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Nickel-catalysed asymmetric S_N2' substitution chemistry of Baylis–Hillman derived allylic electrophiles

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Abstract

Unsymmetrical PhCH=CH(CH_2X)(CO_2Me) (X = Cl, OAc) undergoes regioselective α-substitution with $AlMe_3$ to afford (*E*)-PhCH=CH(Et)(CO_2Me) under Ni(acac)$_2$ catalysis. On the addition of planar chiral Ferrophite ligands [(*R*)-CpFe(1,2-C_5H_3Ar{$P(OR)_2$}) (Ar = Ph, 4-CF_3Ph, 3,5-Me_2Ph, 1-naphthyl; $(OR)_2$ = 1,1′-binaphthylene, 1,1′-biphenylene)] regioselective methylation γ to the leaving group is possible. It is proposed that the bulky Ferrophite ligand leads to an intermediate nickel allyl species Ni^{II}(Me)(Ferrophite){η^3-PhCHCHCH(CO_2Me)} that adopts a configuration whereby the PhCH= terminus of the π-allyl and the Ni–Me are *syn* leading to good regio (up to 6.4:1) and stereo (up to 94% ee) selectivities. ***To cite this article: A. Novak et al., C. R. Chimie 10 (2007).***

Résumé

Le composé asymétrique PhCH=CH(CH_2X)(CO_2Me) (X = Cl, OAc) subit une substitution régiospécifique en position α avec $AlMe_3$, pour produire (*E*)-PhCH=CH(Et)(CO_2Me) en utilisant Ni(acac)$_2$ en tant que catalyseur. Par addition de ligands Ferrophite chiraux planaires (*R*)-CpFe(1,2-C_5H_3Ar{$P(OR)_2$}) (Ar = Ph, 4-CF_3Ph, 3,5-Me_2Ph, 1-naphthyl; $(OR)_2$ = 1,1′-binaphtylène, 1,1′-biphenylène), la méthylation régiosélective γ sur le groupe partant est possible. Il est suggéré que le volumineux ligand Ferrophite conduise à une espèce allyl-nickel intermédiaire Ni^{II}(Me)(Ferrophite){η^3-PhCHCHCH(CO_2Me)}, qui adopte une configuration dans laquelle les groupes PhCH= terminaux du système π-allyl et Ni–Me sont *syn*, conduisant ainsi à de bonnes régio- (jusqu'à 6.4:1) et stéréo- (e.e. atteignant 94%) sélectivités. ***Pour citer cet article : A. Novak et al., C. R. Chimie 10 (2007).***

Keywords: Allylic substitution; Organoaluminium; Monodentate phosphates; Ferrophites

Mots-clés : Substitution allylique ; Organo-aluminium ; Phosphites monodentés ; Ferrophites

1. Introduction

While hundreds of ligands promote asymmetric additions to palladium bound π-allyls [1,2], the analogous asymmetric nickel chemistry is limited to a handful of

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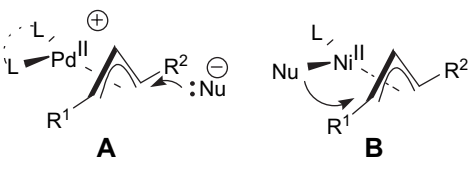
papers [3]. The palladium processes are known to proceed by attack of soft stabilised nucleophiles (often malonate anions) *exo* to the allyl (**A**, Scheme 1). The nature of intermediate **A** dictates that bidentate ligands and symmetrical π-allyls will offer distinct advantages (the combination of P–N chelates and *symmetrical* allyls is particularly effective) [2]. Conversely, the nickel chemistry is normally proposed to proceed via *endo* migration of a Ni-bound nucleophile (normally an alkyl or other organogroup) to the allyl (**B**, Scheme 1) [3]. Intermediate **B** requires the presence of a monodentate chiral ligand for the allyl ligand to π-coordinate in simple square planar geometries. We speculated that under conditions where Nu is 'small' (e.g. a methyl group) and L is 'large' (i.e. a large chiral ligand) that the nickel chemistry might afford a new approach to substitution reactions of *unsymmetrical* π-allyl species (for which far fewer general approaches exist, particularly with non-malonate nucleophiles) [4] provided appropriate matching between the ligand and the derived nickel π-allyl could be attained.

2. Ligand selection and synthesis

We speculated that the recently introduced Ferrophite class of chiral ligands [5] might prove appropriate in attempting to define an effective asymmetric allylation reaction based on intermediate **B** whereby one of the four possible stereoisomers might be favoured. A small library of these compounds was selected for screening purposes (Scheme 2). Ferrophites **L1**–**L7** were prepared either by our literature route or minor modifications thereof [5]. Installation of the phosphite unit used identical procedures to the synthesis of **L1**. Full preparative details of the new ligands **L3** and **L7** are given in the Section 5. To increase the diversity of the library and to compare its performance against known ligands of 'privileged' structure the ferrocenyl phosphine of Kagan (**L8**) [6] was included along with commercially available (*R*)-BINAP and (*R*,*S*)-Josiphos.



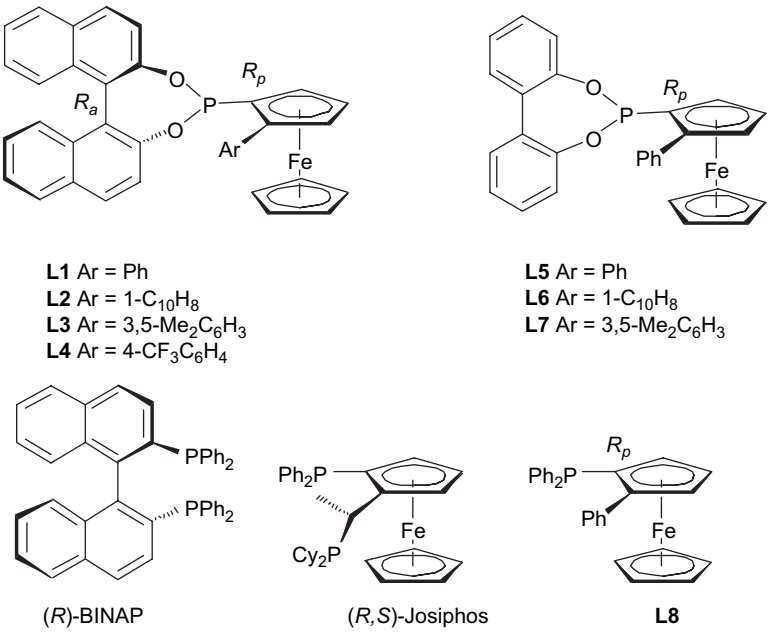
Scheme 1. Comparison of Pd and Ni-catalysed allylation reactions.

3. Catalysis results and mechanistic inferences

We selected the conversion of the allylic chloride (**1a**) and acetate (**1b**) as representative non-symmetrical allylic electrophiles for two reasons: firstly, these species are readily attained through simple Baylis–Hillman chemistry [7], and secondly, a reliable chiral GC assay for the conversion yield and ee determination of product **2** was already available [8] (Scheme 3). The ether **1c** was selected to allow direct comparison with the work of Nobuyoshi and RajanBabu [3a]. Preliminary results revealed that, in contrast to our previously investigated copper chemistry [8], formation of regioisomeric **3** competed with the desired γ product **2**. In the absence of any added ligand, **3** was formed as essentially the sole $AlMe_3$ displacement product (α/γ attack > 60:1). This fortunately enabled a GC assay for **3** to be developed as mixtures of **2/3** co-eluted under normal flash chromatography. The nickel-catalysed reaction required only low loadings [2 mol% $Ni(acac)_2$] but was relatively slow, around 24 h was required at ambient temperature (conditions A) for complete conversion. Most asymmetric screenings were carried out for 3 days at 10 °C to maximise the enantioselectivities realised (conditions B) leading to somewhat lower conversions.

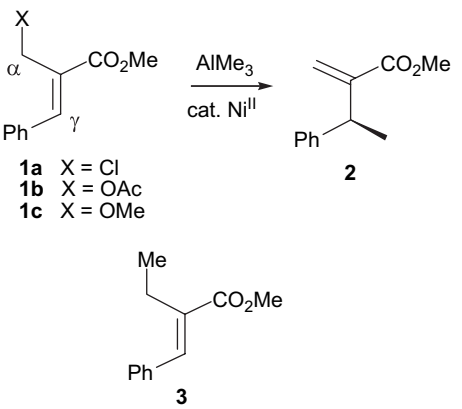
As predicted, based on the structure of intermediate **B**, the chelate ligands BINAP and Josiphos were ineffective (runs 2 and 3). Utilisation of the monodentate Ferrophite ligand family in contrast delivered the desired product **2** with synthetically viable levels of enantioselectivities (up to 94%), though α/γ regioselectivity remained low in the majority of cases.

Comparison of the substrates **1a**–**c** under catalysis by the biphenol ligand **L5** was informative (runs 11–13). All three provided **2** with identical enantioselectivity (71%, *S*) consistent with the formation of a common π-allyl intermediate. The differing α/γ regiochemical ratios observed suggest that the rate of oxidative displacement at the α,γ-related termini of **1** is responsible for the observed regiochemical behaviour. This working model requires that the overall rate of the oxidative addition (and related processes) leading to the isomers **C**, *ent*-**C**, **D** and *ent*-**D** must be similar to the rate of expulsion of the products **2** and **3** from the catalysts. The implication that a mixture of four stereoisomeric π-allyl complexes are present is currently under both NMR and computational investigations. The presence of **D**/*ent*-**D** in the reaction mixture predicts that the bulk of the ligand should effect the regiochemistry (product **3** being achiral) independently of enantioselective events leading to **2**. This notion is



Scheme 2. Preliminary ligand screening library.

supported when using **L2** and **L6** whereby a far superior regioselectivity is observed for substrate **1b** over **1a**. Our working model for the process is that as the bulk of the ligand is increased, the formation of one of the less hindered π-allyls **C**/*ent*-**C** is favoured over diastereomeric **D**/*ent*-**D** (Scheme 4). However, as formation of **C**/*ent*-**C** requires γ attack of the LNi^0 nucleophile on **1** during the oxidative addition if the steric demands of the ligand become too great then the overall reaction rate slows down. These simple ideas are supported by the data of Table 1 in the case of bulky **L2** (low α/γ ratio) and conversely in the absence of any steric bulk (no added Ferrophite, L = solvent, maximum α/γ).



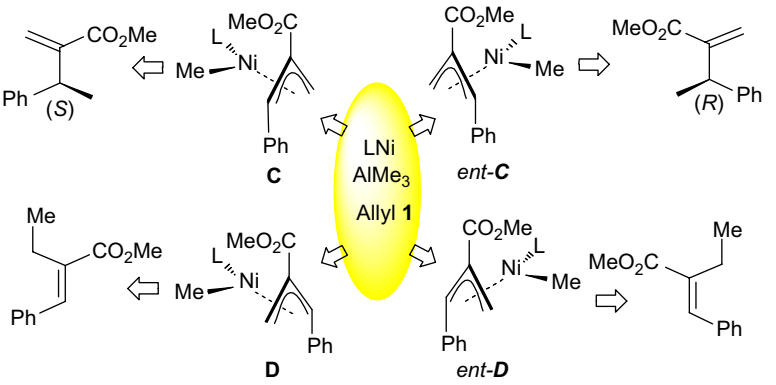
Scheme 3. Methylation of Baylis–Hillman derived electrophiles.

The complete situation is complicated as we do not know if the shown *anti* allyl configuration is preferred and the conformation of the Ferrophite in the enantioselective reductive elimination also remains unknown. At present this creates anomalies in our analysis. For example, increasing the bulk of the aryl group in **L1** from Ph to 3,5-$C_6H_3Me_2$ (**L3**) produced little effect suggesting that the back of these substituents points into 'free space'. However, closely related **L7** did apparently favour formation of **C**/*ent*-**C** leading to improved regio but not enantioselectivity. Having shown that the general approach is valid searching for key π-allyl/ligand interactions by calculative methods will be profitable and this will be discussed in the future.

In addition to this, use of DABAL–Me_3 [9] (an air-stable form of $AlMe_3$) gave increased levels of enantioselectivity, but a loss of α/γ regioselectivity (run 7). This suggests that the stabilising amine (DABCO) remains bound to $AlMe_3$ during both the transmetalation and enantioselective events.

4. Conclusions

We have been able to show a rare example of an enantioselective nickel-catalysed allylation reaction for non-symmetrical allylic electrophiles derived from Baylis–Hillman products. The enantioselectivities realised are significant (49–94%) and partial control of the regiochemistry of the addition can be attained through



Scheme 4. Working model for the observed selectivities.

the ligand (up to $\alpha/\gamma = 0.16$). In the absence of added ligand the reaction is regiospecific leading to the achiral substitution product. Although the reaction is viable at low catalyst loadings (2 mol% Ni/4 mol% ligand) its rate is insufficient and new ligand/condition combinations should be sought to significantly improve the present situation.

5. Experimental

5.1. General experimental

Reactions were carried out under conditions and equipment previously described [5]. Ligands **L1**, **L2**, **L4**–**L6** and **L8** were prepared by literature procedures [5,6]. BINAP and Josiphos were commercial samples. Compounds **1a** and **1b** were prepared according to literature procedures [7,10].

5.2. Preparation of the new ligands

5.2.1. (R_p,S_c)-2-(Tolyl-4-sulfinyl)-1-(3,5methylphenyl)-ferrocene [CpFe{η^5-1,2-C_5H_3(3,5-$CH_3C_6H_3$)[S(O)-4-Tol]}] (precursor to *L3* and *L7*)

To a mixture of [CpFe{η^5-1,2-C_5H_3[$B(OH)_2$][S(O)-4-Tol]}] (1.78 g, 4.82 mmol), palladium(dppf)dichloride $\cdot CH_2Cl_2$ (0.39 g, 0.48 mmol), 5-bromo-*m*-xylene (0.98 mL, 7.24 mmol) and toluene (80 mL) under argon

Table 1
Asymmetric substitution reactions of allylic electrophiles **1**[a]

Run	**1** (X)	Ligand	Method	Time/days	Conv./%	Yield **2** + **3**/%	α/γ	ee **2**
1	**1a** (Cl)	None	A	3	>99	63	>60	–
2	**1a** (Cl)	BINAP	B	2	26	8	1.65	6 (*R*)
3	**1a** (Cl)	Josiphos	B	2	37	16	0.33	4 (*R*)
4	**1a** (Cl)	**L1**	A	1	>99	82	2.04	58 (*S*)
5	**1a** (Cl)	**L2**	A	1	61	36	0.50	84 (*S*)
6	**1a** (Cl)	**L2**	B	3	52	30	0.58	92 (*S*)
7	**1a** (Cl)	**L2**	B[b]	3	>99	41	1.20	94 (*S*)
8	**1b** (OAc)	**L2**	B	3	48[c]	33	0.22	94 (*S*)
9	**1a** (Cl)	**L3**	B	3	>99	71	1.96	52 (*S*)
10	**1a** (Cl)	**L4**	B	3	>99	77	1.14	73 (*S*)
11	**1a** (Cl)	**L5**	B	3	82	73	0.52	71 (*S*)
12	**1b** (OAc)	**L5**	B	2	50[c]	26	0.30	71 (*S*)
13	**1c** (OMe)	**L5**	B	3	31	24	0.85	71 (*S*)
14	**1a** (Cl)	**L6**	B	3	98	43	0.50	91 (*S*)
15	**1b** (OAc)	**L6**	B	3	72[c]	19	0.16	93 (*S*)
16	**1a** (Cl)	**L7**	B	3	70	56	0.75	49 (*S*)
17	**1a** (Cl)	**L8**	B	3	>99	66	4.08	63 (*S*)

[a] Reactions carried out on 0.25 mmol **1** with 0.02/0.04/2 equiv. $Ni(acac)_2$/ligand/$AlMe_3$ in THF (3.0 mL). Conversions, yields and enantioselectivities by GC.
[b] DABAL–Me_3 1.5 equiv. used.
[c] Conversion of acetate **1b** determined by ^1H NMR.

was added sodium hydroxide (2 M, 4.7 mL, 9.41 mmol). The solution was heated at reflux for 4 h, then cooled, concentrated under reduced pressure and purified by column chromatography on silica gel (pentane/EtOAc/CH_2Cl_2, 7:2:1) to give the title compound as an orange solid. Yield: 1.255 g (61%). M.P. 202–204 °C. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.74 (d, 2H, $J = 8.4$ Hz, C_6H_4Me), 7.38 (s, 2H, $C_6H_3Me_2$), 7.33 (d, 2H, $J = 7.6$ Hz, C_6H_4Me), 6.93 (s, 1H, $C_6H_3Me_2$), 4.68–4.67 (m, 1H, C_5H_3), 4.38 (t, 1H, $J = 2.4$ Hz, C_5H_3), 4.13 (s, 5H, C_5H_5), 4.06–4.05 (m, 1H, C_5H_3), 2.44 (s, 3H C_6H_4Me), 2.36 (s, 6H, $C_6H_3Me_2$) ppm. ^{13}C{^{1}H}NMR (100.1 MHz, $CDCl_3$): δ 141.3 ($C_6H_3Me_2$), 140.1 ($C_6H_3Me_2$), 137.6 ($C_6H_3Me_2$), 135.5 ($C_6H_3Me_2$), 129.2 (C_6H_4Me), 129.1 ($C_6H_3Me_2$), 127.6 ($C_6H_3Me_2$), 125.7 (C_6H_4Me), 92.3 (C_5H_3), 90.3 (C_5H_3), 72.1 (C_5H_3), 71.1 (C_5H_5), 69.2 (C_5H_3), 68.9 (C_5H_3), 21.5 (C_6H_4Me), 21.4 ($C_6H_3Me_2$) ppm. IR (CH_2Cl_2): $\nu = 2921$, 1601, 1493, 1108, 1084, 1035, 1015, 853, 828 cm^{-1}. [Found (HRMS, ES): MH^+ 429.0973. $C_{25}H_{25}OSFe$ requires M 429.0970.]

5.2.2. *(R_p,R_a)-2-(3,5-Dioxa-4-phosphacyclohepta [2,1-a;3,4-a′]dinaphthalen-4-yl)-1-m-xyleneferrocene [CpFe{η^5-1,2-C_5H_3(3,5-$CH_3C_6H_3$)[P($O_2C_{20}H_{12}$)]}] (**L3**)*

A solution of sulfoxide precusor (0.45 g, 1.05 mmol) in THF (10 mL) was cooled to −78 °C under argon. To the solution was added ^{t}BuLi (1.7 M in hexanes, 0.68 mL, 1.16 mmol) which caused the solution to darken. After 5 min binaphthyl phosphite was added (0.43 g, 1.05 mmol) as a THF solution (5 mL), causing the solution to lighten in colour. After 5 min, water (1 mL) was added to quench the reaction and was warmed quickly to room temperature. The reaction mixture was extracted with ether and the organic layer dried over $MgSO_4$, concentrated under reduced pressure and purified further by column chromatography on silica gel (pentane/Et_2O, 4:1) to give the title compound as an orange solid. Yield: 0.31 g (54%) $[\alpha]_D = -230$ ($c = 1.00$, CH_2Cl_2). ^{31}P{H}NMR (202.5 MHz, C_6D_6): δ 187.9 ppm. ^{1}H NMR (500.1 MHz, C_6D_6): δ 7.73–7.70 (m, 2H, Ar), 7.68 (s, 2H, Ar), 7.64 (d, 1H, $J = 8.5$ Hz, Ar), 7.62 (d, 1H, $J = 8.0$ Hz, Ar), 7.55 (d, 1H, $J = 8.5$ Hz, Ar), 7.52 (d, 1H, $J = 8.5$ Hz, Ar), 7.48 (d, 1H, $J = 8.5$ Hz, Ar), 7.21–7.14 (m, 2H, Ar), 7.10 (d, 1H, $J = 9.0$ Hz, Ar), 7.02–6.97 (m, 2H, Ar), 6.80 (s, 1H, Ar), 4.59–4.58 (m, 1H, C_5H_3), 4.12 (s, 5H, C_5H_5), 3.92–3.89 (m, 2H, C_5H_3), 2.29 (s, 6H, $C_6H_3Me_2$) ppm. ^{13}C{H}NMR (100.6 MHz, C_6D_6): δ 150.2, 150.1, 138.0, 138.0, 133.7, 133.3, 132.1, 131.5, 131.0, 129.8, 129.2, 128.8, 127.4, 127.2, 126.7, 126.5, 125.7, 125.6, 125.1, 124.9, 124.4, 123.1, 122.2, 94.33 (d, $J = 25$ Hz), 74.1, 74.1, 71.1, 71.0, 21.5 ppm. IR (CH_2Cl_2): $\nu = 2917$, 2855, 1601, 1589, 1510, 1330, 1106, 1070, 950, 851, 827 cm^{-1}. [Found (HRMS, ES): MH^+ 605.1318. $C_{38}H_{30}O_3PFe$ requires M 605.1327.]

5.2.3. *(R_p,R_a)-2-(3,5-Dioxa-4-phosphacyclohepta [2,1-a;3,4-a′]biphenalen-4-yl)-1-m-xyleneferrocene [CpFe{η^5-1,2-C_5H_3(3,5-$CH_3C_6H_3$)[P($O_2C_{12}H_8$)]}] (**L7**)*

A solution of sulfoxide precusor (0.54 g, 1.25 mmol) in THF (15 mL) was cooled to −78 °C under argon. To the solution was added ^{t}BuLi (1.7 M in hexanes, 0.81 mL, 1.38 mmol) which caused the solution to darken. After 5 min biphenyl phosphite was added (0.39 g, 1.25 mmol) as a THF solution (5 mL), causing the solution to lighten in colour. After 5 min, water (1 mL) was added to quench the reaction, and was warmed quickly to room temperature. The reaction mixture was extracted with ether and the organic layer dried over $MgSO_4$, concentrated under reduced pressure and purified further by column chromatography on silica gel (pentane/Et_2O, 4:1) to give the title compound as an orange solid. Yield: 0.05 g (8%) $[\alpha]_D = 22.6$ ($c = 1.00$, CH_2Cl_2). ^{31}P{H}NMR (202.5 MHz, C_6D_6): δ 190.1 ppm. ^{1}H NMR (500.1 MHz, C_6D_6): δ 7.63 (s, 2H, Ar), 7.28 (dd, 2H, $J = 7.5$, 1.5 Hz, Ar), 7.21 (d, 1H, $J = 7.5$ Hz, Ar), 7.12 (dt, 1H, $J = 7.5$, 1.5 Hz, Ar), 7.03 (t, 1H, $J = 7.5$ Hz, Ar), 6.96 (dt, 1H, $J = 7.5$, 1.0 Hz, Ar), 6.91 (dt, 1H, $J = 8.0$, 2.0 Hz, Ar), 6.83 (d, 1H, $J = 8.0$ Hz, Ar), 6.78 (s, 1H, Ar), 4.60–4.58 (m, 1H, C_5H_3), 4.25–4.24 (m, 1H, C_5H_3), 4.14 (s, 5H, C_5H_5), 4.08 (t, 1H, $J = 2.5$ Hz, C_5H_3), 2.26 (s, 6H, $C_6H_3Me_2$) ppm. ^{13}C{H}NMR (100.6 MHz, C_6D_6): δ 152.7, 152.7, 152.1, 152.0, 138.0, 137.9, 133.3, 133.2, 132.2, 132.2, 130.1, 130.0, 129.6, 129.2, 129.1, 125.3, 124.7, 122.8, 122.4, 122.4, 94.36 (d, $J = 25$ Hz), 74.4, 74.0, 74.0, 71.2, 71.1, 71.1 ppm. IR (CH_2Cl_2): $\nu = 3557$, 2922, 1602, 1500, 1332, 1196, 1098, 1039, 1009, 853 cm^{-1}. [Found (HRMS, ES): MNa^+ 523.1111. $C_{30}H_{28}O_3PFeNa$ requires M 523.1120.]

5.2.4. *(E)-Methyl 2-(methoxymethyl)-3-phenylacrylate (**1c**) [11]*

To a stirred solution of NaH (60% dispersion in mineral oil) (0.08 g, 2 mmol) in dry THF (10 mL) at 0 °C under an argon atmosphere was added a solution of precursor alcohol (*E*)-PhCH=C(CH_2OH)(CO_2Me) (0.39 g; 2 mmol) in dry THF (5 mL) over 1 h. To the reaction mixture MeI (150 μL; 2.4 mmol) was added and the mixture stirred for a further 18 h at room

temperature. Quenching the reaction with sat. NH_4Cl (aq) (20 mL) was followed by extraction with Et_2O (50 mL). The combined organic layers were washed with brine (50 mL) and dried over $MgSO_4$. Purification by flash chromatography on silica gel (pentane/Et_2O, 4:1) gave the title compound as a colourless oil. Yield: 0.24 g (58%) ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.68 (s, 2H, Ar), 7.95 (s, 1H, =C*H*), 7.51–7.40 (m, 3H, Ar), 4.25 (s, 2H, CH_2OMe), 3.86 (s, 3H, C(O)O*Me*), 3.45 (s, 3H, O*Me*) ppm. ^{13}C{H}NMR (100.6 MHz, $CDCl_3$): δ 168.1, 144.8, 134.7, 130.1, 129.9, 129.4, 128.6, 66.6, 58.3, 52.2 ppm. [Found (HRMS, ES): MNa^+ 229.0829. $C_{12}H_{14}O_3Na$ requires M 229.0835.]

5.3. General procedure

5.3.1. Nickel-catalysed asymmetric alkylation of Baylis–Hillman derived electrophiles with $AlMe_3$

To a flame-dried Schlenk tube under argon charged with ligand (4 mol %) and $Ni(acac)_2$ (1.2 mg, 2 mol%) anhydrous THF (3 mL) was added and stirred at −10 °C for 5 min. To this the neat allylic chloride or acetate (0.25 mmol) was added and the mixture stirred at −10 °C for 10 min after which time $AlMe_3$ (2 M solution in heptanes, 0.5 mmol, 0.25 mL) was added dropwise. The reaction mixture was warmed to 10 °C, after 3 days at this temperature the yellow reaction was quenched with 2 M HCl (2 mL) followed by addition of the GC internal standard (pentadecane, 25 μL) and extraction with Et_2O (2 × 3 mL). The organic phase was separated and filtered through a plug of silica. A 1 mL sample was removed for GC analysis.

5.3.2. (±)-Methyl 2-methylene-3-phenylbutanoate (**2**)

Pure compound prepared according to literature procedure [7] gave colourless oil. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.30–7.16 (m, 5H, Ar), 6.28 (s, 1H, =C$H_{2\alpha}$), 5.61 (s, 1H, =C$H_{2\beta}$), 4.03 (q, 1H, J = 7.2 Hz, C*H*Me), 3.67 (s, 3H, O*Me*), 1.42 (d, 3H, J = 7.2 Hz, *Me*) ppm. ^{13}C{H}NMR (100.6 MHz, $CDCl_3$): δ 167.6, 145.0, 144.5, 128.6, 127.6, 126.5, 124.0, 52.0, 40.7, 20.9 ppm. IR ($CHCl_3$): ν = 2969m, 1721s, 1627, 1437, 1149, 947 cm^{-1}. [Found (HRMS, EI): M^+ 190.0998. $C_{12}H_{14}O_2$ requires M 190.0998.] The GC assay: 25m 2,6-*O*-dimethyl,3-*O*-pentyl)-γ-cyclodextrin silica column, 120 °C (30 min): 10 °C/min: 200 °C (20 min), He carrier gas, 12 psi, (*S*): 14.8 min. (*R*): 15.2 min. Anal. Calcd. for $C_{12}H_{14}O_2$: C 75.76, H 7.42%; found: C 75.75, H 7.37%.

5.3.3. (E)-Methyl 2-benzylidenebutanoate (**3**) [12]

Prepared according to general procedure A in absence of ligand. Purification by flash chromatography on silica gel (hexane/Et_2O, 9:1) gave the title compound as a colourless oil. Isolated yield: 20 mg (42%) 63% by GC. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.66 (s, 1H, =C*H*), 7.40–7.35 (m, 5H, Ar), 3.83 (s, 3H, O*Me*), 2.57 (q, 2H, J = 7.6 Hz, CH_2Me), 1.18 (t, 3H, J = 7.6 Hz, *Me*) ppm. ^{13}C{H}NMR (100.6 MHz, $CDCl_3$): δ 168.8, 138.6, 135.8, 134.8, 129.2, 128.3, 128.0, 51.9, 20.8, 13.9 ppm. IR ($CHCl_3$): ν = 3027, 2952, 2877, 1698, 1628, 1495, 1435, 1312, 1284, 1238, 1204, 1130, 1045, 810 cm^{-1}. [Found (HRMS, EI): MNa^+ 213.0898. $C_{12}H_{14}O_2Na$ requires MNa 213.0897.] The GC assay: 25m 2,6-*O*-dimethyl,3-*O*-pentyl)-γ-cyclodextrin silica column, 120 °C (30 min): 10 °C/min: 200 °C (20 min), 24.9 min.

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