Tetrahedron Letters,Vol.29,No.8,pp 857-860,1988
Printed in Great Britain

0040-4039/88 $3.00 + .00
Pergamon Journals Ltd.

ALKYLATION OF AMINES USING TRIVALENT BISMUTH DERIVATIVES

Derek H.R. Barton*, Nubar Ozbalik and Manian Ramesh

Department of Chemistry, Texas A&M University,
College Station, TX 77843, U.S.A.

Summary - Mixed alkylaryl Bi^{III} derivatives have been prepared by both anionic and free radical methods. The thermal stability of these compounds permits them to be used in the presence of cupric acetate for the alkylation of amines. Trialkylbismuth compounds can also be used in the same way.

Amines, phenols and enols are all arylated efficiently (on nitrogen or on oxygen as appropriate) using triarylbismuth diacylates and catalysis by a copper reagent[1,2]. An extension of this work was the discovery that triphenylbismuth could N-phenylate amines in the presence of sufficient copper^{II} acetate[3].

Although trialkylbismuth compounds have been known for more than 70 years[4], they have not been used in synthesis. Simple trialkylbismuth derivatives are readily obtained[5] from bismuth trichloride and the appropriate Grignard or organolithium reagents. The mixed alkylaryl bismuth compounds 1 (Ph_2BiR) have recently been reported[6] resulting from the reaction of diphenylbismuth chloride with an alkyl lithium.

Trivalent alkylbismuth species cannot be converted into stable five valent compounds due to spontaneous fragmentation. In consequence, much of the chemistry that we have developed with Bi^{V} arylated compounds cannot be applied. Nevertheless, it seemed possible that oxidation in situ with Cu^{II} acetate might provide reagents which could alkylate, say, the amine function. This communication reports firstly our experiments using mixed alkylaryl bismuth compounds; β-phenylethyldiphenylbismuth (1a), methyldiphenylbismuth (1b)[6] and trialkylbismuth compounds; tri-β-phenylethylbismuth (2a), and trimethylbismuth

	Ph_2BiR		R_3Bi
1a	$R = CH_2CH_2Ph$	2a	$R = CH_2CH_2Ph$
1b	$R = CH_3$	2b	$R = CH_3$

(2b)[4] for alkylation of amines. The bismuth derivatives 1a and 2a were synthesized by reacting Ph_2BiCl and $BiCl_3$ respectively with β-phenylethylmagnesium bromide in ether at 0° in an inert atmosphere (1a: 3h stirring, 76% yield; 2a: 16h stirring, 50% yield). The work-up procedure involved a filtration of the reaction mixture over alumina and then evaporating the solvent. Due to their air-sensitivity, all operations were carried out under an argon atmosphere. The compounds were characterized by spectral measurements and elemental analysis.

Another method of synthesizing 1a involved a free radical substitution reaction on diphenylthiophenyl bismuth 3a[7] in which the weak Bi-X bond was exploited. We have prepared both 3a and 3b *via* diphenylbismuth trifluoroacetate 4[8]. Compounds 3a and 3b were found to be unstable in solution; they underwent disproportionation to give Ph_3Bi and

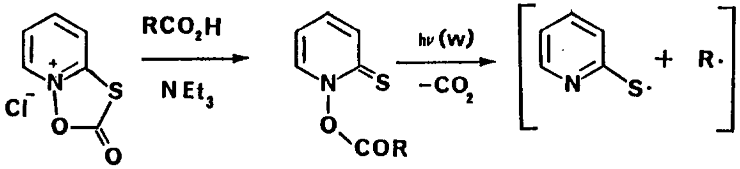
$$Ph_3Bi + CF_3COOH \longrightarrow \underline{4} \xrightarrow{PhXH} Ph_2BiXPh$$

$\underline{3a}$ X = S

$\underline{3b}$ X = Se

$(PhX)_3Bi$. The rate of this reaction was studied in various solvents and under different pH conditions. The reaction was relatively slow in THF and was catalyzed by acids. It was completely inhibited in pyridine and triethylamine.

The β-phenylethyl radical required for the substitution reaction was easily generated by the recently invented method of photolytic decarboxylation of thiohydroxamic esters.[9] Thus, irradiation of 5 in the presence of diphenylthiophenyl derivative 3a (2 eq.), in THF furnished 77% of the expected product (1a) which was identical with the sample obtained from the reaction of Ph_2BiCl with the Grignard reagent. Similarly, good yield of 1a (70%) could also be secured by photolysis of 5 in the presence of diphenylselenophenyl derivative 3b.



$\underline{5}$ R = CH_2CH_2Ph

We performed experiments to study the thermal stability[10] of β-phenylethylbismuth compounds 1a and 2a. Trialkylbismuth 2a upon refluxing in benzene for 8h yielded styrene 48%. The quantities of styrene and recovered trialkylbismuth 2a indicated that all three phenethyl groups are susceptible to β-elimination. Consequently, when a solution of 2a in

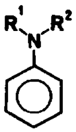
$$\underline{2a} \xrightarrow[\Delta,\ 8h]{C_6H_6,Ar} \underset{48\%}{3\ PhCH{=}CH_2} + \underset{50\%}{\underline{2a}} \qquad \underline{2a} \xrightarrow[\Delta,\ 2h]{toluene,Ar} \underset{100\%}{3\ PhCH{=}CH_2}$$

Table

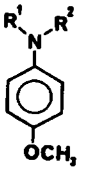
Alkylation of Amines Using R_3Bi or Ph_2BiR $^{a)}$

Amine	Reagent	Product(s) (% Yield)	Amine	Reagent	Product(s) (% Yield)
6	1a	12 (11), 18 (30)	9	2a	15 (53)
8	1a	14 (8), 19 (28)	10	2a	16 (49)
9	1a	15 (51)	11	2a	17 (53)
11	1a	27 (50)	6	2b	20 (trace), 21 (31)
9	1b	24 (31)	7	2b	22 (3), 23 (33)
11	1b	27 (50)	7	2b (excess)	22 (4), 23 (51)
6	2a	12 (27)	9	2b	24 (49)
7	2a	13 (32)	10	2b	25 (47)
8	2a	14 (24)	11	2b	26 (52)

a) Reactions were carried out in CH_2Cl_2 using 1.0 mmole of amine, 1.2 mmole of bismuth reagent and 1.0 mmole of $Cu(OAc)_2$ at room temperature under argon for 24 h.



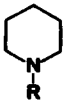
6 $R^1 = R^2 = H$
12 $R^1 = H$; $R^2 = CH_2CH_2Ph$
18 $R^1 = Ph$; $R^2 = CH_2CH_2Ph$
20 $R^1 = H$; $R^2 = CH_3$
21 $R^1 = R^2 = CH_3$



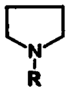
7 $R^1 = R^2 = H$
13 $R^1 = H$; $R^2 = CH_2CH_2Ph$
22 $R^1 = H$; $R^2 = CH_3$
23 $R^1 = R^2 = CH_3$

n-Bu NR^1R^2

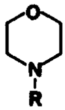
8 $R^1 = R^2 = H$
14 $R^1 = H$; $R^2 = CH_2CH_2Ph$
19 $R^1 = Ph$; $R^2 = CH_2CH_2Ph$



9 $R^1 = H$
15 $R^1 = CH_2CH_2Ph$
24 $R^1 = CH_3$



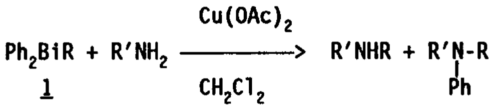
10 $R^1 = H$
16 $R^1 = CH_2CH_2Ph$
25 $R^1 = CH_3$



11 $R^1 = H$
17 $R^1 = CH_2CH_2Ph$
26 $R^1 = CH_3$
27 $R^1 = C_6H_5$

toluene was refluxed for 2 h, a complete consumption of alkylbismuth leading to quantitative formation of styrene was observed. In contrast, 1a was stable even after heating neat at 160°. When subjected to an oxidation reaction with benzoylperoxide in CH_2Cl_2, 1a afforded β-phenylethylbenzoate and triphenylbismuth dibenzoate.

Reaction of the amine (1 eq) and alkyldiphenylbismuth (1.2 eq) in CH_2Cl_2 in the presence of $Cu(OAc)_2$ (1 eq) at room temperature afforded a mixture of mono- and di-substituted amines (Table).



$$\underset{\mathbf{1}}{Ph_2BiR} + R'NH_2 \xrightarrow[CH_2Cl_2]{Cu(OAc)_2} R'NHR + R'\underset{\underset{Ph}{|}}{N}\text{-}R$$

A blank experiment indicated that 1 disproportionates in the presence of $Cu(OAc)_2$ into triphenylbismuth and trialkylbismuth 2, which prompted us to study the alkylation process using trialkylbismuth derivatives. In a typical experiment, a solution of 7 (1 eq), 2a (1.2 eq) and $Cu(OAc)_2$ (1 eq) in CH_2Cl_2 (10 ml) was stirred at room temperature, under argon for 24 h. The solvent was then removed and unreacted 2a and copper salts were destroyed by reduction using lithium aluminum hydride (8 eq) in THF, at 40° during 2 h. The excess of reducing agent was decomposed and the reaction mixture, after filtering over alumina, afforded the amine 13 (32%).

We thank the Welch Foundation for their generous support of this work.

References

1. D.H.R. Barton, J.P. Finet and J.Khamsi, Tetrahedron Letts., 27, 3615 (1986).
2. D.H.R. Barton, J.P. Finet, J. Khamsi and C. Pichon, Tetrahedron Letts., 27, 3619 (1986).
3. D.H.R. Barton, J.P. Finet and J. Khamsi, Tetrahedron Letts., 28, 887 (1987).
4. K. Schaefer and F. Hein, Z. Anorg. Allgem. Chem., 100, 249 (1917).
5. M. Wieber, Gmelin Handbuch der Anorganischen Chemie, Band 47, Springer Verlag, New York, 1977, p.44-60.
6. T. Kauffmann and F. Steinseifer, Chem. Ber., 118, 1031 (1985).
7. H. Gilman and H.L. Yale, J. Am. Chem. Soc.,73, 2880 (1951).
8. G.B. Deacon, W.R. Jackson and J.M. Pfeiffer, Aust. J. Chem., 37, 527 (1984).
9. D.H.R. Barton and S.Z. Zard, Pure and Appl. Chem., 58, 675 (1986) and references cited therein.
10. T. Kauffmann, F. Steinseifer and N. Klas, Chem. Ber., 118, 1039 (1985).

(Received in USA 2 December 1987)