

氮杂环卡宾(NHC)催化的联芳基二醛去对称化构建轴手性醛类化合物

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摘要 在不对称催化合成领域,轴手性醛类化合物因其独特的结构常作为有机催化剂或手性配体的前体,发展其对映选择性与结构多样性的合成方法一直是化学家们的兴趣所在.然而,只有很少的催化方法被开发用于构建结构多样的轴手性醛.利用去对称化策略,通过卡宾催化的氧化酯化反应发展了一类轴手性醛类化合物的新合成方法.该方法条件温和,具有优异的产率和对映选择性,且底物范围较广,官能团兼容性较好.这一策略为轴手性醛及其衍生物的合成提供了新的可能性.

关键词 轴手性;氮杂环卡宾催化;去对称化

N-Heterocyclic Carbene (NHC)-Catalyzed Desymmetrization of Biaryldialdehydes to Construct Axially Chiral Aldehydes

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Abstract In the field of asymmetric catalytic synthesis, axially chiral aldehydes are often used as precursors of organic catalysts or chiral ligands because of their unique structures. The development of synthetic methods with enantioselectivity and structural diversity has always been the interest of chemists. However, only few catalytic methods have been developed for the construction of structurally diverse axially chiral aldehydes. Herein, a N-heterocyclic carbene (NHC)-catalyzed oxidative esterification reaction to synthesize axially chiral aldehydes through desymmetrization strategy was developed. This method features mild conditions (room temperature), excellent yields and enantioselectivity, broad substrate scope and good function group tolerance (26 examples, 54%~97% yields, up to 99% *ee*). All the axially chiral aldehyde products have been fully characterized and the absolute configuration was established by comparing the results from known literature. This strategy provides new possibilities for the synthesis of axially chiral aldehydes and their derivatives.

Keywords axially chiral; N-heterocyclic carbene; desymmetrization

轴手性化合物广泛存在于许多天然产物以及手性药物、材料等功能分子中,在不对称催化合成中也常作为手性的有机小分子催化剂或手性配体^[1].作为重要的一员,轴手性醛类化合物近年来也成为了药物化学家与合成化学家关注的焦点^[2].例如,含轴手性醛单元的天然产物棉酚^[3]作为一种口服的男性和雄性动物的抗生育剂,对艾滋病感染、糖尿病并发症和癌症也显示出潜在

的治疗活性(Scheme 1, a).同时,轴手性醛类化合物及其衍生物经常作为轴手性配体、催化剂与光学材料的前体被广泛使用^[4].最近,郭其祥团队^[5a-5b]和赵宝国团队^[5c-5d]直接以轴手性醛为有机小分子催化剂,成功发展了氨基酸酯的不对称烷基化反应及酮酸的不对称胺化反应等多种不对称转化.为此,化学家们发展了多种有效的方法来合成轴手性醛类化合物,但通常需要使用化

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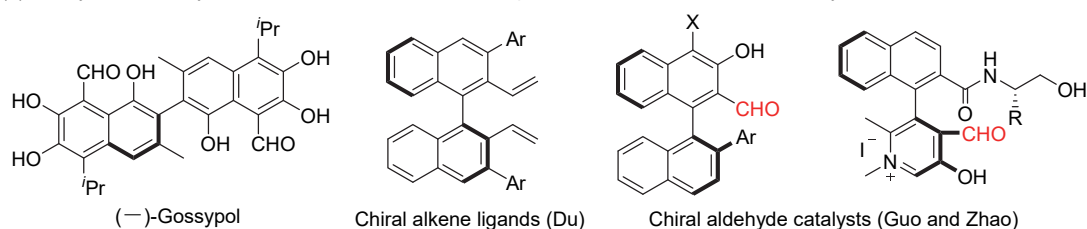
国家自然科学基金(Nos. 21822103, 21820102003, 91956201)、高等学校学科创新引智计划(111 计划, No. B17019)及湖北省自然科学基金(No. 2017AHB047)资助项目.

学计量的手性原料或助剂, 不对称催化合成的方法发展尚不充分. 催化去对称化作为一种具有普适性的策略常被用于合成手性化合物^[6], 2014 年 Turner 和 Clayden 团队^[7]利用该策略发展了酶催化的氧化/还原反应, 成功实现了轴手性醛类化合物的催化不对称合成(Scheme 1, b). 遗憾的是, 该方法在底物普适性与对映选择性方面稍显不足. 不对称碳氢官能化作为一种原子和步骤经济性的策略最近得到快速发展^[8], 2017 年以来史炳锋团队^[9a-9c]和 Ackermann 等^[9d]利用醛基作为导向基团发展了一系列钯催化的碳氢官能化反应, 为轴手性醛的高效、高对映选择性合成提供了新的思路与方法(Scheme 1, c).

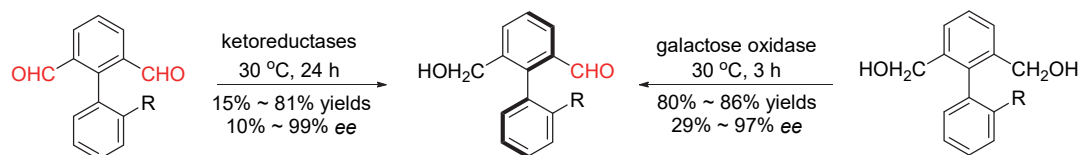
本工作利用去对称化策略, 通过卡宾催化的氧化酯化反应, 成功实现了轴手性醛类化合物的催化不对称合成. 该方法不仅产率高、对映选择性优异, 而且还表现出较广的底物普适性与较好的官能团兼容性.

近年来, 化学家们成功发展了一类协同的氮杂环卡宾与光氧化还原催化策略, 成功实现了几种重要的有机光化学转化^[10-11]. 尤其是, Miyabe 团队^[11c]在 2018 年通过该策略实现了不饱和醛温和条件下的氧化酯化反应, 以较好的收率得到了一系列不饱和酯类化合物. 受到这项工作的启发以及对于不对称光催化反应的研究兴趣^[12], 我们设想能否通过协同的不对称氮杂环卡宾催

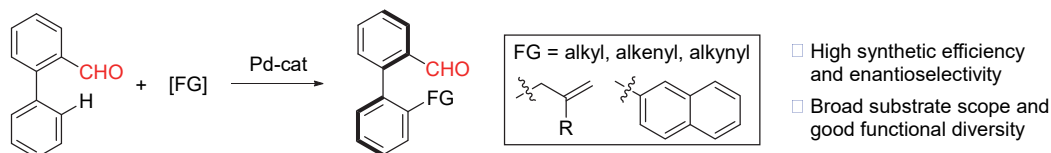
(a) Axially chiral aldehydes and their derivatives in natural products and enantioselective catalysis



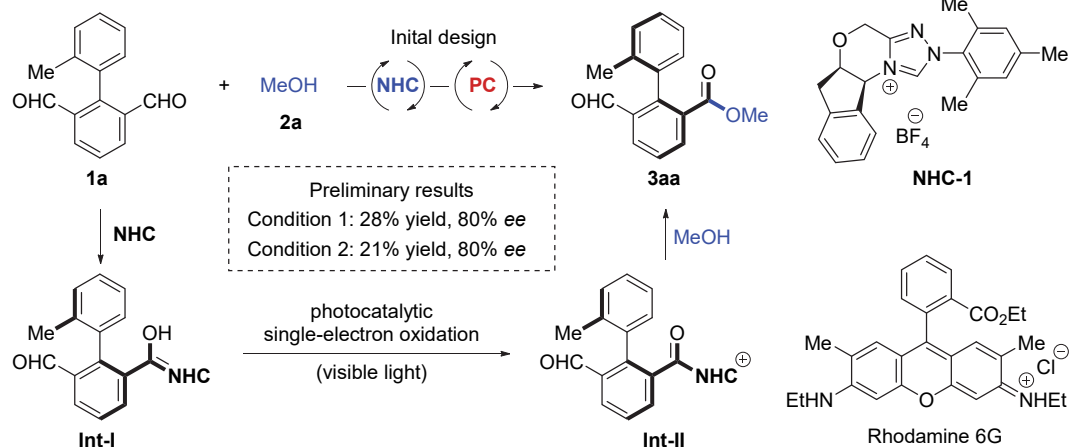
(b) Turner & Clayden's work: enzymatic desymmetrization of biaryldialdehydes



(c) Shi's method: Pd-catalyzed asymmetric C—H functionalization of biaryldialdehydes



(d) This work: NHC-catalyzed desymmetrization of biaryldialdehydes



Condition 1: Rhodamine 6G (5 mol%), **NHC-1** (15 mol%), K_2CO_3 (2.5 equiv.), $BrCCl_3$ (3.0 equiv.), MeOH/toluene (V:V = 1:1, 1 mL), r.t., 24 h, 2 x 3 W white light. Condition 2: the same with condition 1, no light.

图式 1 轴手性醛类的重要性
Scheme 1 Importance of axial chiral aldehydes

化^[13]与可见光诱导的光氧化还原催化^[14], 利用去对称化策略发展联芳基二醛的氧化酯化反应合成轴手性醛类化合物. 我们以联芳基二醛 **1a** 与甲醇为原料, 对这一设想进行了初步尝试, 以三唑噁嗪四氟硼酸盐(**NHC-1**)为手性卡宾催化剂前体, 罗丹明 **6G** 为光催化剂, 在白光照射下反应 8 h, 可以 28% 的收率和 80% *ee* 得到目标产物 **3aa**. 但是, 通过控制实验发现, 该反应在没有光的条件下也可以顺利进行, 收率以及对映选择性基本上不受影响. 因此, 我们通过进一步条件优化, 成功发展了一个卡宾催化的热化学反应, 同样可以以普遍较好的收率与优异的对映选择性合成轴手性化合物^[15].

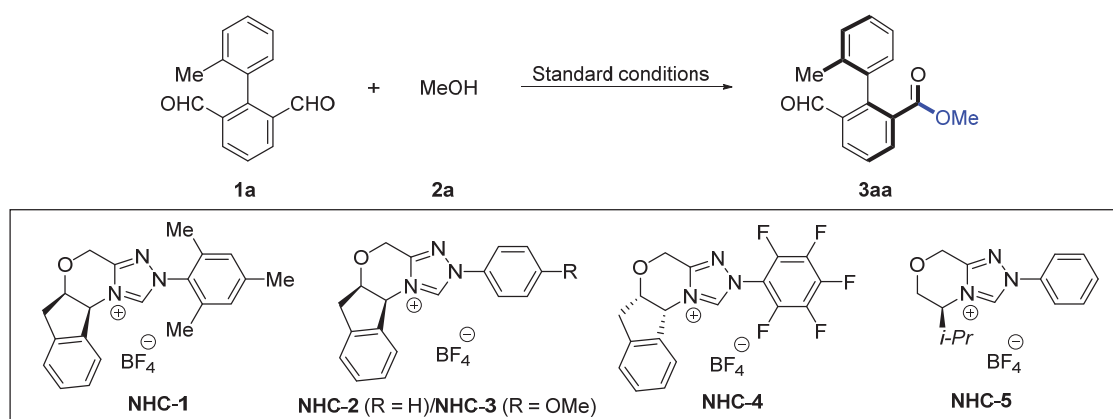
1 结果与讨论

在尝试发展不对称光化学反应失败后, 调整了研究方案: 使用 2'-甲基-[1,1'-联苯]-2,6-二甲醛(**1a**)和甲醇(**2a**)作为模板化合物, 经过一系列的条件优化, 以 **NHC-1** (0.01 mmol, 10 mol%)为催化剂, K_2CO_3 为碱(0.25 mmol, 2.5 equiv.), 3,3',5,5'-四叔丁基二苯醌(DQ, 0.1

mmol, 1.0 equiv.)为氧化剂, 甲苯(1 mL)为溶剂, 在氩气保护及室温下反应 8 h, 以 97% 的收率和 >99% *ee* 得到目标产物 **3aa**(其绝对构型根据参考文献[15], 对比旋光度而确定). 改变卡宾的位阻和骨架会降低催化剂的催化效率与对映选择性(Entries 2~5). 使用 MnO_2 (Entry 6)或 O_2 (Entry 7)作为氧化剂时, 也可以中等的收率得到产物, 但对映选择性有所降低. 该反应在四氢呋喃(Entry 8)和乙腈(Entry 9)等其它溶剂中也能够进行, 但效果没有甲苯作溶剂时理想. 与此同时, 发现碱对反应的影响是非常大的. 当以三乙烯二胺(DABCO) (Entry 11)或 Na_2HPO_4 (Entry 13)作碱时, 反应不发生, 而 Cs_2CO_3 (Entry 12)可以给出一样的对映选择性, 但收率降低.

在确定了最优的反应条件后, 考察了联芳基二醛的底物范围(表 2). 首先, 考察了烷基取代基, 发现带有甲基、乙基以及位阻稍大的异丙基的底物均以较好的收率(75%~97%)和较优的对映选择性(95%~99% *ee*)得到了目标产物 **3aa**~**3ca**. 当底物带有苯基、萘基等芳基取代

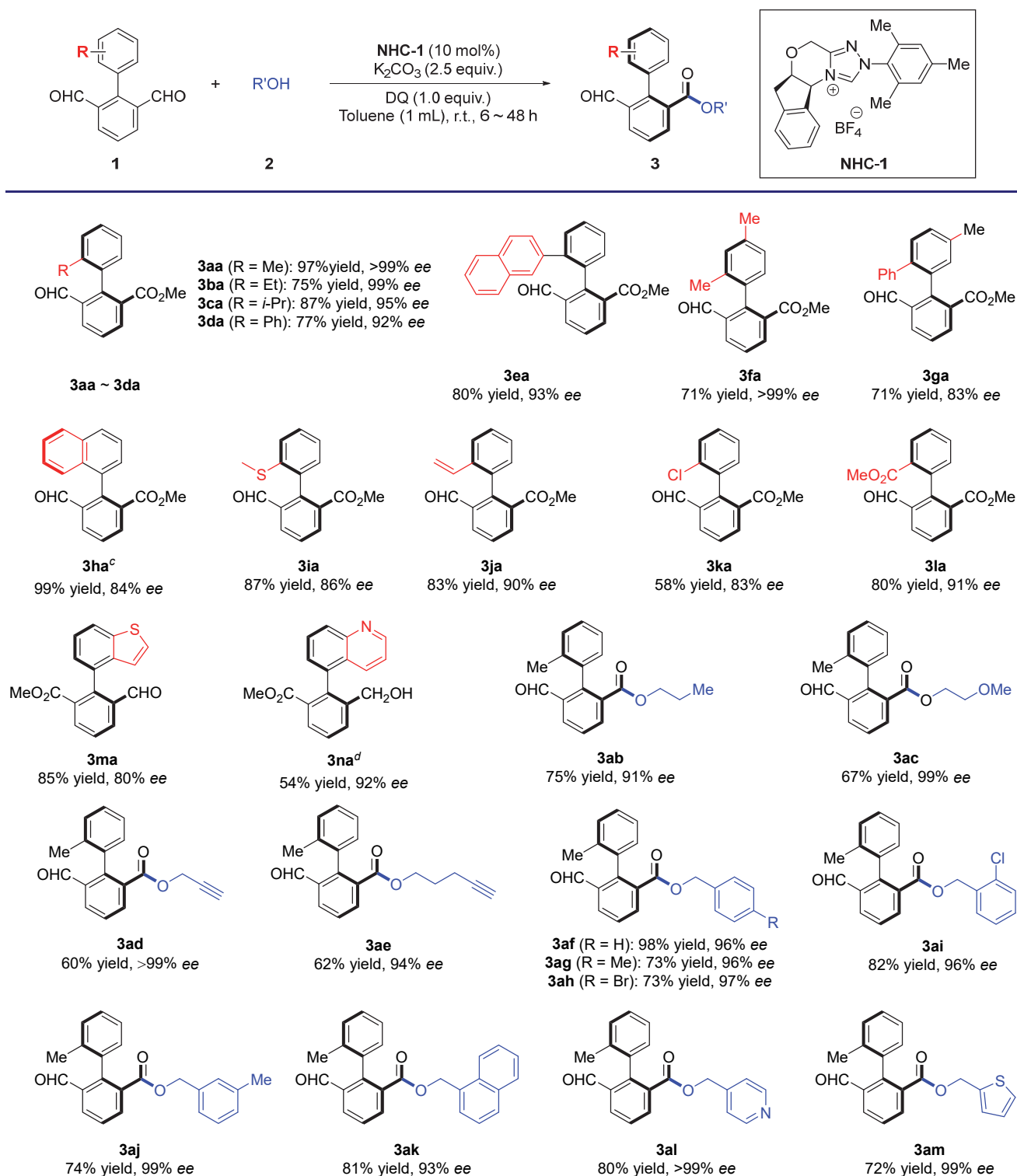
表 1 反应条件的优化^{a,b}
Table 1 Optimization of the reaction conditions



Entry	Deviation from standard conditions	Yield ^b / % of 3aa	<i>ee</i> ^c / % of 3aa
1	None	97	>99
2	NHC-2 instead of NHC-1	27	65
3	NHC-3 instead of NHC-1	56	76
4	NHC-4 instead of NHC-1	5	2
5	NHC-5 instead of NHC-1	33	36
6	MnO_2 instead of DQ	59	80
7	O_2 instead of DQ	64	90
8	THF instead of toluene	86	80
9	CH_3CN instead of toluene	79	99
11	DABCO instead of K_2CO_3	NR	ND
12	Cs_2CO_3 instead of K_2CO_3	85	>99
13	Na_2HPO_4 instead of K_2CO_3	NR	ND
14	Na_2CO_3 instead of K_2CO_3	7	29

^a Standard conditions: **1a** (0.1 mmol), **2a** (1 mmol, 10 equiv.), K_2CO_3 (0.25 mmol, 2.5 equiv.), **NHC-1** (10 mol%), DQ (1.0 equiv.) in toluene (1.0 mL) at room temperature (r.t.). ^b ¹H NMR yield with 1,3,5-trimethoxybenzene as the internal standard. ^c *ee* values were determined by chiral HPLC analysis. NR=no reaction. ND, not detected.

表 2 轴手性二醛的底物范围^{a,b}
Table 2 Scope of synthesis of axially pre-chiral dialdehydes



^a Reaction conditions: **1a** (0.1 mmol), **2a** (1 mmol, 10 equiv.), K_2CO_3 (0.25 mmol, 2.5 equiv.), **NHC-1** (10 mol%), **DQ** (1.0 equiv.) in toluene (1.0 mL) at room temperature. ^b ¹H NMR yield with 1,3,5-trimethoxybenzene as the internal standard. ee values were determined by chiral-phase HPLC analysis. ^c $T = -10\text{ }^\circ\text{C}$. ^d Isolated after reduction with $NaBH_4$.

基时, 同样可以分别以 77% 的收率和 92% ee 以及 80% 的收率和 93% ee 得到轴手性醛产物 **3da** 和 **3ea**. 当在苯环 2,4 位置同时引入甲基时, 可以以 71% 的收率和 >

99% ee 得到相应的产物 **3fa**; 而在苯环对位引入甲基取代基或使用萘环的联芳基二醛时, 反应的对映选择性略有降低, 但仍分别以 83% ee 和 84% ee 得到 **3ga** 和 **3ha**.

接下来,对反应的官能团兼容性进行考察.在联芳基二醛邻位引入杂原子甲基基(3ia)和乙烯基(3ja)时,反应分别以 87% 的收率和 86% *ee* 以及 83% 的收率和 90% *ee* 得到相应的产物.含卤素(3ka)及酯基(3la)等吸电子基团的底物同样适用于该反应,分别以较好对映选择性(83% *ee* 和 91% *ee*)、中等或较好的收率(58%和 80%)进行.通过监测反应发现,含吸电子基的底物反应更快一些,容易导致另一个醛基也发生氧化酯化反应.同时,还对杂环取代的联芳基二醛进行了研究,发现该催化体系同样可以以较好的收率与对映选择性给出目标产物(3ma: 产率 85%, 80% *ee*; 3na: 产率 54%, 92% *ee*).

随后对醇类的底物也进行了考察.简单的长链醇 2b 以及末端有官能团取代的烷基醇,如 2-甲氧基乙醇(2c)和炔丙醇(2d),可以以 60%~75% 的收率和 91%~99% *ee* 得到相应的产物 3ab~3ad.使用炔基取代的 4-戊炔-1-醇,或者引入甲基(3ag)、溴原子(3ah)等基团时,反应可以以 73%~98% 的收率以及 96%~97% *ee* 得到目标化合物,在芳环的邻位和间位分别引入氯原子或甲基时,反应以 82% 收率和 96% *ee* 以及 74% 收率和 99% *ee* 得到轴手性醛产物 3ai 和 3aj.当使用位阻较大的 1-萘甲醇时,以 81% 的产率和 93% 的 *ee* 得到产物 3ak.这表明芳基取代基电性和位置的改变并不会影响反应的收率和对映选择性.此外,4-吡啶甲醇(3al)和 2-噻吩甲醇(3am)等杂芳环苄醇都对反应条件展现了较好的耐受性,以良好的收率(80%, 72%)和优异的对映选择性(>99% *ee*, 99% *ee*)得到产物 3al 和 3am.遗憾的是,该反应对二级醇和三级醇并不兼容.

为了探究该方法的实用性,以联芳基二醛(1a)和甲醇为模型底物进行了克量级实验操作.在标准条件下,将反应放大至 5 mmol 时发现反应收率和对映选择性完全不受影响,最终以 98% 收率和 >99% 的 *ee* 得到 1.10 g 光学纯的目标产物 3aa (Scheme 2).

2 结论

综上所述,利用手性卡宾催化的氧化酯化反应,通过对联芳基二醛的去对称化操作合成轴手性醛类化合

物.在最优条件下,可以将多种不同基团取代的联芳基二醛类化合物以良好的收率和优异的对映选择性转化为相应的轴手性醛类化合物;同时,不同结构的一级醇均能参与该反应,得到优异的收率与对映选择性.该方法具有操作简单、反应条件温和、产率高、对映选择性好、底物范围广以及官能团兼容性好等优点,为轴手性醛类化合物的合成提供了一种新的方法.

3 实验部分

3.1 仪器与试剂

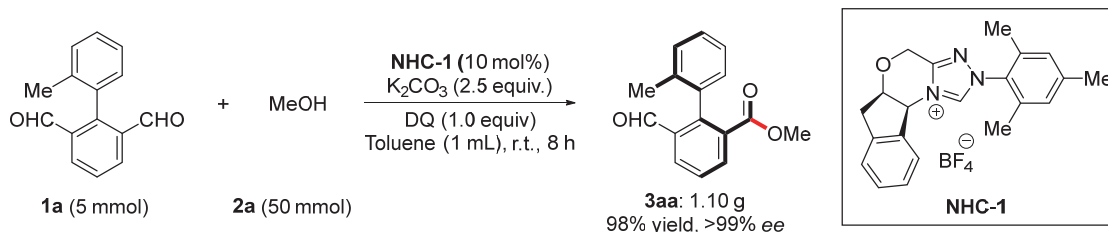
^1H NMR、 ^{13}C NMR 采用 Bruker 400 MHz 型超导核磁共振仪测定,使用氘代氯仿(CDCl_3)为溶剂, TMS 为内标.高分辨质谱用安捷伦液相色谱质谱联用仪.手性测定使用 Agilent 液相色谱仪进行测定,反应中用到的药品来自武汉格奥恒晟发展科技有限公司,卡宾催化剂来自上海大赛璐科技有限公司.

反应体系中试剂均为分析纯药品.反应中用到的溶剂均是经过 JC-Meyer 溶剂纯化系统干燥和脱氧处理的.柱层析使用的是 200~300 目硅胶(青岛海洋化工有限公司).薄层色谱(TLC)使用的是薄层层析硅胶 GF254.底物 1a~1n 参考文献[15]合成.

3.2 实验方法

3.2.1 目标产物 3aa~3oa 和 3ab~3am 的合成方法.

依次向 10 mL 的 Schlenk 管中加入底物 1a (0.1 mmol, 1 equiv.)、无机碱 K_2CO_3 (0.25 mmol, 2.5 equiv.)、卡宾催化剂前体 NHC-1 (0.01 mmol, 10 mol%)、氧化剂 3,3',5,5'-四叔丁基二苯醌(DQ, 0.1 mmol, 1.0 equiv.)、溶剂甲苯(1 mL)以及底物甲醇(1 mmol, 10 equiv.).在室温下反应 8 h,通过薄层色谱监测反应过程.待反应结束后,除去溶剂,使用正己烷/甲苯($V:V=2:1$)作为洗脱剂对反应体系进行柱层析得到目标产物 3aa.化合物 3ba~3ma 和 3ab~3am 也采取相同方法制备.3oa 按照同样的方法合成,使用 0.2 mmol 原料 3o,其他试剂药品相应扩大 2 倍.



图式 2 克量级反应
Scheme 2 A gram-scale reaction

(*R*)-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸甲酯(**3aa**): 反应时间 8 h, 黄色油状液体, 24.6 mg, 产率 97%, 99% *ee*. $[\alpha]_{\text{D}}^{25} + 85.2$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.61 (s, 1H), 8.17 (d, *J*=7.8 Hz, 2H), 7.59 (t, *J*=7.8 Hz, 1H), 7.37~7.20 (m, 3H), 7.09 (d, *J*=7.4 Hz, 1H), 3.61 (s, 3H), 2.04 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ : 191.7, 166.9, 145.5, 136.3, 135.5, 135.2, 134.6, 131.93, 130.3, 129.6, 129.2, 128.3, 127.9, 125.4, 52.2, 20.2; HRMS (ESI) calcd for C₁₆H₁₄NaO₃ [M+Na]⁺ 277.0835, found 277.0816. The enantiomeric excess was determined to be >99% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 1.0 mL/min]: 9.8 min (minor), 10.5 min (major).

(*R*)-6-甲酰基-2'-乙基-[1,1'-联苯]-2-羧酸甲酯(**3ba**): 反应时间 14 h, 黄色油状液体, 20 mg, 产率 75%, >99% *ee*. $[\alpha]_{\text{D}}^{25} + 65$ (*c* 0.76, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.56 (s, 1H), 8.09 (d, *J*=7.8 Hz, 2H), 7.51 (t, *J*=8.1 Hz, 1H), 7.35~7.24 (m, 2H), 7.20~7.14 (m, 1H), 7.01 (d, *J*=7.6 Hz, 1H), 3.52 (s, 3H), 2.27 (dt, *J*=14.3, 7.3 Hz, 2H), 0.96 (t, *J*=7.6 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ : 191.7, 166.9, 145.4, 142.0, 135.1, 134.8, 132.1, 130.2, 129.4, 128.6, 128.5, 127.9, 127.8, 125.3, 52.1, 26.3, 14.3; HRMS (ESI) calcd for C₁₆H₁₄NaO₃ [M+Na]⁺ 291.0992, found 291.0996. The enantiomeric excess was determined to be >99% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 1.0 mL/min]: 10.3 min (minor), 12.1 min (major).

(*R*)-6-甲酰基-2'-异丙基-[1,1'-联苯]-2-羧酸甲酯(**3ca**): 反应时间 14 h, 黄色油状液体, 24.6 mg, 产率 87%, 95% *ee*. $[\alpha]_{\text{D}}^{25} + 95.3$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.65 (s, 1H), 8.17 (dd, *J*=7.8, 1.8 Hz, 2H), 7.59 (t, *J*=7.8 Hz, 1H), 7.41~3.9 (m, 2H), 7.23~7.20 (m, 1H), 7.07 (d, *J*=7.5 Hz, 1H), 3.59 (s, 3H), 2.62~2.47 (m, 1H), 1.13 (d, *J*=6.8 Hz, 3H), 1.04 (d, *J*=6.9 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ : 191.7, 166.8, 146.8, 145.4, 135.1, 135.0, 134.1, 132.2, 130.2, 129.2, 128.8, 127.8, 125.3, 125.1, 52.1, 30.5, 23.8, 23.5; HRMS (ESI) calcd for C₁₈H₁₈NaO₃ [M+Na]⁺ 305.1148, found 305.1155. The enantiomeric excess was determined to be 95% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 1.0 mL/min]: 11.7 min (minor), 16.2 min (major).

(*R*)-6-甲酰基-2'-苯基-[1,1'-联苯]-2-羧酸甲酯(**3da**): 反应时间 14 h, 黄色油状液体, 24.2 mg, 产率 77%, 92% *ee*. $[\alpha]_{\text{D}}^{25} - 59.9$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400

MHz) δ : 9.69 (s, 1H), 8.02 (d, *J*=7.6 Hz, 1H), 7.96 (d, *J*=7.7 Hz, 1H), 7.59~7.41 (m, 4H), 7.28 (d, *J*=7.1 Hz, 1H), 7.15~7.14 (s, 3H), 7.11~7.09 (m, 2H), 3.65 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ : 191.2, 167.3, 145.2, 141.6, 140.2, 134.7, 134.4, 134.2, 132.8, 130.2, 129.7, 129.3, 128.8, 128.0, 127.6, 127.1, 127.0, 52.1; HRMS (ESI) calcd for C₂₁H₁₆NaO₃ [M+Na]⁺ 339.0992, found 339.0995. The enantiomeric excess was determined to be 92% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 1.0 mL/min]: 20.0 min (minor), 24.2 min (major).

(*R*)-6-甲酰基-2'-(2-萘基)-[1,1'-联苯]-2-羧酸甲酯(**3ea**): 反应时间 14 h, 黄色油状液体, 29.2 mg, 产率 80%, 93% *ee*. $[\alpha]_{\text{D}}^{25} - 114.4$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.73 (s, 1H), 7.98 (d, *J*=6.9 Hz, 1H), 7.89 (d, *J*=7.7 Hz, 1H), 7.74~7.69 (m, 1H), 7.69~7.63 (m, 1H), 7.61 (s, 1H), 7.59~7.54 (m, 3H), 7.48~7.44 (m, 1H), 7.44~7.37 (m, 3H), 7.30 (d, *J*=7.5 Hz, 1H), 7.18 (dd, *J*=8.5, 1.4 Hz, 1H), 3.65 (s, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ : 190.8, 167.2, 145.2, 141.6, 137.9, 134.8, 134.6, 134.3, 133.1, 132.7, 132.1, 130.3, 130.2, 130.1, 128.80, 128.5, 128.0, 127.7, 127.6, 127.6, 127.2, 127.2, 126.1, 126.0, 52.1; HRMS (ESI) calcd for C₂₅H₁₈NaO₃ [M+Na]⁺ 389.1148, found 389.1139. The enantiomeric excess was determined to be 93% by HPLC [AD column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 1.0 mL/min]: 13.1 min (minor), 17.4 min (major).

(*R*)-6-甲酰基-2',4'-二甲基-[1,1'-联苯]-2-羧酸甲酯(**3fa**): 反应时间 12 h, 黄色油状液体, 19 mg, 产率 71%, >99% *ee*. $[\alpha]_{\text{D}}^{25} + 13.7$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.62 (s, 1H), 8.15 (dd, *J*=7.7, 3.6 Hz, 2H), 7.57 (t, *J*=7.7 Hz, 1H), 7.10 (s, 1H), 7.05 (d, *J*=7.7 Hz, 1H), 6.97 (d, *J*=7.7 Hz, 1H), 3.64 (s, 3H), 2.38 (s, 3H), 2.00 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ : 191.9, 166.9, 145.7, 138.0, 136.0, 135.0, 134.9, 132.4, 132.1, 130.4, 130.2, 129.1, 127.7, 126.2, 52.2, 21.2, 20.1; HRMS (ESI) calcd for C₁₇H₁₆NaO₃ [M+Na]⁺ 291.0992, found 291.0989. The enantiomeric excess was determined to be >99% by HPLC [AS column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=98:2), 0.45 mL/min]: 25.6 min (minor), 26.6 min (major).

(*R*)-6-甲酰基-5'-甲基-2'-苯基-[1,1'-联苯]-2-羧酸甲酯(**3ga**): 反应时间 15 h, 黄色油状液体, 23.5 mg, 产率 71%, 83% *ee*. $[\alpha]_{\text{D}}^{25} - 66.7$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.69 (s, 1H), 7.96 (dd, *J*=11.5, 8.2

Hz, 2H), 7.43 (t, $J=7.7$ Hz, 1H), 7.34 (q, $J=7.8$ Hz, 2H), 7.16~7.10 (m, 3H), 7.09~7.03 (m, 3H), 3.63 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.4, 167.4, 145.4, 140.2, 138.8, 136.8, 134.6, 134.4, 134.1, 132.8, 130.8, 130.1, 129.6, 129.5, 129.4, 128.0, 127.5, 126.8, 52.2, 21.0; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{18}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 339.0992, found 339.0995. The enantiomeric excess was determined to be 93% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol ($V:V=97:3$), 1.0 mL/min]: 15.4 min (minor), 17.0 min (major).

(*R*)-3-甲酰基-2-(1-萘基)苯甲酸甲酯(**3ha**): 反应时间 22 h, 黄色油状液体, 28.4 mg, 98% yield, 84% *ee*. $[\alpha]_{\text{D}}^{25} -69.3$ (c 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.46 (s, 1H), 8.25 (dd, $J=7.8, 2.8$ Hz, 2H), 7.93 (dd, $J=8.1, 4.6$ Hz, 2H), 7.68 (t, $J=7.5$ Hz, 1H), 7.58~7.47 (m, 2H), 7.40 (t, $J=7.6$ Hz, 1H), 7.33 (dd, $J=11.4, 8.1$ Hz, 2H), 3.38 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.3, 167.2, 144.1, 135.70, 135.2, 133.6, 133.0, 132.9, 132.8, 130.4, 128.6, 128.4, 128.3, 127.5, 126.8, 126.1, 125.4, 124.8, 52.1; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{14}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 313.0835, found 313.0829. The enantiomeric excess was determined to be 84% by HPLC [IC column, 254 nm, *n*-hexane/*iso*-propanol ($V:V=97:3$), 1.0 mL/min]: 18.1 min (minor), 22.0 min (major).

(*R*)-6-甲酰基-2'-(甲硫基)-[1,1'-联苯]-2-羧酸甲酯(**3ia**): 反应时间 11 h, 黄色油状液体, 25 mg, 87% yield, 86% *ee*. $[\alpha]_{\text{D}}^{25} +15.6$ (c 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.60 (s, 1H), 8.20 (t, $J=8.2$ Hz, 2H), 7.61 (t, $J=7.7$ Hz, 1H), 7.43 (t, $J=7.7$ Hz, 1H), 7.30 (d, $J=7.8$ Hz, 1H), 7.27~7.21 (m, 1H), 7.11 (d, $J=7.5$ Hz, 1H), 3.61 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.5, 166.5, 143.9, 137.9, 135.4, 134.8, 134.4, 131.8, 130.4, 129.7, 128.9, 128.4, 124.6, 124.5, 52.2, 15.5; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{14}\text{NaO}_3\text{S}$ $[\text{M}+\text{Na}]^+$ 309.0556, found 309.0548. The enantiomeric excess was determined to be 86% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol ($V:V=95:5$), 1.0 mL/min]: 22.7 min (minor), 24.8 min (major).

(*R*)-6-甲酰基-2'-乙基-[1,1'-联苯]-2-羧酸甲酯(**3ja**): 反应时间 8 h, 黄色油状液体, 22 mg, 83% yield, 90% *ee*. $[\alpha]_{\text{D}}^{25} -40.3$ (c 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.58 (s, 1H), 8.17 (d, $J=7.8$ Hz, 2H), 7.66 (d, $J=7.7$ Hz, 1H), 7.60 (t, $J=7.8$ Hz, 1H), 7.43 (t, $J=7.6$ Hz, 1H), 7.33 (t, $J=7.5$ Hz, 1H), 7.14 (d, $J=6.9$ Hz, 1H), 6.31 (dd, $J=17.4, 11.0$ Hz, 1H), 5.64 (d, $J=17.4$ Hz, 1H),

5.13 (d, $J=11.0$ Hz, 1H), 3.59 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.5, 166.8, 144.5, 136.9, 135.0, 134.4, 132.2, 130.4, 129.8, 128.6, 128.2, 127.3, 124.9, 116.3, 52.2; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{14}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 289.0835, found 289.0831. The enantiomeric excess was determined to be 90% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol ($V:V=97:3$), 1.0 mL/min]: 15.4 min (minor), 18.6 min (major).

(*R*)-2'-氯-6-甲酰基-[1,1'-联苯]-2-羧酸甲酯(**3ka**): 反应时间 8 h, 黄色油状液体, 16 mg, 产率 58%, 83% *ee*. $[\alpha]_{\text{D}}^{25} -18.3$ (c 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.66 (s, 1H), 8.25 (d, $J=7.8$ Hz, 1H), 8.20 (d, $J=7.8$ Hz, 1H), 7.64 (t, $J=7.8$ Hz, 1H), 7.51 (d, $J=7.9$ Hz, 1H), 7.44~7.33 (m, 2H), 7.24 (t, $J=7.3$ Hz, 1H), 3.66 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 190.9, 166.3, 143.0, 135.5, 135.1, 134.7, 133.4, 131.5, 130.9, 130.8, 129.7, 129.2, 128.5, 126.5, 52.3; HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{11}\text{ClNaO}_3$ $[\text{M}+\text{Na}]^+$ 297.0289, found 297.0261. The enantiomeric excess was determined to be 83% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol ($V:V=97:3$), 1.0 mL/min]: 19.3 min (minor), 22.7 min (major).

(*R*)-6-甲酰基-[1,1'-联苯]-2,2'-二羧酸二甲酯(**3la**): 反应时间 10 h, 黄色油状液体, 24 mg, 产率 80%, 91% *ee*. $[\alpha]_{\text{D}}^{25} -31.4$ (c 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.60 (s, 1H), 8.26~8.11 (m, 3H), 7.59 (t, $J=7.7$ Hz, 2H), 7.53 (t, $J=7.1$ Hz, 1H), 7.19 (d, $J=7.3$ Hz, 1H), 3.65 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 190.9, 166.4, 146.1, 138.1, 135.0, 134.7, 132.8, 131.7, 130.8, 130.6, 130.2, 130.0, 128.2, 127.7, 52.0, 51.98; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{14}\text{NaO}_5$ $[\text{M}+\text{Na}]^+$ 321.0733, found 321.0731. The enantiomeric excess was determined to be 91% by HPLC [AD column, 254 nm, *n*-hexane/*iso*-propanol ($V:V=97:3$), 1.0 mL/min]: 11.8 min (minor), 12.6 min (major).

(*R*)-2-(苯并[*b*]噻吩-4-基)-3-甲酰基苯甲酸甲酯(**3ma**): 反应时间 5 h, 黄色油状液体, 25.1 mg, 产率 85%, 80% *ee*. $[\alpha]_{\text{D}}^{25} -69.1$ (c 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.56 (s, 1H), 8.20 (dd, $J=14.8, 7.8$ Hz, 2H), 7.96 (d, $J=8.1$ Hz, 1H), 7.65 (t, $J=7.7$ Hz, 1H), 7.44~7.40 (m, 2H), 7.30~7.19 (m, 2H), 6.85 (d, $J=5.5$ Hz, 1H), 3.44 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.4, 167.1, 143.9, 139.2, 135.1, 135.0, 132.7, 131.1, 130.4, 128.3, 127.5, 125.7, 123.7, 122.6, 122.3, 52.1; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{12}\text{SNaO}_3$ $[\text{M}+\text{Na}]^+$ 319.0399, found 319.0394. The enantiomeric excess was determined

to be 80% by HPLC [IC column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 1 mL/min]: 19.2 min (minor), 20.3 min (major).

(*R*)-1-(邻甲苯基)-2-萘甲酸甲酯(**3oa**): 反应时间 59 h, 黄色油状液体, 22 mg, 产率 40%, 80% *ee*. $[\alpha]_{\text{D}}^{25} + 32.4$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 7.99 (d, *J*=8.7 Hz, 1H), 7.90 (d, *J*=8.5 Hz, 2H), 7.58~7.51 (m, 1H), 7.40~7.26 (m, 5H), 7.07 (s, 1H), 3.63 (s, 3H), 1.94 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ : 168.1, 141.6, 138.6, 136.6, 134.8, 132.3, 129.4, 129.1, 127.9, 127.6, 127.5, 127.4, 126.7, 125.6, 125.3, 51.9, 19.8; HRMS (ESI) calcd for C₁₉H₁₆NaO₂ [M+Na]⁺ 299.1043, found 299.1048. The enantiomeric excess was determined to be 80% by HPLC [IC column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 1 mL/min]: 5.9 min (minor), 6.3 min (major).

(*R*)-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸丙酯(**3ab**): 反应时间 36 h, 黄色油状液体, 17 mg, 产率 61%, 91% *ee*. $[\alpha]_{\text{D}}^{25} + 16.6$ (*c* 0.600, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.64 (s, 1H), 8.16 (dd, *J*=7.7, 1.7 Hz, 2H), 7.59 (t, *J*=7.8 Hz, 1H), 7.32 (d, *J*=7.4 Hz, 1H), 7.28~7.21 (m, 3H), 7.10 (d, *J*=7.5 Hz, 1H), 3.95 (t, *J*=6.6 Hz, 2H), 2.05 (s, 3H), 1.35 (dd, *J*=14.2, 7.1 Hz, 2H), 0.78 (t, *J*=7.4 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ : 191.7, 166.9, 145.1, 136.3, 135.7, 135.2, 134.5, 132.5, 130.2, 129.6, 129.2, 128.3, 127.9, 125.4, 66.9, 21.5, 20.2, 10.3; HRMS (ESI) calcd for C₁₈H₁₈NaO₃ [M+Na]⁺ 305.1148, found 305.1151. The enantiomeric excess was determined to be 91% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 0.7 mL/min]: 21.6 min (minor), 22.7 min (major).

(*R*)-2-甲氧基乙基-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸酯(**3ac**): 反应时间 13 h, 黄色油状液体, 20 mg, 产率 67%, 99% *ee*. $[\alpha]_{\text{D}}^{25} 15.3$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.61 (s, 1H), 8.22~8.13 (m, 2H), 7.59 (t, *J*=8 Hz, 1H), 7.34 (t, *J*=7.4 Hz, 1H), 7.29~7.22 (m, 2H), 7.12 (d, *J*=7.4 Hz, 1H), 4.16~4.10 (m, 2H), 3.311~3.26 (m, 5H), 2.05 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ : 191.7, 166.7, 145.3, 136.5, 135.6, 135.4, 134.5, 132.0, 130.4, 129.6, 129.3, 128.3, 127.9, 125.4, 69.9, 64.0, 58.8, 20.2; HRMS (ESI) calcd for C₁₈H₁₈NaO₄ [M+Na]⁺ 321.1097, found 321.1094. The enantiomeric excess was determined to be 99% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=95:5), 1 mL/min]: 14.7 min (minor), 16.9 min (major).

(*R*)-2-丙炔基-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸酯(**3ad**): 反应时间 21 h, 黄色油状液体, 16.7 mg, 产率 60%, >99% *ee*. $[\alpha]_{\text{D}}^{25} + 62.0$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.62 (s, 1H), 8.20 (t, *J*=8.5 Hz, 2H), 7.61 (t, *J*=7.8 Hz, 1H), 7.34 (t, *J*=7.9 Hz, 1H), 7.26 (m, 2H), 7.10 (d, *J*=7.4 Hz, 1H), 4.68~4.55 (m, 2H), 2.43 (t, *J*=7.9 Hz, 1H), 2.05 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ : 191.3, 165.7, 145.8, 136.3, 135.3, 135.2, 134.8, 131.1, 130.7, 129.7, 129.2, 128.5, 128.0, 125.5, 74.9, 52.1, 19.9; HRMS (ESI) calcd for C₁₈H₁₄NaO₃ [M+Na]⁺ 301.0835, found 3201.0823. The enantiomeric excess was determined to be >99% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 1 mL/min]: 16.0 min (minor), 18.0 min (major).

(*R*)-4-戊炔基-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸酯(**3ae**): 反应时间 14 h, 黄色油状液体, 18.1 mg, 产率 62%, 94% *ee*. $[\alpha]_{\text{D}}^{25} - 23.0$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.59 (s, 1H), 8.23~8.11 (m, 2H), 7.60 (t, *J*=7.8 Hz, 1H), 7.35 (t, *J*=7.4 Hz, 1H), 7.29~7.23 (m, 2H), 7.10 (d, *J*=7.4 Hz, 1H), 4.09 (t, *J*=6.2 Hz, 2H), 2.05 (s, 3H), 2.00 (td, *J*=6 Hz, 2H), 1.93 (t, *J*=2.4 Hz, 1H), 1.58~1.49 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ : 191.6, 166.9, 145.0, 136.3, 135.8, 135.4, 134.7, 132.2, 130.4, 129.7, 129.3, 128.5, 128.0, 125.6, 82.9, 69.0, 63.9, 27.1, 20.2, 15.1; HRMS (ESI) calcd for C₂₀H₁₈NaO₃ [M+Na]⁺ 329.1148, found 329.1145. The enantiomeric excess was determined to be 94% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 1 mL/min]: 16.4 min (minor), 17.5 min (major).

(*R*)-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸苄酯(**3af**): 反应时间 14 h, 黄色油状液体, 32.3 mg, 产率 98%, 97% *ee*. $[\alpha]_{\text{D}}^{25} + 11.6$ (*c* 1.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ : 9.58 (s, 1H), 8.16 (t, *J*=8.0 Hz, 2H), 7.57 (t, *J*=7.8 Hz, 1H), 7.34~7.24 (m, 4H), 7.19 (t, *J*=7.6 Hz, 2H), 7.11~7.07 (m, 3H), 5.02 (q, *J*=12.1 Hz, 2H), 1.97 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ : 191.8, 166.7, 145.3, 136.3, 135.4, 135.3, 135.1, 134.7, 130.3, 129.7, 129.3, 128.5, 128.4, 128.4, 128.3, 127.9, 125.5, 67.0, 20.9; HRMS (ESI) calcd for C₂₂H₁₈NaO₃ [M+Na]⁺ 353.1148, found 353.1140. The enantiomeric excess was determined to be 97% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=97:3), 1.0 mL/min]: 17.9 min (minor), 19.8 min (major).

(*R*)-4-甲基苄基-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸酯(**3ag**): 反应时间 48 h, 黄色油状液体, 25.2 mg, 产

率 73%, 96% *ee*. $[\alpha]_{\text{D}}^{25} + 11.3$ (*c* 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.58 (s, 1H), 8.15 (dd, $J=7.2$, 4.0 Hz, 2H), 7.56 (t, $J=7.8$ Hz, 1H), 7.29 (t, $J=8$ Hz, 1H), 7.20 (t, $J=6.5$ Hz, 2H), 7.12~7.06 (m, 3H), 7.00 (d, $J=7.8$ Hz, 2H), 4.98 (q, $J=12.0$ Hz, 2H), 2.35 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.7, 166.6, 145.3, 138.1, 136.3, 135.4, 135.3, 134.6, 132.2, 132.1, 130.3, 129.7, 129.3, 129.0, 128.6, 128.3, 127.9, 125.4, 67.1, 21.2, 20.2; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{20}\text{NaO}_3$ $[\text{M} + \text{Na}]^+$ 367.1305, found 367.1297. The enantiomeric excess was determined to be 96% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*:*V*=97:3), 1 mL/min]: 15.4 min (minor), 17.6 min (major).

(*R*)-4-溴苄基-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸酯(**3ah**): 反应时间 34 h, 黄色油状液体, 30.0 mg, 产率 73%, 96% *ee*. $[\alpha]_{\text{D}}^{25} + 8.3$ (*c* 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.56 (s, 1H), 8.16 (d, $J=7.8$ Hz, 2H), 7.59 (t, $J=7.8$ Hz, 1H), 7.41 (d, $J=8.3$ Hz, 2H), 7.29 (t, $J=8.0$ Hz, 1H), 7.19 (t, $J=6.9$ Hz, 2H), 7.06 (d, $J=8.4$ Hz, 1H), 6.94 (d, $J=8.3$ Hz, 2H), 5.02~4.88 (m, 1H), 1.96 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.5, 166.6, 145.1, 136.3, 135.4, 135.3, 134.6, 134.0, 131.9, 131.5, 130.5, 130.2, 129.7, 129.2, 128.4, 127.9, 125.5, 122.3, 66.3, 20.1; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{17}\text{BrNaO}_3$ $[\text{M} + \text{Na}]^+$ 431.0253, found 431.0275. The enantiomeric excess was determined to be 96% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*:*V*=97:3), 1 mL/min]: 15.7 min (minor), 16.6 min (major).

(*R*)-2-氯苄基-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸酯(**3ai**): 反应时间 22 h, 黄色油状液体, 29.9 mg, 产率 82%, 96% *ee*. $[\alpha]_{\text{D}}^{25} + 10.7$ (*c* 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.58 (s, 1H), 8.22 (d, $J=7.7$ Hz, 1H), 8.17 (d, $J=9.1$ Hz, 1H), 7.59 (t, $J=8.0$ Hz, 1H), 7.35 (d, $J=7.9$ Hz, 1H), 7.28~7.12 (m, 6H), 7.08 (t, $J=5.4$ Hz, 2H), 5.16 (q, $J=12.8$ Hz, 2H), 2.00 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.6, 166.3, 145.4, 136.3, 135.4, 135.3, 134.7, 133.9, 132.9, 131.8, 130.5, 130.3, 129.6, 129.5, 129.2, 128.3, 127.9, 126.7, 125.4, 64.4, 20.2; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{17}\text{ClNaO}_3$ $[\text{M} + \text{Na}]^+$ 387.0758, found 387.0751. The enantiomeric excess was determined to be 96% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*:*V*=97:3), 1 mL/min]: 35.4 min (minor), 39.6 min (major).

(*R*)-3-甲基苄基-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸酯(**3aj**): 反应时间 13 h, 黄色油状液体, 25.3 mg, 产

率 74%, 99% *ee*. $[\alpha]_{\text{D}}^{25} + 15.4$ (*c* 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.58 (s, 1H), 8.16 (t, $J=7.5$ Hz, 2H), 7.57 (t, $J=7.8$ Hz, 1H), 7.28 (t, $J=7.4$ Hz, 1H), 7.19 (t, $J=7.3$ Hz, 3H), 7.09 (dd, $J=15.3$, 7.5 Hz, 2H), 6.92 (d, $J=6.3$ Hz, 2H), 5.06~4.92 (m, 2H), 2.34 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.7, 166.6, 145.2, 138.0, 136.3, 135.4, 135.3, 135.0, 134.6, 132.2, 130.3, 129.6, 129.2, 129.0, 128.3, 127.8, 125.6, 125.4, 67.2, 21.3, 20.2; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{17}\text{NaO}_3$ $[\text{M} + \text{Na}]^+$ 367.1305, found 367.1300. The enantiomeric excess was determined to be 99% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*:*V*=97:3), 1 mL/min]: 13.0 min (minor), 14.0 min (major).

(*R*)-1-萘甲基-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸酯(**3ak**): 反应时间 11 h, 黄色油状液体, 30.7 mg, 产率 81%, 99% *ee*. $[\alpha]_{\text{D}}^{25} + 13.0$ (*c* 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.52 (s, 1H), 8.13 (dd, $J=11.9$, 7.8 Hz, 2H), 7.87~7.81 (m, 3H), 7.56~7.47 (m, 3H), 7.38 (t, $J=7.6$ Hz, 1H), 7.30 (d, $J=6.9$ Hz, 1H), 7.10~6.97 (m, 3H), 6.93 (d, $J=7.3$ Hz, 1H), 5.49 (dd, $J=33.6$, 12.3 Hz, 2H), 1.86 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.7, 166.6, 145.4, 136.1, 135.4, 135.3, 134.6, 133.6, 132.0, 131.6, 130.7, 130.3, 129.4, 129.0, 128.6, 128.1, 127.9, 127.9, 126.5, 125.9, 125.2, 125.1, 123.5, 65.2, 20.2; HRMS (ESI) calcd for $\text{C}_{26}\text{H}_{20}\text{NaO}_3$ $[\text{M} + \text{Na}]^+$ 403.1305, found 403.1300. The enantiomeric excess was determined to be 99% by HPLC [OD column, 254 nm, *n*-hexane/*iso*-propanol (*V*:*V*=97:3), 1 mL/min]: 19.9 min (minor), 22.4 min (major).

(*R*)-4-吡啶甲基-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧酸酯(**3al**): 反应时间 11 h, 黄色油状液体, 26.9 mg, 产率 80%, >99% *ee*. $[\alpha]_{\text{D}}^{25} + 11.4$ (*c* 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.55 (s, 1H), 8.51 (d, $J=5.1$ Hz, 2H), 8.18 (t, $J=7.4$ Hz, 2H), 7.60 (t, $J=7.8$ Hz, 1H), 7.27 (t, $J=8.0$ Hz, 1H), 7.19 (t, $J=6.2$ Hz, 2H), 7.07 (d, $J=7.3$ Hz, 1H), 6.93 (d, $J=5.4$ Hz, 2H), 5.02 (m, 2H), 1.98 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.4, 166.4, 149.8, 145.2, 143.9, 136.3, 135.4, 135.4, 134.7, 131.5, 130.7, 129.8, 129.3, 128.5, 128.1, 125.6, 122.2, 65.2, 20.2; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{17}\text{NNaO}_3$ $[\text{M} + \text{Na}]^+$ 354.1101, found 354.1087. The enantiomeric excess was determined to be >99% by HPLC [AD column, 254 nm, *n*-hexane/*iso*-propanol (*V*:*V*=95:5), 1 mL/min]: 38.9 min (minor), 42.3 min (major).

(*R*)-2-噻吩甲基-6-甲酰基-2'-甲基-[1,1'-联苯]-2-羧

酸酯(**3am**): 反应时间 12 h, 黄色油状液体, 24.2 mg, 产率 72%, >99% *ee*. $[\alpha]_{\text{D}}^{25} + 18.7$ (*c* 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 9.59 (s, 1H), 8.15 (d, $J=7.8$ Hz, 2H), 7.57 (t, $J=7.7$ Hz, 1H), 7.30~7.27 (m, 2H), 7.23~7.16 (m, 2H), 7.06 (d, $J=7.2$ Hz, 1H), 6.95~6.92 (m, 2H), 5.18 (q, $J=12.7$ Hz, 2H), 1.98 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 191.6, 166.2, 145.5, 136.9, 136.3, 135.2, 134.6, 131.8, 130.4, 129.6, 129.2, 128.6, 128.3, 127.9, 126.9, 126.7, 125.4, 61.0, 20.2; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 359.0712, found 359.0703. The enantiomeric excess was determined to be >99% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=95:5), 1 mL/min]: 12.3 min (minor), 13.5 min (major).

3.2.2 目标产物 **3na** 的合成方法

依次向 10 mL 的 Schlenk 管中加入底物 **1n** (0.2 mmol, 1 equiv.)、无机碱 K_2CO_3 (0.5 mmol, 2.5 equiv.)、卡宾催化剂前体 **NHC-1** (0.02 mmol, 10 mol%)、氧化剂 3,3',5,5'-四叔丁基二苯醌(DQ, 0.2 mmol, 1.0 equiv.)、溶剂甲苯(1 mL)以及底物甲醇(1 mmol, 10 equiv.)。在室温下反应 4 h, 通过薄层色谱监测反应过程。待反应结束后, 除去溶剂, 使用石油醚/乙酸乙酯(*V*: *V*=1:1)作为洗脱剂对反应体系进行柱层析, 浓缩。之后, 加入 NaBH_4 (5.0 equiv.), 缓慢滴加 2 mL 甲醇作为溶剂, 反应 4 h。待反应结束后, 除去溶剂, 使用石油醚/乙酸乙酯(*V*: *V*=2:1)作为洗脱剂对反应体系进行柱层析, 得到目标产物(*R*)-3-(羟甲基)-2-(喹啉-5-基)苯甲酸甲酯(**3na**), 反应时间 4 h, 白色油状液体, 31.4 mg, 产率 54%, 92% *ee*. $[\alpha]_{\text{D}}^{25} - 28.8$ (*c* 1.00, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ : 8.77~8.79 (m, 1H), 8.04 (d, $J=8.4$ Hz, 1H), 7.96 (d, $J=7.8$ Hz, 1H), 7.89 (d, $J=7.5$ Hz, 1H), 7.73~7.62 (m, 2H), 7.58 (t, $J=7.8$ Hz, 1H), 7.32~7.27 (m, 1H), 7.23 (dd, $J=8.5, 4.2$ Hz, 1H), 4.28 (d, $J=13.7$ Hz, 1H), 4.17 (d, $J=13.7$ Hz, 1H), 3.36 (s, 3H), 2.86 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 167.4, 150.1, 147.7, 141.1, 137.3, 137.0, 133.9, 131.6, 130.9, 129.1, 128.8, 128.8, 128.4, 127.3, 126.5, 121.2, 62.1, 51.8; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{15}\text{NNaO}_3$ $[\text{M}+\text{Na}]^+$ 316.0944, found 316.0939. The enantiomeric excess was determined to be 92% by HPLC [IG column, 254 nm, *n*-hexane/*iso*-propanol (*V*: *V*=80:20), 1 mL/min]: 15.6 min (minor), 18.7 min (major).

辅助材料(Supporting Information) 目标化合物 **3aa**~**3na**、**3ba**~**3ma** 的 ^1H NMR 及 ^{13}C NMR 图谱和 Chiral-HPLC 的分析图。这些材料可以免费从本刊网站

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