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Regiodivergent Enantioselective γ-Additions of Oxazolones to 2,3-Butadienoates Catalyzed by Phosphines: Synthesis of α,α-Disubstituted α-Amino Acids and *N,O*-Acetal Derivatives

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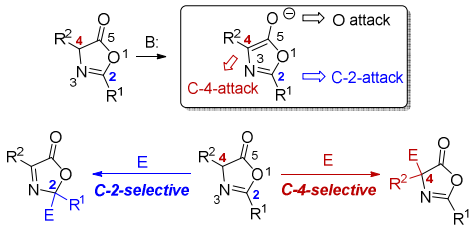
ABSTRACT: Phosphine-catalyzed regiodivergent enantioselective C-2- and C-4-selective γ-additions of oxazolones to 2,3-butadienoates have been developed. The C-4-selective γ-addition of oxazolones occurred in a highly enantioselective manner when 2-aryl-4-alkyl oxazol-5-(4*H*)-ones were employed as pronucleophiles. With the employment of 2-alkyl-4-aryl oxazol-5-(4*H*)-ones as the donor, C-2-selective γ-addition of oxazolones took place in a highly enantioselective manner. The C-4-selective adducts provided a rapid access to optically enriched α,α-disubstituted α-amino acid derivatives, and the C-2-selective products led to facile synthesis of chiral *N,O*-acetals and γ-lactols. Theoretical studies via DFT calculations suggested that the origin of the observed regioselectivity was due to the distortion energy resulted from the interaction between nucleophilic oxazolide and electrophilic phosphonium intermediate.

INTRODUCTION

The chemistry of oxazol-5-(4*H*)-ones (henceforth referred to as oxazolones) has been extensively explored over the past decades, owing to their importance in the synthesis of amino acid derivatives and various heterocyclic structures.[1] Oxazolones have been widely used as a nucleophilic reaction partner due to the relatively high acidity of the α-proton. As shown in Scheme 1, the enolate intermediate generated upon deprotonation of oxazolones may react with electrophiles at different sites, resulting in the formation of different regioisomers. At the outset, we were particularly interested in developing regiodivergent approaches to prepare both C-2-selective and C-4-selective addition products of oxazolones; since the former would allow easy access to disubstituted *N,O*-acetals,[2] and the latter serve as precursors for the synthesis of α,α-disubstituted α-amino acids.[3] A number of transition metal-mediated reactions of oxazolones were reported, and C-4-selectivity was observed exclusively in all the cases.[4] Recently, organocatalytic approaches employing oxazolones have also been developed. All the existing methods focused on conjugate additions of oxazolones to various activated alkenes, e.g. α,β-unsaturated carbonyl compounds,[5] nitroolefins,[6] and vinyl sulfones.[7] It is noteworthy that almost all the above additions of oxazolones took place at the C-4-position, except in two examples whereby C-2-selectivity dominating. While Ooi and co-workers demonstrated that chiral organic ion pair catalyst could effect a C-2-selective addition to α,β-unsaturated acylbenzotriazole,[5b] Jørgensen et al. achieved C-2-selective addition by using acyl phosphonates and chiral thioureas.[5d] To the best of our knowledge, a versatile strategy enabling highly enantioselective additions of oxazolones at both C-2- and C-4-positions is unknown. Given the importance of both classes of adducts, it is highly desirable to develop a regiodivergent approach for oxazolone addition reactions.

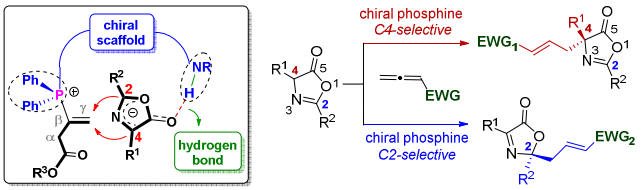
Scheme 1. Regioselectivity in Oxazolone Reactions



Asymmetric phosphine catalysis has been well established as a powerful tool for the creation of chiral molecules.[8] Our group has been intensively investigating this research field in recent years. We designed a series of amino acid-based bifunctional phosphines and applied them to a wide range of reactions, including: (aza)-Morita–Baylis–Hillman reactions,[9] allylic alkylation,[10] Michael addition[11] and various [3+2]/4+2]/[4+1] annulation reactions.[12] Phosphine-catalyzed γ-addition reac

tions[13] are valuable reactions in organic synthesis, and many excellent asymmetric examples emerged in the literature in the past few years.[14] Very recently, we disclosed the utilization of 2,3-butadienoates and prochiral nucleophiles in phosphine-catalyzed γ-addition reactions.[15] Given the acidity of the α-proton in oxazolone structures, we set out to examine whether it is feasible to utilize oxazolones in phosphine-mediated γ-additions.[16a] We envisioned that phosphonium enolate intermediate should be basic enough to activate oxazolones. The subsequently formed ionic pair between phosphonium and oxazolone-derived enoloate, with the assistance of hydrogen bonding network, is expected to have a defined structure. We hypothesize that by tuning the chiral bifunctional phosphines, varying oxazolone structures, and employing different allenoates, we may be able to achieve regiodivergent additions of oxazolones to allenoates (Scheme 2). Herein, we document the first example of regiodivergent C-2-selective and C-4-selective γ-additions of oxazolones to allenoates, leading to highly enantioselective preparation of *N*,*O*-acetal derivatives and α,α-disubstituted α-amino acids, respectively. Moreover, DFT calculations were performed to gain insights into the origin of observed regioselectivity.

Scheme 2. Bifuncitonal Phosphine-catalyzed Enantioselective Regiodivergent γ-Additions of Oxazolones to Allenoates

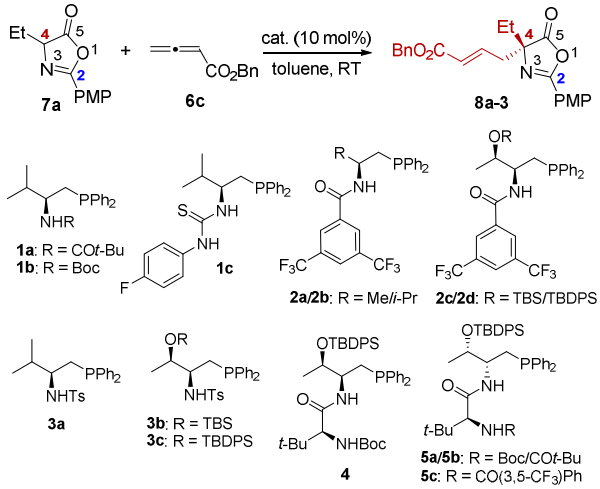


RESULTS AND DISCUSSION

Phosphine-Catalyzed C-4-selective and Enantioselective γ-Addition of Oxazolones. Initially, the γ-addition of 2-(4-methoxyphenyl)-4-ethyloxazol-5(4*H*)-one **7a** to 2,3-butadienoate **6c** was selected as a model reaction, and the catalytic effects of various bifunctional phosphines were evaluated (Table 1). To our delight, all the phosphines examined were effective in promoting the reaction, affording C-4 selective γ-addition adducts as the only product. Bifunctional phosphines with a carbamate, thiourea or amide were found to be ineffective in asymmetric induction, affording the adducts with low ee values (entries 1–7). Bifunctional phosphines with a sulfonamide group were discovered excellent in stereochemical controls (entries 8–10), and dipeptide phosphine catalysts were less effective (entries 11–14). In the presence of O-TBDPS-L-threonine-based phosphine sulfonamide **3c**, C-4 selective γ-addition product was obtained in high yield and with good enantioselectivity (entry 10).

Having identified the best catalyst **3c**, we continued with further optimizations (Table 2). Among all the allenoates examined, the *tert*-butyl ester (**6b**) proved to be the best reaction partner (entries 1–8), and toluene remained to be the solvent of choice (entries 9–12). When the reaction was run with **6b** in toluene at -20 °C, the desired γ-addition adduct was isolated in 94 % yield and with 95 % ee (entry 14).

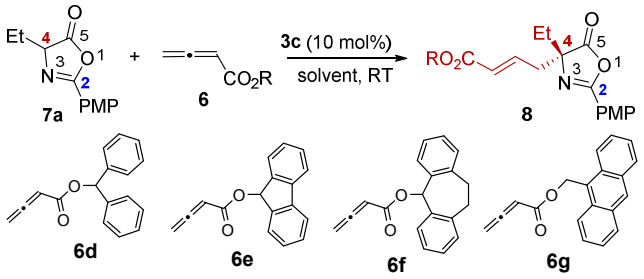
Table 1. Enantioselective C-4 Selective γ-Addition of Oxazolone 7a to Allenoate 6c Catalyzed by Different Phosphines[a]



entry	catalyst	*t* (h)	C-4:C-2[b]	yield (%)[c]	ee (%)[d]
1	**1a**	15	>20:1	84	11
2	**1b**	12	>20:1	91	54
3	**1c**	12	>20:1	93	35
4	**2a**	12	>20:1	90	41
5	**2b**	12	>20:1	87	53
6	**2c**	12	>20:1	91	36
7	**2d**	12	>20:1	91	38
8	**3a**	12	>20:1	92	53
9	**3b**	12	>20:1	95	77
10	**3c**	12	>20:1	96	81
11	**4**	18	>20:1	89	19
12	**5a**	18	>20:1	91	-61
13	**5b**	18	>20:1	90	-45
14	**5c**	18	>20:1	89	-37

[a] Reactions were performed with **7a** (0.1 mmol), **6c** (0.12 mmol) and the catalyst (0.01 mmol) in toluene (1.0 mL) at room temperature. [b] Determined by ^{1}H NMR analysis of the crude mixture. [c] Isolated yield. [d] Determined by HPLC analysis on a chiral stationary phase. TBDPS = tert-butyldiphenylsilyl, TBS = tert-butyldimethylsilyl, Ts = 4-toluenesulfonyl, PMP = 4-methoxyphenyl.

Table 2. Optimization of C-4-Selective γ-Addition Reaction[a]

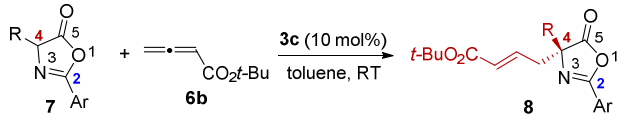


entry	R(**6**)	solvent	**8**	yield (%)[b]	ee (%)[c]
1	Et(**6a**)	toluene	**8a-1**	94	83
2	*t*-Bu(**6b**)	toluene	**8a-2**	95	88
3	Bn(**6c**)	toluene	**8a-3**	96	78
4	**6d**	toluene	**8a-4**	93	75
5	**6e**	toluene	**8a-5**	94	72
6	**6f**	toluene	**8a-6**	94	77
7	**6g**	toluene	**8a-7**	90	70
8	Ph(**6h**)	toluene	**8a-8**	89	72
9	*t*-Bu(**6b**)	xylene	**8a-1**	95	81
10	*t*-Bu(**6b**)	Et_2O	**8a-1**	96	78
11	*t*-Bu(**6b**)	$CHCl_3$	**8a-1**	95	31
12	*t*-Bu(**6b**)	CH_2Cl_2	**8a-1**	93	63
13[d,e]	*t*-Bu(**6b**)	toluene	**8a-1**	96	93
14[d,f]	*t*-Bu(**6b**)	toluene	**8a-1**	94	95

[a] Reactions were performed with **7a** (0.10 mmol), **6** (0.12 mmol) and **3c** (0.01 mmol) in the solvent specified (1.0 mL) at room temperature overnight. [b] Isolated yield. [c] Determined by HPLC analysis on a chiral stationary phase. [d] With 0.15 mmol allenoate. [e] The reaction was run at 0 °C for 20 h. [f] At -20 °C for 48 h.

With the optimized reaction conditions for C-4-selective addition of oxazolones in hand, we explored the scope of the reaction (Table 3). Oxazolones with various aliphatic substituents at the C-4 position could be employed, and the C-4-selective adducts were obtained in high yields and with excellent enantioselectivities (entries 1–11). Both linear and branched alkyl groups at the C-4 position were well-tolerated. Remarkably, when *tert*-butyl substituted oxazolone was used, enantiomerically enriched γ-addition product was isolated in 91% yield, despite the fact that the newly formed stereogenic center was extremely sterically hindered (entry 7). Notably, the reaction was also well-tolerated for sulfur-containing oxazolones (entries 8 and 9). The presence of phenyl group in the C-4-alkyl-substituted oxazolones slightly lowered the enantioselectivity of the reaction (entries 12 and 13). When the oxazolones with different aryl groups at the 2-position were used, the excellent C-4-selectivity and enantioselectivity of the reaction were maintained (entries 14 and 15). However, oxazolones with an aryl substitution at the 4-position were found to be unsuitable;[17] although C-4-selective adduct was obtained in excellent yield, the ee value was very low (entry 16). The absolute configurations of the γ-addition products (**8**) were assigned by comparing the optical rotation of derivative **14** with the value reported in the literature.[18]

Table 3. Substrate Scope for 3c-Catalyzed C-4-Selective Enantioselective γ-Addition of Oxazolones 7 to Allenoate 6b[a]



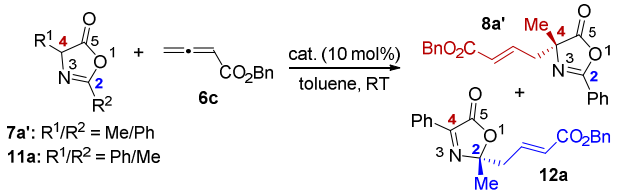
entry	R/Ar	C-4:C-2[b]	prod./yield (%)[c]	ee (%)[d]
1	Et/PMP	>20:1	**8a**/94	95
2	Me/PMP	19:1	**8b**/96	93
3	*n*-Pr/PMP	14:1	**8c**/99	92
4	*i*-Pr/PMP	>20:1	**8d**/94	90
5	*n*-Bu/PMP	>20:1	**8e**/95	91
6	*iso*-Bu/PMP	>20:1	**8f**/94	90
7[e]	*t*-Bu/PMP	>20:1	**8g**/91	94
8	CH_2SCH_3/PMP	>20:1	**8h**/91	91
9	$(CH_2)_2SCH_3$/PMP	>20:1	**8i**/88	93
10	*n*-C_6H_{13}/PMP	>20:1	**8j**/97	95
11	$CH(CH_2)_5$/PMP	>20:1	**8k**/96	91

12	$(CH_2)_2Ph$/PMP	>20:1	**8l**/95	84
13	Bn/PMP	>20:1	**8m**/93	80
14	Et/C_6H_5	19:1	**8n**/94	92
15[f]	Et/4-F-C_6H_4	19:1	**8o**/89	91
16	Ph/PMP (**9**)	>20:1	**10**/89	30

[a] Reactions were performed with **8** (0.1 mmol), **6b** (0.15 mmol) and **3c** (0.01 mmol) in toluene (1.0 mL) at -20 °C for 48 h. [b] Determined by ^{1}H NMR of the crude reaction mixture. [c] Isolated yield. [d] ee of major product and determined by HPLC analysis on a chiral stationary phase. [e] with 0.02 mmol catalyst **3c**. [f] The reaction was stirred for 60 h. PMP = 4-methoxyphenyl.

Phosphine-Catalyzed C-2- Selective and Enantioselective γ-Addition of Oxazolones. Having established the enantioselective pathway to derive C-4-selective γ-addition products, we next focused on developing γ-addition of oxazolones to allenoates in a C-2-selective fashion. We reasoned judicious selection of substrates utilized and careful tuning the catalyst structures may lead to the discovery of an enantioselective C-2-selective γ-addition. Consequently, different substituted oxazolones and benzyl 2,3-butadienoate were employed, and the results are summarized in Table 4. We were delighted to uncover that replacement of 2-phenyl-4-ethyloxazol-5(4*H*)-one **7a'** with 2-methyl-4-phenyloxazol-5(4*H*)-one **11a** completely reverted the regioselectivity, leading to excellent C-2-selective product formation (entries 1 & 2). The above results suggested the nature of the substituents at C-2 and C-4 positions of oxazolones seems crucial for the regioselectivity of the γ-additions to allenes. Various bifunctional phosphines were subsequently screened, aiming to improve enantioselectivity of the reaction. While all the phosphines examined afforded C-2-selective adducts, dipeptide phosphines were found to be more effective for asymmetric induction (entries 3–14). When **5c** was used, the C-2-selective product, *N*,*O*-acetal **12a** was obtained in 92% yield and with 85% ee (entry 15). The substrate scope for C-2-selective γ-addition of oxazolones to allenoates was next evaluated using the optimal conditions identified (Table 5). The reaction worked well for various C-2-substituted oxazolones, although the C-2-selectivities for linear alkyl substituents were superior to those obtained with branched alkyl groups (entries 1–7). Variation of the substituents at the C-4-positions of oxazolones could also be tolerated (entries 8–11). When 2-benzyl-4-phenyl substituted oxazolone was used, the ee value for the C-2-selective product dropped (entry 12).

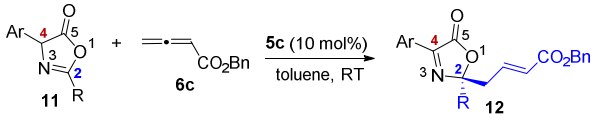
Table 4. Enantioselective C-2-Selective γ-Addition of Oxazolones: Initial Screenings [a]



entry	sub.	cat.	C-2:C-4[b]	prod./yield (%)[c]	ee (%)[d]
1	**7a'**	**3c**	<1:20	**8a'**/91	74
2	**11a**	**3c**	>20:1	**12a**/92	67
3	**11a**	**1a**	7:1	**12a**/83	16
4	**11a**	**1b**	4:1	**12a**/76	19
5	**11a**	**1c**	9:1	**12a**/86	32
6	**11a**	**2a**	10:1	**12a**/88	46
7	**11a**	**2b**	14:1	**12a**/89	50
8	**11a**	**2c**	19:1	**12a**/90	65
9	**11a**	**2d**	>20:1	**12a**/91	73
10	**11a**	**3a**	12:1	**12a**/90	43
11	**11a**	**3b**	19:1	**12a**/94	51
12	**11a**	**4**	>20:1	**12a**/92	60
13	**11a**	**5a**	>20:1	**12a**/91	-70
14	**11a**	**5b**	>20:1	**12a**/92	-62
15	**11a**	**5c**	**>20:1**	**12a/92**	**-85**

[a] Reactions were performed with **11a** or **7a'** (0.1 mmol), **6c** (0.12 mmol) and the catalyst (0.01 mmol) in toluene (1.0 mL) at RT for 12-18 h. [b] Determined by 1H NMR of the crude reaction mixture. [c] Isolated yield. [d] ee of the major product and determined by HPLC analysis on a chiral stationary phase.

Table 5. Substrate Scope for the C-2-Selective γ-Addition [a]

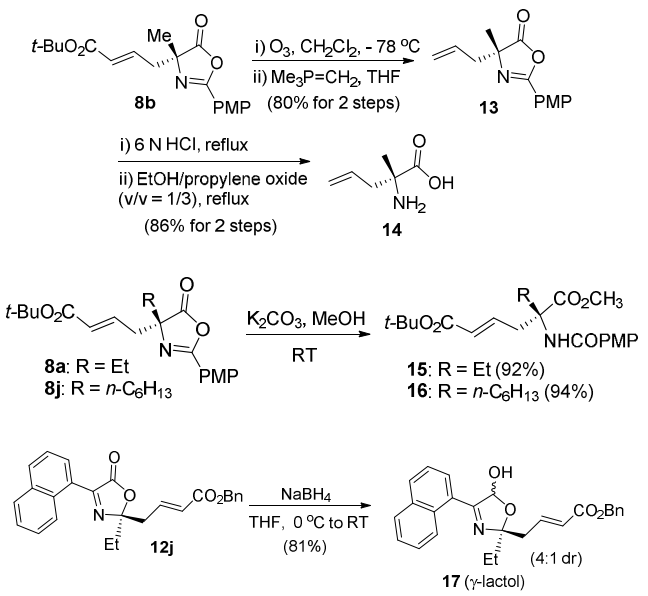


entry	R/Ar	C-2:C-4[b]	**12**/yield (%)[c]	ee (%)[d]
1	Me/Ph	>20:1	**12a**/92	85
2	Et/Ph	>20:1	**12b**/90	85
3[e]	*n*-Pr/Ph	>20:1	**12c**/88	87
4	*i*-Pr/Ph	9:1	**12d**/87	85
5	*n*-Bu/Ph	>20:1	**12e**/93	95
6	*n*-C_5H_{11}/Ph	12:1	**12f**/88	91
7[f]	C_6H_{11}/Ph	6:1(19:1)	**12g**/81(91)	96(80)
8	Et/2-Nap	>20:1	**12h**/95	92
9[e]	*n*-C_5H_{11}/2-Nap	19:1	**12i**/94	88
10	Et/1-Nap	>20:1	**12j**/95	94
11	*n*-Pr/1-Nap	>20:1	**12k**/95	93
12	Bn/Ph	>20:1	**12l**/93	80

[a] Reactions were performed with **11** (0.1 mmol), **6c** (0.12 mmol) and the catalyst **5c** (0.01 mmol) in toluene (1.0 mL) at RT for 12 h. [b] Determined by ^{1}H NMR analysis of the crude mixture. [c] Isolated yield. [d] The ee of the major product and determined by HPLC analysis on a chiral stationary phase. [e] With 0.02 mmol catalyst **5c** at 0 °C for 24 h. [f] With 0.02 mmol catalyst **5c** at -20 °C for 48 h, and the data in parentheses were obtained at room temperature.

Regioselective γ-additions of oxazolones to 2,3-butadienoates offer straightforward synthetic methods to challenging yet valuable molecular architectures. The C-4-selective adducts are not only precursors to α,α-disubstituted α-amino acid derivatives, they are also synthetically useful given the rich functionality in the structure.[16] The C-2-selective adducts of this reaction, on the other hand, represent optically enriched *N,O*-acetals. As illustrated in Scheme 3, adduct **8b** could be readily converted to allyl-substituted oxazolone **13** in high yield.[15] Acidic hydrolysis led to ring opening of **13** and simultaneous cleavage of the 4-methoxybenzoyl group, affording α,α-disubstituted α-amino acid **14** in high yield. Alternatively, ring opening of oxazolone under mild basic conditions yielded the corresponding α,α-disubstituted α-amino acid derivatives **15** and **16** in excellent yields. When C-2-selective γ-addition product **12j** was treated with $NaBH_4$, lactol **17** was readily obtained in good yield.

Scheme 3. Elaboration of γ-Addition Adducts



Mechanistic Studies to Understand the Origin of Observed Regioselectivity. The mechanism of the γ-addition in this report is believed to follow the general mechanism described in the literature,[14,15] and the detailed mechanistic pathways are illustrated in Figure 1. Nucleophilic addition of **3c** to **6c** yields a zwitterionic intermediate **A**, which abstracts the C-4-proton of 2-phenyl-4-methyloxazol-5(4*H*)-one **7a'** to form oxazolide **C1** and phosphonium **B**. The subsequent nucleophilic addition takes place at **C-4** position of **C1** via transition state **TS3-C4**, leading to the formation of intermediate **D1-C4**. A hydride shift then takes place and affords intermediate **E1-C4**, which generates addition product **8** upon elimination of **3c**. On the other hand, when 2-methyl-4-phenyloxazol-5(4*H*)-one **11a** is employed, oxazolide **C2** is generated. In this pathway, the **C-2**-selective addition is favoured, which eventually leads to the formation of **C-2**-selective product **12a**, via a key transition state **TS5-C2**.

It was rather striking to discover in this study that the employment of different alkyl or aryl groups at **C-2-** or **C-4-** position of oxazolones could result in highly regiodivergent γ-additions to allenoates, we thus probed the reaction mechanism[19] by DFT calculations to understand the origin of the observed regioselectivity. The Gibbs free energy profiles of **3c**-catalyzed γ-addition reaction of oxazolones **7a'** or **11a** to allenoate **6c** were calculated,[20] and we focused on the step of adding oxazolide (**7a'-1/2** or **11a-1/2**) to phosphonium (**A**) to understand the observed regioselectivity (Figure 2). When 2-phenyl-4-methyloxazol-5(4*H*)-one **7a'** is used as a substrate, the above addition step can take place via transition state **TS3-*C2-re*** at C-2 position or via transition state **TS3-*C4-re*** at C-4 position. The calculated activation energy for **TS3-*C4-re*** (C-4-selective) is 2.4 kcal/mol lower than the value for **TS3-*C2-re*** (C-2-selective), corresponding to a regioselectivity of

1:56 (C-2:C-4), which is consistent with our experimental observation. Examination of geometries of the two transition states revealed that the bond lengths are comparable, suggesting the steric repulsion is not accountable for the energy difference. To gain more insights, we then applied distortion/interaction model[21] ($\Delta E^{\neq} = \Delta E^{\neq}_{dist} + \Delta E^{\neq}_{int}$) and utilized oxazolide and phosphonium as two fragments to further analyze the reaction. The difference of interaction energy terms ($\Delta E^{\neq}_{int}$) between **TS3-*C2-re*** and **TS3-*C4-re*** is only 1.4 kcal/mol. However, the difference of distortion energy terms ($\Delta E^{\neq}_{dist}$) between the two pathways is 3.7 kcal/mol, suggesting distortion energy played a key role in observed regioselectivity. When **7a'-1** reacts at the C-2-position with phosphonium to form the new C–C bond, the hybridization state of C-2 changes from sp2 to sp3. In transition state **TS3-*C2-re***, the presence of 2-phenyl group reduces the reactivity of C-2 through conjugation, and it also makes the distortion of the reacting C-2 carbon unfavorable. Furthermore, the dihedral angle of $D_{C_3\text{-}C_2\text{-}N_3}$-C4 in **TS3-*C2-re*** is 149.7, 2.8° smaller than that in **TS3-*C4-re***, correlating well with the distortion energy difference between the two transition states. Similar analysis was applied to the γ-addition of **11a**. The calculated free energy difference between the two transition states **TS5-*C2-re*** and **TS5-*C4-re*** is 2.5 kcal/mol, corresponding to a 1:66 (C-4:C-2) selectivity, which is consistent with the experimental observation. In the less-favored **TS5-*C4-re***, the conjugation of the phenyl group leads to a higher distortion energy. On the other hand, the non-conjugated methyl group at C-2- position makes the distortion at C-2 easier and accounts for the observed C-2-selectivity of the γ-addition.

The Origin of Observed Enantioselectivity. We also performed DFT calculations to understand the enantioselectivity of the above phosphine-catalyzed γ-addition reactions (Figure 3). The enantioselectivity of the reaction is determined at the nucleophilic attack step. When **7a'** is employed, the *re*-face attack occurs through transition state **Ts3-*C4-re*** with a barrier of 13.0 kcal/mol, affording intermediate **E1-C4-*R*** with an *R*-configuration. Alternatively, the *Si*-face attack proceeds via transition state **Ts3-*C4-si*** with a higher barrier of 16.1 kcal/mol. The B3LYP-D3 calculations predict a value of 99% ee for *R*-isomer, which is consistent with the experimental observation. When substrate **11a** is employed, a value of 87% ee predicted by the B3LYP-D3 method based on the energy difference of **Ts5-*C2-re*** and **Ts5-*C2-si*** is in good agreement with the experimental result. In the geometry of **Ts2-*C4-si***, the H…O distance of 2.52 Å and H…H distance of 3.06 Å suggests the repulsion between the phenyl group of reactant and the phosphine catalyst, resulting in a higher transition state barrier. Similarly, in the geometry **Ts5-*C2-si***, the short H…H distance of 2.68 Å and H…C distance of 3.14 Å lead to the repulsion between the phenyl group of reactant and the phosphine catalyst, accounting for favorable *re*-face attack.

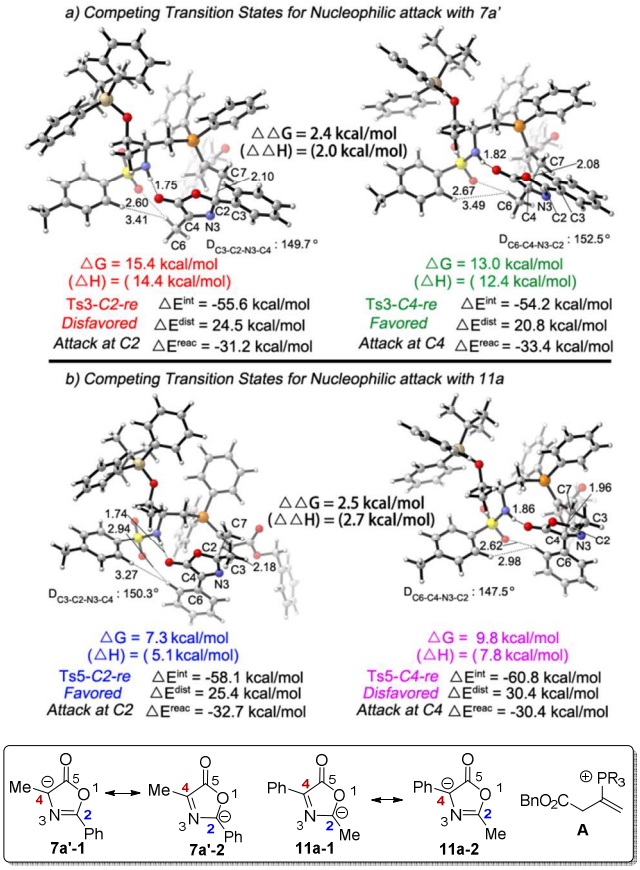


Figure 2. Optimized transition states for **3c**-catalyzed nucleophilic attack with **7a'** and **11a**.

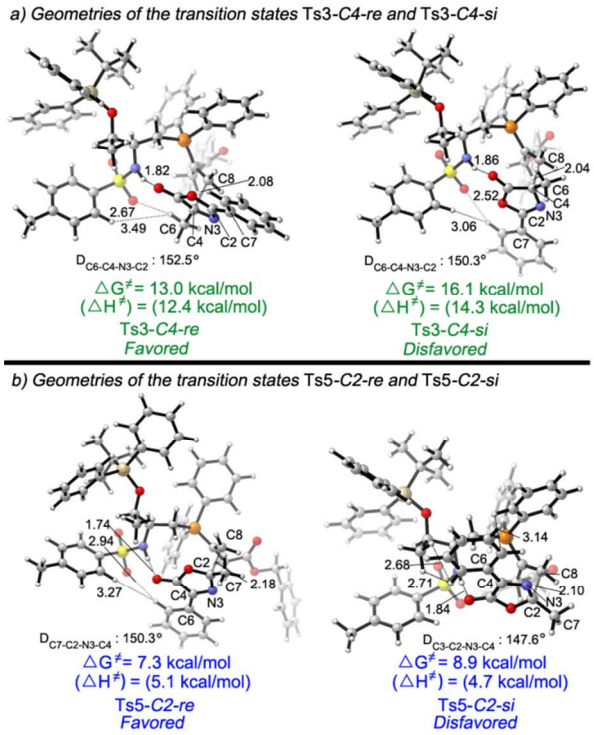


Figure 3. Geometries of the **Ts3-*C4-re***, **Ts3-*C4-si***, **Ts5-*C2-re*** and **Ts5-*C2-si*** transition states with **3c** as catalyst.

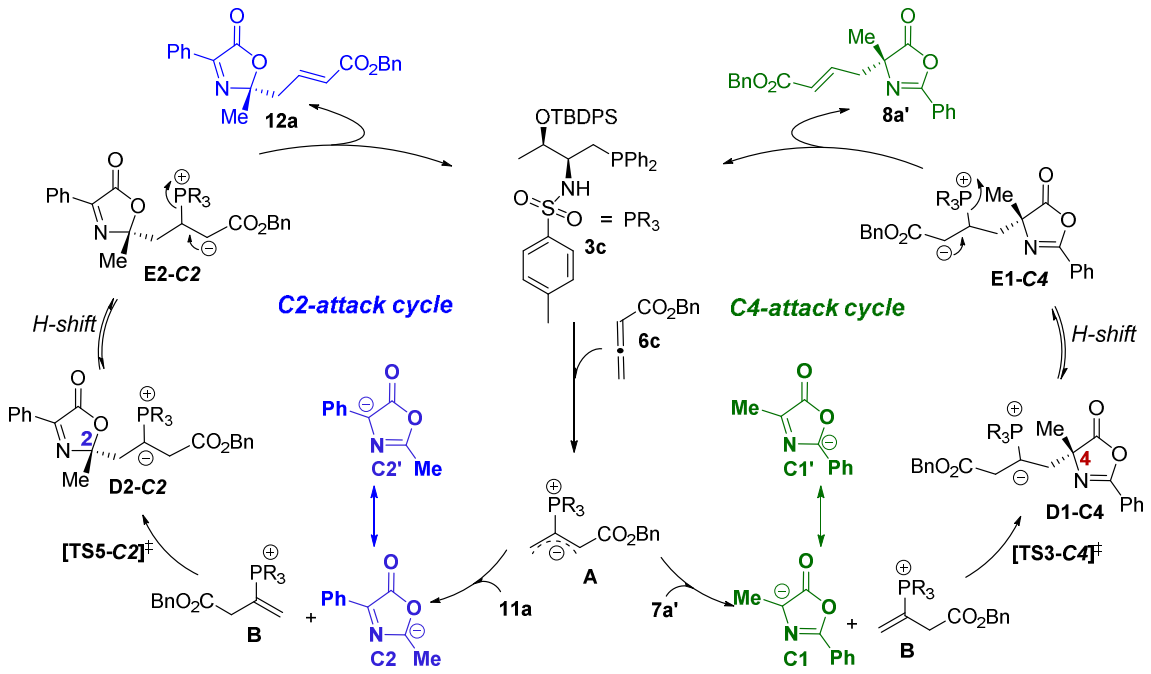


Figure 1. Proposed mechanism for the **3c**-catalyzed γ-addition of oxazolones (**7a'** or **11a**) to allenoate **6c**.

CONCLUSIONS

In conclusion, we have discovered the first regiodivergent enantioselective γ-additions of oxazolones to 2,3-butadienoates catalyzed by chiral phosphines. By employing 2-aryl-4-alkyl-substituted oxazolones as donors, the C-4-selective γ-addition occurred to furnish highly enantiomerically enriched 4,4-disubstituted oxazolones, which are the valuable precursors to α,α-disubstituted α-amino acid derivatives. The employment of 2-alkyl-4-aryl- substituted oxazolones as pronucleophiles led to exclusive C-2-selective γ-addition to 2,3-butadienoates, and the adducts are valuable for creation of chiral *N,O*-acetal and lactols. Disclosed herein is the first practical approach for controlling highly enantioselective C-2 and C-4-selective γ-additions of oxazolones to 2,3-butadienoates, leading to facile synthesis of optically enriched α,α-disubstituted α-amino acid and γ-lactol derivatives. Our theoretical investigations revealed that the regioselectivity was determined by the distortion energy resulted from the interactions between nucleophilic oxazolide and electrophilic phosphonium intermediate, and the mechanistic insights gained may open up new avenues for the design of regioselective addition processes of oxazolones and other similar donors. Such efforts are currently on-going in our laboratory, and will be reported in due course.

ASSOCIATED CONTENT

Supporting Information. Synthetic and experimental details, the characterizations of catalysts, substrates and products, and the analysis of enantioselectivities of γ-addition adducts. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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Graphic Abstract