Solvent-assisted Acetylenic Oxy-Cope Rearrangement: a Novel Synthesis of Ionone and its Analogues

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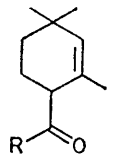
Summary Acetylenic oxy-Cope rearrangement of cyclohex-2-enylprop-2-ynols, a new type of synthetic equivalent of ionone and its analogues, has been investigated in neat and solvent-assisted systems.

ONLY a few examples of triple bond participation in the oxy-Cope rearrangement[1,2] have been reported, particularly in open chain systems, in spite of the extensive studies of reactions of hexa-1,5-dienol systems. Recently we reported the effect of change of solvent on the [3,3] sigmatropic rearrangement of hexa-1,5-dienol systems, which increases the selectivity of the [3,3] shift and causes some variation in the stereochemistry of the $\delta\epsilon$-unsaturated ketone formed.[3] We have now extended the investigation to the acetylenic oxy-Cope process and studied reactions of the cyclohex-2-enylprop-2-ynols (**2**),† synthetic equivalents of ionone and its analogues.

Thermal rearrangement of neat (**2**) at 160 °C for 20 h under nitrogen mainly gives the $\alpha\beta,\delta\epsilon$-unsaturated ketones (**3**) together with the isomeric compounds (**4**) and (**5**), bulky substituents R resulting in increased formation of (**3**). β-Hydroxyacetylene cleavage, which has been reported to

† The alcohol (**2**) was obtained in *ca.* 75% overall yield from cyclogeraniolene, *via* the $\beta\gamma$-unsaturated ketone (**1**), by zinc chloride-catalysed acylation with the appropriate acyl anhydride [J. K. Groves and N. Jones, *J. Chem. Soc.* (*C*), 1968, 2215; E. Klein and W. Rojahn, *Tetrahedron Letters*, 1971, 3607] followed by reaction with acetylene mono-Grignard reagent.



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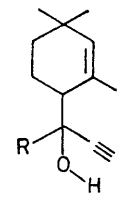

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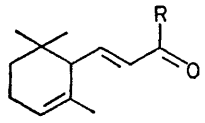

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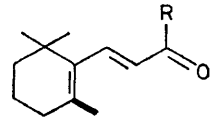

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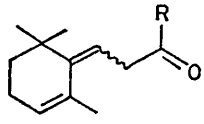

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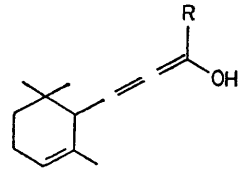

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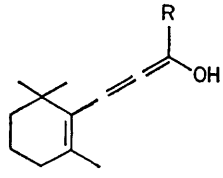

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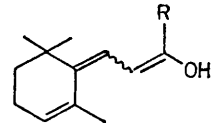

(8)

be absent in this type of vapour-phase acetylenic oxy-Cope reaction,[2] takes place only to a small (*ca.* 2—4%) extent, but it was nevertheless clearly observed as a side reaction.

The use of n-decane as solvent (volume = 2 × volume of reagents) suppresses the formation of (**4**), and increases the yield of (**5**) by an equivalent amount. However, when *N*-methyl-2-pyrrolidone (NMP) is used as solvent, it increases the yield of (**4**). The detailed effect of hexamethylphosphoric triamide (HMPA) solvent, in which little rate acceleration is observed, has not been clarified owing to its ability to isomerize (**3**) and (**4**). These solvents neither influence the β-hydroxyacetylene cleavage nor increase the selectivity of the [3,3] shift.[4] Isomerization of (**3**) to (**4**) occurs under these conditions only in HMPA. The results are presented in the Table.

TABLE. Results of acetylenic oxy-Cope rearrangement of (**2**)[a]

Compound (**2**) R	Solvent[b]	Conversion of (**2**)[c]/%	Selectivity of product[c] /%	Ratio[d] of (**3**):(**4**):(**5**)
Me	None	92	80	61:11:28
"	n-Decane	84	78	61: 0:39
"	NMP	90	78	42:58: 0
"	HMPA	100	67	36:64: 0
Et	None	93	78	68:16:16
"	n-Decane	87	66	73: 2:25
"	NMP	90	75	59:30:11
Pr[i]	None	92	79	87:11: 2
"	n-Decane	91	70	81: 6:13
"	NMP	94	70	68:31: 1

[a] Reactions were carried out at 160 °C for 20 h under nitrogen. [b] Volume = twice volume of reagent. [c] Conversions and selectivities were determined by g.l.c. and selectivity represents [yield of (**3**) + (**4**) + (**5**)]/[conversion of (**2**)]. [d] The figures represent percentages of ionone as determined by g.l.c.

The dienone (**5**), not obtainable by the isomerization of (**3**) or (**4**) under these conditions and, to our knowledge a new type of [3,3] sigmatropic rearrangement product, is probably derived from the intermediate (**8**). We suggest, therefore, that in n-decane the allylic proton shift of (**6**) tends towards structure (**8**) rather than (**7**). In the case of NMP solvent, it is not certain whether the increased formation of (**4**) at the expense of (**3**) is a result of a cyclic transition state for hydroxy proton transfer of (**6**), as proposed by Viola,[2] or whether the allylic proton shift of (**6**) in this solvent is towards (**7**) because the reaction is accompanied by isomerization of (**5**) to a mixture of (**3**) and (**4**).[5]

We thank Dr. M. Shiono for discussions on the mechanism.

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[1] J. W. Wilson and S. A. Sherrod, *Chem. Comm.*, 1968, 143; A. Viola and J. H. MacMillan, *J. Amer. Chem. Soc.*, 1968, **90**, 6141.
[2] A. Viola and J. H. MacMillan, *J. Amer. Chem. Soc.*, 1970, **92**, 2404.
[3] Y. Fujita, T. Onishi, and T. Nishida, *Synthesis*, in the press.
[4] In open-chain 4-isopropenyl-3,7-dimethyloct-6-en-1-yn-3-ol systems (Y. Fujita, F. Wada, T. Onishi, and T. Nishida, *Chem. Letters*, 1977, 943), we have succeeded in increasing the selectivity of the [3,3] shift from *ca.* 40% in the neat system to *ca.* 68% in NMP (Y. Fujita, T. Onishi, and T. Nishida, unpublished results).
[5] A. van Wageningen, P. C. M. van Noort, and H. Cerfontain, *J.C.S. Perkin II*, 1974, 1662.