A New Simple Method for the Benzologation of Heterocycles

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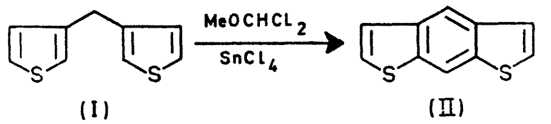
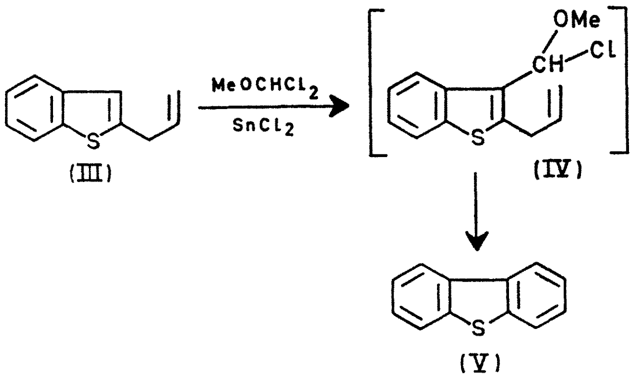
Summary The action of an αα-dichloro-ether and tin(IV) chloride on an allyl-substituted heterocycle such as benzothiophen or benzofuran offers a new simple route to the benzo-derivative of the heterocycle.

WE recently demonstrated[1] that polycyclic heteroaromatic compounds were conveniently synthesised in one step by utilising the 'direct Bradsher reaction', as exemplified in the conversion (I → II). We have now extended this work to the annelation of a terminal benzene ring which may, by suitable choice of reactants, be unsubstituted or specifically substituted.

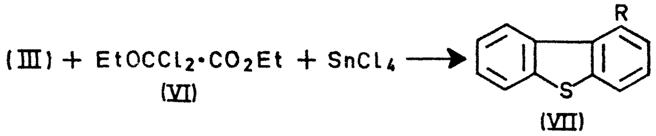


Routes to specifically substituted dibenzothiophens such as 1- or 3-substituted derivatives are long and of low yield and since these compounds are currently of considerable interest[3] we have especially studied their synthesis.

The general reaction sequence is exemplified by the conversion of 2-allylbenzothiophen (III) (readily prepared from 2-lithiobenzothiophen and allyl bromide) into dibenzothiophen (V) in 55% yield under very mild conditions (reaction occurs readily between −50° and 0°).

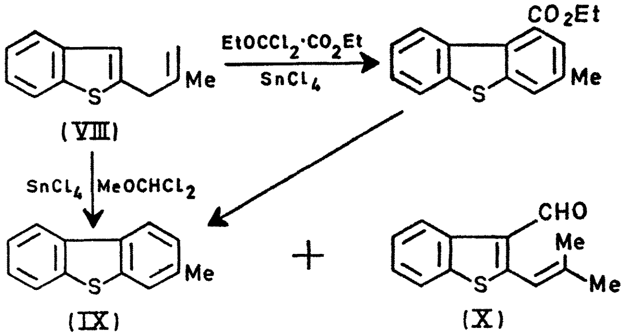


1-Substituted dibenzothiophens are readily prepared in high yield by use of ethyl dichloro-ethoxyacetate (VI) (obtained in high yield by the action of phosphorus pentachloride on ethyl oxalate[4]) and tin(IV) chloride, which with 2-allylbenzothiophen (III) give the ester (VIIa) (m.p. 62·5°) in 61% yield. The ester is a versatile intermediate and gives the alcohol (VIIb) (96%; m.p. 105—107°) with lithium aluminium hydride which in turn was converted into the chloromethyl compound (VIIc) (70%; m.p. 99—100°) with thionyl chloride. The ester on hydrolysis with alkali gives the known[5] acid (VIId) (94%; m.p. 176—177°) from which was prepared the amide (VIIe) (74%; m.p. 258°) and the known methyl compound[6] (VIIf) (70%; m.p. 71°) by reductive silylation with trichlorosilane.[7]



a; R = CO_2Et
b; R = CH_2OH
c; R = CH_2Cl
d; R = CO_2H
e; R = $CONH_2$
f; R = Me

The reported synthesis of 3-substituted derivatives are equally tedious. For example, the synthesis of 3-methyldibenzothiophen requires several steps and gives a very low overall yield.[6] The use of a substituted allyl benzothiophen was thus considered. The compound (VIII) by the usual sequence gave 3-methyldibenzothiophen (IX) (m.p. 78°) though only in 10% yield, the major product being the isomerised and formylated benzothiophen (X). However, the use of ethyl dichloroethoxyacetate gave the ester (m.p. 87—88°) in good yield, which was readily hydrolysed and decarboxylated to the same 3-methyl compound in very high yield.



This synthesis clearly has considerable general potential in the benzologation of aromatic systems in which substitution *ortho* to the allylic group can be assured. Thus 2-allylbenzofuran (III; S=O) gave the highly inaccessible 1-carboxylic ester (VIIa; S=O) (32%) by the action of ethyl dichloroethoxyacetate and tin(IV) chloride. The oily ester gave the known dibenzofuran-1-carboxylic acid[8] on hydrolysis.

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