The Catalytic Effect of Copper lons in the Phenylation Reaction of David and Thieffry

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Several types of bifunctional molecules are smoothly phenylated by triphenylbismuth diacetate in a reaction which has an induction period, a curious solvent dependence, and the need for illumination; however, the addition of a small amount of Cu(OAc)₂ removes all these limitations and accelerates greatly the reaction.

The phenylation of enols and of phenols by Bi^{V} reagents shows a regioselectivity which depends on the structure of the Bi reagent and on the reaction conditions.^{1,2} David and Thieffry recently discovered³ a remarkable reaction of 1,2- to 1,6-glycols. Heating with triphenylbismuth diacetate (1) in methylene dichloride gave mono-O-phenylation of the glycol in yields generally better than 80%. Phenylation of axial hydroxy groups was preferred over that of the corresponding equatorial isomers. The reaction showed an induction period.

Triphenylbismuth diacetate is an inefficient reagent for the phenylation of ordinary alcohols. However, we have found that a number of other neighbouring groups do permit efficient phenylation and the effect of David and Thieffry is not limited only to hydroxy. Thus 2-phenoxyethanol (3) and 2-methoxyethanol (4) were easily O-phenylated (92 and 86% respectively). Ethanolamine (5) gave a mixture of N-phenylaminoethanol (6) (51%), N,N-diphenylaminoethanol (7) (8%), and N,O-diphenylaminoethanol (8) (17%). Mercaptoethanol (9) gave a mixture of bis-(2-phenoxyethyl) disulphide (10) (22%) and 2-hydroxyethyl 2-phenoxyethyl disulphide (11) (58%). Benzoin (12) was also O-phenylated to give (13) (88%). Competition studies between ethylene glycol (2), 2-methoxyethanol (4), and 2-phenoxyethanol (3) gave the relative rates OH: OMe: OPh of 8:4:1. It is clear that the theoretical views of David and Thieffry³ must now be modified.

We have examined further the reaction of David and Thieffry³ using 2,2-dimethylpropane-1,3-diol (14) as substrate. This is monophenylated to give (15) in nearly quantitative yield and the reaction can be followed easily by n.m.r.

Table 1. Reaction of (1) with 3β -cholestanol (17).

Equiv. of Cu(OAc) ₂	Solvent	Temp./°C	Reaction time/h	% Yield of (18)
0	CH ₂ Cl ₂	Reflux	8	36
0.1	CH_2Cl_2	Reflux	8	39
0.1	CH_2Cl_2	Room temp.	48	31
0.1	C_6H_6	Reflux	24	50

Table 2. Effect of $Cu(OAc)_2$ on the reaction of (1) with (14) in CH_2Cl_2 .

Equiv. of Cu(OAc) ₂	Temp./°C	Induction time/h	Reaction time/h	% Yield of (15)
0	60ª	2	4	91
0.0001	60ª	0	0.25	82
0.1	60ь	0	0.25	78
0.1	20ь	0	1	82

^a Ambient light. ^b In the dark.

spectroscopy in CD_2Cl_2 . A second phenylation to give (16) is considerably slower. No reaction occurred in acetone, benzene, bromochloromethane, chloroform, dibromomethane, and tetrahydrofuran. A poor yield of (15) was obtained in 1,2-dichloroethane. Thermal *and* photochemical activation (laboratory lighting) are needed for the reaction. In CH_2Cl_2

$$Ph_{3}Bi(OAc)_{2} + ROCH_{2}CH_{2}OH \rightarrow ROCH_{2}CH_{2}OPh$$

(1) (2) $R = H$ (3) $R = Ph$ (4) $R = Me$	
R ¹ R ² NCH ₂ CH ₂ OR ³	HSCH ₂ CH ₂ OH
(5) $R^1 = R^2 = R^3 = H$ (6) $R^1 = Ph, R^2 = R^3 = H$ (7) $R^1 = R^2 = Ph, R^3 = H$ (8) $R^1 = R^3 = Ph, R^2 = H$	(9)
$R^1O[CH_2]_2S-S[CH_2]_2OR^2$	PhCH(OR)C(:O)Ph
(10) $R^1 = R^2 = Ph$ (11) $R^1 = Ph, R^2 = H$	(12) $R = H$ (13) $R = Ph$

R¹OCH₂CMe₂CH₂OR²

(14)
$$R^1 = R^2 = H$$

(15) $R^1 = Ph, R^2 = H$
(16) $R^1 = R^2 = Ph$

under reflux the induction period was 2 h and the reaction was complete in 4 h. There was no reaction at room temperature and no reaction under reflux in the dark. Irradiation with a 300 W sun lamp reduced the time for reaction to a total of 1.5 h.



Table 3. Reaction of (1) with (14) in various solvents

Solvent	Equiv. of Cu(OAc) ₂	Reaction time/h	% Yield of (15)
CHCl ₃	$\begin{cases} 1 \\ 0.1 \end{cases}$	0.5 0.5	67 66
Tetrahydrofuran	0.1	0.75	75
C ₆ H ₆	0.1	0.1	82
CH ₂ BrCl	0.1	0.25	79

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We recently became aware of the interesting work of Dodonov et al.4 on the phenylation (without solvent) of monohydric alcohols with triphenylbismuth diacetate in the presence of copper salts. In contrast to this work we find (Table 1) that the presence of $Cu(OAc)_2$ has only a small effect on the phenylation of cholestanol (17) to give cholestanyl phenyl ether (18) in solution. Small amounts of $Cu(OAc)_2$ had, however, a dramatic effect on the reaction of David and Thieffry (Table 2). There was no longer an induction period, nor was irradiation needed. The reaction could even be carried out at room temperature. The reaction was no longer dependent on solvent (Table 3). There was again no induction period and no need for irradiation. Without the $Cu(OAc)_2$ the yield was 0% for all the solvents in Table 3. $Co(OAc)_2$, $Ni(OAc)_2$, and $FeCl_3$ had no effect on the reaction.

It would be premature to offer a conclusion as to the mechanism of this reaction. The large rate increase seen is limited to bifunctional molecules which give the reaction of David and Thieffry. We postulate the formation of a copper complex⁵ and, perhaps, the transfer of aryl from bismuth to copper and then to oxygen.

Primary alcohols can be efficiently phenylated with tetra-

phenylbismuth trifluoroacetate without a catalyst:⁶ octadecan-1-ol (76%), 2,2-dimethylpropanol (61%), geraniol (57%) *etc.*

Received, 27th August 1985; Com. 1262

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