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Organocatalytic asymmetric cyclopropanation of α,β-unsaturated aldehydes with arsonium ylides

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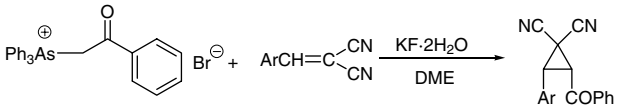
Abstract—A novel organocatalytic asymmetric cyclopropanation of α,β-unsaturated aldehydes with arsonium ylides using diphenylprolinol silylether as a catalyst is described. A variety of chiral cyclopropyl aldehydes are obtained in moderate to good yields with up to 99:1 dr (diastereomeric ratio) and 99% ee under simple and mild reaction conditions.

1. Introduction

Cyclopropanes and their derivatives are not only common structures found in many natural and biologically active compounds,[1] but also versatile building blocks[1a,2] for organic synthesis, because of their unique combination of reactivity and structural properties. Significant progress has been made in the use of a vast array of organometallic carbenoids[3] for the preparation of these types of compounds. On the other hand, several stabilized ylides have also been employed successfully for this purpose. For instance, Corey[4] pioneered the use of sulfonium ylides, while Aggarwal[5] has developed the asymmetric cyclopropanation of electron-deficient alkenes mediated by chiral sulfides. Recently, Dai and Tang[6] utilized chiral telluronium and sulfonium ylides for the enantioselective synthesis of vinylcyclopropanes. Gaunt[7] disclosed an organocatalytic enantioselective cyclopropanation via ammonium ylides. More recently, MacMillan et al.[8] realized a highly enantioselective organocatalytic cyclopropanation reaction between stabilized sulfonium ylides and α,β-unsaturated aldehydes by using 2-carboxylic acid dihydroindole as the catalyst. Most recently, Arvidsson[9] employed (*S*)-(−)-indoline-2-yl-1*H*-tetrazole and novel aryl sulfonamides as new catalysts for the enantioselective organocatalytic cyclopropanation of α,β-unsaturated aldehydes, while Córdava[10] reported a chiral amine catalyzed cyclopropanation reaction between halomalonates or 2-halo-β-keto esters and enals. Our group[11] has accomplished the highly stereoselective synthesis of cyclopropanes with arsonium ylides and electron-deficient olefins (Scheme 1). Still interested in the chemistry of arsonium ylides and inspired by other studies in organocatalytic asymmetric cyclopropanation reactions[4–10] of stabilized ylides and the great achievements of asymmetric iminium catalysis chemistry,[12] we envisioned that a combination of the iminium catalysis with arsonium ylides would provide access to cyclopropanes with high enantioselectivity. Herein we report our studies using this strategy.



Scheme 1. Stereoselective cyclopropanation reaction of electron-deficient olefins.[11b]

2. Results and discussion

Our initial experiment was carried out using 20 mol % of TMS-protected diphenylprolinol **3** as the catalyst, and chloroform as solvent. The reaction between cinnamaldehyde and arsonium salts, in the presence of 4 Å MS, gave the cyclopropane product in very low yield (19%), but with excellent enantioselectivity (95% ee) (Table 1, entry 1).

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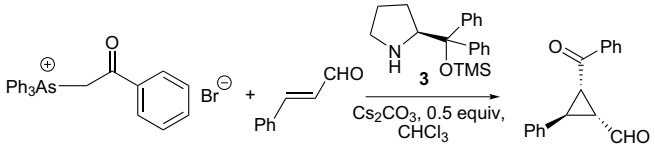
Table 1. Optimization of organocatalytic asymmetric cyclopropanations of α,β-unsaturated aldehydes[a]



1a 2a 4a

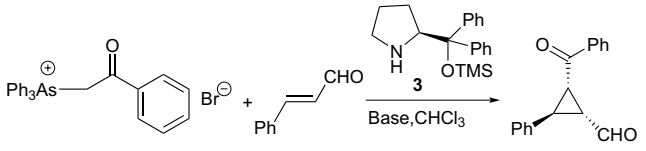
Entry	Catalyst	Solvent	Arsonium salt	Cs_2CO_3	% yield[b]	dr[c]	% ee[d]
1	0.2	$CHCl_3$	1.0	—	19	30:1	95
2	1.0	$CHCl_3$	1.0	—	82	>99:1	98
3	0.2	$CHCl_3$	1.0	0.5	54	16:1	96
4	0.2	$CHCl_3$	1.5	1.5	24	>99:1	96
5	0.2	$CHCl_3$	2.0	2.0	20	32:1	94
6	**0.3**	**$CHCl_3$**	**1.0**	**0.5**	**66**	**18:1**	**99**
7[e]	0.3	$CHCl_3$	1.0	0.5	60	25:1	98
8	0.3	Toluene	1.0	0.5	58	20:1	98
9[e]	0.3	Toluene	1.0	0.5	55	25:1	99
10[f]	0.3	$CHCl_3$	1.0	0.5	52	20:1	98

[a] Reaction conditions: unless specified, a mixture of cinnamaldehyde (0.2 mmol), catalyst, and 4 Å MS (100 mg) in chloroform (4 mL) was stirred for 30 min at room temperature before the arsonium salt and Cs_2CO_3 (50 mol %) were added, and then the stirring was continued for 24 h at room temperature.
[b] Isolated yield.
[c] Determined by chiral HPLC or ^1H NMR analysis.
[d] Determined by chiral HPLC analysis.
[e] Reaction carried out at 0 °C.
[f] No 4 Å MS was added.

Encouraged by this result, we performed another experiment using 1 equiv of catalyst **3**. We were delighted to find that the reaction took place smoothly and gave the product in 82% yield and 98% ee. Based on the above results, we supposed that TMS-protected diphenylprolinol **3** served not only as a catalyst, but also as a base, which deprotonated the arsonium salts to yield arsonium ylides. Therefore, in order to decrease the loading of catalyst and increase the efficiency of the reaction, a base was chosen as an additive for this reaction. As shown in Table 1, when 50 mol % of cesium carbonate was added, the yield increased to 54% and the enantioselective excess was 96% (Table 1, entry 3). Attempts, which increased the amount of arsonium salts to 150 mol % or 200 mol %, or used lesser amounts of base, resulted in low yields[13] (Table 1, entries 4 and 5). When the amount of catalyst was increased to 30 mol %, a 66% yield was obtained. The effects of solvent and reaction temperature were also studied. Under optimized conditions (1.0 equiv cinnamaldehyde, 1.0 equiv arsonium salt, 50 mol % of cesium carbonate, and 30 mol % of catalyst), the desired cyclopropane could be produced in up to 99% ee and in 66% yield (Table 1, entry 6). To the best of our knowledge, this is the first example of enantioselective cyclopropanation based on arsonium salts. A comparison with the literature data of the specific rotation value revealed that the absolute configuration of compound **4a** was (1*R*,2*S*,3*R*) {$[\alpha]_D^{25} = -167.7$ (*c* 1.0, $CHCl_3$), lit. (1*R*,2*S*,3*R*)-**4a** $[\alpha]_D = -165.7$ (*c* 1.0, $CHCl_3$)[7]}.

Next, a variety of organic and inorganic bases were screened for this reaction. The results are summarized in Table 2. Sodium carbonate (50 mol %) gave the best yield (80% yield, Table 2, entry 2) and 98% ee. Other bases also gave nearly the same ee values (98–99% ee) except for potassium hydroxide (80% ee, Table 2, entry 4), while the yields were lower. Additionally, it seems that the diastereoselectivity decreased alongside an increase in the basicity of the bases (Table 2, entries 1–4).

Table 2. Screening of bases for the organocatalytic asymmetric cyclopropanation of α,β-unsaturated aldehydes and arsonium ylides[a]

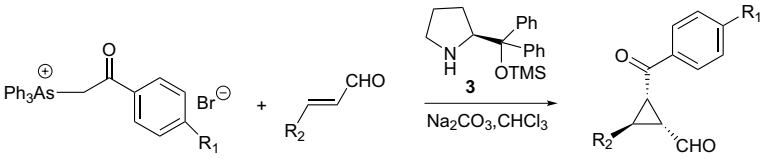


1a 2a 4a

Entry	Base (mol %)		% yield[b]	dr[c]	% ee[d]
1	Li_2CO_3	50	44	53:1	98
2	**Na_2CO_3**	**50**	**80**	**38:1**	**98**
3	K_2CO_3	50	72	29:1	99
4	KOH	100	12	2:1	80
5	CsF	100	54	49:1	99
6	DMAP	50	56	16:1	98
7	Et_3N	100	28	3:1	98
8	Pyridine	100	40	10:1	99
9	DABCO	50	34	5:1	98
10	DBU	100	Trace	ND[e]	ND

[a] Reaction conditions: unless specified, a mixture of cinnamaldehyde (0.2 mmol), catalyst (30 mol %), and 4 Å MS (100 mg) in chloroform (4 mL) was stirred for 30 min at room temperature before the arsonium salt and base were added, and then the stirring was continued for 24 h at room temperature.
[b] Isolated yield.
[c] Determined by chiral HPLC or ^1H NMR analysis.
[d] Determined by chiral HPLC analysis.
[e] Not determined.

Table 3. Scope of the organocatalytic enantioselective asymmetric cyclopropanation reaction of α,β-unsaturated aldehydes[a]



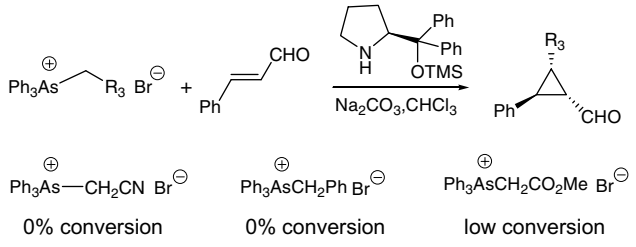
1 2 4

Entry	R_1	R_2	Product	% yield[b]	dr[c]	% ee[d]
1	H	Ph	**4a**	80	38:1	98
2	F	Ph	**4b**	73	11:1	97
3	Cl	Ph	**4c**	65	25:1	96
4	Br	Ph	**4d**	80	19:1	96
5	NO_2	Ph	**4e**	70	>99:1	98
6	Me	Ph	**4f**	51	5:1	98
7	MeO	Ph	**4g**	55	>99:1	98
8	H	Me	**4h**	50	2:1	78
9	H	*n*-Pr	**4i**	67	4:1	96
10	Br	*n*-Pr	**4j**	61	>99:1	95

[a] Reaction conditions: unless specified, a mixture of cinnamaldehyde (0.2 mmol), catalyst (30 mol %), and 4 Å MS (100 mg) in chloroform (4 mL) was stirred for 30 min at room temperature before the arsonium salt and Na_2CO_3 (50 mol %) were added, after which stirring was continued for 24 h at room temperature.
[b] Isolated yield.
[c] Diastereoselectivity determined by chiral HPLC or ^1H NMR analysis.
[d] Determined by chiral HPLC analysis.

Under the optimized reaction conditions above, the scope of the reaction between arsonium ylide reagents and α,β-unsaturated aldehydes was investigated. The results are summarized in Table 3. Generally, by using TMS-protected diphenylprolinol derivative **3** as the catalyst, the reactions between a range of readily available arsonium salts and α,β-unsaturated aldehydes provided cyclopropane products in moderate yields and excellent ee values. For example, arsonium salts **1** bearing electron-withdrawing groups (EWG) (R_1 = EWG) gave the corresponding cyclopropanes **4** in good yields (Table 3, entries 2–5), while arsonium salts **1** bearing electron-donating-groups (EDG) (R_1 = EDG) usually provided slightly lower yields of cyclopropanes **4** (Table 3, entries 6 and 7). In addition, as shown in Table 3, the reactions of aromatic α,β-unsaturated aldehyde worked well to provide the corresponding products with high enantioselectivity (96–98% ee, Table 3, entries 1–7), while the use of crotonaldehyde as a substrate resulted in poorer enantioselectivity (78% ee, Table 3, entry 8).

Other types of arsonium salts were also investigated under similar reaction conditions (Scheme 2). Unfortunately, replacing the benzoyl group with a nitrile group or a phenyl



Scheme 2. Other arsonium ylides applied in the organocatalytic cyclopropanations of α,β-unsaturated aldehydes.

group led to no reaction, and low conversion was observed for the arsonium salts with an ester group. We presume that it was due to the low acidity of the α-proton of these groups.

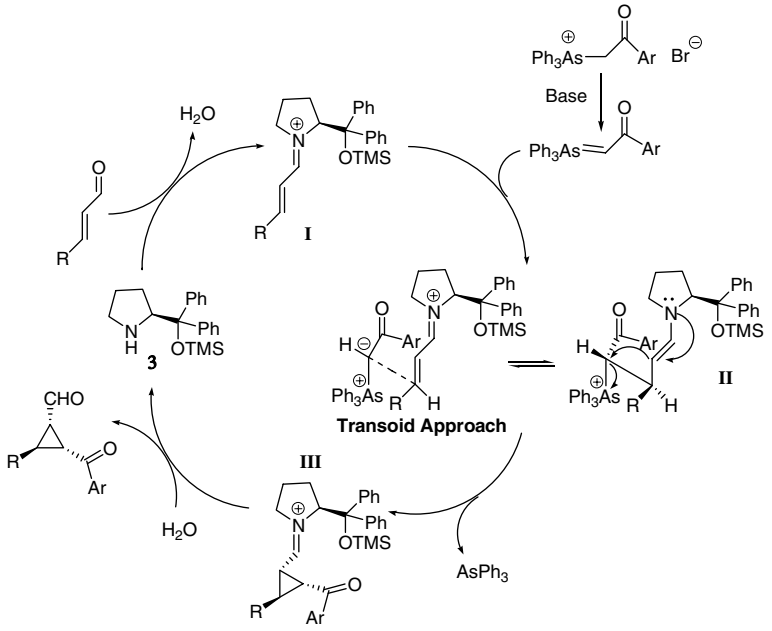
Based on the above results, a possible mechanism for the asymmetric organocatalytic cyclopropanation is proposed (Scheme 3). Firstly, the α,β-unsaturated aldehyde is activated by the amine catalyst **3** through the formation of the reactive iminium intermediate (I).[11c,d] Then, as a nucleophile, the arsonium ylides attack the β-carbon of the α,β-unsaturated aldehyde to form the enamine intermediate (II). An intramolecular S_N2 substitution takes place to form the cyclopropyl enamine intermediate (III). Finally, the intermediate (III) is hydrolyzed to produce the desired cyclopropane and release the amine catalyst **3** simultaneously.

3. Conclusion

In conclusion, we have developed a novel enantioselective organocatalytic cyclopropanation reaction between arsonium ylides and α,β-unsaturated aldehydes with a diphenylprolinol silyl ether as catalyst. The reaction conditions were very mild while the corresponding cyclopropanes could be obtained in moderate to good yields and with high enantioselectivities. Further applications of this new process in asymmetric synthesis are currently in progress.

4. Experimental

General: Analytical TLC was carried out on precoated silica gel plates. Column chromatography was conducted with 300–400 mesh silica gel. NMR spectra were recorded



Scheme 3. Mechanism of the asymmetric organocatalytic cyclopropanation of α,β-unsaturated aldehydes.

at 300 MHz for ^{1}H NMR using $SiMe_4$ as an internal standard in $CDCl_3$ and 75 MHz for ^{13}C NMR. Enantiomeric excesses were determined by chiral HPLC analysis. Optical rotations were measured on a JASCO 1030 polarimeter. All solvents were used directly without further purification.

4.1. General procedure for the organocatalytic asymmetric cyclopropanation of cyclopropyl aldehyde 4a

To a suspension of 100 mg of 4 Å MS in chloroform ($CHCl_3$, 4 mL) were added successively aldehydes (0.2 mmol) and TMS-protected diphenylprolinol derivative (20 mg, 0.06 mmol) at room temperature. After stirring for 30 min, 0.2 mmol of the arsonium salt and sodium carbonate (10.6 mg, 0.1 mmol) was added to the reaction mixture. The mixture was stirred at room temperature for 24 h until the starting material disappeared. The mixture was then eluted with CH_2Cl_2 (20 mL) through Celite; the filtrate was washed successively with HCl (0.5 M, 4 mL), saturated $NaHCO_3$ (2×8 mL), and brine (10 mL), and then dried over $MgSO_4$. Removal of the solvent under reduced pressure afforded the crude product. The latter was directly purified by flash chromatography on silica gel (CH_2Cl_2/hexane 2:3) to afford the pure cyclopropyl **4**, which was confirmed by the comparison of the ^{1}H NMR data with the reported one in the literature. The ee value was determined by chiral HPLC analysis.

4.2. (1*R*,2*S*,3*R*)-2-Benzoyl-3-phenyl- cyclopropanecarbaldehyde 4a[8]

Yellow oil; $[\alpha]_D^{25.5} = -167.7$ (*c* 1.0, $CHCl_3$); IR (film) 3063, 3035, 2855, 1709, 1676, 1598, 1582, 1458, 1377, 1224 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.59 (d, $J = 6.3$ Hz, 1H), 8.01–7.96 (m, 2H), 7.61–7.16 (m, 8H), 3.60 (dd, $J = 6.0$, 6.0 Hz, 1H), 3.48 (dd, $J = 6.0$, 9.1 Hz, 1H), 2.68 (ddd, $J = 6.0$, 6.3, 9.1 Hz, 1H); ^{13}C NMR and MS spectral data were reported in the literature.[8] The diastereomeric and enantiomeric ratios were determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel OJ column (22 °C, 254 nm, 90:10 hexane/2-propanol, 1 mL/min); $t_{major} = 26.8$ min, $t_{minor} = 21.7$ min.

4.3. (1*R*,2*S*,3*R*)-2-(4-Fluorobenzoyl)-3-phenyl-cyclopropanecarbaldehyde 4b

Yellow oil, $[\alpha]_D^{25.0} = -137.1$ (*c* 1.0, $CHCl_3$), IR (film) 3065, 3035, 2856, 2259, 1705, 1674, 1599, 1505, 1424, 1224, 1154, 851, 614 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 9.58 (d, 1H, $J = 6.3$ Hz), 8.01–8.05 (m, 2H), 7.14–7.40 (m, 7H), 3.61 (dd, 1H, $J = 6.0$, 6.0 Hz), 3.42 (dd, 1H, $J = 6.0$, 9.3 Hz), 2.69 (ddd, 1H, $J = 6.0$, 6.3, 9.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9, 193.7, 136.9, 131.3, 131.2, 129.0, 127.8, 126.6, 116.2, 115.9, 40.8, 36.8, 32.5; LRMS (EI): *m*/*e* 123, 95, 145, 239, 115, 212, 75, 117; HRMS (EI) exact mass calculated for ($C_{17}H_{13}FO_2$) requires *m*/*z* 268.0900, found *m*/*z* 268.0907. The diastereomeric and enantiomeric ratios were determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AS-H column (22 °C, 254 nm, 90:10 hexane/2-propanol, 1 mL/min); $t_{major} = 16.7$ min, $t_{minor} = 13.6$ min.

4.4. (1*R*,2*S*,3*R*)-2-(4-Chlorobenzoyl)-3-phenyl-cyclopropanecarbaldehyde 4c

Yellow oil, $[\alpha]_D^{26.3} = -86.4$ (*c* 1.0, $CHCl_3$), IR (film) 3052, 2926, 2844, 1705, 1673, 1589, 1505, 1427, 1403, 1224, 1126, 1092, 1012, 997, 754, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.57 (d, 1H, $J = 6.3$ Hz), 7.92–7.95 (d, 2H, $J = 8.1$ Hz), 7.21–7.48 (m, 7H), 3.61 (dd, 1H, $J = 6.0$, 6.0 Hz), 3.40 (dd, 1H, $J = 6.0$, 9.3 Hz), 2.69 (ddd, 1H, $J = 6.0$, 6.3, 9.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9, 194.0, 140.4, 136.9, 135.2, 129.9, 129.2,

129.0, 127.8, 126.6, 40.9, 36.8, 32.7; LRMS (EI) *m/e* 139, 111, 141, 115, 145, 75, 255, 113; HRMS (EI) exact mass calculated for ($C_{17}H_{13}ClO_2$) requires *m/z* 284.0604, found *m/z* 284.0596. The diastereomeric ratio was determined by ^{1}H NMR; the enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AS-H column (23 °C, 254 nm, 90:10 hexane/2-propanol, 1 mL/min); $t_{major} = 15.7$ min, $t_{minor} = 13.6$ min.

4.5. (1*R*,2*S*,3*R*)-2-(4-Bromobenzoyl)-3-phenyl-cyclopropanecarbaldehyde 4d

Yellow oil, $[\alpha]_D^{26.3} = -80.6$ (*c* 1.0, $CHCl_3$), IR (film) 2926, 2844, 1704, 1671, 1585, 1505, 1428, 1403, 1223, 1071, 996, 753, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.57 (d, 1H, $J = 6.0$ Hz), 7.86–7.84 (d, 2H, $J = 8.1$ Hz), 7.39–7.36 (d, 2H, $J = 8.7$ Hz), 7.39–7.20 (m, 5H), 3.61 (dd, 1H, $J = 6.0$, 6.0 Hz), 3.40 (dd, 1H, $J = 6.0$, 9.3 Hz), 2.69 (ddd, 1H, $J = 6.0$, 6.3, 9.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 197.9, 194.4, 136.7, 135.5, 132.2, 130.0, 129.2, 129.0, 127.8, 126.6, 40.9, 36.8, 32.7; LRMS (EI) *m/e* 183, 185, 115, 145, 155, 157, 192, 76; HRMS (EI) exact mass calculated for ($C_{17}H_{13}BrO_2$) requires *m/z* 328.0099, found *m/z* 328.0105. The diastereomeric and enantiomeric ratios were determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AS-H column (22 °C, 254 nm, 90:10 hexane/2-propanol, 1 mL/min); $t_{major} = 17.4$ min, $t_{minor} = 15.3$ min.

4.6. 1(*R*,2*S*,3*R*)-2-(4-Nitrobenzoyl)-3-phenyl-cyclopropanecarbaldehyde 4e

Yellow oil, $[\alpha]_D^{26.1} = -119.1$ (*c* 1.0, $CHCl_3$), IR (film) 3059, 2925, 2854, 1705, 1681, 1603, 1525, 1500, 1427, 1346, 1319, 1220, 998, 856, 741, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.55 (d, 1H, $J = 6.3$ Hz), 8.29–8.26 (d, 2H, $J = 8.1$ Hz), 8.09–8.06 (d, 2H, $J = 9.0$ Hz), 7.30–7.16 (m, 5H), 3.58 (dd, 1H, $J = 6.0$, 6.0 Hz), 3.38 (dd, 1H, $J = 6.0$, 9.1 Hz), 2.71 (ddd, 1H, $J = 6.0$, 6.3, 9.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.4, 194.2, 141.1, 136.3, 129.9, 129.5, 129.1, 128.1, 126.5, 124.1, 41.0, 37.2, 33.2; LRMS (EI) *m/e* (rel %) 135 (100), 150 (34), 77 (31), 115 (31), 266 (24), 145 (22), 92 (20), 104 (19); HRMS (EI) exact mass calculated for ($C_{17}H_{13}NO_4$) requires *m/z* 295.0845, found *m/z* 295.0836. The diastereomeric ratio was determined by ^{1}H NMR. The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AS-H column (23 °C, 254 nm, 90:10 hexane/2-propanol, 1 mL/min); $t_{major} = 36.2$ min, $t_{minor} = 26.9$ min.

4.7. (1*R*,2*S*,3*R*)-2-(4-Methylbenzoyl)-3-phenyl-cyclopropanecarbaldehyde 4f

Yellow oil, $[\alpha]_D^{25.8} = -81.4$ (*c* 1.0, $CHCl_3$), IR (film) 3030, 2926, 2852, 1704, 1667, 1606, 1500, 1428, 1360, 1231, 1183, 753, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.58 (d, 1H, $J = 6.3$ Hz), 7.91–7.89 (d, 2H, $J = 8.4$ Hz), 7.36–7.21 (m, 7H), 3.60 (dd, 1H, $J = 6.0$, 6.0 Hz), 3.47 (dd, 1H, $J = 6.0$, 9.1 Hz), 2.66 (ddd, 1H, $J = 6.0$, 6.3, 9.1 Hz), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.3, 194.7, 145.2, 137.1, 134.3, 129.6, 129.0, 128.7, 127.6, 126.6, 40.9, 36.8, 32.4, 21.8; LRMS (EI) *m/e* 119, 91, 115, 65, 221, 235, 120, 208; HRMS (EI) exact mass calculated for ($C_{18}H_{16}O_2$) requires *m/z* 264.1150, found *m/z* 264.1157. The diastereomeric ratio was determined by ^{1}H NMR. The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AS-H column (21 °C, 254 nm, 90:10 hexane/2-propanol, 1 mL/min); $t_{major} = 17.8$ min, $t_{minor} = 15.1$ min.

4.8. (1*R*,2*S*,3*R*)-2-(4-Methoxylbenzoyl)-3-phenyl-cyclopropanecarbaldehyde 4g

Yellow oil, $[\alpha]_D^{24.7} = -174.6$ (*c* 1.0, $CHCl_3$), IR (film) 2933, 2837, 1703, 1662, 1585, 1510, 1428, 1355, 1261, 1235, 1167 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.57 (d, 1H, $J = 6.3$ Hz), 8.00–7.97 (d, 2H, $J = 8.7$ Hz), 7.36–7.26 (m, 5H), 6.97–6.94 (d, 2H, $J = 8.7$ Hz), 3.88 (s, 3H), 3.58 (dd, 1H, $J = 6.0$, 6.0 Hz), 3.44 (dd, 1H, $J = 6.0$, 9.1 Hz), 2.68 (ddd, 1H, $J = 6.0$, 6.3, 9.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.4, 193.4, 164.1, 137.2, 130.9, 129.9, 128.9, 127.6, 126.6, 114.0, 55.6, 40.8, 36.7, 32.2; LRMS (EI) *m/e* 135, 77, 115, 107, 92, 136, 251, 224; HRMS (EI) exact mass calculated for ($C_{18}H_{16}O_3$) requires *m/z* 280.1099, found *m/z* 280.1092. The diastereomeric and enantiomeric ratios were determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel OD-H column (22 °C, 254 nm, 90:10 hexane/2-propanol, 1 mL/min); $t_{major} = 18.2$ min and $t_{minor} = 21.3$ min.

4.9. (1*R*,2*S*,3*R*)-2-Benzoyl-3-methyl-cyclopropanecarbaldehyde 4h[8]

Light yellow oil, $[\alpha]_D^{24.9} = -6.1$ (*c* 1.0, $CHCl_3$), IR (film) 3061, 2966, 2931, 1709, 1673, 1598, 1581, 1450, 1226, 1074, 1021 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.36 (d, 1H, $J = 6.3$ Hz), 7.99–7.97 (d, 2H, $J = 7.8$ Hz), 7.63–7.26 (m, 3H), 3.00 (dd, 1H, $J = 6.0$, 8.5 Hz), 2.56 (m, 1H), 2.10 (ddd, 1H, $J = 6.3$, 6.3, 8.7 Hz), 1.36 (d, 3H, $J = 6.0$ Hz); ^{13}C NMR and MS spectral data were reported in the literature.[8] The diastereomeric ratio was determined by ^{1}H NMR. The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel OD column (23 °C, 254 nm, 90:10 hexane/2-propanol, 1 mL/min); $t_{major} = 11.5$ min, $t_{minor} = 10.8$ min.

4.10. (1*R*,2*S*,3*R*)-2-Benzoyl-3-propyl-cyclopropanecarbaldehyde 4i[8]

Light yellow oil, $[\alpha]_D^{25.4} = -16.4$ (*c* 1.0, $CHCl_3$), IR (film) 2959, 2929, 2872, 1706, 1667, 1609, 1579, 1449, 1371, 1264, 1227, 1178, 1011 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.37 (d, 1H, $J = 6.3$ Hz), 8.03–7.97 (m, 2H), 7.63–7.26 (m, 3H), 3.00 (dd, 1H, $J = 5.9$, 8.3 Hz), 2.55–2.53 (m, 1H), 2.16–2.09 (m, 1H), 1.60–1.46 (m, 4H), 0.96 (m, 3H); ^{13}C NMR and MS spectral data were reported in the literature.[8] The diastereomeric ratio was determined by ^{1}H NMR. The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of

the aldehyde, using a Chiracel AD column (21 °C, 254 nm, 90:10 hexane/2-propanol, 1 mL/min); $t_{major} = 13.7$ min, $t_{minor} = 15.1$ min.

4.11. (1*R*,2*S*,3*R*)-2-(4-Bromobenzoyl)-3-propyl-cyclopropanecarbaldehyde 4j

Yellow oil, $[\alpha]_D^{26.5} = -38.6$ (*c* 1.0, $CHCl_3$), IR (film) 2960, 2929, 2872, 1704, 1670, 1585, 1568, 1437, 1400, 1362, 1221, 1174, 1070, 1026, 1008, 994, 844, 784 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.36 (d, 1H, $J = 6.3$ Hz), 7.87–7.83 (dd, 2H, $J = 8.4$, 10.5 Hz), 7.65–7.62 (d, 2H), 2.98–2.94 (dd, 1H, $J = 5.9$, 8.2 Hz), 2.54–2.48 (m, 1H), 2.17–2.10 (m, 1H), 1.62–1.46 (m, 4H), 0.96 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.1, 195.2, 135.8, 132.1, 129.8, 129.0, 40.1, 34.5, 34.1, 29.4, 22.0, 13.7; LRMS (EI) *m*/*e* 183, 253, 144, 157, 41; HRMS (EI) exact mass calculated for ($C_{14}H_{15}BrO_2$) requires *m*/*z* 294.0255, found *m*/*z* 294.0249. The diastereomeric and enantiomeric ratios were determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel OD-H column (21 °C, 254 nm, 90:10 hexane/2-propanol, 1 mL/min); $t_{major} = 16.8$ min, $t_{minor} = 18.4$ min.

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13. Preliminary studies revealed that product **4a** could undergo further Witting type reactions in the presence of an excess of arsonium salt under our reaction conditions. Further thorough study is currently in progress and will be reported in due time.