

SYNLETT Spotlight 270

L-Ascorbic Acid

Compiled by Bernhard Fuger

Bernhard Fuger was born in Berlin, Germany in 1979. After completing his diploma thesis in 2005 at Freie Universitat 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.

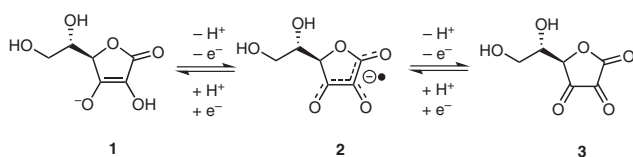
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This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Introduction

L-ascorbic acid, also known as Vitamin C, has an important role in physiology. As an essential vitamin, it has to be taken regularly by mammals which cannot produce it themselves. It serves to prevent diseases 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

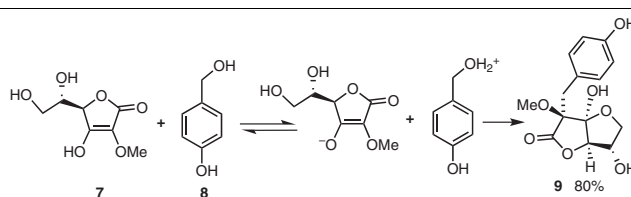


Scheme 1

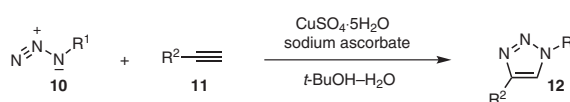
L-ascorbic acid can be synthesized in large amounts from D-glucose by a combination of chemical and microbiological steps in an overall yield of 66%.²

Abstracts

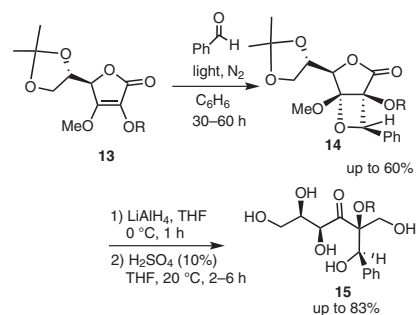
(A) L-Ascorbic acid is able to react selectively as a C-nucleophile. Poss and Belter synthesized bicyclic natural product delesslerine (**9**) from L-ascorbic acid derivative **7** and 4-hydroxybenzyl alcohol (**8**) in good yield. By use of substituted 4-hydroxybenzyl alcohol derivatives, natural products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



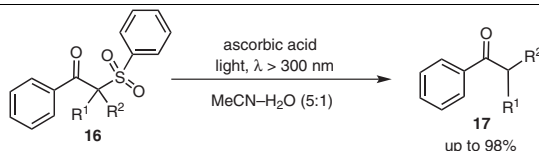
(B) The sodium salt of L-ascorbic acid is used as a reductant in the recently developed and widely applied copper(I)-catalyzed regioselective synthesis of 1,2,3-triazoles **12** from organic azides **10** and alkynes **11**. Among the myriad of reactions of this type, the combination of CuSO₄ hydrate and sodium ascorbate is the most utilized way to produce the catalytically active Cu(I) species.⁵



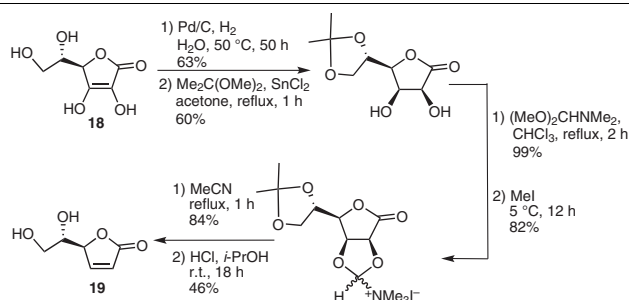
(C) The conjugated electron-rich enediol moiety in L-ascorbic acid is an unusual and interesting functionality. Thopate et al. used a Paterno–Büchi reaction to convert L-ascorbic acid derivatives **13** into chiral oxetanes **14**. These are attractive intermediates for the synthesis of chiral polyols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



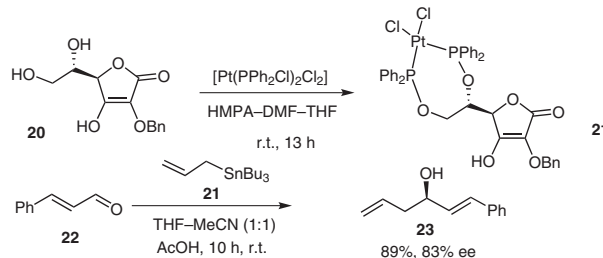
(D) The reductive desulfonation of β -ketosulfones **16** takes place efficiently under irradiation with light ($\lambda > 300$ nm) in the presence of ascorbic acid, as described by Liu et al. Desulfonated products **17** were obtained in excellent yields. Furthermore, double or triple bonds were left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



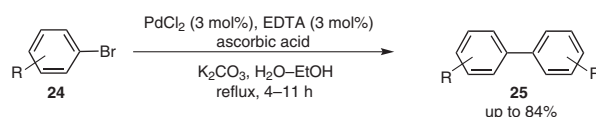
(E) L-Ascorbic acid is an ideal educt for the synthesis of enantiomerically pure 4-substituted butenolides **19**, which are important chiral synthons for the synthesis of natural products. Godefroi and co-workers developed the synthesis of **19** by a didehydroxlation sequence starting from L-ascorbic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



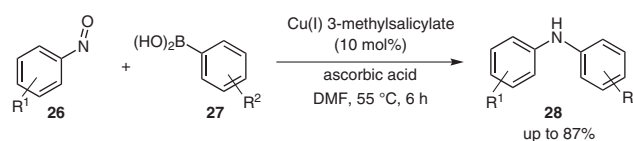
(F) Samuelson and co-workers described the synthesis of chiral platinum-bisphosphinite complexes **21** with a backbone stemming from 2-O-benzylated L-ascorbic acid **20**. These complexes were successfully applied as catalysts in chemical transformations, e.g., in the asymmetric allylation of cinnamaldehyde (**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 environmentally 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

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