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REACTIONS OF FURFURYL ALCOHOLS WITH MALEIC ANHYDRIDE

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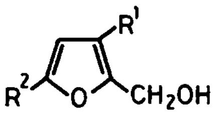
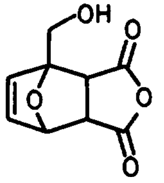
The reactions of some furfuryl alcohols with maleic anhydride have been reinvestigated and, for the first time, conditions defined for the production of intramolecular Diels-Alder adducts. In basic conditions these adducts yield phthalides in high yields.

Intramolecular Diels-Alder (IMDA) reactions of furans, pyrroles and thiophenes offer considerable scope for the synthesis of heterocycles and unusually substituted benzenoids.[1,2,3]

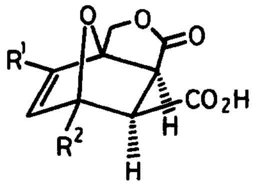
A special case of an IMDA reaction involving a furan nucleus was reported[4] for furanophane and utilised for the synthesis of the cis-indanyl dianion.[5] A striking and more general type of IMDA reaction is that of N-aryl-N-(2-furfuryl)allylamines[6] and the corresponding amides.[7] Despite having an unactivated dienophilic alkene group, the amines undergo spontaneous cyclisation by an IMDA reaction, and this has recently been put to use in chiral synthesis.[8] Attempts to generalise the reaction have met with limited success,[1] and in particular linking the diene and dienophile by an ester grouping gave negative results which were ascribed to conformational effects. Very recently[9] the reactions of furfuryl alcohols (1a) and (1c) with maleic anhydride (MA) in ether or benzene was reported to yield the IMDA adducts (3a) and (3c). No spectroscopic data for the adducts was given but, after hydrogenation they were converted electrochemically[10] to 2-oxabicyclo[2.2.1]-heptane-7-syn-carboxylic lactones, a result taken as proof of structure. However the physical characteristics reported for the adducts leads us to suspect that they are simply the normal Diels-Alder (NDA) adducts (5a) and (5c). This prompts us to briefly report our own work in this area, which is part of a broader investigation, and to describe for the first time the preparation of true IMDA adducts from this reaction.



(1)



(2)



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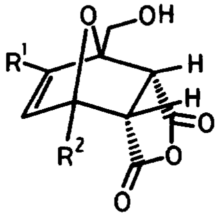

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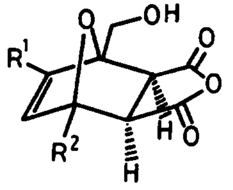


(5)

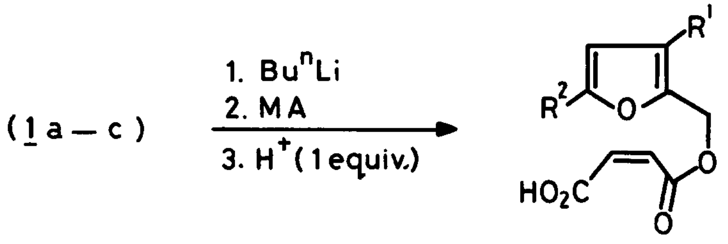
a, $R^1 = R^2 = H$

b, $R^1 = Me, R^2 = H$

c, $R^1 = H, R^2 = Me$

Furfuryl alcohol (1a) has been reported[11] to react with MA to yield an unstable NDA adduct, m.p. 82-83°C formulated as (2) as it yielded a monoacetate. We have reacted equimolar proportions of (1a) and MA at room temperature in various solvents (Et_2O, Me_2CO, EtOAc) to yield only the NDA adduct (5a) m.p. 82-82°C (Kawanisi, m.p. 82°C) fully characterised spectroscopically.[12,13] As a solid (5a) is stable for *ca* 2 days at 25°C, but in solution it rapidly reverts to the components which undergo the extensive polymerisation always found if the reaction is warmed.

When the reaction is carried out in *chloroform* at 25°C for 7 days there results a mixture (60:40)[14] of (5a) and (3a), the long sought tricyclic IMDA lactone, m.p. 123-124°C (d). The NDA (5a) is acetone soluble and readily removed to yield pure (3a). Alternatively a trace of moisture catalyses the conversion of (5a) to (3a) allowing us to formulate (5a) as the *exo*-adduct as well as prepare (3a) directly in 75% isolated yield. The presumed intermediate ester (6a) was prepared as in eq. 1 and cyclised to (3a) in *any* solvent in *ca* 40% yield. Thus the role of the chloroform is to potentiate esterification *versus* NDA reaction in favour of the former.

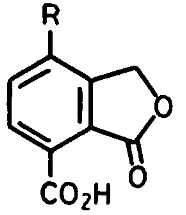


(6)

(1)

Alcohol (1b) reacts with MA in CHCl$_3$ to give (3b)^{12,13} m.p. 123-125°C (d) in 70% yield. The reaction proceeds first to yield the endo-adduct (4b), followed by the exo-adduct (5b) as monitored by ^{1}H n.m.r. The ester (6b) was prepared as in eq. 1 and cyclised to (3b) in 30% yield.

Alcohol (1c) gave only polymeric products when it was reacted with MA in CHCl$_3$, a result in line with the lability of the ester (6c). In ether however the unstable endo-adduct (4c)^{12,13} m.p. 83-84°C was isolable by filtration. From the mother liquors the exo-adduct (5c) m.p. 88-89°C^{12,13} (Kawanisi, m.p. 88°C) was isolated but no IMDA adduct (3c).



(7)

a, R = H

b, R = Me

We were unable to convert the IMDA adducts (3a) and (3b) to the phthalides (7a) and (7b) under acid conditions^6 despite extensive experimentation. However with 3M NaOMe in MeOH or with ^{t}BuLi aromatisation occurs to give (7a) and (7b) in 90% yields. Hence this constitutes a high yielding route to phthalides that is being further explored.

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References and Notes.

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12. I.r. data: (3a) ν_{max}^{KBr} 1710 (-COOH), 1785(lactone) cm^{-1}; (5a) ν_{max}^{nujol} 1790, 1870 anhydride), 3100, 3400 (OH) cm^{-1}; (3b) ν_{max}^{KBr} 1750 (-COOH), 1790 (lactone); (4c) ν_{max}^{nujol} 1780, 1860 (anhydride), 3440 (OH) cm^{-1}; (5c) ν_{max}^{KBr} 1780, 1860 (anhydride), 3380, 3440, 3550 (OH) cm^{-1}.
13. ^{1}H n.m.r. data (δ): (3a) (d_6Me_2CO) 2.96(q,2H,J10Hz), 4.76(q,2H,J12Hz), 5.16(d,1H,J2Hz), 6.56(q,1H,J2;5Hz) and 6.68(d,1H,J5Hz); (5a)(d_6Me_2CO-D_2O) 3.35(q,2H,J7Hz), 3.96(q,2H, J10Hz), 5.23 (broad s,1H) and 6.5(s,2H); (6a) ($CDCl_3$) 5.2(s,2H), 6.3(s,2H), 6.35(m,2H) and 7.4(m,1H); (6b) ($CDCl_3$) 2.1(s,3H,-CH_3), 5.2(s,2H), 6.2(d,1H,J3Hz), 6.3(s,2H) and 7.4(d,1H,J3Hz); (6c) ($CDCl_3$) 2.2(s,3H,-CH_3), 5.15(s,2H), 5.9(d,1H,J3Hz), 6.2(s,2H) and 6.25(d,1H,J3Hz); (3b) (d_6Me_2CO) 1.9(d,3H,J2Hz,-CH_3), 2.97(q,2H,J10Hz), 4.61(q,2H,J12Hz), 4.98(d,1H,J2Hz) and 6.05(quintet,1H,J2Hz); (4c) (d_6Me_2CO) 1.7(s,3H,-CH_3), 3.78(q,2H, J9Hz), 4.05(s,2H) and 6.4(s,2H); (5c) (d_6Me_2CO-D_2O), 1.6(s,3H,-CH_3), 3.4(q,2H,J7Hz), 3.9(q,2H,J10Hz) and 6.4(q,2H,J6Hz).
14. Calculated by integrating the bridge-head hydrogen signal in the ^{1}H n.m.r. spectrum.

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