JOC The Journal of Organic Chemistry

pubs.acs.org/joc Article

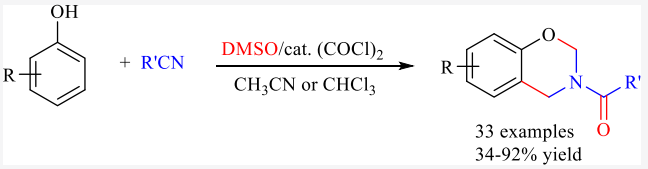
Convenient Preparation of *N*-Acylbenzoxazines from Phenols, Nitriles, and DMSO Initiated by a Catalytic Amount of $(COCl)_2$

Hao Wang, Zeyu Xi, Shuai Huang, Rui Ding, Yang Gao, Yongguo Liu, Baoguo Sun, Hongyu Tian,* and Sen Liang*

Cite This: *J. Org. Chem.* 2021, 86, 4932−4943 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: A convenient preparation method of *N*-acylbenzoxazines has been developed, in which phenols react with nitriles and dimethyl sulfoxide (DMSO) in the presence of a catalytic amount of $(COCl)_2$ in CH_3CN or chloroform to afford the corresponding *N*-acylbenzoxazines in moderate-to-good yields. DMSO acts as a source of HCHO, which is generated in situ from the decomposition of a methoxydimethylsulfonium salt. A regeneration cycle of the methoxydimethylsulfonium salt is proposed, which is initiated by a catalytic amount of $(COCl)_2$.



INTRODUCTION

Dimethyl sulfoxide (DMSO) is primarily utilized as a polar aprotic solvent due to its dissolvability for both polar and nonpolar compounds in organic synthesis. In addition, it is also employed widely as a versatile reagent for a variety of organic transformations, among which its role as a cheap and efficient oxidant should be the most well-known.[1] The application of DMSO as useful synthons has proliferated rapidly in recent years, which can act as sources of oxygen,[2] carbon,[3] or sulfur[4] in a wide range of organic reactions. Several reviews have been dedicated to the utility of DMSO as synthons in organic chemistry.[5]

A series of synthetic methods have been developed in our recent work about the application of the combination reagents of sulfoxide and oxalyl halide,[6] including sulfenyllactonization[6a] or chlorolactonization[6b] of alkenoic acids, bromination,[6c] sulfenylchlorination,[6d] or oxysulfenylation[6e] of alkenes, dehydration of primary amides or aldoximes,[6f] sulfenyletherification of alkenols,[6g] the preparation of unsaturated lactones from 3-alkenoic acids,[6h,i] and methylthiomethylation of carboxylic acids.[6j] During the investigation of oxysulfenylation of alkenes in CH_3CN with DMSO/$(COCl)_2$,[6e] an *N*-acetylbenzoxazine was obtained fortuitously when *p*-cresol was used as a nucleophile. In the following study, we tried to solve the riddle how the *N*-acetylbenzoxazine was formed. It was then discovered that DMSO can decompose in the presence of a catalytic amount of $(COCl)_2$ in CH_3CN under reflux to produce formaldehyde. The addition of phenols to the reaction mixture will lead to the formation of *N*-acetylbenzoxazines. Herein, we would like to share this convenient preparation method of *N*-acylbenzoxazines using DMSO as a source of methylene synthon.

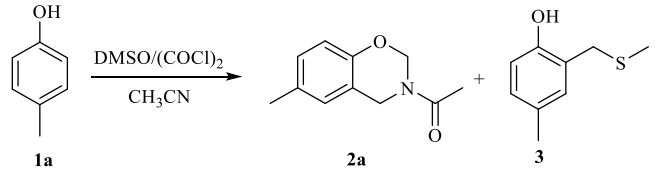
RESULTS AND DISCUSSION

Optimization of Conditions for the Formation of 6-Methyl *N*-Acetylbenzoxazine. 3,4-Dihydro-3-acetyl-6-methyl-2*H*-1,3-benzoxazine was obtained fortuitously as a major product instead of an oxysulfenylated product in our work about oxysulfenylation of alkenes[6e] when 3,3-dimethyl-1-butene was treated with DMSO/$(COCl)_2$ followed by a reaction with *p*-cresol in CH_3CN under reflux. A series of experiments were designed in order to figure out its formation pathway. The formation of benzoxazine in the reaction mixture was semiquantitatively analyzed by gas chromatography−mass spectrometry (GC/MS) with the internal standard method (Table 1). The first control experiment was undertaken referring to the conditions in oxysulfenylation of alkenes. The typical procedure was as follows: to a solution of DMSO (30 mmol, 6 equiv) in acetonitrile (20 mL) cooled at 0 °C was added dropwise a solution of oxalyl chloride (15 mmol, 3 equiv) in acetonitrile (10 mL). Then, *p*-cresol (**1a**) (5 mmol, 1 equiv) was added, and the reaction mixture was allowed to warm to room temperature and heated to reflux. The reaction mixture was monitored by GC/MS, and **1a** disappeared completely after refluxing for 2 h. 3,4-Dihydro-3-acetyl-6-methyl-2*H*-1,3-benzoxazine (**2a**) was found to be produced as the major product (31%) in the reaction mixture, along with a byproduct formed together, 4-methyl-2-methylthiomethylphenol (**3**) (16%) (entry 1, Table 1). When the reaction was tried to be carried out at room temperature with the other conditions the same as those in entry 1, neither **2a** nor

Received: November 18, 2020
Published: March 17, 2021

https://doi.org/10.1021/acs.joc.0c02768
J. Org. Chem. 2021, 86, 4932−4943

Table 1. Investigation on the Conditions for the Formation of *N*-Acetylbenzoxazine



1a 2a 3

entry	conditions	benzoxazine **2a** (yield[a]) (%)	by-product **3** (yield[a]) (%)
1	DMSO/$(COCl)_2$/*p*-cresol (6/3/1), 0 °C-reflux (2 h[b])	31	16
2	DMSO/$(COCl)_2$/*p*-cresol (6/3/1), 0 °C-rt (16 h)	0	0
3	DMSO/$(COCl)_2$/*p*-cresol (6/3/1), 0 °C-reflux (2 h[c]/1.5 h[d])	39	8
4	DMSO/$(COCl)_2$/*p*-cresol (6/0.6/1), 0 °C-reflux (3 h[c]/1.5 h[d])	85	0
5	DMSO/$(COCl)_2$/*p*-cresol (6/0.3/1), 0 °C-reflux (6 h[c]/1.5 h[d])	97	0
6	DMSO/$(COCl)_2$/*p*-cresol (4/0.2/1), 0 °C-reflux (6 h[c]/1.5 h[d])	47	0

[a]GC/MS determined. [b]The reaction mixture was warmed up to reflux after the addition of all the reactants at 0 °C. [c]The refluxing time before the addition of *p*-cresol. [d]The refluxing time after the addition of *p*-cresol.

the byproduct **3** was detected after stirring for 16 h (entry 2, Table 1). It was found by accident that the addition order of **1a** also had obvious impact on the formation of **2a** and the byproduct. The amount of **2a** increased (39%) and the byproduct reduced when the reaction mixture was refluxed for 2 h before the addition of **1a** (entry 3, Table 1). It is interesting to note that **2a** was formed in high yield (85%) and the byproduct was not observed when the DMSO/$(COCl)_2$ ratio increased from 2/1 to 10/1 (entry 4, Table 1). For this reaction, the mixture of DMSO/$(COCl)_2$ was heated to reflux for 3 h until DMSO disappeared and then **1a** was added. No byproduct was observed, and **2a** was produced in 97% yield when the DMSO/$(COCl)_2$ ratio increased further to 20/1 (entry 5, Table 1). It took 6 h for DMSO to be consumed completely before the addition of **1a**. The yield of **2a** reduced obviously (47%) when the DMSO/$(COCl)_2$/**1a** ratio decreased from 6/0.3/1 to 4/0.2/1 (entry 6, Table 1).

Investigation on Generality. The reactions of phenols, nitriles, and DMSO in the presence of a catalytic amount of $(COCl)_2$ were examined in order to investigate the generality of this method for the synthesis of benzoxazine. First, the reactions of a variety of phenols with CH_3CN were carried out according to the optimized conditions (entry 5, Table 1). As shown in Table 2, all the reactions proceeded well to give the corresponding benzoxazines in moderate-to-good yields. Both electron-donating and -withdrawing group-substituted phenols were converted to benzoxazines efficiently (**2a**−**h**). The reactions of *p*-*t*-butyl and *p*-phenyl phenol (**1c** and **1e**) produced benzoxazines **2c** and **2e** in relatively lower yields than **1a**, which might be due to the steric effect of the substituted group on the phenyl ring. Among three halo-substituted phenols (**1f**−**h**), the reaction of *p*-fluorophenol **1f** produced benzoxazine **2f** in the highest yield. However, no benzoxazine was formed in the reaction of *p*-nitrophenol. For the reaction of phenol **1i**, benzoxazine **2i** was produced in the lowest yield of 60%. A few oily drops were observed floating on the surface of the solvent, which was supposed to be polymers. In addition, 2-naphthol **1j** also reacted well to give benzoxazine **2j** in 77% yield. Likewise, 6-cyano-2-naphthol **1k** underwent the reaction smoothly to afford benzoxazine **2k** in 88% yield. Obviously, the cyano group in the substrate did not compete with acetonitrile in the formation of benzoxazine. 7-Hydroxycoumarin **1l** was converted to the corresponding benzoxazine **2l** in 75% yield, in which a little amount of byproduct at the β position was formed. In comparison, 4-methyl-7-hydroxycoumarin **1m** produced an about 2:1 mixture of benzoxazines **2m-1** and **2m-2** at the α and β positions, which was separated on column chromatography to afford **2m-1** in 45% yield and **2m-2** in 22% yield. In contrast, no reaction was observed when 4-hydroxycoumarin was treated under the same conditions.

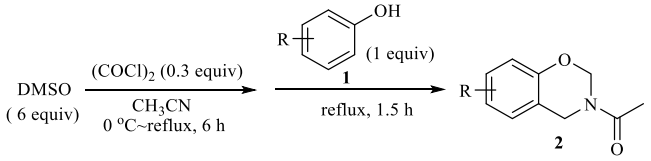
When DMSO-d_6 was used in the reaction, 3,4-dihydro-3-acetyl-6-methyl-2*H*-1,3-benzoxazine-d_4 (**2a**-d_4) was obtained in 83% yield. Meanwhile, 3,4-dihydro-3-acetyl-6-methyl-2*H*-1,3-benzoxazine-d_3 (**2a**-d_3) was obtained in 74% yield when CD_3CN was used with $CHCl_3$ as a solvent. Moreover, 3,4-dihydro-3-acetyl-6-methyl-2*H*-1,3-benzoxazine-d_7 (**2a**-d_7) was obtained in 80% isolated yield when CD_3CN and DMSO-d_6 were used in the reaction.

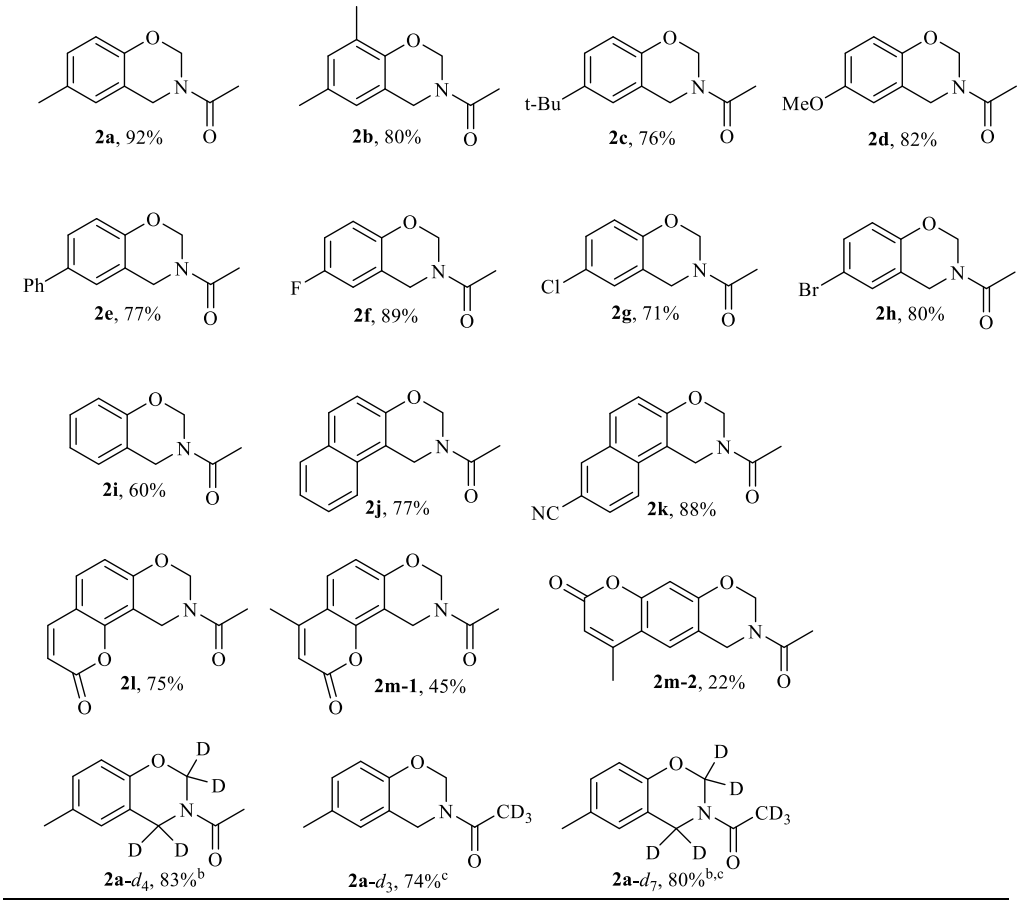
Butyronitrile and cyclopropyl cyanide were also explored as the source of nitrogen of benzoxazines (Table 3). In the abovementioned reactions, CH_3CN was used both as a reagent and solvent. For other nitriles involved in the following reactions, $CHCl_3$ was chosen as a solvent. The general procedure was as follows. To a solution of DMSO (30 mmol, 6 equiv) in $CHCl_3$ (20 mL) cooled at 0 °C was added dropwise a solution of oxalyl chloride (1.5 mmol, 0.3 equiv) in $CHCl_3$ (10 mL) and nitrile (25 mmol, 5 equiv) sequentially. The reaction mixture was allowed to warm to room temperature and heated to reflux for 6 h. Then, phenol (**1**) (5 mmol, 1 equiv) was added, and the mixture was continued to reflux for 1.5 h. For the reactions of butyronitrile, the electron-donating or -withdrawing group-substituted phenols (**1a**−**h**) were converted to the corresponding *N*-butyrylbenzoxazines (**2a′**−**h′**) in 34−65% yields, which were lower than the reactions of acetonitrile. The reaction of *p*-cresol (**1a**) with butyronitrile produced *N*-butyrylbenzoxazine **2a′** in a relatively higher yield of 65%. The reaction of phenol (**1i**) gave *N*-butyrylbenzoxazine **2i′** in 36% yield. 2-Naphthol (**1j**) was converted to *N*-butyrylbenzoxazine **2j′** in 49%. For the reactions of cyclopropyl cyanide, the corresponding *N*-cyclopropylcarbonylbenzoxazines (**2a″**−**j″**) were obtained in 47−90% yields. The reaction of *p*-cresol (**1a**) gave *N*-cyclopropylcarbonylbenzoxazine **2a″** in the highest yield of 90%, whereas phenol (**1i**) afforded *N*-cyclopropylcarbonylbenzoxazine **2i″** in the lowest yield of 47%. In comparison, the yields of the reactions of cyclopropyl nitrile were close to the reactions of CH_3CN.

To demonstrate the practicability of the reaction, a scale-up reaction of *p*-cresol **1a** (50 mmol, 5.4 g) with CH_3CN in the presence of DMSO (0.3 mol, 42.6 mL) with a catalytic amount of $(COCl)_2$ (15 mmol, 2.6 mL) in CH_3CN (150 mL) was

https://doi.org/10.1021/acs.joc.0c02768
J. Org. Chem. 2021, 86, 4932−4943

Table 2. Syntheses of *N*-Acetylbenzoxazines by the Reactions of Phenols with DMSO in the Presence of a Catalytic Amount of $(COCl)_2$ in CH_3CN[a]





[a]Conditions: to a solution of DMSO (30 mmol, 6 equiv) in acetonitrile (20 mL) cooled at 0 °C was added dropwise a solution of oxalyl chloride (1.5 mmol, 0.3 equiv) in acetonitrile (10 mL). After addition, the reaction mixture was allowed to warm to room temperature and heated to reflux for 6 h. Then, phenol (**1**) (5 mmol, 1 equiv) was added, and the mixture was continued to reflux for 1.5 h. The product was obtained by column chromatography. [b]The reaction was carried out with DMSO-d_6. [c]The reaction was carried out with CD_3CN in $CHCl_3$.

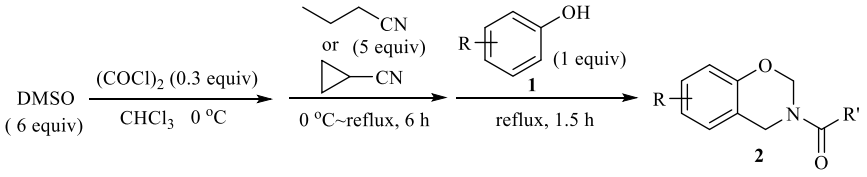
carried out under the optimized conditions. The product **2a** was obtained in 90% yield (8.5 g).

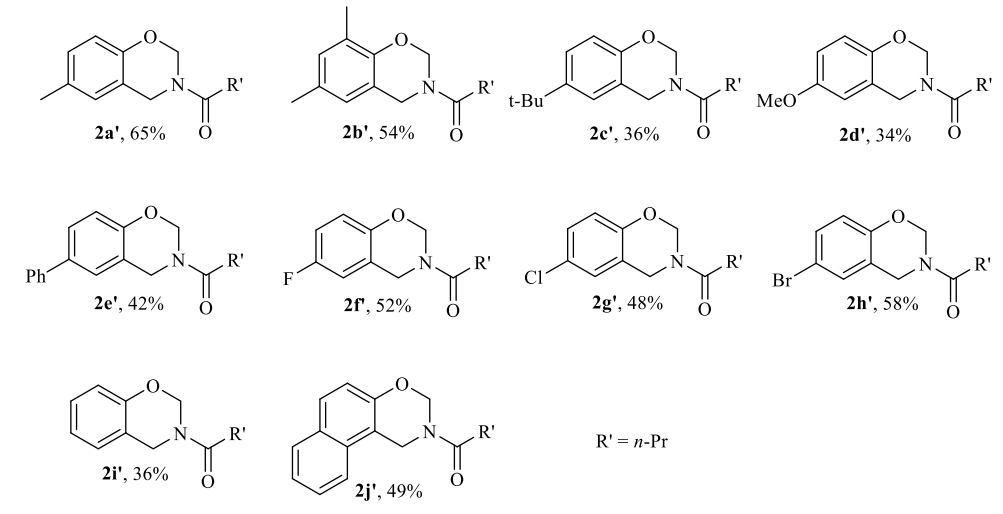
Proposed Mechanisms for the Formation of *N*-Acylbenzoxazines. The formation mechanism of benzoxazine was confusing at first. Some interesting outcomes were observed when 2,4-dimethylphenol (**1b**) was treated with DMSO/$(COCl)_2$ (a ratio of 2/1) at different temperatures (Scheme 1). 2,4-Dimethylphenol (**1b**) was converted to 2,4-dimethyl-6-methylthiomethylphenol (**4**) when the reaction was carried out at −65 °C in CH_2Cl_2 under the typical conditions of Swern oxidation. When the reaction was carried out in CH_3CN and warmed up to refluxing for 2 h after the addition of all the reactants at 0 °C, 2,4-dimethyl-6-methylthiomethylphenol (**4**) was also formed along with 3,4-dihydro-3-acetyl-6,8-dimethyl-2*H*-1,3-benzoxazine (**2b**) with a ratio of about 1/2.

The formation of 2,4-dimethyl-6-methylthiomethylphenol at −65 °C is easily understandable, which should be the same as thiomethoxymethylation of phenols with DMSO/Ac_2O or *N*,*N*′-dicyclohexylcarbodiimide.[7] It is well-known that the reaction of DMSO with $(COCl)_2$ generates an intermediate chlorodimethylsulfonium salt (**5**) very quickly, which is the key active species in Swern oxidation. Chlorodimethylsulfonium salt (**5**) is attacked by 2,4-dimethylphenol (**1b**) followed by an elimination to give a (2,4-dimethylphenyloxy)dimethylsulfonium salt (**6**), which is deprotonated followed by a [2,3] σ rearrangement and a tautomerization to produce 2,4-dimethyl-6-methylthiomethylphenol **4** (Scheme 2). Since the intermediate **5** is unstable above −65 °C, it is impossible that the formation of **4** under reflux in CH_3CN is through the reaction of **1b** with the intermediate **5**. However, it enlightened us that there should be an intermediate at reflux, which can act as an electrophile like the intermediate **5**. Therefore, another pathway for the formation of **4** is proposed as follows. When the reaction was carried out at higher temperature, excess DMSO attacks the methyl group of the chlorodimethylsulfonium salt **5** via a nucleophilic substitution leading to the formation of meth-

https://doi.org/10.1021/acs.joc.0c02768
J. Org. Chem. 2021, 86, 4932−4943

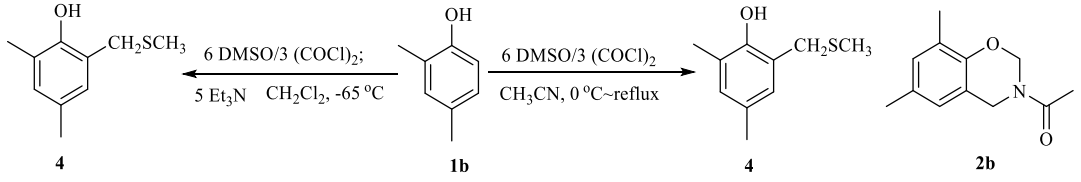
Table 3. Syntheses of *N*-Acylbenzoxazines by the Reactions of Phenols with Nitriles and DMSO in the Presence of a Catalytic Amount of $(COCl)_2$ in $CHCl_3$[a]





[a]Conditions: to a solution of DMSO (30 mmol, 6 equiv) in $CHCl_3$ (20 mL) cooled at 0 °C was added dropwise a solution of oxalyl chloride (1.5 mmol, 0.3 equiv) in $CHCl_3$ (10 mL) and nitrile (25 mmol, 5 equiv) sequentially. The reaction mixture was allowed to warm to room temperature and heated to reflux for 6 h. Then, phenol (**1**) (5 mmol, 1 equiv) was added and the mixture was continued to reflux for 1.5 h.

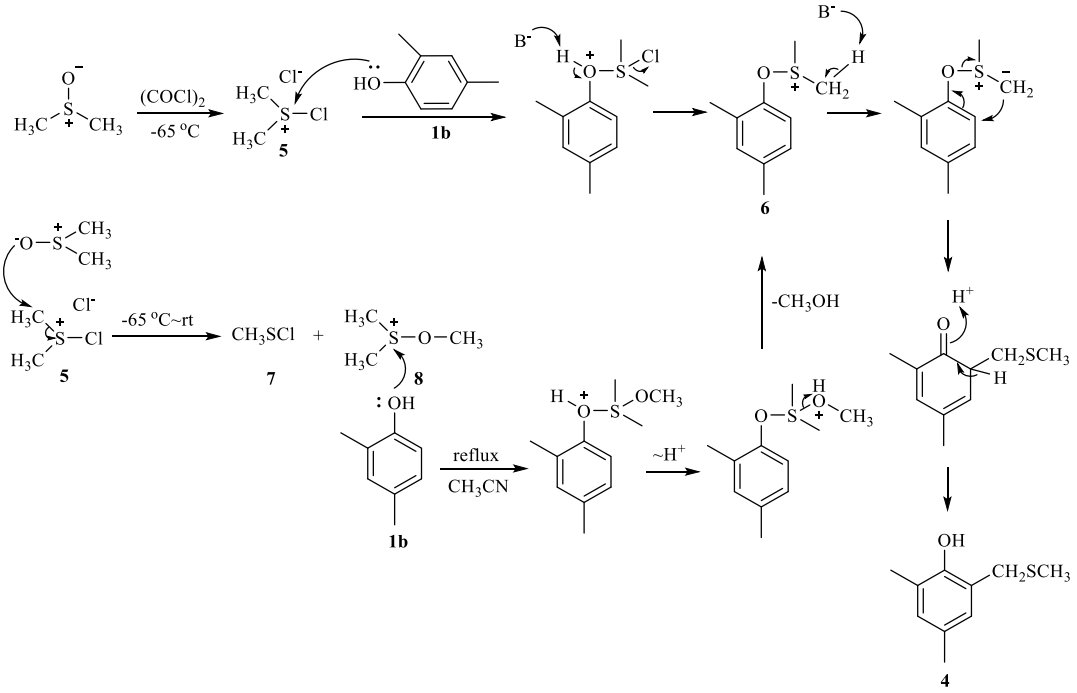
Scheme 1. Reactions of 2,4-Dimethylphenol with DMSO/$(COCl)_2$ at Different Temperatures



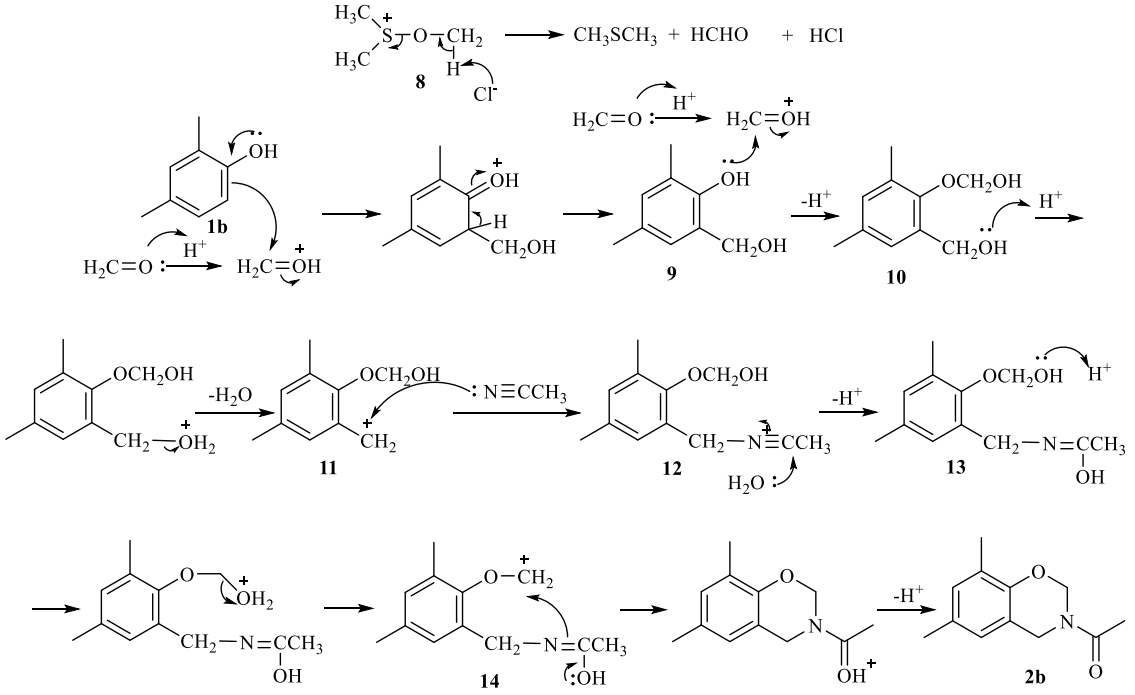
anesulfenyl chloride (**7**) and a methoxydimethylsulfonium salt (**8**), which was reported by Bellesia et al.[8] and also observed in our related work.[6] Just as the intermediate **5**, the intermediate methoxydimethylsulfonium salt (**8**) reacted with **1b** as an electrophile to give an adduct, which lost CH_3OH after a proton transfer to also generate the intermediate (**6**) leading to **4** as mentioned above (Scheme 2).

https://doi.org/10.1021/acs.joc.0c02768
J. Org. Chem. 2021, 86, 4932−4943

Scheme 2. Proposed Mechanisms for the Formation of 2,4-Dimethyl-6-methylthiomethylphenol4



Scheme 3. Proposed Mechanism for the Formation of *N*-Acetylbenzoxazine 2b



As for the formation of 3,4-dihydro-3-acetyl-6,8-dimethyl-2*H*-1,3-benzoxazine (**2b**), produced under reflux with **4** together, the possible pathway is proposed as follows (Scheme 3). The methoxydimethylsulfonium salt (**8**) can decompose to dimethyl sulfide and formaldehyde, which was observed in our previous work.[6g] Formaldehyde was deduced to be the key intermediate for the formation of benzoxazine. 2,4-Dimethylphenol (**1b**) underwent the Friedel−Crafts reaction with formaldehyde to give 2,4-dimethyl-6-hydroxymethylphenol (**9**), which reacted with another formaldehyde to produce 2-hydroxymethyloxy-3,5-dimethylbenzyl alcohol (**10**). The intermediate **10** lost H_2O after protonation to generate a benzyl cation **11**, which was attacked by the nitrogen of CH_3CN to form a nitrilium ion **12**. The nucleophilic addition of H_2O to the nitrilium ion **12** yielded the intermediate **13**, which was protonated and lost H_2O to produce a relatively stable carbocation **14**. Finally, an intramolecular nucleophilic attack on the carbocation led to ring closure to afford benzoxazine **2b**. Obviously, the formation pathway of benzoxazines is similar to the Ritter reaction.[9]

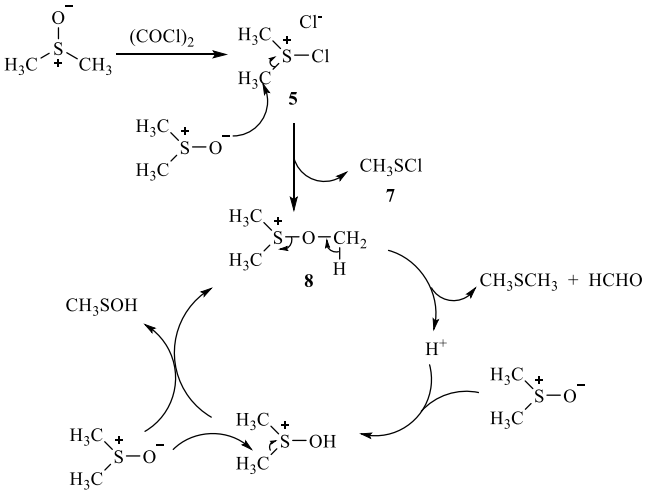
The speculation mentioned above indicated that the formation of both 2,4-dimethyl-6-methylthiomethylphenol (**4**)

https://doi.org/10.1021/acs.joc.0c02768
J. Org. Chem. 2021, 86, 4932−4943

and 3,4-dihydro-3-acetyl-6,8-dimethyl-2*H*-1,3-benzoxazine (**2b**) is related closely to the intermediate methoxydimethylsulfonium salt (**8**). There is a competition between the formation of **4** and benzoxazine **2b**. The results obtained in Table 1 are able to be explained based on the speculation. For the reactions of **1a**, benzoxazine **2a** was produced along with the methylthiomethylated byproduct **3** (entry 1, Table 1). When the reaction mixture was heated to reflux for a certain time before the addition of *p*-cresol, it promoted the decomposition of the intermediate methoxydimethylsulfonium salt (**8**) so that the amount of the methylthiomethylated byproduct **3** decreased (entry 3, Table 1). In addition, it needs higher temperature than room temperature whether the intermediate methoxydimethylsulfonium salt (**8**) decomposes to formaldehyde or acts as an electrophile since neither benzoxazine nor the byproduct was observed at room temperature (entry 2, Table 1).

However, how to explain the formation of benzoxazine **2a** in the presence of a catalytic amount of $(COCl)_2$ (entries 4−6, Table 1)? A regeneration cycle of the intermediate methoxydimethylsulfonium salt (**8**) is proposed, which was initiated by the reaction of DMSO with a catalytic amount of $(COCl)_2$ (Scheme 4). First, a catalytic amount of $(COCl)_2$ reacted with 2

Scheme 4. Proposed Mechanism for the Regeneration of the Methoxydimethylsulfonium Salt (8)



equiv of DMSO to form the intermediate methoxydimethylsulfonium salt (**8**) as discussed above, which decomposed to dimethyl sulfide, formaldehyde, and a proton H^+. The transfer of this proton H^+ to DMSO produced a hydroxydimethylsulfonium salt, which was then attacked by DMSO on the methyl group via a nucleophilic substitution to regenerate a methoxydimethylsulfonium salt (**8**) and release a methanesulfenic acid (CH_3SOH).

The mechanisms proposed above indicate that the formation of 1 equiv of benzoxazine requires 4 equiv of DMSO theoretically, which can explain why the formation of benzoxazine decreased with the reduced ratios of DMSO/*p*-cresol (entry 6, Table 1). The results obtained from DMSO-d_6 or/and CD_3CN were consistent with the speculation mentioned above (**2a**-d_4, **2a**-d_3, and **2a**-d_7, Table 2). For the reaction of *p*-nitrophenol, no benzoxazine was formed, which should be due to the strong deactivation of the nitro group.

The fact that DMSO acts as a methylene synthon can be dated back to Traynelis and Hergenrother's work in 1964, in which formaldehyde from the decomposition of DMSO upon prolonged reflux reacted with diols to form cyclic acetals or with amides to form methylenebisamides.[10] Many milder methods of transferring a methylene unit from DMSO have been developed recently, such as using DMSO with oxidants,[11] transition-metal catalysts,[12] or other activating agents.[13] The method in this present work provides an alternative approach to utilizing DMSO as a source of methylene synthon, which is easily operated and cost-efficient since only a catalytic amount of $(COCl)_2$ is needed.

CONCLUSIONS

In summary, *N*-acylbenzoxazines can be prepared from the reaction of phenols, nitriles, and DMSO in the presence of a catalytic amount of $(COCl)_2$. DMSO acts as a source of methylene synthon by generating HCHO in situ involved in the reactions. The methoxydimethylsulfonium salt is the key precursor for HCHO, which decomposes easily when heated. It is noteworthy that only a catalytic amount of $(COCl)_2$ is needed to initiate the reactions and the methoxydimethylsulfonium salt is able to be regenerated by a catalytic cycle.

EXPERIMENTAL SECTION

General Information. NMR spectra were obtained on a Bruker AV 300 spectrometer (^1H NMR at 300 MHz, $^{13}C\{^1H\}$ NMR at 75 MHz) in $CDCl_3$ using tetramethylsilane as an internal standard. Chemical shifts (δ) were given in ppm and coupling constants (J) in Hz. All the NMR peak assignments were confirmed by the correlation spectroscopy, heteronuclear single-quantum correlation spectroscopy, and heteronuclear multiple bond correlation spectra. High-resolution mass spectrometry (HRMS) data were obtained on a SolariX mass spectrometer or a Micromass GCT mass spectrometer. Thin-layer chromatography (TLC) was performed with precoated TLC plates, silica gel 60 F-254, with a layer thickness of 0.25 mm. Flash chromatography separations were performed on 200−400 mesh silica gel. Reagents and solvents are of commercial grade and were used as supplied. All the substrates (**1a**−**m**) are commercially available and were purchased from Sigma-Aldrich or Innochem.

General Procedure for Syntheses of *N*-Acetylbenzoxazines from Phenols and DMSO in CH_3CN with a Catalytic Amount of $(COCl)_2$. To a solution of DMSO (30 mmol, 6 equiv) in acetonitrile (20 mL) cooled at 0 °C was added dropwise a solution of oxalyl chloride (1.5 mmol, 0.3 equiv) in acetonitrile (10 mL). The mixture was stirred for 10 min at 0 °C. It was then allowed to warm to room temperature and heated to reflux in an oil bath for 6 h. Then, phenol (**1**) (5 mmol, 1 equiv) was added, and the reaction mixture was continued to reflux for 1.5−3 h. After cooling to room temperature, the reaction mixture was then concentrated on a rotary evaporator and the residue was redissolved in CH_2Cl_2 (100 mL). The resulting solution was washed with 1.0 M NaOH and brine. The organic phase was dried over sodium sulfate, filtered, and concentrated, and the residue was purified by flash chromatography on basic alumina (petroleum ether/EtOAc) to give *N*-acetylbenzoxazine (**2a**−**m**).

General Procedure for Syntheses of *N*-Acylbenzoxazines from Phenols, Nitriles, and DMSO in $CHCl_3$ with a Catalytic Amount of $(COCl)_2$. To a solution of DMSO (30 mmol, 6 equiv) in chloroform (20 mL) cooled at 0 °C was added dropwise a solution of oxalyl chloride (1.5 mmol, 0.3 equiv) in chloroform (10 mL). The mixture was stirred for 10 min at 0 °C. Butyronitrile or cyclopropyl cyanide (25 mmol, 5 equiv) was added. The reaction mixture was then allowed to warm to room temperature and heated to reflux in an oil bath for 6 h. Then, phenol (**1**) (5 mmol, 1 equiv) was added, and the reaction mixture was continued to reflux for 2.5−5 h. After cooling to room temperature, the reaction mixture was then concentrated on a rotary evaporator and the residue was redissolved in CH_2Cl_2 (100 mL). The resulting solution was washed with 1.0 M NaOH and brine. The organic phase was dried over sodium sulfate, filtered, and concentrated, and the

https://doi.org/10.1021/acs.joc.0c02768
J. Org. Chem. 2021, 86, 4932−4943

residue was purified by flash chromatography on basic alumina (petroleum ether/EtOAc) to give *N*-acetylbenzoxazine (**2a′−j′** and **2a″−j″**).

Analytical Data. *3,4-Dihydro-3-acetyl-6-methyl-2H-1,3-benzoxazine (**2a**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 101−102 °C, 879 mg, 92% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.99−6.74 (m, 3H, H−C-5, H−C-7 and H−C-8), 5.37 and 5.26 (s, 2H, H−C-2), 4.75 and 4.65 (s, 2H, H−C-4), 2.27 (s, 3H, H−CH_3), 2.24 and 2.19 (s, 3H, H−$COCH_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.4 (C═O), 151.7 and 151.4 (C-8a), 131.3 and 131.0 (C-5), 128.9 and 128.4 (C-6), 127.4 and 126.7 (C-7), 120.1 and 118.8 (C-4a), 117.3 and 116.8 (C-8), 75.1 and 70.7 (C-2), 45.7 and 42.0 (C-4), 21.8 and 20.9 (−CO$\underline{C}H_3$), 20.5 (C6−$\underline{C}H_3$); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{11}H_{14}NO_2$, 192.1019; found, 192.1019.

*3,4-Dihydro-3-acetyl-6,8-dimethyl-2H-1,3-benzoxazine (**2b**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). Colorless viscous oil, 820 mg, 80% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.80 and 6.77 (s, 1H, H−C-7), 6.66 (s, 1H, H−C-5), 5.34 and 5.23 (s, 2H, H−C-2), 4.68 and 4.58 (s, 2H, H−C-4), 2.22 and 2.20 (s, 3H, C−CH_3−C-6), 2.20 and 2.13 (s, 3H, H−$COCH_3$), 2.13 (s, 3H, C−CH_3−C-8); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.0 and 168.8 (C═O), 149.6 and 149.2 (C-8a), 130.1 and 129.8 (C-6), 129.7 and 129.3 (C-7), 126.0 and 125.5 (C-8), 124.4 and 123.8 (C-5), 119.2 and 118.0 (C-4a), 74.6 and 70.1 (C-2), 45.2 and 41.6 (C-4), 21.3 and 20.4 (−CO$\underline{C}H_3$), 20.1 (C6−$\underline{C}H_3$), 15.0 (C8−$\underline{C}H_3$); HRMS (ESI-ICR) m/z: [M + Na]$^+$ calcd for $C_{12}H_{15}NNaO_2$, 228.0995; found, 228.0995.

*4-Dihydro-3-acetyl-6-t-butyl-2H-1,3-benzoxazine (**2c**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). Light-yellow waxy solid, 885 mg, 76% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.21−7.14 (m, 1H, H−C-7), 7.06 (s, 1H, H−C-5), 6.83 and 6.79 (d, J = 9.0 Hz, 1H, H−C-8), 5.36 and 5.26 (s, 2H, H−C-2), 4.78 and 4.68 (s, 2H, H−C-4), 2.23 and 2.19 (s, 3H, H−CH_3CO), 1.29 and 1.27 (s, 9H, H−$C(CH_3)_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.3 (C═O), 151.6 and 151.1 (C-8a), 144.6 and 144.4 (C-6), 125.2 and 124.7 (C-7), 123.6 and 123.0 (C-5), 119.5 and 118.2 (C-4a), 116.9 and 116.4 (C-8), 75.0 and 70.4 (C-2), 45.8 and 42.1 (C-4), 34.0 (−$\underline{C}(CH_3)_3$), 31.3 (−$C(\underline{C}H_3)_3$), 21.7 and 20.8 (−CO$\underline{C}H_3$); HRMS (EI-TOF) m/z: [M]$^+$ calcd for $C_{14}H_{19}NO_2$, 233.1416; found, 233.1418.

*3,4-Dihydro-3-acetyl-6-methoxy-2H-1,3-benzoxazine (**2d**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). Yellow solid, mp = 56−57 °C, 849 mg, 82% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.81−6.65 (m, 2H, H−C-7 and H−C-8), δ 6.56 (d, J = 3 Hz, 1H, H−C-5), 5.31 and 5.20 (s, 2H, H−C-2), 4.72 and 4.62 (s, 2H, H−C-4), 3.71 (s, 3H, H−OCH_3), 2.20 and 2.15 (s, 3H, H−$COCH_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.3 (C═O), 154.3 and 154.2 (C-6), 147.8 and 147.3 (C-8a), 120.8 and 119.5 (C-4a), 118.1 and 117.6 (C-7 or C-8), 114.1 and 113.9 (C-8 or C-7), 111.2 and 110.8 (C-5), 75.0 and 70.5 (C-2), 55.5 (−O$\underline{C}H_3$), 45.6 and 42.0 (C-4), 21.7 and 20.8 (−CO$\underline{C}H_3$); HRMS (EI-TOF) m/z: [M]$^+$ calcd for $C_{11}H_{13}NO_3$, 207.0895; found, 207.0894.

*3,4-Dihydro-3-acetyl-6-phenyl-2H-1,3-benzoxazine (**2e**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 99−102 °C, 974 mg, 77% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51−7.49 (m, 2H, H−*o*-phenyl), 7.42−7.32 (m, 4H, H−*m*-phenyl and H−*p*-phenyl, H−C-7), 7.30−7.27 (m, 1H, H−C-5), 6.97 and 6.92 (d, J = 8.7 Hz, 1H, H−C-8), 5.41 and 5.29 (s, 2H, H−C-2), 4.84 and 4.72 (s, 2H, H−C-4), 2.25 and 2.20 (s, 3H, H−CH_3); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.4 (C═O), 153.4 and 153.0 (C-8a), 140.2 and 140.2 (C1−phenyl), 135.1 and 134.8 (C-6), 128.7 (C−*m*-phenyl), 126.9 (C-7), 126.6 (C−*o*-phenyl), 126.6 and 126.6 (C-5), 125.6 and 125.0 (C−*p*-phenyl), 120.6 and 119.3 (C-4a), 117.8 and 117.3 (C-8), 75.1 and 70.6 (C-2), 45.7 and 42.0 (C-4), 21.7 and 20.8 (−CO$\underline{C}H_3$); HRMS (EI-TOF) m/z: [M]$^+$ calcd for $C_{16}H_{15}NO_2$, 253.1103; found, 253.1100.

*3,4-Dihydro-3-acetyl-6-fluoro-2H-1,3-benzoxazine (**2f**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 85−86 °C, 868 mg, 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.84−6.76 (m, 3H, H−C-5, H−C-7 and H−C-8), 5.35 and 5.27 (s, 2H, H−C-2), 4.75 and 4.67 (s, 2H, H−C-4), 2.24 and 2.19 (s, 3H, H−$COCH_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.2 (C═O), 158.9 and 158.7 (C−F, $^1J_{C-F}$ = 240.0 Hz, C-6), 155.7 and 155.5 (C−F, $^1J_{C-F}$ = 240.0 Hz, C-6), 149.8 and 149.4 (C−F, $^4J_{C-F}$ = 1.5 Hz, C-8a), 121.4 and 120.0 (C−F, $^3J_{C-F}$ = 7.5 Hz, C-4a), 121.3 and 119.9 (C−F, $^3J_{C-F}$ = 7.5 Hz, C-4a), 118.5 and 118.0 (C−F, $^3J_{C-F}$ = 8.3 Hz, C-8), 118.3 and 117.9 (C−F, $^3J_{C-F}$ = 8.3 Hz, C-8), 115.0 and 114.6 (C−F, $^2J_{C-F}$ = 22.5 Hz, C-7), 114.7 and 114.3 (C−F, $^2J_{C-F}$ = 22.5 Hz, C-7), 113.1 and 112.6 (C−F, $^2J_{C-F}$ = 22.5 Hz, C-5), 112.8 and 112.3 (C−F, $^2J_{C-F}$ = 22.5 Hz, C-5), 74.9 and 70.4 (C-2), 45.3 and 41.6 (C-4), 21.5 and 20.6 (−CO$\underline{C}H_3$); HRMS (ESI-ICR) m/z: [M + Na]$^+$ calcd for $C_{10}H_{10}FNNaO_2$, 218.0588; found, 218.0589.

*3,4-Dihydro-3-acetyl-6-chloro-2H-1,3-benzoxazine (**2g**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 122−124 °C, 749 mg, 71% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.10−7.02 (m, 2H, H−C-5 and H−C-7), 6.82 and 6.75 (d, J = 9.0 Hz, 1H, H−C-8), 5.35 and 5.25 (s, 2H, H−C-2), 4.73 and 4.63 (s, 2H, H−C-4), 2.22 and 2.17 (s, 3H, H−$COCH_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.5 (C═O), 152.6 and 152.2 (C-8a), 128.4 and 127.9 (C-7), 126.9 and 126.8 (C-5), 126.5 and 126.3 (C-6), 122.0 and 120.6 (C-4a), 119.0 and 118.5 (C-8), 75.2 and 70.7 (C-2), 45.4 and 41.7 (C-4), 21.8 and 21.9 (−CO$\underline{C}H_3$); HRMS (ESI-ICR) m/z: [M + Na]$^+$ calcd for $C_{10}H_{10}ClNNaO_2$, 234.0292; found, 234.0294.

*3,4-Dihydro-3-acetyl-6-bromo-2H-1,3-benzoxazine (**2h**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 135−136 °C, 1024 mg, 80% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28−7.21 (m, 2H, H−C-5 and H−C-7), 6.81 and 6.73 (d, J = 9.0 Hz, 1H, H−C-8), 5.39 and 5.28 (s, 2H, H−C-2), 4.77 and 4.67 (s, 2H, H−C-4), 2.25 and 2.21 (s, 3H, H−$COCH_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.4 (C═O), 153.2 and 152.6 (C-8a), 131.3 and 130.8 (C-7), 129.8 and 129.2 (C-5), 122.4 and 121.0 (C-4a), 119.4 and 118.9 (C-8), 114.1 and 113.7 (C-6), 75.1 and 70.7 (C-2), 45.3 and 41.6 (C-4), 21.8 and 20.9 (−CO$\underline{C}H_3$); HRMS (EI-TOF) m/z: [M]$^+$ calcd for $C_{10}H_{10}BrNO_2$, 254.9895; found, 254.9890.

*3,4-Dihydro-3-acetyl-2H-1,3-benzoxazine (**2i**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). Yellow solid, mp = 55−57 °C, 531 mg, 60% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18−7.05 (m, 2H, H−C-6 and H−C-7), 6.99−6.85 (m, 2H, H−C-5 and H−C-8), 5.40 and 5.30 (s, 2H, H−C-2), 4.80 and 4.70 (s, 2H, H−C-4), 2.26 and 2.21 (s, 3H, H−$COCH_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.5 and 169.5 (C═O), 154.0 and 153.5 (C-8a), 128.3 and 127.8 (C-5), 127.2 and 126.5 (C-7), 121.9 and 121.6 (C-6), 120.4 and 119.1 (C-4a), 117.6 and 117.0 (C-8), 75.0 and 70.6 (C-2), 45.7 and 42.0 (C-4), 21.8 and 20.9 (−CO$\underline{C}H_3$); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{10}H_{12}NO_2$, 178.0863; found, 178.0860.

*2,3-Dihydro-2-acetyl-1H-naphth[1,2-e][1,3]oxazine (**2j**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). Yellow solid, mp = 60−64 °C, 874 mg, 77% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71−7.66 (m, 1H, H−C-8), 7.61−7.45 (m, 2H, H−C-5 and H−C-4), 7.44−7.31 (m, 2H, H−C-6 and H−C-7), 7.03 and 6.96 (d, J = 9.0 Hz, 1H, H−C-3), 5.38 and 5.20 (s, 2H, H−OCH_2N), 4.98 and 4.79 (s, 2H, H−CH_2N), 2.18 and 2.15 (s, 3H, H−$COCH_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.3 and 169.0 (C═O), 151.5 and 150.9 (C-2), 130.6 and 130.3 (C-4a), 128.8 and 128.7 (C-8a), 128.5 and 128.2 (C-4 or C-5), 128.4 and 128.1 (C-5 or C-4), 126.7 and 126.6 (C-7), 123.8 and 123.8 (C-6), 120.9 and 120.2 (C-8), 118.3 and 117.8 (C-3), 112.1 and 110.6 (C-1), 74.5 and 70.0 (−O$\underline{C}H_2$N), 43.4 and 39.9 (−$\underline{C}H_2$N), 21.6 and 20.6 (−CO$\underline{C}H_3$); HRMS (EI-TOF) m/z: [M]$^+$ calcd for $C_{14}H_{13}NO_2$, 227.0946; found, 227.0942.

*2,3-Dihydro-2-acetyl-8-cyano-1H-naphth[1,2-e][1,3]oxazine (**2k**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 179−180 °C, 1109 mg, 88% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 and 8.15 (s, 1H, H−C-1), 7.81−7.64 (m, 3H, H−C-4, H−C-8 and H−C-3), 7.23 and 7.18 (d, J = 9.0 Hz, 1H, H−C-7), 5.54 and 5.44 (s, 2H, H−OCH_2N), 5.13 and 5.01 (s, 2H, H−CH_2N), 2.33 and 2.31 (s, 3H, H−$COCH_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.4 (C═O), 154.4 and 153.6 (C-6), 134.4 and 134.2 (C-1), 132.6 and 132.3 (C-4a), 129.2 and 128.8 (C-8), 128.0 (C-8a), 127.6 and 127.5 (C-3), 122.4 and 121.7 (C-4), 120.7 and 120.1 (C-

https://doi.org/10.1021/acs.joc.0c02768
J. Org. Chem. 2021, 86, 4932−4943

7), 119.0 (−CN), 112.8 and 111.2 (C-5), 107.3 (C-2), 74.9 and 70.4 (−OCH$_2$N), 43.6 and 39.8 (−CH$_2$N), 21.9 and 20.9 (−COCH$_3$); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{15}H_{13}N_2O_2$, 253.0972; found, 253.0969.

*9-Acetyl-9,10-dihydrochromeno[8,7-e][1,3]oxazin-2(8H)-one (**2l**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 172−173 °C, 919 mg, 75% yield; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.02 and 7.99 (d, J = 9 Hz, 1H, H−C-4), 7.55 and 7.54 (d, J = 9 Hz, 1H, H−C-5), 6.91 and 6.89 (d, J = 9 Hz, 1H, H−C-6), 6.35 and 6.34 (d, J = 9 Hz, 1H, H−C-3), 5.53 and 5.40 (s, 2H, H−OCH$_2$N), 4.82 and 4.77 (s, 2H, H−CH$_2$N), 2.22 and 2.21 (s, 3H, H−COCH$_3$); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 170.0 (C═O), 160.2 (C-2), 157.1 and 156.9 (C-7), 151.7 and 151.7 (C-8a), 145.0 (C-4), 128.0 (C-5), 114.2 and 114.1 (C-8), 113.4 (C-3), 113.1 (C-6), 109.0 and 108.8 (C-6), 75.7 and 70.9 (−OCH$_2$N), 41.5 and 37.6 (−CH$_2$N), 22.2 and 21.2 (−COCH$_3$); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{13}H_{12}NO_4$, 246.0761; found, 246.0759.

*9-Acetyl-4-methyl-9,10-dihydrochromeno[8,7-e][1,3]oxazin-2(8H)-one (**2m-1**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 195−197 °C, 586 mg, 45% yield; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.59 and 7.57 (d, J = 9 Hz, 1H, H−C-5), 6.91 and 6.89 (d, J = 9 Hz, 1H, H−C-6), 6.24 (s, 1H, H−C-3), 5.52 and 5.39 (s, 2H, H−OCH$_2$N), 4.80 and 4.75 (s, 2H, H−CH$_2$N), 2.37 (s, 3H, H−CH$_3$), 2.21 (s, 3H, H−COCH$_3$); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 170.0 (C═O), 160.0 (C-2), 157.0 and 156.8 (C-7), 154.2 and 154.1 (C-4), 151.1 and 151.0 (C-8a), 124.9 and 124.8 (C-5), 113.9 and 113.8 (C-6 or C-4a), 113.8 and 113.7 (C-4a or C-6), 111.9 (C-3), 108.9 and 108.8 (C-8), 75.7 and 70.8 (−OCH$_2$N), 41.7 and 37.8 (−CH$_2$N), 22.2 and 21.3 (−COCH$_3$), 18.7 (−CH$_3$); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{14}H_{14}NO_4$, 260.0917; found, 260.0917.

*3-Acetyl-6-methyl-3,4-dihydrochromeno[6,7-e][1,3]oxazin-8(2H)-one (**2m-2**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 192−193 °C, 290 mg, 22% yield; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.64 and 7.62 (s, 1H, H−C-5), 6.88 and 6.87 (s, 1H, H−C-8), 6.23 (s, 1H, H−C-3), 5.53 and 5.41 (s, 2H, H−OCH$_2$N), 4.84 and 4.79 (s, 2H, H−CH$_2$N), 2.37 (s, 3H, H−CH$_3$), 2.19 and 2.15 (s, 3H, H−COCH$_3$); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 169.9 (C═O), 160.4 (C-2), 156.8 and 156.8 (C-7), 153.6 and 153.5 (C-8a), 153.3 and 153.2 (C-4a), 124.8 and 124.6 (C-5), 118.4 and 117.9 (C-6), 114.5 (C-4), 112.5 (C-3), 104.3 and 104.2 (C-8), 75.9 and 71.1 (−OCH$_2$N), 45.3 and 41.5 (−CH$_2$N), 22.0 and 21.2 (−COCH$_3$), 18.6 (−CH$_3$); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{11}H_7D_7NO_4$, 260.0917; found, 260.0919.

*3,4-Dihydro-3-acetyl-6-methyl-2H-1,3-benzoxazine (**2a**-d_4).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 102−103 °C, 809 mg, 83% yield. ^{1}H NMR (300 MHz, CDCl$_3$): δ 6.98−6.74 (m, 3H, H−C-5, H−C-7 and H−C-8), 2.28 and 2.26 (s, 3H, H−CH$_3$), 2.24 and 2.19 (s, 3H, H−COCH$_3$); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ 169.4 (C═O), 151.8 and 151.4 (C-8a), 131.3 and 131.0 (C-5), 128.9 and 128.4 (C-6), 127.4 and 126.7 (C-7), 119.9 and 118.6 (C-4a), 117.3 and 116.7 (C-8), 21.8 and 20.9 (−COCH$_3$), 20.5 (C6−CH$_3$); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{11}H_{10}D_4NO_2$, 196.1270; found, 196.1269.

*3,4-Dihydro-3-acetyl-6-methyl-2H-1,3-benzoxazine (**2a**-d_3).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 99−100 °C, 718 mg, 74% yield. ^{1}H NMR (300 MHz, CDCl$_3$): δ 6.99−6.74 (m, 3H, H−C-5, H−C-7 and H−C-8), 5.37 and 5.26 (s, 2H, H−C-2), 4.75 and 4.65 (s, 2H, H−C-4), 2.28 and 2.27 (s, 3H, H−CH$_3$); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ 169.5 (C═O), 151.8 and 151.3 (C-8a), 131.4 and 131.0 (C-5), 128.9 and 128.4 (C-6), 127.4 and 126.7 (C-7), 120.1 and 118.7 (C-4a), 117.3 and 116.8 (C-8), 75.1 and 70.6 (C-2), 45.6 and 42.0 (C-4), 20.5 (C6−CH$_3$); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{11}H_{11}D_3NO_2$, 195.1207; found, 195.1206.

*3,4-Dihydro-3-acetyl-6-methyl-2H-1,3-benzoxazine (**2a**-d_7).* It was purified by flash column chromatography (petroleum ether/EtOAc = 8:1). White solid, mp = 103−104 °C, 792 mg, 80% yield. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.02−6.73 (m, 3H, H−C-5, H−C-7 and H−C-8), 2.27 and 2.26 (s, 3H, H−CH$_3$); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ 169.4 (C═O), 151.8 and 151.3 (C-8a), 131.2 and 130.9 (C-5), 128.9 and 128.4 (C-6), 127.3 and 126.7 (C-7), 119.9 and 118.6 (C-4a), 117.2 and 116.7 (C-8), 20.5 and 20.4 (C6−CH$_3$); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{11}H_7D_7NO_2$, 199.1458; found, 199.1461.

*3,4-Dihydro-3-butyryl-6-methyl-2H-1,3-benzoxazine (**2a′**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). White solid, mp = 105−108 °C, 712 mg, 65% yield. ^{1}H NMR (300 MHz, CDCl$_3$): δ 6.97 and 6.94 (d, J = 9.0 Hz, 1H, H−C-7−benzoxazine), 6.88 and 6.86 (s, 1H, H−C-5−benzoxazine), 6.80 and 6.75 (d, J = 9.0 Hz, 1H, H−C-8−benzoxazine), 5.39 and 5.28 (s, 2H, H−C-2−benzoxazine), 4.76 and 4.65 (s, 2H, H−C-4−benzoxazine), 2.46 and 2.39 (t, J = 7.5 Hz, 2H, H−C-2), 2.27 (s, 3H, H−CH$_3$−benzoxazine), 1.75−1.68 (m, 2H, H−C-3), 0.99 (t, J = 7.5 Hz, 3H, H−C-4); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ 172.0 (C═O), 151.9 and 151.4 (C-8a−benzoxazine), 131.2 and 130.9 (C-6−benzoxazine), 128.9 and 128.4 (C-7−benzoxazine), 127.4 and 126.7 (C-5−benzoxazine), 120.3 and 118.9 (C-4a−benzoxazine), 117.3 and 116.7 (C-8−benzoxazine), 74.4 and 70.8 (C-2−benzoxazine), 45.0 and 42.1 (C-4−benzoxazine), 35.6 and 34.9 (C-2), 20.5 (CH$_3$−benzoxazine), 18.6 and 18.2 (C-3), 13.9 (C-4); HRMS (EI-TOF) m/z: [M]$^+$ calcd for $C_{13}H_{17}NO_2$, 219.1259; found, 219.1260.

*3,4-Dihydro-3-butylryl-6,8-dimethyl-2H-1,3-benzoxazine (**2b′**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). Colorless viscous oil, 629 mg, 54% yield. ^{1}H NMR (300 MHz, CDCl$_3$): δ 6.84 and 6.81 (s, 1H, H−C-7−benzoxazine), 6.72 and 6.70 (s, 1H, H−C-5−benzoxazine), 5.40 and 5.29 (s, 2H, H−C-2−benzoxazine), 4.74 and 4.64 (s, 2H, H−C-4−benzoxazine), 2.47 and 2.38 (t, J = 7.5 Hz, 2H, H−C-2), 2.23 (s, 3H, H−CH$_3$−C6−benzoxazine), 2.15 (s, 3H, H−CH$_3$−C8−benzoxazine), 1.78−1.66 (m, 2H, H−C-3), 0.99 and 0.98 (t, J = 7.5 Hz, 3H, H−C-4); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ 172.0 (C═O), 149.6 (C-8a−benzoxazine), 130.6 and 130.2 (C-6−benzoxazine), 130.1 and 129.6 (C-7−benzoxazine), 126.6 and 15.9 (C-5−benzoxazine), 124.8 and 124.1 (C-4a−benzoxazine), 119.7 and 118.3 (C-8−benzoxazine), 74.4 and 70.8 (C-2−benzoxazine), 45.1 and 42.1 (C-4−benzoxazine), 35.6 and 34.9 (C-2), 20.5 (CH$_3$−C-6−benzoxazine), 18.6 and 18.2 (C-3), 15.4 (CH$_3$−C-8−benzoxazine), 13.8 (C-4); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{14}H_{20}NO_2$, 234.1489; found, 234.1486.

*3,4-Dihydro-3-butylryl-6-t-butyl-2H-1,3-benzoxazine (**2c′**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). Light-yellow waxy solid, 470 mg, 36% yield. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.20 and 7.17 (d, J = 9.0 Hz, 1H, H−C-7−benzoxazine), 7.06 (s, 1H, H−C-5−benzoxazine), 6.84 and 6.79 (d, J = 9.0 Hz, 1H, H−C-8−benzoxazine), 5.39 and 5.29 (s, 2H, H−C-2−benzoxazine), 4.79 and 4.69 (s, 2H, H−C-4−benzoxazine), 2.46 and 2.40 (t, J = 7.5 Hz, 2H, H−C-2), 1.78−1.65 (m, 2H, H−C-3), 1.28 (s, 9H, H−C(CH$_3$)), 0.98 (t, J = 7.5 Hz, 3H, H−C-4); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ 171.9 and 171.8 (C═O), 151.7 and 151.2 (C-8a−benzoxazine), 144.5 and 144.3 (C-6−benzoxazine), 125.2 and 124.7 (C-7−benzoxazine), 123.7 and 123.0 (C-5−benzoxazine), 119.7 and 118.3 (C-4a−benzoxazine), 116.9 and 116.3 (C-8−benzoxazine), 74.3 and 70.7 (C-2−benzoxazine), 45.1 and 42.2 (C-4−benzoxazine), 35.5 and 34.8 (C-2), 34.0 (−C(CH$_3$)$_3$), 31.3 (−C(CH$_3$)$_3$), 18.4 and 18.0 (C-3), 13.8 (C-4); HRMS (ESI-ICR) m/z: [M + H]$^+$ calcd for $C_{16}H_{24}NO_2$, 262.1802; found, 262.1800.

*3,4-Dihydro-3-butylryl-6-methoxy-2H-1,3-benzoxazine (**2d′**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). Yellow viscous oil, 400 mg, 34% yield. ^{1}H NMR (300 MHz, CDCl$_3$): δ 6.79−6.66 (m, 2H, H−C-7−benzoxazine and H−C-8−benzoxazine), 6.57 (s, 1H, H−C-5−benzoxazine), 5.34 and 5.23 (s, 2H, H−C-2−benzoxazine), 4.74 and 4.64 (s, 2H, H−C-4−benzoxazine), 3.72 (s, 3H, H−OCH$_3$), 2.43 and 2.36 (t, J = 7.5 Hz, 2H, H−C-2), 1.75−1.63 (m, 2H, H−C-3), 0.96 (t, J = 7.5 Hz, 3H, H−C-4); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ 171.9 and 171.8 (C═O), 154.3 and 154.1 (C-6−benzoxazine), 147.9 and 147.4 (C-8a−benzoxazine), 121.0 and 119.7 (C-4a−benzoxazine), 118.1 and 117.6 (C-7−benzoxazine or C-8−benzoxazine), 114.1 and 113.9 (C-8−benzoxazine or C-7−benzoxazine), 111.2 and 110.9 (C-5−benzoxazine), 74.3 and 70.8 (C-2−benzoxazine), 55.5 (−OCH$_3$), 45.0 and 42.1 (C-4−benzox-

https://doi.org/10.1021/acs.joc.0c02768
J. Org. Chem. 2021, 86, 4932−4943

azine), 35.5 and 34.8 (C-2), 18.4 and 18.0 (C-3), 13.8 (C-4); HRMS (ESI-ICR) m/z: $[M + H]^+$ calcd for $C_{13}H_{18}NO_3$, 236.1281; found, 236.1283.

*3,4-Dihydro-3-butylryl-6-phenyl-2H-1,3-benzoxazine (**2e′**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). White solid, mp = 74−75 °C, 590 mg, 42% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51−7.49 (m, 2H, H−*o*-phenyl), 7.42−7.24 (m, 5H, H−*m*-phenyl, H−*p*-phenyl, H−C7− and H−C5−benzoxazine), 6.96 and 6.92 (d, J = 9.0 Hz, 1H, H−C8−benzoxazine), 5.44 and 5.32 (s, 2H, C2−benzoxazine), 4.85 and 4.73 (s, 2H, C4−benzoxazine), 2.47 and 2.40 (t, J = 7.5 Hz, 2H, H−C-2), 1.76−1.69 (m, 2H, H−C-3), 0.99 (t, J = 7.5 Hz, 3H, H−C-4); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.1 (C═O), 153.7 and 153.2 (C-8a−benzoxazine), 140.4 (C−*i*-phenyl), 135.2 and 134.8 (C6−benzoxazine), 128.8 (C−*m*-phenyl), 127.1 (C−*p*-phenyl), 126.8 (C−*o*-phenyl), 126.6 (C7−benzoxazine), 125.8 and 125.2 (C5−benzoxazine), 120.9 and 119.6 (C4a−benzoxazine), 118.0 and 117.4 (C8−benzoxazine), 74.6 and 71.0 (C2−benzoxazine), 45.2 and 42.2 (C4−benzoxazine), 35.7 and 35.0 (C-2), 18.6 and 18.2 (C-3), 14.0 (C-4); HRMS (ESI-ICR) m/z: $[M + H]^+$ calcd for $C_{18}H_{20}NO_2$, 282.1489; found, 282.1483.

*3,4-Dihydro-3-butylryl-6-fluoro-2H-1,3-benzoxazine (**2f′**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). White solid, mp = 56−58 °C, 580 mg, 52% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.82−6.76 (m, 3H, H−phenyl), 5.36 and 5.27 (s, 2H, H−C-2−benzoxazine), 4.75 and 4.65 (s, 2H, H−C-4−benzoxazine), 2.45 and 2.37 (t, J = 7.5 Hz, 2H, H−C-2), 1.73−1.63 (m, 2H, H−C-3), 0.97 (t, J = 7.5 Hz, 3H, H−C-4); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.0 and 171.9 (C═O), 159.1 and 158.9 (C−F, $^1J_{C-F}$ = 238.5 Hz, C-6−benzoxazine), 155.9 and 155.7 (C−F, $^1J_{C-F}$ = 238.5 Hz, C-6−benzoxazine), 150.1 and 149.6 (C−F, $^4J_{C-F}$ = 1.5 Hz, C-8a−benzoxazine), 121.6 and 120.2 (C−F, $^3J_{C-F}$ = 7.5 Hz, C-4a−benzoxazine), 121.6 and 120.1 (C−F, $^3J_{C-F}$ = 7.5 Hz, C-4a−benzoxazine), 118.7 and 118.1 (C−F, $^3J_{C-F}$ = 8.3 Hz, C-8−benzoxazine), 118.6 and 118.0 (C−F, $^3J_{C-F}$ = 8.3 Hz, C-8−benzoxazine), 115.2 and 114.8 (C−F, $^2J_{C-F}$ = 23.3 Hz, C-7−benzoxazine), 114.9 and 114.5 (C−F, $^2J_{C-F}$ = 23.3 Hz, C-7−benzoxazine), 113.4 and 112.7 (C−F, $^2J_{C-F}$ = 24.0 Hz, C-5−benzoxazine), 113.0 and 112.4 (C−F, $^2J_{C-F}$ = 23.5 Hz, C-5−benzoxazine), 74.4 and 70.8 (C-2−benzoxazine), 44.8 and 41.9 (C-4−benzoxazine), 35.5 and 34.8 (C-2), 18.4 and 18.1 (C-3), 13.8 (C-4); HRMS (EI-TOF) m/z: $[M]^+$ calcd for $C_{12}H_{14}FNO_2$, 223.1009; found, 223.1008.

*3,4-Dihydro-3-butylryl-6-chloro-2H-1,3-benzoxazine (**2g′**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). White solid, mp = 88−89 °C, 574 mg, 48% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.09−7.05 (m, 2H, H−C-5−benzoxazine and H−C-7−benzoxazine), 6.82 and 6.78 (d, J = 9.0 Hz, 1H, H−C-8−benzoxazine), 5.38 and 5.28 (s, 2H, H−C-2−benzoxazine), 4.75 and 4.65 (s, 2H, H−C-4−benzoxazine), 2.45 and 2.37 (t, J = 7.5 Hz, 2H, H−C-2), 1.73−1.64 (m, 2H, H−C-3), 0.97 (t, J = 7.5 Hz, 3H, H−C-4); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.0 and 171.9 (C═O), 152.7 and 152.1 (C-8a−benzoxazine), 128.3 and 127.8 (C-7−benzoxazine), 126.8 and 126.7 (C-5−benzoxazine), 126.3 and 126.2 (C-6−benzoxazine), 122.0 and 120.1 (C-4a−benzoxazine), 118.9 and 118.4 (C-8−benzoxazine), 74.4 and 70.9 (C-2−benzoxazine), 44.7 and 41.7 (C-4−benzoxazine), 35.5 and 34.8 (C-2), 18.4 and 18.1 (C-3), 13.8 (C-4); HRMS (ESI-ICR) m/z: $[M + H]^+$ calcd for $C_{12}H_{15}ClNO_2$, 240.0786; found, 240.0785.

*3,4-Dihydro-3-butylryl-6-bromo-2H-1,3-benzoxazine (**2h′**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). White solid, mp = 98−99 °C, 821 mg, 58% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28−7.21 (m, 2H, H−C-5−benzoxazine and H−C-7−benzoxazine), 6.78 and 6.74 (d, J = 9.0 Hz, 1H, H−C-8−benzoxazine), 5.40 and 5.30 (s, 2H, H−C-2−benzoxazine), 4.77 and 4.67 (s, 2H, H−C-4−benzoxazine), 2.46 and 2.37 (t, J = 7.5 Hz, 2H, H−C-2), 1.78−1.65 (m, 2H, H−C-3), 0.99 (t, J = 7.5 Hz, 3H, H−C-4); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 173.0 and 171.9 (C═O), 153.2 and 152.6 (C-8a−benzoxazine), 131.1 and 130.7 (C-7−benzoxazine), 129.8 and 129.1 (C-5−benzoxazine), 122.6 and 121.2 (C-4a−benzoxazine), 119.3 and 118.8 (C-8−benzoxazine), 114.0 and 113.5 (C-6−benzoxazine), 74.4 and 70.8 (C-2−benzoxazine), 44.6 and 41.6 (C-4−benzoxazine), 35.5 and 34.7 (C-2), 18.4 and 18.1 (C-3), 13.8 (C-4); HRMS (ESI-ICR) m/z: $[M + H]^+$ calcd for $C_{12}H_{15}BrNO_2$, 284.0281; found, 284.0280.

*3,4-Dihydro-3-butylryl-2H-1,3-benzoxazine (**2i′**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). Yellow solid, mp = 37−39 °C, 369 mg, 36% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.16−7.07 (m, 2H, H−C-7−benzoxazine and H−C-6−benzoxazine), 6.98−6.84 (m, 2H, H−C-5−benzoxazine and H−C-8−benzoxazine), 5.42 and 5.31 (s, 2H, H−C-2−benzoxazine), 4.80 and 4.69 (s, 2H, H−C-4−benzoxazine), 2.47 and 2.40 (t, J = 7.5 Hz, 2H, H−C-2), 1.76−1.68 (m, 2H, H−C-3), 0.99 (t, J = 7.5 Hz, 3H, H−C-4); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.0 (C═O), 154.1 and 153.5 (C-8a−benzoxazine), 128.2 and 127.7 (C-5−benzoxazine), 127.2 and 126.5 (C-7−benzoxazine), 121.8 and 121.5 (C-6−benzoxazine), 120.6 and 119.2 (C-4a−benzoxazine), 117.5 and 117.0 (C-8−benzoxazine), 74.4 and 70.8 (C-2−benzoxazine), 45.0 and 42.0 (C-4−benzoxazine), 35.6 and 34.9 (C-2), 18.5 and 18.1 (C-3), 13.8 (C-4); HRMS (ESI-ICR) m/z: $[M + H]^+$ calcd for $C_{12}H_{16}NO_2$, 206.1176; found, 206.1176.

*2,3-Dihydro-2-butyryl-1H-naphth[1,2-e][1,3]oxazine (**2j′**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). Yellow viscous oil, 625 mg, 49% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74−7.71 (m, 1H, H−C-8), 7.68−7.58 (m, 2H, H−C-5 and H−C-4), 7.48−7.32 (m, 2H, H−C-6 and H−C-7), 7.06 and 7.02 (d, J = 9.0 Hz, 1H, H−C-3), 5.46 and 5.30 (s, 2H, H−OCH_2N), 5.06 and 4.90 (s, 2H, H−CH_2N), 2.48 and 2.39 (t, J = 7.5 Hz, 2H, H−C-2), 1.75−1.66 (m, 2H, H−C-3), 0.98 (t, J = 7.5 Hz, 3H, H−C-4); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 171.8 (C═O), 151.9 and 151.2 (C-2−benzoxazine), 130.9 and 130.5 (C-4a−benzoxazine), 129.1 (C-8a−benzoxazine), 128.6 and 128.3 (C-4−benzoxazine or C-5−benzoxazine), 128.2 (C-5−benzoxazine or C-4−benzoxazine), 126.8 (C-7−benzoxazine), 124.0 (C-6−benzoxazine), 121.1 and 120.3 (C-8−benzoxazine), 118.6 and 118.0 (C-3−benzoxazine), 112.4 and 110.8 (C-1−benzoxazine), 74.1 and 70.5 (−O<u>C</u>H_2N), 43.0 and 40.2 (−<u>C</u>H_2N), 35.6 and 34.8 (C-2), 18.4 and 18.0 (C-3), 13.7 (C-4); HRMS (ESI-ICR) m/z: $[M + H]^+$ calcd for $C_{16}H_{18}NO_2$, 256.1332; found, 256.1334.

*3,4-Dihydro-3-cyclopropylcarbonyl-6-methyl-2H-1,3-benzoxazine (**2a″**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). White solid, mp = 77−78 °C, 977 mg, 90% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.95 (d, J = 7.5 Hz, 1H, H−C7−benzoxazine), 6.88 (s, 1H, H−C5−benzoxazine), 6.78 (d, J = 7.8 Hz, 1H, H−C8−benzoxazine), 5.48 and 5.38 (s, 2H, H−C2−benzoxazine), 4.87 and 4.76 (s, 2H, H−C4−benzoxazine), 2.27 (s, 3H, H−CH_3), 1.86 (br s, 1H, H−CH−cyclopropyl), 1.09−1.04 (m, 2H, H−CH_2−cyclopropyl), 0.88−0.82 (m, 2H, H′−CH_2−cyclopropyl); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.4 and 172.1 (C═O), 151.7 and 151.2 (C8a−benzoxazine), 130.7 (C6−benzoxazine), 128.4 and 128.0 (C7−benzoxazine), 127.0 and 126.6 (C5−benzoxazine), 120.0 and 118.9 (C4a−benzoxazine), 116.9 and 116.4 (C8−benzoxazine), 74.1 and 70.7 (C2−benzoxazine), 44.6 and 42.4 (C4−benzoxazine), 20.2 (−<u>C</u>H_3), 11.2 and 10.6 (−<u>C</u>H−cyclopropyl), 7.9 and 7.6 (−<u>C</u>H_2−cyclopropyl); HRMS (EI-TOF) m/z: $[M]^+$ calcd for $C_{13}H_{15}NO_2$, 217.1103; found, 217.1101.

*3,4-Dihydro-3-cyclopropylcarbonyl-6,8-dimethyl-2H-1,3-benzoxazine (**2b″**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). Colorless viscous oil, 739 mg, 64% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.74 (s, 1H, H−C-7), 6.67 and 6.62 (s, 1H, H−C-5), 5.42 and 5.32 (s, 2H, H−C-2), 4.77 and 4.66 (s, 2H, H−C-4), 2.18 and 2.12 (s, 6H, H−CH_3−benzoxazine), 1.84−1.78 (m, 1H, H−CH−cyclopropyl), 1.02−0.97 (m, 2H, H−CH_2−cyclopropyl), 0.81−0.75 (m, 2H, H′−CH_2−cyclopropyl); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 171.8 and 171.5 (C═O), 149.5 and 149.1 (C-8a), 129.6 (C-6), 129.2 and 128.9 (C-7), 125.5 and 125.1 (C-8), 124.0 and 123.7 (C-5), 119.0 and 118.1 (C-4a), 73.6 and 70.2 (C-2), 44.1 and 41.9 (C-4), 19.7 (−<u>C</u>H_3−C6), 14.7 (−<u>C</u>H_3−C8), 10.8 and 10.0 (−<u>C</u>H−cyclopropyl), 7.4 and 7.2 (−<u>C</u>H_2−cyclopropyl); HRMS (ESI-ICR) m/z: $[M + H]^+$ calcd for $C_{14}H_{18}NO_2$, 232.1332; found, 232.1329.

*3,4-Dihydro-3-cyclopropylcarbonyl-6-t-butyl-2H-1,3-benzoxazine (**2c″**).* It was purified by flash column chromatography (petroleum

https://doi.org/10.1021/acs.joc.0c02768
J. Org. Chem. 2021, 86, 4932−4943

ether/EtOAc = 15:1). Light-yellow waxy solid, 907 mg, 70% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.15−6.80 (m, 3H, H−C7−benzoxazine, H−C5−benzoxazine and H−C8−benzoxazine), 5.47 and 5.38 (s, 2H, H−C2−benzoxazine), 4.89 and 4.79 (s, 2H, H−C4−benzoxazine), 1.85 (br s, 1H, H−CH−cyclopropyl), 1.28 (s, 9H, H−*t*Bu), 1.04−1.03 (m, 2H, H−CH_2−cyclopropyl), 0.85−0.81 (m, 2H, H′−CH_2−cyclopropyl); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.3 (C═O), 151.7 and 151.2 (C8a−benzoxazine), 144.4 (C6−benzoxazine), 124.6 (C7−benzoxazine), 123.5 and 123.0 (C5−benzoxazine), 119.6 and 118.5 (C4a−benzoxazine), 116.8 and 116.3 (C8−benzoxazine), 74.2 and 70.8 (C2−benzoxazine), 44.9 and 42.8 (C4−benzoxazine), 33.9 (−C(CH_3)$_3$), 31.2 (−C(CH_3)$_3$), 11.4 and 10.7 (−CH−cyclopropyl), 8.0 and 7.7 (−CH_2−cyclopropyl); HRMS (EI-TOF) *m*/*z*: [M]$^+$ calcd for $C_{16}H_{21}NO_2$, 259.1572; found, 259.1568.

*3,4-Dihydro-3-cyclopropylcarbonyl-6-methoxy-2H-1,3-benzoxazine (**2d″**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). Yellow solid, mp = 70−71 °C, 851 mg, 73% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.80−6.59 (m, 2H, H−C-7 and H−C-8), 6.59 (s, 1H, H−C-5), 5.45 and 5.34 (s, 2H, H−C-2), 4.87 and 4.76 (s, 2H, H−C-4), 3.73 (s, 3H, H−OCH_3), 1.86 (br s, 1H, H−CH−cyclopropyl), 1.07−1.02 (m, 2H, H−CH_2−cyclopropyl), 0.87−0.81 (m, 2H, H′−CH_2−cyclopropyl); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.4 (C═O), 154.3 and 153.4 (C6−benzoxazine), 148.0 and 147.5 (C8a−benzoxazine), 121.0 and 119.9 (C4a−benzoxazine), 118.1 and 117.6 (C5−benzoxazine), 114.0 and 111.2 (C8−benzoxazine and C7−benzoxazine), 74.4 and 71.1 (C2−benzoxazine), 55.5 (−OCH_3), 44.9 and 42.8 (C4−benzoxazine), 11.5 and 10.8 (−CH−cyclopropyl), 8.2 and 7.8 (−CH_2−cyclopropyl); HRMS (ESI-ICR) *m*/*z*: [M + H]$^+$ calcd for $C_{13}H_{16}NO_3$, 234.1125; found, 234.1123.

*3,4-Dihydro-3-cyclopropylcarbonyl-6-phenyl-2H-1,3-benzoxazine (**2e″**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). White solid, mp = 131−134 °C, 837 mg, 60% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54−7.52 (m, 2H, H−*o*-phenyl), 7.45−7.40 (m, 3H, H−*m*-phenyl and H−*p*-phenyl), 7.35−7.31 (m, 2H, H−C7− and H−C5−benzoxazine), 6.97 (d, *J* = 9.0 Hz, 1H, H−C8−benzoxazine), 5.55 and 5.47 (s, 2H, C2−benzoxazine), 4.97 and 4.89 (s, 2H, C4−benzoxazine), 1.89 (br s, 1H, H−CH−cyclopropyl), 1.12−1.07 (m, 2H, H−CH_2−cyclopropyl), 0.91−0.85 (m, 2H, H′−CH_2−cyclopropyl); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.5 (C═O), 153.2 (C-8a−benzoxazine), 140.3 (C−*i*-phenyl), 135.0 (C6−benzoxazine), 128.7 (C−*m*-phenyl), 127.0 (C−*p*-phenyl), 126.7 (C−*o*-phenyl), 126.6 (C7−benzoxazine), 125.7 (C5−benzoxazine), 120.8 (C4a−benzoxazine), 117.4 (C8−benzoxazine), 74.6 and 71.2 (C2−benzoxazine), 45.1 and 42.8 (C4−benzoxazine), 11.0 (−CH−cyclopropyl), 8.0 (−CH_2−cyclopropyl); HRMS (EI-TOF) *m*/*z*: [M]$^+$ calcd for $C_{18}H_{17}NO_2$, 279.1259; found, 279.1261.

*3,4-Dihydro-3-cyclopropylcarbonyl-6-fluoro-2H-1,3-benzoxazine (**2f″**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). White solid, mp = 60−61 °C, 928 mg, 84% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.79−6.73 (m, 3H, H−C-5, H−C-7 and H−C-8), 5.45 and 5.33 (s, 2H, H−C-2), 4.85 and 4.74 (s, 2H, H−C-4), 1.84 (br s, 1H, H−CH−cyclopropyl), 1.03−1.00 (m, 2H, H−CH_2−cyclopropyl), 0.86−0.80 (m, 2H, H′−CH_2−cyclopropyl); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.1 (C═O), 158.6 (C−F, $^1J_{C-F}$ = 238.5 Hz, C-6), 155.4 (C−F, $^1J_{C-F}$ = 238.5 Hz, C-6), 149.8 and 149.4 (C-8a), 121.4 and 120.2 (C−F, $^3J_{C-F}$ = 6.2 Hz, C-4a), 121.3 and 120.3 (C−F, $^3J_{C-F}$ = 6.2 Hz, C-4a), 118.1 and 117.7 (C−F, $^3J_{C-F}$ = 7.1 Hz, C-8), 117.6 (C−F, $^3J_{C-F}$ = 7.1 Hz, C-8), 114.5 and 114.3 (C−F, $^2J_{C-F}$ = 21.5 Hz, C-7), 114.3 and 114.0 (C−F, $^2J_{C-F}$ = 21.5 Hz, C-7), 112.9 and 112.6 (C−F, $^2J_{C-F}$ = 23.9 Hz, C-5), 112.6 and 112.2 (C−F, $^2J_{C-F}$ = 23.9 Hz, C-5), 74.0 and 70.6 (C-2), 44.3 and 42.1 (C-4), 11.1 and 10.4 (−CH−cyclopropyl), 7.8 and 7.6 (−CH_2−cyclopropyl); HRMS (EI-TOF) *m*/*z*: [M]$^+$ calcd for $C_{12}H_{12}FNO_2$, 221.0852; found, 221.0855.

*3,4-Dihydro-3-cyclopropylcarbonyl-6-chloro-2H-1,3-benzoxazine (**2g″**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). White solid, mp = 102−103 °C, 936 mg, 79% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.12−7.07 (m, 2H, H−C-7 and H−C-5), 6.82−6.80 (m, 1H, H−C-8), 5.50 and 5.40 (s, 2H, H−C-2), 4.87 and 4.78 (s, 2H, H−C-4), 1.85 (br s, 1H, H−CH−cyclopropyl), 1.09−1.04 (m, 2H, H−CH_2−cyclopropyl), 0.90−0.84 (m, 2H, H′−CH_2−cyclopropyl); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.4 (C═O), 152.6 and 152.1 (C-8a), 128.0 and 127.7 (C-7), 126.6 and 126.5 (C-5), 126.3 (C-6), 121.9 and 120.8 (C-4a), 118.7 and 118.3 (C-8), 74.4 and 71.0 (C-2), 44.5 and 42.2 (C-4), 11.4 and 10.8 (−CH−cyclopropyl), 8.0 (−CH_2−cyclopropyl); HRMS (EI-TOF) *m*/*z*: [M]$^+$ calcd for $C_{12}H_{12}ClNO_2$, 237.0557; found, 237.0561.

*3,4-Dihydro-3-cyclopropylcarbonyl-6-bromo-2H-1,3-benzoxazine (**2h″**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). White solid, mp = 108−109 °C, 1012 mg, 72% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26−7.22 (m, 2H, H−C-7 and H−C-5), 6.77 (d, *J* = 9.0 Hz, 1H, H−C-8), 5.49 and 5.43 (s, 2H, H−C-2), 4.86 and 4.79 (s, 2H, H−C-4), 1.84 (br s, 1H, H−CH−cyclopropyl), 1.10−1.05 (m, 2H, H−CH_2−cyclopropyl), 0.90−0.84 (m, 2H, H′−CH_2−cyclopropyl); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.5 (C═O), 152.7 (C-8a), 130.7 (C-7), 129.7 (C-5), 122.5 and 121.4 (C-4a), 118.8 (C-8), 113.9 (C-6), 74.4 and 71.0 (C-2), 44.5 and 42.2 (C-4), 11.5 and 10.8 (−CH−cyclopropyl), 8.0 (−CH_2−cyclopropyl); HRMS (EI-TOF) *m*/*z*: [M]$^+$ calcd for $C_{12}H_{12}BrNO_2$, 281.0051; found, 281.0047.

*3,4-Dihydro-3-cyclopropylcarbonyl-2H-1,3-benzoxazine (**2i″**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). Yellow viscous oil, 477 mg, 47% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14−7.05 (m, 2H, H−C-6 and H−C-7), 6.97−6.85 (m, 2H, H−C-5 and H−C-8), 5.49 and 5.39 (s, 2H, H−C-2), 4.89 and 4.79 (s, 2H, H−C-4), 1.86 (br s, 1H, H−CH−cyclopropyl), 1.07−1.02 (m, 2H, H−CH_2−cyclopropyl), 0.87−0.81 (m, 2H, H′−CH_2−cyclopropyl); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.6 and 172.3 (C═O), 154.0 and 153.5 (C-8a), 127.9 and 127.6 (C-5), 127.0 and 126.5 (C-7), 121.6 (C-4a), 120.4 and 119.3 (C-6), 117.4 and 116.9 (C-8), 74.2 and 70.8 (C-2), 44.8 and 42.5 (C-4), 11.4 and 10.8 (−CH−cyclopropyl), 8.2 and 7.8 (−CH_2−cyclopropyl); HRMS (ESI-ICR) *m*/*z*: [M + H]$^+$ calcd for $C_{12}H_{14}NO_2$, 204.1019; found, 204.1015.

*2,3-Dihydro-2-cyclopropylcarbonyl-1H-naphth[1,2-e][1,3]oxazine (**2j″**).* It was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). Yellow waxy solid, 797 mg, 63% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76−7.74 (m, 1H, H−C-8), 7.651−7.62 (m, 2H, H−C-5 and H−C-4), 7.48−7.35 (m, 2H, H−C-6 and H−C-7), 7.07 and 7.04 (d, *J* = 9.0 Hz, 1H, H−C-3), 5.54 and 5.48 (s, 2H, H−OCH_2N), 5.16 and 5.09 (s, 2H, H−CH_2N), 1.94−1.86 (m, 1H, H−CH−cyclopropyl), 1.10−1.06 (m, 2H, H−CH_2−cyclopropyl), 0.88−0.84 (m, 2H, H′−CH_2−cyclopropyl); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 172.6 and 172.1 (C═O), 151.7 and 151.1 (C-2), 130.7 and 130.4 (C-4a), 129.0 and 128.8 (C-8a), 128.5 and 128.4 (C-4 or C-5), 128.2 and 128.1 (C-5 or C-4), 126.6 (C-7), 123.8 (C-6), 120.9 and 120.3 (C-8), 118.6 and 117.9 (C-3), 112.2 and 110.8 (C-1), 73.9 and 70.6 (−OCH_2N), 42.8 and 40.6 (−CH_2N), 11.5 and 10.7 (−CH−cyclopropyl), 8.1 and 7.7 (−CH_2−cyclopropyl); HRMS (ESI-ICR) *m*/*z*: [M + H]$^+$ calcd for $C_{16}H_{16}NO_2$, 254.1176; found, 254.1172.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02768.

Experimental procedures, product characterizations (^{1}H and ^{13}C NMR and HRMS), and copies of NMR and HRMS spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

Hongyu Tian − *Beijing Advanced Innovation Center for Food Nutrition and Human Health, Beijing Key Laboratory of Flavor Chemistry, Beijing Technology and Business University, Beijing 100048, China;* orcid.org/0000-0002-7117-6420; Email: tianhy@btbu.edu.cn; Fax: +8610 68984545

Sen Liang − *Beijing Advanced Innovation Center for Food Nutrition and Human Health, Beijing Key Laboratory of*

Flavor Chemistry, Beijing Technology and Business University, Beijing 100048, China; Email: liangsen@btbu.edu.cn

Authors

Hao Wang − *Beijing Advanced Innovation Center for Food Nutrition and Human Health, Beijing Key Laboratory of Flavor Chemistry, Beijing Technology and Business University, Beijing 100048, China*

Zeyu Xi − *Beijing Advanced Innovation Center for Food Nutrition and Human Health, Beijing Key Laboratory of Flavor Chemistry, Beijing Technology and Business University, Beijing 100048, China*

Shuai Huang − *Beijing Advanced Innovation Center for Food Nutrition and Human Health, Beijing Key Laboratory of Flavor Chemistry, Beijing Technology and Business University, Beijing 100048, China*

Rui Ding − *Beijing Advanced Innovation Center for Food Nutrition and Human Health, Beijing Key Laboratory of Flavor Chemistry, Beijing Technology and Business University, Beijing 100048, China*

Yang Gao − *Beijing Advanced Innovation Center for Food Nutrition and Human Health, Beijing Key Laboratory of Flavor Chemistry, Beijing Technology and Business University, Beijing 100048, China*

Yongguo Liu − *Beijing Advanced Innovation Center for Food Nutrition and Human Health, Beijing Key Laboratory of Flavor Chemistry, Beijing Technology and Business University, Beijing 100048, China*

Baoguo Sun − *Beijing Advanced Innovation Center for Food Nutrition and Human Health, Beijing Key Laboratory of Flavor Chemistry, Beijing Technology and Business University, Beijing 100048, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.0c02768

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors acknowledge financial support from the National Key Research and Development Program (2017YFB0307502).

■ REFERENCES

(1) (a) Epstein, W. W.; Sweat, F. W. Dimethyl sulfoxide oxidations. *Chem. Rev.* **1967**, *67*, 247−260. (b) Tidwell, T. T. Oxidation of alcohols by activated dimethyl sulfoxide and related reactions: an update. *Synthesis* **1990**, *1990*, 857−870. (c) Li, J. J.; Corey, E. J. *Name Reactions for Functional Group Transformations*; The Wiley Bicentennial-Knowledge for Generations: Canada, 2007; pp 291−308. (d) Reddy, P. N.; Reddy, B. V. S.; Padmaja, P. Emerging role of green oxidant I_2/DMSO in organic synthesis. *Curr. Org. Synth.* **2018**, *15*, 815−838. (e) Monga, A.; Bagchi, S.; Sharma, A. Iodine/DMSO oxidations: a contemporary paradigm in C−N bond chemistry. *New J. Chem.* **2018**, *42*, 1551−1576.

(2) (a) Liang, Y.-F.; Wu, K.; Song, S.; Li, X.; Huang, X.; Jiao, N. I_2- or NBS-Catalyzed highly efficient α-hydroxylation of ketones with dimethyl sulfoxide. *Org. Lett.* **2015**, *17*, 876−879. (b) Chebolu, R.; Bahuguna, A.; Sharma, R.; Mishra, V. K.; Ravikumar, P. C. An unusual chemoselective oxidation strategy by an unprecedented exploration of an electrophilic center of DMSO: a new facet to classical DMSO oxidation. *Chem. Commun.* **2015**, *51*, 15438−15441. (c) Cao, Z.; Lv, H.; Liu, Y.; Nie, Z.; Liu, H.; Yang, T.; Luo, W.; Liu, Q.; Guo, C. Dimethyl sulfoxide oxygen donor-based annulation of ketones and ammonium persulfate: regioselective synthesis of 2,4-disubstituted oxazoles. *Adv. Synth. Catal.* **2019**, *361*, 1632−1640. (d) Xu, R.; Wan, J.-P.; Mao, H.; Pan, Y. Facile synthesis of 2-(phenylthio)phenols by copper(I)-catalyzed tandem transformation of C−S coupling/C−H functionalization. *J. Am. Chem. Soc.* **2010**, *132*, 15531−15533. (e) Sultana, F.; Shaik, S. P.; Alarifi, A.; Srivastava, A. K.; Kamal, A. Transition-metal-free oxidative cross coupling of methylhetarenes with imidazoheterocycles towards efficient C(sp2)-H carbonylation. *Asian J. Org. Chem.* **2017**, *6*, 890−897.

(3) (a) Yao, B.; Song, R.-J.; Liu, Y.; Xie, Y.-X.; Li, J.-H.; Wang, M.-K.; Tang, R.-Y.; Zhang, X.-G.; Deng, C.-L. Palladium-catalyzed C-H oxidation of isoquinoline N-oxides: selective alkylation with dialkyl sulfoxides and halogenation with dihalo sulfoxides. *Adv. Synth. Catal.* **2012**, *354*, 1890−1896. (b) Jiang, X.; Wang, C.; Wei, Y.; Xue, D.; Liu, Z.; Xiao, J. A general method for N-methylation of amines and nitro compounds with dimethylsulfoxide. *Chem.—Eur. J.* **2014**, *20*, 58−63. (c) Lv, Y.; Li, Y.; Xiong, T.; Pu, W.; Zhang, H.; Sun, K.; Liu, Q.; Zhang, Q. Copper-catalyzed annulation of amidines for quinazoline synthesis. *Chem. Commun.* **2013**, *49*, 6439−6441. (d) Xie, Z.; Li, P.; Hu, Y.; Xu, N.; Wang, L. Visible-light-induced and iron-catalyzed methylation of N-arylacrylamides with dimethyl sulphoxide: a convenient access to 3-ethyl-3-methyl oxindoles. *Org. Biomol. Chem.* **2017**, *15*, 4205−4211. (e) Jiang, S.; Yang, Z.; Guo, Z.; Li, Y.; Chen, L.; Zhu, Z.; Chen, X. Transition metal-free α-methylation of 1,8-naphthyridine derivatives using DMSO as methylation reagent. *Org. Biomol. Chem.* **2019**, *17*, 7416−7424.

(4) (a) Yuan, G.; Zheng, J.; Gao, X.; Li, X.; Huang, L.; Chen, H.; Jiang, H. Copper-catalyzed aerobic oxidation and cleavage/formation of C-S bond: a novel synthesis of aryl methyl sulfones from aryl halides and DMSO. *Chem. Commun.* **2012**, *48*, 7513−7515. (b) Chu, L.; Yue, X.; Qing, F.-L. Cu(II)-mediated methylthiolation of aryl C-H bonds with DMSO. *Org. Lett.* **2010**, *12*, 1644−1647. (c) Gao, X.; Pan, X.; Gao, J.; Huang, H.; Yuan, G.; Li, Y. Ammonium iodide-induced sulfonylation of alkenes with DMSO and water toward the synthesis of vinyl methyl sulfones. *Chem. Commun.* **2015**, *51*, 210−212. (d) Sharma, P.; Rohilla, S.; Jain, N. Copper acetate-DMSO promoted methylthiolation of arenes and heteroarenes. *J. Org. Chem.* **2015**, *80*, 4116−4122. (e) Chalikidi, P. N.; Uchuskin, M. G.; Trushkov, I. V. V.; Abaev, T.; Serdyuk, O. V. Facile synthesis of β-keto sulfones employing Fenton's reagent in DMSO. *Synlett* **2018**, *29*, 571−575. (f) Chang, M.-Y.; Chen, H.-Y.; Tsai, Y.-L. NH_2OH-HCl-Mediated umpolung α-methylsulfonylation of α-sulfonyl ketones with methylsulfoxides: synthesis of α,β-bissulfonyl arylketones. *Org. Lett.* **2019**, *21*, 1832−1836.

(5) (a) Jones-Mensah, E.; Karki, M.; Magolan, J. Dimethyl sulfoxide as a synthon in organic chemistry. *Synthesis* **2016**, *48*, 1421−1436. (b) Wu, X.-F.; Natte, K. The applications of dimethyl sulfoxide as reagent in organic synthesis. *Adv. Synth. Catal.* **2016**, *358*, 336−352. (c) Tashrifi, Z.; Khanaposhtani, M. M.; Larijani, B.; Mahdavi, M. DMSO: yesterday's solvent, today's reagent. *Adv. Synth. Catal.* **2020**, *362*, 65−86.

(6) (a) Zhang, T.; Dai, Y.; Cheng, S.; Liu, Y.; Yang, S.; Sun, B.; Tian, H. A facile method for the sulfenyllactonization of alkenoic acids using dimethyl sulfoxide activated by oxalyl chloride. *Synthesis* **2017**, *49*, 1380−1386. (b) Ding, R.; Lan, L.; Li, S.; Liu, Y.; Yang, S.; Tian, H.; Sun, B. A novel method for the chlorolactonization of alkenoic acids Using diphenyl sulfoxide/oxalyl chloride. *Synthesis* **2018**, *50*, 2555−2566. (c) Ding, R.; Li, J.; Jiao, W.; Han, M.; Liu, Y.; Tian, H.; Sun, B. A highly efficient method for bromination of alkenes, alkynes, and ketones using dimethyl sulfoxide and oxalyl bromide. *Synthesis* **2018**, *50*, 4325−4335. (d) Lan, L.; Gao, Y.; Ding, R.; Zhang, T.; Liu, Y.; Sun, B.; Tian, H. A facile sulfenylchlorination of alkenes with $Me_2SO/(COCl)_2$. *Synth. Commun.* **2019**, *49*, 539−549. (e) Liu, Y.; Gao, Y.; Wang, Z.; Dong, J.; Ding, R.; Sun, B.; Tian, H. The oxysulfenylation of alkenes with dimethyl sulfoxide/oxalyl chloride. *Synth. Commun.* **2019**, *49*, 2662−2670. (f) Ding, R.; Liu, Y.; Han, M.; Jiao, W.; Li, J.; Tian, H.; Sun, B. Synthesis of nitriles from primary amides or aldoximes under conditions of a substoichiometric Swern oxidation. *J. Org. Chem.* **2018**, *83*, 12939−12944. (g) Gao, Y.; Cheng, S.; Zhang, T.; Ding, R.; Liu, Y.; Sun, B.; Tian, H. Dimethyl sulfoxide/oxalyl chloride: a useful reagent for sulfenyletherification. *Synth. Commun.* **2018**, *48*, 2773−2781. (h) Ding, R.; Li, Y.; Liu, Y.; Sun, B.; Yang, S.; Tian, H. Synthesis of butenolides by reactions of 3-alkenoic acids with diphenyl sulfoxide/

oxalyl chloride. *Flavour Fragrance J.* **2018**, *33*, 397−404. (i) Ding, R.; Liu, Y.; Liu, L.; Li, H.; Tao, S.; Sun, B.; Tian, H. A facile synthesis of γ-butenolides via cyclization of 3-alkenoic acids with dimethyl sulfoxide and oxalyl bromide. *Synth. Commun.* **2019**, *49*, 3001−3007. (j) Wang, Q.; Ding, R.; Huang, S.; Liu, Y.; Sun, B.; Tian, H. Preparation and odor characteristics of methylthiomethyl carboxylates. *Flavour Fragrance J.* **2020**, *35*, 302−308.

(7) (a) Pfitzner, K. E.; Marino, J. P.; Olofson, R. A. The reactions of phenols with oxysulfonium cations. *J. Am. Chem. Soc.* **1965**, *87*, 4658−4659. (b) Hayashi, Y.; Oda, R. Thiomethoxymethylation of phenols by dimethyl sulfoxide and acetic anhydride. *J. Org. Chem.* **1967**, *32*, 457−458.

(8) Bellesia, F.; Boni, M.; Ghelfi, F.; Pagnoni, U. M.; Pinetti, A. β-Chloroalkyl sulfides from $Me_2S/SO_2Cl_2/Me_2SO$ and alkenes. *Synth. Commun.* **1992**, *22*, 1101−1108.

(9) (a) Ritter, J. J.; Minieri, P. P. A new reaction of nitriles. I. Amides from alkenes and mononitriles. *J. Am. Chem. Soc.* **1948**, *70*, 4045−4048. (b) Ritter, J. J.; Kalish, J. A new reaction of nitriles. II. Synthesis of *t*-carbinamines. *J. Am. Chem. Soc.* **1948**, *70*, 4048−4050.

(10) Traynelis, V. J.; Hergenrother, W. L. Decomposition of dimethyl sulfoxide aided by ethylene glycol, acetamide, and related compounds. *J. Org. Chem.* **1964**, *29*, 221−222.

(11) (a) Wang, J.; Rochon, F. D.; Yang, Y.; Hua, L.; Kayser, M. M. Synthesis of oxazolidines using $DMSO/P_4O_{10}$ as a formaldehyde equivalent. *Tetrahedron: Asymmetry* **2007**, *18*, 1115−1123. (b) Patel, O. P. S.; Anand, D.; Maurya, R. K.; Yadav, P. P. H_2O_2/DMSO-promoted regioselective synthesis of 3,3'-bisimidazopyridinylmethanes via intermolecular oxidative C(sp(2))-H bond activation of imidazo-heterocycles. *J. Org. Chem.* **2016**, *81*, 7626−7634. (c) Mahajan, P. S.; Tanpure, S. D.; More, N. A.; Gajbhiye, J. M.; Mhaske, S. B. Ammonium persulfate activated DMSO as the one-carbon synthon for the synthesis of methylenebisamides and other applications. *RSC Adv.* **2015**, *5*, 101641−101646.

(12) (a) Ai, H.-J.; Qi, X.; Peng, J.-B.; Ying, J.; Wu, X.-F. Palladium-catalyzed cross-coupling of arylboronic acid and benzonitriles with DMSO as the methylene source. *Asian J. Org. Chem.* **2018**, *7*, 2045−2048. (b) Sun, K.; Lv, Y.; Zhu, Z.; Zhang, L.; Wu, H.; Liu, L.; Jiang, Y.; Xiao, B.; Wang, X. Oxidative C-S bond cleavage reaction of DMSO for C-N and C-C bond formation: New Mannich-type reaction for β-amino ketones. *RSC Adv.* **2015**, *5*, 3094−3097.

(13) Wang, Q.; Sun, L.; Jiang, Y.; Li, C. Synthesis of methylenebisamides using CC- or DCMT-activated DMSO. *Beilstein J. Org. Chem.* **2008**, *4*, 51.

https://doi.org/10.1021/acs.joc.0c02768
J. Org. Chem. 2021, 86, 4932−4943