Aromatic Nucleophilic Substitution on $Cr(CO)_3$-Complexed Halogenoarenes: A New Synthesis of *O*-Aryloximes and Their Cyclization to Benzofurans

Andreina Alemagna, Clara Baldoli, Paola Del Buttero,* Emanuela Licandro, and Stefano Maiorana*

Dipartimento di Chimica Organica e Industriale, Via Golgi 19, I-20133 Milano, Italy

O-Aryloximes are synthesized by reaction of acetone oxime with $Cr(CO)_3$-complexed halogenoarenes and then cyclized to give benzofurans.

Although there are a limited number of examples, *O*-arylated hydroxylamines and oximes are of interest since the oximes are starting materials in the synthesis of benzofurans *via* a rearrangement analogous to the Fischer indole synthesis.[1] *O*-Arylhydroxylamines, provided they are stable, are usually obtained by hydrolysis of *O*-aryloximes, which in turn are prepared by arylation of oximes or their sodium salts. In the early stages of our work the only arylation methods available seemed to be the nucleophilic substitution of sodium salts of oximes with activated halogeno- or nitro-arenes,[1b,c,2] or the reaction of oximes with diazonium salts.[3] The former is limited to the synthesis of *O*-aryloximes carrying electron-withdrawing substituents in the *O*-aryl moiety, and the latter gives low yields of *O*-aryloximes. The reaction of hydroxylamine-*O*-sulphonic acid with phenolate was reported to give a low yield of *O*-phenylhydroxylamine.[4] The recently reported exchange of an NH_2 group between an amine acceptor phenolate and an amine donor phenoxyamine[5] is limited by the narrow pK_a range for the amino acceptor. We have previously shown that under phase-transfer catalysis (P.T.C.) halogenoarenes activated by $Cr(CO)_3$ complexation allowed S_NAr substitutions to be performed with thiolates[6] and alkoxides[7] under mild conditions.

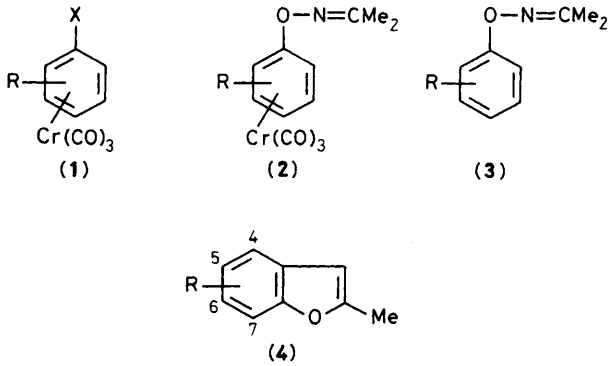
We now report that under analogous conditions halogenobenzenes and -toluenes (**1**) react smoothly with acetone oxime to give the corresponding *O*-aryloximes (**3a**—**e**) in good yields. The reactions were carried out under solid–liquid phase-transfer conditions. Compound (**1**) (4.06 mmol), tetraoctylammonium bromide (1.14 mmol), powdered KOH (12.95 mmol), acetone oxime (6.10 mmol), and benzene (40 ml) were stirred under nitrogen. The reaction was monitored by t.l.c. (silica gel; light petroleum–CH_2Cl_2, 2 : 1, as eluant). When the starting material had disappeared benzene was removed under reduced pressure, the residue dissolved in Et_2O, and the solution filtered on Celite. After evaporation, the residue was crystallized from di-isopropyl ether to give the complexed *O*-aryloximes (**2a**—**e**) (Table 1).

Decomplexation of (**2a**—**e**) with I_2 gave the crude *O*-arylox-

Table 1. Preparation of the complexed (**2**) and decomplexed (**3**) oximes.

Starting material				Complexed *O*-aryloxime			*O*-Aryloxime			
	R	X	Reaction time/h	Complex	% Yield	M.p., *t*/°C	Compound	% Yield from (**2**)	M.p. or b.p., *t*/°C (*p*/Torr)	Ref.
(**1a**)	H	F	0.5	(**2a**)	85	83	(**3a**)	78	115(1)	1a
(**1b**)	*o*-Me	F	1.75	(**2b**)	75	88—89	(**3b**)	56	[a]	—
(**1c**)	*m*-Me	F	1.0	(**2c**)	98	77	(**3c**)	55	77(0.8)	—
(**1d**)	*p*-Me	F	3.5	(**2d**)	89	96	(**3d**)	81	60	3a
(**1e**)	*m*-OMe	Cl	1.75	(**2e**)	84	112—114	(**3e**)	74	[a]	—
(**1f**)	*m*-Me	Cl	3.0	(**2c**)	75	—	—	—	—	—

[a] Thermally unstable oil, purified by column chromatography.



a; R = 7 - Me **d**; R = 5 - Me
b; R = 4 - Me **e**; R = 4 - OMe
c; R = 6 - Me **f**; R = 6 - OMe

imes (**3a**—**e**) which were chromatographed on a silica gel column (light petroleum–CH_2Cl_2, 1:1) followed by distillation or crystallization from suitable solvents. Results are presented in Table 1.

As expected, fluorine is substituted more rapidly than chlorine [see reactions of (**1c**) and (**1f**), Table 1]. Results for the *o*-, *m*-, and *p*-fluorotoluenes show that the reaction is an *ipso* substitution and that the *meta*-isomer is, qualitatively, the most reactive. Yields are always good, even with halogenoarenes carrying electron-donor groups such as *m*-chloroanisole which did not react using the method of ref. 5.

Complexation of the halogenoarene is essential for reaction, and in addition much lower yields were obtained when $Cr(CO)_3$-complexed halogenoarenes were treated with the sodium salts of the oximes without the phase-transfer catalyst, in Me_2SO or tetrahydrofuran solution.

We have shown that the above *O*-aryloximes carrying electron-donor substituents could be transformed into benzofurans, as has already been shown for *O*-aryloximes.[1,8] Treatment of an ice-cold solution of (**3a**—**e**) (3.36 mmol) in EtOH (30 ml) with H_2SO_4 (10.55 mmol) followed by heating under reflux to completion of the reaction (t.l.c.) afforded the crude benzofurans (**4a**—**f**)[9—12] in 45—87% yield.

Acetone *O*-(*m*-methoxyphenyl)oxime gives a 29:71 mixture (identified by ^1H n.m.r. spectroscopy; Varian XL-200) of 2-methyl-4-methoxy-[11] and 2-methyl-6-methoxy-benzofuran,[12] from which the latter, practically pure, could be isolated by column chromatography (silica gel; CH_2Cl_2–light petroleum, 1:1). The *O*-(*m*-tolyl)oxime affords a 42:59 mixture of 2,4-dimethyl- and 2,6-dimethyl-benzofuran, which were identified by ^1H n.m.r. spectroscopy and ^{13}C n.m.r. comparison with literature data.[10]

Attempts to cyclize the $Cr(CO)_3$-complexed aryloximes (**2a** or **d**) under the same conditions failed.

Thus, the *O*-arylation of oximes by $Cr(CO)_3$-complexed halogenoarenes under P.T.C. conditions is of general applicability, even with electron-donor-substituted halogenoarenes, and the scope of the acid-catalysed [3,3] sigmatropic rearrangement of *O*-aryloximes to give benzofurans is extended, owing to the easier availability of the starting oximes.

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