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Intramolecular propargylic reduction in γ -benzyl protected $\text{Co}_2(\text{CO})_6$ - α,γ -acetylenic diols under Nicholas reaction conditions

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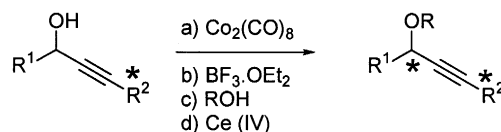
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Abstract

Lewis acid treatment of γ -benzyl protected $\text{Co}_2(\text{CO})_6$ - α,γ -acetylenic diols yielded after cobalt demetallation bishomopropargylic alcohols in good yields. The method works with both primary and secondary benzyl ethers and is compatible with many kinds of protecting groups and functionalities. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: alkynes; cobalt; cobalt compounds; Nicholas reaction.

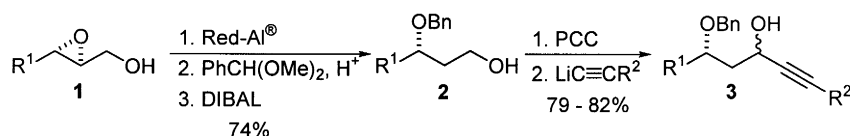
Recently, we reported a new procedure to obtain enantiomerically enriched products using the Nicholas reaction, by trapping the carbocation generated by acid treatment of a chiral $\text{Co}_2(\text{CO})_6$ -complexed propargylic secondary alcohol with nucleophiles.¹ Chirality was introduced at the remote acetylenic substituent R^2 (Scheme 1). In order to gain access to highly oxygenated linear chains with controlled structure, we were interested in the influence of additional hydroxy groups at R^1 on the stereochemistry in the propargylic centre.² As a result of these studies we have recently found that α,β -acetylenic diols afforded homopropargylic ketones under the Nicholas reaction conditions.³



Scheme 1.

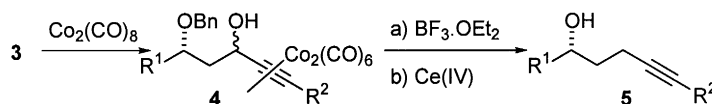
In this communication we present our preliminary results relating to the use of γ -benzyl protected $\text{Co}_2(\text{CO})_6$ - α,γ -acetylenic diols **4** as substrates. The majority of the γ -benzyl protected α,β -propargylic alcohols **3** were obtained by direct addition of a lithium acetylide to suitable carbonyl derivatives in accordance with Scheme 2⁴ or by protecting group exchange.

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Scheme 2.

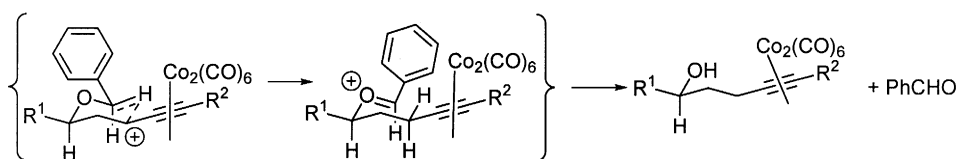
We have found an unexpected participation of the benzyl group that causes reduction at the propargylic position, yielding the unprotected bishomopropargylic alcohol **5** in good yields (Scheme 3).⁵ The method could be considered as an alternative to standard acetylene coupling, avoiding elimination reactions and taking advantage of the high reactivity of acetylide anions towards carbonyl compounds.⁶



Scheme 3.

Representative examples are outlined in Table 1. Lewis acid treatment ($\text{BF}_3 \cdot \text{OEt}_2$, CH_2Cl_2 , -20°C) of γ -benzyl protected $\text{Co}_2(\text{CO})_6$ - α,γ -acetylenic diols **4** provided the corresponding complexed bishomopropargylic alcohol in a straightforward manner. When the benzyl-protected group is located at a secondary position complete integrity of the stereogenic centre was retained. If a THP-ether was present (entry 4) the isolated product showed that this protecting group had been cleaved. The procedure works with additional free hydroxy groups (entry 7), although in this case only moderate yields are obtained. When the hydroxy groups are protected as silyl ethers (TBDPS or TBDMS) (entries 2, 3 and 6) or as an ester (entry 5) satisfactory yields are obtained regardless of the position of the protected hydroxy group relative to the triple bond. The benzyl group can be also located at primary carbons with similar results (entry 9). When a β -oxygen is present (entry 8) only traces of the reduced product were obtained, presumably due to β -elimination of the intermediate carbocation.³ In all cases, the $\text{Co}_2(\text{CO})_6$ -bishomopropargylic alcohols were satisfactorily decomplexed from the metal in the standard manner ($\text{Ce}(\text{NO}_3)_6(\text{NH}_4)_2$, acetone, 0°C vs acetone, rt).⁷

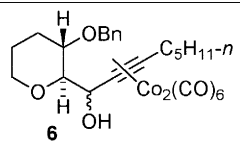
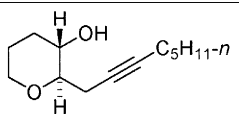
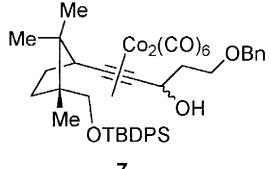
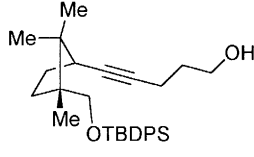
It is noteworthy to mention that the role of the benzyl group is essential to achieving the reported transformation, since when the γ -hydroxy group is unprotected or is a silyl ether (TBDPS or TBDMS) the reduction did not occur. A hydride transfer from a benzylic position to the propargylic carbocation, followed by nucleophilic attack of water to the positive charge thus generated is the basis of our tentative explanation of the facts outlined above (Scheme 4).¹⁰



Scheme 4.

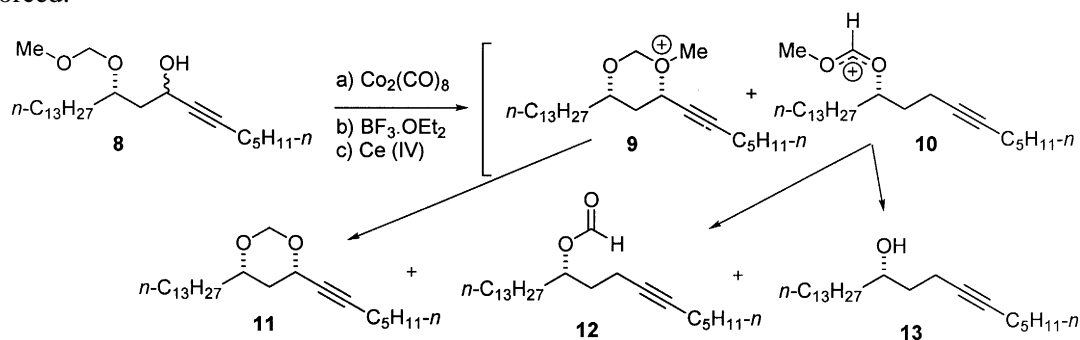
In order to obtain additional evidence about this mechanism we protected the γ -hydroxy group as a MOM-ether, considering that in this group the methylene may have similar features to that of the benzyl group regarding the ability of transfer of hydride. However, in this case when the diastereoisomeric mixture **8** was submitted to the above mentioned conditions a 1:0.8:0.7 mixture of **11:12:13** was obtained in 85% overall yield. The expected bishomopropargylic alcohol **13** was contaminated with the acetal **11** and the formate ester **12** resulting from water attacking the cations **9** and **10**, respectively. Although with

Table 1
Representative examples of propargylic reduction in γ -benzyl protected $\text{Co}_2(\text{CO})_6$ - α,γ -acetylenic diols under Lewis acid treatment

Entry	4	5 (Yield %) ^a
1.	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = n\text{-C}_5\text{H}_{11}$	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = n\text{-C}_5\text{H}_{11}$ 70 (65)
2.	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = (\text{CH}_2)_3\text{OTBDPS}$	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = (\text{CH}_2)_3\text{OTBDPS}$ 78 (69)
3.	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = (\text{CH}_2)_3\text{OTBDMS}$	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = (\text{CH}_2)_3\text{OTBDMS}$ 75 (68)
4.	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = (\text{CH}_2)_3\text{OTHP}$	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = (\text{CH}_2)_3\text{OH}$ 46 (40)
5.	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = (\text{CH}_2)_3\text{OBz}$	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = (\text{CH}_2)_3\text{OBz}$ 80 (74)
6.	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = \text{CH}_2\text{OTBDPS}$	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = \text{CH}_2\text{OTBDPS}$ 77 (69)
7.	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = (\text{CH}_2)_3\text{OH}$	$\text{R}^1 = n\text{-C}_3\text{H}_7, \text{R}^2 = (\text{CH}_2)_3\text{OH}$ 51 (46)
8. ⁸		 --
9. ⁹		 83 (76)

^aYields are not optimized (in brackets the overall yield from 3 to 5).

this protecting group different behaviour was observed, the idea of a six-membered transition state is reinforced.



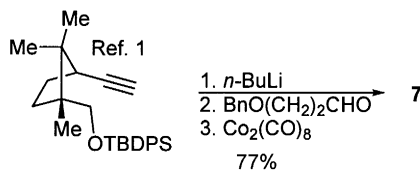
In summary, intramolecular hydride transfer from a benzyl ether, located in a γ -position in $\text{Co}_2(\text{CO})_6$ -complexed α,γ -acetylenic diols, to a propargylic cation generated under Nicholas conditions provides a new method to obtain bishomopropargylic alcohols. The scope and limitation of the procedure to more substituted substrates is under study and will be published in due course.

Acknowledgements

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- Chiral 2,3-epoxy alcohols were regioselectively opened to the corresponding 1,3-diols. Benzylidene protection and regioselective reduction provided the secondary benzyl ether **2**. Oxidation of the primary alcohol furnished the aldehyde that after lithium acetylide addition yielded **3**.
- For other examples of 'ionic hydrogenations' of alcohols, see: (a) Kursanov, D. N.; Parnes, Z. N.; Loim, N. M. *Synthesis* **1974**, 633, and references cited therein. (b) Adlington, M. G.; Orfanopoulos, M.; Fry, J. L. *Tetrahedron Lett.* **1976**, 2955. (c) Carey, F. A.; Tremper, H. S. *J. Org. Chem.* **1971**, *36*, 758. (d) Olah, G. A.; Arvanaghi, M.; Ohannecian, L. *Synthesis* **1987**, 770. (e) Smonou, I.; Orfanopoulos, M. *Tetrahedron Lett.* **1988**, *29*, 5793, and references cited therein.
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- Satisfactory spectroscopic data and combustion analyses were obtained for all new compounds.
- Compound **6** was obtained by a similar sequence to that outlined in Scheme 2 using (3*S*,2*R*)-(hydroxymethyl)perhydro-2*H*-pyran-3-ol as the 1,3-diol. See: Nicolaou, K. C.; Duggan, M. E.; Hwang, C.-K. *J. Am. Chem. Soc.* **1989**, *111*, 6666.
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- We have isolated and characterised the benzaldehyde produced.