Syntheses of Some 2-Substituted Cyclohexenones by Michael-type Reactions on Tetrahydropyran-2′-yloxy-cyclohexenes

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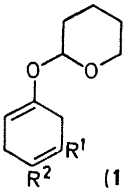
Summary A tetrahydropyran-2-yloxy-group activates a double bond in a cyclohexene or cyclohexadiene system in a similar way to an amino-group, and thermal reactions with αβ-unsaturated carbonyl derivatives result in good yields of 2-substituted cyclohexanones or cyclohexenones.

1-METHOXYCYCLOHEXA-1,4-DIENES, obtainable by metal–ammonia reductions of anisoles, react with dienophiles to give initially 1-methoxycyclohexa-1,3-dienes, conjugation occurring through charge-transfer complexes,[1] and finally to produce Diels–Alder adducts.[2] The tetrahydropyranyl ethers of phenols are similarly reducible,[3] and methyl acrylate has been added to 1-(tetrahydropyran-2′-yloxy)-cyclohexa-1,3-diene to produce the Diels–Alder adduct in low yield, with other unidentified products.[3]

Reaction of the diene (**1**; $R^1 = R^2 = H$) with the *trans*-ketone (**2**) results in a different type of reaction, the product being the diketone (**5**; $R^1 = R^2 = H$). Presumably (**5**) is derived according to the indicated addition mechanism (**3**), yielding (**4**; $R^1 = R^2 = H$), which produces (**5**) upon conjugation. The diene (**1**; $R^1 = H$, $R^2 = Me$) in fact produces initially the βγ-unsaturated ketone (**4**; $R^1 = H$, $R^2 = Me$) which can be converted into (**5**; $R^1 = H$, $R^2 = Me$ by further heating. The diene (**1**; $R^1 = Me$, $R^2 = H$) directly produces the diketone (**5**; $R^1 = Me$, $R^2 = H$). The reaction conditions involve heating in a sealed evacuated tube to 180° for 48 hr. or 210° for 12 hr., and the yields are of the order 60—90% based on the initial phenol.

The 6-methyl-2-(2′-oxocyclohex-6′-enyl)heptan-4-one (**5**; $R^1 = R^2 = H$) had b.p. 125—127°/0·1 mm., ν_{max} 1713, 1674, 1614 cm.$^{-1}$, λ_{max} (EtOH) 236 nm (ε 11,900), and *m/e* (*M*) 222(11), 165(100), 137(60), 123(36), 85(23), and 57(35) arising by expected fragmentations. The structure is supported also by the n.m.r. spectrum: δ ($CDCl_3$) 6·70 (t, 1H, *J* 4 Hz; $-C{=}CH-$), 3·16 (m, 1H; $=CCH\text{Me}CH_2$), 2·6—1·8 (m, 11H), 1·07 (d, 3H, *J* 7 Hz; CH_3CH), 0·90 [d, 6H, *J* 7Hz; $(CH_3)_2CH$]. Double resonance experiments substantiate the assignments, and solvent shifts in perdeuteriobenzene are in accord with those expected[4] in an αβ-unsaturated carbonyl system, Hydrogenation (Pd–C



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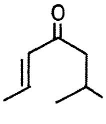

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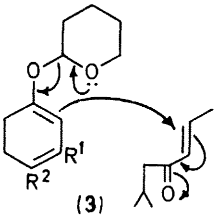

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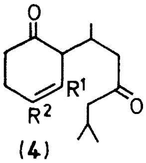

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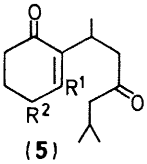

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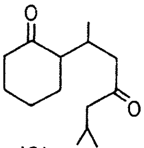

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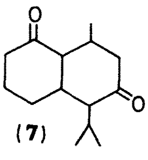

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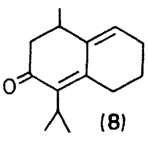

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in acetic acid) gave the diketone (**6**), the spectra (mass, u.v., i.r., n.m.r.) of which are in accord with the structure.

Cyclisation of (**5**; $R^1 = R^2 = H$) with 0·1N-sodium ethoxide in ethanol gives the bicyclic diketone (**7**), and reaction of (**5**; $R^1 = R^2 = H$) with toluene-*p*-sulphonic acid in refluxing benzene gives the bicyclic dienone (**8**), the structures of which are fully supported by analyses and spectra. Similar products were obtained from (**5**; $R^1,R^2 =$ H,Me or Me,H). The second double bond of the cyclohexadiene is not necessary for the initial addition reaction, since 1-(tetrahydropyran-2′-yloxy)cyclohexene obtained by reduction of (**1**; $R^1 = R^2 = H$) using Wilkinson's catalyst,[5] gives the diketone (**6**) directly.

The process, therefore, leads potentially to a number of interesting mono- and bicyclic ketones from readily available materials. Moreover, unlike the unsymmetrical enamines, the double bond can usually be produced in a specific position owing to the known specificities of reduction and isomerisation processes.

We are indebted to Mr. K. B. Chamberlain for technical assistance and to Zoecon Corporation for financial support.

(*Received, October* 31*st*, 1969; *Com.* 1656.)

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