© 1998 The Chemical Society of Japan

Bis(1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane) Peroxodisulfate: A Mild and Efficient Oxidant for Cleavage of Nitrogen Double Bonds and Oxidation of Alcohols under Anhydrous Conditions

Abdol Reza Hajipour,* Iraj Mohammadpoor -Baltork,† and Godaraz Kianfar

College of Chemistry, Isfahan University of Technology, Isfahan, Iran

†Department of Chemistry, Isfahan University, Isfahan 81744, Iran

(Received March 27, 1998)

Bis(1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane) peroxodisulfate (**1**), is readily prepared as an orange solid from commercially available 1,4-diazabicyclo[2.2.2]octane and potassium peroxodisulfate. This reagent easily converts hydrazones, semicarbazones, oximes, and alcohols to the corresponding carbonyl compounds with excellent yields.

Oxidation of organic compounds in an organic solvent under mild conditions is very important in modern organic synthesis. Over the years several new oxidizing reagents have been prepared.[1—29] Unfortunately, most of these reagents suffer from at least one of the following disadvantages: 1) cost of preparation, 2) hygroscopicity, 3) photosensitivity, 4) instability, 5) long reaction time, 6) high acidity, 7) no selectivity, 8) dangerous procedure needed for their preparation, and 9) tedious work-up procedure.

Highly crystalline hydrazone and oxime derivatives constitute a very efficient method for the isolation, purification, and characterization of aldehydes and ketones. Thus the regeneration of the aldehydes and ketones from such derivatives constitutes an important synthetic process. The classical method for the conversion of hydrazones to the corresponding carbonyl compounds involves hydrolysis under acidic conditions and is not suitable for acid-sensitive and asymmetric compounds.[30] Several other reagents[31—36] have been developed, to supplement acid hydrolysis.

As part of an ongoing project, we required an efficient and rapid method for the conversion of compounds such as hydrazones, semicarbazones, and oximes to the corresponding carbonyl compounds. We wish to report the synthesis of bis(1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane) peroxodisulfate (BAABCPS) (**1**) and its reaction with derivatives of carbonyl compounds and alcohols. We have found that the reaction of **1** with carbonyl compounds derivatives in refluxing acetonitrile gave the corresponding carbonyl compounds. The reagent was examined on a wide variety of carbonyl compound derivatives such as oximes **2**, hydrazones, and semicarbazones **4** (Schemes 1 and 2).

Our results show that oximes, hydrazone, and semicarbazones are converted to the corresponding aldehydes and ketones in excellent yields; no further oxidations to their carboxylic acids were observed (Tables 1 and 2).

We have also found that the reagent is able to oxidize the alcohols to the corresponding carbonyl compounds, and α-hydroxy ketones to diketones (Scheme 3).

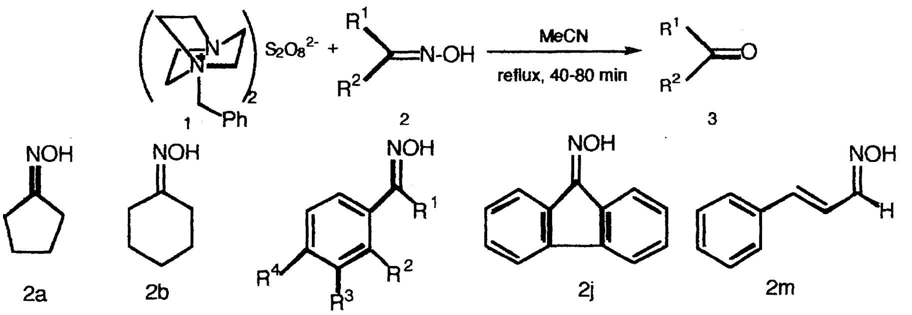
The alcohols and α-hydroxy ketones (**6**) were oxidized with the reagent **1** to the corresponding carbonyl compounds in high yields (Table 3). The oxidation of compounds with unsaturated double bonds was also investigated. It was found that the reagent selectively oxidized the alcohols and was ineffective in oxidizing double bonds (Table 3).

Another noteworthy advantage of the reagent lies in the exclusive formation of the carbonyl compounds irrespective of the presence of other oxidizable functions (alcohol and double bond). When we treated one equimolar amount of oxime in the presence of very reactive benzyl alcohol only the oxime was selectively oxidized (Scheme 4). When we treated α,β-unsaturated alcohols or α,β-unsaturated oximes, only the hydroxyl groups or C=NOH groups was selectively oxidized to the corresponding carbonyl compounds and the reagent was ineffective in oxidizing double bonds (Table 1, oxime 3m and Table 3, alcohols 6r—6u). In order to evaluate the greater chemoselectivity of the reagent, we treated one equimolar amount of oxime in the presence of thiol; only the thiol was selectively oxidized. In the reaction of alcohol in the presence of thiol with the reagent, only the thiol was selectively oxidized. We have also found that the reaction of alcohol in the presence of sulfide with the reagent, only the alcohol was selectively oxidized (Scheme 4).

In conclusion, we report here an efficient, rapid, and inexpensive method for the conversion of oximes, hydrazones, semicarbazones, and alcohols to the corresponding carbonyl compounds which is superior to previously reported methods in terms of selectivity, high yields, purity of products and simple and rapid work-up.

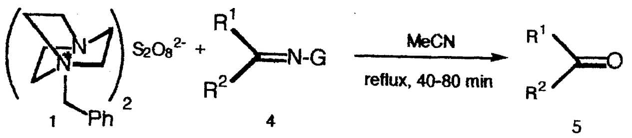
Experimental

All yields refer to isolated products. Products were characterised by comparison with authentic samples (IR and NMR spectrum, thin



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

Scheme 1.



Comound	R^1	R^2	G
4a	Ph	Ph	PhNH
4b	Ph	Me	PhNH
4c	3,4-$(MeO)_2C_6H_3$	Me	PhNH
4d	*p*-PhC_6H_4	Me	PhNH
4e	2-Pyridyl	Ph	PhNH
4f	4-Pyridyl	Me	PhNH
4g	*p*-$MeOC_6H_4$	Me	PhNH
4h	*o*-$MeOC_6H_4$	Me	PhNH
4i	Ph	Ph	*p*-$NO_2C_6H_4$
4j	*p*-$MeOC_6H_4$	H	*p*-$NO_2C_6H_4$
4k	*p*-ClC_6H_4	Me	*p*-$NO_2C_6H_4$
4l	*p*-PhC_6H_4	Me	*p*-$NO_2C_6H_4$
4m	Ph	Ph	Me_2N
4n	Ph	Me	Me_2N
4o	$(MeO)_2C_6H_3$	Me	Me_2N
4p	*p*-$MeOC_6H_4$	Me	Me_2N
4q	Ph	H	NH_2CONH
4r	Ph	Me	NH_2CONH
4s	*p*-$MeOC_6H_4$	Me	NH_2CONH
4t	3,4-$(MeO)_2C_6H_3$	Me	NH_2CONH

Scheme 2.

Table 1. Converting of **2** to Carbonyl Compound **3**

Starting material	Product[a]	Reaction time/min	Yield[b] %	Mp/°C or bp/°C/Torr[c] (lit,[26,29,37])
2a	**3a**	15	95	127—130/760 (127—130)
2b	**3b**	15	95	154—156/760 (154—156)
2c	**3c**	15	98	177/760 (179)
2d	**3d**	20	97	240/760 (240)
2e	**3e**	15	99	42—44 (41—44)
2f	**3f**	15	100	204/760 (203)
2g	**3g**	15	100	49—52 (50—52)
2h	**3h**	15	97	55—57 (55—57)
2i	**3i**	30	95	58—60 (58—60)
2j	**3j**	15	98	80—83 (80—83)
2k	**3k**	20	95	232/760 (234)
2l	**3l**	15	98	117—119 (117—118)
2m	**3m**	25	94	126/760 (125—128)

a) were confirmed by comparison with authentic sample (IR and NMR). b) yield of isolated pure carbonyl compound. c) 1 Torr = 133.322 Pa.

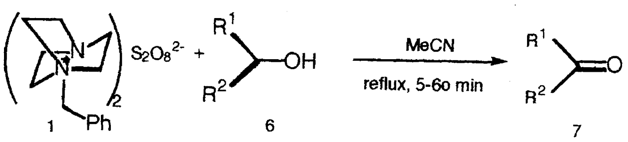
layer chromatography, melting and boiling point).[26,29,37] All reactions proceeded in acetonitrile; all ^{1}H NMR spectra were recorded at 90 MHz in $CDCl_3$ and CCl_4 relative to TMS (0.00 ppm). Elemental analysis was performed by Research Institute of Petroleum Industry, Tehran, I.R. Iran.

General Method. Preparation of BAABCPS (1): The reagent was prepared in two steps: In step one, to a solution of 1, 4-diazabicyclo[2.2.2]octane (DABCO) (0.1 mol, 11.22 g) in acetone (200 ml) was added to benzyl bromide (0.1 mol, 17.1 g) dropwise. 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 mmHg), yield 25.5 g (90%), ^{1}H NMR (D_2O) δ = 7.60 (s, 5H), 4.60 (s, 2H), 3.80 (s, 4H), 3.20 (s, 8H). In step two, to a solution of 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide (0.1 mol, 28.30 g) was added a solution of $K_2S_2O_8$ (0.05 mol, 13.52 g) in H_2O (60 ml) dropwise. 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 mmHg), yield 35.5 g (85%), ^{1}H NMR (DMSO-d_6) δ = 7.60 (s, 5H), 4.80 (s, 2H), 3.90 (s, 4H), 3.30 (s, 8H). The oxidant was titrated three times following this representative procedure: to 2.5 ml of 0.01 M BAABCPS (1 M = 1 mol dm^{-3}) solution in a 20 ml conical flask were added 0.7 ml of 5 M sodium bromide solution and 0.2 ml of 3 M sulfuric acid. Stopper the flask. Swirl the content. Then add excess 0.05 M ammonium iron(II)

Table 2. Converting of **4** to Carbonyl Compounds **5**

Starting material	Product[a)]	Reaction time/min	Yield[b)] %	Mp/°C or bp/°C/Torr (lit,[29,37)])
4a	**5a**	60	90	48 (47—49)
4b	**5b**	45	90	82—85/760 (83—85)
4c	**5c**	80	85	48 (47—50)
4d	**5d**	50	98	118 (117—119)
4e	**5e**	60	96	42 (41—43)
4f	**5f**	45	96	78/760 (76—79)
4g	**5g**	45	96	38 (37—39)
4h	**5h**	45	91	244—249/760 (245—248)
4i	**5i**	80	65	49 (47—49)
4j	**5j**	80	55	120/760 (118—121)
4k	**5k**	80	50	232/760 (232)
4l	**5l**	80	65	118—120 (117—119)
4m	**5m**	40	91	48 (47—49)
4n	**5n**	60	95	84/760 (83—85)
4o	**5o**	45	100	48—49 (47—50)
4p	**5p**	55	98	37—39 (37—39)
4q	**5q**	80	70	178—190/760 (117—179)
4r	**5r**	80	60	84—85 (83—85)
4s	**5s**	80	75	38 (37—39)
4t	**5t**	80	59	47—49 (47—50)

a) were confirmed by comparison with authentic sample (IR and NMR). b) yield of isolated pure carbonyl compound.



1 6 7

Scheme 3.

sulfate (1.5 ml), and allow to stand for 30 min. Add 0.1 ml of 0.001 M ferroin indicator, and titrate the excess of Fe^{2+} ion with 0.02 M cerium(V) sulfate in 0.5 M sulfuric acid to the first color change from orange to yellow. The average of the three trials gave 32.02±0.6% by weight of the active oxidizing agent (BAABCPS). Found: C, 52.20; H, 6.40; N, 9.20; S, 10.60%. Calcd for $C_{26}H_{38}N_4S_2O_8$: C, 52.16; H, 6.40; N, 9.36; S, 10.71%.

Oxidation of 2 to 3: The oxime **2** (2 mmol) was added to a stirred solution of oxidant **1** (2 mmol, 1.2 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 (Table 1). The mixture was cooled and 3 g of silica gel was added to the reaction mixture. It 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 carbonyl compound **3**. The product was purified by short-path distillation or column chromatography on silica gel using a mixture of ethyl acetate and hexane as eluent (90 : 10).

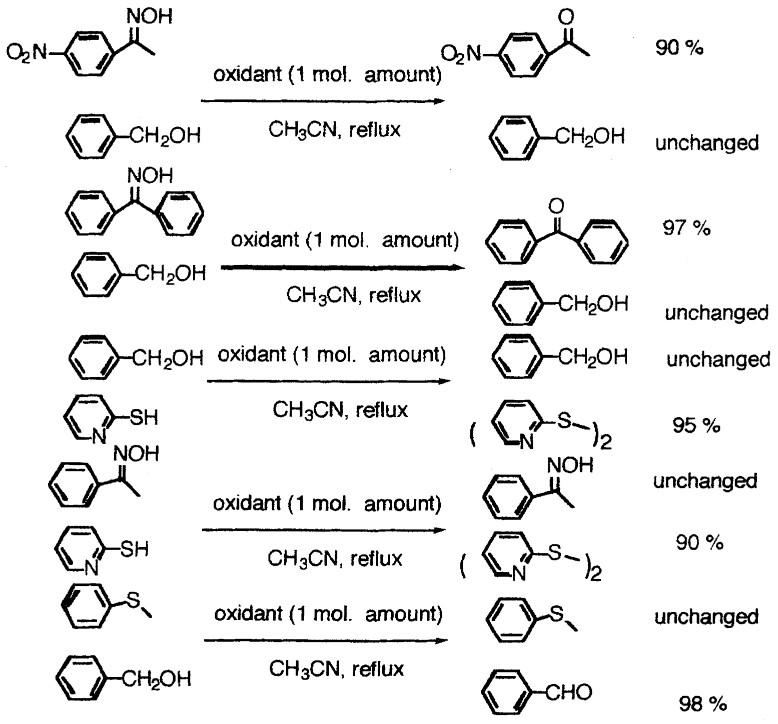
Oxidation of 4 to 5: The compound **4** (2 mmol) was added to a stirred solution of oxidant **1** (2 mmol, 1.2 g) in acetonitrile (15 ml). The mixture was heated at reflux until TLC showed complete disappearance of starting material, which required 40—80 min depending on the substrate (Table 2). The mixture was cooled and 3 g of silica gel was added to the reaction mixture. It 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 carbonyl compound **5**. The product could be further purified by column chromatography on silica gel using a mixture of ethyl acetate and hexane as eluent (90 : 10).

Oxidation of 6 to 7: The alcohol **6** (2 mmol) was added to a stirred solution of oxidant **1** (2 mmol, 1.2 g) in acetonitrile (15 ml). The mixture was heated at reflux until TLC showed complete

Table 3. Oxidation of Alcohols **6** to Carbonyl Compounds **7**[a)]

Alcohols	R^1	R^2	Reaction time/min	Yield[b)] %	Mp/°C or bp/°C/Torr (lit,[29,37)])
6a	Ph	H	10	98	179/760 (178)
6b	$4\text{-}NO_2C_6H_4$	H	20	95	104 (104—105)
6c	$3,4\text{-}(MeO)_2C_6H_3$	H	30	98	82 (81—83)
6d	$4\text{-}PhC_6H_4$	Me	15	97	117—119 (117—119)
6e	2-Pyridyl	Ph	10	96	84/760 (83—85)
6f	Ph	Me	15	96	119/760 (118—121)
6g	$4\text{-}MeOC_6H_4$	H	5	97	35—37 (35—37)
6h	$2\text{-}MeOC_6H_4$	H	30	97	47 (47—49)
6i	Ph	Ph	60	95	102/760 (100—103)
6j	$3\text{-}MeOC_6H_4$	H	10	99	45 (45—47)
6k	$4\text{-}ClC_6H_4$	H	20	94	196/760 (195—198)
6l	$2\text{-}ClC_6H_4$	H	10	96	212/760 (212—214)
6m	Ph	$PhCH_2$	25	98	54 (54—55)
6n	$4\text{-}BrC_6H_4$	Me	30	95	49—50 (49—51)
6o	$4\text{-}ClC_6H_4$	Me	15	100	232/760 (232—234)
6p	Ph	PhCO	25	96	95 (94—96)
6q	$2,3\text{-}(MeO)_2C_6H_3$	H	30	95	49—52 (49—53)
6r	PhCH=CH	Ph	20	95	54—57 (54—57)
6s	PhCH=CH	Me	60	95	39 (39—40)
6t	$4\text{-}NO_2C_6H_4CH{=}CH$	H	40	90	138—142 (139—142)
6u	PhCH=CH	H	60	99	127/760 (125—128)

a) were confirmed by comparison with authentic sample (IR and NMR). b) yield of isolated pure carbonyl compound.



Scheme 4.

disappearance of starting material, which required 10—60 min depending on the substrate (Table 3). The mixture was cooled and 3 g of silica gel was added to the reaction mixture. It 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 carbonyl compound **7**. The crude product was purified by column chromatography on silica gel using a mixture of ethyl acetate and hexane as eluent (90 : 10).

Partial support of this work by the Isfahan University of Technology Research Council is gratefully acknowledged.

References

1) L. F. Fieser and M. Fieser, "Reagent for Organic Synthesis," Wiley, New York (1967), Vol. 1.

2) H. Firouzabadi, A. R. Sardarian, M. Naderi, and B. Vesal, *Tetrahedron*, **23**, 5001 (1984).

3) H. Firuozabadi and I. M. Baltork, *Bull. Chem. Soc. Jpn.*, **65**, 1185 (1992).

4) H. Firuozabadi and Z. Mostafavipoor, *Bull. Chem. Soc. Jpn.*, **56**, 914 (1983).

5) H. Firouzabadi and A. R. Sardarian, *Synth. Commun.*, **13**, 863 (1983).

6) A. Clericl and O. Pona, *J. Chem. Soc.*, *Perkin Trans. 2*, **1988**, 1234.

7) W. E. Fristad and J. R. Peterson, *Tetrahedron Lett.*, **1983**, 4547.

8) P. T. Perumal, *Synth. Commun.*, **20**, 1353 (1990).

9) T. Itahara, Y. Fujii, and M. Tada, *J. Org. Chem.*, **53**, 3421 (1988).

10) T. Itahara, R. Ebihara, Y. Fujii, and M. Tada, *Chem. Lett.*, **1986**, 1319.

11) S. Yamasaki and Y. Yamasaki, *Bull. Chem. Soc. Jpn.*, **63**, 301 (1990).

12) S. Yamasaki, *Chem. Lett.*, **1992**, 823.

13) S. Yamasaki and Y. Yamasaki, *Chem. Lett.*, **1990**, 571.

14) J. C. Jung, H. C. Choi, and Y. H. Kim, *Tetrahedron Lett.*, **1993**, 3581.

15) H. C. Choi and Y. H. Kim, *Synth. Commun.*, **24**, 2307 (1994).

16) F. Chen, J. Yang, H. Zhang, C. Guan, and J. Wan, *Synth. Commun.*, **25**, 3163 (1995).

17) H. C. Choi, K. Cho, and Y. H. Kim, *Synlett*, **1995**, 207.

18) F. Chen, J. Wan, C. Guan, J. Yang, and H. Zhang, *Synth. Commun.*, **26**, 253 (1996).

19) I. Mohammadpoor-Baltork and Sh. Pouranshivani, *Synth. Commun.*, **26**, 1 (1996).

20) I. Mohammadpoor-Baltork and Sh. Pouranshivani, *Synthesis*, **1997**, 756.

21) I. Mohammadpoor-Baltork, M. M. Sadeghi, N. Mahmoodi, and B. Kharamesh, *Indian J. Chem.*, *Sect. B*, **36B**, 438 (1997).

22) R. S. Varma and H. M. Meshram, *Tetrahedron Lett.*, **38**, 7973 (1997).

23) R. S. Varma, R. K. Saini, and R. Dahia, *Tetrahedron Lett.*, **38**, 7823 (1997).

24) R. S. Varma, R. Dahia, and R. K. Saini, *Tetrahedron Lett.*, **38**, 7029 (1997).

25) R. S. Varma, R. K. Saini, and H. M. Meshram, *Tetrahedron Lett.*, **38**, 6525 (1997).

26) A. R. Hajipour and N. Mahboubghah, *J. Chem. Res. (S)*, **1998**, 123.

27) A. R. Hajipour, *Indian J. Chem.*, *Sect. B*, **36B**, 1069 (1997).

28) A. R. Hajipour and N. Mahboubghah, *Indian J. Chem.*, *Sect. B*, **36B**, 285 (1998).

29) H. Firouzabadi, A. R. Sardarian, and H. Badparva, *Bull. Chem. Soc. Jpn.*, **69**, 685 (1996).

30) E. B. Hersberg, *J. Org. Chem.*, **12**, 541 (1948).

31) J. R. Maloney and R. E. Lyle, *Synthesis*, **1978**, 212.

32) L. Singh and R. N. Ram, *Synth. Commun.*, **23**, 3139 (1962).

33) J. Drabowicz, *Synthesis*, **1980**, 125.

34) C. G. Rao, A. S. Radhakrishna, B. B. Singh, and S. P.

Bhatnagar, *Synthesis*, **1983**, 808.
35) S. Satish and N. Kalyanam, *Chem. Ind.* (*London*), **1981**, 809.
36) S. H. Pines, J. M. Chemerda, and M. A. Kozlowski, *J. Org. Chem.*, **31**, 3446 (1966).
37) Aldrich Catalog, "Handbook of Fine Chemicals," 1990-91.