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Research Article

Oxidative Cleavage of β-Keto Sulfones via Nitrous Acid

Hatem A. Abdel-Aziz[1,2]

[1]*Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia*
[2]*Department of Applied Organic Chemistry, National Research Center, Dokki, Cairo 12622, Egypt*

Correspondence should be addressed to Hatem A. Abdel-Aziz; hatem_741@yahoo.com

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The reaction of nitrous acid with 1-aryl-2-(arylsulfonyl)ethanones **3a–e** afforded the unexpected arenecarboxylic acids **12a–e**, formic acid **14**, and benzene/4-toluenesulfinic acid **15a**, **b** through oxidative cleavage reaction. 4-Chlorobenzoic acid (**12a**), [1,1′-biphenyl]-4-carboxylic acid (**12b**), 2-naphthoic acid (**12c**), 2-thiophenecarboxylic acid (**12d**), and 2-benzofurancarboxylic acid (**12e**) were isolated in 72%, 62%, 55%, 58%, and 62% yields, respectively. The reported mechanistic pathways proposed the production of 1-aryl-2-(phenyl/tolylsulfonyl)ethane-1,2-dione **7** instead of arenecarboxylic acids **12**. A mechanistic pathway to explain the reaction of nitrous acid with 1-aryl-2-(arylsulfonyl)ethanones **3a–e** was suggested. In this pathway, the intermediate 1,2-oxazete **10** lost benzene/4-toluenesulfinic acid **15** to produce 1,2-oxazet-3-one **11**. Ring cleavage of the latter intermediate afforded the arenecarboxylic acids **12**.

1. Introduction

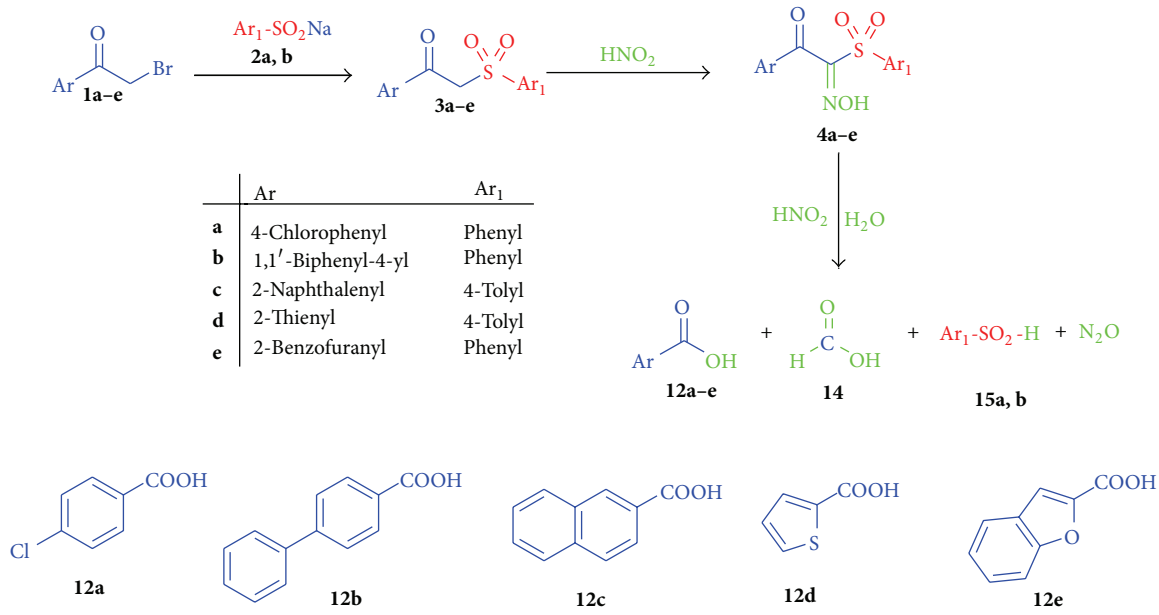
β-Keto sulfones are versatile synthetic intermediates used for the preparation of diverse classes of organic compounds such as substituted acetylenes, olefins, allenes, vinyles, and pyrans. The chemistry of β-keto sulfones achieved a significant peak of interest during the last decades and nowadays constitutes a whole branch of organosulfur chemistry [1–3]. Although the chemistry of β-keto sulfones has been widely investigated, little has appeared in the literature concerning their oximes. Oximes represent an important class of organic compounds with a wide range of practical applications. Oximes can be synthesized by condensation of an aldehyde or a ketone with hydroxylamine. They can also be obtained from reaction of nitrites with active methylene compounds. The latter reaction produces *C*-nitroso compounds which usually rearrange to oximino compounds. This reaction has value as a means of introducing an oximino function in a part of molecule that does not have a carbonyl group for direct oximation [4]. The oxidation of oximes with various inorganic acids is a known procedure for the recovery of aldehydes and ketones from their corresponding oximes [5]. This method has been widely utilized and its reaction mechanism has been reported [6]. In this study and in continuation of our interest in chemistry of β-keto sulfones [7–9], we shall deal with the reaction of nitrous acid with β-keto sulfones **3** and therefore the probable modes of formation of the corresponding carboxylic acids **12**.

2. Experimental

2.1. Chemistry

2.1.1. General. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded as KBr disks using the Perkin Elmer FT-IR Spectrum BX apparatus. NMR spectra were scanned in DMSO-d_6 on a Bruker NMR spectrometer operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C. Chemical shifts are expressed in δ-values (ppm) relative to TMS as an internal standard. Coupling constants (J) are expressed in Hz. D_2O was added to confirm the exchangeable protons. The mass spectra were performed using a Varian MAT CH-5 spectrometer (70 eV).

*2.1.2. Synthesis of 1-Aryl-2-arylsulfonyl Ethanones **3a–f**.* These compounds were prepared according to the reported method [10–15].



	Ar	Ar_1
a	4-Chlorophenyl	Phenyl
b	1,1′-Biphenyl-4-yl	Phenyl
c	2-Naphthalenyl	4-Tolyl
d	2-Thienyl	4-Tolyl
e	2-Benzofuranyl	Phenyl

FIGURE 1: The reaction of nitrous acid with β-keto sulfones **3a–e**.

*2.1.3. Synthesis of Oximes **4a–f**.* To a stirred cold solution of β-keto sulfones **3a–f** [10–15] (10 mmol) in glacial acetic acid (20 mL), sulfuric acid (1 mL, 50%) was added. Then cold solution of sodium nitrite (0.7 g, 10 mmol) in water (5 mL) was added dropwise with stirring at such a rate that the temperature remains in the range 0–5°C. Over a period of 30 min, a light blue solution of nitrous acid is produced. The mixture is stirred for extra 1 h at 25°C. The reaction mixture was poured into cold water and the solid product was filtered off, washed with water, and dried. Recrystallization from EtOH afforded **4a–f** which were used without any further purification in the next step.

*2.1.4. The Reaction of Nitrous Acid with β-Keto Sulfones **3a–e**.* To a stirred cold solution of β-keto sulfones **3a–e** (10 mmol) or oximes **4a–e** (10 mmol) in glacial acetic acid (30 mL), sulfuric acid (5 mL, 50%) was added. Then cold solution of sodium nitrite (2.1 g, 30 mmol) in water (10 mL) was added dropwise with stirring at such a rate that the temperature remains in the range 0–5°C. Over a period of 30 min, a light blue solution of nitrous acid is produced. The mixture is stirred for extra 48 h at 25°C. The solid that precipitated was collected, washed with water, and dried. Recrystallization from EtOH afforded the corresponding carboxylic acids **12a–e** in 55–72% yield. Formic acid (**14**) and benzene/4-toluenesulfinic acid **15** were detected in filtrate using chromatographic analyses. 4-Chlorobenzoic acid (**12a**) was isolated in 65% yield by the reaction of 1-(4-chlorophenyl)-2-[(4-methylphenyl)sulfonyl]ethanone (**3f**) instead of **3a**.

*(1) 4-Chlorobenzoic Acid (**12a**).* This acid was prepared from 1-(4-chlorophenyl)-2-(phenylsulfonyl)ethanone (**3a**) [10] in 65% yield (1.02 g). 1-(4-Chlorophenyl)-2-[(4-methylphenyl)sulfonyl]ethanone (**3f**) [11] afforded 1.13 g (72% yield) of 4-chlorobenzoic acid (**12a**); m.p. 238–240°C (Let. m.p. 238–241°C) [16]; ^{1}H NMR δ 7.57 (d, J = 8.5 Hz, 2H, ArHs), 7.95 (d, J = 8.5 Hz, 2H, ArHs), 13.20 (s, D_2O exchangeable, 1H, OH); ^{13}C NMR δ 128.69 (C3 and C5), 129.72 (C1), 131.10 (C2 and C6), 137.70 (C4), 166.45 (C=O); MS (EI) m/z 156 [M^+], 157 [M^++1], 158 [M^++2].

*(2) [1,1′-Biphenyl]-4-carboxylic Acid (**12b**).* This acid was prepared from 1-(1,1′-biphenyl-4-yl)-2-(phenylsulfonyl)ethanone (**3b**) [12] in 62% yield (1.23 g); m.p. 225–227°C (Let. m.p. 220–225°C) [17]; ^{1}H NMR δ 7.43 (t, J = 7.5 Hz, 1H, ArH), 7.51 (t, J = 7.5 Hz, 2H, ArHs), 7.75 (d, J = 7.5 Hz, 2H, ArHs), 7.79 (d, J = 8.5 Hz, 2H, ArHs), 8.03 (d, J = 8.5 Hz, 2H, ArHs), 13.00 (s, D_2O exchangeable, 1H, OH); ^{13}C NMR δ 126.70 (C3 and C5), 126.91 (C2 and C6), 128.20 (C4 and C4′), 129.04 (C3′ and C5′), 129.90 (C2′ and C6′), 139.07 (C1′), 144.0 (C1), 167.26 (C=O); MS (EI) m/z 198 [M^+].

*(3) 2-Naphthoic Acid (**12c**).* This acid was prepared from 2-[(4-methylphenyl)sulfonyl]-1-(2-naphthalenyl)ethanone (**3c**) [13] in 55% yield (0.95 g); m.p. 186–188°C (Let. m.p. 185–187°C) [18]; ^{1}H NMR δ 7.60–7.68 (m, 2H, ArHs), 7.98–8.03 (m, 3H, ArHs), 8.21 (d, J = 8.0 Hz, 1H, ArH), 8.62 (s, 1H, ArH), 13.11 (s, D_2O exchangeable, 1H, OH); ^{13}C NMR δ 125.25 (C3), 126.69 (C2), 127.60 (C7), 128.01 (C5), 128.14 (C4), 128.63 (C6), 129.20 (C8), 130.34 (C1), 132.14 (C8a), 134.80 (C4a), 167.56 (C=O); MS (EI) m/z 172 [M^+].

*(4) 2-Thiophenecarboxylic Acid (**12d**).* This acid was prepared from 2-[(4-methylphenyl)sulfonyl]-1-(2-thienyl)ethanone (**3d**) [14] in 58% yield (0.74 g); m.p. 124–126°C (Let. m.p. 125–127°C) [19]; ^{1}H NMR δ 7.19 (dd, J = 3.5, 4.8 Hz, 1H, H4), 7.727 (dd, J = 0.7, 3.5 Hz, 1H, H5), 7.91 (dd, J = 0.7, 4.8 Hz, 1H, H3), 13.23 (s, D_2O exchangeable, 1H, OH); ^{13}C NMR δ 135.20 (C2), 133.79 (C3), 128.82 (C4), 133.81 (C5), 163.51 (C=O); MS (EI) m/z 128 [M^+].

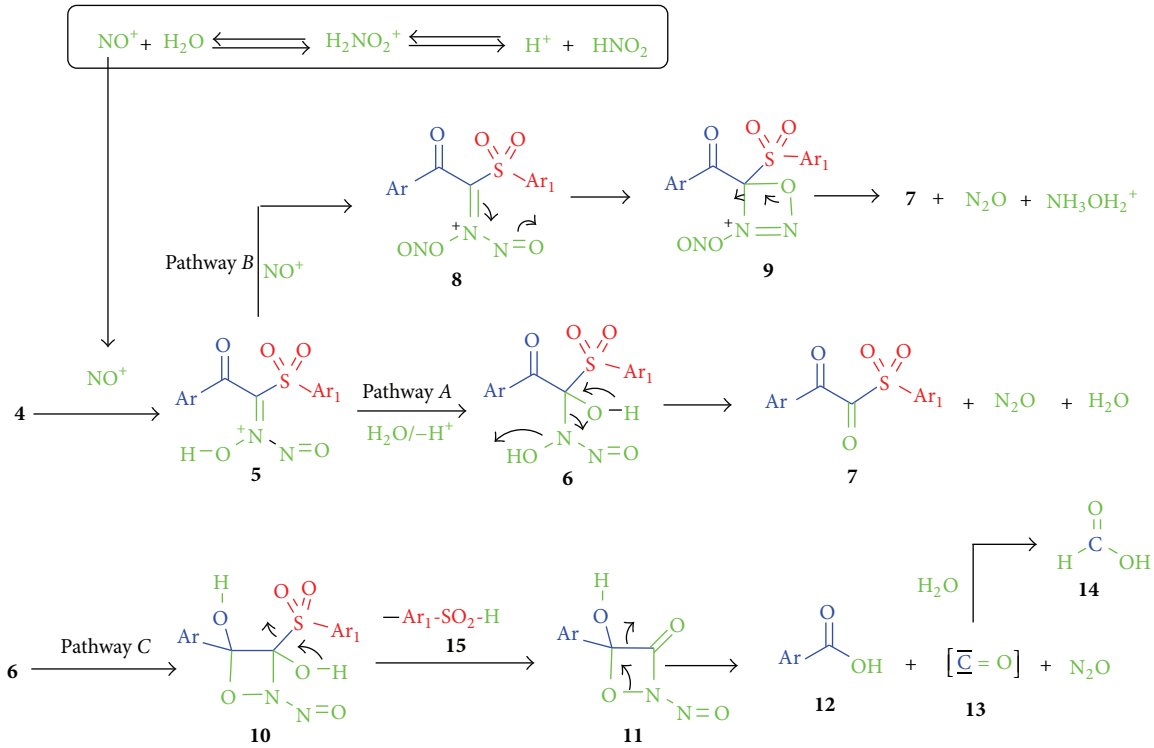


FIGURE 2: The reported mechanistic pathways *A* and *B* [6] for the reaction of nitrous acid with oximes suggested the formation of sulfonyl-diketone **7** during the reaction of nitrous acid with oxime **4**. The proposed mechanistic pathway of the reaction of nitrous acid with *β*-keto sulfones **3** through intermediate 1,2-oxazete **10**, pathway *C*.

*(5) 2-Benzofurancarboxylic Acid (**12e**).* This acid was synthesized from 1-(2-benzofuranyl)-2-(phenylsulfonyl)ethanone (**3e**) [15] in 52% yield (0.84 g); m.p. 193–195°C (Let. m.p. 193–196°C) [20]; ^{1}H NMR δ 7.38 (t, J = 7.5 Hz, 1H, H5), 7.53 (t, J = 7.5 Hz, 1H, H4), 7.71–7.77 (m, 2H, H3+H4), 7.83 (d, J = 7.5 Hz, 1H, H6), 13.80 (s, D_2O exchangeable, 1H, OH); ^{13}C NMR δ 114.35 (C8), 115.82 (C3), 123.00 (C4), 123.91 (C5), 127.04 (C6), 127.84 (C3a), 146.02 (C2), 154.95 (C8a), 160.02 (C=O); MS (EI) m/z 162 [M^+].

3. Results and Discussion

β-Keto sulfones **3a–e** were synthesized by the reaction of 2-bromo-1-arylethanone **1a–e** with the appropriate sodium arylsulfinate **2a**, **b** according to the reported method [10–15]. Treatment of *β*-keto sulfones **3a–e** with sodium nitrite, in acetic acid containing sulfuric acid, afforded the corresponding carboxylic acids **12a–e** in addition to formic acid (**14**) and benzene/4-toluenesulfinic acid **15a**, **b** (Figure 1).

Interestingly, it was found that this method provides the possibility to prepare carboxylic acids through the formation of oximes **4a–e** as intermediates followed by the oxidative cleavage process of C–C bond by nitrous acid under the application of mild reaction conditions. In general, normal ketones are not oxidized except under extremely hard conditions and give several products [21].

4-Chlorobenzoic acid (**12a**), [1,1′-biphenyl]-4-carboxylic acid (**12b**), 2-naphthoic acid (**12c**), 2-thiophenecarboxylic acid (**12d**), and 2-benzofurancarboxylic acid (**12e**) were isolated in 72%, 62%, 55%, 58%, and 62% yields, respectively, by the reaction of *β*-keto sulfones **3a–e** with excess nitrous acid at 0–5°C. 4-Chlorobenzoic acid (**12a**) was isolated in 65% yield by the reaction of 1-(4-chlorophenyl)-2-[(4-methylphenyl)sulfonyl]ethanone (**3f**) instead of **3a**. The structures of carboxylic acids **12a–e** are assigned on the basis of their spectral data and physical constants which are identical with those described for authentic samples of **12a–e** obtained commercially [16–20]. For example, ^{1}H NMR of acids **12a–e** revealed the D_2O exchangeable signal of carboxylic OH in the region δ 13.0–13.8 whereas their ^{13}C NMR showed the signal due to the carbon of carbonyl function in the region δ 160.2–167.56. ^{1}H NMR of **12a** showed the AB system of *Para* substituted benzene ring at δ 7.57 and 7.95 as two doublets with J = 8.5 Hz, whereas the ^{1}H NMR of **15d** revealed three doublets of doublets (dd) signals at δ 7.19 (J = 3.5, 4.8 Hz), 7.727 (J = 0.7, 3.5 Hz), and 7.91 (J = 0.7, 4.8 Hz) for H4, H5, and H3 of thiophene moiety, respectively.

Mechanistic explanation has been reported for the reaction of nitrous acid and nitrosonium ion NO^+ with oximes by Kliegman and Barnes [6]. They proposed two mechanistic pathways using ^{15}N nitrous acid to determine the reaction products. The intermediate product of the reaction of nitrous acid with oxime **4** is the iminoxyl cation **5** which can react in one of these two pathways *A* or *B* (Figure 2).

The nitrosating agent nitrous acid is formed *in situ* by the action of acetic or mineral acid on sodium nitrite and

a further reaction takes place to give the nitrosonium ion NO^+ (Figure 2). The reported mechanistic pathways through hydrolysis of iminoxyl cation **5** to give hydroxy precursor **6** (pathway *A*) or through nitrosation of **5** to give intermediate **8** and then 1,2,3-oxadiazete **9** (pathway *B*) proposed the production of 1-aryl-2-(phenyl/tolylsulfonyl)ethane-1,2-dione **7** instead of arenecarboxylic acids **12** (Figure 2).

These results stimulate our interest to offer a mechanistic pathway (pathway *C*) to explain the formation of acids **12** as main reaction products through oxidative cleavage of β-keto sulfone oximes **4**, keeping in mind the formation of formic acid (**14**) and benzene/4-toluenesulfinic acid **15** (Figure 2). In this pathway, hydroxy precursor **6** cyclized to give the intermediate 1,2-oxazete **10** which lost benzene/4-toluenesulfinic acid **15** to produce 1,2-oxazet-3-one **11**. Ring cleavage of the latter intermediate afforded the arenecarboxylic acids **12** and di-anion **13** [6] which reacted with water to give formic acid (**14**).

4. Conclusion

In conclusion, we studied the reaction of nitrous acid with β-keto sulfones **3a–e**, and we also proposed a mechanistic pathway to explain the formation of unexpected carboxylic acids **12a–e** through the oxidative cleavage reaction.

Conflict of Interests

The author has declared that there is no conflict of interests.

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