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Diastereoselective Three-Component Synthesis of β-Amino Carbonyl Compounds Using Diazo Compounds, Boranes, and Acyl Imines under Catalyst-Free Conditions

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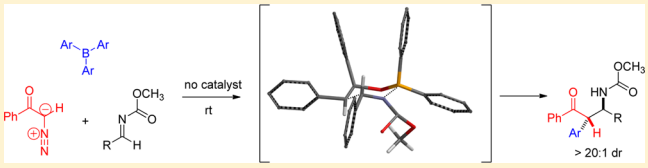
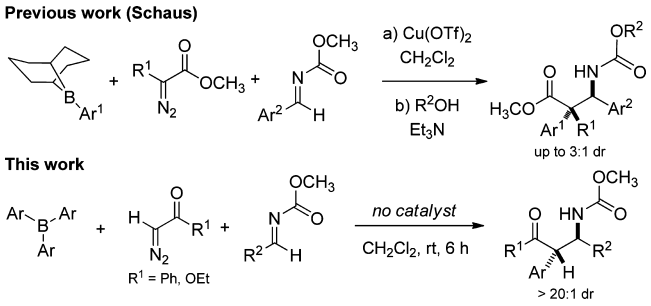
Supporting Information

ABSTRACT: Diazo compounds, boranes, and acyl imines undergo a three-component Mannich condensation reaction under catalyst-free conditions to give the anti β-amino carbonyl compounds in high diastereoselectivity. The reaction tolerates a variety of functional groups, and an asymmetric variant was achieved using the (−)-phenylmenthol as chiral auxiliary in good yield and selectivity. These β-amino carbonyl compounds are valuable intermediates, which can be transformed to many potential bioactive molecules.



The development of new multicomponent coupling processes for complex organic molecules synthesis has attracted intense interest in recent years.[1] Multicomponent coupling processes provide novel and complex molecules with multiple stereocenters in a single reaction vessel, which becomes highly desirable in modern organic and medicinal chemistry.[2] Boronates and boranes can form new C−C bond via carbon migration in the Petasis multicomponent reaction, as well as in other organic transformations.[3] A far less studied methodology is the Hooz three-component reaction between alkylboranes, diazo compounds, and a suitable electrophile (Scheme 1).[4]

Scheme 1. Three-Component Mannich Reactions



Mukaiyama and co-workers applied the Hooz three-component reaction to an aldol-type reaction of benzaldehyde.[5] Miranda developed a two-step synthesis of 1,3-diketones and β-ketoesters taking advantage of Hooz's multicomponent strategy, which was also employed by Wang and Barluenga.[6] Dilman introduced boronic ester as the boron source in the three-component amino ester synthesis.[7] Herein, we report a highly diastereoselective multicomponent Mannich reaction involving boranes, diazo compounds, and acyl imines, which can be used to synthesize β-(protected amino) carbonyl compounds under catalyst-free conditions. These β-amino carbonyl compounds are valuable intermediates, which can be further transformed to biologically active molecules.[8]

A central challenge in the development of the desired sequential process is the reaction between the diazo substrate and organoboron derivative to form a boron enolate.[9] If a single enolate isomer is formed, then the subsequent Mannich-type reaction should proceed via a closed-transition state in a highly diastereoselective manner. In a recent report by Schaus and Luan, copper catalysts were used to develop a unique Mannich−Hooz reaction in excellent yields but substrate-dependent diastereoselectivity.[10] It is reasoned that the use of the Lewis acidic copper in the reaction could erode diastereoselectivity through a number of pathways.[11] Through the use of catalyst-free conditions, we hoped to expand the scope of the reaction and concomitantly improve the diastereoselectivity.[12]

Our investigation began with a screen of phenyl-substituted organoboronic acids and esters as potential partners in the reaction with α-diazoacetophenone **2a** and phenyl methyl carbamate imine **3a**. When using boronic acid **1a** we observed none of the desired product, due to undesired aziridine **5** formation (Table 1, entry 1).[13] Diethoxy phenyl boronate **1b** was unable to participate in this reaction under uncatalyzed conditions (Table 1, entry 2).[14] Use of electron-withdrawing trifluoroethoxy groups on the boronates failed to increase the yield (Table 1, entry 3). A similar low yield was also observed with triphenylboroxine **1d** (Table 1, entry 4).

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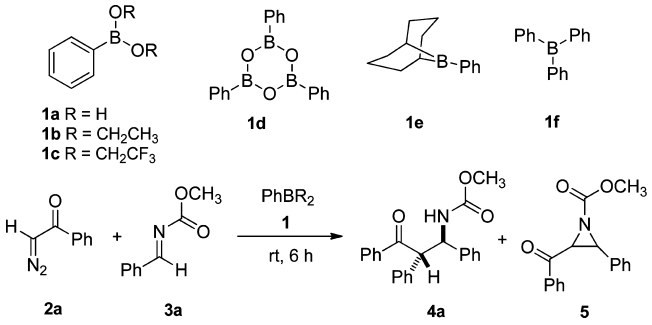
Table 1. Optimization of the Three-Component Mannich Reaction[a]



entry	boron	solvent	yield of **4a**[b] (%)	yield of **5**[b] (%)	dr
1	**1a**	CH_2Cl_2		76	
2	**1b**	CH_2Cl_2	8		
3	**1c**	CH_2Cl_2	10		
4	**1d**	CH_2Cl_2	11		
5	**1e**	CH_2Cl_2		11	
6	**1f**	CH_2Cl_2	**85**		>20:1
7	**1f**	$PhCH_3$	66		>20:1
8	**1f**	THF	52		>20:1

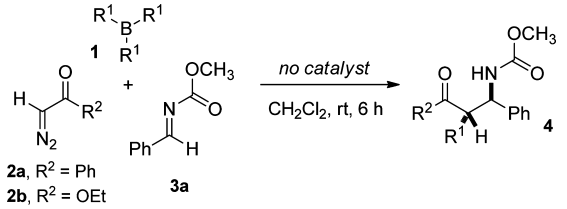
[a]Reactions were run with 1.2 mmol of boron **1**, 1.2 mmol of diazo ketone **2**, and 1.0 mmol of acyl imine **3a** in CH_2Cl_2 (0.2 M) for 6 h under Ar, followed by flash chromatography on silica gel. [b]Isolated yield.

A survey of *B*-phenyl-9-borabicyclo[3.3.1]nonane **1e** resulted in low yield, due to an undesired alkyl migration (*B*-Ph-9-BBN **1e**, Table 1, entry 5). This *B*-alkyl bond migration is similar to what Hooz and Schaus observed in previous multicomponent Mannich reactions.[10,15] To increase the specificity of the migration, the use of triphenyl borane **1f** was applied to the reaction and gave the 85% yield under catalyst-free conditions (Table 1, entry 6). Furthermore, the product is formed in excellent diastereoselectivity (>20:1 dr) as the *anti* diastereomer.[16] A solvent screen showed polar, noncoordinating CH_2Cl_2 gave the best results among other common organic solvents (Table 1, entries 6–8). The optimized reaction conditions utilized a slight excess of borane **1f** and diazoacetophenone **2a** relative to the imine **3a** in CH_2Cl_2 to afford the desired compound in 85% yield.

With the optimal reaction conditions of commercially available triphenyl borane **1f** in hand (Table 2, entry 1), we extended this multicomponent methodology to other boranes and diazocarbonyl compounds. Both electron-rich and electron-deficient triaryl boranes **1b** and **1c** were suitably reactived (Table 2, entries 2 and 3), providing the desired products **4b** and **4c** in 81% and 86% yield, respectively. Ethyl diazoacetate **2b** was also compatible with our system, thereby accessing a *β*-amino acid-type scaffold (4d, Table 2, entry 4).[17] In each instance, the newly formed products were formed in >20:1 dr.

A selection of carbamate-protected imines was tested in the three-component reaction under the optimal conditions. The cinnamaldehyde-derived imine **3a** participated well, providing the 1, 2-addition product in 85% yield at room temperature (Table 3, entry 1). Electron-deficient imines **3b,c** were transformed to the desired three-component adducts in good yields (Table 3, entries 2 and 3). Electron-rich imines **3d,e** worked smoothly, albeit under prolonged reaction time (Table 3, entries 4 and 5). 2-Naphthyl imine **3f** also gave good yield

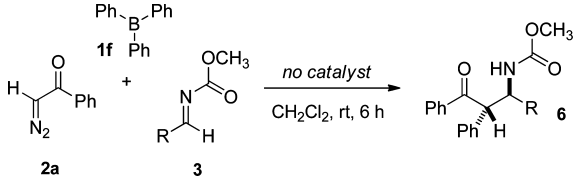
Table 2. Evaluation of Borane and Diazo Components in the Mannich Reaction[a]



entry	R^1	diazo (R^2)	product	yield[b] (%)
1	Ph	**2a** (Ph)	**4a**	85
2	4-$CH_3OC_6H_4$	**2a** (Ph)	**4b**	81
3	4-FC_6H_4	**2a** (Ph)	**4c**	86
4	Ph	**2b** (OEt)	**4d**	84

[a]Reactions were run with 1.2 mmol of triaryl borane **1**, 1.2 mmol of diazo compound **2**, and 1.0 mmol of imine **3a** in CH_2Cl_2 for 6 h under Ar, followed by flash chromatography on silica gel. [b]Isolated yield.

Table 3. Three-Component Mannich Reactions of Various Imines[a]



entry	R	imine	product	yield[b] (%)
1	(*E*)-PhCH=CH	**3a**	**6a**	85
2[c]	4-BrC_6H_4	**3b**	**6b**	82
3	3-FC_6H_4	**3c**	**6c**	89
4[d]	3-$CH_3OC_6H_4$	**3d**	**6d**	81
5[d]	3,4-$(OCH_2O)C_6H_3$	**3e**	**6e**	81
6	2-naphthyl	**3f**	**6f**	84

[a]Reactions were run with 1.2 mmol of triphenyl borane **1a**, 1.2 mmol *α*-diazoacetophenone **2a**, and 1.0 mmol imine **3** in CH_2Cl_2 for 6 h under Ar, followed by flash chromatography on silica gel. [b]Isolated yield. [c]10% DMF as the cosolvent. [d]12 h.

with nearly exclusive anti selectivity in this three-component process (Table 3, entry 6).

An asymmetric variant of multicomponent Mannich reaction involving borane and diazo compounds was developed using chiral diazoesters (Scheme 2).[10,18] Several chiral diazo esters have been evaluated. Among those investigated, the commercially available (−)-phenylmenthol, which can also be synthesized inexpensively over four steps,[19] affords the chiral **8** in over 98:2 dr and 85% yield.[20]

Our proposed mechanism begins with the negatively polarized *α*-carbon of diazo compound **2** attacking electrophilic boron **1f**. The extrusion of nitrogen and migration of phenyl selectively affords boron (*E*)-enolate **9** (Figure 1). Previous reports of boron enolate formation have shown the preferential formation of the (*E*)-conformer, often with high selectivity.[10,21] In agreement with these observations, calculations of the ground-state energies of (*E*)-**9** and (*Z*)-**9** show the (*E*)-isomer to be favorable by 2.9 kcal/mol.[22] Next, the Mannich addition to acyl imine **3** occurs through Zimmerman–Traxler transition state to give the *anti* *β*-keto amine.

To minimize 1,3-diaxial interactions in between the bulky aromatic groups in the transition state, we propose an (*E*)/(*Z*)-imine isomerization occurs to form the more reactive (*Z*)-

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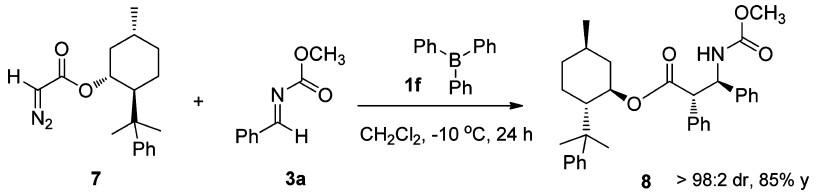
Scheme 2. Asymmetric Multicomponent Mannich Reaction Using a Chiral Diazoester



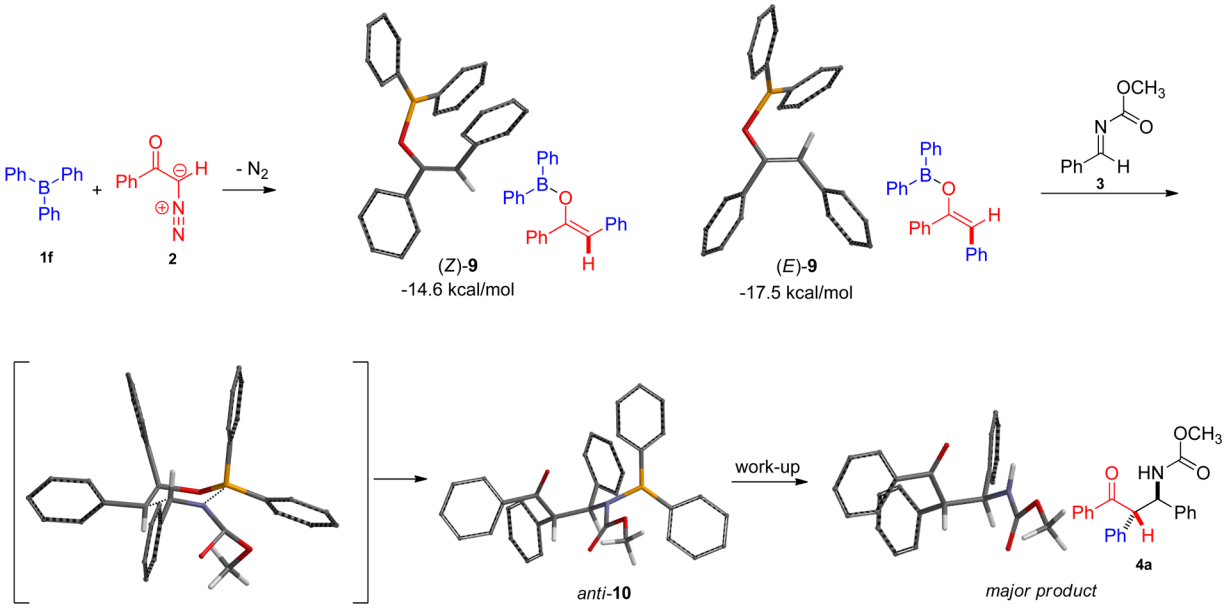


Figure 1. Proposed mechanism for three-component Mannich reaction (hydrogen atoms are partially omitted for clarity).

imine. The thermodynamically less favored (*Z*)-conformer has been previously proposed as an intermediate by Corey and Schaus in reactions with sterically congested closed-transition states.[23]

In conclusion, we have developed a diastereoselective three-component reaction under catalyst-free conditions. This reaction demonstrates a new multicomponent approach to access various β-amino esters. The three-component reaction was conducted asymmetrically employing the (−)-phenylmenthol ester in good diastereoselectivity and yield. A transition-state calculation was performed employing B3LYP/6-31G** set in order to reveal the mechanism of the multicomponent reaction.

EXPERIMENTAL SECTION

General Procedure Used for the Preparation of Amido Ketone under Catalyst-Free Conditions (Table 1). A 10 mL round-bottom flask was charged with a stir bar under Ar (overdried). Triphenylborane (290 mg, 1 mmol) in 2.5 mL of dichloromethane was added to the flask, which was then stirred at room temperature, and a solution of the α-diazoacetophenone (175 mg, 1.2 mmol) and phenyl methyl carbamate imine (163 mg, 1.2 mmol) in 0.5 mL of dichloromethane was added dropwise over 5 min. The solution was further stirred at room temperature for 12 h followed by flash chromatography over silica gel (elution with 98:2, hexanes/EtOAc) to afford the amido ketone **4a** as a colorless oil (305 mg, 85% yield).

*Methyl (3-Oxo-1,2,3-triphenylpropyl)carbamate (Table 2, **4a**).* The crude mixture was purified through flash column chromatography with elution by 98:2−95:5 hexanes/EtOAc. Yield: 305 mg, 85%, liquid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27−6.95 (m, 13H), 6.76 (t, J = 14.5 Hz, 2H), 5.98 (s, 1H), 5.42 (t, J = 15.7 Hz, 1H), 4.86 (d, J = 12.3 Hz, 1H), 3.60 (s, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 193.2, 155.5, 140.6, 139.0, 138.6, 136.4, 130.9, 130.3, 129.9, 129.3, 128.4, 128.1, 128.1, 127. 8, 127.7, 127.6, 127.3, 66.8, 57.9, 52.5. IR (thin film, cm^{-1}): 3421, 1718, 1653, 1486, 1453, 1242, 744, 711. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{23}H_{21}NO_3Na$ 382.1419, found 382.1438.

*Methyl (2-(4-Methoxyphenyl)-3-oxo-1,3-diphenylpropyl)-carbamate (Table 2, **4b**).* The crude mixture was purified through flash column chromatography with elution by 98:2−95:5 hexanes/EtOAc. Yield: 334 mg, 81%, liquid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44−6.97 (m, 11H), 6.96−6.79 (m, 2H), 6.73 (d, J = 8.9 Hz, 1H), 6.07 (s, 1H), 5.45−5.38 (m, 1H), 5.07−4.91 (m, 1H), 3.91−3.57 (s*2, 6H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 195.2, 158.5, 155.5, 139.1, 136.5, 132.5, 131.6, 131.1, 130.1, 129.8, 129.2, 128.5, 128.1, 128.0, 127.9, 127. 7, 127.6, 127.2, 112.9, 77.4, 77.1, 76.8, 66.8, 65.3, 55.2, 52.4. IR (thin film, cm^{-1}): 3421, 2951, 2837, 1712, 1648, 1511, 1495, 1297, 1252, 1186, 1034, 831, 700. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{24}H_{23}NO_4Na$ 412.1525, found 412.1514.

*Methyl (2-(4-Fluorophenyl)-3-oxo-1,3-diphenylpropyl)carbamate (Table 2, **4c**).* The crude mixture was purified through flash column chromatography with elution by 98:2−95:5 hexanes/EtOAc. Yield: 324 mg, 86%, liquid. IR (thin film, cm^{-1}): 3432, 3051, 1715, 1654, 1506, 1310, 1227, 1167, 1083, 838, 755, 599. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{23}H_{20}NO_3FNa$ 400.1325, found 400.1333]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27−6.77 (m, 12H), 6.73 (m, 2H), 5.92 (m, 1H), 5.35−5.26 (m, 1H), 4.83 (d, J = 12.3 Hz, 1H), 3.66−3.44 (s, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz): δ 193.1, 162.4, 160.6, 155.5, 140.6, 138.9, 136.4, 132.2, 131.8, 130.0, 129.8, 129.2, 128.5, 128.2, 128.1, 128.1, 128.0, 127.8, 127.8, 127.7, 127.4, 114.5, 114.3, 66. 9, 65.4, 52.6.

*Ethyl 3-((Methoxycarbonyl)amino)-2,3-diphenylpropanoate (Table 2, **4d**).* The crude mixture was purified through flash column chromatography with elution by 98:2−95:5 hexanes/EtOAc. Yield: 275 mg, 84%, liquid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.45−7.02 (m, 8H), 6.84 (d, J = 7.0 Hz, 2H), 6.06 (d, J = 10.1 Hz, 1H), 5.92 (d, J = 10.0 Hz, 1H), 4.24−3.89 (m, 2H), 3.72 (s, 3H), 1.16 (t, J = 7.1 Hz,

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3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 192.6, 154.3, 140.7, 139.2, 130.4, 129.9, 129.2, 127. 8, 127.6, 127.5, 127.2, 65.9, 61.0, 57.7, 52.4, 14.6. IR (thin film, cm^{-1}): 3432, 1718, 1652, 1496, 1456, 1229, 754, 699. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{19}H_{21}NO_4Na$ 350.1386, found 350.1381.

*Methyl ((E)-5-Oxo-1,4,5-triphenylpent-1-en-3-yl)carbamate (Table 3, **6a**).* The crude mixture was purified through flash column chromatography with elution by 98:2−95:5 hexanes/EtOAc. Yield: 327 mg, 85%, liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56−7.09 (m, 15H), 6.38 (t, J = 21.0 Hz, 1H), 6.08 (dd, J = 15.8, 6.2 Hz, 1H), 5.90−5.73 (m, 1H), 5.20−5.02 (m, 1H), 3.70 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.1, 155.6, 139.6, 136.6, 136.4, 132.6, 130.1, 129.6, 128.6, 128.5, 128.1, 128.0, 127.9, 127.7, 127.5, 127.4, 126.8, 126.5, 66. 9, 65.2, 52.6. IR (thin film, cm^{-1}): 3424, 3041, 2941, 1721, 1643, 1493, 1442, 1307, 1229, 1042, 967, 743, 692. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{25}H_{23}NO_3Na$ 408.1576, found 408.1567.

*Methyl (1-(4-Bromophenyl)-3-oxo-2,3-diphenylpropyl)-carbamate (Table 3, **6b**).* The crude mixture was purified through flash column chromatography with elution by 98:2−95:5 hexanes/EtOAc. Yield: 358 mg, 82%, liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−6.87 (m, 12H), 6.61 (d, J = 8.4 Hz, 2H), 5.93 (s, 1H), 5.46 (d, J = 12.3 Hz, 1H), 4.86 (d, J = 12.3 Hz, 1H), 3.58 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 191.9, 154.4, 139.1, 137.2, 135.3, 130.0, 129.6, 129.1, 128.7, 127.4, 127.1, 127.0, 126.9, 126.7, 126.4, 120.7, 65.9, 64.6, 51.5. IR (thin film, cm^{-1}): 3425, 1725, 1671, 1501, 1303, 1218, 1054, 1021, 742, 699. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{23}H_{20}NO_3BrNa$ 460.0524, found 460.0517.

*Methyl (1-(3-Fluorophenyl)-3-oxo-2,3-diphenylpropyl)carbamate (Table 3, **6c**).* The crude mixture was purified through flash column chromatography with elution by 98:2−95:5 hexanes/EtOAc. Yield: 336 mg, 89%, liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−6.66 (m, 12H), 6.49 (dd, J = 23.2, 9.0 Hz, 2H), 5.96 (m, 2H), 5.43−5.34 (m, 1H), 4.87 (d, 1H), 3.55 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.3, 155.4, 143.9, 143.7, 141.3, 141.1, 140.5, 139.1, 138.8, 130.1, 129.9, 129.2, 129.0, 128.3, 128.0, 127.7, 127.7, 127.6, 127.3, 127.0, 126.9, 125.1, 119.9, 119.9, 67.0, 65.8, 47.1. IR (thin film, cm^{-1}): 3428, 2924, 1715, 1613, 1486, 1459, 1301, 1229, 1166, 1046, 733, 698. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{23}H_{20}NO_3FNa$ 400.1325, found 400.1329.

*Methyl (1-(3-Methoxyphenyl)-3-oxo-2,3-diphenylpropyl)-carbamate (Table 3, **6d**).* The crude mixture was purified through flash column chromatography with elution by 98:2−95:5 hexanes/EtOAc. Yield: 315 mg, 81%, liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−6.88 (m, 10H), 6.67 (dd, J = 8.2, 1.9 Hz, 1H), 6.41 (d, J = 7.8 Hz, 1H), 6.27−6.10 (m, 1H), 5.95 (t, J = 24.5 Hz, 1H), 5.42 (d, 11.3 Hz, 1H), 4.88 (d, J = 12.3 Hz, 1H), 3.63 (s, 3H), 3.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.1, 158.7, 155.5, 140.6, 140.5, 138.6, 136.4, 130.1, 129.9, 128.6, 128. 5, 128.1, 128.0, 127.8, 127.6, 127.6, 127.2, 121.4, 114.5, 113.7, 66.8, 65.8, 55.0, 52.4. IR (thin film, cm^{-1}): 3435, 3063, 2954, 1721, 1642, 1487, 1455, 1224, 1176, 1048, 913, 731, 702. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{24}H_{23}NO_4Na$ 412.1525, found 412.1538.

*Methyl (1-(Benzo[d][1,3]dioxol-5-yl)-3-oxo-2,3-diphenylpropyl)-carbamate (Table 3, **6e**).* The crude mixture was purified through flash column chromatography with elution by 98:2−95:5 hexanes/EtOAc. Yield: 327 mg, 81%, liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−6.89 (m, 11H), 6.49 (d, J = 8.1 Hz, 1H), 6.27 (s, 1H), 6.19 (dd, J = 8.1, 1.5 Hz, 1H), 5.84 (m, 3H), 5.38 (t, J = 13.7 Hz, 1H), 4.88 (d, J = 12.3 Hz, 1H), 3.63 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 191.2, 155.4, 146.9, 146.9, 140.5, 138.6, 136.4, 132.8, 130.2, 129.8, 128.5, 128.1, 127.9, 127.8, 127.7, 127.6, 127.3, 123.0, 109.5, 107.4, 100.9, 66.8, 65.8, 52.5. IR (thin film, cm^{-1}): 3431, 1721, 1657, 1493, 1429, 1311, 1221, 1035, 914, 738, 694. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{24}H_{21}NO_5Na$ 426.1317, found 426.1322.

*Methyl (1-(Naphthalen-2-yl)-3-oxo-2,3-diphenylpropyl)-carbamate (Table 3, **6f**).* The crude mixture was purified through flash column chromatography with elution by 98:2−95:5 hexanes/EtOAc. Yield: 344 mg, 84%, liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−6.98 (m, 16H), 6.92 (d, J = 8.5 Hz, 1H), 6.29 (d, J = 9.9 Hz, 1H), 6.13 (s, 1H), 5.12 (t, J = 22.3 Hz, 1H), 4.99 (t, J = 13.9 Hz, 1H), 3.89−3.50 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.6, 155.5, 140.6, 138.7, 136.5, 136.4, 132.9, 132.6, 130.5, 129.9, 128.9, 128.6, 128.2, 128.2, 128.1, 127.9, 127.9, 127.5, 127.4, 127.1, 126.9, 126.2, 125.9, 66.9, 66.0, 52.5. IR (thin film, cm^{-1}): 3429, 3051, 1719, 1657, 1491, 1454, 1311, 1217, 1178, 1059, 741, 698. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{27}H_{23}NO_3Na$ 432.1576, found 432.1568].

General Procedure Used for Asymmetric Three-Component Reaction Using Chiral Auxiliaries (Figure 1). A 10 mL round-bottom flask was charged with a stir bar under Ar (overdried). To the flask was added triphenylborane (290 mg, 1 mmol) in 2.5 mL of dichloromethane. The mixture was then stirred at room temperature, and a solution of the phenylmenthyl diazoacetate (360 mg, 1.2 mmol) and phenyl methyl carbamate imine (163 mg, 1.2 mmol) in 0.5 mL of dichloromethane was added dropwise over 5 min. The solution was cooled to −10 °C for 24 h followed by flash chromatography over silica gel (elution with 98:2−95:5 hexanes/EtOAc) to afford the chiral carbamate **8** as a colorless oil (436 mg, 85% yield, > 98:2 dr).

*(2S,3R)-(1R,2S,5R)-5-Methyl-2-(2-phenylpropan-2-yl)cyclohexyl 3-((Methoxycarbonyl)amino)-2,3-diphenylpropanoate (**8**).* Yield: 436 mg, 85%, liquid. dr: > 98:2. $[\alpha]^{23}_D$ = −32.8 (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57−6.96 (m, 13H), 6.76 (d, J = 7.3, 2H), 6.03 (s, 1H), 5.56 (d, 1H), 5.25(d, 1H), 4.71 (m, 1H), 4.04 (s, 3H), 1.86 (s, 1H), 1.67 (s, 1H), 1.55 (s, 1H), 1.42 (s, 2H), 1.26 (s, 4H), 0.99 (d, J = 9.5, 6H), 0.74 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 156.0, 138.9, 137.6, 137.3, 132.1, 130.5, 129.7, 129.0, 128.5, 128.3, 128.0, 127.8, 127.6, 127.2, 126.9, 125.9, 125.5, 125.4, 122.8, 78.8, 57.4, 56.2, 51. 8, 50.5, 41.0, 40.1, 34.4, 31.3, 30.3, 27.7, 23.7, 22.7, 21.7. IR (thin film, cm^{-1}): 3037, 2943, 1719, 1605, 1487, 1231, 758, 704. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{33}H_{39}NO_4Na^+$ 536.2777, found 536.2780.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

DFT calculations and copies of ^{1}H and ^{13}C NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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