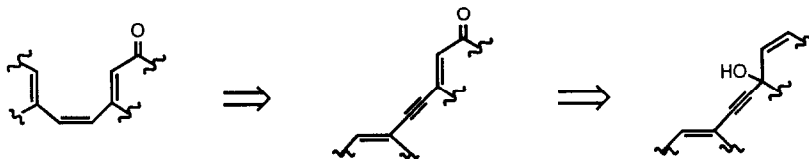


PYRIDINIUM DICHROMATE-INDUCED 1,3-OXIDATIVE REARRANGEMENTS OF ENYNOLS.

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Summary: The pyridinium dichromate-induced oxidative rearrangements of various 1-ene-4-yne-3-ols have been examined. These reactions occur regioselectively at the olefin site and are only synthetically useful with Z-substituted enynols.

The frameworks of many natural products lend themselves to synthetic strategies which have as their key step a 6π thermal electrocyclization process. However, the viability of this approach depends in large part on the availability of general and reliable methods for the preparation of the required trienes. Retrosynthetically, these trienes can be envisaged as being prepared by reduction of dienynes, which, in turn, might conceivably be prepared by oxidative rearrangement of suitably-functionalized tertiary allylic alcohols^{1,2} (*vide infra*). Implicit to the successful use of the latter process is the notion that the oxidative rearrangement will occur regioselectively at the olefinic site.



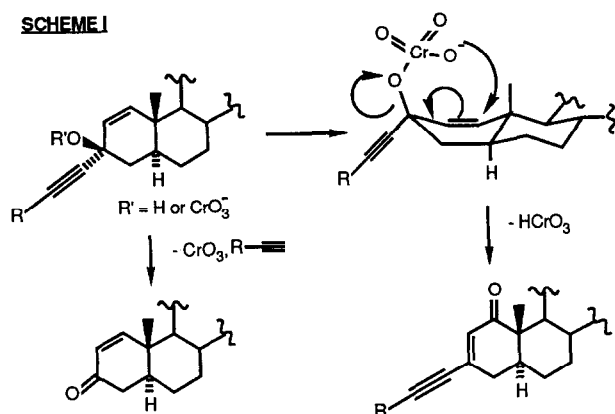
As a means of testing the viability of this approach, we have: (a) prepared a series of enynols and (b) studied their oxidative rearrangement with pyridinium dichromate (PDC).³ Each of the enynols was synthesized by addition of a lithium acetylide to an enone in dry THF at -78°C .⁴ The oxidative rearrangements were carried out using 1.5 equivalents of PDC in methylene chloride at room temperature for times ranging between 16 and 44 hours. The products and yields for each of these sequences are given in Table 1.

For all cases studied these PDC-induced oxidative rearrangements proceeded with complete regioselectivity. In six of the cases (Entries 1-6), the yields of transposed enones were good to excellent. Apparently, this type of rearrangement is capable of tolerating a moderate degree of steric hindrance around either the starting tertiary alcohol (e.g., Entry 6) or the allylic carbon which is ultimately oxygenated (e.g., Entry 2). Since products derived from oxygenation at the acetylenic site were never observed, we conclude that these reactions probably do not involve the intermediacy of any discrete cationic species, but instead proceed through a [3,3]-sigmatropic rearrangement.

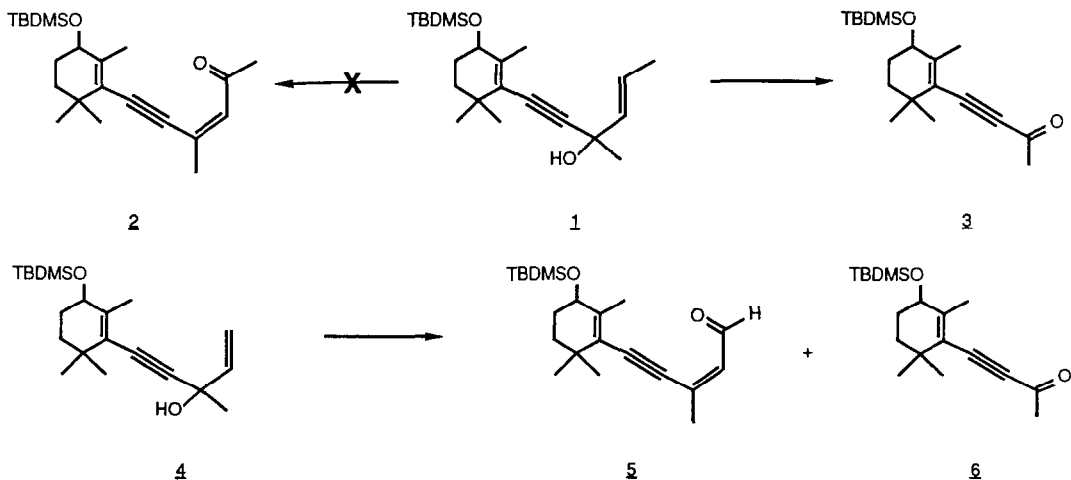
TABLE I

1) $R_1=R_2=H, R_3=Me$ 2) $R_1=R_2=Me, R_3=Me$ 3) $R_1=R_2=R_3=H$	92% 97% 70%	88% 96% 71%
4)		
	90%	78%
5)		
	70%	62%
6)		
	95%	90%
7)		
	96%	23%
8)		
	94%	32%
9)		
	99%	0%

In order to help define the structural limitations of these processes, we have prepared a number of substrates for study. For example, in Entries 7 and 8, the *trans* A-B ring juncture locks the C-3 hydroxyl group in a pseudo-equatorial orientation, thereby requiring the [3,3]-sigmatropic rearrangement to proceed via a boat-like transition state. Although in each case the rearranged enones were produced in fair yields, significant amounts of the starting enones were also observed. Chromate ester formation and subsequent ring flip to an A-ring boat, necessarily creates a severe 1,4-steric (flagpole) interaction. As a consequence of this, the relative population of the required reactive intermediate should be significantly reduced, thereby allowing processes to compete which are not normally competitive with the rearrangement (such as acetylide ejection, see Scheme 1).



Attempted oxidative rearrangement of the alcohol derived from α -ionone (Entry 9) resulted in a complex mixture of products, implying that the procedure may be limited to cyclic allylic alcohols. This is consistent with Dauben's findings that pyridinium chlorochromate (PCC)-induced oxidative rearrangements of simple tertiary allylic alcohols work best in systems containing *Z*-double bonds.^{1a,5} To probe this, we examined the oxidative rearrangements of two additional substrates.



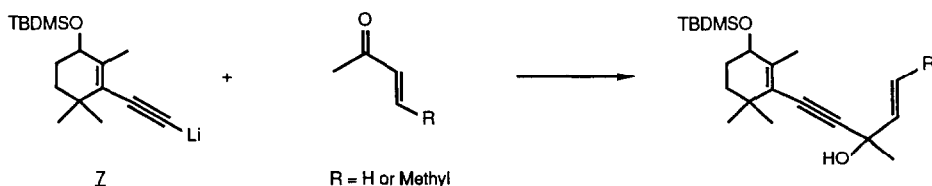
Exposure of **1**⁶ to PDC gave none of the desired oxidative rearrangement product **2**. Instead, ketone **3** was quantitatively produced.⁷ This material appears to be the result of a vinyl hydrogen abstraction, followed by carbon-carbon bond scission. PDC treatment of the unmethylated alcohol **4**⁶ resulted in a 3:1 mixture of **5** and **6**, suggesting that in situations where both E- and Z-vinyl hydrogens are available, the rearrangement and fragmentation processes are competitive.

In conclusion, PDC-induced oxidative rearrangements of enynols have been shown to be completely regiospecific and therefore probably involve a [3,3]-sigmatropic rearrangement. These processes are synthetically useful with Z-substituted enynols. However, with E-substituted enynols, oxidative rearrangement competes with a variety of carbon-carbon bond scission processes.

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- Compounds **1** and **4** were prepared by addition of lithium acetylide **Z** to propenyl methyl ketone and methyl vinyl ketone, respectively (*vide infra*).



- The structure of ketone **3** was unequivocally established by independent synthesis.

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