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Communication

First Pauson–Khand reaction on sugar acetylenes

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Abstract

Pauson–Khand reaction was achieved on the sugar acetylenes having an allylic ether substituent at the two-position of the tetrahydropyran ring to provide tri-cyclic products with high stereospecificity. This is the first example of Pauson–Khand reactions with compounds on carbohydrate or tetrahydropyranose ring, and the scope is described. © 1999 Elsevier Science S.A. All rights reserved.

Keywords: Pauson–Khand reaction; Sugar acetylene; biscobaltoctacarbonyl

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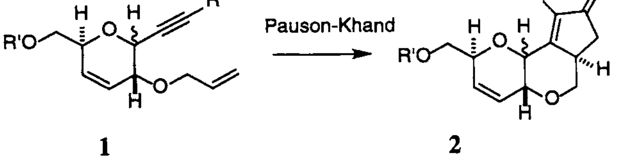
Among synthetic reactions involving organometals as catalysts, the Pauson–Khand reaction has occupied a leading position for synthesis of cyclopentanone or cyclopentenone derivatives. Most of those examples are found in the precursor compounds having no stereogenic centers. We became interested in performing Pauson–Khand reaction, a $[2+2+1]$cyclization with an acetylene and an olefin attached to a pyranose ring at the adjacent position, in order to obtain optically active products that are potentially useful for natural product synthesis. We have recently established a new method to synthesize the sugar acetylenes for use as reagents [1]. The current study of the Pauson–Khand [2] reaction on the sugar acetylene **1** should give the tricyclic products **2** as shown in Eq. (1). These products would also provide some additional aspects for the sugar acetylenes as synthetic intermediates.



1 **2**

(1)

The general precursor sugar acetylenes (**1**) are readily available by *C*-glycosidation of glycals with silylacetylenes in acidic media [1,3]. When 2-acetoxy-glucal **3**, for example, is treated with bis(trimethylsilyl)acetylene in the presence of tin tetrachloride, and then with sodium borohydride in the presence of cerium(III) chloride, the alkynylated product **4** is obtained [4]. This acetylene alcohol (**4**) was then converted into the corresponding allyl ether (**6**) in two steps via the corresponding carbonate (**5**) in the presence of palladium as catalyst [5]. In this case about 23% of the allylic alcohol (**4**) was recovered. The product **6** was obtained with retention of configuration, which suggested the π-allyl complex of palladium and the carbonate **5** took place at the noncyclic allyl ether group rather than the cyclic one. The 1,2-*cis*-en-yne compound (**6**) was first converted to the corresponding biscobalthexacarbonyl complex (**7**), and was then subjected to one of several Pauson–Khand conditions. Treatment of **7** with six equivalents of *N*-methylmorphorine *N*-oxide (NMO) at room temperature under nitrogen [6] yielded the tri-cyclic product **8** as crystals (m.p. 86.3°, $[\alpha]_D = +195°$) in 98% yield. To the best of our knowledge this is the first example of successful Pauson–Khand reaction related to a sugar-based acetylene [7] (Scheme 1).

Such a successful Pauson–Khand reaction with the 1,2-*cis*-en-yne precursor **7** prompted us to examine a 1,2-*trans*-ene-yne precursor **9**, which was obtainable

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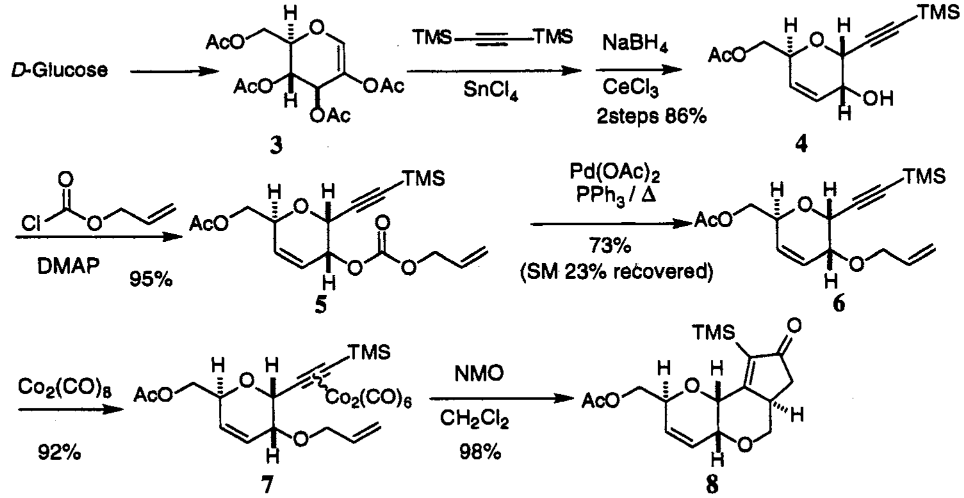
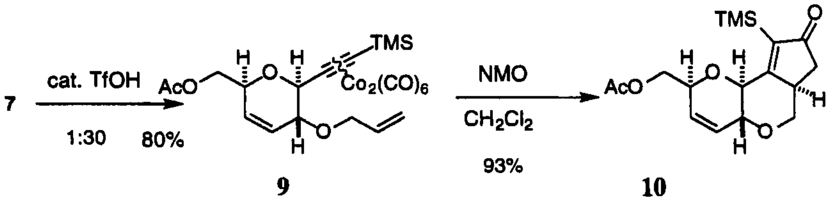
from **7** via acidic epimerization. Treatment with trifluoromethanesulfonic acid (0.1 M solution of TfOH) at room temperature afforded **9** (containing a small amount of **7** as a mixture in a ratio of 30:1). This product was subjected to NMO in dichloromethane under the same conditions as above to provide **10** (m.p. 119°, $[\alpha]_D = +222.1°$) (Scheme 2).

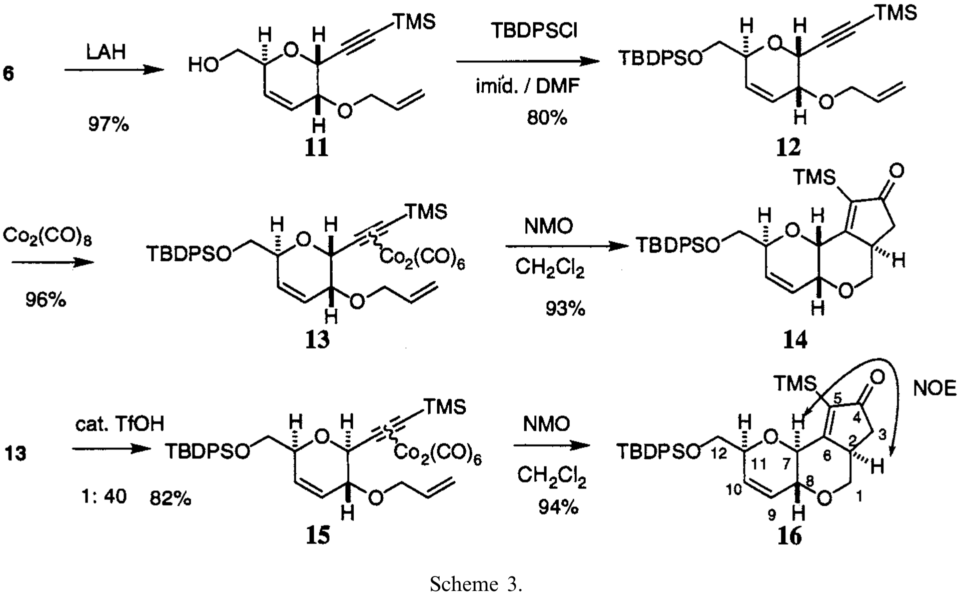
Similar examples were achieved with 1,2-*cis*- and 1,2-*trans*-en-yne precursors of acetylene bis-cobalthexacarbonyl complex having *tert*-butyldiphenylsilyl protection at the six-position as **13** and **15**, which were prepared from the acetate **6**, respectively as shown in Scheme 3. In this case the α–β isomerization took place in 40:1 ratio under the same acidic conditions as the above



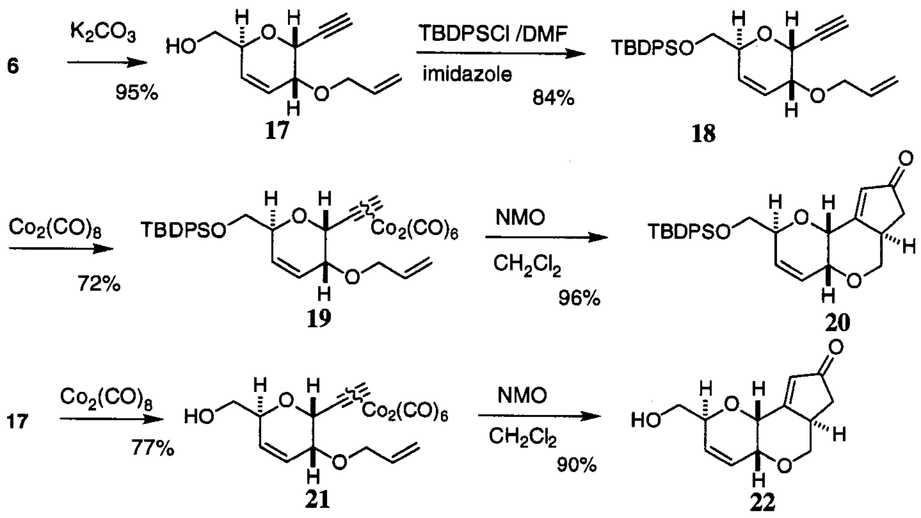
Scheme 1.



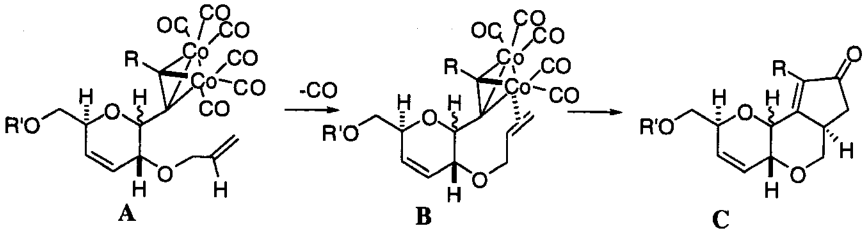
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

case. The P–K reaction to both **13** and **15** again proceeded with NMO to produce the corresponding tricyclic compounds **14** (colorless oil, $[\alpha]_D = +78.8°$) and **16** (m.p. 134.4°, $[\alpha]_D = +115.7°$) in high yields, respectively. Among these P–K tricyclic products the last compound (**16**) from *trans*-ene-yne precursor (**15**) clearly indicated an NOE between 2-H and 7-H so that the stereochemistry of the 2-H should be α. Consequently the stereochemistry of **14**, which showed no NOE, should be assigned as 2-H being α as well.

The third examples are the cases of terminal acetylene (without trimethylsilyl group). Two 1,2-*cis*-precursors (**19** and **21**) were prepared from **6** by hydrolysis of the trimethylsilyl and acetyl groups with dipotassium carbonate (Scheme 4). In this case the α–β epimerization did not take place due to insufficient steric congestion without the trimethylsilyl group, so the P–K reaction was examined only with the 1,2-*cis*-en-yne precursors. Both the TBDPS derivative **19** and the free alcohol **21** afforded the tricyclic P–K products **20** (as oil, $[\alpha]_D = 82.4°$) and **22** (m.p. 168.3°, $[\alpha]_D = 281.1°$) in 96 and 90% yield, respectively.

The stereochemistry of the products was assigned from NMR; thus, all of the P–K products from 1,2-*cis*-precursors showed no NOE between 2-H and 7-H. Only compound **16** indicated a clear NOE. (Compound **10**, in fact, showed an NOE with 2-H, but the 7-H overlapped with other proton signals.) The stereochemical process might be determined by approach of the initial coordination of π-electrons on the side chain to exchange the carbon monoxide ligands to one of the cobalt atoms. Scheme 5 shows one possible process of the P–K reaction [8]; thus, the side chain olefin and one of the cobalt atoms in the starting material **A** approach each other, intramolecular ligand exchanges **A** to **B**. In this case, the terminal olefin is predestined to approach to the cobalt complex such that the subsequent [2 + 2] cycloaddition takes place through a minimum-energy surface. Fig. 1 illustrates the intermediates from 1,2-*trans* materials explaining the stereochemical course, so that 2-H directed to the α orientation, where only one of the two *apical* carbonyl groups can exchange with olefin. Fig. 2 illustrates the 1,2-*cis* cases, where the tetrahydropyran ring takes an inverted conformation, but the approach between the two reaction cite should

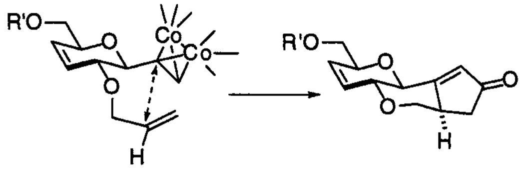


Fig. 1.

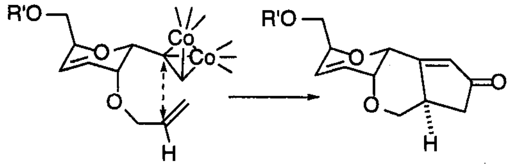


Fig. 2.

happen in a similar manner to the *trans* case. This explanation would lead to the high stereoselective product having 2-H in alpha orientation (Scheme 5).

Additional examples of this reaction including more detailed data will be described in full elsewhere.

Acknowledgements

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