SYNTHESIS OF SUBSTITUTED BENZENOIDS AND BIPHENYLS VIA DIELS-ALDER

CYCLOADDITION OF 6-METHOXY-2-PYRONES

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Summary: A convenient synthesis of substituted 6-methoxy-2-pyrones from alkyl and aryl esters is described. These pyrones undergo Diels-Alder reactions with acetylenic dienophiles to provide an efficient route to polysubstituted benzoates, phthalates and biphenyls.

Although the synthesis of substituted benzenoids has been extensively investigated, 1 there remains a need for efficient general routes to them. A number of syntheses using cycloaddition reactions of pyrones have been described, 1-3 but they are disadvantaged by the lack of a general method for the synthesis of the required pyrones. Recent work on the synthesis of labelled mevalonic acid lactone 4 suggested a convenient route to a wide variety of substituted pyrones, and this route has been applied to the synthesis of isotopically-labelled 6-methoxy-4-methyl-2-pyrone (1a) which naphthoguinones² to reacts with provide а convenient route to isotopically-labelled anthraquinones.⁵ The extension of this work to provide a general route to substituted pyrones eg (la-e) and their reactions with acetylenic dienophiles is now reported.

The carbinols (3a-d) were prepared by treatment of the alkyl and aryl esters (2a-d) with allylmagnesium bromide, and carbinol (3e) was obtained from ethyl acetate and α -methyl-allylmagnesium chloride. Ozonolysis and cyclisation of the resultant β -hydroxyglutaric acids (4a-e) by heating with acetyl chloride give the glutaric anhydrides (5a-e), which on heating in xylene gave the glutaconic anhydrides (6a-e). Treatment with diazomethane² converted these to the desired 6-methoxy-2-pyrones in high overall yields.⁶

Pyrones (1a-e) reacted with dimethyl acetylenedicarboxylate in refluxing toluene to give the phthalates (7a-e) in moderate to good yields.⁶ Pyrones (1a) and (1c) were also converted to the benzoates (7f) and (7g) on reaction with methyl propiolate. The pyrones react much less readily with olefinic dienophiles. Of the variety tested only maleic anhydride proved sufficiently reactive and the initial adduct lost CO2 to give a diene which underwent a second cycloaddition to form a 2:1 adduct in agreement with previous studies.2,3





Reagents: (i) $CH_2 = CHCHR^2Br$, Mg, tetrahydrofuran, Et_2O ; (ii) O_3 , HOAc, CH_2Cl_2 ; (iii) H_2O_2 , HOAc; (iv) AcCl, reflux; (v) xylene, reflux; (vi) CH_2N_2 ; (vii) $R^3C = C.CO_2Me$, toluene, reflux.

<u>References</u>

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- 6. Yields have not been optimised. However the pyrones were formed in overall yields of 60-80% from the starting ester. Yields in the cycloaddition reactions varied from 35% for (7e) to 95% for (7d). All yields refer to isolated recrystallised materials.

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