A Synthon for Epoxyolefin Cyclisation

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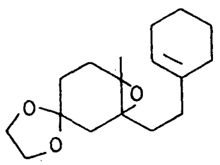
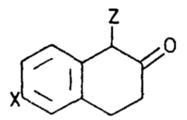
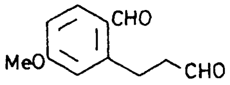
Summary An efficient synthesis of 1,2-epoxy-1-methyl-2-(3-oxopropyl)-4,4-ethylenedioxycyclohexane from 6-methoxy-2-tetralone is described; this aldehyde undergoes Wittig–Schlosser condensation to give epoxyolefins which are possible substrates for epoxyolefin cyclisation.

Previously we have described[1] the efficient cyclisation of (**1**) with BF_3 to an angularly methylated hydrophenanthrene. However, when additional chirality is introduced into compounds of type (**1**) the stereoselective introduction of the epoxide is difficult and diastereoisomeric mixtures are produced on cyclisation. This serious deficiency for stereoselective syntheses could be overcome if an epoxide of type (**1**) could act as an efficient initiator of polyenic cyclisation,[2] as developed by Johnson; here only the carbon atoms of the epoxide ring would be chiral while other chiral centres would be generated from geometrically isomeric double bonds. We now describe the synthesis of a versatile intermediate (**11**) which can be used for the preparation of a variety of polyene epoxides.

The tetralone (**2**) is readily available by Friedel–Crafts reaction of *p*-methoxyphenylacetyl chloride and ethylene;[3] various methods were investigated for the cleavage of the 1,2-bond the most satisfactory being acetoxylation[4] of (**2**) to (**3**) [$Pb(OAc)_4$–C_6H_6–$CaCO_3$; 56%], reduction to a mixture of the corresponding diols ($NaBH_4$–MeOH; 73%), and oxidation ($NaIO_4$; 97%) to the aldehyde (**5**) [τ (CCl_4) 0·08 (1H, s) and 0·25 (1H, t, *J* 1·2 Hz); ν_{max} (CCl_4) 1725 and 1690 cm^{-1}]. Reduction[5] of the aldehyde (**5**) ($LiAlH_4$–$4AlCl_3$–Et_2O; 90%) gave the alcohol (**6**) [τ CCl_4) 6·5 (2H, t; *J* 7 Hz) and 7·85 (3H, s)] which on Birch reduction (Li–NH_3–EtOH; 90%) gave the enol-ether (**8**), readily converted [$(CH_2OH)_2$–C_6H_6–TsOH; 80%] into the corresponding ethylene acetal [τ(CCl_4) 6·2 (4H, s), 6·6 (2H, t, *J* 7 Hz), and 8·43 (3H, s)]. Epoxidation of the acetal (*m*-$ClC_6H_4CO_3H$–K_2CO_3–CH_2Cl_2;


(1)


(2); X = OMe, Z = H
(3); X = OMe, Z = OAc
(4); X = Z = H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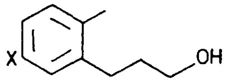
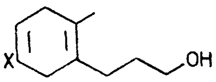
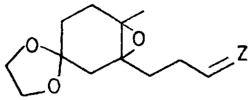
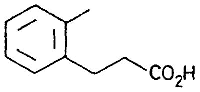

(6); X = OMe
(7); X = H


(8); X = OMe
(9); X = H


(10); Z = H, OH
(11); Z = O
(12); Z = CH_2
(13); Z = CHMe
(14); Z = $CH[CH_2]_2C(Me)=CH_2$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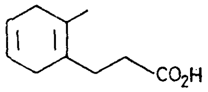
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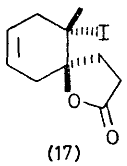
(17)

93%) yielded the epoxide (**10**) [τ(CCl_4) 6·5 (2H, m) and 8·75 (3H, s)] which on oxidation with Collins's reagent (CrO_3–C_5H_5N–CH_2Cl_2) formed the aldehyde (**11**) [τ (CCl_4) 0·25 (1H, t, *J* 1·5 Hz) and 8·8 (3H, s); ν_{max} (CCl_4) 1730 cm^{-1}]. Using the Schlosser modification[6] of the Wittig reaction the (*E*)-olefins (**12**), (**13**), and (**14**) could be prepared in good yield. Thus the aldehyde (**11**) is a useful precursor for the preparation of epoxyolefins.

In an attempt to prepare a more readily available synthon 2-tetralone was cleaved† [NaOH–KOH (2:1), 250 °C; 70%] to the acid (**7**) which on Birch reduction [Li–NH_3–EtOH] gave mainly (**16**) [τ (CCl_4) 4·4 (2H, m) and 8·4 (3H, s)] together with varying proportions of starting material and tetrahydro-product. Reduction of the alcohol (**7**) [from $LiAlH_4$ reduction of (**15**)] gave similar results. The unreduced aromatic acid (**15**) could be separated by conversion of (**16**) into the neutral (**17**) [τ (CCl_4) 4·4 (2H, m) and 8·05 (3H, s); ν_{max} (CCl_4) 1790 cm^{-1}] ($NaHCO_3$–KI_3); however, regeneration of (**16**) from (**17**) (Zn–AcOH) was always accompanied by the formation of *ca.* 5% of (**15**). Hydrogenation of (**9**) (H_2–Pd–$CaCO_3$) yielded the expected dihydro-derivative, but attempts to monoepoxidise (**9**) and the dihydro-derivative led to mixtures of the required monoepoxides and ethers derived from cyclisation of the side chain on to the epoxide. It is not clear why these epoxides are more readily cyclised than the acetal (**10**).

We thank the S.R.C. for financial support (to J. W. S.).

(*Received*, 25*th April* 1977; *Com.* 381.)

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† The methoxytetralone could not be cleaved by this method.

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