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REGIOSPECIFIC ARYLATION BY ACID/BASE CONTROLLED REACTIONS OF TETRAPHENYLBISMUTH ESTERS

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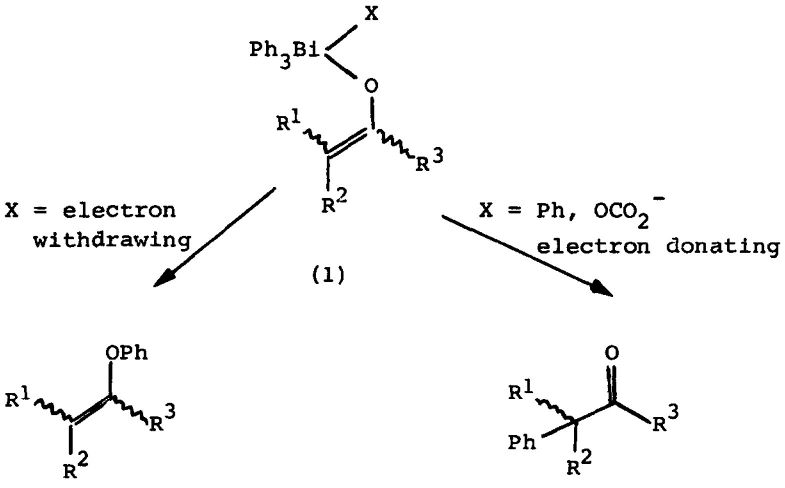
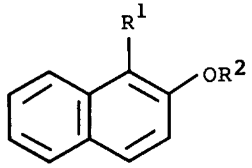
SUMMARY.- Tetraphenylbismuth V reagents react with enolic systems under acidic or basic conditions to give predictably different intermediates; these fragment with variable, but anticipated, regioselectivity.

We have previously suggested that arylation reactions of phenols and enols with pentavalent organobismuth reagents involve initial formation of an intermediate (1) possessing a covalent bismuth-oxygen bond[1,2]. A preliminary study[3] also indicated that the breakdown of this intermediate may be controlled by the nature of the ancillary groups around the bismuth atom, with electron withdrawing groups favouring reductive α-elimination (Scheme). In contrast to other arylation reagents[4], the formation and decomposition of a predetermined intermediate confers upon organobismuth compounds the potential for regiospecific reactions.

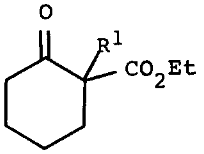




(2) $R^1 = R^2 = H$

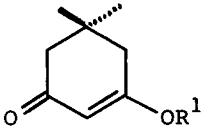
(5) $R^1 = Ph$, $R^2 = H$

(6) $R^1 = H$, $R^2 = Ph$



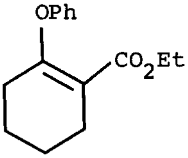
(3) $R^1 = H$

(7) $R^1 = Ph$



(4) $R^1 = H$

(8) $R^1 = Ph$



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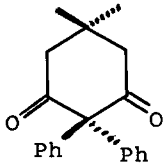

(10)

The present communication describes the reactivity of a series of tetraphenylbismuth esters of increasing acidity (OCOCH$_3$, OCOCF$_3$, OSO$_2$-C$_6$H$_4$-p-Me, OSO$_2$CF$_3$) which were readily prepared by addition of the appropriate acid (1 mol. equiv.) to a solution of pentaphenylbismuth[5] in benzene. With the exception of the acetate all esters are white crystalline solids of indefinite stability and readily soluble in organic solvents.

Three ambident substrates, β-naphthol (2), 2-carboethoxycyclohexanone (3), and dimedone (4), were chosen for study. Based on our previous observations with tetraphenylbismuth trifluoroacetate[3], we anticipated that the acidic proton of the substrate would react to give intermediate (1, X = OCOCF$_3$) with liberation of benzene.

Formation of the enolate or phenolate anion under strongly basic conditions however should preclude the formation of benzene and we reasoned that preferential nucleophilic displacement of trifluoroacetate anion should occur to give a new intermediate (1, X = Ph). The first conditions then should give[3] O-phenylation and the second C-phenylation. The results presented in the Table confirm this analysis of the factors involved.

Table[a)]

Ph_4BiX	pH[b)]	PRODUCTS (% Yield)		
		Substrate (2)	(3)	(4)[c)]
X = $OCOCH_3$	A	(2) 19, (5) 25, (6) 26	(7) 47, (3), 21	Complex
	C	(5) 90[d)]	(7) 89	Complex
X = $OCOCF_3$	A	(6) 75	(7) 10, (9) 30	(8) 55
	B	(6) 90	(9) 57	(8) 88
	C	(5) 90	(7) 91	(10) 15
X = $OSO_2-C_6H_4$-*p*-Me	A	(2) 58, (6) 42	(3) 82	(4) 50, (8) 40
	B	(2) 83, (6) 11	(3) 90	(4) 26, (8) 55
	C	(5) 90	(7) 72	(10) 81
X = OSO_2CF_3	A	(2) 95	(3) 90	(4) 70, (8) 5
	B	(2) 96	(3) 85	(4) 60, (8) 10
	C	(5) 86	(7) 89	(10) 69

a) All reactions were carried out at 60°C in benzene unless specified otherwise.

b) A = neutral conditions; B = addition of trichloroacetic acid (0.6 mol. equiv.); C = preformed anion using *N*-*tert*-butyl-*N*',*N*"-tetramethylguanidine.

c) Reactions to form (10) were carried out using > 2 mol. equiv. of reagent.

d) Reactions performed at room temperature.

Under neutral conditions, the generation of intermediate (1) requires the loss of one molecule of benzene. This was confirmed for the reaction of β-naphthol with tetraphenylbismuth monotrifluoroacetate to give the enol ether (6) (75%) and benzene (90%, by n.m.r.). Triphenylbismuth was not detected in this experiment. As the strength of the organic acid increases this initial step becomes increasingly difficult and the trifluoromethanesulphonate ester is practically inert. The nature of the ester group also plays a pivotal role in controlling the breakdown of the intermediate. Thus, β-naphthol with the acetate gave a mixture of 1-phenyl-2-naphthol (5) (25%) and the ether (6) (26%) whereas use of the trifluoroacetate led to exclusive *O*-arylation (75%).

We have also found that the formation of intermediates (1) is subject to acid catalysis. In several instances, addition of trichloroacetic acid (0.6 equiv.) leads to significantly improved yields, particularly in the reactions of the trifluoroacetate. We do not consider at the present time, that the addition of the acid leads to formation of a mixed *tri*-arylbismuth *di*ester[6].

The behaviour of the corresponding anions, generated by treatment with N-tert-butyl-N',N"-tetramethylguanidine[7] as base, completely changes the regiochemical course of the reaction. In all cases studied, the formation of the aryl ether was entirely suppressed and exclusive formation of a new carbon-phenyl bond was observed. Clearly, under these conditions, the previously recalcitrant ester function now becomes an excellent leaving group, with resultant generation of the intermediate (1, X = Ph) normally formed in the reactions of pentaphenylbismuth[2]. The formation of triphenylbismuth (78%) in the reaction of the trifluoromethanesulphonate with the anion of β-naphthol supports this mechanistic interpretation. The ester displacement route to the tetraphenylated intermediate can however be advantageous. Thus, dimedone with pentaphenylbismuth gave a complex mixture, while reaction of its anion with the esters gives the C-diarylated product (10) in high yield.

The above examples demonstrate that an unusually high degree of predictable regioselectivity can be achieved under a variety of conditions by the appropriate choice of covalent organobismuth intermediate and of acid or base.

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