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1,3-Cycloaddition of Benzyne to Thiophens

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Summary Benzyne, generated from diphenyliodonium-2carboxylate, reacts with various thiophens by addition to the sulphur and β -carbon to give, after loss of an acetylene moiety, benzo[b]thiophens in low but reproducible yields.

DURING a study¹ of the solution-phase reactions of various thiophens (1) with benzyne generated from diphenyliodonium-2-carboxylate,² the formation of benzo[b]thiophens in low but reproducible yields was repeatedly observed (Table). A similar observation was reported some years ago from the gas-phase reaction of thiophen and benzyne generated from phthalic anhydride, and was rationalized by a mechanism which predicted that both β -carbons of the thiophen were lost and both α -carbons were retained in the product (2).³ Aside from the improbability of portions of this mechanism as revealed by more recent studies,⁴ the substitution patterns of the benzo[b]thiophens (2) in the Table clearly contradict this prediction. Instead, it appears that adjacent α - and β -carbons of the thiophens (1) are either retained as C-2 and C-3 of the product (2), respectively, or they are lost entirely.

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TABLE.	Yields ^a	of	benzo[b]thic	ophens (2). ¹
Thiophen (1) R		Benzo[b]thiophen (2) R % Yield		
a; b;	H 2-Br		H H 9 Dr	0.5 1.5
с; d;	3,4-Br ₂ 2-Me		3-Вг 2-Ме Н	3·8 ca. 0·5° 0·5
e; f; g:	3-Me 2,5-Me₂ 2-OMe		Н 2-Ме Н	$0.5 \\ 3.0 \\ 1.0$

 $^{\rm a}$ Identification based on g.c.-m.s. comparison with authentic materials. Yields are g.c.-determined. $^{\rm b}$ Conditions and major products are given in ref. 2. c Incomplete resolution from other components of the reaction mixture.

Although details such as the sequence and timing of the steps cannot be specified as yet, the mechanism must involve a 1,3-cycloaddition of benzyne to the sulphur and β -carbon of the thiophen ring and expulsion of an acetylene moiety composed of the α - and β -carbons of the unattacked side of the thiophen ring. With monosubstituted thiophens, the unsubstituted side is preferentially attacked for (1b, e, and g) but for 2-methylthiophen (1d) either side may react. An illustrative mechanism incorporating these features is shown in the Scheme.[†]

Benzyne is known to participate in 1,3-cycloaddition reactions,⁵ including several with mesoionic five-membered heterocycles.⁶ Two recent examples closely related to the mechanism in the Scheme involve the stepwise attack of benzyne on the sulphur atoms of dithiin dioxides' or 2,1,3-benzothiadiazoles,⁸ followed by attack at a β -carbon and elimination of an acetylene or a nitrile, respectively. All these examples, however, involve species relatively more



dipolar or less aromatic than thiophen. Although 1,3cycloaddition to a thiophen ring had previously been considered to explain certain photochemical reactions, this hypothesis was eliminated⁹ thereby leaving the present reaction as the first apparent example of this phenomenon.

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+ Added in proof. A similar mechanism has been recently proposed to explain the reactions of cyclic thioenol ethers with di methyl acetylenedicarboxylate (K. Gollnick and S. Fries, Angew. Chem., Int. Ed. Engl., 1980, 19, 832).

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