A Tandem Oxidation–Intramolecular Diels–Alder Reaction

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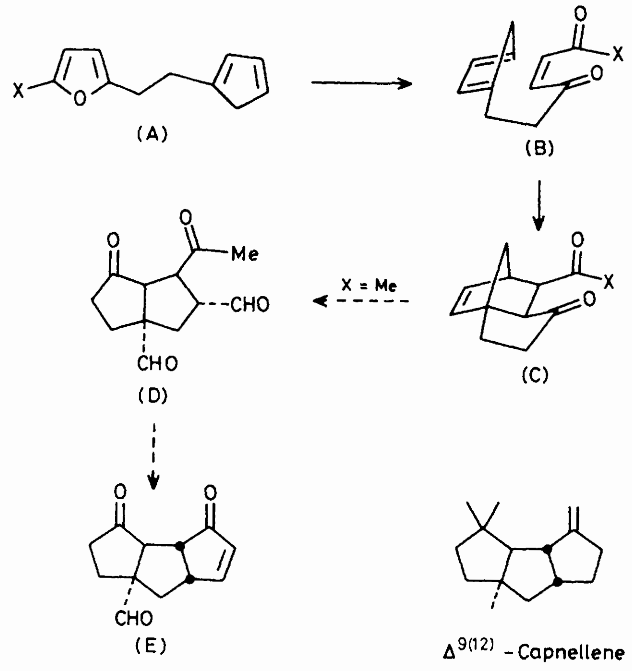
Oxidation of the furan (**4**) with pyridinium chlorochromate gave the intramolecular Diels–Alder cycloadduct (**6**) as the major product, presumably *via* the intermediate (**5**).

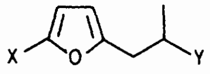
There is considerable current interest in the intramolecular Diels–Alder reaction and it has been applied to a number of synthetic objectives with notable success.[1] Recently several research groups have reported[2] that oxidation of the furan ring gives the corresponding enedione, a good dienophile. In an effort to synthesise the capnellene type skeleton, we have designed an approach which utilizes the furan ring as an enedione precursor for the intramolecular Diels–Alder reaction, Scheme 1. A similar sequence has recently been reported to afford the hydrindenone skeleton.[3] To our knowledge there are very few examples[4] of an oxidation reaction spontaneously followed by an intramolecular Diels–Alder reaction at room



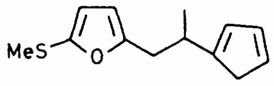
Scheme 1

temperature. In this communication we report the results of such a reaction.

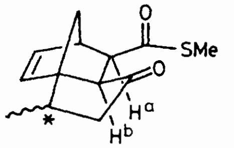
Metallation[5] of furan with Bu^{n}Li in dry tetrahydrofuran (THF) at room temperature followed by addition of propylene oxide gave the alcohol (**1**) in high yield (90%).† Reaction of (**1**) with 2.5 equiv. of Bu^{n}Li followed by addition of dimethyl disulphide gave compound (**2**) (60—70%) which was converted into the *p*-toluenesulphonate derivative (**3**) (85%). Reaction of compound (**3**) with the cyclopentadienyl anion[6] gave compound (**4**) (68%). Oxidation of compound (**4**) with 2 equiv. of pyridinium chlorochromate (PCC)[2] in CH_2Cl_2 at room temperature for 2 hours gave compound (**6**) as the major product in 40% yield (unoptimized yield). From the ^1H and ^{13}C n.m.r. spectra, product (**6**) was shown to be a mixture of two epimers (ratio 1 : 1); its epimeric centre is denoted by an asterisk. The product (**6**) was presumably formed by an intramolecular Diels–Alder reaction of the intermediate (**5**) formed by oxidation of compound (**4**) with PCC. Attempts to isolate the intermediate (**5**) were not successful. Interrupting the oxidation of (**4**) also gave (**6**) as the major product with unreacted starting material (**4**).



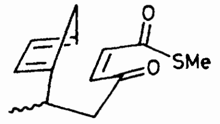
(**1**) X = H, Y = OH
(**2**) X = SMe, Y = OH
(**3**) X = SMe, Y = p-$MeC_6H_4SO_3$



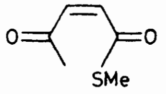
(**4**)



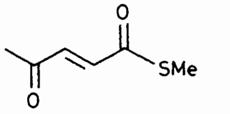
(**6**)



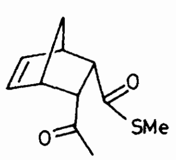
(**5**)



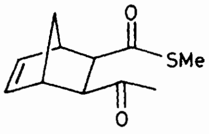
(**7**)



(**8**)



(**9**)



(**10**)

In order to ensure oxidation of the furan ring of (**4**) to give the α,β-unsaturated carbonyl ester function of (**5**) and then rapid cycloaddition of this dienophile function with the cyclopentadiene ring in the same molecule at room temperature, the following procedure was carried out. Oxidation of 2-methylthio-5-methylfuran (prepared by reaction of 2-methylfuran with Bu^{n}Li in THF followed by addition of dimethyl disulphide) with two equiv. of PCC at room temp. for 2 h gave a single product (**7**) in 70% isolated yield. A longer oxidation reaction time (24 h) gave the *cis*-isomer (**7**) and the *trans*-isomer (**8**) in a ratio of 1 : 2.‡ It is known that PCC can cause *cis–trans* isomerization during the oxidation of furan.[2a] Reaction of the *cis*-isomer (**7**) with cyclopentadiene at room temp. for 6 h gave the *endo* adduct (**9**) as the major product and the *exo* adduct (**10**) as the minor product in a ratio of 6 : 1 in 80% yield.§

Since under the same reaction conditions the conversion of (**4**) into (**6**) (2 h) is faster than the isomerization of the *cis*-isomer (**7**) to the *trans*-isomer (**8**), the stereochemistry of the enedione alkene bond of the intermediate (**5**) was assigned as *cis*. Models show the transition state for *exo* addition to be much more readily available than that for *endo* addition. Therefore it is reasonable to assume that (**6**) is the *exo* adduct with the stereochemistry as suggested.

The stereochemistry of (**6**) can also be assigned by

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† *Spectral data.* (**1**): i.r., $\nu_{max.}$ (CHCl$_3$) 3400 cm^{-1}; n.m.r., δ 1.23 (d, 3H), 2.10 (br, 1H), 2.73 (d, 2H), 4.05 (sextet, 1H), 6.06 (d, 1H), 6.26 (dd, 1H), 7.30 (d, 1H); mass, M^+ 126. (**2**): i.r. 3400 cm^{-1}; n.m.r., δ 1.23 (d, 3H), 1.80 (br., 1H), 2.40 (s, 3H), 2.75 (d, 2H), 4.10 (sextet, 1H), 6.15 (d, 1H), 6.37 (d, 1H); mass, M^+ 172. (**3**): i.r., $\nu_{max.}$ (CHCl$_3$) 1360, 1180 cm^{-1}; n.m.r., δ 1.33 (d, 3H), 2.34 (s, 3H), 2.43 (s, 3H), 2.90 (dd, 2H), 4.85 (sextet, 1H), 6.08 (d, 1H), 6.33 (d, 1H), 7.29 (d, 2H), 7.70 (d, 2H); mass, M^+ 326. (**4**): i.r., 3080, 1615 cm^{-1}; n.m.r., δ 1.17 (d, 3H), 2.35 (s, 3H), 2.60—3.10 (m, 5H), 6.00—6.50 (m, 5H); mass, M^+ 220. (**6**): i.r., 1750, 1700, 1030 cm^{-1}; n.m.r. two doublets (3H) at δ 1.14 and 1.21, δ 1.30—1.45 (m, 1H), 1.90—2.30 (m, 3H), 2.34 (s, 3H), 2.38—2.75 (m, 2H), 2.85 (dd, 1H), 3.07 (m, 1H), 6.15—6.25 (m, 1H), two doublets (1H) at δ 6.35 and 6.50; mass, M^+ 236. (**7**): i.r., 1705, 1670, 1615 cm^{-1}; n.m.r., δ 2.35 (s, 3H), 2.42 (s, 3H), 6.24 (s, 2H); mass, M^+ 144. (**8**): i.r., 1695, 1665, 1610 cm^{-1}; n.m.r., δ 2.37 (s, 3H), 2.45 (s, 3H), 6.90 (s, 2H); mass, M^+ 144. (**9**): i.r., 1710, 1685 cm^{-1}; n.m.r., δ 1.30—1.50 (m, 2H), 2.03 (s, 3H), 2.26 (s, 3H), 3.10—3.35 (m, 3H), 3.72 (dd, 1H), 6.08 (dd, 1H), 6.48 (dd, 1H); mass, M^+ 210. (**10**): i.r., 1710, 1685 cm^{-1}; n.m.r., δ 1.36—1.56 (m, 1H), 1.96—2.10 (m, 1H), 2.12 (s, 3H), 2.32 (s, 3H), 2.62 (dd, 1H), 2.92—3.20 (m, 3H), 6.25 (m, 2H); mass, M^+ 210.

‡ The ratio was determined by n.m.r. spectroscopy and column chromatography separation of the crude oxidation products. The alkene protons of the *cis*-isomer (**7**) resonate at δ 6.24 (s, 2H) whereas those of the *trans* isomer (**8**) resonate is at δ 6.90 (s, 2H).

§ The ratio was determined by n.m.r. spectroscopy. The yield (80%) was the total yield of (**9**) and (**10**) from (**7**).

comparing its ^1H n.m.r. spectrum with the spectra of compounds (**9**) and (**10**). Compound (**9**) showed two separate sets of peaks at δ 6.08 (dd, 1H) and 6.48 for the two alkene protons since these two protons are affected by the two different functional groups in the *endo* configuration. Compound (**10**), the *exo* adduct, showed peaks at δ 6.25 (m, 2H) for the alkene protons. It is known that in the norbornene system[7] the *exo* protons show absorption at lower field (larger δ value) than that of the *endo* protons. Compound (**9**) showed two sets of peaks (dd) at δ 3.72 and 3.24 for the *exo* protons whereas compound (**10**) showed peaks at δ 2.62 and 2.96 for the *endo* protons. Compound (**6**) showed peaks for H^a and H^b at δ 2.60 and 2.85, chemical shift values similar to those of (**10**) rather than (**9**). The coupling constant, 8 Hz, between H^a and H^b indicates a *cis* configuration between these two protons. Thus, it was confirmed that (**6**) was formed by *exo* addition with a *cis*-configuration between H^a and H^b.

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