Selective Method for the Conversion of Oximes to their Corresponding Carbonyl Compounds under Microwave Irradiation by N-Bromo-N-phenyl-para-toluenesulfonamide

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In this work, oximes are converted to their corresponding carbonyl compounds in good yields using N-bromo-N-phenyl-para-toluenesulfonamide, under microwave irradiation. The simple work-up procedure minimizes loss of product.

Keywords: Carbonyl compounds; Oximes; N-Bromo-N-phenyl-para-toluenesulfonamide; Selective.

INTRODUCTION

In recent years, oxime compounds have been used as intermediates for a number of synthetic products, and have also been proved to be important and useful reagents in organic syntheses.[1-3] These compounds are also useful protecting groups in organic syntheses[4] and have found extensive application in the isolation of carbonyl compounds.[5-6] Several methods based on reductive, hydrolytic, and oxidative reactions have been developed for the cleavage of oximes.[7-9] Owing to the considerable importance of such compounds there is still scope for newer methods as the existing oxidative methods suffer from disadvantages such as long reaction time,[10] formation of over oxidation products and difficulties in isolation of products.[11] Also many deoximating reagents are relatively expensive and difficult to prepare. We have previously reported convenient methods for the deoximation of oximes to their corresponding carbonyl compounds.[12] We now describe a new method for the selective cleavage of oximes to their carbonyl compounds under microwave irradiation with the use of N-bromo-N-phenyl-para-toluenesulfonamide as an effective oxidizing agent that overcomes the disadvantages associated with oxidative methods developed so far. Microwave-promoted reactions occur with dramatic decreases in reaction times[13-14] and in some cases cleaner reactions with easier work-ups than observed when using conventional heating. Microwave reactions involve selective absorption of MW energy by polar molecules, non-polar molecules being inert to MW dielectric loss.[15-16]

In microwave dielectric heating, the microwave energy is introduced into the chemical reactor remotely and direct access by the energy source to the reaction vessel is obtained. The microwave radiation passes through the walls of the vessel and heats only the reactants and solvent, not the reaction vessel itself. If the apparatus is properly designed, the temperature increase will be uniform throughout the sample, which can lead to less by-products and/or decomposition products. In order to understand why this phenomenon occurs, it is necessary to comprehend the underlying mechanisms of microwave dielectric heating. As with all electromagnetic radiation, microwave radiation can be divided into an electric field component and a magnetic field component. The former component is responsible for the dielectric heating, which is effected via the following mechanism.

One of the interactions of the electric field component with the matrix is called the dipolar polarization mechanism. For a substance to generate heat when irradiated with microwaves it must possess a dipole moment, as has a water molecule. A dipole is sensitive to external electric fields and will attempt to align itself with the field by rotation. The applied field provides the energy for this rotation. Under low frequency irradiation, the molecule will rotate in phase with the oscillating electric field. The molecule gains some energy by this behaviour, but the overall heating ef-

fect by this full alignment is small. Alternatively, under the influence of a high frequency electric field the dipoles do not have sufficient time to respond to the oscillating field and do not rotate. Since no motion is induced in the molecules, no energy transfer takes place and therefore no heating occurs. If the applied field is in the microwave radiation region, however, a phenomenon occurs between these two extremes. In the microwave radiation region, the frequency of the applied irradiation is low enough so that the dipoles have time to respond to the alternating electric field and therefore rotate. The frequency is, however, not high enough for the rotation to precisely follow the field. Therefore, as the dipole re-orientates to align itself with the electric field, the field is already changing and generates a phase difference between the orientation of the field and that of the dipole. This phase difference causes energy to be lost from the dipole by molecular friction and collisions, giving rise to dielectric heating.[17]

RESULTS AND DISCUSSION

In continuation of our studies on application of N-halo compounds in organic chemistry,[18] we now found a novel and efficient protocol for the deoximation of a variety of oximes using N-bromo-N-phenyl-para-toluenesulfonamide under microwave irradiation conditions. This reagent was prepared from N-phenyl-para-toluenesulfonamide (Scheme I).

The reagent **2** has low toxicity, low cost and is easily prepared. The best results are achieved using aqueous acetone as the solvent; also the use of an inert atmosphere is not required for this reaction (Scheme II).

Deoximation of different types of oximes (acyclic, cyclic, and benzylic) and sterically hindered oximes were investigated. The results are summarized in Table 1. The aldoximes were converted to the corresponding aldehydes and no carboxylic acid was formed due to overoxidation of the regenerated aldehyde (entries 3, 6).

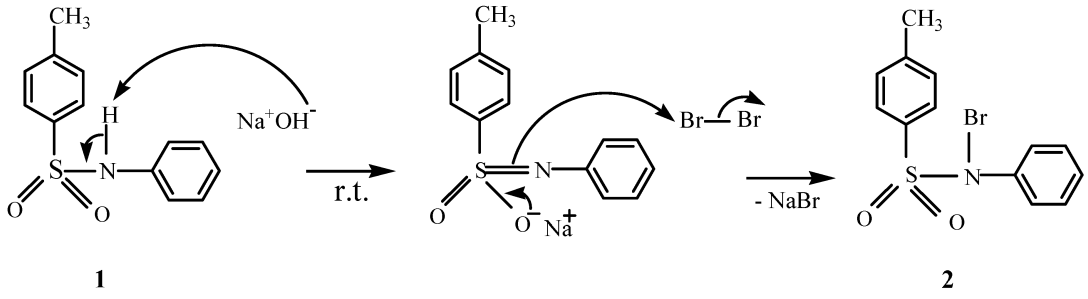
Interestingly, camphor oxime was also converted to the corresponding carbonyl compound as a model for deoximation of the sterically hindered ketone oxime (entry 10). In addition, benzoin oxime (entry 1) was cleaved to the corresponding carbonyl compounds smoothly without affecting the other functionality. Therefore this method is useful for the chemoselective oxidative deoximation of oximes in the presence of alcohols or for oximes that contain an OH functional group. Thus we also used this procedure for the selective deoximation of acetophenone oxime in the presence of an equimolar amount of benzyl alcohol. The only observed product was acetophenone in 94% conversion. We observed the competitive oxidation of oximes in the presence of alkenes. For this purpose, equimolar mixtures of cyclohexanone oxime and cyclohexene in acetone and water were allowed to react with N-bromo-N-phenyl-para-toluenesulfonamide under microwave irradiation. The deoximation of cyclohexanone oxime took place (96% conversion), whereas the cyclohexene was recovered unchanged.

This reagent **2** is stable for a couple of months at 25 °C and can be stored in the refrigerator almost permanently. One of the advantages of this method is that, after the reaction was completed, N-bromo-N-phenyl-para-toluenesulfonamide **2** converted to the N-phenyl-para-toluenesulfonamide **1**, which can be recovered, brominated and reused many times.

CONCLUSION

In conclusion, in this study, we have demonstrated the efficiency of N-bromo-N-phenyl-para-toluenesulfonamide

Scheme I



1 **2**

Scheme II

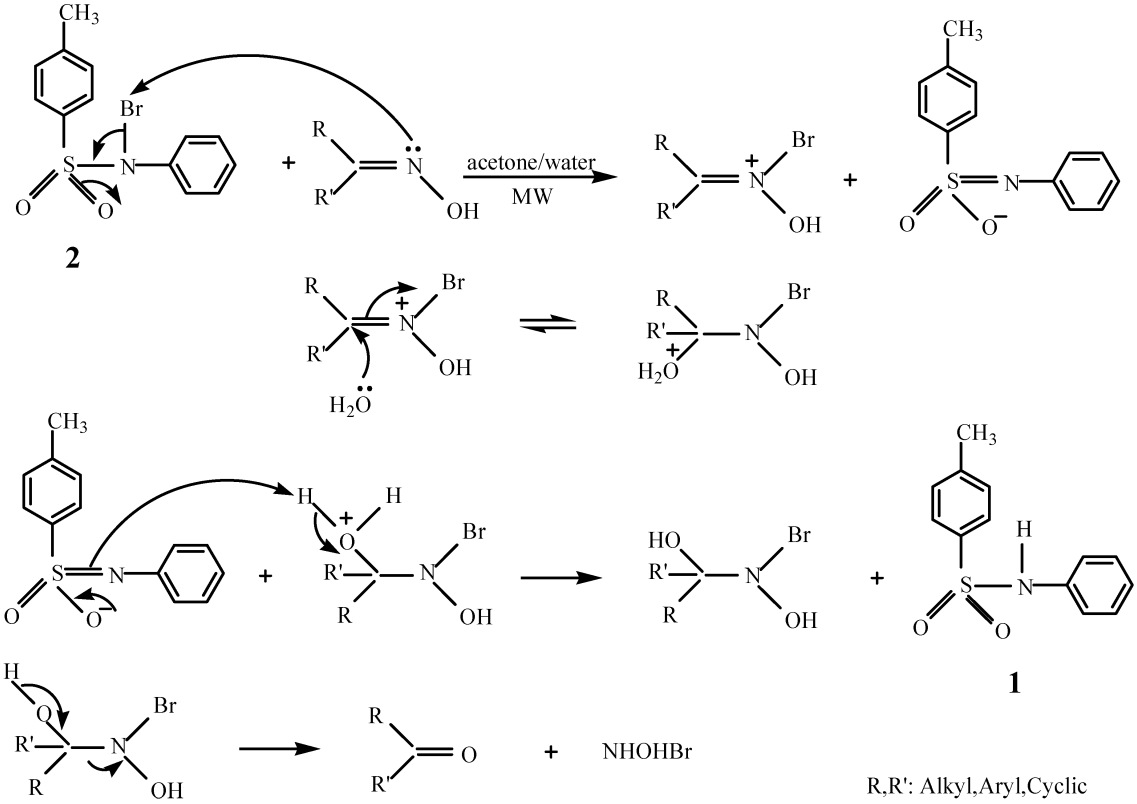


Table 1. Deoximation with N-bromo-N-phenyl-para-toluenesulfonamide under microwave irradiation

Entry	Substrate	Carbonyl compound	Time (min)	Yield (%)[a,b]
1	benzoin oxime	benzoin	1.6	90
2	4-methyl acetophenone oxime	4-methyl acetophenone	1	95
3	benzaldehyde oxime	benzaldehyde	1	94
4	acetophenone oxime	acetophenone	1	94
5	cyclohexanone oxime	cyclohexanone	1	96
6	cinnamaldehyde oxime	cinnamaldehyde	1.5	93
7	diisopropyl ketone oxime	diisopropyl ketone	1.4	92
8	isobutyl methyl ketone oxime	isobutyl methyl ketone	1.3	93
9	cyclopentanone oxime	cyclopentanone	2	90
10	camphor oxime	camphor	2.1	89
11	ethyl methyl ketone oxime	ethyl methyl ketone	2	90

[a] Products were characterized by their physical constants, comparision with authentic samples and by their IR and ^{1}H NMR spectra.
[b] Isolated yields.

towards the cleavage of oximes to their corresponding carbonyl compounds. The notable special features of this methodology are: selectivity, excellent yields of products, low cost reagent, easy preparation, easy work up, very short reaction times and no formation of over oxidation products due to the chemoselectivity and mild nature of re-

agent **2**.

EXPERIMENTAL

IR and ^{1}H NMR spectra were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and a 90 MHz Jeol FT-NMR spectrometer, respectively. ^{1}H NMR chemical shifts were measured relative to TMS (int; 1H).

Synthesis of N-phenyl-para-toluenesulfonamide

In a beaker (10.0 g, 53 mmol) of 4-methylbenzenesulfonyl chloride was placed. The beaker was heated on a water bath (75 ^{o}C) until 4-methylbenzenesulfonyl chloride became a liquid. Then aniline (4.9 mL, 53 mmol) was added dropwise, with stirring. The mixture was stirred for 40 minutes at 60 ^{o}C. The mixture was cooled and distilled water (70 mL) was added. The product was collected by suction on a Büchner funnel, and washed with cold distilled water (30 mL). Recrystallizaton with ethanol afforded pure product in 90% yield. mp 120-121 ^{o}C; IR (KBr): 3260, 2920, 1593, 1465, 1325, 1148, 1080, 816 cm^{-1}; ^{1}H NMR (acetone-d_6/TMS): δ = 2.35 (s, 3H), 6.90 (1H), 7.37-7.82 (m, 9H); Anal. Calcd. for $C_{13}H_{13}NO_2S$: C, 63.15; H, 5.26; N, 5.66. Found: C, 63.35; H, 5.50; N, 5.85%.

Synthesis of N-bromo-N-phenyl-para-toluenesulfonamide

N-phenyl-para-toluenesulfonamide (10 g, 40.5 mmol) was dissolved in a solution of NaOH (0.06 mol, 2.4 g) in water (40 mL) at room temperature. Then a solution of bromine (6.4 mL) in CCl_4 (12 mL) was added with vigorous stirring. The resulting precipitate was filtered and washed with cold distilled water (20 mL) and then recrystallization with ethanol afforded pure reagent in 87 % yield, mp 129-130 ^{o}C. IR (KBr): 2910, 1590, 1436, 1350, 1161, 812 cm^{-1}; ^{1}H NMR (acetone-d_6/TMS): δ = 2.35 (s, 3H), 7.25-7.80 (m, 9H); Anal. Calcd. for $C_{13}H_{12}NO_2SBr$: C, 48; H, 3.69; N, 4.30. Found: C, 48.13; H, 3.76; N, 4.47%.

General procedure for deoximation of oximes

A mixture of the oxime (3 mmol), N-bromo-N-phenyl-para-toluenesulfonamide (1.1 g, 3.3 mmol), acetone (12 mL) and distilled water (2 mL) were placed in a 250 mL round-bottomed flask and refluxed under microwave irradiation in a microwave oven at a power output of 200 W for the appropriate time as indicated in Table 1. The reaction was monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure, and then Et_2O (15 mL) was added to the mixture and stirred for 15 min. The sulfonamide was removed by filtration and the product was purified by column chromatography [(hexane-Et_2O)(4:1)] (Table 1). Products were characterized by their physical constants, by comparison with authentic samples and by their IR and ^{1}H NMR spectra.

DATA OF THE PRODUCTS

1: **Benzoin**, mp 131-133 ^{o}C, IR: 3416, 3380, 3030, 1670, 1573, 1460, 1375, 1275, 1190, 980, 850, 610 cm^{-1}; ^{1}H NMR (DMSO-d_6/TMS): δ 6 (s, 1H), 6.1 (s, 1H), 7-7.5 (m, 8H), 8 (d, 2H).

2: **4-Methyl acetophenone**, bp 219-221^{o}C, IR: 3300, 3080, 3000, 2960, 1680, 1640, 1420, 1210, 954, 840, 750, 690 cm^{-1}; ^{1}H NMR (DMSO-d_6/TMS): δ 2.3 (s, 3H), 2.7 (s, 3H), 7.2 (d, 2H), 7.8 (d, 2H).

3: **Benzaldehyde**, bp 176-178 ^{o}C, IR: 3050, 3030, 2850, 2710, 1950, 1900, 1820, 1705, 1450, 1250, 920, 830, 740 cm^{-1}, ^{1}H NMR ($CDCl_3$/TMS): δ 7.5 (m, 2H), 7.6 (m, 1H), 7.9 (m, 2H), 10 (s, 1H).

4: **Acetophenone**, bp 81-83 ^{o}C, IR: 3600, 3345, 3050, 3020, 2960, 2850, 1680, 1635, 1580, 1450, 1260, 1070, 960, 730, 620 cm^{-1}, ^{1}H NMR ($CDCl_3$/TMS): δ 2.6 (s, 3H), 7.2-7.7 (m, 3H), 7.9 (m, 2H).

5: **Cyclohexanone**, bp 152-155 ^{o}C, IR: 3600, 3420, 2950, 2600, 1850, 1800, 1760, 1710, 1670, 1440, 1320, 1220, 1060, 990, 750 cm^{-1}, ^{1}H NMR ($CDCl_3$/TMS): δ 1.5-2 (m, 6H), 2.5 (m, 4H).

6: **Cinnamaldehyde**, bp 124-127 ^{o}C, IR: 3330, 3060, 2990, 2800, 1670, 1620, 1606, 1570, 1350, 1210, 1070, 970, 750, 620 cm^{-1}, ^{1}H NMR ($CDCl_3$/TMS): δ 6.5 (m, 1H), 7 (m, 1H), 7.1-7.7 (m, 5H), 10 (d, 1H).

7: **Diisopropyl ketone**, bp 120-122 ^{o}C, IR: 3600, 3450, 3100, 2870, 1710, 1630, 1450, 1220, 1130, 980, 890, 610 cm^{-1}, ^{1}H NMR ($CDCl_3$/TMS): δ 1 (d, 12H), 2.5 (m, 2H).

8: **Isobutyl methyl ketone**, bp 114-116 ^{o}C, IR: 3350, 2940, 1710, 1450, 1290, 1110, 970, 830, 620 cm^{-1}, ^{1}H NMR ($CDCl_3$/TMS): δ 0.9 (d, 6H), 2-2.2 (m, 4H), 2.4 (d, 2H).

9: **Cyclopentanone**, bp 126-129 ^{o}C, IR: 3400, 2960, 2800, 1970, 1740, 1620, 1450, 1230, 950, 890, 810, 710, 460 cm^{-1}, ^{1}H NMR ($CDCl_3$/TMS): δ 1.7-2.4 (m, 8H).

10: **Camphor**, mp 165-168 ^{o}C, IR: 3450, 2940, 2870,

1740, 1430, 1380, 1250, 1080, 950, 730, 610 cm^{-1}, ^1H NMR ($CDCl_3$/TMS): δ 0.8-1 (t, 9H), 1.3-1.7 (m, 3H), 1.9-2.5 (m, 4H).

11: **Ethyl methyl ketone**, bp 77-79 ^oC, IR: 3010, 2950, 2870, 1720, 1450, 1255, 940, 510, 450 cm^{-1}, ^1H NMR ($CDCl_3$/TMS): δ 1 (t, 3H), 2.2 (s, 3H), 2.5 (q, 2H).

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