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Formal [3+2] Cycloaddition of Nitrosoallenes with Carbonyl and Nitrile Compounds to Form Functional Cyclic Nitrones

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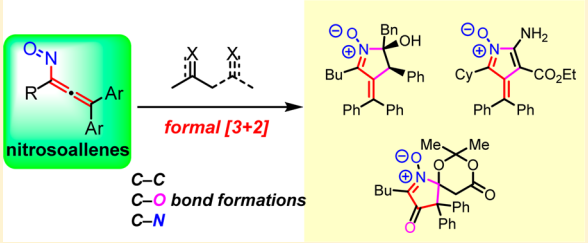
Supporting Information

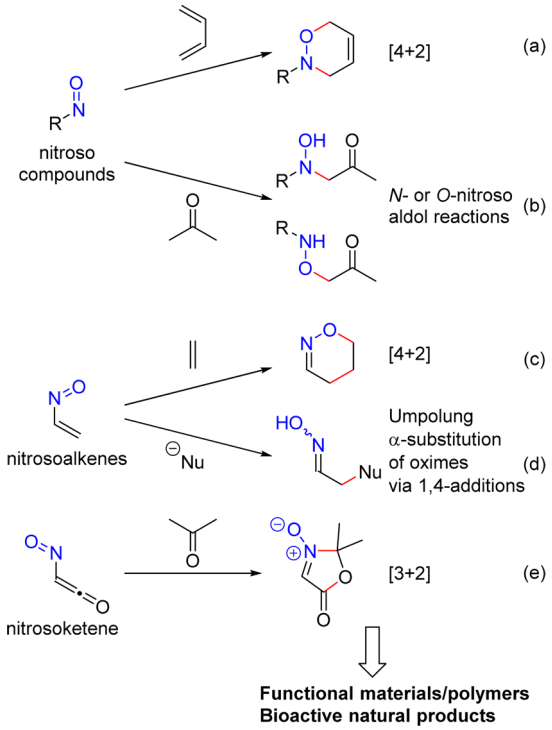
ABSTRACT: The synthesis of functional cyclic nitrones via [3+2] cycloadditions of allenamide-derived nitrosoallenes with carbonyl/nitrile compounds, including ketones, esters, and nitriles, is presented herein. Rapid carbon−carbon, carbon−oxygen, and carbon−nitrogen bond formations were achieved with *in situ* prepared nitrosoallenes, and densely substituted oxacyclic and carbocyclic nitrones containing tetrasubstituted carbon centers were successfully synthesized. The spirocyclic nitrone products synthesized from cyclic dicarbonyl compounds underwent the unique skeletal rearrangements to cyclic α-ketonitrones.



INTRODUCTION

The development of methodologies that employ reactive species, which enable the synthesis of valuable molecules because of their unique reactivity is of great importance in synthetic organic chemistry. Among them, nitroso compounds are well-known to be highly fascinating reactive species due to their strong electron-withdrawing ability.[1,2] The behavior of nitroso compounds has been widely studied because of the ease with which they form nitrogen-containing compounds as a result of their unique reactivity (Scheme 1). Thus, to date, a variety of *C*-nitroso compounds have been applied to the syntheses of various alkaloids and heterocycles.[3−8] Conventional nitroso molecules, including acyl nitroso compounds, are one of the most studied nitroso groups to date. These compounds undergo [4+2] cycloadditions with dienes to afford 3,4-dihydro-2*H*-oxazines (Scheme 1a).[3] Moreover, because of the efficiency of α-hydroxyamino- and α-aminoxy carbonyl compounds, nitroso compounds, especially aryl nitroso and alkoxycarbonyl nitroso compounds, have been utilized in nitroso aldol reactions (Scheme 1b).[4] The selective carbon−nitrogen or carbon−oxygen bond formations can be carried out in asymmetric metal- and organo-catalyzed reactions. With nitrosoalkenes as diene units, [4+2] cycloaddition can deliver 1,2-oxazines (5,6-dihydro-4*H*-oxazines) that are different from those derived from simple nitroso compounds (Scheme 1c).[5] These nitrosoalkenes also allow the umpolung α-substitution of ketones and oximes with nucleophiles through 1,4-addition. Thus, these reactions have been applied to the synthesis of natural products (Scheme 1d).[6] Although nitroso compounds conjugated with sp-carbon atoms are rare,[2a−c,7] Kaneko et al. reported a nitrosoketene that undergoes a formal [3+2] cycloaddition with ketones (Scheme 1e).[8a−c] Although the reaction mechanism is still under discussion,[8d−f] the afforded butenolide-like cyclic nitrones were also demonstrated as efficient precursors of α-amino acids through further [3+2] cycloaddition reactions. Because of the unique molecular

Scheme 1. Nitroso Compounds and Their Reactions



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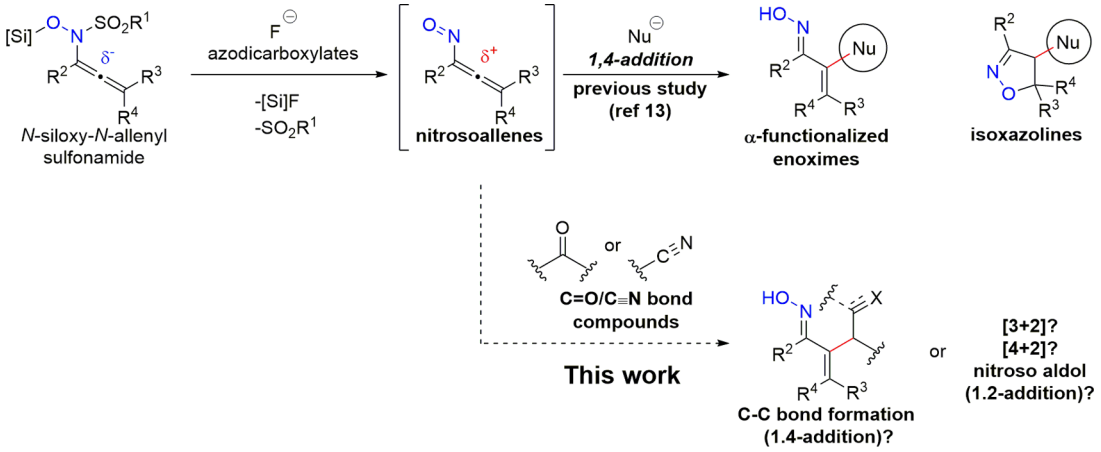
Scheme 2. Outline of the Synthetic Pathways, Including Nitrosoallene-Mediated Synthesis, in This Work



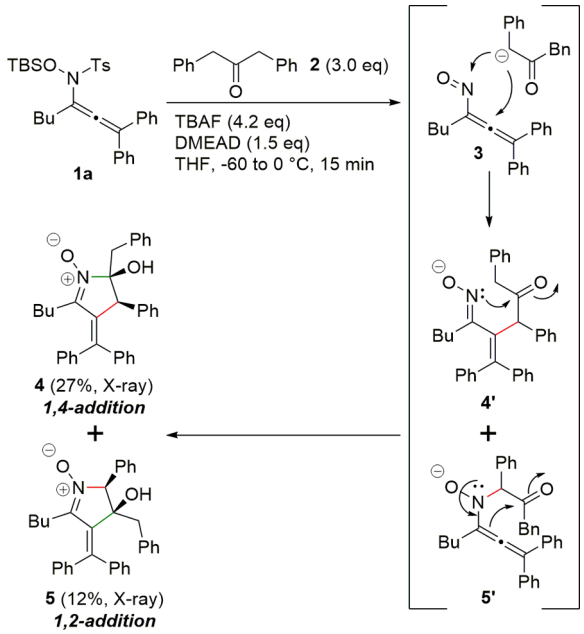
transformation ability of nitroso species, we believe that the effect of their strong reactivity on the synthesis of heterocycles should be explored. The use of these novel nitroso functional compounds is envisioned in the development of new synthetic procedures that supply nitrogen−containing functional molecules, especially heterocycles toward functional materials and bioactive molecules. Moreover, nitrones have long been known as versatile intermediates in organic synthesis, and have been in reported various reactions including concerted cycloadditions.[9−12]

Very recently, we reported the nitrosoallene-mediated synthesis of α-functionalized enoximes representing the umpolung reactivity of allenamides (Scheme 2).[13] These nitrosoallenes demonstrated very unique reactivities to produce α-functionalized enoximes and isoxazolines through 1,4-additions of the nucleophiles.[14] Additionally, the nature of nitrosoallenes were found to be distinct from those of known nitroso compounds. These favorable results encouraged us to further investigate other possible synthetic pathways that these novel reactive species may undergo to form polycyclic compounds. Thus, following the outcome of previous research on nitrosoalkenes and nitrosoketenes,[6,8] new reactivity patterns between the current nitrosoallenes and carbonyl compounds were predicted. Hence, nitrogen-containing compounds were expected to be formed by carbon−carbon bond formation through 1,4-additions, and by nitroso aldol reactions through 1,2-additions, as well as [3+2] and [4+2] reactions. Moreover, as demonstrated in our previous study,[13] synthetic methods using nitrosoallenes can be performed under mild conditions, and can be completed in a short period of time, due to the strong reactivities of these compounds. To further reveal the potential of these novel nitrosoallenes, we herein report the addition reactions of nitrosoallenes with carbonyl/nitrile compounds to produce cyclic nitrones, and investigate their reaction patterns through DFT calculations. We also examine the skeletal rearrangement of the afforded spirooxacyclic nitrones to spiro- and bicyclic α-ketonitrones.

RESULTS AND DISCUSSION

Based on the preceding examples of nitroso-utilizing reactions, especially those with nitrosoalkenes and nitrosoketenes (Scheme 1d,e), we initially tested the reactions of nitrosoallenes with monoketone compounds. As established in our previous study,[13] the nitrosoallenes were prepared by TBAF in the presence of the azodicarboxylate reagent dimethoxyethyl azodicarboxylate (DMEAD),[15] a scavenger of the *in situ* generated sulfinates. Acetophenone or cyclohexanone of simple ketones did not produce any adducts in the presence or absence of base reagents, as reported in cases with nitrosoalkenes.[6f] Instead, cycloaddition reactions forming carbon−oxygen and carbon−nitrogen bonds proceeded with nitrosoketenes (Scheme 1e).[8a,b] On the other hand, with dibenzyl ketone **2**, the addition reaction of nitrosoallene **3** from **1a** successfully proceeded to afford carbocyclic nitrones **4** and **5**. These were produced from 1,4- and 1,2-additions to **3**, respectively (Scheme 3). Thus,

Scheme 3. Cycloaddition Reactions with Ketones



1,4-addition product **4** could be synthesized as a cyclic nitrone through **4′**. The oxacyclic nitrone products afforded with nitrosoketenes (Scheme 1e)[8] were not afforded in this case. Although the product yields were fair, we accomplished carbon−carbon bond formation with a ketone and *C*-nitroso species. We postulated that this success was due to the pK_a values of the hydrogen atom at the α-position of the ketones (pK_a = 19 for **2**, and acetophenone pK_a = 25 and 26 for acetophenone and cyclohexanone in DMSO, respectively).[16] Therefore, we opted to use 1,3-diketones and β-ketoesters because of their more acidic α-hydrogen atoms (Scheme 4).

With 1,3-cyclohexanediones **6a** and **6c** (pK_a = 10 in DMSO for 1,3-cyclohexanedione),[16] when the reaction was performed

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Scheme 4. Cycloaddition Reactions with Cyclic 1,3-Diketones and Their Skeletal Rearrangements

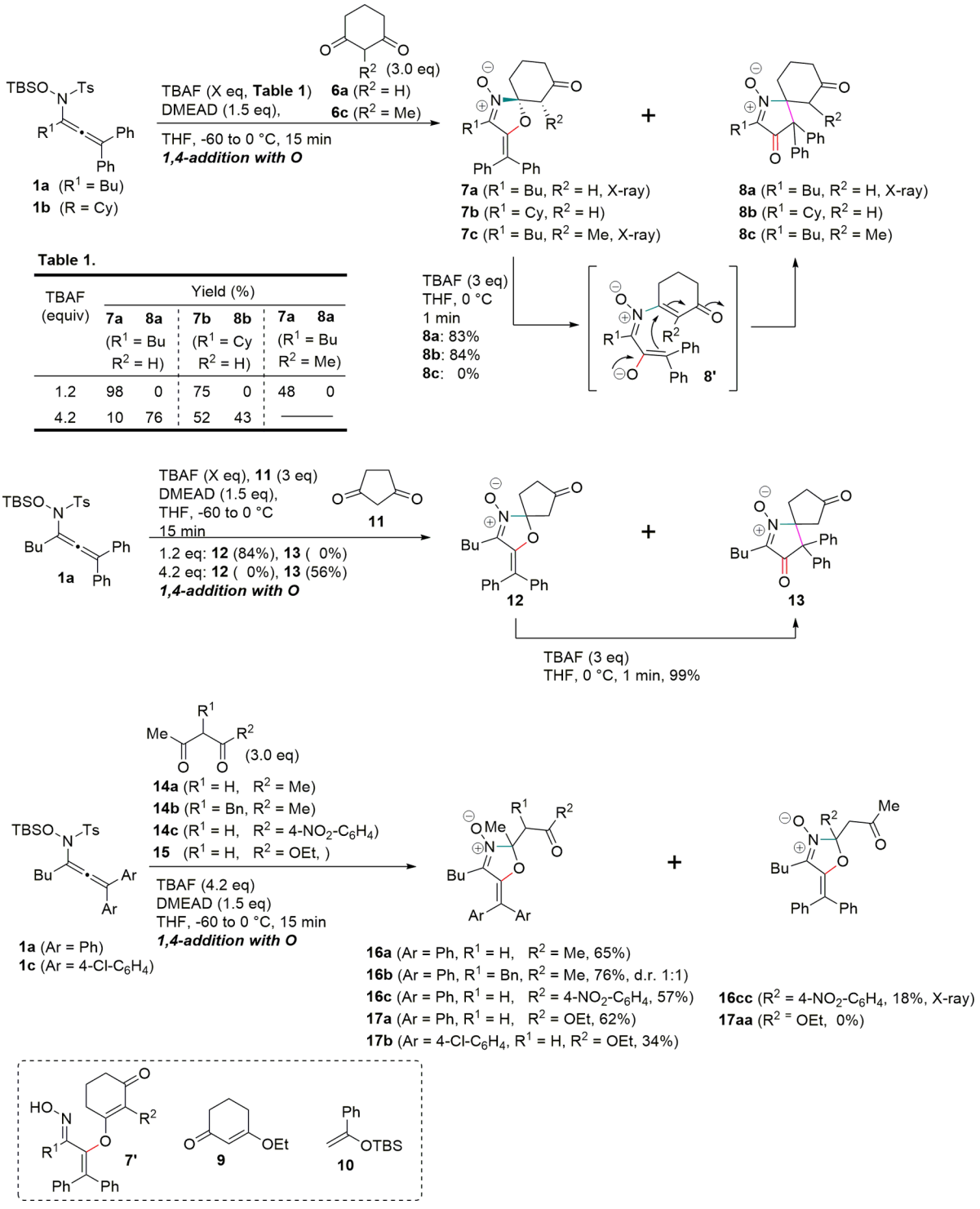

Table 1.

TBAF (equiv)	Yield (%)					
	7a (R^1 = Bu, R^2 = H)	**8a**	**7b** (R^1 = Cy, R^2 = H)	**8b**	**7a** (R^1 = Bu, R^2 = Me)	**8a**
1.2	98	0	75	0	48	0
4.2	10	76	52	43	———	

with 1.2 equiv of TBAF, [3+2] product nitrones **7a–c** were afforded in good to excellent yield. However, the afforded [3+2] products were not carbocyclic nitrones from carbon–carbon bond formations (as in **2**), but oxacyclic nitrones **7a–c** through carbon–oxygen bond formations via enol ether **7′**. It should be noted that 1,3-diketones are reported as failing to undergo addition reactions with nitrosoalkenes.[6e] Interestingly, spirocyclic α-keto nitrone products **8a–b** were isolated as major products when 4.2 equiv of TBAF were used (Scheme 4, Table 1). The structures of **7a**, **7c**, and **8a** were confirmed by X-ray crystallography. Oxacyclic nitrones **7a–b** were successfully converted to **8a–b** in good yield under basic conditions. Thus, α-ketonitrones **8a–b** can be afforded from **7a–b** via β-elimination followed by ring closure of **8′** by 1,4-addition of the resulting enolate. This mechanism is supported by the results obtained for compounds **7c** to **8c** via **8′** possessing sterically repulsive methyl substitute. We also investigated base reagents to discover whether potassium *tert*-butoxide and TBAF work well in this skeletal rearrangement (See Supporting Information). Although potassium *tert*-butoxide afforded the best yields,

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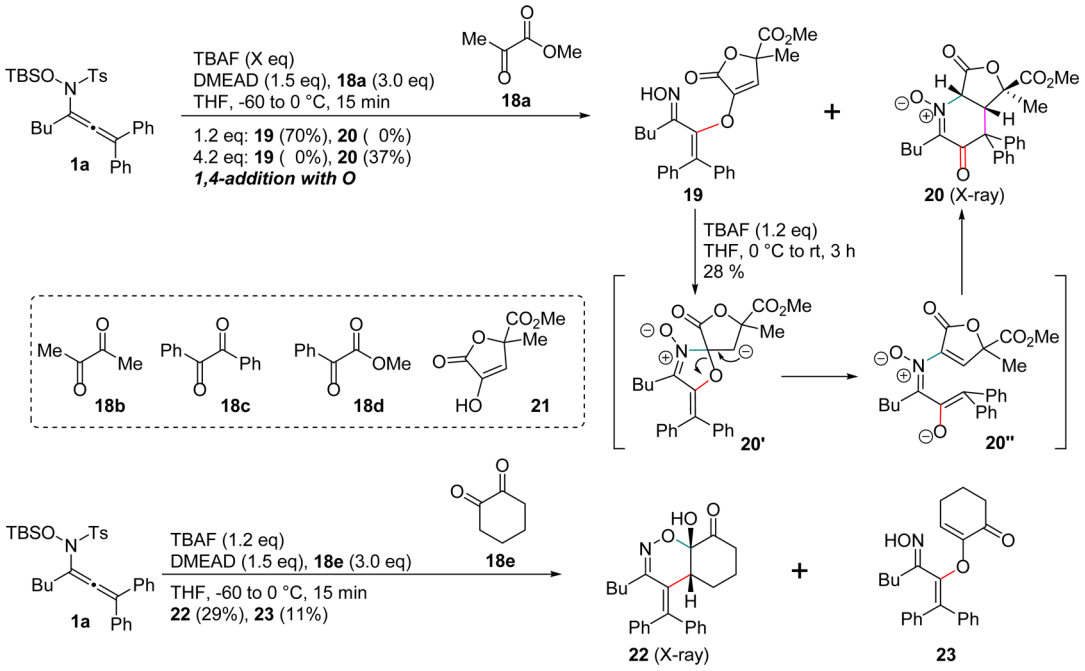
Scheme 5. Cycloaddition Reactions with 1,2-Dicarbonyl Compounds



we chose TBAF for its rapid conversion and initial coupling conditions. Similar to base-treated enolates, the use of enol ethers **9** or **10** for dienophiles, dipolarophiles, and the *in situ*-generated enolates did not produce any coupling products. A similar transformation was also observed in the reaction with 1,3-cyclopentanedione **11**.

The reaction of **1a** with acyclic diketone acetylacetone **14a** (pK_a = 13 in DMSO)[16] also afforded the [3+2] products oxacyclic nitrones **16a** in moderate yield. The cycloaddition product **16b** was also afforded with α-substituted acetylacetone **14b**[17] in higher yields. With unsymmetrical 1,3-diketone **14c**,[18] nitrone **16c** combined at the less hindered carbonyl position and was afforded as the major product. The structure of the minor product **16cc**, coupled at the hindered carbonyl group, was confirmed by X-ray crystallography. β-ketoester ethyl acetoacetate **15** only afforded cyclic nitrone **17a** through the reaction at the ketone position, while simple 1,4-addition via carbon−carbon bond formation was reported with nitrosoalkenes.[6e] Allenamide with electron-withdrawing arenes **1c** also afforded oxacyclic nitrones **17b** in fair yield. Interestingly, skeletal rearrangements were not observed in the case of acyclic diketone adducts even in the presence of excess base reagents. From the crystallographic data of oxacyclic nitrones **7a** and **7c** (see Supporting Information), antiperiplanar conformations and axial directions of carbon−oxygen moieties in the cyclic dione adducts are expected to favor rapid elimination to form **8′**, followed by a cyclization process. Probably, the conformation of the enolates of the acyclic dione adducts, suitable for β-elimination, would be thermodynamically disfavored due to steric repulsion.

In the reported case of nitrosoketene (Scheme 1e),[8] for the structurally similar chemical component nitrosoallenes, [3+2] reactions with 1,3-dicarbonyl compounds only afforded trace amounts of cyclic nitrones. On the other hand, simple ketones produced the desired compound in moderate to good yields under reflux conditions. These different reactivities showcase the unique character of nitrosoallenes. Thus, it is suggested that the reaction mechanisms of the [3+2] cycloaddition of nitrosoallenes with carbonyl compounds should be considered separately from those of the discussed nitrosoketene reactions.[8] From the results in Scheme 3, these cycloaddition reactions should consist of a stepwise pathway via the enolization of ketones, followed by carbon−oxygen bond formation through 1,4-addition to nitrosoallenes, and finally cyclization with the oxime nitrogen atoms.

To compare the reactivity, we next conducted reactions with 1,2-dicarbonyl compounds (Scheme 5). With methyl pyruvate **18a** of the α-ketoester, **1a** was converted to α-alkenoxy enoxime **19** and bicyclic α-oxonitrone **20**. Since pyruvic acid has been reported to dimerize under base conditions,[19] and diacetyl **18b** did not afford the addition product, oxime **19** should have been formed by the oxa-Michael addition of lactone **21**, the dimerization product from **18a**. Excess TBAF gave only **20**, and enol adduct **19** was certainly transformed into **20**, probably through a cascade process including cyclization to spirocyclic nitrone **20′** followed by β-elimination to **20″** and the 1,4-addition or 6π electrocyclization/isomerization of nitrone. The absence of isolable oxacyclic nitrone would be due to the instability of the carbanion in **20′** when compared to the carbanions in the 1,3-dicarbonyl adducts. Benzil **18c** and methyl benzoyl formate **18d** could not afford carbonyls in the enol form. Thus, coupling products were not isolated in this case. A different product was afforded from α-diketone 1,2-cyclohexanedione **18e**, and bicyclic oxime ether **22** was afforded along with enol ether oxime **23** by carbon−oxygen bond formation through enolization. Because the type of cyclization is different from that of nitrone **20**, **22** is probably formed by a concerted or stepwise [4+2] reaction with the enol form of **18e**. The reaction with the monomethyl enol ether of **18e** did not afford any addition products.

In the case of ketones, the high electron density of the enolates tends to be on the electronegative oxygen. This would promote carbon−oxygen bond formations with the nitrosoallenes. We therefore introduced malonates and malononitriles to reduce the contribution of the heteroatom anions, and to encourage

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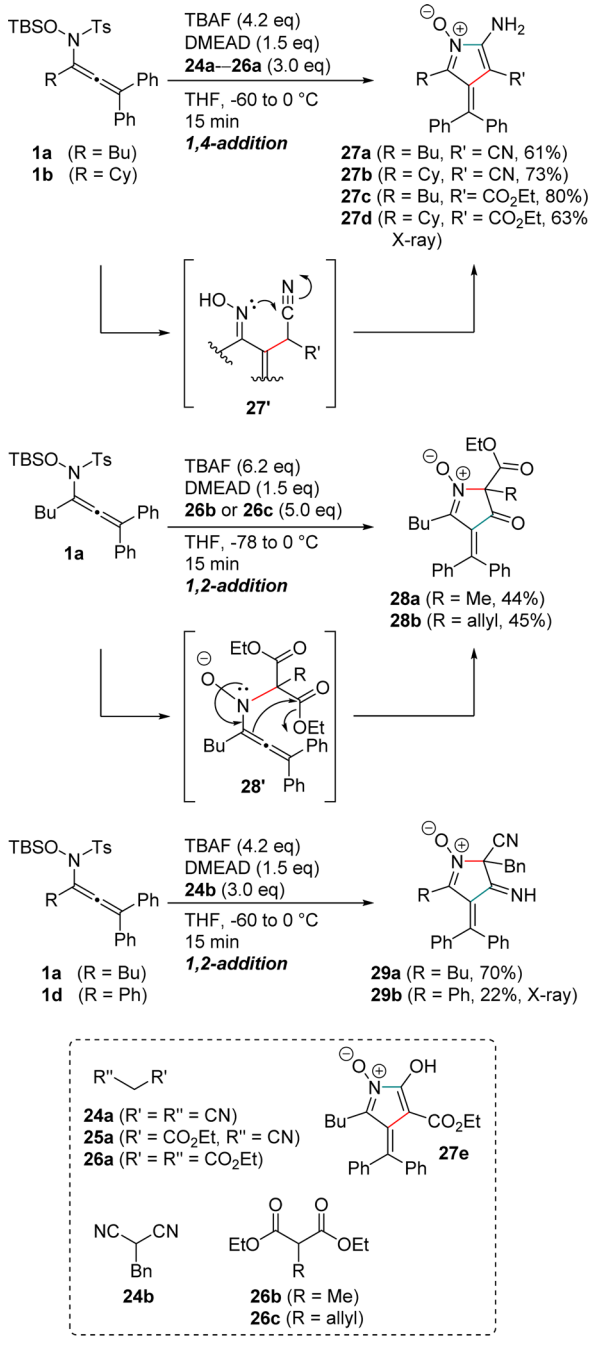
Scheme 6. Cycloaddition Reactions with Malonates and Malononitriles

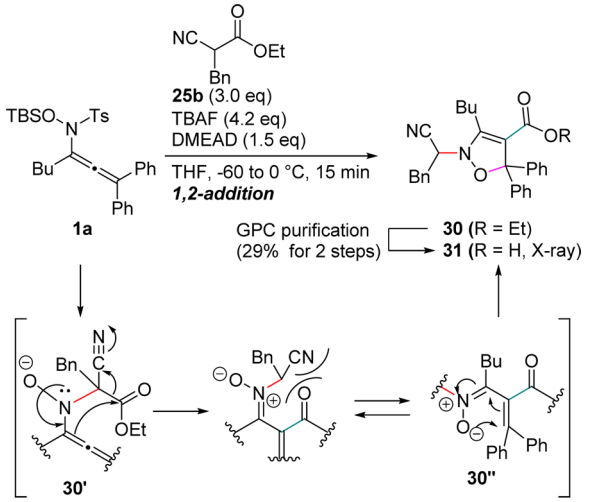


nucleophilic additions at the active methylene positions of the soft nucleophiles (Scheme 6). Unsubstituted malononitrile **24a** (pK_a = 11 in DMSO)[16] and ethyl cyanoacetate **25a** afforded 2-azafulvene derivatives (cyclic *C*,*N*-divinyl nitrones) **27a**,**b**. It is postulated that these products are afforded by initial carbon−carbon bond formation through 1,4-addition to nitrosoallenes followed by cyclization to form nitrones. Cyanoacetate **25a** selectively afforded 3-amino-2-azafulvene **27c** by cyclization with the cyano group. While Weinreb et al. reported a 6-membered ring 4*H*-1,2-oxazine product in the reaction with nitrosoalkene and sulfonylacetonitrile,[6e] we exclusively created 5-membered ring products, probably due to the presence of allene moieties. The structure of aminoazafulvene **27d**, afforded from **1b** and **25a** were confirmed by X-ray crystallography. Although diethyl malonate **26a** (pK_a = 16 in DMSO)[16] did not afford any stable products (decomposed under concentration during purification), we propose that the decomposed unstable product is **27e**, related to products **27a**−**d**. Acetonitrile, even when used as solvent, did not attach to the substrates.

We also introduced the substituted malonates **26b**,**c** to the addition reaction and the coupling products were successfully afforded in moderate yields. However, the resultant products were not nitrones from 1,4-addition to nitrosoallenes, but carbocyclic nitrones **28a**,**b**. These compounds were postulated to be generated by initial carbon−nitrogen bond formation via 1,2-addition to the nitrosoallenes, and successive Dieckmann condensation of hydroxyallenamine **28′**. With benzyl malononitrile **24b**, iminocyclic nitrones **29a**,**b** were isolated in 70% and 22% yields, respectively. The low yield of **29b**, whose structure was determined by X-ray crystallography, would be due to the large steric repulsion between phenyl groups.[13] From these results, steric repulsion between aryl groups on the allene moiety, necessary to prepare the nitrosoallene precursor substrates,[13] could also enhance regioselectivity. The results from 1,2-addition to the nitrosoallenes are contrary to those reported for nitrosoalkene reactions. The latter reactants afforded carbon−carbon bond formation between nitrosoalkenes and malonates.[6]

We further investigated benzylated α-cyanoester **25b** to test the chemoselectivity of cyclization where **25b** afforded addition product **30** in ca. 50% yield (Scheme 7). Purification of **30** by

Scheme 7. Cycloaddition Reactions with α-Cyanoester



gel permeation column (GPC) chromatography hydrolyzed the ester to afford carboxylic acid **31**. This was submitted for X-ray crystallographic analysis. Isoxazoline product **31** was delivered by 1,2-addition to nitrosoallene followed by Dieckmann condensation of **30′** at the ester moiety. However, due to the presence of the electron-withdrawing cyano group, carbon−carbon bond cleavage—instead of elimination of the alkoxide—occurred, followed by cyclocondensation of *C*-vinyl nitrone **30″**.

As shown above, addition reactions of the diesters occurred at the carbon atoms. On the other hand, the reaction with Meldrum's acid **32** exhibited a different reactivity from those of malonates and dinitriles (Scheme 8). Similar to 1,3-diketones, Meldrum's acid **32** underwent [3+2] cycloaddition reaction through carbon−oxygen bond formation to afford the very unique cyclic nitrone **33** containing an orthoamido structure.

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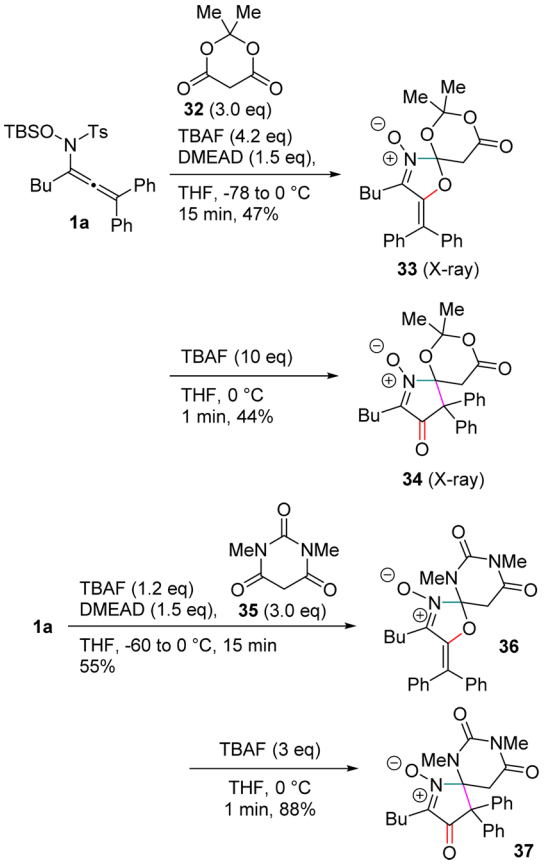
Scheme 8. Cycloadditions with Meldrum's Acid and Dimethyl Barbituric Acid



It can be postulated that the strong acidity of **33** (pK_a = 7 in DMSO),[16] compared to that of the malonates by orbital interaction,[20] increased the electron density of its anion on the oxygen atoms to undergo oxa-Michael addition to nitrosoallenes. **33** also successfully transformed to carbocyclic α-oxonitrone **34**. This latter is analogous to the products afforded from 1,3-diketones. A similar compound, *N*,*N*′-dimethylbarbituric acid **35**, also produced [3+2] adduct orthoimidate **36** that was similarly converted to **37**.

Overall, in conjunction with our previous study,[13] the nature of nitrosoallenes was found to be distinct from that of nitrosoalkenes and nitrosoketenes. With respect to the reactivities of nitrosoallenes based on the classical HSAB principle,[21] carbon atoms at the β-position in nitrosoallene seem to be "hard" and nitrogen atoms "soft" electrophiles.[13] On the other hand in the case of nitrosoalkenes, soft carboanions like malonates have been reported to generate carbon−carbon bonds at the β-carbon atoms of the nitrosoalkenes.[6] The difference between nitrosoalkene and nitrosoallene can be partially explained by DFT calculations (See Table S1 in Supporting Information). LUMO levels of unsaturated nitroso molecules demonstrate that they have a much higher reactivity than conjugated carbonyl compounds. A comparison between the LUMO coefficients of the nitrogen and β-carbon atoms shows that nitrosoallene appears between nitrosoalkene and nitrosoketene, while the value of the nitrogen atom is larger than that of the sp-carbon atom. On the other hand, the inverse was observed for nitrosoethene. This could be one of the reasons why there is minimal carbon−carbon bond formation at the β-carbon centerwhen compared to nitrosoalkenes. In the case of ketones, including Meldrum's acid and barbituric acid, the anion population tends to occur mainly on the oxygen atoms. These atoms are incompatible with the nitrogen atoms of nitroso compounds, and thus, carbon−oxygen bond formation reactions would be preferred. On the other hand, the negative charges of both nitriles and esters are mainly on the α-carbon atoms due to the instability of the ketene acetal and ketenimine anions. For this reason, the unsubstituted malononitrile achieved carbon−carbon bond formation on the sp-carbon center. However, C−N bond formations may occur with α-substituted malonates and nitriles. Thus, the regioselectivity may also be considered through steric repulsion with the substituents on the allenes. In the case of the [3+2] reaction of nitrosoketene under heating conditions,[8] a pericyclic mechanism is proposed. In our study of nitrosoallenes, the cyclization reaction is expected to proceed stepwise through enolate formation, as previously discussed.

We also consider the pK_a values of the nucleophiles. The pK_a table of tested carbonyl compounds—heteroatom and carbon nucleophiles including previously tested substrates[13]—is illustrated in Figure 1, while the addition reactions with the

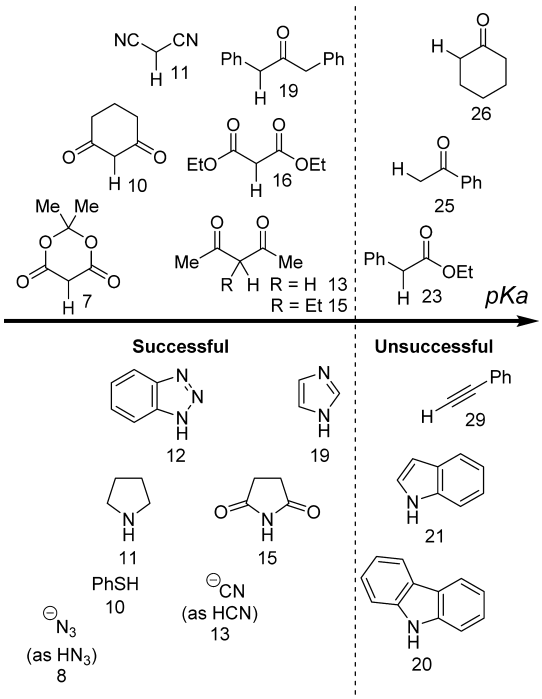


Figure 1. pK_a table of tested carbonyl compounds and other nucleophiles[13] in DMSO.

new azoles (imidazole pK_a = 19; benzotriazole pK_a = 12)[16] are illustrated in Scheme 9. In the case of dibenzylketone **2** (pK_a = 19), both 1,2- and 1,4-additions occurred in fair yield, unselectively. Because it has been reported that nitrosoalkenes do not afford any adducts with simple ketones, the reactivity of ketones with a C(sp^2)-nitroso compound that have higher pK_a values would simply be reduced, or they would favor 1,2-additions that afford unstable enamine products. The nucleophilicity of the compounds,[22] together with factors, should also be considered in the assessment of the results obtained from the addition of base reagents or the use of enol ethers (Schemes 3−4). However, borderline results of acceptable and unacceptable nucleophiles are clearly found at a pK_a value between 19 and 20. Because the precursors of nitrosoallenes to be investigated are limited due to the preparation methods,

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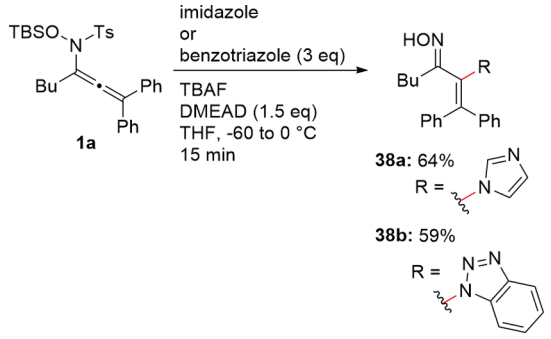
Scheme 9. Synthesis of α-Azole-Attached Enoximes



global research of acceptable nucleophiles on nitrosoallenes including comparison to the theoretical analyses should be reported by developing new synthetic methods of aminoallenes, the nitrosoallene precursors, in near future.

CONCLUSION

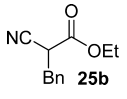
The formal [3+2] cycloadditions of nitrosoallenes with carbonyl compounds including ketones, esters, and nitriles are demonstrated herein. The synthesis of densely functionalized cyclic nitrones was achieved along with a further ring rearrangement cascade to form carbocyclic nitrones. From experimental studies, nitrosoallenes were observed to accept both 1,2- and 1,4-additions to afford cyclic nitrones. The cycloaddition reaction is thought to have proceeded through a stepwise process. Our work revealed the reaction behavior of novel chemical nitrosoallene species, and the [3+2] cycloaddition reaction mechanism was indicative of a stepwise process. We believe that our research, based on the synthesis of a characteristic chemical species and functional carbocyclic nitrones, can further assist the development of organic chemistry on alkaloid and heterocycle synthesis.

EXPERIMENTAL SECTION

General Information. ^{1}H, and ^{13}C NMR were recorded at 500 MHz for ^{1}H NMR, 126 MHz for ^{13}C NMR. Chemical shifts were reported as δ values in ppm and calibrated from residual solvent peaks ($CDCl_3$: δ 7.26 for ^{1}H NMR, δ 77.00 for ^{13}C NMR, CD_2Cl_2: δ 5.32 for ^{1}H NMR, δ 53.84 for ^{13}C NMR), or tetramethylsilane (δ 0 for ^{1}H NMR). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), br (broad peak), m (complex multiplet). Mass spectra were realized by EI (70 eV), CI, FAB, or ESI using a double-focusing mass spectrometer. The materials which were hard to be purified by silica gel column chromatography were purified by a recycling preparative gel permeation chromatography (GPC).

Allenamides of Nitrosoallene Precursors (1a–d). Prepared in accordance with our previous report.[13]

Preparation of Ethyl 2-Cyano-3-phenylpropionate (25b). **25b** was prepared in accordance with the reported procedure for the

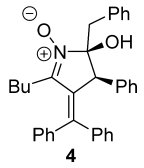


25b

synthesis of 1,3-diketones.[17] Potassium carbonate (1.11 g, 8.0 mmol) and benzyl bromide (478 μL, 4.0 mmol) were added to a stirred solution of ethyl cyanoacetate (1.28 mL, 12 mmol) in acetonitrile (8 mL) at room temperature. After 2 h, the mixture was extracted with diethyl ether and the organic layer was washed with 1 N HCl and brine. The combined organic layers were dried over sodium sulfate and concentrated in vacuo. The resultant residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 10/1) to afford **25b**. Colorless oil; R_f value 0.20 (hexane/ethyl acetate = 10/1); IR (NaCl, neat) ν_{max} 2984, 2251, 1743, 1455, 1261, 1207, 1030, 857, 748 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.27 (m, 5H), 4.24 (m, 2H), 3.72 (dd, 1H, J = 8.5, 6.0 Hz), 3.28 (dd, 1H, J = 13.5, 6.0 Hz), 3.20 (dd, 1H, J = 13.5, 8.5 Hz), 1.27 (t, 3H, J = 6.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5, 135.2, 129.0, 128.9, 127.8, 116.1, 62.9, 39.7, 35.7, 13.9; LRMS (EI) m/z 203 (M^+, 15%), 130 (20), 91 (100); HRMS (EI) calcd for $C_{12}H_{13}NO_2$ (M^+) 203.0946, found 203.0945.

General Procedure of [3+2] and 1,4-Addition Reactions with Nitrosoallene Intermediates. A tetrabutylammonium fluoride (TBAF) THF solution (equivalents used are noted in the section relevant to each product) was added to a stirred solution of allenamide and azodicarboxylate (1.5 equiv) in THF (0.05 M for allenamide) at −60 °C under nitrogen atmosphere. After 5 min, a nucleophile (equivalents used are noted for each product are noted in the relevant sections) was added at the same temperature, and the reaction mixture was warmed up to 0 °C. After 10 min, the reaction was quenched with water. The mixture was extracted with diethyl ether and washed with water and brine. The combined organic layers were dried over sodium sulfate and concentrated in vacuo. The resultant residue was purified by flash silica gel column chromatography to afford nitrones or α-substituted enoximes. When necessary, the purified materials were further treated with GPC.

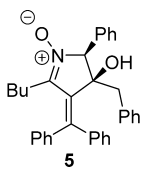
*(±)-(2R,3R)-2-Benzyl-5-butyl-4-(diphenylmethylene)-2-hydroxy-3-phenyl-3,4-dihydro-2H-pyrrole 1-Oxide (**4**, CCDC 1471114).*



4

13.7 mg (27%) of **4** and 5.7 mg (12%) of **5** were afforded from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (420 μL, 1.0 m in THF, 0.42 mmol), and 1,3-diphenyl-2-propanone (63.1 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 3/1 followed by GPC: chloroform). Recrystallization for X-ray crystallographic analysis was performed with ethyl acetate. Yellow solid; R_f value 0.28 (hexane/ethyl acetate = 2/1); mp 225.1–226.3 °C; IR (NaCl, neat) ν_{max} 3187, 3060, 2956, 1738, 1540, 1494, 1454, 1380, 1291, 1237, 1165, 747 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.41 (m, 3H), 7.36–7.28 (m, 3H), 7.22–7.16 (m, 7H), 7.11–7.08 (m, 1H), 7.05–7.01 (m, 2H), 6.78–6.77 (m, 2H), 6.49–6.47 (m, 2H), 4.08 (s, 1H), 3.44 (d, 1H, J = 14.0 Hz), 3.06 (d, 1H, J = 14.0 Hz), 2.34–2.28 (m, 1H), 1.76–1.68 (m, 1H), 1.35–1.25 (m, 3H), 0.99–0.87 (m, 2H), 0.69 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.5, 141.3, 140.5, 139.8, 138.9, 134.7, 132.9, 130.5, 128.89, 128.87, 128.82, 128.76, 128.64, 128.53, 128.48, 128.25, 128.1, 127.8, 127.7, 127.6, 127.5, 127.2, 127.0, 99.1, 53.2, 45.1, 26.9, 25.2, 22.8, 13.5; HRMS (ESI) calcd for $C_{34}H_{33}NNaO_2$ $[M+Na]^+$ 510.24090, found 510.24086.

*(±)-(2S,3S)-3-Benzyl-5-butyl-4-(diphenylmethylene)-3-hydroxy-2-phenyl-3,4-dihydro-2H-pyrrole 1-Oxide (**5**, CCDC 1471113).*



5

Obtained as above. Recrystallization for X-ray crystallographic analysis was performed with ethyl acetate. White solid; R_f value 0.28 (hexane/ethyl acetate = 2/1); mp 188.3–189.4 °C; IR (NaCl, neat) ν_{max} 3176, 2928, 1550, 1494, 1442, 1378, 1230, 1116, 758, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.20 (m, 18H), 6.88–6.86 (m, 2H), 5.08 (s, 1H), 3.28 (d, 1H, J = 14.0 Hz), 3.02 (d, 1H, J = 14.0 Hz), 2.28–2.22 (m, 1H), 1.93–1.87 (m, 1H), 1.44–1.28 (m, 3H), 1.05–0.98 (m, 2H), 0.73 (t, 3H, J = 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.1, 142.0, 140.8, 140.3, 138.0, 135.4, 132.4, 130.7, 129.5, 129.2, 128.73, 128.68, 128.5, 128.3, 128.14, 128.09, 127.84, 127.79, 127.3,

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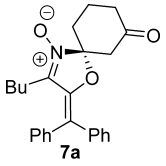
81.2, 79.3, 47.2, 26.9, 25.3, 22.7, 13.6; HRMS (ESI) calcd for $C_{34}H_{33}NNaO_2$ $[M+Na]^+$ 510.2409, found 510.2408.

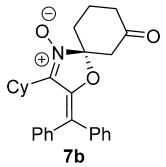
*(±)-(R)-3-Butyl-2-(diphenylmethylene)-7-oxo-1-oxa-4-azaspiro-[4.5]dec-3-ene 4-Oxide (**7a**, CCDC 1471104).* 38.1 mg (98%) of **7a**



7a

was afforded from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 m in THF, 0.12 mmol), and 1,3-cyclohexanedione (33.6 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 2/1). A single crystal for X-ray analysis was afforded by recrystallization from hexane. White solid; R_f value 0.28 (hexane/ethyl acetate = 2/1); mp 117−118 °C; IR (NaCl, neat) ν_{max} 2957, 1725, 1536, 1443, 1258, 1186, 1058, 766, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41−7.38 (m, 3H), 7.33 (d, 2H, J = 7.5 Hz), 7.29−7.25 (m, 4H), 7.20 (t, 1H), 3.33 (d, 1H, J = 15.0 Hz), 2.67 (d, 1H, J = 15.0 Hz), 2.60−2.53 (m, 2H), 2.45 (ddd, 1H, J = 13.5, 13.5, 6.0 Hz), 2.25−2.19 (m, 1H), 2.07−2.01 (m, 2H), 1.85 (m, 2H), 1.20 (tt, 2H, J = 7.0, 6.0 Hz), 0.95 (td, 2H, J = 7.0, 7.0 Hz), 0.71 (t, 3H, J = 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.4, 145.2, 139.2, 138.1, 137.3, 131.2, 129.4, 128.3, 128.2, 127.9, 127.0, 118.1, 105.2, 49.2, 39.7, 32.7, 26.8, 24.1, 22.4, 19.8, 13.5; HRMS (ESI) calcd for $C_{25}H_{27}NNaO_3$ $[M+Na]^+$ 412.1889, found 412.1885.

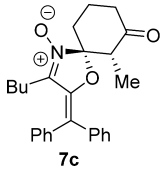
*(±)-(R)-3-Cyclohexyl-2-(diphenylmethylene)-7-oxo-1-oxa-4-azaspiro[4.5]dec-3-ene 4-Oxide (**7b**).* 31.3 mg (75%) of **7c** was



7b

afforded from allenamide **1b** (57.4 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 m in THF, 0.12 mmol), and 1,3-cyclohexanedione (33.6 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 3/1). White solid; R_f value 0.30 (hexane/ethyl acetate = 2/1); mp 203.9−204.9 °C; IR (NaCl, neat) ν_{max} 2927, 1721, 1531, 1443, 1297, 1253, 1186, 1061, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43−7.36 (m, 3H), 7.33−7.31 (m, 2H), 7.27−7.16 (m, 5H), 3.27 (d, 1H, J = 15.0 Hz), 2.63 (d, 1H, J = 15.0 Hz), 2.53−2.48 (m, 2H), 2.44−2.38 (m, 1H), 2.21−2.08 (m, 3H), 2.04−1.93 (m, 2H), 1.58−1.56 (m, 2H), 1.43−1.41 (m, 1H), 1.28−1.21 (m, 3H), 1.10 (ddt, 1H, J = 3.5, 3.5, 13.0, 13.0 Hz), 0.55 (ddddd, 2H, J = 3.5, 3.5, 13.0, 13.0, 13.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.7, 145.3, 140.7, 138.3, 138.0, 130.8, 129.4, 128.4, 128.1, 127.9, 127.0, 118.0, 105.0, 49.3, 39.7, 35.1, 32.8, 25.6, 25.1, 24.2, 24.0, 19.8; HRMS (ESI) calcd for $C_{27}H_{29}NNaO_3$ $[M+Na]^+$ 438.2045, found 438.2042.

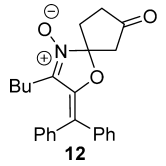
*(±)-(5R,6R)-3-Butyl-2-(diphenylmethylene)-6-methyl-7-oxo-1-oxa-4-azaspiro[4.5]dec-3-ene 4-Oxide (**7c**, CCDC 1471115).* 19.3 mg



7c

(48%) of **7c** was obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 m in THF, 0.12 mmol), and 2-methyl-1,3-cyclohexanedione (37.8 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 4/1 followed by gel permeation chromatography: chloroform). Recrystallization for X-ray analysis was performed with hexane/ethyl acetate. White solid; R_f value 0.30 (hexane/ethyl acetate = 2/1); mp 116.5−117.1 °C; IR (NaCl, neat) ν_{max} 2931, 1720, 1536, 1443, 1258, 1188, 982, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41−7.36 (m, 3H), 7.30−7.22 (m, 6H), 7.19−7.16 (m, 1H), 3.34 (q, 1H, J = 6.5 Hz), 2.65 (td, 1H, J = 14.0, 4.5 Hz), 2.58−2.54 (m, 1H), 2.46 (td, 1H, J = 14.0, 6.0 Hz), 2.15−2.09 (m, 1H), 2.06−1.93 (m, 3H), 1.70−1.64 (m, 1H), 1.30−1.09 (m, 2H), 1.01−0.86 (m, 5H), 0.69 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.9, 146.4, 140.2, 138.2, 137.4, 131.3, 129.3, 128.3, 128.2, 128.0, 127.0, 117.5, 107.8, 50.5, 40.2, 33.5, 26.7, 24.2, 22.6, 20.2, 13.5, 5.9; HRMS (ESI) calcd for $C_{26}H_{29}NNaO_3$ $[M+Na]^+$ 426.2045, found 426.2039.

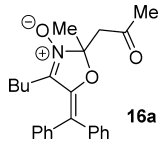
*3-Butyl-2-(diphenylmethylene)-7-oxo-1-oxa-4-azaspiro[4.4]non-3-ene 4-Oxide (**12**).* 31.4 mg (84%) of **12** was obtained from



12

allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 M in THF, 0.12 mmol), and 1,3-cyclopentanedione (29.4 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 2/1). White solid; R_f value 0.45 (hexane/ethyl acetate = 2/1); mp 123−124 °C; IR (NaCl, neat) ν_{max} 2956, 1754, 1537, 1492, 1443, 1307, 1262, 1179, 1002, 760, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26−7.23 (m, 3H), 7.22−7.20 (m, 2H), 7.16−7.11 (m, 4H), 7.09−7.06 (m, 1H), 3.04 (d, 1H, J = 18.5 Hz), 2.70−2.45 (m, 4H), 2.30−2.25 (m, 1H), 1.75−1.70 (m, 2H), 1.07 (m, 2H), 0.81 (qt, 2H, J = 7.0 Hz), 0.56 (t, 3H, J = 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.9, 145.6, 139.8, 138.1, 137.3, 131.2, 129.4, 128.4, 128.3, 128.0, 127.2, 118.2, 107.1, 47.0, 37.7, 33.1, 26.8, 24.2, 22.5, 13.5; HRMS (ESI) calcd for $C_{24}H_{25}NNaO_3$ $[M+Na]^+$ 398.17321, found 398.17322.

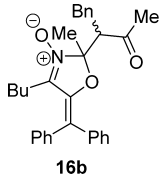
*4-Butyl-5-(diphenylmethylene)-2-methyl-2-(2-oxopropyl)-2,5-dihydrooxazole 3-Oxide (**16a**).* 24.5 mg (65%) of **16a** was obtained



16a

from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (420 μL, 1.0 M in THF, 0.42 mmol), and acetylacetone (31 μL, 0.30 mmol) (silica gel column chromatography: hexane/diethyl ether = 3/2). Pale yellow oil; R_f value 0.13 (hexane/ethyl acetate = 3/1); IR (NaCl, neat) ν_{max} 2957, 1721, 1543, 1259, 1185, 1069, 704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39−7.34 (m, 5H), 7.29−7.25 (m, 4H), 7.19 (tt, 1H, J = 7.5, 1.5 Hz), 3.23 (d, 1H, J = 16.0 Hz), 3.05 (d, 1H, J = 16.0 Hz), 2.19 (s, 3H), 1.93 (ddd, 1H, J = 13.0, 11.0, 5.0 Hz), 1.78−1.72 (m, 4H), 1.31−1.15 (m, 2H), 1.01−0.87 (m, 2H), 0.69 (t, 3H, J = 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.7, 146.4, 139.8, 138.6, 137.7, 131.3, 129.4, 128.2, 128.0, 127.8, 126.8, 117.4, 102.2, 48.1, 31.5, 26.4, 24.8, 24.1, 22.5, 13.4; HRMS (ESI) calcd for $C_{24}H_{27}NO_3Na$ $[M+Na]^+$ 400.18886, found 400.18886.

*4-Butyl-5-(diphenylmethylene)-2-methyl-2-(3-oxo-1-phenylbutan-2-yl)-2,5-dihydrooxazole 3-Oxide (**16b**, 1:1 Inseparable Diastereomixture).* 35.5 mg (76%) of **16b** was obtained from allenamide



16b

1a (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (420 μL, 1.0 M in THF, 0.42 mmol), and 3-benzyl-2,4-pentanedione **14b** (57.1 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 4/1 followed by gel permeation chromatography: chloroform). Colorless oil; R_f value 0.28 (hexane/ethyl acetate = 4/1);

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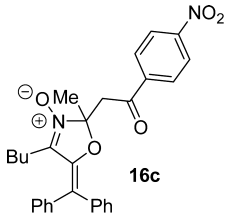
IR (NaCl, neat) ν_{max} 2957, 1716, 1538, 1495, 1444, 1257, 1190, 1068, 968 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 (m, 4H), 7.42−7.17 (m, 26H), 3.61 (dd, 1H, J = 10.5, 5.0 Hz), 3.56 (dd, 1H, J = 12.0, 3.5 Hz), 3.17−3.03 (m, 3H), 2.84 (dd, 1H, J = 13.5, 3.5 Hz), 1.97−1.90 (m, 5H), 1.86 (s, 3H), 1.79−1.66 (m, 8H), 1.31−1.10 (m, 4H), 1.00−0.85 (m, 4H), 0.69 (t, 3H, J = 7.5 Hz), 0.67 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.9, 206.9, 146.3, 146.2, 140.0, 139.6, 138.8, 138.3, 138.1, 137.7, 137.5, 137.4, 131.3, 129.6, 129.5, 128.90, 128.87, 128.71, 128.67, 128.4, 128.23, 128.18, 128.0, 127.9, 127.1, 127.0, 126.7, 117.7, 117.4, 104.2, 104.1, 60.1, 58.5, 34.0, 33.5, 33.1, 32.9, 26.7, 26.5, 24.1, 23.9, 23.2, 22.6, 22.5, 22.3, 13.50, 13.48; HRMS (ESI) calcd for $C_{31}H_{33}NO_3Na$ $[M+Na]^+$ 490.2358, found 490.2352.

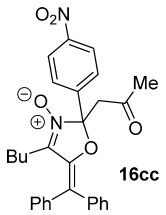
*4-Butyl-5-(diphenylmethylene)-2-methyl-2-(2-(4-nitrophenyl)-2-oxoethyl)-2,5-dihydrooxazole 3-Oxide (**16c**).* 27.7 mg (57%) of **16c**



16c

and 8.8 mg (18%) of the isomer **16cc** were obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.0 mg, 0.15 mmol), TBAF (420 μL, 1.0 M in THF, 0.42 mmol), and 1-(4-nitrophenyl)butane-1,3-dione (62 mg, 0.30 mmol)[17] (silica gel column chromatography: hexane/ethyl acetate = 5/1 to 2/1). Yellow oil; R_f value 0.19 (hexane/ethyl acetate = 2/1); IR (NaCl, neat) ν_{max} 2957, 1689, 1526, 1345, 1184, 748 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, 2H, J = 8.5, 2.0 Hz), 8.06 (dd, 2H, J = 9.0, 2.0 Hz), 7.38−7.34 (m, 3H), 7.22−7.15 (m, 7H), 3.70 (d, 1H, J = 15.0 Hz), 3.61 (d, 1H, J = 15.0 Hz), 1.87 (s, 3H), 1.85−1.72 (m, 2H), 1.21−1.07 (m, 2H), 0.95−0.85 (m, 2H), 0.67 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.3, 150.2, 145.8, 141.1, 140.0, 138.1, 137.3, 131.1, 129.4, 129.3, 128.3, 128.2, 127.8, 127.1, 123.6, 117.9, 102.5, 44.5, 26.5, 25.0, 24.1, 22.5, 13.5; HRMS (ESI) calcd for $C_{29}H_{28}N_2O_5Na$ $[M+Na]^+$ 507.1896, found 507.1892.

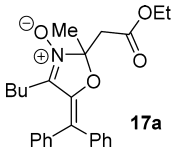
*4-Butyl-5-(diphenylmethylene)-2-(4-nitrophenyl)-2-(2-oxopropyl)-2,5-dihydrooxazole 3-Oxide (**16cc**, CCDC 1471116).* Yellow



16cc

crystal; recrystallization for X-ray crystallographic analysis was performed with ethyl acetate/hexane; R_f value 0.29 (hexane/ethyl acetate = 2/1); mp 138−140 °C; IR (NaCl, neat) ν_{max} 2958, 1728, 1524, 1349, 1187, 1062, 856, 754 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.24 (dd, 2H, J = 9.0, 2.0 Hz), 7.90 (dd, 2H, J = 9.0, 2.0 Hz), 7.45−7.24 (m, 10H), 3.68 (d, 1H, J = 17.5 Hz), 3.43 (d, 1H, J = 17.5 Hz), 2.23 (s, 3H), 1.97 (ddd, 1H, J = 13.0, 11.5, 5.5 Hz), 1.68 (ddd, 1H, J = 13.0, 11.5, 5.0 Hz), 1.30−1.13 (m, 2H), 0.92 (tq, 2H, J = 7.5, 6.0 Hz), 0.66 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.4, 148.4, 146.1, 143.5, 140.1, 138.1, 137.1, 131.2, 129.5, 128.3, 128.1, 127.4, 126.3, 123.7, 119.3, 101.1, 48.1, 31.4, 26.3, 24.2, 22.5, 13.4; HRMS (ESI) calcd for $C_{29}H_{28}N_2O_5Na$ $[M+Na]^+$ 507.1896, found 507.1898.

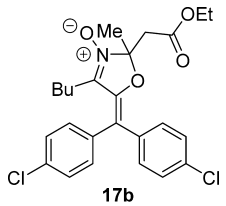
*4-Butyl-5-(diphenylmethylene)-2-(2-ethoxy-2-oxoethyl)-2-methyl-2,5-dihydrooxazole 3-Oxide (**17a**).* 25.3 mg (62%) of **17a** was obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (420 μL, 1.0 M in THF, 0.42 mmol), and ethyl acetoacetate (38.2 μL, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 2/1). Pale yellow oil; R_f value 0.23 (hexane/ethyl acetate = 3/1); IR (NaCl, neat) ν_{max} 2958, 1739,



17a

1543, 1259, 704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38−7.36 (m, 5H), 7.28−7.25 (m, 4H), 7.19 (tt, 1H, J = 7.5, 1.5 Hz), 4.21−4.12 (m, 2H), 3.21 (d, 1H, J = 15.5 Hz), 2.97 (d, 1H, J = 15.5 Hz), 1.90 (ddd, 1H, J = 13.0, 10.5, 5.0 Hz), 1.81−1.75 (m, 4H), 1.30−1.17 (m, 5H), 1.00−0.88 (m, 2H), 0.69 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.5, 146.5, 139.7, 138.6, 137.7, 131.3, 129.5, 128.3, 128.0, 127.9, 127.8, 126.9, 117.2, 102.1, 61.0, 41.4, 26.5, 24.8, 24.2, 22.6, 14.1, 13.5; HRMS (ESI) calcd for $C_{25}H_{29}NO_4Na$ $[M+Na]^+$ 430.1994, found 430.1992.

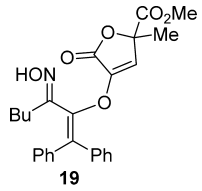
*5-(Bis(4-chlorophenyl)methylene)-4-butyl-2-(2-ethoxy-2-oxoethyl)-2-methyl-2,5-dihydrooxazole 3-Oxide (**17b**).* 16.2 mg (34%) of



17b

17b was obtained from allenamide **1c** (61.7 mg, 0.10 mmol), DMEAD (35.0 mg, 0.15 mmol), TBAF (320 μL, 1.0 M in THF, 0.32 mmol), and ethyl acetoacetate (25.5 μL, 0.20 mmol) (silica gel column chromatography: hexane/diethyl ether = 3/1 to 1/1). Pale yellow oil; R_f value 0.23 (hexane/ethyl acetate = 3/1); IR (NaCl, neat) ν_{max} 2958, 1739, 1541, 1490, 1259, 1091, 832 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, 2H, J = 8.0 Hz), 7.27−7.22 (m, 4H), 7.18 (d, 2H, J = 8.0 Hz), 4.15 (q, 2H, J = 7.5 Hz), 3.19 (d, 1H, J = 16.0 Hz), 2.96 (d, 1H, J = 16.0 Hz), 1.97 (ddd, 1H, J = 13.5, 11.0, 5.5 Hz), 1.83 (ddd, 1H, J = 13.5, 11.0, 5.0 Hz), 1.75 (s, 3H), 1.30−1.15 (m, 5H), 1.06−0.95 (m, 2H), 0.72 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 147.2, 139.2, 136.7, 135.8, 134.4, 132.7, 130.7, 128.7, 128.1, 114.5, 102.3, 61.0, 41.1, 26.4, 24.8, 24.2, 22.6, 14.1, 13.4; HRMS (ESI) calcd for $C_{25}H_{27}Cl_2NO_4Na$ $[M+Na]^+$ 498.12148, found 498.12146.

*Methyl (E)-4-((3-(Hydroxyimino)-1,1-diphenylhept-1-en-2-yl)-oxy)-2-methyl-5-oxo-2,5-dihydrofuran-2-carboxylate (**19**).* 24.6 mg



19

(70%) of **19** was obtained from allenamide **1a** (54.8 mg, 0.10 mmol) and DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 M in THF, 0.12 mmol), and methyl pyruvate (30.3 μL, 0.30 mmol) (silica gel column chromatography: hexane/diethyl ether = 2/1 followed by gel permeation chromatography: chloroform). White solid; R_f value 0.43 (hexane/ethyl acetate = 2/1); mp 129.0−130.8 °C; IR (NaCl, neat) ν_{max} 2957, 1791, 1653, 1444, 1202, 1115, 967, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31−7.24 (m, 7H), 7.19−7.16 (m, 4H), 6.26 (s, 1H), 3.67 (s, 3H), 2.17 (m, 2H), 1.50 (s, 3H), 1.44 (dd, 2H, J = 7.5, 7.0 Hz), 1.23 (qt, 2H, J = 7.5, 7.5 Hz), 0.84 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9, 165.3, 156.4, 143.9, 143.2, 138.5, 138.0, 134.3, 130.1, 129.3, 128.3, 128.24, 128.22, 128.1, 122.5, 82.0, 53.2, 27.8, 26.7, 22.8, 22.6, 13.6; HRMS (ESI) calcd for $C_{26}H_{27}NNaO_6$ $[M+Na]^+$ 472.1736, found 472.1739.

*(±)-(4aR,8aS)-3-Butyl-4-(diphenylmethylene)-8a-hydroxy-4a,6,7,8a-tetrahydro-4H-benzo[e][1,2]oxazin-8(5H)-one (**22**, CCDC 1471110).* 11.4 mg of **22** (29%) and 4.1 mg of **23** (11%) were obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 M in THF, 0.12 mmol), and 1,2-cyclohexanedione (33.6 mg, 0.30 mmol) (silica gel column

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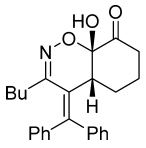
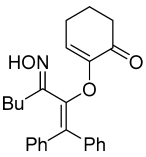


22

chromatography: hexane/ethyl acetate = 4/1). Single crystal for X-ray analysis was obtained by recrystallization from diethyl ether. White solid; R_f value 0.58 (hexane/ethyl acetate = 2/1); mp 127.6−128.9 °C; IR (NaCl, neat) ν_{max} 2955, 2860, 1732, 1443, 1124, 1075, 906 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.45 (br, 1H), 7.34−7.32 (m, 6H), 7.11 (br, 2H), 6.93 (br, 1H), 4.77 (s, 1H), 2.87 (dt, 1H, J = 14.5, 14.5, 6.5 Hz), 2.60 (dd, 1H, J = 12.0, 5.0 Hz), 2.49 (td, 1H, J = 14.5, 1.5, 1.5 Hz), 2.09−1.82 (m, 4H), 1.69−1.53 (m, 2H), 1.41−1.25 (m, 2H), 1.18−1.00 (m, 2H), 0.73 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.2, 157.8, 148.2, 141.5, 140.8, 128.8, 128.3, 128.2, 122.3, 96.7, 43.5, 36.8, 33.1, 30.5, 27.6, 24.1, 22.3, 13.7; HRMS (ESI) calcd for $C_{25}H_{27}NNaO_3$ $[M+Na]^+$ 412.1889, found 412.1888.

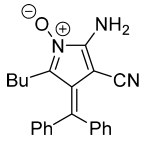
*(E)-2-((3-(Hydroxyimino)-1,1-diphenylhept-1-en-2-yl)oxy)-cyclohex-2-en-1-one (**23**).* Obtained as above. Colorless oil; R_f value



23

0.40 (hexane/ethyl acetate = 2/1); IR (NaCl, neat) ν_{max} 3313, 2928, 1691, 1443, 1194, 1122, 963, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29−7.14 (m, 10H), 6.31 (t, 1H, J = 4.5 Hz), 2.40 (t, 2H, J = 6.5 Hz), 2.35 (ddt, 2H, J = 6.0, 6.0, 4.5 Hz), 2.22 (dd, 2H, J = 8.0 Hz), 1.86 (tt, 2H, J = 6.5, 6.0 Hz), 1.48 (m, 2H), 1.26 (m, 2H), 0.86 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.9, 157.1, 148.8, 143.2, 139.9, 139.0, 132.5, 130.2, 129.5, 128.0, 127.9, 127.5, 127.1, 126.0, 38.6, 27.7, 26.8, 24.6, 23.0, 22.7, 13.7; HRMS (ESI) calcd for $C_{25}H_{27}NNaO_3$ $[M+Na]^+$ 412.1889, found 412.1880.

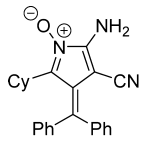
*5-Amino-2-butyl-4-cyano-3-(diphenylmethylene)-3H-pyrrole 1-oxide (**27a**).* 21.0 mg (61%) of **27a** was obtained from allenamide



27a

1a (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (420 μL, 1.0 M in THF, 0.42 mmol), and malononitrile (19.8 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 3/2). Red oil; R_f value 0.40 (hexane/ethyl acetate = 1/1); IR (NaCl, neat) ν_{max} 3268, 3195, 2955, 2203, 1679, 1488, 1381, 1225, 756 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.49−7.25 (m, 6H), 7.26−7.22 (m, 2H), 7.210−7.207 (m, 2H), 6.16 (br, 2H), 2.06 (m, 2H), 1.32 (m, 2H), 0.94 (m, 2H), 0.66 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 156.1, 150.9, 145.1, 141.0, 140.6, 132.4, 131.7, 130.5, 130.4, 128.7, 128.6, 128.4, 114.7, 66.5, 28.3, 26.0, 23.0, 13.6; HRMS (ESI) calcd for $C_{22}H_{22}N_3O$ $[M+H]^+$ 344.1763, found 344.1762.

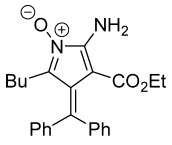
*5-Amino-4-cyano-2-cyclohexyl-3-(diphenylmethylene)-3H-pyrrole 1-Oxide (**27b**).* 27.0 mg (73%) of **27b** was obtained from



27b

allenamide **1c** (57.4 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (420 μL, 1.0 M in THF, 0.42 mmol), and malononitrile (19.8 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 4/1). Red oil; R_f value 0.50 (hexane/ethyl acetate = 1/1); IR (NaCl, neat) ν_{max} 3268, 3195, 2925, 2382, 2205, 1680, 1487, 1400, 1292, 1177, 755 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.52−7.40 (m, 6H), 7.28 (dd, 2H, J = 7.0, 1.5 Hz), 7.20 (d, 2H, J = 7.0 Hz), 6.00 (brs, 2H), 2.24 (m, 2H), 1.61−1.54 (m, 3H), 1.45−1.10 (m, 4H), 0.587 (m, 2H); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 156.4, 150.7, 141.5, 140.8, 132.7, 131.6, 130.51, 130.45, 128.7, 128.6, 128.4, 114.7, 67.1, 37.5, 26.5, 25.89, 25.7; HRMS (ESI) calcd for $C_{24}H_{23}N_3O$ $[M+Na]^+$ 392.1739, found 392.1745.

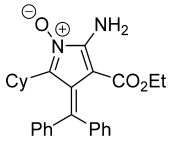
*5-Amino-2-butyl-3-(diphenylmethylene)-4-(ethoxycarbonyl)-3H-pyrrole 1-Oxide (**27c**).* 31.1 mg (80%) of **27c** was obtained from



27c

allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 M in THF, 0.12 mmol), and ethyl cyanoacetate (32 μL, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 3/2). Red oil; R_f value 0.38 (hexane/ethyl acetate = 1/1); IR (NaCl, neat) ν_{max} 2954, 2362, 1684, 1487, 1295, 1224, 1104 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.50−7.47 (m, 1H), 7.41−7.29 (m, 5H), 7.27−7.25 (m, 2H), 7.21−7.20 (m, 2H), 6.44 (s, 2H), 3.59 (q, 2H, J = 7.0 Hz), 1.96 (m, 2H), 1.34 (m, 2H), 0.93 (tq, 2H, J = 7.5, 7.5 Hz), 0.75 (t, 3H, J = 7.0 Hz), 0.67 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 155.1, 150.9, 147.0, 143.9, 142.0, 132.3, 132.2, 130.0, 129.2, 129.1, 128.1, 127.8, 86.8, 59.6, 28.5, 25.9, 22.8, 13.8, 13.5; HRMS (ESI) calcd for $C_{24}H_{27}N_2O_3$ $[M+H]^+$ 391.2022, found 391.2023.

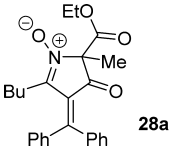
*5-Amino-2-cyclohexyl-3-(diphenylmethylene)-4-(ethoxycarbonyl)-3H-pyrrole 1-Oxide (**27d**, CCDC 1471112).* 31.1 mg (80%) of **27d**



27d

was obtained from allenamide **1c** (57.4 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 M in THF, 0.12 mmol), and ethyl cyanoacetate (32 μL, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 2/1). Recrystallization for X-ray analysis was performed with ethyl acetate. Dark yellow solid; R_f value 0.23 (hexane/ethyl acetate = 2/1); mp 69.4−70.3 °C; IR (NaCl, neat) ν_{max} 2926, 1683, 1481, 1300, 1191, 1104, 755, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (t, 1H, J = 7.5 Hz), 7.40 (t, 2H, J = 7.5 Hz), 7.35−7.30 (m, 3H), 7.24−7.23 (m, 4H), 6.45 (brs, 2H), 3.58 (q, 2H, J = 7.5 Hz), 2.30 (dddd, 2H, J = 12.5, 12.5, 12.5, 3.5 Hz), 1.59−1.56 (m, 2H), 1.43−1.39 (m, 2H), 1.29−1.26 (m, 3H), 1.19−1.12 (m, 1H), 0.76 (t, 3H, J = 7.5 Hz), 0.51 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 155.5, 150.6, 148.9, 144.1, 142.5, 132.4, 132.0, 130.0, 129.4, 129.1, 128.1, 127.8, 87.0, 59.5, 37.1, 26.3, 25.7, 25.2, 13.8; HRMS (ESI) calcd for $C_{26}H_{29}N_2O_3$ $[M+H]^+$ 417.2178, found 417.2179.

*5-Butyl-4-(diphenylmethylene)-2-(ethoxycarbonyl)-2-methyl-3-oxo-3,4-dihydro-2H-pyrrole 1-Oxide (**28a**).* 13.3 mg (44%) of **28a**



28a

was obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.0 mg, 0.15 mmol), TBAF (620 μL, 1.0 M in THF, 0.62 mmol), and diethyl methylmalonate (83.0 μL, 0.50 mmol) (silica gel column chromatography: hexane/diethyl ether = 4/3). Red oil; R_f value 0.23

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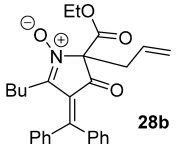
(hexane/ethyl acetate = 3/1); IR (NaCl, neat) ν_{max} 2957, 1760, 1730, 1506, 1390, 1256, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.49−7.33 (m, 6H), 7.20−7.18 (m, 4H), 4.32−4.22 (m, 2H), 2.34 (ddd, 1H, J = 13.5, 10.0, 5.5 Hz), 2.12 (ddd, 1H, J = 13.5, 9.5, 5.5 Hz), 1.76 (s, 3H), 1.38−1.25 (m, 5H), 1.06−0.99 (m, 2H), 0.69 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.4, 164.1, 153.7, 150.2, 139.9, 139.2, 131.2, 130.6, 130.3, 130.2, 128.34, 128.32, 128.30, 127.9, 126.0, 79.5, 63.1, 26.5, 24.9, 22.3, 16.6, 13.9, 13.5; LRMS (EI, M = $C_{25}H_{27}NO_4$) m/z 405 (M^+, 55%), 363 (100), 362 (80); HRMS (EI) calcd for $C_{25}H_{27}NO_4$ (M^+) 405.1940, found 405.1932.

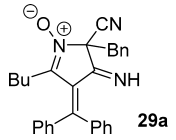
*2-Allyl-5-butyl-4-(diphenylmethylene)-2-(ethoxycarbonyl)-3-oxo-3,4-dihydro-2H-pyrrole 1-Oxide (**28b**).* 14.7 mg (45%) of **28b**



28b

was obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.0 mg, 0.15 mmol), TBAF (620 μL, 1.0 M in THF, 0.62 mmol), and diethyl allylmalonate (99.0 μL, 0.50 mmol) (silica gel column chromatography: hexane/ethyl acetate = 6/1). Red oil; R_f value 0.29 (hexane/ethyl acetate = 3/1); IR (NaCl, neat) ν_{max} 2958, 1760, 1730, 1506, 1389, 1238, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.49−7.38 (m, 4H), 7.34 (t, 2H, J = 7.5 Hz), 7.16−7.15 (m, 4H), 5.59 (dddd, 1H, J = 17.5, 10.5, 7.5, 7.5 Hz), 5.28 (dd, 1H, J = 17.5, 2.0 Hz), 5.23 (dd, 1H, J = 10.5, 2.0 Hz), 4.26 (m, 2H), 3.20 (dd, 1H, J = 14.5, 7.5 Hz), 2.96 (dd, 1H, J = 14.5, 7.5 Hz), 2.27−2.13 (m, 2H), 1.37−1.25 (m, 5H), 1.00 (m, 2H), 0.68 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.8, 163.7, 155.3, 149.5, 140.0, 139.2, 131.4, 130.7, 130.4, 130.2, 129.0, 128.3, 127.8, 127.0, 121.8, 82.5, 63.1, 34.2, 26.6, 24.9, 22.4, 13.9, 13.5; LRMS (EI, M = $C_{27}H_{29}NO_4$) m/z 431 (M^+, 26%), 389 (50), 388 (42), 83 (53), 57 (100); HRMS (EI) calcd for $C_{27}H_{29}NO_4$ (M^+) 431.2097, found 431.2099.

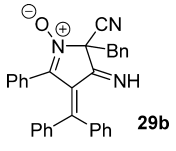
*2-Benzyl-5-butyl-2-cyano-4-(diphenylmethylene)-3-imino-3,4-dihydro-2H-pyrrole 1-Oxide (**29a**).* 30.4 mg (70%) of **29a** was



29a

obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (420 μL, 1.0 M in THF, 0.42 mmol), and 2-benzylmalononitrile (46.9 mg, 0.30 mmol)[19] (silica gel column chromatography: toluene/ethyl acetate = 20/1). Single crystal for X-ray analysis was obtained by recrystallization from ethyl acetate. Yellow oil; R_f value 0.38 (toluene/ethyl acetate = 20/1); IR (NaCl, neat) ν_{max} 3288, 2957, 1654, 1515, 1385, 1250, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.70 (s, 1H), 7.49−7.19 (m, 13H), 6.98 (br, 1H), 6.15 (br, 1H), 3.97 (d, 2H, J = 14.0 Hz), 3.49 (d, 2H, J = 14.0 Hz), 1.97−1.84 (m, 2H), 1.24−1.15 (m, 1H), 1.01−0.92 (m, 1H), 0.90−0.73 (m, 2H), 0.61 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 153.0, 145.6, 139.6, 138.7, 131.1, 131.0, 130.1, 129.6, 129.5, 128.41, 128.38, 124.1, 115.0, 74.0, 41.7, 26.2, 25.2, 22.4, 13.3; HRMS (ESI) calcd for $C_{29}H_{27}N_3ONa$ $[M+Na]^+$ 456.2052, found 456.2056.

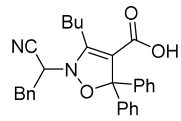
*2-Benzyl-2-cyano-4-(diphenylmethylene)-3-imino-5-phenyl-3,4-dihydro-2H-pyrrole 1-Oxide (**29b**, CCDC 1471108).* 10.1 mg (22%)



29b

of **29b** was obtained from allenamide **1c** (56.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (420 μL, 1.0 M in THF, 0.42 mmol), and 2-benzyl malononitrile (46.9 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 10/1). Recrystallization for X-ray crystallographic analysis was performed with hexane. Yellow solid; R_f value 0.48 (hexane/ethyl acetate = 2/1); mp 70.3−71.1 °C; IR (NaCl, neat) ν_{max} 3288, 3060, 2927, 2360, 1653, 1487, 1444, 1392, 1236, 1169, 885, 759, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.55−7.47 (m, 4H), 7.36−7.27 (m, 8H), 7.05−6.86 (m, 8H), 4.09 (d, 1H, J = 13.0 Hz), 3.58 (d, 1H, J = 13.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 147.8, 146.5, 138.8, 138.6, 131.1, 131.0, 130.4, 130.3, 129.4, 129.1, 128.9, 128.7, 128.5, 127.4, 126.4, 123.4, 114.9, 75.4, 42.6; HRMS (ESI) calcd for $C_{31}H_{24}N_3O$ $[M+H]^+$ 454.1919, found 454.1913.

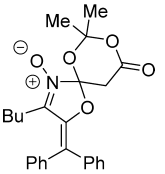
*3-Butyl-2-(1-cyano-2-phenylethyl)-5,5-diphenyl-2,5-dihydroisoxazole-4-carboxylic Acid (**31**, CCDC 1471111).* 12.9 mg (29%) of **31**



31

was obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 M in THF, 0.12 mmol), and ethyl 2-benzyl-2-cyanoacetate **25b** (61.0 mg, 0.50 mmol) (silica gel column chromatography: hexane/ethyl acetate = 5/1 followed by gel permeation chromatography:chloroform). Single crystal for X-ray analysis was obtained by recrystallization from hexane. Pale yellow solid; R_f value 0.45 (hexane/ethyl acetate = 2/1); mp 149.2−149.7 °C; IR (NaCl, neat) ν_{max} 2958, 2931, 1661, 1447, 1155, 911, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.50−7.45 (m, 4H), 7.35−7.27 (m, 9H), 7.17−7.16 (m, 2H), 4.45 (t, 1H, J = 7.5 Hz), 3.24 (dq, 2H, J = 14.0, 7.5 Hz), 3.03−2.97 (m, 1H), 2.35 (m, 1H), 1.22−1.13 (m, 4H), 0.76 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.8, 142.3, 141.3, 134.6, 129.42, 129.37, 128.7, 128.1, 127.84, 127.80, 127.6, 127.5, 116.3, 109.9, 92.7, 54.7, 37.1, 29.8, 24.9, 22.1, 13.5; HRMS (ESI) calcd for $C_{29}H_{28}N_2NaO_3$ $[M+Na]^+$ 475.1998, found 475.1997.

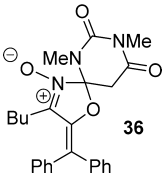
*3-Butyl-2-(diphenylmethylene)-7,7-dimethyl-9-oxo-1,6,8-trioxa-4-azaspiro[4.5]dec-3-ene 4-Oxide (**33**, CCDC 1471105).* 39.5 mg



33

(47%) of **33** was obtained from allenamide **1a** (109.6 mg, 0.20 mmol), DMEAD (70.3 mg, 0.30 mmol), TBAF (840 μL, 1.0 M in THF, 0.84 mmol) and Meldrum's acid (86.5 mg, 0.60 mmol) (silica gel column chromatography: hexane/ethyl acetate = 2/1 with 10% toluene). Single crystal for X-ray analysis was obtained by recrystallization from hexane. White solid; R_f value 0.38 (hexane/ethyl acetate = 2/1); mp 137−138 °C; IR (NaCl, neat) ν_{max} 2957, 1768, 1542, 1293, 1039, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42−7.24 (m, 10H), 3.64 (d, 1H, J = 18.0 Hz), 3.05 (d, 1H, J = 18.5 Hz), 1.93−1.84 (m, 2H), 1.78 (s, 3H), 1.75 (s, 3H), 1.28−1.18 (m, 2H), 0.96 (tq, 2H, J = 7.5, 7.5 Hz), 0.70 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8, 143.5, 139.3, 137.6, 136.8, 130.9, 129.8, 128.6, 128.4, 128.0, 127.9, 121.5, 112.7, 106.3, 34.7, 28.33, 28.27, 26.7, 24.3, 22.5, 13.4; HRMS (ESI) calcd for $C_{25}H_{27}NNaO_5$ $[M+Na]^+$ 444.1787, found 444.1779.

*3-Butyl-2-(diphenylmethylene)-6,8-dimethyl-7,9-dioxo-1-oxa-4,6,8-triazaspiro[4.5]dec-3-ene 4-Oxide (**36**).* 23.9 mg (55%) of **36** was obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 M in THF, 0.12 mmol),



36

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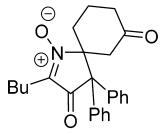
and *N*,*N*′-dimethyl barbituric acid (46.8 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 3/1). Colorless oil; R_f value 0.38 (hexane/ethyl acetate = 2/1); IR (NaCl, neat) ν_{max} 2957, 1730, 1681, 1544, 1445, 1351, 1178, 1054, 754 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41−7.35 (m, 3H), 7.29−7.20 (m, 7H), 3.49 (d, 1H, J = 16.5 Hz), 3.22 (s, 3H), 3.14 (d, 1H, J = 16.0 Hz), 2.90 (s, 3H), 2.01−19.5 (ddd, 1H, J = 13.0, 11.0, 5.5 Hz), 1.73−1.67 (ddd, 1H, J = 13.0, 11.5, 5.0 Hz), 1.27−1.10 (m, 2H), 0.97−0.84 (m, 2H), 0.65 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 152.6, 143.6, 140.2, 137.4, 136.7, 130.9, 129.7, 128.7, 128.5, 128.2, 128.0, 121.2, 105.3, 39.4, 28.1, 27.7, 26.7, 24.3, 22.5, 13.4; HRMS (ESI) calcd for $C_{25}H_{27}N_3NaO_4$ $[M+Na]^+$ 456.1899, found 456.1900.

General Procedure for Skeletal Rearrangement to Spirocyclic Nitrones. A TBAF THF solution (equivalents used are noted in the section relevant to each product) was added to a stirred THF solution of oxacyclic nitrone (0.05 M) at 0 °C. After 1 min, the reaction mixture was concentrated in vacuo, and the residue was purified by silica gel column chromatography to afford the rearranged carbocyclic nitrone.

*2-Butyl-3,7-dioxo-4,4-diphenyl-1-azaspiro[4.5]dec-1-ene 1-Oxide (**8a**, CCDC 1471109). From Allenamide.* According to the general



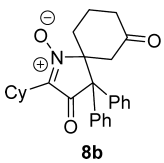
8a

procedure of [3+2] reactions with nitrosoallene intermediates, 29.5 mg (76%) of **8a** was afforded from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (450 μL, 1.0 M in THF, 0.42 mmol), and 1,3-cyclohexanedione (33.6 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 5/1 to 2/1).

*From Oxacyclic Nitrone (**1**).* According to the general procedure for the skeletal rearrangement, 16.2 mg (83%) of **8a** was afforded from oxacyclic nitrone **7a** (19.5 mg, 0.050 mmol) and TBAF (150 μL, 1.0 M in THF, 0.15 mmol) (silica gel column chromatography: hexane/ethyl acetate = 2/1).

*From Oxacyclic Nitrone (**2**).* Potassium *t*-butoxide (6.2 mg, 0.055 mmol) was added to a stirred solution of **7a** (19.5 mg, 0.050 mmol) in THF (1.0 mL) at 0 °C. After 3 h, a saturated ammonium chloride aqueous solution was added to the reaction mixture. The mixture was extracted with diethyl ether and washed with brine. The combined organic layers were dried over sodium sulfate and concentrated in vacuo. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 2/1) to afford **8a** (18.8 mg, 96%). Recrystallization for X-ray analysis was performed with ethyl acetate. White solid; R_f value 0.45 (hexane/ethyl acetate = 2/1); mp 111−112 °C; IR (NaCl, neat) ν_{max} 2957, 2931, 2873, 1709, 1558, 1387, 1103, 922, 760, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43−7.37 (m, 5H), 7.31−7.28 (m, 3H), 7.11−7.10 (m, 2H), 3.32 (d, 1H, J = 15.0 Hz), 2.56−2.49 (m, 3H), 2.40 (d, 1H, J = 15.0 Hz), 2.13−2.06 (m, 1H), 2.02−1.96 (m, 1H), 1.88−1.85 (m, 1H), 1.70−1.65 (m, 1H), 1.56−1.42 (m, 3H), 1.28 (m, 2H), 0.88 (t, 3H, J = 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.8, 194.7, 142.5, 137.2, 136.8, 129.5, 129.4, 128.8, 128.7, 128.2, 128.0, 84.5, 69.7, 44.6, 38.7, 38.4, 26.1, 22.7, 21.9, 20.3, 13.6; HRMS (ESI) calcd for $C_{25}H_{27}NNaO_3$ $[M+Na]^+$ 412.1889, found 412.1882.

*2-Cyclohexyl-3,7-dioxo-4,4-diphenyl-1-azaspiro[4.5]dec-1-ene 1-Oxide (**8b**). From Allenamide.* According to the general procedure for

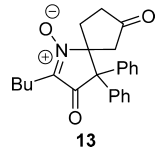


8b

[3+2] reactions with nitrosoallene intermediates, 21.5 mg (52%) of **8b** was afforded from allenamide **1b** (57.4 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (150 μL, 1.0 M in THF, 0.42 mmol), and 1,3-cyclohexanedione (33.6 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 6/1 to 4/1).

From Oxacyclic Nitrone. According to the general procedure of skeletal rearrangement, 17.5 mg (84%) of **8b** was afforded from oxacyclic nitrone **7b** (20.8 mg, 0.050 mmol) and TBAF (420 μL, 1.0 M in THF, 0.15 mmol) (silica gel column chromatography: hexane/ethyl acetate = 2/1). Colorless oil; R_f value 0.48 (hexane/ethyl acetate = 2/1); IR (NaCl, neat) ν_{max} 2929, 1710, 1550, 1388, 1103, 914, 760, 730 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44−7.37 (m, 5H), 7.30−7.24 (m, 3H), 7.12−7.08 (m, 2H), 3.33 (d, 1H, J = 16.0 Hz), 2.86 (tt, 1H, J = 12.0, 3.5 Hz), 2.54 (m, 1H), 2.38 (d, 1H, J = 16.0 Hz), 2.11−2.05 (m, 1H), 2.00−1.65 (m, 8H), 1.52−1.43 (m, 3H), 1.29−1.21 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.8, 194.4, 144.1, 137.3, 136.8, 129.5, 129.4, 128.75, 128.69, 128.1, 127.9, 84.3, 69.5, 44.2, 38.9, 38.7, 33.6, 25.83, 25.79, 25.7, 25.6, 25.4, 20.2; HRMS (ESI) calcd for $C_{27}H_{29}NNaO_3$ $[M+Na]^+$ 438.2045, found 438.1044.

*2-Butyl-3,7-dioxo-4,4-diphenyl-1-azaspiro[4.4]non-1-ene 1-Oxide (**13**). From Allenamide.* According to the general procedure

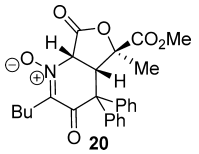


13

for [3+2] reactions with nitrosoallene intermediates, 21.1 mg (56%) of **13** was afforded from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (420 μL, 1.0 M in THF, 0.42 mmol), and 1,3-cyclopentanedione (29.4 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 2/1).

From Oxyacyclic Nitrone. 19.0 mg (quant) of **13** was obtained from oxacyclic nitrone **12** (18.8 mg, 0.050 mmol) and TBAF (150 μL, 1.0 M in THF, 0.15 mmol) (silica gel column chromatography: hexane/ethyl acetate = 3/1). White solid; R_f value 0.58 (hexane/ethyl acetate = 2/1); mp 146−147 °C; IR (NaCl, neat) ν_{max} 2957, 2931, 1751, 1710, 1558, 1495, 1385, 1264, 704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41−7.37 (m, 3H), 7.33−7.27 (m, 5H), 7.07−7.03 (m, 2H), 3.52 (d, 1H, J = 19.0 Hz), 2.77 (d, 1H, J = 19.0 Hz), 2.57−2.48 (m, 2H), 2.43 (m, 1H), 2.34 (m, 1H), 2.06 (m, 1H), 1.54−1.37 (m, 3H), 1.24 (m, 2H), 0.86 (t, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.6, 194.6, 142.7, 139.4, 136.5, 129.6, 129.3, 128.80, 128.77, 128.4, 128.0, 86.5, 68.7, 44.2, 36.3, 36.1, 26.1, 22.6, 22.0, 13.6; HRMS (ESI) calcd for $C_{24}H_{25}NNaO_3$ $[M+Na]^+$ 398.1732, found 398.1736.

*(±)-(4aR,5R,7aS)-2-Butyl-5-(methoxycarbonyl)-5-methyl-3,7-dioxo-4,4-diphenyl-3,4,4a,5,7,7a-hexahydrofuro[3,4-b]pyridine 1-Oxide (**20**, CCDC 1471106). From Allenamide.* According to the



20

general procedure for [3+2] reactions with nitrosoallene intermediates, 16.6 mg (37%) of **20** was obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (420 μL, 1.0 M in THF, 0.42 mmol), and methyl pyruvate (30 μL, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 10/1 to 5/1 followed by gel permeation chromatography: chloroform).

*From Oxime **19**.* 5.0 mg (28%) of **20** was afforded from oxime **19** (17.6 mg, 0.040 mmol) and TBAF (120 μL, 1.0 M in THF, 0.12 mmol) after stirring at 0 °C for 1.5 h followed by rt for 1.5 h (silica gel column chromatography: hexane/ethyl acetate = 2/1). Single crystal for X-ray analysis was obtained by recrystallization from hexane. Pale yellow solid; R_f value 0.40 (hexane/ethyl acetate = 2/1); mp 102.8−104.5 °C; IR (NaCl, neat) ν_{max} 2955, 1805, 1667, 1529, 1291, 1219, 752 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.51−7.50 (m, 2H), 7.42−7.35 (m, 4H), 7.32−7.25 (m, 3H), 7.22−7.18 (m, 1H), 5.15 (d, 1H, J = 8.0 Hz), 4.80 (d, 1H, J = 8.0 Hz), 3.31 (s, 3H), 2.73 (m, 2H), 1.59 (s, 3H), 1.41−1.21 (m, 4H), 0.85 (t, 3H, J = 7.5 Hz); ^{13}C NMR

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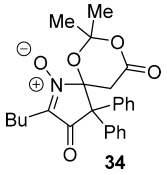
(126 MHz, $CDCl_3$) δ 185.5, 168.6, 163.9, 150.7, 138.2, 137.8, 129.7, 129.2, 128.7, 128.3, 127.6, 126.5, 85.6, 66.6, 53.5, 52.9, 47.5, 26.3, 24.6, 22.7, 19.9, 13.6; HRMS (ESI) calcd for $C_{26}H_{27}NNaO_6$ $[M+Na]^+$ 472.1736, found 472.1733.

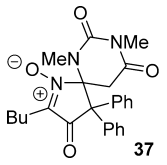
*2-Butyl-7,7-dimethyl-3,9-dioxo-4,4-diphenyl-6,8-dioxa-1-azaspiro[4.5]dec-1-ene 1-Oxide (**34**, CCDC 1471107).* 9.3 mg (44%)



34

of **34** was afforded from oxacyclic nitrone **33** (21.1 mg, 0.050 mmol) and TBAF (500 μL, 1.0 M in THF, 0.50 mmol) (silica gel column chromatography: hexane/ethyl acetate = 2/1). Recrystallization for X-ray analysis was performed with hexane. White solid; R_f value 0.58 (hexane/ethyl acetate = 2/1); mp 184−185 °C; IR (NaCl, neat) ν_{max} 2958, 2359, 1767, 1714, 1563, 1387, 1284, 985, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39−7.35 (m, 3H), 7.30−7.22 (m, 7H), 3.34 (d, 1H, J = 17.5 Hz), 2.81 (d, 1H, J = 17.5 Hz), 2.52 (t, 2H, J = 7.5 Hz), 1.82 (s, 3H), 1.45 (tdd, 2H, J = 7.5, 7.5, 2.5 Hz), 1.34 (s, 3H), 1.20 (m, 2H), 0.84 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.8, 163.7, 142.8, 137.1, 136.0, 130.0, 129.5, 129.0, 128.7, 128.2, 127.8, 106.9, 103.8, 69.8, 34.4, 29.0, 28.4, 26.0, 22.5, 21.9, 13.6; HRMS (ESI) calcd for $C_{25}H_{27}NNaO_5$ $[M+Na]^+$ 444.1787, found 444.1784.

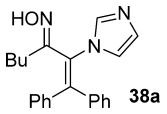
*2-Butyl-6,8-dimethyl-3,7,9-trioxo-4,4-diphenyl-1,6,8-triazaspiro-[4.5]dec-1-ene 1-Oxide (**37**).* 21.1 mg (88%) of **37** was obtained from



37

oxacyclic nitrone **36** (24.1 mg, 0.056 mmol) and TBAF (168 μL, 1.0 M in THF, 0.168 mmol). Pure material was obtained without silica gel chromatography. Colorless oil; R_f value 0.43 (hexane/ethyl acetate = 2/1); IR (NaCl, neat) ν_{max} 2958, 1713, 1674, 1568, 1452, 1386, 754 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.72−7.70 (m, 2H), 7.45−7.40 (m, 3H), 7.29−7.24 (m, 3H), 6.81−6.78 (m, 2H), 3.187 (s, 3H), 3.186 (d, 1H, J = 16.5 Hz), 3.11 (d, 1H, J = 16.5 Hz), 2.77−2.66 (m, 2H), 2.34 (s, 3H), 1.65 (ddt, 2H, J = 15.5, 7.5, 7.5 Hz), 1.45 (tq, 2H, J = 7.5, 7.5 Hz), 0.97 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.3, 165.2, 153.3, 145.1, 139.1, 134.7, 129.3, 129.0, 128.73, 128.66, 128.5, 128.2, 93.1, 63.7, 36.2, 31.3, 27.9, 26.6, 23.1, 21.9, 13.6; HRMS (ESI) calcd for $C_{25}H_{27}N_3NaO_4$ $[M+Na]^+$ 456.1899, found 456.1892.

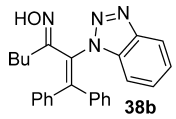
Synthesis of 2-Azolyl Enoximes. *2-(1H-Imidazol-1-yl)-1,1-diphenylhept-1-en-3-one Oxime (**38a**).* According to the general



38a

procedure for [3+2] reactions, 22.2 mg (64%) of **38a** was afforded from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (450 μL, 1.0 M in THF, 0.42 mmol), and imidazole (20.4 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 1/1). White solid; R_f value 0.20 (hexane/ethyl acetate = 1/1); mp 161−162 °C; IR (NaCl, neat) ν_{max} 2957, 2859, 1490, 1230, 996 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 10.4 (brs, 1H), 7.32−7.14 (m, 9H), 6.92−6.91 (m, 2H), 6.85 (s, 1H), 6.71 (s, 1H), 2.13 (m, 2H), 1.38 (m, 2H), 1.22 (tq, 2H, J = 7.5, 7.5 Hz), 0.82 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5, 140.4, 140.1, 139.5, 138.1, 129.9, 129.3, 128.7, 128.4, 128.2, 128.0, 120.0, 28.0, 27.2, 23.0, 13.6; HRMS (ESI) calcd for $C_{22}H_{24}N_3O$ $[M+H]^+$ 346.1919, found 346.1913.

*2-(1H-Benzo[d][1,2,3]triazol-1-yl)-1,1-diphenylhept-1-en-3-one Oxime (**38b**).* According to the general procedure for [3+2] reactions,



38b

23.4 mg (59%) of **38b** was obtained from allenamide **1a** (54.8 mg, 0.10 mmol), DMEAD (35.1 mg, 0.15 mmol), TBAF (120 μL, 1.0 M in THF, 0.12 mmol), and benzotriazole (35.7 mg, 0.30 mmol) (silica gel column chromatography: hexane/ethyl acetate = 6/1). Colorless oil; R_f value 0.50 (hexane/ethyl acetate =2/1); IR (NaCl, neat) ν_{max} 3172, 2957, 2871, 1491, 1282, 1012 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (brs, 1H), 7.91 (d, 1H, J = 8.5 Hz), 7.90−7.21 (m, 8H), 7.01−6.94 (m, 3H), 6.86−6.84 (m, 2H), 2.07 (m, 2H), 1.41 (m, 2H), 1.16 (tq, 2H, J = 7.5, 7.5 Hz), 0.74 (t, 3H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.4, 145.2, 145.1, 139.5, 139.1, 133.1, 130.1, 129.1, 128.7, 128.4, 128.3, 128.0, 127.7, 127.6, 123.8, 119.8, 110.1, 27.8, 27.0, 22.8, 13.5; HRMS (ESI) calcd for $C_{25}H_{24}N_4NaO$ $[M+Na]^+$ 419.1848, found 419.1841.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00758.

^1H and ^{13}C NMR spectra (PDF)

Crystallographic data of new compounds (CCDC numbers 1471114 for **4**; 1471113 for **5**; 1471104 for **7a**; 1471109 for **8a**; 1471116 for **16cc**; 1471106 for **20**; 1471110 for **22**; 1471112 for **27c**; 1471108 for **29b**; 1471111 for **31**; 1471105 for **33**; 1471107 for **34**) (CIF)

Computational data [Gaussian09 B3LYP/6-31G(d,p)] (XYZ)

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Notes

The authors declare no competing financial interest.

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