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LETTERS

Selective electrochemical reduction of cinnamyl ethers in the presence of other allylic C–O bonds

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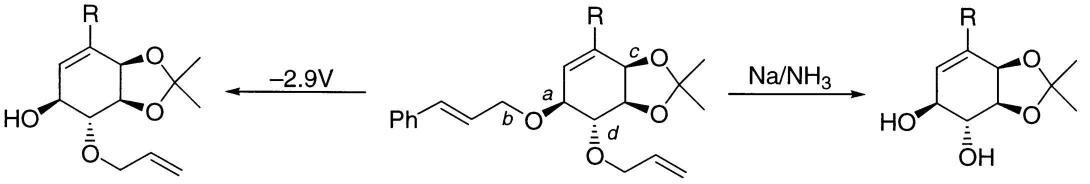
Abstract—Several conduritol derivatives protected as allyl and cinnamyl ethers were subjected to electrochemical reduction at a mercury cathode, resulting in selective removal of the cinnamyl group. © 2001 Published by Elsevier Science Ltd.

The use of allyl and cinnamyl ethers as protecting groups for alcohols is well known[1] as are the methods for their removal.[2,3] These can involve oxidative removal, as in the case of deallylations with Ce(IV),[4] for example, a reaction proceeding via cationic or radical cationic intermediates, thus also allowing a further substitution of such intermediates. In such 'deprotections', the oxygen of the original alcohol is replaced with one from the trapping nucleophile, with the potential for scrambling of stereochemical configuration. Reductive removal is most frequently accomplished by such means as dissolving metal reduction, where the original alcohol oxygen and its configuration remain intact. For cinnamyl groups, their electrochemical reduction in the presence of Ni(II) is preferred to radical cyclization from neighboring aryl halides.[5] Such has been our experience in attempted electrochemical cyclizations of vinyl bromides onto cinnamyl ethers,[6] where cleavage of the cinnamyl group and reduction of a vinyl[6] or aryl[5] bromide occur essentially simultaneously. Recently palladium-catalyzed electrochemical reduction of both allyl and cinnamyl groups in the presence of aryl halides has been reported.[7]

We found no mention in the literature of any attempts to control selectively a cleavage of only one of several allylic systems or attempts to control allylic versus cinnamyl cleavage. A comparison of allylic and benzylic reduction has been published.[2i] We chose several examples for study, the most complex being the conduritol derivative **1** containing an endocyclic (position (*a*)), as well as exocyclic (*b*) cinnamyl units in addition to endocyclic (*c*) and exocyclic (*d*) allyl groups. In most of the cases shown in Table 1, the dissolving metal reduction of the two 'exocyclic' groups occurs without selectivity, whereas the electrochemical reduction at −2.9 V (Hg or C cathode) cleaves only the *exo* cinnamyl ether to afford **3**.

Other examples of selective removal are shown in Table 1. In most cases the treatment of the cinnamyl–allyl ethers with excess Na in NH_3 resulted in the removal of both groups. In attempts with a 'stoichiometric' amount of the metal (2 equiv.), cinnamyl cleavage occurred at a faster rate, but the reaction mixtures contained starting material, allyl ether, and diol in all cases. However, the electrochemical reduction of the



3a R = H
3b R = Ph

1a R = H
1b R = Ph

1a R = H
1b R = Ph

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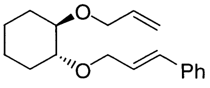
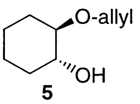
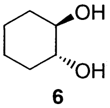
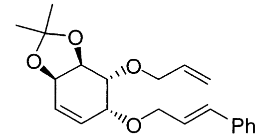
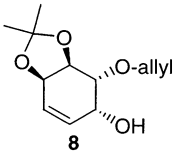
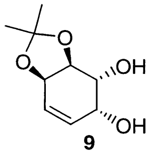
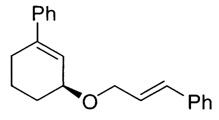
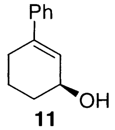
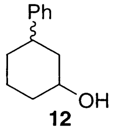
cinnamyl group was in all cases selective. In the cases of the phenyl-substituted conduritol **1b** and a simpler model **10**, the Na–NH_3 reaction yielded only recovered starting material (in the case of **1b**) or over reduction of both cinnamyl groups (in the case of **10**). Electrochemical reduction, on the other hand, gave clearly the deprotected alcohols. We attribute these results to solubility problems and a different reduction regime. With co-solvents (THF) the reduction was sluggish and non-selective, and in the case of **10** it provided alcohol **12** (mixture of diastereomers) exclusively.

In spite of the fact that these experiments were not optimized, it is clear that the electrochemical removal offers advantages over other methods. First, it retains the stereochemical configuration of the alcohol, which is not possible by employing methods performed under oxidizing conditions. Second, it is selective not only with respect to allyl groups but also with respect to other cinnamyl units where the reductively generated anion would be more basic (i.e. at secondary cyclic carbon as in *a* in **1**). Third, alkylative methods of removal, such as the recently reported TMSCl/NaI procedure,[8] offer no selectivity in differentiating between allylic and cinnamyl carbons.

The electrochemical reductions were performed with a Hg pool cathode or a vitrified carbon cathode at the indicated potentials. The linear sweep voltammograms (LSV) of the starting materials showed reduction waves around −2.9 V for the cinnamyl C–O bond cleavage and the reduction to 1-phenyl-1-propene. Additional reduction wave, assumed to be that corresponding to the reduction of an allyl group, was separated by ca. 300 mV.

Cyclic and linear sweep measurements were determined with a platinum glassy carbon electrode and a platinum auxiliary electrode. Measurements were referenced to a Ag/Ag^+ couple, constructed by placing a silver wire in a 0.1 M solution of silver nitrate in CH_3CN, producing a reference electrode 0.5785 V versus NHE (normal hydrogen electrode). The voltammetry of all compounds was hampered by adsorption of material to the working electrode, shown by the cathodic shift and the decrease in current exhibited in the reduction waves of successive sweeps. Reproducible voltammograms were obtained by polishing the electrode surface between successive sweeps, and at the same time stirring and degassing the solution. Several general characteristics were observed in the voltammograms, such as typically broad reduc-

Table 1. Electrochemical versus dissolving metal reductions of cinnamyl–allyl systems

Ether	Method	Products, Isolated Yield, %		
		**4**	 **5**	 **6**
4	Na (2 eq), NH_3	22	34	5
	excess Na, NH_3	0	0	62
	−2.8 V (Hg)	0	62	5
1b		**1b**	**3b**	**2b**
	Na (2 eq), NH_3	85	0	0
	excess Na, NH_3	80	0	0
	−2.9 V (Hg)	20	78	0
		**7**	 **8**	 **9**
7	Na (4 eq), NH_3	37	40	48
	excess Na, NH_3	17	4	44
	−2.8 V (Hg)	12	83	2
1a		**1a**	**3a**	**2a**
	Na (4 eq), NH_3	40	31	55
	excess Na, NH_3	14	<1	47
	−2.7 V (Hg)	17	83	1
		**10**	 **11**	 **12**
10	Na (4 eq), NH_3	65	10	25
	excess Na, NH_3, THF	—	—	100
	−2.7 V (Hg)	10	78	—

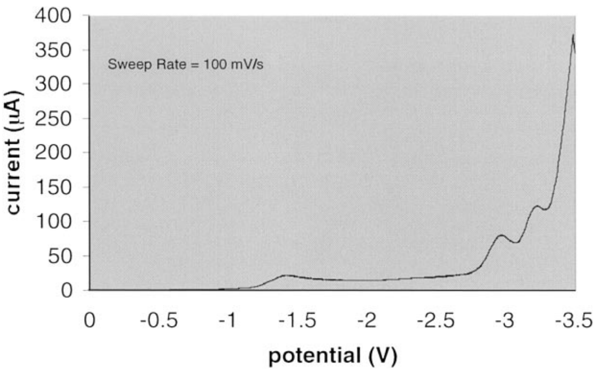


Figure 1. Linear sweep voltammogram of **7**.

tion waves with half peak potentials greater than 100 mV and with a cathodic shift that increased with sweep rate.

The linear sweep voltammogram of conduritol derivative **7** is shown in Fig. 1. The voltammogram is characterized by two broad reduction waves at $E_1 = -2.9$ V and $E_2 = -3.2$ V (half-peak potentials). These reduction waves were found to be irreversible through cyclic voltammetric analysis. Attempts to extend the preparative reductions to carbon electrodes have thus far not succeeded.

In conclusion, we have shown selectivity in removal of cinnamyl groups over allyl groups under extremely mild conditions. Because the cinnamyl unit is inexpensive and because the deprotection occurs in an environmentally benign manner, this method is superior to the classical procedures reported in the literature.

Worthwhile future endeavors include the study of multiple selectivities to determine the ease of removal of cinnamyl versus cinnamate, cinnamyl (or cinnamate) or benzoate, for example. Since hydrogenations of benzyl groups are sometimes troublesome, cinnamyl group offers the advantages of easy removal. We will report on these endeavors in due course.

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