1-Benzyl-4-aza-1-azoniabicyclo[2.2.2]octane Periodate: a Mild and Efficient Oxidant for the Cleavage of Oxime Double Bonds under Anhydrous Conditions†

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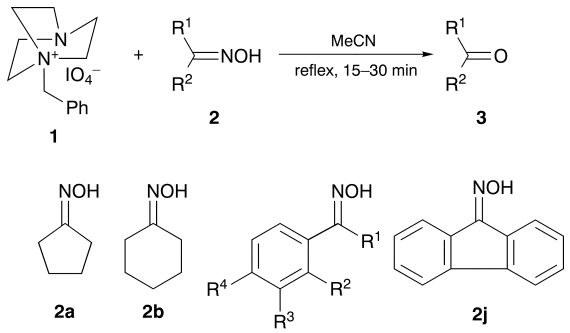
1-Benzyl-4-aza-1-azoniabicyclo[2.2.2]octane periodate (BAABCP) (**1**), readily prepared from commercially available 1,4-diazabicyclo[2.2.2]octane (DABCO) and sodium periodate, converts oximes and α-sulfinyl oximes to the corresponding carbonyl compounds and β-keto sulfoxides, respectively, in high yields and high enantiomeric purity.

The conversion of carbonyl derivatives such as oximes and α-sulfinyl oximes to the corresponding carbonyl compounds is a useful transformation and is important synthetically.

The classical method for the conversion of these compounds to the corresponding carbonyl compounds is hydrolysis under acidic conditions. This method, however, is not suitable for acid sensitive and asymmetric compounds.[1] Several new methods have been developed that have advantages over the classical method.[2–5]

As part of an ongoing asymmetric synthetic project we required an efficient and rapid method for the conversion of oximes and α-sulfinyl oximes to the corresponding carbonyl compounds. We found that the reaction of BAABCP (**1**) in acetonitrile under reflux gave the corresponding carbonyl compounds. The reagent was tested on a wide array of oximes (Scheme 1).



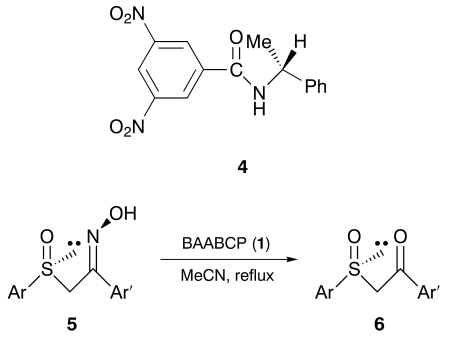
	R^1	R^2	R^3	R^4
2c	H	H	H	H
b	H	OMe	H	H
e	H	H	OMe	OMe
f	Me	H	H	H
g	Ph	H	H	H
h	$PhCH_2$	H	H	H
i	H	H	NO_2	H
k	H	H	H	Cl
l	H	H	H	Ph

Scheme 1 Oxidation of oximes **2** to the corresponding carbonyl compound **3**

The results (Table 1) show that the oximes **2** on treatment with **1** in acetonitrile under reflux gave the corresponding aldehydes and ketones **3** and no further oxidation to the carboxylic acid was observed.

β-Keto sulfoxides are very important starting materials in asymmetric synthesis,[6,7] and can be synthesised by the cleavage of the C=N bond of α-sulfinyl oximes, which are readily prepared *via* the addition of aryl methyl sulfoxides to aryl *N*-oxides.[8] The hydrolysis of the C=N bond of α-sulfinyl oximes by the Annunzian method[10] was attempted but the optical purity and yield by this method were low (ee < 35 and yield < 50%).

We found that the cleavage of the C=N bond of α-sulfinyl oximes[8] by **1** in acetonitrile under reflux is rapid (20–30 min) and almost quantitative with high optical purity as shown by ^{1}H NMR analysis in the presence of a chemical shift reagent (> 95%) (Table 2).[6] The general reaction is shown in Scheme 2 and Table 2. In all cases, the crude product was judged to be of > 95% purity based on ^{1}H NMR and TLC analysis. As shown in Table 1, the corresponding sulfones are not formed in this reaction. The enantiomeric purity of **6** was determined to be > 95% from ^{1}H NMR chiral shift studies using (−)-(*R*)-*N*-(3,5-dinitrobenzoyl)-α-phenylethylamine **4** as a chiral shift reagent[6] and comparing the optical rotation of the products with known compounds.[6,11] To determine the enantiomeric purity of **6** it was mixed with 1 equiv. of the chiral reagent **4** in an NMR tube.



a Ar = phenyl, Ar′ = phenyl
b Ar = phenyl, Ar′ = 3,4-diethoxyphenyl
c Ar = *p*-tolyl, Ar′ = phenyl
d Ar = *p*-tolyl, Ar′ = 3,4-dimethoxyphenyl
e Ar = 2-methoxy-1-naphthyl, Ar′ = phenyl
f Ar = 2-methoxy-1-naphthyl, Ar′ = 3,4-diethoxyphenyl

Scheme 2

In conclusion, we have found 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 the optical purity and yield of these reactions are high.

Experimental

General Method. Preparation of **1**.—The reagent **1** was prepared in two steps. *Step 1*. To a solution of DABCO (0.1 mol, 11.22 g) in acetone (200 ml) was added benzyl bromide (0.1 mol, 17.1 g) dropwise. A white solid of 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]-octane bromide was precipitated, the crystals were collected, washed

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Table 1 Conversion of **2** to the corresponding carbonyl compound **3**

Starting material	Product	Reaction time/min	Yield (%)[a]	Mp/°C or bp/°C/torr (lit.[9])
2a	**3a**	15	95	127–130/760 (127–130)
2b	**3b**	15	95	154–156/760 (154–156)
2c	**3c**	15	98	179/760 (178)
2d	**3d**	20	97	240/760 (238)
2e	**3e**	15	99	41–44 (41–44)
2f	**3f**	15	100	203/760 (203)
2g	**3g**	15	100	50–52 (49–51)
2h	**3h**	15	97	55–57 (55–57)
2i	**3i**	30	95	58–60 (57–59)
2j	**3j**	15	98	80–83 (80–83)
2k	**3k**	20	95	234/760 (232)
2l	**3l**	15	98	117–118 (117–119)

[a]Isolated yields.

Table 2 Oxidation of **5** to **6**

Starting material	Product	Reaction time/min	Yield (%)[a]	ee (%)
5a	**6a**	15	98	95
5b	**6b**	20	95	96
5c	**6c**	20	96	96
5d	**6d**	25	99	98
5e	**6e**	30	95	98
5f	**6f**	30	95	100

[a]Isolated yields.

with acetone (20 ml) and then dried under high vacuum (0.01 mm Hg). Yield 25.5 g (90%). *Step 2*. To a solution of 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide (0.05 mol, 14.15 g) was added a solution of $NaIO_4$ (0.05 mol, 10.70 g) in H_2O (20 ml) dropwise. An orange solid of **1** was precipitated and 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 19.90 g (80%) ($C_{13}H_{19}IN_2O_4$ requires: C, 39.61; H, 4.86; N, 7.11%. Found: C, 39.59; H, 4.93; N, 7.6%).

Oxidation of **2** *to* **3**.—The oxime **2** (1 mmol) was added to a stirred solution of oxidant **1** (1 mmol, 0.394 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. The reaction mixture and was stirred for 5 min, the solid was then separated by filtration through Celite and washed with acetonitrile (2 × 10 ml). Evaporation of the solvent gave the carbonyl compound **3** which was >95% pure (TLC, ^{1}H NMR). The product could be further purified by short-path distillation or column chromatography on silica gel using mixture of ethyl acetate as eluent.

Preparation of β-Keto Sulfoxides **6**.—The α-sulfinyl oxime **5**[8] (1 mmol) was added to a stirred solution of oxidant **1** (1 mmol, 0.394 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 which was stirred for 5 min and the resulting solid separated by filtration through Celite and washed with acetonitrile (2 × 10 ml). Evaporation of the solvent gave the β-keto sulfoxides **6** which were >95% pure (TLC, ^{1}H NMR). The product could be further purified by column chromatography on silica gel using mixture of ethyl acetate as eluent.

(+)-(*R*)-2-(*Phenylsulfinyl*)*acetophenone* (**6a**).—Mp 70–71 °C (lit.,[12] 70.5–71.5 °C); δ_H 7.1–7.9 (m, 10 H), 4.48 and 4.28 (AB q, *J* 13.8 Hz, 2 H); *m*/*z*, 244.30 (80%, M^+), 105 (100) ($C_{14}H_{12}O_2S$ requires: C, 68.83; H, 4.95%. Found: C, 68.77; H, 5.02%) $[\alpha]_D^{28}$ + 161.65 (*c* 1.2, $CHCl_3$).

(+)-(*R*)-3′,4-*Dimethoxy*-2-(*phenylsulfinyl*)*acetophenone* (**6b**).—Mp 88–89 °C; δ_H 7.1–7.9 (m, 8 H), 4.48 and 4.28 (AB q, *J* 13.6 Hz, 2 H), 3.92 (s, 6 H, 2 × OMe); *m*/*z* 304.36 (65%, M^+), 165 (100) ($C_{16}H_{16}O_4S$ requires: C, 63.14; H, 5.30%. Found: C, 63.06; H, 5.46%) $[\alpha]_D^{28}$ + 146.65 (*c* 1.2, $CHCl_3$).

(+)-(*R*)-2-(p-*Tolylsulfinyl*)*acetophenone* (**6c**).—Mp 84–85 °C (lit.,[13] 82–83.5 °C); 7.0–7.9 (m, 9 H), 4.52 and 4.28 (AB q, *J* 14 Hz, 2 H), 2.35 (s, 1 H); $[\alpha]_D^{28}$ + 180.20 (*c* 1.2, $CHCl_3$) [lit.,[13] $[\alpha]_D^{26}$ + 227.70 (*c* 1.00, acetone)].

(+)-(*R*)-3′,4′-*Dimethoxy*-2-(p-*tolylsulfinyl*)*acetophenone* (**6d**).—Mp 96–98 °C; δ_H 7.1–7.9 (m, 7 H), 4.95 and 4.39 (AB q, *J* 13.6 Hz, 2 H), 3.88 (s, 6 H, 2 × OMe), 242 (s, 3 H); *m*/*z* 318.39 (70%, M^+), 165 (100) ($C_{17}H_{18}O_4S$ requires: C, 64.13; H, 5.50%. Found: C, 68.08; H, 5.73%) $[\alpha]_D^{28}$ + 202.20 (*c* 1.2, acetone).

(+)-(*R*-2-(2-*Methoxy*-1-*naphthylsulfinyl*)*acetophenone* (**6e**).—Mp 89–90 °C; δ_H 8.92 (d, 1 H), 7.1–7.9 (m, 10 H), 5.05 and 4.82 (AB q, *J* 13.2 Hz, 2 H), 3.90 (s, 3 H, OMe); *m*/*z* 325.5 (80%, M^+), 226.3 (25), 141 (100) ($C_{19}H_{16}O_3S$ requires: C, 70.35; H, 4.97%. Found: C, 70.41; H, 4.88%) $[\alpha]_D^{28}$ + 97.5 (*c* 1.2, CH_2Cl_2).

(+)-(*R*)-3′,4′-*Dimethoxy*-2-(2-*Methoxy*-1-*naphthylsulfinyl*)*acetophenone* (**6f**).—Mp 119–121 °C; δ_H 8.95 (d, 1 H), 6.8–8 (m, 7 H), 5.02 and 4.85 (AB q, *J* 13.2 Hz, 2 H), 4.00 (s, 3 H, OMe), 3.95 (s, 3 H, OMe), 3.80 (s, 3 H, OMe); *m*/*z* 385.1 (50%, M^+), 288.3 (25), 205 (100). ($C_{21}H_{20}O_5S$ requires: C, 65.61; H, 5.24%. Found: C, 65.70; H, 5.38%) $[\alpha]_D^{28}$ + 90.8, (*c* 1.3, CH_2Cl_2).

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