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SOLVOLYTIC CYCLIZATION OF 6-PHENYL-5-HEXENYL AND 6-PHENYL-5-HEXYNYL BROSYLATES IN ACETIC ACID

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Recent reports concerning triple bond involvement in solvolytic cyclization reactions[2,3] prompt us to report some observations on acetolysis of phenyl-substituted hexenyl and hexynyl systems. The cationic cyclization of 6-phenyl-5-hexynyl brosylate under the relatively mild conditions of acetolysis is particularly noteworthy.

Preparation of trans-6-phenyl-5-hexen-1-ol was achieved by homologation (through the cyanide and carboxylic acid) of 5-phenyl-4-penten-1-yl bromide.[4] Various 6-aryl-5-hexenols were also prepared by the Wittig reaction of the appropriate benzyltriphenylphosphonium ylid with 5-hydroxypentanal. Acetolysis of 5-phenyl-4-pentenyl bromide[4b] and hydrolysis of the resulting ester afforded trans-5-phenyl-4-penten-1-ol. Treatment of the sodium salt of ethynylbenzene with 3-chloropropyl tosylate and homologation of the resulting chloride yielded 6-phenyl-5-hexyn-1-ol. Acetolysis rate constants of the brosylates are shown in Table I; acetolysis products are presented in Chart I

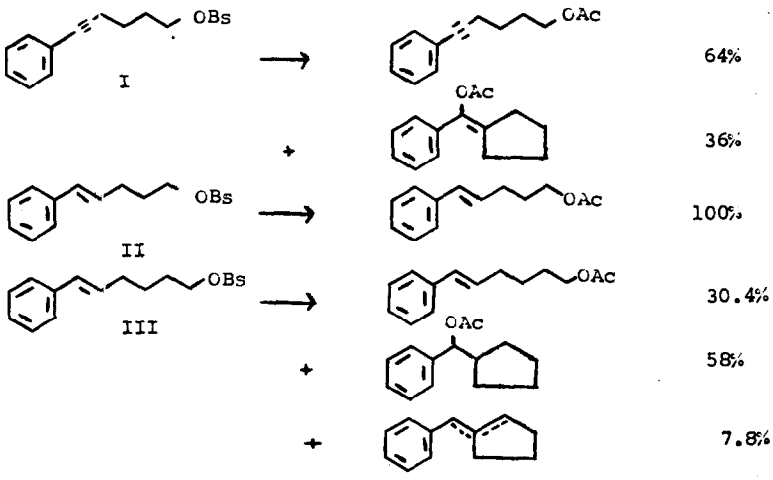
Table I

Rates of Acetolysis at 80°[a]

Brosylate	10^5 k, $sec.^{-1}$
6-phenylhexyl (V)	0.392 ± 0.008
trans-5-phenyl-4-pentenyl (II)	0.309 ± 0.003
trans-6-phenyl-5-hexenyl (III)	1.27 ± 0.01
trans-6-p-anisyl-5-hexenyl (IV)	3.12 ± 0.03
6-phenyl-5-hexynyl (I)	0.37 ± 0.01[b]

[a]Solutions were initially 0.03 M in brosylate and 0.036 M in sodium acetate. [b]Downward drifting rate constant.

Chart I[a]



[a]Product studies made under same conditions as used for kinetic measurements (see Table I). Products were isolated by gas chromatography and identified by comparison with authentic samples.

Most interesting is the 6-phenyl-5-hexynyl system (I) where a 36% yield of the enol acetate of phenyl cyclopentyl ketone on acetolysis indicates intramolecular displacement by the triple bond competes well with attack of solvent and acetate ion on the brosylate. The importance of the phenyl group in aiding and orienting the cyclization reaction is apparent since only the five-ring product is formed. This contrasts with the 6-heptyn-2-yl system where solvolysis of the tosylate in trifluoroacetic acid yields principally 3-methylcyclohexenyl product[3] and to 4-pentyn-1-yl tosylate which does not cyclize on acetolysis.[5] Synthetic implications of this reaction are considerable since such facile cyclization of a hexynyl system in buffered acetic acid indicates that the strong acid solvents (formic and trifluoroacetic acids) used in previous cases[2,3] and the frequent side reactions encountered in these solvents, may be avoided in adapting cationic alkyne cyclization to the synthesis of cyclic and polycyclic structures.

As in several similar cases where the double bond is between carbons 4 and 5 from the reaction center,[6] trans-5-phenyl-4-pentenyl brosylate (II) does not cyclize on acetolysis. However, as shown in Chart I, trans-6-phenyl-5-hexenyl brosylate (III) yields 66% of phenylcyclopentylcarbinyl products. Under similar conditions the 5-hexenyl system affords only 16% of cyclized product (exclusively cyclohexene and cyclohexyl acetate)[6a] indicating

the trans-styryl double bond to be about ten times as efficient as an internal nucleophile as the vinyl group. This is similar to the effects seen in comparing formolysis of 6-methyl-5-heptenyl nitrobenzenesulfonate[6e] (where a tertiary cation may be formed on cyclization) with that of the 5-hexenyl ester.[7] The propensity for five-membered ring formation, noted in the 6-methyl-5-heptenyl system[6e] and in I, is also observed here and is clearly a result of formation of the more stable cyclized carbonium ion. Increased stabilization of the intermediate cation, as would be present in the case of trans-6-p-anisyl-5-hexenyl brosylate (IV), should be reflected in a higher yield of cyclized product. A 90% yield of anisylcyclopentylcarbinyl products is obtained on acetolysis of IV. It would be expected that use of a more polar, less nucleophilic solvent should result in complete cyclization of III and IV, though competing addition of solvent to the double bond may also become important.

Assuming that the reaction products in these cases are the result of two parallel reactions, one can evaluate the rate of the "normal" acetolysis reaction and the rate of the cyclization process from the overall acetolysis rate constant and the product composition. While crude, since these estimated rate constants depend on accuracy of product analysis, the data are interesting. The "normal" acetolysis rates for III and IV are 0.43 and 0.32, x 10^{-5} $sec.^{-1}$, respectively, probably within experimental error of the measured rate for 6-phenylhexyl brosylate (V). This lack

of inductive effect of distant double bonds has been observed in cyclopentenylalkyl brosylates, also.[8] (With respect to the phenyl group, it should be noted that V and 3-cyclopentylpropyl brosylate have identical acetolysis rates.)[6b] The acetylenic system, I, has an estimated "normal" rate of 0.24×10^{-5} sec.$^{-1}$, indicating a 40% reduction in rate on changing a phenylethyl substituent to phenylethynyl. This is in keeping with previous observations of appreciable inductive effects by remote triple bonds.[9] Whether this inductive effect is responsible for the six-fold difference in the calculated rates of the cyclization reactions for I and III (0.13 and 0.84, $\times 10^{-5}$ sec.$^{-1}$, respectively), or whether steric differences and differences in carbonium ion stability are more important is not clear.

Further studies of stereochemistry and substituent effects in these systems are in progress.

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