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Synthesis of dibromo ketones by the reaction of the environmentally benign H_2O_2-HBr system with oximes

Research Article

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Abstract: It was found that oximes undergo deoximation in the presence of the H_2O_{2aq}-HBr_{aq} system to form ketones and bromo ketones. This reaction provided the basis for the synthesis of dibromo ketones in yields varying from 40% to 94%. This method is environmentally friendly, sustainable, and easy to perform. The results of this investigation extend the potential of the use of oximes for the protection of carbonyl group, thus offering the ability to perform not only conventional deoximation but also the subsequent bromination of ketones. The reaction is easily scaled up and dibromo ketones can be prepared in gram amounts.

Keywords: *Oximes • Dibromo ketones • Bromination • Hydrogen peroxide • Hydrobromic acid*

1. Introduction

Oximes belong to one of the most important classes of compounds in organic chemistry. Due to their availability and diverse reactivity, these compounds are used in the synthesis of amines, amides (lactams), nitriles, halo nitroso derivatives and halo nitro derivatives, as complex-forming agents, chelating agents, *etc*.

The oximation of the carbonyl group is a convenient way of protecting this group; numerous procedures for the deoximation were described in the literature [1]. All these procedures are, as a rule, limited to the formation of the starting carbonyl compounds from oximes.

In the present study, we show that oximes **1** can be used as the starting reagents for the synthesis of bromo ketones **3-5** (apparently, through the intermediate formation of ketones **2**) by performing the reaction of **1** with the H_2O_{2aq}-HBr_{aq} reaction system. The latter is non-hazardous and convenient to handle and it acts as the deoximating and brominating agent with respect to oximes **1a-l**. We found the conditions of the synthesis, in which dibromo ketones **4a-l** are formed as the major reaction products (Scheme 1).

This result was quite unpredictable. We expected that the reaction would afford geminal bromo nitroso and bromo nitro products in view of the fact that, as shown earlier, the reactions of oximes with the related H_2O_2-HCl system performed under similar conditions (AcOH, dioxane, benzene, and dichloromethane as the solvents; 38-50°C) give geminal chloronitroso and chloronitro products with a good selectivity and in high yields (Scheme 2) [2].

It should be noted that, since in comparison with elemental halogens the H_2O_2-HHal systems are non-hazardous, environmentally friendly, and easy to produce, their use follows modern trends in organic synthesis and these systems were widely used in the last decades [3-7]. These systems are most extensively used for halogenation of arenes [4], alkenes [5], ketones [6], and alkylarenes [7]. The diversity of halogenation and oxidation reactions associated with the generation of several active species (HHalO, H_2HalO^+, Hal_2) in the

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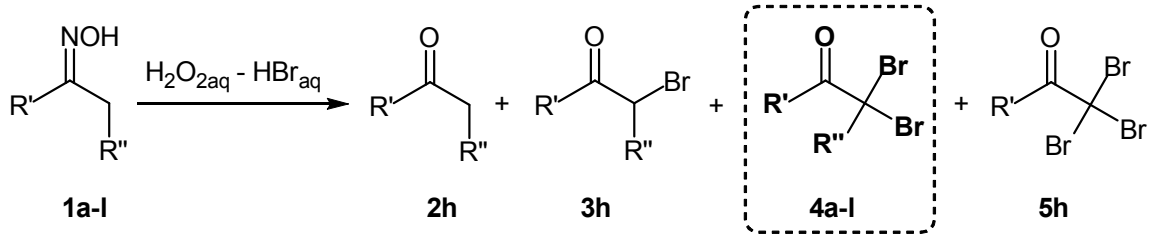
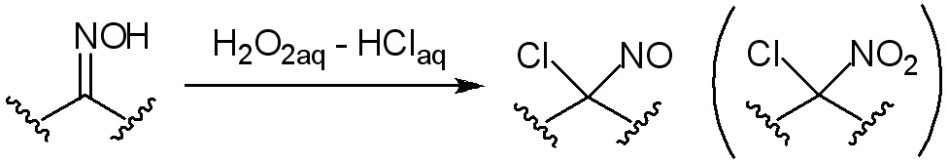


a: R' = Ph, R'' = H; **b**: R' = 2-naphtyl, R'' = H; **c**: R' = R'' = 2-tetralin; **d**: R' = 4-MeC_6H_4, R'' = H;
e: R' = 4-MeC_6H_4, R'' = H; **f**: R' = 4-HOC_6H_4, R'' = H; **g**: R' = 4-ClC_6H_4, R'' = H;
h: R' = 4-BrC_6H_4, R'' = H; **i**: R' = 3-BrC_6H_4, R'' = H; **j**: R' = 3-$NO_2C_6H_4$, R'' = H;
k: R' = 4-$NO_2C_6H_4$, R'' = H; **l**: R' = *tert*-butyl, R'' = H

Scheme 1. Transformations of oximes **1a-l** in reactions with the H_2O_2-HBr system.



Scheme 2. Chlorination of oximes with an H_2O_2-HCl system: facile synthesis of gem-chloronitroso- and gem-chloronitro compounds.

H_2O_2-HHal systems [8] offers the ability to control the pathway and selectivity of the reactions.

The results of this investigation extend the potential of the application of oximes for the protection of the carbonyl group, thus offering the ability to perform not only conventional deoximation but also the subsequent bromination of ketones. This approach can be useful in a multistage synthesis in which oxime fragment is introduced temporarily for the protection of carbonyl group or prepared not from the carbonyl group as well as in transformations, which are possible only in the presence of the oxime group.

2. Experimental procedure

The NMR spectra were recorded on Bruker AM-300 (300.13 MHz for ^1H and 75.48 MHz for ^{13}C), Bruker WM-250 (250.13 MHz for ^1H and 62.9 MHz for ^{13}C), and Bruker AC-200 (200.13 MHz for ^1H and 50.32 MHz for ^{13}C) spectrometers in $CDCl_3$. The TLC analysis was carried out on chromatographic Silufol UV-254 plates. Column chromatography was performed with the use of 63-200 mesh silica gel (Merk).

The melting points were determined on a Kofler hot stage and are uncorrected.

Ketones and hydroxylamine hydrochloride were commercial reagents (Acros). An aqueous 36% H_2O_2 solution and an aqueous 48% HBr solution of high purity grade were used without additional purification. All oxime substrates **1a-l** used in this investigation were quantitatively synthesized by refluxing a mixture of 1 equiv of the corresponding ketone, 2.3 equiv of hydroxylamine hydrochloride, and 2.5 equiv of sodium acetate trihydrate in aqueous methanol. Their purities were confirmed by measuring the melting points and NMR spectra.

Dioxane, AcOH, MeCN, $CHCl_3$, CH_2Cl_2, PhH, and petroleum ether (PE, 40-70) of high purity grade were used as is from commercial sources.

Synthesis of 2,2-dibromo-3,4-dihydronaphthalen-1(2*H*)-one, 4c.

3,4-Dihydro-1(2*H*)-naphthalenone oxime **1c** (200 mg, 1.24 mmol) was dissolved in CH_3COOH (3.5 mL). Then a 36% aqueous H_2O_2 solution (469 mg, 4.96 mmol) and a 48% aqueous HBr solution (2.09 g, 12.4 mmol) were successively added with cooling on a water bath to 15-20°C. The reaction mixture was refluxed for 20 min (96-106°C) and then cooled to room temperature. Water (20 mL) was added, and the reaction products were extracted with $CHCl_3$ (2×10 mL). The combined organic extracts were washed with water (2×20 mL), dried over Na_2SO_4, filtered, and concentrated. 2,2-Dibromo-3,4-dihydronaphthalen-1(2*H*)-one **4c** was isolated by column chromatography on SiO_2 with the use of CH_2Cl_2/PE = 1/1 as the eluent; the yield was 72% (272 mg, 0.893 mmol).

Synthesis of 2,2-dibromo-1-(2-naphthyl) ethanone, 4b.

1-(2-Naphthalenyl)-1-ethanone oxime **1b** (200 mg, 1.08 mmol) was dissolved in dioxane (3 mL). Then a 36% aqueous H_2O_2 solution (408 mg, 4.32 mmol) and a 48% aqueous HBr solution (1.82 g, 10.8 mmol) were successively added with cooling on a water bath to

15-20°C. The reaction mixture was refluxed for 20 min (89-92°C) and then cooled to room temperature. Water (20 mL) was added, and the reaction products were extracted with $CHCl_3$ (2×10 mL). The combined organic extracts were washed with water (2×20 mL), dried over Na_2SO_4, filtered, and concentrated. 2,2-Dibromo-1-(2-naphthyl)ethanone **4b** was isolated by column chromatography on SiO_2 with the use of CH_2Cl_2/PE = 4/3 as the eluent; the yield was 83% (294 mg, 0.896 mmol).

Synthesis of 5,7-dibromo-undecan-6-one, mixture of *meso*- and *rac*-isomers (7).

Undecan-6-one oxime **6** (200 mg, 1.08 mmol) was dissolved in dioxane (3 mL). Then a 36% aqueous H_2O_2 solution (306 mg, 3.24 mmol) and a 48% aqueous HBr solution (1.28 g, 7.59 mmol) were successively added with cooling on a water bath to 15-20°C. The reaction mixture was refluxed for 20 min (89-92°C) and then cooled to room temperature. The isolation was carried out as described in previous experiment. The yield of 5,7-dibromo-undecan-6-one **7** was 76% (269 mg, 0.82 mmol).

4'-Bromoacetophenone (2h) [9]

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.54 (s, 3H, CH_3), 7.56 (d, *J* = 8.4 Hz, 2H, CH), 7.80 (d, *J* = 8.4 Hz, 2H, CH).

^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 26.5, 128.2, 129.8, 131.8, 135.8, 197.0.

2-Bromo-1-(4-bromophenyl)ethanone (3h) [10]

White crystals; mp = 106-108°C ([10] mp 107 - 110°C).

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 4.4 (s, 2H), 7.65 (m, 2H, CH), 7.86 (m, 2H, CH).

^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 30.1, 129.1, 130.2, 132.0, 132.3, 190.2.

2,2-Dibromo-1-phenylethanone (4a) [11]

White crystals; mp = 35-36°C ([11] mp 35.5-36°C).

^{1}H NMR (250MHz, $CDCl_3$): δ = 6.74 (s, 1H, CH), 7.46-7.59 (m, 2H, ArH), 7.59-7.70 (m, 1H, ArH), 8.09 (m, 2H, ArH).

2,2-Dibromo-1-(2-naphthyl)ethanone (4b) [12]

Pale yellow crystals; mp = 100-101.5°C ([12] mp 101-102°C).

^{1}H NMR (250MHz, $CDCl_3$): δ = 6.89 (s, 1H, CH), 7.55-7.70 (m, 2H, ArH), 7.86-8.01 (m, 3H, ArH), 8.06-8.11 (m, 1H, ArH), 8.62 (s, 1H, ArH).

^{13}C NMR (62.9MHz, $CDCl_3$): δ = 39.9, 124.7, 127.2, 127.9, 128.1, 128.9, 129.5, 129.8, 131.8, 132.2, 136.0, 186.0.

2,2-Dibromo-3,4-dihydronaphthalen-1(2*H*)-one (4c) [13]

White crystals; mp =57-59°C ([13] mp 59-60°C)

^{1}H NMR (300.13MHz, $CDCl_3$): δ = 2.95-3.15 (m, 4H, CH_2-CH_2), 7.22-7.29 (m, 1H, ArH), 7.30-7.40 (m, 1H, ArH), 7.49-7.57 (m, 1H, ArH) 8.09-8.16 (m, 1H, ArH).

^{13}C NMR (50.32MHz, $CDCl_3$): δ = 29.1, 45.6, 67.4, 126.9, 127.0, 128.5, 129.8, 134.3, 141.9, 183.9.

2,2-Dibromo-1-(4-methylphenyl)ethanone (4d) [12]

Pale yellow crystals; mp = 97-98°C ([12] mp 98-99°C).

^{1}H NMR (250.13MHz, $CDCl_3$): δ = 2.43 (s, 3H, CH_3), 6.72 (s, 1H, CH), 7.30 (d, 2H, *J* = 7.9 Hz, ArH), 7.97 (d, 2H, J = 7.9 Hz, ArH).

2,2-Dibromo-1-(3-bromo-4-methoxyphenyl) ethanone (4e) [6b]

Slightly yellow crystals; mp = 103-104°C ([6b] 104-105°C)

^{1}H NMR (200.13MHz, $CDCl_3$): δ = 3.98 (s, 3H, CH_3), 6.63 (s, 1H, CH), 6.96 (d, 1H, *J* = 8.7 Hz, ArH), 8.10 (dd, 1H, *J* = 8.7, 2.3 Hz, ArH), 8.30 (d, 1H, *J* = 2.3 Hz, ArH).

^{13}C NMR (50.32MHz, $CDCl_3$): δ = 39.5, 56.7, 111.3, 112.3, 124.2, 131.1, 135.0, 160.5, 183.7.

2,2-Dibromo-1-(3,5-dibromo-4-hydroxyphenyl) ethanone (4f) [6b]

White crystals; mp = 104.5-105°C ([6b] 104-105°C)

^{1}H NMR (250MHz, $CDCl_3$): δ = 6.54 (s, 1H, CH), 6.43-6.55 (br.s., 1H, OH), 8.24 (s, 2H, ArH).

^{13}C NMR (62.9MHz, $CDCl_3$): δ = 38.7, 110.3, 125.3, 134.1, 154.5, 182.7.

2,2-Dibromo-1-(4-chlorophenyl)ethanone (4g) [12]

White crystals; mp = 92.5-93.5°C ([12] mp 93-94°C).

^{1}H NMR (200.13MHz, $CDCl_3$): δ = 6.62 (s, 1H, CH), 7.48 (d, 2H, *J* = 8.5 Hz, ArH), 8.04 (d, 2H, *J* = 8.5 Hz, ArH).

2,2-Dibromo-1-(4-bromophenyl)ethanone (4h) [12]

White crystals; mp = 92-93 °C ([12] mp 93-94°C).

^{1}H NMR (250.13MHz, $CDCl_3$): δ = 6.61 (s, 1H, CH), 7.65 (d, 2H, *J* = 8.7Hz, ArH), 7.97 (d, 2H, *J* = 8.7Hz, ArH).

^{13}C NMR (75.47MHz, $CDCl_3$): δ = 39.4, 129.7, 129.9, 131.2, 132.3, 185.1).

2,2-Dibromo-1-(3-bromophenyl)ethanone (4i) [14]

Pale yellow crystals; mp = 42.5-44°C ([14] mp 43-44°C).

^{1}H NMR (250MHz, $CDCl_3$): δ = 6.65 (s, 1H, CH), 7.37 (m, 1H, ArH), 7.75 (m, 1H, ArH), 8.01 (m, 1H, ArH), 8.20 (m, 1H, ArH).

^{13}C NMR (62.9MHz, $CDCl_3$): δ = 39.6, 123.2, 128.2, 130.3, 132.5, 134.4, 137.3, 184.7.

2,2-Dibromo-1-(3-nitrophenyl)ethanone (4j) [12]

Pale yellow crystals; mp = 55-56 °C ([12] mp 55-56°C).

^{1}H NMR (300.13 MHz, $CDCl_3$): δ =6.66 (s, 1H, CH), 7.76 (m, 1H, ArH), 8.42-8.55 (m, 2H, ArH), 8.94 (s, 1H, ArH).

^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 38.7, 124.8, 128.6, 130.3, 132.2, 135.4, 148.5, 148.1.

2,2-Dibromo-1-(4-nitrophenyl)ethanone (4k) [15]

Pale yellow crystals; mp = 62-64°C ([15] mp 60°C).

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 6.62 (s, 1H, CH), 8.22-8.41 (m, 4H, ArH).

1,1-Dibromo-3,3-dimethylbutan-2-one (4l) [16]

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.29 (s, 9H, $3CH_3$), 6.34 (s, 1H, CH).

^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 26.5 (CH_3), 37.0, 43.7, 201.2 (C=O)

2,2,2-Tribromo-1-(4-bromophenyl)ethanone (5h)

Slightly yellow solid; mp = 104-105°C.

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.63 (d, 2H, CH, $J_{1,2}$ = 8.81 Hz), 8.21 (d, 2H, CH, $J_{1,2}$ = 8.81 Hz).

^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 41.3, 127.1, 129.5, 131.7, 133.3, 180.7.

Anal. Calcd for $C_8H_4Br_4O$: C, 22.05; H, 0.93; Br, 73.35. Found: C, 22.15; H, 0.95; Br, 73.38.

5,7-Dibromo-undecan-6-one, mixture of *meso*- and *rac*-isomers (7) [17]

Slightly yellow oil.

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 0.92 (m, 6H, CH_3), 1.26-1.56 (m, 8H, CH_2), 1.89-2.25 (m, 4H, CH_2), 4.58 (m, 0.5H, CHBr), 4.72 (m, 1.5H, CHBr).

^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 13.9 (CH_3), 22.1, 22.3, 29.4, 29.5, 32.4, 34.5 (CH_2), 50.3, 50.7 (CHBr), 194.4, 197.9 (CO).

3. Results and discussion

The present study consists of two parts. First, we examined the influence of the reaction factors on the yields of the products **2h-5h** by an example of the model compound, *p*-bromoacetophenone oxime **1h**. Second, we performed the preparative synthesis of dibromo ketones **4a-l** from oximes **1a-l** taking into account the optimized conditions.

In the first part of the study, the reaction of *p*-bromoacetophenone oxime **1h** with H_2O_{2aq}-HBr_{aq} system was performed in single- and two-phase systems with the use of the following solvents: acetic acid, dioxane, acetonitrile, chloroform, and benzene. A 36% aqueous H_2O_2 solution was added to a suspension or solution of oxime **1h** followed by the addition of a 48% aqueous HBr solution with stirring and cooling. Then the reaction mixture was heated to the boiling point and refluxed during a preset period of time. Depending on the reaction conditions, acetophenone **2h** and consecutively brominated monobromoacetophenone **3h**, dibromoacetophenone **4h**, and tribromoacetophenone **5h** were prepared (Table 1).

The influence of the following three parameters on the yield of products **2h-5h** was examined: the nature of the solvent and the amounts of H_2O_2 and HBr.

In runs 1-9, where acetic acid was used as the solvent, the amounts of H_2O_2 and HBr were optimized with the aim of achieving selective deoximation and preparing one of bromoacetophenones. It was shown that the reaction affords mono- (**3h**) and dibromoacetophenone **4h** as the major reaction products as the amount of H_2O_2 increases from 0.5 to 2.5 mol per mole of **1h** in the presence of an excess of HBr varying from 3 to 10 mol per mole of **1h** (runs 1-7). In runs 6 and 7, dibromoacetophenone **4h** was prepared with selectivity, allowing the use of this procedure for synthetic purposes. A comparison of the results of runs 5-7 showed that an excess of HBr suppresses the bromination reaction to a certain extent. This is consistent with the data on the reversibility of the bromination of ketones [18].

In run 8 (in the absence of HBr), acetophenone **2h** was obtained in good yield (80%); the H_2O_2 – AcOH system acts as the deoximating agent.

An unexpected result was obtained in run 9, where H_2O_2 was not used as the oxidizing agent; instead, air was bubbled through the reaction mixture and, as a result, monobromoacetophenone **3h** was synthesized as the major product (yield 66%). It is known that HBr is not oxidized by atmospheric oxygen; however, arenes, alkenes, and ketones can be brominated by the HBr/$NaNO_2$/air system.[3a,19] Presumably, in the case under consideration HBr is oxidized by nitrogen oxides that are formed in the course of deoximation of oxime.

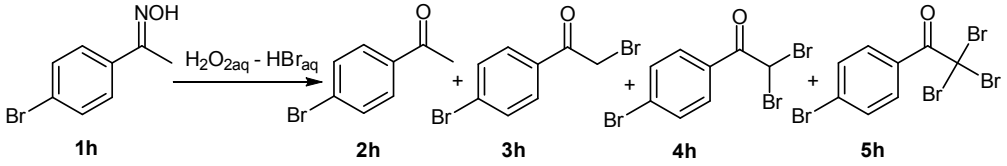
The use of dioxane as the solvent (runs 10-12) allowed us to prepare monobromoacetophenone **3h** (run 11) and dibromoacetophenone **4h** (run 12) in satisfactory yields.

In the case of acetonitrile (runs 13 and 14), we failed to selectively synthesize products **2h-4h**. The synthesis in the two-phase system consisting of chloroform or benzene (runs 15-17) also holds little promise for the selective preparation of bromo ketones even with the use of the acid catalyst TsOH (run 16).

Taking into account the reaction conditions optimized for the preparation of dibromoacetophenone **4h**, we synthesized dibromo ketones **4a-l** from oximes **1a-l** (Table 2).

The above-described method for the synthesis of dibromo ketones from oximes proved to be quite general and gives products in preparative yields.

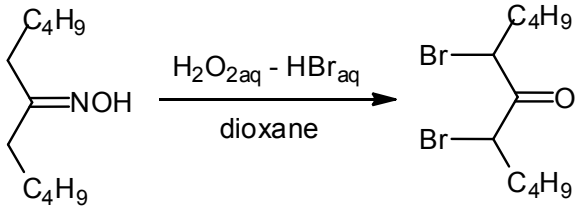
Table 1. Influence of the reaction conditions on the results of the reaction of oxime 1h with the H_2O_{2aq}-HBr_{aq} system[a].



1h **2h** **3h** **4h** **5h**

Run	Mol H_2O_2/ mol 1h	Mol HBr/ mol 1h	Solvent	Reaction time (min)	Yield, % 2h	3h	4h	5h
1	0.5	5	AcOH	20	32	62	3	-
2	1.5	3	AcOH	20	27	67	3	-
3	1.5	5	AcOH	20	13	73	9	-
4	2	5	AcOH	40	2.3	62	31	-
5	2.5	4	AcOH	90	-	-	68	16
6	2.5	5	AcOH	20	-	-	87	9
7	2.5	10	AcOH	20	-	16	77	-
8	2.5	0	AcOH	20	80	-	-	-
9 [b]	0	5	AcOH	120	24	66	4	-
10	1.5	3	dioxane	20	49	46	-	-
11	2	4	dioxane	20	11	73	5	-
12	2.5	5	dioxane	30	-	18	69	-
13	1.5	3	MeCN	20	50	47	-	-
14	2.5	5	MeCN	60	-	46	53	1
15	2.5	5	$CHCl_3$	210	71	13	2	-
16	2.5 [c]	5	$CHCl_3$	210	11	59	18	-
17	2.5	5	PhH	60	3	65	26	2

[a] *General procedure: a 36% aqueous H_2O_2 solution (44-221 mg, 0.47-2.34 mmol) (except run 9) and a 48% aqueous HBr solution (0.47-1.57g, 2.8-9.34 mmol) (except run 8) were added with stirring and water-bath cooling (15-20°C) to a solution of p-bromoacetophenone oxime 1h (200 mg, 0.934 mmol) in the solvent (2 mL), and the reaction mixture was refluxed.*
[b] *The total volume of acetic acid was 4 mL; air was bubbled through the reaction mixture.*
[c] *TsOH (53.3 mg, 0.28 mmol, 0.3mol / mol 1h) was added to the reaction mixture.*



6 **7**

Scheme 3. Bromination of oxime 6 in the reaction with the H_2O_2-HBr system.

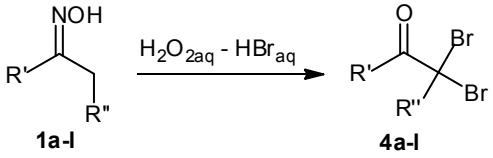
Dibromoacetophenones **4a-d** containing no functional groups were synthesized in good yield (66-83%) in runs 1-4. The bromination of methoxy- **(1e)** and hydroxyacetophenone **(1f)** oximes (runs 5 and 6, respectively) resulted in the bromination not only of the side chain but also of the aryl ring. Noteworthy is the high yield of product **4e** (94%), whose synthesis involves the following three reactions: deoximation, bromination of the side chain, and bromination of the ring, each reaction occurring in quantitative yield. The introduction of electron-withdrawing substituents, such as chlorine and bromine, into the ring (oximes **1g-i,** runs 7-9) does not interfere with the synthesis of dibromo ketones **4g-i** in good yields. The presence of the strong electron-withdrawing nitro group in the nucleus of acetophenone oxime (runs 10-11) leads to a decrease in the yield of target dibromoacetophenones **4j** (59%) and **4k** (44%). Aliphatic ketone oxime **1l** is selectively transformed into dibrominated product **4l** (87% yield).

It is interesting to note that in the reaction of undecan-6-one containing two methylene groups in the α- and α'-positions relatively to the carbonyl group with H_2O_2-HBr system bromination occurs of both these positions. α-,α'–Dibromoketone **7** is prepared in 76% yield, formation of α,α–dibromoketone is not observed (Scheme 3).

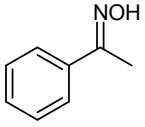
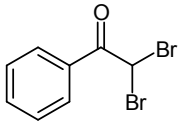
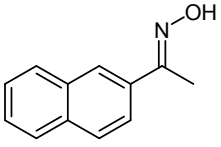
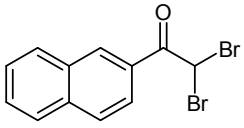
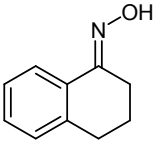
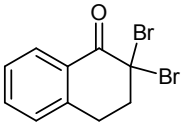
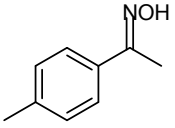
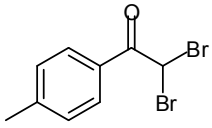
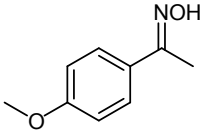
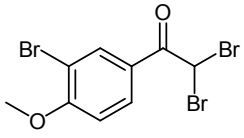
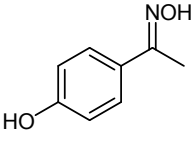
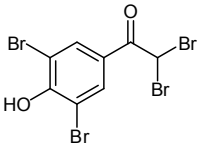
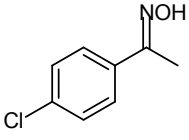
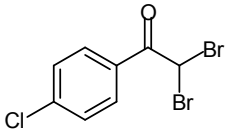
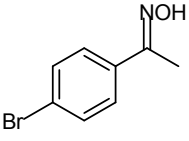
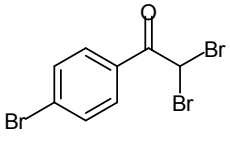
4. Conclusions

To sum up, we developed an easy-to-perform, environmentally friendly and facile method for the synthesis of dibromo ketones in yields varying from 40

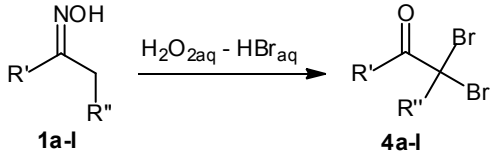
Table 2. Synthesis of dibromo ketones **4a-l** by the reaction of oximes **1a-l** with the H_2O_{2aq}-HBr_{aq} system[a].



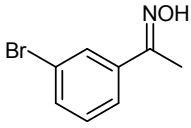
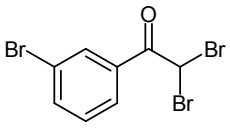
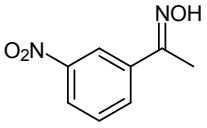
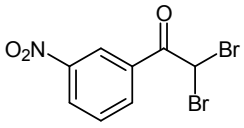
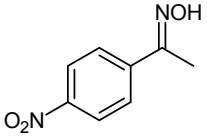
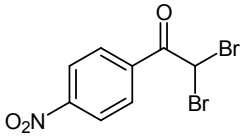
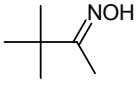
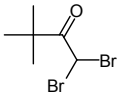
1a-l **4a-l**

Run	Oxime 1	Mol H_2O_2 / mol 1	Mol HBr / mol 1	Dibromo ketone 4, yield %
1	 1a	3	6	 4a, 66 (68)[b]
2[c]	 1b	4	10	 4b, 83
3	 1c	4	10	 4c, 72
4	 1d	3	6	 4d, 74
5	 1e	4.5	10	 4e, 94
6	 1f	4.5	10	 4f, 40
7	 1g	3	6	 4g, 75 (73)[b]
8	 1h	2.5	5	 4h, 84

Continued **Table 2.** Synthesis of dibromo ketones **4a-l** by the reaction of oximes **1a-l** with the H_2O_{2aq}-HBr_{aq} system[a].



1a-l **4a-l**

Run	Oxime 1	Mol H_2O_2 / mol 1	Mol HBr / mol 1	Dibromo ketone 4, yield %
9	 1i	3	8	 4i, 75
10	 1j	4.5	11	 4j, 59
11	 1k	5	10	 4k, 44
12	 1l	4	8	 4l, 87

[a] *General procedure: a 36% aqueous H_2O_2 solution (2.34-6.95 mmol; 2.5-5 mol H_2O_2 per mole of 1a-l) and a 48% aqueous HBr solution (4.67-13.9 mmol; 6-11 mol HBr per mole of 1a-l) were added with stirring and water-bath cooling (15-20°C) to a solution of oxime 1a-l (200 mg, 0.934-1.74 mmol) in AcOH (2-4mL), and the reaction mixture was refluxed (89-106°C) for 20 min.*
[b] *The synthesis was scaled up by a factor of 10.*
[c] *Dioxane as the solvent.*

to 94% based on the reactions of oximes with the H_2O_{2aq}-HBr_{aq} system. The results of the present study extend the potential of the use of oximes for the protection of the carbonyl group, which offers the ability to perform not only conventional deoximation but also the subsequent *in situ* bromination of the resulting ketones. The process can be scaled up and dibromo ketones can be prepared in gram amounts.

Acknowledgments

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