Aza-Baylis–Hillman Reactions of *N*-(Arylmethylene) diphenylphosphinamides with Activated Olefins in the Presence of Various Lewis Bases

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Abstract: The aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides with methyl vinyl ketone (MVK), methyl acrylate, acrylonitrile, ethyl vinyl ketone (EVK), phenyl vinyl ketone (PVK), phenyl acrylate, 2-cyclopenten-1-one, 2-cyclohexen-1-one have been systemically investigated in the presence of various Lewis bases. The Lewis base and solvent effects in these reactions have been discussed. A new class of double aza-Baylis–Hillman reactions (in some cases exclusively) and their further transformations including catalytic, asymmetric version in the presence of chiral nitrogen and phosphine Lewis bases have been disclosed in this paper.

Keywords: *N*-(arylmethylene)diphenylphosphinamide; aza-Baylis–Hillman reactions; DABCO, Lewis bases; organic catalysis; phosphanes

Introduction

Great progress has been made in the execution of Baylis–Hillman reaction,[1] for which several catalytic, asymmetric versions have been published,[2] since Baylis and Hillman first reported the reactions of acetaldehyde with ethyl acrylate and acrylonitrile in the presence of catalytic amounts of strong Lewis base such as 1,4-diazabicyclo[2.2.2]octane (DABCO) in 1972.[3] Besides the traditional Baylis–Hillman reactions,[4] recently, the scope and limitations of aza-Baylis–Hillman reactions have been extensively investigated.[5] Some unprecedented reaction patterns and a catalytic, asymmetric version of the aza-Baylis–Hillman reaction using *N*-sulfonated imines as the substrates have been disclosed by our group.[6] *N*-(Arylmethylene)diphenylphosphinamides **1** are another well-known class of electron-deficient imines.[7] Therefore, it will be of interest to investigate their aza-Baylis–Hillman reactions with various activated olefins in the presence of Lewis base promoter. Previously, we reported the aza-Baylis–Hillman reactions of **1** with methyl vinyl ketone, methyl acrylate, and acrylonitrile catalyzed by various Lewis bases to give the adducts in good yields in a short communication.[6d,8] Herein, we wish to report the comprehensive aza-Baylis–Hillman reaction patterns of *N*-(arylmethylene)diphenylphosphinamides **1** with various activated olefins including methyl vinyl ketone (MVK), methyl acrylate, acrylonitrile, ethyl vinyl ketone (EVK), phenyl vinyl ketone (PVK), phenyl acrylate, 2-cyclopenten-1-one, and 2-cyclohexen-1-one in the presence of various Lewis base promoters. The Lewis base and solvent effects in these aza-Baylis–Hillman reactions have been investigated. Some unprecedented reaction patterns derived from double aza-Baylis–Hillman reactions are disclosed in this paper. In addition, the catalytic, asymmetric version in the presence of chiral nitrogen and phosphine Lewis bases has been investigated.

Results and Discussion

Aza-Baylis–Hillman Reactions of 1 with MVK

The Lewis base promoters and solvents for the aza-Baylis–Hillman reactions of *N*-(benzylidene)diphenylphosphinamide **1a** with MVK were first systematically examined (Scheme 1). The results are summarized in Table 1. We found that the Lewis base and solvent played very important roles for this reaction. For example, using 10 mol% of PPh_3 as the Lewis base in DMF or MeCN, the reaction proceeded very well to give the corresponding normal aza-Baylis–Hillman adduct **2a** in 81% and 99% yields, respectively (Table 1, entries 2 and 4). Using PPh_2Me as the Lewis base, **2a** was produced in a relative-

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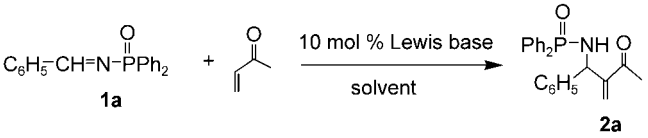
ly low yield (76%) under the same conditions (Table 1, entry 5). Using PBu_3 or $PPhMe_2$ as the Lewis base, traces of **2a** were produced along with many unidentified products (Table 1, entries 6 and 7). The well established strong nitrogen Lewis base, DABCO, gave a lower yield of **2a** in many solvents under the same conditions as those catalyzed by PPh_3 (Table 1, entries 8–11). In dichloromethane, **2a** was obtained in moderate yield (66%) (Table 1, entry 11). On use of DMAP as a nitrogen Lewis base in DMF, **2a** was produced in 72% within 96 h (Table 1, entry 12). In all these cases, the normal aza-Baylis–Hillman adduct **2a** was formed exclusively.

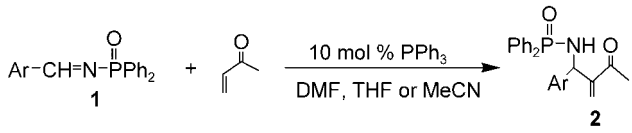
For aza-Baylis–Hillman reactions of other *N*-(arylmethylene)diphenylphosphinamides **1** with MVK using PPh_3 as Lewis base under the optimized reaction conditions, the adducts **2** were obtained in good to excellent yields (Scheme 2). The results are summarized in Table 2. For *N*-(arylmethylene)diphenylphosphinamides **1** having an electron-donating group on the phenyl ring, the corresponding aza-Baylis–Hillman adducts **2b** and **2c** were obtained in low yields in DMF (Table 2, entries 1 and 2), but in MeCN or THF, **2b** and **2c** were formed in 77 and 80% yields (Table 2, entries 8 and 10) or 90% and 70% yield (Table 2, entries 9 and 11), respectively. For *N*-(arylmethylene)diphenylphosphinamides **1** having an electron-withdrawing group on the phenyl ring, the corresponding aza-Baylis–Hillman adducts **2d** – **h** were produced in high yields (Table 2, entries 3–7, 12–15). In some cases, the reactions proceeded smoothly to furnish adduct **2** quantitatively.

Aza-Baylis–Hillman Reactions of 1 with Methyl Acrylate

We next examined the aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** with methyl acrylate in the presence of various Lewis bases (Scheme 3). Using PPh_3 or DABCO as the Lewis base, the reaction was sluggish (Table 3, entries 1–7). By use of the nitrogen Lewis base DMAP, **3a** was produced in traces (Table 3, entry 14). Most of starting materials were recovered and no other product was detected. But, we were pleased to find that on using PPh_2Me as the Lewis base in dichloromethane, the corresponding aza-Baylis–Hillman adduct **3a** was obtained in 71% yield (Table 3, entry 10). In fact, *N*-(arylmethylene)diphenylphosphinamides **1** are more soluble in dichloromethane than in other solvents such as THF or DMF. In addition, dichloromethane contains less free oxygen,



Scheme 1.



Scheme 2.

Table 1. Aza-Baylis–Hillman reactions of *N*-(benzylidene)-diphenylphosphinamide (**1a**; 1.0 equiv.) with MVK (1.2 equivs.) in the presence of a Lewis base (10 mol %) at room temperature in various solvents.

Entry	Lewis base	Solvent	Time [h]	Yield [%][a] **2a**
1	PPh_3	THF	48	52
2	PPh_3	DMF	48	81
3	PPh_3	CH_2Cl_2	72	27
4	PPh_3	MeCN	48	99
5	PPh_2Me	MeCN	72	76
6	$PPhMe_2$	MeCN	72	trace
7	PBu_3	MeCN	72	trace
8	DABCO	THF	144	30
9	DABCO	DMF	144	37
10	DABCO	MeCN	144	35
11	DABCO	CH_2Cl_2	144	66
12	DMAP	DMF	96	72

[a] Yield of isolated products.

Table 2. Aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** (1.0 equiv.) with MVK (1.2 equivs.) in the presence of PPh_3 (10 mol %) in DMF, THF or MeCN.

Entry	Ar	Solvent	Time [h]	Yield [%][a] **2**
1	*p*-EtC_6H_4 (**1b**)	DMF	48	**2b**, 20
2	*p*-$MeOC_6H_4$ (**1c**)	DMF	72	**2c**, 19
3	*p*-FC_6H_4 (**1d**)	DMF	48	**2d**, 76
4	*p*-ClC_6H_4 (**1e**)	DMF	48	**2e**, 67
5	*p*-BrC_6H_4 (**1f**)	DMF	48	**2f**, 99
6	*p*-$NO_2C_6H_4$ (**1g**)	DMF	4	**2g**, 60
7	C_6H_5CH=CH (**1h**)	DMF	72	**2h**, 67
8	*p*-EtC_6H_4 (**1b**)	MeCN	48	**2b**, 77
9	*p*-EtC_6H_4 (**1b**)	THF	48	**2b**, 90
10	*p*-$MeOC_6H_4$ (**1c**)	MeCN	48	**2c**, 80
11	*p*-$MeOC_6H_4$ (**1c**)	THF	48	**2c**, 70
12	*p*-FC_6H_4 (**1d**)	MeCN	36	**2d**, 99
13	*p*-ClC_6H_4 (**1e**)	MeCN	48	**2e**, 87
14	*p*-BrC_6H_4 (**1f**)	MeCN	24	**2f**, 99
15	*p*-$NO_2C_6H_4$ (**1g**)	MeCN	48	**2g**, 99

[a] Yield of isolated products.

which can oxidize a phosphine Lewis base during the reaction, than other solvents such as THF or DMF. Therefore, dichloromethane is the solvent of choice for this reaction. It should be emphasized here that when using PBu_3 or $PPhMe_2$ as the Lewis base, **3a** was obtained only in 38% or 31% yields (Table 3, entries 8 and 9). Upon further careful investigations such as HPLC separation and X-ray diffraction, we found that when using PBu_3 or $PPhMe_2$ as the Lewis base promoter, the major product was a double aza-Baylis–Hillman adduct **4** as mixtures of *syn*- and *anti*-isomers along with the normal Baylis–Hillman adduct **3** (Scheme 4). Therefore, we found out different reaction conditions for the production of either the normal or the abnormal aza-Baylis–Hillman adduct by change of the employed Lewis base under mild reaction conditions.

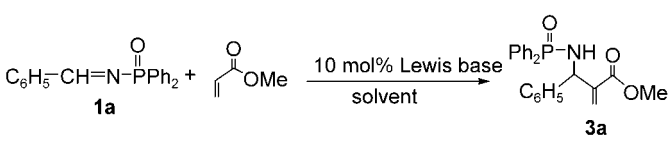
For the aza-Baylis–Hillman reactions of other *N*-(arylmethylene)diphenylphosphinamides **1** with methyl acrylate using PPh_2Me as a Lewis base under the optimized reaction conditions, the normal adducts **3** were obtained in moderate to good yields (Scheme 5). The results are summarized in Table 4. The aliphatic aza-Baylis–Hillman adduct **3 h** was formed in moderate yield (Table 4, entry 7).

In fact, the formation of **4**, the abnormal aza-Baylis–Hillman adduct derived from a double aza-Baylis–Hillman reaction, has never been disclosed before in such a reaction using methyl acrylate as a Michael acceptor.[9] Using *N*-benzylidenediphenylphosphinamide **1a** (no substituent on the phenyl ring) as the substrate, we carefully examined the reaction conditions for this reaction including Lewis bases and solvents (see Scheme S1 in Supporting Information). The results are summarized in Supporting Information as Table S1. Using $PPhMe_2$ or PBu_3 as a Lewis base in THF, the abnormal aza-Baylis–Hillman adduct **4a** can be obtained as the major product along with minor normal aza-Baylis–Hillman product **3a** (Table S1 in Supporting Information, entries 4, 8). Using PMe_3 as a Lewis base, the reaction became sluggish, but also can produce the abnormal aza-Baylis–Hillman adduct **4a** in 32% yield along with a 37%

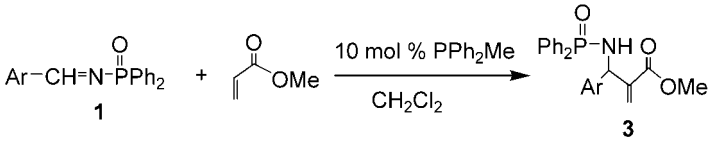
Table 3. Aza-Baylis–Hillman reactions of *N*-benzylidenediphenylphosphinamide (**1a**; 1.0 equiv.) with methyl acrylate (1.2 equivs.) in the presence of a Lewis base (10 mol %) at room temperature in various solvents.

entry	Lewis base	Solvent	Time [h]	Yield [%][a] **3a**
1	PPh_3	DMF	48	trace
2	PPh_3	CH_2Cl_2	480 (20 d)	12
3	DABCO	THF	120	12
4	DABCO	DMF	120	12
5	DABCO	CH_2Cl_2	120	trace
6	DABCO	MeCN	120	26
7	DABCO	MeCN[b]	120	58
8	$PPhMe_2$	MeCN	72	38
9	PBu_3	CH_2Cl_2	72	31
10	PPh_2Me	CH_2Cl_2	42	71
11	PPh_2Me	THF	42	39
12	PPh_2Me	MeCN	42	36
13	PPh_2Me	DMF	42	30
14	DMAP	DMF	96	trace

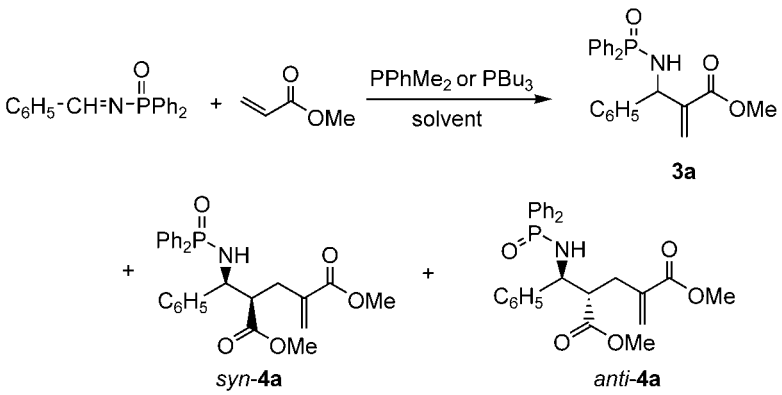
[a] Yield of isolated products.
[b] The reaction was carried out at 60 °C.



Scheme 3.



Scheme 5.



Scheme 4.

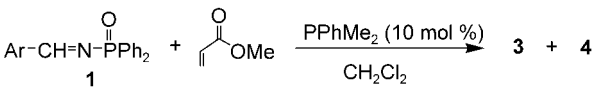
Table 4. Aza-Baylis–Hillman reactions of *N*-(arylmethyene)-diphenylphosphinamides **1** (1.0 equiv.) with methyl acrylate (1.2 equivs.) in the presence of Ph^2PMe (10 mol %) in dichloromethane.

Entry	Ar	Time [h]	Yield [%][a] 3
1	*p*-EtC_6H_4 (**1b**)	96	**3b**, 50
2	*p*-$MeOC_6H_4$ (**1c**)	96	**3c**, 78
3	*p*-FC_6H_4 (**1d**)	42	**3d**, 92
4	*p*-ClC_6H_4 (**1e**)	48	**3e**, 50
5	*p*-BrC_6H_4 (**1f**)	48	**3f**, 60
6	*p*-$NO_2C_6H_4$ (**1g**)	4	**3g**, 63
7	C_6H_5CH=CH (**1h**)	42	**3h**, 40

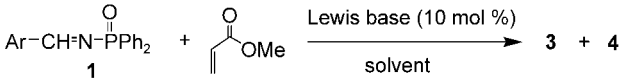
[a] Yield of isolated products.

yield of **3a** in THF (see Table S1 in Supporting Information, entry 9). These results suggest that with Lewis bases having stronger nucleophilicity, the abnormal adduct **4** can be produced. However, during further investigations, we found that the substituents on the phenyl ring of **1** and the employed solvents can significantly affect the formation of **4a**. For example, with *N*-(*p*-chlorobenzylidene)diphenylphosphinamide **1e** having an electron-withdrawing group on the phenyl ring, the corresponding normal aza-Baylis–Hillman adduct **3e** was obtained as the sole product using $PPhMe_2$ and PBu_3 as Lewis bases in MeCN and THF, respectively (see Scheme S2 in Supporting Information, Table S2 in Supporting Information, entries 2, 8). But, in dichloromethane, **4e** can be formed in moderate yields along with the corresponding normal adduct **3e** (see Table S2 in Supporting Information, entries 1, 5). $PPhMe_2$ gave higher yields of **3e** and **4e** under the same conditions (see Table S2 in Supporting Information, entries 1, 5). Thus, for starting materials **1** having electron-withdrawing groups on the phenyl ring, we used $PPhMe_2$ as a Lewis base and carried out these reactions in dichloromethane (Scheme 6). The double aza-Baylis–Hillman adducts **4** were produced as the major products in good yields (Table 5, entries 1–4). In some cases, adducts **4** were produced exclusively (Table 5, entries 1 and 3). On the other hand, for starting material *N*-(*p*-methoxybenzylidene)diphenylphosphinamide **1c** having a strongly electron-donating methoxy group on the phenyl ring, using $PPhMe_2$ as a Lewis base in dichloromethane, the reaction became sluggish (Scheme 7, Table 6, entry 1). Using PBu_3 as a Lewis base in acetonitrile, DMF or CH_2Cl_2, the corresponding abnormal aza-Baylis–Hillman adduct **4c** was obtained as the major product (Table 6, entries 3–5). However, a prolonged time was required for this reaction. In THF, the corresponding normal aza-Baylis–Hillman adduct **3c** was obtained in 70% yield exclusively (Table 6, entry 2). From *N*-(*p*-methylbenzylidene)diphenylphosphinamide **1b**, **4b** was obtained along with the normal aza-Baylis–Hillman adduct **3b** in THF (Table 6, entry 7). It should be emphasized here that using the strongest nucleophilic Lewis base PMe_3, **4** was obtained in moderate yield along with product **3** in moderate yield as well (Table 6, entries 6 and 8). The ratio of **3**:**4** is variable with the employed different Lewis bases, solvents and reaction time (see Table S2 in Supporting Information and Table S3 in Supporting Information, entry 5). Using PMe_3 as a Lewis base, the total yields of **3** and **4** were higher than others. Thus we carried out the Baylis–Hillman reactions of other *N*-(arylmethylene)diphenylphosphinamides **1** with methyl acrylate in the presence of PMe_3 (see Scheme S3 in Supporting Information). The results are summarized in Supporting Information as Table S3. However, using MVK or acrylonitrile as a Michael acceptor, no double Baylis–Hillman adduct was formed at all. The relative configuration of abnormal aza-Baylis–Hillman adduct **4** was determined by X-ray crystal diffraction. An ORTEP drawing of *anti*-**4f** is shown in Figure 1.[10] The ratios of *syn* and *anti* were determined by ^1H NMR spectroscopic data (see Supporting Information: Scheme S1, Table S1, Scheme S2, Table S2, Scheme S3, Table S3).

Concerning the route of formation of **4**, we confirmed that the abnormal aza-Baylis–Hillman adduct **4** was formed from the reaction of **3** with methyl acrylate in the presence of PBu_3 Lewis base by means of the control experiments shown in Scheme 8. The plausible reaction mechanism for the double aza-Baylis–Hillman reaction



Scheme 6.



Scheme 7.

Table 5. Aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** (1.0 equiv.) with methyl acrylate (2.5 equivs.) in the presence of $PPhMe_2$ (10 mol %) in dichloromethane.

Entry	Ar	Time [h]	Yield [%][as] 3	Yield [%][a] 4 (*syn*:*anti*)[b]
1	*p*-FC_6H_4 (**1d**)	24	0	**4d**, 82 (1:3.8)
2	*p*-BrC_6H_4 (**1f**)	48	9	**4f**, 70 (1:10)
3	*p*-$NO_2C_6H_4$ (**1g**)	48	0	**4g**, 47 (1:2.6)
4	C_6H_5CH=CH (**1h**)	48	15	**4h**, 46 (1:17.5)

[a] Yield of isolated products.
[b] The *syn*:*anti* ratio was determined by ^1H NMR spectroscopy.

Table 6. Aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** (1.0 equiv.) having an electron-donating group with methyl acrylate (2.5 equivs) in the presence of Lewis base (10 mol %) in various solvents.

Entry	Ar	Lewis base	Solvent	Time [h]	Yield [%][a] **3**	Yield [%][a] **4** (*syn*:*anti*)[b]
1	*p*-$MeOC_6H_4$ (**1c**)	$PPhMe_2$	CH_2Cl_2	96	**3c**, <10	**4c**, 0
2	*p*-$MeOC_6H_4$ (**1c**)	PBu_3	THF	48	**3c**, 70	**4c**, 0
3	*p*-$MeOC_6H_4$ (**1c**)	PBu_3	MeCN	96	**3c**, 0	**4c**, 60 (1:1.1)
4	*p*-$MeOC_6H_4$ (**1c**)	PBu_3	DMF	96	**3c**, 6	**4c**, 90 (1:8)
5	*p*-$MeOC_6H_4$ (**1c**)	PBu_3	CH_2Cl_2	96	**3c**, 11	**4c**, 80 (1:1.7)
6	*p*-$MeOC_6H_4$ (**1c**)	PMe_3	THF	48	**3c**, 33	**4c**, 43 (1:5.5)
7	*p*-EtC_6H_4 (**1b**)	PBu_3	THF	17	**3b**, 39	**4b**, 37 (1:2)
8	*p*-EtC_6H_4 (**1b**)	PMe_3	THF	48	**3b**, 53	**4b**, 20 (1:12.5)

[a] Yields of isolated products.

[b] The *syn*:*anti* ratio was determined by ^1H NMR spectroscopy.

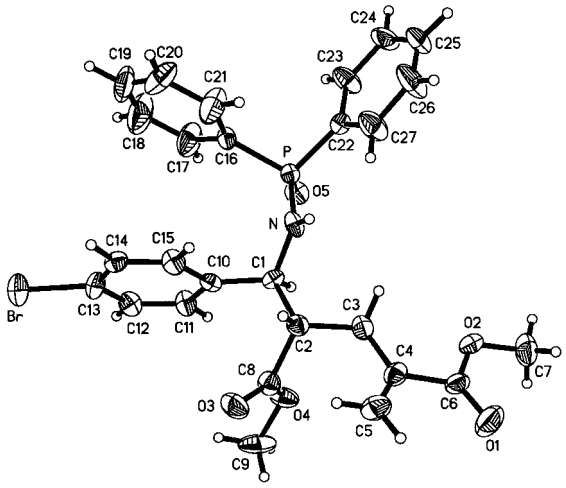
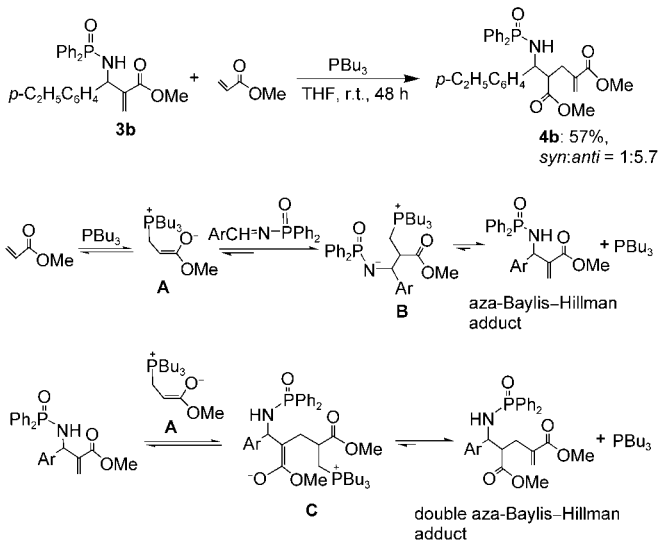


Figure 1. The X-ray crystal structure of *anti*-**4f**.

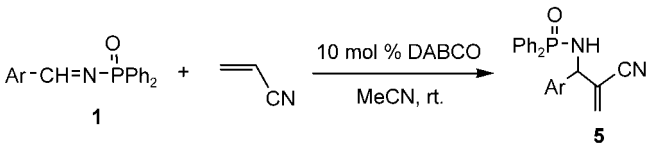


Scheme 8. The plausible reaction mechanism for the double Baylis–Hillman reaction

is described in Scheme 8. The first step is an aldol condensation to form the normal Baylis–Hillman adduct *via* intermediates **A** and **B** and the second step is a Michael addition of a Lewis base-generated enolate **A** from methyl acrylate.[9a] The Michael addition reaction (1,4-addition) takes place preferentially to give the double aza-Baylis–Hillman adduct **4** because the enolate **A** is a hindered nucleophile (Scheme 8). The nucleophilicity of the nitrogen Lewis base is too weak to promote such a double Baylis–Hillman reaction. With methyl vinyl ketone as a Michael acceptor in the presence of stronger Lewis bases, this reaction produced a complicated mixture of unidentified products.

Aza-Baylis–Hillman Reactions of 1 with Acrylonitrile

For the aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** with acrylonitrile, we examined many Lewis bases in a similar manner as described above in DMF at room temperature, but we found that DABCO can effectively catalyze this reaction to give the corresponding aza-Baylis–Hillman adduct **5a** in high yield (see Scheme S4 in Supporting Information, Table S4 in Supporting Information, entry 2). Using PPh_3, $PPhMe_2$, PBu_3 or PPh_2Me as the Lewis base, the reaction mixture immediately became dark and the reaction gave **5a** in traces or relatively low to moderate yields (24–60%) along with many unidentified products (see Table S4 in Supporting Information, entries 1, 3–5). With another nitrogen Lewis base, DMAP, no reaction occurred (see Table S4 in Supporting Information, entry 6). The solvent effects have been also examined using DABCO as Lewis base. The results are shown in Supporting Information as Table



Scheme 9.

Table 7. Aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** (1.0 equiv.) with acrylonitrile (1.2 equivs.) in the presence of DABCO (10 mol %).

Entry	Ar	Solvent	Time [h]	Yield [%][a] 5
1	*p*-EtC_6H_4 (**1b**)	MeCN	72	**5b**, 41
2	*p*-$MeOC_6H_4$ (**1c**)	MeCN	72	**5c**, 28
3	*p*-FC_6H_4 (**1d**)	MeCN	48	**5d**, 69
4	*p*-ClC_6H_4 (**1e**)	MeCN	48	**5e**, 59
5	*p*-BrC_6H_4 (**1f**)	MeCN	48	**5f**, 64
6	*p*-$NO_2C_6H_4$ (**1g**)	MeCN	24	**5g**, 27
7	C_6H_5CH=CH (**1h**)	MeCN	72	**5h**, 53

[a] Yields of isolated products.

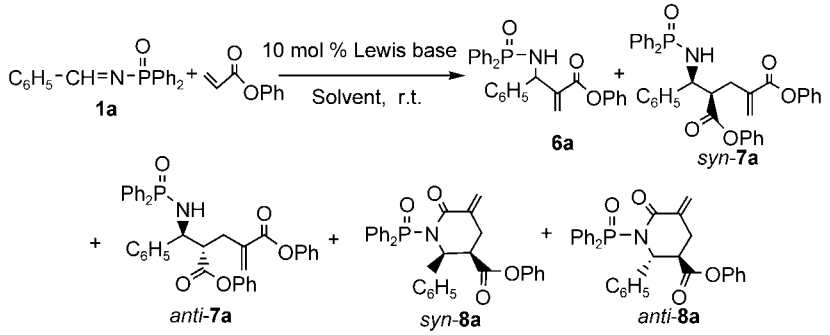
S5. In MeCN, the aza-Baylis–Hillman adduct **5a** was produced in 86% yield (see Table S5 in Supporting Information, entry 2).

Under the optimized reaction conditions, we next examined the aza-Baylis–Hillman reactions of other *N*-(arylmethylene)diphenylphosphinamides **1** with acrylonitrile (Scheme 9). The results are summarized in Table 7. The normal aza-Baylis–Hillman adducts **5** were obtained in moderate to good yields in most cases (Table 7).

Aza-Baylis–Hillman Reactions of 1 with Phenyl Acrylate

The interesting finding in this paper is in the aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** with phenyl acrylate (Scheme 10). At the beginning, this version of the reaction was examined with various Lewis bases. Using PPh_3, DABCO, $PPhMe_2$, PPh_2Me PMe_3, or DBU as a Lewis base in this reaction, the corresponding aza-Baylis–Hillman adduct **6a** was obtained in trace to moderate yields (56%) (Table 8, entries 1–6). Using DABCO as the nitrogen Lewis base in this reaction, we found that the adduct **6a** was obtained in 17% along with the double aza-Baylis–Hillman adduct **7a** as a mixture of *syn* and *anti*-isomers in 25% (Table 8, entry 2). By means of HPLC analysis and X-ray crystal structure diffraction (Figure 2),[11] we found that when using PBu_3 as a Lewis base, **6a** was formed in traces and the reaction gave the double adduct **7a** as a mixture of *syn* and *anti*-isomers and the unexpected cyclized product **8a** similarly as a mixture of *syn*- and *anti*-isomers at the same time (Scheme 10, Table 8, entry 10). Next we carefully examined the unusual reaction pattern in the reaction of **1a** with phenyl acrylate using PBu_3 as Lewis base. In order to improve the yields of **7a** and **8a**, the solvent effects were examined. The best solvents were THF, Et_2O, DME, and 1,4-dioxane (Table 8, entries 10, 13, 15 and 16). Increasing the reaction temperature did not improve the yields of **7a** and **8a** (Table 8, entries 11, 12, 14 and 17).

PPh_3 and DBU are the best promoters for the formation of the normal aza-Baylis–Hillman adduct **6a** (Table 8, entries 1 and 6). The solvent effect was also clarified by use of PPh_3 as a Lewis base (see Scheme S5 in Supporting Information, Table S6 in Supporting Information, entries 1–4). The best result was obtained in MeCN using PPh_3 as a Lewis base (see Table S6 in Supporting Information, entry 2). Under the optimized reaction conditions, we next examined the aza-Baylis–Hillman reactions of other *N*-(arylmethylene)diphenylphosphinamides **1** with phenyl acrylate (Scheme 11). The results are summarized in Table 9. For *N*-(arylmethylene)diphenylphosphinamides **1** derived from aryl aldehydes, the normal aza-Baylis–Hillman adducts **6** were obtained in moderate yields (Table 9, entries 1–6). For *N*-(arylmethylene)diphenylphosphinamide **1 h** derived from an aliphatic aldehyde, the corresponding adduct **6 h** was obtained in low yield (19%) (Table 9, entry 7).



Scheme 10.

Table 8. Aza-Baylis–Hillman reactions of *N*-benzylidenediphenylphosphinamide (**1a**; 1.0 equiv.) with phenyl acrylate (2.5 equivs.) in the presence of Lewis base PBu_3 (10 mol %) in THF.

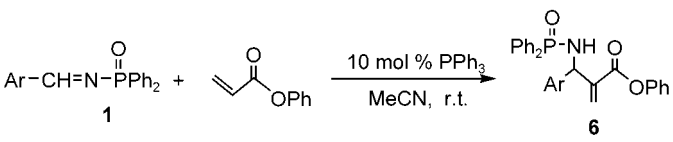
Entry	Lewis base	Solvent	Time [h]	Yield [%][a] **6a**	Yield [%][a] **7a** (*syn*:*anti*)[b]	Yield [%][a] **8a** (*syn*:*anti*)[b]
1	PPh_3	THF	24	54	0	0
2	DABCO	THF	24	17	25 (1:10)	0
3	$PhPMe_2$	THF	24	40	0	0
4	Ph_2PMe	THF	12	25	0	0
5	PMe_3	THF	12	Trace	0	0
6	DBU	THF	1/6	56	0	0
7	PBu_3	CH_2Cl_2	24	0	Trace	0
8	PBu_3	DMF	24	0	Trace	0
9	PBu_3	MeCN	24	0	Trace	0
10	PBu_3	THF	24	trace	53 (1:1.3)	20 (1:5.1)
11	PBu_3	THF[c]	12	0	52 (1:1.7)	9 (1:5.1)
12	PBu_3	THF[d]	12	0	Trace	18 (1:5.9)
13	PBu_3	Et_2O	1/6	0	59 (1:4.5)	11 (1:6.9)
14	PBu_3	Et_2O[d]	1/6	0	Trace	20 (1:6.4)
15	PBu_3	DME	1/6	0	27 (1:1.3)	12 (1:7.0)
16	PBu_3	1,4-dioxane	1/6	0	69 (1:1.9)	9 (1:5.2)
17	PBu_3	1,4-dioxane[c]	1/6	0	53 (1:2.1)	6 (1:5.0)
18	PBu_3	CH_3OH	24	0	0	0

[a] Yields of isolated productss.
[b] The *syn*:*anti* ratio was determined by ^{1}H NMR spectroscopy.
[c] The reaction was carried out at 40°C.
[d] The reaction was carried out under reflux conditions.

Table 9. Aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** (1.0 equiv.) with phenyl acrylate (2.5 equivs.) in the presence of PPh_3 (10 mol %) at room temperature in MeCN.

Entry	Ar	Solvent	Time [h]	Yield [%][a] **6**
1	*p*-EtC_6H_4 (**1b**)	MeCN	72	**6b**, 38
2	*p*-$MeOC_6H_4$ (**1c**)	MeCN	72	**6c**, 58
3	*p*-FC_6H_4 (**1d**)	MeCN	48	**6d**, 48
4	*p*-ClC_6H_4 (**1e**)	MeCN	48	**6e**, 59
5	*p*-BrC_6H_4 (**1f**)	MeCN	48	**6f**, 66
6	*p*-$NO_2C_6H_4$ (**1g**)	MeCN	24	**6g**, 52
7	C_6H_5CH=CH (**1h**)	MeCN	72	**6h**, 19

[a] Yield of isolated products.

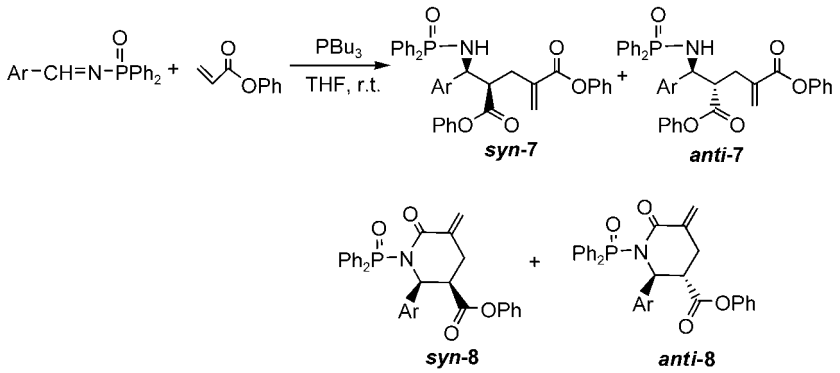


Scheme 11.

Under the optimized conditions, namely in THF at room temperature, we carried out the reactions of various *N*-(arylmethylenediphenylphosphinamides) **1** with phenyl acrylate using PBu_3 as a Lewis base (Scheme 12). The results are listed in Table 10. In all cases, the double aza-Baylis–Hillman adduct **7** as mixtures of *syn*- and *anti*-isomers, except for **7 h**, and the cyclized abnormal aza-Baylis–Hillman product **8** also as mixtures of *syn*- and *anti*-isomers, except for **8f** and **8 h**, were obtained at the same time (Table 10, entries 1–7). The *syn* and *anti* ratios of **7** were determined by ^{1}H NMR spectroscopy. The configuration of the cyclized abnormal aza-Baylis–Hillman product *anti*-**8a** was confirmed by X-ray crystal diffraction (Figure 2). In order to confirm the route of formation of **8**, the control experiments shown in Table 11 were carried out in the presence of various bases or solid acids. In the presence of organic bases such as DBU, PBu_3, BSA [bis(trimethylsilyl)acetamide] or solid acids such as montmorillonite KSF clay, no reactions occurred with **7a** (Table 11, entries 1, 2, 4, 5). The stronger base NaOMe caused the decomposition of **7a** (Table 11, entry 6). Only in the presence of PBu_3 and phenyl acrylate was **8a** formed in moderate yield (Table 11, entry 3). This result suggests that the intermediate enolate **D**, derived from nucleophilic attack of PBu_3 to phenyl acrylate (the Baylis–Hillman reaction intermediate) during the reaction, plays a very important role in the formation of **8**. The proton of the NH group is abstracted by enolate **D**[12] to give the intermediate **E** which produces **8** *via* an intramolecular nucleophilic attack of N^- to the carboxylate (Scheme 13). The *syn*- and *anti*-isomeric ratios of **8** were determined by ^{1}H NMR spectroscopy data (see Supporting Information). We believe that the different *syn*/*anti* ratios between **7** and **8** are due to the different transformation rates of *syn*- and *anti*-isomers **7** to **8**. In most cases the *anti*-**7** is more easily converted to *anti*-**8**. At the present stage, we cannot explain these different transformation rates.

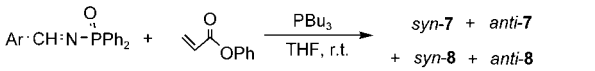
Aza-Baylis–Hillman Reactions of 1 with Ethyl Vinyl Ketone

In the aza-Baylis–Hillman reactions of **1a** with ethyl vinyl ketone (EVK), we found that only in the presence of PPh_3 did the reaction proceed smoothly and the corresponding normal aza-Baylis-Hillman adduct **9a** was obtained as sole product (see Scheme S6 in Supporting Information). On using stronger Lewis bases such as PBu_3 or PPh_2Me, this reaction gave many unidentified products as well as the double aza-Baylis–Hillman adduct. We have not yet been able to purify or isolate these products by a column chromatography. Using DABCO, DMAP, or DBU as a Lewis base, this reaction is sluggish. The solvent effects were examined using PPh_3 as a Lewis base. The results are summarized in Supporting Information as Table S7. The best result is obtained in THF



Scheme 12.

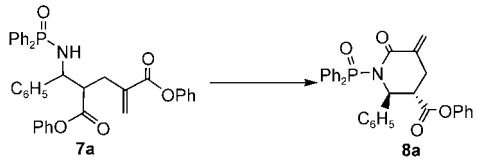
Table 10. Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** (1.0 equiv.) with phenyl acrylate (2.5 equivs.) in the presence of PBu_3 (10 mol %) in THF.



Entry	Ar	Time [h]	Yield [%][a] 7 (*syn*:*anti*)[b]	Yield [%][a] 8 (*syn*:*anti*)[b]
1	*p*-$MeOC_6H_4$ (**1c**)	72	**7c**, 40 (1:2.0)	**8c**, 10 (1:10.0)
2	*p*-FC_6H_4 (**1d**)	48	**7d**, 34 (1:2.1)	**8d**, 14 (1:11.0)
3	*p*-ClC_6H_4 (**1e**)	48	**7e**, 34 (1:10.0)	**8e**, 16 (1:11.0)
4	*p*-BrC_6H_4 (**1f**)	48	**7f**, 36 (1:1.3)	**8f**, 13 (*anti*)
5	*p*-$NO_2C_6H_4$ (**1g**)	24	**7g**, 32 (1:1.7)	**8g**, 12 (1:8.3)
6	C_6H_5CH=CH (**1h**)	72	**7h**, 39 (*anti*)	**8h**, 12 (*anti*)
7	*p*-MeC_6H_4 (**1i**)	72	**7i**, 44 (1:1.7)	**8i**, 13 (1:5.9)

[a] Yields of isolated products.
[b] The *syn*:*anti* ratio was determined by ^{1}H NMR spectroscopy.

Table 11. Synthesis of lactam **8**.



Entry	Reaction conditions	Time [h]	Yield [%][a] 8a
1	PBu_3, THF	72	NR
2	DBU, THF	72	NR
3	PBu_3, THF,  (2.0 equivs.)	72	41
4	KSF, THF	72	NR
5	BSA, THF	72	NR
6	$NaOCH_3$, THF	72	0[b]

[a] Yields of isolated products.
[b] **7a** disappeared, but **8a** was not observed.

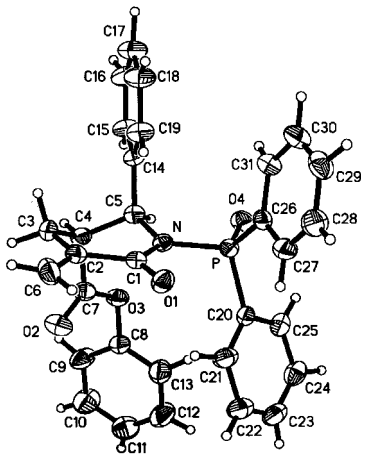
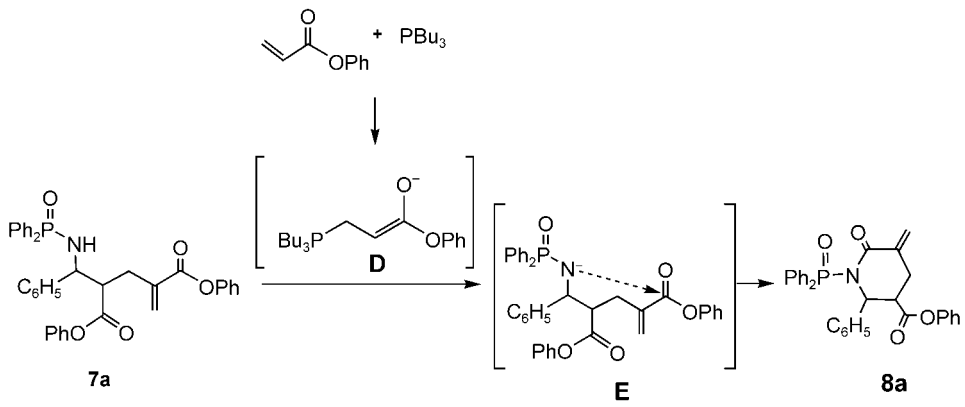


Figure 2. The X-ray crystal structure of *anti*-**8a**.

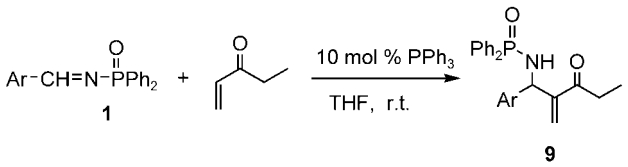
(see Table S7 in Supporting Information, entry 4). Under the optimized conditions, we carried out the aza-Baylis–Hillman reactions of various imines **1** with EVK (Scheme 14). The results are shown in Table 12. The corresponding normal aza-Baylis–Hillman adducts **9** were formed in moderate yields (Table 12, entries 1–5).

Aza-Baylis–Hillman Reactions of 1 with Phenyl Vinyl Ketone

On the other hand, for the aza-Baylis–Hillman reactions of **1a** with phenyl vinyl ketone (PVK) (see Scheme S7 in Supporting Information), we found that only when using PPh_2Me as a Lewis base in THF was the corresponding normal aza-Baylis–Hillman adduct **10a** obtained in 23% along with the double aza-Baylis–Hillman adduct **11a** in 28% (see Table S8 in Supporting Information, entry 5). Using DABCO or $PPhMe_2$ as a Lewis base in this reaction, adduct **11a** was formed exclusively in 13% and 10%



Scheme 13. A plausible mechanism for the formation of **8**.



Scheme 14.

Table 12. The aza-Baylis–Hillman reaction of **1** (1 equiv.) with EVK (1.2 equivs.) in the presence of PPh_3 (10 mol %) at room temperature in THF.

Entry	Ar	Solvent	Time [h]	Yield [%][a] 9
1	*p*-$MeOC_6H_4$ (**1c**)	THF	72	**9c**, 59
2	*p*-ClC_6H_4 (**1e**)	THF	48	**9e**, 47
3	*p*-BrC_6H_4 (**1f**)	THF	48	**9f**, 61
4	*p*-$NO_2C_6H_4$ (**1g**)	THF	24	**9g**, 38
5	*p*-MeC_6H_4 (**1i**)	THF	72	**9i**, 50

[a] Yields of isolated products.

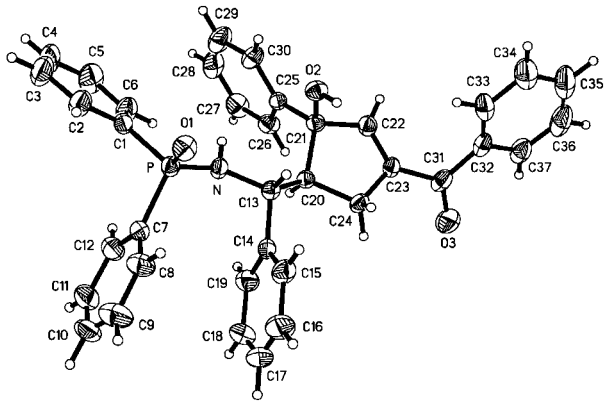
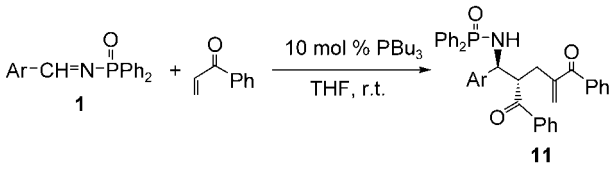


Figure 3. The X-ray crystal structure of *anti*-**12a**.

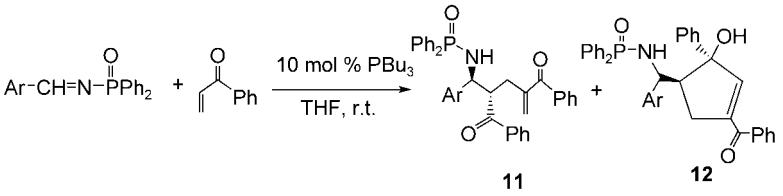


Scheme 15.

yield in THF, respectively (see Table S8 in Supporting Information, entries 1, 6). In CH_2Cl_2, MeCN, and DMF using PPh_2Me as a Lewis base in this reaction, the adducts **11a** were formed in low yields (see Table S8 in Supporting Information, entries 2–4). The best result was obtained in THF using PBu_3 as a Lewis base (see Table S8 in Supporting Information, entry 7). In all these cases the double adduct **11a** was formed in the *anti*-configuration.[13] In other solvents, this reaction became sluggish using PBu_3 as a Lewis base (see Table S8 in Supporting Information, entries 9–12). The interesting finding in this reaction is that when the reaction time is prolonged to 120 h, a cyclized abnormal aza-Baylis–Hillman adduct **12a** was formed as the *anti*-conformer (see Scheme S7 in Supporting Information, Table S8 in Supporting Information, entry 8 and 12). Its configuration was confirmed by X-ray crystal diffraction (Figure 3).[14]

In Scheme 15 and Table 13, we show that the double aza-Baylis–Hillman adducts **11** could be exclusively formed in the presence of PBu_3 in moderate yields within 3 days from various imines **1**. In Scheme 16 and Table 14, we indicate that with a prolonged reaction time, the cyclized abnormal aza-Baylis–Hillman adducts **12** were produced from various imines **1** along with double aza-Baylis–Hillman adducts **11**. In general, the reaction rates in this type of aza-Baylis–Hillman reaction are slow and the yields of **11** and **12** are moderate. The *anti*-configuration of **11** was determined by ^1H NMR spectroscopy (see Supporting Information).

The formation route for the cyclized abnormal aza-Baylis–Hillman adducts **12** was determined by the control experiments shown in Table 14. In the presence of PBu_3, the double adduct **11** can be transformed into



Scheme 16.

Table 13. The double aza-Baylis–Hillman reaction of **1** (1 equiv.) with PVK (2.5 equivs.) catalyzed by PBu_3 (10 mol %) in THF.

Entry	Ar	Time [h]	Yield [%][a] 11
1	C_6H_5 (**1a**)	72	**11a**, 62
2	*p*-$MeOC_6H_4$ (**1c**)	96	**11c**, 23
3	*p*-FC_6H_4 (**1d**)	48	**11d**, 37
4	*p*-ClC_6H_4 (**1e**)	48	**11e**, 55
5	*p*-BrC_6H_4 (**1f**)	48	**11f**, 43
6	*p*-$NO_2C_6H_4$ (**1g**)	24	**11g**, 40
7	C_6H_5CH=CH (**1h**)	72	**11h**, 20
8	*p*-MeC_6H_4 (**1i**)	72	**11i**, 34

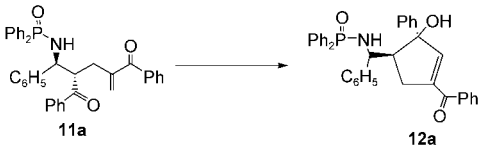
[a] Yields of isolated products.

Table 14. The aza-Baylis–Hillman reaction of **1** (1 equiv.) with PVK (2.5 equivs.) in the presence of PBu_3 (10 mol %) for a longer reaction time in THF.

Entry	Ar	Time [h]	Yield [%][a] 11	Yield [%][a] 12
1	C_6H_5 (**1a**)	120	**11a**, 24	**12a**, 20
2	*p*-$MeOC_6H_4$ (**1c**)	120	**11c**, 20	**12c**, 10
3	*p*-FC_6H_4 (**1d**)	120	**11d**, 27	**12d**, 17
4	*p*-ClC_6H_4 (**1e**)	120	**11e**, 40	**12e**, 15
5	*p*-BrC_6H_4 (**1f**)	120	**11f**, 41	**12f**, 20
6	*p*-$NO_2C_6H_4$ (**1g**)	96	**11g**, 32	**12g**, 10
7	C_6H_5CH=CH (**1h**)	120	**11h**, 30	**12h**, 15
8	*p*-MeC_6H_4 (**1i**)	120	**11i**, 26	**12i**, 11

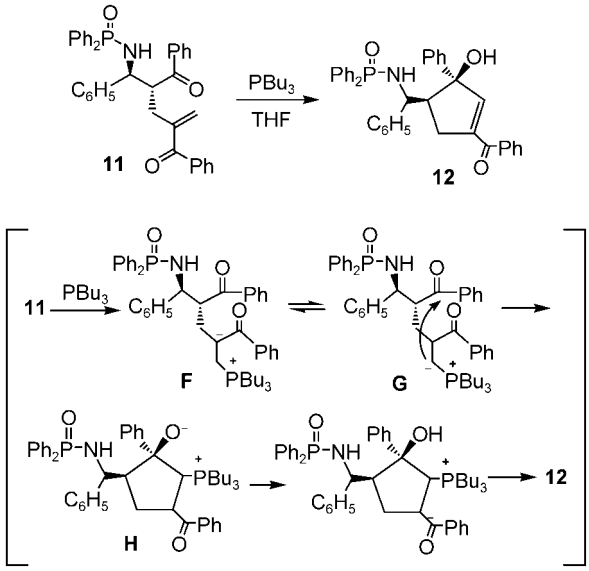
[a] Yields of isolated products.

Table 15. Mechanistic rationale for the formation of **12**.



Entry	Reaction conductions	Time [h]	Yield [%][a] 12a
1	PBu_3, THF	72	40
2	K_2CO_3, THF	72	NR
3	KSF, THF	72	NR

[a] Yields of isolated products.

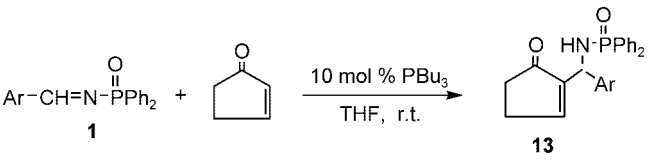


Scheme 17. A plausible reaction mechanism for the formation of **12**.

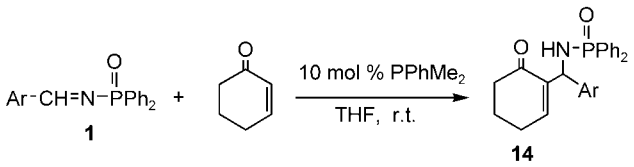
the cyclized abnormal adducts **12** after a prolonged reaction period. Other bases or solid acids did not promote this transformation (Table 15, entries 2 and 3). A possible mechanism for the formation of **12** is shown in Scheme 17. The formed phosphonium enolate **F** derived from the phenyl vinyl ketone moiety in **12** with PBu_3 is in an equilibrium with the zwitterionic intermediate **G**[15] which produces the cyclized zwitterionic intermediate **H** *via* an intramolecular nucleophilic addition. Proton transfer and elimination of PBu_3 then furnish the cyclized product **12** (Scheme 17).

Aza-Baylis–Hillman Reactions of 1 with 2-Cyclopenten-1-one and 2-Cyclohexen-1-one

For cyclic enones, we examined the aza-Baylis–Hillman reactions of **1** with 2-cyclopenten-1-one or 2-cyclohexen-1-one in the presence of various Lewis bases in dichloromethane (see Scheme S8 in Supporting Information). For 2-cyclopenten-1-one, the Lewis bases DABCO and PPh_3 showed no catalytic activity in this reaction (see Table S9 in Supporting Information, entries 1 and 2). The Lewis bases PBu_3 and PPh_2Me gave good results in dichloromethane (see Table S9 in Supporting Infor-



Scheme 18.



Scheme 19.

Table 16. Aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** (1.0 equiv.) with 2-cyclopenten-1-one (1.2 equivs.) in the presence of PBu_3 (10 mol %) at room temperature in THF.

Entry	Ar	Solvent	Time [h]	Yield [%][a] **13**
1	*p*-EtC_6H_4 (**1b**)	THF	24	**13b**, 66
2	*p*-$MeOC_6H_4$ (**1c**)	THF	24	**13c**, 97
3	*p*-FC_6H_4 (**1d**)	THF	12	**13d**, 83
4	*p*-ClC_6H_4 (**1e**)	THF	12	**13e**, 91
5	*p*-BrC_6H_4 (**1f**)	THF	12	**13f**, 60
6	*p*-$NO_2C_6H_4$ (**1g**)	THF	6	**13g**, 65
7	C_6H_5CH=CH (**1h**)	THF	12	**13h**, 80

[a] Yields of isolated products.

Table 17. Aza-Baylis–Hillman reactions of N-(arylmethylene)diphenylphosphinamides **1** (1.0 equivs.) with 2-cyclohexen-1-one (1.2 equivs.) in the presence of $PPhMe_2$ (10 mol %) at room temperature in THF.

Entry	Ar	Solvent	Time [h]	Yield [%][a] **14**
1	*p*-EtC_6H_4 (**1b**)	THF	72	**14b**, 62
2	*p*-$MeOC_6H_4$ (**1c**)	THF	72	**14c**, 42
3	*p*-FC_6H_4 (**1d**)	THF	48	**14d**, 85
4	*p*-ClC_6H_4 (**1e**)	THF	48	**14e**, 65
5	*p*-BrC_6H_4 (**1f**)	THF	48	**14f**, 70
6	*p*-$NO_2C_6H_4$ (**1g**)	THF	24	**14g**, 53
7	C_6H_5CH=CH (**1h**)	THF	48	**14h**, 79

[a] Yields of isolated products.

mation, entries 3 and 6). The corresponding normal aza-Baylis–Hillman adduct **13a** was obtained in 92% yield using PBu_3 as Lewis base promoter (see Scheme S8 in Supporting Information, Table S9 in Supporting Information, entry 6). After examination of the solvent effects, we found that when this reaction was carried out in THF, the yield of **13a** can be improved to 97% at room temperature (see Table S10 in Supporting Information entry 4). For other *N*-diphenylphosphorylimines **1** under the optimized reaction conditions, the corresponding adducts **13** were obtained in good to excellent yields (Scheme 18). The results are summarized in Table 16.

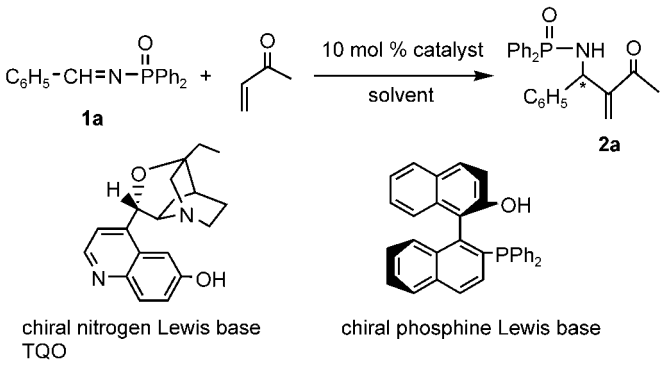
However, for 2-cyclohexen-1-one, the stronger Lewis bases $PPhMe_2$ or PMe_3 gave the best result in dichloromethane and the corresponding normal aza-Baylis–Hillman adduct **14a** was formed in 49% and 48% yields, respectively (see Scheme S9 in Supporting Information, Table S11 in Supporting Information, entries 4 and 5). The Lewis bases DABCO, PPh_3 and PPh_2Me did not catalyze this reaction (see Table S11 in Supporting Information, entries 1–3). Upon examination of the solvent effect, it was found that THF is also the best solvent for this reaction because **14a** was isolated in 81% (see Table S12 in Supporting Information, entry 4). For the reaction of 2-cyclohexen-1-one with various *N*-(arylmethylene)diphenylphosphinamides **1** under the optimized reaction conditions, the aza-Baylis–Hillman adducts **14** were obtained in moderate to good yields (Scheme 19, Table 17, entries 1–7).

In all cases, only the corresponding normal aza-Baylis-Hillman adducts **13** and **14** were formed, respectively.

Catalytic, Asymmetric Aza-Baylis–Hillman Reactions

Furthermore, we have examined the catalytic, asymmetric aza-Baylis–Hillman reactions of *N*-(arylmethylene)-diphenylphosphinamides **1** with MVK in the presence of the chiral nitrogen Lewis base 4-(3-ethyl-4-oxa-1-azatricyclo[4.4.0.$0^{3,8}$]dec-5-yl)-quinolin-6-ol (TQO)[2a,c,14] and the phosphine Lewis base (*R*)-2′-diphenylphosphanyl-[1,1′]binaphthalenyl-2-ol (Scheme 20).[6f] The results are summarized in Table 18. We first used TQO[16] (10 mol %) as the chiral Lewis base in this aza-Baylis–Hillman reaction in various solvents. The reaction is sluggish in DMF and acetonitrile at room temperature. The corresponding adduct **2a** was obtained in low yields and low enantioselectivities (23% ee and 12% ee), respectively (Table 18, entries 1 and 3). Lowering the reaction temperature to $-20\,^{\circ}C$ did not improve the enantioselectivity (Table 18, entry 4). In dichloromethane, the adduct **2a** was obtained in 73% yield, but still in only 28% ee (Table 18, entry 2). At $-20\,^{\circ}C$, a trace of **2a** was obtained (Table 18, entry 5). When the chiral phosphine Lewis base (10 mol %) was used as the catalyst in dichloromethane (Scheme 20), the reaction proceeded smoothly to give **2a** in 82% yield with 47% ee, although in DMF or THF this reaction was sluggish and the achieved ee was low under the same conditions (Table 18, entries 6, 7 and 10).[17] At $-20\,^{\circ}C$, this catalytic, asymmetric reaction was sluggish in dichloromethane and DMF (Table 18, entries 8 and 9). The chiral HPLC charts are shown in Supporting Information.

The catalytic, asymmetric aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1**

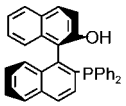


Scheme 20.

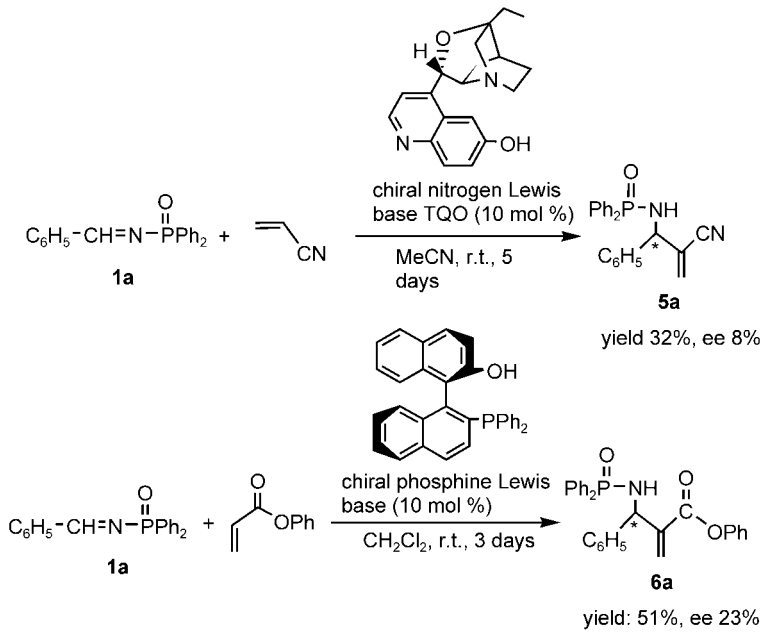
with acrylonitrile was carried out in the presence of the chiral nitrogen Lewis base TQO with MeCN as the solvent to give the adduct in 31% yield with 8% ee (Scheme 21). This reaction is sluggish using the phosphine Lewis base (*R*)-2′-diphenylphosphanyl-[1,1′]binaphthalenyl-2-ol. We also carried out the reaction of *N*-(arylmethylene)diphenylphosphinamides **1** with phenyl acrylate in the presence of the chiral phosphine Lewis base (*R*)-2′-diphenylphosphanyl-[1,1′]binaphthalenyl-2-ol in dichloromethane (Scheme 21) (this reaction is sluggish using TQO as chiral Lewis base). The adduct was obtained in 51% yield with 23% ee. All of the adducts were obtained in low ee and yields. Thus, reactions under other conditions were not further examined.

In summary, moderate ee has been achieved in this catalytic, asymmetric aza-Baylis–Hillman reactions using MVK as Michael acceptor in the presence of a chiral phosphine Lewis base in dichloromethane at room temperature. For other simple Michael acceptors, these reactions are sluggish in the presence of sterically bulky chiral Lewis base promoters.

Table 18. Catalytic, asymmetric aza-Baylis–Hillman reactions of *N*-benzylidenediphenylphosphinamide (**1a**; 1.0 equiv.) with MVK (1.2 equiv.) in the presence of chiral phosphine and nitrogen catalysts (10 mol %).

Entry	Catalyst	Solvent	Temp. [°C]	Time [h]	Yield [%][a] **2a**	ee [%][b]	$[\alpha]_D$[c]
1	TQO	DMF	r.t.	48	43	23	+7.7
2		CH_2Cl_2	r.t.	48	73	28	+8.0
3		MeCN	r.t.	48	13	12[d]	+3.0
4		DMF	–20	72	32	23	+8.4
5		CH_2Cl_2	–20	120	<10	ND[e]	ND
6		DMF	r.t.	48	27	38	+9.7
7		CH_2Cl_2	r.t.	48	82	47	+14.6
8		CH_2Cl_2	–20	120	<10	ND	ND
9		DMF	–20	72	15	43[d]	+13.2
10		THF	r.t.	72	26	31[d]	+8.9

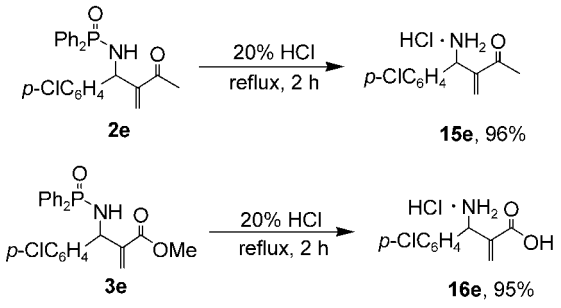
[a] Yields of isolated products.
[b] Determined by chiral HPLC.
[c] Measured in chloroform at 20 °C.
[d] Calculated by comparing the optical rotation.
[e] Not determined.



Scheme 21.

Conclusion

We have comprehensively examined the aza-Baylis–Hillman reactions of *N*-(arylmethylene)diphenylphosphinamides **1** with various activated olefins. The Lewis bases and solvents can significantly affect the reaction products. We found that, when using stronger Lewis bases such as $PPhMe_2$ or PBu_3 as promoters in the of **1** with methyl acrylate, phenyl acrylate or PVK, the double aza-Baylis–Hillman adducts **4**, **7**, and **11** and the abnormal aza-Baylis–Hillman adducts **8** or **12**, derived from the further reactions of the double adducts, can be obtained either as the major products or as the sole products depending on the reaction conditions. This is first report to disclose the formation of abnormal aza-Baylis–Hillman adducts **8** and **12** in aza-Baylis–Hillman reactions under mild conditions. In addition, the catalytic, asymmetric version of this reaction using simple Michael acceptors such as MVK, acrylonitrile or phenyl acrylate has been investigated. Moderate ee in the aza-Baylis–Hillman reaction of *N*-benzylidenediphenylphosphinamide (**1a**) with MVK has been achieved. On the basis of our previous results of the aza-Baylis–Hillman reactions using *N*-sulfonated imines (ArCH=NTs or ArCH=NMs) as the electrophiles, it is clear that the reaction rate of this reaction is slow for many Michael acceptors under the same conditions. The significant advantage in this type of aza-Baylis–Hillman reaction is the ease of removal of the diphenylphosphinyl group from the corresponding adduct because the sulfonyl group (Ts or Ms) in the adducts derived from *N*-sulfonated imines (ArCH=NTs or ArCH=NMs) is usually very difficult to remove. A typical procedure is as follows: upon heating in 10–20% aqueous HCl solution for several hours, the diphenylphosphinyl group can be removed perfectly to give the corresponding β-aminocarbonyl products (Scheme 22).[2d] Efforts are underway to elucidate the mechanistic details of this reaction and the key factors of the Lewis base for different substrates of the Baylis-Hillman reaction. Work along this line is currently in progress.



2e **15e**, 96%

3e **16e**, 95%

Scheme 22.

Experimental Section

General Remarks

Unless otherwise stated, all reactions were carried out under an argon atmosphere. All solvents were purified by distillation. Methyl vinyl ketone and tributylphosphine were obtained from Tokyo Chemical Industry (Tokyo Kasei Co. Ltd.) and used without purification. All *N*-tosyl imines were prepared according to the literature. Infrared spectra were measured on a Perkin-Elmer 983 spectrometer. ^{1}H-NMR spectra were recorded on a 300 MHz spectrometer in $CDCl_3$ using tetramethylsilane as the internal standard. Mass spectra were recorded with an HP-5989 instrument and HRMS were measured on a Finnigan MA + mass spectrometer. Satisfactory CHN microanalyses were obtained with a Carlo-Erba 1106 analyzer. Melting points were obtained by means of a micromelting point apparatus and are uncorrected.

Typical Reaction Procedure for Triphenylphosphine-Catalyzed Baylis–Hillman Reaction of *N*-Benzylidenediphenylphosphinamide (1a) with Methyl Vinyl Ketone

To a Schlenk tube containing **1a** (76 mg, 0.25 mmol) and triphenylphosphine (7 mg, 0.03 mmol) in DMF (0.5 mL) was added methyl vinyl ketone (MVK) (21 mg, 24.4 μL, 0.30 mmol) under an argon atmosphere and the reaction mixture was stirred for 48 h at room temperature (20 °C). The mixture was then washed with water (3 × 10 mL) and extracted with dichloromethane (2 × 10 mL). The organic layer was dried over anhydrous Na_2SO_4, the solvent removed under reduced pressure and the residue purified by silica gel column chromatography (eluent: EtOAc/petroleum=1/4) to give **2a** as a colorless solid; yield: 72 mg (81%).

Acknowledgements

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[10] The crystal data of *anti*-**4f** have been deposited under CCDC 191599. Empirical Formula: $C_{27}H_{27}NO_5PBr$, formula weight: 556.38, crystal color/habit: colorless/prismatic, crystal dimensions: $0.20 \times 0.20 \times 0.30$ mm, crystal System: monoclinic, lattice type: primitive, lattice parameters: $a = 5.4081(6)$ Å, $b = 20.733(2)$ Å, $c = 23.224(3)$ Å, $\alpha = 90°$, $\beta = 95.707(2)°$, $\gamma = 90°$, $V = 2591.1(5)$ Å^3, space group: Cc, $Z = 4$, $D_{calc} = 1.426$ g/cm^3, $F_{000} = 1144$; diffractometer: Rigaku AFC7R, residuals: R, Rw: 0.0596, 0.1531.

[11] The crystal data of **8a** have been deposited under CCDC 198221. Empirical formula: $C_{31}H_{26}NO_4P$, formula weight: 507.50, crystal color/habit: colorless/prismatic, crystal dimensions: $0.626 \times 0.153 \times 0.062$ mm, crystal system: orthorhombic, lattice type: primitive, lattice parameters: $a = 19.439(2)$ Å, $b = 14.4410(17)$ Å, $c = 9.3305(10)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $V = 2619.2(5)$ Å^3, space group: Pna2(1), $Z = 4$, $D_{calc} = 1.287$ g/cm^3, $F_{000} = 1064$, diffractometer: Rigaku AFC7R, residuals: R, Rw: 0.0552, 0.1087.

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[14] The crystal data of **12a** has been deposited under CCDC 195448. Empirical formula: $C_{37}H_{34}NO_4P$, formula weight: 587.62, crystal color/habit: colorless/prismatic, crystal dimensions: $0.368 \times 0.288 \times 0.151$ mm, crystal system: triclinic, lattice type: primitive, lattice parameters: $a = 11.6753(18)$ Å, $b = 11.9784(18)$ Å, $c = 12.1491(18)$ Å, $\alpha = 107.856(3)°$, $\beta = 91.723(3)°$, $\gamma = 97.974(4)°$, $V = 1596.8(4)$ Å^3, space group: P-1; $Z = 2$, $D_{calc} = 1.222$ g/cm^3, $F_{000} = 620$; diffractometer: Rigaku AFC7R, residuals: R, Rw: 0.0695, 0.1730.

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