Tetrahedron Letters,Vol.27,No.31,pp 3615-3618,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

METALLIC COPPER CATALYSIS OF N-ARYLATION OF AMINES BY TRIARYLBISMUTH DIACYLATES

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Abstract -- The N-arylation of aliphatic and aromatic amines by triarylbismuth diacylates under neutral conditions is strongly catalysed by copper powder at room temperature.

Following the interesting observation[1] that copper ions catalyse the phenylation of simple alcohols (no solvent) by triphenylbismuth diacetate 1, we recently showed[2] that Cu^{II} ions had a much greater catalytic effect in the same O-phenylation reaction on a number of bifunctionalised molecules. In studying the role of the second heteroatom involved in the selective mono O-phenylation of glycols,[3] the preferential phenylation of nitrogen vs. oxygen was noted in the reaction of 2-aminoethanol with 1.[2] At the same time, we became aware of a Russian report by Dodonov et al. succinctly describing a copper diacetate catalysed N-phenylation[4] of amines by 1. The reaction, performed in THF at room temperature, was slow (> 60 hrs) and required a large excess of the amine (5 equiv.). Moreover, diphenylamine was converted to the triphenyl derivative in a very poor yield (< 3%). In the preceding paper,[5] we have reported the catalytic activity of metallic copper in the O-phenylation of phenols and enolic compounds. We now report a high yielding mild N-phenylation of amines by various triarylbismuth diacylates in the presence of a catalytic amount of metallic copper.

Reaction of the amine and triphenylbismuth diacetate 1 in methylene dichloride in the presence of metallic copper (0.1 equiv.) at room temperature afforded the corresponding phenyl derivative. Thus, aniline 2, 1 (1.1 equiv.) and metallic copper powder (0.1 equiv.) gave 3 in 96% yield in 2 hrs. When the reaction was performed in the absence of metallic copper, no trace of N,N-diphenylamine was detected after 2 hrs. Similarly, various aromatic amines were smoothly N-phenylated in high yields (Table 1). The 2,6-disubstituted aniline 10 required an excess of 1 to give a high yield of 11 (92% in 24 hrs). ortho-Nitroaniline 12 and para-nitroaniline 14 were also slowly phenylated (24 hrs), and 14 required an excess of 1 (2.2 equiv.). Triarylamines were also obtained by pour procedure, in a good yield for 8 (78%), and a lower yield for 4 (23%). An excess of 1 was again needed.

Table 1. Arylation of Amines by Triphenylbismuth Diacylates in the Presence of Metallic Copper[a,b]

Substrate	$Ph_3Bi(OAc)_2$ 1 (equiv.)	Reaction Time (h)	Product, Isolated Yield (%)
2	1.1	2	3 (96)
3	1.1	48	4 (23)
5	1.02	0.75	6 (97)
7	1.02	0.25	8 (91)
7	2.2	7	8 (48) , 9 (43)
7	3.3[c]	24	8 (28) , 9 (68)
8	2.2[d]	72	9 (78)
10	2.2	24	11 (92)
12	1.1	20	13 (90)
14	1.02	2	14 (74) , 15 (23)
14	2.2	16	15 (90)
23	1.1	4	24 (60) , 25 (20)
23	2.2	3	25 (70)
26	1.1	48	27 (0)
28	1.1	4	29 (90)
30	2.2	24	31 (70) , 32 (18)
35	1.1	24	36 (90)

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a) All reactions performed in methylene dichloride at room temperature in the presence of metallic copper (0.1 equiv.) with agitation. b) All new compounds were fully characterised by analytical and spectral data. c) 1 was added in three portions of 1.1 equiv. at t = 0, t = 4 hrs and t = 8.5 hrs. d) Reaction performed with 1 (1.1 equiv.) for 24 hrs. A second portion (1.1 equiv.) was then added.

Ph_3BiXY

1 X = Y = $OCOCH_3$
16 X = Y = $OCOCF_3$
17 X , Y = CO_3
18 X = Y = OTos

19 X = Ph , Y = $OCOCF_3$
20 X = Ph , Y = OTos
21 X = Y = Ph

Ar	$Ar-NH_2$	ArNHPh	$Ar-NPh_2$
C_6H_5	2	3	4
$4-CH_3-C_6H_4$	5	6	
$4-CH_3O-C_6H_4$	7	8	9
$2,4,6-(CH_3)_3-C_6H_2$	10	11	
$2-O_2N-C_6H_4$	12	13	
$4-O_2N-C_6H_4$	14	15	

$$(4\text{-}CH_3\text{-}C_6H_4)_3Bi(OAc)_2$$

22

Various pentavalent phenylbismuth derivatives can be used as efficient N-phenylating agents : the bis-trifluoroacetate derivative 16 was the most efficient, while 17 and 21 were not active (Table 2). Reaction of tri-p-tolylbismuth diacetate 22 showed that the Bi-bonded carbon atom becomes bonded to the nitrogen atom.

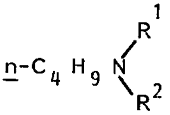
Table 2. Influence of the Organobismuth Compound on the Arylation of Aromatic Amines[a]

Substrate	Bismuth Compound	Reaction Time (h)	Product. Isolate Yield (%)
2	1	2	3 (96)
	16	0.5	3 (99)
	17	24	3 (0)
	18	1.5	3 (38)
	19	1	3 (92)
	20	1.5	3 (56)
	21	24	3 (0)
	22	11[b]	6 (98)
10	1	0.75	11 (40)
	16	0.75	11 (95)
14	1	0.75	15 (26)
	16	0.75	15 (98)
33	16	24	34 (32)

a) All reactions performed in methylene dichloride with 1.1 equiv. of organobismuth and 0.1 equiv. of metallic copper, at room temperature with agitation. b) Non optimised reaction time.

Aliphatic primary amines are also smoothly N-phenylated to the mono- and di-phenyl derivatives (Table 1). In this case, bulky aliphatic substituents inhibited the reaction. Aliphatic and heterocyclic secondary amines were not phenylated by 1 or 16 in the presence of metallic copper. However, as in the case of 2-aminoethanol, morpholine was slowly phenylated, only by 16, in a low yield (32%). Benzophenone hydrazone was also smoothly mono-phenylated (90%) in 24 hrs. Imines, enamines, oximes, amides, N,N,N',N'-tetramethylguanidine and semicarbazones were inert to the reagent $Ph_3Bi(OAc)_2$ + Cu°.

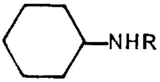
Thus, addition of a catalytic amount of copper to triphenylbismuth diacetate 1 allows high yielding selective N-phenylation of primary aliphatic amines and of variously substituted aniline derivatives.



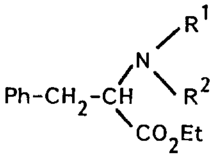
23 $R^1 = R^2 = H$
24 $R^1 = Ph$, $R^2 = H$
25 $R^1 = R^2 = Ph$

t-C_4H_9NHR

26 R = H
27 R = Ph



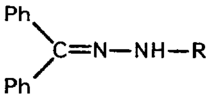
28 R = H
29 R = Ph



30 $R^1 = R^2 = H$
31 $R^1 = Ph$, $R^2 = H$
32 $R^1 = R^2 = Ph$

$(C_2H_5)_2N$-R

33 R = H
34 R = Ph



35 R = H
36 R = Ph

We have recently examined the arylation reactions of Bi^V compounds for the participation of aryl radicals in the mechanism of the process.[6] All tests so far have been negative. In the case of the present and preceding[2,5] copper catalysed reactions, the addition of large amounts of 1,1-diphenylethylene had no effect on the reaction. A radical mechanism is again excluded.

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(Received in France 2 June 1986)