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TRIPHENYLCARBENIUM AND TRIS(*P*-BROMOPHENYL)AMMONIUMYL ION INDUCED LACTONIZATIONS OF ω-BENZYLOXY AND ω-*P*-METHOXYBENZYLOXY METHYL ESTERS

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The title reaction leads to smooth generation of five and six membered lactones via direct nucleophilic participation of the carbomethoxy group in intermediates of type 3.

Triphenylcarbenium ion will abstract hydride ions from the benzylic carbon of benzyl ethers.[1] *tris*(*p*-Bromophenyl)amine cation radical (ammoniumyl ion) generates cations at the benzylic carbon of *p*-methoxybenzyl ethers by sequential electron transfer, proton loss, and electron transfer.[2] Both processes lead after reaction with water to arylaldehyde and alcohol and thus serve as methods of benzyl ether deprotection.

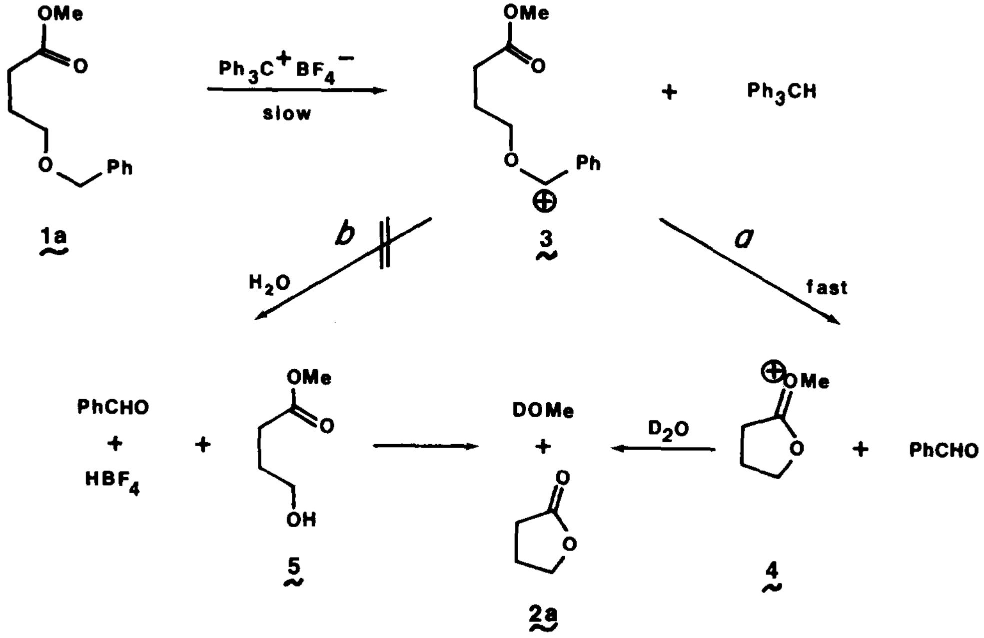
We reasoned that in the absence of water, appropriately situated intramolecular nucleophilic functional groups might interact with these benzylic carbenium ions in an interesting and useful fashion. Indeed, carbomethoxy groups lead to the formation of γ- and δ-lactones by displacement of arylaldehyde, and we have used this reaction as a key step in a recently reported synthesis of *dl*-aplysistatin.[3] Herein are reported additional examples and limitations of this lactonization reaction as well as the results of an nmr study which offer insight to the mechanism of the transformation.

Substrates 1a-g[4] (see Table) containing methyl ester and benzyl or *p*-methoxybenzyl ether functionalities were prepared by reaction of the appropriate lactone with excess potassium hydroxide in refluxing toluene in the presence of excess benzyl or *p*-methoxybenzyl chloride[5] followed by Fischer esterification with methanol. Exposure of ester ether 1a to trityl cation (1.1 eq) in $CDCl_3$ or CD_3CN (reagents are more soluble and reaction rate is greater in acetonitrile) leads to a reaction which can be monitored by the appearance of ^1H-NMR resonances for $Ph_3C\underline{H}$ (δ5.5) and $PhC\underline{H}O$ (δ9.9) and the disappearance of starting material material absorptions. A new methyl resonance appeared at δ3.75, and this shifted to δ3.42

upon the addition of D_2O at which time the absorptions for γ-butyrolactone (2a) were also present.

Our interpretaion of this sequence of events (see Scheme) is that hydride abstraction was followed by internal displacement of benzaldehyde by the carbomethoxy group in cation 3 (see path *a*) to generate the methylated oxonium ion 4 (δ_{Me}3.75) which then collapsed to lactone 2a and methanol (δ_{Me}3.42) upon the addition of D_2O. An alternative pathway (path *b*) leading via hydroxy ester 5 seems unlikely since that intermediate would have had to have been formed by reaction with adventitious water present in the reaction medium (recall that PhCHO was present *before* the addition of D_2O in the nmr experiment), and trityl cation reacts rapidly with water in acetonitrile.[6] Moreover, had 5 been an intermediate, it should have lactonized rapidly to generate 2a and methanol *before* the addition of D_2O in the nmr study.

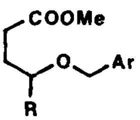
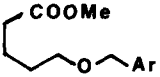
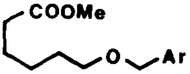
Scheme



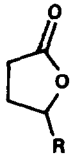
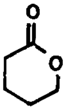
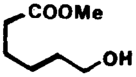
It is also indicated in the Scheme that hydride abstraction from 1a is a slow process relative to the rate of cyclization (3 → 4). This is consistent with the observations that i) $PhC\underline{H}O$ and $Ph_3C\underline{H}$ peaks grow in the nmr analysis in equal intensities and ii) substrates 1a and 1d are consumed at equal rates (gc analysis of loss of starting materials) when a 1:1 mixture of the two is treated with $Ph_3C^+BF_4^-$.

The results of attempted lactonization of substrates 1a-g are summarized in the Table. The volatility of product lactones 2a and 2c prevented obtention of meaningful isolated yields after chromatographic purification although they were the only products observed by direct nmr and gc analysis. Successful lactonization of 1b indicates the compatability of a secondary carbon center in the cyclization reaction. Ester ethers 1f and 1g did not yield the corresponding ε-caprolactone. Only methyl 6-hydroxyhexanoate (6) was obtained after the addition of water to these reaction mixtures. This failure to cyclize could be due to either kinetic or thermodynamic aspects of the relationship of the seven membered analog of 4 and the corresponding precursor cation 3.

Table

	Substrate	Method[a]	Yield[b]	Product
1a	R = H Ar = Ph	$\xrightarrow{A}$	78% (28%)	2a R = H
1b	R = nBu Ar = Ph	$\xrightarrow{A}$	-- (67%)	2b R = nBu
1c	R = H Ar = p-MeOPh	$\xrightarrow{B}$	91%	2a R = H
1d	Ar = Ph	$\xrightarrow{A}$	71%	2c
1e	Ar = p-MeOPh	$\xrightarrow{B}$	81%	2c
1f	Ar = Ph	$\xrightarrow{A}$	--	6
1g	Ar = p-MeOPh	$\xrightarrow{B}$	--	6

a) Method A: 1 in dry acetonitrile was treated with $Ph_3C^+BF_4^-$ (1.1 eq) at RT until gc showed no 1 (one to several hours); water was added; gc yield analysis or standard workup and column chromatography on SiO_2 was performed. Method B: same as method A except that $(p\text{-}BrPh)_3N^{+\cdot}\ SbCl_6^-$ (2.2 eq) was used instead of $Ph_3C^+BF_4^-$.
b) Yields were determined by gc analysis (isolated yields in parentheses).

Finally, in full accord with expectations arising from the results of Steckhan,[2] reaction of a 1:1 mixture of benzyl and *p*-methoxybenzyl ethers 1a and 1c with the *tris*(*p*-bromophenyl)-ammoniumyl ion led to exclusive consumption of 1c as determined by gc analysis, thus further demonstrating the selectivity available with this reagent.[2]

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References and Notes:

1. Barton, D. H. R.; Magnus, P. D.; Streckert, G.; Zurr, D. *J. Chem. Soc. Chem. Comm.* 1971, 1109.
2. Schmidt, W.; Steckhan, E. *Ang. Chem. Int. Ed. Engl.* 1978, 17, 673.
3. Hoye, T. R.; Kurth, M. J. *J. Am. Chem. Soc.* 1979, 101, 5065.
4. These compounds gave ir, nmr, and mass spectral and elemental combustion data entirely consistent with their structures.
5. Eyre, D. H.; Harrison, J. W.; Lythgoe, B. *J. Chem. Soc. (C)* 1967, 452.
6. Archie, William Councill, Jr., *Diss. Abst. Int. B.* 1971, 32, 816.

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