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Efficient Rh^{II} binaphthol phosphate catalysts for enantioselective intramolecular tandem carbonyl ylide formation–cycloaddition of α-diazo-β-keto esters

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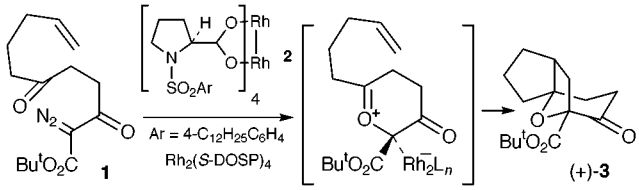
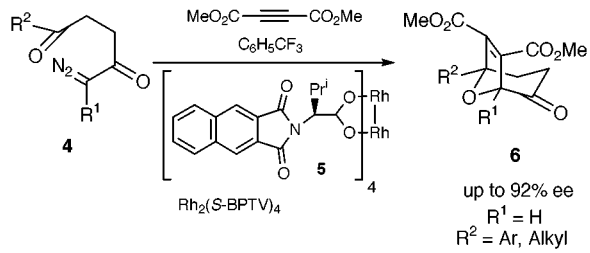
Catalytic enantioselective tandem carbonyl ylide formation–cycloadditions of α-diazo-β-keto ester 1 using 0.5 mol% dirhodium tetrakis(1,1′-binaphthyl-2,2′-diyl phosphate) catalysts 7–9 and 14 to give the cycloadduct 3 in good yields and up to 90% ee are described.

There are currently few methods to achieve catalytic enantioselective 1,3-dipolar cycloadditions, despite the potential utility of such asymmetric transformations.[1] In 1997 we reported the first observations of catalytic enantioselective tandem carbonyl ylide formation–cycloaddition (up to 53% ee) using unsaturated α-diazo-β-keto esters.[2] For example, reaction of α-diazo-β-keto ester **1** using 1 mol% Rh_2(*S*-DOSP)$_4$ **2** in hexane at room temperature gave cycloadduct (+)-**3**† in 93% yield and 52% ee (Scheme 1).[3]



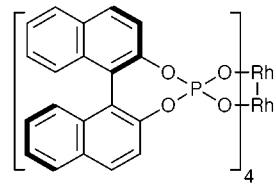
Scheme 1

More recently, research groups led by Doyle,[4] Ibata[5] and Hashimoto[6] have reported conceptually related (but intermolecular) asymmetric carbonyl ylide cycloadditions. The asymmetric induction in these cycloadditions was low (< 30% ee), aside from the work by Hashimoto using α-diazo ketones with DMAD as the dipolarophile, where ees up to 92% were reported (Scheme 2, R^1 = H, R^2 = Ph, absolute sense of asymmetric induction not determined).

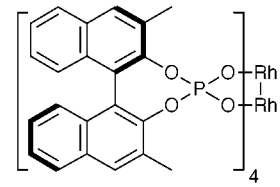


Scheme 2

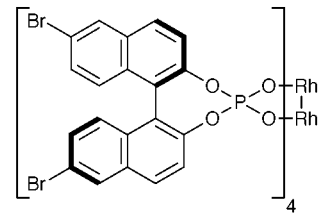
Although we have screened a number of chiral rhodium carboxylate catalysts with α-diazo-β-keto ester **1**,[7] none have delivered asymmetric induction levels close to those observed with Rh_2(*S*-DOSP)$_4$ **2**. Also, applying the optimised catalyst–solvent combination for intermolecular cycloaddition of α-diazo ketones with DMAD reported by Hashimoto[6] [Rh_2(*S*-BPTV)$_4$ **5**, $PhCF_3$, *cf*. Scheme 2] to α-diazo-β-keto ester **1** at 25 °C resulted in only essentially racemic cycloadduct **3** (90% yield, 1% ee). Furthermore, cycloadduct **6** (R^1 = CO_2Et, R^2 = Me) was obtained in only 33% ee under the same conditions in the reaction of α-diazo-β-keto ester **4** (R^1 = CO_2Et, R^2 = Me) with DMAD [α-diazo ketone **4** (R^1 = H, R^2 = Me) gave cycloadduct in 80% ee].[6] These latter results indicate that ee is rather sensitive to variation in the electronic structure of the dipole. A variety of chiral, non-racemic dirhodium carboxylates and carboxamidates have been extensively examined as asymmetric catalysts in a number of diazocarbonyl transformations.[4] However, in seeking to develop more efficient catalysts for asymmetric carbonyl ylide formation–cycloaddition, we were attracted to the isolated reports in 1992 by Pirrung[8] and McKervey[9] concerning 1,1′-binaphthyl-2,2′-diyl phosphate (BNP) catalysts Rh_2(*S*-BNP)$_4$ (*ent*-**7**) and Rh_2(*R*-BNP)$_2$(O_3CH)$_2$·5H_2O respectively for diazocarbonyl decomposition. C–H insertion and cyclopropanation were among the asymmetric processes investigated (up to 60% ee). Here we communicate our preliminary studies on such catalysts which lead to improved enantioselectivities in tandem carbonyl ylide formation–cycloaddition of α-diazo-β-keto esters.



Rh_2(*R*-BNP)$_4$ **7**



Rh_2(*R*-DMBNP)$_4$ **8**



Rh_2(*R*-DBBNP)$_4$ **9**

Initial investigation of Pirrung's structurally well-defined catalyst Rh_2(*R*-BNP)$_4$ **7** with α-diazo-β-keto ester **1** in hexane at 25 °C gave an immediate improvement in ee of the cycloadduct (+)-**3** (64% ee, Table 1, entry 1) compared with Rh_2(*S*-DOSP)$_4$ **2** (52% ee), even though Rh_2(*R*-BNP)$_4$ **7** was only partially soluble in hexane at 25 °C. Interestingly, asymmetric induction was maintained in CH_2Cl_2 at 25 °C (65% ee, entry 2); this compares with 8% ee previously obtained using Rh_2(*S*-DOSP)$_4$ **2** in CH_2Cl_2.[2] Whilst Rh_2(*R*-BNP)$_4$ **7** remained soluble in CH_2Cl_2 at 0 °C, no improvement in ee was observed (64%, entry 3). The results with Rh_2(*R*-BNP)$_4$ **7** prompted a study of the effects of structural variation of the binaphthyl core on enantioselectivity.

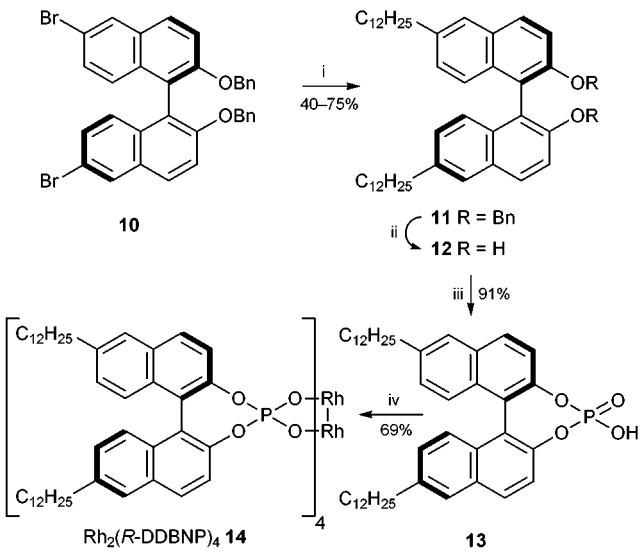
Substitution at the 3,3′-positions was first examined using Rh_2(*R*-DMBNP)$_4$ **8**, which was prepared (79%) by an analo-

Table 1 Effect of catalyst on the yields and enantioselectivities of formation of cycloadduct **3** from α-diazo-β-keto ester **1**

Entry	Catalyst	Solvent	*T*/°C	Yield of **3** (%)	Ee of **3** (%)[a]
1	**7**	hexane	25	65	64
2	**7**	CH_2Cl_2	25	83	65
3	**7**	CH_2Cl_2	0	55	64
4	**8**	CH_2Cl_2	25	50	7
5	**9**	hexane	25	34	66
6	**9**	CH_2Cl_2	25	67	58
7	**9**	CH_2Cl_2	0	36	61
8	**14**	CH_2Cl_2	25	80	68
9	**14**	hexane	25	76	81
10	**14**	hexane	0	81	88 (89)
11	**14**	hexane	−15	66	90 (90)

[a] Ees were determined on the methyl ester [obtained from **3** by hydrolysis–esterification (TFA, CH_2Cl_2, then MeOH, TsOH)] by ^{1}H NMR analysis of the split methoxy signal using Pr(hfc)$_3$. Ees in parentheses were determined on the benzyl oxime ether (*O*-benzylhydroxylamine hydrochloride, NaOAc, MeOH) of the methyl ester by HPLC analysis (Daicel Chiralpak AD, 10% EtOH–hexane) of the major geometric isomer.

gous procedure[8] to Rh_2(*R*-BNP)$_4$ from $Rh_2(OAc)_4$ by ligand exchange using the known 3,3′-dimethyl-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate.[10] However, reaction of Rh_2(*R*-DMBNP)$_4$ **8** with α-diazo-β-keto ester **1** led to no cycloadduct in hexane and a low ee (7%) of (+)-**3** in CH_2Cl_2 (Table 1, entry 4), possibly due to steric congestion at the axial binding sites on the dirhodium core, which (in CH_2Cl_2) might also facilitate catalyst release to give the free ylide for cycloaddition. Substitution at the 6,6′-positions has been a successful tactic to alter asymmetric induction with binaphthyl-based catalysts.[11] Rh_2(*R*-DBBNP)$_4$ **9**, available from 6,6′-dibromo-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate,[12] induced similar ees to Rh_2(*R*-BNP)$_4$ **7** (entries 5–7). With the primary aim of investigating a more hydrocarbon-soluble catalyst, Rh_2(*R*-DDBNP)$_4$ was synthesised according to Scheme 3.



Scheme 3 *Reagents and conditions*: i, $C_{12}H_{25}MgBr$, $Ph_2P(CH_2)_3PPh_2$–$NiCl_2$ (1 mol%), Et_2O, reflux, 48 h; ii, TMSCl, NaI, MeCN, $PhCH_3$, 40 °C, 2 h (89%); iii, $POCl_3$, Py, 25 °C, 1 h, then H_2O, $NaHCO_3$; iv, $Rh_2(OAc)_4$, PhCl, reflux, 5 h.

The known bisether **10**[13] was cross-coupled[14] with commercially available dodecylmagnesium bromide (40–75%, Scheme 3). Deprotection of the resultant didodecyl bisether **11** using TMSI[15] gave diol **12** (89%). Formation of the acid **13** (91%) from the diol **12** under standard conditions followed by ligand exchange[16] gave Rh_2(*R*-DDBNP)$_4$ **14** (69%).‡ Although only a slight rise in the ee of (+)-**3** was noted with Rh_2(*R*-DDBNP)$_4$ **14** in CH_2Cl_2 (Table 1, entry 8) compared with Rh_2(*R*-BNP)$_4$ **7** at 25 °C, the new catalyst was significantly more effective in hexane (81% ee, entry 9). Moreover, catalyst solubility and activity were maintained in hexane at 0 °C and asymmetic induction rose to give the cycloadduct (+)-**3** in 81% yield and 89% ee (entry 10). A similar ee (90%) was observed on conducting the reaction at −15 °C (entry 11) whereas reaction at −30 °C was very slow and gave a complex product mixture from which no cycloadduct was isolable.

Our results indicate that dirhodium tetrakis(1,1′-binaphthyl-2,2′-diyl phosphate) catalysts can be superior to the more commonly utilised carboxylates and carboxamidates in asymmetric transformations of diazocarbonyl compounds and deserve to be more fully investigated.

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Notes and references

† The absolute configuration of the predominant cycloadduct enantiomer (+)-**3** formed using α-diazo-β-keto ester **1** and Rh_2(*S*-DOSP)$_4$ **2** is as shown in Scheme 1 and was determined by crystallographic analysis following hydrolysis using TFA, esterification with (1*S*)-*endo*-(−)-borneol, oxime formation using $HONH_2$ with the major diastereomer and finally reaction with 3,5-dinitrobenzoyl chloride. *Crystal data* for (+)-**3**: $C_{28}H_{33}N_3O_9$, M = 555.58, orthorhombic, a = 6.415(2), b = 19.871(5), c = 21.298(8) Å, U = 2714.8 Å^3, T = 190 K, space group $P2_12_12_1$ (no. 19), Z = 4, μ(Cu-K) = 0.81 mm^{-1}; R_w = 0.040 (3133 independent reflections), R = 0.046 [$I > 3\sigma(I)$]. CCDC 182/1422. See http://www.rsc.org/suppdata/cc/1999/2185/ for crystallographic data in .cif format.

‡ *Selected data* for **14**: $[\alpha]_D^{25}$+60.9 (c 0.03 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$; $CHCl_3$) 0.89 (24H, t, J 6.7), 1.21–1.34 (144H, m), 1.68–1.71 (16H, m), 2.75 (16H, t, J 7.5), 7.18 (8H, d, J 8.7), 7.43 (8H, d, J 8.7), 7.56 (8H, d, J 8.9), 7.65 (8H, s) and 7.77 (8H, d, J 8.9); δ_C(100 MHz; $CDCl_3$; $CDCl_3$) 14.1 (Me), 22.7, 29.4, 29.5, 29.6, 29.6, 29.7, 31.2, 31.9, 35.8 (11 × CH_2), 121.2 (CH), 121.6 (quat.), 126.7 (CH), 127.1 (CH), 128.0 (CH), 130.4 (CH), 130.7 (quat.), 132.0 (quat.), 139.9 (quat.) and 147.2 (quat.).

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