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PRELIMINARY NOTE

Novel Diels-Alder Cycloaddition Involving two α,β-Unsaturated Esters in the Formation of Isocoumarins from the Reaction of Ethyl Propynoate with 3,4-Bis(trifluoromethyl)furan

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SUMMARY

Reaction of ethyl propynoate with 3,4-bis(trifluoromethyl)furan (4) at 150°C affords a mixture of ethyl 6,7-bis(trifluoromethyl)isocoumarin-3-carboxylate (7) and the corresponding 4-carboxylate (8) in the ratio 52:9, produced by Diels-Alder cycloaddition of the alkyne to the α,β-unsaturated ester function of the initially-formed 1:1 adduct, the

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oxanorbornadiene (9), followed by opening of the oxygen bridge and elimination of ethanol. The corresponding reaction involving dimethyl acetylenedicarboxylate gives the expected oxanorbornadiene (5).

Thermal reactions of furan and its derivatives with acetylenic esters have been widely investigated since that between furan and dimethyl acetylenedicarboxylate (DMAD) was first reported in 1931 [1]. Products from the DMAD reactions are temperature and reactant ratio dependent, e.g. Diels-Alder 1:1, 2:1, and 3:1 furan : DMAD adducts have been isolated and characterised [1,2].

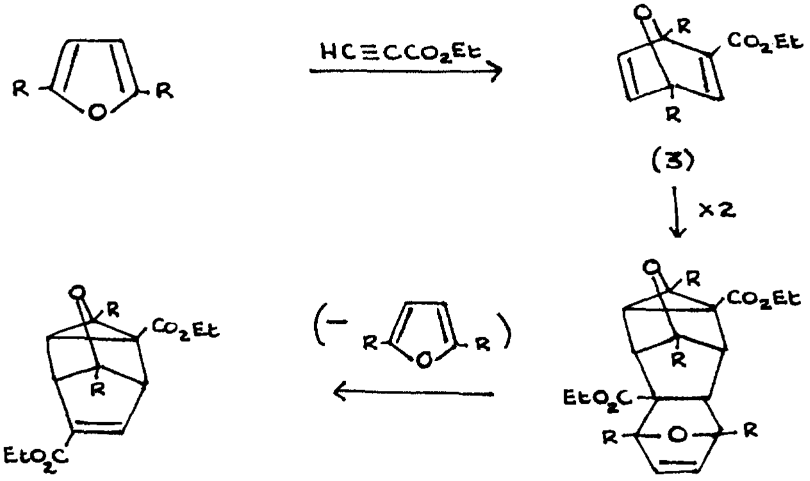
Reactions involving ethyl propynoate (EP) are less facile than those with DMAD and the only product isolated from the reaction with furan at 130° C was the 1:2 adduct (1) [3]; 2,5-dimethylfuran afforded the analogous compound (2) as the major product [4]. Compounds (1) and (2) were considered to arise by dimerisation of the initially-formed 1:1 adduct, the oxanorbornadiene (3), by a ${}_{\pi}2_{s} + {}_{\pi}2_{s} + {}_{\pi}2_{s}$ mechanism followed by retrocleavage of furan or 2,5-dimethylfuran [4] (Scheme 1).

In the present work the reactions of 3,4-bis(trifluoromethyl)furan (4) [5,6] with DMAD and EP have been carried out as part of a general investigation of the chemistry of this furan derivative.

The reaction with DMAD (1:1 molar ratio) proceeded smoothly at 100 °C (7 days) to afford the expected Diels-Alder adduct, oxanorbornadiene (5) (81%); 2:1 and 3:1 adducts were not detected. Compound (5) has been prepared previously in good yield (80%) from reaction of hexafluorobut-2-yne with dimethyl furan-3,4-dicarboxylate [7]. The only Diels-Alder cycloaddition reported involving furan (4) was that with hexafluorobut-2-yne to give the tetrakis(trifluoromethyl)oxanorbornadiene (6) (86%) [5].

The reaction with EP did not proceed at an appreciable rate below 150°C, but at this temperature (14 days) a 1:1 molar ratio of reactants (*in vacuo* in Pyrex) afforded a volatile mixture of unchanged furan (4) and ethanol together with a residue. Treatment of the residue with anhydrous ether followed by filtration gave ethyl 6,7-bis(trifluoromethyl)isocoumarin-3-carboxylate (7) (52%), while removal of the ether from the filtrate followed by purification by dry column flash chromatography [eluant: petrol (b.p. 40 - 60°C)/CH_2Cl_2 3:1 v/v] yielded the 4-carboxylate isomer (8) (9%).

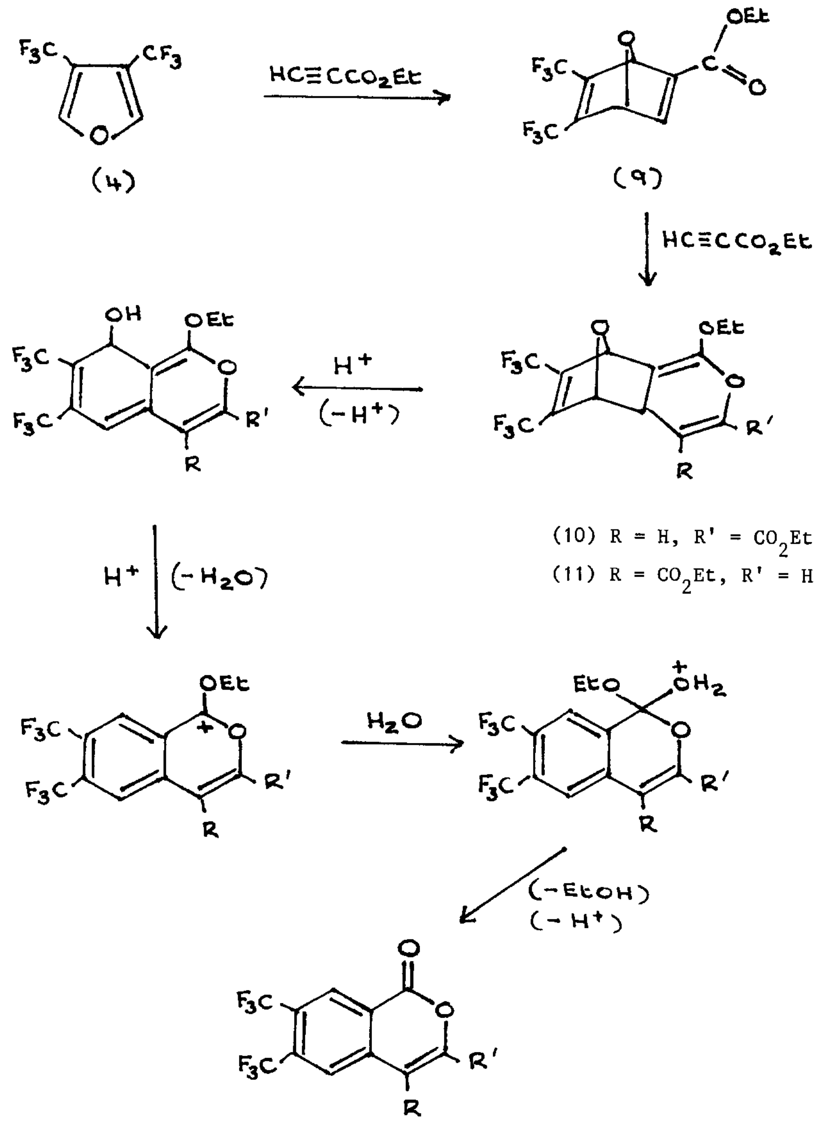
Compounds (7) and (8) were identified by elemental analysis and their n.m.r. (^{1}H, ^{13}C, and ^{19}F) and mass spectra, and the structure of the major isomer (7) was confirmed by an X-ray study.



(1) R = H

(2) R = Me

Scheme 1



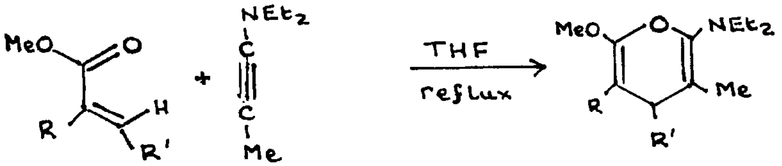
(10) R = H, R' = CO_2Et
(11) R = CO_2Et, R' = H

(7) R = H, R' = CO_2Et
(8) R = CO_2Et, R' = H

Scheme 2

These compounds are formed by Diels-Alder cycloaddition of **EP** to the initial adduct, the oxanorbornadiene (**9**), in which the α,β-unsaturated ester grouping functions as the diene component, to afford the 2:1 adducts (**10**) and (**11**) followed by acid-catalyzed opening of the oxygen bridge (by traces of protons on the walls of the Pyrex reaction tube) and elimination of water and ethanol (Scheme 2).

The isocoumarins formed in the present work contrast markedly with the products obtained from reaction of furan and 2,5-dimethylfuran with **EP** [3,4]. To the best of our knowledge only one report of an α,β-unsaturated ester acting as a diene in the Diels-Alder reaction has been published hitherto, i.e. reaction of the acrylate derivatives (**12**) with the ynamine (**13**) to afford the γ-pyrans (**14** - **16**) (35 - 60%) [8] (Scheme 3), although reactions of α,β-unsaturated aldehydes and ketones with dienophiles are



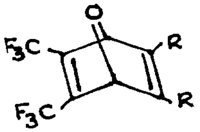
(12) (13)

(14) R = R' = H

(15) R = H, R' = Me

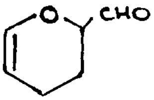
(16) R = Me, R' = H

Scheme 3



(5) R = CO_2Me

(6) R = CF_3



(17)

well documented [9]. Therefore, this is the first report of Diels-Alder cycloaddition involving two α,β-unsaturated esters.

Frontier orbital coefficients calculated by Houk and Strozier [10] have been used to explain the regioselectivity observed in the dimerisation of acrolein to give cycloadduct (**17**) and in the reactions of acrolein and α,β-unsaturated ketones with various dienophiles; both HOMO (diene) / LUMO (dienophile) and LUMO (diene) / HOMO (dienophile) interactions predict correctly the products formed [11]. By analogy, Diels-Alder reaction of EP with the 1:1 adduct (**9**) would be expected to afford 2:1 adduct (**10**) mainly which would lead to the observed major product, isocoumarin (**7**).

Further investigation of this novel type of reaction is being pursued and will be reported in a full paper in due course.

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