Nickel-Catalyzed [2π + 2π + 2π] (Homo-Diels−Alder) and [2π + 2π] Cycloadditions of Bicyclo[2.2.1]hepta-2,5-dienes

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Abstract: Active catalysts which promote the homo-Diels−Alder (HDA) cycloaddition with a variety of electron-deficient olefins with bicyclo[2.2.1]hepta-2,5-diene (norbornadiene, NBD) have been developed. The nickel complex and the additives (e.g., ligands, reducing agents) influence the activity of the catalyst. Dienophiles which participate in this cycloaddition include acyclic and cyclic enones, lactones, sulfones, and sulfoxides. The dienophile substituent, the catalyst, and the temperature affected the *exo/endo* selectivity in the HDA reaction. A diastereoselective reaction with an optically enriched vinyl sulfoxide led to the synthesis of an optically active deltacyclane. The regio- and stereoselectivity of the HDA reaction between 2-substituted norbornadienes and electron-deficient dienophiles has also been studied. The substituents on the diene and dienophile as well as the ligands were found to exert a dramatic effect on the selectivity. With very reactive dienophiles, an alternative [2π + 2π] cycloaddition was discovered for 2-substituted norbornadienes. In some cases, the [2π + 2π] cycloaddition can occur with high chemo- and regioselectivity and moderate levels of stereoselectivity.

Introduction

The discovery that metal catalysts promote cycloaddition reactions has become a powerful tool in organic synthesis. Metal-catalyzed [2 + 2], [3 + 2], [4 + 2], and higher order cycloadditions have been studied with encouraging results.[1−4] We have focused on determining the scope and limitations of the metal-catalyzed [2π + 2π + 2π] homo-Diels−Alder (HDA) reaction as a method for the synthesis of strained polycyclic compounds.[5−11]

The first example of the HDA reaction was reported in 1958 by Ullman,[11a] when a "small amount" of adduct **2** was obtained when norbornadiene (NBD, **1**) and maleic anhydride were heated at 205 °C (eq 1). The reaction was referred to as the *homo*-Diels−Alder reaction due to the sp^3 center separating the olefins of the bicyclic diene. Since the diene was not

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(2) For metal-catalyzed [3 + 2] cycloadditions , see: (a) Binger, P.; Buch, H. M. *Top. Curr. Chem.* **1987**, *135*. 77. (b) Trost, B. M. *Pure Appl. Chem.* **1988**, *60*, 1615 and references cited therein. (c) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 77 and references cited therein. (d) Motherwell, W. B.; Shipman, M. *Tetrahedron Lett.* **1991**, *32*, 1103. (e) Lautens, M.; Ren, Y.; Delanghe, P. H. M. *J. Am. Chem. Soc.* **1994**, *116*, 8821.

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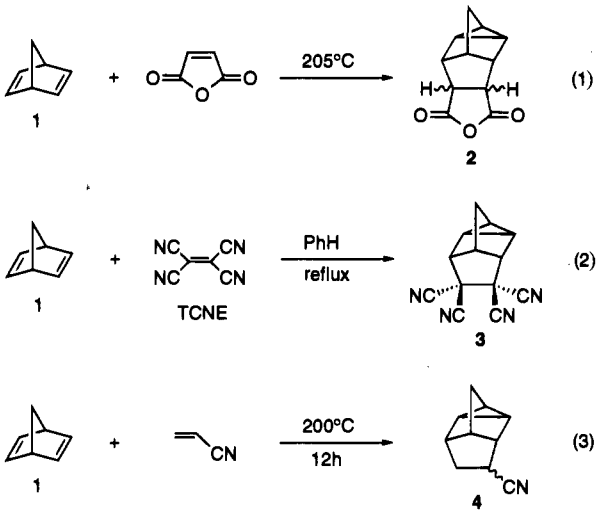
conjugated, a cyclopropane was created in lieu of a double bond. Following Ullman's observation, Blomquist and Meinwald reported a similar reaction between NBD and tetracyanoethylene (TCNE), leading to deltacyclane **3** in quantitative yield (eq 2).[11b] Unfortunately, less reactive dienophiles gave lower yields and required high temperature to provide any cycloadduct. For example, on prolonged heating at 200 °C, a mixture of NBD and acrylonitrile gave a 12% yield of deltacyclane **4** (eq 3).[11c]



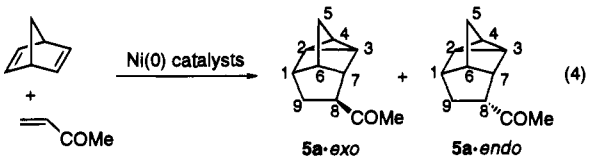
(1) (2) (3)

The limitations of the thermal homo-Diels–Alder reaction[11] led several groups to examine the utility of transition metals in promoting the cycloaddition.[6-8] Schrauzer discovered that nickel complexes catalyzed the reaction of NBD with less reactive olefins such as acrylonitrile or methyl acrylate to give the corresponding deltacyclane in moderate yields.[6a] Other metals were found to be much less effective catalysts for the cycloaddition of electron-deficient olefins, but low-valent cobalt complexes did catalyze the HDA reaction of certain unactivated acetylenes.[7,8] We expanded the scope of cobalt-catalyzed HDA reactions of NBD with acetylenes, developed an asymmetric variant using chiral phosphine ligands, and reported the first examples of the intramolecular reaction.[7f,g,8a]

Although the question of stereoselectivity in the HDA reaction has been examined for both thermal and metal-catalyzed reactions of NBD (**1**) with some olefins (acrylonitrile and methyl acrylate), the reported stereoselectivities were poor (*exo/endo* ratios of 1.5:1 to 4:1 commonly observed).[12] Unlike the Diels–Alder reaction where predictable and high regioselectivity is expected in a cycloaddition between an electron-rich diene and an electron-poor dienophile,[13] little was known about the regiochemical outcome of an unsymmetrical analogous HDA reaction. In this paper we provide a full account of our work in this area. An active nickel catalyst is reported which provides improved stereoselectivity. The range of olefins which participate in the HDA reaction has been expanded. We also examine the regioselectivity of these reactions using 2-substituted norbornadienes and various unsymmetrical dienophiles.

Search for an Active Catalyst

We investigated the cycloaddition between methyl vinyl ketone (MVK) and norbornadiene (eq 4), which had previously been accomplished in low yield.[6a] $NiCl_2(PPh_3)_2$ in the presence of Et_3Al is known to catalyze the HDA reaction between NBD and acrylonitrile to afford the corresponding deltacyclane in moderate yield.[6b] However, this catalytic system was not suitable



(4)

Table 1. Ni-Catalyzed HDA Reaction of NBD with Methyl Vinyl Ketone

entry	catalyst[a]	temp (°C)	*exo:endo* (**5a**)	yield (%)
1	$NiCl_2(PPh_3)_2/Et_3Al$	rt		NR
2	$NiCl_2(PPh_3)_2/Et_3Al$	80		NR
3	$Ni(CO)_2(PPh_3)_2$	80	2:1	90
4	$Ni(CO)_2(PPh_3)_2$	60	9:1	62
5	$Ni(CO)_2(PPh_3)_2$ (+ Me_3NO)	80	5:1	44
6	$Ni(CO)_2(PPh_3)_2$ (+ CuI)	80	8:1	23
7	$Ni(acac)_2/Et_3Al/2PPh_3$	10	>20:1	30
8	$Ni(acac)_2/Et_3Al/2PPh_3$	rt	19:1	62
9	$Ni(acac)_2/Et_3Al/2PPh_3$	80	3:1	37
10	$Ni(acac)_2/Et_3Al/2PPh_3$ (+ COD)[b]	rt	43:1	58
11	$Ni(COD)_2/2PPh_3$	rt	14:1	85
12	$Ni(COD)_2/2PPh_3$	80	**>20:1**	**99**

[a] 5 mol % Ni(0). [b] COD ligand stabilizes the complex formed by reduction, but is labile enough to allow catalytic activity. [c] For entries 3–6, no solvent. [d] For entries 7–12, 1,2-dichloroethane was the solvent.

for the reaction with MVK (Table 1, entries 1 and 2). In the presence of 5 mol % $Ni(CO)_2(PPh_3)_2$ at 80 °C, deltacyclane **5a** was isolated in 90% yield as a 2:1 mixture of *exo/endo* isomers (Table 1, entry 3). Improvement in the *exo* stereoselectivity was noted when the reaction temperature was lowered to 60 °C although the yield of **5a** decreased (Table 1, entry 4). Any further decrease in temperature led to long reaction times and low (<10%) yields. Attempted activation of $Ni(CO)_2(PPh_3)_2$ by the addition of cuprous iodide (which might complex a phosphine and free a coordination site)[14] or trimethylamine *N*-oxide (which converts a CO ligand by oxidation to CO_2)[15] (entries 5 and 6) was unsuccessful. The *exo* selectivity was somewhat enhanced by these methods, but the yield of cycloadduct was reduced. In considering more reactive complexes, Yoshikawa had demonstrated that low-valent nickel complexes generated by reduction of $Ni(acac)_2$ with sodium borohydride were catalysts, but no yields were given.[6b] Sodium borohydride was incompatible with an enone, and therefore an alternative reducing agent was required. Triethylaluminum proved to be very convenient; reaction of 5–10 mol % $Ni(acac)_2$ with 2 equiv of the reducing agent in the presence of a phosphine ligand (2 equiv) under the usual conditions gave deltacyclane **5a** in 62% yield as a 19:1 mixture of stereoisomers (entry 8), and importantly, the reaction had taken place at room temperature. Changing the reaction temperature led to lower yields and varying levels of selectivity (entries 7 and 9). Addition of a stoichiometric amount of cyclooctadiene (COD) relative to nickel improved the selectivity (entry 10), but at the expense of a more difficult purification step. As expected, an atmosphere of CO(g) gave lower yields, and the addition of a coordinating solvent such as THF lowered the yield with no change in selectivity.[16]

(12) (a) Reference 6b. (b) Reference 11h. The splitting pattern for H^8 in monosubstituted *exo*-deltacyclanes showed three to four lines (t or dd), while for the *endo* compound, there were six or eight lines (dt or ddd) due to the additional coupling to the proton on the adjacent bridgehead.

(13) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley Interscience: New York, 1992.

(14) Kauffman, G.; Teter, L. A. *Inorg. Synth.* **1963**, *6*, 9.

(15) Luh, T.-Y. *Coord. Chem. Rev.* **1984**, *60*, 255.

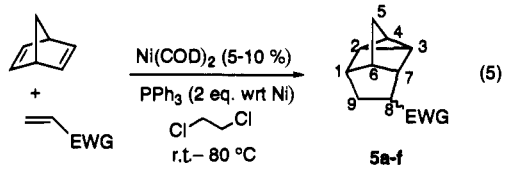
(16) Wender, P. A.; Jenkins, T. E. *J. Am. Chem. Soc.* **1989**, *111*, 6432.

The most effective catalyst was obtained by combining Ni(COD)$_2$ with triphenylphosphine.[17] Excellent yields of the HDA adduct with high *exo* selectivity (entries 11−12) were obtained, and furthermore the *exo/endo* ratios are highly dependent on the dienophile and the phosphine ligands, *vide infra.*

The most convenient method to assign and distinguish the two stereoisomeric adducts relied on the different splitting patterns of H^8 in the *exo* and *endo* cycloadducts in the ^{1}H NMR spectra.[12] H^8 of the *exo* cycloadducts couples with the two protons at C^9, giving a dd pattern while in the *endo* cycloadducts, H^8 is a ddd due to an additional coupling with H^7.

Nickel-Catalyzed HDA Reaction of Norbornadiene with Various Dienophiles: Scope and Stereoselectivity

In order to determine the compatibility of various functional groups using the Ni(COD)$_2$/Ph$_3$P catalyst, other electron-deficient alkenes were examined (eq 5). The yields and selectivities observed under the optimized conditions are shown in Table 2.



(5)

Table 2. Ni-Catalyzed HDA Reaction of NBD with Electron-Deficient Olefins

entry	deltacyclane	EWG	temp (°C)	yield (%)	*exo:endo*
1	**5a**	COMe	80	99	**>20:1**
2	**5b**	CHO	rt	58	3:1
3	**5c**	CO^{t}Bu	60	69	1.5:1
4	**5d**	CN	80	82	4:1
5	**5e**	SO_2Ph	rt	75	1:1
6	**5f**	SOPh	rt	65	7:1
7	**5f**	SOPh	rt	73	**>19:1**[a]

[a] P(OPh)$_3$ was used instead of PPh$_3$.

Unlike thermal HDA reactions in which *endo* adducts predominate[11h] (ascribed to the more favorable "*endo* transition state" as in a typical Diels−Alder reaction), nickel-catalyzed HDA reactions of acyclic electron deficient dienophiles give *exo* isomers as the major cycloadducts. The *exo/endo* selectivities are highly dependent on the nature of the dienophile, the phosphine ligands, and the reaction temperature.

Acrolein, an extremely reactive dienophile, had not been successfully used in the HDA reaction.[18] Using Ni(COD)$_2$/Ph$_3$P, deltacyclane **5b** was obtained in moderate yield and selectivity (Table 2, entry 2). (*Caution!* Temperature control was essential in this reaction since spontaneous heating occurred when the cooling bath was removed. This appears to be due to the rapid polymerization of acrolein under the reaction conditions.) At < 10 °C, low yields of cycloadduct were isolated.

We were surprised to find that *tert*-butyl vinyl ketone[19] gave poorer *exo* selectivity than methyl vinyl ketone (entry 3). When the reaction temperature was lowered from 60 °C to room temperature, the *exo* selectivity improved (3:1) but the yield was only 17%. While the cycloaddition with phenyl vinyl sulfone was nonselective (entry 5), phenyl vinyl sulfoxide gave an adduct which was predominantly *exo*, and the selectivity was found to be highly dependent on the nature of the phosphine used, *inter alia.*

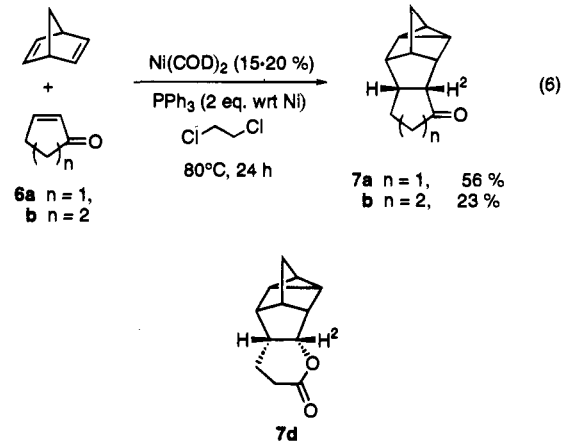
Table 3

entry	EWG	*exo:endo*	entry	EWG	*exo:endo*
1[a]	COOMe	1.4:1	3	SO_2Ph	1:1
2	COMe	14:1	4	SOPh	19:1

[a] Data taken from ref 6c.

An interesting comparison can be made between our results and previous studies carried out by Noyori.[6c] Removal of one oxygen in the electron-withdrawing group (EWG) on the dienophile resulted in a dramatic increase in the *exo/endo* selectivity (Table 3). Thus, changing the EWG on the dienophile from a methyl ester (COOMe) to a methyl ketone (COMe) or a sulfone (SO_2Ph) versus a sulfoxide (SOPh) resulted in a 10−20-fold improvement in the *exo/endo* selectivity.

Cyclic enones have not been previously examined as dienophiles in the HDA reaction. We found this class of compounds to be moderately reactive in the presence of Ni(COD)$_2$/PPh$_3$. One feature of the cycloaddition is that pentacyclic compounds **7a,b** are created with high stereoselectivity in a single step (>20:1 ratio of stereoisomers). However, in contrast to reactions with acyclic enones, the stereochemistry of the newly formed rings in **7a** and **7b** was shown to be *endo* (eq 6). The change in stereoselectivity may be associated with the *s-cis* vs *s-trans* conformation of the dienophile.



(6)

Figure 1.

The ^{1}H NMR spectra of **7a** and **7b** were complex and failed to provide coupling information which could be used to assign the mode of cycloaddition. The resonance for the proton at C^2 of **7a** was split by more than two protons, the maximum observed with all other deltacyclanes. Long-range coupling with the protons α to the carbonyl may explain the unusual multiplicity of this signal. Conversion of ketone **7a** to the corresponding lactone **7d** (Figure 1) by Baeyer−Villiger oxidation[20] permitted unambiguous assignment of the stereochemistry since it effectively isolated the resonance for H^2, removing long-range couplings and shifting the signal downfield from the other proton resonances. This signal now had a dd splitting pattern, characteristic of the *endo* adduct.

We extended these studies to include an investigation of a lactone and a maleimide. The cycloaddition of 2-buten-4-olide (**8**)[21] with NBD was more sluggish than that of 2-cyclopentenone

(17) For the preparation of Ni(COD)$_2$, see: (a) Schunn, R. A.; Ittel, S. D.; Cushing, M. A. *Inorg. Synth.* **1990**, *28*, 94. (b) Schunn, R. A. *Inorg. Synth.* **1974**, *15*, 5.

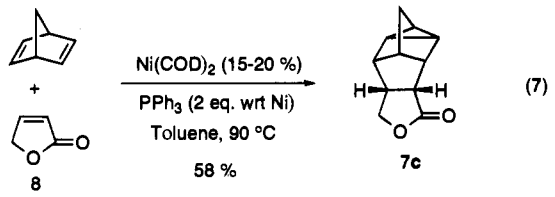
(18) (a) Schrauzer, G. N.; Glockner, P. *Chem. Ber.* **1964**, *97*, 2451. (b) Schrauzer, G. N. *Adv. Catal.* **1968**, *18*, 378.

(19) *tert*-Butyl vinyl ketone was prepared by Weinreb's procedure via the *N*-methoxy-*N*-methyl amide: Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.

(20) (a) Trost, B. M.; Fleming, I. In *Comprehensive Organic Synthesis*; Krow, G. R., Ed.; Pergamon Press: New York, 1991; Vol. 7, Chapter 5.1. (b) Krow, G. R. *Tetrahedron* **1981**, *37*, 2697.

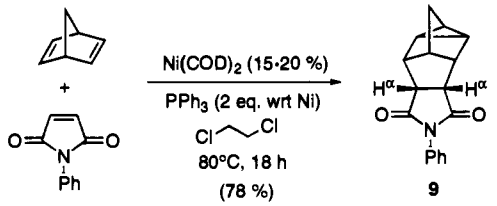
(21) Tanaka, S.; Ogasawara, K. *Synthesis* **1974**, 42.

(**6a**). Under the usual conditions, the cycloadduct (28%) was contaminated by unreacted starting material which was difficult to remove. However, when **8** was heated at 90 °C in toluene, the reaction went to completion and the yield of *endo* lactone **7c** was 58% (eq 7).



(7)

The cycloaddition of NBD with *N*-phenylmaleimide (NPM) provided high yields of the *endo* adduct **9** with both $Ni(CO)_2(PPh_3)_2$ and $Ni(COD)_2/PPh_3$ (eq 8). The two α-hydrogens showed a dd splitting pattern which is similar to that of the *endo* adducts **7a**–**c**. Thus cyclic enones, lactones, and maleimides follow the same pattern of favoring the *endo* addition.



(8)

Most of the nickel-catalyzed HDA reactions were carried out in 1,2-dichloroethane at room temperature to 80 °C. In some cases, however, the cycloadditions were slow and so they were carried out in the absence of solvent. Excess dienophile was typically employed in the cycloadditions (1.5–2.5 equiv) in order to minimize the formation of norbornadiene dimers. However, when the dienophile was expensive, norbornadiene was used in excess and the yield was based on dienophile.

1,1- and 1,2-disubstituted electron-deficient dienophiles such as methacrylonitrile, crotonitrile, and dimethyl maleate have been previously shown to undergo HDA reaction with norbornadiene under nickel catalysis.[6a–d] An extensive study on the effect of the electronic and steric components of the phosphine ligand on the stereoselectivity has also been reported.[6b]

Cycloaddition Reactions of Norbornadiene with Vinyl Sulfoxide and Vinyl Sulfones

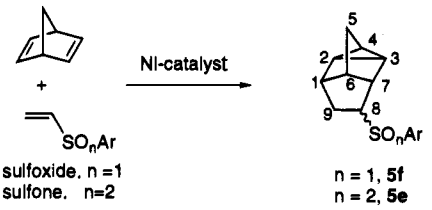
Sulfoxides and sulfones were of interest since they are versatile intermediates for organic synthesis. Maignan and Rafael reported the Diels–Alder cycloaddition of optically active (*R*)-*p*-tolyl vinyl sulfoxide with cyclopentadiene, but the level of asymmetric induction (diastereoselectivity) for the ring formation was poor (2–3.5:1), and the ratio of *exo* to *endo* isomers was low (1:2).[22] Kagan has shown that improved selectivity accompanies formation of the sulfonium salt prior to addition of the diene.[23] We found that phenyl vinyl sulfoxide and sulfone undergo the HDA cycloaddition in the presence of nickel catalysts (eq 9). With the sulfone, high yields of HDA adduct **5e** were obtained even with $Ni(CO)_2(PPh_3)_2$ (Table 4, entry 1). Phenyl vinyl sulfoxide was not reactive with this catalyst, but the HDA reaction occurred smoothly using $Ni(acac)_2/Et_3Al$ or $Ni(COD)_2$ (Table 4, entries 2–5).

Sulfone **5e** was nonselectively formed regardless of the catalyst or temperature. Fortunately this was not a serious limitation since the mixture of stereoisomers was readily epimerized in the presence of potassium *tert*-butoxide in THF to give a high yield of **5e** enriched in the *exo* isomer (*exo*:*endo* = 9:1). Lower selectivity (83:17) was observed when the mixture was treated with *n*-BuLi at −78 °C followed by a low-temperature quench using camphorsulfonic acid in THF. The *endo* isomer was conveniently obtained by recrystallization of the enriched mixture.

Table 4. HDA for Phenyl Vinyl Sulfone and Sulfoxide with NBD

entry[a]	catalyst	**5e** yield (%) (*exo*:*endo*)	**5f** yield (%) (*exo*:*endo*)	*exo*-(*R*,*S*)-5f yield[b] (%)
1	$Ni(CO)_2(PPh_3)_2$	87 (1:1)	NR	
2	$Ni(acac)_2/PPh_3/Et_3Al$	77 (1:1)	33 (1:1)[c,d]	20
3	$Ni(COD)_2/PPh_3$	75 (1:1)	65 (7:1)[c]	35
4	$Ni(COD)_2/P(OPh)_3$	[e](1:1)	~59 (>19:1)[f]	56
5	$Ni(COD)_2/P(OPh)_3$		~73% (>19:1)[f,g]	69

[a] Entries 1–4, Ar = Ph; entry 5, Ar = Tol. [b] Isolated yield of the *exo*-(*R*,*S*)-**5f** isomer. [c] Ratio measured after oxidation to **5f**. [d] An unidentified material was also formed. [e] The reaction went to completion at room temperature or 80 °C. [f] At 80 °C, the yield decreased to 45% but the ratio was unchanged. A small amount of [2 + 2] adduct was isolated with the minor HDA isomers. [g] The optically enriched tolyl vinyl sulfoxide was used in place of racemic phenyl vinyl sulfoxide.



(9)

The stereochemical outcome of the sulfoxide cycloaddition was remarkably sensitive to subtle changes in the catalyst. Phenyl vinyl sulfoxide was nonselective (1:1) with $Ni(acac)_2/PPh_3/Et_3Al$, but the *exo* isomer predominated when $Ni(COD)_2/PPh_3$ was used (65% yield, 7:1, Table 4, entry 3). Perhaps this change is due to the presence of a Lewis acid under the former conditions. Sulfoxide **5f** was a complex mixture of diastereomers since the starting phenyl vinyl sulfoxide was racemic and the reaction was nonselective. The *exo*/*endo* selectivity was readily determined by oxidizing a crude portion of the product with *m*-chloroperoxybenzoic acid (MCPBA) to sulfone **5e**. This simplified the mixture, and the *exo*/*endo* ratio was measured by ^1H NMR. The ratio of (*R*,*S*) to (*S*,*S*) was difficult to determine due to a byproduct which was present, but the reaction with $Ni(COD)_2/2PPh_3$ appeared to be nonselective by examination of the crude ^1H NMR of the sulfoxide mixture.

The 7:1 ratio of *exo*/*endo* isomers obtained using $Ni(COD)_2/Ph_3P$ was encouraging, and further studies revealed that changing the ligand from PPh_3 to $P(OPh)_3$ improved the *exo*/*endo* selectivity to >19:1 and favored the (*R*,*S*) diastereomer as well (Table 4, entry 4). When optically active (*S*)-(−)-*p*-tolyl vinyl sulfoxide[24] was used in the cycloaddition, similar levels of selectivity were observed and the major product was isolated in 69% yield (entry 5). Crystals of the major adduct obtained by recrystallization from hot ether were suitable for X-ray analysis, and the structure of the major diastereomer was determined to be (R_c,S_s) (Figure 2).[25]

Several pieces of evidence indicate that the stereochemistry of the sulfoxide was unaffected by the reaction conditions. The

(22) Maignan, C.; Rafael, R. A. *Tetrahedron* **1983**, *39*, 3245.
(23) (a) Ronan, B.; Kagan, H. B. *Tetrahedron: Asymmetry* **1991**, *2*, 75. (b) Ronan, B.; Kagan, H. B. *Tetrahedron: Asymmetry* **1992**, *3*, 115.
(24) (a) Abbott, D. J.; Colonna, S.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 1* **1976**, 493. (b) Drabowicz, J.; Bujnicki, B.; Mikolajczyk, M. *J. Org. Chem.* **1982**, *47*, 3325. (c) Andersen, K. K. *Tetrahedron Lett.* **1962**, 93. (d) Hulce, M.; Mallamo, J. P.; Frye, L. L.. Kogan, T. P.; Posner, G. H. *Org. Synth.* **1985**, *64*, 196.
(25) Details of the X-ray analyses for compounds **5f**, **25**, and **28** have been submitted for publication in *Acta Crystallogr., Sect. C.*

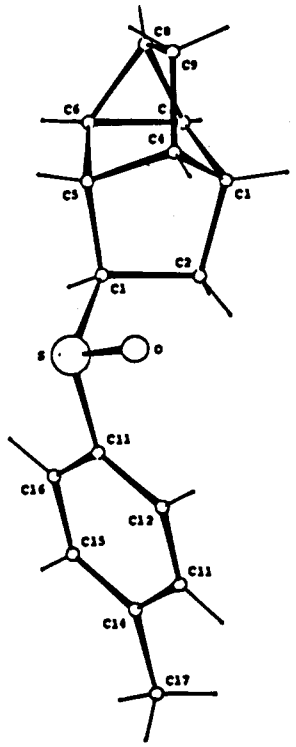


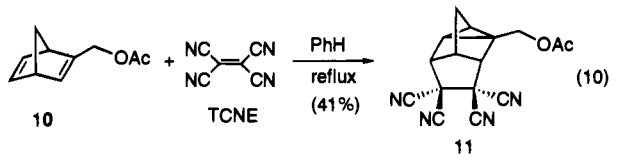
Figure 2. X-ray structure of (−)-**5f**.

optical rotation of sulfoxide **5f** was high ($[\alpha]_D = -263°$ (c = 0.96, acetone)), and the optical rotation of recovered vinyl sulfoxide was unchanged. Dispersion analysis of the X-ray data also supported the S_s configuration of **5f**, which is identical to that of the starting vinyl sulfoxide. Optically enriched sulfone **5e** ($[\alpha]_D = -19.7°$ (c = 0.6, acetone)), obtained by oxidation of sulfoxide **5f**, was studied using the chiral NMR shift reagent (+)-Eu(hfc)$_3$.[26] The signal due to *endo* proton H^{9n} (1.85 ppm, dd) for the racemic sulfone was doubled upon addition of the shift reagent. The optically enriched material did not show any doubling of lines with several additions of (+)-Eu(hfc)$_3$. Unfortunately a lack of baseline resolution prevented a quantitative determination of the diastereomeric excess (de) by this method. However, the doubling was absent with the enriched sample, indicating that the de is high. Studies using either (+)-Eu(hfc)$_3$ or (+)-Yb(hfc)$_3$ with the sulfoxide were not informative.[26]

Nickel-Catalyzed HDA Reaction of Substituted Norbornadienes: Regio- and Stereoselectivity

Unlike the Diels−Alder reaction (where predictable and high regioselectivity is expected in a cycloaddition between an electron-rich diene and an electron-poor dienophile), little was known about the regiochemical outcome of an unsymmetrical analogous HDA reaction. In fact, prior to our studies,[6e] reports of successful cycloadditions using substituted norbornadienes were rare in the literature.[11f,i] In one instance, TCNE, a symmetrical and highly reactive dienophile, reacted on the distal side of the 2-substituted NBD **10** to give the substituted cyclopropane product **11** (eq 10).[11i] Other attempts to promote the cycloaddition with substituted norbornadienes or other types of homoconjugated dienes have been unsuccessful.[11i,27]

We began our investigation of the regioselectivity of the homo-Diels−Alder reaction with 2-substituted norbornadienes bearing an electron-donating or electron-withdrawing group and various electron-deficient dienophiles. From the outset of this



10 TCNE 11

study, we were aware that as many as eight isomers could be formed when both the diene and dienophile were unsymmetrical; thus, high levels of regioselectivity would be necessary before the reaction could become synthetically useful. The structures of the regioisomers, designated *ortho*, *meta*, *meta'*, and *para*, are shown in Scheme 1. *Exo* and *endo* stereoisomers are possible for each cycloadduct.

The reaction of electron-deficient 2-substituted NBD **12a** (Y = COOMe) with acrylonitrile (EWG = CN) gave exclusively the *para* isomers regardless of the reaction conditions (Table 5). Ni(COD)$_2$/2PPh$_3$ gave the optimum yields and selectivities of cycloadducts at 80 °C (entry 4) whereas at lower temperatures, the reaction was incomplete after 48 h (entries 2 and 3), and at 90 °C, the starting material was completely consumed but the yield and selectivity were slightly lower (entry 5).

The results of the HDA reaction between electron-deficient 2-substituted NBD **12a** (Y = COOMe) with various dienophiles are shown in Table 6. The best yields and the selectivities were obtained at 80 °C using Ni(COD)$_2$ (10−20%) and PPh$_3$ (2 equiv with respect to Ni) in 1,2-dichloroethane. At lower temperatures, the reactions were incomplete after two days. At 90−100 °C in toluene, the substituted diene was completely consumed but the yields and selectivities were lower.

A few ligands were examined for the HDA reaction of NBD **12a** with MVK, and PPh$_3$ gave the best results. The addition of PBu$_3$ or 1,4-bis(diphenylphosphino)butane (dppb) to Ni(COD)$_2$ provided complexes that were ineffective as catalysts. With 1,2-bis(diphenylphosphino)ethane (dppe), the product was isolated in low yield and the reaction was less selective. P(O^{i}Pr)$_3$ also formed catalysts that approached the activity of those generated with PPh$_3$ (Table 6, entry 4). While the overall yield for the reaction was lower than with PPh$_3$, an interesting effect was noted in the regioselectivity of this cycloaddition. The minor *ortho-endo* product from the reaction with PPh$_3$ became the major adduct with P(O^{i}Pr)$_3$. With the electron-rich NBD **12b**, cycloaddition occurred selectively to give the *ortho-endo* adduct with either PPh$_3$ or P(O^{i}Pr)$_3$, *inter alia*.

The homo-Diels−Alder reaction often gives high levels of stereoselectivity, but it remains difficult to predict which isomer will predominate. Acrylonitrile was moderately stereoselective with either the parent NBD (**1**) or 2-substituted NBD **12a**; however, the selectivity was reversed for the two adducts. The *endo* isomer predominates (2.3:1) in the *para* adducts from NBD **12a** (Table 6, entry 1) while the *exo* adduct was favored (4:1) from NBD (**1**) (Table 2, entry 4). The sulfone cycloadditions were nonselective with NBD (**1**) (Table 2, entry 5), while the cycloaddition with a substituted NBD such as **12a** was remarkably *exo* selective (Table 6, entry 2).

The regioselectivity was more consistent. The *para* isomer was favored for all dienophiles examined with **12a**. The substituent Y appears as a substituent on the cyclopropane in most of the adducts isolated. The *ortho* and *meta'* isomers were minor products, but the *meta* adduct was not observed. The stepwise nature of the reaction and the questions concerning the mechanism make direct comparisons to the concerted Diels−Alder reaction invalid. Furthermore, these trends in reactivity may be complicated by a change in the rate-determining step, with different factors controlling the various rates for each substrate. Further experimental work coupled with calculations may shed light on these results.

(26) Parker, D. *Chem. Rev.* **1991**, *91*, 1441.
(27) Kelly, T. R. *Tetrahedron Lett.* **1973**, *14*, 437.

Scheme 1

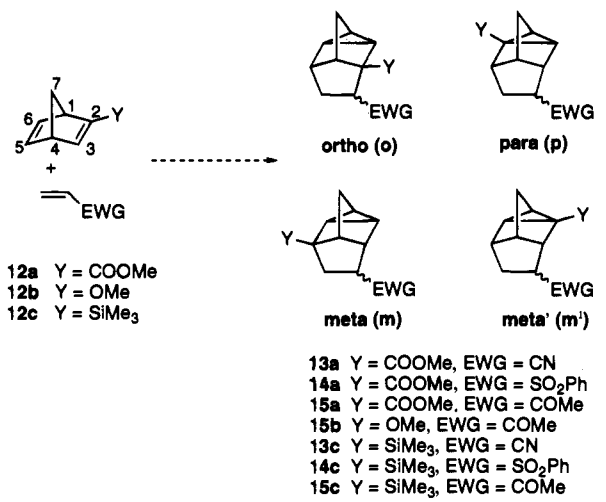


Table 5. HDA Reaction of 2-Substituted NBD **12a** with Acrylonitrile

entry	temp (°C)	catalyst[a]	yield (*p*-**13a**)	*exo*:*endo*
1	60	$Ni(CO)_2(PPh_3)_2$	65%	1:1
2	rt	$Ni(COD)_2/2PPh_3$	*b*	1:1
3	40	$Ni(COD)_2/2PPh_3$	*c*	1:1.7
4	80	$Ni(COD)_2/2PPh_3$	94%	1:2.3
5	90[d]	$Ni(COD)_2/2PPh_3$	74%	1:2

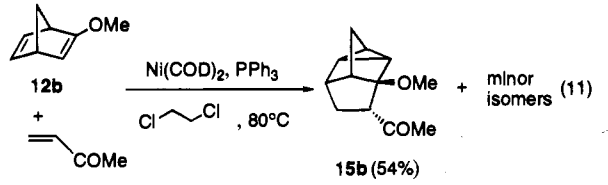
[a] For entries 1–4, reactions run in 1,2-dichloroethane. [b] The reaction was ~25% complete after 48 h. [c] The reaction was ~50% complete after 48 h. [d] Toluene was employed as the solvent.

Table 6. HDA Reaction of NBD **12a** with Different Dienophiles Catalyzed by $Ni(COD)_2/PPh_3$

				ratio of regioisomers (*exo*:*endo*)			
entry	EWG	adduct	yield (%)	para	*meta'*	meta	ortho
1	CN	**13a**	94	100 (1:2.3)			
2	SO_2Ph	**14a**	75	66 (>20:1)	33 (>20:1)		
3	COMe	**15a**	84	70 (3:1)	10 (1:1.4)		20 (0:1)
4[a]	COMe	**15a**	49	35 (2.4:1)	8 (0:1)		57 (0:1)

[a] $P(O^iPr)_3$ was used instead of PPh_3.

Similar studies were carried out with electron-rich 2-substituted NBD **12b** (Y = OMe). With methyl vinyl ketone (MVK) at 80 °C using $Ni(COD)_2$ (10–20%), PPh_3 (2 equiv with respect to Ni) in 1,2-dichloroethane, deltacyclane **15b** was formed in moderate yield, accompanied by minor isomers (eq 11). The



selectivity in this reaction was high, with the *ortho-endo* HDA adduct **15b** making up >80% of the total product (54% isolated yield). However, few other dienophiles underwent the HDA reaction with this substrate. In contrast to the reaction between MVK and NBD (**1**), in which the *exo* isomer predominated, the *endo* isomer was formed as the major product in the reaction between MVK and NBD **12b**. The origin of the regioselectivity should be electronic in nature, since steric factors should result in approach to the unsubstituted side of the NBD as in electron-deficient NBD **12a**.

Other dienol ethers gave poor results in the cycloaddition reaction. For example, substituting the methyl for an allyl or benzyl group was desirable since they could be easily converted back to the free alcohol, but both were sluggish in the HDA reaction, and low yields of cycloadducts were obtained (<5%).

Table 7. Competition Results for Dienophiles with NBD (**1**)

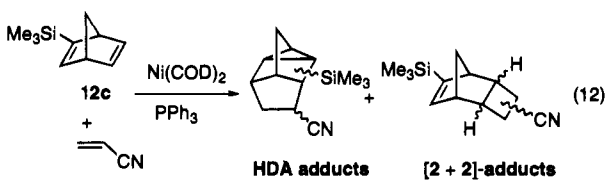
entry	dienophile	% incorporation	relative reactivity
1	MA	4.2	1.0
2	MVK	39.1	11.1
3	AN	55.5	16.3

Table 8. Competition Results for 2-Substituted NBDs with MVK

entry	NBD	reactivity relative to **12b**
1	**1**	7.6
2	**12a**	4.5
3	**12b**	1.0

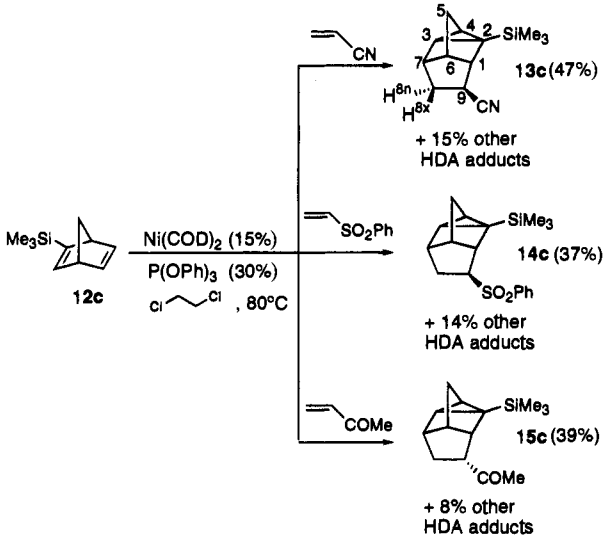
Unlike the Diels–Alder reaction, both electron-deficient and electron-rich dienes were less reactive than the parent NBD (**1**) in the nickel-catalyzed HDA reaction, indicating that substitution is more important than any electronic effect. Fewer classes of dienophiles underwent cycloadditions with the substituted dienes studied even with the active catalysts based on $Ni(COD)_2$ and $Ni(acac)_2$. Several competition experiments were carried out to confirm these qualitative observations and to shed light on the differing selectivities observed for NBD **12a** and **12b**. The first competition study employed 5 equiv of equimolar amounts of acrylonitrile (AN), methyl vinyl ketone (MVK), and methyl acrylate (MA) in a competition for NBD (**1**) to determine the relative reactivities of these three dienophiles (Table 7). The reactivity of each dienophile was assessed by evaluation of the product ratio by capillary gas chromatography. The results show that acrylonitrile was the most reactive, and methyl acrylate was the least reactive. To evaluate the relative reactivity of norbornadienes **1**, **12a**, and **12b**, two sets of competition reactions were carried out (i) between **1** and **12a** with MVK and (ii) between **1** and **12b** with MVK. An equimolar amount of each diene (2–3 equiv each with respect to MVK) was used with respect to MVK in order to approach pseudo-first-order conditions. The approximate value of the relative reactivity toward the cycloaddition with MVK can be calculated by comparison of the ratios of adducts from each diene. These competition studies confirmed that both electron-rich **12b** and electron-deficient **12a** were significantly less reactive than the parent, unsubstituted NBD (**1**) (Table 8) and that electron-poor dienes react faster than electron-rich ones.

When a 2-silyl-substituted NBD (Y = $SiMe_3$) was subjected to the above cycloaddition conditions (using $Ni(COD)_2/2PPh_3$) with acrylonitrile, a complex mixture of HDA adducts and [$2\pi + 2\pi$] adducts was obtained (eq 12).



By varying the cycloaddition conditions (including changing the reaction temperature, varying the ratio of the reactants and the ratio of Ni/phosphine, using different phosphine ligands, etc.), we found that $P(OPh)_3$ at 80 °C with 10–15% of $Ni(COD)_2$ led to the elimination of the [$2\pi + 2\pi$] adducts and the selectivities in the HDA reactions were optimized (Scheme 2). Thus, under these conditions with a 2-silyl-substituted NBD, *meta'* isomers predominate. In most cases however the yields were lower than with other dienes.

Scheme 2



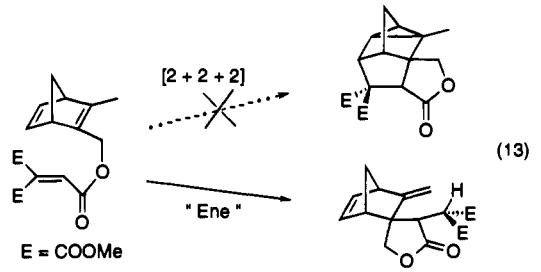
The stereochemistry of the cycloadducts was assigned by using a combination of ^{13}C (APT) NMR and ^{1}H NMR decoupling techniques. The presence of two cyclopropane CH groups and one quaternary cyclopropane carbon in the ^{13}C (APT) NMR indicated that the $SiMe_3$ group was attached to the cyclopropane. Several decouplings revealed that H^7 (dt) was coupled to H^3 (dd) and H^{8x} (dt), but H^1 (d) was not coupled to either cyclopropane resonance. The dd splitting pattern of H^9 in the cycloadducts **13c** and **14c** and the ddd splitting pattern of H^9 in the cycloadduct **15c** allowed an unambiguous assignment of the *exo* and *endo* isomers as described previously.

To summarize our studies of the Ni-catalyzed HDA reaction with 2-substituted norbornadienes, an electron-withdrawing group attached to the 2-position of the NBD favors the *para* regioisomer (Table 6), while an electron-donating group favors the *ortho* regioisomer (eq 11) and a silyl group favors the *meta'* regioisomer (Scheme 2). We have also carried out studies of the regio- and stereoselectivity for the HDA reaction of 7-substituted norbornadienes with various electron-deficient olefins. Moderate to very high levels of selectivities were observed, and these studies point to a strong electronic influence on regioselectivity in HDA reactions.[6f]

Attempted Nickel-Catalyzed Intramolecular HDA Reaction: Alkyl-Tethered Trienes as Substrates

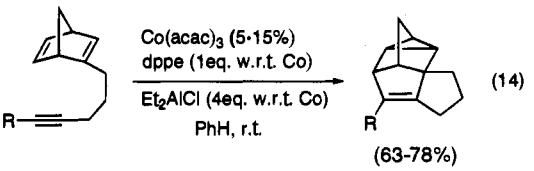
The decrease in entropy associated with tethering the two reactive components suggests that the intramolecular reaction would be significantly more facile than the intermolecular reaction.[28] However, this potential rate enhancement is compromised by the dramatic decrease in rate associated with intermolecular cycloadditions with substituted norbornadienes as described in the previous section. In fact, prior to our studies,[7f] there was only one reported example of an attempted intramolecular HDA reaction in the literature (eq 13).[27] Instead of undergoing a $[2\pi + 2\pi + 2\pi]$ cycloaddition, an intramolecular ene reaction occurred.[28,29]

The failure of this substrate to undergo the HDA reaction is not difficult to rationalize given the results of our earlier studies which indicated that the reactivity of a 2,3-disubstituted NBD



in a HDA reaction would be very low.[30] The presence of the methyl substituent on the norbornadiene also allowed an alternative reaction pathway (the ene reaction) to occur.

On the basis of the success we achieved on the cobalt-catalyzed intramolecular HDA reaction of dienynes (eq 14),[7f] we attempted the nickel-catalyzed intramolecular HDA reaction of trienes. An efficient route to the synthesis of trienes **19**–**22**



has been developed (Scheme 3). Deprotonation of NBD using Schlosser's base,[32a] followed by trapping with 1,4-dibromobutane, generates bromide **16**. This bromide was easily converted to aldehyde **18** which was a common intermediate in the synthesis of several electron-deficient olefins tethered to the diene. The *E*- and *Z*-unsaturated esters were prepared by varying the phosphonate reagent and reaction temperature. Using the Horner–Wadsworth–Emmons modification[33b] of the Wittig olefination[33a] with methyl (diethylphosphono)acetate, the *E*-isomer **19** was obtained. The Still modification[33c] of the Wadsworth–Emmons reaction (bis(2,2,2-trifluoroethyl)[(methoxycarbonyl)methyl]phosphonate in potassium hexamethyldisilazide (KHMDS) and 18-crown-6 at −78 °C) furnished the *Z*-isomer **20**. Nitrile **21** was obtained as an *E/Z* mixture from the corresponding (diethylphosphono)acetonitrile.

Several attempts to achieve an intramolecular HDA cycloaddition with these substrates were unsuccessful, providing only recovered substrate or decomposition of the trienes on prolonged heating. These substrates failed to undergo the desired reaction thermally (up to 170 °C) or under nickel catalysis. Attempts were made using the $Ni(COD)_2$ catalyst with various ligands (PPh_3, $P(OPh)_3$, $P(O^iPr)_3$, and dppe) and at temperatures ranging from room temperature to 110 °C. The ligand to nickel ratio and the concentration of the reaction were also varied, but again no desired cycloaddition was observed.

Considering the reduced reactivity of 1,2-disubstituted enones and lactones in the intermolecular cycloaddition, we decided to prepare a monosubstituted enone to test its reactivity. This triene **22** was easily prepared from aldehyde **18** using vinylmagnesium bromide followed by a Swern oxidation of the resulting alcohol, but once again no reaction was observed under a variety of conditions. In addition to the use of various nickel catalysts, we also employed complexes based on other metals

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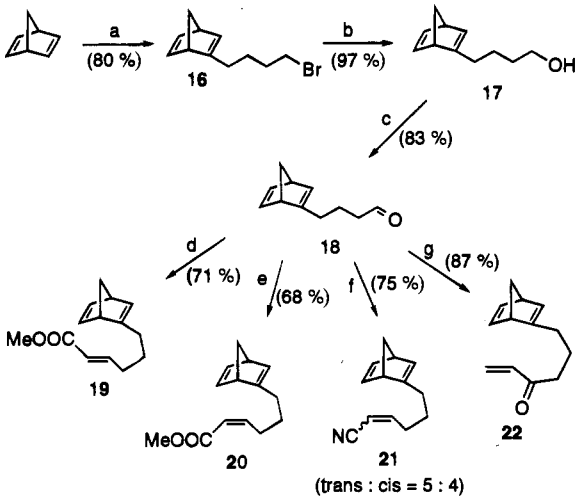
Scheme 3[a]



[a] Conditions: (a) (i) ^{t}BuOK/^{n}BuLi, −78 °C; (ii) $Br(CH_2)_4Br$; (b) HMPA−H_2O (85:15), $NaHCO_3$, 100 °C, 24 h; (c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C; (d) NaH, $(EtO)_2P(O)CH_2COOMe$, PhH, 60 °C; (e) KHMDS, 18-crown-6, $(CF_3CH_2CH_2O)_2P(O)CH_2COOMe$, −78 °C; (f) NaH, $(EtO)_2P(O)CH_2CN$, PhH, 60 °C; (g) (i) vinylmagnesium bromide, THF; (ii) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C.

(e.g., $Co(acac)_3$/dppe/Et_2AlCl, $Fe(acac)_3$/Et_3Al, SmI_2, and some Rh-based catalysts), but no cycloaddition was observed.

Nickel-Catalyzed [2π + 2π] Cycloadditions of Substituted Norbornadienes

During the studies of the nickel-catalyzed HDA reactions between substituted norbornadienes with various dienophiles, we noticed that some dienes underwent a [2π + 2π] cycloaddition instead of a [2π + 2π + 2π] cycloaddition.[10] For example 2-(TMS)NBD (**12c**) (TMS = trimethylsilyl) reacted with acrylonitrile in the presence of $Ni(COD)_2$/2PPh_3 to afford a mixture of [2π + 2π + 2π] and [2π + 2π] adducts (eq 12). In some cases, this [2π + 2π] cycloaddition can occur exclusively with high chemo- and regioselectivity and moderate levels of stereoselectivity. The [2π + 2π] cycloaddition between an unsymmetrical dienophile and a monosubstituted NBD could produce up to 16 products (eq 15). Two regioisomers are possible for the reaction with either olefin of the NBD. Four stereoisomers could result for each regioisomer by *exo* or *endo* attack, with *cis-syn-cis* or *cis-anti-cis* stereochemistry (Figure 3) possible for the cyclobutane.

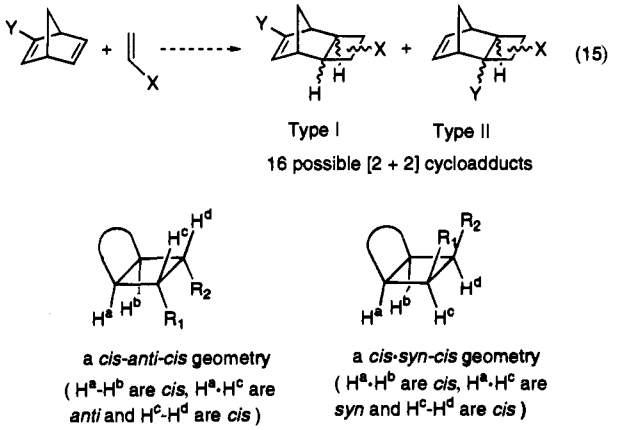


Figure 3. Geometries of cyclobutane.

We have investigated the substituent effects on the olefin and enophile that lead to cyclobutane formation. Reaction occurred

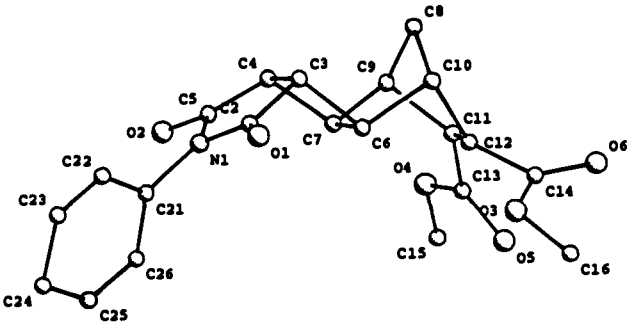
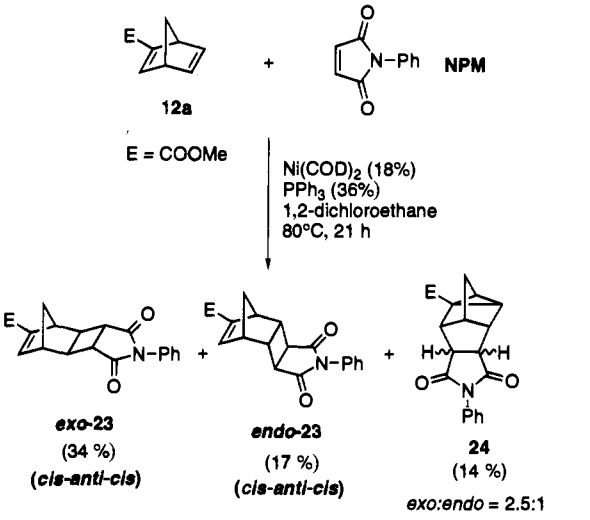


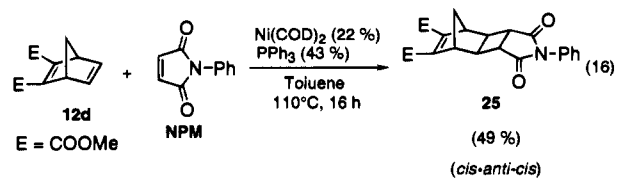
Figure 4. X-ray structure of **25**.

Scheme 4



exclusively with the unsubstituted double bond of the NBD irrespective of the electronic nature of the substituent (Y), giving type I [2π + 2π] adducts (eq 15). In addition, only two of the remaining isomers were observed in most cases. We find that cyclobutane formation appears to be particularly facile when unreactive dienes react with very reactive alkenes. We have also observed a clear trend between the *exo* vs *endo* mode of reaction and the electron density on the remote nonreacting alkene of the NBD. The specific examples are outlined below.

Cyclobutane formation was first observed in our studies of the cycloadditions between an electron-deficient NBD, **12a** (Y = COOMe), and dimethyl maleate.[30] A small amount of [2π + 2π] cycloadduct accompanied the expected [2π + 2π + 2π] adduct (ratio 1:4.5). When the more reactive olefin *N*-phenylmaleimide (NPM) was used, the major product was cyclobutane *exo*-**23** (34%) accompanied by *endo*-**23** (17%) and two [2π + 2π + 2π] adducts **24** (14%, *exo:endo* = 2.5:1) (Scheme 4). Cycloaddition of electron-deficient 2,3-disubstituted NBD **12d** with NPM afforded *exo*-cyclobutane **25** (eq 16) which was free from other [2π + 2π] or [2π + 2π + 2π] cycloadducts. The structure of **25** was confirmed by X-ray crystallography (Figure 4).[25]



Cycloaddition between the electron-rich 2-substituted NBD **12b** and acrylonitrile or *N*-phenylmaleimide (NPM) gave exclusive formation of [2π + 2π] adducts (Scheme 5). Unlike

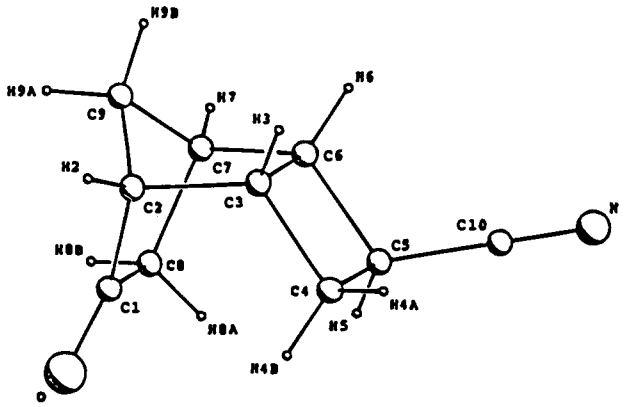
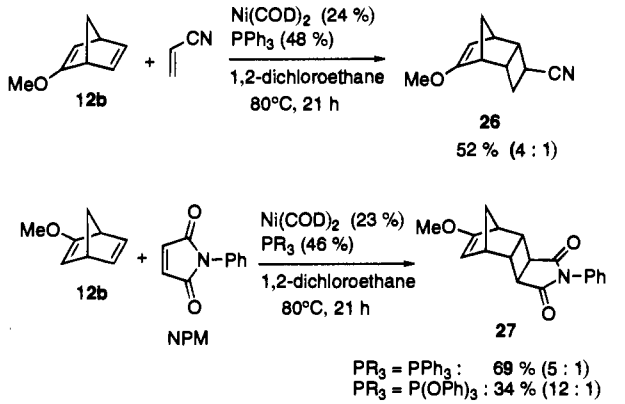


Figure 5. X-ray structure of **28**.

Scheme 5



the cycloadditions with electron-deficient norbornadienes **12a** and **12d** which gave the major adducts with an *exo-(cis-anti-cis)* geometry (***exo*-23** and **25**), cycloaddition with electron-deficient NBD **12b** afforded the *endo-(cis-anti-cis)* adducts **26** and **27** as the major products. As shown in Scheme 5, improvement in the *endo* stereoselectivity to 12:1 was achieved by changing the phosphine from PPh_3 to $P(OPh)_3$.

The structure of **26** was elucidated by X-ray crystallography of the ketone **28** (eq 17, Figure 5),[25] and the structure of **27** was confirmed by using ^1H NMR techniques (nuclear Overhauser effect (NOE) and decoupling experiments) on the corresponding tricyclic diester **29b** (eq 18): irradiation at 3.16 ppm (H^e); H^T δ 2.53, 14% enhancement vs H^C δ 2.39, 0% enhancement. The product arising from the *endo-(cis-anti-cis)* adduct was the only one of the four possible stereoisomers that was expected to show this enhancement.

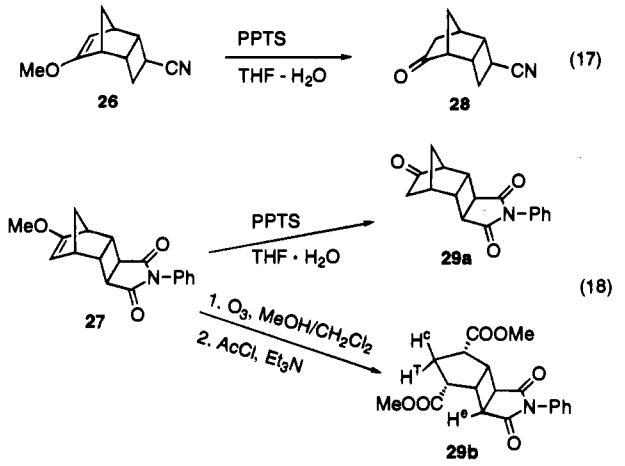
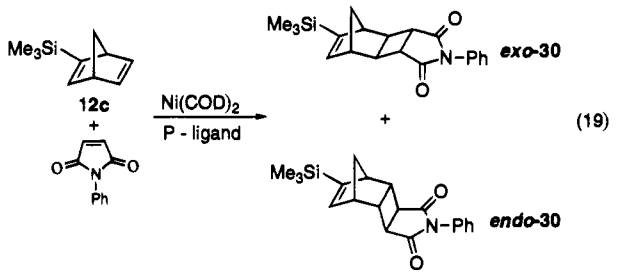


Table 9. Effect of Temperature and Phosphines on [2π + 2π] cycloaddition with NBD **12c**

entry	ligand	temp (°C)	yield (%)	***endo*-30:*exo*-30**
1	2 PPh_3	110	69[a]	1:4.7
2	2 $P(OPh)_3$	110	71	1:3.7
3	2 $P(OPh)_3$	80	42	1.8:1
4	1 $P(OPh)_3$	80	62	1:1

[a] An additional 7−10% [2 + 2 + 2] HDA adducts complicated the mixture with this ligand.

2-Silyl-substituted NBD **12c** also underwent a [2π + 2π] cycloaddition with NPM, giving cyclobutanes ***exo*-30** and ***endo*-30** (eq 19). This reaction was more complicated since the stereochemistry varied as a function of the temperature and ligand (Table 9). At higher temperatures (110 °C) the *exo* adduct



predominated regardless of the phosphine ligand used, but the chemoselectivity for the [2π + 2π] vs [2π + 2π + 2π] reaction was increased by using $P(OPh)_3$ instead of PPh_3. Lower temperatures led to reduced selectivity with a slight preference for the *endo* adduct.

Thus, although as many as 16 possible [2π + 2π] cycloadducts could be formed in these cycloadditions, only one or two of these products were observed in most cases. In all the [2π + 2π] adducts isolated, the reaction occurred on the less substituted olefin of the norbornadienes, and the stereochemistry of the cyclobutanes formed favored the less hindered *cis-anti-cis* geometry. Electron-deficient norbornadienes **12a** and **12d** favored *exo-(cis-anti-cis)* adducts ***exo*-23** and **25**, while the *endo-(cis-anti-cis)* adducts **26** and **27** were preferred with electron-deficient NBD **12b**. 2-Silyl-substituted NBD **12c** afforded both *exo-* and *endo-(cis-anti-cis)* adducts, and their ratios varied with the conditions.

Nickel-Catalyzed [2π + 2π] Cycloadditions of Strained Polycyclic Olefins

The $Ni(COD)_2$-catalyzed *exo* [2π + 2π] reaction of strained olefins with electron-deficient olefins (acrylates, acrylonitrile, and dimethyl maleate) was reported in low to moderate yields and varying levels of *syn/anti* selectivity (2−7:1).[34] We examined two related substrates (**31** and **32**) and found that $Ni(COD)_2/PPh_3$ catalyzes a highly selective *exo* [2π + 2π] cycloaddition with *N*-phenylmaleimide (NPM) to give adducts **33** and **34** (Scheme 6). Only one adduct was isolated from each of these cycloadditions. At 110 °C, the selectivity of the reaction decreased and a small amount of a minor isomer was formed (Table 10). Homoconjugation to the benzene ring or the *exo*-cyclopropyl group with the olefin was proposed to explain the observed [2π + 2π] reaction.[34]

[2π + 2π] vs [2π + 2π + 2π] Cycloadditions: Mechanistic Considerations

Noyori proposed that the mechanism of the metal-catalyzed HDA cycloaddition involves a series of metallacycle intermedi-

(34) Noyori, R.; Takaya, H.; Yamakawa, M. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 852.

Scheme 6

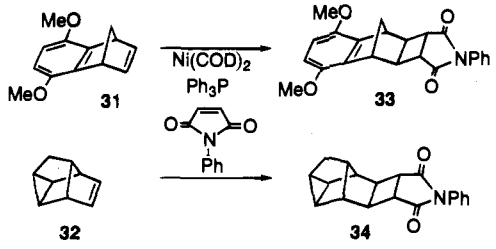


Table 10. $[2\pi + 2\pi]$ Cycloadditions of **31** and **32** with NPM

entry	substrate	adduct	temp (°C)	yield (%)
1	31	33	80	60[a]
2			110	54[b]
3	32	34	80	25
4			rt	10[c]

[a] No reaction in the absence of catalyst. [b] Contained a small amount of a minor isomer. [c] With $Ni(COD)_2$ in the absence of phosphine, no product was obtained.

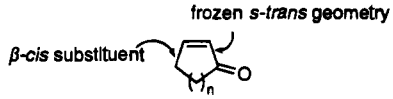
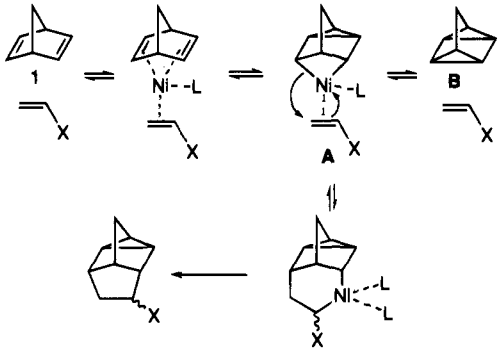


Figure 6. Geometry of cyclic enones.

Scheme 7. Proposed Mechanism of Ni-Catalyzed HDA Reaction



ates (Scheme 7).[6c,34] Initial coordination of the three olefins to the metal center is followed by formation of the cyclopropane and the metallacyclobutane **A**. Carbometalation on the olefin of the dienophile provided a metallacyclohexane that undergoes a reductive elimination to give the observed adduct. Thus, a common intermediate, **A**, was proposed to explain the formation of the same product(s) from different starting materials (NBD (**1**) and quadricyclane (**B**)).[34,35]

The development of active catalysts and the exploration of cycloadditions with substituted dienes and dienophiles have provided additional information on the mechanism of the reaction. The formation of $[2\pi + 2\pi]$ and HDA adducts indicates that several reaction pathways are possible and that small changes in substitution significantly influence the course of the reaction. A pathway which incorporates all the known information is presented in Scheme 8. The reaction between one olefin of the diene and the dienophile would give rise to metallacyclopentane **III**. Reductive elimination would give a cyclobutane-containing product equivalent to the *endo* [2 + 2] reaction mode. Alternatively, **III** could undergo carbometalation on the norbornenyl olefin, giving metallacycle **IV**. Reductive elimination would then generate the HDA adduct. These

(35) For $[\sigma^2 + \sigma^2 + \pi^2]$ cycloadditions of quadricyclanes, see: (a) Smith, C. D. *J. Am. Chem. Soc.* **1966**, *88*, 4273. (b) Prinzbach, H. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 1068. (c) Kaupp, G. *Chem. Ber.* **1971**, *104*, 182. (d) Tabushi, I.; Yamamura, K.; Yoshida, Z. *J. Am. Chem. Soc.* **1972**, *94*, 787.

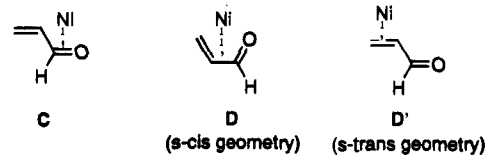
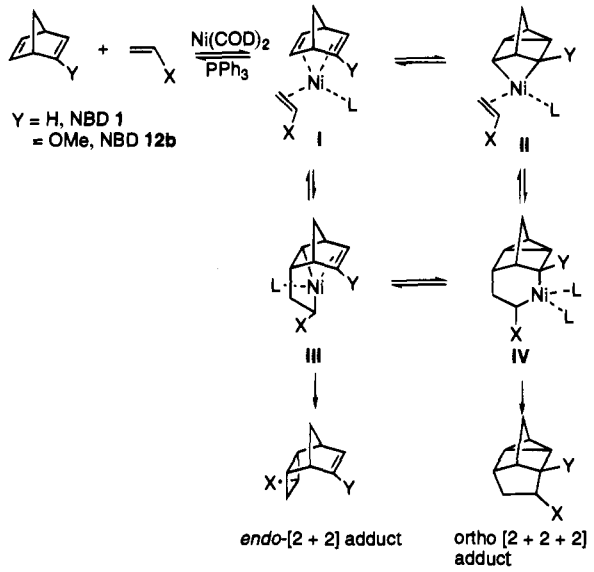


Figure 7. Different types of coordinations between a metal complex and an enone.

Scheme 8. Partitioning between [2 + 2] and [2 + 2 + 2] Cycloadditions



proposals do not preclude Noyori's mechanism, but incorporate this sequence as one of the possible pathways. Thus, these cycloadditions may occur via pathway **I** → **II** → **IV** → deltacyclane as proposed by Noyori or by the alternative pathway **I** → **III** → **IV** → deltacyclane.

Support for the intermediate **III** comes from the formation of the *endo* $[2\pi + 2\pi]$ cycloadduct from the reaction of electron-rich NBD **12b** with acrylonitrile or *N*-phenylmaleimide as described previously. Changing to a different dienophile (X = COMe) favors **IV** and eventual formation of the *ortho* $[2\pi + 2\pi + 2\pi]$ adduct. These routes appear to be competing pathways that are influenced by the substitution patterns of the olefin and diene. Clearly the substituents on the dienophile exert an effect on the coordinating ability of the olefin, and thus on the cycloaddition reaction.

The Ni-catalyzed HDA reaction of acyclic and cyclic enones provides some additional information. The reaction of MVK (an acyclic enone) with NBD (**1**) was highly *exo* selective (eq 5, Table 2), while the cyclic enones and lactones gave *endo* adducts (eqs 6 and 7). Two differences are noteworthy: the presence of the *β-cis*-substituent and the frozen *s-trans* geometry for cyclic dienophiles (Figure 6).

Enones often coordinate initially to the carbonyl group as in **C**, with migration of the metal to the olefin to give **D** or **D'** (Figure 7).[36,37] The *s-cis* complex **D** of the metal to both the carbonyl and olefin of acyclic enones was also known for related complexes.[37] This suggested that the *s-cis* vs *s-trans* difference was important to the difference in the *exo/endo* selectivities that we observed.

With cyclic enones, two possible metallacycle intermediates, $\mathbf{M_1}$ and $\mathbf{M_2}$, can be considered (Figure 8). The *β-cis*-methylene

(36) Jolly, P. W.; Wilke, G. *The Organic Chemistry of Nickel*; Academic Press: New York, 1974; Vol. I.

(37) (a) Tolman, C. A. *J. Am. Chem. Soc.* **1970**, *92*, 2953, 1956. (b) Tolman, C. A.; Seidel, W. C.; Gosser, L. W. *J. Am. Chem. Soc.* **1974**, *96*, 53.

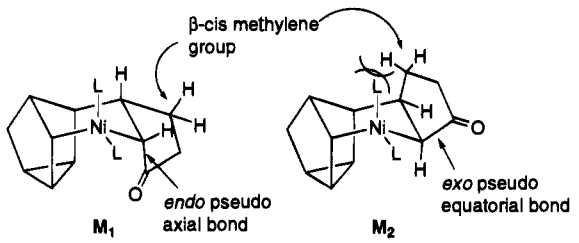


Figure 8. Two possible metallocycles in the Ni-catalyzed HDA reaction of NBD and a cyclic enone.

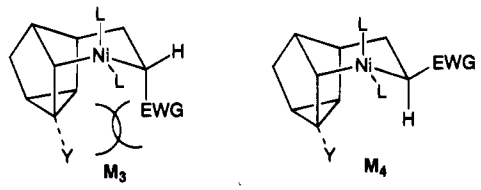


Figure 9. Two possible metallocycles in the Ni-catalyzed HDA reaction of NBD and an acyclic dienophile.

substituent in the chair conformation of $\mathbf{M_1}$ (leading to the favored *endo* adduct) occupies an equatorial position with the ketone group in an adjacent axial position. The *endo* axial substituent is tied back in the ring, decreasing 1,3-diaxial interactions. The interaction of the ligand on the nickel with the axial CH_2 for the *exo* precursor $\mathbf{M_2}$ would be greater than the interaction between the ligand and the axial H in $\mathbf{M_1}$. This unfavorable interaction would favor formation of the *endo* adduct for the cyclic enones.

With acyclic enones or other acyclic dienophiles the EWG occupies an equatorial position in intermediate $\mathbf{M_4}$ due to less severe 1,3-diaxial interactions (Figure 9, Y = H). Metallacyclohexane $\mathbf{M_4}$ reductively eliminates to give the *exo* HDA adduct, which accounts for the preference for this stereochemistry in the reaction with NBD (**1**) (Table 2).[46]

The regioselectivities of the reaction with substituted norbornadienes observed in both the [2π + 2π] and the HDA cycloadditions were moderate to high, and were influenced by substituents attached to the reacting olefin as well as by the other ligands attached to the metal. The direct substituent effect with the homo-Diels–Alder reactions of the 2-substituted dienes appeared to be primarily electronic in nature since the electron-withdrawing group favored the *para* isomer (Table 6) while the electron-donating methoxy group favored the *ortho* isomer (eq 11). 2-(TMS)NBD **12c** gave the *meta'* isomer as the major adduct (Scheme 2), suggesting that steric effects also play a role.

The stereoselectivity of the HDA cycloaddition with substituted norbornadienes ranges from nonselective to highly *exo* or *endo* selective (Table 6). Both steric and stereoelectronic preferences may be important to this aspect of the cycloaddition. In the case of the *para* and *meta'* isomers, the *exo* product predominates (except for acrylonitrile which is a linear nonbulky group).

The presence of a substituent on the cyclopropane, which occupies one of the axial positions, leads to a further increase in steric hindrance between the ligands on the metal and the equatorial substituent which might account for the formation of the *endo* isomer in the case of the 2-(MeO)NBD **12b** (eq 11) (Figure 9, Y = OMe).

The ligand also influenced the selectivity, particularly to those cycloadditions which were nonselective with PPh_3. The reaction of vinyl sulfoxides with **1** in the presence of $P(OPh)_3$ resulted in increased *exo*-(*R*,*S*) selectivity, indicating that a steric effect and/or an electronic effect was also possible. The appropriate choice of ligand was also found to influence the reaction pathway followed in borderline cases. The reaction of the silyl diene with the $P(OPh)_3$ ligand gave a high selectivity for the *meta'* HDA isomer with acrylonitrile (Scheme 2), while a similar reaction using PPh_3 afforded a complex mixture of [2 + 2] and HDA adducts (eq 12). The reason for the difference in the phosphorus ligand was not clear, since both steric and electronic parameters were changed between these ligands (PPh_3, $P(O^i\text{-}Pr)_3$, and $P(OPh)_3$). Further studies may be warranted in order to optimize a specific cycloaddition, the product of which is going to be carried further in a synthetic sequence.

Conclusion

We have expanded the scope of HDA reaction of norbornadiene with various electron-deficient olefins including acyclic and cyclic enones, lactones, sulfones, and sulfoxides. Moderate to high levels of regio- and stereoselectivity were achieved for the HDA reaction between various substituted norbornadienes with a variety dienophiles. An alternative [2π + 2π] cycloaddition was discovered for 2-substituted norbornadienes with reactive dienophiles. Many problems arise in finding trends in reactivity or making generalizations for this reaction because of the multistep nature of the reaction mechanism. The factors affecting each step must be considered, and for each substrate, the rate-determining step of the reaction may be different, with different factors controlling these various rates. Nevertheless, these cycloadditions are very powerful and efficient for the construction of highly strained polycyclic molecules. Our current investigations are focused on the fragmentation of these cycloadducts and the applications of this cycloaddition–fragmentation protocol to the synthesis of polycyclic natural products. Preliminary results in our laboratory show that selective cleavage of the cyclopropane in the deltacyclene is possible by selective insertion of a metal into one of the cyclopropane bonds. Details of these fragmentation studies will follow shortly.

Experimental Section

General Procedures. Standard column chromatography was performed using 230–400 mesh silica gel obtained from Toronto Research Chemicals.[38] Infrared spectra were taken on a Nicolet 8210E FTIR spectrophotometer. ^{1}H NMR spectra were recorded at 200 MHz using a Varian Gemini NMR spectrometer and at 400 MHz using a Varian XL400 spectrometer. Chemical shifts for ^{1}H NMR spectra are reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform: δ 7.24 ppm). ^{13}C NMR spectra were recorded at 50 and 100 MHz. Chemical shifts for ^{13}C NMR spectra are reported in parts per million from tetramethylsilane with the solvent as the internal standard (deuteriochloroform: δ 77.00 ppm). For mixtures, the peaks due to the major isomer were identified when possible. High-resolution mass spectra were recorded with a VG 70-250S (double focusing) mass spectrometer at 70 eV. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. Optical rotations were taken with a Perkin-Elmer 243B polarimeter at 589 nm. Capillary GC analyses were obtained with a Hewlett-Packard Model 5890A gas–liquid chromatograph, using a HP 20M Carbowax column, equipped with a Hewlett-Packard Model 3396A digital integrator. All glassware was flame dried under an inert atmosphere of dry nitrogen or argon.

Reagents. Unless stated otherwise, commercial reagents were used without purification. Tetrahydrofuran and diethyl ether were distilled immediately prior to use from sodium wire/benzophenone. Pyridine and dichloromethane were distilled immediately prior to use from calcium hydride. Bicyclo[2.2.1]hepta-2,5-diene (**1**), 2-cyclohexenone (**6b**), and 2-cyclopentenone (**6a**) were distilled prior to use. Acrolein was distilled immediately prior to each use and stabilized with a crystal

(38) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

of butylated hydroxytoluene (BHT) to inhibit radical polymerization. Methyl vinyl ketone (MVK) was distilled under reduced pressure and stabilized with hydroquinone (0.5 wt %). 2-Buten-4-olide (**8**) was prepared by the method of Tanaka and Ogasawara.[21] *N*-Phenylmaleimide (NPM) was used as obtained from Aldrich, or was sublimed under high vacuum to prevent contamination of the product with a minor impurity that was later detected. Phenyl vinyl sulfone (PVS) was recrystallized from hot hexanes prior to use.[39] Racemic phenyl vinyl sulfoxide[39] was distilled twice to remove traces of sulfide and sulfone. Enantiomerically enriched (*S*)-(−)-*p*-tolyl vinyl sulfoxide was prepared by a literature procedure via (*R*)-(+)-menthyl *p*-toluenesulfinate, prepared from (+)-menthol[40,41] [vinyl sulfoxide: $[\alpha]_D = -409°$ (c = 1.35, EtOH); lit.[40] (*R*)-(+)-*p*-tolyl vinyl sulfoxide: $[\alpha]_D = +396°$ (c = 1, EtOH) starting from (−)-menthol]. The vinyl sulfoxide was repurified by flash chromatography to remove all traces of (+)-menthol. $Ni(CO)_2(PPh_3)_2$ was used as obtained from Aldrich. $Ni(COD)_2$ was prepared by a literature method.[17a] $Ni(acac)_2$ was dried prior to use by azeotropic removal of water with toluene. Substituted norbomadienes **12a**−**c** were prepared as described in the literature.[42−44]

General Cycloaddition Procedure. Method A (with $Ni(CO)_2(PPh_3)_2$ as Catalyst). The dienophile was added to a flask containing the diene and $Ni(CO)_2(PPh_3)_2$ (3−5 mol %). With a water-cooled condenser in place, the reaction mixture was stirred at the desired temperature for approximately 16 h. The product was then filtered through silica gel with dichloromethane (50 mL) as eluent, and the solvent was removed *in vacuo* to give the crude product. This crude material was purified by Kugelrohr (bulb to bulb) distillation or by flash chromatography on silica gel.

General Cycloaddition Procedure. Method B (with $Ni(COD)_2$ as Catalyst). The method of addition was as follows: $Ni(COD)_2$ (10−25 mol %) was added to a flame-dried flask equipped with a magnetic stir bar and a rubber septum in the glovebox. The ligand (triphenylphosphine, 2 mol equiv with respect to Ni) was introduced with a positive flow of N_2(g), and the diene (1 mmol) was added in 1,2-dichloroethane or toluene followed by the dienophile (2 mmol for acrylonitrile, acrolein, and methyl vinyl ketone, 0.5−1 mmol for the cyclic enones and lactones) as a neat liquid. Reactions with phenyl vinyl sulfone and *N*-phenylmaleimide, which were solids, were carried out in the following manner. The dienophile (PVS or NPM, 1 mmol) was added directly to the nickel catalyst prior to addition of the diene, or as a solution in 1,2-dichloroethane immediately following the addition of diene. Reactions with *tert*-butyl vinyl ketone, 2-buten-4-olide, and phenyl vinyl sulfoxide were modified slightly, with addition of a solution of the diene and dienophile (0.5−1 mmol) in the solvent to the flask containing the catalyst. When a phosphite ligand was used instead of triphenylphosphine, the diene and ligand were mixed with the solvent, and added via cannula to the flask containing $Ni(COD)_2$ [or $Ni(COD)_2$−dienophile for solids]. The mixture was stirred at the desired temperature under nitrogen for 16−48 h.

The workup was as follows: The catalyst was oxidized by stirring with the flask open to the air for 1−2 h. The reaction mixture was filtered through a plug of silica using dichloromethane (100 mL) as the eluant. Evaporation of the solvent gave a crude product, which was purified by Kugelrohr (bulb to bulb) distillation or flash chromatography on silica gel.

General Cycloaddition Procedure. Method C (with $Ni(acac)_2$/Et_3Al as Catalyst). Triethylaluminum (9−36 mol %) was added dropwise to a flask containing $Ni(acac)_2$ (5−20 mol %), PPh_3 (10−40 mol %), and bicyclo[2.2.1]hepta-2,5-diene. The dienophile was added to this activated catalyst as a neat liquid or as a solution in 1,2-dichloroethane. This mixture was stirred at the desired temperature for 16−48 h. The catalyst was then oxidized by stirring with the flask open to the air for 1−2 h. The reaction mixture was filtered through a plug of silica using dichloromethane (100 mL). Evaporation of the solvent gave a crude product, which was purified by Kugelrohr (bulb to bulb) distillation or flash chromatography on silica gel.

Representative Examples of Nickel-Catalyzed HDA Cycloadditions. Cycloaddition of Norbornadiene (1) with MVK (Table 1, Entries 11 and 12). The reaction was carried out using method B with methyl vinyl ketone (0.32 mL, 4.0 mmol), NBD (**1**) (0.22 mL, 2.0 mmol), $Ni(COD)_2$ (36 mg, 0.13 mmol, 6.5 mol %), and PPh_3 (69 mg, 0.26 mmol, 13 mol %) at room temperature ovemight. Bulb to bulb distillation as above gave **5a** (280 mg, 85%, *exo*:*endo* = 14:1). The same reaction was carried out at 80 °C to afford **5a** (99%, *exo*:*endo* > 20:1). The spectra were in accord with those reported in the literature.[6c]

Cycloaddition of Norbornadiene (1) with Acrolein (Table 2, Entry 2). The reaction was carried out as in general procedure B using acrolein (0.34 mL, 5.0 mmol), NBD (**1**) (0.27 mL, 2.5 mmol), $Ni(COD)_2$ (68 mg, 0.25 mmol, 10 mol %), and PPh_3 (134 mg, 0.51 mmol, 20 mol %). Spontaneous heating and solidification were observed as the acrolein was added to the other reagents. (*Caution!* Due to the highly exothermic nature of the polymerization of acrolein under the reaction conditions, slow addition of the acrolein to the recation mixture with the control of a water bath is required.) After the solid was broken up to prevent trapping of the product inside the polymer, filtration and bulb to bulb distillation provided **5b** (1 mmHg, 90 °C, 220 mg, 58%, *exo*:*endo* = 3:1).

Tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonane-8-carboxaldehyde (5b). ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.8 (d, 0.25H), 9.65 (d, 0.75H), 2.85 (br m, 1H), 2.30 (br s, 1H), 2.09 (br s, 1H), 2.0 (m, 1H), 1.83 (br m, 1H), 1.7 (br s, 1H), 1.56 (s, 2.1H), 1.50 (s, 0.75H), 1.12 (t, 1H), 1.0 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): (major isomer) δ 183.08, 46.48, 44.16, 42.09, 39.64, 31.11, 14.56, 14.38, 13.19; (smaller peaks) δ 182.24, 45.64, 44.63, 42.52, 42.31, 28.74, 14.28, 12.66, 10.69. IR (neat): 3058, 2947, 2865, 2800, 2720, 1720, 1708 cm^{-1}. HRMS for $C_{10}H_{12}O$: *m/e* calcd 148.0888, found 148.0886.

Cycloaddition of Norbornadiene (1) with *tert*-Butyl Vinyl Ketone (Table 2, Entry 3). The reaction was carried out as in general procedure B using 4,4-dimethyl-1-penten-3-one (230 mg, 2.0 mmol), NBD (**1**) (0.44 mL, 4.0 mmol), 1,2-dichloroethane (0.50 mL), $Ni(COD)_2$ (54 mg, 0.2 mmol, 10 mol %), and PPh_3 (105 mg, 0.4 mmol, 20 mol %) at 60 °C overnight. Bulb to bulb distillation (0.5 mmHg, 90−100 °C) gave **5c** (280 mg, 69%, *exo*:*endo* = 1.5:1).

***tert*-Butyl 8-Tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonyl Ketone (5c).** ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.46 (ddd, 0.33H, J = 10.5, 5.0, 3.8 Hz), 3.25 (dd, 0.66H, J = 8.1, 6.1 Hz), 2.20 (m, 0.33H), 2.16 (s, 0.33H), 2.12 (br s, 0.66H), 2.01 (m, 1.0H), 1.94 (m, 0.66H), 1.86 (m, 0.33H), 1.80 (br s, 0.33H), 1.78 (br s, 0.33H), 1.76−1.58 (m, 1.4H), 1.50 (m, 2H), 1.24 (m, 0.33H), 1.15 (s, 9H), 1.05 (m, 1H), 0.92 (m, 1H), 0.80 (m, 0.33H). ^{13}C NMR (50 MHz, $CDCl_3$): (major isomer) δ 219.69, 46.92, 45.37, 42.03, 39.55, 32.85, 31.03, 26.18, 25.87, 14.89, 14.30, 12.69;

(39) Paquette, L. A.; Carr, R. V. C. *Org. Synth.* **1985**, *64*, 157.

(40) Enantiomerically enriched (*S*)-(−)-*p*-tolyl vinyl sulfoxide was prepared by S. Walden by a literature procedure via (*R*)-(+)-menthyl *p*-toluenesulfinate: Abbot, D. J.; Colonna, S.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 1* **1976**, 493.

(41) (a) Drabowicz, J.; Bujnicki, B.; Mikolajczyk, M. *J. Org. Chem.* **1982**, *47*, 3325. (b)Andersen, K. K. *Tetrahedron Lett.* **1962**, 93. (c) Hulce, M.; Mallamo, J. P.; Frye. L. L.; Kogan, T. P.; Posner, G. H. *Org. Synth.* **1985**, *64*, 196.

(42) Substituted NBD (**12a**) was prepared by a Diels−Alder reaction carried out by adsorbing cyclopentadiene and methyl propiolate on activated silica gel in the ratio of reactants:silica gel = 1:20 by weight. After seven days at room temperature, the product was isolated by elution from the silica gel using ether, followed by purification by flash chromatography. We found this method superior to the more traditional methods. (a) Graham, P. J.; Buhle, E. L.; Pappas, N. *J. Org. Chem.* **1961**, *26*, 4658. (b) Corey, E. J.; Shibasaki, M.; Nicolaou, K. C.; Malmstan, C. L.; Samuelsson, B. *Tetrahedron Lett.* **1976**, 737. Adsorbents have been employed to accelerate other Diels−Alder cycloadditions. (c) Hondrogiannis, G.; Pagni, R. M.; Kabalka, G. W.; Anosike, P.; Kurt, R. *Tetrahedron Lett.* **1990**, *31*, 5433. (d) Veselovsky, V. V.; Gybin, A. S.; Lozanova, A. V.; Moiseenkov, A. M.; Smit, W. A.; Caple, R. *Tetrahedron Lett.* **1988**, *29*, 175. Alternatively, **12a** can also be prepared in good yield by deprotonation of norbornadiene with Schlosser's base (ref 32a), followed by trapping with methyl chloroformate.

(43) Dienol ether **12b** was prepared via the literature procedure from the ketone via the dimethyl acetal, with elimination of methanol using $AlCl_3$−Et_3N in ether. (a) Jefford, C. W.; Huy, P. T. *Tetrahedron Lett.* **1980**, *21*, 755. (b) Barbot, F.; Miginiac, P. *Helv. Chim. Acta* **1979**, *62*, 1451. The allyl and benzyl dienol ethers were prepared in the same way via the corresponding acetals, which were made by using TMSOR and TMSOTf at −78 °C. Tsunoda, T.; Suzuki, M.; Noyori , R. *Tetrahedron Lett.* **1980**, *21*, 1357.

(44) Silyl-substituted NBD **12c** was prepared by deprotonation of norbornadiene with Schlosser's base (ref 32a), followed by trapping with chlorotrimethylsilane.

(smaller peaks) δ 219.73, 47.32, 46.85, 43.80, 43.69, 48.61, 42.400, 35.17, 34.92, 30.42, 29.88, 28.31, 27.51, 27.22, 25.77, 14.45, 12.38, 10.30. IR (neat): 3058, 2960, 2865, 1698 cm^{-1}. HRMS for $C_{14}H_{20}O$: *m/e* calcd 204.1514, found 204.1513.

Cycloaddition of Norbornadiene (1) with Acrylonitrile (Table 2, Entry 4). The reaction was carried out using method B with acrylonitrile (0.36 mL, 5.5 mmol), NBD (**1**) (0.25 mL, 2.3 mmol), $Ni(COD)_2$ (28.9 mg, 0.10 mmol, 4.5 mol %), and PPh_3 (65 mg, 0.25 mmol, 10 mol %) at 80 °C for 16 h. Bulb to bulb distillation gave 8-cyanotetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonane (**5d**) (2−4 mmHg, 80−90 °C, 278 mg, 82%, *exo:endo* ≈4:1 measured from capillary gas chromatography (CGC)). The spectra were in accord with those reported in the literature.[6a,45]

Cycloaddition of Norbornadiene (1) with 2-Cyclopentenone (6a). The reaction was carried out as in general procedure B using 2-cyclopentenone (**6a**) (0.19 mL, 2.3 mmol), NBD (**1**) (0.36 mL, 3.3 mmol), $Ni(COD)_2$ (62.5 mg, 0.23 mmol, 10 mol %), and PPh_3 (118 mg, 0.45 mmol, 20 mol %) at 70 °C ovemight. Flash chromatography (10% ethyl acetate in hexanes) of the distilled material (0.1 mmHg, ≤110 °C) gave **7a** (220 mg, 56%, >97% pure by CGC). This product was identified as the *endo* isomer by Baeyer−Villiger oxidation and analysis of the coupling pattern for H^2 in the oxidation product 3-oxapentacyclo[7.4.0.0^{2,7}.0^{8,12}.0^{11,13}]tridecan-4-one (**7d**). MCPBA (80%, Aldrich, 272.5 mg, 1.26 mmol) was added to a solution of ketone **7a** (134.9 mg, 0.77 mmol) in dichloromethane (4.0 mL) and stirred for several minutes. Solid sodium bicarbonate (157.8 mg, 1.9 mmol) was then added to this mixture, and the suspension was stirred for seven days at room temperature. The mixture was partitioned between dichloromethane (100 mL) and aqueous sodium hydroxide (1.5 M, 50 mL), and washed sequentially with aqueous sodium hydroxide (2 × 30 mL), water (40 mL), and brine (40 mL). The crude product was dried over magnesium sulfate and the solvent removed *in vacuo*, yielding an impure lactone (150 mg, ^1H NMR resonance of H^2 shows one peak at δ 4.79, dd, J = 9.6, 4.5 Hz, indicating that the *endo* product was formed). Further attempts at purification resulted in loss of material but did not provide a pure product.

***endo*-Pentacyclo[6.4.0.0^{2,6}.0^{7,11}.0^{10,12}]dodecan-3-one (7a).** ^1H NMR (400 MHz, $CDCl_3$): δ 2.87 (tdd, 1H, J = 9.8, 4.4, 3.0 Hz), 2.61 (ddd, 1H, J = 10.5, 5.3, 1.7 Hz), 2.44 (d_{AB}t, 1H, J = 18.7, 10.1 Hz), 2.28 (d_{AB}ddd, 1H, J = 18.8, 9.8, 4.3, 1.9 Hz), 2.22 (dt, 1H, J = 4.7, 2 Hz), 2.12 (dt, 1H, J = 4.3, 2.1 Hz), 2.05−1.88 (m, 3H), 1.48 (d_{AB}t, 1H, J = 10.8, 1.5 Hz), 1.43 (d_{AB}, 1H, J = 10.8 Hz), 1.15 (t, 1H, J = 4.9 Hz), 0.97 (td, 1H, J = 5.3, 1.9 Hz), 0.88 (td, 1H, J = 5.2, 1.8 Hz). ^{13}C NMR and APT data (50 MHz, $CDCl_3$): δ 52.25 (CH), 48.41 (CH), 45.41 (CH), 44.56 (CH), 41.64 (CH), 39.98 (CH_2), 29.87 (CH_2), 22.09 (CH_2), 13.16 (CH), 11.79 (CH), 10.24 (CH). IR (neat): 3064, 2940, 2864, 1731 cm^{-1}. HRMS for $C_{12}H_{14}O$: *m/e* calcd 174.1045, found 174.1002.

Cycloaddition of Norbornadiene (1) with 2-Cyclohexenone (6b). The reaction was carried out as in general procedure B using 2-cyclohexenone (**6b**) (0.27 mL, 2.7 mmol), NBD (**1**) (0.57 mL, 5.3 mmol), $Ni(COD)_2$ (74 mg, 0.27 mmol, 10 mol %), and PPh_3 (147 mg, 0.56 mmol, 21 mol %) at 80 °C ovemight. Flash chromatography gave **7b** (110 mg, 23%, >95% pure by CGC). The major product was identified as the *endo* isomer by comparison with the adduct from **7a**.

***endo*-Pentacyclo[7.4.0.0^{2,7}.0^{8,12}.0^{11,13}]tridecan-3-one (7b).** ^1H NMR (400 MHz, $CDCl_3$): δ 2.67 (dd, 1H, J = 11.7, 4.3 Hz), 2.55 (tdd, 1H, J = 11.2, 6.1, 3.7 Hz), 2.38 (dm, 1H, J = 18.5 Hz), 2.32 (m, 1H), 2.14 (br m, 1H), 2.03 (m, 1H), 1.90 (m, 2H), 1.73 (m, 1H), 1.71−1.64 (m, 1H), 1.47 (m, 2H), 1.35 (m, 1H), 1.06 (m, 2H), 0.88 (m, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 216.49, 50.85, 47.16, 44.69, 40.48, 40.11, 39.43, 30.06, 26.91, 21.60, 13.05, 11.77, 10.16. IR (neat): 3060, 2940, 2865, 2240, 1698 cm^{-1}. HRMS for $C_{13}H_{16}O$: *m/e* calcd 188.1201, found 188.1199.

Cycloaddition of Norbornadiene (1) with 2-Buten-4-olide (8). The reaction was carried out as in general procedure B using 2-buten-4-olide (**8**)[21] (80.3 mg, 0.95 mmol), NBD (**1**) (0.20 mL, 1.8 mmol), $Ni(COD)_2$ (89.3 mg, 0.32 mmol, 33 mol %), and PPh_3 (173.5 mg, 0.66 mmol, 67 mol %) in toluene (0.30 mL) at 110 °C for 19 h. Bulb to bulb distillation (0.03 mmHg, 100−110 °C) and flash chromatography (0−40% ethyl acetate in hexanes) yielded **7c** (97.0 mg, 58%).

***endo*-4-Oxapentacyclo[6.4.0.0^{2,6}.0^{7,11}.0^{10,12}]dodecan-3-one (7c).** ^1H NMR (400 MHz, $CDCl_3$): δ 4.34 (d_{AB}d, 1H, J = 9.6, 8.2 Hz), 4.27 (d_{AB}d, 1H, J = 9.6, 3.1 Hz), 3.06 (d_{AB}d, 1H, J = 10.9, 5.1 Hz), 2.99 (m or d_{AB}ddd, 1H, J = 10.9, 8.2, 4, 3.1 Hz), 2.38 (ddd, 1H, J = 4.4, 2.4, 2.0 Hz), 2.16 (ddd, 1H, J = 4, 2.1, 1.9 Hz), 2.01 (br s, 1H), 1.55 (t, 2H, J = 1.4 Hz), 1.21 (dd, 1H, J ≈ 5 Hz), 1.12 (ddm, 1H, J ≈ 5 Hz), 1.08 (ddm, 1H, J ≈ 5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.97 (COO), 69.99 (CH_2O), 47.12, 45.81, 45.24, 44.86, 40.98, 30.97, 13.01, 12.11, 9.64. IR (neat): 3072, 3060, 2980, 2957, 2941, 2919, 2864, 1754 cm^{-1}. HRMS for $C_{11}H_{12}O_2$: *m/e* calcd 176.0837, found 176.0833.

Cycloaddition of Norbornadiene (1) with *N*-Phenylmaleimide. The reaction was carried out using method B with unpurified *N*-phenylmaleimide (154.0 mg, 0.89 mmol), NBD (**1**) (0.15 mL, 1.4 mmol), $Ni(COD)_2$ (40.0 mg, 0.14 mmol, 15 mol %), and PPh_3 (75.3 mg, 0.29 mmol, 32 mol %) in 1,2-dichloroethane (0.50 mL) at 80 °C for 18 h. Flash chromatography (20% ethyl acetate in hexanes) yielded 4-phenyl-4-azapentacyclo[6.4.0.0^{2,6}.0^{7,11}.0^{10,12}]dodeca-3,5-dione (**9**) (184.0 mg, 78%, traces of an impurity from the starting dienophile were detected in the ^1H NMR).

***endo*-4-Phenyl-4-azapentacyclo[6.4.0.0^{2,6}.0^{7,11}.0^{10,12}]dodeca-3,5-dione (9).** ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (m, 2H), 7.36 (m, 1H), 7.22 (m, 2H), 3.35 (dd, 2H, J = 2.9, 1.8 Hz), 2.57 (br s, 2H), 2.19 (br s, 1H), 1.61 (br s, 2H), 1.29 (t, 1H, J = 4.7 Hz), 1.12 (dd, 2H, J = 5.1, 1.1 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 178.29, 132.08, 129.34, 128.74, 126.85, 47.11, 45.21, 44.52, 30.51, 12.37, 10.62. IR (neat): 3065, 2980, 2960, 2870, 1710 cm^{-1}. HRMS for $C_{17}H_{15}O_2N$: *m/e* calcd 265.1102, found 265.1098.

Cycloaddition of Norbornadiene (1) with Phenyl Vinyl Sulfone (Table 4, Entry 1). The reaction was carried out as in general procedure A using $Ni(CO)_2(PPh_3)_2$ (47 mg, 0.075 mmol, 3 mol %), NBD (**1**) (0.50 mL, 4.6 mmol), and phenyl vinyl sulfone (380 mg, 2.3 mmol) in 1,2-dichloroethane (0.50 mL) at 80 °C ovemight. Flash chromatography (20% ethyl acetate in hexanes) gave **5e** (520 mg, 87%, *exo:endo* = 1:1). Pure *endo*-**5e** was obtained by recrystallization from a mixture of chloroform and hexanes.

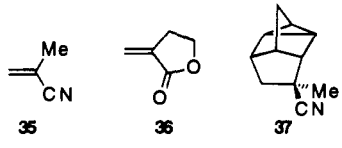
***endo*-8-(Phenylsulfonyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (*endo*-5e).** ^1H NMR (200 MHz, $CDCl_3$): δ 7.92 (m, 2H), 7.60 (m, 3H), 3.62 (ddd, 1H, J = 11.0, 5.8, 3.6 Hz), 2.16 (br m, 3H), 1.90 (br m, 2H), 1.50 (m, 1H), 1.48 (s, 2H), 1.20 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$, *endo* isomer, peaks for *exo* isomer subtracted): δ 133.42, 128.41, 128.12, 66.42, 44.42, 42.52, 42.30, 29.77, 27.02, 13.09, 10.21. IR (neat): 3056, 2975, 2940, 2875, 1435 cm^{-1}. HRMS for $C_{15}H_{16}O_2S$: *m/e* calcd 260.0871, found 260.0857.

***exo*-8-(Phenylsulfonyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (*exo*-5e).** ^1H NMR (200 MHz, $CDCl_3$): δ 7.87 (d, 2H, J = 7.7 Hz), 7.61 (t, 1H, J = 7.3 Hz), 7.54 (d, 1H, J = 7.3 Hz), 7.52 (d, 1H, J = 7.7 Hz), 3.42 (dd, 1H, J = 5.2, 8.6 Hz), 2.40 (s, 1H), 2.17 (s, 1H), 2.14 (m, obscured, 1H), 2.09 (s, 1H), 1.87 (dd, 1H, J = 9.1, 13.2 Hz), 1.54 (s, 2H), 1.12 (m, 1H), 0.92 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 133.56, 129.30, 128.61, 65.47 , 43.89, 42.17, 39.06, 31.01, 29.19, 14.73, 14.73, 13.21. HRMS for $C_{15}H_{16}O_2S$: *m/e* calcd 260.0871, found 260.0867.

Cycloaddition of Norbornadiene (1) with (*S*)-(−)-*p*-Tolyl Vinyl Sulfoxide (Table 4, Entry 5). A mixture of NBD (**1**) (0.15 mL, 1.4 mmol), (*S*)-(−)-*p*-tolyl vinyl sulfoxide (98.2 mg, 0.59 mmol) and $P(OPh)_3$ (0.06 mL, 0.25 mmol, 42 mol %) in 1,2-dichloroethane (1.0 mL) was added to $Ni(COD)_2$ (35.0 mg, 0.13 mmol, 21 mol %). The mixture was stirred at room temperature for 2.5 days. After exposing the reaction mixture to air for 3 h, the product was filtered through

(45) Kauffman, G.; Teter, L. A. *Inorg. Synth.* **1963**, *6*, 9.

(46) As suggested by a reviewer, we have attempted the cycloadditions between norbornadiene and methacrylonitrile (**35**) and α-methylene-γ-butyrolactone (**36**) under the nickel-catalyzed conditions. Methacrylonitrile (**35**) afforded 48% of the *exo* HDA adduct **37** accompanied by trace amounts of some [2 + 2] adducts. The assignment of the stereochemistry was supported by NOE experiments. Cycloaddition with **36** gave a complicated mixture of products which were inseparable.



35 **36** **37**

silica gel with dichloromethane (175 mL), and the solvent was removed *in vacuo*. Flash chromatography (10–40% ethyl acetate in hexanes) gave 8-(*R,S*)-(−)-(*p*-tolylsulfinyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane [(−)-**5f**] (104.7 mg, 69%, $[\alpha]^D = -268°$ (c = 0.66, acetone)). A second fraction (8.5 mg, maximum 5.5%) contained a mixture of the starting vinyl sulfoxide, the product tentatively assigned as the minor *exo*-(*S,S*)-deltacyclane (maximum 4% calculated by ^{1}H NMR subtracting the starting material only), and the unknown product similar to that formed with the racemic sulfoxide. The *exo*-(*S,S*) HDA adduct had peaks in the ^{1}H NMR corresponding to H^8 (δ 3.13, J = 8.3, 5.3 Hz), H^1, H^6, and H^7 (δ 2.58, br s, 1H, d; 2.06, br s, 2H); the data for cyclopropanes are as follows: (δ 1.14, t, $J \approx 5$ Hz; 0.95, tm, $J \approx 5$ Hz; 0.90, tm, $J \approx 5$ Hz). The signals for the tolyl methyl group at δ 2.38 and the H^5 and H^9 signals at δ 1.55 were larger than expected due to the impurities. The *endo*-sulfoxides were not detected.

***exo*-8-(*R,S*)-(−)-(*p*-Tolylsulfinyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane [(−)-5f].** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, 2H, J = 8.1 Hz), 7.29 (d, 2H, J = 8.1 Hz), 2.96 (dd, 1H J = 8.6, 4.9 Hz), 2.40 (s, 3H), 2.30 (t, 1H, J = 2.1 Hz), 2.16 (dt, 1H, J = 13, 4.3 Hz), 2.11 (br s, 1H), 2.07 (m, 1H), 1.56 (m, 2H), 1.54 (dd, 1H, J =13, 8.6 Hz), 1.14 (t, 1H, J = 4.8 Hz), 0.98 (tm, 1H, $J \approx 5$ Hz), 0.93 (tm, 1H, $J \approx 5$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 141.13, 140.39, 129.82, 124.46, 65.55, 45.81, 42.17, 39.15, 31.24, 25.44, 20.87, 15.39, 15.08, 13.55. IR (neat): 3058, 2958, 2945, 2865, 1477, 1443 cm^{-1}. HRMS for $C_{16}H_{18}OS$: *m/e* calcd 258.1078, found 258.1077. A crystal suitable for X-ray analysis was obtained by recrystallization from hot ether.

HDA Reaction of Electron-Deficient Norbornadiene (12a) with Acrylonitrile (Table 5, Entry 4). The reaction was carried out as in general procedure B using NBD **12a** (150.5 mg, 1.0 mmol) and acrylonitrile (0.15 mL, 2.3 mmol) dissolved in 1,2-dichloroethane (0.5 mL) with Ni(COD)$_2$ (32.8 mg, 0.13 mmol, 13 mol %) and PPh_3 (62.1 mg, 0.24 mmol, 24 mol %). Kugelrohr distillation (0.15 mmHg, 100–110 °C) of the crude product provided a mixture of ***p-exo*-13a** and ***p-endo*-13a** (192.0 mg, 94%, ratio 1:2.3 by ^{1}H NMR). IR (neat): 3070, 2955, 2885, 2872, 2236, 1722, 1716 cm^{-1}. HRMS for $C_{12}H_{13}O_2N$: *m/e* calcd 203.0946, found 203.0966. Crystallization from pentane produced pure ***p-endo*-13a** (mp = 67.5–69 °C). Flash chromatography of the ***p-exo*-13a** enriched sample using 15% dioxane in hexanes provided a sample of pure ***p-exo*-13a**, which solidified after further purification by Kugelrohr distillation (0.05 mmHg, 90–95 °C, mp = 74.5–78 °C).

Methyl *p-endo*-8-Cyanotetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane-2-carboxylate (*p-endo*-13a). ^{1}H NMR and decouplings (400 MHz, $CDCl_3$): δ 3.66 (s, 3H, OMe), 2.91 (dt, 1H, J = 11.2,4.7 Hz, H^8), 2.43 (m, 1H, H^7), 2.38 (t, 1H, J = 3.2 Hz, H^1), 2.20 (d_{AB}d, 1H, J = 13.2, 4.7 Hz, H^{9n}), 2.12 (d_{AB}dd, 1H, J = 13.2, 11.2, 3.2 Hz, H^{9x}), 2.06 (dm, 1H, J = 5.1 Hz, H^3), 1.99 (d, 1H, J = 5.1 Hz, H^4), 1.92 (m, 1H, H^6), 1.72 (d_{AB}t, 1H, J = 11.3, 1.4 Hz, H^5), 1.66 (d_{AB}, 1H, J = 11.3 Hz, H$^{5'}$). ^{13}C NMR and APT (50 MHz, $CDCl_3$): δ 173.06 (COO), 122.34 (CN), 51.18 (OCH_3), 46.54, 43.02, 42.51, 30.91 (CH_2), 30.67 (CH_2), 28.45 (C_{quat}), 27.49, 24.77, 24.33. Anal. Calcd for $C_{12}H_{13}O_2N$: C, 70.92; H, 6.45. Found: C, 70.63; H, 6.50.

Methyl *p-exo*-8-Cyanotetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane-2-carboxylate (*p-exo*-13a). ^{1}H NMR and decouplings (500 MHz [Varian Labs], $CDCl_3$): δ 3.63 (s, 3H, OMe), 2.81 (dd, 1H, J = 9.3, 4.9 Hz, H^8), 2.49 (t, 1H, J = 1.8 Hz, H^7), 2.44 (dd, 1H, J = 3.7, 2.5 Hz, H^1), 2.39 (d_{AB}d, 1H, J = 13.2, 9.3 Hz, H^{9n}), 2.22 (br s, 1H, H^6), 2.02 (d_{AB}tm, 1H, J = 13.2, 4.9 Hz, H^{9x}), 1.99 (dm, 1H, J = 5.0 Hz, H^4), 1.77 (d_{AB}m, 1H, J = 11.4 Hz, H^5), 1.74 (dt, 1H, J = 5.0, 1.8 Hz, H^3), 1.69 (d_{AB}m, 1H, J = 11.4 Hz, H$^{5'}$). ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.15, 122.90, 51.00, 48.06, 42.40, 41.88, 31.57, 30.12936, 27.99, 27.25, 26.32, 25.26. Anal. Calcd for $C_{12}H_{13}O_2N$: C, 70.92; H, 6.45. Found: C, 70.71; H, 6.52.

HDA Reaction of Electron-Deficient Norbornadiene 12a with Phenyl Vinyl Sulfone (Table 6, Entry 2). The reaction was carried out as in general procedure B using NBD **12a** (350.1 mg, 2.3 mmol) and phenyl vinyl sulfone (390.0 mg, 2.3 mmol) dissolved in 1,2-dichloroethane (0.8 mL) with Ni(COD)$_2$ (64.6 mg, 0.24 mmol, 10 mol %) and PPh_3 (125.6 mg, 0.48 mmol, 21 mol %). Flash chromatography (0–40% ethyl acetate in hexanes) gave recovered starting materials **12a** (45.9 mg, 13%), phenyl vinyl sulfone (84.0 mg, 21%), and a mixture of ***p*-14a** and ***m'*-14a** as a viscous oil (550 mg, 75%, ratio 2:1 by ^{1}H NMR).

***p*- and *m'*-8-(Phenylsulfonyl)tetracyclo[4.3.0.02,4.03,7]nonane (*p*- and *m'*-14a).** ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.93–7.81 (m, 2H), 7.68–7.49 (m, 3H), 3.72 (dd, 0.33H, J = 9.1, 5.2 Hz), 3.57 (s, 2H), 3.49 (s, 1H), 3.42 (dd, 0.66H, J = 8.3, 6.2 Hz), 2.60 (br s, 0.6H), 2.42 to 2.36 (m, 2H), 2.27 (m, 0.6H), 2.17 to 2.09 (m, 1.3H), 1.96 to 1.93 (m, 1.3H), 1.71 to 1.57 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.43, 173.01, 139.02, 138.81, 133.76, 133.62, 129.36, 129.21, 128.49, 128.39, 64.16, 63.31, 51.10, 44.69, 43.26, 42.73, 42.61, 40.88, 40.52, 30.25, 28.95, 28.81, 28.27, 28.19, 27.72, 27.15, 25.49, 25.30, 24.87. IR (neat): 3067, 2950, 2872, 1721, 1714 cm^{-1}. HRMS for $C_{17}H_{18}O_4S$: *m/e* calcd 318.0926, found 318.0924. Anal. Calcd for $C_{17}H_{18}O_4S$: C, 64.13; H, 5.70. Found: C, 64.20; H, 5.98.

HDA Reaction of Electron-Deficient Norbornadiene 12a with Methyl Vinyl Ketone (Table 6, Entry 3). The reaction was carried out as in general procedure B using NBD **12a** (144.5 mg, 0.96 mmol) and methyl vinyl ketone (0.20 mL, 2.5 mmol) dissolved in 1,2-dichloroethane (0.50 mL) with Ni(COD)$_2$ (49.5 mg, 0.18 mmol, 19 mol %) and PPh_3 (99.0 mg, 0.38 mmol, 39 mol %). The crude material was purified by Kugelrohr distillation (0.1 mmHg, 90–100 °C) to give a mixture of five products (197.5 mg, 93%, ratio 50:22:18:6:4 as determined by integration of resonances for H$^\alpha$ and OCH_3). IR (neat, cm^{-1}): 2950 (w), 2896 (s), 2871 (m), 1720 (s), 1713 (s) cm^{-1}. HRMS for $C_{13}H_{16}O_3$: *m/e* calcd 220.1099, found 220.1099. Flash chromatography (189.0 mg, 10% ethyl acetate in hexanes) provided four fractions containing the isomers shown above. The first fraction contained ***o-endo*-15a** and ***m'-exo*-15a**, (37.1 mg, 18%, ratio 6.3:1 by integration of resonances for H^9 and OCH_3) (15.5% ***o-endo*-15a**, 2.5% ***m'-exo*-15a**). The second fraction contained ***p-exo*-15a** and ***o-endo*-15a** (68.0 mg, 34%, ratio 16:1 by integration of resonance for OCH_3) (32% ***p-exo*-15a**, 2% ***o-endo*-15a**). The third fraction contained ***p-exo*-15a** and ***m'-endo*-15a** (34.0 mg, 17%, ratio 4:1 by integration of resonances for H$^{8/9}$ and OCH_3) (13.5% ***p-exo*-15a**, 3.5% ***m'-endo*-15a**). The fourth and final fraction contained ***p-endo*-15a** with an unidentified product containing vinylic peaks (41.1 mg, 20%, ratio 3:1 by integration of resonances for H^8 vs two total vinylic H's) (15% ***p-endo*-15a**, 5% unknown). Total yields of HDA cycloadducts are as follows: ***p-exo*-15a**, 45.5%; ***o-endo*-15a**, 17.5%; ***p-endo*-15a**, 15%; ***m'-endo*-15a**, 3.5%; ***m'-exo*-15a**, 2.5%. *para*:*meta'*:*ortho* ≈ 70:10:20. The total yield is 84%.

***p-exo*-8-Acetyltetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (*p-exo*-15a).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.64 (s, 3H), 2.89 (dd, 1H, J = 9.3, 5.5 Hz), 2.31 (t, 1H, J = 2.0 Hz), 2.29 (dd, 1H, J = 3.8, 2.3 Hz), 2.12 (s, 3H), 2.11 (d_{AB}d, 1H, J = 12.5, 9.3 Hz), 1.92 - 1.86 (m, 3H), 1.72 (dm, 1H, J = 4.3 Hz), 1.65 (d_{AB}, 1H, J = 11.3 Hz), 1.57 (d_{AB}, 1H, J = 11.3 Hz). ^{13}C NMR and APT (50 MHz, $CDCl_3$): δ 210.73 (C=O), 174.37 (COO), 51.36, 51.07, 45.84, 42.63, 41.09, 30.47 (CH_2), 29.12 (C_{quat}), 29.01 (CH_2), 28.44, 28.20, 26.03. Anal. Calcd for $C_{13}H_{16}O_3$ (mixture of **15a** isomers): C, 70.89; H, 7.32. Found: C, 70.99; H, 7.49.

***o-endo*-8-Acetyltetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (*o-endo*-15a).** ^{1}H NMR (400 MHz, C_6D_6): δ 3.40 (dd, 1H, J = 11.6, 5.1 Hz, H^9), 3.35 (s, 3H, OMe), 1.88 (d_{AB}d, 1H, J = 12.1, 5.1 Hz, H^{8n}), 1.86 (br s, 1H), 1.82 (m, 1H), 1.80 (s, 3H, Me), 1.60 (m, 2H, H^{8x} and H^5), 1.48 (t, 1H, J = 5 Hz), 1.30 (d_{AB}t, 1H, J = 11.0, 1.3 Hz, H$^{5'}$), 1.06 (t, 1H, J = 5 Hz), 0.84 (tm, 1H, J = 5 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 208.80, 175.39, 59.50, 56.59, 51.54, 48.51, 44.36, 29.47, 28.87, 27.95, 15.50, 13.38, 12.66. Anal. Calcd for $C_{13}H_{16}O_3$ (mixture of **15a** isomers): C, 70.89; H, 7.32. Found: C, 70.99; H, 7.49.

***p-endo*-8-Acetyltetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (*p-endo*-15a).** ^{1}H NMR and decouplings (400 MHz, $CDCl_3$): δ 3.62 (s, 3H, OMe), 3.03 (dt, 1H, J = 11.0, 4.5 Hz, H^8), 2.41 (dt, 1H, J = 4.0, 2.0 Hz, H^7), 2.28 (dd overlap, 1H, J = 13, 4.6 Hz, H^{9n}), 2.26 (m, 1H, H^1), 2.11 (s, 3H, Me), 1.98 (br s, 1H, H^6), 1.85 (d, 1H, J = 4.9 Hz, H^4), 1.72 (d_{AB}dd, 1H, J = 13, 11.0, 4.1 Hz, H^{9x}), 1.61 (d overlap, 1H, J = 4.9 Hz, H^3), 1.60 (d_{AB} overlap, 1H, J = 11.1 Hz, H^5), 1.54 (d_{AB}, 1H, J = 11.1 Hz, H$^{5'}$). ^{13}C NMR (50 MHz, $CDCl_3$): δ 209.59, 173.93, 52.47, 51.11, 46.42, 44.24, 42.76, 30.03, 28.87, 26.03, 25.08, 23.71. Anal. Calcd for $C_{13}H_{16}O_3$ (mixture of **15a** isomers): C, 70.89; H, 7.32. Found: C, 70.99; H, 7.49.

***m'-endo*-8-Acetyltetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (*m'-endo*-15a).** ^{1}H NMR and decouplings (400 MHz, $CDCl_3$): δ 3.52 (s, 3H, OMe), 3.18 (ddd, 1H, J = 10.0, 5.3, 4.0 Hz, H^9), 2.66 (dd, 1H, J = 3.8, 2.3 Hz), 2.24 (s, 3H, Me), 2.15 (dd overlap, 1H, J = 13, 5.3 Hz, H^{8n}),

2.13 (m overlap, 1H), 2.01 (br s, 1H), 1.89 (d, 1H, J = 4.7 Hz), 1.79 (d, 1H, J = 4.7 Hz), 1.64 (d_{AB}, 1H, J = 11.2 Hz, H^5), 1.55 (d_{AB}dd, 1H, J = 13, 10.0, 4.7 Hz, H^{8x}), 1.53 (d_{AB} overlap, 1H, J = 11.2 Hz, $H^{5'}$). ^{13}C NMR (50 MHz, $CDCl_3$): δ 210.40, 174.09, 53.24, 50.74, 46.75, 45.41, 43.75, 30.18, 30.04, 27.13, 26.88, 25.92 (sm), 25.75. Anal. Calcd for $C_{13}H_{16}O_3$ (mixture of **15a** isomers): C, 70.89; H, 7.32. Found: C, 70.99; H, 7.49.

HDA Reaction of Electron-Rich 2-Substituted Norbornadiene 12b with Methyl Vinyl Ketone. The reaction was carried out as in general procedure B using 2-methoxybicyclo[2.2.1] hepta-2,5-diene (**12b**) (320.2 mg, 2.6 mmol) and methyl vinyl ketone (0.42 mL, 5 mmol) dissolved in 1,2-dichloroethane (0.10 mL) with $Ni(COD)_2$ (133.0 mg, 0.48 mmol, 18 mol %) and PPh_3 (241.9 mg, 0.92 mmol, 35 mol %). The crude material was purified by Kugelrohr distillation (0.1 mmHg, 90−100 °C) and flash chromatography (10% ethyl acetate in hexanes) to give the product (90% major isomer **15b**, 256.0 mg, 51%). A second fraction containing several isomers was isolated (15.0 mg, 3%).

***o-endo*-1-Methoxy-9-acetyltetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (15b).** ^1H NMR and decouplings (400 MHz, C_6D_6, fraction 1): δ 2.94 (s, 3H, OMe), 2.85 (dd, 1H, J = 10.8, 4.3 Hz, H^9), 2.46 (dd, 1H, J = 12.5, 4.3 Hz, H^{8n}), 2.02 (s, 3H, Me), 1.65 (dt, 1H, J = 4.3, 2.1 Hz, H^7), 1.60−1.58 (m, 2H, H^6 and H^5), 1.43 (ddd, 1H, J = 12.5, 10.8, 4.3 Hz, H^{8x}), 1.30 (dt, 1H, J = 10.8, 1.5 Hz, $H^{5'}$), 1.04 (br m, 2H, H^3 and H^4), 0.90 (t, 1H, J = 5.4, H^2). ^{13}C NMR (50 MHz, $CDCl_3$): δ 209.62, 94.24, 51.09, 49.25, 42.42, 39.09, 29.85, 28.90, 26.78, 17.12, 14.16, 12.83. IR (neat): 3060, 2973, 2940, 2866, 2830, 1707 cm^{-1}. HRMS for $C_{12}H_{16}O_2$: *m/e* calcd 192.1150, found 192.1147. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.94; H, 8.41. Key coupling constants that enabled identification of the *endo* stereochemistry are as follows: $J(H^{8n-9})$ = 4.3 Hz, $J(H^{8x-9})$ = 10.8 Hz, $J(H^{8x-7})$ = 4.3 Hz, $J(H^{8x-8n})$ = 12.5 Hz. Since $J(H^{9-8n})$ was small and $J(H^{9-8x})$ was large, this indicated that H^9 was *trans* to H^{8n} and *cis* to H^{8x}.

HDA Reaction of 2-Silyl-Substituted Norbornadiene 12c with Acrylonitrile. The reaction was carried out as in general procedure B using NBD **12c** (163.1 mg, 1.0 mmol) in 1,2-dichloroethane (1.0 mL) with $Ni(COD)_2$ (40.3 mg, 0.15 mmol, 15 mol %) and $P(OPh)_3$ (0.04 mL, 0.15 mmol, 15 mol %). Acrylonitrile (0.20 mL, 3.0 mmol) was added, and the mixture was stirred at 80 °C for 36 h. Bulb to bulb distillation (0.03 mmHg, 75 °C) gave mainly HDA isomers (133.5 mg, 62%, ~75% *meta'-exo* isomer **13c** from integration of H^1 and H^3 compared to the total integration, assuming all compounds in the mixture had the same molecular formula). The *meta'-exo* isomer **13c** was recrystallized selectively from the mixture using hot pentane, and cooling at 0 °C for up to one week. This isomer was identified as the *meta'-exo* isomer by H^9 (dd), and by several decouplings that revealed H^7 (dt) was coupled to H^3 (dd) and H^{8x} (dt), but H^1 (d) was not coupled to either cyclopropane resonance.

***m'-exo*-2-(Trimethylsilyl)-9-cyanotetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane-(13c).** ^1H NMR and decouplings (400 MHz, $CDCl_3$): δ 2.75 (dd, 1H, J = 9.1, 4.7 Hz, H^9), 2.21 (d, 1H, J = 2.2 Hz, H^1), 2.13 (dt, 1H, J = 4, 2 Hz, H^7), 2.08 (br s, 1H, H^6), 1.99 (d_{AB}d, 1H, J = 12.8, 9.1 Hz, H^{8n}), 1.91 (d_{AB}t, 1H, J = 12.8, 4.2 Hz, H^{8x}), 1.61 (d_{AB}, 1H, H^5), 1.51 (d_{AB}, 1H, J = 11.0 Hz, $H^{5'}$), 1.08 (d, 1H, J = 4.6 Hz, H^4), 0.95 (dd, 1H, J = 4.6, 2.0 Hz, H^3), −0.03 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$): δ 123.68, 50.09, 42.88, 41.71, 32.91, 31.31, 28.82, 20.21, 19.53, 9.82, −1.60. IR (neat): 3056, 3046, 3022, 2950, 2896, 2882, 2867, 2235 cm^{-1}. HRMS for $C_{13}H_{19}NSi$: *m/e* calcd 217.1286, found 217.1275.

HDA Reaction of 2-Silyl-Substituted Norbornadiene 12c with Phenyl Vinyl Sulfone. A solution of 2-(trimethylsilyl)bicyclo[2..2.1]-hepta-2,5-diene (**12c**) (196.0 mg, 1.19 mmol), phenyl vinyl sulfone (100.0 mg, 0.59 mmol), and $P(OPh)_3$ (0.05 mL, 0.19 mmol, 32 mol %) in 1,2-dichloroethane (0.7 mL) was added to a flame-dried flask containing $Ni(COD)_2$ (24.4 mg, 0.09 mmol, 15 mol %). The reaction mixture was then stirred at 80 °C for 24 h, and the crude product was purified by flash chromatography (50% ether in hexanes). The first fraction (69.5 mg, 7:1 ratio, *meta'-exo* isomer 37%, *para-exo* isomer 4.4%), and the second fraction contained three or more isomers (20.0 mg, 9.5%). The major isomer was identified as the *meta'-exo* adduct by ^{13}C (APT) NMR and ^1H decouplings experiments.

***m'-exo*-2-(Trimethylsilyl)-9-(phenylsulfonyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]-nonane (14c).** ^1H NMR (400 MHz, C_6D_6): (major isomer) (*meta'-exo*) δ 3.46 (dd, 1H, J = 9.1, 5.4 Hz), 2.46 (br s, 1H), 2.33 (d, 1H, J = 2.3), 2.30 (m, 1H), 1.85 (m, 1H), 1.69 (dd, 1H, J = 13.3, 9.0 Hz), 1.34 (m, 2H), 0.83 (d, 1H, J = 4.5 Hz), 0.69 (dd, 1H, J = 4.6, 1.9 Hz), −0.10 (s, 9H); (visible peaks for the minor isomer) (*para-exo*) δ 3.34 (dd, 1H, J = 8.9, 5.8 Hz), 2.38 (br s, 1H), 1.77 (t, 1H, 2.5 Hz), 0.54 (dd, 1H, J = 4.6, 2.1 Hz), −0.22 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): (major isomer) (*meta'-exo*) δ 139.21, 133.39, 129.15, 128.40, 65.66, 47.02, 43.16, 40.19, 31,39, 28.71, 20.64, 19.38, 11.06, −1.79; (visible peaks for the minor isomer) (*para-exo*) δ 128.48, 65.52, 45.08, 45.03, 40.51, 31.26, 29.67, 20.80, −1.61. IR (neat): 3051, 2945, 2868, 1448, 1307, 1286, 1251, 1145, 1089 cm^{-1}. HRMS for $C_{18}H_{24}O_2SSi$: *m/e* calcd 332.1266, found 332.1272.

HDA Reaction of 2-Silyl-Substituted Norbornadiene 12c with Methyl Vinyl Ketone. A solution of 2-(trimethylsilyl)bicyclo[2..2.1]-hepta-2,5-diene (**12c**) (80.0 mg, 0.49 mmol), methyl vinyl ketone (0.10 mL, 1.20 mmol), and $P(OPh)_3$ (0.04 mL, 0.15 mmol, 30 mol %) in toluene (0.6 mL) was added to a flame-dried flask containing $Ni(COD)_2$ (20.1 mg, 0.07 mmol, 15 mol %). The reaction mixture was then stirred at 110 °C for 24 h and purified by flash chromatography (10% ether in hexanes), affording **15c** (*meta'-endo* adduct, 44.0 mg, 39%) and two inseparable *exo* adducts (9.0 mg, 8%, 4.3:1). The major isomer was identified as the *meta'-endo* adduct by ^{13}C (APT) NMR and ^1H decouplings experiments.

***m'-endo*-2-(Trimethylsilyl)-9-acetyltetracyclo[4.3.0.0^{2,4}.0^{3,7}]-nonane (15c).** ^1H NMR (200 MHz, $CDCl_3$): δ 2.95 (ddd, 1H, J = 10.4, 6.9, 3.7 Hz), 2.30 (dd, 1H, J = 3.5, 2.1 Hz), 2.14 (s, 3H), 2.01−1.80 (m, 3H), 1.62 (ddd, 1H, J = 12.4, 10.7, 4.7 Hz), 1.41 (br s, 2H), 1.01 (br s, 2H), −0.14 (s, 9H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 210.16, 56.15, 49.30, 45.02, 43.20, 30.27, 29.85, 26.20, 21.52, 20.76, 18.91, −0.91. IR (neat): 3057, 2952, 2807, 1708, 1456, 1427, 1356, 1251 cm^{-1}. HRMS for $C_{14}H_{22}OSi$: *m/e* calcd 243.1440, found 243.1430.

Representative Examples of Nickel-Catalyzed [2π + 2π] Cycloadditions. Cycloaddition of Electron-Deficient NBD 12d with *N*-Phenylmaleimide (NPM). The reaction was carried out as in general procedure B using $Ni(COD)_2$ (43.0 mg, 0.16 mmol, 22 mol %), PPh_3 (81.1 mg, 0.31 mmol, 43 mol %), and *N*-phenylmaleimide (127.5 mg, 0.7 mmol). Dimethyl bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (**12d**) (149.5 mg, 0.7 mmol) in toluene (1.0 mL) was added, and the mixture was stirred at 110 °C for 16 h. Flash chromatography (15−50% ethyl acetate in hexanes) gave the ***exo-(cis-anti-cis)*-25** (133.6 mg, 49%). Crystals obtained by recrystallization from hot ether−dichloromethane were analyzed by Dr. A. Lough using X-ray crystallography and identified as the *exo-(cis-anti-cis)* adduct.

[2 + 2] *exo-(cis-anti-cis)*-25. mp: 189 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (m, 2H), 7.42 (m, 1H), 7.31 (m, 1H), 7.29 (m, 1H), 3.77 (s, 6H), 3.48 (br s, 2H), 2.96 (sharp m, 2H), 2.67 (br s, 2H), 1.83 (d_{AB}, 1H, J = 10.6 Hz), 1.79 (d_{AB}, 1H, J = 10.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.84, 164.17, 143.51, 131.79, 129.21, 128.78, 126.40, 52.19, 47.66, 41.93, 40.68, 39.75. IR (neat): 3070, 2980, 2950, 2925, 2870, 1774, 1737, 1731, 1721, 1713, 1705, 1619 cm^{-1}. HRMS for $C_{21}H_{19}O_6N$: *m/e* calcd 381.1212, found 381.1227.

Cycloaddition of Electron-Rich NBD 12b with Acrylonitrile. The reaction was carried out as in general procedure B using NBD **12b** (151.4 mg, 1.05 mmol, ~85% pure by CGC) in 1,2-dichloroethane (0.50 mL) with $Ni(COD)_2$ (68.4 mg, 0.25 mmol, 24 mol %) and PPh_3 (129.2 mg, 0.49 mmol, 47 mol %). Acrylonitrile (0.20 mL, 3.0 mmol) was added, and the mixture was stirred at 80 °C for 21 h. Bulb to bulb distillation (0.1 mmHg, 100 °C) provided [2 + 2] adduct **26** (116.7 mg, 63%, ratio ~5:1 by integration of the ^1H NMR resonances for the enol ether protons at δ 4.84 and 4.78 ppm). ^1H NMR (200 MHz, $CDCl_3$): δ 4.84 (m, 0.15H), 4.78 (m, 0.85H), 3.63 (s, 3H), 2.92 (br m, 3H), 2.70 (m, 1H), 2.35 (br m, 2H), 1.77 (d_{AB}m, 1H, J = 8.3 Hz), 1.58 (br m, 2H), 1.02 (d_{AB}m, 1H, J = 8.3 Hz). This enol ether was unstable, and it was converted to the corresponding ketone **28** prior to further characterizations.

Conversion of Enol Ether 26 to Ketone 28. Pyridinium *p*-toluenesulfonate (PPTS) (12.4 mg, 0.05 mmol) was added to **26** (49.3 mg, 0.28 mmol) in THF (3.0 mL) and water (0.75 mL). The mixture was stirred for 7 h before partitioning between dichloromethane (50 mL) and water (25 mL). The organic layer was washed with water (25 mL) and brine (25 mL), and dried over $MgSO_4$. The solvent was removed *in vacuo*, and bulb to bulb distillation (0.1 mmHg, 90−100

°C) and flash chromatography (20–60% ethyl acetate in hexanes) gave **28** (36.4 mg, 80%). Crystallization from hot ether provided the major product for analysis. X-ray analysis by Dr. A. Lough identified the product as the *para-endo-(cis-anti-cis)* isomer **28** (see text). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.10 (br m, 2H), 2.80 (br m, 2H), 2.53 (br m, 1H), 2.24 (m, 2H), 2.00 (ddd, 1H, $J \approx 15$, 10, 5 Hz), 1.89 (d_{AB}m, 1H, $J = 10.7$ Hz), 1.54 (d_{AB}m, 1H, $J = 10.7$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 212.59, 122.64, 54.40, 42.20, 40.45, 38.69, 36.45, 35.52, 26.30, 19.43. IR (neat): 2978, 2950, 2920, 2893, 2875, 2233, 1740 cm^{-1}. HRMS for $C_{10}H_{11}ON$: *m/e* calcd 161.0841, found 161.0842.

Cycloaddition of Electron-Rich NBD 12b with *N*-Phenylmaleimide. The reaction was carried out as in general procedure B using $Ni(COD)_2$ (66.5 mg, 0.24 mmol, 23 mol %), PPh_3 (127.0 mg, 0.48 mmol, 46 mol %), and *N*-phenylmaleimide (198.1 mg, 1.1 mmol). A solution of NBD **12b** (148 mg, 1.04 mmol, ~85% pure by CGC) in 1,2-dichloroethane (0.50 mL) was then added, and the mixture was stirred at 80 °C for 21 h. The unstable crude [2 + 2] adduct **27** (265 mg) was converted to ketone **29a** and diester **29b** for further characterization. The ^{1}H NMR (200 MHz, $CDCl_3$) of the crude material revealed signals for an enol ether (δ 4.85 (major), 4.60 (minor) ppm, ratio ~4.5:1). A low yield of the major product **27** was obtained by crystallization from ethyl acetate–hexanes. ^{1}H NMR (200 MHz, $CDCl_3$, crystals): δ 7.43 (m, 3H), 7.29 (m, 2H), 4.85 (d, 1H, $J = 3.3$ Hz), 3.63 (s, 3H), 3.08 (m, 1H), 2.95 (m, 3H), 2.78 (d_{AB}m, 1H, $J = 6.0$ Hz), 2.67 (d_{AB}m, 1H, $J = 6.0$ Hz), 1.84 (d_{AB}, 1H, $J = 8.5$ Hz), 1.14 (d_{AB}, 1H, $J = 8.5$ Hz).

Conversion of Enol Ether 27 to Ketone 29a. PPTS (13.8 mg, 0.05 mmol) was added to a mixture of the crude enol ether **27** (63.0 mg) in THF (3.0 mL) and water (0.75 mL). The mixture was stirred for 7 h before partitioning between dichloromethane (50 mL) and water (25 mL). The organic layer was washed with water (25 mL) and brine (25 mL), and dried over $MgSO_4$. After the solvent was removed *in vacuo*, flash chromatography (30–50% ethyl acetate in hexanes) gave the major product **29a** (34.8 mg, 50% for both steps). ^{1}H NMR (400 MHz, C_6D_6): δ 2.48 (m, 1H), 2.29 (d, 1H, $J = 5.4$ Hz), 2.20 (m, 3H), 1.93 (br s, 1H, width at half-height ~10 Hz), 1.68 (d_{AB}d, 1H, $J = 18.4$, 4.5 Hz), 1.53 (d_{AB}d, 1H, $J = 18.4$, 4.9 Hz), 1.03 (sharper d_{AB}m, 1H, $J = 10.8$ Hz), 0.69 (br d_{AB}m, 1H, $J \approx 10$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 215.21, 178.14, 177.28, 132.00, 129.31, 128.86, 126.47, 53.82, 41.74, 41.45, 41.25, 40.90, 39.67, 39.08, 38.63. ^{13}C NMR (100 MHz, partial scan only for HETCOR spectrum, C_6D_6): δ 56.06, 43.93, 43.91, 43.63, 42.96, 42.03, 41.15, 38.92. IR (neat): 3068, 2980, 2950, 2870, 1765, 1745, 1720, 1680, 1598 cm^{-1}. HRMS for $C_{17}H_{15}O_3N$: *m/e* calcd 281.1052, found 281.1060. Anal. Calcd for $C_{17}H_{15}O_3N$: C, 72.58; H, 5.37. Found: C, 72.40; H, 5.69.

Cycloaddition of Silyl-Substituted NBD 12c with *N*-Phenylmaleimide (Table 9, Entry 3). The reaction was carried out as in general procedure B using $Ni(COD)_2$ (54.0 mg, 0.20 mmol, 17 mol %) and *N*-phenylmaleimide (208 mg, 1.2 mmol). A solution of 2-(trimethylsilyl)-bicyclo[2.2.1]hepta-2,5-diene **12c** (298.5 mg, 1.8 mmol) and $P(OPh)_3$ (0.10 mL, 0.38 mmol, 32 mol %) in 1,2-dichloroethane (1.5 mL) was added, and the mixture was stirred at 80 °C for 18 h. Several fractions containing two [$2\pi + 2\pi$] cycloadducts were obtained by flash chromatography (10–20% ethyl acetate in hexanes). The first fraction contained the *endo* [$2\pi + 2\pi$] adduct ***endo*-30** (63.5 mg, 16%). A second fraction contained the *endo* [$2\pi + 2\pi$] adduct with $PO(OPh)_3$ (51.0 mg, ~85% pure by weight from integration of the phenyl region, 11% yield), and a third fraction contained mainly $PO(OPh)_3$. The final fraction contained the *exo* [$2\pi + 2\pi$] adduct ***exo*-30** and *N*-phenylmaleimide (130.6 mg, ~45% by weight adduct from integration of the ^{1}H NMR, 15% yield). This sample was purified by crystallization from hot ether for analysis. The calculated overall ratio *endo*:*exo* [$2\pi + 2\pi$] adducts = 1.8:1.

[2 + 2] *endo*-30. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.35 (m, 5H), 6.71 (d, 1H, $J = 3.0$ Hz), 3.21 (br s, 1H, width at half-height ~10 Hz), 3.15 (br s, 1H, width at half-height ~10 Hz), 2.91 (br m, 2H), 2.61 (d_{AB}d, 1H, $J = 6.3$, 2.6 Hz), 2.53 (d_{AB}d, 1H, $J = 6.3$, 2.5 Hz), 1.64 (d_{AB}, 1H, $J = 8.8$ Hz), 1.24 (d_{AB}, 1H, $J = 8.8$ Hz), 0.16 (s, 9H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 179.06, 178.90, 152.18, 146.60, 132.40, 129.31, 128.68, 126.62, 52.02, 47.64, 46.19, 42.52, 42.06, 41.31, −1.94. IR (neat, cm^{-1}): 3066 (w), 3045 (w), 3035 (w), 2956 (s), 2896 (w), 2865 (w), 1771 (m), 1720 (s), 1713 (s), 1598 (m), 1556 (m), 1497 (s). Anal. Calcd for $C_{20}H_{23}O_2NSi$ (mixture of *exo* and *endo* isomers): C, 71.18; H, 6.87. Found: C, 70.59; H, 6.78.

[2 + 2] *exo*-30. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.35 (m, 5H), 6.33 (d, 1H, $J = 3.0$ Hz), 3.10 (br s, 1H, width at half-height ~4 Hz), 3.04 (br s, 1H, width at half-height ~5 Hz), 2.85 (sharp m, 2H), 2.30 (d_{AB}m, 1H, $J = 6.7$ Hz), 2.13 (d_{AB}m, 1H, $J = 6.7$ Hz), 1.65 (d_{AB}, 1H, $J = 9.9$ Hz), 1.46 (d_{AB}, 1H, $J = 9.9$ Hz), 0.05 (s, 9H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 178.54, 178.45, 150.48, 145.12, 132.28, 129.33, 128.77, 126.64, 46.67, 45.32, 41.20, 41.05, 40.85, 40.67, 40.49, −2.27. IR (neat): 2952 (s), 2925 (s), 2870 (m), 2865 (m), 2852 (m), 1706 (s), 1680 (s), 1580 (w), 1480 (m) cm^{-1}. Anal. Calcd for $C_{20}H_{23}O_2NSi$ (mixture of *exo* and *endo* isomers): C, 71.18; H, 6.87. Found C, 70.59; H, 6.78.

Cycloaddition of Dimethoxybenzonorbornadiene 31 with *N*-Phenylmaleimide (Table 10, Entry 1). The reaction was carried out as in general procedure B using $Ni(COD)_2$ (44.2 mg, 0.16 mmol, 20 mol %), PPh_3 (86.0 mg, 0.33 mmol, 41 mol %), and *N*-phenylmaleimide (138.5 mg, 0.8 mmol). A solution of **31** (167.1 mg, 0.8 mmol) in 1,2-dichloroethane (1.5 mL) was added, and the mixture was stirred at 80 °C for 48 h. Cycloadduct ***exo*-33** (180.1 mg, 60%) was obtained by flash chromatography (20–30% ethyl acetate in hexanes).

[2 + 2] Adduct *exo*-33. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.40 (m, 3H), 7.22 (m, 2H), 6.59 (s, 2H), 3.74 (s, 8H), 3.01 (br s, 2H, width at half-height 5 Hz), 2.48 (br s, 2H, width at half-height 5 Hz), 2.00 (br d_{AB}, 1H, 10.3 Hz), 1.84 (br d_{AB}, 1H, $J = 10.3$ Hz). ^{13}C NMR and APT (50 MHz, $CDCl_3$): δ 178.14 (C=O), 148.40 (C_{quat}), 134.37 (C_{quat}), 132.26 (C_{quat}), 129.34 (CH), 128.78 (CH), 126.61 (CH), 109.93 (CH), 55.56 (OMe), 42.92 (CH), 42.31 (CH), 40.90 (CH_2), 0.64 (CH). IR (neat): 3065, 2960, 2850, 1770, 1714, 1707, 1602 cm^{-1}. HRMS for $C_{23}H_{21}O_4N$: *m/e* calcd 375.1470, found 375.1456.

Cycloaddition of Deltacyclene 32 with *N*-Phenylmaleimide (Table 10, Entry 3). The reaction was carried out as in general procedure B using $Ni(COD)_2$ (46.0 mg, 0.17 mmol, 17 mol %), PPh_3 (88.6 mg, 0.34 mmol, 34 mol %), and *N*-phenylmaleimide (177.0 mg, 1.0 mmol). A solution of deltacyclene **32** (199.0 mg, 1.7 mmol) in 1,2-dichloroethane (1.5 mL) was added, and the mixture was stirred at 80 °C for 40 h. Cycloadduct **34** (72.8 mg, 25%, >90% pure) was obtained by flash chromatography (10–20% ethyl acetate in hexanes). The major product **34** was assumed to have the *exo* stereochemistry of the cyclobutane by analogy with the literature result using the cyclopropyl-substituted norbomene.

[2 + 2] Adduct *exo*-34. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.35 (m, 5H), 2.95 (m, 2H), 2.86 (sharp m, 2H), 2.24 (br s, 2H), 2.12 (br s, 1H), 1.66 (br s, 2H), 1.20 (tm, 1H, $J \approx 5$ Hz), 0.87 (dm, 2H, $J \approx 5$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 178.50, 132.28, 129.22, 128.61, 126.53, 45.92, 45.08, 42.75, 36.13, 30.98, 13.58, 12.89. IR (neat): 3065, 2930, 2860, 1771, 1704 cm^{-1}.

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Supporting Information Available: Text describing the details of experimental procedures and compound characterization data that are not included in the Experimental Section (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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