Pergamon

Tetrahedron Letters, Vol. 35, No. 15, pp. 2393-2396, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0255-V

Reaction of Nitromethane with Aluminium Phenolates: Mild Synthesis of Salicylaldoximes

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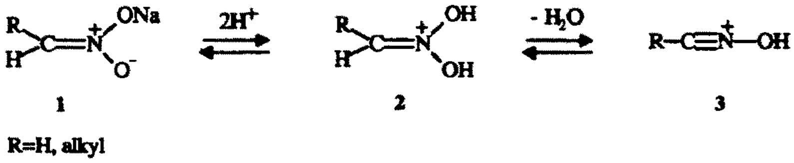
Abstract: A mild synthesis of phenolic oximes has been performed by heating $AlCl_3$ in nitromethane with suitable phenols (molar ratio 2 : 1).

Sodium nitronates are known to react with aromatics affording arylated oximes[1]. The reaction requires large amounts of strong acids such as TFSA, HF or $HF \cdot SbF_5$. Under these conditions, diprotonation of the nitronate anion **1** produces the N,N-dihydroxyiminium ion **2** which reacts as an electrophilic species equivalent to the N-hydroxynitrilium ion **3** (after losing H_2O).

Scheme 1

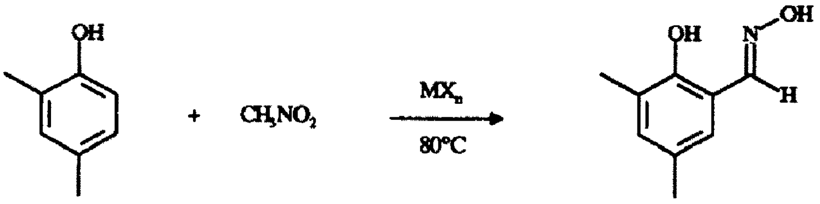


By a synthetic point of view the reaction has some severe limitations; in fact dry alkali metal salts of nitrocompounds **1** are capable of decomposing explosively if heated or subjected to mild shock[2]. Moreover large amounts of superacidic promoters are needed when nitroalkanes are utilized instead of the corresponding nitronates[3].

In the course of our study on the electrophilic bis-acylation of aluminium phenolates with phthaloyl chlorides we have found a dramatic solvent effect by carrying out the reaction in nitromethane or nitrobenzene[4]. Intrigued by this, we studied by multinuclear NMR analysis and by X-ray analysis of single crystal structure the 1:1 complexes $AlCl_3 \cdot CH_3NO_2$ and $AlCl_3 \cdot C_6H_5NO_2$[5]. In this study we have now found that the adduct between aluminium trichloride and nitromethane reacts with phenols producing phenolic oximes thus avoiding the use of strongly acidic media[6].

First we examined the reaction of 2,4-dimethylphenol **4e**, selected as the model substrate, with nitromethane under different experimental conditions, in order to obtain the best yield of oxime **5e** (Table1).

Table 1. Reaction between 2,4-dimethylphenol and nitromethane under different experimental conditions.



4e

5e

Entry	MX$_n$	MX$_n$: 4e^a	Solvent	t (h)	5e Yield (%)	5e Select.^{b} (%)
a	$SnCl_4$	1 : 1	CH_3NO_2	1	-	-
b	$TiCl_4$	"	"	"	8	90
c	BCl_3	"	"	"	-	-
d	$AlCl_3$	"	"	"	30	94
e	$ZnCl_2$	"	"	"	-	-
f	$AlCl_3$	2 : 1	"	"	45	92
g	"	3 : 1	"	"	40	89
h	"	2 : 1	$CHCl{=}CCl_2$^{c}	"	-	-
i	"	"	CH_3NO_2	5	70	97

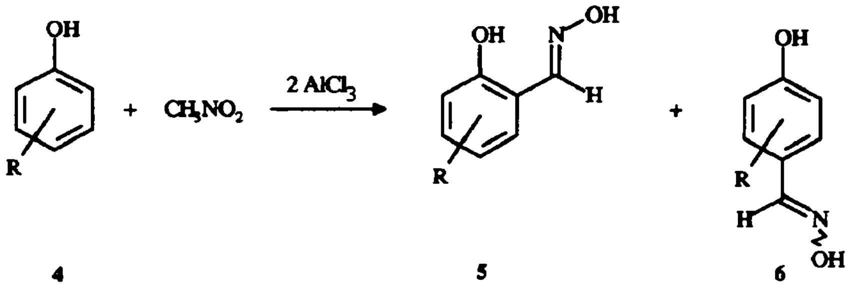
^{a} Molar concentration of 4e = 0.35; ^{b} Selectivity = Yield/Reacted phenol x 100; ^{c} CH_3NO_2/4e molar ratio = 5/1.

Among the Lewis acids employed $AlCl_3$ was found to be the best promoter (entry **d**) among different catalysts less reactive or completely inert. Two equivalents of $AlCl_3$ were needed to obtain a better yield, but yet use of a large excess of such Lewis acid would cause some undesired side reactions (entries **f** and **g**). Dehydration of the oxime **5e** to the corresponding nitrile may be a case. As a limitation actually observed, the reaction with nitroethane and higher nitroalkanes only produces traces of the corresponding oxime. Finally the use of nitromethane as the reagent in different solvents normally utilized in Friedel-Crafts reactions completely inhibits the process (entry **h**).

Successively the reaction was extended to different phenols under the optimum conditions (Table 1, entry **i**).

As shown in Table 2 various substituted phenols react with nitromethane to give the expected oximes **5** and **6**. The process is extremely sensitive to the steric effect of the substituent R. For example 2-isopropyl-5-methylphenol is converted into the oxime **5f** (E + Z isomers) in 85% yield, while 2-methyl-5-isopropylphenol affords the oxime **5g** (E isomer) in only 14% yield. In cases when both *ortho* and *para* positions are accessible, a mixture of regioisomers is obtained. The *ortho*-oxime is only produced as the E isomer whereas the *para*-oxime is constituted of a mixture of E + Z isomers. Stereochemistry of the products was determined by ^1H NMR analysis of the N-protonated derivatives as previously described by Jacquesy[7].

Table 2. Reaction between different phenols and nitromethane.



Entry	R	Conv. (%)	Yield **5** (%)	Yield **6** (%)	
			E	E	Z
a	3-CH_3	82	38	25	16
b	4-CH_3	45	40	-	
c	3-OCH_3	65	40	13	7
d	4-nC_9H_{19}	85	80	-	
e	2,4-CH_3	72	70	-	
f	2-$(CH_3)_2CH$-5-CH_3	90	-	70	15
g	2-CH_3-5-$(CH_3)_2CH$	20	-	14	
h	3,4-(CH=CH-CH=CH)	60	50	-	

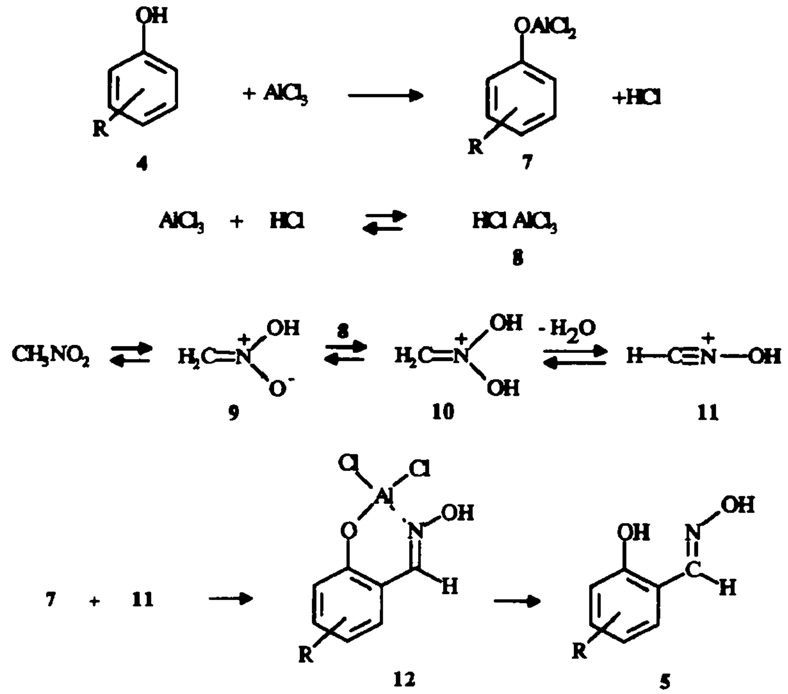
Typical Procedure. A magnetically stirred solution of $AlCl_3$ (2.66g, 0.02 mol) and the selected phenol (0.01 mol) in dry nitromethane (30 ml) was heated at 80°C for 5 hours under nitrogen. Treatment with aqueous 10% oxalic acid, extraction with Et_2O and drying with Na_2SO_4 followed by chromatography on SiO_2, eluant hexane-ethyl acetate (5-30%) afforded the solid products.

On the basis of reports from the literature[1,3,6] and our results, the mechanism of the present reaction might be proposed as described in the Scheme 2: the first step is the reaction of the phenol **4** with $AlCl_3$ to afford the corresponding dichloroaluminium phenolate **7** and HCl[8] which in turn reacts with the excess of $AlCl_3$ producing the superacid adduct **8**[9]. The complex **8** then reacts with the aci-nitromethane **9**[10] to give the actual electrophilic species **11** which reacts with the dichloroaluminium phenolate **7** producing the final oxime.

Concerning the stereochemistry of products **5** and **6**, the intermediacy of ion **11** implies the initial formation of the Z isomer, the nucleophilic addition of the aromatic being kinetically controlled; rapid isomerization of the resulting benzaldoximes is in agreement with the formation of E + Z isomeric products **6**, while the exclusive formation of the E isomer in products **5** is due to the chelation effect in complexes **12** (Scheme 2).

In conclusion we have shown that nitromethane reacts with phenols in the presence of $AlCl_3$ affording the corresponding oximes thus avoiding the use of superacids or strongly acidic promoters.

Scheme 2



Acknowledgements

This work was supported by the Consiglio Nazionale delle Ricerche (C.N.R., Roma), Progetto Finalizzato Chimica Fine e Secondaria II and by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (M.U.R.S.T.).

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(*Received in UK* 6 *December* 1993; *revised* 28 *January* 1994; *accepted* 4 *February* 1994)