

# Tavs Reactions of *o*-Halobenzaldimines with Ethyl Diphenylphosphinite. Synthesis and Crystal Structure of a Bis(phosphine Oxide)

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**ABSTRACT:** *The reactions of a series of o-halobenzaldimines with ethyl diphenylphosphinite in ethanol, in the presence of nickel(II), proceed with a coordination template-assisted Tavs phosphorylation at the carbon to which the halogen was attached and addition of diphenylphosphine oxide to the imino bond, to form a bis(phosphine oxide), the structure of which has been confirmed by X-ray crystallography. Carrying out the reaction in acetonitrile, in the presence of copper(I) iodide, results only in a Tavs replacement of halogen by phosphorus, to give an o-diphenylphosphinylaryl imine.* © 2005 Wiley Periodicals, Inc. Heteroatom Chem 16:242–245, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20117

## INTRODUCTION

The nickel-promoted phosphonation of aryl halides by alkyl phosphite esters is commonly known as the Tavs reaction [1,2]. The reaction usually involves heating the aryl halide with an alkyl phosphite (or related tervalent phosphorus ester) in the presence of a nickel(II) halide at around 200°C (and in the absence of a solvent). The overall course of the reaction is broadly similar to the more familiar Michaelis–

Arbuzov phosphonation of alkyl halides, in that the displaced halogen appears as a volatile alkyl halide, the alkyl group of which arises from the alkyl phosphite reagent [3,4]. However, the Michaelis–Arbuzov reaction does not require the presence of a transition metal compound, whereas the Tavs reaction only proceeds in the presence of such a component. The mechanism is usually considered to involve in situ reduction of nickel(II) to a nickel(0) phosphite complex which then undergoes oxidative insertion into the carbon–halogen bond of the aryl halide to form an arylnickel(II) intermediate. This then undergoes reductive elimination of an aryl(alkoxy)phosphonium salt, which then collapses to form the phosphonylated arene product [5,6]. The Tavs reaction is strongly disfavored by simple substituents in the ortho position to the halogen [1,2]. However, if the ortho substituent bears one or more donor groups capable of coordinating to the metal ion, then a coordination-template assisted phosphonation mechanism is possible, and replacement of the halogen is facilitated. Thus, e.g., the nickel(II)-promoted Tavs reaction of *o*-bromoacetanilides with triethylphosphite proceeds normally at ca 160°C [7], and, even more remarkably, the reaction of *o*-haloarylazobenzenes with triethylphosphite in the presence of copper(II) acetate yields the related *o*-diethylphosphonatoarylazobenzenes in refluxing ethanol in good yield, via the intermediate formation of copper(I)-phosphite complexes [8,9]. Following our work, and that of others, on the coordination

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template-assisted formation of aryl-phosphonium, -arsonium, and -stibonium salts from the metal ion-promoted reactions of tertiary phosphines, arsines, and stibines with aryl halides bearing an appropriate donor group in close proximity to the halogen [10–14], we were interested in studying the reactivity of such template aryl halides in the Tavs reaction with ethyl diphenylphosphinite, which might provide a new route to some interesting chelating phosphine oxide ligands with additional heterodonor centers.

## RESULTS AND DISCUSSION

In our earlier studies of coordination template-assisted displacement of aryl halogen, we focused on the nickel(II)-promoted reactions of the *o*-haloarylimines **1**, X = hal, R = alkyl or aryl, with tertiary phosphines, which proceed in good yield in refluxing ethanol, to give the related phosphonium salts **2**, R<sup>1</sup>, R<sup>2</sup> = alkyl or aryl [10]. Normally, the nickel-promoted reactions of simple aryl halides with tertiary phosphines only take place at ca 200°C, and so it is clear that the *o*-iminogroup in **1** is providing a significant kinetic template effect. In the present study, the imines **1**, X = Cl, Br, or I, R = *p*-MeOC<sub>6</sub>H<sub>4</sub> were heated for several hours under reflux in ethanol with ethyl diphenylphosphinite and nickel(II) bromide (0.5 mol per mol of

imine). On cooling, each solution deposited a white solid, mp 206–208°C, irrespective of the nature of the original halogen present. An X-ray crystallographic study of the solid, recrystallized from dichloromethane ether, revealed that the product was the bis(phosphine oxide) **3** rather than the expected *o*-iminoarylphosphine oxide **4**. Compound **3** is of interest in that it is a chelating bis(phosphine oxide) which has an additional donor nitrogen, and which also possesses a chiral carbon atom, although the compound was isolated as a racemate, and no attempt was made to resolve it into its enantiomers. The infrared spectrum of the product showed an absence of any absorption in the region of 1600 cm<sup>-1</sup> attributable to the presence of the imine group, but instead showed a broad absorption at 3300 cm<sup>-1</sup>, attributable to NH stretching, implying that the imine group had been reduced. The <sup>31</sup>P NMR spectrum showed two singlets at δ = 34.59 and 34.70 ppm, consistent with the presence of two diphenylphosphinyl moieties in different locations. The integration of the <sup>1</sup>H NMR spectrum indicated that two such groups were present with respect to the *p*-methoxyphenyl group. The molecular structure of **3** is displayed in Fig. 1, and is consistent with the spectroscopic data. The structure contains one molecule of dichloromethane where the central carbon atom is disordered over two positions. The absolute structure has been determined and the chiral

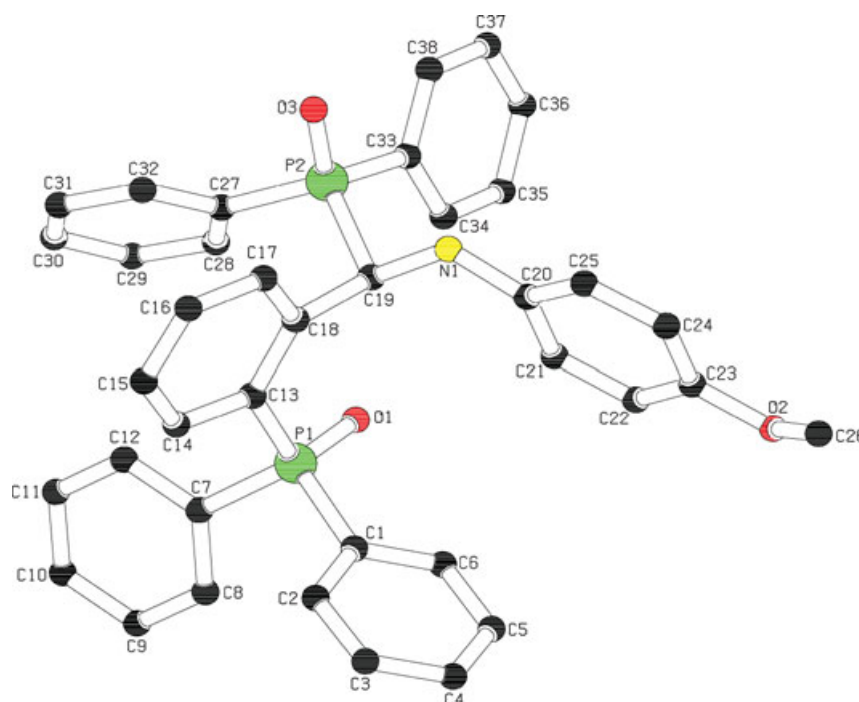


FIGURE 1 Molecular structure of **3** with the disordered CH<sub>2</sub>Cl<sub>2</sub> solvent removed for clarity.

center depicted is in the R form, whilst the centrosymmetric nature of the space group generates the S form through the inversion center to give a racemic pair. One phosphoryl group is intramolecularly hydrogen bonded to the nitrogen–hydrogen bond, as shown in Fig. 1, with a donor–acceptor distance  $O3 \cdots N1 = 2.886(8)$  Å. In the crystal structure two of these interactions form a discrete head to tail dimer. Crystal data are given in Table 1, and selected bond length and bond angle data are given in Table 2. A possible pathway for the formation of **3** is the addition of the P–H bond of diphenylphosphine oxide (formed in situ by a nickel-catalyzed Michaelis–Arbuzov solvolytic dealkylation of the phosphinite ester by ethanol) to the imine bond of the initially formed, expected product **4**. Such hydrophosphination reactions of imines are well established [15].

In order to confirm the above suggestion, we then sought to prepare compound **4** by another route. Following the work of Price et al. on the copper-promoted reactions of *o*-haloarylazobenzenes with triethylphosphite [8,9], and our recent use of copper(I) iodide in acetonitrile in the formation of

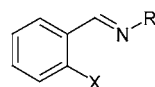
TABLE 1 Crystal Data and Structure Refinement for **3**

Empirical formula	$C_{39}H_{35}Cl_2NO_3P_2$
Formula weight	698.52
Temperature	120(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/n$
Unit cell dimensions	$a = 13.148(2)$ Å $b = 17.0897(6)$ Å $c = 16.544(3)$ Å $\beta = 110.771(16)^\circ$
Volume	$3475.5(8)$ Å <sup>3</sup>
Z	4
Density (calculated)	1.335 mg/m <sup>3</sup>
Absorption coefficient	0.318 mm <sup>-1</sup>
$F(000)$	1456
Crystal	Prism; pale yellow
Crystal size	$0.30 \times 0.14 \times 0.10$ mm <sup>3</sup>
$\theta$ range for data collection	$2.90$ – $27.47^\circ$
Index ranges	$-16 \leq h \leq 17$ , $-21 \leq k \leq 22$ , $-21 \leq l \leq 21$
Reflections collected	42720
Independent reflections	7900 ( $R_{int} = 0.0449$ )
Completeness to $\theta = 27.47^\circ$	99.4%
Max. and min. transmission	0.9689 and 0.9106
Data/restraints/parameters	7900/12/440
Goodness-of-fit on $F^2$	1.024
Final $R$ indices [ $F^2$ $\checkmark$ $2\sigma(F^2)$ ]	$R1 = 0.0611$ , $wR2 = 0.1448$
$R$ indices (all data)	$R1 = 0.0746$ , $wR2 = 0.1557$
Extinction coefficient	0.0018(15)
Largest diff. peak and hole	1.677 and $-1.776$ eÅ <sup>-3</sup>

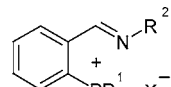
TABLE 2 Selected Bond Lengths (Å) and Angles (°)

C13–P1	1.825(5)	O1–P1	1.498(4)
C19–N1	1.454(5)	O3–P2	1.491(3)
C19–P2	1.841(5)		
N1–C19–C18	116.4(4)	C7–P1–C1	106.9(2)
N1–C19–P2	105.4(3)	C1–P1–C13	105.0(2)
C18–C19–P2	109.1(3)	O3–P2–C33	112.4(2)
C20–N1–C19	122.5(4)	O3–P2–C27	110.2(2)
O1–P1–C7	111.2(2)	C33–P2–C27	107.5(2)
O1–P1–C1	111.1(2)	O3–P2–C19	112.5(2)
O1–P1–C13	115.3(2)	C33–P2–C19	105.5(2)
C7–P1–C13	106.7(2)	C27–P2–C19	108.4(2)

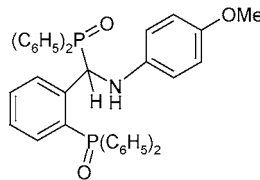
aryl-arsonium and aryl-stibonium salts from the reactions of template aryl halides and triaryl-arsines and triaryl-stibines [12,13], we studied the reaction of the *o*-haloimine **1**,  $X = Br$ ,  $R = p\text{-MeOC}_6\text{H}_4$  with ethyl diphenylphosphinite in acetonitrile, in the presence of copper(I) iodide. After several hours under reflux, a yellow solid was isolated from the reaction mixture in 25% yield. The infrared spectrum showed a band at  $1600\text{ cm}^{-1}$  attributable to the imine group, and both <sup>1</sup>H and <sup>31</sup>P NMR and mass spectrometry were consistent with structure **4**. Clearly, in acetonitrile, the phosphinite ester is not suffering metal-promoted solvolysis, and hence no diphenylphosphine oxide is present to add to the imine bond. To confirm that such an addition takes place in ethanol, compound **4** was treated with ethyl diphenylphosphinite in ethanol containing nickel(II) bromide. The bis(phosphine oxide) **3** was formed rapidly.



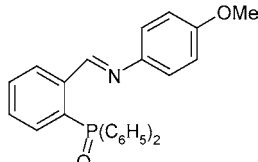
1



2



3



4

## EXPERIMENTAL

<sup>31</sup>P, <sup>1</sup>H, and <sup>13</sup>C NMR studies were carried out using a Bruker AC250 FTNMR spectrometer. Accurate mass

measurements were carried out using a VG7070E mass spectrometer, at a resolution of 5000. Perfluorokerosene was used as the internal standard.

*Reactions of o-haloarylimines 1, X = Cl, Br, I; R = p-methoxyphenyl with ethyl diphenylphosphinite*

*In the Presence of Nickel(II).* The *o*-haloimine ( $3.5 \times 10^{-3}$  mol), ethyl diphenylphosphinite ( $7 \times 10^{-3}$  mol), and nickel(II) bromide ( $1.75 \times 10^{-3}$  mol) were heated together under reflux in ethanol ( $10 \text{ cm}^3$ ) in a nitrogen atmosphere for 6 h. The reaction mixture was then poured into water, and the organic products extracted into chloroform. Evaporation of the dried extract gave a solid which was recrystallized from ethanol to give  $\alpha$ -(4-methoxyphenylamino)-(*o*-diphenylphosphinyl)benzylidiphenylphosphine oxide **3**, as a white crystalline solid, mp  $206^\circ\text{C}$ , in yields of 39, 39, and 45% (from **1**, X = Cl, Br, and I, respectively). IR (nujol):  $1175, 1160 \text{ cm}^{-1}$  (P=O).  $\delta^{31}\text{P}$  ( $\text{CDCl}_3$ ) = 34.70 and 34.59 ppm.  $\delta^1\text{H}$  ( $\text{CDCl}_3$ ) = 8.4 (m, 2ArH), 8.2 (m, 1ArH), 7.7–7.1 (m, 18ArH), 6.85 (m, 3ArH), 6.2 (AB pattern, 4ArH), 5.15, (br.m, benzylic CH), 3.55 (s, 3H,  $\text{CH}_3$ ), and 2.1 (broad, NH, exchanges with  $\text{D}_2\text{O}$ ) ppm.  $^{13}\text{C}$  ( $\text{CDCl}_3$ ) showed a benzylic carbon as a doublet ( $^1J_{\text{PC}} = 74.7 \text{ Hz}$ ) at  $\delta = 53.5$  ppm. ESMS (+ve ion mode): Calcd. for  $(\text{M} + \text{Na})^+$ : 635. Found: 635  $(\text{M} + \text{Na})^+$ . Crystals for X-ray diffraction were grown from dichloromethane ether. Anal. Calcd. for  $\text{C}_{38}\text{H}_{33}\text{NO}_3\text{P}_2 \cdot \text{CH}_2\text{Cl}_2$ : C, 67.06, H, 5.05, N, 2.00. Found: C, 67.35, H, 5.09, N, 2.00%.

*In the Presence of Copper(I).* The *o*-bromophenylimine ( $1.0 \times 10^{-3}$  mol), ethyl diphenylphosphinite ( $1 \times 10^{-3}$  mol), and copper(I) iodide ( $1.0 \times 10^{-3}$  mol) were heated together under reflux in acetonitrile ( $5 \text{ cm}^3$ ) in a nitrogen atmosphere for 6 h. The reaction mixture was then poured into water, and the organic products extracted into chloroform. Evaporation of the dried extract gave a solid which was recrystallized from acetonitrile to give *N*-(*o*-diphenylphosphinylbenzylidene)-4-methoxyphenylamine **4**, as bright yellow crystals, mp  $148^\circ\text{C}$ , in 25% yield. IR (nujol):  $1191 \text{ cm}^{-1}$  (P=O).  $\delta^{31}\text{P}$  ( $\text{CDCl}_3$ ) = 30.88 ppm.  $\delta^1\text{H}$  ( $\text{CDCl}_3$ ) = 9.28 (s, 1H, CH=N), 8.45 (m, 1ArH), 7.75–7.4 (m, 12ArH), 7.15 (m, 1ArH), 7.0–6.7 (AB pattern, 4ArH), 3.8 (s, 3H,  $\text{CH}_3$ ). Calcd for  $\text{C}_{26}\text{H}_{22}\text{NO}_2\text{P}$ ,  $\text{M}^+ = 411.13882$ . Found:  $\text{M}^+ = 411.13586$  (3 mmu).

*X-ray Crystallography.* Data were collected by means of combined phi and omega scans on a Nonius KappaCCD area detector situated at the window of a Nonius FR591 rotating anode ( $\lambda\text{Mo K}_\alpha = 0.71073 \text{ \AA}$ ). The structures were solved by direct methods, SHELXS-97 and refined using SHELXL-97 [16]. Hydrogen atoms were included in the refinement, but thermal parameters and geometry were constrained to ride on the atom to which they are bonded. The data were corrected for absorption effects using SORTAV [17,18]. A solvent molecule of dichloromethane was found to be present in the asymmetric unit with the central carbon atom disordered over two sites which refined to give an occupancy ratio of 63:37. Supplementary data in the form of CIF files have been deposited with the Cambridge Crystallographic Data Centre (deposition number: CCDC256344)

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