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Enantioselective Amine-Catalyzed [4 + 2] Annulations of Allene Ketones and 2,3-Dioxopyrrolidine Derivatives: Synthesis of 4*H*-Pyran Derivatives

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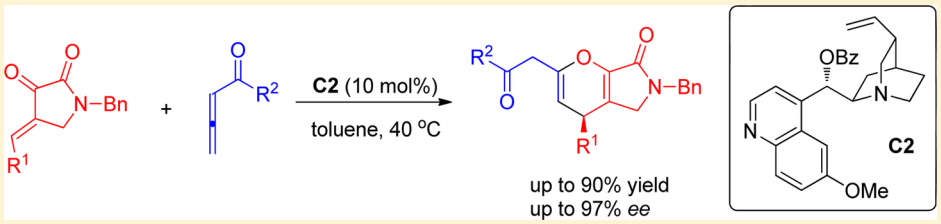
Supporting Information



ABSTRACT: An efficient cinchona alkaloid-derived amine catalyzed asymmetric [4 + 2] cycloaddition is successfully developed. 4*H*-Pyran fused pyrrolin-2-one products are readily obtained in moderate to high yields with good enantioselectivites by employing allene ketones and 2,3-dioxopyrrolidine derivatives as substrates.

The pyran structural motif has been widely found in a large number of bioactive molecules and natural products,[1] and pyran derivatives also serve as versatile intermediates in organic synthesis.[2] Therefore, many methods have been developed to afford substituted pyrans.[3] Pyrrolin-2-one skeletons are featured in plenty of natural products and biologically active drug candidates.[4] Compounds which contain the pyrrolin-2-one moiety often have significant pharmaceutical activities.[5]

Over the past decades, the phosphine promoted cycloaddition reaction of allenoate has achieved remarkable progress.[6] Since Lu disclosed the first phosphine-catalyzed [3 + 2] cyclization between allenoates and electron-deficient olefins in 1995,[7] corresponding synthetic methods have been developed rapidly in the past few years. However, it is noteworthy that the development of the amine-catalyzed cycloaddition reaction was still slow paced. As Lewis base promoters, tertiary amines could smoothly catalyze the reactions of allenoates with various substrates carrying polarized C═X bands (X = N, O, and C), such as [2 + 2][8] and [4 + 2][9] annulations. In 2011, Masson and Zhu reported the first enantioselective formal [2 + 2] cycloadditions of allenoates and imines catalyzed by cinchona alkaloid amide.[8b] Subsequently, the groups of Tong, Bohan, Ye, and Shi have independently described [4 + 2] annulations of allenoates with activated olefins.[9a−d] Recently, Cheng reported chiral tertiary amine-catalyzed asymmetric [4 + 2] cycloadditions of allenoates with 2-olefinic benzofuran-3-ones to afford dihydropyran fused benzofuran derivatives.[9g]

While allenoates have been extensively used, the corresponding allene ketones have only been reported in a few cases.[10] In 2007, the Wallace group have demonstrated the first phosphine-catalyzed [3 + 2] cycloadditions of allene ketones in good yield and diastereoselectivity.[10b] In 2009, the Loh group introduced the silicon group at the α-position of allene ketones, which was the key to obtaining cross-cyclized [3 + 2] products.[10c] Recently, Antonchick and Waldmann reported a phosphine-catalyzed [3 + 2] annulation of isoquinolinium methylides with allene ketones.[10g] Lu's group developed a novel phosphine-catalyzed [4 + 2] annulation employing allene ketones as C_2 synthons, which was the first time that an allene ketone was used in a asymmetric phosphine-catalyzed annulation reaction.[10h] To the best of our knowledge, there is no report on the asymmetric amine-catalyzed annulation using allene ketones to synthesize chiral pyran skeletons. We envisioned that a [4 + 2] annulation reaction could be developed by employing allene ketones and activated alkenes via asymmetric amine catalysis. In an effort to continue our studies of the synthesis of chiral heterocyclic compounds,[11] herein we report a chiral amine-catalyzed enantioselective [4 + 2] cycloaddition between allene ketones and 2,3-dioxopyrrolidine derivatives.[12]

We initiated our investigations using (*E*)-1-benzyl-4-benzylidenepyrrolidine-2,3-dione (**1a**) and 1-phenylbuta-2,3-dien-1-one (**2a**) with different amine catalysts and solvents (Table 1). In the presence of **C1**, the desired [4 + 2] annulation occurred smoothly to yield **3a** in 76% yield with 95% *ee* (entry 1). Then, a number of widely used cinchona alkaloid derived catalysts **C2**−**C15** were tested (entries 2−15), and we were

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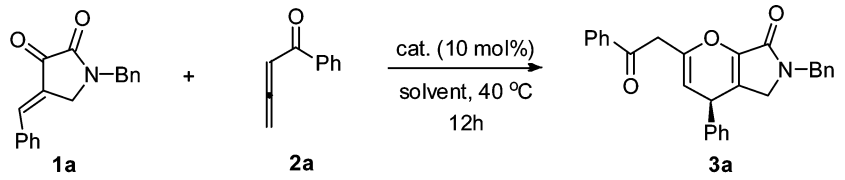
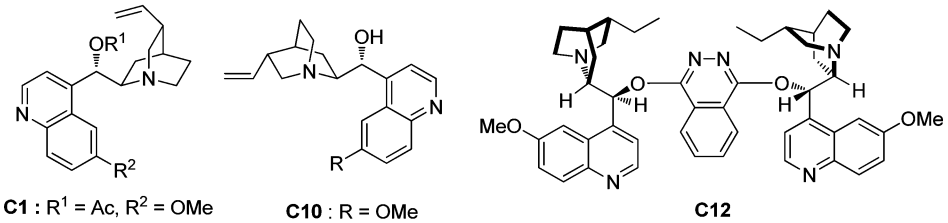
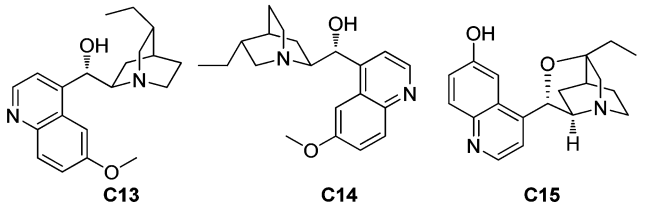
Table 1. Screening for the [4 + 2] Cycloaddition[a]





C1 : R^1 = Ac, R^2 = OMe
C2 : R^1 = Bz, R^2 = OMe
C3 : R^1 = TMS, R^2 = OMe
C4 : R^1 = TES, R^2 = OMe
C5 : R^1 = TBDPS, R^2 = OMe
C6 : R^1 = TBDMS, R^2 = OMe
C7 : R^1 = TIPS, R^2 = OMe
C8 : R^1 = H, R^2 = OMe
C9 : R^1 = H, R^2 = H

C10 : R = OMe
C11 : R = H



C12 C13 C14 C15

entry	cat.	solvent	yield (%)[b]	*ee* (%)[c]
1	**C1**	toluene	76	95
2	**C2**	toluene	88	97
3	**C3**	toluene	76	89
4	**C4**	toluene	86	90
5	**C5**	toluene	31	91
6	**C6**	toluene	80	85
7	**C7**	toluene	80	87
8	**C8**	toluene	80	88
9	**C9**	toluene	75	19
10	**C10**	toluene	70	−56
11	**C11**	toluene	64	−31
12	**C12**	toluene	69	96
13	**C13**	toluene	80	80
14	**C14**	toluene	64	−66
15	**C15**	toluene	90	32
16	**C2**	DCE	83	95
17	**C2**	THF	20	92
18	**C2**	CH_3CN	59	93
19[d]	**C2**	toluene	71	96

[a]The reactions were conducted with 0.2 mmol of **1a**, 0.3 mmol of **2a**, and 10 mol % catalyst in 2.0 mL of solvent at 40 °C. [b]Isolated yields. [c]Determined by chiral HPLC analysis. [d]5 mol % catalyst was added..

delighted to find that all of the amine catalysts worked well for the [4 + 2] cycloaddition. **C2** could give products in 88% yield and 97% *ee* (entry 2). Silicon group substituted catalysts (**C3**−**C7**) gave no better results than **C2**. Under the catalysis of **C5**, the *ee* value was not improved, but the yield of **3a** was lower, which indicated that big O-substitution could not improve enantioselectivity but decrease the reactivity of the catalyst. As expected, the enantiomer of **4a** was formed when the chirality-inversed catalysts (**C10**, **C11**, and **C14**) were employed, although the enantioselectivities were lower. We were surprised to find that *β*-ICD (**C15**) gave a higher yield but a lower *ee* value. Next, a quick solvent screening identified toluene as the best solvent (entries 16−18). At last, we decreased the amount of **C2** to 5 mol % (entry 19) and found that the yield was significantly reduced but that the *ee* value was nearly unchanged.

Having established the optimal reaction conditions, we next surveyed the substrate scope of the reaction by varying the structures of 2,3-dioxopyrrolidine derivatives **1** and allene ketones **2**. As exhibited in Table 2, the reaction was applicable to a wide range of 2,3-dioxopyrrolidine derivatives bearing different aromatic groups (entries 2−14). In most cases, the corresponding products were obtained in moderate to good yield (59−90%) with good enatioselectivities (80−95% *ee*). The substituents on the phenyl rings affected the yields apparently, for example, *ortho*-Me, *ortho*-F, and 2-naphthyl-containing substrates gave lower yields (entries 2, 12 and 14). Subsequently, different allene ketones were employed in the reaction (entries 15−20), and good results were obtained.

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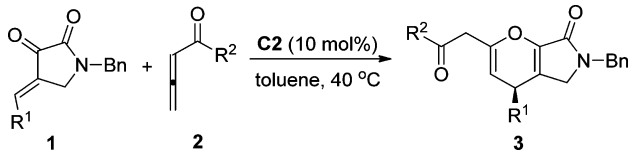
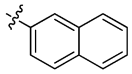
Table 2. Substrate Scope of the C2-Catalyzed Asymmetric [4 + 2] Cyclization of 1 and 2[a]



Entry	R^1	R^2	t (h)	3, Yield (%)[b]	*ee* (%)[c]
1	Ph	Ph	12	**3a**, 88	97
2	2-MeC_6H_4	Ph	24	**3b**, 62	89
3	3-MeC_6H_4	Ph	12	**3c**, 86	94
4	4-MeC_6H_4	Ph	24	**3d**, 88	95
5	2-BrC_6H_4	Ph	17	**3e**, 84	80
6	3-BrC_6H_4	Ph	12	**3f**, 90	92
7	4-BrC_6H_4	Ph	17	**3g**, 82	92
8	2-ClC_6H_4	Ph	16	**3h**, 89	86
9	3-ClC_6H_4	Ph	12	**3i**, 79	91
10	4-ClC_6H_4	Ph	18	**3j**, 78	91
11	3,4-diClC_6H_3	Ph	12	**3k**, 77	89
12	2-FC_6H_4	Ph	12	**3l**, 59	95
13	4-CNC_6H_4	Ph	15	**3m**, 81	89
14		Ph	53	**3n**, 63	95
15	Ph	3-MeC_6H_4	12	**3o**, 79	93
16	Ph	4-MeC_6H_4	12	**3p**, 89	93
17	Ph	3-BrC_6H_4	12	**3q**, 87	94
18	Ph	4-BrC_6H_4	12	**3r**, 86	91
19	Ph	4-ClC_6H_4	12	**3s**, 89	95
20	Ph	3,4-diClC_6H_3	12	**3t**, 88	89
21	Ph	*n*-C_6H_{13}	72	23	-
22	Ph	OBn	48	8	-

[a]The reactions were conducted with 0.2 mmol of **1**, 0.3 mmol of **2**, and 10 mol % **C2** in 2.0 mL of toluene at 40 °C. [b]Isolated yields. [c]Determined by chiral HPLC analysis.

Then, an alkyl-substituted allene ketone was tested, but no good result was achieved (entry 21). Lastly, an allenoate substrate was also tested in this reaction, which only gave product in 8% yield (entry 22). We believe that this result may be due to the different reactivities between allene ketone and allenoate substrates. The absolute configuration of products **3** was unequivocally assigned as R by X-ray diffraction of **3a**.[13]

On the basis of the above experimental results and the previous mechanistic investigations,[14] a plausible mechanism has been proposed as shown in Scheme 1. Addition of the **C2** to the allene ketone **2a** will generate zwitterionic intermediates **A1** and **A2**. Then, the activated olefin **1a**, which is stabilized by the $\pi-\pi$ stacking between the phenyl ring and the quinolone moiety, is attacked by the intermediate **A1** from the *Si*-face to obtain the intermediate **C**. Subsequently, the intermediate **C** undergoes a ring-closed reaction, and the elimination of catalyst **C2** affords the product **3a′**, which then isomerizes to form the final product **3a**.

In summary, we have developed an efficient amine catalyzed [4 + 2] annulation between allene ketones and 2,3-dioxopyrrolidine derivatives. By utilizing cinchona alkaloid derived catalysts, 4*H*-pyran derivatives could be obtained in moderate to high yields with good enantioselectivities. To the best of our knowledge, this is the first asymmetric amine-catalyzed annulation employing allene ketones as substrates. This method provides an efficient way to construct 4*H*-pyran skeletons, which are widely found in natural products.

EXPERIMENTAL SECTION

General Information. All reactions were carried out in glassware with magnetic stirring. Purification of reaction products was carried out by flash chromatography using silica gel at high pressure. ^{1}H NMR and ^{13}C NMR spectra were recorded using $CDCl_3$ as the solvent and TMS as an internal standard. The peak patterns of ^{1}H NMR are indicated as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublet; and m, multiplet. The coupling constants, *J*, are reported in hertz (Hz). Data for ^{13}C NMR are reported in terms of chemical shift and multiplicity. High resolution mass spectra (HRMS) were recorded using ESI (FT-ICR). IR spectra were recorded by a FT-IR instrument and are reported in wavenumbers (cm^{-1}). HPLC analyses were conducted on the ID colunm and eluting with *n*-hexane/CH_2Cl_2/

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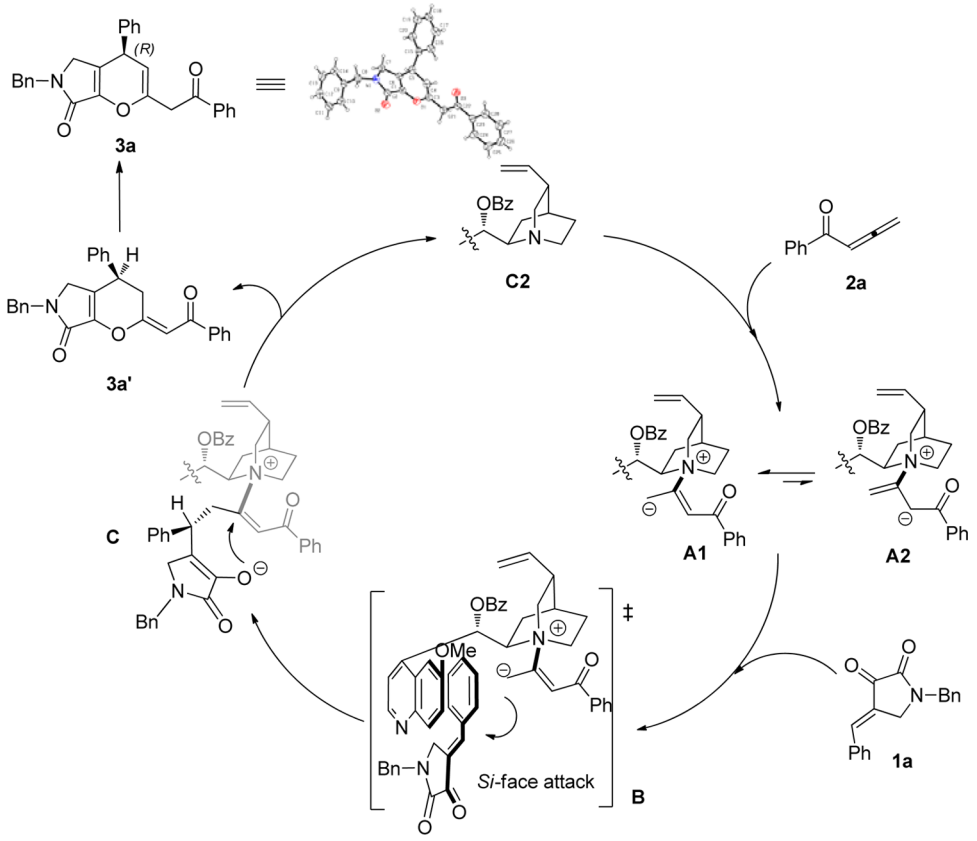
Scheme 1. Proposed Mechanism of the Reaction of 1a and 2a



MeOH. 2,3-Dioxopyrrolidine derivative **1**,[12] allene ketone **2**,[10b] and catalyst **C2**[15] were synthesized according to the previously reported methods.

General Procedure for the Synthesis of 3. To a suspension of compound **1** (0.2 mmol) in toluene (2 mL), were sequentially added catalyst **C2** (0.02 mmol) and compound **2** (0.3 mmol), and the mixture was then stirred and heated with an oil bath at 40 °C. The reaction was monitored by TLC analysis, and when the reaction was completed, the mixture was subjected directly to flash column chromatography on silica gel (200−300 mesh, petroleum ether/ethyl acetate 3:1) to yield the corresponding products.

*(R)-6-Benzyl-2-(2-oxo-2-phenylethyl)-4-phenyl-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3a**).* Red solid; 88% yield (74 mg); 97% *ee*; $[\alpha]_D^{20}$ = 23.0; (*c* 1.0, $CHCl_3$); mp 74.4−75.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99−7.97 (m, 2H), 7.59−7.44 (m, 3H), 7.31−7.16 (m, 10H), 4.86 (d, *J* = 3.2 Hz, 1H), 4.81 (d, *J* = 15.2 Hz, 1H), 4.32 (d, *J* = 2.4 Hz, 1H), 4.28 (d, *J* = 15.2 Hz, 1H), 3.95 (d, *J* = 16.8 Hz, 1H), 3.89 (d, *J* = 16.8 Hz, 1H), 3.56 (d, *J* = 19.2 Hz, 1H), 3.36 (d, *J* = 18.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.7, 163.8, 145.9, 142.8, 141.7, 136.6, 136.1, 133.3, 128.8, 128.6, 128.6, 128.2, 127.9, 127.7, 127.5, 127.3, 123.6, 103.8, 47.2, 46.2, 42.7, 38.8 ppm. IR (KBr): ν 3358, 3061, 2919, 1692, 1598, 1451, 1339, 1242, 1203, 1144, 992, 756, 736, 701 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{23}NO_3$ $[M + Na]^+$, 444.1570; found, 444.1565. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 7.8 min, t_{minor} = 9.4 min.

*(R)-6-Benzyl-2-(2-oxo-2-phenylethyl)-4-(o-tolyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3b**).* Yellow solid; 62% yield (54 mg); 89% *ee*; $[\alpha]_D^{20}$ = 33.0; (*c* 1.0, $CHCl_3$); mp 56.9−58.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99−7.97 (m, 2H), 7.60−7.45 (m, 3H), 7.32−7.10 (m, 9H), 4.81 (d, *J* = 3.6 Hz, 1H), 4.80 (d, *J* = 15.2 Hz, 1H), 4.62 (d, *J* = 2.4 Hz, 1H), 4.33 (d, *J* = 15.2 Hz, 1H), 3.96 (d, *J* = 16.4 Hz, 1H), 3.87 (d, *J* = 16.8 Hz, 1H), 3.58 (dd, *J* = 18.4 Hz, *J* = 0.8 Hz, 1H), 3.41 (d, *J* = 18.0 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.8, 163.9, 145.9, 142.3, 140.7, 136.7, 136.2, 134.6, 133.4, 130.5, 129.1, 128.7, 128.6, 128.3, 127.9, 127.6, 127.0, 126.8, 123.5, 103.6, 47.3, 46.3, 42.7, 34.8, 19.3 ppm. IR (KBr): ν 3370, 3062, 2919, 1694, 1598, 1451, 1339, 1241, 1145, 992, 735, 701 cm^{-1}. ESI-HRMS: calcd for $C_{29}H_{25}NO_3$ $[M + Na]^+$, 458.1727; found, 458.1721. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 55/44/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 20.0 min, t_{minor} = 25.1 min.

*(R)-6-Benzyl-2-(2-oxo-2-phenylethyl)-4-(m-tolyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3c**).* Orange solid; 86% yield (75 mg); 94% *ee*; $[\alpha]_D^{20}$ = 22.0; (*c* 1.0, $CHCl_3$); mp 50.8−53.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00- 7.98 (m, 2H), 7.60−7.46 (m, 3H), 7.32−7.16 (m, 6H), 7.05−6.97 (m, 3H), 4.84 (s, 1H), 4.83 (d, *J* = 14.4 Hz, 1H), 4.29 (d, *J* = 2.0 Hz, 1H), 4.29 (d, *J* = 14.8 Hz, 1H), 3.97 (d, *J* = 16.8 Hz, 1H), 3.89 (d, *J* = 16.8 Hz, 1H), 3.56 (d, *J* = 18.4 Hz, 1H), 3.37 (d, *J* = 18.4 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.7, 163.9, 145.8, 142.8, 141.7, 138.6, 136.7, 136.1, 133.4, 128.7, 128.6, 128.5, 128.3, 128.1, 127.9, 127.6, 124.8, 123.8, 103.9, 47.3, 46.3, 42.8, 38.8, 21.3 ppm. IR (KBr): ν 3362, 3059, 2921, 2371, 1693, 1604, 1450, 1242, 1197, 1140, 1029, 995, 737, 701 cm^{-1}. ESI-HRMS: calcd for $C_{29}H_{25}NO_3$ $[M + Na]^+$, 458.1727; found, 458.1722. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 12.2 min, t_{minor} = 16.4 min.

*(R)-6-Benzyl-2-(2-oxo-2-phenylethyl)-4-(p-tolyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3d**).* Red solid; 88% yield (77 mg); 95% *ee*; $[\alpha]_D^{20}$ = 26.0; (*c* 1.0, $CHCl_3$); mp 55.6−56.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99−7.97 (m, 2H), 7.60−7.46 (m, 3H), 7.31−7.06 (m, 9H), 4.84−4.80 (m, 2H), 4.31−4.28 (m, 2H), 3.95 (d, *J* = 16.8 Hz, 1H), 3.89 (d, *J* = 16.8 Hz, 1H), 3.55 (d, *J* = 18.4 Hz, 1H), 3.37 (d, *J* = 18.0 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.8, 163.9, 145.8, 141.7, 139.9, 137.0, 136.7, 136.2, 133.4, 129.5, 128.7, 128.6, 128.3, 128.0, 127.6, 127.6, 123.9, 104.0, 47.3, 46.3, 42.8, 38.4, 21.0 ppm. IR (KBr): ν 3364, 3059, 2921, 2373, 1693, 1662, 1450, 1241, 1203, 1143, 1031, 994, 754, 702 cm^{-1}. ESI-HRMS: calcd for $C_{29}H_{25}NO_3$ $[M + Na]^+$, 458.1727; found, 458.1722. HPLC analysis:

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Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 45/54/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 10.2 min, t_{minor} = 12.9 min.

*(S)-6-Benzyl-4-(2-bromophenyl)-2-(2-oxo-2-phenylethyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3e**).* Yellow solid; 84% yield (84 mg); 80% *ee*; $[\alpha]_D^{20}$ = −7.0; (*c* 1.0, $CHCl_3$); mp 61.6−62.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00−7.98 (m, 2H), 7.60−7.41 (m, 5H), 7.33−7.06 (m, 7H), 4.92 (s, 1H), 4.85 (d, *J* = 3.2 Hz, 1H), 4.77 (d, *J* = 15.2 Hz, 1H), 4.36 (d, *J* = 14.8 Hz, 1H), 3.98 (d, *J* = 16.8 Hz, 1H), 3.93 (d, *J* = 16.8 Hz, 1H), 3.77 (d, *J* = 18.8 Hz, 1H), 3.46 (d, *J* = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.6, 163.6, 146.8, 142.1, 141.6, 136.7, 136.1, 133.4, 132.5, 130.9, 128.8, 128.6, 128.6, 128.3, 128.3, 127.8, 127.5, 122.8, 122.7, 102.7, 47.4, 46.2, 42.7, 37.7 ppm. IR (KBr): ν 3373, 3060, 2919, 2371, 1688, 1597, 1450, 1339, 1241, 1273, 1202, 1144, 1025, 992, 737, 702 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{22}BrNO_3$ $[M+Na]^+$, 522.0675; found, 522.0669. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 60/39/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 12.1 min, t_{minor} = 15.0 min.

*(R)-6-Benzyl-4-(3-bromophenyl)-2-(2-oxo-2-phenylethyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3f**).* Orange solid; 90% yield (90 mg); 92% *ee*; $[\alpha]_D^{20}$ = 27.0; (*c* 1.0, $CHCl_3$); mp 61.5−63.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99−7.97 (m, 2H), 7.60−7.46 (m, 3H), 7.37−7.14 (m, 9H), 4.84−4.81 (m, 2H), 4.33−4.28 (m, 2H), 3.97 (d, *J* = 16.4 Hz, 1H), 3.90 (d, *J* = 16.8 Hz, 1H), 3.57 (d, *J* = 18.4 Hz, 1H), 3.37 (d, *J* = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.6, 163.6, 146.4, 145.1, 142.0, 136.6, 136.1, 133.5, 130.8, 130.5, 130.5, 128.7, 128.7, 128.3, 127.9, 127.6, 126.5, 123.0, 122.8, 103.2, 47.1, 46.3, 42.7, 38.6 ppm. IR (KBr): ν 3370, 3060, 2921, 2371, 1691, 1594, 1450, 1242, 1202, 1144, 1092, 1030, 785, 737, 696 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{22}BrNO_3$ $[M+Na]^+$, 522.0675; found, 522.0669. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 13.1 min, t_{minor} = 21.0 min.

*(R)-6-Benzyl-4-(4-bromophenyl)-2-(2-oxo-2-phenylethyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3g**).* Orange solid; 82% yield (82 mg). 92% *ee*; $[\alpha]_D^{20}$ = 51.0; (*c* 1.0, $CHCl_3$); mp 59.2−61.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99−7.97 (m, 2H), 7.61−7.58 (m, 1H), 7.50−7.42 (m, 4H), 7.32−7.08 (m, 7H), 4.83−4.79 (m, 2H), 4.34−4.30 (m, 2H), 3.93 (s, 2H), 3.56 (d, *J* = 18.0 Hz, 1H), 3.35 (d, *J* = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.7, 163.7, 146.3, 141.9, 141.8, 136.6, 136.1, 133.5, 132.0, 129.5, 128.7, 128.7, 128.3, 128.0, 127.7, 123.0, 121.3, 103.3, 47.2, 46.3, 42.7, 38.4 ppm. IR (KBr): ν 3365, 2921, 2373, 1693, 1485, 1450, 1242, 1203, 1143, 1010, 754, 697 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{22}BrNO_3$ $[M+Na]^+$, 522.0675; found, 522.0669. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 13.7 min, t_{minor} = 22.1 min.

*(S)-6-Benzyl-4-(2-chlorophenyl)-2-(2-oxo-2-phenylethyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3h**).* Yellow solid; 89% yield (81 mg); 86% *ee*; $[\alpha]_D^{20}$ = −5.0; (*c* 1.0, $CHCl_3$); mp 86.0−87.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00−7.98 (m, 2H), 7.60−7.41 (m, 4H), 7.31−7.14 (m, 8H), 4.93 (d, *J* = 2.8 Hz, 1H), 4.84 (d, *J* = 3.6 Hz, 1H), 4.77 (d, *J* = 15.2 Hz, 1H), 4.36 (d, *J* = 15.2 Hz, 1H), 3.98 (d, *J* = 16.8 Hz, 1H), 3.93 (d, *J* = 16.8 Hz, 1H), 3.74 (d, *J* = 18.8 Hz, 1H), 3.45 (d, *J* = 18.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.7, 163.6, 147.0, 142.2, 139.9, 136.7, 136.1, 133.4, 132.3, 130.6, 129.2, 128.7, 128.6, 128.4, 128.3, 127.9, 127.7, 127.6, 122.8, 102.5, 47.4, 46.3, 42.7, 34.9 ppm. IR (KBr): ν 3372, 3062, 2917, 2371, 1695, 1597, 1450, 1339, 1242, 1202, 992, 756, 701 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{22}ClNO_3$ $[M+Na]^+$, 478.1180; found, 478.1175. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 60/39/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 11.4 min, t_{minor} = 14.1 min.

*(R)-6-Benzyl-4-(3-chlorophenyl)-2-(2-oxo-2-phenylethyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3i**).* Orange solid; 79% yield (72 mg); 91% *ee*; $[\alpha]_D^{20}$ = 26.0; (*c* 1.0, $CHCl_3$); mp 60.1−62.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99−7.97 (m, 2H), 7.61−7.46 (m, 3H), 7.32−7.09 (m, 9H), 4.84 (s, 1H), 4.83 (d, *J* = 15.2 Hz, 1H), 4.32 (d, *J* = 2.8 Hz, 1H), 4.31 (d, *J* = 15.2 Hz, 1H), 3.97 (d, *J* = 16.4 Hz, 1H), 3.91 (d, *J* = 16.4 Hz, 1H), 3.57 (d, *J* = 18.8 Hz, 1H), 3.37 (d, *J* = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.6, 163.6, 146.4, 144.8, 142.0, 136.6, 136.1, 134.7, 133.5, 130.1, 128.7, 128.7, 128.3, 127.9, 127.9, 127.6, 127.6, 126.0, 122.8, 103.2, 47.1, 46.3, 42.7, 38.6 ppm. IR (KBr): ν 3363, 3061, 2920, 2372, 1694, 1595, 1450, 1339, 1243, 1203, 995, 756, 737, 696 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{22}ClNO_3$ $[M+Na]^+$, 478.1180; found, 478.1175. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 60/39/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 11.6 min, t_{minor} = 17.8 min.

*(R)-6-Benzyl-4-(4-chlorophenyl)-2-(2-oxo-2-phenylethyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3j**).* Orange solid; 78% yield (71 mg); 91% *ee*; $[\alpha]_D^{20}$ = 42.0; (*c* 1.0, $CHCl_3$); mp 54.1−55.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98−7.96 (m, 2H), 7.60−7.57 (m, 1H), 7.49−7.45 (m, 2H), 7.32−7.23 (m, 5H), 7.19−7.13 (m, 4H), 4.83 (d, *J* = 3.2 Hz, 1H), 4.79 (d, *J* = 14.8 Hz, 1H), 4.32 (d, *J* = 14.8 Hz, 1H), 4.32 (d, *J* = 2.0 Hz, 1H), 3.93 (s, 2H), 3.70 (d, *J* = 18.4 Hz, 1H), 3.35 (d, *J* = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.6, 163.6, 146.2, 141.8, 141.3, 136.5, 136.1, 133.4, 133.1, 129.1, 128.9, 128.7, 128.6, 128.2, 127.9, 127.6, 123.1, 103.4, 47.1, 46.2, 42.7, 38.2 ppm. IR (KBr): ν 3367, 3061, 2919, 2371, 1692, 1597, 1489, 1450, 1409, 1243, 1203, 1144, 1089, 1015, 832, 737, 700 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{22}ClNO_3$ $[M+Na]^+$, 478.1180; found, 478.1175. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 13.6 min, t_{minor} = 21.5 min.

*(R)-6-Benzyl-4-(3,4-dichlorophenyl)-2-(2-oxo-2-phenylethyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3k**).* Red solid; 77% yield (75 mg); 89% *ee*; $[\alpha]_D^{20}$ = 38.0; (*c* 1.0, $CHCl_3$); mp 54.4−56.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98−7.96 (m, 2H), 7.59−7.07 (m, 11H), 4.81 (d, *J* = 15.2 Hz, 2H), 4.34 (d, *J* = 15.2 Hz, 2H), 3.94 (s, 2H), 3.58 (d, *J* = 18.0 Hz, 1H), 3.36 (d, *J* = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.5, 163.5, 146.7, 143.0, 142.1, 136.5, 136.0, 133.5, 132.9, 131.5, 130.8, 129.7, 128.7, 128.7, 128.3, 128.0, 127.7, 127.2, 122.4, 102.9, 47.1, 46.3, 42.7, 38.1 ppm. IR (KBr): ν 3370, 2923, 2368, 1690, 1597, 1466, 1450, 1243, 1223, 1144, 1030, 738, 700 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{21}Cl_2NO_3$ $[M+Na]^+$, 512.0791; found, 512.0785. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 45/54/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 10.3 min, t_{minor} = 18.1 min.

*(S)-6-Benzyl-4-(2-fluorophenyl)-2-(2-oxo-2-phenylethyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3l**).* White solid; 59% yield (52 mg); 95% *ee*; $[\alpha]_D^{20}$ = 22.0; (*c* 1.0, $CHCl_3$); mp 150.9−151.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00−7.98 (m, 2H), 7.61−7.36 (m, 3H), 7.34−7.01 (m, 8H), 6.98−6.96 (m, 1H), 4.83 (d, *J* = 3.2 Hz, 1H), 4.78 (d, *J* = 14.8 Hz, 1H), 4.75 (s, 1H), 4.35 (d, *J* = 14.8 Hz, 1H), 4.48 (d, *J* = 16.8 Hz, 1H), 3.93 (d, *J* = 16.8 Hz, 1H), 3.68 (d, *J* = 18.4 Hz, 1H), 3.45 (d, *J* = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.7, 163.7, 160.8, 158.4, 147.2, 142.2, 136.7, 136.2, 133.4, 130.1, 130.1, 129.4, 129.3, 128.8, 128.7, 128.7, 128.7, 128.3, 127.9, 127.6, 124.9, 124.8, 122.7, 115.2, 114.9, 101.9, 47.4, 47.4, 46.3, 42.7, 30.9, 30.8 ppm. IR (KBr): ν 3370, 3062, 2917, 1695, 1487, 1452, 1340, 1243, 1198, 1094, 992, 758, 701 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{22}FNO_3$ $[M+Na]^+$, 462.1476; found, 462.1472. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 55/44/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 16.4 min, t_{minor} = 19.9 min.

*(R)-4-(6-Benzyl-7-oxo-2-(2-oxo-2-phenylethyl)-4,5,6,7-tetrahydropyrano[2,3-c]pyrrol-4-yl)benzonitrile (**3m**).* Yellow solid; 81% yield (74 mg); 89% *ee*; $[\alpha]_D^{20}$ = 59.0; (*c* 1.0, $CHCl_3$); mp 61.8−64.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98−7.96 (m, 2H), 7.62−7.47 (m, 5H), 7.37−7.17 (m, 7H), 4.85 (d, *J* = 3.6 Hz, 1H), 4.78 (d, *J* = 14.8 Hz, 1H), 4.42 (d, *J* = 2.4 Hz, 1H), 4.35 (d, *J* = 14.8, 1H), 3.97 (d, *J* = 17.2 Hz, 1H), 3.92 (d, *J* = 16.8 Hz, 1H), 3.59 (d, *J* = 18.8 Hz, 1H), 3.33 (d, *J* = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.5, 163.4, 147.8, 146.8, 142.3, 136.4, 136.0, 133.5, 132.7, 128.7, 128.7, 128.6, 128.2, 127.9, 127.7, 122.0, 118.4, 111.3, 102.6, 47.0, 46.3, 42.6, 39.0 ppm. IR (KBr): ν 3356, 3061, 2920, 2228, 1692, 1606, 1450, 1339, 1243, 1204, 1144, 992, 847, 737, 701 cm^{-1}. ESI-HRMS: calcd for $C_{29}H_{22}N_2O_3$ $[M+Na]^+$, 469.1523; found, 469.1517. HPLC analysis: Chiralpak ID, *n*-hexane/CH_2Cl_2/MeOH = 60/39/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 20.4 min, t_{minor} = 34.6 min.

*(R)-6-Benzyl-4-(naphthalen-2-yl)-2-(2-oxo-2-phenylethyl)-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3n**).* Orange solid; 63% yield (59 mg); 95% *ee*; $[\alpha]_D^{20}$ = 42.0; (*c* 1.0, $CHCl_3$); mp 55.4−57.6 °C. ^{1}H

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NMR (400 MHz, $CDCl_3$): δ = 8.01−7.99 (m, 2H), 7.81−7.75 (m, 3H), 7.61−7.57 (m, 2H), 7.50−7.44 (m, 4H), 7.37−7.15 (m, 6H), 4.93 (d, J = 3.2 Hz, 1H), 4.82 (d, J = 15.2 Hz, 1H), 4.50 (s, 1H), 4.26 (d, J = 15.2 Hz, 1H), 3.99 (d, J = 16.4 Hz, 1H), 3.93 (d, J = 16.4 Hz, 1H), 3.59 (d, J = 18.4 Hz, 1H), 3.34 (d, J = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.7, 163.9, 146.2, 141.9, 140.1, 136.6, 136.2, 133.4, 133.3, 132.6, 128.8, 128.7, 128.4, 128.0, 127.7, 127.6, 127.6, 126.4, 126.3, 126.0, 125.8, 123.6, 103.8, 47.3, 46.3, 42.8, 39.1 ppm. IR (KBr): ν 3368, 3057, 2922, 2375, 1691, 1598, 1450, 1242, 1143, 1031, 995, 749, 738, 702 cm^{-1}. ESI-HRMS: calcd for $C_{32}H_{25}NO_3$ [M + Na]$^+$, 494.1727; found, 494.1730. HPLC analysis: Chiralpak ID, n-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 14.8 min, t_{minor} = 21.3 min.

*(R)-6-Benzyl-2-(2-oxo-2-(m-tolyl)ethyl)-4-phenyl-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3o**).* Red solid; 79% yield (69 mg); 93% *ee*; $[\alpha]_D^{20}$ = 12.0; (c 1.0, $CHCl_3$); mp 55.2−57.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79−7.77 (m, 2H), 7.40−7.17 (m, 12H), 4.85 (d, J = 3.2 Hz, 1H), 4.82 (d, J = 15.2 Hz, 1H), 4.32 (d, J = 1.6 Hz, 1H), 4.29 (d, J = 14.8 Hz, 1H), 3.94 (d, J = 16.8 Hz, 1H), 3.88 (d, J = 16.8 Hz, 1H), 3.56 (d, J = 18.4 Hz, 1H), 3.36 (d, J = 18.0 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.9, 163.8, 146.0, 142.8, 141.7, 138.4, 136.7, 136.2, 134.1, 128.8, 128.6, 128.5, 127.9, 127.7, 127.5, 127.3, 125.5, 123.6, 103.7, 47.2, 46.2, 42.8, 38.8, 21.3 ppm. IR (KBr): ν 3361, 3059, 2920, 1691, 1603, 1452, 1240, 1158, 1090, 1038, 995, 735, 702 cm^{-1}. ESI-HRMS: calcd for $C_{29}H_{25}NO_3$ [M + Na]$^+$, 458.1727; found, 458.1722. HPLC analysis: Chiralpak ID, n-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 13.1 min, t_{minor} = 16.3 min.

*(R)-6-Benzyl-2-(2-oxo-2-(p-tolyl)ethyl)-4-phenyl-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3p**).* Red solid; 89% yield (77 mg); 93% *ee*; $[\alpha]_D^{20}$ = 19.0; (c 1.0, $CHCl_3$); mp 62.5−63.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89−7.87 (m, 2H), 7.31−7.16 (m, 12H), 4.85 (d, J = 2.8 Hz, 1H), 4.81 (d, J = 14.8 Hz, 1H), 4.32 (s, 1H), 4.29 (d, J = 15.2 Hz, 1H), 3.92 (d, J = 16.8 Hz, 1H), 3.86 (d, J = 16.8 Hz, 1H), 3.56 (d, J = 18.4 Hz, 1H), 3.36 (d, J = 18.4 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.3, 163.8, 146.1, 144.2, 142.8, 141.7, 136.7, 133.7, 129.3, 128.8, 128.6, 128.4, 127.9, 127.7, 127.5, 127.2, 123.6, 103.6, 47.2, 46.2, 42.6, 38.8, 21.6 ppm. IR (KBr): ν 3350, 3029, 2920, 1693, 1606, 1452, 1242, 1201, 1181, 995, 814, 735, 702 cm^{-1}. ESI-HRMS: calcd for $C_{29}H_{25}NO_3$ [M + Na]$^+$, 458.1727; found, 458.1722. HPLC analysis: Chiralpak ID, n-hexane/CH_2Cl_2/MeOH = 52/47/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 16.0 min, t_{minor} = 21.6 min.

*(R)-6-Benzyl-2-(2-(3-bromophenyl)-2-oxoethyl)-4-phenyl-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3q**).* Orange solid; 87% yield (87 mg); 94% *ee*; $[\alpha]_D^{20}$ = 27.0; (c 1.0, $CHCl_3$); mp 62.4−64.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (s, 1H), 7.90 (d, J = 7.6 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.37−7.17 (m, 11H), 4.86 (d, J = 3.2 Hz, 1H), 4.81 (d, J = 15.2 Hz, 1H), 4.32 (d, J = 1.6 Hz, 1H), 4.29 (d, J = 15.2 Hz, 1H), 3.92 (d, J = 16.8 Hz, 1H), 3.86 (d, J = 16.8 Hz, 1H), 3.56 (d, J = 18.4 Hz, 1H), 3.36 (d, J = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.4, 163.7, 145.5, 142.6, 141.7, 137.8, 136.6, 136.2, 131.2, 130.2, 128.8, 128.6, 127.9, 127.7, 127.6, 127.3, 126.9, 123.6, 122.9, 104.1, 47.2, 46.2, 42.8, 38.8 ppm. IR (KBr): ν 3370, 3062, 2918, 2372, 1692, 1452, 1420, 1242, 1201, 1143, 994, 736, 701 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{22}BrNO_3$ [M + Na]$^+$, 522.0675; found, 522.0668. HPLC analysis: Chiralpak ID, n-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 13.9 min, t_{minor} = 17.4 min.

*(R)-6-Benzyl-2-(2-(4-bromophenyl)-2-oxoethyl)-4-phenyl-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3r**).* Yellow solid; 86% yield (86 mg); 91% *ee*; $[\alpha]_D^{20}$ = 27.0; (c 1.0, $CHCl_3$); mp 67.6−70.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 8.4 Hz, 2H), 7.32−7.17 (m, 10H), 4.85 (d, J = 3.2 Hz, 1H), 4.80 (d, J = 15.2 Hz, 1H), 4.32 (s, 1H), 4.29 (d, J = 15.6 Hz, 1H), 3.91 (d, J = 16.8 Hz, 1H), 3.85 (d, J = 16.8 Hz, 1H), 3.56 (d, J = 18.4 Hz, 1H), 3.36 (d, J = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.7, 163.7, 145.5, 142.6, 141.6, 136.6, 134.8, 131.9, 129.8, 128.8, 128.6, 128.5, 127.9, 127.7, 127.5, 127.3, 123.6, 104.0, 47.2, 46.2, 42.7, 38.8 ppm. IR (KBr): ν 3367, 3061, 2917, 2371, 1692, 1585, 1452, 1396, 1242, 1203, 1143, 1072, 989, 736, 702 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{22}BrNO_3$ [M + Na]$^+$, 522.0675; found, 522.0669. HPLC analysis: Chiralpak ID, n-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 14.1 min, t_{minor} = 16.8 min.

*(R)-6-Benzyl-2-(2-(4-chlorophenyl)-2-oxoethyl)-4-phenyl-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3s**).* Orange solid; 89% yield (81 mg); 95% *ee*; $[\alpha]_D^{20}$ = 27.0; (c 1.0, $CHCl_3$); mp 63.3−65.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.32−7.17 (m, 10H), 4.86 (d, J = 3.2 Hz, 1H), 4.81 (d, J = 15.2 Hz, 1H), 4.32 (s, 1H), 4.29 (d, J = 15.2 Hz, 1H), 3.92 (d, J = 16.8 Hz, 1H), 3.86 (d, J = 16.4 Hz, 1H), 3.56 (d, J = 18.4 Hz, 1H), 3.37 (d, J = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.6, 163.7, 145.6, 142.7, 141.7, 139.8, 136.6, 134.4, 129.7, 128.9, 128.8, 128.6, 127.9, 127.7, 127.6, 127.3, 123.6, 104.0, 47.2, 46.2, 42.7, 38.8 ppm. IR (KBr): ν 3372, 3061, 2920, 2373, 1688, 1589, 1452, 1400, 1242, 1203, 1143, 1092, 1034, 991, 738, 701 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{22}ClNO_3$ [M + Na]$^+$, 478.1180; found, 478.1175. HPLC analysis: Chiralpak ID, n-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 14.3 min, t_{minor} = 16.9 min.

*(R)-6-Benzyl-2-(2-(3,4-dichlorophenyl)-2-oxoethyl)-4-phenyl-5,6-dihydropyrano[2,3-c]pyrrol-7(4H)-one (**3t**).* Orange solid; 88% yield (86 mg); 89% *ee*; $[\alpha]_D^{20}$ = 29.0; (c 1.0, $CHCl_3$); mp 61.1−63.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, J = 2.0 Hz, 1H), 7.81 (dd, J = 8.4 Hz, J = 2.0 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.33−7.16 (m, 10H), 4.86 (d, J = 3.2 Hz, 1H), 4.80 (d, J = 15.2 Hz, 1H), 4.32 (d, J = 2.8 Hz, 1H), 4.29 (d, J = 15.2 Hz, 1H), 3.90 (d, J = 16.8 Hz, 1H), 3.85 (d, J = 17.2 Hz, 1H), 3.57 (d, J = 18.4 Hz, 1H), 3.37 (d, J = 18.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.6, 163.7, 145.3, 142.6, 141.7, 137.9, 136.6, 135.6, 133.3, 130.8, 130.2, 128.8, 128.6, 127.9, 127.7, 127.6, 127.4, 127.4, 123.7, 104.2, 47.2, 46.2, 42.8, 38.8 ppm. IR (KBr): ν 3374, 3063, 3029, 2918, 2374, 1693, 1584, 1494, 1453, 1388, 1241, 1201, 1143, 1031, 1000, 735, 701 cm^{-1}. ESI-HRMS: calcd for $C_{28}H_{21}Cl_2NO_3$ [M + Na]$^+$, 512.0791; found, 512.0785. HPLC analysis: Chiralpak ID, n-hexane/CH_2Cl_2/MeOH = 50/49/1, flow rate 1.0 mL/min, λ = 245 nm, t_{major} = 15.0 min, t_{minor} = 17.4 min.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

HPLC chromatograms of **3**, X-ray crystallographic data for **3a** (CIF), and ^{1}H and ^{13}C NMR spectra. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00961.

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Notes

The authors declare no competing financial interest.

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