic potential of *R*-carvone favored its widespread use as a chiral matrix in targeted synthesis.[1,2] In a search for new chiral synthons, in this work we studied the reaction of *R*-carvone with $Pb(OAc)_4$. This salt can act as a radical or ionic oxidant and participate in substitution, elimination, fragmentation, and other reactions.[3–5] In our hands, the reaction of *R*-carvone **1** with $Pb(OAc)_4$ in refluxing benzene produced compound **2** in 59% yield (Scheme 1) as a mixture of diastereomers at the side quaternary methyl-containing center in a 1 : 1.2 ratio [^{1}H NMR, based on the intensity of the signals of sp^2-H at C(3)]. The configuration of chiral centers in diastereomers **2** was not determined. We explain the observed chemoselectivity, *i.e.*, oxygenation in the side isopropenyl moiety instead of the possible α-acetoxylation, by the fact that the carvone keto group is not enolized under the experimental conditions.

As for the reported close precedents of this outcome, we found only a single example of carvone acetoxylation with lead tetraacetate to give 8-hydroxy derivative **3a** and its acetate **3b**.[5] We also failed to find structures with topology similar to **2**. As concerns the reactions of $Pb(OAc)_4$ with olefins, it is of note that, depending on the solvent (AcOH, MeOH, PhH), the formation of products of double bond, such as vicinal diacetates, methoxy acetates, hydroxy acetates, monoacetates, *gem*-diacetoxy derivatives, *etc*., is not unknown.[6–8] In fact, *p*-methoxystyrene reacts with $Pb(OAc)_4$ to give *gem*-diacetate $MeOC_6H_4CH_2CH(OAc)_2$ in a high yield. The reactions of $Pb(OAc)_4$ with ketones bring about their α-acetoxy derivatives.[3,9]

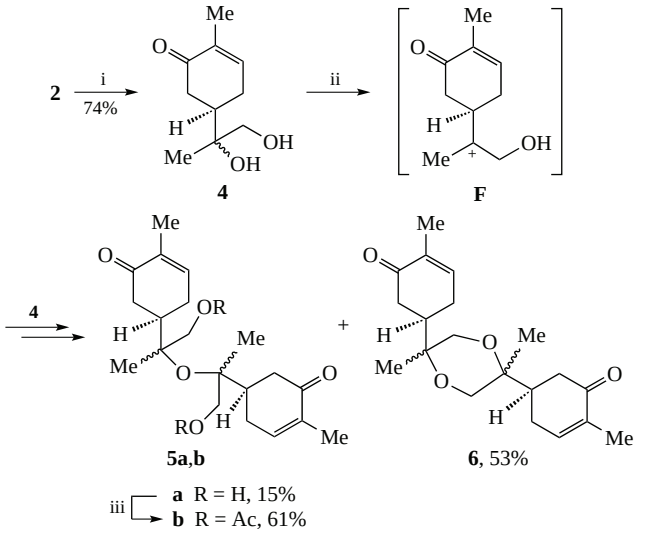
The main difficulties in justifying the suggested mechanism of this reaction are related to the 'formation' of the tertiary alcohol function in abnormal product **2** (Scheme 2). Regardless of the ionic or radical nature of the reaction, one should expect that cationoid intermediate **A** appears at the initial stages, which *via* delocalized cation **B** is converted to ketene ethylenedioxy acetal **C** with release of H^+ and then $Pb(OAc)_2$. Electron rich compound **C** readily undergoes a substitution reaction with $Pb(OAc)_4$ to give intermediate **D**. Further, H^+-catalyzed acetolysis of **D** and ring opening in ortho ester **E** gives stabilized cation, which collapses by recombination with AcO^- to afford final product **2** and Ac_2O.



Scheme 1 *Reagents and conditions*: i, $Pb(OAc)_4$ (4 equiv.), PhH, 60 °C, 48 h; ii, $Pb(OAc)_4$ (ref. 5).



Scheme 2



Scheme 3 *Reagents and conditions*: i, K_2CO_3–MeOH, room temperature, 4 h; ii, $CDCl_3$–HCl (cat.), room temperature, 12 h; iii, AcCl, Et_3N, CH_2Cl_2, room temperature, 3 h.

Methanolysis of ester **2** (MeOH–K_2CO_3) furnishes diol **4** in 74% yield (Scheme 3). In the $CDCl_3$–HCl (cat.) medium, diol **4** smoothly gives bis-hydroxy ether **5a** and 1,4-dioxane derivative **6**. Acylation of diol **5a** affords diacetate **5b**. The isomeric composition (~1 : 1.1–1.2) established at the stage of the synthesis of **2** is nearly retained upon transition from diol **4** to ethers **5a**,**b** and dioxane **6**. This situation is explained by the fact that these reactions occur through planar carbocationic intermediates **A** and **F** (Schemes 2 and 3), and the nucleophile can approach with equal probability from both sides (in an intramolecular way, among others). The possible pathways for the formation of products **5a** and **6** from diol **4** are outlined in Online Supplementary Materials.

To sum up, instead of the possible C^6-acetoxylation of carvone, the reaction with $Pb(OAc)_4$ led to anomalous product **2** with involvement of the lateral double bond. The suggested pathways for its formation and fragmentation of acyclic diacetate **5b** and 1,4-dioxane derivative **6** in the mass spectra are also of interest.

This work was supported by the Ministry of Education and Science of the Russian Federation (state task program no. AAAA-A17-117011910032-4) and by the Russian Foundation for Basic Research (grant no. 20-33-90039).

Spectral studies were performed using equipment available at the Center for Collective Use ‘Chemistry’, Ufa Institute of Chemistry, Ufa Federal Research Center, Russian Academy of Sciences.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.09.034.

References

1 H. Hagiwara, *Nat. Prod. Commun*., 2016, **11**, 1391.
2 H. Hagiwara, *Nat. Prod. Commun*., 2013, **8**, 935.
3 M. L. Mihailović, Ž. Čeković and B. M. Mathes, *Lead(IV) Acetate*, Wiley, 2005, doi: 10.1002/047084289x.rl007.
4 M. L. Mihailović, L. Lorenc, M. Gašić, M. Rogić, M. Melera and A. Stefanović, *Tetrahedron*, 1966, **22**, 2345.
5 T. J. De Pascual and B. I. Sanchez, *An. Quim*., 1976, **7a**, (I), 76.
6 R. Criegee, P. Dimroth, K. Noll and R. Simon, *Chem. Ber*., 1957, **90**, 1070.
7 A. Lethbridge, R. O. C. Norman and C. B. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1929.
8 A. Lethbridge, R. O. C. Norman, C. B. Thomas and W. J. E. Parr, *J. Chem. Soc., Perkin Trans. 1*, 1975, 231.
9 E. M. Sanchez Fernandez, J. I. Candela Lena, E. Altinel, N. Birlirakis, A. F. Barrero and S. Arseniyadis, *Tetrahedron: Asymmetry*, 2003, **14**, 2277.

Received: 13th April 2021; Com. 21/6521