Tetrahedron Letters,Vol.27,No.31,pp 3619-3622,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

# COPPER CATALYSED O-PHENYLATION OF PHENOLS AND ENOLS BY PENTAVALENT ORGANOBISMUTH COMPOUNDS

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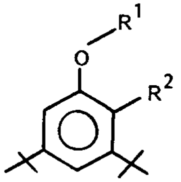
Abstract — The O-phenylation of phenols under neutral conditions by $Bi^V$ reagents is strongly catalysed by copper salts and by copper powder, even at room temperature. Enolic systems are also subject to copper powder catalysis and give exclusively O-phenylation.

Regioselective phenylation of many phenols and enols by various pentavalent organobismuth reagents can be obtained by proper choice of the bismuth reagent and the reaction conditions.[1,2] Thus, O- or C-phenylation can be selectively performed. The reactivity of triphenylbismuth diacylates with phenols and enols was not extensively studied.[1] However in the course of mechanistic studies on the David and Thieffry glycol O-arylation,[3,4] we examined the reactivity of triphenylbismuth diacetate 1 with various substrates,[5] among them phenols and enolic compounds.

Reaction of 1 with phenols in methylene dichloride under reflux yielded the O-phenyl derivatives, whereas reaction of 2 in the presence of a base led to C-phenylated derivatives.[1] Following the discovery of a strong copper salt catalysis in the David and Thieffry[4] glycol O-phenylation reaction and a lesser catalysis in the O-phenylation of alcohols,[6] we studied the effect of cupric diacetate on the phenylation of phenols. Addition of copper diacetate $Cu(OAc)_2$ in catalytic amount (0.1 equiv.) improved the reaction rate in such a way that the reaction could be run at room temperature (Table 1). An optimum yield was obtained after 1 hr, instead of 23 hours under reflux without catalyst.

| | | |
|---|---|---|
| $Ph_3Bi(OAc)_2$ | $Ph_3Bi(OCOCF_3)_2$ | $Ph_4BiOCOCF_3$ |
| 1 | 2 | 3 |



4 $R^1 = R^2 = H$
5 $R^1 = Ph$, $R^2 = H$
6 $R^1 = H$, $R^2 = Ph$

Table 1. Phenylation of Phenol 4 with Triphenylbismuth Diacetate[a]

| Entry | Reaction Time (hr) | Catalyst (eq.) | BTMG[b] (eq.) | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| 1 | 23[c] | - | 0 | 14 | 86 | 0 |
| 2 | 24[c] | - | 1.2 | 60 | trace | 20 |
| 3 | 1 | $Cu(OAc)_2$, (0.1) | 0 | 15 | 77 | 0 |
| 4 | 24 | $Cu(OAc)_2$, (0.1) | 0 | 13 | 80 | 0 |
| 5 | 24 | $Cu(OAc)_2$, (0.1) | 1.2 | 34 | 53 | 6 |
| 6 | 4 | Cu, (0.1) | 0 | 0 | 90 | 0 |

a) All reactions performed with 1 (1.2 eq.) in $CH_2Cl_2$ under argon at room temperature unless specified otherwise. b) BTMG = N-t-butyl-N',N',N'',N''-tetramethylguanidine. c) Reaction performed under reflux.

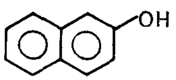
In the reaction under basic conditions, the original regioselectivity was reversed to give (Entry 5) mostly the O-phenyl ether, although in moderate yield (53%). A further modification of the reaction system made possible a high yielding reaction under mild conditions : addition of metallic copper powder (0.1 equiv.) to a mixture of 1 and 4 at room temperature in $CH_2Cl_2$ with stirring yielded 5 in 90% after 1 hr. The reaction was then performed on a series of phenols (Table 2). Only 2,4-di-t-butylphenol gave a poor yield and 2,4,6-tri-t-butylphenol did not react. The purity of the copper powder was not critical. 98.5% Pure copper had the same effect as Aldrich Gold Label 99.995% copper.

Table 2. Metallic Copper Catalysed O-Phenylation of Phenols.[a,b]

ArOH + 1 + Cu -> Ar-OPh
7 8

| 7 | Reaction Time (hr) | 8 |
|---|---|---|
| 9 | 5 | 84 |
| 10 | 5 | 88 |
| 11 | 24 | 73 |
| 12 | 3 | 67 |
| 13 | 4 | 90 |
| 14 | 5 | 80 |
| 15 | 3 | 26 |
| 16 | 24 | 0 |
| 17 | 5 | 90 |
| 18 | 15 | 97 |

a) Reaction conditions : 1 (1.2 eq.), Cu (0.1 eq.), $CH_2Cl_2$, room temperature, under argon. b) All new compounds were fully characterised by analytical and spectroscopic data.



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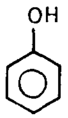

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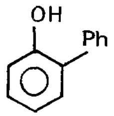

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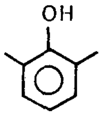

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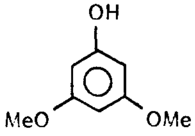

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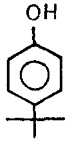

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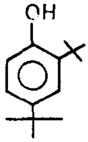

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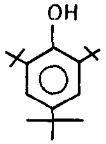

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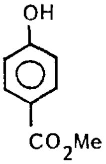

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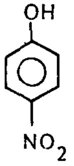

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The effect of copper salts appeared also in the previously described O-phenylation of phenols[1] with tetraphenylbismuth trifluoroacetate 3. Reaction of 3 with phenols 4 and 9 in benzene at room temperature gave after 24 hours poor to moderate yields of the corresponding O-phenyl ethers. However, addition of 0.1 equiv. of Cu(OAc)$_2$ gave a high yield (Table 3).

Table 3. Copper Salt Catalysis of the Reaction of Phenol O-Phenylation with 3[a]

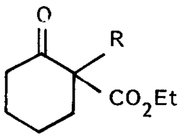
| Phenol | Cu(OAc)$_2$ (eq.) | Unreacted phenol (%) | Phenyl ether (%) |
|---|---|---|---|
| 4 | 0 | 60 | 27 |
| 4 | 0.1 | - | 85 |
| 9 | 0 | 36 | 50 |
| 9 | 0.1 | 12 | 80 |

a) All reactions performed with 3 (1.2 eq.) in benzene at room temperature for 24 hrs, under argon.

Table 4. Copper Catalysis of the Phenylation Reaction of Enols.

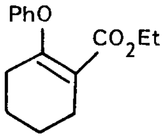
| Entry | Substrate | Method[a] | Reaction Time (hr) | Catalyst (eq.) | S.M. (%) | O-phenyl ether (%) |
|---|---|---|---|---|---|---|
| 1 | 19 | A | 20 | - | 19, (56) | 21, (27) |
| 2 | 19 | A | 40 | Cu(OAc)$_2$, (0.1) | 19, (55) | 21, (40) |
| 3 | 22 | B | 24 | Cu, (0.1) | 22, (22) | 23, (45) |
| 4 | 22 | C | 24 | Cu, (0.1) | - | 23, (88) |
| 5 | 24 | D | 4 | Cu, (0.1) | - | 25, (70) |
| 6 | 24 | B | 4 | Cu, (0.1) | - | 25, (96) |

a) A: 3 (1.2 equiv.), $C_6H_6$, 50°C; B: 2 (1 equiv.), $CH_2Cl_2$, room temperature; C: 2 (2 equiv.), $CH_2Cl_2$, room temperature; D: 1 (1 equiv.), $CH_2Cl_2$, room temperature.



19 R = H

20 R = Ph



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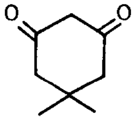

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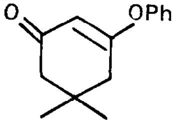

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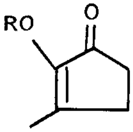

24 R = H
25 R = Ph

Enolic systems show a similar arylation behaviour to phenols.[2] Cupric acetate did not have a major catalytic effect on the O-phenylation of 19 (Table 4, entries 1 and 2). However, no C-phenyl derivative 20 was observed. Dimedone 22 was also converted to its O-phenyl derivative 23 in the presence of copper powder (Table 4, entries 3 and 4) which was markedly faster than the uncatalysed reaction.[2] The diosphenol 24 reacted very smoothly with the diacetate 1 or the reagent 2, again with distinct catalysis, to furnish the O-phenyl derivative 25.

The oxidation of thiols to disulphides by triphenylbismuth carbonate gives high yields.[7] A similar oxidation is effected by the diacetate 2 and the reaction is not changed by the addition of copper powder.

The scope and mechanism of this catalysis by metallic copper in the O-arylation reactions of $Bi^V$ compounds is currently under study and will be reported in full in due course.

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(Received in France 2 June 1986)