COPPER SALTS CATALYSIS OF <u>N</u>-PHENYLATION OF AMINES BY TRIVALENT ORGANOBISMUTH COMPOUNDS

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<u>Abstract</u> - The N-arylation of aliphatic and aromatic amines by Ph_3Bi and $Cu(OCOR)_2$ gives high yield of the mono- or di-phenylated amines under mlld conditions.

Amines can be mono- or di-phenylated by action of $Ph_3Bi(OCOR)_2$ in the presence of metallic copper or various copper salts under very mild conditions.^{1,2} Similarly, phenols and enols are <u>O</u>-phenylated under these conditions.^{2,3} During the study of the scope and mechanism of the amine phenylation, we sometimes obtained yields better than 100% with respect to the Bi^V reagent and assuming the transfer of one phenyl per mole of reagent. Therefore the second phenylation had to be effected by a trivalent bismuth species. As dismutation of Ph_2BiX yields Ph_3Bi ,⁴ the observation could be explained by Ph_3Bi being a phenylating agent in the presence of copper(II) salts. Although not general,⁵ dismutation of Ph_2BiOAc has been described to occur under special circumstances.⁶

We investigated further this reaction and found that amines react smoothly with Ph_3Bi in the presence of copper(II) acetate (0.5 equiv.) to give high yields of the mono- or di-phenylated derivatives (Table 1). Whereas in the previously described systems $[Ph_3Bi(OCOR)_2$ and Cu, Cu^I or Cu^{II}] the yields were mostly related to the steric hindrance of the amine, the $Ph_3Bi + Cu(OAc)_2$ system shows also a dependence on the basicity of the amine. <u>n</u>-Butylamine gave a good yield of the <u>N</u>-diphenyl derivative but <u>p</u>-nitroaniline reacted poorly. On the other hand, a secondary amine such as tetrahydroisoquinoline gave a higher yield (90%) of the <u>N</u>-phenyl derivative than in the reaction with $Ph_3Bi(OCOCF_3)_2$ and Cu (30%).

It must be noted that only copper (II) diacylates ($R = CH_3$ or CF_3) were efficient catalysts. Other copper compounds, such as metallic copper, copper oxides, chlorides or triflates gave no N-phenylation.

Substrate	Reaction Time (h)	Product (%)	
<u><u>1</u></u>	24	2 (82)	
<u>3</u>	24	<u>4</u> (60)	
5	20	6 (48)	
<u>7</u>	20	<u>8</u> (25)	
9	24	<u>10</u> (6)	
<u>11</u>	24	<u>12</u> (60), <u>13</u> (38)	
<u>14</u>	20	<u>15</u> (76)	
16	24	<u>17</u> (60)	
<u>18</u>	20	19 (16)	
20	24	21 (90)	
22	18	23 (56)	

Table 1. Phenylation of Amines by Ph₃Bi and Cu(OAc)₂^{a)}

a) All reactions performed in methylene dichloride with Ph_3Bi (1.2 equiv.), $Cu(OAc)_2$ (0.5 equiv.), at room temperature under argon.



Although good yields are obtained with 0.5 equiv. of $Cu(OAc)_2$, stoichiometric $Cu(OAc)_2$ gave the best yields of <u>N</u>-phenylated amines, in contrast to the catalytic amount required in the $Ph_3Bi(OAc)_2$ + Cu species system.¹ Alcohols and phenols did not react under these conditions. Dodonov <u>et al.</u>⁷ recently reported that when Ph_3Bi is decomposed in neat aliphatic alcohols in the presence of $Cu(OAc)_2$, a slow <u>O</u>-phenylation of the alcohol occurred, which was improved under oxygen atmosphere. In our case, the reaction can be performed under an atmosphere of argon and air. An oxygen atmosphere scarcely affected the yield. Addition of a large excess of the radical trap, 1,1-diphenylethylene⁸ did not change the yield.

However, when rigorous exclusion of oxygen traces was performed, the yield of \underline{N} -phenylated product was dependent upon the amount of $Cu(OAc)_2$ (Table 2). When Ph_3Bi was treated with $Cu(OAc)_2$ (1-3 equiv.) for 24 h in CH_2CI_2 , no reaction occurred and Ph_3Bi was recovered (92-95%). But when phenol 24 was reacted with Ph_3Bi (1.2 equiv.) $Cu(OAc)_2$, and triethylamine (6 equiv.) for 24 h at room temperature, the \underline{O} -phenvl ether 25 was obtained : $Cu(OAc)_2$ 0.1 equiv., 25, 0%; $Cu(OAc)_2$ 0.5 equiv., 25, 21% and $Cu(OAc)_2$ 1 equiv., 25 44%. A possible mechanism implies the formation of a copper diacetate-amine complex which reacts with Ph_3Bi to give either a phenyl copper derivative by transmetallation, followed by \underline{N} -phenylation (Scheme 1), or to give $Ph_3Bi(OAc)_2$ which secondly reacts with a copper(1) species to give a phenyl copper (11) species, which phenylates the amine (Scheme 1). This mechanism bears some similarity to copper catalysis in diaryliodonium chemistry.⁹ Further studies are new under way and will be reported in due course.

$$[Cu(OAc)_2, mRNH_2] + Ph_3Bi \longrightarrow Ph_3Bi(CAc)_2 + Cu^{IOAc}, nRNH_2$$

 $Ph_{3}Bi(OAc)_{2} + RNH_{2} + Cu^{I}X \xrightarrow{A_{c}O} Cu^{I}X \xrightarrow{Ph} RNHPh + Cu^{I}X$

Scheme 1

Cu(OAc) ₂ (equiv.)	0.5	1	1.5	2	
<u>2</u> (%)	25	42	60	59	

Table 2. Phenylation of p-Anisidine 1 under Oxygen-free Conditions.^{a,h}

a) All reaction performed in methylene dichloride with Ph₃Bi (1.2 equiv.) at room temperature for 24 hours.

b) Freeze-thaw decassed methylene dichloride was added to the decassed mixture of 1, Ph₃Bi and Cu(OAc)₂.

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