Bis(1-benzyl-4-aza-1-azonia-bicyclo[2.2.2]octane) persulfate: A mild and efficient oxidant for cleavage of oxime double bonds under anhydrous conditions

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Bis(1-benzyl-4-aza-1-azonia-bicyclo[2.2.2]octane) persulfate (BAABCP) readily prepared as orange solid from commercially available 1,4-diazabicyclo[2.2.2]octane (DABCO) and potassium persulfate, converts oximes and \(\alpha\)-sulfinyl oximes to the corresponding carbonyl compounds and \(\beta\)-keto sulfoxides respectively, the yields and enantiomeric purity are excellent.

Regeneration of carbonyl compounds from stable and readily prepared aldoximes and ketal oximes has received attention in recent years. Since oximes can be prepared from non-carbonyl compounds, the regeneration of carbonyl compounds from oximes provides an alternative method for the preparation of aldehydes and ketones. However, many of these methods to generate carbonyl compounds from oximes involve reagents which are either expensive or not readily available.

The classical method for the conversion of these compounds to the corresponding carbonyl compounds is hydrolysis of these compounds under acidic conditions; this method is not suitable for acid sensitive and asymmetric compounds.

As part of an ongoing asymmetric synthetic project we required an efficient and rapid method for the conversion of oximes and \(\alpha\)-sulfinyl oximes to the corresponding carbonyl compounds. We have found that reaction of BAABCP with oximes in acetonitrile under reflux gave the corresponding carbonyl compounds. The reagent was tested on a wide array of oximes (Scheme I).

Our results show that oximes 2 converted to the corresponding aldehydes and ketones 3 and no further oxidation to their carboxylic acid was observed by treatment with BAABCP under reflux condition (Table I).

Optical active \(\beta\)-keto sulfoxides are very important starting material in the asymmetric synthesis. These compounds can be synthesised by the cleavage of C=N of optical active \(\alpha\)-sulfinyl oximes, which are readily prepared via the addition of aryl methyl sulfoxides to aryl N-oxides. We tried to hydrolyse the C=N of optical active \(\alpha\)-sulfinyl oximes by the Annunzian method, in our hand the optical purity...
and yield of the cleavage of C=N of α-sulfinyl oximes by this method was low (i.e. e.e<35 and yield <50 %).

We found that cleavage of C=N of optical active α-sulfinyl oximes 34, by BAABCPS 1 in acetonitrile at reflux condition is rapid (20-30 min), and almost quantitative with high optical purity (Table II)31 from as revealed by 1H NMR analysis in the presence of chemical shift reagent (> 95 %). The general reaction is detailed in Scheme II and Table II. In all cases, the crude product was judged to be of >95% purity based on 1H NMR and TLC analysis.

In conclusion, we report here an efficient, rapid and inexpensive method for the conversion of oximes and α-sulfinyl oximes to the corresponding carbonyl compounds and β-keto sulfoxides respectively; the reactions are clean, rapid and of optical purity and yield of these reaction are high.

### Experimental Section

#### General method: Preparation of BAABCPS 1.

To a solution of DABCO (0.1 mole, 11.22 g) in acetone (200 mL) at room temperature was added benzyl bromide (0.1 mole, 17.1 g) dropwise, when the white solid of 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide was precipitated. The crystals were collected, washed with acetone (20 mL) and then dried under high vacuum (0.01 mm Hg), yield 25.5 g (90%).

To a solution of 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide (0.1 mole, 28.305 g) was added a solution of K2S2O8 (0.05 mole, 13.52 g) in H2O (20 mL) dropwise, when the orange solid of BAABCPS 1 was precipitated. The reaction mixture was stirred at -5°C for 30 min, the crystals were collected, washed with water (20 mL) and then dried under high vacuum (0.01 mm Hg), yield 25.45 g (85%).

### Oxidation of 5 to 6

The oxime 2 (1 mmole) was added to a stirred solution of oxidant 1 (1 mmole, 0.60 g) in acetonitrile (15 mL). The mixture was heated at reflux until TLC showed complete disappearance of starting material, which required 15-30 min depending on the substrate. The mixture was cooled and to it 3 g silica gel was added. The reaction mixture was filtered through Celite and washed with acetonitrile (2×10 mL). Evaporation of the solvent gave carbonyl compound 3 which was >95% pure from 1H NMR analysis. The product could be further purified by short-path distillation or column chromatography on silica gel using mixture of ethyl acetate/n-hexane (20/80) as eluent.

### Preparation of β-keto sulfoxides 6.

The α-sulfinyl oxime 534 (1 mmole) was added to a stirred solution of oxidant 1 (1 mmole, 0.60 g) in acetonitrile (15 mL). The mixture was heated at reflux until TLC showed complete disappearance of starting material, which required 15-30 min depending on the substrate.
The mixture was cooled and 3 g silica gel was added to the reaction mixture. It was stirred for 5 min, the sbjul was then separated by filtration through Celite and washed with acetonitrile (2x10 mL). Evaporation of the solvent gave β-keto sulfoxides which was >95% pure from 1H NMR analysis. The product could be further purified by column chromatography on silica gel using ethyl acetate as eluent.

(+)-(R)-2-(Phenyl-1'-sulfinyl)-acetophenone 6a: m.p. 70-71°C (Lit. 37 70.5-71.5°C); 1H NMR: δ 7.1-7.9 (m, 10H), 4.48, and 4.28 (AB quartet system, J=13.6 Hz, 2H); MS: m/z 244.30 (80%, M'), 105 (100%). Anal. Calcd for C15H12O2S: C, 68.83; H, 4.95. Found: C, 68.77; H, 5.02%. [α]D20 +161.65 (c 1.2 CHCl3).

(+)-(R)-2-(Phenyl-1'-sulfinyl)-3,4-dimethoxyacetophenone 6b: m.p. 88-89°C; 1H NMR: δ 7.1-7.9 (m, 8H), 4.48, and 4.28 (AB quartet system, J=13 Hz, 2H), 3.92 (s, 6H, 2xOMe); MS: m/z 304.36 (100%). Anal. Calcd for C16H14O2S: C, 63.14; H, 3.50. Found: C, 63.06; H, 5.46%. [α]D20 +146.65 (c 1.2 CHCl3).

(+)-(R)-(2-(Tolyl-1'-sulfinyl)-3,4-dimethoxyacetophenone 6c: m.p. 96-98°C; 1H NMR: δ 7.0-7.9 (m, 7H, 4.95 and 4.39 (AB quartet system, J=13 Hz, 2H), 3.88 (s, 6H, 2xOMe), 242 (s, 3H, MS: m/z 316.39 (70%, M'), 165 (100%). Anal. Calcd for C17H16O2S: C, 64.13; H, 5.70. Found: C, 68.08; H, 5.73%. [α]D28 +202.20 (c 1.2, acetone).

(+)-(R)-2-(2'-Methoxynaphthyl-1'-sulfinyl)-acetophenone 6e: m.p. 79-80°C; 1H NMR: δ 8.92 (d, 1H), 7.1-7.9 (m, 10H), 5.05 and 4.82 (AB quartet system, J=13 Hz, 2H), 3.90 (s, 3H, OMe); MS: m/z 325.5 (80%, M'), 226.3 (25%), 141 (100%). Anal. Calcd for C17H16O2S: C, 70.35; H, 4.97. Found: C, 70.41; H, 4.88%. [α]D28 +97.5 (c 1.2, DCM).

(+)-(R)-2-(2'-Methoxynaphthyl-1'-sulfinyl)-3,4-dimethoxyacetophenone 6f: m.p. 119-21°C; 1H NMR: δ 8.95 (d, 1H), 6.8-8.0 (m, 7H), 5.02 and 4.85 (AB quartet system, J=13.2 Hz, 2H), 4.00 (s, 3H, OMe), 3.95 (s, 3H, OMe), 3.80 (s, 3H, OMe); MS: m/z 385.1 (50%, M'), 288.3 (25%), 205 (100%). Anal. Calcd for C21H20O2S: C, 65.61; H, 5.24. Found: C, 65.70; H, 5.38%. [α]D28 +90.8, (c 1.3, DCM).

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