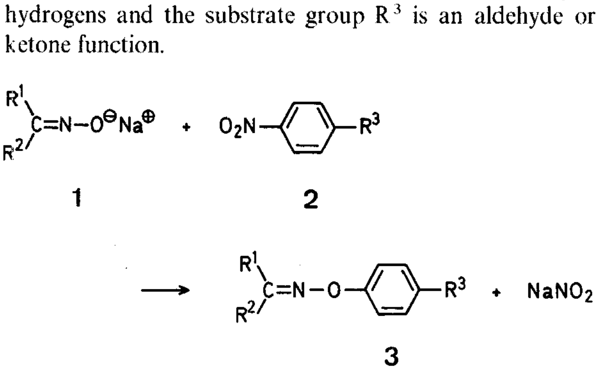
O-Arylation of Ketoximes by Aromatic Nitro Compounds

Jacob B. Baumann

Department of Chemistry, Pennsylvania State University, Schuylkill Campus, Schuylkill Haven, Pennsylvania 17972, U.S.A.

O-Arylketoximes are useful as intermediates in the synthesis of benzofurans, via a cyclization analogous to the Fischer indole synthesis[1,2,3]. They have been prepared by the reaction of *O*-phenylhydroxylamines with ketones[1] and by interaction of sodium salts of oximes with halonitrobenzenes, forming *O*-nitrophenyloximes[2,3].

We have devised a process for the preparation of *O*-arylketoximes (**3**) by the direct arylation of sodium salts (**1**) of ketoximes with various 4-substituted nitrobenzenes (**2**). This reaction proceeds readily at room temperature with the loss of the nitro group, and usually affords the desired product in good yield. Several functional groups survive the reaction unchanged. The reaction is limited to ketoximes, since *O*-arylaldoximes undergo further change to form the aryl nitrile[4,5]. Further, we did not isolate any *O*-arylketoxime from the reaction of the sodium salt of acetone oxime with either 4-nitrobenzaldehyde or 4-nitroacetophenone. Thus a limitation apparently exists when the ketoxime contains alpha hydrogens and the substrate group R^3 is an aldehyde or ketone function.



The details of the preparation of twelve *O*-arylketoximes are given in Table 1. All were stable solids whose identity was confirmed by analysis, infrared spectroscopy, and mass spectroscopy. The mass spectroscopy data was used to establish the molecular weight and to show the presence of the *O*-aryl bond in each compound. The abundant ions in the mass spectrum, in addition to the parent, included both ions expected from the fission of the *N*—*O* bond. Also observed was an ion of one mass unit larger than the aryloxy ion, probably resulting from the gain of a hydrogen. The formation of these fragments substantiates the formulation of the products as oxime ethers, rather than nitrones. Other abundant ions resulted from cleavage within the functional group R^3. Infrared frequencies are given to substantiate the presence of the unchanged functional group R^3.

Preparation of *O*-Arylketoximes (3): Method A: A solution of sodium methoxide was prepared by the addition of sodium (0.02 mol) to methanol (7.5 ml). Dimethyl sulfoxide (42.5 ml) was added, followed by the oxime (0.020 mol) and the nitro compound (0.020 mol). The reaction mixture was stirred at room temperature for 24 h. The solvents were removed by distillation at reduced pressure and the crude solid mixture was purified by recrystallization. Sodium nitrite was washed out in the preparation of compounds **b** and **f** but not of **d**, **e**, **i**, and **j**.

Method B: Identical to method A, except that at the end of 24 h the reaction mixture was diluted by the addition of distilled water (100 ml). The precipitated solid was suction-filtered and then recrystallized.

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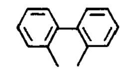
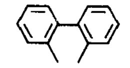
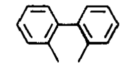
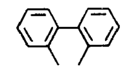
Table 1. Preparation of *O*-Arylketoximes (**3**)

Compound[a] **3**	R^1	R^2	R^3	Yield (%)	Method	M.p.	Recrystallization Solvent	M.S.[b] (*m/e*)	I.R.[c] cm^{-1}
a	$-(CH_2)_5-$		$COOCH_3$	7	B	84–86°	CH_3OH/H_2O	247, 216, 188, 152, 151, 96	1700
b	$-(CH_2)_5-$		CN	22	A	73–75°	CH_3OH/H_2O	214, 119, 118, 96	2220
c	CH_3	CH_3	$COOCH_3$	12	B	78–80°	pet. ether (30–60°)	207, 176, 152, 151, 96	1715
d	CH_3	CH_3	CN	24	A	100–102°	CH_3OH/pet. ether (30–60°)	174, 119, 118, 56	2210
e	C_6H_5	C_6H_5	$COOCH_3$	28	A	107–109°	CH_3OH	331, 300, 180, 152, 151	1710
f	C_6H_5	C_6H_5	CN	61	A	95–97°	CH_3OH	290, 180, 119, 118	2215
g	C_6H_5	C_6H_5	C_6H_5CO	66	B	116–118°	CH_3OH/C_3H_7OH	377, 300, 198, 180, 105, 77	1685
h	C_6H_5	C_6H_5	CHO	59	B	85–88°	CH_3OH	301, 180, 122, 121	1690
i			$COOCH_3$	31	A	166–168°	$CH_3OH/C_6H_5CH_3$	329, 298, 270, 178, 152, 151	1720
j			CN	73	A	166–168°	$CH_3OH/C_6H_5CH_3$	296, 178, 119, 118	2210
k			C_6H_5CO	37	B	118–121°	C_3H_7OH	375, 298, 270, 198, 197, 178, 105, 77	1650
l			CHO	48	B	135–137°	C_3H_7OH	299, 270, 178, 122, 121	1680

[a] All products gave satisfactory elemental analyses (C ±0.27%), (H ±0.17%), (N ±0.28%).
[b] Recorded at 70 eV.
[c] KBr disks.