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Chiral Bisphosphazides as Dual Basic Enantioselective Catalysts

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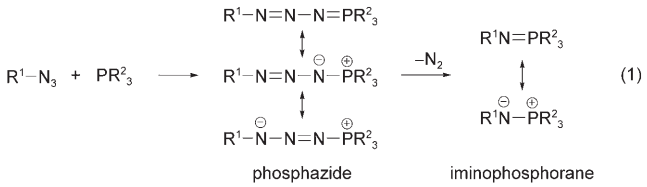
Abstract: Chiral bisphosphazides complexed with lithium salts efficiently catalyze the direct enantioselective 1,4-addition of dialkyl malonates to acyclic enones. Spectroscopic studies on the stoichiometry of the bisphosphazide and lithium salt have indicated the formation of a 1:1 species as the active enantioselective catalyst. It is suggested that the catalyst generates a complex of the protonated phosphazide and the chiral nucleophile as the key intermediate. The phosphazide moiety appears to be a promising dual basic functionality for stereo- and chemoselective catalytic transformations.

Keywords: asymmetric catalysis · basicity · lithium · Michael addition · phosphazene base

Introduction

Phosphazene compounds are employed as strong neutral organic bases,[1] functional materials,[2] and chemoselective synthetic reagents.[3] The utilization of Schwesinger's phosphazene bases[1] as strongly basic reagents for the chemoselective deprotonation of acidic and even less acidic C–H protons has been extensively investigated.[4] More recently, applications in the catalytic regulation of organometallic[5] and organosilicon[6] species have been reported. Most of these studies have dealt exclusively with simple iminophosphoranes ($R^1N{=}PR^2{}_3$), and several examples of chiral phosphazene-catalyzed enantioselective reactions have been reported.[4i,5b,c,7]

However, little attention has been paid to phosphazides ($R^1N{=}N{-}N{=}PR^2{}_3$), which are generally considered to be unstable intermediates in the Staudinger reaction,[8] although they are also potentially attractive as Lewis and/or Brønsted basic functionalities [Eq. (1)].



(1)

Verkade et al. recently reported that several azidoproazaphosphatranes resist thermal denitrogenation and may be used as catalytic bases in base-mediated reactions.[9] It was noted that appropriate steric bulkiness and electronic properties of the substituents were required for sufficient stabilization of the phosphazide intermediates.[9]

These findings motivated us to investigate the possible reactivity of the phosphazide moiety in base-catalyzed asymmetric reactions. Preparation of chiral phosphazides through the Staudinger reaction is attractive, because simply by mixing chiral azides with bulky and electron-donating tris(-dialkylamino)phosphines, chiral phosphazides are generated, which may be used directly for asymmetric reactions without further purification.[10]

We report here the first enantioselective catalysis using a chiral bisphosphazide (**1a**) complexed with lithium salts, by which direct, enantioselective 1,4-addition of dialkyl malonates to acyclic enones can be efficiently accomplished (Scheme 1). The asymmetric direct Michael addition of malonates to enones is a representative reaction in modern asymmetric catalysis,[11] and known metallic[12] and non-metallic[13,14] catalysts developed for this purpose are also effective for other base-catalyzed asymmetric processes.[11] We also present a possible application of the phosphazide

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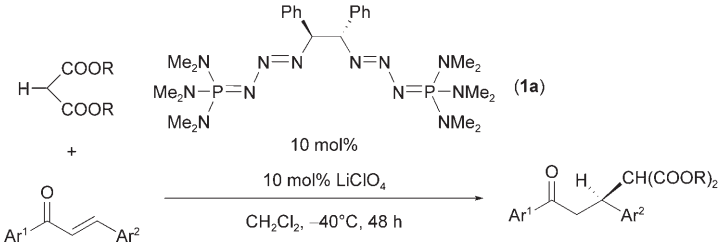
Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author: Preparation of bisazide, chiral HPLC charts for products, and NMR spectra for the titration experiments.

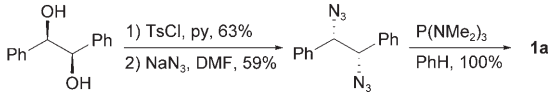
moiety as a promising *dual basic* functionality (both a Brønsted and Lewis base) in stereo- and chemoselective catalytic transformations.



Scheme 1. Direct conjugate addition of dialkyl malonates to enones catalyzed by bisphosphazide **1a** and a lithium salt.

Results and Discussion

First, we prepared the chiral bisphosphazide **1a** by simply mixing tris(dimethylamino)phosphine and the requisite asymmetrically functionalized bisazide at room temperature. The bisazide precursor was easily prepared in two steps from commercially available (*R*,*R*)-hydrobenzoin (Scheme 2, Figure 1).[15]



Scheme 2. Preparation of bisphosphazide **1a**.

1a was found to be stable at room temperature, both in pure form and in benzene solution, and no decomposition to reduced diamine **2** or denitrogenated iminophosphorane **3a** was observed. When heated at 80 °C for 18 h in toluene, **1a** was quantitatively transformed to iminophosphorane **3a** (as estimated by ^{31}P NMR).[5c] Derivatives **1b–d** were also prepared, following the same method as described for **1a** (Figure 1). From the viewpoints of simplicity and availability, **1a** was used for initial investigations.

Thus, we first applied **1a** for the direct conjugate addition of dimethyl malonate to *trans*-chalcone (Table 1). Although only slight asymmetric induction was observed, the reaction proceeded directly in the presence of a catalytic amount of **1a** (10 mol%) to form the 1,4-adduct **4a** (Table 1, entries 1–3). With the aim of obtaining higher stereoselectivity, we tested several additives. After many trials, we found that the addition of lithium *tert*-butoxide to bisphosphazide **1a** remarkably enhanced the stereoselectivity (entries 4–6), whereas other alkali metal *tert*-butoxides gave only poor selectivities (entries 7 and 8). In all cases, the *S* product was obtained as the major enantiomer.

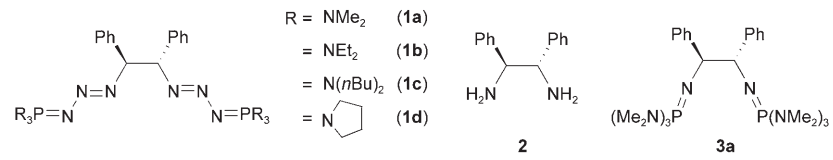
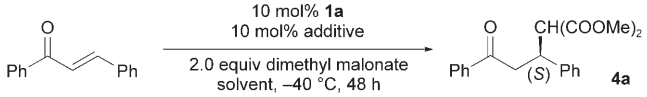


Figure 1. Structures of the prepared chiral phosphazides **1a–d**, the related diamine **2**, and the analogous iminophosphorane **3a**.

Table 1. Effects of solvent and additives on the reactivity and selectivity.

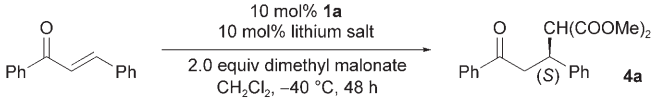


Entry	Additive	Solvent	Yield[a]	*ee*[b]
1	–	THF	21	8
2	–	toluene	56	13
3	–	CH_2Cl_2	98	10
4	LiO*t*Bu	THF	45	55
5	LiO*t*Bu	toluene	78	52
6	LiO*t*Bu	CH_2Cl_2	63	79
7	NaO*t*Bu	CH_2Cl_2	84	25
8	KO*t*Bu	CH_2Cl_2	43	1

[a] Isolated yield. [b] Determined by chiral HPLC.

The effect of the counter anion of the lithium salt was also investigated (Table 2). It was found that relatively acidic lithium salts gave better enantioselectivities. Among the lithium salts that we tested, $LiClO_4$ gave the best result (Table 2, entry 8).

Table 2. Effect of the counter anion of the lithium salt.



Entry	Lithium salt	Yield[a]	*ee*[b]
1	LiCl	89	60
2	LiBr	62	79
3	LiI	51	77
4	$LiBF_4$	52	85
5	$LiPF_6$	86	78
6	LiOTf	75	88
7	$LiNTf_2$	85	85
8	$LiClO_4$	95	88

[a] Isolated yield. [b] Determined by chiral HPLC.

Using $LiClO_4$ as an additive, reactions using **1b**, **1c**, **2**, and **3** were examined (Table 3). The bisphosphazides with diethylamino (**1b**) and pyrrolidyl (**1d**) substituents also gave good enantioselectivity, similar to that seen with **1a** (entries 2 and 4), whereas dibutylamino-substituted phosphazide **1c** gave poor selectivity (entry 3). The corresponding diamine **2** with the same chiral framework was completely ineffective, giving no selectivity at all (entry 5). The analogous iminophosphorane **3a**[5c] was also found to give poor selectivity (entries 6 and 7). The reaction did not proceed without the phosphazide (entry 8).

Table 3. Catalysis using other bases.[a]

Entry	Base	Yield[b]	*ee*[c]
1	**1a**	95	88
2	**1b**	82	88
3	**1c**	99	34
4	**1d**	82	89
5	**2**	3	1
6	**3a**	68	12
7	**3a**[d]	92	2
8	–	0	–

[a] Unless otherwise noted, reactions were carried out at −40 °C for 48 h in the presence of *trans*-chalcone (1.0 equiv), dimethyl malonate (2.0 equiv), base (10 mol %), and $LiClO_4$ (10 mol %). [b] Isolated yield of **4a**. [c] Determined by chiral HPLC. [d] Without $LiClO_4$.

Next, we tested the conjugate addition of various kinds of nucleophiles to chalcone derivatives (Table 4). The reactions of various dialkyl malonates proceeded in excellent yields with good selectivities (entries 1–3). Di-*tert*-butyl malonate could also be employed when Li*O*t*Bu was used in place of $LiClO_4$ (entry 4). Interestingly, the reaction did not proceed with more acidic 1,3-dicarbonyl compounds such as ketoesters, diketones, or cyclic esters (data not shown). Bisnitrile gave the addition product but with no enantioselectivity (entry 5). Using dimethyl malonate as the nucleophile, the scope of the reaction was investigated in terms of the electrophiles that could be applied (entries 6–14). Chalcone derivatives with both electron-donating (Me, OMe) and electron-withdrawing (Cl, F, NO_2) substituents on their aryl moieties could be successfully used as substrates without altering the enantioselectivity (entries 6–11). Reaction with coordinative substrates, such as those bearing 2-furyl and 2-pyridyl substituents, proceeded without any decrease in selectivity (entries 12 and 13). Substitution of the aryl ring at the α-position was also tolerated (entry 14).

To shed light on the possible structure of the catalyst and the catalytic mechanism, we first examined the ^1H and ^{31}P NMR spectra of complexes of **1a** and $LiClO_4$ in various stoichiometric ratios (Figure 2). The chemical shift of the benzylic proton changed when 0.5 equiv of $LiClO_4$ was added to **1a** (Figure 2a), implying the formation of a **1a**:Li chemical species with a molar ratio of 2:1 when less than 1.0 equiv of lithium salt was added. In both the ^1H and ^{31}P NMR spectra, saturation was observed when 1.0 equiv of $LiClO_4$ was added to **1a**, indicating 1:1 stoichiometric complexation of $LiClO_4$ and **1a**.

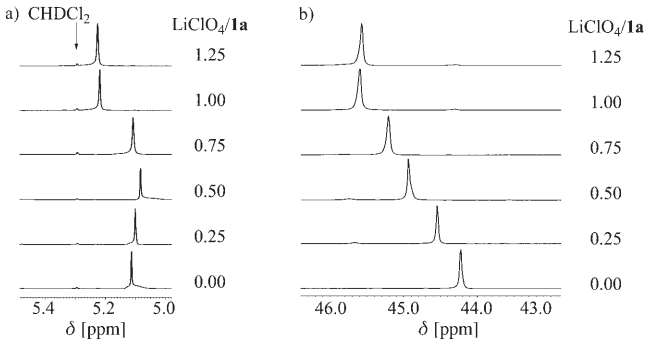
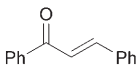
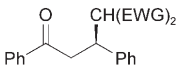
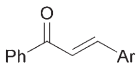
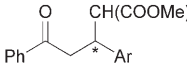
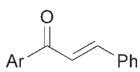
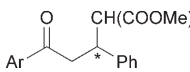


Figure 2. a) ^1H NMR titration of **1a** with $LiClO_4$ in CD_2Cl_2 (benzylic region) at 25 °C. b) ^{31}P NMR titration of **1a** with $LiClO_4$ in CD_2Cl_2 at 25 °C.

Table 4. Bisphosphazide-catalyzed conjugate additions of nucleophilic enols to enones.[a]

Entry	Substrate	Product	Yield[b]	*ee*[c]
				
1		EWG = COOEt (**4b**)	>99	79 (*S*)
2		= COO*i*Pr (**4c**)	96	84 (*S*)
3		= COOBn (**4d**)	85	80 (*S*)
4[d]		= COO*t*Bu (**4e**)	94	71
5		= CN (**4f**)	>99	1
				
6	Ar = 4-MeC_6H_4	Ar = 4-MeC_6H_4 (**4g**)	66	87
7	= 4-$MeOC_6H_4$	= 4-$MeOC_6H_4$ (**4h**)	84	88
8	= 4-ClC_6H_4	= 4-ClC_6H_4 (**4i**)	86	84
9	= 4-FC_6H_4	= 4-FC_6H_4 (**4j**)	54	85
10	= 4-$NO_2C_6H_4$	= 4-$NO_2C_6H_4$ (**4k**)	>99	88
11	= 2-ClC_6H_4	= 2-ClC_6H_4 (**4l**)	>99	89
12	= 2-furyl	= 2-furyl (**4m**)	41	88
13	= 2-pyridyl	= 2-pyridyl (**4n**)	98	88
				
14	Ar = 4-ClC_6H_4	Ar = 4-ClC_6H_4 (**4o**)	92	83

[a] Unless otherwise noted, reactions were carried out at −40 °C for 48 h in the presence of *trans*-chalcone (1.0 equiv), dimethyl malonate (2.0 equiv), **1a** (10 mol %), and $LiClO_4$ (10 mol %). [b] Isolated yield. [c] Determined by chiral HPLC. [d] Li*O*t*Bu (10 mol %) was used instead of $LiClO_4$.

We next investigated the dependence of the yield and *ee* on the **1a**/$LiClO_4$ ratio (Figure 3). In accordance with the ^{31}P and ^1H NMR findings, the selectivity was highest when a 1:1 ratio of **1a** and $LiClO_4$ was used. A loading of $LiClO_4$ of less than 1.0 equiv with respect to **1a** resulted in a significant decrease in the yield.

Combined with the above NMR findings, this result could be interpreted as follows. In the presence of 0.5 equiv of Li salt, **1a** forms an inactive 2:1 **1a**/$LiClO_4$ species, whereas when 1.0 equiv of Li salt is added to **1a**, an active and stereoselective 1:1 **1a**/$LiClO_4$ complex is generated (Scheme 3).

Because the bisphosphazide had to be added to achieve product formation, it presumably deprotonates the dialkyl

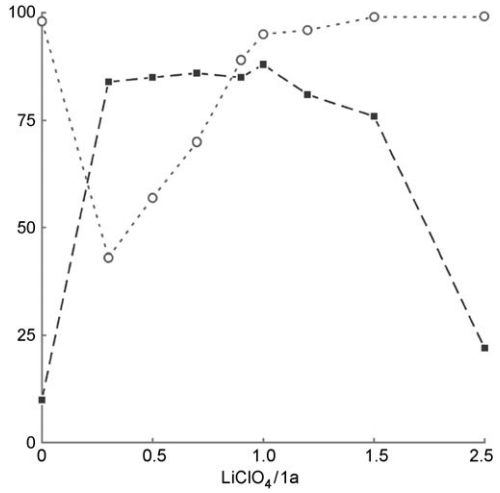
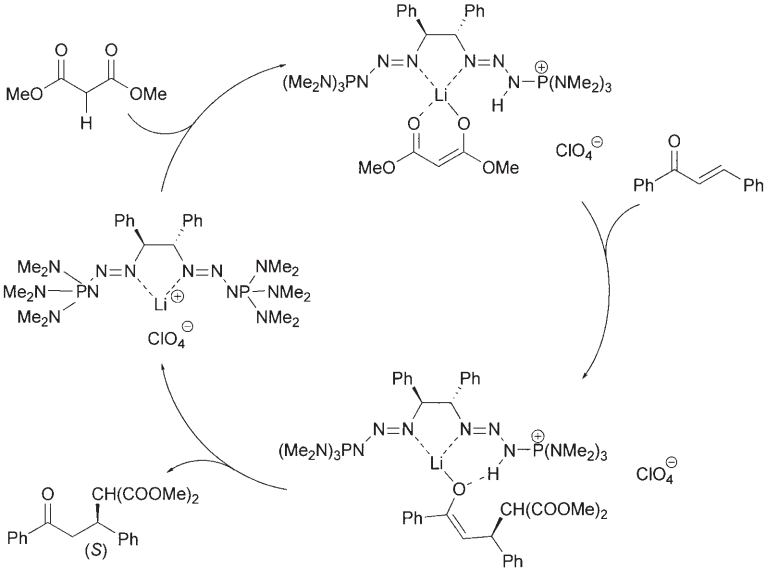


Figure 3. Dependence of yield (○) and *ee* (■) on the $LiClO_4$/**1a** ratio. The reaction was carried out at −40 °C for 48 h in the presence of 1.0 equiv of chalcone, 2.0 equiv of dimethyl malonate, 10 mol % of **1a**, and 0, 3, 5, 7, 9, 10, 12, 15, or 20 mol % of $LiClO_4$.

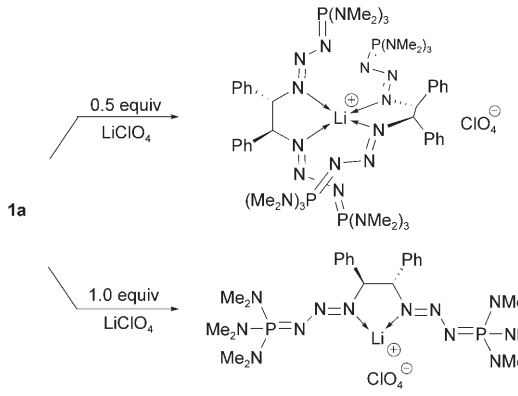
malonate to form an enolate nucleophile. The reaction with the bisphosphazide catalyst alone gave poor enantioselectivity; equimolar addition of the lithium salt to the bisphosphazide was necessary for high enantioselectivity. This result suggests that the 1:1 **1a**/$LiClO_4$ complex (Scheme 3) is involved in the catalytic cycle. The fact that relatively acidic lithium salts gave better enantioselectivities further implies that the lithium cation complexed with the bisphosphazide plays a Lewis acidic role in the efficient stereoselective reaction. Although details of the reaction mechanism of this enantioselective conjugate addition remain unclear, a possible catalytic cycle is shown in Scheme 4.

In the reaction mixture, the 1:1 **1a**/$LiClO_4$ complex readily reacts with the dialkyl malonate to form a chiral enolate species and protonated phosphazide. The chiral enolate species reacts with the chalcone, possibly through acid-base dual activation,[11b] whereby the protonated phosphazenium center serves as an acid for the electrophilic activation of the enone, and the bisphosphazide serves as a base for the lithium enolate (Scheme 5a). A putative transition state is presented in Scheme 5b.

Overall, the bisphosphazide serves as a dual base, as a Lewis base for the lithium enolate, and as a Brønsted base for the deprotonation of the dialkyl malonate to form a chiral nucleophile. The resulting protonated bisphosphazide may thus serve as an acid-base dual activator. Further crystallographic, spectroscopic, and computational studies aimed at elucidating the origin of the selectivity are underway.



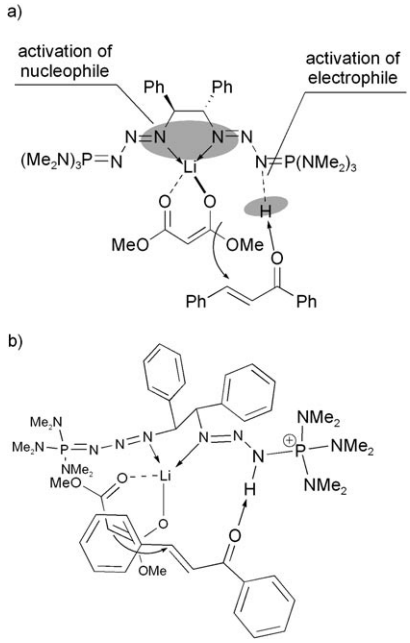
Scheme 4. Proposed catalytic cycle.



Scheme 3. Possible species formed from **1a** and $LiClO_4$ (0.5 or 1.0 equiv).

Conclusion

A novel chiral bisphosphazide (**1a**) has been developed for the enantioselective catalytic 1,4-addition of malonates to acyclic enones using controlled complexation with lithium salts. Spectroscopic studies on the stoichiometry of the complex formed between the bisphosphazide and the lithium salt suggest the formation of a 1:1 species as the active and selective catalyst. Both the bisphosphazide and the lithium salt proved necessary for obtaining high catalytic activity and enantioselectivity, suggesting that the bisphosphazide serves as a dual base, that is, both as a Lewis base and as a Brønsted base. We suggest that the phosphazide moiety represents a promising dual basic functionality for stereoselec-



Scheme 5. a) Acid-base dual activation in a putative transition state. b) 3D representation of the putative transition state.

tive catalytic transformations. Further studies to extend the scope of the reaction and to improve the enantioselectivity, employing phosphazides with other chiral frameworks, are underway.

Experimental Section

Reactions were carried out under Ar atmosphere using dry solvents. Melting points (m.p.) were determined with a Yazawa micro melting point apparatus and are uncorrected. Infrared (IR) data were recorded on a SensIR ATR (attenuated total reflectance) FT-IR spectrometer. The spectra were each acquired in 32 scans at a resolution of four using the ReactIR 2.20 software system. Absorbance frequencies are reported in cm^{-1}. NMR data were recorded on either a JEOL AL400 spectrometer (395.75 MHz for ^1H, 99.50 MHz for ^{13}C) or a JEOL ECA600 spectrometer (600.172 MHz for ^1H, 150.907 for ^{13}C, 242.956 MHz for ^{31}P). Chemical shifts are expressed in δ values (parts per million, ppm), and coupling constants are expressed in Hertz (Hz). ^1H NMR spectra were referenced to tetramethylsilane as an internal standard or to a solvent signal ($CHCl_3$ in $CDCl_3$: 7.26 ppm, $CHDCl_2$ in CD_2Cl_2: 5.32 ppm, or C_6HD_5 in C_6D_6: 7.15 ppm). ^{13}C NMR spectra were referenced to tetramethylsilane as an internal standard or to a solvent signal ($CDCl_3$: 77.0 ppm, CD_2Cl_2: 53.8 ppm, or C_6D_6: 128.0 ppm). ^{31}P NMR spectra were referenced to external 85% H_3PO_4 in D_2O. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet, dt = double triplet, td = triple doublet, dq = double quartet, brs = broad singlet. Low- and high-resolution mass spectra (LRMS and HRMS) were obtained on JEOL JMS-DX303 and JMS-700 spectrometers, respectively, at the Mass Spectrometry Resource, Graduate School of Pharmaceutical Sciences, Tohoku University. Analytical HPLC was performed using Daicel Chiralpak AD. The samples of **4** subjected to HPLC were the purified products from column chromatography on silica gel.

Materials: Unless otherwise noted, materials were purchased from Tokyo Kasei Co., Aldrich Inc., or other commercial suppliers, and were used after appropriate purification (distillation or recrystallization). (*R*,*R*)-(+)-Hydrobenzoin was obtained from Kanto Chemical Co. Ltd. Flash column chromatographies were performed on Kanto silica gel 60N (spherical, neutral, 70–230 mesh).

Representative procedure for the preparation of catalysts: **(1*S*,2*S*)-Bis-[tris(dimethylamino)phosphazido]-1,2-diphenylethane (1a)**: **For use as a reagent**: Under Ar atmosphere, tris(dimethylamino)phosphine (325.9 mg, 2.0 mmol) was added to a solution of (+)-(1*S*,2*S*)-1,2-diphenylethane-1,2-diazide (264.3 mg, 1.00 mmol) in benzene (1.5 mL) at room temperature. After stirring the mixture for 20 h at the same temperature, further dry benzene (1.0 mL) was added to give a 0.20 M solution of **1a**. Quantitative conversion was confirmed by ^{31}P NMR analysis.

For analysis: Under Ar atmosphere, tris(dimethylamino)phosphine (325.9 mg, 2.00 mmol) was added to a solution of (+)-(1*S*,2*S*)-1,2-diphenylethane-1,2-diazide (263.0 mg, 0.995 mmol) in benzene (1.5 mL) in a 20 mL Schlenk tube at room temperature. The mixture was stirred for 21 h at the same temperature. It was then concentrated under reduced pressure and **1a** was isolated in a glove box (517.0 mg, 88%). The product was recrystallized from toluene/hexane as colorless needles. M.p. 96–97 °C; ^1H NMR (400 MHz, CD_2Cl_2): $\delta = 2.61$ (d, $J = 9.2$ Hz, 36H), 5.13 (s, 2H), 6.95–7.12 (m, 6H), 7.15–7.25 ppm (m, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, CD_2Cl_2): $\delta = 36.8$, 78.7, 125.4, 127.0, 128.7, 141.9 ppm; $^{31}P\{^1H\}$ NMR (243 MHz, CD_2Cl_2): $\delta = 41.5$ ppm (s); ^{31}P NMR (243 MHz, CD_2Cl_2): $\delta = 41.5$ ppm (septet, $J = 9.2$ Hz); IR (neat): $\tilde{\nu} = 2917$, 2890, 2846, 2806, 1451, 1293, 1109, 974, 737, 699 cm^{-1}; LRMS (FAB): *m*/*z*: 591 $[M+1]^+$; HRMS: *m*/*z*: calcd for $C_{26}H_{49}N_{12}P_2$: 591.3678; found: 591.3683.

(1*S*,2*S*)-Bis[tris(diethylamino)phosphazido]-1,2-diphenylethane (1b): Yellow oil; ^1H NMR (400 MHz, $CDCl_3$/TMS): $\delta = 1.00$ (t, $J = 7.1$ Hz, 36H), 2.98–3.09 (m, 24H), 5.30 (s, 2H), 6.92–7.05 (m, 6H), 7.15–7.22 ppm (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, C_6D_6/TMS): $\delta = 13.8$ (d, $J = 2.5$ Hz), 39.7 (d, $J = 3.3$ Hz), 80.8, 125.8, 127.6, 129.8, 143.7 ppm; $^{31}P\{^1H\}$ NMR (243 MHz, CD_2Cl_2): $\delta = 42.4$ ppm (s); ^{31}P NMR (243 MHz, CD_2Cl_2): $\delta =$ 42.5 ppm (nonet, $J = 9.7$ Hz); IR (neat): $\tilde{\nu} = 2917$, 2890, 2846, 2806, 1451, 1293, 1109, 974, 737, 699 cm^{-1}; LRMS (FAB): *m*/*z*: 760 $[M+1]^+$; HRMS: *m*/*z*: calcd for $C_{38}H_{73}N_{12}P_2$: 759.5556; found: 759.5552.

(1*S*,2*S*)-Bis[tris(dibutylamino)phosphazido]-1,2-diphenylethane (1c): Yellow oil; ^1H NMR (400 MHz, $CDCl_3$/TMS): $\delta = 0.95$ (t, $J = 7.2$ Hz, 36H), 1.16–1.34 (m, 24H), 1.54–1.67 (m, 24H), 3.00–3.14 (m, 24H), 5.61 (s, 2H), 6.94–7.01 (m, 2H), 7.06–7.27 (m, 6H), 7.52–7.56 ppm (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, C_6D_6/TMS): $\delta = 14.3$, 20.9, 31.1 (d, $J = 2.5$ Hz), 46.5 (d, $J = 2.5$ Hz), 81.0, 125.8, 127.6, 129.8, 144.1 ppm; $^{31}P\{^1H\}$ NMR (243 MHz, CD_2Cl_2): $\delta = 41.9$ ppm (s); ^{31}P NMR (243 MHz, CD_2Cl_2): $\delta =$ 41.9 ppm (nonet, $J = 9.9$ Hz); IR (neat): $\tilde{\nu} = 2958$, 2933, 2873, 1617, 1455, 1329, 1160, 1034, 926, 812, 698, 677 cm^{-1}; LRMS (FAB): *m*/*z*: 1096 $[M+1]^+$; HRMS: *m*/*z*: calcd for $C_{62}H_{121}N_{12}P_2$: 1095.9312; found: 1095.9342.

(1*S*,2*S*)-Bis[tris(pyrrolidino)phosphazido]-1,2-diphenylethane (1d): Yellow oil; ^1H NMR (400 MHz, $CDCl_3$/TMS): $\delta = 1.67$–1.75 (m, 24H), 3.10–3.20 (m, 24H), 5.26 (s, 2H), 6.93–7.06 (m, 6H), 7.15–7.21 ppm (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS): $\delta = 26.5$ (d, $J = 6.4$ Hz), 47.2 (d, $J = 2.5$ Hz), 81.6, 125.9, 127.7, 129.7, 143.6 ppm; $^{31}P\{^1H\}$ NMR (243 MHz, $CDCl_3$): $\delta = 31.5$ ppm (s); ^{31}P NMR (243 MHz, $CDCl_3$): $\delta =$ 31.3–31.6 ppm (m); IR (neat): $\tilde{\nu} = 2958$, 2865, 2850, 1445, 1204, 1111, 1069, 1009, 754, 697 cm^{-1}; LRMS (FAB): *m*/*z*: 748 $[M+1]^+$; HRMS: *m*/*z*: calcd for $C_{38}H_{61}N_{12}P_2$: 747.4617; found: 747.4630.

Representative procedure for the conjugate addition of dialkyl malonates to chalcones: **2-(3-Oxo-1,3-diphenyl-propyl)-malonic acid dimethyl ester (4a)**:[12a,13b,14] A solution of *trans*-chalcone (104.1 mg, 0.50 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise to a mixture of $LiClO_4$ (5.3 mg, 0.05 mmol), **1a** (0.25 mL, 0.20 M in benzene, 0.05 mmol), and dimethyl malonate (132.1 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) at −40 °C under an Ar atmosphere. The reaction mixture was stirred for 48 h, then quenched with saturated NH_4Cl solution and extracted with AcOEt. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated using a rotary evaporator to afford the crude product. Purification by column chromatography on silica gel (0→15% AcOEt in hexane) afforded **4a**. The product was recrystallized from Et_2O/hexane as colorless needles. M.p. 84–85 °C; $[\alpha]_D^{29} = +24.20$ ($c = 1.01$ in $CHCl_3$) (lit.:[14] $[\alpha]_D^{25} = +17.7$ ($c = 1.2$ in $CHCl_3$)); ^1H NMR (400 MHz, $CDCl_3$/TMS): $\delta = 3.48$ (dd, $J =$

16.8, 8.8 Hz, 1H), 3.51 (s, 3H), 3.55 (dd, J=16.8, 5.2 Hz, 1H), 3.73 (s, 3H), 3.86 (d, J=9.6 Hz, 1H), 4.19 (dt, J=9.2, 5.2 Hz, 1H), 7.14–7.29 (m, 5H), 7.42 (t, J=7.6 Hz, 2H), 7.53 (tt, J=7.6, 1.6 Hz, 1H), 7.87–7.92 ppm (m, 2H); IR (neat): $\tilde{\nu}$=2954, 2844, 1727, 1681, 1432, 1233, 1158, 1025, 747, 687 cm^{-1}; LRMS (EI): m/z: 340 [M^+]; HRMS: m/z: calcd for $C_{20}H_{20}O_5$: 340.1311; found: 340.1307; elemental analysis calcd (%) for $C_{20}H_{20}O_5$: C 70.57, H 5.92; found: C 70.45, H 5.97; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=28.4 min (minor enantiomer), t_R=35.2 min (major enantiomer).

2-(3-Oxo-1,3-diphenyl-propyl)-malonic acid diethyl ester (4b):[13b,14] Recrystallized from Et_2O/hexane, colorless needles; m.p. 73–74 °C; $[\alpha]_D^{31}$=+22.50 (c=1.01 in $CHCl_3$) (lit.:[14] $[\alpha]_D^{25}$=+17.5 (c=0.8 in $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ=1.01 (t, J=7.1 Hz, 3H), 1.24 (t, J=7.1 Hz, 3H), 3.45 (dd, J=16.6, 9.0 Hz, 1H), 3.54 (dd, J=16.6, 4.6 Hz, 1H), 3.82 (d, J=9.8 Hz, 1H), 3.95 (q, J=7.1 Hz, 2H), 4.13–4.24 (m, 3H), 7.13–7.30 (m, 5H), 7.38–7.55 (m, 3H), 7.86–7.92 ppm (m, 2H); IR (neat): $\tilde{\nu}$=2983, 1721, 1679, 1293, 1239, 1167, 1030, 745, 700, 687 cm^{-1}; LRMS (EI): m/z: 368 [M^+]; HRMS: m/z: calcd for $C_{22}H_{24}O_5$: 368.1624; found: 368.1612; elemental analysis calcd (%) for $C_{22}H_{24}O_5$: C 71.72, H 6.57; found: C 71.72, H 6.42; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=22.4 min (minor enantiomer), t_R=39.1 min (major enantiomer).

2-(3-Oxo-1,3-diphenyl-propyl)-malonic acid diisopropyl ester (4c):[13b,14] Recrystallized from Et_2O/hexane, colorless needles; m.p. 88–89 °C; $[\alpha]_D^{31}$=+15.80 (c=1.01 in $CHCl_3$) (lit.:[14] $[\alpha]_D^{25}$=+21.3 (c=0.7 in $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ=0.97 (d, J=6.3 Hz, 3H), 1.04 (d, J=6.3 Hz, 3H), 1.24 (d, J=6.3 Hz, 6H), 3.43 (dd, J=16.5, 9.5 Hz, 1H), 3.53 (dd, J=16.5, 4.1 Hz, 1H), 4.15 (dt, J=9.7, 4.1 Hz, 1H), 4.79 (sept, J=6.3 Hz, 1H), 5.07 (sept, J=6.3 Hz, 1H), 7.12–7.28 (m, 5H), 7.38–7.44 (m, 2H), 7.49–7.54 (m, 1H), 7.86–7.91 ppm (m, 2H); IR (neat): $\tilde{\nu}$=2983, 2935, 1721, 1683, 1281, 1235, 1104, 750, 702, 691 cm^{-1}; LRMS (EI): m/z: 396 [M^+]; HRMS: m/z: calcd for $C_{24}H_{28}O_5$: 396.1937; found: 396.1928; elemental analysis calcd (%) for $C_{24}H_{28}O_5$: C 72.70, H 7.12; found: C 72.58, H 7.09; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=12.88 min (minor enantiomer), t_R=24.82 min (major enantiomer).

2-(3-Oxo-1,3-diphenyl-propyl)-malonic acid dibenzyl ester (4d):[13b,14] Recrystallized from Et_2O/hexane, colorless needles; m.p. 106–107 °C; $[\alpha]_D^{31}$=+16.20 (c=1.01 in $CHCl_3$) (lit.:[14] $[\alpha]_D^{25}$=+18.4 (c=1.0 in $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ=3.49 (d, J=6.4 Hz, 2H), 3.94 (d, J=9.5 Hz, 1H), 4.18–4.25 (m, 1H), 4.90 (s, 2H), 5.11 (d, J=12.2 Hz, 1H), 5.16 (d, J=12.2 Hz, 1H), 7.04–7.42 (m, 17H), 7.48–7.53 (m, 1H), 7.77–7.82 ppm (m, 2H); IR (neat): $\tilde{\nu}$=3346, 3031, 1733, 1681, 1229, 1152, 1011, 965, 741, 699 cm^{-1}; LRMS (EI): m/z: 492 [M^+]; HRMS: m/z: calcd for $C_{32}H_{28}O_5$: 492.1937; found: 492.1957; elemental analysis calcd (%) for $C_{32}H_{28}O_5$: C 78.03, H 5.73; found: C 77.99, H 5.86; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=38.86 min (minor enantiomer), t_R=73.36 min (major enantiomer).

2-(3-Oxo-1,3-diphenylpropyl)-malonic acid di-*tert*-butyl ester (4e):[16] Recrystallized from Et_2O/hexane, colorless needles; m.p. 117–118 °C; $[\alpha]_D^{31}$=+8.57 (c=0.75 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ=1.19 (s, 9H), 1.46 (s, 9H), 3.39 (dd, J=16.4, 9.9 Hz, 1H), 3.51 (dd, J=16.4, 3.9 Hz, 1H), 3.64 (d, J=10.1 Hz, 1H), 4.07 (dt, J=10.0, 3.9 Hz, 1H), 7.11–7.17 (m, 1H), 7.19–7.27 (m, 4H), 7.38–7.44 (m, 2H), 7.49–7.54 (m, 1H), 7.87–7.91 ppm (m, 2H); IR (neat): $\tilde{\nu}$=2979, 1735, 1719, 1683, 1368, 1246, 1138, 741, 700, 687 cm^{-1}; LRMS (EI): m/z: 368 [M−56]$^+$; HRMS: m/z: calcd for $C_{26}H_{32}O_5$: 368.1624; found: 368.1635; elemental analysis calcd (%) for $C_{26}H_{32}O_5$: C 73.56, H 7.60; found: C 73.57, H 7.57; HPLC (Daicel Chiralpak AD, isopropanol/hexane 5:95, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=12.15 min (minor enantiomer), t_R=41.15 min (major enantiomer).

2-(3-Oxo-1,3-diphenylpropyl)-malononitrile (4f):[13b,14] Recrystallized from CH_2Cl_2/hexane, colorless needles; m.p. 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ=3.65 (dd, J=18.6, 5.3 Hz, 1H), 3.72 (d, J=18.6, 8.5 Hz, 1H), 3.96 (dt, J=8.5, 5.1 Hz, 1H), 4.66 (d, J=5.1 Hz, 1H), 7.35–7.54 (m, 7H), 7.60–7.66 (m, 1H), 7.96–8.00 ppm (m, 2H); IR (neat): $\tilde{\nu}$=2919, 2900, 2256, 1681, 1449, 1233, 762, 748, 700, 690 cm^{-1}; LRMS (EI): m/z: 274 [M^+]; HRMS: m/z: calcd for $C_{18}H_{14}N_2O$: 274.1106; found: 274.1099; elemental analysis calcd (%) for $C_{18}H_{14}N_2O$: C 78.81, H 5.14, N 10.21; found: C 78.81, H 5.34, N 10.07; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=20.10 min (major enantiomer), t_R=27.67 min (minor enantiomer).

2-[3-Oxo-3-phenyl-1-(4-tolyl)-propyl]-malonic acid dimethyl ester (4g):[17] Recrystallized from Et_2O/hexane, colorless needles; m.p. 75–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ=2.26 (s, 3H), 3.40–3.57 (m, 5H), 3.72 (s, 3H), 3.83 (d, J=9.5 Hz, 1H), 4.15 (dt, J=9.1, 5.1 Hz, 1H), 7.04 (d, J=8.3 Hz, 2H), 7.13 (d, J=8.3 Hz, 2H), 7.39–7.46 (m, 2H), 7.50–7.56 (m, 1H), 7.88–7.93 ppm (m, 2H); IR (neat): $\tilde{\nu}$=2954, 1729, 1681, 1233, 1208, 1194, 1160, 1025, 820, 688 cm^{-1}; LRMS (EI): m/z: 354 [M^+]; HRMS: m/z: calcd for $C_{21}H_{22}O_5$: 354.1467; found: 354.1478; elemental analysis calcd (%) for $C_{21}H_{22}O_5$: C 71.17, H 6.26; found: C 70.71, H 6.10; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=24.0 min (minor enantiomer), t_R=31.6 min (major enantiomer).

2-[1-(4-Methoxyphenyl)-3-oxo-3-phenylpropyl]-malonic acid dimethyl ester (4h):[17,18] Recrystallized from Et_2O/hexane, colorless needles; m.p. 81–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ=3.43 (dd, J=16.6, 8.9 Hz, 1H), 3.52 (dd, J=16.6, 4.8 Hz, 1H), 3.52 (s, 3H), 3.73 (s, 3H), 3.74 (s, 3H), 3.82 (d, J=9.4 Hz, 1H), 4.10–4.18 (m, 1H), 6.75–6.81 (m, 2H), 7.14–7.20 (m, 2H), 7.40–7.46 (m, 2H), 7.50–7.56 (m, 1H), 7.88–7.92 ppm (m, 2H); IR (neat): $\tilde{\nu}$=2954, 1729, 1681, 1515, 1231, 1179, 1158, 1025, 754, 729, 686 cm^{-1}; LRMS (EI): m/z: 370 [M^+]; HRMS: m/z: calcd for $C_{21}H_{22}O_6$: 370.1416; found: 370.1413; elemental analysis calcd (%) for $C_{21}H_{22}O_6$: C 68.10, H 5.99; found: C 67.63, H 6.00; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=51.76 min (minor enantiomer), t_R=75.66 min (major enantiomer).

2-[1-(4-Chlorophenyl)-3-oxo-3-phenylpropyl]-malonic acid dimethyl ester (4i): Recrystallized from Et_2O/hexane, colorless needles; m.p. 87–88 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ=3.45 (dd, J=17.0, 8.9 Hz, 1H), 3.53 (dd, J=17.0, 4.8 Hz, 1H), 3.53 (s, 3H), 3.74 (s, 3H), 3.82 (d, J=9.2 Hz, 1H), 4.17 (dt, J=9.2, 4.8 Hz, 1H), 7.18–7.26 (m, 4H), 7.40–7.47 (m, 2H), 7.52–7.58 (m, 1H), 7.87–7.92 ppm (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS): δ=40.1, 42.1, 52.5, 52.7, 57.0, 128.0, 128.6, 128.6, 129.5, 133.0, 133.2, 136.6, 139.0, 168.0, 168.5, 197.2 ppm; IR (neat): $\tilde{\nu}$=2956, 1729, 1681, 1235, 1162, 1023, 827, 752, 685, 665 cm^{-1}; LRMS (EI): m/z: 374 [M^+]; HRMS: m/z: calcd for $C_{20}H_{19}O_5Cl$: 374.0921; found: 374.0904; elemental analysis calcd (%) for $C_{20}H_{19}O_5Cl$: C 64.09, H 5.11; found: C 63.97, H 5.11; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=32.86 min (minor enantiomer), t_R=52.03 min (major enantiomer).

2-[1-(4-Fluorophenyl)-3-oxo-3-phenylpropyl]-malonic acid dimethyl ester (4j): Recrystallized from Et_2O/hexane, colorless needles; m.p. 85–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ=3.44 (dd, J=16.9, 8.9 Hz, 1H), 3.40–3.57 (m, 5H), 3.72 (s, 3H), 3.83 (d, J=9.5 Hz, 1H), 4.15 (dt, J=9.1, 5.1 Hz, 1H), 7.04 (d, J=8.3 Hz, 2H), 7.13 (d, J=8.3 Hz, 2H), 7.39–7.46 (m, 2H), 7.50–7.56 (m, 1H), 7.88–7.93 ppm (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS): δ=40.1, 42.3, 52.4, 52.7, 57.2, 115.3 (d, J=21.3 Hz), 128.1, 128.6, 129.7 (d, J=7.8 Hz), 129.8, 133.1 (d, J=3.3 Hz), 136.7, 161.8 (d, J=245.8 Hz), 168.0, 168.6, 197.3 ppm; IR (neat): $\tilde{\nu}$=2954, 1729, 1681, 1233, 1208, 1194, 1160, 1025, 820, 688 cm^{-1}; LRMS (EI): m/z: 354 [M^+]; HRMS: m/z: calcd for $C_{21}H_{22}O_5$: 354.1467; found: 354.1478; elemental analysis calcd (%) for $C_{21}H_{22}O_5$: C 67.03, H 5.34; found: C 66.74, H 5.37; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=24.0 min (minor enantiomer), t_R=31.6 min (major enantiomer).

2-[1-(4-Nitrophenyl)-3-oxo-3-phenylpropyl]-malonic acid dimethyl ester (4k):[18] Recrystallized from Et_2O/hexane, colorless needles; m.p. 77–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ=3.50–3.63 (m, 5H), 3.75 (s, 3H), 3.89 (d, J=9.1 Hz, 1H), 4.31 (dt, J=8.9, 5.1 Hz, 1H), 7.41–7.50 (m, 4H), 7.53–7.79 (m, 1H), 7.86–7.92 (m, 2H), 8.10–8.16 ppm (m, 2H); IR (neat): $\tilde{\nu}$=2954, 1731, 1684, 1517, 1345, 1256, 1152, 856, 748, 688 cm^{-1}; LRMS (EI): m/z: 385 [M^+]; HRMS: m/z: calcd for $C_{20}H_{19}NO_7$: 385.1162; found: 385.1154; elemental analysis calcd (%) for $C_{20}H_{19}NO_7$: C 62.33, H 4.97, N 3.63; found: C 62.08, H 5.05, N 3.40; HPLC (Daicel Chiralpak AD, isopropanol/hexane 30:70, flow rate 1.0 mL min^{-1}, λ=254 nm): t_R=29.3 min (minor enantiomer), t_R=59.7 min (major enantiomer).

2-[1-(2-Chlorophenyl)-3-oxo-3-phenylpropyl]-malonic acid dimethyl ester (4l):[18] Pale-yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$/TMS): $\delta = 3.57$–3.76 (m, 8H), 4.10 (d, $J = 8.4$ Hz, 1H), 4.67 (dt, $J = 8.6$, 4.8 Hz, 1H), 7.10–7.19 (m, 2H), 7.27–7.37 (m, 2H), 7.40–7.46 (m, 2H), 7.51–7.57 (m, 1H), 7.90–7.95 ppm (m, 2H); IR (neat): $\tilde{\nu} = 2954$, 1733, 1684, 1436, 1227, 1154, 1021, 750, 690 cm^{-1}; LRMS (EI): m/z: 374 [M^+]; HRMS: m/z: calcd for $C_{20}H_{19}ClO_5$: 374.0921; found: 374.0929; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, $\lambda = 254$ nm): $t_R =$ 17.5 min (minor enantiomer), $t_R = 19.6$ min (major enantiomer).

2-(1-Furan-2-yl-3-oxo-3-phenylpropyl)-malonic acid dimethyl ester (4m): Recrystallized from Et_2O/hexane, colorless crystals; m.p. 40–41 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS): $\delta = 3.47$ (dd, $J = 17.1$, 4.8 Hz, 1H), 3.58 (dd, $J = 17.1$, 8.5 Hz, 1H), 3.64 (s, 3H), 3.73 (s, 3H), 4.30–4.37 (m, 1H), 6.09–6.13 (m, 1H), 6.21–6.24 (m, 1H), 7.25–7.28 (m, 1H), 7.42–7.48 (m, 2H), 7.51–7.58 (m, 1H), 7.92–7.98 ppm (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS): $\delta = 10.9$, 34.3, 39.6, 52.6, 54.8, 107.0, 110.3, 128.1, 128.6, 133.2, 136.6, 141.7, 153.4, 168.2, 168.4, 197.2 ppm; IR (neat): $\tilde{\nu} = 2960$, 2921, 1744, 1735, 1683, 1256, 1158, 1146, 1007, 760, 727, 686 cm^{-1}; LRMS (EI): m/z: 330 [M^+]; HRMS: m/z: calcd for $C_{18}H_{18}O_6$: 330.1103; found: 330.1103; elemental analysis calcd (%) for $C_{18}H_{18}O_6$: C 65.45, H 5.49; found: C 65.56, H 5.62; HPLC (Daicel Chiralcel OD, isopropanol/hexane 5:95, flow rate 1.0 mL min^{-1}, $\lambda = 254$ nm): $t_R = 15.80$ min (minor enantiomer), $t_R = 16.92$ min (major enantiomer).

2-[3-Oxo-3-phenyl-1-(pyridin-2-yl)-propyl]-malonic acid dimethyl ester (4n): Recrystallized from Et_2O/hexane, colorless crystals; m.p. 74–75 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS): $\delta = 3.42$ (dd, $J = 17.6$, 3.9 Hz, 1H), 3.54 (s, 3H), 3.74 (s, 3H), 3.79 (dd, $J = 17.6$, 9.5 Hz, 1H), 4.11 (d, $J =$ 9.6 Hz, 1H), 4.32 (dt, $J = 9.5$, 3.9 Hz, 1H), 7.05–7.09 (m, 1H), 7.34–7.45 (m, 3H), 7.49–7.60 (m, 2H), 7.88–7.93 (m, 2H), 8.44–8.47 ppm (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS): $\delta = 41.5$, 41.7, 52.3, 52.6, 55.8, 121.9, 124.8, 128.1, 128.5, 133.0, 136.2, 136.7, 149.0, 160.3, 168.4, 169.0, 197.7 ppm; LRMS (EI): m/z: 341 [M^+]; HRMS: m/z: calcd for $C_{19}H_{19}NO_5$: 341.1263; found: 341.1254; elemental analysis calcd (%) for $C_{19}H_{19}NO_5$: C 66.85, H 5.61, N 4.10; found: C 66.82, H 5.84, N 3.85; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, $\lambda = 254$ nm): $t_R = 30.6$ min (minor enantiomer), $t_R = 52.2$ min (major enantiomer).

2-[3-(4-Chlorophenyl)-3-oxo-1-phenylpropyl]-malonic acid dimethyl ester (4o): Recrystallized from Et_2O/hexane, colorless needles; m.p. 71–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS): $\delta = 3.42$ (dd, $J = 16.9$, 8.9 Hz, 1H), 3.51 (s, 3H), 3.53 (dd, $J = 16.9$, 4.8 Hz, 1H), 3.73 (s, 3H), 3.84 (d, $J =$ 9.2 Hz, 1H), 4.16 (dt, $J = 9.2$, 4.8 Hz, 1H), 7.15–7.28 (m, 5H), 7.36–7.43 (m, 2H), 7.81–7.86 ppm (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS): $\delta = 40.8$, 42.3, 52.4, 52.6, 57.2, 127.3, 128.0, 128.5, 128.9, 129.5, 135.1, 139.5, 140.2, 168.1, 168.7, 196.4 ppm; IR (neat): $\tilde{\nu} = 2954$, 1727, 1681, 1235, 1210, 1154, 1090, 1025, 825, 702 cm^{-1}; LRMS (EI): m/z: 374 [M^+]; HRMS: m/z: calcd for $C_{20}H_{19}O_5Cl$: 374.0921; found: 374.0931; elemental analysis calcd (%) for $C_{20}H_{19}O_5Cl$: C 64.09, H 5.11; found: C 63.92, H 5.07; HPLC (Daicel Chiralpak AD, isopropanol/hexane 10:90, flow rate 1.0 mL min^{-1}, $\lambda = 254$ nm): $t_R = 36.86$ min (minor enantiomer), $t_R =$ 51.84 min (major enantiomer).

NMR spectroscopic analyses for the titration of 1a with $LiClO_4$: ^{1}H and ^{31}P NMR spectra were obtained on a JEOL ECA600 spectrometer (600.172 MHz for ^{1}H, 242.956 MHz for ^{31}P). Unless otherwise noted, spectra were recorded from approximately 0.10 M solutions of the samples in CD_2Cl_2 at 25 °C. ^{1}H NMR spectra were referenced to a solvent signal ($CHDCl_2$, 5.32 ppm). ^{31}P NMR spectra were referenced to external 85% H_3PO_4 in D_2O.

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[1] a) R. Schwesinger, H. Schlemper, *Angew. Chem.* **1987**, *99*, 1212–1214; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 1167–1169; b) R. Schwesinger, H. Schlemper, C. Hasenfratz, F. Willaredt, T. Dambacher, T. Breuer, C. Ottaway, M. Fletschinger, F. Boele, J. Fritz, D. Putzas, J. W. Rotter, F. G. Bordwell, A. V. Satish, G.-Z. Ji, E.-M. Peters, K. Peters, H. G. von Schnering, L. Walz, *Liebigs Ann.* **1996**, 1055–1081.

[2] a) H. R. Allcock, "*Chemistry and Applications of Polyphosphazenes*", Wiley, Hoboken, **2003**; b) J. Paulsdorf, N. Kaskhedikar, M. Burjanadze, S. Obeidi, N. A. Stolwijk, D. Wilmer, H.-D. Wiemhofer, *Chem. Mater.* **2006**, *18*, 1281–1288; c) J. X. Zhang, L. Y. Qiu, Y. Jin, K. J. Zhu, *Macromolecules* **2006**, *39*, 451–455; d) K. Huynh, A. J. Lough, I. Manners, *J. Am. Chem. Soc.* **2006**, *128*, 14002–14003.

[3] a) F. Palacios, E. Herran, C. Alonso, G. Rubiales, B. Lecea, M. Ayerbe, F. P. Cossio, *J. Org. Chem.* **2006**, *71*, 6020–6030; b) A. Solladie-Cavallo, M. Roje, R. Welter, V. Sunjic, *J. Org. Chem.* **2004**, *69*, 1409–1412.

[4] a) M. O'Donnell, F. Delgado, C. Hostettler, R. Schwesinger, *Tetrahedron Lett.* **1998**, *39*, 8775–8778; b) M. Caldarelli, J. Habermann, S. V. Ley, *J. Chem. Soc. Perkin Trans. 1* **1999**, 107–110; c) G. A. Kraus, N. Zhang, J. G. Verkade, M. Nagarajan, P. B. Kisanga, *Org. Lett.* **2000**, *2*, 2409–2410; d) A. Clark, D. Patel, M. J. Broadhurst, *Tetrahedron Lett.* **2003**, *44*, 7763–7765; e) T. Imahori, Y. Kondo, *J. Am. Chem. Soc.* **2003**, *125*, 8082–8083; f) T. Imahori, C. Hori, Y. Kondo, *Adv. Synth. Catal.* **2004**, *346*, 1090–1092; g) D. Bensa, T. Constantieux, J. Rodriguez, *Synthesis* **2004**, 923–927; h) V. Raab, E. Gauchenova, A. Merkoulov, K. Harms, J. Sundermeyer, B. Kovacevic, Z. B. Maksic, *J. Am. Chem. Soc.* **2005**, *127*, 15738–15743; i) D. Uraguchi, S. Sakaki, T. Ooi, *J. Am. Chem. Soc.* **2007**, *129*, 12392–12393.

[5] a) M. T. Reetz, E. Bohres, *Chem. Commun.* **1998**, 935–936; b) J. M. Brunel, O. Legrand, S. Reymond, G. Buono, *J. Am. Chem. Soc.* **1999**, *121*, 5807–5808; c) M. Sauthier, J. Fornies-Camer, L. Toupet, R. Reau, *Organometallics* **2000**, *19*, 553–562; d) U. Köhn, M. Schulz, A. Schramm, W. Günther, H. Görls, S. Schenk, E. Anders, *Eur. J. Org. Chem.* **2006**, 4128–4134; e) M. Ueno, A. E. H. Wheatley, Y. Kondo, *Chem. Commun.* **2006**, 3549–3550.

[6] a) M. Ueno, C. Hori, K. Suzawa, M. Ebisawa, Y. Kondo, *Eur. J. Org. Chem.* **2005**, 1965–1968; b) K. Kobayashi, M. Ueno, Y. Kondo, *Chem. Commun.* **2006**, 3128–3130; c) K. Suzawa, M. Ueno, A. E. H. Wheatley, Y. Kondo, *Chem. Commun.* **2006**, 4850–4852; d) M. Ueno, M. Yonemoto, M. Hashimoto, A. E. H. Wheatley, H. Naka, Y. Kondo, *Chem. Commun.* **2007**, 2264–2266.

[7] Synthesis of chiral phosphazenes: a) X. Liu, P. Ilankumaran, I. A. Guzei, J. G. Verkade, *J. Org. Chem.* **2000**, *65*, 701–706; b) P. Ilankumaran, G. Zhang, J. G. Verkade, *Heteroat. Chem.* **2000**, *11*, 251–253; c) U. Köhn, M. Schulz, A. Schramm, W. Günther, S. Schenk, E. Anders, *Eur. J. Org. Chem.* **2006**, 4128–4134.

[8] a) H. Staudinger, *Helv. Chim. Acta* **1919**, *2*, 635–646; reviews: b) Y. G. Gololobov, I. N. Zhmurova, L. F. Nasukhin, *Tetrahedron* **1981**, *37*, 437–472; c) Yu. G. Gololobov, I. N. Zhmurova, L. F. Kasukhin, *Tetrahedron* **1992**, *48*, 1353–1406; recent theoretical studies: d) W. Q. Tian, Y. A. Wang, *J. Org. Chem.* **2004**, *69*, 4299–4308; e) W. Q. Tian, Y. A. Wang, *J. Chem. Theory Comput.* **2005**, *1*, 353–362.

[9] a) J. G. Verkade, P. B. Kisanga, *Tetrahedron* **2003**, *59*, 7819–7858, and references therein; b) X. Liu, N. Thirupathi, I. A. Guzei, J. G. Verkade, *Inorg. Chem.* **2004**, *43*, 7431–7440; c) Ch. Venkat Reddy, J. G. Verkade, *J. Org. Chem.* **2007**, *72*, 3093–3096; d) Ch. Venkat Reddy, B. M. Fetterly, J. G. Verkade, *Energy Fuels* **2007**, *21*, 2466–2472.

[10] Conventional preparation of phosphazene bases generally requires deprotonation of phosphonium salts and purification of the product. The use of an in situ deprotonated phosphonium salt as a catalyst has also recently been reported, see ref. [4i].

[11] a) *Comprehensive Asymmetric Catalysis* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**; b) J.-A. Ma, D. Cahard, *Angew. Chem.* **2004**, *116*, 4666–4683; *Angew. Chem. Int.*

Ed. **2004**, *43*, 4566–4583; c) H. Li, Y. Wang, L. Tang, L. Deng, *J. Am. Chem. Soc.* **2004**, *126*, 9906–9907; d) H. Huang, E. N. Jacobsen, *J. Am. Chem. Soc.* **2006**, *128*, 7170–7171; e) S. B. Tsogoeva, *Eur. J. Org. Chem.* **2007**, 1701–1716.

[12] a) H. Sasai, T. Arai, Y. Satow, K. N. Houk, M. Shibasaki, *J. Am. Chem. Soc.* **1995**, *117*, 6194–6198; b) M. Shibasaki, N. Yoshikawa, *Chem. Rev.* **2002**, *102*, 2187–2210.

[13] a) T. Ooi, K. Maruoka, *Acc. Chem. Res.* **2004**, *37*, 526–533; b) T. Ooi, D. Ohara, K. Fukumoto, K. Maruoka, *Org. Lett.* **2005**, *7*, 3195–3197.

[14] J. Wang, H. Li, L. Zu, W. Jiang, H. Xie, W. Duan, W. Wang, *J. Am. Chem. Soc.* **2006**, *128*, 12652–12653.

[15] D. Pini, A. Iuliano, C. Rosini, P. Salvadori, *Synthesis* **1990**, 1023–1024.

[16] N. End, L. Macko, M. Zehnder, A. Pfaltz, *Chem. Eur. J.* **1998**, *4*, 818–824.

[17] B. M. Choudary, M. Lakshmi Kantam, B. Kavita, Ch. Venkat Reddy, F. Figueras, *Tetrahedron* **2000**, *56*, 9357–9364.

[18] W. Ye, J. Xu, C.-T. Tan, C.-H. Tan, *Tetrahedron Lett.* **2005**, *46*, 6875–6878.

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