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N-Heterocyclic Carbene-Catalyzed [3 + 4] Annulation of Enals and Alkenyl Thiazolones: Enantioselective Synthesis of Thiazole-Fused ε-Lactones

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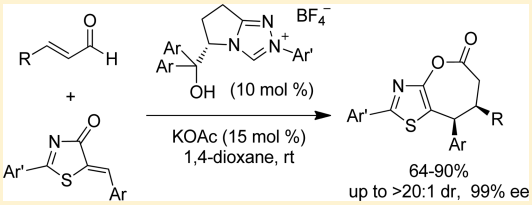
Supporting Information

ABSTRACT: The bifunctional N-heterocyclic carbene catalyzed [3 + 4] annulation of enals and 5-alkenyl thiazolones was developed, giving the corresponding thiazole-fused ε-lactones in high yields with excellent diastereoselectivties and enantioselectivities. The thiazole-fused ε-lactone could be isomerized to the spirocyclic thiazolone−cyclopentanone without erosion of enantioselectivity.



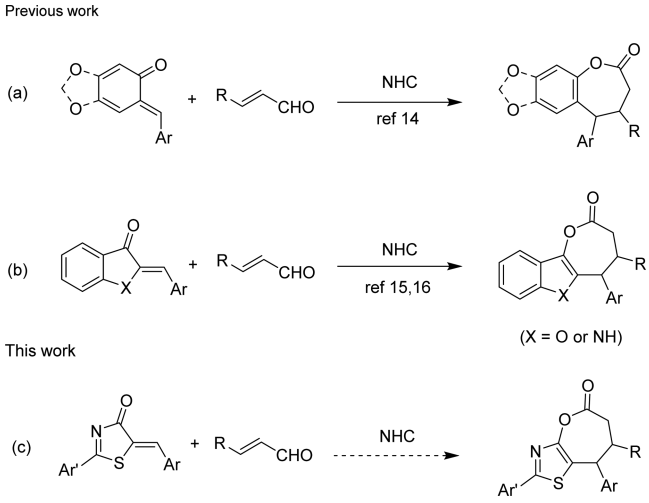
Thiazole is a significant motif in various biologically active natural products and pharmaceuticals.[1] For example, thiamin, also called vitamin B1, is effective for metabolic disorders, thiamine deficiency, and brain disorders.[2] Furthermore, bleomycin, tallysomycin, and zorbamycin, containing the same motif, are used as antitumor antibiotics.[3] On the other hand, ε-lactones are also core structures of numerous biological active compounds.[4] Combined with these two motifs, thiazole-fused ε-lactones are interesting from biological and synthetic points of view.

Over the past decades, N-heterocyclic carbenes (NHCs) have been demonstrated as powerful organic catalysts for a range of reactions.[5] The NHC-catalyzed reactions of enals have gained popularity since the first example established by Bode et al. and Glorius et al. in 2004.[6] Then, various reactions of enals were developed via the Breslow intermediate,[7] homoenolate,[8] enolate,[9] vinyl enolate,[10] α,β-unsaturated acyl azolium,[11] δ-carbon activation[12] and single electron oxidation.[13]

In 2013, Scheidt et al. and our group independently reported the NHC-catalyzed enantioselective [3 + 4] annulation of enals with *o*-quinone methides to give the corresponding benzo-ε-lactones (Scheme 1, reaction a).[14] Zhao et al. developed the NHC-catalyzed [3 + 4] annulation with aurone for the synthesis of indole-fused ε-lactones under the regulation of Lewis acid.[15] Meanwhile, our group revealed that [3 + 4] annulation products are kinetically favored when a bifunctional NHC bearing the free hydroxyl group was used (Scheme 1, reaction b).[16] It is noted that only quinones and benzoheterocycles are used for these reactions. Thus, it would be interesting and useful to extend the reactant to simple heterocycles without benzene. In this note, the [3 + 4] annulation of enals with 5-alkenyl thiazolones was developed for the synthesis of thiazole-fused ε-lactones (Scheme 1, reaction c).

The model reaction of the *n*-hexenal (**1a**) with 5-benzylidene thiazolone (**2a**) was investigated under NHC catalysis (Table 1). It was found that no desired [3 + 4] annulation product **3a**

Scheme 1. NHC-Catalyzed Synthesis of ε-Lactones



or competitive [3 + 2] annulation product **4a** was formed for the reaction in the presence of 10 mol % of NHC precursor **A1** or **A2** with a silyl ether group (entries 1 and 2).[17] We were encouraged to find that the [3 + 4] product **3a** was obtained in 14% yield with exclusive *cis*-selectivity and 92% ee when preNHC **B1** with a free hydroxyl group was used (entry 3).[18] Interestingly, the yield was dramatically improved to 86% with essentially single enantiomer when the preNHC **B2** with *N*-2-isopropylphenyl group was used (entry 4). The base is also found to play an important role for the reaction. The yield of ε-lactone **3a** was decreased when NaOAc was used instead of KOAc (entry 5), and the competitive [3 + 2] cycloadduct **4a** was observed when Cs_2CO_3 or DBU was used (entries 6 and

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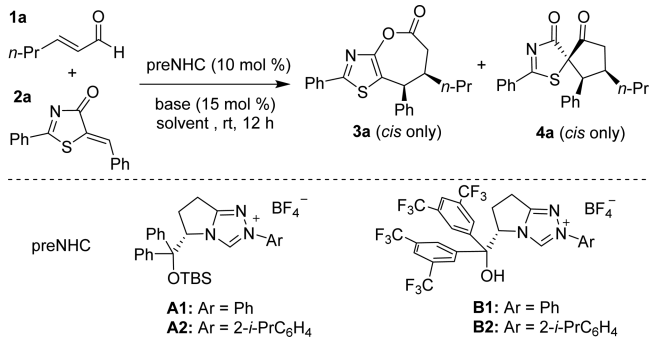
Table 1. Optimization of the Reaction Conditions[a]



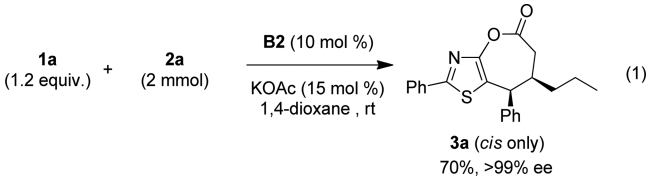
				3a		4a	
entry	preNHC	base	solvent	yield[b] (%)	ee[c] (%)	yield[b] (%)	ee[c] (%)
1	**A1**	KOAc	1,4-dioxane	NR			
2	**A2**	KOAc	1,4-dioxane	NR			
3	**B1**	KOAc	1,4-dioxane	14	92	0	
4	**B2**	KOAc	1,4-dioxane	86 (80)[d]	>99	0	
5	**B2**	NaOAc	1,4-dioxane	72	>99	trace	
6	**B2**	Cs_2CO_3	1,4-dioxane	29	>99	22	>99
7	**B2**	DBU	1,4-dioxane	18	99	<5	
8	**B2**	KOAc	CH_2Cl_2	72	>99	12	>99
9	**B2**	KOAc	ethyl ether	44	>99	24	>99
10	**B2**	KOAc	toluene	75	>99	0	

[a]General conditions: **1a** (0.24 mmol), **2a** (0.20 mmol), preNHC **A-B** (10 mol %), base (15 mol %), solvent (2 mL), room temperature. [b]Yield determined by ^{1}H NMR spectroscopy. [c]Determined by HPLC on a chiral column. [d]Isolated yield in parentheses. NR = no reaction.

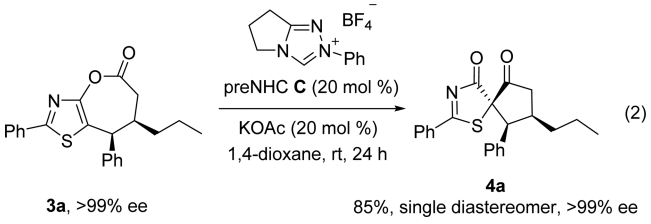
7).[19] Screening of solvent resulted in no better solvent than 1,4-dioxane (entry 4 vs entries 8−10).

With the optimized reaction conditions in hand, the substrate scope of this reaction was then investigated using various 5-alkenyl thiazolones **2** with enals **1** (Scheme 2). It was found that both electron-donating (Ar = 4-MeC_6H_4, 4-$MeOC_6H_4$) and electron-withdrawing (Ar = 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-$NO_2C_6H_4$) substituents of 5-alkenyl thiazolones worked well, giving the desired cycloadducts **3b−g** in good yields with excellent diastereo- and enantioselectivities. *Meta*-substituents (Ar = 3-ClC_6H_4) and 1-naphthyl were tolerable with preservation of good yields and excellent diastereo- and enantioselectivities (**3h,i**). Enals with different substituents were also explored. Enals with both short and long alkyl chains worked well (**3j,k**). The reaction of aryl enals gave the products (**3l,m**) in high yields and with excellent enantioselectivities but decreased diastereoselectivities (4:1 dr). The 5-alkenyl thiazolones with different substituted aryls on the 2-carbon were also investigated. It was found that both the electron-donating and electron-withdrawing substituents (Ar′ = 4-MeC_6H_4, 4-ClC_6H_4) were tolerable, giving the desired products **3n,o** in good yields with excellent enantioselectivities.

The reaction could be carried out at 2 mmol scale in good yield with exclusive *cis*-selectivity and excellent enantioselectivity (eq 1).



In the presence of ordinary triazolium NHC precursor **C**, the thiazole-fused ε-lactone **3a** could be transformed to the corresponding spirocyclic product **4a** in good yield with excellent diastereoselectvity (eq 2).



The absolute structures of thiazole-fused ε-lactone **3l** and spirocyclic cyclopentanone **4a** were established by the X-ray analysis of their single crystals (Figures S1 and S2, Supporting Information).

The proposed catalytic cycle is depicted in Figure 1. The addition of NHC to enals **1** generates the vinyl Breslow intermediate **I**, in which the *Z*-configuration of the enol is favored possibly due to repulsion of the sterically demanded diarylmethyl of the NHC and the hydroxyl of *E*-enol.[20] The Michael addition of intermediate **I** to 5-alkenyl thiazolones **2** via a transition state (TS A), featuring with the H-bonding between the hydroxyl of the NHC and 5-alkenyl thiazolone, gave adduct **II**. The intramolecular *O*-acylation of adduct **II** gives the desired [3 + 4] cycloadduct **3** and regenerates NHC catalyst (path a). Alternatively, the *C*-acylation of adduct **II** may afford the [3 + 2] cycloadduct **4** (path b). In our optimized reaction conditions, the *O*-acylation is overwhelmingly favored with no *C*-acylation observed. The possible H-bonding may make the carbonyl a harder Lewis acid and thus favors the hard Lewis basic *O*-acylation over the soft Lewis basic *C*-acylation.

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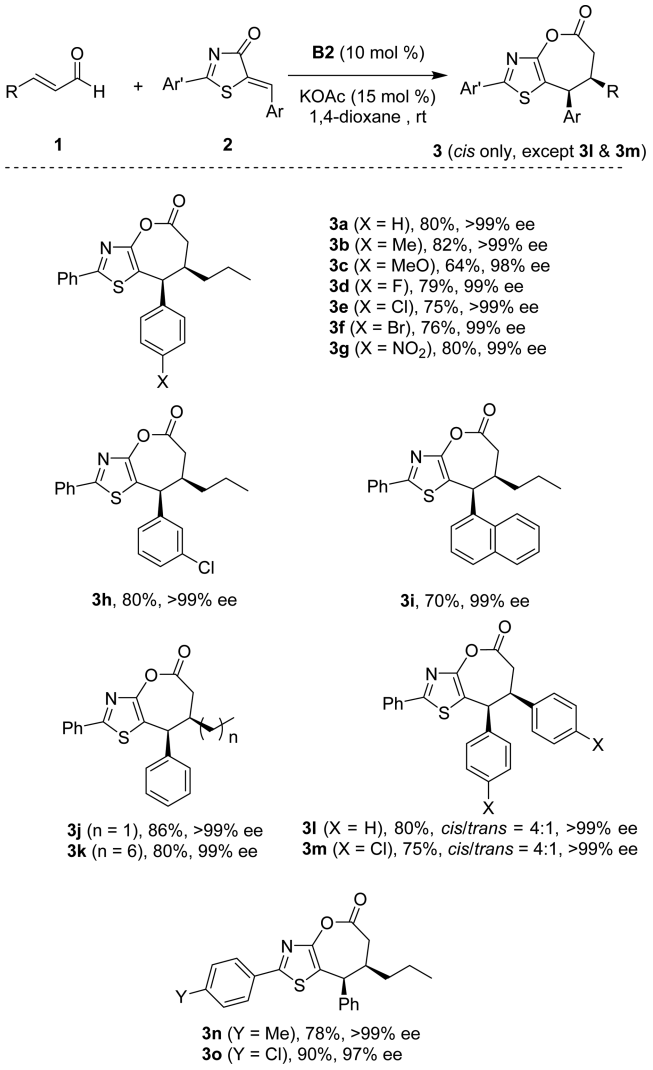
Scheme 2. Substrate Scope



In summary, the N-heterocyclic carbene catalyzed [3 + 4] annulation of enals and 5-alkenyl thiazolones was developed. The reaction worked well for various 5-alkenyl thiazolones and enals, giving the corresponding thiazole-fused ε-lactones in high yields with excellent diastereoselectivities and enantioselectivities under the optimized conditions using a bifunctional chiral triazolium NHC precursor with a free hydroxyl group. The thiazole-fused ε-lactone could be transformed to the corresponding spirocyclic cyclopentanone under ordinary NHC catalysis.

EXPERIMENTAL SECTION

General Considerations. All reactions were carried out under nitrogen atmosphere in oven-dried glassware with magnetic stirring. All solvents were dried and distilled by standard procedures. Column chromatography was performed on silica gel 200−300 mesh. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were recorded in $CDCl_3$, with tetramethylsilane as an internal standard and reported in parts per million (ppm, δ). Optical rotations were measured on a digital polarimeter operating at the sodium D line with a 100 mm path cell and are reported as follows: $[\alpha]_D^T$ (concentration (g/100 mL), solvent). High-resolution mass spectrometry (HRMS) data were obtained using electrospray ionization (ESI), and an orbitrap mass analyzer was used. Melting points were determined on a melting point apparatus and are uncorrected.

General Procedure for the Synthesis of Thiazole-Fused ε-Lactones. To the solution of NHC precursor **B2** (15.4 mg, 0.02 mmol), KOAc (3.0 mg, 0.03 mmol), and 5-alkenyl thiazolone **2** (0.20 mmol) in 1,4-dioxane (2 mL) was added enal **1** (0.24 mmol). The reaction mixture was stirred at room temperature overnight. The reaction mixture was passed through a pad of silica gel and washed with ethyl acetate. A small portion of the mixture was collected for ^{1}H NMR to determine the ratio of *cis*-**3**/*trans*-**3**. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (ethyl ether/petroleum ether, typically 1/10) to give the thiazole-fused ε-lactone **3** with exclusive *cis*-selectivtivities for all cases except compounds **3l** and **3m**. Racemic samples for standard of chiral HPLC were prepared using 10 mol % of racemic NHC precursor *rac*-**B2** as the preNHC.

*(7R,8S)-2,8-Diphenyl-7-propyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3a**).* Yield: 59 mg (80%), viscous solid, R_f = 0.20 (petroleum ether/ethyl ether, 8:1). $[\alpha]_D^{20}$ −43.5 (*c* 0.52, $CHCl_3$).

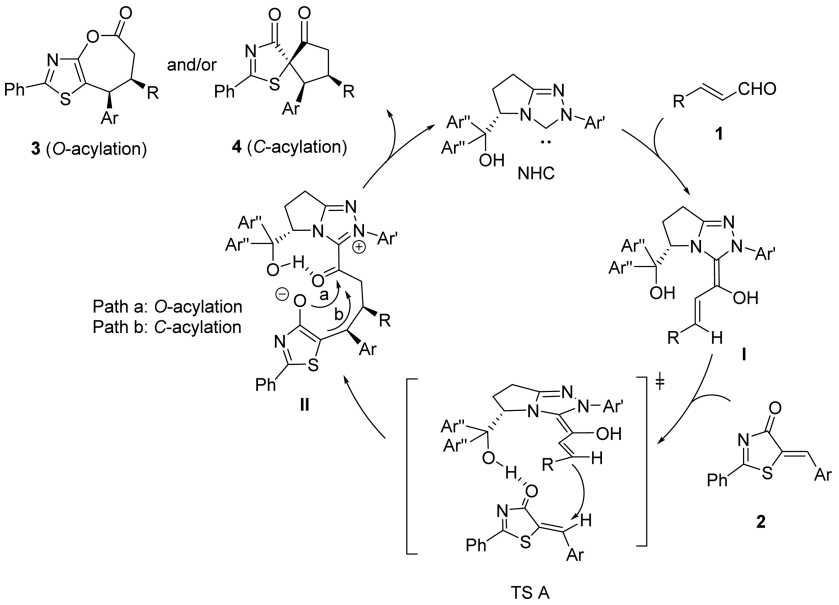


Figure 1. Plausible catalytic cycle.

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HPLC analysis: 99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 14.1 min (major), 18.0 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06−7.66 (m, 2H), 7.43−7.30 (m, 6H), 7.24 (d, *J* = 6.6 Hz, 2H), 4.53 (d, *J* = 5.9 Hz, 1H), 2.98 (dd, *J* = 14.7, 9.2 Hz, 1H), 2.75 (dd, *J* = 14.8, 2.2 Hz, 1H), 2.57 (m, 1H), 1.52−1.39 (m, 1H), 1.38−1.27 (m, 1H), 1.26−1.07 (m, 2H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.0, 163.8, 153.2, 140.1, 132.8, 130.7, 129.4, 129.1, 128.7, 128.0, 125.9, 118.3, 47.5, 39.1, 37.3, 33.3, 20.4, 14.0. IR (KBr): ν 2980, 1647, 1453 cm^{-1}. HRMS (ESI) *m*/*z*: [M + H] $^+$ calcd for $C_{22}H_{22}NO_2S^+$ 364.1371, found 364.1361.

(7R,8S)-2-Phenyl-7-propyl-8-(p-tolyl)-7,8-dihydrooxepino[2,3-d]-thiazol-5(6H)-one (**3b**). Yield: 62 mg (82%), viscous solid, R_f = 0.21 (petroleum ether/ethyl ether, 8:1). $[\alpha]_D^{20}$ −58.5 (*c* 1.25, $CHCl_3$). HPLC analysis: >99% ee, [Daicel CHIRALPAK IA column, 20 °C, 254 nm *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 18.5 min (major), 20.1 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−7.77 (m, 2H), 7.39 (dd, *J* = 5.5, 1.8 Hz, 3H), 7.23−7.05 (m, 4H), 4.49 (d, *J* = 5.7 Hz, 1H), 2.97 (dd, *J* = 14.7, 9.3 Hz, 1H), 2.73 (dd, *J* = 14.8, 2.2 Hz, 1H), 2.57−2.52 (m, 1H), 2.36 (s, 3H), 1.51−1.38 (m, 1H), 1.38−1.28 (m, 1H), 1.25−1.10 (m, 2H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.0, 163.7, 153.1, 137.7, 137.1, 132.8, 130.6, 129.3, 129.3, 129.0, 125.9, 118.6, 47.1, 39.1, 37.2, 33.4, 21.2, 20.4, 14.0. IR (KBr): ν 2959, 1644, 1455 cm^{-1}. HRMS (ESI) *m*/*z*: [M + H] $^+$ calcd for $C_{23}H_{24}NO_2S^+$ 378.1522, found 378.1519.

(7R,8S)-8-(4-Methoxyphenyl)-2-phenyl-7-propyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3c**). Yield: 52 mg (62%), viscous solid, R_f = 0.14 (petroleum ether/ethyl ether, 8:1). $[\alpha]_D^{20}$ −46.0 (*c* 0.61, $CHCl_3$). HPLC analysis: 98% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 17.0 min (major), 22.8 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92−7.72 (m, 2H), 7.40 (dd, *J* = 5.2, 2.1 Hz, 3H), 7.21−7.08 (m, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 4.48 (d, *J* = 5.7 Hz, 1H), 3.82 (s, 3H), 2.96 (dd, *J* = 14.7, 9.3 Hz, 1H), 2.73 (dd, *J* = 14.7, 2.1 Hz, 1H), 2.61−2.44 (m, 1H), 1.52−1.39 (m, 1H), 1.38−1.30 (m, 1H), 1.27−1.07 (m, 2H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.0, 163.7, 159.2, 153.0, 132.8, 132.2, 130.7, 130.4, 129.1, 125.9, 118.9, 114.0, 55.4, 46.7, 39.2, 37.2, 33.4, 20.4, 14.0. IR (KBr): ν 1636, 1511 cm^{-1}. HRMS (ESI) *m*/*z*: [M + H] $^+$ calcd for $C_{23}H_{24}NO_3S^+$ 394.1471, found 394.1465.

(7R,8S)-8-(4-Fluorophenyl)-2-phenyl-7-propyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3d**). Yield: 60 mg (79%), viscous solid, R_f = 0.18 (petroleum ether/ethyl ether, 8:1). $[\alpha]_D^{20}$ −30.5 (*c* 0.56, $CHCl_3$). HPLC analysis: 99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 16.0 min (major), 17.7 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (dd, *J* = 7.6, 2.2 Hz, 2H), 7.42−7.40 (m, 3H), 7.30−7.14 (m, 2H), 7.07 (t, *J* = 8.6 Hz, 2H), 4.53 (d, *J* = 5.9 Hz, 1H), 2.96 (dd, *J* = 14.8, 9.2 Hz, 1H), 2.76 (dd, *J* = 14.8, 2.2 Hz, 1H), 2.58−2.52 (m, 1H), 1.53−1.38 (m, 1H), 1.35−1.25 (m, 1H), 1.23−1.11 (m, 2H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.7, 164.0, 162.4 (d, *J* = 247.2 Hz), 161.1, 153.2, 136.0 (d, *J* = 3.3 Hz), 132.7, 130.9 (t, *J* = 2.0 Hz), 129.1, 126.0, 118.0, 115.7 (d, *J* = 21.3 Hz), 46.9, 39.0, 37.2, 33.2, 20.4, 14.0. IR (KBr): ν 2981, 1644, 1508 cm $^{-1}$. HRMS (ESI) *m*/*z*: [M + H_3O]$^+$ calcd for $C_{22}H_{23}NO_3FS^+$ 400.1377, found 400.1375.

(7R,8S)-8-(4-Chlorophenyl)-2-phenyl-7-propyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3e**). Yield: 60 mg (75%), white solid. Mp: 94−96 °C. R_f = 0.15 (petroleum ether/ethyl ether, 6:1). $[\alpha]_D^{20}$ −46.9 (*c* 1.0, $CHCl_3$). HPLC analysis: >99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 14.8 min (major), 19.5 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (dt, *J* = 7.8, 2.7 Hz, 2H), 7.48−7.31 (m, 5H), 7.21−7.15 (m, 2H), 4.52 (d, *J* = 5.9 Hz, 1H), 2.96 (dd, *J* = 14.8, 9.2 Hz, 1H), 2.76 (dd, *J* = 14.8, 2.2 Hz, 1H), 2.58−2.52 (m, 1H), 1.54−1.39 (m, 1H), 1.36−1.22 (m, 1H), 1.26−1.07 (m, 2H), 0.84 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.6, 164.1, 153.2, 138.7, 133.9, 132.6, 130.8, 130.7, 129.1, 128.9, 126.0, 117.6, 47.0, 38.8, 37.1, 33.1, 20.4, 14.0. IR (KBr): ν 2970, 1636, 1489 cm^{-1}. HRMS (ESI) *m*/*z*: [M + H]$^+$ calcd for $C_{22}H_{21}NO_2SCl^+$, 398.0976, Found 398.0973.

(7R,8S)-8-(4-Bromophenyl)-2-phenyl-7-propyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3f**). Yield: 67 mg (76%), white solid. Mp: 99−103 °C. R_f = 0.2 (petroleum ether/ethyl ether, 4:1). $[\alpha]_D^{20}$ −45.3 (*c* 0.92, $CHCl_3$). HPLC analysis: 99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 15.8 min (major), 21.0 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−7.76 (m, 2H), 7.56−7.42 (m, 2H), 7.40 (d, *J* = 6.5 Hz, 3H), 7.18−7.02 (m, 2H), 4.50 (d, *J* = 5.7 Hz, 1H), 2.96 (dd, *J* = 14.8, 9.2 Hz, 1H), 2.76 (dd, *J* = 14.9, 2.1 Hz, 1H), 2.60−2.49 (m, 1H), 1.56−1.38 (m, 1H), 1.34−1.06 (m, 3H), 0.84 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.6, 164.0, 153.2, 139.2, 132.6, 131.9, 131.0, 130.8, 129.1, 125.9, 122.0, 117.5, 47.1, 38.7, 37.1, 33.1, 20.4, 14.0. IR (KBr): ν 1636, 1486, 1465 cm^{-1}. HRMS (ESI) *m*/*z*: [M + H]$^+$ calcd for $C_{22}H_{21}BrNO_2S^+$ 442.0471, found 442.0462.

(7R,8S)-8-(4-Nitrophenyl)-2-phenyl-7-propyl-7,8-dihydrooxepino-[2,3-d]thiazol-5(6H)-one (**3g**). Yield: 63 mg (77%), viscous solid. R_f = 0.1 (petroleum ether/ethyl ether, 4:1). $[\alpha]_D^{20}$ −48.6 (*c* 0.5, $CHCl_3$). HPLC analysis: 99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 13.5 min (major), 22.2 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, *J* = 8.8 Hz, 2H), 7.84 (dd, *J* = 7.9, 1.8 Hz, 2H), 7.50−7.35 (m, 5H), 4.68 (d, *J* = 6.0 Hz, 1H), 3.01 (dd, *J* = 14.8, 8.9 Hz, 1H), 2.84 (dd, *J* = 14.9, 2.1 Hz, 1H), 2.64−2.62 (m, 1H), 1.57−1.42 (m, 1H), 1.30−1.13 (m, 3H), 0.84 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.1, 164.5, 153.4, 147.6, 147.6, 132.4, 131.1, 130.2, 129.2, 126.0, 124.0, 116.2, 47.5, 38.5, 37.2, 32.9, 20.4, 13.9. IR (KBr): ν 2975, 1637, 1490 cm^{-1}. HRMS (ESI) *m*/*z*: [M + H]$^+$ calcd for $C_{22}H_{21}N_2O_4S^+$ 409.1217, found 409.1213.

(7R,8S)-8-(3-Chlorophenyl)-2-phenyl-7-propyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3h**). Yield: 63 mg (80%), viscous solid. R_f = 0.2 (petroleum ether/ethyl ether, 6:1). $[\alpha]_D^{20}$ −48.7 (*c* 0.53, $CHCl_3$). HPLC analysis: >99% ee, [Daicel CHIRALPAK IA column, 20 °C, 254 nm *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 14.7 min (major), 18.1 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (dd, *J* = 7.6, 2.1 Hz, 2H), 7.47−7.36 (m, 3H), 7.41−7.26 (m, 2H), 7.24 (s, 1H), 7.18−7.08 (m, 1H), 4.51 (d, *J* = 5.9 Hz, 1H), 2.98 (dd, *J* = 14.9, 9.2 Hz, 1H), 2.78 (dd, *J* = 14.8, 2.1 Hz, 1H), 2.63−2.50 (m, 1H), 1.55−1.39 (m, 1H), 1.35−1.08 (m, 3H), 0.85 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.6, 164.2, 153.2, 142.2, 134.7, 132.6, 130.9, 123.0, 129.4, 129.1, 128.2, 127.6, 126.0, 117.3, 47.3, 38.7, 37.2, 33.1, 20.4, 14.0. IR (KBr): ν 2982, 1640, 1409 cm^{-1}. HRMS (ESI) *m*/*z*: [M + H] $^+$ calcd for $C_{22}H_{21}NO_2SCl^+$ 398.0976, found 398.0973.

(7R,8S)-8-(Naphthalen-1-yl)-2-phenyl-7-propyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3i**). Yield: 60 mg (73%), white solid. Mp: 143−147 °C. R_f = 0.2 (petroleum ether/ethyl ether, 10:1). $[\alpha]_D^{20}$ −90.4 (*c* 0.75, $CHCl_3$). HPLC analysis: 99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 15.2 min (major), 18.3 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 8.4 Hz, 1H), 7.87 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.78−7.76 (m, 3H), 7.56−7.44 (m, 2H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.35−7.31 (m, 4H), 5.41 (d, *J* = 5.0 Hz, 1H), 3.09 (dd, *J* = 14.4, 8.1 Hz, 1H), 2.99 (dd, *J* = 14.5, 2.1 Hz, 1H), 2.75−2.59 (m, 1H), 1.33−1.30 (m, 2H), 1.06−0.94 (m, 1H), 0.84−0.78 (m, 1H), 0.58 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.7, 164.1, 153.6, 136.7, 134.0, 132.8, 131.2, 130.7, 129.5, 129.1, 128.6, 128.1, 127.0, 126.1, 126.0, 125.2, 122.2, 119.4, 43.9, 38.3, 37.1, 31.7, 20.4, 13.9. IR (KBr): ν 2979, 1636, 1385 cm^{-1}. HRMS (ESI) *m*/*z*: [M + H]$^+$ calcd for $C_{26}H_{26}NO_3S^+$ 432.1628, found 432.1625.

(7R,8S)-7-Ethyl-2,8-diphenyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3j**). Yield: 60 mg (86%), viscous solid. R_f = 0.3 (petroleum ether/ethyl ether, 8:1). $[\alpha]_D^{20}$ −47.8 (*c* 0.45, $CHCl_3$). HPLC analysis: 99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 14.7 min (major), 19.7 min (major)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89−7.80 (m, 2H), 7.47−7.29 (m, 6H), 7.30−7.21 (m, 2H), 4.55 (d, *J* = 5.9 Hz, 1H), 3.00 (dd, *J* = 14.7, 9.2 Hz, 1H), 2.78 (dd, *J* = 14.7, 2.3 Hz, 1H), 2.53−2.40 (m, 1H), 1.47−1.41 (m, 1H), 1.28−1.08 (m, 1H), 0.92 (t, *J* = 7.4 Hz, 3H).

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^{13}C NMR (101 MHz, $CDCl_3$): δ 168.9, 163.9, 153.2, 140.2, 132.8, 130.7, 129.4, 129.1, 128.7, 128.0, 125.9, 118.3, 47.5, 41.2, 36.9, 24.2, 12.0. IR (KBr): ν 2965, 1648, 1454 cm^{-1}. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{21}H_{20}NO_2S^+$ 350.1209, found 350.1207.

*(7R,8S)-7-Heptyl-2,8-diphenyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3k**).* Total yield: 62 mg (80%), viscous solid. R_f = 0.31 (petroleum ether/ethyl ether, 8:1). $[\alpha]_D^{20}$ −39.7 (*c* 0.6, $CHCl_3$). HPLC analysis: 99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 10.9 min (major), 13.8 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (dd, *J* = 7.5, 2.4 Hz, 2H), 7.40−7.26 (m, 6H), 7.24 (d, *J* = 6.9 Hz, 2H), 4.53 (d, *J* = 5.7 Hz, 1H), 2.99 (dd, *J* = 14.8, 9.3 Hz, 1H), 2.76 (dd, *J* = 14.7, 2.3 Hz, 1H), 2.64−2.44 (m, 1H), 1.44−1.29 (m, 2H), 1.26−1.19 (m, *J* = 5.3 Hz, 10H), 0.85 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.0, 163.8, 153.2, 140.2, 132.8, 130.7, 129.4, 129.1, 128.7, 128.0, 125.9, 118.3, 47.5, 39.3, 37.3, 31.8, 31.2, 29.5, 29.2, 27.3, 22.7, 14.2. IR (KBr): ν 2966, 1650, 1453 cm^{-1}. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{26}H_{30}NO_2S^+$ 420.1997, found 420.1995.

*(7R,8S)-2,7,8-Triphenyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3l**).* Total yield: 62 mg (80%, *cis:trans* = 4:1), viscous solid. R_f = 0.1 (petroleum ether/ethyl ether, 8:1). HPLC analysis: >99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 17.8 min (major), 25.1 min (minor)]. DATA of *cis*-**3l** (obtained by recrystallization). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (dd, *J* = 6.6, 3.2 Hz, 2H), 7.43−7.42 (m, 3H), 7.26−7.09 (m, 6H), 6.76−6.72 (m, 4H), 4.73 (d, *J* = 5.9 Hz, 1H), 4.02 (ddd, *J* = 10.3, 6.1, 3.8 Hz, 1H), 3.43 (dd, *J* = 13.9, 11.1 Hz, 1H), 3.01 (dd, *J* = 13.9, 3.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.9, 163.9, 153.9, 141.9, 139.4, 138.4, 132.8, 130.8, 129.5, 129.2, 128.5, 128.2, 127.9, 127.9, 126.0, 117.9, 49.4, 47.9, 38.0. IR (KBr): ν 2980, 1645, 1458 cm^{-1}. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{25}H_{20}NO_2S^+$ 398.1209, found 398.1207.

*(7R,8S)-7,8-Bis(4-chlorophenyl)-2-phenyl-7,8-dihydrooxepino-[2,3-d]thiazol-5(6H)-one (**3m**).* Total yield: 70 mg (75%, *cis/trans* = 4:1). R_f = 0.15 (petroleum ether/ethyl acetate, 10:1). HPLC analysis: >99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 24.4 min (major), 39.1 min (minor)]. Data of *cis*-**3m** (obtained by recrystallization). White solid. Mp: 188−190 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84−7.78 (m, 2H), 7.38−7.36 (m, 3H), 7.16−7.10 (m, 2H), 7.10−7.04 (m, 2H), 6.63 (t, *J* = 8.0 Hz, 4H), 4.62 (d, *J* = 5.9 Hz, 1H), 3.91 (ddd, *J* = 9.9, 6.1, 3.7 Hz, 1H), 3.27 (dd, *J* = 14.1, 11.1 Hz, 1H), 2.91 (dd, *J* = 13.9, 3.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.2, 164.2, 153.9, 137.6, 136.6, 134.2, 134.0, 132.6, 131.0, 130.7, 129.8, 129.2, 128.9, 128.7, 128.7, 126.0, 116.8, 76.8, 48.5, 47.18, 37.9. IR (KBr): ν 2923, 1770, 1490, 1130 cm^{-1}. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{25}H_{18}Cl_2NO_2S^+$ 466.0430, found 466.0423.

*(7R,8S)-8-Phenyl-7-propyl-2-(p-tolyl)-7,8-dihydrooxepino[2,3-d]-thiazol-5(6H)-one (**3n**).* Yield: 60 mg (78%), viscous solid. R_f = 0.2 (petroleum ether/ethyl ether, 8:1). $[\alpha]_D^{20}$ −5.4 (*c* 0.5, $CHCl_3$). HPLC analysis: >99% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 16.4 min (major), 22.4 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.42−7.32 (m, 3H), 7.26−7.17 (m, 4H), 4.52 (d, *J* = 5.7 Hz, 1H), 2.98 (dd, *J* = 14.7, 9.3 Hz, 1H), 2.75 (dd, *J* = 14.7, 2.2 Hz, 1H), 2.63−2.50 (m, 1H), 2.37 (s, 3H), 1.50−1.41 (m, 1H), 1.38−1.27 (m, 1H), 1.25−1.08 (m, 2H), 0.83 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$): δ 169.1, 164.1, 153.1, 141.1, 140.2, 130.2, 129.8, 129.4, 128.7, 128.0, 125.9, 117.6, 47.5, 39.2, 37.3, 33.3, 21.6, 20.4, 14.0. IR (KBr): ν 2926, 1764, 1542, 1220 cm^{-1}. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{23}H_{24}NO_2S^+$ 378.1522, Found 378.1514.

*(7R,8S)-2-(4-Chlorophenyl)-8-phenyl-7-propyl-7,8-dihydrooxepino[2,3-d]thiazol-5(6H)-one (**3o**).* Yield: 71 mg (90%), viscous solid. R_f = 0.19 (petroleum ether/ethyl ether, 8:1). $[\alpha]_D^{20}$ −28.0 (*c* 0.6, $CHCl_3$). HPLC analysis: 97% ee [Daicel CHIRALPAK IA column, 20 °C, 254 nm hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 20.0 min (major), 22.1 min (minor)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 6.2 Hz, 2H), 7.37 (m, 4H), 7.28−7.21 (m, 3H), 4.53 (d, *J* = 3.4 Hz, 1H), 2.98 (dd, *J* = 14.6, 5.5 Hz, 1H), 2.77−2.74 (m, 1H), 2.62−2.52 (m, 1H), 1.48−1.36 (m, 1H), 1.36−1.31 (m, 1H), 1.25−1.17 (m, 2H), 0.83 (t, *J* = 5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.8, 162.5, 153.3, 140.1, 136.8, 131.3, 129.4, 129.4, 128.8, 128.1, 127.2, 118.8, 47.6, 39.1, 37.3, 33.3, 20.4, 14.0. IR (KBr): ν 2928, 1767, 1535, 1221 cm^{-1}. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{22}H_{21}ClNO_2S^+$ 398.0976, found 398.0969.

*NHC-Catalyzed Isomerization of **3a** to **4a**.* A solution of NHC precursor C (5.5 mg, 0.02 mmol), KOAc (2.0 mg, 0.02 mmol), and **3a** (>20:1 dr, > 99% ee, 36.3 mg, 0.10 mmol) in 1,4-dioxane (1 mL) was stirred at room temperature for 24 h. The reaction mixture was passed through a pad of silica gel and washed with ethyl acetate. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl ether, 10:1) to give cycloadduct **4a** as a white solid.

*(5R,8R,9S)-2,9-Diphenyl-8-propyl-1-thia-3-azaspiro[4.4]non-2-ene-4,6-dione (**4a**).* Yield: 30.8 mg (85%), white solid. Mp: 146−148 °C. R_f = 0.4 (petroleum ether/ethyl ether, 8:1). $[\alpha]_D^{20}$ −10.4 (*c* 0.5, $CHCl_3$). HPLC analysis: >99% ee, [Daicel CHIRALPAK IA column, 20 °C, 254 nm *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm, 14.8 min (minor), 16.5 min (major)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10−7.94 (m, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.26−7.19 (m, 3H), 6.92 (dd, *J* = 6.4, 3.2 Hz, 2H), 3.92 (d, *J* = 7.3 Hz, 1H), 3.58−3.41 (m, 1H), 2.89 (dd, *J* = 19.7, 9.2 Hz, 1H), 2.36 (dd, *J* = 19.7, 11.6 Hz, 1H), 1.26−1.22 (m, 2H), 1.15−1.11 (m, 1H), 0.91−0.79 (m, 1H), 0.76 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 207.9, 196.9, 188.6, 140.4, 135.6, 131.7, 129.2, 129.1, 129.0, 128.5, 127.9, 80.4, 55.6, 41.1, 37.2, 34.8, 21.4, 14.3. IR (KBr): ν 2957, 1706, 1515 cm^{-1}. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{22}H_{22}NO_2S^+$ 364.1371, found 364.1361.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00313.

NMR spectra and HPLC for obtained compounds (PDF)

X-ray data for **3l** (CIF)

X-ray data for **4a** (CIF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Zheludkevich, M. L.; Yasakau, K. A.; Poznyak, S. K.; Ferreira, M. G. S. *Corros. Sci.* **2005**, *47*, 3368. (b) Jin, Z. *Nat. Prod. Rep.* **2006**, *23*, 464. (c) Choi, H.; Pereira, A. R.; Cao, Z.; Shuman, C. F.; Engene, N.; Byrum, T.; Matainaho, T.; Murray, T. F.; Mangoni, A.; Gerwick, W. H. *J. Nat. Prod.* **2010**, *73*, 1411. (d) Lin, L.; Yang, Y.; Wang, M.; Lai, L.; Guo, Y.; Wang, R. *Chem. Commun.* **2015**, *51*, 8134.

(2) (a) Ahn, I. P.; Kim, S.; Lee, Y. H. *Plant Physiol.* **2005**, *138*, 1505. (b) Park, J. H.; Dorrestein, P. C.; Zhai, H.; Kinsland, C.; McLafferty, F. W.; Begley, T. P. *Biochemistry* **2003**, *42*, 12430. (c) Bonner, J.; Spar, B. *Science* **1937**, *85*, 183. (d) Lonsdale, D. *Evid-Based Compl. Alt.* **2006**, *3*, 49.

(3) (a) Stubbe, J.; Kozarich, J. W. *Chem. Rev.* **1987**, *87*, 1107. (b) Kross, J.; Henner, W. D.; Hecht, S. M.; Haseltine, W. A. *Biochemistry* **1982**, *21*, 4310. (c) Galm, U.; Wendt-Pienkowski, E.; Wang, L.; Huang, S.-X.; Unsin, C.; Tao, M.; Coughlin, J. M.; Shen, B. *J. Nat. Prod.* **2011**, *74*, 526. (d) Galm, U.; Wendt-Pienkowski, E.;

DOI: 10.1021/acs.joc.6b00313
J. Org. Chem. 2016, 81, 4841−4846

Wang, L.; George, N. P.; Oh, T.-J.; Yi, F.; Tao, M.; Coughlin, J. M.; Shen, B. *Mol. BioSyst.* **2009**, *5*, 77.
(4) (a) Lukacova, V.; Polonsky, J.; Moretti, C.; Pettit, G. R.; Schmidt, J. M. *J. Nat. Prod.* **1982**, *45*, 288. (b) Koul, O.; Daniewski, W. M.; Multani, J. S.; Gumulka, M.; Singh, G. *J. Agric. Food Chem.* **2003**, *51*, 7271. (c) Lin, B.-D.; Chen, H.-D.; Liu, J.; Zhang, S.; Wu, Y.; Dong, L.; Yue, J.-M. *Phytochemistry* **2010**, *71*, 1596. (d) Zhang, Y.; Wang, J.-S.; Wang, X.-B.; Gu, Y.-C.; Wei, D.-D.; Guo, C.; Yang, M.-H.; Kong, L.-Y. *J. Agric. Food Chem.* **2013**, *61*, 2171.
(5) For selected reviews, see: (a) Enders, D.; Balensiefer, T. *Acc. Chem. Res.* **2004**, *37*, 534. (b) Hopkinson, M. N.; Richter, C.; Schedler, M.; Glorius, F. *Nature* **2014**, *510*, 485. (c) Mahatthananchai, J.; Bode, J. W. *Acc. Chem. Res.* **2014**, *47*, 696. (d) Flanigan, D. M.; Romanov-Michailidis, F.; White, N. A.; Rovis, T. *Chem. Rev.* **2015**, *115*, 9307.
(6) (a) Sohn, S. S.; Rosen, E. L.; Bode, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 14370. (b) Burstein, C.; Glorius, F. *Angew. Chem., Int. Ed.* **2004**, *43*, 6205.
(7) For selected examples, see: (a) DiRocco, D. A.; Rovis, T. *J. Am. Chem. Soc.* **2011**, *133*, 10402. (b) Fang, X. Q.; Chen, X. K.; Lv, H.; Chi, Y. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 11782. (c) Sun, L. H.; Liang, Z. Q.; Jia, W. Q.; Ye, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 5803.
(8) For selected examples, see: (a) He, M.; Uc, G. J.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 15088. (b) Nair, V.; Vellalath, S.; Poonoth, M.; Suresh, E. *J. Am. Chem. Soc.* **2006**, *128*, 8736. (c) Chiang, P.-C.; Kaeobamrung, J.; Bode, J. W. *J. Am. Chem. Soc.* **2007**, *129*, 3520. (d) He, M.; Bode, J. W. *J. Am. Chem. Soc.* **2008**, *130*, 418. (e) Phillips, E. M.; Reynolds, T. E.; Scheidt, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 2416. (f) Wang, M. H.; Cohen, D. T.; Schwamb, C. B.; Mishra, R. K.; Scheidt, K. A. *J. Am. Chem. Soc.* **2015**, *137*, 5891. (g) Menon, R. S.; Biju, A. T.; Nair, V. *Chem. Soc. Rev.* **2015**, *44*, 5040. (h) Nair, V.; Vellalath, S.; Babu, B. P. *Chem. Soc. Rev.* **2008**, *37*, 2691. (i) Chen, X.; Fang, X.; Chi, Y. R. *Chem. Sci.* **2013**, *4*, 2613.
(9) For selected examples, see: (a) He, M.; Struble, J. R.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 8418. (b) Phillips, E. M.; Wadamoto, M.; Chan, A.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3107. (c) Li, Y.; Wang, X.-Q.; Zheng, C.; You, S.-L. *Chem. Commun.* **2009**, 5823. (d) Fu, Z.; Sun, H.; Chen, S.; Tiwari, B.; Li, G.; Robin Chi, Y. *Chem. Commun.* **2013**, *49*, 261.
(10) For selected examples, see: (a) Chen, X. Y.; Xia, F.; Cheng, J. T.; Ye, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 10644. (b) Mo, J.; Chen, X.; Chi, Y. R. *J. Am. Chem. Soc.* **2012**, *134*, 8810.
(11) For selected examples, see: (a) De Sarkar, S.; Studer, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 9266. (b) Rong, Z. Q.; Jia, M. Q.; You, S. L. *Org. Lett.* **2011**, *13*, 4080. (c) Bera, S.; Samanta, R. C.; Daniliuc, C. G.; Studer, A. *Angew. Chem., Int. Ed.* **2014**, *53*, 9622. (d) Bera, S.; Daniliuc, C. G.; Studer, A. *Org. Lett.* **2015**, *17*, 4940. (e) Liang, Z. Q.; Wang, D. L.; Zhang, H. M.; Ye, S. *Org. Lett.* **2015**, *17*, 5140. (f) Mao, J.-H.; Wang, Z.-T.; Wang, Z.-Y.; Cheng, Y. *J. Org. Chem.* **2015**, *80*, 6350. (g) Xie, D.; Yang, L.; Lin, Y.; Zhang, Z.; Chen, D.; Zeng, X.; Zhong, G. *Org. Lett.* **2015**, *17*, 2318. (h) Yetra, S. R.; Mondal, S.; Suresh, E.; Biju, A. T. *Org. Lett.* **2015**, *17*, 1417.
(12) Zhu, T.; Mou, C.; Li, B.; Smetankova, M.; Song, B.-A.; Chi, Y. R. *J. Am. Chem. Soc.* **2015**, *137*, 5658.
(13) (a) White, N. A.; Rovis, T. *J. Am. Chem. Soc.* **2014**, *136*, 14674. (b) White, N. A.; Rovis, T. *J. Am. Chem. Soc.* **2015**, *137*, 10112. (c) Zhang, Y.; Du, Y.; Huang, Z.; Xu, J.; Wu, X.; Wang, Y.; Wang, M.; Yang, S.; Webster, R. D.; Chi, Y. R. *J. Am. Chem. Soc.* **2015**, *137*, 2416.
(14) (a) Izquierdo, J.; Orue, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2013**, *135*, 10634. (b) Lv, H.; Jia, W. Q.; Sun, L. H.; Ye, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 8607.
(15) Wang, M.; Rong, Z.-Q.; Zhao, Y. *Chem. Commun.* **2014**, *50*, 15309.
(16) Liang, Z.-Q.; Gao, Z.-H.; Jia, W.-Q.; Ye, S. *Chem. - Eur. J.* **2015**, *21*, 1868.
(17) (a) Zhang, Y.-R.; He, L.; Wu, X.; Shao, P.-L.; Ye, S. *Org. Lett.* **2008**, *10*, 277. (b) Enders, D.; Han, J. *Tetrahedron: Asymmetry* **2008**, *19*, 1367. (c) Enders, D.; Han, J. *Synthesis* **2008**, *2008*, 3864.
(18) (a) He, L.; Zhang, Y.-R.; Huang, X.-L.; Ye, S. *Synthesis* **2008**, *2008*, 2825. (b) Huang, X.-L.; He, L.; Shao, P.-L.; Ye, S. *Angew. Chem., Int. Ed.* **2009**, *48*, 192. (c) Huang, X.-L.; Ye, S. *Chin. Sci. Bull.* **2010**, *55*, 1753.
(19) Guo, C.; Schedler, M.; Daniliuc, C. G.; Glorius, F. *Angew. Chem., Int. Ed.* **2014**, *53*, 10232.
(20) According to the literature (refs 14 and 15), the *E*-configuration of the enol is favored when less sterically demanded NHC is used.

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