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无金属条件下芳基酮与二甲亚砜的 α-C(sp³)—H 亚甲基化反应合成 γ-酮亚砜

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摘要 芳基酮通过 C(sp³)—H 键官能化与二甲亚砜发生直接的 α-C(sp³)—H 亚甲基化反应生成 γ-酮亚砜, 该方法适用于各种芳基酮. 此外, 二甲基亚砜(DMSO)在反应中不仅用作溶剂, 而且用作含硫单元. 这种转化的实际价值在于 γ-酮亚砜的高效和稳健的一锅合成法, 并在初步实验的基础上, 提出了一种可能的反应机理.

关键词 芳基酮; C(sp³)—H 亚甲基化; 无金属; γ-酮亚砜; 区域选择性

Metal-Free α-C(sp³)—H Methylenation of Aryl Ketones to Form γ-Keto Sulfoxides with Dimethyl Sulfoxide

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Abstract A direct α-C(sp³)—H methylenation of aryl ketones to form γ-keto sulfoxides via C(sp³)—H functionalization with dimethyl sulfoxide has been developed. This method is applicable to a wide range of aryl ketones. Moreover, dimethyl sulfoxide (DMSO) in this reaction is used not only as solvent but also as a sulfur-containing unit. The practical value of this transformation highlights the efficient and robust one-pot synthesis of γ-keto sulfoxides. Based on the preliminary experiments, a plausible reaction mechanism is proposed.

Keywords aryl ketone; C(sp³)—H methylenation; metal-free; γ-keto sulfoxides; regioselectivity

1 Introduction

Organosulfur compounds play a significant role in organic chemistry and the drug discovery process due to their unique properties and potential pharmaceutical applications,[1] as well as serving as important intermediates in synthetic organic chemistry.[2] In light of the importance of the organosulfur compounds, many methods for the generation of these organosulfur compounds have been established over recent years.[3] However, most of the synthetic procedures suffer from a number of limitations, such as the requirement for a metal and complicated procedures. Consequently, it is highly desirable to explore novel and sustainable approaches that can access multifunctional organosulfur compounds from simple starting materials.

As a cheap and commercially available solvent, dimethyl sulfoxide (DMSO) has been widely used in organic synthesis owing to its low cost, great dissolving capacity, good stability and low toxicity. Furthermore, it has the ability to introduce O,[4] =CH—,[5] Me,[6] SMe,[7] SOMe,[8] SO_2Me,[9] $MeSCH_2$[10] and $MeSOCH_2$[11] fragments into molecules, and it also plays crucial role as oxidant.[12] Recently, direct C(sp³)—H functionalization is considered as a promising approach for the α-functionalization of ketone due to its atom economy and step economy.[13] Based on this strategy, the formation of organosulfur compounds via α-C(sp³)—H functionalization of ketones has been provided. In 2017, a novel acid-promoted direct cross-coupling reaction of methyl ketones and DMSO to prepare β-acyl allylic sulfones was reported by Wen and co-workers (Scheme 1, a).[9c] In the same year, Guo's group[10a] disclosed a coupling of methyl groups under transition metal-free reaction conditions, which enabled a double cross-coupling of C(sp³)—H

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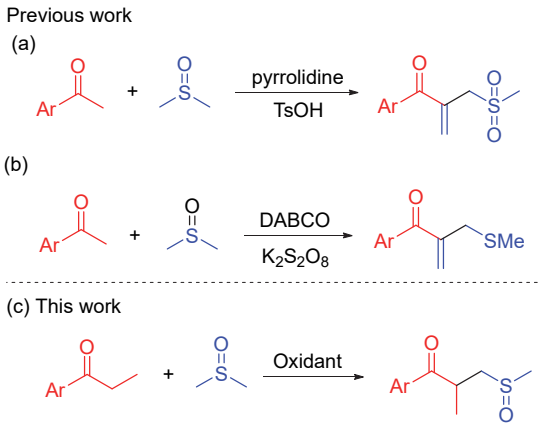
bonds by the reaction of methyl ketones with DMSO in one pot (Scheme 1, b).

We envisaged that simple sulfoxide reagents, combined with organic peroxide, could act as a convenient source of $MeSOCH_2$ radicals.[14] It should be noted that it is challenging to control the regioselectivity for achieving CH_2-$SOCH_3$ functional transformations from DMSO. To the best of our knowledge, there have been very few reports to date involving DMSO as a sulfoxide source to realize C(sp^3)—H methylenation for the C—C bond formation via cross dehydrogenative coupling.[15] In this context, and in line with our current research interests,[16] herein we report an unprecedented reaction, which could achieve a α-C(sp^3)—H methylenation for the C—C bond formation between aryl ketones and DMSO under metal-free conditions (Scheme 1, c). It is noteworthy that DMSO in this reaction is used not only as a solvent but also as a source of CH_2SOCH_3 unit.



Scheme 1 Synthetic application of DMSO

2 Results and discussion

Propiophenone **1a** was chosen as the model substrate to study the reaction. Initially, DMSO was used as the solvent and sulfoxide source in the presence of 3.0 equiv. of peroxide at 120 ℃ (Table 1). Firstly, $(NH_4)_2S_2O_8$ was used as the oxidant, and the mixtures were stirred for 5, 7 and 9 h. To our delight, the desired product, 2-methyl-3-(methylsulfinyl)-1-phenylpropan-1-one (**2a**) was obtained in 49%, 69% and 69% yields, respectively (Entries 1～3), which were in good accordance with a deprotonative cross-coupling procedure. To our disappointment, attempts to improve the product yields by lowering the reaction temperature failed (Entries 4 and 5). Next, various oxidants, such as benzoyl peroxide, peroxide isobutylbenzene, $K_2S_2O_8$, di-*tert*-butyl peroxide (DTBP), *tert*-butyl hydroperoxide (TBHP) were also screened (Entries 6～10). However, no γ-keto sulfoxide **2a** could be detected, except with $K_2S_2O_8$, which gave a 15% yield (Entry 8). There was a slight decrease in yield when the amount of $(NH_4)_2S_2O_8$ was reduced (Entry 11). Gratifyingly, the efficiency of this conversion was improved by increasing the amount of $(NH_4)_2S_2O_8$, indicating that $(NH_4)_2S_2O_8$ plays an essential role in this transformation (Entry 12). It was noted that the product yield remained almost unchanged when the reactions were performed under an atmosphere of O_2 or N_2 (Entries 13 and 14).

Table 1 Optimization of the reaction conditions[a]

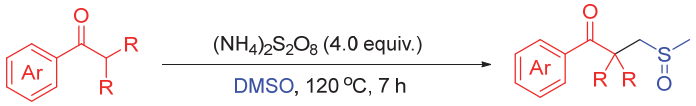
Entry	Peroxide	T/℃	t/h	Yield[b]/%
1	$(NH_4)_2S_2O_8$	120	5	49
2	$(NH_4)_2S_2O_8$	120	7	69
3	$(NH_4)_2S_2O_8$	120	9	69
4	$(NH_4)_2S_2O_8$	70	7	—
5	$(NH_4)_2S_2O_8$	r.t.	7	—
6	Benzoyl peroxide	120	7	—
7	Peroxide isobutylbenzene	120	7	—
8	$K_2S_2O_8$	120	7	15
9	DTBP	120	7	—
10	TBHP	120	7	—
11[c]	$(NH_4)_2S_2O_8$	120	7	54
12[d]	**$(NH_4)_2S_2O_8$**	**120**	**7**	**77**
13[d,e]	$(NH_4)_2S_2O_8$	120	7	77
14[d,f]	$(NH_4)_2S_2O_8$	120	7	77

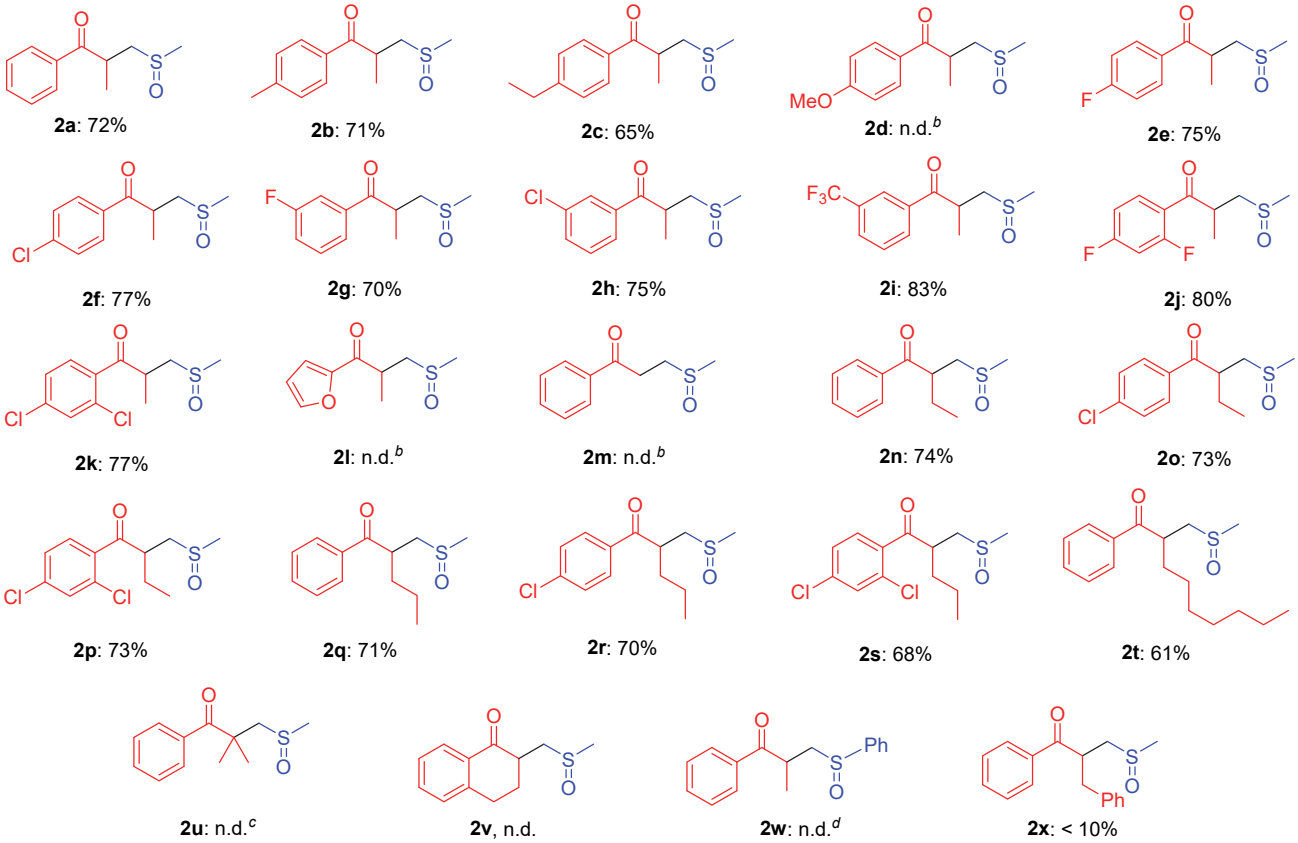
[a] Reaction conditions: **1a** (0.25 mmol), peroxide (3.0 equiv.), DMSO (2.0 mL). [b] GC yield. [c] $(NH_4)_2S_2O_8$: 2.0 equiv. [d] $(NH_4)_2S_2O_8$: 4.0 equiv. [e] O_2 balloon. [f] N_2 balloon.

With the optimized reaction conditions established (Table 1, Entry 12), the scope and generality of this unique reaction were investigated. As shown in Table 2, the process can be successfully applied to an array of simple aryl ketones. For example, substituents with different electronic properties at the *para*-position of the phenyl ring of propiophenone were examined, and all proceeded well to give the desired products in moderate to good yields (**2a**～**2c**, **2e**, **2f**). Propiophenone **1d**, bearing a *para*-methoxyl group, was also used as a substrate. However, it decomposed and did not yield the expected compound **2d**. Next, propiophenones with a *meta*-substituent on the phenyl ring (**1g**～**1i**) were converted into γ-keto sulfoxides. These reactions proceeded smoothly to deliver the target products **2g**～**2i** in 70%～83% yields. Furthermore, the reactions also tolerated disubstituted substrates **2j**～**2k**.

1-(Furan-2-yl)propan-1-one (**1l**) was not compatible with these reaction conditions, as the furan group can be easily oxidized by $(NH_4)_2S_2O_8$. In addition, it was found that acetophenone **1m** could not be converted into the corresponding γ-keto sulfoxide due to its dimerization process.[17] Compound **1n** was compatible, providing the desired product **2n** in 74% yield. With this promising result, other aryl ketones (**1o**～**1t**) were examined, and the desired products were generated in good yields (**2o**～**2t**). Unfortunately, **2u** was not obtained when **1u** was used, possibly due to the greater steric hindrance of the dimethyl group. The reaction was also unsuccessful for the preparation of cyclohexanone **2v** and methyl phenyl sulfoxide **2w**. When 3-phenylpropiophenone **1x** was employed in this reaction, less than 10% yield of **2x** was obtained.

Table 2 Substrate scope[a]

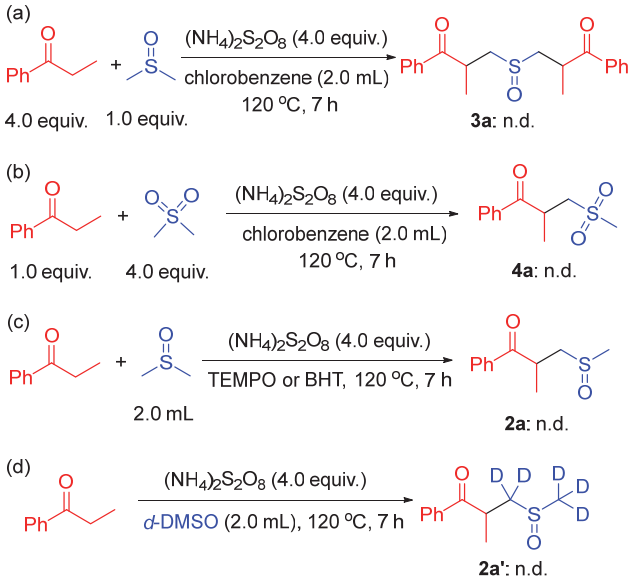




[a] Unless otherwise specified, all the reactions were carried out on 1.0 mmol scale in 2.0 mL of DMSO; isolated yield; [b] The starting material was decomposed; [c] 30% of **1u** was recovered; [d] 2.0 mL of methyl phenyl sulfoxide was used instead of DMSO.

To gain insight into the reaction mechanism, some control reactions were conducted (Scheme 2). Firstly, we investigated whether two molecules of propiophenone **1a** could react with DMSO,[11b] so 4.0 equiv. of **1a** was added to the reaction with 2.0 mL of chlorobenzene as the solvent, but none of the desired product **3a** was obtained (Scheme 2, a). Furthermore, treatment of 4.0 equiv. of dimethyl sulfones under the standard reaction conditions in chlorobenzene led to none of the desired product **4a** being obtained (Scheme 2, b). The reaction was completely suppressed when 2,2,6,6-tetramethylpiperidoxyl (TEMPO) or butylated hydroxytoluene (BHT) was used as the radical scavenger under the standard conditions (Scheme 2, c). Finally, a deuterium experiment was carried out, and replacing DMSO with DMSO-d_6 under standard reaction conditions failed to give the desired product **2a'** (Scheme 2, d).

Density functional theory (DFT) calculations were performed to identify the energy barriers between DMSO and DMSO-*d* in this transformation. As shown in Figure 1, DMSO overcomes an energy barrier of 151.2 kJ•mol^{-1} via an isomerization transition state, in which the vibrational



Scheme 2 Control experiments for the mechanism study

mode clearly indicates a rupture of a C—H bond and the simultaneous formation of an O—H bond. In this process, DMSO is transformed into the thioenol. Meanwhile, deuterated DMSO also undergoes the same isomerization process. However, the energy barrier to overcome has increased to 201.5 kJ•mol^{-1}, 50.3 kJ•mol^{-1} higher than that of DMSO. The activation energy has a great influence on the reaction rate and it demonstrated that the reaction rates between DMSO and *d*-DMSO are different.

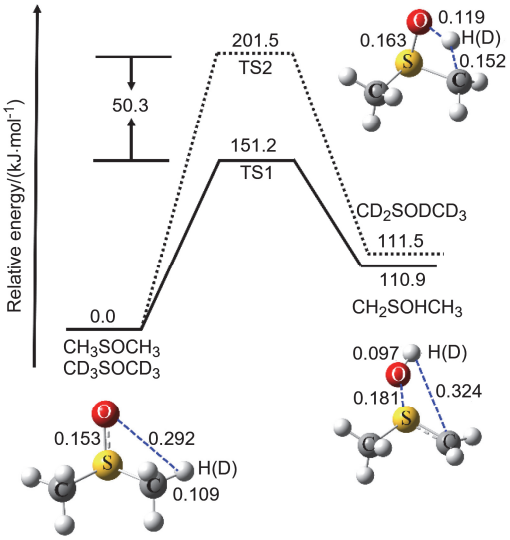
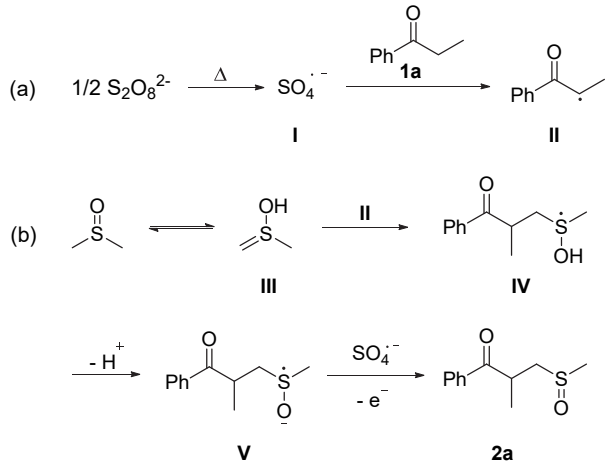


Figure 1 Energy profile and optimized structures of DMSO and deuterated DMSO isomerization at the M062X/6-311+G(d,p)-PCM(DMSO)//M062X/6-311+G(d,p) level (bond length: nm)

On the basis of the above results and related work, a plausible mechanism for the formation of *γ*-keto sulfoxides is shown in Scheme 3. First, sulfate radical anion ($SO_4^{\bullet -}$) **I** is generated under heating, then single electron oxidation of propiophenone **1a** by $SO_4^{\bullet -}$ provides *α*-carbonyl radical **II**.[18] At the same time, DMSO undergoes keto-enol tautomerism to form enol **III**, which enables the radical addition with intermediate **II**, forming intermediate **IV**. Then, intermediate **IV** undergoes deprotonation to give **V**. Finally, intermediate **V** furnishes the final product by the aid of $SO_4^{\bullet -}$.



Scheme 3 Proposed mechanism

3 Conclusions

In summary, a practical $(NH_4)_2S_2O_8$-promoted metal-free *α*-C(sp^3)—H methylenation of aryl ketones to construct *γ*-keto sulfoxides using DMSO as the methylenation agent with high selectivity has been developed. The operationally simple and practical protocol is inexpensive and exhibits excellent regioselectivity and good functional group tolerance. Preliminary mechanistic studies suggest that a keto-enol tautomerism process of DMSO is involved. We expect that this unique transformation will provide new routes to access to *γ*-keto sulfoxides with versatile uses in synthetic and medicinal chemistry applications. Further studies in this area are in progress in our laboratory.

4 Experimental section

4.1 General experimental information

All the reactions were carried out at 120 ℃ for 7 h in a round-bottom flask equipped with a magnetic stir bar. Unless otherwise stated, all reagents and solvents were purchased from commercial suppliers and used without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker model Bruker AV-400 spectrometer in solutions of $CDCl_3$ using tetramethylsilane as the internal standard. HRMS spectra were obtained on a Bruker micro-TOFQII ESI mass spectrometer.

4.2 General procedure for the synthesis of *γ*-keto sulfoxides

A mixture of propiophenone (**1a**) (134 mg, 1.0 mmol), $(NH_4)_2S_2O_8$ (918 mg, 4.0 mmol) and dimethyl sulfoxide (DMSO) (2.0 mL) was added successively into a round-bottom flask, and the resulting solution was stirred for 7 h at 120 ℃. The mixture was purified by column chromatography on silica gel to afford product **2a** with petroleum ether/aether (V ∶ V = 20 ∶ 1) as the eluent. Compounds **2b**～**2t** were synthesized using the same method.

2-Methyl-3-(methylsulfinyl)-1-phenylpropan-1-one (**2a**): 72% yield (151 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) *δ*: 7.98 (d, J=8.4 Hz, 2H), 7.58 (t, J=7.6 Hz,1H), 7.49 (t, J=7.6 Hz, 2H), 3.75～3.70 (m, 1H), 3.00 (br, 1H), 2.61 (br, 1H), 2.13 (s, 3H), 1.30 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) *δ*: 202.8, 36.2, 133.1, 128.7, 128.3, 41.0, 37.6, 17.7, 16.5; HRMS (ESI) calcd for $C_{11}H_{14}NaO_2S$ [M+Na^+] 233.0606, found 233.0611.

2-Methyl-3-(methylsulfinyl)-1-*p*-tolylpropan-1-one (**2b**): 71% yield (159 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) *δ*: 7.89 (d, J=8.0 Hz, 2H), 7.29 (d, J=8.8 Hz, 2H), 3.76～3.67 (m, 1H), 2.99 (dd, J=6.8, 13.2 Hz, 1H), 2.61 (dd, J=7.6, 13.2 Hz, 1H), 2.13 (s, 3H), 1.30 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) *δ*: 202.4, 144.0, 133.7, 129.4, 128.4, 40.8, 37.6, 21.6, 17.8, 16.5; HRMS (ESI) calcd for $C_{12}H_{16}NaO_2S$ [M + Na^+] 247.0763, found

247.0766.

1-(4-Ethylphenyl)-2-methyl-3-(methylsulfinyl)propan-1-one (**2c**): 65% yield (154 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.91 (d, J=8.4 Hz, 2H), 7.31 (d, J=8.4 Hz, 2H), 3.75～3.67 (m, 1H), 2.99 (dd, J=6.80, 13.2 Hz, 1H), 2.72 (q, J=7.6 Hz, 2H), 2.60 (dd, J=7.6, 13.2 Hz, 1H), 2.17 (s, 3H), 1.31～1.27 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 202.4, 150.1, 133.9, 128.5, 128.2, 40.8, 37.6, 28.9, 17.8, 16.5, 15.1; HRMS (ESI) calcd for $C_{13}H_{18}NaO_2S$ [M+Na^+] 261.0919, found 261.0922.

1-(4-Fluorophenyl)-2-methyl-3-(methylsulfinyl)propan-1-one (**2e**): 75% yield (171 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 8.00 (dd, J=8.8, 5.6 Hz, 2H), 7.15 (d, J=8.8 Hz, 2H), 3.71～3.62 (m, 1H), 2.98 (dd, J=12.8, 7.2 Hz,1H), 2.60 (dd, J=12.8, 7.2 Hz, 1H), 2.12 (s, 3H), 1.29 (d, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 201.2, 165.5 (d, $^1J_{C\text{-}F}$=255.0 Hz), 132.7 (d, $^4J_{C\text{-}F}$=3.4 Hz), 130.9 (d, $^3J_{C\text{-}F}$=9.3 Hz), 115.8 (d, $^2J_{C\text{-}F}$=21.7 Hz), 41.0, 37.6, 17.8, 16.5; HRMS (ESI) calcd for $C_{11}H_{13}FNaO_2S$ [M+Na^+] 251.0512, found 251.0517.

1-(4-Chlorophenyl)-2-methyl-3-(methylsulfinyl)propan-1-one (**2f**): 77% yield (187 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.91 (d, J=8.8 Hz, 2H), 7.46 (d, J=8.8 Hz, 2H), 3.71～3.62 (m, 1H), 2.98 (dd, J=6.8, 13.2 Hz, 1H), 2.62 (dd, J=7.6, 13.2 Hz, 1H), 2.12 (s, 3H), 1.29 (d, J=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 201.1, 139.5, 134.4, 129.7, 129.0, 41.1, 37.5, 17.7, 16.5; HRMS (ESI) calcd for $C_{11}H_{13}ClNaO_2S$ [M + Na^+] 267.0217, found 267.0219.

1-(3-Fluorophenyl)-2-methyl-3-(methylsulfinyl)propan-1-one (**2g**): 70% yield (160 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.77～7.74 (m, 1H), 7.67～7.63 (m, 1H), 7.50～7.45 (m, 1H), 7.31～7.26 (m, 1H), 3.71～3.62 (m, 1H), 2.99 (br, 1H), 2.62 (br, 1H), 2.13 (s, 3H), 1.30 (d, J=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 201.6, 162.7 (d, $^1J_{C\text{-}F}$=254.0 Hz), 138.3(d, $^4J_{C\text{-}F}$=3.7 Hz), 130.3 (d, $^3J_{C\text{-}F}$=8.4 Hz), 123.9 (d, $^2J_{C\text{-}F}$=32.8 Hz), 120.2 (d, $^3J_{C\text{-}F}$=12.8 Hz), 115.1 (d, $^2J_{C\text{-}F}$=21.2 Hz), 41.3, 37.4, 17.7, 16.5; HRMS (ESI) calcd for $C_{11}H_{13}FNaO_2S$ [M+Na^+] 251.0512, found 251.0506.

1-(3-Chlorophenyl)-2-methyl-3-(methylsulfinyl)propan-1-one (**2h**): 75% yield (193 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.94 (s, 1H), 7.86～7.83 (m, 1H), 7.57～7.54 (m, 1H), 7.46～7.42 (m, 1H), 3.71～3.62 (m, 1H), 2.98 (br, 1H), 2.62 (br, 1H), 2.13 (s, 3H), 1.30 (d, J=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 201.4, 137.8, 135.8, 130.09, 130.0, 128.4, 126.3, 41.3, 37.4, 17.7, 16.5; HRMS (ESI) calcd for $C_{11}H_{13}ClNaO_2S$ [M + Na^+] 267.0217, found 267.0224.

1-(3-(Trifluoromethyl)phenyl)-2-methyl-3-(methylsulfinyl)propan-1-one (**2i**): 83% yield (230 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 8.20 (s, 1H), 8.16 (d, J=7.6 Hz, 1H), 7.84 (d, J=7.6 Hz, 1H), 7.64 (d, J=7.6 Hz, 1H), 3.78～3.69 (m, 1H), 3.02 (dd, J=6.8, 13.2 Hz, 1H), 2.64 (dd, J=7.6, 13.2 Hz, 1H), 2.15 (s, 3H), 1.33 (t, J=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 201.4, 150.5, 136.8, 131.4, 129.5, 129.9, 129.51, 129.4, 125.141.3, 37.4, 17.7, 16.5; HRMS (ESI) calcd for $C_{12}H_{13}F_3NaO_2S$ [M+Na^+] 301.0480, found 301.0488.

1-(2,4-Difluorophenyl)-2-methyl-3-(methylsulfinyl)propan-1-one (**2j**): 80% yield (197 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.92～7.86 (m, 2H), 7.00～6.96 (m, 1H), 6.91～6.86 (m, 1H), 3.02 (br, 1H), 2.58 (br, 1H), 2.13 (s, 3H), 1.28 (d, J=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 200.0, 165.8 (d, $^1J_{C\text{-}F}$=254.0 Hz), 165.1 (d, $^1J_{C\text{-}F}$=254.0 Hz), 112.35 (dd, $^4J_{C\text{-}F}$=3.4 Hz, $^2J_{C\text{-}F}$=21.2 Hz), 122.2 (d, $^2J_{C\text{-}F}$=23.1 Hz), 112.3 (dd, $^4J_{C\text{-}F}$=3.4 Hz, $^3J_{C\text{-}F}$=21.3 Hz), 104.7 (dd, $^2J_{C\text{-}F}$=25.3 Hz, $^2J_{C\text{-}F}$=27.8 Hz), 45.3, 37.2, 29.6, 16.7; HRMS (ESI) calcd for $C_{11}H_{12}F_2NaO_2S$ [M+Na^+] 269.0418, found 269.0414.

1-(2,4-Dichlorophenyl)-2-methyl-3-(methylsulfinyl)propan-1-one (**2k**): 77% yield (213 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.46～7.41 (m, 2H), 7.32 (dd, J=8.0, 1.6 Hz, 1H), 3.58～3.49 (m, 1H), 2.95 (dd, J=6.8, 13.2 Hz, 1H), 2.58 (dd, J=7.6, 13.2 Hz, 1H), 2.10 (s, 3H), 1.27 (d, J=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 204.8, 137.7, 137.2, 131.6, 130.2, 130.0, 127.3, 45.3, 37.1, 37.0, 16.4; HRMS (ESI) calcd for $C_{11}H_{12}Cl_2NaO_2S$ [M+Na^+] 300.9827, found 300.9822.

2-(Methylsulfinyl)methyl)-1-phenylbutan-1-one (**2n**): 74% yield (165 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.98 (d, J=8.4 Hz, 2H), 7.58 (t, J=7.6 Hz, 1H), 7.43 (t, J=7.6 Hz, 2H), 3.69～3.62 (m, 1H), 2.96 (br, 1H), 2.70 (br, 1H), 2.11 (s, 3H), 1.90～1.79 (m, 1H), 1.75～1.66 (m, 1H), 0.90 (t, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 202.5, 137.3, 133.1, 128.6, 128.2, 47.6, 35.7, 16.8, 11.4; HRMS (ESI) calcd for $C_{12}H_{16}NaO_2S$ [M+Na^+] 247.0763, found 247.0771.

1-(4-Chlorophenyl)-2-(methylsulfinyl)methyl)butan-1-one (**2o**): 73% yield (188 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.92 (d, J=8.8 Hz, 2H), 7.46 (d, J=8.8 Hz, 2H), 3.62～3.56 (m, 1H), 2.99 (dd, J=6.8, 13.2 Hz, 1H), 2.67 (dd, J=7.6, 13.2 Hz, 1H), 2.09 (s, 3H), 1.87～1.78 (m, 1H), 1.72～1.63 (m, 1H), 0.88 (d, J=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 201.7, 139.6, 135.7, 129.6, 129.0, 47.7, 35.7, 25.7, 16.6, 11.4; HRMS (ESI) calcd for $C_{12}H_{15}ClNaO_2S$ [M+Na^+] 281.0373, found 281.0379.

1-(2,4-Dichlorophenyl)-2-(methylsulfinyl)methyl)butan-1-one (**2p**): 73% yield (213 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.48～7.45 (m, 2H), 7.32 (dd, J=8.0, 1.6 Hz, 1H), 3.49～3.43 (m, 1H), 2.93 (dd, J=6.8, 13.2 Hz, 1H), 2.66 (dd, J=7.6, 13.2 Hz, 1H), 2.11 (s, 3H), 1.87～1.78 (m, 1H), 1.67～1.62 (m, 1H), 0.92 (t, J=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 203.9, 137.4, 137.1, 132.1, 130.5, 130.2, 127.2, 51.8, 34.7, 24.3, 16.5, 11.1; HRMS (ESI) calcd for $C_{12}H_{14}Cl_2NaO_2S$ [M+Na^+] 2314.9983, found 314.9985.

2-(Methylsulfinyl)methyl)-1-phenylpentan-1-one (**2q**): 71% yield (169 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.97 (d, J=8.4 Hz, 2H), 7.56 (t, J=7.6 Hz, 1H), 7.49 (t, J=7.6 Hz, 2H), 3.75～3.68 (m, 1H), 2.97 (br, 1H), 2.69 (br, 1H), 2.11 (s, 3H), 1.81～1.74 (m, 1H), 1.64～1.61 (m, 1H), 1.35～1.30 (m, 2H), 0.88 (t, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 203.0, 137.4, 133.1, 128.6, 128.2,

46.2, 36.2, 34.8, 29.6, 20.4, 14.1; HRMS (ESI) calcd for $C_{13}H_{18}NaO_2S$ [M+Na^+] 261.0919, found 261.0912.

1-(4-Chlorophenyl)-2-(methylsulfinyl)methyl)pentan-1-one (**2r**): 70% yield (190 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.92 (d, J=8.8 Hz, 2H), 7.46 (d, J=8.8 Hz, 2H), 3.68～3.62 (m, 1H), 2.93 (dd, J=6.8, 13.2 Hz, 1H), 2.66 (dd, J=7.6, 13.2 Hz, 1H), 2.09 (s, 3H), 1.79～1.72 (m, 1H), 1.65～1.55 (m, 1H), 1.34～1.28 (m, 2H), 0.88 (t, J=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 201.8, 139.2, 135.3, 129.6, 129.0, 46.2, 36.2, 34.9, 20.4, 16.6, 14.1; HRMS (ESI) calcd for $C_{13}H_{17}ClNaO_2S$ [M+Na^+] 295.0530, found 295.0534.

1-(2,4-Dichlorophenyl)-2-(methylsulfinyl)methyl)pentan-1-one (**2s**): 68% yield (208 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.48～7.45 (m, 2H), 7.33 (dd, J=8.0, 1.6 Hz, 1H), 3.55～3.49 (m, 1H), 2.93 (dd, J=6.8, 13.2 Hz, 1H), 2.65 (dd, J=7.6, 13.2 Hz, 1H), 2.10 (s, 3H), 1.80～1.71 (m, 1H), 1.38～1.28 (m, 3H), 0.89 (t, J=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 203.9, 137.4, 137.1, 133.6, 130.5, 130.2, 127.2, 50.4, 35.3, 35.5, 20.1, 16.6, 14.1; HR-MS (ESI) calcd for $C_{13}H_{16}Cl_2NaO_2S$ [M+Na^+] 329.0140, found 329.0148.

2-(Methylsulfinyl)methyl)-1-phenylbutan-1-one (**2t**): 61% yield (179 mg), a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 Hz) δ: 7.99 (d, J=8.4 Hz, 2H), 7.52 (t, J=7.6 Hz, 1H), 7.48 (t, J=7.6 Hz, 2H), 3.74～3.67 (m, 1H), 2.97 (br, 1H), 2.70 (br, 1H), 2.11 (s, 3H), 1.84～1.77 (m, 1H), 1.66～1.59 (m, 1H), 1.28～1.23 (m, 10H), 0.87 (t, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ: 202.2, 137.1, 133.0, 128.6, 128.2, 46.3, 36.2, 32.7, 31.7, 29.7, 29.6, 29.0, 27.1, 22.5, 14.0; HRMS (ESI) calcd for $C_{17}H_{26}NaO_2S$ [M+Na^+] 317.1546, found 317.1555.

4.3 Computational details

All the geometries were optimized with M062X functional at the level of 6-311+G(d,p).[19] The same level was used for the frequency and solvation calculations adopting the polarizable continuum model (PCM). The sum of electronic and zero-point energies were used for reactants, products and transition states (TS) to obtain the activation energy barriers. There is only one imaginary frequency for TS and zero for reactants and products. Internal reaction coordinate (IRC) calculations were carried out to verify correct TS. All the calculations were carried out in Gaussian 09 program suite.[20]

Supporting Information ^{1}H NMR and ^{13}C NMR spectra of all the new compounds. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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