Highly Efficient Asymmetric Hetero-Diels−Alder Reactions of Carbonyl Compounds Catalyzed by Lewis Acid Platinum Complexes of Conformationally Flexible NUPHOS-Type Diphosphines

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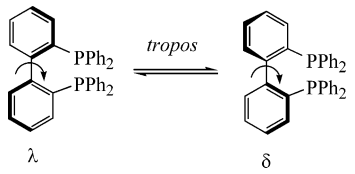
Conformationally flexible NUPHOS-type diphosphines have been resolved as their diastereopure platinum BINOLate complexes δ- and λ-[(NUPHOS)Pt{(*S*)-BINOL}] and the corresponding enantiopure Lewis acids δ- and λ-[(NUPHOS)Pt$(OTf)_2$], being generated by protonation with trifluoromethanesulfonic acid, act as highly efficient catalysts for the hetero-Diels−Alder reaction of nonactivated conjugated dienes with aryl glyoxals and glyoxylate esters, giving ee's as high as 99%.

Advances in the area of platinum-group asymmetric catalysis have traditionally been guided by the premise that conformationally rigid enantiopure diphosphines are required to achieve high selectivities.[1] Recently, though, numerous reports have appeared that use either achiral or meso ligands to convey asymmetry in enantioselective catalysis.[2] In this approach an enantiopure ligand (L*), sometimes referred to as a chiral activator, interacts with an achiral or meso ligand (L) and causes the latter to preferentially adopt one of its chiral conformations, which is ultimately responsible for the transmission of asymmetry in an enantioselective transformation. One such ligand is 2,2′-bis(diphenylphosphino)biphenyl (BIPHEP),[3] a biaryl diphosphine whose axial chiral conformations cannot be resolved due to rapid off-metal rotation about the biaryl axis; such ligands are now commonly termed *tropos*.[4]



Mikami and Noyori were first to demonstrate that BIPHEP could replace its atropisomeric counterpart BINAP in the highly enantioselective ruthenium-catalyzed asymmetric hydrogenation of ketones.[5] In this approach, the 1:1 mixture of *S*/*S*,S and *R*/*S*,*S* diastereoisomers that formed as a result of addition of (*S*,*S*)-1,2-diphenylethylenediamine ((*S*,*S*)-DPEN) to *rac*-[(DM-BIPHEP)$RuCl_2(dmf)_n$] (DM-BIPHEP = 2,2′-bis((3,5-dimethylphenyl)phosphino)biphenyl) slowly equilibrated to a 1:3 thermodynamic mixture which catalyzed the hydrogenation of 1′-acetonaphthone to give an ee of 84%, a marked improvement on the performance of the corresponding catalyst generated from *rac*-BINAP. In this case, effective catalysis relied on the combination of BIPHEP and another enantiopure ligand defining the chiral environment at the metal. Shortly after, Gagné demonstrated that BIPHEP could be used as the sole source of chirality to achieve high ee's in platinum group asymmetric catalysis.[6] This was possible, since coordi-

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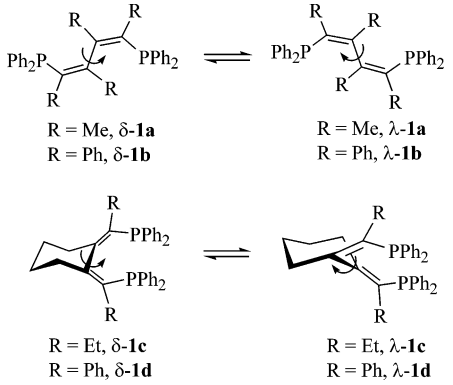
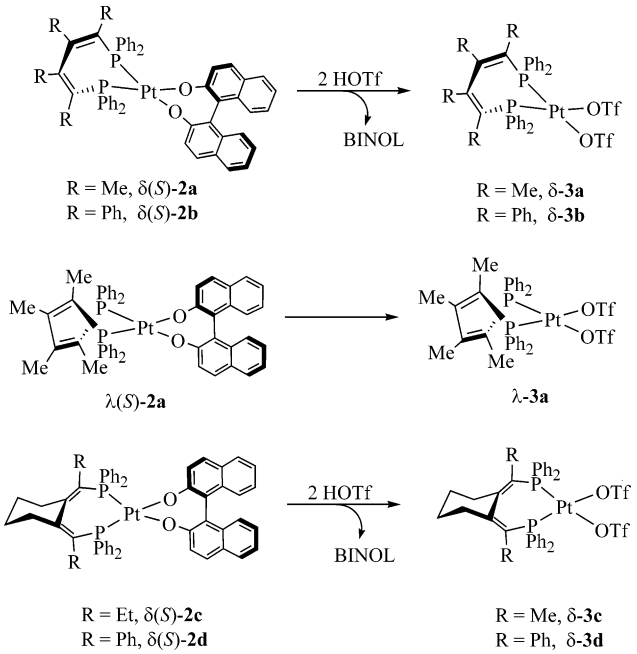
Chart 1



nation of BIPHEP to platinum slows atropinterconversion such that the diastereoisomeric complexes δ- and λ-[(BIPHEP)Pt{(*S*)-BINOL}] can each be isolated, the BINOL liberated, and the resulting enantiopure Lewis acid δ- or λ-[(BIPHEP)Pt$(OTf)_2$] used to catalyze the Diels−Alder and glyoxylate-ene reactions, with ee's of 94 and 72%, respectively. Following this, Mikami used 3,3′-dimethyl-2,2′-diamino-1,1′-binaphthyl (DM-DABN) to resolve palladium complexes of BIPHEP and showed that the enantiopure Lewis acid (*R*)-[(BIPHEP)Pd$(MeCN)_2$]$[SbF_6]_2$ catalyzed the Diels−Alder reaction between 1,3-cyclohexadiene and ethyl glyoxylate, to give an ee of 82%.[7] Most surprisingly, the diastereopure DABN complex (*R*)-[(BIPHEP)Pd{(*R*)-DABN}]$[SbF_6]_2$ proved to be a highly activated catalyst and gave an ee of 94% in the same Diels−Alder reaction. Similarly, (*R*)-DABN has been used to control axial chirality in Pt, Pd, and Ni complexes of (diphenylphosphino)ferrocene (dppf), the (dppf)Ni/(*R*)-DABN combination giving markedly higher ee's than their Pd and Pt counterparts in the glyoxylate-ene reaction.[8]

We have recently prepared a new class of conformationally flexible diphosphine, NUPHOS, which bears a close structural similarity to BIPHEP.[9] Indeed, preliminary studies have shown that both acyclic and monocyclic NUPHOS-type diphosphines (Chart 1) behave in much the same manner as BIPHEP in that coordination slows atropinterconversion[10] such that enantiopure conformations can be resolved and the resulting Lewis acid fragment δ-[(NUPHOS)Pt$(OTf)_2$] used to catalyze the Diels−Alder reaction between acryloyl-*N*-oxazolidinones and cyclopentadiene, in some cases with excellent enantioselectivities.[11] On the basis of this similarity, we have recently begun to explore the applications of this new class of diphosphine in asymmetric catalysis and

Scheme 1



herein report that Lewis acid platinum complexes of NUPHOS diphosphines are highly efficient catalysts for a range of hetero-Diels−Alder reactions of nonactivated conjugated dienes with aryl glyoxals and glyoxylate esters.

Each of the BINOLate complexes δ/λ-[(NUPHOS)Pt{(*S*)-BINOL}] (**2a**−**d**) is typically prepared as a 1:1 mixture of diastereoisomers by reaction of [(NUPHOS)-$PtCl_2$] with Na_2-(*S*)-BINOL, as previously described.[10] Diastereopure samples of these complexes are obtained either by thermal interconversion followed by crystallization of the diastereoenriched mixture to give the thermodynamically favored δ-[(NUPHOS)Pt{(*S*)-BINOL}] (δ-**2a**−**d**) or, in the case of **1a**, by fractional crystallization of a 1:1 diastereoisomeric mixture to give the thermodynamically less favored λ-[(Me_4-NUPHOS)Pt-{(*S*)-BINOL}] (λ-**2a**). Compounds δ-**2a**−**d**/λ-**2a** are typically deep golden yellow or red-orange air- and moisture-stable solids that can be stored in the atmosphere for several months without noticeable decomposition. Thus, although δ-**2a**−**d**/λ-**2a** can be converted into the corresponding enantiopure dichlorides by reaction with hydrogen chloride, it is far more convenient to store the catalyst as its BINOLate complex and generate the active species, δ-**3a**−**d**/λ-**3a**, in situ by liberating the BINOL with a strong acid of a weakly coordinating anion: e.g., trifluoromethanesulfonic acid (Scheme 1). Moreover, solutions of δ-**2a**−**d**/λ-**2a** are considerably more stable with respect to atropinterconversion than their dichloride counterparts, which begin to racemize within hours at room temperature.

A single-crystal X-ray study of one of these BINOLate precursors, [{1,2-bis(1-diphenylphosphinoprop-1-ylidene)-cyclohexane}Pt{(*S*)-BINOL}] (δ-**2c**), has been undertaken, a perspective view of which is shown in Figure 1. Figure 1 clearly shows that the NUPHOS diphosphine coordinates to platinum to form a seven-membered ring with a δ-skew conformation, typical of this ligand type, and a dihedral angle between the least-squares planes containing C(2)C(21)C(3)C(31) and C(4)C-

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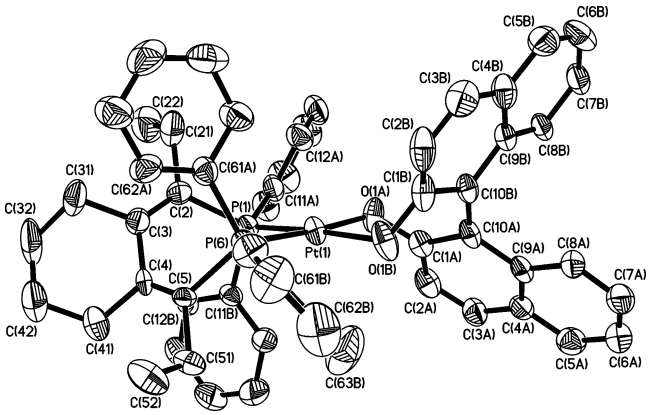
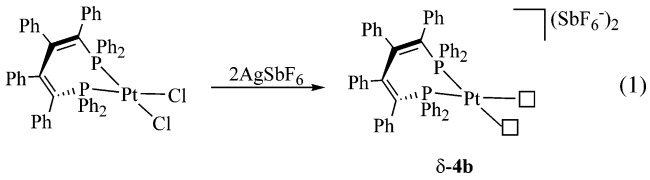


Figure 1. Molecular structure of δ-[(1,4-Et_2-2,3-cyclo-C_6H_8-NUPHOS)Pt{(*S*)-BINOL}] (δ-**2c**), highlighting the alternating edge−face arrangement of the diphenylphosphino phenyl rings. Hydrogen atoms and toluene molecules of crystallization have been omitted for clarity. Ellipsoids are at the 30% probability level. Selected bond lengths (Å) and angles (deg): Pt(1)−P(1), 2.227(3); Pt(1)−P(6), 2.225(3); Pt(1)−O(1A), 2.025(7); Pt(1)−O(1B), 2.028(7); C(2)−C(3), 1.344(14); C(3)−C(4), 1.501(14); C(4)−C(5), 1.312(14); P(1)−Pt(1)−P(6), 90.51(10); O(1A)−Pt(1)−O(1B), 88.5(3); P(6)−Pt(1)−O(1A), 176.0(2); P(6)−Pt(1)−O(1B), 93.06(19); P(1)−Pt(1)−O(1B), 174.5(3); P(1)−Pt(1)−O(1A), 88.24(19); C(2)−C(3)−C(4), 125.3(9); C(3)−C(4)−C(5), 123.7(8); C(2)−C(3)−C(31), 122.8(10); C(31)−C(3)−C(4), 111.7(9); C(41)−C(4)−C(5), 124.0(10); C(3)−C(4)−C(41), 112.0(9).

(41)C(5)C(51) of 55.2°, similar to that reported for a number of related conformationally restricted diphosphines.[12] The platinum atom in δ-**2c** is distorted from an ideal square-planar geometry with a dihedral angle of 5.6° between the PtP_2 and PtO_2 planes. The phenyl rings of the diphenylphosphino groups adopt the familiar alternating edge−face arrangement with the two pseudoaxial rings C(61A)−C(66A) and C(11B)−C(16B) exposing their edges toward the platinum center to form torsion angles of 18.8 and 11.3°, respectively, and the equatorial phenyl rings C(61B)−C(66B) and C(11A)−C(16A) exposing their faces toward platinum to form torsion angles of 43.5 and 44.1°, respectively. The endocyclic bond angles of 111.7(9) and 112.0(9)° for C(31)−C(3)−C(4) and C(3)−C(4)−C(41), respectively, are significantly smaller than the ideal value of 120° for an sp^2-hybridized carbon and reflect the strong tendency of this carbon atom to adopt an angle close to 109.5° required by a cyclohexane ring. The Pt(1)−P(1) and Pt(1)−P(6) bond lengths of 2.227(3) and 2.225(3) Å, respectively, are essentially the same, as are the Pt(1)−O(1A) and Pt(1)−O(1B) distances of 2.025(7) and 2.028(7) Å. The natural bite angle of 90.51(10)° is close to the ideal value of 90° and is comparable to those in related complexes, including [(1,4-Ph_2-*cyclo*-C_6H_8-NUPHOS)$PtCl_2$] (92.26(6)°),[9b] [{(*R*)-BINAP}$PdCl_2$] (92.69(8)°),[13] and [Pt(BINAP)$_2$] (92.3(1)°).[14]

The enantiopure Lewis acids δ-[(NUPHOS)Pt$(OTf)_2$] (δ-**3a**−**d**) and λ-[(NUPHOS)Pt$(OTf)_2$] (λ-**3a**) are highly efficient catalysts for hetero-Diels−Alder reactions of nonactivated conjugated dienes with ethyl glyoxylate and aryl glyoxals. The active catalysts are conveniently generated in situ by protonation of a dichloromethane solution of δ−/λ-**2a**−**d** prior to addition of the substrates, which is performed at low temperature to limit racemization of the resulting Lewis acid. In a typical procedure a dichloromethane solution of δ-**2a**−**d** and 4 Å molecular sieves was treated with trifluoromethanesulfonic acid at 0 °C for 10 min to generate δ-[(NUPHOS)Pt$(OTf)_2$], after which time both substrates were added and the resulting solution was warmed to room temperature. After 5 h the reaction mixture was filtered through a short silica plug with ethyl acetate and the Diels−Alder adduct purified by column chromatography and analyzed by ^1H NMR spectroscopy and either HPLC or GC. All reactions were performed in the presence of 4 Å molecular sieves, since it is commonly accepted that they improve catalyst performance, in particular enantioselectivity, by removing trace amounts of water and acid impurities.[15]

The benchmark hetero-Diels−Alder reactions between 1,3-cyclohexadiene and ethyl glyoxylate and aryl glyoxals were first to be examined, and the results are summarized in Table 1. In each case δ-**3a**−**d** were found to be effective and selective catalysts for this transformation, giving high conversions, near complete endo selectivities, and good to excellent endo enantioselectivities (81−99%, 1*S*,*3R*,*4R* configuration). Although the BINOLate precursors offer a practical advantage in terms of storage and ease of catalyst generation, we have examined the performance of the Lewis acid δ-**4b**, generated by treatment of the corresponding enantiopure δ-[(Ph_4-NUPHOS)$PtCl_2$] with silver hexafluoroantimonate (eq 1) and obtained an ee of 93% and a



(1)

conversion of 99% for the Diels−Alder reaction between 1,3-cyclohexadiene and ethyl glyoxylate (entry 4), which compares favorably to that obtained using δ-**3b** (entry 3). Comparable conversions and enantioselectivities were also obtained with aryl glyoxal substrates (entries 11 and 17).

In a limited examination of the catalyst loading for δ-**3b** and ethyl glyoxylate, it was found that loadings as low as 0.2 mol % may be achieved (endo:exo 92:8, 93% ee, conversion 89%); however, 2 mol % catalyst loadings were routinely used for practical reasons. The absolute configuration of each cycloadduct was determined by comparison of samples generated using catalysts formed by activation of [M{(*S*)-BINAP}Cl_2] (M = Pd, Pt) with $AgSbF_6$, as previously described.[16] In this

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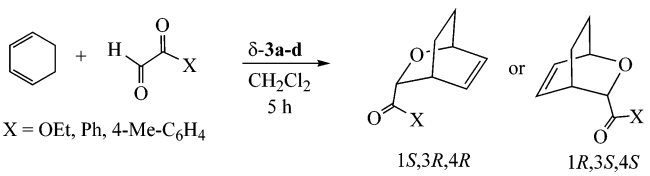
Table 1. Asymmetric Hetero-Diels–Alder Reaction of 1,3-Cyclohexadiene with Ethyl Glyoxylate and Aryl Glyoxals Catalyzed by δ-3a–d and δ-4b

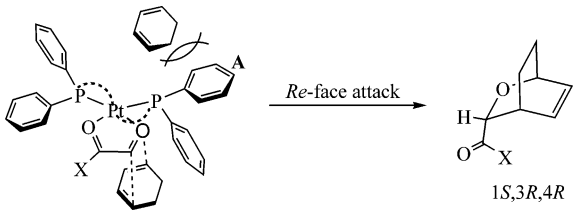


entry[a]	substrate	catalyst (mol %)	conversn (%)[b]	endo:exo ratio[c]	endo % ee (config)[d,e]
1	OEt	λ-**3a**	99	98:2	98 (1*R*,3*S*,4*S*)[d]
2	OEt	δ-**3a**	99	98:2	96 (1*S*,3*R*,4*R*)[d]
3	OEt	δ-**3b**	99	98:2	95 (1*S*,3*R*,4*R*)[d]
4	OEt	δ-**4b**	99	98:2	93 (1*S*,3*R*,4*R*)[d]
5	OEt	δ-**3c**	99	98:2	99 (1*S*,3*R*,4*R*)[d]
6	OEt	δ-**3d**	98	97:3	99 (1*S*,3*R*,4*R*)[d]
7	OEt	Pt{(*S*)-BINAP}	99	98:2	93 (1*S*,3*R*,4*R*)[d]
8	Ph	λ-**3a**	86	99:1	95 (1*R*,3*S*,4*S*)[e]
9	Ph	δ-**3a**	60	99:1	92 (1*S*,3*R*,4*R*)[e]
10	Ph	δ-**3b**	62	99:1	93 (1*S*,3*R*,4*R*)[e]
11	Ph	δ-**4b**	66	99:1	94 (1*S*,3*R*,4*R*)[e]
12	Ph	δ-**3c**	75	99:1	96 (1*S*,3*R*,4*R*)[e]
13	Ph	δ-**3d**	88	99:1	99 (1*S*,3*R*,4*R*)[e]
14	Ph	Pt{(*S*)-BINAP}	85	99:1	97 (1*S*,3*R*,4*R*)[e]
15	4-MeC$_6$H$_4$	λ-**3a**	67	99:1	81 (1*R*,3*S*,4*S*)[e]
16	4-MeC$_6$H$_4$	δ-**3b**	71	99:1	91 (1*S*,3*R*,4*R*)[e]
17	4-MeC$_6$H$_4$	δ-**4b**	65	99:1	90 (1*S*,3*R*,4*R*)[e]
18	4-MeC$_6$H$_4$	δ-**3c**	74	99:1	98 (1*S*,3*R*,4*R*)[e]
18	4-MeC$_6$H$_4$	δ-**3d**	69	99:1	94 (1*S*,3*R*,4*R*)[e]
20	4-MeC$_6$H$_4$	Pt{(*S*)-BINAP}	73	99:1	99 (1*S*,3*R*,4*R*)[e]

[a] Reaction conditions: 2 mol % catalyst, 1,3-cyclohexadiene (0.63 mmol) and dienophile (2.93 mmol) in 1.0 mL of CH_2Cl_2, room temperature. [b] Conversions for a 5 h run determined by GLC using Chrompak Chirasil-DEX CB. [c] Determined by ^{1}H NMR spectroscopy. [d] Enantiomeric excess determined by chiral GLC using a Chrompak Chirasil DEX CB column. [e] Enantiomeric excess determined by chiral HPLC using a Diacel Chiracel OD-H column. Average of three runs.

study, Oi and co-workers showed that palladium catalysts of (*S*)-BINAP gave the hetero Diels–Alder product with 3*R* absolute configuration by reduction to the corresponding alcohol, followed by reaction with (a,*S*)-2′-methoxy-1,1′-binaphthyl-2-carboxylic acid and a single-crystal X-ray crystal structure determination of the resulting ester.[17] While Lewis acids δ-**3a**–**d** all gave the Diels–Alder cycloadducts with 3*R* configuration, that based on λ-**3a** gave the cycloadduct with opposite absolute configuration and an enantioselectivity comparable to that obtained with δ-**3a**. In this regard, NUPHOS-type diphosphines behave in a manner similar to BINAP in that the absolute stereochemistry is that expected for a δ-(*S*)-BINAP like diphosphine, according to the stereochemical model recently proposed by Oi to account for the high level of enantiofacial selection obtained in the palladium (*S*)-BINAP catalyzed hetero-Diels–Alder reaction between 1,3-cyclohexadiene and phenyl glyoxal.[17] In this model, the dienophile coordinates in a bidentate manner through both carbonyl oxygen atoms to form a square-planar adduct, in much the same manner as the catalyst–substrate complex formed between ethyl glyoxylate and copper-

Scheme 2



(II) bis(oxazoline) catalysts.[18] Thus, if δ-NUPHOS diphosphines behave in a (*S*)-BINAP-like manner, the pseudoequatorial phenyl ring labeled A will be oriented above the PtP_2 plane and prevent attack of the diene at the *Si* face, thus rendering endo-*Re* face attack to give cycloaddition with 3*R* absolute configuration the favored pathway (Scheme 2). Examination of the results in Table 1 clearly shows that the performance of NUPHOS-type diphosphines approaches that of BINAP-based catalysts, which suggests that this easy-to-prepare, relatively inexpensive, and air-stable conformationally flexible diphosphine could offer a practical alternative to more expensive and often synthetically more demanding enantiopure ligands. In this regard, Gagné has recently used palladium catalysts stabilized by various labile electron-poor benzonitriles and based on the relatively expensive (*S*)-MeO-BIPHEP to obtain ee's of 99% in the hetero-Diels–Alder reaction of 1,3-cyclohexadiene with ethyl glyoxylate and phenyl glyoxal.[19]

Lewis acids δ-**3a**–**d** also catalyze the hetero Diels–Alder reactions between 2,3-dimethyl-1,3-butadiene and ethyl glyoxylate, phenyl glyoxal, and *p*-tolyl glyoxal, the results of which are summarized in Table 2. In the case of ethyl glyoxylate, formation of the dihydropyran was accompanied by minor amounts of hetero-ene byproduct, and although the enantioselectivities of the Diels–Alder product were good to excellent (71–90%, 2*R*), the ee's of the ene product were low (15–36%). The formation of ene byproduct has previously been observed in hetero-Diels–Alder reactions with palladium–BINAP[17] and Cu(II)–bis(oxazoline) catalysts.[20] In the former, Oi investigated the effect on enantioselectivity and product distribution of increasing the size of the glyoxylate ester substituent and reported that the ee's of both the hetero-Diels–Alder product and the ene product increased with increasing size of the alkyl group. Earlier Jørgensen reported that the alkyl group of the glyoxylate ester has a dramatic influence on the hetero-Diels–Alder to ene product ratio but only a limited influence on the ee of the reaction.[20] Although the enantioselectivities of the ene byproduct are at best modest, Lewis acid palladium complexes of enantiopure diphosphines, including (*S*)-Tol-BINAP and (*S*)-MeO-BIPHEP, have been used for the enantioselective synthesis of α-hydroxy esters via the glyoxylate-ene reaction of 1,1-disubstituted and trisubstituted olefins and ee's as high as 98% have been obtained, albeit with an ene-specific substrate such as methylenecyclohexane.[21]

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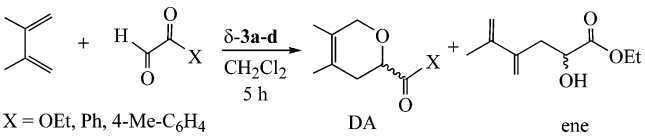
Table 2. Asymmetric Hetero-Diels–Alder Reaction of 2,3-Dimethyl-1,3-butadiene with Ethyl Glyoxylate Aryl and Glyoxals Catalyzed by δ-3a–d



			Diels–Alder		ene	
entry[a]	substrate	catalyst (mol %)	yield (%)[b]	% ee (confign)[c,d]	yield (%)[b]	% ee[f]
1	OEt	λ-**3a**	42	86 (*S*)[c]	14	36
2	OEt	δ-**3a**	44	83 (*R*)[c]	15	32
3	OEt	δ-**3b**	49	71 (*R*)[c]	22	15
4	OEt	δ-**3b**	47	89 (*R*)[c,e]	nd[g]	
5	OEt	δ-**3c**	41	90 (*R*)[c]	3	23
6	OEt	δ-**3d**	39	74 (*R*)[c]	18	21
7	OEt	Pt{(*S*)-BINAP}	49	90 (*R*)[c]	28	57
8	Ph	λ-**3a**	77	88 (*S*)[d]		
9	Ph	δ-**3a**	74	87 (*R*)[d]		
10	Ph	δ-**3b**	79	82 (*R*)[d]		
11	Ph	δ-**3b**	74	93 (*R*)[d,e]		
12	Ph	δ-**3c**	74	97 (*R*)[d]		
13	Ph	δ-**3d**	66	88 (*R*)[d]		
14	Ph	Pt{(*S*)-BINAP}	65	96 (*R*)[d]		
15	4-MeC$_6$H$_4$	λ-**3a**	67	89 (*S*)[d]		
16	4-MeC$_6$H$_4$	δ-**3b**	72	73 (*R*)[d]		
17	4-MeC$_6$H$_4$	δ-**3c**	70	93 (*R*)[d]		
18	4-MeC$_6$H$_4$	δ-**3d**	71	78 (*R*)[d]		
19	4-MeC$_6$H$_4$	Pt{(*S*)-BINAP}	68	93 (*R*)[d]		

[a] Reaction conditions: 2 mol % catalyst, 2,3-dimethyl-1,3-butadiene (0.32 mmol) dienophile (0.25 mmol) in 1.0 mL of CH_2Cl_2, room temperature. [b] Conversion for a 5 h run measured by GC. [c] Enantiomeric excess determined by chiral GLC using a Chrompak Chirasil-DEX CB column. Average of three runs. [d] Enantiomeric excess determined by chiral HPLC using a Daicel Chiralpak AD column. [e] Reaction conducted at −20 °C for 15 h. [f] Not determined. [g] None detected.

In contrast, we found no evidence for the ene byproduct in the hetero-Diels–Alder reaction of 2,3-dimethyl-1,3-butadiene with phenyl or *p*-tolyl glyoxal catalyzed by δ-**3a**–**d**, and reactions with these substrates gave good conversions (68–77%) and excellent enantioselectivities (73–96%, 2*R*). As expected, λ-**3a** gave the Diels–Alder adduct of opposite absolute stereochemistry (2*S*) with an enantioselectivity comparable to that obtained with δ-**3a** (entries 7 and 8) consistent with the BINAP-like stereoinduction model depicted in Figure 2. The effect of temperature on the performance of catalyst δ-**3b** was also investigated, since it consistently gave the lowest enantioselectivities in the hetero-Diels–Alder reactions with 2,3-dimethyl-1,3-butadiene. As expected, enantioselectivity improved at lower temperatures, and at −20 °C the ee's of 89 and 93% for ethyl glyoxlate and phenyl glyoxal, respectively, were significantly higher than those of 71 and 82%, respectively, obtained at room temperature.

Finally, for selected substrate combinations ionic liquids appear to provide a marked enhancement in enantioselectivity. For instance, the Diels–Alder reaction of 2,3-dimethyl-1,3-butadiene with phenyl and *p*-tolyl glyoxal catalyzed by δ-**3b** gave ee's of 82 and 73%, respectively, in dichloromethane at room temperature and 89 and 84%, respectively, in [emim][NTf_2]. It should be noted that an enhancement in enantioselectivity was not obtained for all substrate combinations; however, in such cases enantioselectivities were comparable to those obtained in dichloromethane. Enhancement of enantioselectivity has previously been reported for ruthenium-catalyzed asymmetric hydrogenations[22] as well as platinum group catalyzed Diels–Alder reactions,[11b,23] and the effect of ionic liquids on enantioselective reactions has recently been reviewed.[24] Interestingly, in these reactions the rate is slower in ionic liquids than in dichloromethane. This may be associated with strong hydrogen bonding of the dienophile with the cation, which lowers its reactivity. In contrast, in the Diels–Alder reactions reported to date, large increases in the reaction rate are commonly observed in ionic liquid compared with the rates in organic solvents and water.

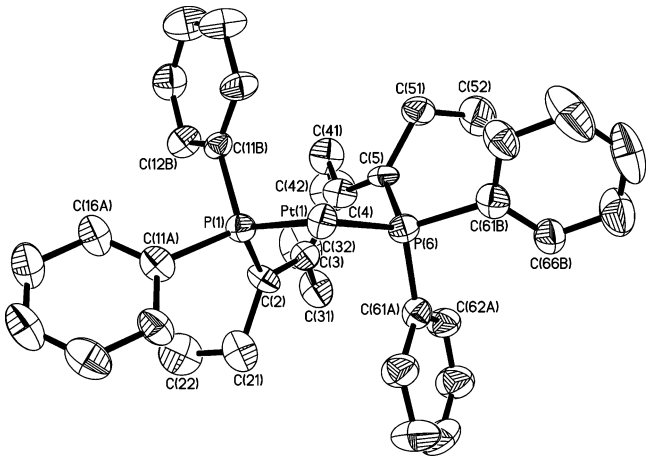


Figure 2. Perspective view of the molecular structure of δ-**2c** to emphasize the asymmetric environment at platinum. The BINOL fragment, hydrogen atoms, and toluene molecules of crystallization have been omitted for clarity. Ellipsoids are at the 30% probability level.

In summary, enantiopure Lewis acid platinum metal complexes of conformationally flexible NUPHOS-type diphosphines are highly efficient catalysts for the hetero-Diels–Alder reaction between nonactivated dienes and glyoxylate esters and aryl glyoxals. This study has shown that the performance of NUPHOS-based catalysts approaches and can even rival that of BINAP, and, since bidentate phosphines are central to platinum group catalysis, it could be possible to apply this strategy to a range of asymmetric transformations. Moreover, NUPHOS diphosphines could also replace BINAP and related ligands in achiral transformations, for instance, in the palladium-catalyzed carbonylation of heteroaromatic chlorides[26] and the rhodium-catalyzed chemo- and regioselective intramolecular cyclotrimerization of alkynes,[27] two recent examples in which the optimum catalyst was based on a BINAP-like diphosphine.

Experimental Section

General Procedures. All manipulations involving air-sensitive materials were carried out in an inert-atmosphere

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glovebox or using standard Schlenk line techniques under an atmosphere of nitrogen or argon in oven-dried glassware. Diethyl ether was distilled from potassium/sodium alloy and dichloromethane from calcium hydride, and [emim][NTf_2] was prepared following the method of Bonhôte et al.[25] (*S*)-BINAP was purchased from Strem. Unless otherwise stated, commercially purchased materials were used without further purification. Deuteriochloroform was predried with calcium hydride, vacuum-transferred, and stored over 4 Å molecular sieves. The platinum complexes [(NUPHOS)Pt{(*S*)-BINOL}] (**2a**−**e**) and [Pt{(*S*)-BINAP)Cl_2][17] were prepared as previously described. Ethyl glyoxylate and phenyl glyoxal were purchased from Lancaster, and *p*-tolyl glyoxal was prepared as described in the literature;[26] all were distilled immediately prior to use. ^{1}H and ^{31}P{^{1}H} and ^{13}C{^{1}H} NMR spectra were recorded on a JEOL LAMBDA 500 or Bruker AC 200, AMX 300, and DRX 500 machines. Purification of reaction products was carried out by column chromatography on reagent silica gel (60−200 mesh). Analytical high-performance liquid chromatography (HPLC) was performed on an Agilent 110 Series HPLC equipped with a variable-wavelength detector using either a Daicel Chiralcel OD-H or a Chiralpak AD column. Chiral GLC was performed on a Agilent 6890N series GC using a Chrompak Chirasil DEX CB column. Enantiomeric excesses were calculated from the HPLC and GC profiles.

***δ*-[{1,4-bis(diphenylphosphino)-1,2,3,4-tetraphenyl-1,3-butadiene}$PtCl_2$] (*δ*-4b).** A solution of enantiopure *δ*-[{1,4-bis(diphenylphosphino)-1,2,3,4-tetraphenyl-1,3-butadiene}-platinum{(*S*)-BINOL}] (*λ*-**2b**; 1.1 g, 0.91 mmol) in dichloromethane (20 mL) was treated with a diethyl ether solution of HCl (2.5 mL, 2.5 mmol, 1.0 M solution in diethyl ether). Addition of HCl resulted in an immediate color change from deep yellow to near colorless. After 10 min the solution was filtered, the solvent removed under vacuum, and the resulting residue washed with diethyl ether (5 × 10 mL) and hexane (5 × 10 mL). Crystallization of the product by slow diffusion of a dichloromethane solution layered with hexane at room temperature gave pale yellow *λ*-**4b** in 67% yield (0.61 g). ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$, *δ*): 1.9 (t, J_{PtP} = 3607 Hz, PPh_2). ^{1}H NMR (500.13 MHz, $CDCl_3$, 232 K, *δ*): 9.57 (br m, 4H, C_6H_5), 7.9 (br m, 6H, C_6H_5), 7.2 (m, 6H, C_6H_5), 6.88, (m, 4H, C_6H_5), 6.7 (t, J = 7.3 Hz, 2H, C_6H_5), 6.65 (m, 6H, C_6H_5), 6.54 (t, J = 7.9 Hz, 4H, C_6H_5), 6.18 (br, 4H, C_6H_5), 6.11 (d, J = 7.3 Hz, 4H, C_6H_5). Anal. Calcd for $C_{52}H_{40}Cl_2P_2Pt$: C, 62.91; H, 4.06. Found: C, 63.23; H, 4.44. $[\alpha]_D$ = −9.07 (*c* 1.0, $CHCl_3$).

General Procedure for Platinum-Catalyzed Enantioselective Hetero-Diels−Alder Reactions between Ethyl Glyoxylate and 1,3-Cyclohexadiene with Catalyst Precursors 2a−d. A flame-dried Schlenk flask charged with *δ*-**2b** (0.0154 g, 0.0127 mmol) and 4 Å molecular sieves (ca. 0.025 g) was cooled to 0 °C and dichloromethane added (1 mL). The resulting solution was treated with trifluoromethanesulfonic acid (2.1 *μ*L, 0.024 mmol) to give an immediate color change from deep red-orange to near colorless. After the mixture was stirred for 5 min, freshly distilled ethyl glyoxylate (0.390 mL, 2.93 mmol) was added, followed by 1,3-cyclohexadiene (0.060 mL, 0.63 mmol). The resulting mixture was warmed to room temperature and stirred for a further 5 h, after which time the solution was filtered through a short plug of silica with ethyl acetate, the solvent removed, and the residue purified by column chromatography over silica gel (60−200 mesh, 25% ethyl acetate/75% hexane). The endo/exo ratio was obtained from ^{1}H NMR spectroscopy, and the enantiomeric excess was determined by GC using a Chrompak Chirasil DEX CB column (90 °C for 7 min ramp to 125 °C at 4 °C/min; hold 15 min, pressure 11 psi). The retention times of the enantiomers of *endo*- and *exo*-ethyl 2-oxabicyclo[2.2.2]oct-5-ene-3-carboxylate were 13.81 min (exo_1), 14.12 min (exo_2), 14.67 min ($endo_{3S}$), 15.13 min ($endo_{3R}$). The absolute configuration of the endo cycloadduct was assigned by comparison with the retention times of samples prepared from [{(*S*)-BINAP}$PtCl_2$].

General Procedure for Platinum-Catalyzed Enantioselective Hetero-Diels−Alder Reactions between Ethyl Glyoxylate and 2,3-Dimethyl-1,3-butadiene using Catalyst Precursors 2a−d. Catalyst mixtures were prepared as described above for 1,3-cyclohexadiene. After 5 h the solution was filtered through a short plug of silica with ethyl acetate, the solvent removed, and the resulting residue purified by column chromatography over silica gel (60−200 mesh, 20% ethyl acetate/80% hexane) to give the Diels−Alder and ene products as colorless oils. The enantiomeric excess was determined by GC using a Chrompak Chirasil-DEX CB column (90 °C for 7 min ramp to 125 °C at 4 °C/min; hold 15 min, pressure 11 psi). The retention times of the Diels−Alder product ethyl 4,5-dimethyl-3,6-dihydro-2*H*-pyran-2-carboxylate were 17.02 min (2*R*) and 17.49 min (2*S*), and those of the ene product ethyl 2-hydroxy-5-methyl-4-methylene-5-hexenoate were 17.14 and 18.16 min.

General Procedure for Platinum-Catalyzed Enantioselective Hetero-Diels−Alder Reactions between Aryl Glyoxals and 1,3-Cyclohexadiene using Catalyst Precursors 2a−d. A flame-dried Schlenk flask charged with **2c** (0.0126 g, 0.0127 mmol) and 4 Å molecular sieves (ca. 0.025 g) was cooled to 0 °C and dichloromethane added (1 mL). The resulting solution was treated with trifluoromethanesulfonic acid (2.1 *μ*L, 0.024 mmol) to give an immediate color change from golden yellow to near colorless. After the mixture was stirred for 5 min, freshly distilled phenyl glyoxal (0.032 mL, 0.25 mmol) was added, followed by 1,3-cyclohexadiene (0.031 mL, 0.33 mmol). The reaction mixture was warmed to room temperature and stirred for a further 5 h, after which the solution was filtered through a short plug of silica with ethyl acetate, the solvent removed, and the resulting residue purified by column chromatography over silica gel (60−200 mesh, 10% ethyl acetate/90% hexane). The endo/exo ratio was obtained from ^{1}H NMR spectroscopy, and the enantiomeric excess was determined from the HPLC profile using a Daicel Chiralcel OD-H column (0.75 mL/min flow rate, hexane/propan-2-ol 90/10). The retention times of the enantiomers of *endo*-3-benzoyl-2-oxabicyclo[2.2.2]oct-5-ene were 11.61 min ($endo_{3S}$) and 12.70 min ($endo_{3R}$), while those of 3-(4′-methylbenzoyl)-2-oxabicyclo-[2.2.2]oct-5-ene were 10.96 min ($endo_{3S}$) and 12.72 min ($endo_{3R}$). The absolute configuration of the endo cycloadduct was assigned by comparison with the retention times of samples prepared from (*R*)- and [{(*S*)-BINAP}$PtCl_2$].

General Procedure for Platinum-Catalyzed Enantioselective Hetero-Diels−Alder Reactions between Aryl Glyoxals and 2,3-Dimethyl-1,3-butadiene using Catalyst Precursors 2a−d. Catalyst mixtures were prepared as described above for 1,3-cyclohexadiene and the products purified by column chromatography over silica gel. The enantiomeric excess was determined by HPLC using a Chiralpak AD column (1 mL/min flow rate, hexane/propan-2-ol 95/5). The retention times of the two enantiomers of 2-benzoyl-4,5-dimethyl-3,6-dihydro-2*H*-pyran were 9.30 min ($endo_{2S}$) and 12.47 min ($endo_{2R}$), and those of 4,5-dimethyl-2-(4′-methylbenzoyl)-3,6-dihydro-2*H*-pyran were 12.05 min ($endo_{2S}$) and 17.27 min ($endo_{2R}$).

General Procedure for Platinum-Catalyzed Enantioselective Hetero-Diels−Alder Reactions between Aryl Glyoxals and 2,3-Dimethyl-1,3-butadiene using Catalyst Precursors [{(*S*)-BINAP)$PtCl_2$]. A solution of [{(*S*)-BINAP)-$PtCl_2$] (0.0111 g, 0.0125 mmol) and 4 Å molecular sieves (0.025 g) in dichloromethane (2 mL) was treated with silver hexafluoroantimonate (0.0086 g, 0.025 mmol) and stirred for 30 min. The resulting catalyst solution was cooled to 0 °C, and freshly distilled phenyl glyoxal (0.057 mL, 0.625 mmol) was added, followed by 1,3-cyclohexadiene (0.078 mL, 0.825 mmol). The reaction mixture was warmed to room temperature and stirred for a further 5 h, after which the solution was filtered through a short plug of silica with ethyl acetate, the solvent removed, and the resulting residue purified by column chromatography

Table 3. Summary of Crystal Data and Structure Determination Details for Compound 2c

formula	$C_{70}H_{66}O_2P_2Pt$
M_r	1196.26
cryst color	yellow
cryst size (mm)	0.30 × 0.26 × 0.25
temp, K	297(2)
cryst syst	orthorhombic
space group	$P2_12_12_1$
a, Å	17.095(8)
b, Å	17.629(8)
c, Å	19.234(9)
α	90
β	90
γ	90
V, Å^3	5795(5)
Z	4
D_{calcd} (g cm^{-3})	1.371
F(000)	2440
μ(Mo Kα) (mm^{-1})	2.521
θ_{max}, deg	23.38
no. of rflns measd	49 429
no. of unique rflns	8395
R_{int} (on F^2)	0.1166
no. of params	639
R^a ($F^2 > 2\sigma(F^2)$)	0.0515
$R_w{}^b$ (all data)	0.1163
GOF^c (S)	1.059
max, min diff map, e Å^{-3}	0.735, −1.523

[a] Conventional $R = \sum||F_o| - |F_c||/\sum|F_o|$ for "observed" reflections having $F_o^2 > 2\sigma(F_o^2)$. [b] $R_w = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$ for all data. [c] GOF = $[\sum w(F_o^2 - F_c^2)^2/((\text{no. of unique rflns}) - (\text{no. of params}))]^{1/2}$.

over silica gel. The product was analyzed by ^{1}H NMR spectroscopy and either GC or HPLC as described above.

Crystal Structure Determinations of 2c. Data were collected on a Bruker-AXS SMART diffractometer using the SAINT-NT software with graphite-monochromated Mo Kα radiation using ψ/ω scans. A crystal was mounted onto the diffractometer at room temperature (ca. 297 K). Crystal stabilities were monitored via re-collection of the first set of frames. There were no significant variations (<±1%). Lorentz and polarization corrections were applied. The structures were solved using direct methods and refined with the SHELXTL program package, and the non-hydrogen atoms were refined with anisotropic thermal parameters. Table 3 gives further details. Hydrogen atoms were added at idealized positions, and a riding model was used for subsequent refinement. The function minimized was $\sum[w(|F_o|^2 - |F_c|^2)]$ with reflection weights $w^{-1} = [\sigma^2|F_o|^2 + (g_1P)^2 + (g_2P)]$, where $P = [\max|F_o|^2 + 2|F_c|^2]/3$. Additional material available from the Cambridge Crystallographic Data Center comprises relevant tables of atomic coordinates, bond lengths and angles, and thermal parameters.

Acknowledgment. We gratefully acknowledge the EPSRC (R.K.R.), CenTACat (HKL), and the McClay Trust (C.R.N.) for funding and Johnson Matthey for loans of palladium salts.

Supporting Information Available: For **3c,** tables of crystal data and structure solution and refinement details, atomic coordinates, bond distances, bond angles, and anisotropic thermal parameters. This material is available free of charge via the Internet at http://pubs.acs.org. Observed and calculated structure factor tables are available from the authors upon request.

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