

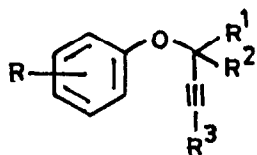
A NOVEL SYNTHESIS OF FLAV-3-ENES BY CLAISEN REARRANGEMENT

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ABSTRACT : 1-Arylprop-2-ynyl aryl ethers (6) undergo a facile Claisen rearrangement in N,N-diethylaniline/o-dichlorobenzene to give flav-3-enes in good yields.

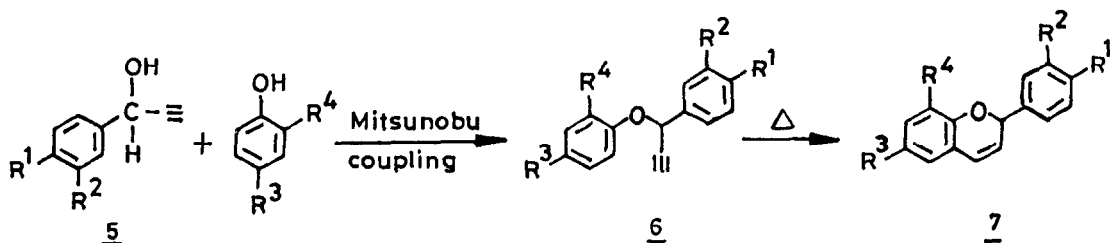
Though the aryl propargyl ether Claisen rearrangement has been recognised as one of the simple routes for the synthesis of 2H-1-benzopyrans¹ there are hardly any reports about its application for the synthesis of flav-3-enes. Among the aryl substituted aryl propargyl ethers only the rearrangement of a few 3-phenylprop-2-ynyl aryl ethers (1) to the respective 2H-1-benzopyrans is known². The rearrangement of but-3-yn-2-yl aryl ethers (2) and 2-methylbut-3-yn-2-yl aryl ethers (3), particularly the latter, proceed with great facility furnishing the corresponding benzopyrans³. In the light of these reports one could expect that 1-arylprop-2-ynyl aryl ethers (6) should rearrange readily to the flav-3-enes. Further, the development of conjugation in the transition state in these cases should provide additional driving force for the initial 3,3-sigmatropic rearrangement⁴. Surprisingly there are no reports in the literature even about the preparation of 1-arylprop-2-ynyl aryl ethers.



1. R¹, R² = H; R³ = Ph
2. R¹ = CH₃; R², R³ = H
3. R¹, R² = CH₃; R³ = H
4. R¹, R², R³ = Ph

Against this literature background we sought to prepare and investigate the Claisen rearrangement of 1-arylprop-2-ynyl aryl ethers. While these ethers could not be prepared by nucleophilic displacements on the chloride of 1-phenylprop-2-yn-1-ol with phenols, application of the Mitsunobu method for the coupling of the alcohols 5 with phenols afforded the desired 1-arylprop-2-ynyl aryl ethers 6a - 6k in moderately good yields, free from complications due to acetylene-allene rearrangements⁵. Heating these ethers at 180°C in N,N-diethylaniline or poly(ethylene glycol)-200 for 30 minutes yielded the

flav-3-enes 7a-7k in 84-95% yield (Table). All these flav-3-enes have been thoroughly characterised by spectral data, and in the case of 7a and 7f the structures were further confirmed by comparison with the respective authentic samples prepared by the method of Marathe et al⁶.



Table

Entry	R ¹	R ²	R ³	R ⁴	Yield of <u>6</u> (%)	Yield of <u>7</u> (%)
a	H	H	H	H	52	93
b	H	H	CH ₃	H	51	95
c	H	H	Cl	H	50	94
d	H	H	OCH ₃	H	46	92
e	H	H	H	CH ₃	51	94
f	OCH ₃	H	H	H	51 ⁺	93
g	OCH ₃	H	CH ₃	H	55 ⁺	90
h	OCH ₃	H	Cl	H	45 ⁺	90
i	OCH ₃	H	OCH ₃	H	45 ⁺	91
j	OCH ₃	OCH ₃	CH ₃	H	50 ⁺	93
k	H	H	NO ₂	H	40	84

⁺ The ethers were found to contain 30-40% of the corresponding flav-3-enes. The mixtures were subjected to rearrangement as such.

Though 3-nitroflav-3-enes are well known, there are hardly any reports in literature on the synthesis of flav-3-enes with nitro groups in either of the aromatic rings. These compounds could be potential intermediates in the synthesis of amino flavanoids⁷. The Mitsunobu coupling of 1-phenylprop-2-yn-1-ol with 4-nitrophenol furnished the ether 6k in 40% yield. Attempted rearrangement of 6k in N,N-diethylaniline led to extensive decomposition.

However, rearrangement of 6k in *o*-dichlorobenzene⁸ at 180°C furnished the 6-nitroflav-3-ene (7k) in 84% yield.

Monitoring the progress of the rearrangement prop-2-ynyl aryl ether, but-3-yn-2-yl aryl ether and 1-phenylprop-2-ynyl aryl ether by ¹H nmr indicates the relative rates of the rearrangement to be 1:9:63. This demonstrates the significant rate acceleration attendant upon the introduction of one phenyl group in the α -position. Full kinetic investigations are in progress.

The facility with which the 1-arylprop-2-ynyl aryl ethers rearrange to the flav-3-enes prompted us to reinvestigate one of the earlier works of Hurd et al⁹ on the Claisen rearrangement of 1,1,3-triphenylprop-2-ynyl aryl ether (4). It was reported by these workers that attempted rearrangement of 4 neat at 350°C led only to 9-phenylethynylfluorene in 45% yield. The rearrangement of 4 in a solvent like *N,N*-diethylaniline¹⁰ or poly(ethylene glycol)-200¹¹, the solvents recommended for propargyl Claisen rearrangement, has not been investigated. The ether 4, prepared by the Mitsunobu coupling of 1,1,3-triphenylprop-2-yn-1-ol with phenol, underwent a facile Claisen rearrangement in *N,N*-diethylaniline at 180°C during 20 minutes to furnish the known 2,2,4-triphenylbenzopyran¹² in 85% yield. The product was characterised by ¹H nmr, ir, uv and mass spectral data.

Flav-3-enes are important starting materials in the synthesis of other classes of flavanoids¹³. The most widely adopted route to the synthesis of flav-3-enes is through the 2'-hydroxychalcones¹³, while other routes involve 4-bromoflavans¹⁴, chrom-2-ene¹⁵ and *o*-cinnamylphenols¹⁶. The route discussed in this communication provides a short, facile and general entry to the flav-3-enes via a facile 3,3-sigmatropic rearrangement.

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