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HETEROCYCLIC SYNTHESES WITH ALLENE-1,3-DICARBOXYLIC ESTERS AND ACIDS : NEW CHROMENE, CHROMONE, QUINOLONE, α-PYRONE AND COUMARIN SYNTHESES

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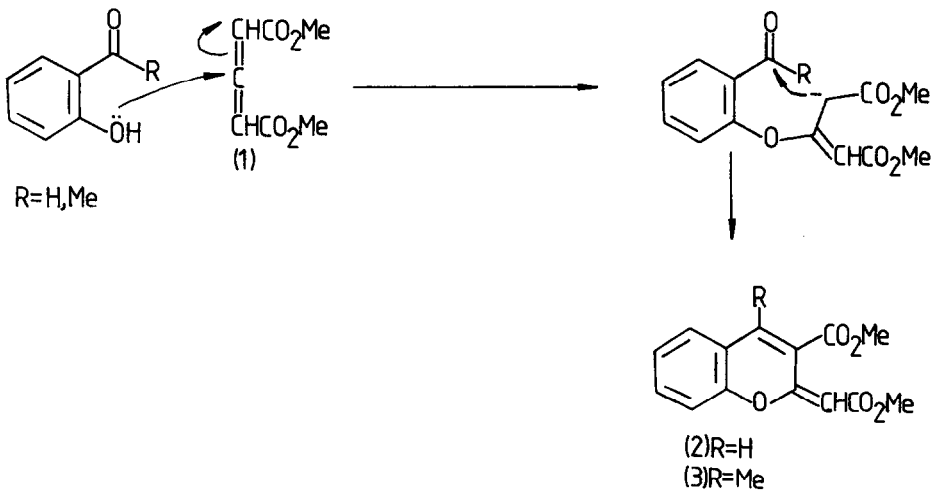
SUMMARY: Allene 1,3-dicarboxylic esters and acids have been converted into chromenes, chromones, an α-pyrone and a coumarin by reactions with phenols and to quinolones by reaction with aniline derivatives. A novel chromene → coumarin rearrangement is also reported.

We have previously demonstrated reactions of dimethyl penta-2,3-dienedioate (DPDD) (1) with substrates having two adjacent nucleophiles.[1] We have now extended the synthetic utility of DPDD by reaction with salicylaldehyde, o-hydroxyacetophenone, and methyl salicylate whereby the phenolic group acts as the nucleophile and the adjacent carbonyl as an electrophile. A novel rearrangement and other heterocyclic syntheses are also reported.

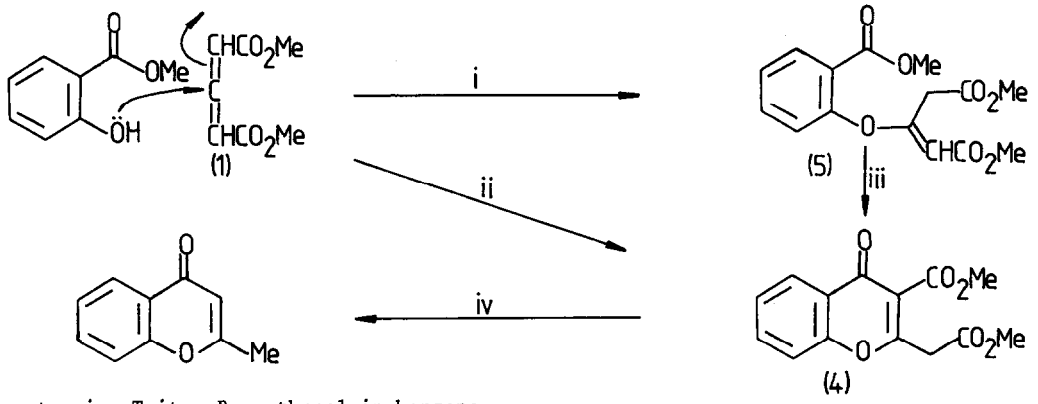
DPDD reacts at ambient temperatures with salicylaldehyde in benzene in the presence of benzyl trimethylammonium hydroxide (triton B) to give the chromene (2;61%)+ directly. Under similar conditions o-hydroxyacetophenone gave only a low yield of the chromene (3), but with potassium t-butoxide in t-butanol the desired product (3:38%) was more readily obtained.



Scheme 1.

+ The yields given in this paper have not been optimised.

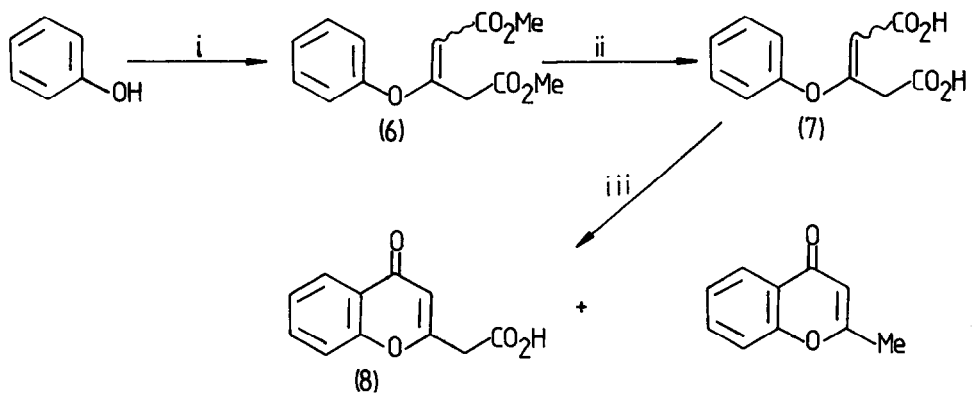
DPDD also reacts with methyl salicylate under the latter conditions to give the chromone (4;16%). The intermediate (5) was not isolated, but it could be prepared by reaction with methyl salicylate in benzene with DPDD in the presence of triton B and methanol in 11% yield. The enol ether (5) cyclised to the chromone (4;56%) in the presence of lithium diisopropylamide in tetrahydrofuran. The product was hydrolysed and decarboxylated to 2-methyl chromone (84%) with aqueous acetic acid containing a trace of sulphuric acid.



Reagents i. Triton B, methanol in benzene
ii. Potassium t-butoxide in t-butanol, iii. Lithium diisopropylamide in tetrahydrofuran. iv. Sulphuric acid in aqueous acetic acid.

Scheme 2.

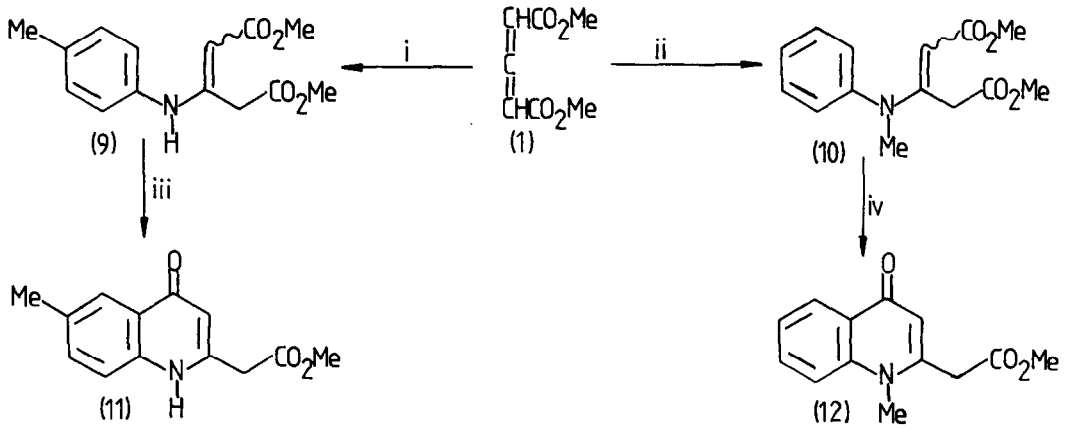
Heterocyclic synthesis may also be achieved from phenols and aromatic amines without the necessity of an adjacent carbonyl group (c.f. reaction of acetylenedicarboxylic esters[2 - 4]) Thus, reaction of phenol with DPDD in benzene with triton B as catalyst gave the enol ether (6;81%) which was hydrolysed with aqueous methanolic potassium hydroxide to the dibasic acid (7;93%). Cyclisation in the presence of polyphosphoric acid at 100° gave the chromone (8;23%), and also 2-methylchromone (23%).



Reagents i. DPDD, triton B in benzene, ii. Aqueous methanolic potassium hydroxide, iii. Polyphosphoric acid.

Scheme 3.

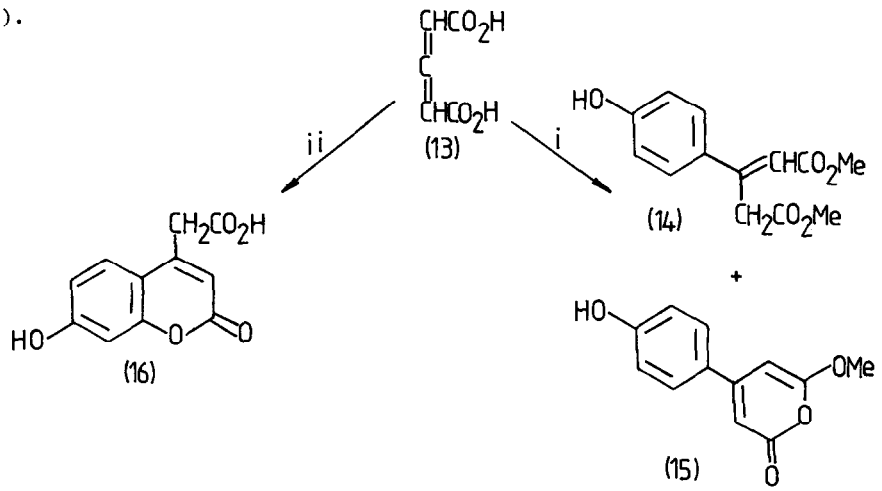
In a similar manner, DPDD reacts with p-toluidine in boiling methanol and N-methylaniline in boiling benzene to give the enamines (9;83%) and (10;80%) respectively. The enamine (9) cyclised in boiling 1,2-dichlorobenzene (180°) to give the quinolone (11;40%), whereas the enamine (10) derived from N-methylaniline failed to cyclise under these conditions, but in the presence of polyphosphoric acid at 100° the quinolone (12;71%) was formed.



Reagents i. p-Toluidine, methanol, ii. N-Methylaniline, benzene, iii. 1,2-Dichlorobenzene, iv. Polyphosphoric acid 100°.

Scheme 4.

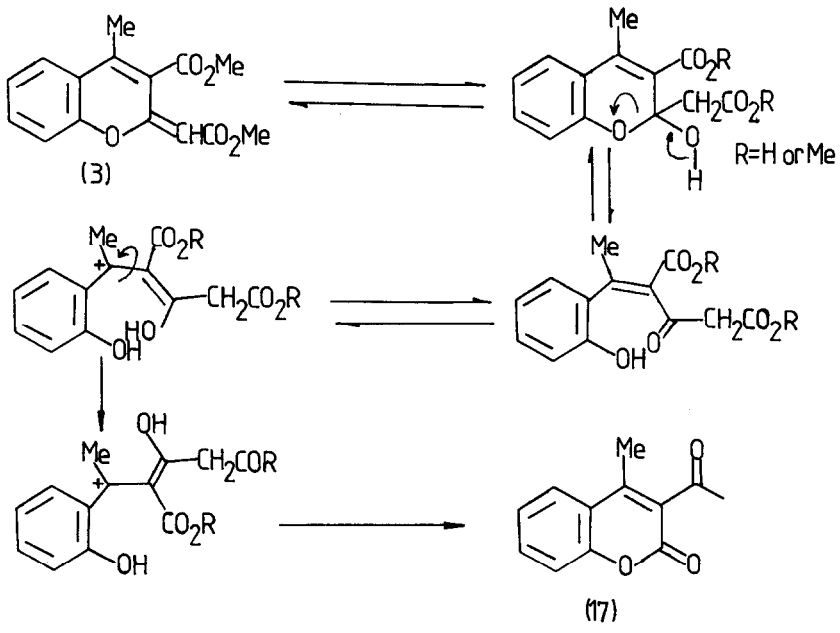
In the presence of methanesulphonic acid and phosphorus pentoxide phenols appear to react with penta-2,3-dienedioic acid (PDDA) (13) in a different mode, whereby nucleophilic attack by the benzene ring occurs in preference to reaction with the phenolic group. Thus, reaction of PDDA and phenol in the presence of methanesulphonic acid and phosphorus pentoxide, followed by reaction with diazomethane leads to formation of the diester (14; 24%) and the α-pyrone (15; 17%)[5]. Under the same acidic conditions resorcinol gave the coumarin (16;40%).



Reagents i. Phenol, phosphorus pentoxide in methanesulphonic acid, diazomethane
ii. Resorcinol, phosphorus pentoxide in methanesulphonic acid.

Scheme 5.

A coumarin (17) was obtained by rearrangement of the chromene (3) with aqueous acid. Thus boiling 50% aqueous acetic acid causes hydrolysis, decarboxylation and rearrangement to 3-acetyl-4-methyl coumarin (17; 42%) probably by hydration of the chromene (3), ring opening, double bond isomerisation and recyclisation as suggested in Scheme 6.



Scheme 6

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