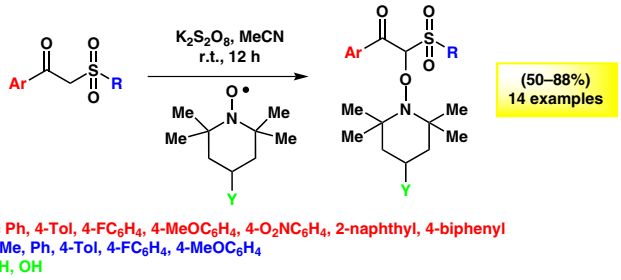
Synlett C.-K. Chan, M.-Y. Chang Letter

Potassium Persulfate Mediated Conjugation of β-Ketosulfones with TEMPO

C.-K. Chan
M.-Y. Chang*

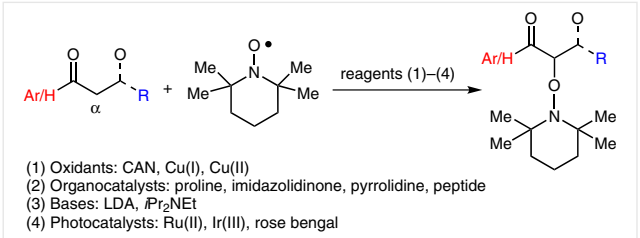
Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung 807, Taiwan
mychang@kmu.edu.tw



Received: 13.07.2016
Accepted after revision: 28.08.2016
Published online: 09.09.2016
DOI: 10.1055/s-0036-1588317; Art ID: st-2016-w0454-l

Abstract We report a simple route for the preparation of α-aminoxy-β-ketosulfones in high yields by a potassium persulfate mediated α-aminoxylation of β-ketosulfones with TEMPO in acetonitrile at room temperature for 12 hours.

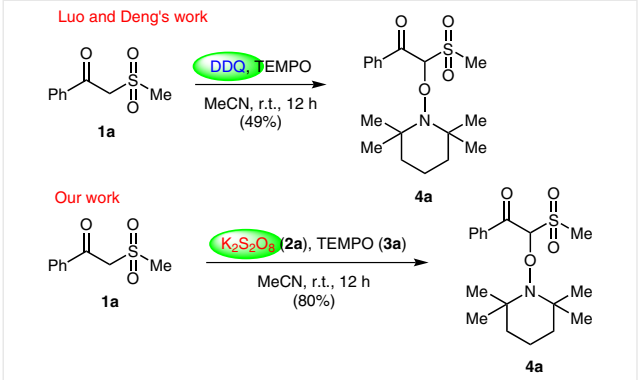
Key words ketosulfones, alkoxyamines, aminoxylation, potassium persulfate, TEMPO, quinoxalines



Scheme 1 Synthetic routes to alkoxyamines

α-Alkoxyamination (α-aminoxylation) can serve as a direct method for the activation of carbon atoms in the positions α to a functional group and subsequent coupling with an oxyamino radical to generate a new carbon–oxyamino bond under oxidative conditions.[1] This is not only a key step in the preparation of functionalized materials such as fireproofing agents or rheology modifiers, but it can also be employed as a valuable route for the formation of useful building blocks or carbon-radical precursors in organic chemistry. Over the past decade, tremendous progress has been made in the oxidative radical α-alkoxyamination of carbonyl compounds (aldehydes and ketones) and 1,3-dicarbonyl synthons (β-keto esters and β-diketones) with TEMPO. Generally, these reactions are induced by oxidant-mediated direct conjugation,[2,3] organocatalyst-promoted cross-coupling of enamine intermediates,[4] base-promoted alkylation of enolate intermediates,[5] or by a photoinduced route (Scheme 1).[6] Although many efforts have been devoted to synthesizing alkoxyamines, there is still a continuing need to provide a new and efficient oxidative reagent for the conjugation of 1,3-dicarbonyl synthons with TEMPO.

In continuation of our investigations on synthetic applications of β-ketosulfones,[7] we developed the $K_2S_2O_8$ (**2a**)-mediated α-alkoxyamination of the β-ketosulfone **1a** with TEMPO (**3a**) in MeCN at room temperature for 12 hours. Recently, Luo and Deng reported a synthetic route to vicinal tricarbonyl compounds through DDQ-mediated C–H activated α-oxidation of β-keto esters with TEMPO; however, they only examined one case of a β-ketosulfone skeleton under these conditions (Scheme 2).[8] Although DDQ is a common oxidant and is often used in various oxidations, the reported isolated yield was low (49%). On the basis of our work, potassium persulfate ($K_2S_2O_8$) provides a better yield (80%). Taking into account the yield of the conjugated



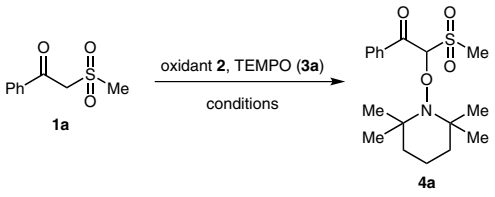
Scheme 2 α-Alkoxyamination of a β-ketosulfone with TEMPO

adducts and the costs of the reagents DDQ and $K_2S_2O_8$, we believe that $K_2S_2O_8$ is the optimal reagent for the overall process.

Initially, the reaction of β-ketosulfone **1a** with 1.1 equivalents of $K_2S_2O_8$ (**2a**) and 1.2 equivalents of TEMPO (**3a**) in MeCN at room temperature for 12 hours gave the alkoxyamine **4a** in 80% yield (Table 1, entry 1). When we performed the same reaction with 1.1 equivalents of DDQ (**2b**), *t*-BuOOH (**2c**), H_2O_2 (**2d**), Oxone (**2e**), *i*-BuONO (**2f**), NaOCl (**2g**), or (diacetoxyiodo)benzene (DIB; **2h**), we did not obtain better yields of the desired alkoxyamine **4a** (entries 2–8). When CAN (**2i**) was used as the oxidant, we obtained a 39% yield of alkoxyamine **4a** along with a 21% yield of benzoic acid (entry 9). These studies confirmed that $K_2S_2O_8$ (**2a**) is an appropriate oxidant for the formation of alkoxyamine **4a**. On increasing the amount of TEMPO from 1.1 to 2.0 equivalents, no obvious increase in the yield was observed (entry 10). When MeCN was replaced by CH_2Cl_2 or EtOAc, the yields were 37% and 45%, respectively (entries 11 and 12). A reduction in the reaction time from 12 to 5 hours, gave only a 36% yield of **4a**, with 48% recovery of **1a** (entry 13) whereas increasing the reaction time to 40 h gave a slightly reduced yield of **4a** of 52% (entry 14). Increasing the temperature from room temperature to the reflux temperature gave a better yield (65%) after five hours, whereas the yield fell to 35% after 12 hours (entries 15 and 16). Interestingly, traces of **4a** (8%) were isolated at room temperature after 40 hours in the absence of $K_2S_2O_8$ (**2a**) in open-vessel conditions (entry 17). On the basis of a higher yield, we believe that $K_2S_2O_8$ (1.1 equiv) and MeCN are an optimal combination for the conjugation of β-ketosulfones with TEMPO.

Having determined the optimal reaction conditions (Table 1, entry 1), we explored the conversion of other substrates (Table 2).[9] The $K_2S_2O_8$ (**2a**)-mediated α-aminoxylation of β-ketosulfones **1a–k** with TEMPO analogues **3a** and **3b** in MeCN at room temperature for 12 h provided the corresponding α-aminoxy-β-ketosulfones **4a–n** in yields of 50–88%. A diversity of electron-withdrawing and electron-

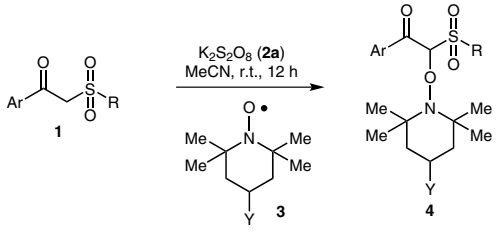
Table 1 . Optimization of the Reaction Conditions[a]



Entry	Oxidant (equiv)	Solvent	Temp (°C)	Time (h)	Yield[b] (%) of **4a**
1	$K_2S_2O_8$ (**2a**) (1.1)	MeCN	25	12	80
2	DDQ (**2b**) (1.1)	MeCN	25	12	45
3	*t*BuOOH (**2c**) (1.1)	MeCN	25	12	<5[c]
4	H_2O_2 (**2d**) (1.1)	MeCN	25	12	<5[c]
5	Oxone (**2e**) (1.1),	MeCN	25	12	<5[c]
6	*i*-BuONO (**2f**) (1.1),	MeCN	25	12	<5[c]
7	NaOCl (**2g**) (1.1),	MeCN	25	12	<5[c]
8	DIB (**2h**) (1.1),	MeCN	25	12	<5[c]
9	CAN (**2i**) (1.1)	MeCN	25	12	39[d]
10	$K_2S_2O_8$ (**2a**) (2.0)	MeCN	25	12	75
11	$K_2S_2O_8$ (**2a**) (1.1)	CH_2Cl_2	25	12	37
12	$K_2S_2O_8$ (**2a**) (1.1)	EtOAc	25	12	45
13	$K_2S_2O_8$ (**2a**) (1.1)	MeCN	25	5	36[e]
14	$K_2S_2O_8$ (**2a**) (1.1)	MeCN	25	40	52
15	$K_2S_2O_8$ (**2a**) (1.1)	MeCN	82	5	65
16	$K_2S_2O_8$ (**2a**) (1.1)	MeCN	82	12	35
17	$K_2S_2O_8$ (**2a**) (0)	MeCN	25	40	8[f]

[a] Reaction conditions: **1a** (1.0 mmol), TEMPO (1.2 equiv), solvent (5 mL), open vessel.
[b] Isolated yields.
[c] **1a** was recovered (85–92%).
[d] 21% of benzoic acid was isolated.
[e] 48% of **1a** was recovered.
[f] 81% of **1a** was recovered.

Table 2 Synthesis of Alkoxyamines **4a–n**[a]

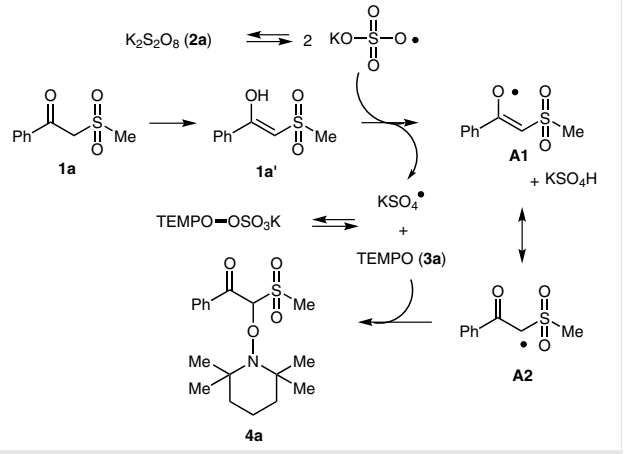


Entry		Ar	R		Y	Product	Yield[b] (%)
1	**1a**	Ph	Me	**3a**	H	**4a**	80
H	**1b**	Ph	Me	**3a**	H	**4b**	83
H	**1c**	Ph	4-Tol	**3a**	H	**4c**	83
H	**1d**	4-Tol	4-Tol	**3a**	H	**4d**	85
H	**1e**	4-FC_6H_4	4-Tol	**3a**	H	**4e**	80
H	**1f**	4-$MeOC_6H_4$	4-Tol	**3a**	H	**4f**	56
H	**1g**	4-$O_2NC_6H_4$	4-Tol	**3a**	H	**4g**	80
H	**1h**	2-naphthyl	4-Tol	**3a**	H	**4h**	85
H	**1i**	Ph	4-FC_6H_4	**3a**	H	**4i**	81
H	**1j**	Ph	4-$MeOC_6H_4$	**3a**	H	**4j**	52
H	**1a**	Ph	4-Tol	**3b**	OH	**4k**	81
H	**1e**	4-FC_6H_4	4-Tol	**3b**	OH	**4l**	88
H	**1f**	4-$MeOC_6H_4$	4-Tol	**3b**	OH	**4m**	50
H	**1k**	4-biphenyl	4-Tol	**3b**	OH	**4n**	80

[a] Reaction conditions: **1** (1.0 mmol), **2a** (1.1 mmol), **3** (1.2 mmol), MeCN (5 mL), 12 h, r.t.
[b] Isolated yield.

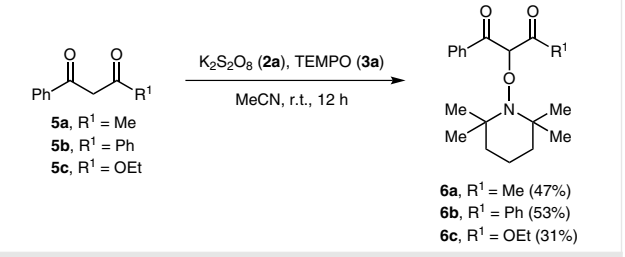
neutral groups Ar and R on the sulfone **1** were well tolerated; however, when Ar or R was an electron-donating group, the corresponding products **4f**, **4j**, and **4m** were obtained in slightly lower yields (56, 52, and 50%, respectively; Table 2, entries 6, 10, and 13).

One the basis of these results, we propose a mechanism in which the reaction proceeds by a single-electron transfer (SET) process (Scheme 3).[10] Initially, an $SO_4^{\cdot-}$ anion radical is formed by hemolytic cleavage of $K_2S_2O_8$. **1a'**, the enol form of **1a** formed by keto–enol tautomerization, undergoes SET with the $SO_4^{\cdot-}$ to give radical **A1**. Resonance of the delocalized electron in the radical **A1** then gives the secondary carbon radical **A2**. Finally, coupling of **A2** and TEMPO (**3a**) affords **4a**.[2a] During the process, O–O bond-forming and bond-cleavage reactions of TEMPO and $KSO_4^{\cdot-}$ also occur.



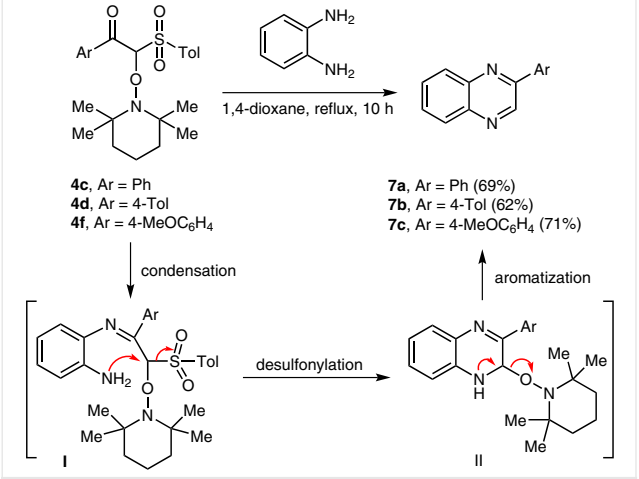
Scheme 3 Plausible mechanism

By changing the α-substituent from a sulfonyl group to a carbonyl group (β-diketones **5a** and **5b**) or an ethyl ester group (β-keto ester **5c**), we obtained the alkoxyamines **6a–c** in 47, 53, and 31% yield, respectively (Scheme 4). The α-aminoxy-β-ketosulfones **4a–n** provided better yields (50–88%) than did the α-aminoxy-β-diketones **6a** and **6b**[6d] or the α-aminoxy-β-keto ester **6c**.[2d]



Scheme 4 Synthesis of alkoxyamines **6a–c**

As an extension of our $K_2S_2O_8$-mediated α-alkoxyamination of β-ketosulfones with TEMPO, we prepared a series of quinoxalines **7a–c** (Scheme 5). Quinoxaline is a versatile scaffold present in useful synthetic intermediates[11] and bioactive molecules.[12] The most popular reported procedures for syntheses of quinoxalines involve the condensation of 1,2-diaminobenzenes with various polar *ortho*-carbon units, such as α-methylene aldehydes or ketones, 1,2-diketones, epoxides, vicinal diols, diazoketones, alkenes, or alkynes.[13] Among these starting substrates, no examples of an α-aminoxy-β-ketosulfone has been reported for the formation of a quinoxaline. Condensation of α-aminoxy-β-ketosulfone **4c**, **4d**, or **4f** with benzene-1,2-diamine in refluxing 1,4-dioxane for 10 hours gave the corresponding quinoxaline **7a–c** (62–71%)[14] through a tandem process involving condensation of **4c**, **4d**, or **4f** with benzene-1,2-diamine and sequential intramolecular desulfonylation of intermediate **I** and aromatization of intermediate **II**.



Scheme 5 . Synthesis of **7a–c**

In summary, we have developed a simple route to α-aminoxy-β-ketosulfones by $K_2S_2O_8$-mediated α-aminoxylation of β-ketosulfones **1** with TEMPO **3** in MeCN at room temperature for 12 hours. The products **4** were obtained in good to high yields. The $K_2S_2O_8$-mediated α-aminoxylation of 1,3-dicarbonyl synthons **5** (β-diketones and β-keto ester) gave the corresponding products **6** in moderate yields. Moreover, quinoxalines **7** were synthesized by condensation of the α-aminoxy-β-ketosulfone products **4** with 1,2-diaminobenzene. Further investigations on synthetic applications of β-ketosulfones will be conducted and published in due course.

Acknowledgment

The authors would like to thank the Ministry of Science and Technology of the Republic of China for its financial support (MOST 105-2113-M-037-001).

Supporting Information

Supporting information (experimental procedures and scanned photocopies of NMR ($CDCl_3$) spectral data) for this article is available online at http://dx.doi.org/10.1055/s-0036-1588317.

References and Notes

(1) For reviews on α-alkoxyamination (α-aminoxylation), see: (a) Hawker, C. J. *Acc. Chem. Res.* **1997**, *30*, 373. (b) Korolev, G. V.; Marchenko, A. P. *Russ. Chem. Rev.* **2000**, *69*, 409. (c) Studer, A. *Chem. Soc. Rev.* **2004**, *33*, 267. (d) Studer, A.; Schulte, T. *Chem. Rec.* **2005**, *5*, 27. (e) Sciannamea, V.; Jérôme, R.; Detrembleur, C. *Chem. Rev.* **2008**, *108*, 1104. (f) Vogler, T.; Studer, A. *Synthesis* **2008**, 1979. (g) Megiel, E. *J. Appl. Polym. Sci.* **2013**, *127*, 4858. (h) Merino, P.; Tejero, T.; Delso, I.; Matute, R. *Synthesis* **2016**, *48*, 653. (i) Tebben, L.; Studer, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 5034.

(2) Oxidant-mediated conjugation of 1,3-dicarbonyl synthons with TEMPO. For $CuCl_2$/β-keto esters, see: (a) Luo, X.; Wang, Z.-L.; Jin, J.-H.; An, X.-L.; Shen, Z.; Deng, W.-P. *Tetrahedron* **2014**, *70*, 8226. For alkenes/β-diesters, see: (b) Wetter, C.; Jantos, K.; Woithe, K.; Studer, A. *Org. Lett.* **2003**, *5*, 2899. For CAN/β-keto esters, see: (c) Feng, P.; Sun, X.; Su, Y.; Li, X.; Zhang, L.-H.; Shi, X.; Jiao, N. *Org. Lett.* **2014**, *16*, 3388. (d) Feng, P.; Song, S.; Zhang, L.-H.; Jiao, N. *Synlett* **2014**, *25*, 2717.

(3) Oxidant-mediated conjugation of carbonyl synthons with TEMPO. For CuCl/aldehydes, see: (a) Schoening, K.-U.; Fischer, W.; Hauck, S.; Dichtl, A.; Kuepfert, M. *J. Org. Chem.* **2009**, *74*, 1567. For Cu/Fe/α-alkoxyketones, see: (b) Xie, Y.-X.; Song, R.-J.; Liu, Y.; Liu, Y.-Y.; Xiang, J.-N.; Li, J.-H. *Adv. Synth. Catal.* **2013**, *355*, 3387.

(4) Organocatalyst-mediated α-alkoxyamination of aldehydes via enamine intermediates. For proline, see: (a) Hayashi, Y.; Yamaguchi, J.; Hibino, K.; Shoji, M. *Tetrahedron Lett.* **2003**, *44*, 8293. (b) Brown, S. P.; Brochu, M. P.; Sinz, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 10808. For imidazolidinone, see: (c) Sibi, M. P.; Hasegawa, M. *J. Am. Chem. Soc.* **2007**, *129*, 4124. For pyrrolidine/electrolysis, see: (d) Bui, N.-N.; Ho, X.-H.; Mho, S.-i.; Jang, H.-Y. *Eur. J. Org. Chem.* **2009**, 5309. For imidazolidinone/$CuCl_2$, see: (e) Simonovich, S. P.; Van Humbeck, J. F.; MacMillan, D. W. C. *Chem. Sci.* **2012**, *3*, 58. (f) Abeykoon, G. A.; Chatterjee, S.; Chen, J. S. *Org. Lett.* **2014**, *16*, 3248. For pyrrolidine/$FeCl_3$, see: (g) Van Humbeck, J. F.; Simonovich, S. P.; Knowles, R. R.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2010**, *132*, 10012. For peptide/$FeCl_2$, see: (h) Akagawa, K.; Fujiwara, T.; Sakamoto, S.; Kudo, K. *Org. Lett.* **2010**, *12*, 1804.

(5) Base-mediated α-alkoxyamination of carbonyl synthons via enolate intermediates. For pyridine/ketones, see: (a) Li, Y.; Pouliot, M.; Vogler, T.; Renaud, P.; Studer, A. *Org. Lett.* **2012**, *14*, 4474. For LDA/esters, see: (b) Jahn, U. *J. Org. Chem.* **1998**, *63*, 7130. (c) Jahn, U.; Hartmann, P.; Dix, I.; Jones, P. G. *Eur. J. Org. Chem.* **2001**, 3333. For $TiCl_4$/DIPEA/ketones, see: (d) Gómez-Palomino, A.; Pellicena, M.; Romo, J. M.; Solà, R.; Romea, P.; Urpi, F.; Font-Bardia, M. *Chem. Eur. J.* **2014**, *20*, 10153.

(6) Photolytic conjugation of carbonyl or 1,3-dicarbonyl synthons: For Ru(II)/aldehydes, see: (a) Koike, T.; Akita, M. *Chem. Lett.* **2009**, *38*, 166. For Ru(II)/Ir(III)/β-keto esters, see: (b) Koike, T.; Yasu, Y.; Akita, M. *Chem. Lett.* **2012**, *41*, 999. For rose bengal/β-keto esters, see: (c) Liu, H.; Feng, W.; Kee, C. W.; Zhao, Y.; Leow, D.; Pan, Y.; Tan, C.-H. *Green Chem.* **2010**, *12*, 953. For Ru(II)/β-diketones, see: (d) Schroll, P.; König, B. *Eur. J. Org. Chem.* **2015**, 309. For Ru(II)/β-keto esters, see: (e) Daniel, M.; Fensterbank, L.; Goddard, J.-P.; Ollivier, C. *Org. Chem. Front.* **2014**, *1*, 551.

(7) Synthetic applications on β-ketosulfones. For styrylsulfones, see: (a) Chang, M.-Y.; Chen, Y.-C.; Chan, C.-K. *Synlett* **2014**, *25*, 1739. For vinylcyclopropanes, see: (b) Chang, M.-Y.; Chen, Y.-C.; Chan, C.-K. *Tetrahedron* **2014**, *70*, 8908. For tetrahydrofurans, see: (c) Chang, M.-Y.; Cheng, Y.-C. *Synlett* **2016**, *27*, 854. For tetrahydropyrans, see: (d) Chang, M.-Y.; Lu, Y.-J.; Cheng, Y.-C. *Tetrahedron* **2015**, *71*, 1192. For dihydropyrans, see: (e) Chang, M.-Y.; Chen, Y.-H.; Cheng, Y.-C. *Tetrahedron* **2016**, *72*, 518. For pyrroles, see: (f) Chang, M.-Y.; Cheng, Y.-C.; Lu, Y.-J. *Org. Lett.* **2014**, *16*, 6252. For vinylfurans, see: (g) Chan, C.-K.; Lu, Y.-J.; Chang, M.-Y. *Tetrahedron* **2015**, *71*, 9544. For arylfurans, see: (h) Chang, M.-Y.; Cheng, Y.-C.; Lu, Y.-J. *Org. Lett.* **2015**, *17*, 1264. For arenes, see: (i) Chang, M.-Y.; Cheng, Y.-C.; Lu, Y.-J. *Org. Lett.* **2015**, *17*, 3142. For arylpyridazines, see: (j) Chang, M.-Y.; Lu, Y.-J.; Cheng, Y.-C. *Tetrahedron* **2015**, *71*, 6840. For tetralins and benzosuberans, see: (k) Chang, M.-Y.; Cheng, Y.-C. *Org. Lett.* **2016**, *18*, 608. For aryltetralins, see: (l) Chang, M.-Y.; Cheng, Y.-C. *Org. Lett.* **2016**, *18*, 1682. For arylnaphthalenes, see: (m) Chang, M.-Y.; Huang, Y.-H.; Wang, H.-S. *Tetrahedron* **2016**, *72*, 1888. For phenanthrenes, see: (n) Chang, M.-Y.; Chen, Y.-C.; Chan, C.-K. *Tetrahedron* **2015**, *71*, 782. For phenanthrofurans, see: (o) Chan, C.-K.; Chen, Y.-C.; Chen, Y.-L.; Chang, M.-Y. *Tetrahedron* **2015**, *71*, 9187.

(8) For DDQ-mediated oxidation of β-keto esters, see: Wang, Z.-L.; An, X.-L.; Ge, L.-S.; Jin, J.-H.; Luo, X.; Deng, W.-P. *Tetrahedron* **2014**, *70*, 3788.

(9) **Alkoxyamines 4; General Procedure**

$K_2S_2O_8$ (**2a**, 300 mg, 1.1 mmol) was added to a solution of the appropriate β-keto sulfone **1** (1.0 mmol) and TEMPO analogue **3** (1.2 mmol) in MeCN (5 mL) at r.t., and the mixture was stirred at r.t. for 12 h. The solvent was evaporated and the residue was diluted with H_2O (10 mL). The mixture was extracted with EtOAc (3 × 20 mL) and the organic layers were combined, washed with brine, dried, filtered, and concentrated to afford the crude product, which was purified by chromatography [silica gel, hexanes–EtOAc (10:1 to 6:1)]

2-(Methylsulfonyl)-1-phenyl-2-[(2,2,6,6-tetramethylpiperidin-1-yl)oxy]ethanone (4a)

Colorless gum; yield: 282 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 7.2 Hz, 2 H), 7.66 (t, *J* = 7.6 Hz, 1 H), 7.54 (t, *J* = 7.6 Hz, 2 H), 6.22 (s, 1 H), 3.11 (s, 3 H), 1.57 (br s, 6 H), 1.43 (br s, 2 H), 1.31 (br s, 4 H), 1.18 (br s, 3 H), 0.86 (br s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.15, 136.34, 133.71 (2 C), 128.65 (2 C), 128.43 (2 C), 94.78, 61.70, 60.26, 40.46, 40.25, 37.16, 33.52, 32.57, 19.81, 16.25. HRMS (ESI): *m/z* $[M + 1]^+$ calcd for $C_{18}H_{28}NO_4S$: 354.1739; found: 354.1743;

(10) (a) Luke, T. L.; Mohan, H.; Manoj, V. M.; Manoj, P.; Mittal, J. P.; Aravindakumar, C. T. *Res. Chem. Intermed.* **2003**, *29*, 379. (b) Laha, J. K.; Tummalalli, K. S. S.; Nair, A.; Patel, N. *J. Org. Chem.* **2015**, *80*, 11351.

(11) (a) Song, H. J.; Lee, T. H.; Han, M. H.; Lee, J. Y.; Moon, D. K. *Polymer* **2013**, *54*, 1072. (b) Liu, X. M.; Zhao, Q.; Li, Y.; Song, W.-C.; Li, Y.-P.; Chang, Z.; Bu, X.-H. *Chin. Chem. Lett.* **2013**, *24*, 962. (c) Shi, J.; Chai, Z.; Su, J.; Chen, J.; Tang, R.; Fan, K.; Zhang, L.; Han, H.; Qin, J.; Peng, T.; Li, Q.; Li, Z. *Dyes Pigm.* **2013**, *98*, 405. (d) Li, H.; Koh, T. M.; Hagfeldt, A.; Grätzel, M.; Mhaisalkar, S. G.; Grimsdale, A. C. *Chem. Commun.* **2013**, *49*, 2409. (e) Venkateswararao, A.; Tyagi, P.; Thomas, K. R. J.; Chen, P.-W.; Ho, K.-C. *Tetrahedron* **2014**, *70*, 6318.

(12) For recent reports on biological activities of quinoxalines, see: (a) Kotharkar, S. A.; Shinde, D. B. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 6181. (b) Rodrigues, F. A. R.; Bomfim, I. da S.; Cavalcanti, B. C.; Pessoa, C. Ó do.; Wardell, J. L.; Wardell, S. M. S. V.; Pinheiro, A. C.; Kaiser, C. R.; Nogueira, T. C. M.; Low, J. N.; Gomes, L. R.; de Souza, M. V. N. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 934. (c) Parhi, A. K.; Zhang, Y.; Saionz, K. W.; Pradhan, P.; Kaul, M.; Trivedi, K.; Pilch, D. S.; LaVoie, E. J. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 4968. (d) Guillon, J.; Moreau, E.; Mouray, S.; Sinou, V.; Forfar, I.; Fabre, S. B.; Desplat, V.; Millet, P.; Parzy, D.; Jarry, C.; Grellier, P. *Bioorg. Med. Chem.* **2008**, *16*, 9133.

(13) For examples of syntheses of quinoxalines, see: (a) Zhang, C.; Xu, Z.; Zhang, L.; Jiao, N. *Tetrahedron* **2012**, *68*, 5258. (b) Cho, C. S.; Ren, W. X.; Shim, S. C. *Tetrahedron Lett.* **2007**, *48*, 4665. (c) Robin, R. S.; Taylor, R. J. K. *Synlett* **2005**, 1003. (d) Meshram, H. M.; Ramesh, P.; Kumar, G. S.; Reddy, B. C. *Tetrahedron Lett.* **2010**, *51*, 4313. (e) Chang, M. Y.; Lee, T. W.; Hsu, R. T.; Yen, T. L. *Synthesis* **2011**, 3143. (f) Kim, S. Y.; Park, K. H.; Chung, Y. K. *Chem. Commun.* **2005**, 1321. (g) Pan, F.; Chen, T.-M.; Cao, J.-J.; Zou, J.-P.; Zhang, W. *Tetrahedron Lett.* **2012**, *53*, 2508. (h) Meshram, H. M.; Ramesh, P.; Kumar, G. S.; Reddy, B. C. *Tetrahedron Lett.* **2010**, *51*, 4313. (i) Qi, C.; Jiang, H.; Huang, L.; Chen, Z.; Chen, H. *Synthesis* **2011**, *19*, 387. (j) Akkilagunta, V. K.; Reddy, V. P.; Kakulapati, R. R. *Synlett* **2010**, 2571. (k) Tingoli, M.; Mazzella, M.; Panunzi, B.; Tuzi, A. *Eur. J. Org. Chem.* **2011**, 399. (l) Yang, Y.; Zhang, S.; Wu, B.; Ma, M.; Chen, X.; Qin, X.; He, M.; Hussain, S.; Jing, C.; Ma, B.; Zhu, C. *ChemMedChem* **2012**, *7*, 823. (m) Schmidt, B.; Krehl, S.; Hauke, S. *J. Org. Chem.* **2013**, *78*, 5427. (n) Huang, T.-Q.; Qu, W.-Y.; Ding, J.-C.; Liu, M.-C.; Wu, H.-Y.; Chen, J.-X. *J. Heterocycl. Chem.* **2013**, *50*, 293. (o) Edayadulla, N.; Lee, Y. R. *RSC Adv.* **2014**, *4*, 11459. (p) Dandia, A.; Parewa, V.; Maheshwari, S.; Rathore, K. S. *J. Mol. Catal. A: Chem.* **2014**, *394*, 244. (q) Xie, C.; Zhang, Z.; Yang, B.; Song, G.; Gao, H.; Wen, L.; Ma, C. *Tetrahedron* **2015**, *71*, 1831. (r) Go, A.; Lee, G.; Kim, J.; Bae, S.; Lee, B. M.; Kim, B. H. *Tetrahedron* **2015**, *71*, 1215. (s) Nasar, M. K.; Kumar, R. R. Perumal S. *Tetrahedron Lett.* **2007**, *48*, 2155. (t) Climent, M. J.; Corma, A.; Hernández, J. C.; Hungria, A. B.; Iborra, S.; Martínez-Silvestre, S. *J. Catal.* **2012**, *292*, 118. (u) Martin, L. J.; Marzinzik, A. L.; Ley, S. V.; Baxendale, I. R. *Org. Lett.* **2011**, *13*, 320. (v) Castillo, J.-C.; Presset, M.; Abonia, R.; Coquerel, Y.; Rodriguez, J. *Eur. J. Org. Chem.* **2012**, 2338. (w) Wang, W.; Shen, Y.; Meng, X.; Zhao, M.; Chen, Y.; Chen, B. *Org. Lett.* **2011**, *13*, 4514. (x) Xu, Y.; Wan, X. *Tetrahedron Lett.* **2013**, *54*, 642. (y) Shi, S.; Wang, T.; Yang, W.; Rudolph, M.; Hashmi, A. S. K. *Chem. Eur. J.* **2013**, *19*, 6576.

(14) Song, J.; Li, X.; Chen, Y.; Zhao, M.; Dou, Y.; Chen, B. *Synlett* **2012**, *23*, 2416.