Organic & Biomolecular Chemistry

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Cite this: *Org. Biomol. Chem.*, 2012, **10**, 773

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PAPER

Phosphine-catalyzed [4 + 2] annulation and vinylogous addition reactions between 1,4-dien-3-ones and 1,1-dicyanoalkenes†

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Received 17th July 2011, Accepted 5th October 2011
DOI: 10.1039/c1ob06187a

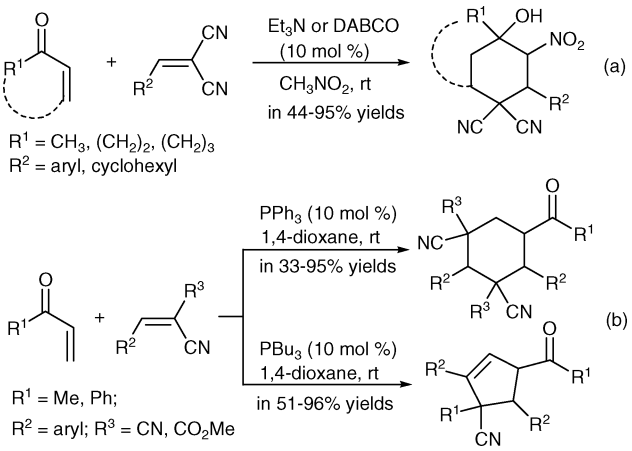
Phosphine-catalyzed [4 + 2] annulation and vinylogous Michael addition reactions between 1,4-dien-3-ones and 1,1-dicyanoalkenes are presented. Under the catalysis of PBu_3 (20 mol %), 1,4-dien-3-ones like styryl ketones with 2-aryl 1,1-dicyanoalkenes as doubly activated alkenes readily undergo a formal [4 + 2] cycloaddition reaction, affording polysubstituted cyclohexanones in satisfactory yield and good diastereoselectivity; with the doubly activated alkenes bearing an acidic methyl or methylene at the 2-position, a vinylogous Michael addition of 1,4-dien-3-ones occurs under the same reaction conditions, giving a non-cyclized multifunctional adduct in good yield. These two phosphine-catalyzed transformations represent atom economical carbon–carbon bond forming reactions capable of rapid construction of molecular complexity. Based on experimental results, formation of the products has been mechanistically rationalized, and a phosphonium activation is proposed.

Introduction

The carbon–carbon bond forming reaction is fundamental to organic synthesis, with enormous research efforts engaged in improving reaction efficiency, stereoselectivity, and chemoselectivity.[1] Over the past decade, nucleophilic phosphine organocatalysis,[2] as a powerful strategy for efficient C–C bond formation, has become one of the hot research topics in the field of synthetic chemistry. A number of phosphine-catalyzed reactions, typically including the Morita–Baylis–Hillman (MBH) reaction,[3a,3b] the Rauhut–Currier (RC) reaction,[3c] and many important annulation reactions of electron-deficient allenes or alkynes,[2c,2d] have been actively explored as efficient and atom economical synthetic methods.

In those reactions, carbonyl-activated alkenes, such as conjugated enones and enoates, are the most popular substrates, acting as latent enolates (nucleophiles) and/or Michael acceptors (electrophiles). A common phosphine-catalyzed reaction of carbonyl-activated alkenes encompasses generation of a latent enolate *via* nucleophilic addition of a catalyst phosphine and subsequent coupling of the enolate with an electrophile, like aldehydes, imines, or Michael acceptors, to fulfill a new C–C bond formation. The chemoselective coupling between an activated alkene (acting as a latent enolate) and an aldehyde (or imine) could be readily achieved under the influence of a nucleophilic phosphine, as evidenced in the reported MBH reactions.[3a] However, a highly chemo-controlled phosphine-catalyzed cross-coupling between two different Michael acceptors remains a challenging goal,[4] although encouraging progress has been made in recent years, particularly with regard to intramolecular versions of the RC reaction.[3c]

Recently, we have successfully developed a conjugated enone–doubly activated alkene strategy to achieve highly chemoselective cross-couplings between two different Michael acceptors (Scheme 1).[5] Under the catalysis of a tertiary amine Lewis base, a highly diastereoselective three-component cascade annulation reaction has been realized in a Michael–Michael–Henry sequence from



Scheme 1 Lewis base-catalyzed cross-couplings between two different activated alkenes.

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† Electronic supplementary information (ESI) available: experimental details for Scheme 4; X-ray crystal structure data and ORTEP drawings for (*trans*, *E*)-**3b** and **4b**; copies of ^1H and ^{13}C NMR spectra for **3**, **4**, **5** and **6**; copies of 2D-NMR spectra for representative compounds. CCDC reference numbers 827159 and 827760. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob06187a

enones, 1,1-dicyanoalkenes and nitromethane, providing an efficient synthetic method for densely functionalized cyclohexanes and some bicyclic compounds (Scheme 1, a).[5a] Interestingly, under the mediation of tertiary phosphines possessing different leaving group abilities, highly chemoselective cascade [2 + 2 + 2] and [2 + 2 + 1] annulation reactions occurred, respectively, between two molecules of 1,1-dicyanoalkenes (or 2-cyanoacrylates) and one molecule of enones, leading to highly diastereoselective syntheses of polysubstituted cyclohexanes and cyclopentenes (Scheme 1, b).[5b] The effectiveness of this strategy may be attributed to the decent reactivity difference between enones and doubly activated alkenes: an enone is a better latent enolate (nucleophile) under the catalysis of a nucleophilic organic Lewis base; a doubly activated alkene acts as a more reactive Michael acceptor (electrophile).

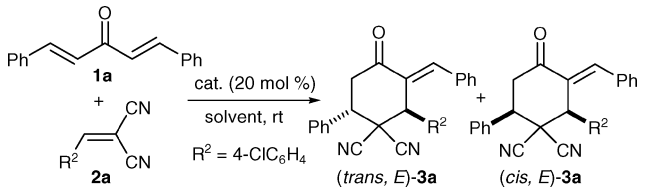
As a reasonable extension of our prior work, we further investigated the feasibility of phosphine-catalyzed cross-couplings between 1,4-dien-3-ones and 1,1-dicyano alkenes. As a group of versatile multifunctional building blocks, 1,4-dien-3-ones are widely used in many important organic transformations,[6,7] like the Nazarov cyclization[6a] and the Diels–Alder cycloaddition,[6b,6c] to build molecular ring systems. A pioneering example of a phosphine-mediated homo-coupling reaction of 1,4-dien-3-ones was also disclosed by Schaus *et al.*, leading to an efficient and diastereoselective synthesis of bicyclo[3.2.1]octenones through a tandem [4 + 2] cycloaddition–Wittig olefination process.[8] Encouragingly, our investigation unveiled that, under the catalysis of nuleophilic phosphines, two cross-couplings of 1,4-dien-3-ones and 1,1-dicyanoalkenes could be highly chemoselectively realized, which was embodied in phosphine-catalyzed [4 + 2] annulation and vinylogous Michael addition reactions, respectively. These two reactions represent atom economical C–C forming reactions capable of efficiently constructing molecular complexity. Herein we wish to report the detail.

Results and discussion

Our research was initiated with symmetric styryl ketone **1a** and a doubly activated alkene 2-(4-chlorophenylmethylidene) malononitrile **2a**. In the presence of PPh_3 (20 mol%), a reaction mixture of **1a** (0.6 mmol) and **2a** (0.5 mmol) in CH_2Cl_2 (2.0 mL) was stirred at room temperature for 24 h. To our delight, two separable isomeric products (*trans*, *E*)-**3a** and (*cis*, *E*)-**3a** were collected from the reaction mixture in 48% combined yield with the *trans*-isomer being the major product after column chromatographic isolation (Table 1, entry 1). Structural identification of **3a** revealed that a formal [4 + 2] cycloaddition reaction between dienone **1a** and doubly activated alkene **2a** occurred. This reaction represents a new phosphine-catalyzed reactivity pattern of dienones.[8,9] It also offers a convenient access to highly functionalized cyclohexanones, which are common structural components in many natural products and pharmaceutically interesting compounds.[10]

A brief survey on the reaction conditions was carried out by using the reaction of **1a** and **2a** as a probe (Table 1). Among a series of chosen tertiary phosphines (entries 1–5), electron-rich PBu_3 gave the best result regarding the yield and diastereoselectivity, although others were all effective for the reaction. Air-stable and strongly nucleophilic 1,3,5-triaza-7-phosphaadamantane (PTA), often used as a convenient alternative phosphine for the air-sensitive PBu_3,[11] only brought about much inferior yields in this

Table 1 Survey on the reaction conditions[a]



Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]	dr[c]
1	PPh_3	CH_2Cl_2	24	41(7)	6 : 1
2	PPh_2Me	CH_2Cl_2	24	46(9)	5 : 1
3	$PPhMe_2$	CH_2Cl_2	24	51(9)	6 : 1
4[d]	PTA	CH_2Cl_2	24	14(15)	1 : 1
5	PBu_3	CH_2Cl_2	24	58(8)	7 : 1
6	PBu_3	CH_2Cl_2	24	60(9)	7 : 1
7	DABCO	CH_2Cl_2	24	—	—
8	DBU	CH_2Cl_2	24	—	—
9	PBu_3	$CHCl_3$	24	62(13)	6 : 1
10	PBu_3	THF	48	60(15)	4 : 1
11	PBu_3	toluene	24	55(14)	4 : 1
12	PBu_3	CH_3CN	48	20(14)	2 : 1
13	PBu_3	ethanol	48	—	—
14[e]	PBu_3	$CHCl_3$	24	69(10)	7 : 1

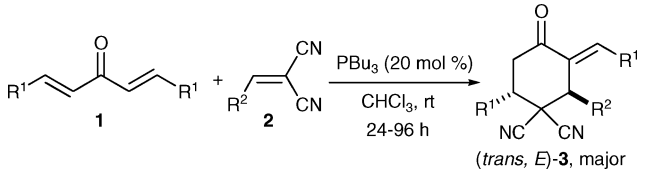
[a] Typical conditions: under N_2 atmosphere, dienone **1a** (for entries 1–5, 0.6 mmol; for entries 6–14, 0.5 mmol), activated alkene **2a** (for entries 1–5, 0.5 mmol; for entries 6–14, 0.6 mmol) and catalyst (0.1 mmol) in solvent (2 mL) were stirred at rt. [b] Isolated yield of the isomer (*trans*, *E*)-**3a** and data in parentheses for the isomer (*cis*, *E*)-**3a**. [c] Determined by ^{1}H NMR assay of the crude product. [d] PTA = 1,3,5-triaza-7-phosphaadamantane. [e] $CHCl_3$ (5 mL) was used.

reaction (entry 4). Adjusting the molar ratio of **1a**/**2a** to 1 : 1.2 resulted in a slight improvement of yield in the PBu_3-catalyzed reaction (entry 6). Common tertiary amine catalysts, like DABCO and DBU, were completely ineffective for the transformation (entries 7 and 8). Choosing PBu_3 as the catalyst, several common solvents other than CH_2Cl_2 were further surveyed (entries 9–13). $CHCl_3$ emerged as the best solvent with respect to the yield and diastereoselectivity (entry 9), although THF and toluene also gave comparable results (entries 10, 11). The polar solvent CH_3CN and protic solvent ethanol were detrimental to the reaction (entries 12, 13). A dilute substrate concentration was found to be good for the reaction. When the reaction was run at 0.1 M concentration of **1a**, the yield of **3a** was considerably improved (entry 14).

Under the optimized conditions, the generality of the reaction was examined (Table 2). With dienone **1a** employed, a variety of 1,1-dicyanoalkenes **2** were explored. Phenyl-substituted alkenes **2** bearing either electron-donating or -withdrawing groups on the benzene ring readily afforded their corresponding [4 + 2] annulation products **3** in moderate to good yields and good to high diastereoselectivities (entries 1–10). Heteroaryl-substituted alkenes **2k** and **2l** were also suitable substrates in the annulation reaction with **1a**, giving corresponding cyclohexanones **3** in moderate yields and excellent diastereoselectivities (entries 11 and 12). *E*-styryl-substituted activated alkene **2m** was also examined, readily affording the annulation product **3m** in 86% yield and high diastereoselectivity (entry 13). However, ethyl-substituted alkene **2n** was not an effective candidate for the annulation reaction with **1a** (entry 14).

Choosing activated alkenes **2a** and **2e** as two representative reactants, several differently substituted dienones **1** were also tested

Table 2 Synthesis of cyclohexanones **3** from dienones **1** and 1,1-dicyanoalkenes **2**[a]



Entry	R^1 in **1**	R^2 in **2**	Yield (%)[b]	dr[c]
1	Ph (**1a**)	4-ClC_6H_4 (**2a**)	**3a**, 69 (10)	7 : 1
2	Ph (**1a**)	4-$MeOC_6H_4$ (**2b**)	**3b**, 81	11 : 1
3	Ph (**1a**)	2-$MeOC_6H_4$ (**2c**)	**3c**, 84	7 : 1
4	Ph (**1a**)	4-MeC_6H_4 (**2d**)	**3d**, 86	7 : 1
5	Ph (**1a**)	Ph (**2e**)	**3e**, 70	7 : 1
6	Ph (**1a**)	2-ClC_6H_4 (**2f**)	**3f**, 70	20 : 1
7	Ph (**1a**)	2-BrC_6H_4 (**2g**)	**3g**, 69	14 : 1
8	Ph (**1a**)	2,4-ClC_6H_3 (**2h**)	**3h**, 58	8 : 1
9	Ph (**1a**)	4-FC_6H_4 (**2i**)	**3i**, 48	7 : 1
10	Ph (**1a**)	4-$CF_3C_6H_4$ (**2j**)	**3j**, 51	5 : 1
11	Ph (**1a**)	2-furyl (**2k**)	**3k**, 55	12 : 1
12	Ph (**1a**)	2-thiofuryl (**2l**)	**3l**, 62	20 : 1
13	Ph (**1a**)	*E*-styryl (**2m**)	**3m**, 86	14 : 1
14	Ph (**1a**)	Et (**2n**)	trace	—
15	4-$MeOC_6H_4$ (**1b**)	4-ClC_6H_4 (**2a**)	**3n**, 74	5 : 1
16	4-$MeOC_6H_4$ (**1b**)	Ph (**2e**)	**3o**, 43	5 : 1
17	4-MeC_6H_4 (**1c**)	4-ClC_6H_4 (**2a**)	**3p**, 56	7 : 1
18	4-MeC_6H_4 (**1c**)	Ph (**2e**)	**3q**, 57 (11)	5 : 1
19	4-FC_6H_4 (**1d**)	4-ClC_6H_4 (**2a**)	**3r**, 62	7 : 1
20	4-FC_6H_4 (**1d**)	Ph (**2e**)	**3s**, 80	7 : 1
21	4-$CF_3C_6H_4$ (**1e**)	Ph (**2e**)	**3t**, 46	8 : 1

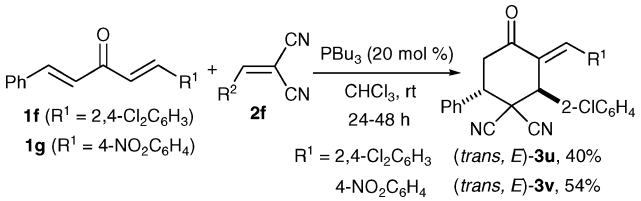
[a] For a typical procedure, see Experimental section. [b] Isolated yield of the major product (*trans*, *E*)-**3** and data in parentheses for isolated minor products (*cis*, *E*)-**3**. [c] Ratio of (*trans*, *E*)-**3**/(*cis*, *E*)-**3**, determined by ^{1}H NMR assay of the crude product.

(Table 2, entries 15–21). Under the standard conditions, phenyl-substituted dienones **1b–1e** bearing either electron-donating or -withdrawing groups readily underwent the PBu_3-catalyzed [4 + 2] annulations with activated alkenes **2a** or **2e**, affording their corresponding cyclohexanones **3** in moderate to good yields and good diastereoselectivities.

In all cases listed in Table 2, the [4 + 2] annulation reaction furnished the cyclohexanone product **3** in a pair of diastereomers with a varying ratio, as determined by ^{1}H NMR measurement of the crude product. However, in most of cases, only the major products (*trans*, *E*)-**3** were isolated as pure compounds by column chromatography on silica gel. Except **3a** and **3q** (entries 1 and 18), the minor products (*cis*, *E*)-**3** were all obtained as impure fractions in column chromatographic isolation.

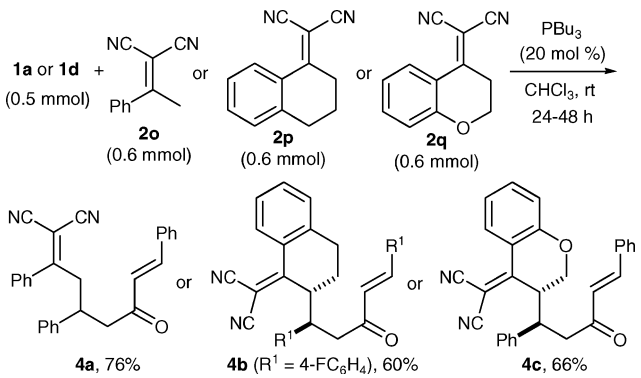
Asymmetric 1,4-dien-3-ones were also examined (Scheme 2). Under the standard conditions, the regioselective annulation products (*trans*, *E*)-**3u** and (*trans*, *E*)-**3v** were successfully obtained in modest yields from the respective reactions of asymmetric 1,4-dien-3-ones **1f** and **1g** with doubly activated alkene **2f**. Apparently, the regioselectivity of the annulation reactions depends on the electronic property difference between two aryl substituents of asymmetric dienones **1**.

Although monoalkyl-substituted activated alkene **2n** was ineffective for the PBu_3-catalyzed [4 + 2] annulation with dienone **1a** (Table 2, entry 14), however, under the catalysis of PBu_3 (20 mol%), a highly chemoselective cross-coupling between dienones **1** and



Scheme 2 Regioselective annulations of asymmetric 1,4-dien-3-ones **1f** and **1g**.

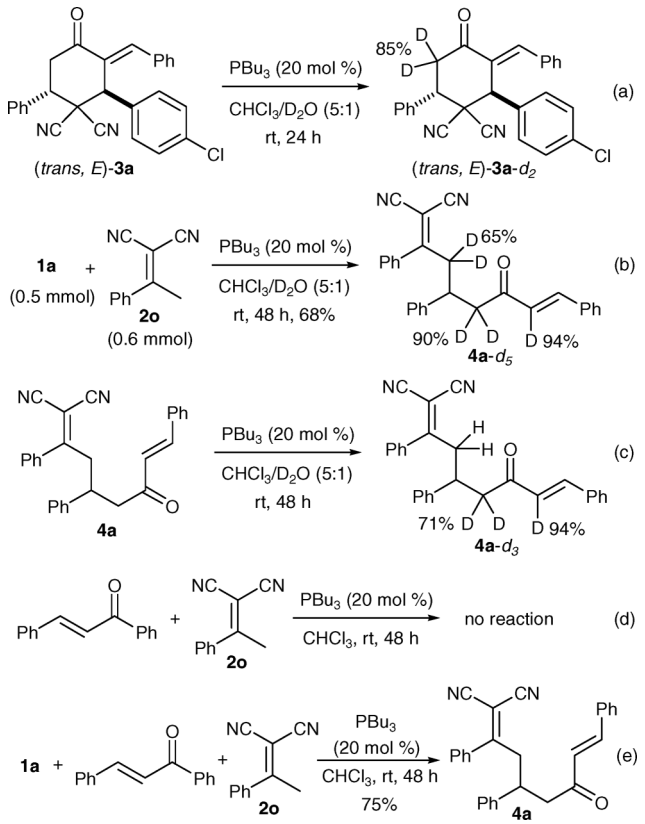
aryl-substituted alkenes **2** bearing an acidic methyl or methylene at the 2-position readily occurred, producing vinylogous Michael addition products **4** as a single diastereomer in satisfactory yields (Scheme 3). Recently, many amine-catalyzed vinylogous Michael additions between 1,1-dicyanoalkenes like **2o–q** and various Michael acceptors were documented as an efficient C–C bond forming protocol.[12] In contrast, similar phosphine-catalyzed vinylogous Michael additions were seldom reported.[13] The PBu_3-catalyzed vinylogous Michael addition of dienones **1a** and **1d** with activated alkenes **2o–q** indeed represents a new example of the phosphine-catalyzed reaction, as well as provides an efficient method to construct molecular complexity.



Scheme 3 Phosphine-catalyzed vinylogous Michael additions.

The structures of cyclohexanones **3** and Michael addition products **4** were fully identified by spectrometric methods, including IR, NMR (^{1}H and ^{13}C), and HRMS-ESI. The structural assignments, including relative configuration determination, were further confirmed by NOSEY and X-ray crystallographic analyses for representative compounds. The crystal structures of (*trans*, *E*)-**3b** (CCDC 827159) and **4b** (CCDC 827760) are shown in the Supplementary Information.†

In order to better interpret the mechanisms of the PBu_3-catalyzed [4 + 2] annulation and vinylogous Michael addition reactions between dienones **1** and activated alkenes **2**, the following experiments were deliberately conducted (Scheme 4, for detail, also see the Supplementary Information†). A H/D exchange experiment was first carried out to probe the mechanism. In the presence of PBu_3 (20 mol%), the annulation product (*trans*, *E*)-**3a** was stirred at room temperature for 24 h in a mixture of $CHCl_3$–D_2O (5 : 1), giving a partially deuterated product (*trans*, *E*)-**3a**-d_2 (Scheme 4, a). According to the reported work by Bergman, *et al.*,[14] the H/D exchange at the α-position of the carbonyl of **3a** most likely proceeded through an enolate intermediate generated from the nucleophilic addition of PBu_3 to the alkene unit. It was also found that no isomerization was observed in the H/D



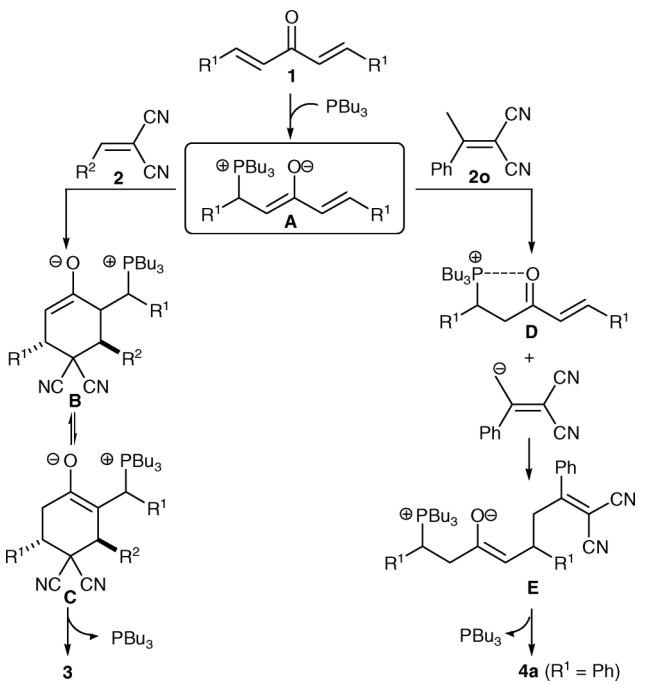
Scheme 4 Experiments for mechanistic investigation.

exchange of **3a**, particularly with regard to the configuration of the alkene unit, although addition of the phosphine PBu_3 to the alkene unit and subsequent elimination were presumably involved in the H/D exchange process. This result implies that the reversible addition of PBu_3 to the alkene unit is a highly stereoselective process.

The H/D exchange strategy was also applied in the case of the vinylogous Michael addition. Under the standard conditions, the PBu_3-catalyzed vinylogous Michael addition reaction of styryl ketone **1a** and activated alkene **2o** was run in a media of $CHCl_3$–D_2O (5 : 1), producing a partially deuterated adduct **4a**-d_5 in 68% yield with substantial deuterium incorporations at the α- and γ-positions of the carbonyl (Scheme 4, b). In contrast, the normal adduct **4a** was treated under the same conditions, giving a deuterated product **4a**-d_3 with comparable deuterium incorporations only at the α-positions of the carbonyl (Scheme 4, c). This fact strongly supports a hypothesis that an allylic carbanion intermediate is formed through deprotonation of the acidic methyl of the activated alkene **2o** in the vinylogous Michael addition reaction.

Additional experiments provide more clues about the mechanism of the vinylogous Michael addition (Scheme 4, d and e). Under the standard conditions, chalcone, as a monoenone that is structurally in close proximity to the dienone **1a**, did not undergo any similar vinylogous Michael addition reaction with the activated alkene **2o**; meanwhile, in the presence of the equivalent chalcone, only the adduct **4a** from dienone **1a** and alkene **2o** was formed in 75% yield. These results indicate that monoenones like chalcone do not possess enough reactivity to couple with the activated alkene **2o** or its corresponding allylic carbanion.

Based on the above results, a plausible mechanism to account for the formation of **3** and **4** is depicted in Scheme 5. Initially, nucleophilic addition of PBu_3 to dienone **1** generates a phosphonium dienolate intermediate **A**. When the doubly activated alkene **2** does not possess an acidic group, intermediate **A** undergoes a formal [4 + 2] cycloaddition with alkene **2** predominantly in an *exo* fashion,[15] producing intermediate **B**. Intermediate **B** interconverts with intermediate **C**, which undertakes an elimination of PBu_3 to furnish the [4 + 2] annulation product **3**. In another scenario, when the alkene **2**, like **2o**, bears an acidic methyl group at the 2-position, the dienolate intermediate **A** as a strong base is readily protonated with the activated alkene **2**, producing a β-phosphonium-substituted monoenone **D** and an allylic carbanion. Considering a possible activation effect of the phosphonium unit on the monoenone moiety through a Coulombic interaction between the phosphonium unit and the adjacent carbonyl in intermediate **D**,[16] we postulate that a Michael addition between intermediate **D** and the allylic carbanion takes place, resulting in the formation of intermediate **E**. Finally, **E** undergoes proton transfer and elimination of PBu_3 to give out the vinylogous Michael addition product **4**.

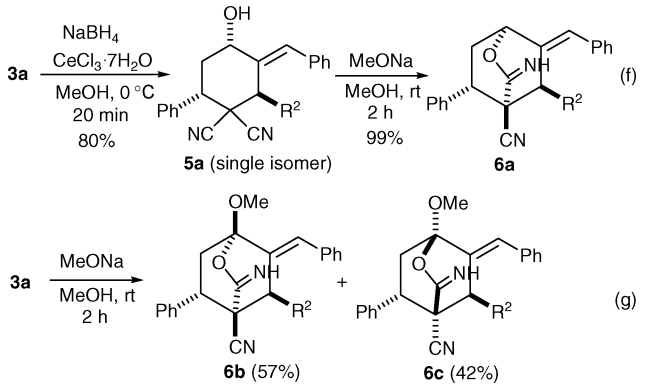


Scheme 5 A plausible mechanism for the formation of **3** and **4**.

To illustrate the synthetic application of the cross-coupling products, the following chemical transformations were performed (Scheme 6). Starting from the [4 + 2] cycloaddition product (*trans*, *E*)-**3a**, a complex bicyclic substructure 3-imino-2-oxabicyclo[2.2.2]octane[17] in **6** could be readily accessed in high yields.

Conclusions

In summary, two kinds of PBu_3-catalyzed cross-couplings between 1,4-dien-3-ones and 1,1-dicyanoalkenes have been realized, which



Scheme 6 The construction of a bicyclic substructure from **3a** (R^2 = 4-ClC_6H_4).

consist of a formal [4 + 2] cycloaddition reaction and a vinylogous Michael addition reaction, respectively. These two reactions represent atom economical C–C forming reactions that are capable of efficiently constructing multifunctional cyclohexanones and acyclic carbonyl compounds. On the basis of the experimental results in this study, the reactions are supposed to proceed through a key intermediate phosphonium dienolate, and an activation effect of the phosphonium unit presumably plays a key role in the vinylogous Michael addition reaction. Future efforts in our laboratory will be directed toward the potential application in organic synthesis and detailed mechanism of these two reactions.

Experimental section

General information

Unless otherwise noted, all reactions were carried out in a nitrogen atmosphere under anhydrous conditions. Solvents were purified according to standard procedures. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AV 400 spectrometer with tetramethylsilane as an internal standard. NOESY spectra were obtained on a Varian 300 spectrometer in $CDCl_3$. High resolution ESI mass spectra were acquired with an IonSpec QFT-ESI instrument. Infrared spectra were recorded on a JASCO FT/IR-480 spectrophotometer. Elemental analyses were performed on a Yanaco CHN Corder MT-3 automatic analyzer. X-ray crystal diffraction data were collected on a Nonius Kappa CCD diffractometer with Mo-Kα radiation (λ = 0.7107 Å) at room temperature. Column chromatography was performed on silica gel (200–300 mesh) using a mixture of petroleum ether/ethyl acetate as eluant.

General procedure for PBu_3-catalyzed [4 + 2] annulation reaction between dienone 1 and activated alkene 2 (Table 2 and Scheme 2)

Under a N_2 atmosphere, to a solution of dienone **1** (0.5 mmol) and activated alkene **2** (0.6 mmol) in chloroform (5 mL) was added PBu_3 (25 uL, 0.1 mmol). The resulting mixture was stirred at room temperature for a specified time (Table 2) till dienone **1** was completely consumed, as monitored by TLC. The solvent was removed on a rotary evaporator under reduced pressure and the residue was subjected to column chromatographic isolation on silica gel (gradient elution, petroleum ether (60–90 °C)/ethyl acetate 20 : 1–10 : 1) to give the annulation product **3**.

3-Benzylidene-2-(4-chlorophenyl)-4-oxo-6-phenyl cyclohexane-1,1-dicarbonitrile (3a). Prepared from **1a** (117 mg, 0.5 mmol) and **2a** (113 mg, 0.6 mmol) and isolated as two pure diastereomers. (*trans*, *E*)-**3a**: yellow solid; yield 145 mg, 69%; m.p. 198–200 °C; IR (KBr): *ν* 3062, 1687, 1597, 1492, 1410, 1263, 1175, 1094, 823, 738, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.50 (d, J = 8.4 Hz, 2H), 7.45–7.26 (m, 10H), 7.13 (d, J = 6.9 Hz, 2H), 4.95 (s, 1H), 3.57 (dd, J = 13.2, 5.2 Hz, 1H), 3.31 (dd, J = 18.6, 13.2 Hz, 1H), 3.13 (dd, J = 18.6, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.7, 143.7, 135.9, 134.9, 134.3, 133.3, 131.4, 131.3, 130.4, 129.9, 129.8, 129.6, 129.3, 128.9, 128.2, 113.7, 113.1, 49.9, 45.2, 42.1, 42.0; Anal. Calcd for $C_{27}H_{19}ClN_2O$: C 76.68, H 4.53, N 6.62; found: C 76.26, H 4.36, N 6.51. (*cis*, *E*)-**3a**: yellow solid; yield 21 mg, 10%; m.p. 95–98 °C; IR (KBr): ν 3061, 2917, 1703, 1594, 1493, 1264, 1093, 831, 749, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.54–7.42 (m, 5H), 7.35–7.18 (m, 7H), 7.11 (d, J = 7.5 Hz, 2H), 5.00 (s, 1H), 3.74 (dd, J = 13.6, 4.5 Hz, 1H), 3.45 (dd, J = 19.4, 13.8 Hz, 1H), 3.04 (dd, J = 19.5, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.2, 144.2, 135.15, 135.12, 134.7, 133.3, 132.4, 130.5, 129.97, 129.91, 129.7, 129.5, 129.2, 128.5, 128.1, 114.4, 112.3, 52.3, 47.9, 45.6, 40.7; HRMS-ESI Calcd for $C_{27}H_{19}ClN_2O$ [M + Na]$^+$ 445.1078, found 445.1075.

(*E*)-3-Benzylidene-2-(4-methoxyphenyl)-4-oxo-6-phenyl cyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3b). Prepared from **1a** (117 mg, 0.5 mmol) and **2b** (110 mg, 0.6 mmol). Yellow solid; yield 169 mg, 81%; m.p. 143–144 °C; IR (KBr): *ν* 3062, 2934, 1687, 1608, 1512, 1254, 1182, 1031, 829, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.46–7.26 (m, 10H), 7.17 (d, J = 6.9 Hz, 2H), 7.02 (d, J = 8.6 Hz, 2H), 4.94 (s, 1H), 3.86 (s, 3H), 3.65 (dd, J = 13.2, 5.2 Hz, 1H), 3.29 (dd, J = 18.5, 13.2 Hz, 1H), 3.12 (dd, J = 18.6, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.0, 160.3, 142.9, 135.3, 133.6, 132.0, 131.3, 130.2, 130.0, 129.5, 129.2, 128.8, 128.2, 127.6, 114.9, 114.0, 113.4, 55.4, 50.0, 45.5, 42.1, 41.9; elemental analysis: $C_{28}H_{22}N_2O_2$ requires C, 80.36; H, 5.30; N, 6.69; found: C, 79.92; H, 4.98; N 6.52.

(*E*)-3-Benzylidene-2-(2-methoxyphenyl)-4-oxo-6-phenyl cyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3c). Prepared from **1a** (117 mg, 0.5 mmol) and **2c** (110 mg, 0.6 mmol). Yellow solid; yield 176 mg, 84%; m.p. 178–179 °C; IR (KBr): *ν* 3062, 2840, 1690, 1600, 1492, 1457, 1250, 1025, 763, 737, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (s, 1H), 7.47 (t, J = 7.7 Hz, 1H), 7.43–7.30 (m, 8H), 7.24 (d, J = 10.7 Hz, 1H), 7.17 (d, J = 7.1 Hz, 2H), 7.09 (dd, J = 16.7, 8.0 Hz, 2H), 5.26 (s, 1H), 3.82 (s, 3H), 3.78 (dd, J = 13.0, 5.1 Hz, 1H), 3.26 (dd, J = 18.3, 13.1 Hz, 1H), 3.10 (dd, J = 18.4, 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.3, 157.4, 141.7, 135.7, 133.7, 132.1, 131.8, 131.2, 130.1, 129.9, 129.4, 129.1, 128.6, 128.3, 124.3, 121.6, 114.1, 113.2, 112.5, 55.2, 45.1, 43.1, 42.2; HRMS-ESI Calcd for $C_{28}H_{22}N_2O_2$ [M + Na]$^+$ 441.1574, found 441.1575.

(*E*)-3-Benzylidene-4-oxo-6-phenyl-2-*p*-tolylcyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3d). Prepared from **1a** (117 mg, 0.5 mmol) and **2d** (100 mg, 0.6 mmol). Yellow solid; yield 172 mg, 86%; m.p. 100–101 °C; IR (KBr): *ν* 3060, 1687, 1597, 1264, 1117, 750, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.41–7.27 (m, 11H), 7.21–7.13 (m, 2H), 4.93 (s, 1H), 3.66 (dd, J = 13.1, 5.3 Hz, 1H), 3.30 (dd, J = 18.6, 13.2 Hz, 1H), 3.14 (dd, J = 18.6, 5.4 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ

196.0, 142.9, 139.7, 135.3, 133.5, 132.7, 131.9, 130.3, 130.2, 129.98, 129.92, 129.5, 129.2, 128.8, 128.2, 114.0, 113.3, 50.3, 45.4, 42.2, 42.0, 21.2; elemental analysis: $C_{28}H_{22}N_2O$ requires C, 83.56; H, 5.51; N, 6.96; found: C, 83.75; H, 5.37; N 6.79.

(*E*)-3-Benzylidene-4-oxo-2,6-diphenylcyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3e). Prepared from **1a** (117 mg, 0.5 mmol) and **2e** (93 mg, 0.6 mmol). Yellow solid; yield 135 mg, 70%; m.p. 208–209 °C; IR (KBr): *ν* 3005, 2838, 1679, 1583, 1511, 1260, 1173, 1030, 831, 758, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.91 (s, 1H), 7.61–7.45 (m, 3H), 7.45–7.25 (m, 10H), 7.15 (d, *J* = 6.7 Hz, 2H), 4.98 (s, 1H), 3.65 (dd, *J* = 13.1, 5.3 Hz, 1H), 3.31 (dd, *J* = 18.6, 13.1 Hz, 1H), 3.14 (dd, *J* = 18.6, 5.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.9, 143.2, 135.9, 135.2, 133.5, 131.7, 130.2, 130.1, 129.9, 129.8, 129.6, 129.5, 129.2, 128.9, 128.2, 113.9, 113.2, 50.6, 45.3, 42.1; HRMS-ESI Calcd for $C_{27}H_{20}N_2O$ [M + Na]$^+$ 411.1468, found 411.1468.

(*E*)-3-Benzylidene-2-(2-chlorophenyl)-4-oxo-6-phenyl cyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3f). Prepared from **1a** (117 mg, 0.5 mmol) and **2f** (113 mg, 0.6 mmol). Yellow solid; yield 148 mg, 70%; m.p. 93–95 °C; IR (KBr): *ν* 3063, 1688, 1593, 1262, 761, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.90 (s, 1H), 7.60 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.48–7.29 (m, 10H), 7.22–7.11 (m, 3H), 5.64 (s, 1H), 3.82 (dd, *J* = 13.4, 5.0 Hz, 1H), 3.36 (dd, *J* = 18.4, 13.4 Hz, 1H), 3.18 (dd, *J* = 18.4, 5.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.7, 144.2, 135.6, 134.9, 133.6, 133.2, 131.6, 131.5, 131.3, 130.9, 130.2, 129.7, 129.6, 129.2, 128.9, 128.4, 127.6, 113.8, 112.4, 46.7, 43.7, 42.6, 42.1; HRMS-ESI Calcd for $C_{27}H_{19}ClN_2O$ [M + Na]$^+$ 445.1078, found 445.1069.

(*E*)-3-Benzylidene-2-(2-bromophenyl)-4-oxo-6-phenyl cyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3g). Prepared from **1a** (117 mg, 0.5 mmol) and **2g** (140 mg, 0.6 mmol). Yellow solid; yield 160 mg, 69%; m.p. 74–76 °C; IR (KBr): *ν* 3062, 1689, 1596, 1259, 1179, 1025, 761, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.91 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.51–7.30 (m, 10H), 7.23–7.09 (m, 3H), 5.61 (s, 1H), 3.82 (dd, *J* = 13.4, 5.0 Hz, 1H), 3.36 (dd, *J* = 18.3, 13.4 Hz, 1H), 3.19 (dd, *J* = 18.3, 5.0 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.8, 144.4, 135.0, 134.8, 133.1, 131.7, 131.4, 131.0, 130.2, 129.7, 129.6, 129.2, 129.0, 128.4, 128.2, 126.6, 113.8, 112.4, 48.9, 43.6, 42.6, 42.0; HRMS-ESI Calcd for $C_{27}H_{19}BrN_2O$ [M + Na]$^+$ 489.0573, found 489.0566.

(*E*)-3-Benzylidene-2-(2,4-dichlorophenyl)-4-oxo-6-phenyl cyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3h). Prepared from **1a** (117 mg, 0.5 mmol) and **2h** (112 mg, 0.6 mmol). Yellow solid; yield 132 mg, 58%; m.p. 90–91 °C; IR (KBr): *ν* 3064, 1689, 1587, 1471, 1257, 766, 750, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.91 (s, 1H), 7.63 (d, *J* = 1.8 Hz, 1H), 7.51–7.30 (m, 9H), 7.19–7.06 (m, 3H), 5.57 (s, 1H), 3.74 (dd, *J* = 13.3, 4.9 Hz, 1H), 3.36 (dd, *J* = 18.4, 13.4 Hz, 1H), 3.18 (dd, *J* = 18.4, 4.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.5, 144.6, 136.5, 136.4, 134.6, 133.0, 132.2, 131.9, 131.3, 131.2, 130.4, 129.7, 129.5, 129.3, 129.0, 128.4, 128.0, 113.6, 112.2, 46.3, 43.6, 42.6, 41.9; HRMS-ESI Calcd for $C_{27}H_{18}C_{l2}N_2O$ [M + Na]$^+$ 479.0688, found 479.0684.

(*E*)-3-Benzylidene-2-(4-fluorophenyl)-4-oxo-6-phenyl cyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3i). Prepared from **1a** (117 mg, 0.5 mmol) and **2i** (103 mg, 0.6 mmol). Yellow solid; yield 97 mg, 48%; m.p. 199–200 °C; IR (KBr): *ν* 3063, 1687, 1604, 1509, 1238, 832, 738, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.91 (s, 1H), 7.46–7.27 (m, 10H), 7.27–7.19 (m, 2H), 7.13 (d, *J* = 6.9 Hz, 2H), 4.97 (s, 1H), 3.59 (dd, *J* = 13.2, 5.2 Hz, 1H), 3.31 (dd, *J* = 18.6, 13.2 Hz, 1H), 3.13 (dd, *J* = 18.6, 5.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.7, 163.2 (d, *J* = 250.9 Hz), 143.5, 135.0, 133.4, 131.9 (d, *J* = 8.3 Hz), 131.7 (d, *J* = 3.2 Hz), 131.6, 130.3, 129.8, 129.6, 129.3, 128.9, 128.2, 116.8 (d, *J* = 21.8 Hz), 113.8, 113.1, 49.9, 45.3, 42.0; elemental analysis: $C_{27}H_{19}FN_2O$ requires C, 79.79; H, 4.71; N, 6.89; found: C, 80.07; H, 4.57; N 7.19.

(*E*)-3-Benzylidene-4-oxo-6-phenyl-2-(4-(trifluoromethyl) phenyl)cyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3j). Prepared from **1a** (117 mg, 0.5 mmol) and **2j** (133 mg, 0.6 mmol). Yellow solid; yield 116 mg, 51%; m.p. 189–190 °C; IR (KBr): *ν* 3064, 1688, 1598, 1326, 1124, 832, 740, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.95 (s, 1H), 7.80 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.46–7.34 (m, 6H), 7.34–7.27 (m, 2H), 7.11 (d, *J* = 7.0 Hz, 2H), 5.02 (s, 1H), 3.56 (dd, *J* = 13.1, 5.2 Hz, 1H), 3.34 (dd, *J* = 18.6, 13.1 Hz, 1H), 3.17 (dd, *J* = 18.5, 5.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.4, 144.1, 139.8, 134.7, 133.2, 131.9 (q, *J* = 32.9 Hz), 130.9, 130.6, 130.5, 129.7, 129.3, 128.9, 128.1, 126.6 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.5), 113.5, 112.9, 50.2, 45.1, 42.2, 42.0; elemental analysis: $C_{28}H_{19}F_3N_2O$ requires C, 73.68; H, 4.20; N, 6.14; found: C, 73.82; H, 4.34; N, 6.13.

(*E*)-3-Benzylidene-2-(2-furyl)-4-oxo-6-phenylcyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3k). Prepared from **1a** (117 mg, 0.5 mmol) and **2k** (86 mg, 0.6 mmol). Yellow solid; yield 103 mg, 55%; m.p. 79–80 °C; IR (KBr): *ν* 3062, 1692, 1609, 1496, 1245, 1016, 740, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.86 (s, 1H), 7.59 (s, 1H), 7.49–7.30 (m, 9H), 7.28–7.18 (m, 2H), 6.55 (dd, *J* = 12.9, 2.4 Hz, 2H), 5.10 (s, 1H), 3.59 (dd, *J* = 12.8, 5.5 Hz, 1H), 3.23 (dd, *J* = 18.3, 12.9 Hz, 1H), 3.10 (dd, *J* = 18.3, 5.5 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.1, 148.1, 144.6, 142.7, 135.2, 133.3, 130.2, 129.9, 129.7, 129.6, 129.3, 129.0, 128.2, 113.14, 113.13, 112.2, 111.4, 45.2, 44.7, 43.6, 41.9; HRMS-ESI Calcd for $C_{25}H_{18}N_2O$ [M + Na]$^+$ 401.1261, found 401.1260.

(*E*)-3-Benzylidene-4-oxo-6-phenyl-2-(2-thiofuryl)cyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3l). Prepared from **1a** (117 mg, 0.5 mmol) and **2l** (96 mg, 0.6 mmol). Yellow solid; yield 122 mg, 62%; m.p. 74–76 °C; IR (KBr): *ν* 3062, 1689, 1600, 1244, 1199, 737, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.90 (s, 1H), 7.49 (dd, *J* = 5.1, 0.8 Hz, 1H), 7.46–7.32 (m, 8H), 7.31 (d, *J* = 3.6 Hz, 1H), 7.25–7.21 (m, 2H), 7.19 (dd, *J* = 5.1, 3.7 Hz, 1H), 5.27 (s, 1H), 3.72 (dd, *J* = 12.9, 5.5 Hz, 1H), 3.26 (dd, *J* = 18.6, 12.9 Hz, 1H), 3.10 (dd, *J* = 18.6, 5.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.0, 143.4, 137.9, 135.2, 133.3, 132.1, 130.4, 129.9, 129.6, 129.5, 129.3, 129.0, 128.22, 128.17, 127.9, 113.6, 113.5, 46.1, 45.7, 42.5, 41.8; HRMS-ESI Calcd for $C_{25}H_{18}N_2OS$ [M + Na]$^+$ 417.1032, found 417.1036.

(*E*)-3-Benzylidene-4-oxo-6-phenyl-2-styrylcyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3m). Prepared from **1a** (117 mg, 0.5 mmol) and **2m** (108 mg, 0.6 mmol). Yellow semi-solid; yield 178 mg, 86%; IR (KBr): *ν* 3061, 1689, 1604, 1448, 1200, 769, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.95 (s, 1H), 7.51 (d, *J* = 6.8 Hz, 2H), 7.48–7.36 (m, 13H), 6.70 (d, *J* = 16.3 Hz, 1H), 6.65 (d, *J* = 16.2 Hz, 1H), 4.68 (d, *J* = 1.9 Hz, 1H), 3.75 (dd, *J* = 13.1, 5.2 Hz, 1H), 3.20 (dd, *J* = 18.3, 13.2 Hz, 1H), 3.00 (dd, *J* = 18.3, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.9, 143.5,

138.7, 135.2, 135.0, 133.3, 130.43, 130.37, 129.65, 129.62, 129.4, 129.3, 129.1, 128.9, 128.1, 127.1, 122.4, 113.48, 113.45, 47.7, 44.2, 43.1, 42.1; HRMS-ESI Calcd for $C_{29}H_{22}N_2O$ [M + Na]$^+$ 437.1624, found 437.1617.

(*E*)-2-(4-Chlorophenyl)-3-(4-methoxybenzylidene)-6-(4-methoxyphenyl)-4-oxocyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3n). Prepared from **1b** (147 mg, 0.5 mmol) and **2a** (113 mg, 0.6 mmol). Yellow solid; yield 179 mg, 74%; m.p. 188–190 °C; IR (KBr): *ν* 3004, 2838, 1681, 1585, 1512, 1260, 1173, 830 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.89 (s, 1H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.14 (d, *J* = 8.7 Hz, 2H), 6.88 (dd, *J* = 8.7, 6.4 Hz, 4H), 4.95 (s, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.52 (dd, *J* = 13.1, 5.4 Hz, 1H), 3.26 (dd, *J* = 18.7, 13.1 Hz, 1H), 3.10 (dd, *J* = 18.7, 5.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.5, 161.5, 160.3, 143.7, 135.9, 134.4, 132.4, 131.5, 129.8, 129.3, 128.7, 127.0, 125.8, 114.6, 114.5, 113.9, 113.3, 55.4, 55.3, 49.9, 45.6, 41.9, 41.3; elemental analysis: $C_{29}H_{23}ClN_2O_3$ requires C, 72.12; H, 4.80; N, 5.80; found: C, 71.85; H, 4.48; N, 5.34.

(*E*)-3-(4-Methoxybenzylidene)-6-(4-methoxyphenyl)-4-oxo-2-phenylcyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3o). Prepared from **1b** (147 mg, 0.5 mmol) and **2e** (93 mg, 0.6 mmol). Yellow solid; yield 96 mg, 43%; m.p. 202–203 °C; IR (KBr): *ν* 3030, 2922, 1685, 1594, 1511, 1175, 816, 756, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.89 (s, 1H), 7.56–7.45 (m, 3H), 7.43–7.37 (m, 2H), 7.21–7.12 (m, 6H), 7.07 (d, *J* = 8.1 Hz, 2H), 4.98 (s, 1H), 3.61 (dd, *J* = 13.1, 5.4 Hz, 1H), 3.28 (dd, *J* = 18.6, 13.1 Hz, 1H), 3.11 (dd, *J* = 18.6, 5.4 Hz, 1H), 2.35 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.8, 161.4, 160.3, 143.2, 135.9, 132.4, 130.2, 129.6, 129.5, 129.4, 129.3, 127.3, 126.0, 114.5, 114.4, 114.1, 113.4, 55.4, 55.3, 50.5, 45.7, 42.0, 41.3; elemental analysis: $C_{29}H_{24}N_2O$ requires C, 83.63; H, 5.81; N, 6.73; found: C, 83.19; H, 5.70; N, 6.52.

(*E*)-2-(4-Chlorophenyl)-3-(4-methylbenzylidene)-4-oxo-6-*p*-tolylcyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3p). Prepared from **1c** (131 mg, 0.5 mmol) and **2a** (113 mg, 0.6 mmol). Yellow solid; yield 126 mg, 56%; m.p. 179–180 °C; IR (KBr): *ν* 3030, 2922, 1685, 1594, 1492, 1409, 1174, 1095, 819, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.89 (s, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 6H), 7.05 (d, *J* = 8.0 Hz, 2H), 4.95 (s, 1H), 3.54 (dd, *J* = 13.1, 5.2 Hz, 1H), 3.28 (dd, *J* = 18.6, 13.2 Hz, 1H), 3.11 (dd, *J* = 18.6, 5.3 Hz, 1H), 2.37 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.8, 143.9, 141.1, 139.6, 135.8, 134.4, 131.9, 131.4, 130.5, 130.3, 130.1, 129.9, 129.8, 129.7, 128.0, 113.8, 113.2, 49.9, 45.4, 41.9, 41.7, 21.5, 21.2; elemental analysis: $C_{29}H_{23}ClN_2O$ requires C, 77.24; H, 5.14; N, 6.21; found: C, 76.87; H, 5.20; N, 6.09.

3-(4-Methylbenzylidene)-4-oxo-2-phenyl-6-*p*-tolyl cyclohexane-1,1-dicarbonitrile (3q). Prepared from **1c** (131 mg, 0.5 mmol) and **2e** (93 mg, 0.6 mmol) and isolated as two pure diastereomers. (*trans*, *E*)-**3q**: yellow solid; yield 119 mg, 57%; m.p. 202–203 °C; IR (KBr): *ν* 3030, 2922, 1685, 1594, 1511, 1175, 816, 756, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.89 (s, 1H), 7.56–7.45 (m, 3H), 7.43–7.37 (m, 2H), 7.21–7.12 (m, 6H), 7.07 (d, *J* = 8.1 Hz, 2H), 4.98 (s, 1H), 3.61 (dd, *J* = 13.1, 5.4 Hz, 1H), 3.28 (dd, *J* = 18.6, 13.1 Hz, 1H), 3.11 (dd, *J* = 18.6, 5.4 Hz, 1H), 2.35 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 196.0, 143.4, 140.9, 139.4, 135.9, 132.3, 130.8, 130.7, 130.21, 130.17, 129.9, 129.6, 129.5, 128.0, 114.0, 113.3, 50.6, 45.5, 42.1, 41.7, 21.5, 21.2; Anal. Calcd for $C_{29}H_{24}N_2O$: C 83.63, H 5.81, N 6.73; found: C 83.19, H 5.70, N 6.52. (*cis*, *E*)-**3q**: yellow solid; yield 23 mg, 11%; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.75 (s, 1H), 7.43–7.34 (m, 4H), 7.34–7.21 (m, 5H), 7.08 (d, *J* = 7.6 Hz, 2H), 7.01 (d, *J* = 7.7 Hz, 2H), 5.02 (s, 1H), 3.67 (dd, *J* = 13.7, 3.7 Hz, 1H), 3.41 (dd, *J* = 19.3, 13.9 Hz, 1H), 2.96 (dd, *J* = 19.2, 3.9 Hz, 1H), 2.37 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 197.3, 143.3, 140.6, 139.5, 136.9, 132.3, 131.9, 130.7, 130.4, 130.0, 129.2, 129.13, 129.08, 128.9, 128.1, 115.1, 112.4, 52.7, 48.3, 45.2, 40.7, 21.4, 21.2; HRMS-ESI Calcd for $C_{29}H_{24}N_2O$ [M + Na]$^+$ 439.1781, found 439.1781.

(*E*)-2-(4-Chlorophenyl)-3-(4-fluorobenzylidene)-6-(4-fluoro phenyl)-4-oxocyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3r). Prepared from **1d** (135 mg, 0.5 mmol) and **2a** (113 mg, 0.6 mmol). Yellow solid; yield 142 mg, 62%; m.p. 188–190 °C; IR (KBr): *ν* 3057, 1688, 1602, 1510, 1410, 1243, 1069, 1014, 835 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.87 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.37–7.28 (m, 4H), 7.19–7.01 (m, 6H), 4.90 (s, 1H), 3.57 (dd, *J* = 13.0, 5.4 Hz, 1H), 3.26 (dd, *J* = 18.6, 13.1 Hz, 1H), 3.13 (dd, *J* = 18.6, 5.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.1, 163.7 (d, *J* = 253.3 Hz), 163.3 (d, *J* = 149.5 Hz), 142.7, 136.2, 133.9, 132.1 (d, *J* = 8.6 Hz), 131.3, 130.9, 130.6 (d, *J* = 3.2 Hz), 130.0, 129.99 (d, *J* = 8.6 Hz), 129.3 (d, *J* = 3.2 Hz), 116.4 (d, *J* = 21.7 Hz), 116.3 (d, *J* = 21.9 Hz), 113.5, 112.9, 49.8, 45.3, 41.9, 41.4; elemental analysis: $C_{27}H_{17}ClF_2N_2O$ requires C, 70.67; H, 3.73; N, 6.10; found: C, 70.43; H, 3.59; N, 6.04.

(*E*)-3-(4-Fluorobenzylidene)-6-(4-fluorophenyl)-4-oxo-2-phenylcyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3s). Prepared from **1d** (135 mg, 0.5 mmol) and **2e** (93 mg, 0.6 mmol). Yellow solid; yield 170 mg, 80%; m.p. 179–180 °C; IR (KBr): *ν* 3062, 1687, 1601, 1510, 1239, 1161, 836, 738, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.87 (s, 1H), 7.59–7.48 (m, 3H), 7.42–7.34 (m, 2H), 7.32–7.23 (m, 2H), 7.16 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.06 (dd, *J* = 15.5, 8.6 Hz, 4H), 4.92 (s, 1H), 3.65 (dd, *J* = 13.0, 5.5 Hz, 1H), 3.26 (dd, *J* = 18.6, 13.0 Hz, 1H), 3.14 (dd, *J* = 18.6, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 195.3, 163.6 (d, *J* = 252.9 Hz), 163.2 (d, *J* = 249.2 Hz), 142.2, 135.5, 132.1 (d, *J* = 8.6 Hz), 131.3, 130.9 (d, *J* = 3.3 Hz), 130.01, 130.00 (d, *J* = 8.3 Hz), 129.9, 129.8, 129.5 (d, *J* = 3.1 Hz), 116.3 (d, *J* = 21.7 Hz), 116.2 (d, *J* = 21.8 Hz), 113.7, 113.0, 50.4, 45.4, 42.0, 41.3; elemental analysis: $C_{27}H_{18}F_2N_2O$ requires C, 76.40; H, 4.27; N, 6.60; found: C, 76.28; H, 4.46; N, 6.44.

(*E*)-4-Oxo-2-phenyl-3-(4-(trifluoromethyl)benzylidene)-6-(4-(trifluoromethyl)phenyl)cyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3t). Prepared from **1e** (185 mg, 0.5 mmol) and **2e** (93 mg, 0.6 mmol). Yellow solid; yield 120 mg, 46%; m.p. 90–92 °C; IR (KBr): *ν* 2925, 1693, 1610, 1325, 1170, 1129, 1070, 908, 735, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.91 (s, 1H), 7.64 (t, *J* = 9.0 Hz, 4H), 7.56 (d, *J* = 5.7 Hz, 3H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 7.5 Hz, 2H), 7.30–7.20 (m, 2H), 4.88 (s, 1H), 3.73 (dd, *J* = 13.0, 5.3 Hz, 1H), 3.32 (dd, *J* = 18.5, 13.1 Hz, 1H), 3.19 (dd, *J* = 18.5, 5.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 194.7, 141.5, 138.7, 136.8, 135.2, 133.4, 131.88 (q, *J* = 32.9 Hz), 131.85 (q, *J* = 32.9 Hz), 130.1, 129.9, 129.87, 129.81, 128.7, 126.3 (q, *J* = 3.6 Hz), 125.8 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.3 Hz), 113.5, 112.6, 50.5, 44.8, 41.86, 41.78; HRMS-ESI Calcd for $C_{29}H_{18}F_6N_2O$ [M + Na]$^+$ 547.1216, found 547.1210.

(*E*)-2-(2-Chlorophenyl)-3-(2,4-dichlorobenzylidene)-4-oxo-6-phenylcyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3u). Prepared from **1f** (151 mg, 0.5 mmol) and **2f** (113 mg, 0.6 mmol). Yellow solid; yield 98 mg, 40%; m.p. 182–184 °C; IR (KBr): *ν* 3064, 1688, 1590, 1474, 1260, 1178, 1052, 756, 657 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.95 (s, 1H), 7.64 (dd, *J* = 16.8, 8.3 Hz, 2H), 7.48–7.34 (m, 7H), 7.23–7.13 (m, 3H), 5.64 (s, 1H), 4.77 (dd, *J* = 12.7, 5.6 Hz, 1H), 3.18 (dd, *J* = 18.3, 13.3 Hz, 1H), 3.10 (dd, *J* = 18.3, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 194.4, 144.9, 135.9, 135.6, 135.5, 133.2, 133.1, 131.7, 131.5, 131.4, 131.1, 131.0, 130.4, 130.3, 129.8, 129.0, 128.5, 128.4, 127.6, 113.8, 111.6, 47.0, 42.4, 41.8, 36.5; HRMS-ESI Calcd for $C_{27}H_{17}Cl_3N_2O$ $[M + Na]^+$ 513.0299, found 513.0297.

(*E*)-2-(2-Chlorophenyl)-3-(4-nitrobenzylidene)-4-oxo-6-phenylcyclohexane-1,1-dicarbonitrile ((*trans*, *E*)-3v). Prepared from **1g** (139 mg, 0.5 mmol) and **2f** (113 mg, 0.6 mmol). Yellow solid; yield 126 mg, 54%; m.p. 132–134 °C; IR (KBr): *ν* 3081, 2922, 1691, 1599, 1525, 1347, 855, 758, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.25 (d, *J* = 8.6 Hz, 2H), 7.93 (s, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.50–7.32 (m, 6H), 7.16 (t, *J* = 5.3 Hz, 3H), 5.67 (s, 1H), 3.96 (dd, *J* = 13.2, 5.0 Hz, 1H), 3.35 (dd, *J* = 18.3, 13.4 Hz, 1H), 3.21 (dd, *J* = 18.3, 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 194.2, 148.6, 144.9, 141.7, 135.6, 133.2, 132.9, 131.7, 131.2, 130.9, 130.5, 129.75, 129.66, 129.1, 127.8, 124.4, 113.3, 112.0, 46.7, 43.0, 42.4, 41.5; HRMS-ESI Calcd for $C_{27}H_{18}ClN_3O_3$ $[M + Na]^+$ 490.0929, found 490.0925.

General procedure for PBu_3-catalyzed vinylogous Michael addition reaction between dienone 1 and activated alkene 2 (Scheme 3)

Under a N_2 atmosphere, to a solution of dienone **1** (0.5 mmol) and activated alkene **2** (0.6 mmol) in chloroform (5 mL) was added PBu_3 (25 uL, 0.1 mmol). The resulting mixture was stirred at room temperature until the dienone was completely consumed as monitored by TLC. The solvent was removed on a rotary evaporator under reduced pressure, and the residue was subjected to column chromatographic isolation on silica gel (gradient elution, petroleum ether–ethyl acetate 20 : 1–10 : 1) to yield vinylogous Michael addition product **4** as a single diastereomer.

(*E*)-2-(5-Oxo-1,3,7-triphenylhept-6-enylidene)malononitrile (4a). Prepared from **1a** (117 mg, 0.5 mmol) and **2o** (101 mg, 0.6 mmol). White solid; yield 152 mg, 76%; m.p. 127–128 °C; IR (KBr): *ν* 3061, 3029, 2958, 2229, 1688, 1660, 1603, 1494, 1449, 1332, 1177, 977, 760, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.61–7.45 (m, 6H), 7.44–7.34 (m, 5H), 7.33–7.21 (m, 3H), 7.04–6.96 (m, 2H), 6.65 (d, *J* = 16.2 Hz, 1H), 3.56 (dd, *J* = 13.5, 4.5 Hz, 1H), 3.32 (dd, *J* = 13.4, 10.5 Hz, 1H), 3.28–3.20 (m, 1H), 3.07 (dd, *J* = 17.4, 8.3 Hz, 1H), 2.99 (dd, *J* = 17.3, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 197.7, 178.1, 143.4, 140.8, 134.1, 133.9, 132.3, 130.8, 129.1, 129.0, 128.9, 128.4, 128.0, 127.6, 127.4, 125.8, 112.8, 112.6, 85.7, 47.0, 42.7, 40.0; elemental analysis: $C_{28}H_{22}N_2O$ requires C, 83.56; H, 5.51; N, 6.96; found: C, 83.29; H, 5.73; N, 7.00.

2-(2-((*E*)-1,5-Bis(4-fluorophenyl)-3-oxopent-4-enyl)-3,4-dihydro-2*H*-naphthalen-1-ylidene)malononitrile (4b). Prepared from **1d** (135 mg, 0.5 mmol) and **2p** (116 mg, 0.6 mmol). White solid; yield 140 mg, 60%; m.p. 208–209 °C; IR (KBr): *ν* 3070, 2935, 2226, 1689, 1659, 1599, 1509, 1231, 1159, 765, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.05 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.46 (dd, *J* = 8.4, 5.5 Hz, 2H), 7.42–7.24 (m, 5H), 7.11–6.99 (m, 4H), 6.46 (d, *J* = 16.1 Hz, 1H), 3.57 (dt, *J* = 11.2, 3.2 Hz, 1H), 3.31 (td, *J* = 10.6, 4.2 Hz, 1H), 3.15 (dd, *J* = 16.4, 9.9 Hz, 1H), 3.03 (ddd, *J* = 18.0, 11.8, 6.0 Hz, 1H), 2.85 (dd, *J* = 18.4, 6.2 Hz, 1H), 2.74 (dd, *J* = 16.4, 4.2 Hz, 1H), 2.02–1.89 (m, 1H), 1.75 (d, *J* = 14.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 196.6, 176.9, 164.2 (d, *J* = 252.6 Hz), 161.9 (d, *J* = 246.3 Hz), 142.1, 139.9, 136.5 (d, *J* = 3.1 Hz), 134.2, 130.3 (d, *J* = 8.6 Hz), 130.2 (d, *J* = 3.4 Hz), 129.9, 129.4 (d, *J* = 7.9 Hz), 128.7, 128.4, 127.1, 125.3, 116.2 (d, *J* = 22.0 Hz), 115.9 (d, *J* = 21.2 Hz), 113.8, 113.5, 80.5, 47.3, 45.6, 40.9, 25.6, 24.3; elemental analysis: $C_{30}H_{22}F_2N_2O$ requires C, 77.57; H, 4.77; N, 6.03; found: C, 77.47; H, 4.74; N, 5.96.

2-(3-((*E*)-3-Oxo-1,5-diphenylpent-4-enyl)chroman-4-ylidene) malononitrile (4c). Prepared from **1a** (117 mg, 0.5 mmol) and **2q** (118 mg, 0.6 mmol). Yellow solid; yield 141 mg, 66%; m.p. 161–162 °C; IR (KBr): *ν* 3060, 2925, 2223, 1691, 1607, 1450, 1327, 1258, 765, 749, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.21 (d, *J* = 8.1 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.51–7.32 (m, 10H), 7.31–7.22 (m, 1H), 7.10 (t, *J* = 7.7 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 16.2 Hz, 1H), 4.14–3.99 (m, 2H), 3.57 (td, *J* = 10.4, 5.0 Hz, 1H), 3.36–3.21 (m, 2H), 2.88 (dd, *J* = 16.5, 5.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 196.5, 167.9, 156.4, 143.4, 140.2, 137.1, 134.1, 130.8, 129.1, 128.9, 128.4, 128.2, 128.0, 127.8, 125.7, 121.9, 118.4, 115.5, 113.8, 113.3, 78.4, 66.8, 45.4, 44.2, 40.9; HRMS-ESI Calcd for $C_{29}H_{22}N_2O_2$ $[M + Na]^+$ 453.1574, found 453.1579.

3-Benzylidene-2-(4-chlorophenyl)-4-hydroxy-6-phenyl cyclohexane-1,1-dicarbonitrile (5a). To a stirred solution of **3a** (235 mg, 0.56 mmol) in methanol (9 mL) at 0 °C were added $CeCl_3 \cdot 7H_2O$ (238 mg, 0.64 mmol) and $NaBH_4$ (39 mg, 1.03 mmol). After the resulting mixture was stirred for 20 min, the reaction was quenched by addition of water (5 mL) and the solvent was removed on a rotary evaporator under reduced pressure. The residue was extracted with dichloromethane (3 × 8 mL), and the combined extracts were washed with brine (8 mL), and dried over anhydrous Na_2SO_4. After filtration and concentration on a rotary evaporator under reduced pressure, the crude product was subjected to column chromatography isolation on silica gel (gradient elution, petroleum ether–ethyl acetate 10 : 1–3 : 1) to give **5a** as a single diastereomer. White Solid; yield 188 mg, 80%; m.p. 202–203 °C; IR (KBr): *ν* 3060, 2932, 1493, 1265, 1098, 741, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.46–7.28 (m, 13H), 7.12 (d, *J* = 7.0 Hz, 2H), 4.97 (dd, *J* = 10.5, 5.0 Hz, 1H), 4.82 (s, 1H), 3.53 (dd, *J* = 13.2, 3.0 Hz, 1H), 2.55 (ddd, *J* = 13.0, 5.3, 3.3 Hz, 1H), 2.42 (dd, *J* = 24.9, 13.0 Hz, 1H), 2.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 135.9, 135.6, 135.3, 135.0, 134.7, 130.9, 130.3, 129.5, 129.3, 129.1, 128.7, 128.4, 128.3, 127.9, 113.9, 113.7, 68.6, 50.2, 46.2, 43.4, 37.9; HRMS-ESI Calcd for $C_{27}H_{21}ClN_2ONa$ $[M + Na]^+$ 447.1235, found 447.1234.

6-Benzylidene-5-(4-chlorophenyl)-3-imino-8-phenyl-2-oxabicyclo[2.2.2]octane-4-carbonitrile (6a). To a stirred solution of **5a** (42 mg, 0.1 mmol) in absolute methanol (1 mL) at 0 °C was dropwise added a freshly prepared MeONa solution (0.3 mmol, 0.15 mL) through a microsyringe. After stirred at rt for 2 h, the reaction was quenched by addition of water (3 mL). The resulting solution was extracted with dichloromethane (3 × 5 mL), and the

combined extracts were washed with brine (5 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated on a rotary evaporator under reduced pressure and the residue was subjected to column chromatography isolation on silica gel (gradient elution, petroleum ether–ethyl acetate 10 : 1–3 : 1) to give **6a** as a white solid. White solid; yield 42 mg, 99%; m.p. 210–214 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.20 (m, 8H), 7.21–7.05 (m, 5H), 7.00 (s, 2H), 6.79 (s, 1H), 5.09 (s, 1H), 4.75 (s, 1H), 3.38–3.21 (m, 1H), 2.79–2.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4, 138.9, 134.5, 133.9, 133.0, 130.8, 129.0, 128.9, 128.7, 128.2, 128.1, 116.2, 80.9, 51.0, 49.4, 39.5, 33.7; HRMS-ESI Calcd for $C_{27}H_{22}ClN_2O$ $[M + H]^+$ 425.1415, found 425.1409.

6-Benzylidene-5-(4-chlorophenyl)-3-imino-1-methoxy-8-phenyl-2-oxabicyclo[2.2.2]octane-4-carbonitrile (6b) and its diastereomer (6c). To a stirred solution of **3a** (42 mg, 0.1 mmol) in absolute methanol (1 mL) at 0 °C was dropwise added a freshly prepared MeONa solution (0.3 mmol, 0.15 mL) through a microsyringe. After stirred at rt for 2 h, the reaction was quenched by addition of water (3 mL). The resulting solution was extracted with dichloromethane (3 × 5 mL). The combined extracts were washed with brine (5 mL), dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated on a rotary evaporator under reduced pressure and the residue was subjected to column chromatography isolation on silica gel (gradient eluant, petroleum ether–ethyl acetate 10 : 1–3 : 1) to yield **6b** and **6c** as two separable diastereomers. For **6b**, semi-solid; yield 26 mg, 57%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.35 (m, 5H), 7.26 (d, J = 6.8 Hz, 1H), 7.17–6.96 (m, 7H), 6.89 (d, J = 8.5 Hz, 2H), 4.26 (d, J = 1.4 Hz, 1H), 3.76 (s, 3H), 3.54 (dd, J = 10.7, 5.3 Hz, 1H), 2.49–2.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 138.6, 136.2, 135.3, 135.1, 133.8, 130.5, 129.4, 128.9, 128.6, 128.4, 128.4, 128.2, 127.4, 125.3, 116.1, 88.0, 54.5, 50.0, 45.7, 43.7, 41.2; HRMS-ESI Calcd for $C_{28}H_{23}ClN_2O_2Na$ $[M + Na]^+$ 477.1340, found 477.1345. For **6c**, semi-solid; yield 19 mg, 42%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.16 (m, J = 8.6 Hz, 8H), 7.11 (d, J = 2.3 Hz, 1H), 7.09–6.91 (m, 7H), 4.44 (d, J = 2.2 Hz, 1H), 3.92 (s, 3H), 3.21 (dd, J = 10.4, 5.2 Hz, 1H), 2.67 (dd, J = 13.5, 10.5 Hz, 1H), 2.31 (dd, J = 13.5, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4, 139.3, 137.3, 134.9, 134.2, 132.2, 128.8, 128.7, 128.3, 128.2, 127.9, 127.3, 124.2, 115.9, 87.3, 54.6, 49.7, 49.1, 41.3, 40.1; HRMS-ESI Calcd for $C_{28}H_{23}ClN_2O_2Na$ $[M + Na]^+$ 477.1340, found 477.1345.

Acknowledgements

Financial support from National Natural Science Foundation of China (grant nos. 20872063; 21072100) is gratefully acknowledged.

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