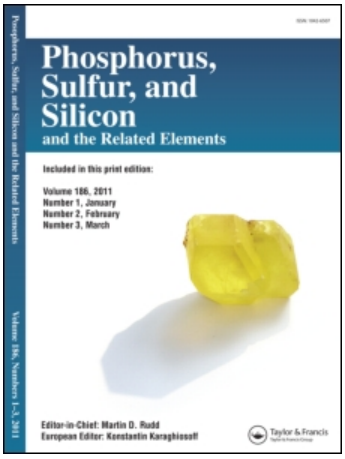

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HIGHLY ENANTIOMERIC PURITY CONVERSION OF α-SULFINYL OXIMES AND α-SULFINYL HYDRAZONES TO THE CORRESPONDING β-KETO SULFOXIDES WITH BUTYLTRIPHENYLPHOSPHONIUM PERIODATE (BUTPPPI)

A. R. Hajipour[a,b] *and A. E. Ruoho*[b]
University of Wisconsin Medical School, Madison, Wisconsin, USA[a] *and Isfahan University of Technology, Isfahan, Iran*[b]

Butyltriphenylphosphonium periodate ($Ph_3P^+BuIO_4^-$) ***1*** *is readily prepared as a white solid from butyltriphenylphosphonium chloride, performs conversion of* α*-sulfinyl oximes (****2****) and* α*-sulfinyl hydrazones (****4****) to the corresponding* β*-keto sulfoxides (****3****) in high yields and high enantiomeric purity.*

Keywords: α-Sulfinyl hydrazones; α-sulfinyl oximes; β-keto sulfoxides; chiral nonracemic synthesis; high enantiomeric purity

β-Keto sulfoxides are very important starting materials in asymmetric synthesis,[1,2] and can be synthesis by the cleavage of the C=N bonds of α-sulfinyl oximes and α-sulfinyl hydrazones. These compounds prepared via the addition of aryl methyl sulfoxides to aryl *N*-oxides[3] or the addition of lithiated *N*,*N*-dimethyl hydrazones to menthyl sulfinate esters[4] respectively. The hydrolysis of C=N double bond of α-sulfinyl oximes (**2**) and α-sulfinyl hydrazones (**4**) by a classical method[5] was attempted but the optical purity and yield by this method were low (ee <35 and yield <50%).

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Address correspondence to A. R. Hajipour, Department of Pharmacology, University of Wisconsin Medical School, 1300 University Ave., Madison, WI 53706-1532. E-mail: arhajipour@facstaff.wisc.edu

RESULTS AND DISCUSSION

Butyltriphenylphosphonium periodate ($Ph_3P^+BuIO_4^-$) is a mild, efficient, stable, and inexpensive reagent, that has been used for our studies under nonaqueous conditions. This reagent is a white powder, which is prepared by the dropwise addition of an aqueous solution of $NaIO_4$ to an aqueous solution of butyltriphenylphosphonium chloride at room temperature. Filtration and drying of the precipitate produced a white powder, which could be stored for months without losing its oxidation ability. This reagent is quite soluble in polar solvents such as methylene chloride, chloroform, acetone, and acetonitrile and insoluble in nonpolar solvents such as carbon tetrachloride, n-hexane, and diethylether. We found that the cleavage of C=N double bond of α-sulfinyl oximes (**2**) and α-sulfinyl hydrazones (**4**) by this reagent in acetonitrile under reflux is rapid (50–70 min). The reaction is very fast and almost quantitative with high optical purity from ^{1}H NMR analysis in the presence of chemical shift reagent (>92) (Tables I and II). The general reaction is detailed in Scheme 1. In all case, the crude product was judged to be of >95% purity based on ^{1}H NMR and TLC analysis. Because of the mildness of the reagent, as shown in Tables I and II, the corresponding sulfones are not formed in these reactions. At this stage the mechanism of the reaction is not clear to us. The enantiomeric purity of (**3**) was determined to be >92 from ^{1}H NMR chiral shift studies using (−)-(R)-*N*-(3,3-dinitrobenzoyl)-α-phenylethylamine (**5**) as a chiral shift reagent[6] and comparing the optical rotation of the products

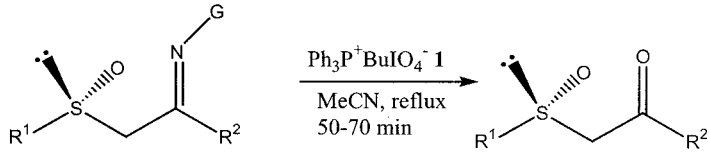
TABLE I Conversion of (**2**) to the Corresponding Carbonyl Compounds (**3**)

Starting material	Product	Reaction time/min	Yield %[a]	e.e. %
2a	**3a**	50	96	92
2b	**3b**	55	95	95
2c	**3c**	60	98	98
2d	**3d**	55	95	100
2e	**3e**	65	99	100
2f	**3f**	65	97	99
2g	**3g**	55	99	96
2h	**3h**	55	96	97
2I	**3I**	70	96	97

[a]Confirmed by comparison with authentic samples (IR, TLC, and ^{1}H-NMR).[1–5]

[b]Substrate/reagent (1:1).

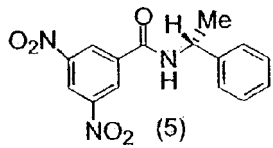
[c]Yield of isolated pure product after purification.



2: G = OH (R_S)
4: G = N-N(Me)$_2$ (R_S)

3 (R_S)

2a R^1 = phenyl, R^2 = phenyl
4a R^1 = phenyl, R^2 = phenyl
2b R^1 = phenyl, R^2 = 3,4-dimethoxyphenyl
4b R^1 = phenyl, R^2 = 3,4-dimethoxyphenyl
2c R^1 = *p*-tolyl, R^2 = phenyl
4c R^1 = *p*-tolyl, R^2 = phenyl
2d R^1 = *p*-tolyl l, R^2 = 3,4-dimethoxyphenyl
4d R^1 = *p*-tolyl, R^2 = 3,4-dimethoxyphenyl
2e R^1 = 2-*methoxy-1-naphthyl*, R^2 = phenyl
4e R^1 = 2-*methoxy-1-naphthyl*, R^2 = phenyl
2f R^1 = 2-*methoxy-1-naphthyl*, R^2 = 3,4-dimethoxyphenyl
4f R^1 = 2-*methoxy-1-naphthyl*, R^2 = 3,4-dimethoxyphenyl
2g R^1 = *p*-tolyl, R^2 = 2,4,6-trimethylphenyl
4g R^1 = *p*-tolyl, R^2 = H
2h R^1 = *p*-tolyl, R^2 = 2,4,6-trimethyl-3,5-dichlorophenyl
4h R^1 = *p*-tolyl, R^2 = Me
2I R^1 = *p*-tolyl, R^2 = 4-methoxyphenyl
4I R^1 = *p*-tolyl, R^2 = Et



(5)

SCHEME 1

with known compounds.[1–5] To determine the enantiomeric purity of (**3**) we mixed it with one equivalent of chiral shift reagent (**5**) in a NMR tube.

In conclusion, we report here an efficient, rapid, mild, and inexpensive method for the conversion of α-sulfinyl oximes (**2**) and α-sulfinyl hydrazones (**4**) by butyltriphenylphosphonium periodate $BuP^+Ph_3IO_4^-$ (**1**) in acetonitrile under refluxing conditions to the corresponding β-keto sulfoxides (**3**).

TABLE II Conversion of (**4**) to the Corresponding Carbonyl Compounds (**3**)

Starting material	Product	Reaction time/min	Yield %[a]	e.e. %
4a	**3a**	60	98	92
4b	**3b**	65	98	94
4c	**3c**	60	95	95
4d	**3d**	60	97	94
4e	**3e**	65	97	96
4f	**3f**	70	99	97
4g	**3g**	60	96	98
4h	**3h**	55	99	95
4I	**3I**	70	98	99

[a]Confirmed by comparison with authentic samples (IR, TLC, and ^{1}H-NMR).[1–5]

[b]Substrate/reagent (1:3).

[c]Yield of isolated pure product after purification.

EXPERIMENTAL

General

All yields refer to isolated products after purification. Starting materials were synthesis by known methods.[1–5] Products were characterized by comparison with authentic samples[1–5] and by spectroscopy data (IR, NMR spectrum, tin layer chromatography, melting and boiling points). All reactions were carried out in acetonitrile. All m.p.s were taken on a Gallenkamp melting apparatus and are uncorrected. Research Institute of Petroleum Industry, Tehran, Iran performed elemental analysis. ^{1}H NMR spectra were recorded at 300 MHz. The spectra were measured in $CDCl_3$ unless otherwise stated, relative to TMS (0.00 ppm). Optical rotations were recorded with a JASCO, DIP-370, Digital Polarimeter.

Preparation of Butyltriphenylphosphonium Periodate (1) (BTPPPI)

A solution of butyltriphenylphosphonium chloride (17.37 g, 49 mmol) in 100 ml of water was prepared, then $NaIO_4$ (10.49 g, 49 mmol) in water (100 ml) was added dropwise to the above solution and stirred for 30 min at room temperature. The resulting white precipitate was filtered and washed with cooled distilled water (50 ml), and dried in a desiccator under vacuum over calcium chloride to afford a white powder (24.49 g, 98% yield), which decomposed at 150–153°C to a dark brown material. ^{1}H-NMR: δ 7.89–7.72 (m, 15H), 3.23 (m, 2H), 1.68 (m, 4H), 0.92 (t, 3H). ^{13}C—NMR: δ 136.03, 136.00, 134.62, 134.54, 131.27, 131.17,

119.72, 119.04, 118.26, 24.92 (d, J = 298,5 Hz, C—P). IR (KBr). Anal Calcd for $C_{22}H_{24}IO_4P$: C, 51.76; H 4.70%. Found: 52.00; H, 4.68%.

Oxidation of (2) or (4) to (3)

General Procedure

The α-sulfinyl oximes (**2**) or α-sulfinyl hydrazones (**4**) (1 mmol) was added to a stirred solution of the oxidant (1) (1 mmol, 0.51 g) in acetonitrile (20 ml). The mixture was heated at reflux until TLC showed complete disappearance of starting material, which required 50–70 min depending on substrate (Tables I and II). The mixture was cooled and 2 g of silica gel was added to the reaction mixture and the reaction mixture was stirred for 5 min. The solid was then separated by suction filtration through Celite and washed with acetonitrile (2×10 ml). Evaporation of the solvent gave the β-keto sulfoxides (**3**). The crude products were purified by column chromatography on silica gel using a mixture of ethyl acetate and hexane as eluent (90:10).

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