Tetrahedron Letters,Vol.30,No.11,pp 1377-1380,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

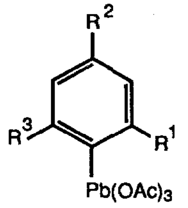
ARYLATION OF AMINES BY ARYLLEAD TRIACETATES USING COPPER CATALYSIS.

Derek H.R. Barton[a], Dervilla M.X. Donnelly[b],
Jean-Pierre Finet[c], and Patrick J. Guiry[b,c]

[a]Department of Chemistry, Texas A&M University,
College Station, Texas 77843. U.S.A.
[b]Department of Chemistry, University College, Dublin, Ireland.
[c]Faculté des Sciences St. Jérôme, 13397 Marseille Cedex 13, France.

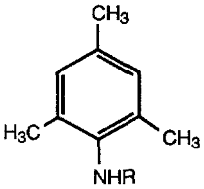
Abstract: The selective monoarylation of aliphatic, heterocyclic and aromatic amines has been performed with a variety of aryllead triacetates **1-4** under copper diacetate catalysis.

Arylation is an important reaction which can be performed by a variety of methods. The synthesis of arylamines can be realised by reaction of amines with diaryliodonium salts[1], or with aryl halides under copper catalysis[2], by reaction of acetanilides with aryl halides under copper iodide catalysis[3] or with activated fluoroarenes and arylamines containing electron-releasing groups[4]. These methods require harsh reaction conditions and are not always high yielding or selective. A milder method is the reaction of amines with arynic compounds generated from aryl halides and alkali amides[5] or complex bases[6]. In the case of carbon and oxygen atoms, the selectivity and mildness of some recently described methods have greatly facilitated their arylation[7]. The copper catalysed reaction of amines with organobismuth reagents[8] or with phenyllead triacetate[9] allows the phenylation of aliphatic and aromatic amines under very mild conditions. The range of available aryllead compounds[10] would increase the interest of the latter reaction for the synthesis of dissymetrically substituted diarylamines. We now report our results on the arylation of a variety of aliphatic, heterocyclic and aromatic amines with aryllead derivatives **1-4** under copper catalysis.



1 $R^1 = R^2 = R^3 = H$
2 $R^1 = R^3 = H$, $R^2 = CH_3O$
3 $R^1 = R^2 = CH_3O$, $R^3 = H$
4 $R^1 = R^2 = R^3 = CH_3O$

The arylation reactions were performed at room temperature in the presence of a catalytic amount of copper diacetate (0.1eq), in methylene dichloride. In all cases, only the monoarylation took place with primary aliphatic and aromatic amines. Good yields were obtained with variously substituted anilines. As noted for the N-phenylation reaction[9], the best yields were obtained with anilines substituted with electron-releasing groups, whereas *p*-nitroaniline and ethyl *p*-aminobenzoate failed to give any of the corresponding N-aryl derivatives. The steric hindrance of the *ortho* substituents had only a moderate influence, as the 2,4,6-trimethoxy-2',4',6'-trimethyldiphenylamine **8** was easily obtained.

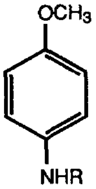


5 R = H

6 R = $4\text{-}CH_3O\,C_6H_4$

7 R = $2,4\text{-}(CH_3O)_2\,C_6H_3$

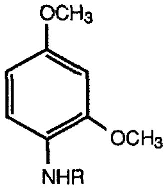
8 R = $2,4,6\text{-}(CH_3O)_3\,C_6H_2$



9 R = H

10 R = $4\text{-}CH_3O\,C_6H_4$

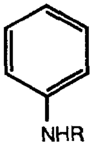
11 R = $2,4\text{-}(CH_3O)_2\,C_6H_3$



12 R = H

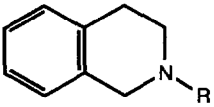
13 R = C_6H_5

14 R = $2,4\text{-}(CH_3O)_2\,C_6H_3$



15 R = H

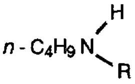
16 R = $4\text{-}CH_3O\,C_6H_4$



17 R = H

18 R = $2,4\text{-}(CH_3O)_2\,C_6H_3$

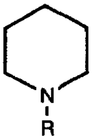
19 R = $2,4,6\text{-}(CH_3O)_3\,C_6H_2$



20 R = H

21 R = $2,4\text{-}(CH_3O)_2\,C_6H_3$

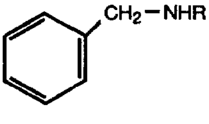
22 R = $2,4,6\text{-}(CH_3O)_3\,C_6H_2$



23 R = H

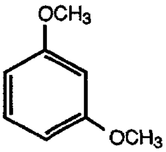
24 R = $2,4\text{-}(CH_3O)_2\,C_6H_3$

25 R = $2,4,6\text{-}(CH_3O)_3\,C_6H_2$



26 R = H

27 R = $2,4\text{-}(CH_3O)_2\,C_6H_3$



28

In the case of the most oxidisable anilines, such as **9** and **12**, reaction with polymethoxyphenyllead reagents **3** and **4** followed a different path. Oxidation of the aniline by the lead reagent took place instead of the N-arylation. When the copper catalyst was omitted, a slow oxidation of the aniline by the lead reagent occurred. Thus the reaction of *p*-anisidine **9** with the dimethoxyphenyllead derivative **3** led only to the recovery of the arene **28**. However, if the copper amine complex was formed before addition of the lead reagent, N-arylation took place. For the more oxidisable **12**, only the N-phenylation with **1** was possible. The better oxidising reagent **3** led only to recovery of the oxidation-reduction products, whatever the reaction conditions.

Heterocyclic amines led to moderate to good yields of their substituted aryl derivatives. Among the aliphatic amines, only the primary linear aliphatic amines were arylated, in poor yields. The steric influence of the alkyl substituent is in this case very important: the bulky *tert*-butylamine and 1-adamantanamine were not arylated. In the same way as with the phenyllead reagent[9], indole and carbazole remained inert, as well as phenols[9].

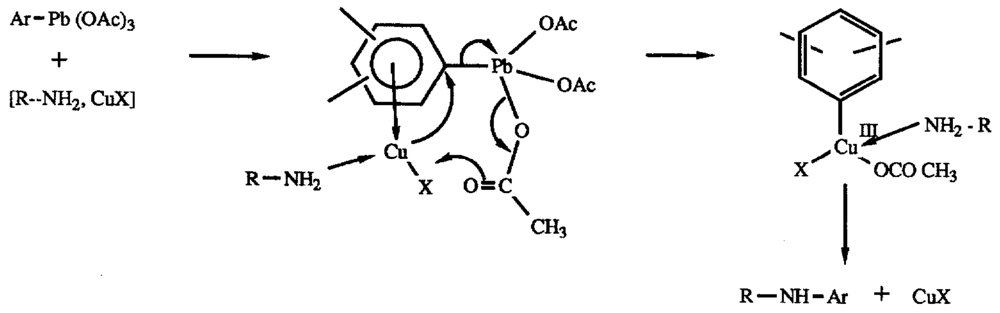
Table: Arylation of Amines by Aryllead Triacetates in the presence of Copper Diacetate[a].

Amine	$ArPb(OAc)_3$	Method of Addition[b]	Reaction Time (h)	Products(%)
5	**2**	A	2	**6** (65)
5	**3**	A	2	**7** (74)
5	**4**	A	2.5	**8** (18)
9	**2**	A	2	**10** (91)
9	**3**	A	4	**11** (0), **28** (60)
9	**3**	B	1.5	**11** (25)
12	**1**	C	1	**13** (34)
12	**3**	C	4	**14** (0), **28** (68)
15	**2**	C	2	**16** (72)
15	**3**	A	2	**13** (78)
17	**3**	A	12	**18** (67)
17	**4**	A	12	**19** (55)
20	**3**	A	16	**21** (16)
20	**4**	A	16	**22** (7)
23	**3**	A	16	**24** (60)
23	**4**	A	16	**25** (35)
26	**3**	A	16	**27** (15)

a-All reactions were carried out in CH_2Cl_2 (1 ml per 0.1 mmole of substrate) under an atmosphere of argon. The amount of the reagents was : Amine (1eq), $ArPb(OAc)_3$ (1.1eq), and $Cu(OAc)_2$ (0.1eq).

b-A: $Cu(OAc)_2$ was added to a mixture of amine and lead reagent.
B: $ArPb(OAc)_3$ was added to a cooled mixture of amine and $Cu(OAc)_2$ and the reaction was performed at 0-5°C.
C: As for B, except reaction was performed at room temperature.

The mild synthesis of a range of alkylaryl amines and dissymetric diarylamines substituted with a variety of different groups can now be easily performed by this copper catalysed reaction with aryllead triacetates. The proper choice of the amine and the lead reagent can avoid side reactions, such as oxidation of the amines. This method compares favourably with arynic methods by the neutral conditions, useful for the arylation of base sensitive substrates and by the synthesis of *ortho*-substituted arylamines which cannot be made *via* aryne methods. Moreover these results reinforce the mechanism postulated in the arylbismuth-copper reaction: oxidative addition on a Cu(I) species followed by reductive elimination of the Cu(III) intermediate.



Acknowledgments: This work was made possible by grants from CNRS/EOLAS/RIA exchange program and from the Ministère Français des Affaires Etrangères to J.P.F. and P.J.G.

REFERENCES

1. A. Varvoglis, *Synthesis*, 1984, 709; M.C. Caserio, D.L. Glusker, and J.D. Roberts, *J. Am. Chem. Soc.*, 1959, **81**, 336; R.A. Scherrer and H.R. Beatty, *J. Org. Chem.*, 1980, **47**, 2127.
2. R.G.R. Bacon and H.A.O. Hill, *Quart. Rev.*, 1965, **19**, 95; J. Lindley, *Tetrahedron*, 1984, **40**, 1433.
3. H.S. Freeman, J.R. Butler, and L.D. Freedman, *J. Org. Chem.*, 1978, **43**, 4975.
4. R.L. Lantz and P. Obelianne, *Bull. Soc. Chim. Fr.*, 1956, 311; J.J. Kulagowski and C.W. Rees, *Synthesis*, 1980, 215; J.H. Garvin, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1331.
5. H. Heaney, Chem. Rev., 1962, **62**, 81.
6. M.F. Moreau-Hochu and P. Caubère, *Tetrahedron*, 1977, **33**, 955 and references therein. For a review see P. Caubère, *Top. Curr. Chem.*, 1978, **73**, 49.
7. R.A. Abramovitch, D.H.R. Barton, and J.P.Finet, *Tetrahedron*, 1988, **44**, 3039.
8. D.H.R. Barton, J.P. Finet, and J. Khamsi, *Tetrahedron Lett.*, 1986, **27**, 3615; 1987, **28**, 887.
9. D.H.R. Barton, N.Yadav-Bhatnagar, J.P. Finet, and J. Khamsi, *Tetrahedron Lett.*,1987, **28**, 3111.
10. R.P. Kozyrod and J.T. Pinhey, *Aust. J. Chem.*,1985, **38**, 713, and references therein.

(Received in France 28 November 1988)