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An Electrophilic Aromatic Substitution by N-Methoxyamides *via* Hypervalent Iodine Intermediates

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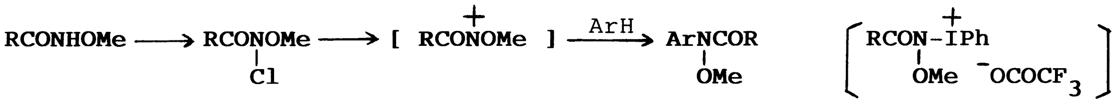
Treatment of N-methoxyamides with hypervalent iodine compounds generates electron deficient nitrogen species which react intra- or intermolecularly with an aromatic group to give N-aryl-N-methoxyamides in good yields.

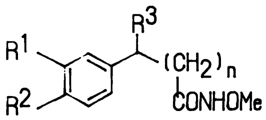
It has been reported that N-methoxy-N-acylnitrenium ions (**A**) generated by treatment of N-chloro-N-methoxyamides (**2**) with silver or zinc salts$^{1)}$ react with arenes to give N-aryl-N-methoxyamides (**3**) in good yields. Recently, Cherest and Lusinchi have reported$^{2)}$ that the action of ferric chloride on N-acetoxyamides leads to generation of electron deficient nitrogen which is trapped intramolecularly by an aromatic group to give oxindoles and analogues. Their procedure is simple in the respect that it does not require prior chlorination of amides.



$$\mathrm{RCONHOMe} \longrightarrow \mathrm{RCO}\underset{\mathrm{Cl}}{\mathrm{N}}\mathrm{OMe} \longrightarrow [\ \mathrm{RCO}\overset{+}{\mathrm{N}}\mathrm{OMe}\ ] \xrightarrow{\mathrm{ArH}} \mathrm{Ar}\underset{\mathrm{OMe}}{\mathrm{N}}\mathrm{COR} \qquad \left[\ \mathrm{RCO}\underset{\mathrm{OMe}}{\mathrm{N}}\text{-}\overset{+}{\mathrm{I}}\mathrm{Ph}\ \ {}^{-}\mathrm{OCOCF_3}\ \right]$$

1 **2** **A** **3** **B**

In this article, we wish to report that N-methoxyamides (**1**) react with hypervalent iodine compounds$^{3)}$ to give intermediates (**B**) in which the electron deficient nitrogen atom is attacked intra- or intermolecularly by arenes to give nitrogen heterocyclic compounds bearing a N-methoxy group or N-aryl-N-methoxyamides. In a typical procedure, a solution of **1** or **4** (2 mmol) in $CHCl_3$ (5 ml) was added to a stirred solution of $PhI(OCOCF_3)_2$ (2.6 mmol) in $CHCl_3$ (10 ml) at 65 °C for 3 min, under an argon atmosphere. The mixture was stirred for 3 min and then poured into saturated aqueous sodium hydrogencarbonate, extracted with CH_2Cl_2 and dried over anhydrous sodium sulfate. Evaporation of the solvent and chromatographic purification afforded the corresponding product as shown in Table 1. Among the hypervalent iodine compounds examined [$PhI(OCOCF_3)_2$, $PhI(OCOCH_3)_2$, $PhIO$-$BF_3 \cdot OEt_2$, $PhIO$-HCO_2H and PhI(OH)OTs], $PhI(OCOCF_3)_2$ usually gives best



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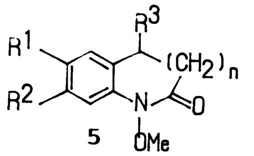

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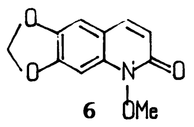
a: n=0; $R^1=R^2=R^3=H$
b: n=1; $R^1=R^2=R^3=H$
c: n=0; $R^1=H$; $R^2=OMe$; $R^3=Me$
d: n=1; $R^1-R^2=OCH_2O$; $R^3=H$



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RCONHOMe

1a: R=Me
b: $R=C_7H_{15}$
c: $R=C_6H_5CH_2O$
d: R=t-BuO
e: $R=C_6H_5$ 

$$\underset{OMe}{ArNCOR}$$

3a: $Ar=C_6H_5$; R=Me
b: $Ar=C_6H_5$; $R=C_7H_{15}$
c: $Ar=C_6H_5$; $R=C_6H_5CH_2O$
d: $Ar=C_6H_5$; R=t-BuO
e: $Ar=C_6H_5$; $R=C_6H_5$ 
f: Ar=o-$MeOC_6H_4$; R=Me
g: Ar=p-$MeOC_6H_4$; R=Me

Table 1. Electrophilic Aromatic Substitution by N-Methoxyamides

Substrate	Product (yield/%)[a]
4a	**5a**(83)
4b	**5b**(74)
4c	**5c**(81)
4d	**5d**(60) + **6**(24)
1a + benzene[b]	**3a**(70)
1b + benzene[b]	**3b**(67)
1c + benzene[b,c]	**3c**(75)
1d + benzene[b,c]	**3d**(73)
1e + benzene[b,c]	**3e**(64)
1a + anisole[d]	**3f**(53) + **3g**(29)

a) Isolated yield. b) 50 molar equiv. with respect to **1**. c) $MeNO_2$ was used as solvent. d) 10 molar equiv. with respect to **1**.

results. Various solvents such as $CHCl_3$, CH_2Cl_2, CCl_4, $MeNO_2$, $ClCH_2CH_2Cl$, and $(CF_3)_2CHOH$ are usable; among them $CHCl_3$ and $MeNO_2$ are the solvent of choice for this reaction, while little or no reaction takes place in tetrahydrofuran or dioxane.

According to the previous method,[1e] N-chloro-N-methoxyamides are the starting materials and chlorination of **1** or **4** bearing electron releasing substituent groups often brought about not only N-chlorination but also aromatic chlorination.[4] The present method makes considerable improvement avoiding undesirable aromatic chlorination because prior chlorination is not required. This reaction does not proceed with N-methylamides and N-acyloxyamides under the similar reaction conditions, which indicates that the N-methoxy group plays an important role for the formation of a hypervalent iodine intermediate (**B**) and the stabilization of a positively charged nitrogen atom generated by release of a phenyliodonium group.

References

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2) M. Cherest and X. Lusinchi, Tetrahedron Lett., 30, 715 (1989).
3) For recent review on hypervalent iodine reagents: R. M. Moriarty and O. Prakash, Acc. Chem. Res., 19, 244 (1986).
4) The N-chloride of **4d** afforded only aromatic chlorination product (64%) and the N-chloride of **1a** could not be used for this reaction due to its high volatility.

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