Tetrahedron Letters,Vol.23,No.39,pp 3987-3990,1982 0040-4039/82/393987-04$03.00/0
Printed in Great Britain

AN ELECTROCHEMICAL KETAL SYNTHESIS FROM 2-CARBOXY-2-ALLYL-TETRAHYDROPYRANS

Peter G. M. Wuts* and Colin Sutherland
Department of Chemistry, The University of Michigan,
Ann Arbor, Michigan 48109

Summary: 2-Substituted tetrahydropyranyl-2-carboxylates have been converted to mixed ketals by electrochemical oxidative decarboxylation.

The ubiquity of spiroketals in both the plant and animal kingdoms is becoming ever more apparent. They constitute key fragments of antibiotics,[1] pheromones,[2] steroids[3] and antiparasitic agents.[4] As a prelude to the synthesis of several spiroketal containing natural products, we chose to examine an electrochemical approach to ketal formation which takes advantage of the ready availability of uronic acid derivatives.[5] Electrochemical oxidative decarboxylation of alpha-alkoxycarboxylic acids to give ketone and aldehyde derived products was initially discovered during investigations of the Kolbe reaction[6] in the early nineteenth century and has received little attention since. Our interest in the synthesis of spiroketal natural products has led us to explore the oxidative decarboxylation of tetrahydropyranyl carboxylates as a route to spiroketal precursors.

As a model substrate, we chose acid 1 but in order to develop suitable precursors to spiroketals an additional substituent at the 2 position of the tetrahydropyranyl ring was required. After several disappointing attempts to introduce a suitable substituent, R, by direct alkylation of either the acid 1 or the esters 2,[7] attention was turned to the ester enolate Claisen rearrangement to append the necessary side chain. A variety of allyl esters 3 (Table I) were prepared by standard methods (RCOCl, ROH, pyridine) and subjected to the conditions outlined by Ireland for the enolate Claisen.[8] The resulting acids 4 were submitted to electrolytic decarboxylation in a divided cell in anhydrous methanol with Et_4NClO_4 and K_2CO_3 as supporting electrolytes to afford ketals 5.[9] The decarboxylations were run at 0.1 ampere (30+/-5 V) until disappearance of the starting acids 3. The ketals were isolated by chloroform extraction followed by distillation of the crude product.

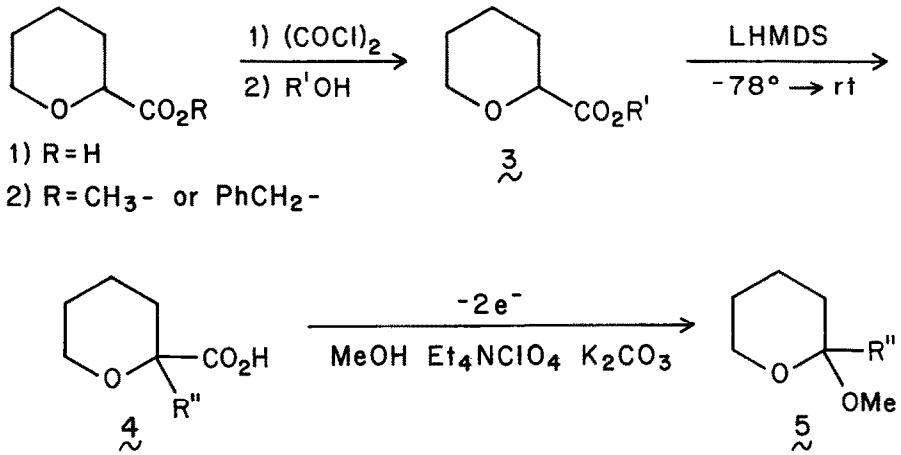
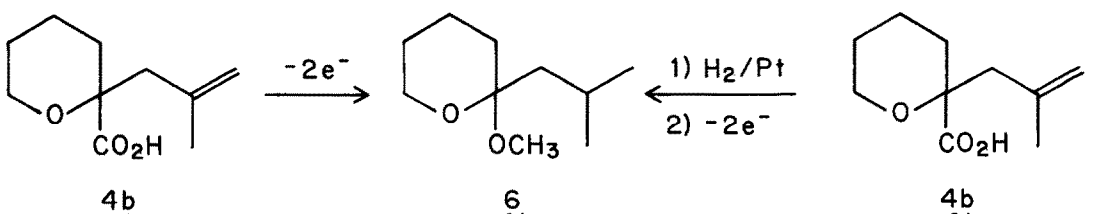


Table I. Results of Electrochemical Decarboxylations[a]

Entry	R'OH	% Yield 3	4 (R=)	% Yield 4	% Yield 5
a	$CH_2=CHCH_2OH$	90	$CH_2=CHCH_2-$	91	87
b	$CH_2=CH(CH_3)CH_2OH$	79	$CH_2=CH(CH_3)CH_2-$	89	75
c	$CH_3CH=CHCH_2OH$	84	$CH_2CH=CH(CH_3)-$	85	90
d	Cyclohexenol	90	3-Cyclohexenyl-	77	67

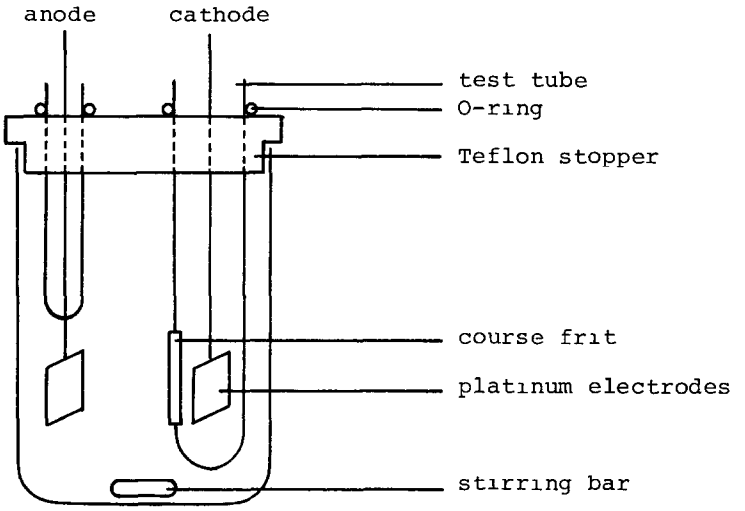
[a]All yields refer to isolated distilled material.

The use of the divided cell was necessary in that initial attempts to carry out the reaction in an undivided cell resulted in alkene reduction as demonstrated by the production of ketal 6 which was prepared independently by hydrogenation of acid 4b and electrolytic oxidative decarboxylation.



Since the Kolbe reaction is run under similar conditions and is compatible with a large number of functional groups, it is expected that the electrolytic ketal formation also has extensive functional group compatibility.

An illustration of the cell used in our electrolysis and a sample experimental procedure should illustrate the ease with which these reactions can be performed.



Sample Experimental Procedure. A solution of 2.0 g of K_2CO_3 and 5.0 g of Et_4NClO_4 in 20 ml of methanol was prepared and allowed to equilibrate between the anode and cathode compartment. Acid 4a (1.60 g, 9.4 mmol) was then added to the anode compartment and a current of 0.1 ampere was applied to the electrodes with a constant current power supply. When TLC (24% EtOAc, 1% AcOH, 75% hexane) analysis indicated the disappearance of acid 4a (~10 hr), the mixture was poured into H_2O and extracted with $CHCl_3$. Kugelrohr distillation (130°, 760 mm) of the crude product afforded 1.27 g (81%) of ketal 5a. IR (film): 3180, 2950, 1650, 1870, 1280, 1220, 1110, 1065, 1040, 980, 920, 880, 850, 815, 750 cm^{-1}. NMR ($CDCl_3$-360 MHz): 6.62 (m, 1H, vinyl), 6.06 (m, vinyl, 2H), 3.60 (m, 2H, CH_2O), 3.20 (s, 3H, CH_3O-), 2.33 (ABq split into doublets, $\Delta\nu$ = 83.8 Hz, J_{ab} = 21.5 Hz, J = 6.8 Hz, 2H, CH_2-CH=), 1.5 (m, 6H) ppm. C-13 ($CDCl_3$): 178.2, 131.0, 118.6, 80.0, 64.8, 44.0, 32.1, 25.1, 20.5 ppm. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.01; H, 10.12.

In conclusion, we have shown that uronic acids may readily be converted to ketals electrochemically. Work is currently in progress to utilize this approach in the synthesis of a variety of spiroketal containing natural products.

Acknowledgment. The authors are indebted to the Research Corporation for support of this work.

References

1. J. W. Westley, Adv. Appl. Microbiol., 22, 177 (1977).
2. W. Franke, V. Heemann, B. Gerken, J. A. A. Renwick and J. P. Vite, Naturwissenschaften, 64, 590 (1977); Von H. Redlich and W. Francke, Angew. Chem., 92, 640 (1980).
3. R. E. Marker and E. Rohrmann, J. Am. Chem. Soc., 61, 846 (1939).
4. C. C. Wang, Ann. Rep. Med. Chem., 16, 269 (1981); I. W. Sherman, Microbiol. Rev., 43, 453 (1979).
5. Carbohydrates provide an excellent source of uronic acid derivatives with suitable functionality for elaboration into spiroketal containing natural products.
6. H. J. Kolbe, Annalen., 69, 257 (1849).
7. Alkylations resulted in yields of <10% with n-alkyl halides and yields of <40% with allylic halides.
8. R. E. Ireland and C. S. Wilcox, Tetrahedron Lett., 2839 (1977) and references cited therein.
9. Note these results are in contrast to those of H. G. Thomas and E. Katzer [Tetrahedron Lett., 887 (1974)] who found that simple unsubstituted α-alkoxycarboxylic acids gave products that resulted from trapping the intermediate carbonium ion with substrate carboxylates.

$$ROCH_2CO_2H \xrightarrow[CH_3CN]{-2e^-} ROCH_2O\overset{O}{\overset{\|}{C}}CH_2OR$$

(Received in USA 1 June 1982)