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Atropselective alkylation of biaryl compounds by means of transition metal-catalyzed C–H/olefin coupling

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Abstract

The reaction of 2-(1-naphthyl)-3-methylpyridine with olefins in the presence of $[RhCl(coe)_2]_2$ and PCy_3 as the catalyst resulted in the alkylation of the naphthyl ring at the 2-position in good yield. The replacement of PCy_3 with the chiral ferrocenyl phosphine, (*R*),(*S*)-PPFOMe, as the ligand resulted in atropselective alkylation of the naphthylpyridine derivatives. Ethylene reacted with the biaryl compounds to give the corresponding addition products in moderate yields with fair to good ee's (up to 49% ee).

Considerable efforts have been made by a number of research groups to synthesize and utilize biaryl compounds which possess axial chirality.[1] Chiral biaryl compounds, e.g. BINAP[2] and BINOL,[3] have been the subject of particular attention because of their potential for use in asymmetric syntheses as a chiral auxiliary. In many cases, chiral compounds such as these can be obtained by the resolution of a racemic mixture. Several other approaches exist for the synthesis of chiral biaryl compounds. One is a transition metal-catalyzed[4] or a transition metal-mediated coupling[5] of two aryl compounds using a chiral auxiliary. Another approach involves the desymmetrization of prochiral biaryl compounds.[6,7] The other approach is an atropselective ring-opening of biaryl lactones with chiral nucleophiles, leading to chiral biaryl compounds with high enantiomeric excess.[8] As an alternative approach, we propose that if the catalytic alkylation of an achiral biaryl compound via C–H bond cleavage takes place in an asymmetric fashion, then rotational restriction between the corresponding atropisomers should be reflected in the alkylated biaryl compounds.[9] In this communication, we describe such an asymmetric induction of axial chirality by means of the transition metal-catalyzed addition of C–H bonds in naphthyl pyridines and naphthyl quinolines to olefins.

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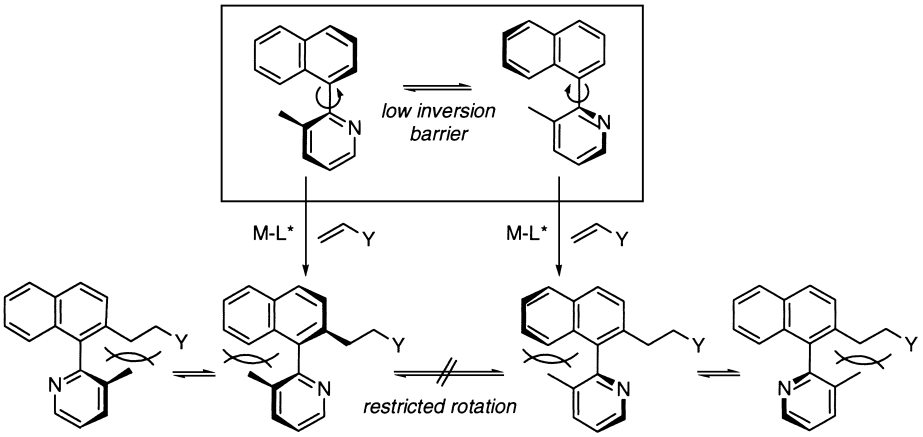
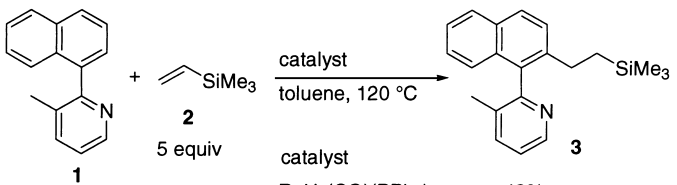
Our approach is shown in Scheme 1. Alkylations of 2-(1-naphthyl)-3-methylpyridine and 1-(1-naphthyl)isoquinoline, in which interconversions between the corresponding atropisomers take place easily because of the low inversion barriers of these types of biaryl compounds,[10,11] by means of transition metal-catalyzed C–H/olefin coupling, should make the interconversion of the atropisomers difficult. Thus, if this reaction was carried out with the aid of a chiral ligand, the atropselective alkylations of the biaryl compounds would be predicted to arise from rotational restriction. This procedure, if successful, could provide a unique approach for the direct preparation of an optical active biaryl compound.



Scheme 1.

The reaction of 2-(1-naphthyl)-3-methylpyridine **1** with trimethylvinylsilane **2** was examined in the presence of an achiral ligand (Eq. (1)). The ruthenium–phophine complex, i.e. $RuH_2(CO)(PPh_3)_3$, which shows a high catalytic activity for the reaction of aromatic ketones with olefins, was fairly effective (43% yield), but $Ru_3(CO)_{12}$ was not (Eq. (1)). Of the various transition metal complexes examined, the $[RhCl(coe)_2]_2/PCy_3$ system[12] showed an acceptable level of catalytic activity for the reaction shown in Eq. (1). Other complexes, including $RhCl(PPh_3)_3$, $RhCl(CO)(PPh_3)_3$ and $IrCl(CO)(PPh_3)_3$, were ineffective for this type of C–H/olefin coupling.

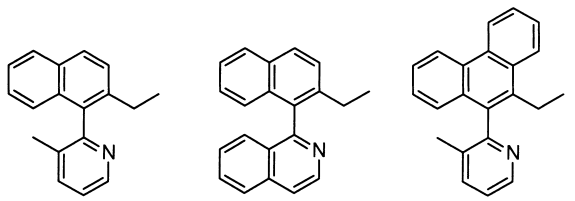


catalyst	
$RuH_2(CO)(PPh_3)_3$	43%
$Ru_3(CO)_{12}$	no reaction
$[RhCl(coe)_2]_2/PCy_3$	55%
$RhCl(PPh_3)_3$	trace
$RhCl(CO)(PPh_3)_2$	no reaction
$IrCl(CO)(PPh_3)_2$	no reaction

(1)

The reaction of some selected biaryl compounds with ethylene was also examined using the $[RhCl(coe)_2]_2/PCy_3$ catalytic system (Fig. 1). For the reaction of **1** with ethylene, the yield of the coupling product **4** was increased to 92%. In the case of the reaction of isoquinoline derivative **5**,

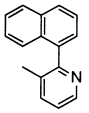
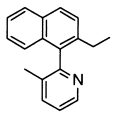
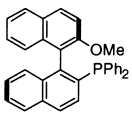
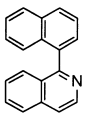
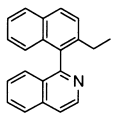
the expected ethylation of the naphthalene ring proceeded with good efficiency, giving **6** as the product in 89% yield. When a phenanthrene derivative was used, the yield was drastically reduced to 5%.



4 92% (20 h) **6** 89% (20 h) 5% (20 h)

Figure 1.

Table 1
Reactions of biaryl compounds with olefins using transition metal complexes and a chiral ligand system[a]

run	biaryl compound	ligand	product	yield	ee[b]
1	 **1**	(*R*),(*S*)-PPFOMe	 **4**	37%[c]	49% ee
2	**1**	(*R*),(*S*)-PPFOMe	**4**	trace[d,e]	—
3[f]	**1**	(*R*),(*S*)-PPFOMe	**4**	15%[g]	15% ee
4	**1**	(*R*)-BINAP	**4**	no reaction	
5	**1**	 (*R*)-MeO-MOP	**4**	49%[h]	0% ee
6	 **5**	(*R*),(*S*)-PPFOMe	 **6**	33%	22% ee
7	**5**	(*R*)-MeO-MOP	**6**	60%	3% ee

[a]Reaction conditions: biaryl compound (0.5 mmol), ethylene (7 kg/cm^2), $[RhCl(coe)_2]_2$ (0.025 mmol), ligand (0.15 mmol), toluene (2.5 mL), 120 °C, 20 h. [b]All enantioselectivities were determined by HPLC analysis on a Daicel OD-H column. [c]The biaryl compound **1** was recovered in 52% yield. [d]The reaction was carried out at 60 °C for 72 h. [e]The biaryl compound **1** was recovered in 90% yield. [f]Ru(cod)(cot) and (*R*),(*S*)-PPFOMe catalyst system was used. [g]The biaryl compound **1** was recovered in 67% yield. [h]The biaryl compound **1** was recovered in 45% yield.

In place of the PCy_3 ligand, several chiral ligands were employed for the present C–H/olefin coupling and some selected results are listed in Table 1. We previously reported[13] that (*R*)-1-[(*S*)-2-(diphenylphosphino)ferrocenyl]ethyl methyl ether **7**[14] (abbreviated as (*R*),(*S*)-PPFOMe) showed a good chiral induction for the rhodium-catalyzed intramolecular cyclization of 1,*n*-pyridyldienes. In the case of the use of ethylene as the olefin, the coupling product (+)-**4**[15,16] was obtained in 34% yield with 49% ee (run 1). This result suggests that one of the atropisomers is preferentially obtained, as the result of restricted rotation of the two aryl groups. To improve the optical yield, the reaction temperature was lowered to 60°C. Unfortunately, under these reaction conditions, the rate of the reaction was quite slow (run 2). A combination of Ru(cod)(cot) and the chiral ferrocenyl phosphine **7** was ineffective in the coupling reaction, although a low valent ruthenium complex showed good catalytic activity for the coupling reaction of aromatic compounds such as aromatic ketones,[18] iminies,[19] and imidates,[20] with olefins (run 3). The complete suppression of the coupling reaction was observed when BINAP was used as the ligand (run 4). Although a biaryl monodentate phosphine ligand, i.e. MeO-MOP,[21] increased the chemical yield to 45%, a racemic mixture was obtained (run 5). Naphthyl isoquinoline **5** also reacted with ethylene using the $[RhCl(coe)_2]_2$/(*R*),(*S*)-PPFOMe catalyst system to give the product (+)-**6**[15,17] (run 6), but the chemical yields and enantiomeric excesses were slightly lower (33% yield and 22% ee, respectively) compared with those of run 1. The MeO-MOP ligand showed catalytic activity but was not effective for the asymmetric induction.

The results described above indicate that the alkylation of achiral biaryl compounds via C–H/olefin coupling results in the induction of axial chirality, as the result of restricted rotation between the aryl groups. Although the efficiencies and the enantioselectivities of the reactions were not high, our present protocol provides a new approach for the preparation of optically active biaryl compounds. Defining the parameters which influence the reactivity of the catalyst, as well as overall enantioselectivity are among our current objectives.

Acknowledgements

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16. Spectral data of **4**: ^{1}H NMR ($CDCl_3$) δ 1.13 (t, $J=7.56$ Hz, 3H, CH_3), 1.96 (s, 3H, CH_3), 2.45 (m, 2H, CH_2), 7.0–7.9 (m, 8H, ArH), 8.62 (dd, $J=4.59$, 1.08 Hz, 1H, pyridyl-H); ^{13}C NMR ($CDCl_3$) δ 15.04, 18.65, 26.51, 122.30, 124.82, 124.96, 126.07, 127.03, 127.89, 128.14, 131.81, 132.04, 132.92, 135.35, 137.45, 139.03, 147.15, 158.08 (Ar); HRMS Found: m/z 247.1364. Calcd for $C_{18}H_{17}N$:M, 247.1361. The specific rotation was determined using 39% ee product. $[\alpha]_D^{20}=+7.2$ (c 0.320, chloroform).
17. Spectral data of **6**: ^{1}H NMR ($CDCl_3$) δ 1.06 (t, $J=7.56$ Hz, 3H, CH_3), 2.38 (q, $J=7.56$ Hz, 2H, CH_2), 6.9–8.0 (m, 11H, ArH), 8.74 (d, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 15.82 (CH_3), 27.35 (CH_2), 120.49, 125.45, 126.25, 126.60, 127.35, 127.49, 127.76, 127.89, 128.30, 129.18, 130.75, 132.47, 133.35, 134.63, 136.66, 140.79, 143.09, 160.88 (Ar); HRMS Found: m/z 283.1356. Calcd for $C_{21}H_{17}N$: M, 283.1361. The optical rotation was determined using 5% ee product. $[\alpha]_D^{20}=+1.9$ (c 0.582, chloroform).
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