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Pseudo-C_3-symmetric trisoxazolines as ligands in copper catalyzed enantioselective Diels–Alder reaction

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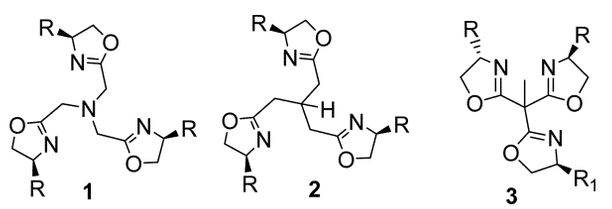
Air- and water-stable chiral catalyst trisoxazolines **4**–**6**/$Cu(ClO_4)_2 \cdot 6H_2O$ have been used in the Diels–Alder reaction of cyclopentadiene with acryloyl-2-oxazolidinones or ketoesters. The reaction is carried out in air and up to 82% ee was achieved.

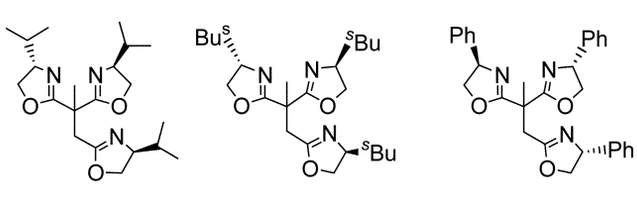
Introduction

The creation of new ligand motifs is very important in the design of superior catalysts.[1] Inspired by the great success of C_2-symmetric ligands in asymmetric catalysis,[2] there is burgeoning interest in the invention of C_3-symmetric chiral ligands and their applications in asymmetric catalysis.[3] Considering that chiral oxazoline ligands are attractive as a consequence of their topography and ease of synthesis and modification,[4] together with the wide application of bisoxazolines,[5] the development and application of trisoxazolines have received more and more attention.[6] The most notable C_3-symmetric trisoxazolines **1**,[6a] **2**,[6e] **3**[6h] have been developed by Katsuki's and Gade's groups respectively (Scheme 1). Although several trisoxazoline ligands have been applied to asymmetric reactions,[6a–e, 6g–h] the successful application of trisoxazolines in asymmetric catalysis is still very limited.



Scheme 1

Recently, we developed a novel pseudo-C_3-symmetric trisoxazoline **4**, and successfully applied it into copper catalyzed indole alkylation[7] and the Kinugasa reaction.[8] In both cases, trisoxazoline **4**/$Cu(ClO_4)_2 \cdot 6H_2O$ was found to be air- and water-stable. The reaction could even be carried out in air. To further explore the utility of trisoxazoline **4** derived chiral catalysts, we synthesized analogues **5** and **6** (Scheme 2), and examined them in the Diels–Alder reactions of cyclopentadiene **7** with acryloyl-2-oxazolidinones **8**[9] and ketoesters **9**.[10] In this article, we wish to report the first example employing trisoxazolines as chrial ligands in the asymmetric Diels–Alder reaction.



Scheme 2

Results and discussion

Trisoxaozlines **5** and **6** were readily prepared according to our previously reported procedures.[7] For the Lewis acid catalyzed Diels–Alder reactions of cyclopentadiene **7** with bidentate dienophiles **8**, the metal–ligand complex was prepared by the reaction of 6 mol% of ligand and 5 mol% of metal salt in appropriate solvents at room tempature under a N_2 atmosphere. The resulting solution of the catalyst was stirred for two hours at room temperature and then the dienophile was added. The mixture was stirred for another 15 minutes and then cooled to the appropriate temperature, followed by the addition of 5–10 equivalents of freshly cracked cyclopentadiene. Trisoxazoline **4** was first evaluated in combination with different metal perchlorate hydrates $M(ClO_4)_2 \cdot 6H_2O$ using acetone as the solvent (Table 1). Of which, as is shown in Table 1, the $Cu(ClO_4)_2 \cdot 6H_2O$ catalyzed reaction proceeded with the most promising reactivity and selectivity. And up to 92 : 8 *endo* selectivity and 67% (*endo* ee) were achieved.

Next, we examined the solvent effect. Considering that trisoxazoline **4**/$Cu(ClO_4)_2 \cdot 6H_2O$ had a poor solubility in weak coordinating solvent, the screening of solvents was carried out using trisoxazoline **4**/$Cu(OTf)_2$ as the catalyst. Generally, solvents such as dichloromethane, THF and CH_3NO_2,[9d] gave high enantiofacial control when bisoxazoline derived chiral Lewis acids were used. However, in these solvents, trisoxazoline **4**/$Cu(OTf)_2$ could promote the reaction smoothly only in poor selectivity (entries 1–5, Table 2). Interestingly, when CH_3CN or acetone was used, the obvious improvement in selectivity was observed (entries 6 and 7). Considering that Evans and coworkers described that fine tuning of counterions of copper(II) could not only increase the reactivity greatly but also improve the enantioselectivity in the bisoxazoline/Cu(II) catalyzed Diels–Alder reaction,[11] we next examined the effect of counterions of copper centers on the selectivity in our screened conditions (entries 5–8). Although all copper salts gave high diastereoselectivity, copper perchlorate hexahydrate proved to be the best copper salt because it provided the best enantioselecitvity in combination with acetone as the solvent. Moreover, when chiral catalyst **4**/$Cu(ClO_4)_2 \cdot 6H_2O$ was used, the reaction could be carried out in atmosphere of air. Thus, $Cu(ClO_4)_2 \cdot 6H_2O$ was the optimal Lewis acid due to its cheapness, easy handling and good enantioselectivity.

To further improve the enantioselectivity, different substituted trisoxazolines **4**–**6** were also examined in acetone using $Cu(ClO_4)_2 \cdot 6H_2O$ as Lewis acid. As shown in Table 3, all of the three trisoxaozolines derived copper complexes could promote the reaction smoothly (entries 1–3, Table 3). Of them, *sec*-butyltrixoazoline **5** was found to be the most promising ligand.

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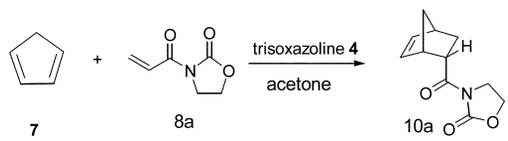
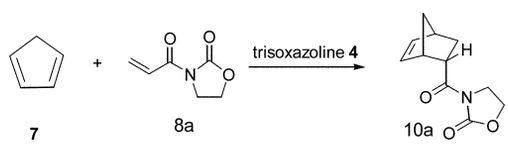
Table 1 Reaction of cyclopentadiene **7** with acryloyl-2-oxazolidinones **8a**[a]



Entry	Lewis Acid	Time/h	Yield[b] (%)	*Exo* : *endo*[c]	Ee[c] (%)
1	$Zn(ClO_4)_2 \cdot 6H_2O$	16	85	10 : 90	13
2	$Mg(ClO_4)_2 \cdot 6H_2O$	16	50	9 : 91	8
3	$Co(ClO_4)_2 \cdot 6H_2O$	16	70	17 : 83	24
4	$Ni(ClO_4)_2 \cdot 6H_2O$	16	92	18 : 82	24
5	$Cu(ClO_4)_2 \cdot 6H_2O$	3	99	8 : 92	67

[a] Reactions were run with 6 mol% of ligand **4** and 5 mol% of metal salt at −20 °C. [b] Isolated yield. [c] *Endo : exo* ratios and enantiomer ratios were determined by HPLC.

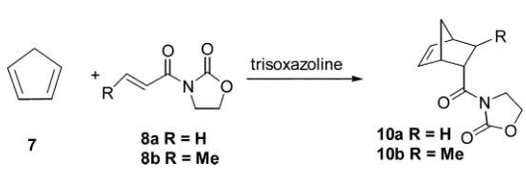
Table 2 Solvents and counter ion effects[a]



Entry	Catalyst	Solvent	Yield[b] (%)	*Exo*[c] : *endo*	Ee[c] (%)
1	$Cu(OTf)_2$	CH_2Cl_2	99	13 : 87	31
2	$Cu(OTf)_2$	$CHCl_3$	89	13 : 87	12
3	$Cu(OTf)_2$	CH_3NO_2	75	14 : 86	7
4	$Cu(OTf)_2$	CH_2ClCH_2Cl	70	11 : 89	42
5	$Cu(OTf)_2$	THF	92	14 : 86	11
6	$Cu(OTf)_2$	CH_3CN	99	6 : 94	62
7	$Cu(OTf)_2$	Acetone	99	3 : 97	61
8	$Cu(ClO_4)_2 \cdot 6H_2O$	Acetone	99	8 : 92	67
9	$Cu(ClO_4)_2 \cdot 6H_2O$	CH_3CN	99	7 : 93	62
10	$Cu(BF_4)_2$[d]	Acetone	80	5 : 95	62
11	$Cu(SbF_2)_2$[d]	Acetone	99	6 : 94	55

[a] Reactions were run with 6 mol% of ligand **4** and 5 mol% of metal salt at −20 °C. [b] Isolated yield. [c] *Endo : exo* ratios and enantiomer ratios were determined by HPLC. [d] Prepared from anhydrous $CuBr_2$ and 2 eq. Ag X_2.

Table 3 Ligand survey and substrate scope



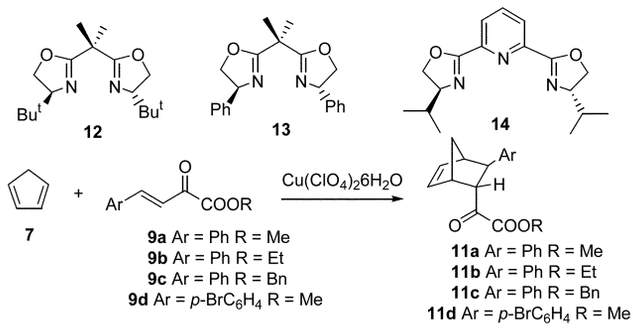
Entry	L	**8**	Temp./°C	Time/h	Yield[b] (%)	*Exo* : *endo*[c]	Ee[c] (%)
1	**4**	**8a**	−20	3	99	8 : 92	67
2	**5**	**8a**	−20	3	99	7 : 93	75
3	**6**	**8a**	−20	3	99	12 : 88	41[d]
4	**5**	**8a**	−45	6	99	4 : 96	80
5	**5**	**8a**	−78	24	20	4 : 96	82
6	**5**	**8b**	0	48	90	19 : 81	74
7	**5**	**8b**	−20	48	21	10 : 90	81

[a] Reactions were run in acetone under *air atmosphere* with 12 mol% of ligand and 10 mol% of $Cu(ClO_4)_2 \cdot 6H_2O$; [b] Isolated yield. [c] *Endo*/*exo* ratios and enantiomer ratios were determined by HPLC. [d] Opposite enantiomer.

When reaction was carried out at −20 °C, up to 75% ee for the *endo* product with 93 : 7 *endo* selectivity was achieved (entry 2). Lowering the temperature to −45 °C improved the enantioselectivity for the *endo* product to 80% ee with full conversion (entry 4). Further lowering of the temperature to −78 °C increased the ee to 82%, but the reaction was slowed down and low conversion was observed probably due to the poor solubility of **8a** in acetone at −78 °C (entry 5). Compared with dienophile **8a**, β-methyl dienophile **8b** is much less reactive. The reaction between cyclopentadiene and **8b** went for completion at 0 °C for 48 hours, and good enantioselectivity (74% ee) for the endo product was obtained (entry 6). Although lowering the temperature could increase the ee up to 81%, only 21% conversion was obtained. It should be noted that all the reactions were carried out under an atmosphere of air.

Subsequently, we examined the Diels–Alder reaction of cyclopentadiene with ketoesters **9**. Although ketoesters **9** have been used in a series of asymmetric reactions,[12] the Diels–Alder

Table 4 Reaction of cyclopentadiene **7** with ketoester **9**[a]

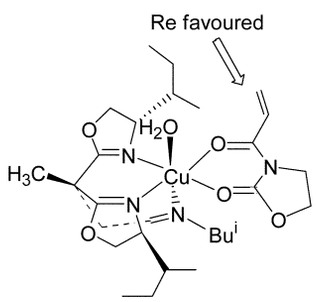


Entry	L	9	Temp./°C	Time/h	Yield[b] (%)	*Exo* : *endo*[c]	Ee[c] (%)
1	**4**	**9a**	−20	20	64	6 : 94	51
2	**5**	**9a**	−20	20	66	8 : 92	53
3	**6**	**9a**	−20	20	73	12 : 88	24[d]
4	**5**	**9a**	−35	48	64	3 : 97	71
5	**12**	**9a**	−35	48	52	8 : 92	53
6	**13**	**9a**	−35	48	58	8 : 92	0
7	**14**	**9a**	0	48	63	12 : 88	4[d]
8	**5**	**9b**	−35	48	82	3 : 97	64
9	**5**	**9c**	−35	48	47	3 : 97	62
10	**5**	**9d**	−35	48	56	nd[e]	nd[e]

[a] Reactions were run in acetone in air with 12 mol% of ligand and 10 mol% of $Cu(ClO_4)_2 \cdot 6H_2O$. [b] Isolated yield. [c] *Endo : exo* ratios and enantiomer ratios were determined by HPLC. [d] Opposite enantiomer. [e] Not determined. Diastereomers and enantiomers cannot be resolved.

reaction of cyclopentadiene with ketoesters **9** was less explored. The best result in literature was achieved by employing DBPHOX/$Cu(SbF_6)_2$ as the catalyst, in which up to 68% ee for the *endo* product (*endo* : *exo* = 94 : 6) was obtained in the reaction of cyclopentadiene with ester **9a**.[10] First, trisoxazolines **4**–**6** were all evaluated in combination with $Cu(ClO_4)_2 \cdot 6H_2O$ in the reaction of ketoester **9a** with cyclopentadiene. When the reaction was carried out at −20 °C, trisoxazolines **4**–**6** derived chiral catalysts gave the product in excellent yields in 24 hours (Table 4). Once again, trisoxazoline **5** was found to be the best ligand and 53% ee was obtained. When the temperature was lowered to −35 °C, up to 71% ee for the *endo* product (*endo* : *exo* = 97 : 3) was obtained. Comercially available bisoxazolines **12**–**14** were also examined under the same reaction conditions, but the enantioselectivity was also unsatisfactory in these conditions. The commonly used *tert*-butylbisoxazoline **12** provided the D–A reaction adduct in 53% ee for the *endo* product (*endo* : *exo* = 92 : 8, entry 5). The (*S*)-phenylbisoxaozline **13** afforded racemic products even at −35 °C (entry 6), while the (*R*)-phenyltrisoxaozline **6** could provided the *endo* product in 24% ee at a higher temperature (−20 °C, entry 3). Surprisingly, isopropylpybox **14** was far less reactive than other ligands in combination with $Cu(ClO_4)_2 \cdot 6H_2O$, and the reaction needed to be carried out at 0 °C for full conversion. Other ketoesters **9b** and **9c** worked well under the same reaction conditions with excellent diastereoselectivity and good enantioselectivity (entries 8 and 9). Aryl substituented ketoester **9d** was also tested in this reaction. Unfortunately, although the reaction proceeded well to afford the desired Diels–Alder reaction product (entry 10), the diastereoselectivity and the enantioselectivity of the product could not be determined by chiral HPLC.

The absolute configuration of the major product **10a** was assigned to be 2*S* by comparing its rotation with the known compound. Based on the absolute configuration of the product, a stereomodel with a distorted octahedral geometry at the copper center was proposed to account for the stereoselectivity of the Diels–Alder reaction (Scheme 3) and it is supported by all of the experimental data. In this model, the *si*-face of acryloyl-2-oxazolidinone was obstructed by the isobutyl substituent on the ligand, permitting that the diene attack was favored only from the *re*-face to afford *S*-enantiomers.



Scheme 3

In conclusion, we demonstrated that pseudo-C_3-symmetric trisoxazolines **4**–**6** could serve as ligands in the copper catalysed Diels–Alder reaction. To the best of our knowledge, this is the first example of employing trisoxazoline derived chiral catalysts in the Diels–Alder reaction. Although the enantioselectivity was not very satisfactory (up to 82%), the outstanding character of this process is that chiral catalysts can be prepared under air, and the reactions can be carried out in air. Investigation into extending the cheap, easy acess and air- and water-stable catalyst system to other asymmetric reactions are currently under way.

Experimental

$Cu(OTf)_2$ was purchased from TCI and $Cu(ClO_4)_2 \cdot 6H_2O$ from Fluka. Purification of the reaction products was carried out by flash chromatography on silica gel. Ether was dried by distillation over sodium-benzophenone ketyl prior to use. Acetonitrile and carbon tetrachloride were distilled over P_2O_5 then over calcium hydride under nitrogen, and stored over 4 Å MS; Triethylamine was distilled over calcium hydride under nitrogen, and stored over 4 Å MS. Acetone was first distilled over anhydrous $CaSO_4$ and stored over 4 Å MS.

General procedures for catalytic asymmetric Diels–Alder reaction

To a Schlenk tube was added $Cu(ClO_4)_2 \cdot 6H_2O$ (0.10 eq.), followed by trisoxazoline **5** (0.12 eq.), then acetone in air. The

solution was stirred at room temperature for two hours, and acryloyl-2-oxazolidinones or ketoester (1.0 eq.) was added. The concentration of Cu^{2+} was maintained at about 0.02 mol mL^{-1}. The resulting mixture was kept stirring for 15 minutes, then cooled to the indicated temperature and stirred for another 15 minutes before the cyclopentadiene (5 eq.) was added. After the reaction was complete (monitored by TLC), the solution was concentrated. The residue was purified by flash column chromatography on silica gel to afford the desired product.

New compounds have been characterized by ^{1}H NMR, ^{13}C NMR, MS, IR and HRMS (or elemental analysis).

(*S*)-1,2,2–Tris[2-(4-*s*-butyl–1,3–oxazolinyl)]propane 5

The ligand was synthesized according to the literature,[7] and purified by flash chromatography on silica gel (acetone–petroleum ether, 1 : 4, v/v) to afford crude **5** as a pale yellow oil. The pure product was obtained by flash column chromatography on silica gel (ethyl acetate–petroleum ether, 1 : 1, v/v then ethyl acetate). $[\alpha]_D^{20} = -110.5$ (20.6 mg 2 mL^{-1} $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.78 (t, J = 7.8 Hz, 9H), 0.91 (t, J = 7.8 Hz, 9H), 1.11–1.20 (m, 3H), 1.39–1.69 (m, 6H), 1.74 (s, 3H), 2.94 (ABd, J = 14.7 Hz, 1H), 3.07 (ABd, J = 14.7 Hz, 1H), 3.87 (t, J = 7.8 Hz, 1H), 3.82–4.34 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): 166.84, 166.82, 163.52, 70.62, 70.43, 70.04, 69.70, 69.35, 69.29, 40.76, 38.75, 38.59, 38.40, 34.89, 26.09, 26.02, 26.00, 21.20, 14.26, 13.94, 13.55, 11.70, 11.62, 11.44. IR (KBr): 2963, 2878, 1663, 1463, 1380, 1354, 1235, 1180, 1095, 981, 927, 776cm^{-1}. MS (EI): 419 (M^+, 4.7), 362 (100), 225 (37), 363 (18), 235 (19), 262 (15), 155 (13), 55 (12), 223 (11). Anal. calcd. for $C_{24}H_{41}O_3N_3$: C, 68.70; H, 9.85; N, 10.01. Found: C, 68.72; H, 9.75; N, 9.75%.

(*R*)-1,2,2–Tris[2-(4-phenyl–1,3–oxazolinyl)]propane 6

The ligand was synthesized according to the literature,[7] and purified by flash chromatography on silica gel (THF–petroleum ether, 1 : 4, v/v) to afford crude **6** as a pale yellow oil. The pure product was obtained by flash column chromatography on silica gel (ethyl acetate–petroleum ether, 1 : 1, v/v). $[\alpha]_D^{20} = +149.7$ (13.2 mg 2 mL^{-1} $CHCl_3$).^{1}H NMR (300 MHz, $CDCl_3$): δ 1.86 (s, 3H), 3.25 (ABd, J = 14.1 Hz, 1H), 3.31 (ABd, J = 14.1 Hz, 1H), 4.03–4.19 (m, 3H), 4.67–4.70 (m, 3H), 5.10–5.32 (m, 3H), 7.23–7.31 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$): 168.29, 168.25, 164.61, 142.01, 142.00, 141.98, 128.38, 128.32, 127.24, 127.20, 126.59, 126.42, 75.31, 74.22, 69.40, 69.41, 69.28, 41.05, 34.90, 30.10, 21.52; IR(KBr): 3063, 3030, 2960, 2901, 1736, 1658, 1604, 1494, 1455, 1355, 1171, 1099, 982, 919, 761, 700cm^{-1}; MS (EI): 479 (M^+, 10), 480 [$(M + 1)^+$, 14], 205 (100), 265 (48), 220 (35), 104 (30), 201 (30); HRMS (EI): exact mass calcd for $C_{30}H_{29}O_3N_3$ $[M]^+$: 479.22090. Found: 479.21840.

3-(Bicyclo[2.2.1]hept-5-en-2-ylcarbonyl)-2-oxazolidinone 10a [10]

The reaction was carreid out at −45 °C to afford the product as a colorless solid in 99% yield, mp 87–88 °C. HPLC analysis [Chiralcel OD–H, ^{i}PrOH–hexanes = 5 : 95, 1.0 mL min^{-1}, 205 nm; t_r (*exo*) = 50.32 min, t_r (*endo*, major) = 54.78 min, t_r (*endo*, minor) = 61.70 min] gave the isomeric composition of the product: 80.0% ee. $[\alpha]_D^{20} = -112.9$ (23.4 mg 2 mL^{-1} $CHCl_3$).^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32–1.44 (m, 3H), 1.84–1.92 (m, 1H), 2.87 (s, 1H), 3.24 (s, 1H), 3.85–4.02 (m, 3H), 4.31–4.39 (m, 2H), 5.80 (dd, J = 5.4, 3.0Hz, 1H), 6.18 (dd, J = 5.4, 2.7 Hz, 1H).

3-(3-Methylbicyclo[2.2.1]hept-5-en-2-ylcarbonyl)-2-oxazolidinone 10b [10]

The reaction was carreid out at 0 °C to afford the product as a colorless solid in 90% yield, mp. 93–94 °C. HPLC analysis (Chiralcel OD–H, ^{i}PrOH–hexanes = 1 : 50, 1.0 mL min^{-1}, 205 nm; t_r (*exo*) = 52.05 min, t_r (*endo*, major) = 62.86 min, t_r (*endo*, minor) = 70.21 min) gave the isomeric composition of the product: 74.0% ee. $[\alpha]_D^{20} = -132.8$ (37.0 mg 2 mL^{-1} $CHCl_3$).^{1}H NMR (300 MHz, $CDCl_3$) for *endo* isomer: 1.13 (d, J = 6.9 Hz, 3H), 1.43–1.48 (m, 1H), 1.71 (d, J = 9.0 Hz, 1H), 2. 06–2.12 (m, 1H), 2.53 (d, J = 1.5 Hz, 1H), 3.28 (br s, 1H), 3.54 (dd, J = 4.5, 3.7 Hz, 1H), 3.89–4.07 (m, 2H), 4.38–4.44 (m, 2H), 5.79 (dd, J = 5.7, 2.7 Hz, 1H), 6.38 (dd, J = 5.7, 2.7 Hz, 1H).

Methyl 3-phenylbicyclo[2.2.1]hept-5-en-2-ylglyoxylate 11a [10]

Colorless oil. HPLC analysis (Chiralpak AD, ^{i}PrOH–hexanes = 1 : 50, 1.0 mL min^{-1}, 254 nm; t_r (*exo*) = 8.66 min, t_r (*endo*, minor) = 9.55 min, t_r (*exo*) = 10.76 min, t_r (*endo*, major) = 11.86 min) gave the isomeric composition of the product: 71.0% ee. $[\alpha]_D^{20} = -110.0$ (27.0 mg 2 mL^{-1} $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.63 (d, J = 10.2 Hz, 1H), 1.94 (d, J = 8.4 Hz, 1H), 3.06 (s, 1H), 3.24 (d, J = 4.2 Hz, 1H), 3.49 (br s, 1H), 3.75 (t, J = 3.0, 4.8 Hz, 1H), 3.85 (s, 3H), 5.94 (t, J = 3.0, 2.4 Hz, 1H), 6.44 (d, J = 3.6 Hz, 1H), 7.21–7.31 (m, 5H).

Ethyl 3-phenylbicyclo[2.2.1]hept-5-en-2-ylglyoxylate 11b

Colorless oil. HPLC analysis (Chiralpak AD, ^{i}PrOH–hexanes = 1 : 50, 1.0 mL min^{-1}, 254 nm; t_r (*exo*) = 10.43 min, t_r (*endo*, minor) = 11.66 min, t_r (*exo*) = 13.75 min, t_r (*endo*, major) = 15.60 min) gave the isomeric composition of the product: 64.0% ee. $[\alpha]_D^{20} = -79.8$ (22.8 mg 2 mL^{-1} $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34 (t, J = 6.9 Hz, 3H), 1.63 (dd, J = 1.8, 8.7 Hz, 1H), 1.94 (d, J = 8.7 Hz, 1H), 3.06 (d, J = 0.9 Hz, 1H), 3.25 (d, J = 5.1 Hz, 1H), 3.49 (s, 1H), 3.74 (dd, J = 3.3, 4.8 Hz, 1H), 4.30 (q, J = 6.9 Hz, 2H), 5.98 (dd, J = 1.8, 5.1 Hz, 1H), 6.44 (dd, J = 3.3, 5.4 Hz, 1H), 7.21–7.31 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): 194.45, 161.84, 143.39, 139.67, 132.76, 128.44, 127.35, 126.12, 62.22, 56.67, 48.96, 47.53, 46.96, 45.40, 13.89. IR (KBr): 3434, 3063, 2982, 2943, 1724, 1602, 1498, 1453, 1369, 1333, 1248, 1086, 1038, 750, 701, 519cm^{-1}; MS (EI): 270 (M^+, 0.07), 131 (100), 66 (52), 205 (48), 103 (23), 77 (13), 91 (12), 132(11), 206(7). HRMS (EI): exact mass calcd for $C_{15}H_{13}O_3$ $[M - C_2H_5]^+$: 241.08734. Found: 241.08794.

Benzyl 3-phenylbicyclo[2.2.1]hept-5-en-2-ylglyoxylate 11c

Colorless oil. HPLC analysis (Chiralpak AD, ^{i}PrOH–hexanes = 1 : 100, 1.0 mL min^{-1}, 254 nm; t_r (*exo*) = 11.94 min, t_r (*endo*, minor) = 13.82 min, t_r (*exo*) = 14.83 min, t_r (*endo*, major) = 17.07 min) gave the isomeric composition of the product: 64.0% ee. $[\alpha]_D^{20} = -62.5$ (16.0 mg 2 mL^{-1} $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.61 (dd, J = 1.8, 9.0 Hz, 1H), 1.91 (d, J = 8.4 Hz, 1H), 3.04 (dd, J = 1.2, 3.0 Hz, 1H), 3.23 (dd, J = 1.2, 4.8 Hz, 1H), 3.43 (m, 1H), 3.70 (dd, J = 3.0, 4.8 Hz, 1H), 5.26 (d, J = 1.5 Hz, 2H), 5.93 (dd, J = 2.4, 5.7 Hz, 1H), 6.42 (dd, J = 3.0, 6.0 Hz, 1H), 7.19–7.32 (m, 5H), 7.36–7.38 (m, 5H).^{13}C NMR (75 MHz, $CDCl_3$): 194.24, 161.81, 143.36, 139.79, 134.47, 132.83, 128.76, 128.69, 128.60, 128.54, 127.42, 126.22, 109.73, 67.80, 56.81, 48.98, 47.60, 46.96, 45.44. IR (KBr): 3064, 3031, 2977, 2877, 1724, 1602, 1498, 1456, 1333, 1245, 1083, 748, 698.cm^{-1}; MS (ESI): 350.2 $(M + NH_4)^+$, 355.2 $(M + Na)^+$ HRMS (ESI): exact mass calcd for $C_{15}H_{13}O_3$ $[M + Na]^+$: 355.1308730. Found: 355.1304656.

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