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The first organocatalyst-mediated enantioselective substitution of racemic iodoalkanes under radical conditions

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ABSTRACT

We have demonstrated for the first time an organocatalyst-mediated enantioselective substitution of racemic iodoalkanes at either a tertiary or a secondary stereogenic center leading to the corresponding optically active products with a tertiary or a quaternary allylated stereogenic center under radical conditions.

1. Introduction

Asymmetric induction in radical reactions has been a focus in synthetic organic chemistry over the last few decades.[1] There have been reports of a number of stereoselective radical reactions, some of which have led to the establishment of optically active products.[2] However, there were no reports concerning asymmetric induction in organocatalyst-mediated radical reactions, until we reported the enantioselective allylation of some racemic precursors under radical conditions in the presence of an organocatalyst.[3] In principle, radical reactions proceed under neutral conditions without the requirement of any metallic catalysts serving as a Lewis acid or a Lewis base, which were previously used in enantioselective radical reactions. We, therefore, explored a radical method allowing introduction of tertiary and quaternary stereogenic centers in an enantioselective manner by using a chiral organocatalyst in place of a metallic catalyst, in order to extend radical methods of enantiocontrolled synthesis.[4] In this paper, we report our finding that the expected enantioselective reaction took place when a racemic iodoalkane was allylated under radical conditions in the presence of a chiral organocatalyst having a Bronsted acidic nature to give rise to the optically active products carrying either a tertiary or a quaternary stereogenic center. Herein, we also report this first example of an organocatalyst-mediated enantioselective radical allylation in detail.

2. Results and discussion

We have already established a chiral Lewis acid-mediated enantioselective allylation via a prochiral radical center generated from racemic 3-iodo-3,4-dihydrocoumarins **1** with allyltributylstannane.[5] The enantioselectivity in this reaction is ascribed to coordination between the carbonyl oxygen of the radical intermediates generated from the racemic **1** and the chiral Lewis acid, which endows chirality to the prochiral radical center (Fig. 1a). If we use a catalyst which is presumed to be capable of allowing hydrogen bonding at the appropriate center(s), a similar effect to that brought about by Lewis acid coordination may be expected (Fig. 1b).[6] Thus, we sought a chiral organic molecule capable of hydrogen bonding under the radical allylation conditions of the prochiral radical intermediates, using the racemic 3-iodo-3,4-dihydrocoumarin derivatives **1a–d** as substrates (Scheme 1, Fig. 2).

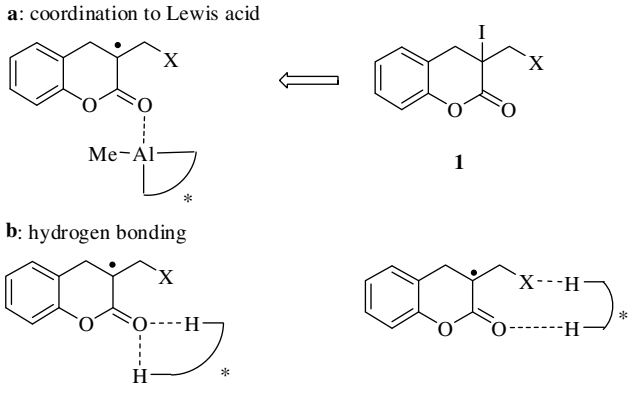

Figure 1. Radicals complexed with chiral compounds.

We chose five *C*2-symmetric chiral molecules **3a–e** carrying two active hydrogens as the organic catalysts so as to form the hydrogen bonding required for chiral induction.[7] Thus, in each reaction, a 1.2 M excess of catalyst was present, together with 1.0 M equiv of dihydrocoumarin substrates **1a–d**, allyltributyltin,

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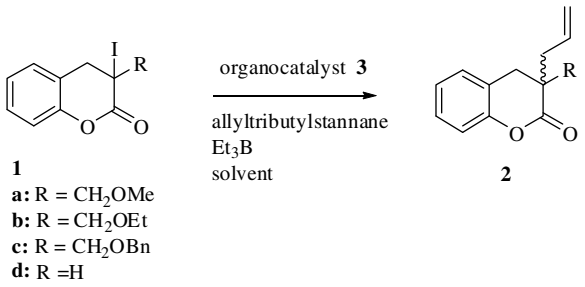
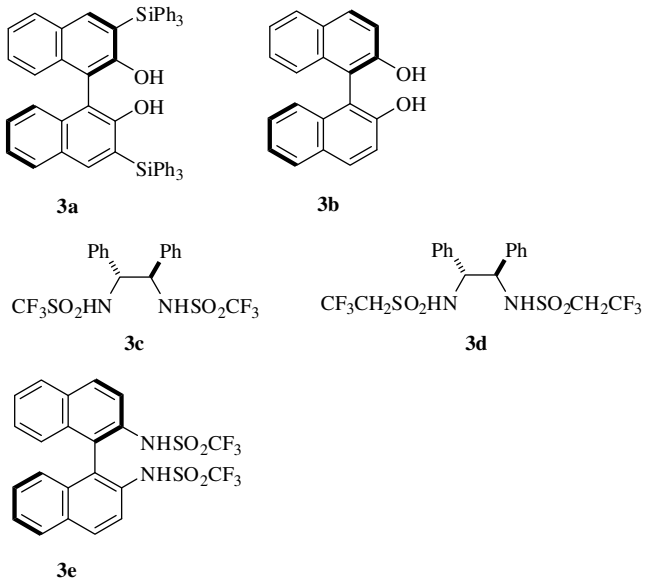


1
a: R = CH_2OMe
b: R = CH_2OEt
c: R = CH_2OBn
d: R =H

2

Scheme 1. Enantioselective allylations of **1** under radical conditions in the presence of organocatalysts **3**.



3a **3b** **3c** **3d** **3e**

Figure 2. Structures of organocatalysts **3**.

and the radical initiator triethylborane.[8] The results are summarized in Table 1.

The reaction was first examined using two BINOL derivatives **3a**,**b** as organocatalysts. The reaction of the substrate iodide **1a** with (*R*)-triphenylsilyl BINOL **3a**, [the Al(III) complex of which generates **2a** with high enantioselectivity[5a]] exhibited no enantioselective induction in CH_2Cl_2 at −78 °C, although the expected transformation proceeded to give the racemic quaternary allylation product **2a** in satisfactory yield (entry 1). However, when (*R*)-BINOL **3b** was used under the same conditions, the expected chiral induction took place to give optically active **2a** in 72% yield, which was found to be a 4% ee (entry 2). The reaction in the presence of sulfonamides **3c–e** was examined next.[9] When bis-trifluoromethylsulfonamide **3c** was present in the reaction of **1a** in CH_2Cl_2 at −78 °C, the chiral induction ratio was increased to give product **2a** in 72% yield with 15% ee (entry 3). Under the same conditions, benzyl ether **1c** afforded the expected product **2c** in 75% yield with 10% ee (entry 4). The enantiomeric induction ratios observed with these two reactions were too low to be of practical use. However, these should be noted as the first instances involving not only organocatalyst-mediated asymmetric induction, but also the generation of a prochiral radical stereogenic center directly from a racemic halogeno-carbon stereogenic center.[10] Although some organocatalyst-mediated enantioselective radical reactions have been reported since our findings, no chiral induction reaction at the racemic stereogenic center via a prochiral radical intermediate has been reported to date.

Table 1
Enantioselective allylations of iododihydrocoumarins **1** to generate **2** under radical conditions in the presence of oraganocatalysts **3**[a]

Entry	Substrate **1**	Organocatalyst **3**	Solvent	Product **2** yield[b] (%)	ee (%)	Confign
1	**1a**	**3a**	CH_2Cl_2	71	0	—
2	**1a**	**3b**	CH_2Cl_2	72	4	(*R*)
3	**1a**	**3c**	CH_2Cl_2	72	15	(*R*)
4	**1c**	**3c**	CH_2Cl_2	75	10	(*R*)
5	**1a**	**3d**	CH_2Cl_2	68	1	(*R*)
6	**1a**	**3e**	CH_2Cl_2	75	30	(*S*)
7[c]	**1a**	**3e**	CH_2Cl_2	71	29	(*S*)
8	**1b**	**3e**	CH_2Cl_2	77	16	(*S*)
9	**1c**	**3e**	CH_2Cl_2	68	11	(*S*)
10	**1a**	**3e**	Toluene	69	11	(*S*)
11[d]	**1a**	**3e**	Toluene	50	6	(*S*)
12	**1d**	**3e**	CH_2Cl_2	63	20	(*S*)

[a] 1.2 equiv of catalysts were used (**3**:**1** = 1.2:1). All reactions were carried out by using 1.0 equiv each of allyltributyltin and Et_3B for a substrate at −78 °C, unless otherwise noted.
[b] Isolated yield.
[c] The reaction was carried out by using 3.0 equiv of allyltributyltin.
[d] Reaction was carried out at −50 °C.

Encouraged by these findings, and to improve the chiral induction ratio we further examined the reaction of **1a** using other organocatalysts **3d** and **e**. Among these, the best result was obtained when the reaction was carried out in the presence of a 1.2 M equiv of the bistrifluorosulfonamide-substituted binapthyl **3e** (entry 6) though the enantioselectivity of **2a** attained (at best 30% ee) was still less than satisfactory. It is noteworthy that the use of an excess of allyltributyltin (3 equiv) did not affect either chemical yield or enantioselectivity (entry 7), which seemed to support a hydrogen bonding mechanism (Fig. 1b); in the absence of such a mechanism, a reduced enantiomeric excess would be expected.[11]

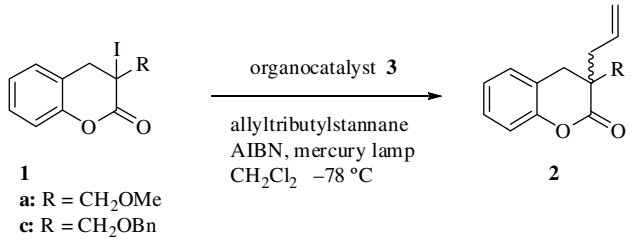
The same catalyst also brought about chiral induction when both the ethyl analogue **1b** and the benzyl analogue **1c** were treated under the same conditions to give the corresponding optically active products **2b** and **2c**, although both were obtained with lower enantioselectivity than **1a** (entries 8 and 9). On the other hand, organocatalyst **3d**, a one-carbon homologue of **3c**, was found to bring about chiral induction under the same conditions. However, it could not compete with the corresponding nor-analogue **3c**, either in chemical yield or in enantiomeric excess (entries 5). These findings indicate that the homologation prevented the formation of the favorable hydrogen bonding (Fig. 1b) by increasing steric congestion of both the substrates and the catalyst and by diminishing the amide acidity of the catalysts.

Owing to the insolubility of the organocatalyst **3e**, the reaction could not be fully examined in toluene, although tighter hydrogen bonding leading to better enantiomeric induction would be expected in this solvent (Fig. 1b) (entries 10 and 11).

The present method was also found to be promising for the enantiocontrolled construction of a tertiary stereogenic center. Thus, the secondary iodide **1d** treated under the same conditions as for **1a** in the presence of the organocatalyst **3e** afforded product **2d** with a tertiary stereogenic center in 63% yield with chiral induction of 20% ee (entry 12).

It is known that borane species derived from triethylborane during the reaction act as Lewis acids.[12] Thus, chiral borane species could have been generated under the present radical conditions by the reaction with chiral organocatalysts **3** present in the reaction medium. We therefore examined the organocatalyst-mediated reaction using AIBN as the radical initiator under photolysis conditions in place of using the boron radical initiator, to alleviate the possibility of the generation of a boron complex serving as a Lewis

acid. Thus, both **1a** and **1c** were reacted with allyltributylstannane in the presence of AIBN and the organocatalyst **3** under irradiation using a mercury lamp in CH_2Cl_2 at −78 °C. The expected reaction occurred to give the allylated products, **2a** with 23% ee from **1a** with **3e**, and **2c** with 8% ee from **1c** with **3c**, respectively. Since the enantioselectivities observed were comparable to those observed by using triethylborane (entries 4 and 6), it can be concluded that the boron radical initiator does not participate in the enantiocontrol (Scheme 2).



Scheme 2. Photochemical enantioselective organocatalyst-mediated allylations of **1** using **3**.

The absolute configuration of the optically active product with a tertiary stereogenic center **2d** was determined by correlation with (*S*)-propyldihydrocoumarin **9**, which was prepared from (*R*)-2-benzyl-3-hydroxypropyl acetate **4**[13] as follows: compound (*R*)-**4** was first converted into tosyloxypropyl acetate **5** whose tosyloxy group was next replaced by an ethyl group using a cuprate reagent, to give 2-benzylpentanol **6** after deacetylation. Jones oxidation of **6** gave carboxylic acid **7**, which after transformation into the acid chloride was subjected to a Friedel–Crafts reaction to readily yield indanone **8**, though some racemization occurred. Baeyer–Villiger oxidation of **8** with *m*-CPBA proceeded regioselectively to afford (*S*)-3-propyl-3,4-dihydrocoumarin **9** whose enantiomeric purity was determined to be 61% ee by HPLC analysis. This compound was compared with product **9** generated by catalytic hydrogenation of **2d** to determine the absolute configuration of the latter as (*S*) (Scheme 3).

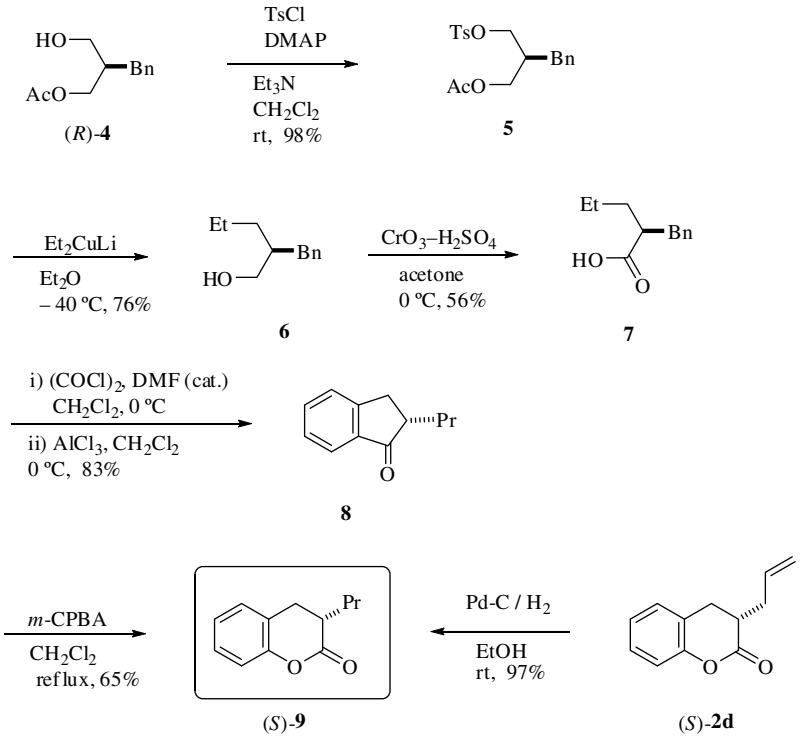
3. Conclusion

In conclusion, we have demonstrated an enantioselective allylation reaction which formed quaternary and tertiary stereogenic centers through generation of prochiral radical centers starting from a corresponding racemic iodo-alkane precursor in the presence of an optically active organocatalyst having Bronsted acidic nature. Although the enantioselectivity attained is still too low to be of practical use, the demonstration of the present reaction which allows the enantioselective modification of a tertiary and a quaternary prochiral radical center is noteworthy and promising for its future use in radical chemistry.

4. Experimental

4.1. General

All melting points were measured on a Yanagimoto (hot plate) melting point apparatus, and are uncorrected. IR spectra were obtained with a Horiba FT-210 spectrophotometer or a JASCO FT/IR-410 spectrophotometer. ^{1}H NMR (270 MHz, 400 MHz or 500 MHz) and ^{13}C NMR (67.5 MHz, 100 MHz or 125 MHz) spectra were recorded with a JEOL EX 270 spectrometer, a JEOL JNM-LA400 spectrometer or a JEOL JNM-LA500 spectrometer in CDCl3 solution using tetramethylsilane as an internal standard, unless otherwise noted. Mass spectra were measured on a JEOL JMS-SX102A spectrometer. Specific rotation was measured on a JASCO P-1030 digital polarimeter. The enantiomeric excess (ee) of **2** and **9** was determined by HPLC analysis using chiral columns (DAICEL). Column chromatography was performed on silica gel. Thin-layer chromatography was carried out on precoated (0.2 mm) Merck Silica Gel F-254 plates. Photochemical reactions were performed by using micro photochemical reaction assembly (Sigma–Aldrich).



Scheme 3. Determination of the absolute configuration of **2d**.

4.2. Preparation of 3-iodo-3,4-dihydrocoumarins 1a–d and organocatalysts 3a–e

3-Iodo-3,4-dihydrocoumarins **1a–c** and organocatalysts **3a**, **c–e** were prepared according to the method described in the literature.[5,8]

(*R*)-BINOL **3b** was obtained from commercial sources and used without further purification.

4.2.1. 3-Iodo-3,4-dihydrocoumarin 1d

Under an argon atmosphere, a solution of 3,4-dihydrocoumarin (3 g, 20.3 mmol) in THF (30 mL) was added to a preformed solution of LDA (22.3 mmol) in THF (50 mL) at −78 °C, and the mixture was stirred for 30 min. This solution was added to a solution of I_2 (7.7 g, 30.3 mmol) in THF (30 mL) at −78 °C, and the mixture was stirred at the same temperature for 30 min. After the addition of 10% HCl, the resulting solution was extracted with Et_2O (100 mL × 2). The organic layer was washed with water, 5% aqueous $Na_2S_2O_3$, aqueous $NaHCO_3$, and brine successively, and dried over $MgSO_4$. Concentration followed by purification through silica gel column chromatography (benzene) gave **1d** (4.2 g, 76%). Colorless crystals: mp 165–166 °C. ^{1}H NMR (270 MHz) δ 3.11 (1H, dd, J = 17.5, 2.7 Hz), 3.49 (1H, dd, J = 17.5, 4.4 Hz), 4.95 (1H, dd, J = 4.4, 2.7 Hz), 7.10–7.20 (3H, m), 7.32–7.40 (1H, m). ^{13}C NMR (67.5 MHz) δ 12.6, 34.9, 116.8, 120.3, 125.0, 128.6, 129.0, 151.5, 165.0. IR (KBr) 3066, 2950, 1751, 1728, 1616, 1171 cm^{-1}. MS m/z 274 (M^+); HRMS calcd for $C_9H_7IO_2$ 273.9491 (M^+), found 273.9499 (M^+).

4.3. Enantioselective allylations

The ees and configurations of **2a–c** were determined directly by HPLC using a chiral column. Spectroscopic data were identical with those for the products described in the literature.[5a] The ee of **2d** was determined directly by HPLC using Chiralcel OD. The configuration was determined by chemical correlation with (*S*)-3-propyl-3,4-dihydrocoumarin **9**. See Scheme 3 for the determination of the absolute configuration of **2d**.

4.3.1. Enantioselective allylations with triethylborane: typical procedure

A solution of (±)-3-iodo-3-methoxymethyldihydrocoumarin **1a** (31.8 mg, 0.1 mmol) and organocatalyst (*R*)-**3e** (65.8 mg, 0.12 mmol) in CH_2Cl_2 (2 mL) was cooled to −78 °C, and the mixture was stirred for 30 min at −78 °C. Allyltributyltin (31 μL, 0.1 mmol) and a solution of triethylborane in hexane (1 M: 0.1 mL, 0.1 mmol) were added successively at −78 °C, and the mixture was allowed to stand for 1 h at the same temperature. After the addition of AcOH (0.1 mL) at −78 °C, the mixture was stirred for 1 h. H_2O was added, and the mixture was extracted with CH_2Cl_2 (20 mL × 2). The organic layer was washed with saturated aqueous $NaHCO_3$ and brine successively, and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure. The residue was taken up in MeCN. The mixture was washed with hexane. Concentration followed by purification through column chromatography (benzene) gave (*S*)-**2a** as colorless oil [17.4 mg, 75%, 30% ee (HPLC: Chiralcel OD, hexane–2-propanol = 50:1, flow rate 0.5 mL/min, Rt 16 min for (*R*)-isomer and 18 min for (*S*)-isomer)].

(*S*)-2d. Colorless oil: bp 130–150 °C/1.5 mmHg (bulb-to-bulb distillation). $[\alpha]_D^{23} = +11.4$ (c 1.47, $CHCl_3$); 20% ee (HPLC: Chiralcel OD, hexane–2-propanol = 50:1, flow rate 0.5 mL/min, Rt 20 min for (*R*)-isomer and 22 min for (*S*)-isomer)]. ^{1}H NMR (270 MHz) δ 2.30–2.41 (1H, m), 2.66–2.87 (3H, m), 2.93–3.07 (1H, m), 5.10–5.17 (2H, m), 5.77–5.92 (1H, m), 7.02–7.28 (4H, m). ^{13}C NMR (67.5 MHz) δ 28.6, 33.9, 38.7, 116.6, 118.2, 122.5, 124.3, 128.1, 128.2, 134.3, 151.6, 170.4. IR (NaCl) 3078, 3014, 2980, 2920, 2848, 1770, 1643, 1615, 1589, 1147 cm^{-1}. MS m/z 188 (M^+); HRMS calcd for $C_{12}H_{12}O_2$ 188.0836 (M^+), found 188.0827 (M^+).

4.3.2. Enantioselective allylations by photochemical reactions (without triethylborane)

Compound (*S*)-**2a**. A solution of (±)-3-iodo-3-methoxymethyldihydrocoumarin **1a** (31.8 mg, 0.1 mmol) and organocatalyst (*R*)-**3e** (65.8 mg, 0.12 mmol) in CH_2Cl_2 (4 mL) was cooled to −78 °C, and the mixture was stirred for 30 min at −78 °C. Allyltributyltin (31 μL, 0.1 mmol) and AIBN (7 mg, 0.04 mmol) were added successively at −78 °C. The resulting solution was irradiated (5.5 W, mercury lamp) at −78 °C for 2 h. Additional AIBN (7 mg, 0.04 mmol) was added, and then the solution was irradiated (5.5 W, mercury lamp) at −78 °C for 60 min. The solvent was removed under reduced pressure. Concentration followed by purification through column chromatography (benzene) gave (*S*)-**2a** as colorless oil [10.6 mg, 46%, 23% ee [HPLC: Chiralcel OD, hexane–2-propanol = 50:1, flow rate 0.5 mL/min, Rt 17 min for (*R*)-isomer and 19 min for (*S*)-isomer)].

Compound (*R*)-**2c**. The reaction was carried out by the same method described for (*S*)-**2a** using α-iodo-α-benzyloxymethyldihydrocoumarin **1c** (39.7 mg, 0.1 mmol) and organocatalyst (*S,S*)-**3c** (52.8 mg, 0.11 mmol) in CH_2Cl_2 (4 mL). The crude product was purified by column chromatography (benzene) and gave (*R*)-**2c** as a colorless oil [10.3 mg, 41%, 8% ee [HPLC: Chiralcel OJ, hexane–2-propanol = 9:1, flow rate 1.0 mL/min, Rt 16 min for (*S*)-isomer and 23 min for (*R*)-isomer)].

4.4. Determination of the absolute configuration of 2d

The absolute configuration of **2d** was determined by chemical correlation with (*S*)-3-propyldihydrocoumarin **9** as shown in Scheme 3. Authentic (*S*)-**9** was synthesized from (*R*)-2-benzyl-3-hydroxypropyl acetate **4** {enantiomeric excess: 97%; $[\alpha]_D$ = +28 (c 1.32, $CHCl_3$)} prepared according to the literatures.[13]

4.4.1. (*S*)-2-Benzyl-3-toluenesulfonyloxypropyl acetate 5

Colorless solid. $[\alpha]_D$ = +4.8 (c 1.13, $CHCl_3$). ^{1}H NMR (270 MHz) δ 1.96 (3H, s), 2.22–2.32 (1H, m), 2.46 (3H, s), 2.64 (2H, dd, J = 7.6, 2.3 Hz), 3.89–5.30 (4H, m), 7.04–7.07 (2H, m), 7.19–7.28 (3H, m), 7.34 (2H, d, J = 8.3 Hz), 7.77 (2H, d, J = 8.3 Hz). ^{13}C NMR (67.5 MHz) δ 20.7, 21.6, 33.9, 39.5, 63.0, 68.9, 126.6, 128.0, 128.6, 128.95, 129.86, 132.7, 138.0, 144.9, 177.6. IR (KBr) 3089, 3060, 3032, 2972, 2960, 2929, 2901, 2867, 1733, 1654, 1561, 1544 cm^{-1}. MS m/z 363 (M^+); HRMS calcd for $C_{19}H_{23}O_5S$ 363.1266 (M+), found 363.1259 (M^+).

4.4.2. (*S*)-2-Benzylpentanol 6

Colorless oil: bp 145–155 °C/2 mm Hg (bulb-to-bulb distillation). $[\alpha]_D$ = −9.9 (c 1.09, MeOH). ^{1}H NMR (270 MHz) δ 0.90 (3H, t, J = 6.9 Hz), 1.25–1.46 (4H, m), 1.74–1.88 (1H, m), 2.63 (2H, d, J = 7.3 Hz), 3.52 (2H, d, J = 5.0 Hz), 7.17–7.21 (3H, m), 7.27–7.31 (2H, m). ^{13}C NMR (67.5 MHz) δ 14.3, 20.1, 33.1, 37.7, 42.4, 64.9, 125.8, 128.3, 129.2, 140.9. IR (NaCl) 3349, 3085, 3062, 3025, 2958, 2927, 2869, 1603 cm^{-1}. MS m/z 178 (M^+); HRMS calcd for $C_{12}H_{18}O$ 178.1357 (M^+), found 178.1362 (M^+).

4.4.3. (*S*)-2-Benzylpentanoic acid 7

Colorless oil. $[\alpha]_D$ = +19.5 (c 2.21, c-hexane). ^{1}H NMR (270 MHz) δ 0.90 (3H, t, J = 7.1 Hz), 1.28–1.71 (4H, m), 2.62–2.70 (1H, m), 2.75 (1H, dd, J = 13.2, 6.9 Hz), 2.97 (1H, dd, J = 13.2, 7.6 Hz), 7.16–7.31 (5H, m). ^{13}C NMR (67.5 MHz) δ 13.9, 20.4, 33.9, 38.1, 47.2, 126.4, 128.4, 128.9, 139.2, 182.1. IR (NaCl) 3366, 3028, 2960, 2926, 2871, 1705, 1603 cm^{-1}. MS m/z 192 (M^+); HRMS calcd for $C_{12}H_{16}O_2$ 192.1149 (M^+), found 192.1140 (M^+).

4.4.4. (*S*)-2-Propylindanone 8

Colorless oil: bp 140–150 °C/4 mm Hg (bulb-to-bulb distillation). $[\alpha]_D$ = +32.5 (*c* 0.71, benzene). ^{1}H NMR (270 MHz) δ 0.96 (3H, t, *J* = 7.1 Hz), 1.39–1.54 (3H, m), 1.83–2.01 (1H, m), 2.61–2.72 (1H, m), 2.81 (1H, dd, *J* = 17.2, 3.8 Hz), 3.31 (1H, dd, *J* = 17.2, 7.9 Hz), 7.33–7.76 (4H, m). ^{13}C NMR (67.5 MHz) δ 14.1, 20.7, 32.9, 33.6, 47.3, 123.9, 126.5, 127.3, 134.6, 136.9, 153.8, 209.1. IR (NaCl) 3072, 2961, 2928, 2870, 1712, 1609, 1589 cm^{-1}. MS *m*/*z* 174 (M^+); HRMS calcd for $C_{12}H_{14}O$ 174.1045 (M^+), found 174.1047 (M^+).

4.4.5. (*S*)-3-Propyldihydrocoumarin 9

Colorless oil: bp 140–150 °C/3 mm Hg (bulb-to-bulb distillation). $[\alpha]_D$ = −12.4 (*c* 1.25, $CHCl_3$); 61% ee (HPLC: Chiralcel OD, hexane–2-propanol = 50:1, flow rate 0.5 mL/min, Rt 18 min for (*R*)-isomer and 20 min for (*S*)-isomer)]. ^{1}H NMR (270 MHz) δ 0.95 (3H, t, *J* = 7.1 Hz), 1.41–1.62 (3H, m), 1.84–1.96 (1H, m), 2.64–2.84 (2H, m), 3.03 (1H, dd, *J* = 15.1, 5.3 Hz), 7.00–7.11 (2H, m), 7.16–7.26 (2H, m). ^{13}C NMR (125 MHz) δ 13.8, 20.0, 29.2, 31.8, 38.9, 116.5, 122.6, 124.2, 128.1, 128.2, 151.6, 171.0. IR (NaCl) 3043, 2960, 2930, 2871, 1769, 1724, 1615, 1589 cm^{-1}. MS *m*/*z* 190 (M^+); HRMS calcd for $C_{12}H_{14}O_2$ 190.0992 (M^+), found 190.0980 (M^+).

4.4.6. Conversion of (*S*)-3-allyldihydrocoumarin 2d into (*S*)-3-propyldihydrocoumarin 9

A solution of (*S*)-**2d** (obtained by enatioselective allylation; 20% ee; 9.4 mg, 0.05 mmol) in EtOH (3 mL) was hydrogenated over 10% Pd–C (10 mg) under H_2 (1 atm) at room temperature for 3 h. After filtration, the solvent was removed under reduced pressure to give (*S*)-**9** as a colorless oil [9.2 mg, 97%, 20% ee (HPLC: Chiralcel OD, hexane–2-propanol = 50:1, flow rate 0.5 mL/min, Rt 18 min for (*R*)-isomer and 20 min for (*S*)-isomer)]. Spectroscopic data were identical with those for the product (*S*)-**9** obtained from (*R*)-2-benzyl-3-hydroxypropyl acetate **4**.

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7. Although it was found that the chiral molecules were required in more than a stoichiometric amount to induce the enantioselectivity effectively, we use the term 'catalyst' or 'organocatalyst' for each of these compounds as an external substance that leads a substrate to a particular product without changing itself.
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9. These chiral sulfonamides gave moderate enantiomeric excess in the enantioselective allylations catalyzed by an aluminum reagent, see: Ref. 5b.
10. After this observation, some organocatalyst-mediated enantioselective radical syntheses have appeared, but they did not intervene in a prochiral radical stereogenic center directly generated from a racemic halogeno-carbon stereogenic center, see: Ref. 4b.
11. The enantioselectivity would decrease under excess tin reagent conditions when chiral tin reagents, formed by coordination of (*R*)-**3e**, are responsible for enantioselection, because achiral tin exists much more in stoichiometric conditions. However, the enantioselectivity in entry 7 strongly indicates that chiral tin reagents did not produce and/or influence the asymmetric induction in this system.
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