SYNLETT
Spotlight 270

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

L-Ascorbic Acid

Compiled by Bernhard Füger

Bernhard Füger was born in Berlin, Germany in 1979. After completing his diploma thesis in 2005 at Freie Universität Berlin under the supervision of Prof. Dr. P. Roesky he joined the research group of Prof. Dr. C. Bolm at RWTH Aachen University, Germany. As a member of DFG research training group (GRK 440) he is currently pursuing his doctoral work. His research is focused on new methods for the synthesis of heterocyclic sulfoximines.

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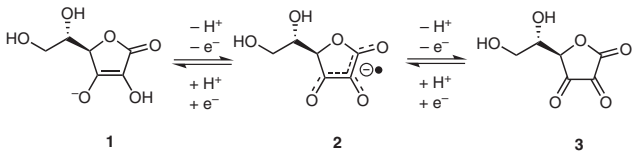
Introduction

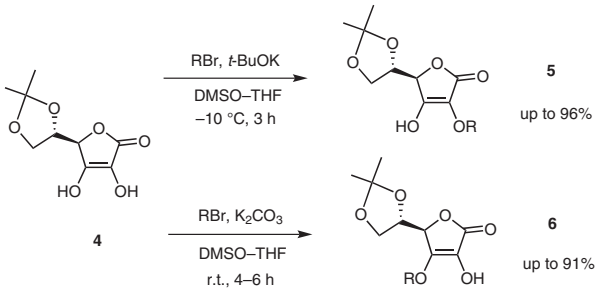
L-ascorbic acid, also known as Vitamin C, has an important role in physiology. As an essential vitamin, it has to be taken regulary by mammals which cannot produce it themselves. It serves to prevent deseases and has proven to act beneficially in the human body. Moreover, it is used in large amounts in the food industry as a nutritional additive and as a radical scavenger to e.g. prevent the oxidative degradation of lipids in food. The oxidation of L-ascorbic acid (or its monoanion **1**) proceeds via monodehydro-L-ascorbic acid (radical anion **2**), which disproportionates to L-ascorbate (**1**) and dehydro-L-ascorbic acid (**3**) (Scheme 1).[1]



Scheme 1

L-ascorbic acid can be synthesized in large amounts from D-glucose by a combination of chemical and microbiological steps in an overall yield of 66%.[2]

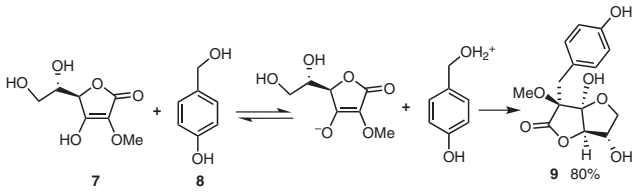
Despite its physiological significance, the chemistry of L-ascorbic acid remained unexplored for a long time. This is probably due to its many reaction possibilities and the resulting lack of chemo- and/or regioselectivity. Procedures for selective functionalization of L-ascorbic acid had to be developed before any further utilization was possible. For example, highly regioselective O-alkylation was described recently: 5,6-*O*-Isopropylidene protected L-ascorbic acid **4** reacts with many electrophiles to yield 2-O-substituted products **5** or 3-O-substituted products **6** in excellent yields and regioselectivities, depending on the reaction conditions (Scheme 2).[3]



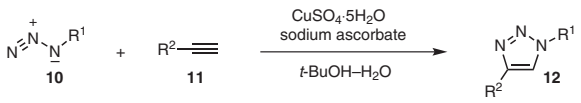
Scheme 2

Abstracts

(A) L-Ascorbic acid is able to react selectively as a C-nucleophile. Poss and Belter synthesized bicyclic natural product delesserine (**9**) from L-ascorbic acid derivative **7** and 4-hydroxybenzyl alcohol (**8**) in good yield. By use of substituted 4-hydroxybenzyl alcohol derivatives, natural products rhodomelol and methylrhodomelol could also be obtained.[4]



(B) The sodium salt of L-ascorbic acid is used as a reductant in the recently developed and widely applied copper(I)-catalyzed regioselective synthesis of 1,2,3-triazoles **12** from organic azides **10** and alkynes **11**. Among the myriad of reactions of this type, the combination of $CuSO_4$ hydrate and sodium ascorbate is the most utilized way to produce the catalytically active Cu(I) species.[5]



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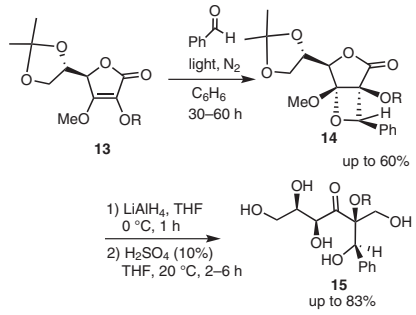
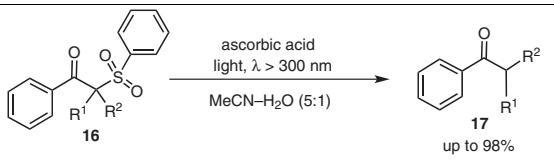
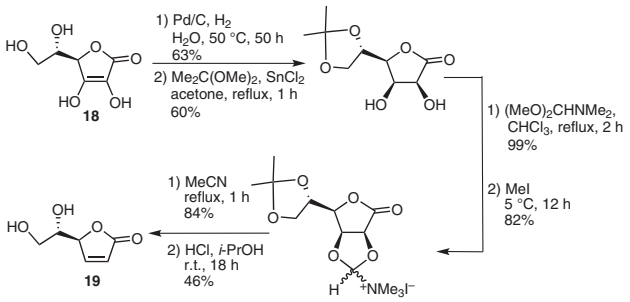
(C) The conjugated electron-rich enediol moiety in L-ascorbic acid is an unusual and interesting functionality. Thopate et al. used a Paterno–Büchi reaction to convert L-ascorbic acid derivatives **13** into chiral oxetanes **14**. These are attractive intermediates for the synthesis of chiral polyols **15** through ring-opening reactions.[6]



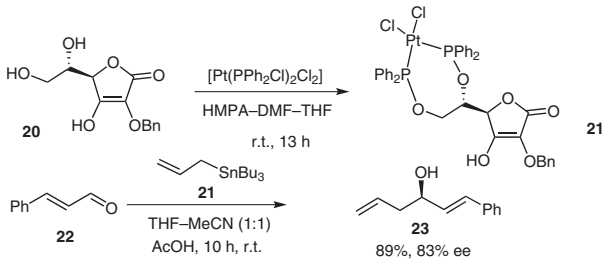
(D) The reductive desulfonylation of β-ketosulfones **16** takes place efficiently under irradiation with light ($\lambda > 300$ nm) in the presence of ascorbic acid, as described by Liu et al. Desulfonylated products **17** were obtained in excellent yields. Furthermore, double or triple bonds were left intact under these reaction conditions.[7]



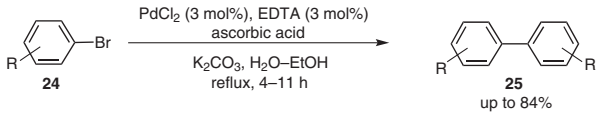
(E) L-ascorbic acid is an ideal educt for the synthesis of enantiomerically pure 4-substituted butenolides **19**, which are important chiral synthons for the synthesis of natural products. Godefroi and co-workers developed the synthesis of **19** by a didehydroxlation sequence starting from L-ascorbic acid (**18**).[8]



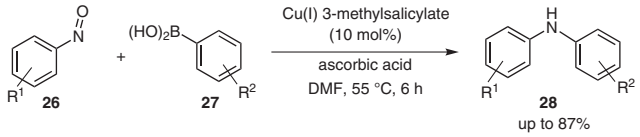
(F) Samuelson and co-workers described the synthesis of chiral platinum-bisphosphinite complexes **21** with a backbone stemming from 2-O-benzylated L-ascorbic acid **20**. These complexes were successfully applied as catalysts in chemical transformations, e.g., in the asymmetric allylation of cinnamaldehyde (**22**) yielding chiral alcohol **23** in high yield and with good enantioselectivity.[9]



(G) Singh and Ram reported the palladium(II) chloride/EDTA catalyzed biaryl homocoupling of both electron-deficient and electron-rich aryl bromides **24** in the presence of L-ascorbic acid as reductant. Homocoupled products **25** with various substitution patterns were obtained in yields up to 84%.[10] Compared to other homocoupling procedures, this method is enviromentally safer, more selective and does not require an inert atmosphere.



(H) The reductive copper(I)-mediated amination of aromatic nitroso compounds **26** with aryl boronic acids **27** was described by Liebeskind and co-workers. Here, the use of L-ascorbic acid as the terminal reductant proved to be very beneficial and superior to other reducing agents. Diarylamines **28** were obtained with a variety of functional groups in good yields.[11]



References

(1) (a) Deifel, A. *Chem. Unserer Zeit* **1993**, *27*, 198. (b) Liao, M.-L.; Seib, P. A. *Food Chemistry* **1988**, *30*, 289.
(2) Grüssner, A.; Reichstein, T. *Helv. Chim. Acta* **1934**, *17*, 311.
(3) Olabisi, A. O.; Wimalasena, K. *J. Org. Chem.* **2004**, *69*, 7026.
(4) Belter, R. K.; Poss, A. J. *J. Org. Chem.* **1988**, *53*, 1535.
(5) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51.
(6) Thopate, S. R.; Kulkarni, M. G.; Puranik, V. G. *Angew. Chem. Int. Ed.* **1998**, *37*, 1110.
(7) Liu, Q.; Han, B.; Liu, Z.; Yang, L.; Liu, Z.-L.; Yu, W. *Tetrahedron Lett.* **2006**, *47*, 1805.
(8) Vekemans, J. A. J. M.; Boerekamp, J.; Godefroi, E. F.; Chittenden, G. J. F. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 266.
(9) (a) Sharma, R. K.; Samuelson, A. G. *Tetrahedron: Asym.* **2007**, *18*, 2387. (b) Sharma, R. K.; Nethaji, M.; Samuelson, A. G. *Tetrahedron: Asym.* **2008**, *19*, 655.
(10) Ram, R. N.; Singh, V. *Tetrahedron Lett.* **2006**, *47*, 7625.
(11) Yu, Y.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2004**, *6*, 2631.