Stereoselectivity in the Homo-Diels–Alder Reaction: Effect of a Remote 7-Substituent on Nickel-catalysed Cycloadditions

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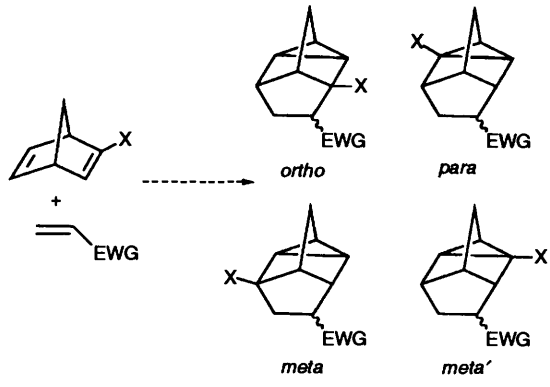
7-Substituted norbornadienes have been shown to undergo highly stereoselective homo-Diels–Alder reactions with a variety of dienophiles. Excellent *exo/endo* selectivity (always >97:3) was observed when methyl vinyl ketone was used as dienophile. Increasing *anti/syn* selectivity (up to 95:5 when Y = OBu^t) was observed as the electronegativity of the 7-substituent increased.

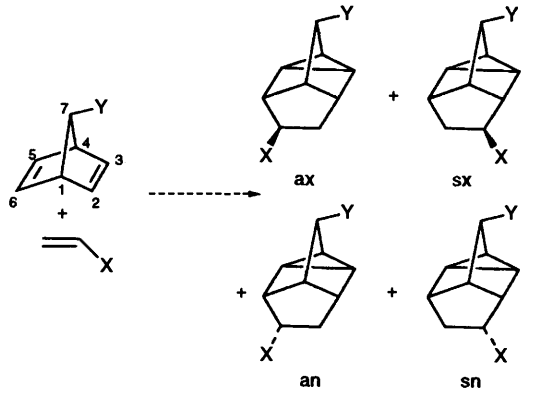
We have recently described regioselective homo-Diels–Alder (HDA) cycloadditions of substituted norbornadienes (NBDs) where the substituent was directly attached to the olefin of the bicyclic diene[1–3] (Scheme 1). High levels of regioselectivity were observed in cycloadditions with electron-rich and electron-deficient dienes. The nature of the substituent controlled the isomer that was formed in these reactions. One difficulty encountered in these studies was the decrease in reactivity associated with increasing substitution on the olefin. In some cases this led to a change in reaction pathway and a [2 + 2] process became dominant.[4] An intriguing possibility is to control the selectivity of the HDA reaction by remote substituents which may be less prone to inhibiting the cycloaddition process.

Our overall objective is to investigate the HDA reaction as a route to polycyclic natural products by a cycloaddition–fragmentation sequence. This strategy requires efficient routes to cycloadducts bearing leaving groups α to the cyclopropane bonds which will undergo bond cleavage under appropriate conditions.[5] We now report our investigation into the regioselectivity of the cycloaddition process between a 7-substituted norbornadiene and a dienophile. Four possible homo-Diels–Alder adducts may be formed in this reaction, namely *anti-exo* (ax), *anti-endo* (an), *syn-exo* (sx) and *syn-endo* (sn) (Scheme 2).

While remote substituents might be expected to have less control over the selectivity compared to a substituent which is directly attached to the reacting centre, literature reports indicate that certain reactions of bicyclo[2.2.1]heptanes systems exhibit moderate to high levels of stereo- and regiochemical control.[6] Some examples include the stereoselective Diels–Alder reaction between hexachlorocyclopentadiene and norbornadienes as reported by Battiste and co-workers[6a] and the regioselective carbene insertions on 7-oxygenated norbornadienes as reported by the Jefford[6i] and Klumpp groups.[6j] In this paper we examine the change in selectivity as the substituent at the 7-position is systematically varied. Remarkably levels of regio- and stereo-control have been observed.



Scheme 1



Scheme 2

Results

The required 7-substituted norbornadienes **1a–h** were prepared according to literature procedures.[7] Oxygenation of norbornadiene by treatment with *tert*-butyl perbenzoate or benzoyl peroxide in the presence of a copper(I) bromide gave **1g** and **1d**, respectively. Conversion of **1g** into **1a** and **1b** was achieved by treatment with the corresponding Grignard reagent. Reaction of HCl(g) with **1g** gave **1c**. Treatment of **1d** with MeMgI gave 7-hydroxynorbornadiene which was protected with triisopropylsilyl chloride (TIPSCl) or 2-methoxyethoxymethyl chloride (MEMCl) to provide **1e** and **1f**.

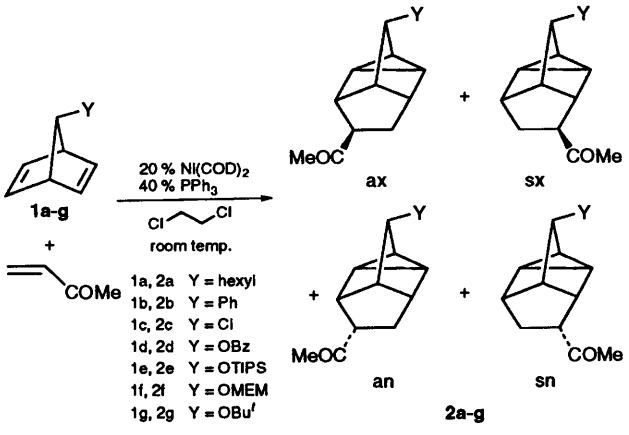
The reactive nickel catalyst formed *in situ* from Ni(COD)$_2$/PPh_3 was found to be most effective in the HDA cycloaddition as reported previously.[2,3b] Typical reaction conditions involved stirring a mixture of the 7-substituted norbornadiene, dienophile and catalyst in 1,2-dichloroethane overnight either at room temperature or at 80 °C.

Effect of the 7-Substituent in the HDA Reaction with Methyl Vinyl Ketone as Dienophile.—In Table 1 are shown the results of the HDA reactions between various 7-substituted NBDs with methyl vinyl ketone (MVK). In general, high yields were obtained. Although four possible products could be formed in this reaction (Scheme 3), little of the *endo* products (an and sn) were detected in most cases. In other words, all 7-substituted NBDs were highly *exo* selective (always >97:3) when allowed to react with MVK. Interestingly the *anti* to *syn* ratio increases gradually as the group electronegativity[8] increases eventually giving 95:5 in favour of the *anti* isomer.

In order to prove that there was no epimerization under the

Table 1 Effect of the 7-substituent in the homo-Diels–Alder reaction with MVK

	Product	Y	Yield (%)	ax:sx:an:sn	*anti*:*syn*	*exo*:*endo*
	2a	Hexyl	83	40:58:1.6:0.4	42:58	98:2
	2b	Ph	84	54:45:0.8:0.2	55:45	99:1
	2c	Cl	60	71:28:0.8:0.2	72:28	99:1
	2d	OBz	97	80:20:0:0	80:20	100:0
	2e	OTIPS	90	90:9:1:0	91:9	99:1
	2f	OMEM	89	88:9:3:0	91:9	97:3
	2g	OBu^t	95	95:5:0:0	95:5	100:0



Scheme 3

reaction conditions, two control experiments were conducted. The isolated *anti-endo* HDA adduct of **2a** was resubjected to the original reaction conditions (20% $Ni(COD)_2$/40% PPh_3 in 1,2-dichloroethane at 80 °C for 24 h), which caused no change in the stereochemistry as monitored by ^1H NMR. The inseparable mixture of **4h** (with *anti*/*syn* ratio 81:19 and *exo*/*endo* ratio 67:33) was converted into the corresponding benzoate derivative by desilylation and esterification as described in the Experimental section. This benzoate, which has a different product distribution from the benzoate **4d** (made *via* the homo-Diels–Alder reaction between NBD **1d** and phenyl vinyl sulfone) was subjected to the same reaction conditions (20% $Ni(COD)_2$/40% PPh_3 in 1,2-dichloroethane at 80 °C for 24 h). Again, no change in the product distribution was observed.

To illustrate the necessity of the catalyst in the HDA reaction, three thermal HDA reactions were attempted. When 7-phenylnorbornadiene **1b** or 7-*tert*-butoxynorbornadiene **1g** was heated with MVK in 1,2-dichloroethane at 80 °C for 2 days in the absence of catalysts, no reaction was observed and starting materials were recovered. The same observation was made for the attempted thermal reaction between 7-*tert*-butoxynorbornadiene **1g** and acrylonitrile (AN). Thus $Ni(COD)_2/PPh_3$ is essential for the cycloaddition reaction.

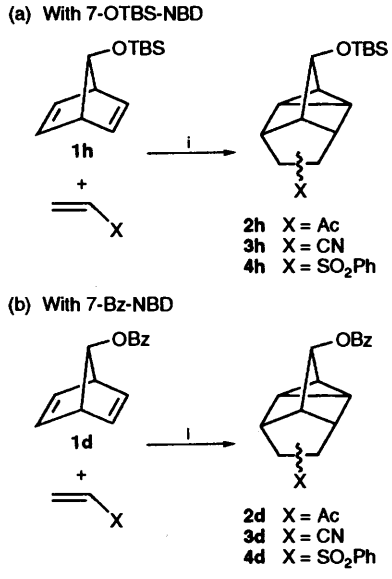
Effect of Temperature.—As shown in Table 2, temperature changes from 22 to 80 °C had little effect on either the yield or the *anti*:*syn* and *exo*:*endo* ratios.

Effect of the Dienophiles in the HDA Reaction.—The regio- and stereo-selectivity of three different dienophiles in the HDA reaction with two different 7-substituted NBDs was investigated (Scheme 4). As we observed for MVK, both AN and phenyl vinyl sulfone (PVS) gave excellent yields of the HDA products. However, a modest drop in *anti*:*syn* ratios was observed while the *exo*:*endo* ratios decreased dramatically as the dienophile changed from MVK to AN or PVS (Table 3).

Table 2 Effect of temperature in cycloaddition with MVK

Product	Y	Temp.*	Yield (%)	*anti*:*syn*	*exo*:*endo*
2a	Hexyl	RT	83	42:58	98:2
		80 °C	85	47:53	96:4
2b	Ph	RT	84	54:46	99:1
		80 °C	87	50:50	98:2
2d	OBz	RT	97	80:20	100:0
		80 °C	95	77:23	96:4
2g	OBu^t	RT	95	95:5	100:0
		80 °C	97	95:5	100:0

* RT = room temperature.



Scheme 4 Effect of the dienophile on the regioselectivity: *Reagents and conditions:* i, 20% $Ni(COD)_2$, 40% PPh_3, $Cl(CH_2)_2Cl$, 80 °C

Table 3 Effect of the dienophile on the regioselectivity

(a) With 7-OTBS-NBD

Product	X	Yield (%)	*anti*:*syn*	*exo*:*endo*
2h	Ac	93	90:10	98:2
3h	CN	93	89:11	79:21
4h	SO_2Ph	95	81:19	67:33

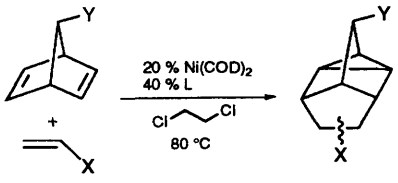
(b) With 7-Bz-NBD

Product	X	Yield (%)	*anti*:*syn*	*exo*:*endo*
2d	Ac	95	77:23	96:4
3d	CN	95	75:25	75:25
4d	SO_2Ph	97	70:30	70:30

Table 4 Effect of phosphine ligands

Product	X	Y	L	Yield (%)	*anti*:*syn*	*exo*:*endo*
2d	Ac	OBz	PPh_3	95	77:23	96:4
			$P(OPr^i)_3$	95	80:20	75:25
3d	CN	OBz	PPh_3	95	75:25	75:25
			$P(OPr^i)_3$	95	85:15	60:40

Effect of Phosphine Ligand.—Unlike the substrates with substituents directly attached to olefin of NBD, which show dramatic changes in stereoselectivity in the HDA reaction,[2,4] little effect was observed on the selectivity by changing the ligand from PPh_3 to $P(OPr^i)_3$ (Scheme 5, Table 4). While the yield of the cycloadditions remained high, the *anti*:*syn* ratios were improved slightly but lower *exo*:*endo* ratios were observed when $P(OPr^i)_3$ was used instead of PPh_3.



Scheme 5 Effect of phosphine ligands

Discussion

A substituent at the 7-position in an NBD derivative breaks one of the planes of symmetry and leads to a differentiation of the two olefins. One of the double bonds is *syn* to the substituent (denoted as *syn*-π) and another is *anti* (denoted as *anti*-π). For a [2π + 2π + 2π] HDA reaction to occur, the dienophile has to approach the NBD from the *endo* face of the double bonds (Fig. 1). Although we do not know which step in the cycloaddition is rate determining, the 7-substituent will clearly exert an electronic effect on the two alkenes and on each of the intermediates in the reaction pathway.

A direct through-space interaction between the 7-substituent with the neighbouring double bond is possible. This interaction could involve either orbital overlap[9] or a field effect. The substituent orbitals could also interact with the π orbitals through bonds rather than through space. For example, the ability of the C(1)–C(7)–C(4) bridge of NBD to hyperconjugate with the two π orbitals could be altered by the 7-substituent.

From the *ab initio* calculations of various 7-substituted norbornadienes using the STO-3G basis set reported by Mazzocchi, Houk and co-workers,[10] there is a shift of electron density from the *anti*-π olefin to the *syn*-π olefin as the substituent group electronegativity increases (Fig. 2). Based on the mechanism of deltacyclane formation proposed by Noyori,[11] metallacycles **B** are formed *via* complex **A** (Scheme 6). The larger the substituent group electronegativity, the greater the shift of electron density from the *anti*-π olefin to the *syn*-π olefin in the **A**. One can rationalize that the *syn*-σ metal-carbon has a greater electron density than the *anti*-σ metal-carbon in the metallacycles **B** as the group electronegativity of Y increases. Thus, the more reactive metallacycle $\mathbf{B}_2$ leads to the major *anti*-product.

The above discussion is based on examining the electronic effect of the 7-substituents on the two olefins of the starting dienes. Steric effects can also be anticipated between the C-7 substituent and the two vinylic hydrogens following complexation of the nickel to the diene. This steric effect may influence which bond then forms. Further investigations to resolve this question by *ab initio* calculations on the presumed nickel π and σ complexes are in progress.[12]

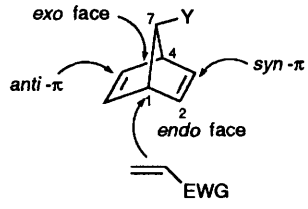


Fig. 1

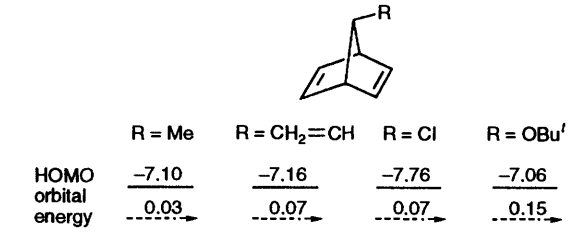


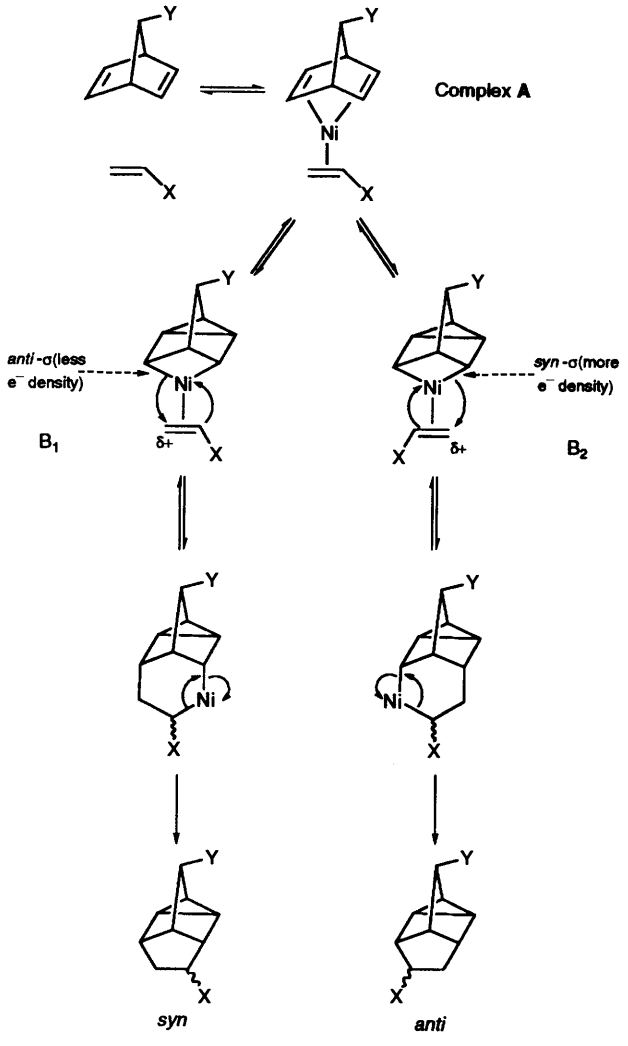
Fig. 2 Data taken from Mazzocchi *et al.*[10] Orbital energies are in eV. The numbers and arrows represent the shift in orbital density.

exo Products were found to be thermodynamically more stable than the corresponding *endo* products. When potassium *tert*-butoxide (5 equiv.) was stirred with a mixture of *exo* and *endo* products of **4h** (*exo*:*endo* = 67:33) at room temperature for 24 h, an increase of *exo*/*endo* ratio in the mixture was observed (*exo*:*endo* ratio increased to 91:9). Thus, *endo* products epimerized to the corresponding *exo* products when treated with a strong base. This observation illustrated not only the fact that *exo* products are more stable than the corresponding *endo* products, but also showed that the *exo*/*endo* ratios can be improved by epimerizing the mixture with a base. Thus, in spite of the lower *exo*/*endo* selectivity when acrylonitrile and phenyl vinyl sulfone were used instead of methyl vinyl ketone as the dienophile (see Table 3), treatment of the adducts with $KOBu^t$ resulted in an increase in the *exo*/*endo* ratio to about 10:1.

Identification of the Cycloadducts.—The structure of each of the four homo-Diels–Alder cycloadducts shown in Fig. 3 were assigned using ^1H NMR techniques. *exo* Cycloadducts (ax and sx) were distinguished from the *endo* cycloadducts by the different splitting pattern of H^8 in the ^1H NMR spectrum. H^8 of the *exo* cycloadducts coupled only with H^9 and H^{10} (but did not couple with H^7 in ax or H^1 in sx) to give a dd pattern. In the *endo* cycloadducts (an and sn), H^8 was a ddd due to an additional coupling with H^7 (in an) or H^1 (in sn). Nuclear Overhauser effect (NOE) and decoupling experiments were used to distinguish ax and sx. In ax, H^1 coupled with H^9 and showed no NOE with H^5 while a positive NOE was observed for H^4 (6–8%), H^6 (8–10%) and H^7 (10–12%) when H^5 was irradiated. In sx, H^7 coupled with H^9 and H^{10} and showed a positive NOE (5–8%) when H^5 was irradiated.

Conclusions

In summary, we have found that 7-substituted norbornadienes undergo a remarkably stereoselective HDA reaction with



Scheme 6

several dienophiles. The *anti-syn* selectivity increased with the increasing electronegativity of the 7-substituent, while less effect was observed as the temperature and the nature of the phosphine ligands were changed. These results, in concert with our studies on intramolecular cycloadditions[3f] and the effect of substituents on the alkene positions[2] indicate the considerable potential of this methodology to construct selectively polycyclic compounds.

Experimental

Triphenylphosphine, triisopropyl phosphate, acrylonitrile and phenyl vinyl sulfone were commercially available and used without additional purification. Methyl vinyl ketone and all the solvents were distilled prior to use. Bis(cycloocta-1,5-diene)-nickel(0), $Ni(COD)_2$, was made according to the procedure described in the literature[13] and was stored under a nitrogen atmosphere inside a glove box. 7-Substituted norbornadienes, **1a–h**, were synthesized by methods described in the literature.[7] ^1H NMR spectra were recorded at 400 MHz using a Varian XL 400 spectrometer or at 200 MHz using a Varian Gemini 200 NMR spectrometer. ^{13}C NMR spectra were recorded at 100 or 50 MHz. IR spectra were obtained using a Nicolet DX FT-IR spectrometer. Combustion analyses were submitted to Galbraith Laboratories Inc., Knoxville, TN. High resolution mass spectra were obtained on a VG 70-250S (double focusing) mass spectrometer at 70 eV.

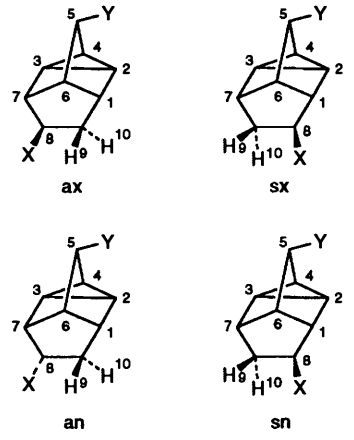


Fig. 3 Identification of the cycloadducts

General Cycloaddition Procedures.—$Ni(COD)_2$ (10–25 mol%) was added to a flame-dried flask equipped with a magnetic stir bar and a rubber septum in the glove box. The ligand (triphenylphosphine, 2 mol equiv. w.r.t Ni) was introduced with a positive flow of N_2(g), and a premixed solution of the 7-substituted norbornadiene (NBD), the dienophile and 1,2-dichloroethane was added to the $Ni(COD)_2/PPh_3$ solid mixture *via* a cannula. Reactions with phenyl vinyl sulfone as dienophile, which was a solid, were modified slightly, with the phenyl vinyl sulfone added to the solid mixture of $Ni(COD)_2/PPh_3$ prior to the addition of the 7-substituted NBD. When a liquid phosphite ligand was used instead of the solid triphenylphosphine, the phosphite was premixed with the diene/solvent/dienophile and then transferred to the $Ni(COD)_2$ *via* a cannula. The reaction mixture was stirred at the desired temperature under nitrogen for 12 to 24 h. The catalyst was then oxidized by stirring the mixture exposed to air for 1 to 2 h. The reaction mixture was filtered through a plug of silica using dichloromethane as eluent. Evaporation of the solvent gave a crude product, which was purified by bulb-to-bulb distillation or flash column chromatography on silica gel.

8-Acetyl-5-hexyltetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]*nonane* **2a**.—The cycloaddition was carried out as in general procedure described above, using 7-hexylbicyclo[2.2.1]hepta-2,5-diene **1a** (164.8 mg, 0.94 mmol), methyl vinyl ketone (0.19 cm^3, 2.34 mmol) in 1,2-dichloroethane (0.5 cm^3) with $Ni(COD)_2$ (51.6 mg, 0.19 mmol, 20 mol%) and PPh_3 (98.3 mg, 37.5 mmol, 40 mol%). The orange–brown reaction mixture was stirred at room temperature for 18 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 10% ether in hexanes as eluent) to afford a separable mixture of **2a** (ax:sx:an:sn = 40:58:1.6:0.4) with total yield of 190.4 mg (83%); ν_{max}(neat)/cm^{-1} 3058m, 2952s, 2924s, 2854s, 1708s, 1448m, 1427w, 1356m, 1314w, 1223w, 1173m, 1145m, 801m and 730w; δ_H($CDCl_3$, 400 MHz) ax: 2.88 (1 H, dd, *J* 8.79 and 4.88), 2.30 (1 H, m), 2.14 (3 H, s), 2.03 (1 H, m), 1.89 (1 H, ddd, *J* 12.21, 9.28 and 4.88), 1.83 (1 H, t, *J* 7.32), 1.68 (1 H, dd, *J* 12.21 and 8.79), 1.58 (1 H, m), 1.25 (8 H, m), 1.14 (2 H, m), 1.02 (1 H, m), 0.95 (2 H, m) and 0.87 (3 H, t, *J* 6.84); δ_H($CDCl_3$, 400 MHz) sx: 2.79 (1 H, dd, *J* 9.07 and 5.12), 2.17 (1 H, m), 2.15 (1 H, m), 2.11 (3 H, s), 1.88 (1 H, ddd, *J* 12.17, 9.07 and 5.12), 1.80 (1 H, t, *J* 7.69), 1.77 (1 H, dd, *J* 12.17 and 9.07), 1.58 (1 H, m), 1.23 (8 H, m), 1.12 (2 H, m), 1.00 (1 H, m), 0.96 (1 H, m), 0.91 (1 H, m) and 0.85 (3 H, t, *J* 6.90); δ_C($CDCl_3$, 100 MHz) ax: 210.84, 52.63, 44.86, 43.58, 43.14, 42.96, 31.88, 31.10, 29.68, 29.61, 29.08, 28.55, 22.69, 18.93, 16.42, 15.17 and 14.14; δ_C($CDCl_3$, 100 MHz) sx: 210.86, 52.67, 46.22, 44.76, 43.58, 39.46, 31.88, 31.10, 29.73, 29.61, 28.98, 28.47, 22.66, 18.94, 16.54, 14.99 and 14.12 (Found: M^+, 246.1986. $C_{17}H_{26}O$ requires *M*, 246.1984).

8-*Acetyl*-5-*phenyltetracyclo*[4.3.0.0^{2,4}.0^{3,7}]*nonane* **2b**.—The cycloaddition was carried out as in general procedure described above, using 7-phenylbicyclo[2.2.1]hepta-2,5-diene **1b** (175.6 mg, 1.04 mmol), methyl vinyl ketone (0.21 cm^3, 2.59 mmol) in 1,2-dichloroethane (0.5 cm^3) with Ni(COD)$_2$ (57.7 mg, 0.21 mmol, 20 mol%) and PPh_3 (109.9 mg, 0.42 mmol, 40 mol%). The orange–brown reaction mixture was stirred at room temperature for 18 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 10% ether in hexanes as eluent) to afford a separable mixture of **2b** (ax:sx:an:sn = 54:45:0.8:0.2) with total yield of 208.5 mg (84%); ν_{max}(neat)/cm^{-1} 3058m, 3030m, 2945s, 2868m, 1708s, 1602m, 1497m, 1448m, 1427w, 1356m, 1314w, 1173m, 801m, 766w and 702m; δ_H($CDCl_3$, 400 MHz) ax: 7.26 (5 H, m), 3.21 (1 H, m), 2.89 (1 H, dd, *J* 8.42 and 6.23), 2.45 (1 H, m), 2.16 (3 H, s), 2.05 (1 H, m), 1.90 (1 H, m), 1.84 (2 H, m), 1.41 (1 H, m), 1.21 (2 H, m); δ_H($CDCl_3$, 400 MHz) sx: 7.25 (5 H, m), 3.21 (1 H, m), 2.93 (1 H, dd, *J* 8.79 and 4.88), 2.29 (1 H, m), 2.18 (1 H, m), 2.07 (3 H, s), 2.02 (1 H, ddd, *J* 12.20, 9.28 and 4.88), 1.88 (1 H, m), 1.72 (1 H, dd, *J* 12.21 and 8.79), 1.40 (1 H, m), 1.27 (1 H, m) and 1.15 (1 H, m); δ_C($CDCl_3$, 50 MHz) ax: 210.23, 142.51, 127.91, 127.28, 125.87, 52.82, 49.08, 46.74, 46.65, 39.82, 29.97, 29.22, 17.94, 16.09 and 16.06; δ_C($CDCl_3$, 100 MHz) sx: 209.97, 142.37, 127.95, 127.28, 125.84, 52.41, 49.09, 46.09, 44.05, 43.44, 29.63, 29.48, 18.09 and 16.43 (Found: C, 85.8; H, 7.8. $C_{17}H_{18}O$ requires C, 85.67; H, 7.61%).

8-*Acetyl*-5-*chlorotetracyclo*[4.3.0.0^{2,4}.0^{3,7}]*nonane* **2c**.—The cycloaddition was carried out as in general procedure described above, using 7-chlorobicyclo[2.2.1]hepta-2,5-diene **1c** (359.5 mg, 2.84 mmol), methyl vinyl ketone (0.57 cm^3, 7.03 mmol) in 1,2-dichloroethane (0.5 cm^3) with Ni(COD)$_2$ (92.2 mg, 0.33 mmol, 12 mol%) and PPh_3 (175.0 mg, 0.67 mmol, 24 mol%). The orange–brown reaction mixture was stirred at room temperature for 18 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 20% ether in hexanes as eluent) to afford a separable mixture of **2c** (ax:sx:an:sn = 71:28:0.8:0.2) with total yield of 336.6 mg (60%); ν_{max}(neat)/cm^{-1} 3065m, 2959s, 2875m, 1708s, 1448w, 1420m, 1363s, 1300m, 1173m, 913m, 808m, 766m and 730m; δ_H($CDCl_3$, 400 MHz) ax: 4.13 (1 H, m), 2.84 (1 H, dd), 2.63 (1 H, m), 2.33 (1 H, m), 2.10 (3 H, s), 1.99 (1 H, m), 1.89 (2 H, m). 1.47 (1 H, m), 1.27 (1 H, m), 1.20 (1 H, m); δ_H($CDCl_3$, 400 MHz) sx: 4.13 (1 H, m). 2.93 (1 H, dd, *J* 8.06 and 4.04), 2.75 (1 H, m), 2.18 (1 H, m), 2.14 (3 H, s), 2.00 (1 H, ddd, *J* 12.98, 8.07 and 4.04), 1.95 (1 H, m), 1.68 (1 H, dd, *J* 12.98 and 8.06), 1.46 (1 H, m), 1.31 (1 H, m) and 1.18 (1 H, m); δ_C($CDCl_3$, 100 MHz) ax: 209.54, 63.81, 53.02, 47.13, 43.78, 41.80, 29.27, 28.76, 21.69, 17.64 and 16.13; δ_C($CDCl_3$, 100 MHz) sx: 209.48, 63.64, 51.42, 46.68, 45.26, 41.35, 29.97, 29.09, 21.81, 17.89 and 16.31 (Found: C, 67.7; H, 6.8. $C_{11}H_{13}ClO$ requires C, 67.18; H, 6.66%).

8-*Acetyltetracyclo*[4.3.0.0^{2,4}.0^{3,7}]*nonan*-5-*yl Benzoate* **2d**.—The cycloaddition was carried out as in general procedure described above, using bicyclo[2.2.1]hepta-2,5-dien-7-yl benzoate **1d** (140.1 mg, 0.66 mmol), methyl vinyl ketone (0.15 cm^3, 1.85 mmol) in 1,2-dichloroethane (1.0 cm^3) with Ni(COD)$_2$ (41.3 mg, 0.15 mmol, 23 mol%) and PPh_3 (81.8 mg, 0.31 mmol, 47 mol%). The orange–brown reaction mixture was stirred at room temperature for 26 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 20% ethyl acetate in hexanes as eluent) to afford an inseparable mixture of **2d** (ax:sx = 80:20) with total yield of 180.8 mg (97%); ν_{max}(neat)/cm^{-1} 3065w, 3000m, 2954m, 2871w, 1721s, 1714s, 1705s, 1699s and 1601m; δ_H($CDCl_3$, 400 MHz) 8.00 (2 H, m), 7.52 (1 H, m), 7.41 (2 H, m), 5.19 (0.2 H, m), 5.17 (0.8 H, m), 2.99 (0.2 H, dd, *J* 8.9 and 5.2), 2.82 (0.8 H, dd, *J* 8.8 and 5.8), 2.79 (0.2 H, m), 2.67 (0.8 H, m), 2.45 (0.8 H, t, *J* 2.1), 2.30 (0.2 H, m), 2.16 (0.6 H, s), 2.13 (2.4 H, s), 2.02 (1 H, br s), 1.93 (1.8 H, m), 1.76 (0.2 H, dd, *J* 12.5 and 9.0), 1.5 (1 H, tm) and 1.25 (2 H, m); δ_C($CDCl_3$, 50 MHz) 209.36, 166.30, 132.66, 130.45, 139.40, 128.15, 79.92, 52.74, 43.12, 41.88, 29.50, 17.56, 16.32 and 15.88; small peaks: 79.79, 52.04, 44.98, 42.85, 40.37, 30.03 and 28.73 (Found: M$^+$, 282.1251. $C_{18}H_{18}O_3$ requires *M*, 282.1255).

8-*Acetyl*-5-*triisopropylsiloxytetracyclo*[4.3.0.0^{2,4}.0^{3,7}]*nonane* **2e**.—The cycloaddition was carried out as in the general procedure described above, using 7-triisopropylsiloxybicyclo-[2.2.1]hepta-2,5-diene, **1e** (70.8 mg, 0.27 mmol), methyl vinyl ketone (0.10 cm^3, 1.20 mmol) in 1,2-dichloroethane (0.35 cm^3) with Ni(COD)$_2$ (17.7 mg, 0.06 mmol, 24 mol%) and PPh_3 (34.8 mg, 0.13 mmol, 48 mol%). The reaction mixture was stirred at room temperature for 72 h. After work-up as described in the general procedure, the crude product was purified by bulb-to-bulb distillation (0.1 mmHg, 100 °C) and flash column chromatography (using 5% ether in hexanes as eluent) to afford an inseparable mixture of **2e** (ax:sx:an = 90:9:1) with a total yield of 78.3 mg (88%); ν_{max}(neat)/cm^{-1} 3068w, 2960s, 2943s, 2892s, 2866s and 1712s; δ_H($CDCl_3$, 400 MHz) 4.21 (1 H, br s), 2.92 (0.1 H^{sx}, dd, *J* 8.7 and 4.4), 2.72 (1 H, t, *J* 7.2), 2.58 (1 H, m), 2.22 (0.9 H^{ax}, t, *J* 2.0), 2.15 (0.3 H^{sx}, s), 2.11 (0.03 H^{an}, s), 2.10 (2.7 H^{ax}, s), 2.06 (0.1 H, m), 1.95 (0.1 H^{sx}, dt, *J* 12.3 and 4.2), 1.94 (0.1 H, br s), 1.86 (1.8 H, m), 1.66 (0.9 H, br s), 1.64 (0.1 H, m), 1.56 (0.1 H^{sx}, dd, *J* 12.3 and 8.8), 1.17 (0.3 H, br m), 1.12 (1.8 H, m) and 1.00 (22 H, s). In C_6D_6, several areas of the ^{1}H NMR were better resolved; δ_H(C_6D_6, 400 MHz) 4.26 (0.9 H^{ax}, br s), 4.21 (0.1 H^{sx}, br s), 2.84 (0.1 H^{sx}, t, *J* 2), 2.69 (1 H^{ax}, dt, *J* 4 and 2), 2.52 (0.1 H^{sx}, dd, *J* 8.7 and 4.4), 2.28 (0.9 H^{ax}, dd, *J* 9.2 and 5), 2.15 (0.9 H^{ax}, t, *J* 2), 2.04 (0.1 H^{sx}, dt, *J* 8.7 and 4.5), 1.90 (0.9 H, br s), 1.84 (1 H, dt, *J* 12.3 and 5), 1.73 (0.3 H^{sx}, s), 1.67 (2.7 H^{ax}, s), 1.60 (1 H, dd, *J* 12.3 and 9.2), 1.10 (21 H, m), 0.95 (1 H, tm, *J* ~ 5) and 0.74 (1 H, tm, *J* ~ 5); δ_C($CDCl_3$, 100 MHz) peaks of major isomer 77.50, 53.38, 46.48, 42.63, 41.30, 29.78, 28.80, 20.79, 18.01, 16.27, 15.79, 15.70, 12.28 and 12.19; visible smaller peaks: 52.3, 46.1, 45.1, 40.0 and 28.9; ν_{max}(neat)/cm^{-1} 3068w, 2960s, 2943s, 2892s, 2866s and 1712s (Found: C, 72.0; H, 10.5. $C_{20}H_{34}O_2Si$ requires C, 71.80; H, 10.24%).

8-*Acetyl*-5-*methoxyethoxymethoxytetracyclo*[4.3.0.0^{2,4}.0^{3,7}]-*nonane* **2f**.—The cycloaddition was carried out as in the general procedure described above, using 7-methoxyethoxymethoxybicyclo[2.2.1]hepta-2,5-diene **1f** (77.8 mg, 0.40 mmol), methyl vinyl ketone (0.10 cm^3, 1.23 mmol) in 1,2-dichloroethane (0.5 cm^3) with Ni(COD)$_2$ (25.3 mg, 0.09 mmol, 23 mol%) and PPh_3 (48.2 mg, 0.18 mmol, 46 mol%). The orange–brown reaction mixture was stirred at room temperature for 18 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 50% ether in hexanes as eluent) to afford an inseparable mixture of **2f** (ax:sx:an = 88:9:3) with total yield 93.8 mg (89%); ν_{max}(neat)/cm^{-1} 3058m, 2929s, 2887s, 1708s, 1452m, 1359s, 1321m, 1299m, 1176s, 1116s, 1060s, 917m, 849m, 819m, 803m and 730m; δ_H($CDCl_3$, 200 MHz) ax: 4.69 (2 H, dd, *J* 9.89 and 6.96), 4.04 (1 H, br s), 3.64 (2 H, m), 3.52 (2 H, m), 3.35 (3 H, s), 2.73 (1 H, t, *J* 6.96), 2.49 (1 H, m), 2.27 (1 H, m), 2.08 (3 H, s), 1.85 (1 H, m), 1.83 (2 H, m), 1.27 (1 H, m), 1.16 (1 H, m) and 1.07 (1 H, m); δ_C($CDCl_3$, 100 MHz) 209.82, 94.61, 86.14, 82.13, 71.73, 66.76, 58.96, 52.97, 43.06, 41.38, 29.74, 18.02, 15.94 and 15.70 (Found: M$^+$, 266.1528. $C_{15}H_{22}O_4$ requires *M*, 266.1518).

8-*Acetyl*-5-tert-*butoxytetracyclo*[4.3.0.0^{2,4}.0^{3,7}]*nonane* **2g**.—The cycloaddition was carried out as in the general procedure described above, using 7-*tert*-butoxybicyclo[2.2.1]hepta-2,5-

diene **1g** (150.8 mg, 0.92 mmol), methyl vinyl ketone (0.21 cm^3, 2.59 mmol) in 1,2-dichloroethane (0.5 cm^3) with $Ni(COD)_2$ (57.7 mg, 0.21 mmol, 23 mol%) and PPh_3 (110.0 mg, 0.42 mmol, 46 mol%). The orange–brown reaction mixture was stirred at room temperature for 18 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 20% ether in hexanes as eluent) to afford a separable mixture of **2c** (ax:sx = 95:5) with total yield of 204.0 mg (95%); ν_{max}(neat)/cm^{-1} 3065m, 2973s, 2938s, 2868m, 1708s, 1462w, 1427w, 1363s, 1251m, 1202s, 1173s, 1082s, 984m, 906m, 801 and 730w; δ_H($CDCl_3$, 400 MHz) ax: 3.96 (1 H, br s), 2.71 (1 H, dd, *J* 6.06 and 8.62), 2.53 (1 H, m), 2.24 (1 H, m), 2.09 (3 H, s), 1.84 (2 H, m), 1.64 (1 H, br s), 1.15 (10 H, m), 1.06 (1 H, m) and 0.99 (1 H, m); δ_H($CDCl_3$, 400 MHz) sx: 3.97 (1 H, br s), 2.92 (1 H, dd, *J* 4.74 and 8.79), 2.67 (1 H, m), 2.15 (3 H, s), 2.08 (1 H, m), 1.99 (1 H, ddd, *J* 12.49, 9.16 and 4.74), 1.63 (1 H, br s), 1.59 (1 H, dd, *J* 12.49 and 8.79), 1.23 (1 H, m), 1.16 (9 H, s), 1.07 (1 H, m) and 0.99 (1 H, m); δ_C($CDCl_3$, 50 MHz) ax: 209.93, 76.76, 73.20, 53.33, 45.72, 43.11, 41.49, 30.23, 29.04, 28.78, 19.82, 16.19 and 15.81; δ_C($CDCl_3$, 100 MHz) sx: 210.36, 76.60, 73.16, 52.45, 45.07, 44.99, 40.28, 29.65, 29.24, 28.52, 19.57, 16.34 and 15.61 (Found: M^+, 234.1613. $C_{15}H_{22}O_2$ requires *M*, 234.1620) (Found: C, 77.0; H, 9.6. $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46%).

8-*Acetyl*-5-tert-*butyldimethylsiloxytetracyclo*[4.3.0.$0^{2,4}$.$0^{3,7}$]-*nonane* **2h**.—The cycloaddition was carried out as in the general procedure described above, using 7-*tert*-butyldimethylsiloxybicyclo[2.2.1]hepta-2,5-diene **1h** (202.8 mg, 0.91 mmol), methyl vinyl ketone (0.20 cm^3, 3.3 mmol) in 1,2-dichloroethane (0.5 cm^3) with $Ni(COD)_2$ (80.0 mg, 0.29 mmol, 32 mol%) and PPh_3 (149.7 mg, 0.57 mmol, 63 mol%). The reaction mixture was stirred at 80 °C for 16 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 5% ethyl acetate in hexanes as eluent) to yield two fractions. The first fraction (228.4 mg, 85.6%) contained two products in a ratio of *anti-exo*:*syn-exo* = 8:1; δ_H($CDCl_3$, 400 MHz) 4.12 (1 H, br s), 2.92 (0.11 H^{sx}, dd, *J* 8.8 and 4.8), 2.72 (0.89 H^{ax}, t, *J* 7.7), 2.68 (0.11 H^{sx}, t, *J* 1.8), 2.55 (0.89 H^{ax}, br s), 2.22 (0.89 H^{ax}, t, *J* 2.2), 2.15 (0.33 H^{sx}, s), 2.10 (2.67 H^{ax}, s), 2.06 (0.11 H^{sx}, m), 1.94 (0.11 H, d_{AB}t, *J* 12.4 and 4.7), 1.86 (1.8 H, m), 1.63 (0.89 H, br s), 1.58 (0.11 H, m-d_{AB}d), 1.23 (0.11 H, m), 1.20 (0.11 H, tm, *J* ~ 5), 1.14 (0.89 H, tm, *J* ~ 5), 1.10 (0.89 H, tm, *J* ~ 5), 1.01 (1 H, tm, *J* ~ 5), 0.85 (9 H, s, Bu^t), 0.03 (3 H, s) and 0.01 (3 H, s). The second fraction (18.6 mg, 7%) contained two products in a ratio of *anti-exo*:*anti-endo* = 2:1; δ_H($CDCl_3$, 400 MHz) 4.12 (0.98 H, br s), 4.10 (0.02 H, br s), 2.98 (0.02 H, m), 2.92 (0.33 H^{an}, dt, *J* 10.7 and 4.4), 2.84 (0.02 H, m), 2.72 (0.63 H^{ax}, t, *J* 7.7), 2.68 (0.05 H, t, *J* 1.8), 2.53 (0.9 H, m), 2.37 (0.3 H, m), 2.22 (0.63 H, t, *J* 2.2), 2.19 (0.06 H, s), 2.15 (0.15 H^{sx}, s), 2.11 (0.87 H^{an}, s), 2.10 (1.89 H^{ax}, s), 2.06 (0.05 H, m), 1.94 (0.05 H, d_{AB}t), 1.86 (1.3 H, m), 1.72 (0.3 H, br s), 1.63 (0.63 H, br s), 1.59 (0.4 H, m), 1.23 (0.05 H, br s), 1.12 (2.3 H, br m), 1.01 (0.7 H, tm), 0.86–0.85 (total 9 H, s) and 0.04–0.01 (total 6 H, s). Total calculated ratio of *anti-exo*:*anti-endo*:*syn-exo* (ax:an:sx) = 88:2:10 with total yield (247.0 mg, 93%). In order to identify and distinguish the different isomers (ax, an and sx) in the inseparable mixture, the mixture of silyl ethers, **2h**, was then converted and compared to the benzoates, **2d**, in which the different isomers (ax, sx, an and sn) had already been distinguished.

5-tert-*Butyldimethylsiloxy*-8-*cyanotetracyclo*[4.3.0.$0^{2,4}$.$0^{3,7}$]-*nonane* **3h**.—The cycloaddition was carried out as in general procedure described above, using 7-*tert*-butyldimethylsiloxybicyclo[2.2.1]hepta-2,5-diene **1h** (196.8 mg, 0.88 mmol), acrylonitrile (0.14 cm^3, 2.1 mmol) in 1,2-dichloroethane (0.5 cm^3) with $Ni(COD)_2$ (72.2 mg, 0.26 mmol, 29 mol%) and PPh_3 (135.9 mg, 0.52 mmol, 59 mol%). The reaction mixture was stirred at 80 °C for 16 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 5% ethyl acetate in hexanes as eluent) to afford an inseparable mixture of **3h** (ax:sx:an:sn = 70:9:19:2) with a total yield of 226.9 mg (93%). The major *anti-exo* isomer was identified by conversion into the benzoate **3d** (see procedure below), and the minor *syn-exo* isomer was identified by elimination (H^8 dd = *exo*). The minor *anti-endo* was identified by the dt pattern for H^8, and the downfield shift of H^1 compared to H^7, as determined by decoupling in C_6D_6. The smallest isomer (2%) was detected only by the ^1H NMR in C_6D_6; δ_H($CDCl_3$, 400 MHz) 4.20 (0.1 H, br s), 4.18 (0.9 H, br s), 2.85 (0.1 H, br s), 2.81 (0.1 H, dd, obscured), 2.79 (0.2 H, dt, obscured), 2.66 (0.7 H, dt, *J* 4 and 2), 2.63 (0.9 H^{ax}, dd, *J* 9.1 and 4.9), 2.37 (0.7 H^{ax}, t, *J* 2.1), 2.31 (0.2 H^{an}, dt, *J* 4 and 2), 2.14 (0.9 H^{ax}, dd^{ax} and m^{an}, *J* 13.2 and 9.2), 2.05 (0.2 H^{an}, ddd, *J* 12.8, 11.2 and 3.9), 1.93 (1.8 H, m), 1.66 (0.2 H, br s), 1.39 (0.2 H, tm, *J* ~ 5), 1.31 (0.2 H, tm, *J* ~ 5), 1.21 (0.2 H, tm, *J* ~ 5), 1.16 (1.5 H, m), 1.03 (0.8 H, tm, *J* ~ 5), 0.87–0.86 (total 9 H, 2 s) and 0.04 (6 H, m); δ_H(C_6D_6, 400 MHz) 3.96 (0.1 H, br s), 3.90 (0.7 H, br s), 3.87 (0.2 H, br s), 2.71 (0.1 H, t, *J* 2), 2.55 (0.02 H^{sn}, m), 2.39 (0.7 H, br s), 2.34 (0.19 H^{an}, dt, *J* 4 and 2), 2.09 (0.1 H, dd, *J* 9.2 and 4.4), 2.00 (0.19 H^{an}, dt, *J* 11.5 and 4.3), 1.89 (1.4 H, m), 1.73 (0.8 H, br s), 1.69 (0.19 H^{an}, m), 1.50 (2 H, br m), 1.35 (0.7 H, br m), 1.20 (0.1 H, tm, *J* ~ 5), 1.15 (0.2 H, br m), 0.94 (9 H, m), 0.85 (1.2 H, m), 0.78 (0.02 H, tm, *J* ~ 5), 0.68 (0.04 H, tm, *J* ~ 5), 0.62 (1.2 H, tm, *J* ~ 5), 0.58 (0.1 H, tm, *J* ~ 5), 0.51 (0.3 H, m), 0.43 (0.1 H, tm, *J* ~ 5), 0.37 (1.2 H, tm, *J* ~ 5) and 0.01 (6 H, m) (Found: M^+, 275.1696. $C_{16}H_{25}NOSi$ requires *M*, 275.1705). In order to identify and distinguish the different isomers (ax, an, sx and sn) in the inseparable mixture, the mixture of silyl ethers, **3h**, was then converted and compared to the benzoates, **3d**, in which the different isomers (ax, sx, an and sn) had already been distinguished.

5-tert-*Butyldimethylsiloxy*-8-*phenylsulfonyltetracyclo*[4.3.-0.$0^{2,4}$.$0^{3,7}$]*nonane* **4h**.—The cycloaddition was carried out as in general procedure described above, using 7-*tert*-butyldimethylsiloxybicyclo[2.2.1]hepta-2,5-diene **1h** (200.2 mg, 0.90 mmol), phenyl vinyl sulfone (155.5 mg, 0.92 mmol) in 1,2-dichloroethane (0.5 cm^3) with $Ni(COD)_2$ (100.7 mg, 0.36 mmol, 40 mol%) and PPh_3 (189.4 mg, 0.72 mmol, 80 mol%). The reaction mixture was stirred at 80 °C for 16 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 20% ethyl acetate in hexanes as eluent) to afford an inseparable mixture of **3h** (ax:sx:an:sn = 54:13:27:6) with total yield of 333.0 mg (95%); δ_H($CDCl_3$, 400 MHz) 7.87 (2 H, m), 7.62 (1 H, m), 7.54 (2 H, m), 4.14 (0.67 $H^{ax,sx}$, br s), 4.08 (0.27 H^{an}, br s), 4.05 (0.06 H^{an}, br s), 3.56 (0.06 H^{sn}, ddd, *J* 11.0, 5.4 and 3.6), 3.48 (0.4 $H^{an,sx}$, m), 3.29 (0.54 H^{ax}, dd, *J* 8.7 and 5.5), 2.81 (0.13 H^{sx}, t, *J* 2.1), 2.72 (0.06 H^{sn}, m), 2.68 (0.27 H^{an}, dt, *J* 4, 2), 2.63 (0.54 H^{ax}, br s), 2.51 (0.54 H^{ax}, t, *J* 2.1), 2.25 (0.27 H, m), 2.22 (0.27 H, dd, *J* 13.2 and 5.8), 2.16 (0.27 H, m), 2.10 (0.54 H, ddd, *J* 13.4, 5.4, 4.0), 2.00 (0.67 H, m), 1.91 (0.54 H, dd, *J* 13.3 and 8.6), 1.84 (0.36 H, m), 1.71 (0.06 H, tm, *J* ~ 5), 1.68 (0.06 H, m), 1.65 (0.27 H, br s), 1.57 (1 H, m), 1.40 (0.20 H, tm, *J* ~ 5), 1.15 (1.6 H, m), 1.01 (0.6 H, tm, *J* ~ 5), 0.86 (1.2 H^{sx}, s), 0.85 (4.8 H^{ax}, s), 0.84 (s, 2.4 H^{an}), 0.83 (0.6 H^{sn}, s) and 0.01 (6 H, br m). In order to identify and distinguish the different isomers (ax, an, sx and sn) in the inseparable mixture, the mixture of silyl ethers, **4h**, was then converted and compared to the benzoates, **4d**, in which the different isomers (ax, sx, an and sn) had already been distinguished.

8-*Cyanotetracyclo*[4.3.0.$0^{2,4}$.$0^{3,7}$]*nonan*-5-*yl Benzoate* **3d**.—The cycloaddition was carried out as in general procedure

described above, using bicyclo[2.2.1]hepta-2,5-dien-7-yl benzoate **1d** (153.5 mg, 0.72 mmol), acrylonitrile (0.10 cm^3, 1.50 mmol) in 1,2-dichloroethane (0.75 cm^3) with $Ni(COD)_2$ (47.3 mg, 0.17 mmol, 24 mol%) and PPh_3 (94.0 mg, 0.36 mmol, 50 mol%). The reaction mixture was stirred at 80 °C for 18 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 15% ethyl acetate in hexanes as eluent) to afford an inseparable mixture of **3d** (ax:sx:an:sn = 55:20:20:5) with total yield of 181.2 mg (95%); δ_H($CDCl_3$, 400 MHz) 8.00 (2 H, m), 7.54 (1 H, m), 7.42 (2 H, m), 5.24 (0.25 H, m), 5.21 (0.75 H, m), 2.97 (0.2 H, t, *J* 2.1), 2.89 (0.45 $H^{an,sn,sx}$, m), 2.78 (0.55 H^{ax}, dt, *J* 4 and 2), 2.73 (0.75 H, m includes dd, J^{dd} 9.2 and 4.8, H^{ax}), 2.61 (0.55 H^{ax}, t, *J* 2.1), 2.56 (0.20 H, m), 2.42 (0.20 H, dt, *J* 4 and 2), 2.39 (0.05 H, dt, *J* 4 and 2), 2.32 (0.75 H, br s), 2.22 (0.75 H, dd, *J* 13.0 and 9.2), 2.10 (0.8 H, br m), 1.98 (0.9 H, m), 1.66 (0.05 H, tm, *J* ~ 5), 1.59 (1.15 H, m), 1.46 (0.20 H, tm, *J* ~ 5), 1.39 (0.05 H, tm, *J* ~ 5), 1.29 (0.75 H, tm, *J* ~ 5) and 1.24 (0.75 H, tm, *J* ~ 5); δ_C($CDCl_3$, 50 MHz): major isomer 133.09, 129.61, 128.43, 78.99, 44.82, 43.67, 41.44, 32.21, 28.22, 16.94, 14.62 and 14.51; medium sized signals for two isomers: 166.62, 130.30, 122.58, 79.14, 46.69, 44.69, 42.90, 39.74, 32.78, 31.59, 28.42, 27.69, 17.02, 16.42, 15.07, 14.91, 14.21 and 12.40; smallest signals: 167.66, 130.23, 122.89, 39.96, 16.50, 15.36 and 12.33. Some regions resolved better in C_6D_6; δ_H(C_6D_6, 400 MHz) 8.11 (2 H, m), 7.08 (3 H, m), 5.04 (0.1 H, br s), 4.98 (0.9 H, m), 2.61 (0.1 H^{sx}, t, *J* 2.0), 2.32 (0.05 H, dt, *J* 4 and 2), 2.19 (0.5 H, br s), 2.13 (0.35 H, dt, *J* 4 and 2), 2.04 (0.1 H^{sx}, dd, *J* 9.5 and 4.8), 2.01 (0.05 H^{sn}, dt, *J* 11.4 and 4.2), 1.92 (0.35 H^{an}, dt, *J* 11.4 and 4.2), 1.93 (0.05 H, br s), 1.84 (0.95 H, br s), 1.81 (0.5 H^{ax}, dd, *J* 8.9 and 5.1), 1.70 (0.35 H, m), 1.56 (0.1 H, dt, *J* 4 and 2), 1.53 (0.05 H, m), 1.45 (1.5 H, br m), 1.36 (0.8 H, m), 1.25 (0.8 H, br m), 1.19 (1.2 H, m), 0.87 (0.35 H, tm, *J* ~ 5), 0.69 (0.05 H, tm, *J* ~ 5), 0.56 (0.5 H, tm, *J* ~ 5), 0.53 (0.1 H, tm, *J* ~ 5), 0.42 (0.1 H, tm, *J* ~ 5) and 0.36 (0.4 H, tm, *J* ~ 5) (Found: M^+, 265.1105. $C_{17}H_{15}NO_2$ requires *M*, 265.1102).

The major isomer (ax) was crystallized selectively using a mixture of hot pentane and cooling in the freezer overnight. This compound was identified as the *anti-exo* isomer by analysis of the HCOSY and NOE (irradiation at 5.21 ppm, H^5, enhancements: H^7 12%; H^6 9%; H^4 8%; H^1 0%) spectra; δ_H($CDCl_3$, 400 MHz) 8.00 (2 H, m), 7.54 (1 H, m), 7.42 (2 H, m), 5.21 (1 H, m, H^5), 2.78 (1 H, dt, *J* 4 and 2, H^1), 2.73 (1 H, dd, *J* 9.2 and 4.9 Hz, H^8), 2.61 (1 H, t, *J* 2.1, H^7), 2.32 (1 H, br s, H^6), 2.22 (1 H, dd, *J* 13.1 and 9.2, H^{10}), 1.99 (1 H, dt, *J* 13.1 and 4.5, H^9), 1.58 (1 H, t, *J* ~ 5, H^4), 1.29 (1 H, tm, *J* ~ 5, H^2) and 1.24 (1 H, tm, *J* ~ 5, H^3); δ_C($CDCl_3$, 50 MHz) 166.79, 133.21, 130.45, 129.76, 128.54, 122.69, 79.11, 44.96, 43.81, 41.58, 32.37, 28.39, 17.09, 14.78 and 14.65.

8-Phenylsulfonyltetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]*nonan-5-yl Benzoate* **4d**.—The cycloaddition was carried out as in general procedure described above, using bicyclo[2.2.1]hepta-2,5-dien-7-yl benzoate **1d** (157.6 mg, 0.74 mmol), phenyl vinyl sulfone (136.9 mg, 0.81 mmol) in 1,2-dichloroethane (1.5 cm^3) with $Ni(COD)_2$ (53.3 mg, 0.19 mmol, 26 mol%) and PPh_3 (101.8 mg, 0.39 mmol, 53 mol%). The reaction mixture was stirred at 80 °C for 18 h. After work-up as described in the general procedure, the crude product was purified by flash column chromatography (using 20% ethyl acetate in hexanes as eluent) to afford an inseparable mixture of **4d** (ax:sx:an:sn = 50:20:20:10) with total yield of 273.0 mg (97%); δ_H($CDCl_3$, 400 MHz) 7.97 (2 H, m), 7.90 (2 H, m), 7.64 (1 H, m), 7.54 (3 H, m), 7.41 (2 H, m), 5.20 (0.2 H^{sx}, br s), 5.19 (0.5 H^{ax}, br s), 5.10 (0.3 $H^{an,sn}$, m), 3.57 (0.5 $H^{an,sn,sx}$, m), 3.37 (0.5 H^{ax}, dd, *J* 13.5, 4.4), 3.12 (0.2 H, br s), 2.86 (0.1 H, dt, *J* 4 and 2), 2.77 (0.7 H, m), 2.64 (0.5 H, t, *J* 2.2), 2.48 (0.2 H, dt, *J* 4 and 2), 2.45 (0.5 H, br s), 2.42 (0.1 H, dt, *J* 4 and 2), 2.38 (0.5 H, m), 2.30 (0.2 H, dd, *J* 13.3 and 5.5), 2.23 (0.5 H, dt, *J* 13.5 and 4.4), 2.14 (0.6 H, m), 2.02 (0.55 H, dd, *J* 13.5 and 8.8), 1.91 (0.2 H, ddd, *J* 13.5 and 8.8), 1.87 (0.3 H, m), 1.83 (0.2 H, dd, *J* 13.5 and 8.8), 1.80 (0.2 H, dm, *J* ~ 5), 1.57 (0.7 H, m), 1.45 (0.1 H, tm, *J* ~ 5), 1.28 (0.8 H, m) and 1.20 (0.8 H, m); δ_C($CDCl_3$, 50 MHz) 166.66, 138.75, 133.80, 133.69, 133.06, 130.41, 130.37, 129.65, 129.41, 129.08, 128.55, 128.45 and 127.99; peaks for major isomer: 79.22, 64.95, 42.66, 41.69, 41.53, 28.45, 16.97, 15.66 and 15.22; medium peaks: 78.05, 65.21, 64.41, 45.23, 43.33, 42.34, 42.15, 41.64, 39.81, 29.29, 26.19, 16.34, 15.59, 13.48 and 11.73; ν_{max}(neat)/cm^{-1} 3067w, 3036w, 3020w, 2965w, 2950s, 2882w, 2870m, 1721s and 1714s (Found: M^+, 380.1062. $C_{22}H_{20}O_4S$ requires *M*, 380.1082).

The major isomer (ax) was crystallized selectively using a mixture of hot pentane–dichloromethane and cooling in the freezer overnight. This compound was identified as *anti-exo* by analysis of H–H decouplings and NOE spectra (irradiation at 5.19 ppm, enhancements: H^7 9%; H^6 9%; H^4 9%; H^1 0%); δ_H($CDCl_3$, 400 MHz) 7.99 (2 H, m), 7.88 (2 H, m), 7.64 (1 H, m), 7.55 (3 H, m), 7.41 (2 H, m), 5.19 (1 H, br s, H^5), 3.37 (1 H, dd, *J* 8.8 and 5.5, H^8), 2.77 (1 H, m, H^1), 2.64 (1 H, t, *J* 2.2, H^7), 2.45 (1 H, br s, H^6), 2.22 (1 H, dt, *J* 13.5 and 4.4, H^9), 2.01 (1 H, dd, *J* 13.5 and 8.8, H^{10}), 1.57 (1 H, t, *J* ~ 5, H^4), 1.28 (1 H, tm) and 1.20 (1 H, tm); δ_C($CDCl_3$, 50 MHz) 166.66, 138.75, 133.81, 133.06, 130.44, 129.65, 129.41, 128.58, 128.44, 79.22, 64.95, 42.66, 41.69, 41.53, 28.45, 16.97, 15.66 and 15.22.

Conversion of **2h** (*Silyl Ethers*) *into* **2d** (*Benzoates*).—Tetrabutylammonium fluoride (1 mol dm^{-3} in THF; 0.11 cm^3, 0.11 mmol) was added to a solution of TBDMS ethers **2h** (28.8 mg, 0.10 mmol) in THF (1.0 cm^3) and the reaction mixture was stirred overnight at room temperature before being partitioned between dichloromethane (15 cm^3) and brine (10 cm^3). The organic layer was then dried ($MeSO_4$) and evaporated under reduced pressure. The product was purified by flash column chromatography (20–40% ethyl acetate in hexane) to give 8-acetyl-5-hydroxytetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonane (16.5 mg, 94%).

Pyridine (0.06 cm^3, 0.7 mmol) and benzoyl chloride (0.05 cm^3, 0.4 mmol) were added to a solution of the alcohol (16.5 mg, 0.09 mmol) and DMAP (7.2 mg, 0.06 mmol) in dichloromethane (0.25 cm^3) at 0 °C. After 1 h, the reaction mixture was partitioned between dichloromethane (20 cm^3) and aqueous sodium hydroxide (0.5 mol dm^{-3}; 10 cm^3). The organic layer was washed with saturated aqueous copper(II) sulfate (15 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The product was purified by flash column chromatography (10% ethyl acetate in hexane) to give a yield of 22.9 mg (87.6%). The major product from this reaction was identical with the major cycloadduct **2d** (ax) from the reaction of **1d** with MVK.

Conversion of **3h** (*Silyl Ethers*) *into* **3d** (*Benzoates*).—Tetrabutylammonium fluoride (1 mol dm^{-3} in THF; 0.12 cm^3, 0.12 mmol) was added to a solution of TBDMS ethers **3h** (29.6 mg, 0.107 mmol) in THF (1.0 cm^3) and the reaction mixture was stirred at room temperature overnight after which it was partitioned between dichloromethane (15 cm^3) and brine (10 cm^3). The organic layer was then dried ($MgSO_4$) and evaporated under reduced pressure. Flash column chromatography (30–60% ethyl acetate in hexane) of the residue gave 8-cyano-5-hydroxytetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonane. The major fraction (12.4 mg, 72%) was esterified (below). The second fraction (3.1 mg, 18%) contained mainly the *anti-endo* isomer (~ 75% of mixture, indicated by ^1H NMR at 200 MHz in $CDCl_3$ (H^8 at δ 2.83, ddd, *J* 9.8, 5.4 and 4.0).

Pyridine (0.04 cm^3, 0.50 mmol) and benzoyl chloride (0.04 cm^3, 0.35 mmol) were added to a solution of the major fraction (12.4 mg, 0.08 mmol) and DMAP (6.0 mg, 0.05 mmol) in

dichloromethane (0.25 cm^3) at 0 °C. After 1 h, the reaction was partitioned between dichloromethane (20 cm^3) and aqueous sodium hydroxide (0.5 mol dm^{-3}; 10 cm^3). The organic layer was washed with saturated aqueous copper(II) sulfate (15 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The product was purified by flash column chromatography (10–20% ethyl acetate in hexane, 14.2 mg, 70%, *anti-exo*:*syn-exo* 6.5:1). The major product was identical with the major cycloadduct **3d** (ax) from the reaction of **1d** with acrylonitrile.

Conversion of **4h** (*Silyl Ethers*) *into* **4d** (*Benzoates*).—Tetrabutylammonium fluoride (1 mol dm^{-3} in THF; 0.11 cm^3, 0.11 mmol) was added to a solution of TBDMS ethers **4h** (39.7 mg, 0.10 mmol) in THF (1.0 cm^3). The reaction mixture was stirred overnight at room temperature before being partitioned between dichloromethane (15 cm^3) and brine (10 cm^3). The organic layer was then dried ($MgSO_4$) and evaporated under reduced pressure. The product was purified by flash column chromatography (20–75% ethyl acetate in hexane) to give 5-hydroxy-8-phenylsulfonyltetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonane in two fractions. The first fraction (14.7 mg, 52%) contained both *exo* products (ratio = 4.5:1 by ^1H NMR). The second fraction (11.0 mg, 39%) contained a mixture of all four isomers.

Pyridine (0.03 cm^3, 0.4 mmol) and benzoyl chloride (0.03 cm^3, 0.3 mmol) were added to a solution of the major fraction (14.7 mg, 0.05 mmol) and DMAP (5.5 mg, 0.05 mmol) in dichloromethane (0.25 cm^3) at 0 °C. After 2 h, the reaction was partitioned between dichloromethane (20 cm^3) and aqueous sodium hydroxide (0.5 mol dm^{-3}; 10 cm^3). The organic layer was washed with saturated aqueous copper(II) sulfate (15 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The product was purified by flash column chromatography (20% ethyl acetate in hexane, 19.2 mg, 95%). The major product was identical with the major cycloadduct **4d** (ax) from the reaction of **1d** with phenyl vinyl sulfone.

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